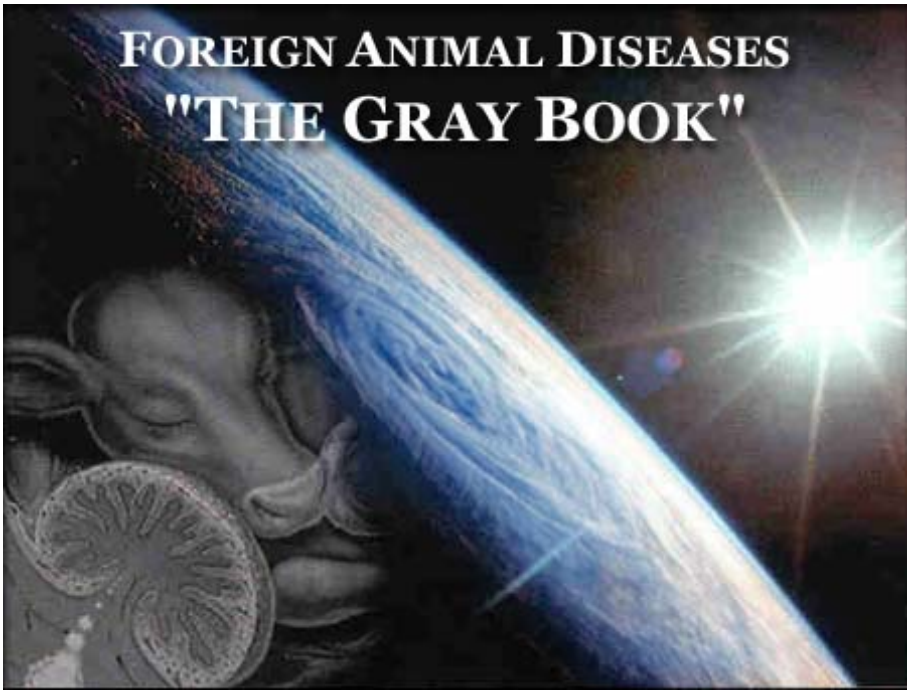

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The views expressed in this publication represent those of the author and do not necessarily reflect those of Bayer or Bayer subsidiaries.

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1998 EDITION

FOREIGN ANIMAL DISEASES

REVISED 1998

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DEDICATION TO

Charles A. Mebus, DVM, PhD

This book is dedicated to Dr. Charles A. Mebus, a world renown authority on animal diseases foreign to the United States. Through his untiring efforts, this edition of the United States Animal Health Association's book on Foreign Animal Diseases has been possible. We are indebted to the professional, exemplary work of Dr. Mebus, a true gentleman and scholar.

PREFACE

This sixth edition of Foreign Animal Diseases appears 44 years after the first edition in 1954. The second, third, forth, and fifth editions were published in 1964, 1975, 1984, and 1992, respectively.

With each edition, new and important information supports the established mission formulated in 1954; namely, to bring together in one document the latest information on those foreign animal diseases considered to be the greatest threat to the livestock and poultry industries in the United States. In keeping with this philosophy, the objectives of the Foreign Animal Diseases Committee of the United States Animal Health Association remain unchanged; i.e., to provide up-to-date information on foreign animal diseases; how they are diagnosed; how they are spread, and how they may be prevented, controlled, and eradicated.

Less restrictive trade between countries will likely increase. This brings with it the requirements for increased vigilance in countries that have achieved a high degree of freedom from many animal diseases.

Historically, practicing veterinarians are among the first to come into contact with or suspect a foreign animal disease either in their hospitals, homes of pet owners, zoological gardens, research institutions, wild-life studies, stockyards, or on farms and ranches. Unfortunately, many of our veterinary teaching institutions (schools and colleges) are giving little if any formal attention to foreign animal diseases. Visual teaching aids, available in the form of slides, films, or electronic sources, can be most informative and leave a more lasting impression of clinical signs than that obtained from lectures alone.

The Council on Education of the American Veterinary Medical Association should emphasize the importance of including foreign animal diseases in the curriculum during their reviews of veterinary teaching institutions. In addition, the USDA should require some level of documented training in foreign animal diseases as an essential element for granting federal accreditation of veterinarians.

In this edition, we have revised the format, added a glossary, and again included colored photographs in an attempt to make the book more user-friendly to individuals engaged in work with livestock and poultry. The photographs are not intended for making a definitive diagnosis but for helping to recognize some of the signs and lesions that may be seen in foreign animal diseases and prompting those who observe such signs to seek assistance from trained foreign animal disease diagnosticians. For the most part, suspected foreign animal diseases create emergency situations. Thus, time is critical in efforts to prevent spread of suspect diseases and to obtain a definitive diagnosis.

It is difficult to prepare a document that is acceptable to all concerned. Some will say it should be more practical and others that it should be more scientific; desired contents depends on one's responsibilities and interests. Our goal was to publish a book that is primarily for those engaged in field activities. We believe this edition has come closer to attaining that goal. This book would not be possible without the input of so many individuals who have unselfishly donated their time to writing the chapters, appendices, and other information.

Finally, we encourage those who use this book to send helpful or critical comments to the United States Animal Health Association. There will be future editions, and constructive comments are always appreciated.

William W. Buisch
John L. Hyde

Charles A. Mebus

COMMITTEE ON FOREIGN ANIMAL DISEASES and others working with animals or having an interest

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PART II
CRITICAL FOREIGN ANIMAL DISEASE ISSUES FOR THE 21st CENTURY

CRITICAL FOREIGN ANIMAL DISEASE ISSUES FOR THE 21st CENTURY

Animal health officials define an exotic or foreign animal disease (FAD) as an important transmissible livestock or poultry disease believed to be absent from the United States and its territories that has a potential significant health or economic impact. The United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) is working vigilantly with State animal health officials and veterinary professionals to identify, control, and eradicate these animal diseases and diminish their impact. As a preface to the updated disease information, this introductory article will provide an overview of the ways in which FAD's may impact U.S. consumers and producers. It will also highlight the new challenges facing those involved in prevention, management, and recovery from FAD threats to the United States.

IMPACTS OF FAD's ON THE U.S. ECONOMY

Foreign animal diseases are considered a threat to the United States when they significantly affect human health or animal production and when there is an appreciable cost associated with disease control and eradication efforts. Diseases such as hog cholera, foot-and- mouth disease (FMD), and highly pathogenic avian influenza (HPAI) can cause high death rates or severe illness and production losses. This loss of productivity can increase the cost of food products obtained from those animal sources. For example, during the 1983-84 outbreak of HPAI, the average cost of one dozen eggs increased by 5 percent (1). McCauley et al. predicted that the price of beef would increase by $0.19 per pound because of an outbreak of FMD (2). Other diseases such as tuberculosis (TB) and brucellosis affect human and animal health. These two diseases, although very prevalent in other countries, will soon be eradicated from U.S. domestic livestock and will thus become exotic.

To protect the long-term health and profitability of U.S. animal agriculture, incursions of a FAD must be rapidly controlled. In the United States, control usually means disease eradication. These eradication efforts can present significant short-term costs to industry and government. For example, in 1983-84 the control and eradication of a highly pathogenic avian influenza outbreak cost the USDA $60 million. In the final stages of hog cholera eradication (1971-1977), the U.S. government spent $79 million (3).

In addition to control costs, one of the most immediate and severe consequences of a FAD occurrence in the United States will be the loss of export markets. U.S. animal agriculture is becoming more dependent on exports. The long-term strategic plans of these industries call for increasing the amount of goods sold abroad. As the percentage of total production destined for export grows, the impact of a domestic FAD outbreak also grows. Other countries will not allow the importation of animals or animal products that pose a risk to their industry. In 1997, the total value of exported U.S. animals and animal products exceeded $7 billion: $2.3 billion in poultry, $1 billion in pork, and $2.6 billion in cattle and cattle products. Theoretically, the long-term trade impacts of a FAD occurrence can be reduced by applying regionalization concepts. A country could, during a FAD outbreak, recognize specified regions of the United States as affected with the disease. The remaining unaffected areas might be free to continue exporting. However, it would take considerable time to have these regions identified and other regions certified as disease-free. In the meantime, all trade in that commodity would be stopped.

NEW CHALLENGES FOR THE MANAGEMENT OF FAD's

As we move into the 21st century, many new issues and factors are affecting FAD prevention, control, management, and recovery. These factors include free trade agreements, free trade blocks, regionalization, increased international passenger travel, intensification of animal production, the constant evolution of infectious agents, and the uncertain impact of biotechnology and bioterrorism.

Evidence is accumulating that these factors are having an impact. For example, hog producers in Taiwan recently experienced a devastating outbreak of FMD for the first time since 1929. Over four million animals were destroyed. Virtually all export markets were lost. The Netherlands recently sustained an outbreak of hog cholera that resulted in major export losses of 65 percent of their production. Other countries in the European Union struggle to eradicate hog cholera. As this book goes to press, hog cholera is active in the Dominican Republic, which is situated only 150 miles from the continental United States.

The world is moving toward more open market access. Free trade agreements such as GATT (General Agreement on Tariffs and Trade) and NAFTA (North American Free Trade Agreement) stipulate that trade in animals and animal products should only be restricted if there is a valid human or animal health risk to the importing country. To stop trade, the importing country must show, with a scientifically valid analysis, that a risk exists. This policy will increase responsibility for the United States to evaluate risks carefully . It also will probably increase the flow of animals and animal products into the United States.

A related element of free trade agreements is the concept of regionalization. As an importing country, the United States is required to evaluate geographic regions of potential importers. More effort and information will be required for the United States to evaluate the risk of a disease from a region that may be smaller than or larger than an area defined by political borders. The United States must have some methods to evaluate the security of the region's boundaries. The acceptance of regionalization puts increased pressure on the United States to remain vigilant for the presence of disease at home and in various countries exporting or hoping to export, to our shores. Examples of regionalization include recognizing the northern U.S. states as Bluetongue free, northern Spain as free from African horse sickness, and portions of Argentina as FMD free.

Around the world countries are joining into free trade blocks. They hope these alliances will give them a competitive advantage against other trading blocks such as the European Union and the NAFTA countries. Problems arise as livestock or animal products are allowed to move freely within these blocks because we may not always know the origin of the products we import.

The volume of international passenger travel is steadily increasing. In 1980, 20 million passengers arrived in the United States on international flights. In 1995, this number rose 131 percent to 47 million (4). The airline industry expects this trend to continue. International travelers may unknowingly bring contaminated animal products from FAD infected countries. Contaminated foodstuffs have often served as a source of a FAD in the United States and other countries (5).

As the world population grows and animal production intensifies, the risks and impacts of FAD incursions increase. Today, infection at one premises can affect 300,000 laying hens, 100,000 hogs, or 100,000 feedlot cattle. When one company owns a large number of animals, frequent and rapid interstate movement occurs. This movement can spread infection across many states before clinical signs are manifest in the source herd.

Lastly, the infectious disease agents and vectors are changing. For example, as the importation of reptilian pets increases, potential disease-transmitting vectors such as Amblyomma ticks are finding new routes of entry. Also, natural selection pressures predict that the FAD of the next decade will be different from the last. Recent examples include the swine-specific FMD virus in Taiwan, Salmonella DT104, and Salmonella enteritidis. Actions and information that accurately prevented disease or predicted risk in the past may not be effective in the future. Around the world, new agents never before a threat to U.S. agriculture have become an important human health or economic concern. Examples include bovine spongiform encephalopathy and porcine

reproductive and respiratory syndrome. Today's new emerging disease may be tomorrow's significant exotic disease.

U.S. RESPONSES TO CHANGING EXOTIC ANIMAL DISEASE THREATS

The Animal and Plant Health Inspection Service has taken the lead in publishing a rule on regionalization expectations. This rule will contribute to international negotiations on animal trade. To define optimal methodologies for conducting risk analyses, APHIS is working with universities, consultants, and the Economic Research Service (ERS). Also, APHIS is beginning to educate animal health officials, the animal agricultural industry, and our trading partners about the concepts and impacts of regionalization.

Disease surveillance data are a critical element for early FAD detection and for accurate risk analyses. Consequently, APHIS is constantly exploring different methodologies for monitoring the health of the U.S. livestock and poultry population. As traditional program diseases such as tuberculosis and brucellosis are eradicated and funding decreases, new surveillance systems will be needed. The U.S. animal health surveillance systems are therefore being reviewed by APHIS to achieve the highest efficiency and breadth without compromising disease detection abilities. Also, APHIS is working with our Latin American trading partners to design feasible surveillance systems for the region. In protecting American agriculture, APHIS is playing a key role in collaborating with international health organizations such as OIE (Office of International Epizootics), IICA (Inter-American Institute for Cooperation on Agriculture), FAO (Food and Agriculture Organization), and others to harmonize trading regulations, risk analysis methods, disease surveillance, and diagnostic methods.

The USDA, state animal health officials, universities, and the animal agricultural industry are taking many steps in response to these changing threats and risks. The diagnostic laboratory system is constantly improving and applying state of the art technology for FAD diagnosis and differentiation. International contacts are used to maintain awareness of disease occurrence. Consolidating the Agriculutural Research Service (ARS) and APHIS and remodeling laboratory facilities at Plum Island will strengthen the opportunities for collaboration on FAD reseach and diagnostic programs.

The emergency management plan is being revised with greater involvement of partners to ensure rapid detection and response. These efforts are discussed in Part III, Protecting Livestock and Poultry Industries from Foreign Animal Diseases, in this publication. Veterinary Services (VS) has downsized just like other U.S. government agencies. In that process, we have gone from four regional emergency response teams to two. However, in doing this, we have also created small Rapid Response Teams that can quickly be deployed to investigate possible FAD outbreaks. Additionally, VS is working more with State departments of agriculture, private veterinary practitioners, and other veterinary specialty groups to formulate better responses to these new threats. Moreover, VS has been examining the distribution of specially trained diagnosticians to determine any needed changes to improve the availability of these individuals. Key diagnosticians to be sent to outbreaks in other countries have also been indentified by VS. This adds to our current knowledge base of the disease outside the laboratory and of the real-life problems involved in control and eradication.

Finally, VS has made efforts to create a manageable data base to collect information on all potential FAD investigations. This begins by having the diagnostician corps enter the most accurate and inclusive data into a computer data base. The future goal is to be able to look at trends and give values back to the reporting producer and veterinary practitioner. The trends may help VS to distribute and train its corps of diagnosticians better. It is hoped that the returned added value will stimulate more reporting by the private sector.

CONCLUSION

Exotic or emerging animal diseases continue to threaten the health and productivity of U.S. livestock and poultry. All of those with the potential of being affected are working to manage these threats by responding to these new challenges.

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GUIDE TO THE LITERATURE

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PART III
PROTECTING LIVESTOCK AND POULTRY INDUSTRIES FROM FOREIGN ANIMAL DISEASES

PROTECTING LIVESTOCK AND POULTRY INDUSTRIES FROM FOREIGN ANIMAL DISEASES

Protecting the livestock and poultry industries of the United States from foreign animal diseases (FAD's) involves four basic principles or phases of emergency management. They are prevention, preparedness, response, and recovery. To be effective, these principles require the support and cooperation of persons, groups, and organizations at the local, State, regional, and national levels. Livestock and poultry owners, veterinarians in private clinical practice, industry groups, the Federal government, State government, State universities, veterinary diagnostic laboratories, and the traveling public must all be included.

PREVENTING THE INTRODUCTION OF FOREIGN ANIMAL DISEASES

The responsibility for preventing the introduction of FAD' into the United States has been assigned to several Government agencies. The U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS) (Fig. 1) has the primary responsibility for preventing the introduction of FAD's through importation regulations governing animals, poultry, and animal and poultry products. To accomplish this objective, APHIS cooperates with other Federal agencies, including the U.S. Customs Service, the U.S. Fish and Wildlife Service, and the U.S. Department of Agriculture's Food Safety and Inspection Service.

Plant Protection and Quarantine (PPQ) within APHIS is responsible for inspecting ships and planes and their cargo, passengers, and luggage arriving from foreign countries. Working closely with customs inspectors, this unit intercepts animals, poultry, animal and poultry products, and disease vectors at U. S. ports of entry.

Veterinary Services (VS) within APHIS administers laws and regulations pertaining to the importation of animals, poultry, pet birds, semen, embryos, hatching eggs, and other animal products to ensure that those imported from foreign countries are free from certain disease agents.

International Services (IS) within APHIS cooperates with its counterparts in foreign countries to reduce the international spread of animal and poultry diseases. The focus is to protect U.S. livestock and poultry by reducing the disease risk through participation in disease-management strategies before animals and poultry are imported into the United States.

PROTECTING THE LIVESTOCK AND POULTRY INDUSTRIES FROM DISEASE INCURSIONS

The responsibility for rapidly detecting and effectively responding to incursions of FAD's is primarily that of the livestock and poultry owners, veterinarians in private clinical practice, the animal health organization of each State, and APHIS. The State animal health official, usually the State Veterinarian, and the Federal Veterinarian, VS, APHIS, routinely conduct surveillance activities to detect any FAD outbreaks quickly. These activities require the support of State veterinary diagnostic laboratories, the Cooperative Extension Service of the USDA, State and Federal meat and poultry inspection services, animal scientists, market operators, and again, livestock and poultry producers and their private veterinarians.

To detect FAD outbreaks quickly, suspicious signs of a FAD must be promptly reported to the State Veterinarian, the VS Federal Veterinarian, or both. Private veterinarians in clinical practice are conversant with the occurrences of domestic animal diseases in their area and will probably be the first to suspect the presence of a FAD. Prompt reporting of suspicious FAD signs will

enable responsible agencies to conduct an investigation, obtain a diagnosis, and contain a FAD outbreak before it spreads.

When suspicious FAD cases are reported, an investigation of the affected herd or flock is immediately conducted by a specially trained FAD diagnostician. On the basis of history, signs, lesions, and species involved, specimens are collected and submitted to the National Veterinary Services Laboratories (NVSL), VS, Ames, IA, or to the Foreign Animal Disease Diagnostic Laboratory (FADDL), Plum Island, NY, to confirm the presence or absence of a FAD.

On the basis of initial FAD investigation findings, often before the laboratory has completed testing of the samples, State and Federal officials in the affected State will take action to quarantine stricken animals or poultry, increase area surveillance, and initiate steps to characterize and control the outbreak. An Early Response Team (ERT) composed of a senior FAD diagnostician, a senior laboratory pathologist from NVSL, and a senior epidemiologist can be called upon to provide greater technical assistance in the investigation, further assessment of the situation, and assistance in identifying needs of local officials to combat the problem.

LEADERSHIP, PARTNERSHIP, AND MEMORANDUMS OF UNDERSTANDING

Veterinary Services has the critical leadership role for the rapid detection of and the effective response to incursions of potentially devastating FAD's. Veterinary Services is also responsible for providing FAD training, maintaining an awareness of FAD threats, and conducting test exercises of the Regional Emergency Animal Disease Eradication Organization (READEO). To maintain the best possible detection and response capabilities into the future, VS has embarked on developing a new Emergency Management System that will incorporate the military, State agriculture, and industry to a greater extent. The Animal Agriculture Coalition, United States Animal Health Association (USAHA) and the National Assembly, and the American Veterinary Medical Association are helping to develop this new Emergency Management System.

Veterinary Services has established Memorandums of Understanding (MOU's) to obtain resources and cooperation from State animal health and wildlife agencies and the Department of Defense. Wildlife specialists from all 50 States and the Commonwealth of Puerto Rico have agreed to assist in FAD's involving wildlife. In addition, MOU's have been signed with State veterinary diagnostic laboratories to provide for FAD surveillance and laboratory support in the event of an outbreak.

EMERGENCY RESPNOSE TO A FAD OUTBREAK

When field investigations and laboratory tests confirm that a FAD exists in the United States and poses a threat to the livestock or poultry industries, the Secretary of the USDA may declare an emergency. This declaration provides Federal funds and enables USDA to invite State authorities to cooperate in the control and elimination of the disease.

Veterinary Services, for the purpose of FAD animal diseasecontrol and eradication, has divided the United States into two geographic regions. A READEO (Fig. 2) has been established by VS in each region to manage Government, State, and industry cooperation for eradicating foreign animal and poultry disease outbreaks. The regions are referred to as the Eastern READEO and Western READEO. They are staffed by veterinarians, technicians, disease specialists, and administrative and clerical personnel selected because of their experience, training, and interest. The organizational structure is as follows:

Director's Office

Assistant Director

State Director(s)

Secretary

Emergency Programs Liaison

Industry Liaison

Meat and Poultry Inspection Liaison
Laboratory Coordination
Legal
Military Liaison
Legislative and Public Affairs

Administration

Administrative Officer
Contracts and Leases
Finance
Information Resources Management
Personnel
Employee Relations
Procurement, Property and Supply
Vehicles

Field Operations

Field Operations Officer
Appraisal
Cleaning and Disinfection
Diagnosis and Inspection
Epidemiology
Euthanasia
Disposal
Regulatory Enforcement
Security and Disease Prevention
Surveillance
Vaccination
Vector Control

Technical Support

Technical Support
Data Base Systems
Disease Reporting Officer
Disease Specialist
Economics
Environmental Impact
Orientation and Training
Risk Assessment
Vaccination Evaluation
Wildlife

These individuals may be employed by the Federal or State governments, the military, and universities.

When a FAD outbreak occurs, READEO personnel immediately report to the affected area and begin emergency operations. In a response to a small animal or poultry disease problem, only a few READEO components may be activated, whereas the entire READEO may be activated in a large animal or poultry disease problem.

When activated, the READEO's use automated systems to record operational data in a data base that is then available to the national Emergency Programs Staff, VS, Riverdale, MD, and each READEO that is in operation.

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Plant Protection and Quarantine
Veterinary Services
Wildlife Services
Information Technology Community
Legislative and Public Affairs
Management and Budget
Organizational and Professional Development
Policy and Program Development

FIGURE 1

United States Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services READEO Regions

FIGURE 2

PART IV
FOREIGN ANIMAL DISEASES

AFRICAN ANIMAL TRYPANOSOMIASIS

(Nagana, Tsetse Disease, Tsetse Fly Disease)

Definition

African animal trypanosomiasis (AAT) is a disease complex caused by tsetse-fly-transmitted *Trypanosoma congolense*, *T. vivax*, or *T. brucei brucei*, or simultaneous infection with one or more of these trypanosomes. African animal trypanosomiasis is most important in cattle but can cause serious losses in pigs, camels, goats, and sheep. Infection of cattle by one or more of the three African animal trypanosomes results in subacute, acute, or chronic disease characterized by intermittent fever, anemia, occasional diarrhea, and rapid loss of condition and often terminates in death. In southern Africa the disease is widely known as nagana, which is derived from a Zulu term meaning "to be in low or depressed spirits"— a very apt description of the disease.

Etiology

African animal trypanosomiasis is caused by protozoa in the family Trypanosomatidae genus *Trypanosoma*. *T. congolense* resides in the subgenus *Nannomonas*, a group of small trypanosomes with medium-sized marginal kinetoplasts, no free flagella, and poorly developed undulating membranes. In east Africa, *T. congolense* is considered to be the single most important cause of AAT. This trypanosome is also a major cause of the disease in cattle in west Africa. Sheep, goats, horses, and pigs may also be seriously affected. In domestic dogs, chronic infection often results in a carrier state.

T. vivax is a member of the subgenus *Duttonella*, a group of trypanosomes with large terminal kinetoplasts, distinct free flagella, and inconspicuous undulating membranes. *T. vivax* is a large (18-26 µm long) monomorphic organism that is very active in wet-mount blood smears. Cattle, sheep, and goats are primarily affected. Although this organism is considered to be less pathogenic for cattle than *T. congolense*, it is nevertheless the most important cause of AAT in west African cattle. This trypanosome readily persists in areas free of tsetse flies (for example, in Central and South America and in the Caribbean), where it is transmitted mechanically by biting flies or contaminated needles, syringes, and surgical instruments.

T. brucei brucei resides in the subgenus *Trypanozoon. T. b. brucei* is an extremely polymorphic typanosome occurring as short, stumpy organisms without flagella, long slender organisms with distinct flagella, and intermediate forms that are usually flagellated. Horses, dogs, cats, camels and pigs are very susceptible to *T. b. brucei* infection. Infection of cattle, sheep, goats and sometimes pigs results in mild or chronic infection. This last observation, although widely accepted, has been called into question by Moulton and Sollod (13), who cite evidence that this organism is widespread in east and west Africa and that it can cause serious disease and high mortality in cattle, sheep, and goats.

Host Range

Cattle, sheep, goats, pigs, horses, camels, dogs, cats, and monkeys are susceptible to AAT and may suffer syndromes ranging from subclinical mild or chronic infection to acute fatal disease. Rats, mice, guinea pigs, and rabbits are useful laboratory species.

More than 30 species of wild animals can be infected with pathogenic trypanosomes, and many of these remain carriers of the organisms. Ruminants are widely known to be active reservoirs of the trypanosomes. Wild Equidae, lions, leopards, and wild pigs are all susceptible and can

also serve as carriers of trypanosomes.

Geographic Distribution

The tsetse-fly-infested area of Africa extends from the southern edge of the Sahara desert (lat. 15° N.) to Angola, Zimbabwe, and Mozambique (lat. 20° S.). Of the three African animal trypanosomes, only *T. vivax* occurs in the Western Hemisphere in at least 10 countries in the Caribbean and South and Central America

Transmission

In Africa, the primary vector for *T. congolense*, *T. vivax*, and *T. b. brucei* is the tsetse fly. These trypanosomes replicate in the tsetse fly and are transmitted through tsetse fly saliva when the fly feeds on an animal. The three main species of tsetse flies for transmission of trypanosomes are *Glossina morsitans*, which favors the open woodland of the savanna; *G. palpalis*, which prefers the shaded habitat immediately adjacent to rivers and lakes; and *G. fusca*, which favors the high, dense forest areas. Trypanosomiasis is also mechanically transmitted by tsetse and other biting flies through the transfer of blood from one animal to another. The most important mechanical vectors are flies of the genus *Tabanus*, but *Haematopota, Liperosia, Stomoxys*, and *Chrysops* flies have also been implicated. In Africa, both *T. vivax* and *T. b. brucei* have spread beyond the "tsetse fly belts" (20), where transmission is principally by tabanid and hippoboscid flies.

The vector for *T. vivax* in the Western Hemisphere remains unknown, but several species of hematophagous (especially tabanid and hippoboscid) flies are believed to serve as mechanical vectors.

Incubation Period

The incubation period for *T. congolense* varies from 4 to 24 days; for *T. vivax*, from 4 to 40 days; and for *T. b. brucei*, from 5 to 10 days.

Pathogenesis

Initial replication of trypanosomes is at the site of inoculation in the skin; this causes a swelling and a sore (chancre). Trypanosomes then spread to the lymph nodes and blood and continue to replicate. *T. congolense* localizes in the endothelial cells of small blood vessels and capillaries. *T. b. brucei* and *T. vivax* localize in tissue. Antibody developed to the glycoprotein coat of the trypanosome kills the trypanosome and results in the development of immune complexes. Antibody, however, does not clear the infection, for the trypanosome has genes that can code for many different surface-coat glycoproteins and change its surface glycoprotein to evade the antibody. Thus, there is a persistent infection that results in a continuing cycle of trypanosome replication, antibody production, immune complex development, and changing surface-coat glycoproteins.

Immunologic lesions are significant in trypanosomiasis, and it has been suggested that many of the lesions (e.g., anemia and glomerulonephritis) in these diseases may be the result of the deposition of immune complexes that interfere with, or prevent, normal organ function. The most significant and complicating factor in the pathogenesis of trypanosomiasis is the profound immunosuppression that occurs following infection by these parasites. This marked immunosuppression lowers the host's resistance to other infections and thus results in secondary disease, which greatly complicates both the clinical and pathological features of trypanosomiasis.

Clinical Signs

Because simultaneous infections with more than one trypanosome species are very common (18), and simultaneous infection with trypanosomes and other hemoparasites (*Babesia* spp., *Theileria* spp., *Anaplasma* spp., and *Ehrlichia* spp.) frequently occurs, it is difficult to conclude

which clinical signs are attributable to a given parasite. Few adequately controlled studies have been made, and thus a "typical" clinical response to each trypanosome is difficult to reconstruct. What follows is a summation of the syndromes observed in field and experimental cases of trypanosomiasis caused by each of the three African animal trypanosomes.

The cardinal clinical sign observed in AAT is anemia. Within a week of infection with the hematic trypanosomes (*T. congolense* and *T. vivax*) there is usually a pronounced decrease in packed cell volume, hemoglobin, red blood cell, and white blood cell levels, and within 2 months these may drop to below 50 percent of their preinfection values. Also invariably present are intermittent fever, edema and loss of condition (Fig. 2). Abortion may be seen, and infertility of males and females may be a sequel. The severity of the clinical response is dependent on the species and the breed of affected animal and the dose and virulence of the infecting trypanosome. Stress, such as poor nutrition or concurrent disease, plays a prominent role in the disease process, and under experimental conditions, where stress may be markedly reduced, it is difficult to elicit clinical disease.

T. congolense is a hematic trypanosome found only in the blood vessels of the animals it infects. It does not localize and multiply outside blood vessels. Infection with *T. congolense* may result in peracute, acute, or chronic disease in cattle, sheep, goats, horses, and camels. Pigs often develop a milder disease; chronic disease is common in dogs. The incubation period is followed by intermittent febrile episodes, depression, lethargy, weakness, loss of condition, anemia, salivation, lacrimation, and nasal discharge. As the disease progresses, loss of condition and hair color changes from black to metallic brown are seen. The back is often arched and the abdomen "tucked up." Accelerated pulse and jugular pulsation occur and breathing is difficult. Anemia is a prominent sign. Early in the infection, the organisms are readily demonstrable in blood smears, but, as the disease progresses to its acute and chronic forms, organisms are most readily demonstrated in lymph node smears.

T. vivax has a variable incubation period, and, although it is considered to be less virulent for cattle than *T. congolense*, mortality rates of over 50 percent can occur. There seems to be a marked variation in the virulence of different strains of *T. vivax*, but it remains the most important cause of trypanosomiasis of cattle, sheep, and goats in west Africa. It causes mild disease in horses and chronic disease in dogs. *T. vivax* is often difficult to find in blood smears and can also be demonstrated in lymph node smears.

T. brucei brucei has a relatively short incubation period and causes severe to fatal infection in horses, camels, dogs, and cats. It usually causes mild, chronic, or subclinical disease in cattle, sheep, goats, and pigs. A febrile response occurs in the horse 4-14 days after infection. This is followed by recurrent febrile reactions. The heartbeat and respiration may be accelerated, and loss of condition and weakness are seen, whereas the appetite remains good. Progressive anemia and icterus, and edema of the ventral regions, especially the male genitalia, are characteristic. The organisms are not always easily perceived in blood smears and are best demonstrated in tissue smears or sections, (e.g., lymph nodes). Infected animals die in a few weeks or several months, depending on the virulence of the strain of *T. b. brucei.*

The marked immunosuppression resulting from trypanosome infection lowers the host's resistance to other infections and causes in secondary disease, which greatly complicates both the clinical and pathological features of trypanosomiasis.

Gross Lesions

No pathognomonic change is seen in AAT. Anemia, edema, and serous atrophy of fat are commonly observed. Subcutaneous edema is particularly prominent and is usually accompanied by ascites, hydropericardium, and hydrothorax. The liver may be enlarged, and edema of lymph nodes is often seen in the acute disease, but they may be reduced in size in the chronic disease. The spleen and lymph nodes may be swollen, normal, or atrophic. Necrosis of the kidneys and heart muscle and subserous petechial hemorrhages commonly occur. Gastroenteritis is common, and focal polioencephalomalacia may be seen. A localized lesion (chancre) may be noted at the site of fly bite, especially in goats. The anemic blood changes are

anisocytosis, poikilocytosis, polychromasia, and punctate basophilia. All, some, or none of the above may be seen.

The lesions caused by the trypanosomes in susceptible host species vary considerably, depending on the species and strain of trypanosome and the species and breed of host animal affected. The hematic trypanosomes (*T. congolense* and *T. vivax*) cause injury to the host mainly by the production of severe anemia, which is accompanied in the early stages of the disease by leukopenia and thrombocytopenia. In the terminal stages of the disease caused by the hematic trypanosomes, focal polioencephalomalacia probably results from ischemia due to massive accumulation of the parasites in the terminal capillaries of the brain.

The lesions resulting from *T. b. brucei* (a tissue parasite) are remarkably different from those seen with the hematic trypanosomes. Anemia is an important lesion, but much more dramatic are the inflammation, degeneration, and necrosis resulting from cellular invasion of various organs. Marked proliferative changes reflecting immunologic response are observed in most body tissues.

Diagnosis

Field Diagnosis

Trypanosomiasis should be suspected when an animal in an endemic area is anemic and in poor condition. Confirmation depends on the demonstration of the organism in blood or lymph node smears.

In the early phases of infection, especially with *T. vivax* and *T. congolense*, the parasite can readily be observed by microscopic examination of a wet-mount of blood slides. Thick blood films and stained with Giemsa are also a good technique (Fig. 1), but in thin fixed blood films, which are favored for species identification, the parasites may be hard to demonstrate. When parasitemia is low, smears of buffy coat (obtained by microhematocrit centrifugation) can be useful for demonstration of the parasites. Because *T. congolense* tends to associate with the erythrocytes, it is essential that buffy coat and adjacent erythrocytes be included in the smear to ensure demonstration of the parasite.

Stained lymph node smears are a very good method for diagnosis, especially for *T. vivax* and *T. b. brucei*. In chronic *T. congolense* infection, the parasites localize in the microcirculation of the lymph nodes and in other capillary beds, allowing diagnosis by examination of lymph node smears or smears made with blood collected from the ear. Early in infection, blood smears are optimal for the demonstration of *T. congolense*.

These conventional techniques of microscopic examination for the presence of trypanosomes are still widely used, but newer and far more sensitive methods are beginning to supplant them. The antigen-detecting enzyme-linked immunosorbent assay is extremely sensitive for the detection of trypanosomiasis in cattle and goats (12, 25), and species-specific DNA probes have been shown to detect simultaneous infection of cattle with *T. vivax*, *T. b. brucei*, and *T. congolense* when conventional methods revealed only single infections (18).

Specimens for the Laboratory

To perform the preceding and more sensitive procedures, the following specimens should be submitted to the laboratory from several animals: serum, blood with the anticoagulant EDTA, dried thin and thick blood smears, and smears of needle lymph node biopsies.

Control and Eradication

Vector Control

Fly eradication and drug prophylaxis are the only effective trypanosomiasis control methods now available. Several approaches to fly control have been used with varying degrees of

success.

Discriminative bush clearing, extensively used in early tsetse fly eradication campaigns, has been locally useful because it eliminates the breeding places of the tsetse. But, to be completely effective, bush clearing requires ecologically unacceptable destruction of vast areas of brush and forest. It is still a useful procedure when used locally in conjunction with other control methods.

Game elimination, and thus elimination of the main source of bloodmeals for the tsetse, was used in early eradication campaigns.

This was an ineffective and wasteful procedure.

Application of the sterile male technique (as used in screwworm eradication in the United States) received considerable attention in the 1980's. Early problems with breeding of the male flies have been overcome, and field trials have been done in both east and west Africa to determine the effectiveness of this approach in vector control. In limited trials, this procedure has reduced fly populations.

Ground and aerial spraying with insecticides and the use of synthetic pyrethroids on cattle have lowered fly densities in some areas, but widespread use would require considerable international cooperation and expense. Widespread application of insecticide has the tremendous disadvantage of also eradicating many other arthropods, several of which are desirable. The recent introduction of odor-baited targets impregnated with insecticides is proving promising as a means of reducing the tsetse fly.

Chemotherapy and Chemoprophylaxis

The use of drugs for the prevention and treatment of trypanosomiasis has been important for many decades, but the rapidity with which the trypanosomes have developed resistance to each drug introduced has tremendously complicated this approach to controlling the disease. In spite of this, some of the older chemoprophylactic drugs such as the quinapyramine derivatives Antrycide and Antrycide Prosalt are still used and give effective protection against *T. b. brucei* infection in horses, camels, and cattle for up to 3 months. The drug pyrithidium bromide (Prothidium and AD2801) is useful in the prophylaxis of *T. vivax* and *T. congolense* infections in cattle, sheep, and goats and can give protection for up to 6 months. The most widely used of the newer chemoprophylactic drugs (and also the least expensive) is isometamidium chloride (26). This drug, in use for over 20 years and sold under the trade names Samorin, Trypamidium, and M&B 4180A, is excellent for the prophylaxis of all three African animal trypanosomes, and gives protection for 3-6 months. The development of resistance to this drug has been reported in both east and west Africa. Homidium bromide has also been found to be an effective chemophrophylactic drug in Kenya, and the newly introduced arsenical Cymelarsan is effective in treatment of *T. b. brucei* infection.

A very widely used chemotherapeutic drug is diminazine aceturate (Berenil), which is effective against all three African animal trypanosomes. The isometamidium drugs are also excellent chemotherapeutic agents as are the quaternary ammonium trypanocides Antrycide, Ethidium and Prothidium.

Although extensively used in trypanosomiasis control, chemoprophylaxis is an expensive, time-consuming, and thus unsatisfactory long-term solution to the problem of African animal trypanosomiasis.

Immunization

No vaccine is currently available for African animal trypanosomiasis.

Trypanotolerance

It has long been recognized that certain breeds of African cattle are considerably more resistant to African trypanosomiasis that others. This is especially true of the west African short-horned cattle (Muturu, Baoule, Laguna, Samba, and Dahomey) and the N'Dama, which is also of west Africa. These cattle have existed in the region for over 5,000 years. Susceptibility studies have shown the N'Dama to be the most resistant breed followed by the smaller west African short-horned cattle, but the large and more recently introduced Zebu is the most susceptible (15). The mechanisms of trypanotolerance have been extensively studied, and it is now well established that trypanotolerance has a genetic basis (13, 17). Trypanotolerance in sheep and goats has also been described, but the mechanisms of the tolerance phenomenon have not been defined.

Public Health

The three AAT trypanosomes are considered to be nonpathogenic for humans. *T. b. brucei*, although not causing human disease, is closely related to *T. b. gambiense* and *T. b. rhodesiense*. The latter is the cause of human sleeping sickness, a very debilitating and often fatal disease considered to be of major public health significance in 36 sub-Saharan countries of west, central, and east Africa with 50 million people at risk (18). In west and central Africa, a chronic form of human sleeping sickness is caused by *T. b. gambiense*, which uses humans as its major host but also infects pigs. In east and southern Africa, *T. b. rhodensiense* is the cause of a much more acute form of human sleeping sickness. This trypanosome also infects cattle, bushbuck (*Tragelaphus scriptus*), and probably many other wild animals that may serve as reservoirs of the parasite.

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Fig. 2. African trypanosomiasis - Severe emaciation

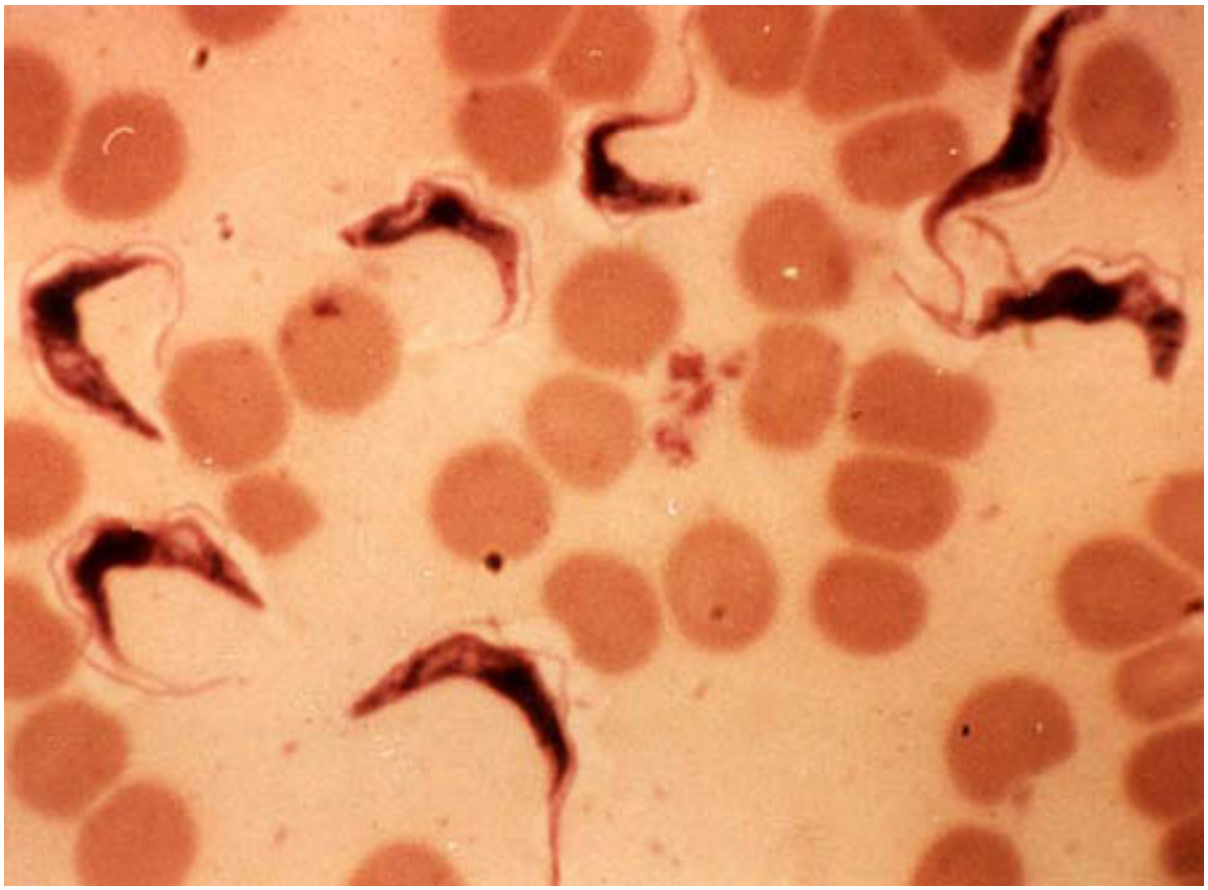

Fig. 1. African trypanosomiasis - Parasites in a blood smear.

PART IV
FOREIGN ANIMAL DISEASES

AFRICAN HORSE SICKNESS

(Perdesiekte, Pestis Equorum, La Peste Equina)

Definition

African horsesickness (AHS) is a highly fatal, viscerotropic, insect-borne viral disease of horses and mules and generally a subclinical disease in other Equidae. The clinical signs and lesions result from selective increased vascular permeability and are characterized by an impairment of the respiratory and circulatory systems.

Etiology

The etiological agent of AHS is a typical orbivirus measuring 68-70 nm in diameter, and the virion is composed of a double-layered protein shell.

The virus is present in the blood and certain organs such as spleen, lung, and lymph nodes in reasonably high concentration, whereas only traces are found in serum, tissue fluids, excretions, and secretions (10). Viremia generally lasts for about 4-8 days and roughly parallels the febrile reaction. In exceptional cases, viremia may last as long as 17 days in the horse and 28 days in zebra and donkeys.

The AHS virus is relatively heat stable, particularly in the presence of protein. It can be stored for at least 6 months at 4° C in saline containing 10 percent serum. Blood in OCG preservative (500 ml glycerin, 500 ml distilled water, 5 g sodium oxalate, and 5 g carbolic acid) can remain infective for more than 20 years; lyophilization may preserve infectivity for as long as 40 years. The virus is readily inactivated at pH values lower than 6.3, but it is relatively stable between values ranging from 6.5 to 8.5.

Nine distinct serotypes of AHS virus are known, the last of which was isolated in 1960. This suggests that, despite its segmented genome, the virus can be regarded as genetically stable and that new serotypes do not readily develop. The present nine serotypes probably evolved over many centuries.

Host Range

Horses, mules, and donkeys have historically been known as hosts for AHS virus, as reflected in the name of the disease. In view of the high mortality rate suffered by horses and mules, these species should be regarded as accidental or indicator hosts. That AHS failed to establish itself outside the tropical regions of Africa tends to indicate that neither horses nor mules or donkeys remain long-term carriers of AHS virus and are therefore not essential for the permanent persistence of the infection in a particular region. Zebra may fulfill this role, but no irrevocable proof has been found to substantiate this view.

The dog has long been known to be susceptible to experimental infection (23). Infection of dogs also readily occurs following ingestion of infected horse meat (3). However, it is extremely unlikely that this species becomes infected by insect bites, and it is generally accepted that dogs play no role in the spread or maintenance of AHS (16).

Camels can ostensibly become inapparently infected with AHS virus, but few details are available as to the level and duration of viremia in this species and its role, if any, in the epizootiology of the disease. A high percentage of African elephant serum samples reacted positively against AHS virus in complement fixation tests (7), but no neutralizing antibodies

could be demonstrated in such samples. No evidence of virus replication could be found in elephants artificially infected with AHS virus (12). It can therefore be concluded that the African elephant is not susceptible to infection and that the putative serological evidence resulted from abnormal reactions of elephant sera in a complement fixation test.

Geographic Distribution

African horse sickness appears to be endemic in tropical regions of central Africa from where it regularly spreads southwards to southern Africa. The Sahara Desert forms a formidable barrier against northward spread. Occasionally the infection does reach northern African countries, either by spread along the Nile valley or along the West Coast of Africa. The disease has also occurred outside Africa on a few occasions, the most notable of which was the major outbreak in the Near and Middle East from 1959 through 63 and in Spain (1966 and 1987-1990) (15).

In temperate regions such as South Africa, AHS has a definite seasonal occurrence. The first cases are usually noticed towards midsummer, and the disease disappears abruptly after the onset of cold weather in autumn. The disease is most prevalent in warm, low-lying moist areas such as valleys and marshes.

Transmission

African horse sickness is a noncontagious disease, and the virus was the first shown to be transmitted by midges (*Culicoides* spp.) (9). The most significant vector seems to be *Culicoides imicola*, but other species, such as *C. variipennis*, which is common in many parts of the United States, should also be considered as potential vectors (4).

The virus is transmitted biologically by midges, and these insects are most active just after sunset and at about sunrise.

Although other insects such as mosquitoes have been implicated as biological vectors, and large biting flies (e.g., *Stomoxys*, *Tabanus*) may transmit AHS virus mechanically, the role of these insects in the epizootiology of the disease is regarded as absolutely minimal compared with that played by the *Culicoides* species.

Generally, midges disperse only a few kilometers from their breeding sites, but it has been postulated that they can be borne for longer distances on air currents (21). Analysis of field observations on the progression of outbreaks indicates that wind-borne spread of midges may assist the short-distance spread of the disease but that long-distance jumps of the infection are invariably the result of movement of infected Equidae.

Incubation Period

In experimentally induced cases the incubation period usually varies between 5 and 7 days, but it may be as short as 2 days and rarely as long as 14 days. Circumstantial evidence indicates that, following natural infection, the incubation period varies from 7 to 14 days.

Clinical Signs

Four clinical forms of AHS can be distinguished (10).

The Peracute or Pulmonary Form

This form is characterized by very marked and rapidly progressive respiratory involvement. An acute febrile reaction may be the only clinical sign for a day or two, reaching a maximum of about 104-106° F (40-41° C). This is followed by various degrees of respiratory distress. The breathing may increase to 60 or even 75 respirations per minute, and the animal tends to stand with its forelegs spread apart, its head extended, and the nostrils fully dilated. Expiration is frequently forced with the abdomen showing heave lines. Profuse sweating is common, and spasmodic coughing may be observed terminally with frothy, serofibrinous fluid exuding from

the nostrils (Fig. 3). The onset of dyspnea is usually very sudden, and death often occurs within 30 minutes to a few hours after its appearance.

The Subacute Edematous or Cardiac Form

The incubation period of this form varies between 7 and 14 days, and the onset of the clinical disease is marked by a febrile reaction of 102-106° F (39-41° C) that lasts for 3-6 days. Shortly before the decline of the fever, characteristic edematous swellings appear. These initially involve the supraorbital fossae and the eyelids (Figs. 4, 5, and 6) and later extend to the lips, cheeks, tongue, intermandibular space, and laryngeal region. Subcutaneous edema sometimes extends a variable distance down the neck towards the chest, often obliterating the jugular groove. Interestingly, no edema of the lower limbs is observed. Terminally, petechial hemorrhages develop in the conjunctivae and under the ventral surface of the tongue. The animal becomes very depressed and may lie down frequently but for very short periods only. Occasionally, signs of colic may develop. Finally, the animal remains prostrate and dies from cardiac failure about 4-8 days after the onset of the febrile reaction. In cases that recover, swellings gradually subside within a period of 3-8 days.

The Acute or Mixed Form

This form represents a mixture of the pulmonary and cardiac forms. Although seldom diagnosed clinically, it is seen at necropsy in the majority of fatal cases of AHS in horses and mules. The disease manifests itself in various ways. Initial pulmonary signs of a mild nature that do not progress are followed by edematous swellings and effusions, and death results from cardiac failure. In the majority of cases, however, the subclinical cardiac form is suddenly followed by marked dyspnea and other signs typical of the pulmonary form.

Horsesickness Fever

This is the mildest form and is frequently overlooked in natural outbreaks. The febrile reaction is usually of the remittent type, with morning remissions and afternoon exacerbation, and lasts for 3-8 days but rarely exceeds 104° F (40° C). Apart from the febrile reaction, other clinical signs are rare and inconspicuous. The conjunctivae may be slightly congested, the pulse rate may be increased, and a certain degree of anorexia and depression may be present. This form of the disease is usually observed in donkeys and zebra or in immune horses infected with a heterologous serotype of AHS virus.

Gross Lesions

The lesions observed at necropsy examination depend largely on the clinical form of disease manifested by the animal before death (10). In the peracute form the most characteristic changes are edema of the lungs or hydrothorax (Figs. 7 and 8). In very peracute cases, extensive alveolar edema and mottled hyperemia of the lungs are seen, whereas in cases with a somewhat more protracted course extensive interstitial and subpleural edema is also present, but hyperemia is less evident. Occasionally the lungs may appear reasonably normal, but the thoracic cavity may contain as much as 8 L of fluid. Other less commonly observed lesions are periaortic and peritracheal edematous infiltration, diffuse or patchy hyperemia of the glandular fundus of the stomach, hyperemia and petechial hemorrhages in the mucosa and serosa of the small and large intestines (Fig. 9 and 10), subcapsular hemorrhages in the spleen, and congestion of the renal cortex. Most of the lymph nodes are enlarged and edematous, especially those in the thoracic and abdominal cavities. Cardiac lesions are usually not conspicuous, but epicardial and endocardial petechial hemorrhages are sometimes evident.

In the cardiac form the prominent lesion is a yellow gelatinous infiltration in the subcutaneous and intermuscular fascia primarily of the head, neck, and shoulders (Fig. 11). Occasionally the lesion may also involve the brisket, ventral abdomen and rump. Hydropericardium (Fig. 12) is a common feature, and there are extensive petechial and ecchymotic hemorrhages on the epicardium and endocardium, particularly of the left ventricle. The lungs are usually normal or

only slightly engorged, and the thoracic cavity rarely contains excess fluid. The lesions in the gastrointestinal tract are generally similar to those found in the pulmonary form, except that submucosal edema of the cecum, large colon, and rectum tends to be far more pronounced.

In the mixed form the lesions seem to represent a combination of those found in the pulmonary and cardiac forms.

Morbidity and Mortality

In susceptible horse populations, the fatalities range between 70 and 95 percent, and the prognosis is extremely poor. In mules, the mortality rate is about 50 percent and in the European and Asian donkey about 5-10 percent. No mortality is observed among African donkeys and zebra.

In enzootic regions, the mortality rate is modified in proportion to the immunity acquired by the equine population as a result of previous vaccination or exposure to natural infection.

Diagnosis

Field Diagnosis

During the early febrile phase of AHS, a field diagnosis may be virtually impossible. However, a presumptive diagnosis should be possible once the characteristic clinical signs have developed and, more particularly, at necropsy.

Specimens for the Laboratory

Confirmation of a presumptive diagnosis is based on virus isolation and identification. This is of particular importance whenever outbreaks occur outside the enzootic regions. The AHS virus can be isolated quite readily from blood collected during the early febrile phase (preferably in heparin or else in other anticoagulants) as well as from spleen, lung, and lymph nodes collected at necropsy (10).

Specimens for virus isolation should be shipped to the laboratory refrigerated, NOT FROZEN.

Horses that survive infection develop specific antibodies within 10-14 days after infection that reach a peak about 10 days later. It is always advisable to use paired (acute and convalescent phase) serum samples. Serological tests can demonstrate AHS antibodies for 1 to 4 years after infection.

Differential Diagnosis

The clinical signs of AHS, particularly when not fully developed, may be confused with other infections, notably equine encephalosis and equine viral arteritis (EVA). The former disease occurs under the same epizootiological conditions as AHS, and in South Africa the two diseases frequently occur simultaneously. Horses suffering from equine encephalosis usually do not have characteristic lung edema or subcutaneous edema, and the mortality rate is considerably lower than in AHS.

Severe cases of EVA may readily be confused with AHS. The presence of ventral edema (in EVA), particularly of the lower limbs, and the much lower mortality rate should allow differentiation. In countries where piroplasmosis occurs, the early stage of this disease, before blood parasites can be demonstrated and anemia develops, may be confused with AHS.

The necropsy lesions of AHS can be confused with those found in cases of purpura hemorrhagica. In the latter condition, the hemorrhages and edema seem to be more severe and widely distributed than in AHS and usually involve the limbs and lower abdomen. The highly sporadic occurrence of purpura also aids in differentiation.

Vaccination

The work of Alexander and de Toit (1,2) has resulted in the development of a live attenuated vaccine that has been used successfully for several decades. However, the adaptation of the virus to the brains of adult mice resulted in a neurotropic vaccine that occasionally caused encephalitis in horses mules and particularly in donkeys (20). This necessitated an alternate and safer method of attenuation achieved by plaque selection in Vero cell cultures (11). The vaccine currently used in South Africa consists of two quadrivalent vaccines that are administered 3 weeks apart. Strategic reserves of monovalent vaccines are also maintained.

Extensive work is presently under way to develop potent inactivated and recombinant vaccines that should widen the choice in the near future.

Control and Eradication

Preventive Measures

The most important means of introducing AHS into a hitherto disease free country is by the introduction of equid animals incubating the disease. Zebra and African donkeys that do not develop any clinical sign of disease are particularly dangerous. Equid animals imported from infected countries should be quarantined in insect-proof facilities at the point of entry. At present, there is a minimum 60-day quarantine period for horses brought into the United States from Asia, Africa, and the Mediterranean countries.

Once the disease is introduced into a country, several preventive measures should be taken to prevent further spread and eventually to eradicate the scourge in the shortest possible time. It is essential to isolate and identify the causal virus, but it is imperative that control measures be implemented even before the final diagnosis has been made.

Officials should delineate area of control, taking into consideration geographical borders such as mountains and rivers. The movement of all equid animal within, into, and out of the control zone should be stopped and this restriction rigidly enforced. Furthermore, all equid animals should be stabled, at least from dusk to dawn, and sprayed with insect repellents to reduce the risk of insects feeding on the animals. If sufficient stabling facilities are not available, barns could be used. Even if not insect-proof, such housing will reduce the risk of infection. Additionally, the rectal temperatures of all equid animals in the zone should be taken regularly (preferably twice daily) to detect infected animals as early as possible because overt disease is generally preceded by viremia for about 3 days. Animals with fever should be killed or housed in insect-free stables until the cause of the fever has been established.

Once the diagnosis has been finalized, vaccination of all susceptible animals with the relevant monovalent AHS vaccine should be considered. This decision will be guided largely by the success of measures already taken.

Natural Immunity

Animals that recovere from the disease develop a solid life-long immunity against the infecting virus and a partial immunity against heterologous serotypes. Foals from immune dams have a passive immunity that may protect them for up to 6 months.

Public Health

There is no evidence that man can become infected with field strains of AHS virus, either through contact with infected animals or from working in laboratories. However, it has been shown that certain neurotropic vaccine strains may cause encephalitis and retinitis in humans following transnasal infection (22).

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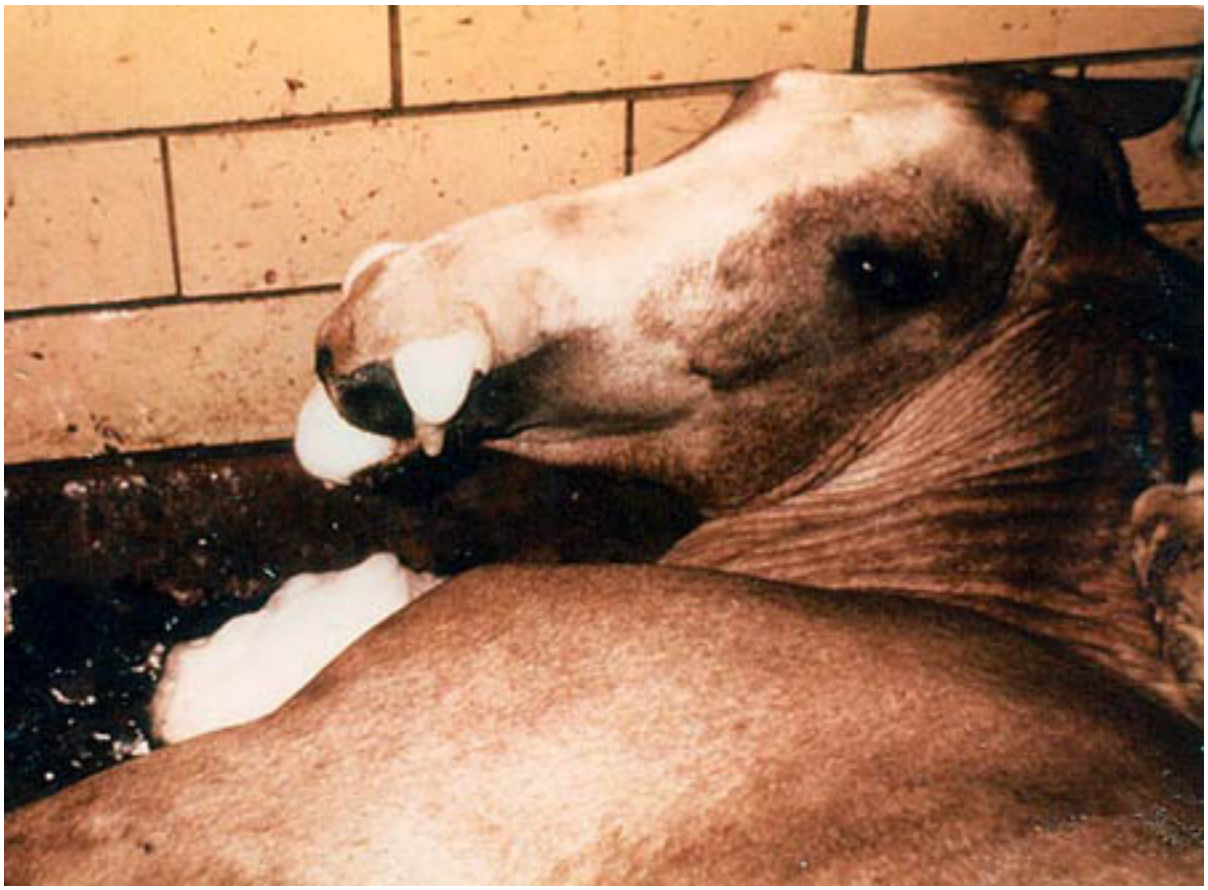

Fig. 3. AHS - Foam from the nares is due to pulmonary edema.

Fig. 4. AHS - Depressed horse; note the bilateral supraorbital edema.

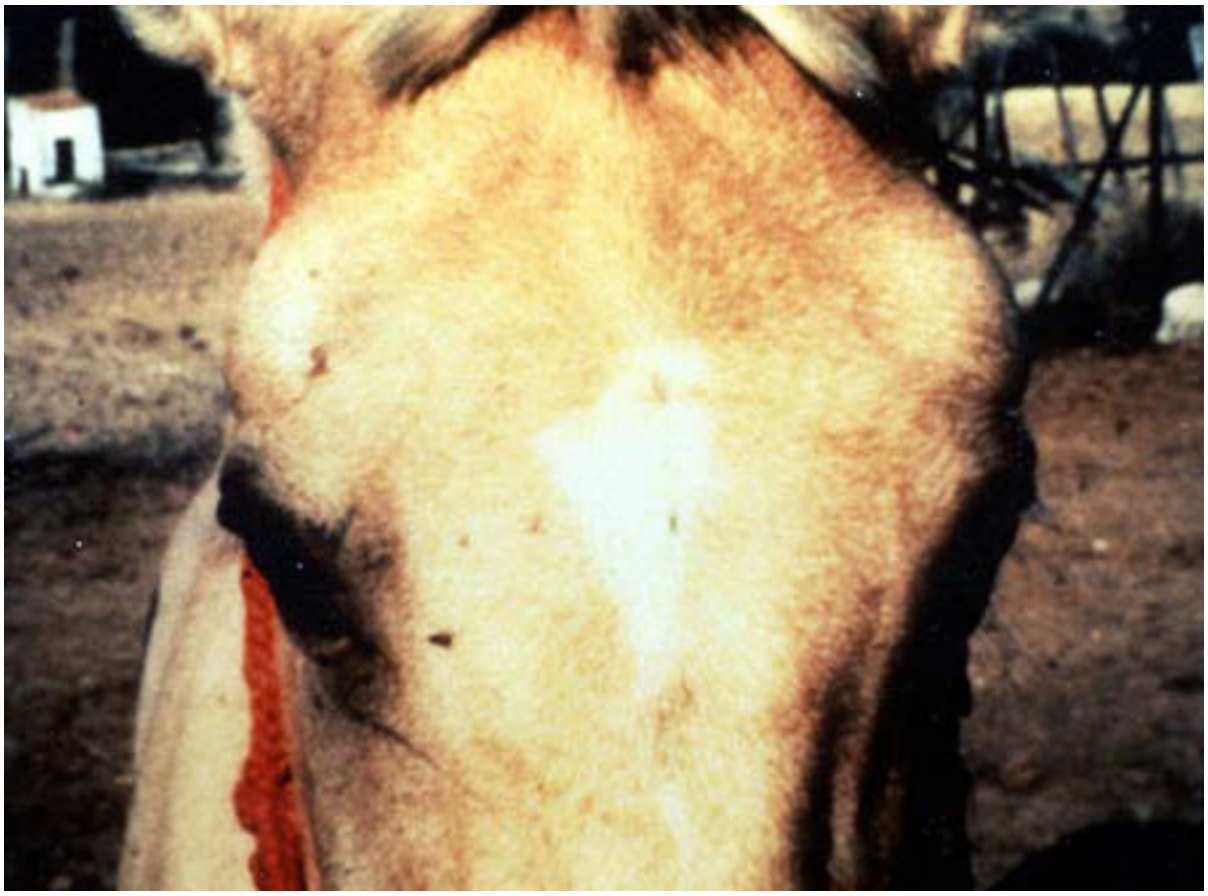

Fig. 5. AHS - Supraorbital edema.

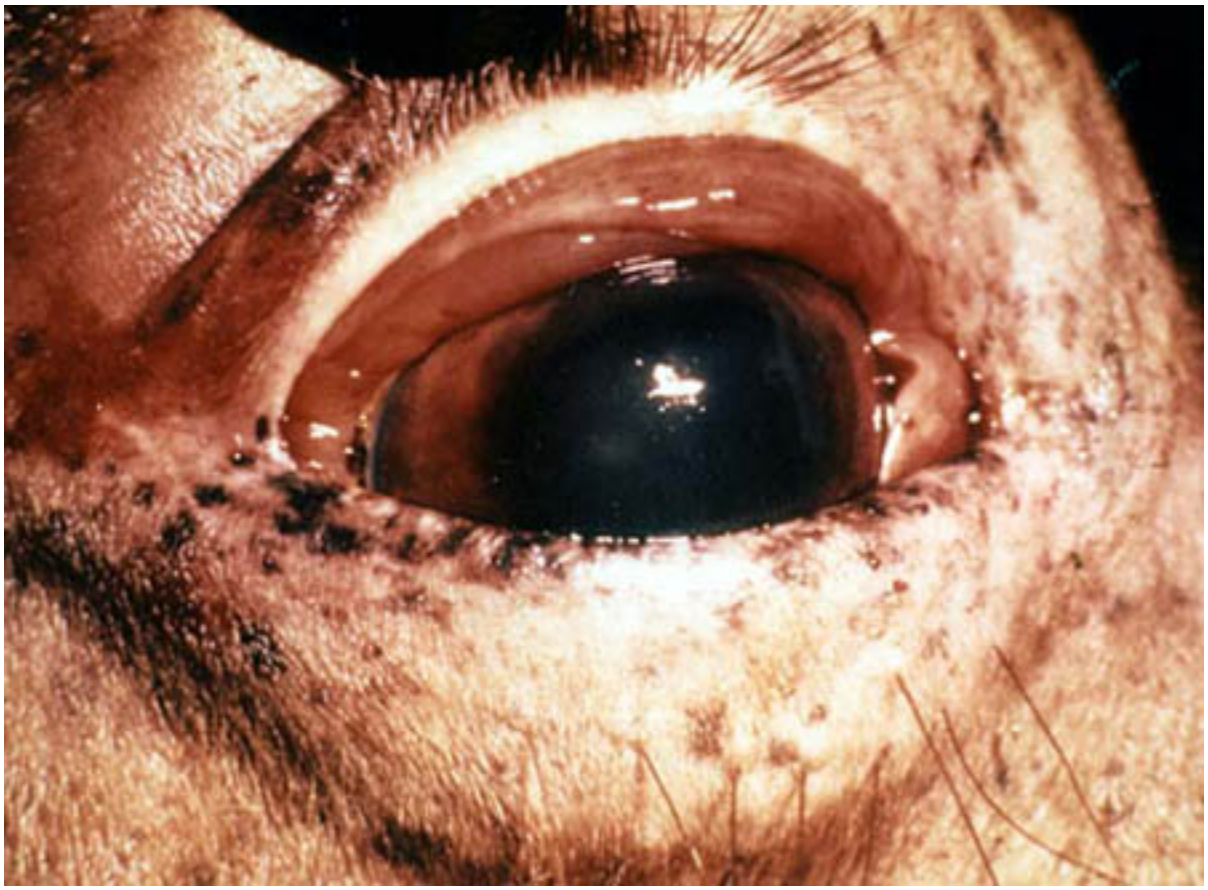

Fig. 6. AHS - Congestion and edema of the conjunctiva. Congestion is a consistent clinical finding in AHS.

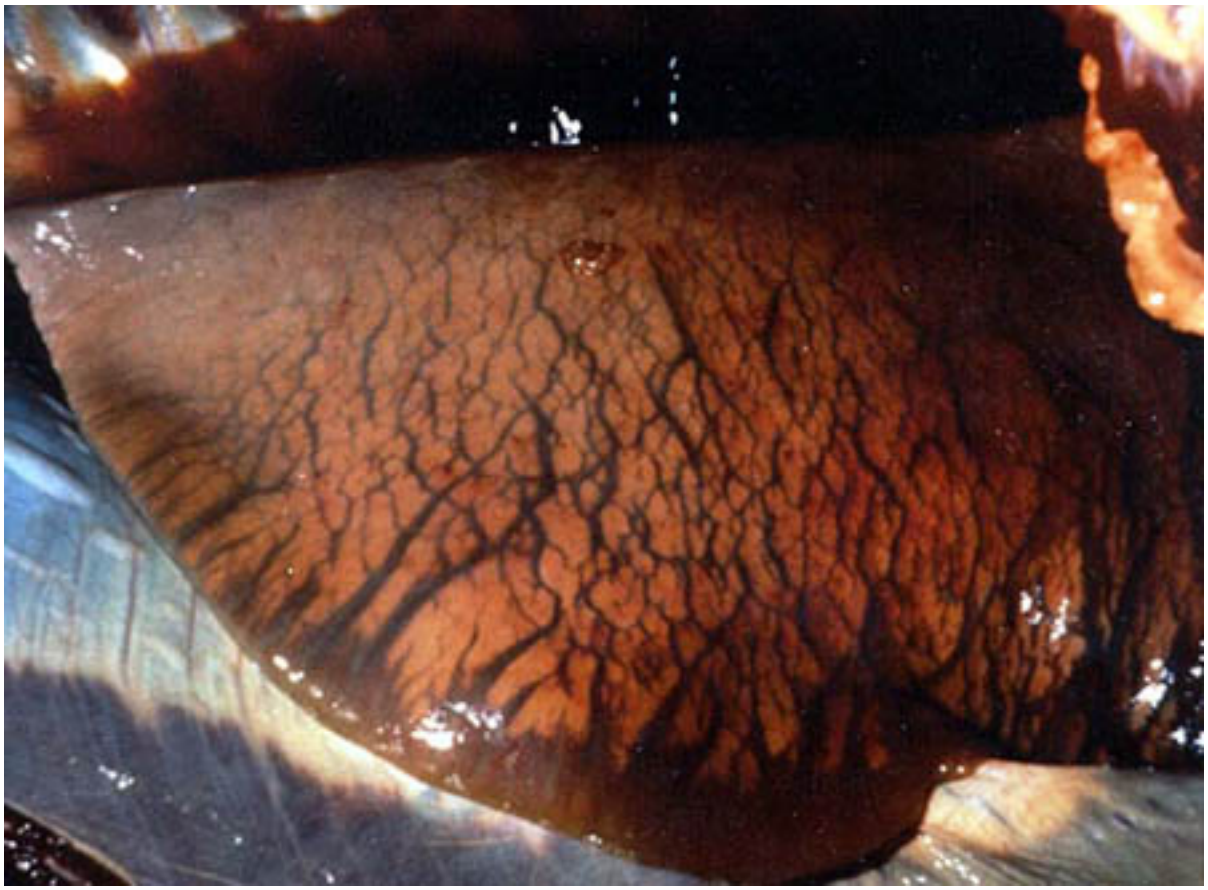

Fig. 7. AHS - Excessive fluid in the thoracic cavity and pulmonary edema; note the distended interlobular septa.

Fig. 8. AHS - Cut surface of an edematous lung; note the distended interlobular septa.

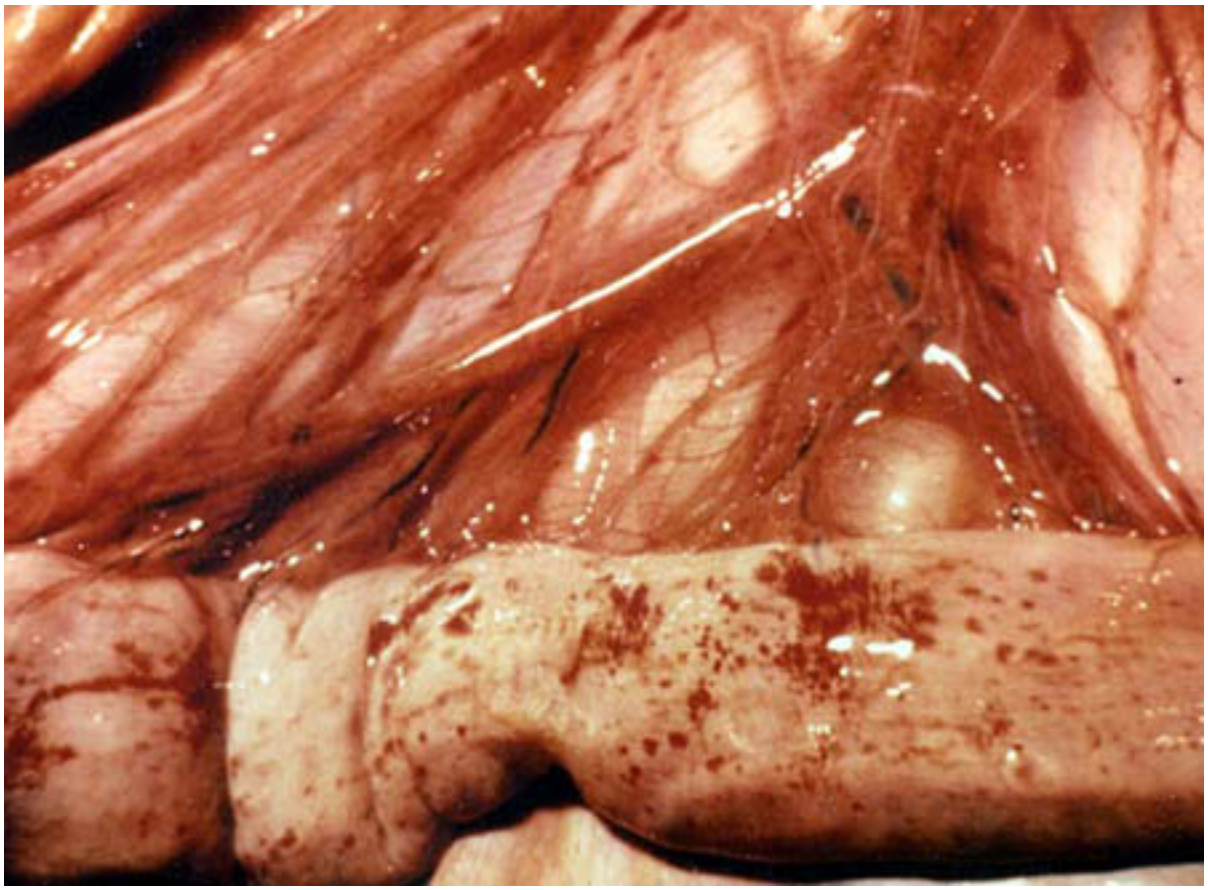

Fig. 9. AHS - Petechial hemorrhages on the serosa are indicative of a viremic or septicemic condition.

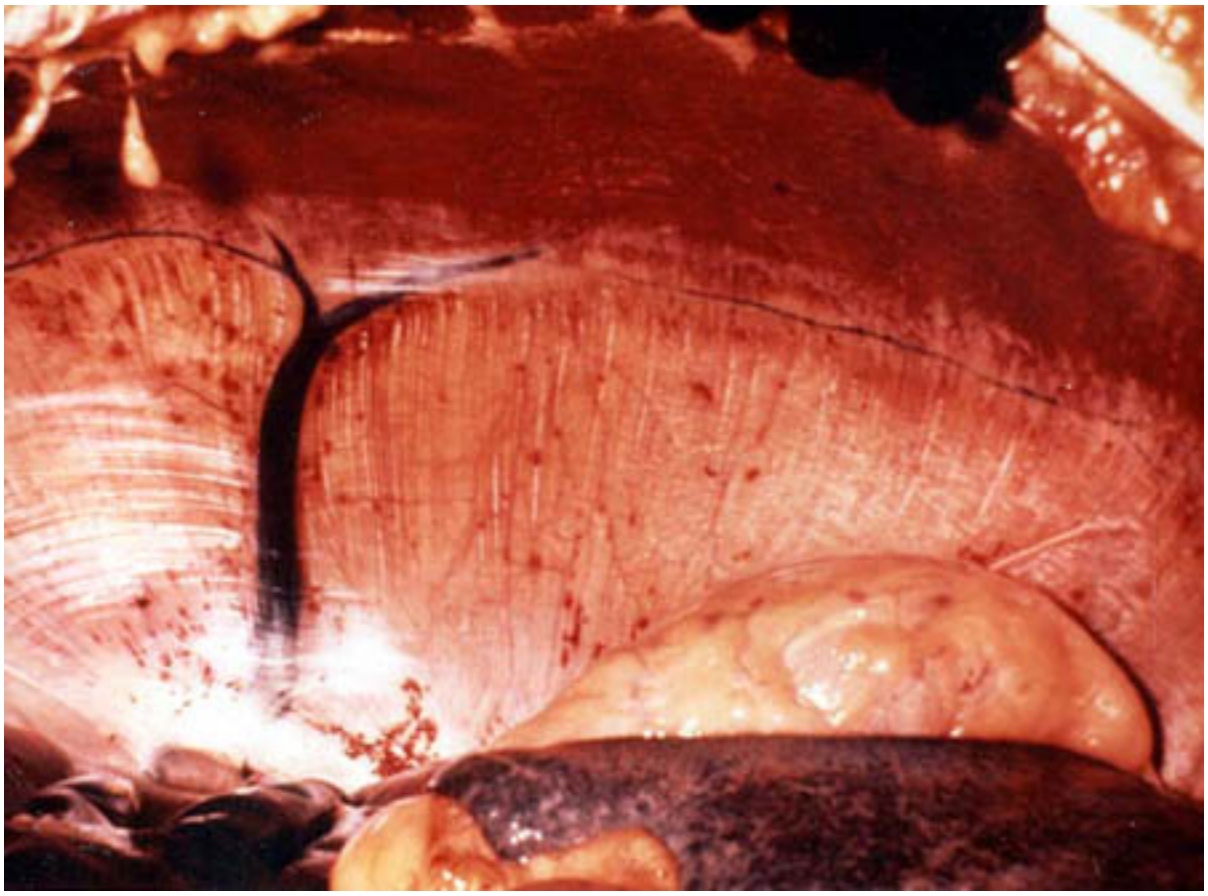

Fig. 10. AHS - Petechial hemorrhages on the diaphragm are indicative of a viremic or septicemic condition.

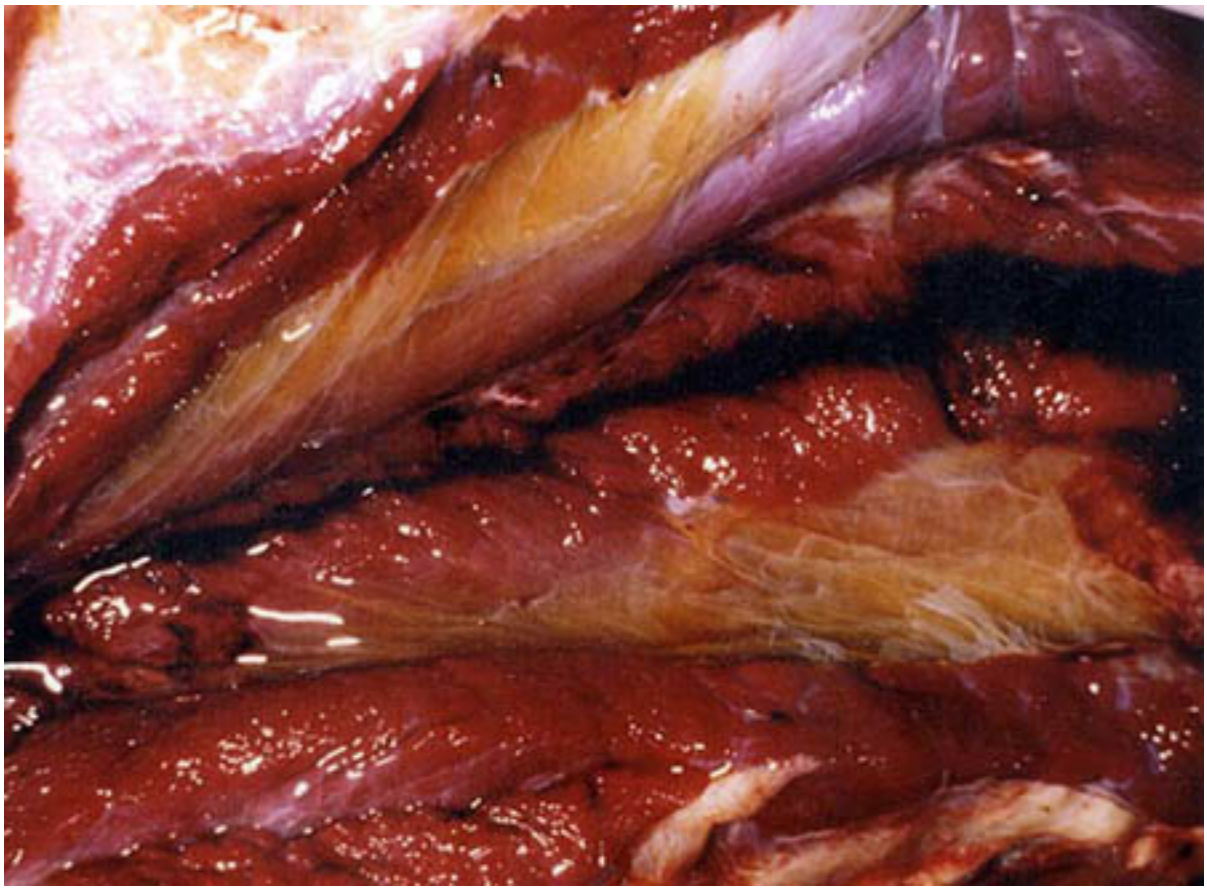

Fig. 11. AHS - Edema in the intermuscular fascia of the neck may be the only lesion in AHS.

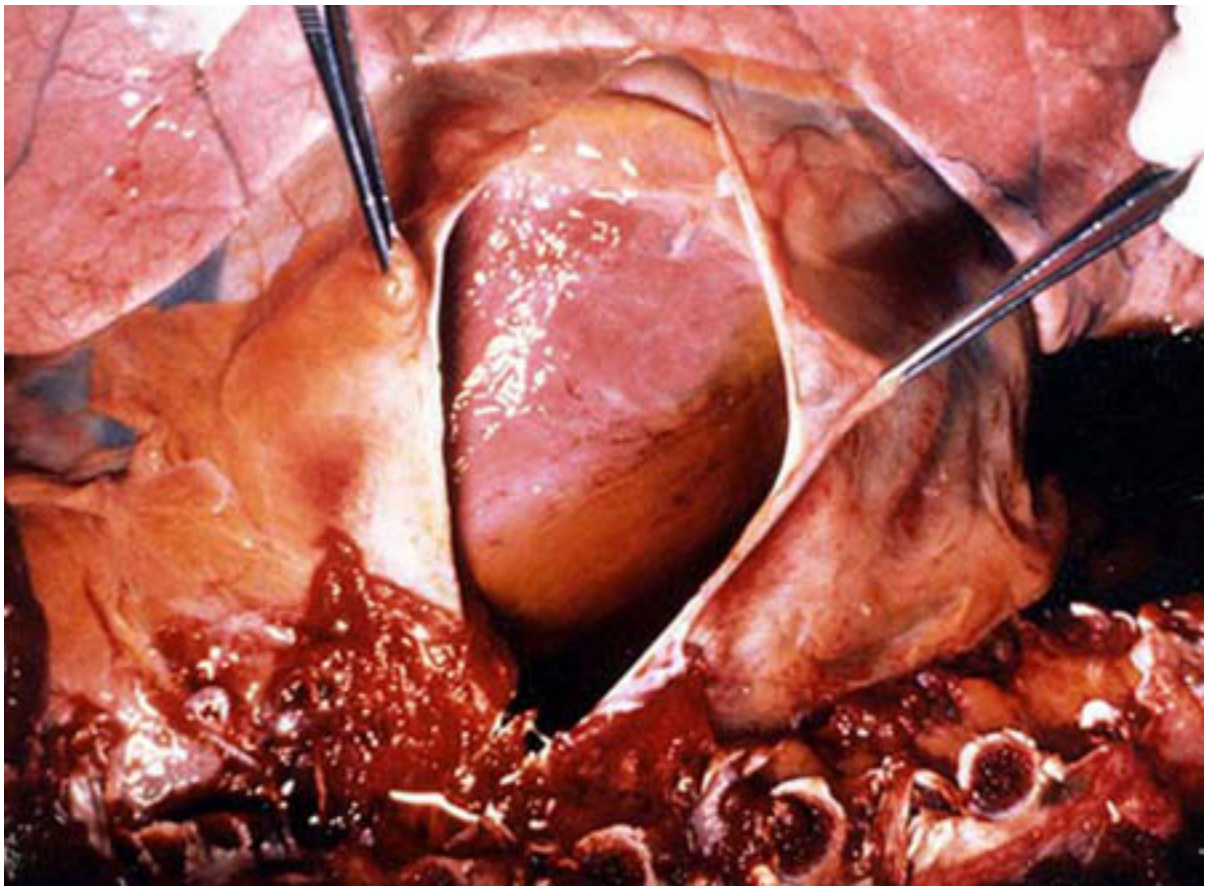

Fig. 12. AHS - Hydopericardium.

PART IV
FOREIGN ANIMAL DISEASES

AFRICAN SWINE FEVER

(Peste porcine Africaine, fiebre porcina Africana, maladie de Montgomery)

Definition

African swine fever (ASF) is a tickborne and contagious, febrile, systemic viral disease of swine .

Etiology

The ASF virus is a large (about 200 nm) lipoprotein-enveloped, icosahedral, double-stranded DNA virus. For many years the agent was classified as an iridovirus (3), but in recent years it was found to have many characteristics of poxvirus; thus, researchers have suggested establishment of a new family for ASF virus (ASFV) (19).

This virus is quite stable and will survive over a wide range of pH. In serum-free medium, ASFV is inactivated at pH 3.9 or lower and at pH 11.5 or higher. In the presence of 25 percent serum, ASFV will remain viable for 7 days at pH 13.4 (17). The virus will survive for 15 weeks in putrefied blood, 3 hours at 50º C, 70 days in blood on wooden boards, 11 days in feces held at room temperature, 18 months in pig blood held at 4º C, 150 days in boned meat held at 39º F, and 140 days in salted dried hams (8A).

Over the years, ASFV isolates with lower virulence have emerged — particularly in the Iberian peninsula. Virulence of isolates varies from highly virulent (essentially 10 percent mortality in 7-10 days after exposure), to moderately virulent (acute illness in which a high percentage of the pigs survive) , to low virulence (only seroconversion occures).

Host Range

Initially, domestic and wild pigs (Africa: warthog, bush pig, and giant forest hog; Europe: feral pig) were thought to be the only hosts of ASFV (1,16). In 1963, Spanish workers isolated ASFV from the soft tick *Ornithodoros erraticus* collected from ASF-infected farms (13). Subsequently, researchers showed that ASFV replicates in the tick and that there is transstadial, transovarial, and sexual transmission in *Ornithodoros* ticks. *O. moubata* collected from warthog burrows in Africa were shown to be infected with ASFV (5). African swine fever in wild pigs in Africa is now believed to cycle between soft ticks living in warthog burrows and newborn warthogs (18). *Ornithodoros* ticks collected from Haiti, the Dominican Republic, and southern California have been shown to be capable vectors of ASFV (4,5), but in contrast to the African ticks, many of the ticks from California died after being infected with ASFV. Many researchers believe that ASFV is really a tick virus and the pig is an accidental host (11).

Because ASFV-infected ticks can infect pigs, ASFV is the only DNA virus that can qualify as an arbovirus.

Geographic Distribution

African swine fever is present in several African countries and on the island of Sardinia.

Transmission

Even though the soft tick has been shown to be a vector (and in Africa probably the reservoir of ASFV), the primary method of spread from country to country has been through the feeding of

uncooked garbage containing ASFV-infected pork scraps to pigs. Once a pig becomes infected, ASFV spreads by direct contact, and contaminated people, equipment, vehicles, and feed. The role of carrier pigs has been difficult to prove experimentally, but circumstantial evidence from the field incriminates carrier pigs. An outbreak of ASF in a contained swine operation in Africa was traced to workers feeding the entrails of guinea fowl to pigs. It was shown that the guinea fowl feed on soft ticks; thus, ASFV was present in the guinea fowl intestines fed to the pigs.

The amount of ASFV needed to infect a pig depends on the route of exposure. Experimentally, a pig can be infected by intramuscular or intravenous inoculation with a 0.13 hemadsorbing dose (HAD_{50}); intranasal-oral inoculation required 18,200 HAD_{50}.

In an ASF endemic area where there are soft ticks, ticks can be the source of infection. However, in these areas in Africa, pigs can be very successfully raised in confinement with double fencing, proper isolation, and sanitary procedures. In Africa, the production system with the highest risk of ASF is the village pig, for these pigs roam. The owners do not practice isolation procedures when the pigs are confined.

In other areas, the disease has to be introduced by infected live pigs or by feeding uncooked garbage containing ASFV-infected pork. Once the disease is introduced into a herd, it spreads by direct and indirect contact with secretions and excretions from infected pigs. Aerosol transmission is not important in the spread of ASF. Because ASFV does not replicate in epithelial cells, the amount of virus shed by an ASF-infected pig is much less than the amount of virus shed by a hog-cholera-infected pig. The blood of a recently infected pig contains a very high ASFV titer: $10^{5.3}$ to $10^{9.3}$ HAD_{50} per milliliter (7). Therefore, if pigs fight, an infected pig develops bloody diarrhea, or an infected pig is necropsied, blood is shed, and there is massive environmental contamination.

Piglets born of ASF-convalescent dams are free of ASFV and ASF antibody at birth but seroconvert after ingesting colostrum (14,15). When piglets from noninfected (control) and ASF-convalescent dams were challenge-inoculated when 7 weeks old, the control piglets developed an average viremia of $10^{7.6}$ and died, whereas the piglets from convalescent gilts developed an average viremia of $10^{4.9}$ and survived. However, because of persistent infection by ASFV, reestablishing a herd using pigs from convalescent animals will not result in an ASFV-free herd. When farmers in Cameroon repopulated their herds using ASF-convalescent animals, the herds experienced recurring periods of high mortality due to ASF.

Incubation Period

After intranasal-oral exposure, pigs usually develop fever and leukopenia in 48 to 72 hours.

Clinical Signs

Highly and Moderately Virulent ASF Isolates

The clinical signs of ASF are influenced by the virulence of the virus and the physiological state (age and pregnancy) of the pig. After inoculation of feeder pigs with either a highly virulent or moderately virulent isolate, the clinical course for both isolates is similar for the first 4-6 days post infection. About 2 DPI, the pigs will develop a fever of 105-107º F (40.5-41.7º C) and white pigs will have a reddened skin, moderate anorexia, and leukopenia. When disturbed the pigs will get up and move about but if left alone will after a short time lie down.

After 4-6 DPI, a difference between the pigs inoculated with the different isolates will become apparent.

Highly Virulent Isolate

The pigs become progressively sicker (eat and move less), and most die between 7 and 10 DPI. It is not unusual to see a pig walking and a short time later to find it dead.

Moderately Virulent Isolate

Pigs infected by moderately virulent ASFV usually have a high fever for 10-12 DPI. Some mortality usually occurs at this time. After 12-14 DPI, temperatures and leukocyte counts start to return to normal levels. It is not unusual to have one or more pigs die as early as 7-8 DPI, but when these pigs are necropsied, the cause of death is frequently hemorrhage into the stomach; the underlying mechanism of death was that ASFV infection caused a thrombocytopenia, resulting in a prolonged bleeding time and hemorrhage from a preexisting gastric ulcer (2). Very young pigs may have a high mortality and have lesions similar to infection by highly virulent virus.

Pigs affected with either isolate, in addition to the reddened skin, may develop dark red to purple discoloration of the skin on the ears (Fig. 13), tail, extremities of the legs, or skin on the hams. This is a nonspecific sign also seen in other diseases. Some groups of pigs will develop diarrhea; this is probably due to disturbed gut physiology and flora rather than a direct effect of the virus because the virus does not replicate in epithelium. In contrast to hog cholera, ASFV-infected pigs do not develop a conjunctivitis or encephalitis, and, despite the high fever, the ASFV- infected pigs stay in good condition, whereas hog cholera-infected pigs quickly lose much weight.

Pregnant animals infected with a high-, moderate-, or low-virulence ASF isolate abort.

Low Virulence Isolates

Nonpregnant animals infected by certain low-virulence ASFV may only seroconvert; pregnant animals will abort.

Other low-virulence ASFV isolates will cause a low fever for 2-3 weeks and then reddened areas 1 cm^2 to many centimeters in size may develop in the skin. These areas then become raised and necrotic. These pigs may also have painless enlargements of joints—particularly the carpal and tarsal joints. This form is referred to as chronic ASF (10). Many of these pigs will have recurring episodes of a more acute disease and eventually die during an acute episode.

Gross Lesions

Highly Virulent ASFV Infection

Pigs that die peracutely from an infection with a highly virulent ASFV may have poorly developed lesions. Animals that die 7 or more DPI have more classic lesions. Three lesions most consistently found and highly suggestive of ASF infection are as follows:

Greatly enlarged dark red to black friable spleen (Fig. 14)

Very enlarged hemorrhagic gastrohepatic lymph nodes (Fig. 15)

Very enlarged hemorrhagic renal lymph nodes (Fig. 16).

Other lesions described for ASF are more variable and are as follows:

Dark red to purple areas of skin on ears, feet, and tail

Petechial hemorrhages on serosal surfaces (Fig. 17)

Petechial to ecchymotic hemorrhages in the renal cortex

Perirenal edema

Edema of the gall bladder (Fig. 18)

Swollen liver

Edema of the lung.

In pigs infected orally, the submandibular lymph node may be enlarged and have some

hemorrhage. Other peripheral lymph nodes may have only edema.

Moderately Virulent Virus

The gross lesions 8-12 DPI in pigs infected with a moderately virulent ASFV are similar to those infected by a highly virulent ASFV. The main difference in the lesions between these two types of isolates is that in infections by a moderately virulent ASFV, the spleen although enlarged, has a more normal color and is not friable.

Low Virulent Virus

The most common lesions in chronic ASF are necrotic skin lesions (Fig. 21, 22), consolidated lobules in the lung (Fig. 19), generalized lymphadenopathy (Fig. 20), swollen joints, and pericarditis.

Aborted fetuses may be anasarcous, and there may be petechial hemorrhages in the placenta, skin, and myocardium, and a mottled liver.

Morbidity and Mortality

The warthog and bush pig develop a viremia but have a very mild or subclinical disease, whereas ASF infection in domestic pigs and European feral pigs can cause a high mortality.

Morbidity in a previously unexposed herd will usually be 100 percent in pigs that have contact with each other. Mortality varies with the virulence of the isolate. Highly virulent isolates will cause about a 100 percent mortality. Infection by lesser virulent isolates can cause mortality that varies from a low percentage to 60-70 percent . Factors that can increase mortality in infections by the lesser virulent isolates are concurrent disease, a young age, and pregnancy.

Diagnosis

Field Diagnosis

The highly virulent form of ASF will be easiest to diagnose because essentially 100 percent of the pigs will die. African swine fever caused by the lesser virulent isolates will be more difficult to diagnose but should always be suspected when there are febrile pigs and necropsy findings include the following:

Greatly enlarged dark red to black spleen

Very enlarged hemorrhagic gastrohepatic lymph nodes

Very enlarged hemorrhagic renal lymph nodes.

African swine fever has frequently been misdiagnosed as hog cholera. In contrast to hog cholera, ASFV-infected pigs do not develop a conjunctivitis or encephalitis, and despite the high fever, the ASFV-infected pigs stay in good condition. In contrast, hog cholera-infected pigs are severely depressed and quickly lose much weight; moreover, they usually have a foul smelling diarrhea.

Specimens for Laboratory

The ASFV is present in the blood starting about 2 DPI. In infections by lesser virulent isolates, ASFV can usually be isolated from the blood for 25 or more DPI. Specimens for laboratory diagnosis are as follows:

Heparinized blood

Clotted blood or serum

Submandibular lymph node

Inguinal lymph node

Tonsil
Spleen
Gastrohepatic lymph node
Lung
Liver
Kidney.

Bone marrow should be submitted if there are considerable postmortem changes.

The specimens should be shipped refrigerated or frozen. Pieces of the preceeding tissues, the brain, and any other gross lesion should be submitted in 10 percent buffered formalin.

Aborted fetuses are usually free of virus; therefore, it is necessary to submit a blood sample from the dam.

Laboratory Diagnosis

The initial diagnosis of ASF in a free area requires isolation and identification of the virus. After the initial diagnosis, confirmation of a diagnosis can be made by demonstrating ASF antigen in tissue or ASF antibody.

Differential Diagnosis

Differential diagnoses for ASF should include hog cholera, erysipelas, salmonellosis, and eperythrozoonoisis.

Vaccination

There is no vaccine.

Control and Eradication

Prevention

Introduction of the disease into free areas can be prevented by cooking all garbage fed to pigs (this applies to commercial and backyard pigs and pets [potbellied pigs]) and importing only ASF-disease free pigs.

Eradication

Control and eradication of ASF in developed countries can be accomplished by slaughter and disposal of all acutely infected pigs, widespread testing and elimination of all seropostive animals, and good herd isolation and sanitary practices.

Today (1996), ASF is not as great a threat to the United States as it was several years ago. The major pork-exporting countries have eradicated the disease in domestic pigs.

Public Health

Human beings are not susceptible to ASFV infection.

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Fig. 13. ASF - Reddened skin on the extremities is a non-specific lesion associated with a septicemic/viremic condition.

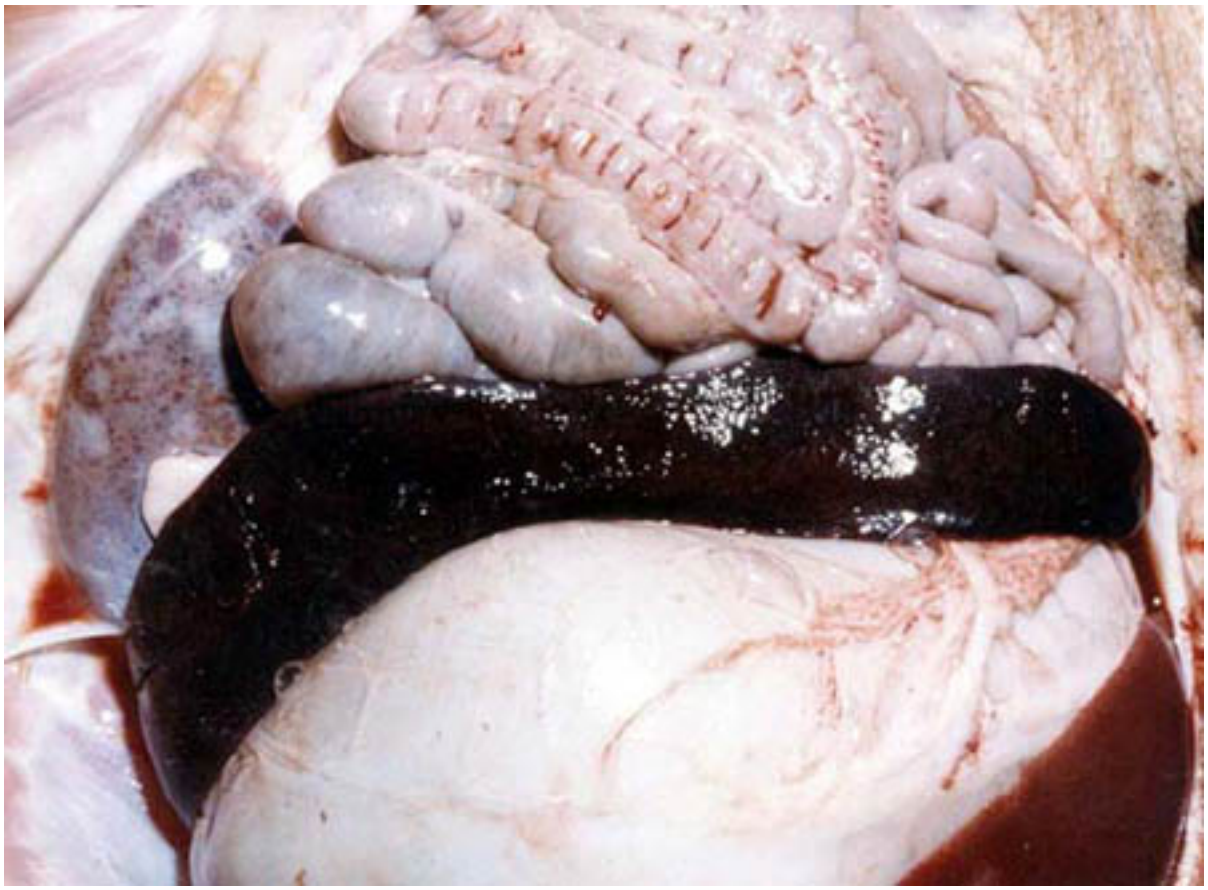

Fig. 14. ASF - A greatly enlarged dark red to black spleen from a pig infected with a highly virulent ASFV isolate. There are petechial hemorrhages in the renal cortex.

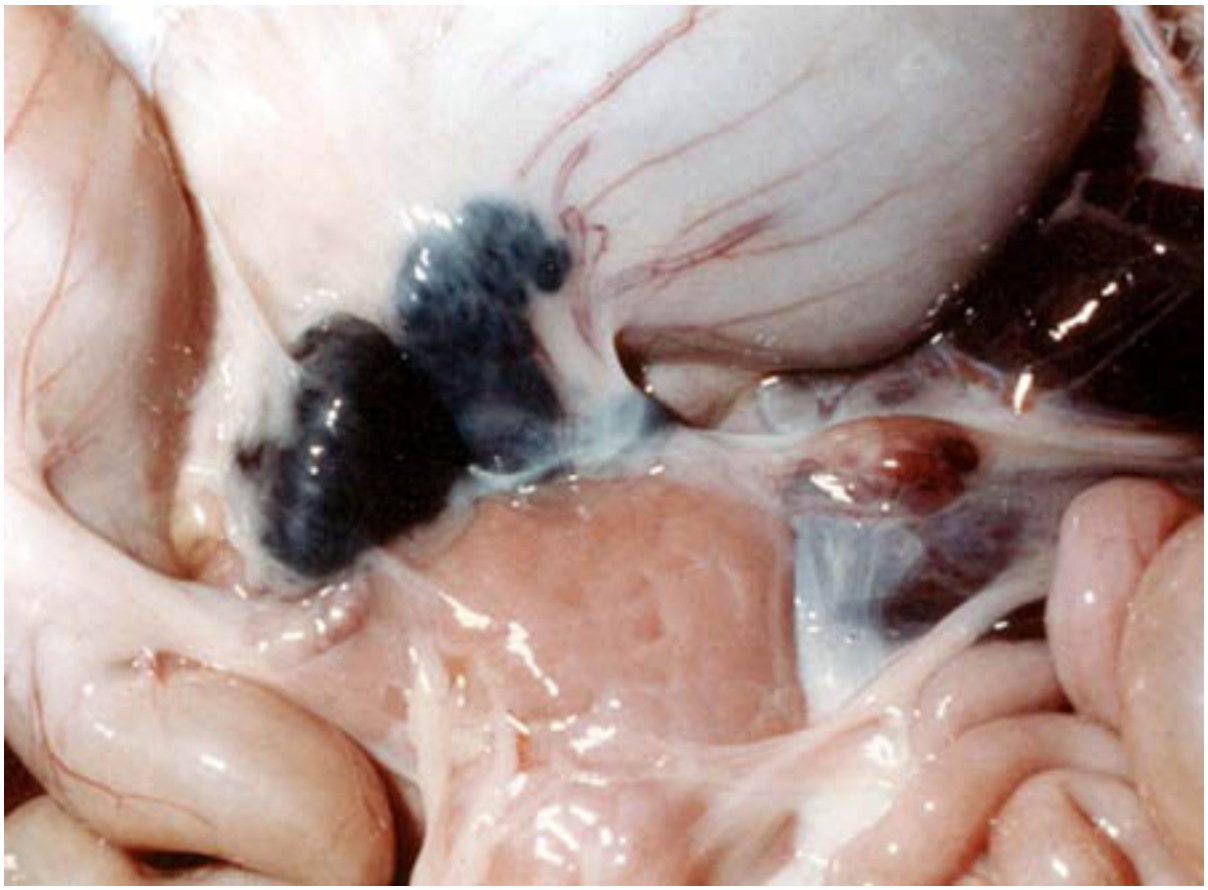

Fig 15. ASF - Very enlarged dark red (hemorrhagic) gastrohepatic lymph nodes from a pig infected with a highly virulent isolate of ASFV.

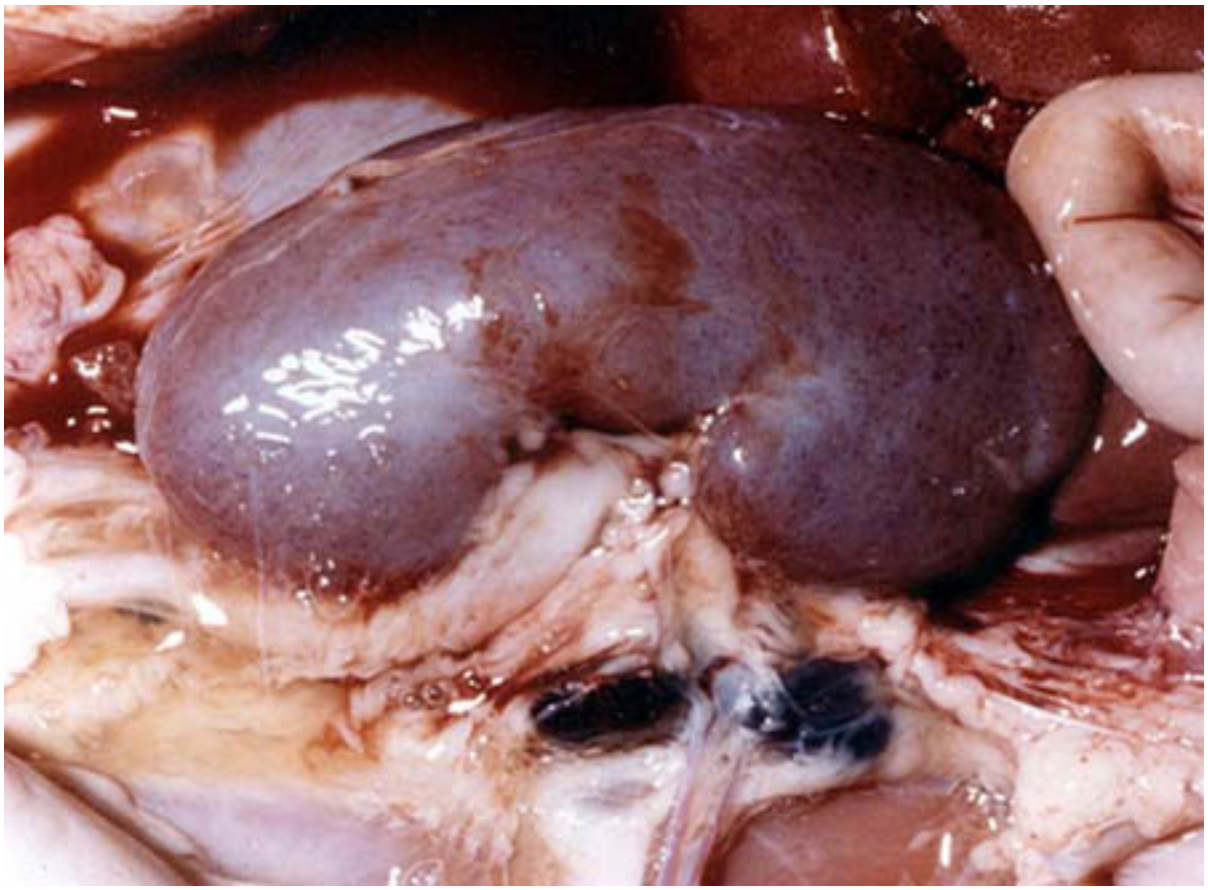

Fig. 16. ASF - Enlarged dark red renal lymph nodes, petechial hemorrhages in the renal cortex, and perirenal edema.

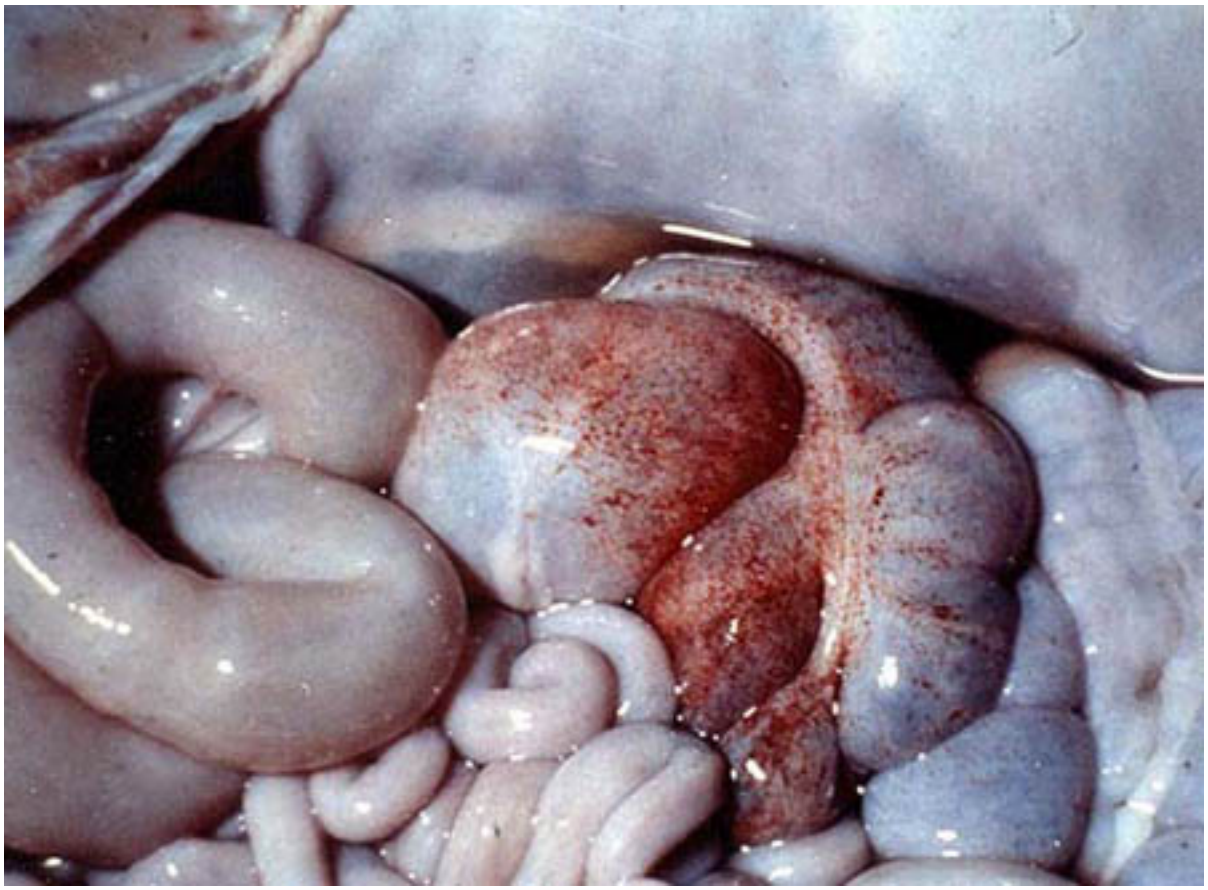

Fig. 17. ASF - Petechial hemorrhages on the serosal surface are indicative of a viremic/septicemic condition.

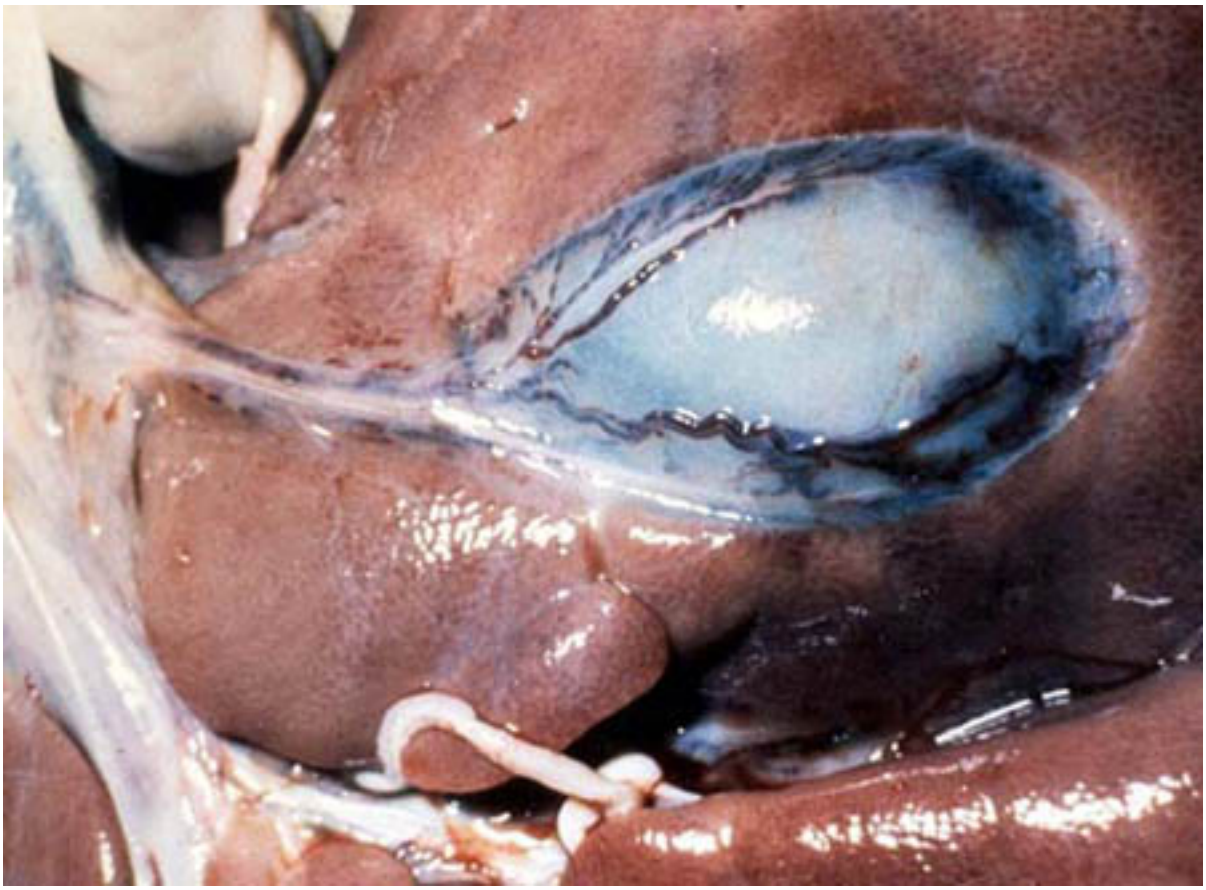

Fig. 18. ASF - Edema of the gall bladder.

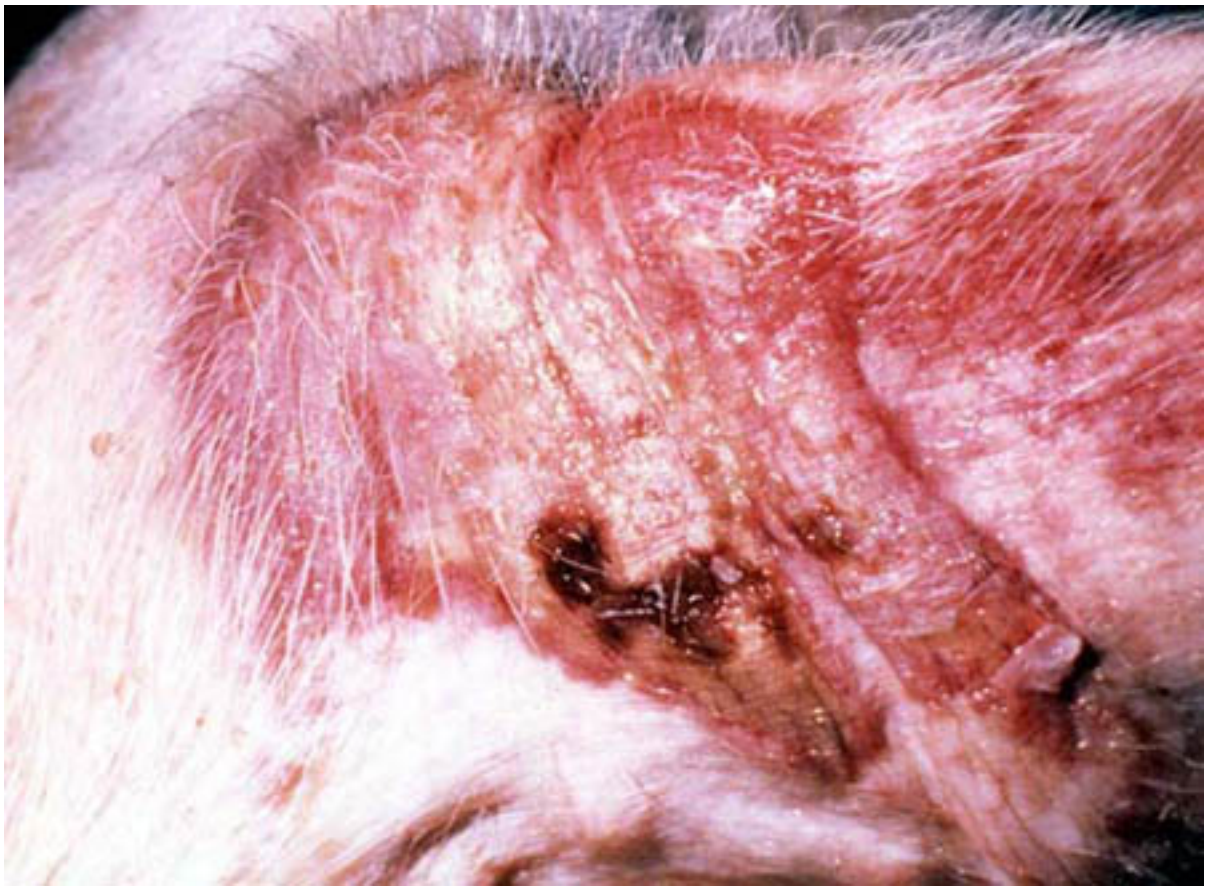

Fig. 21. ASF - Necrosis of the skin is a frequent lesion in chronic ASF.

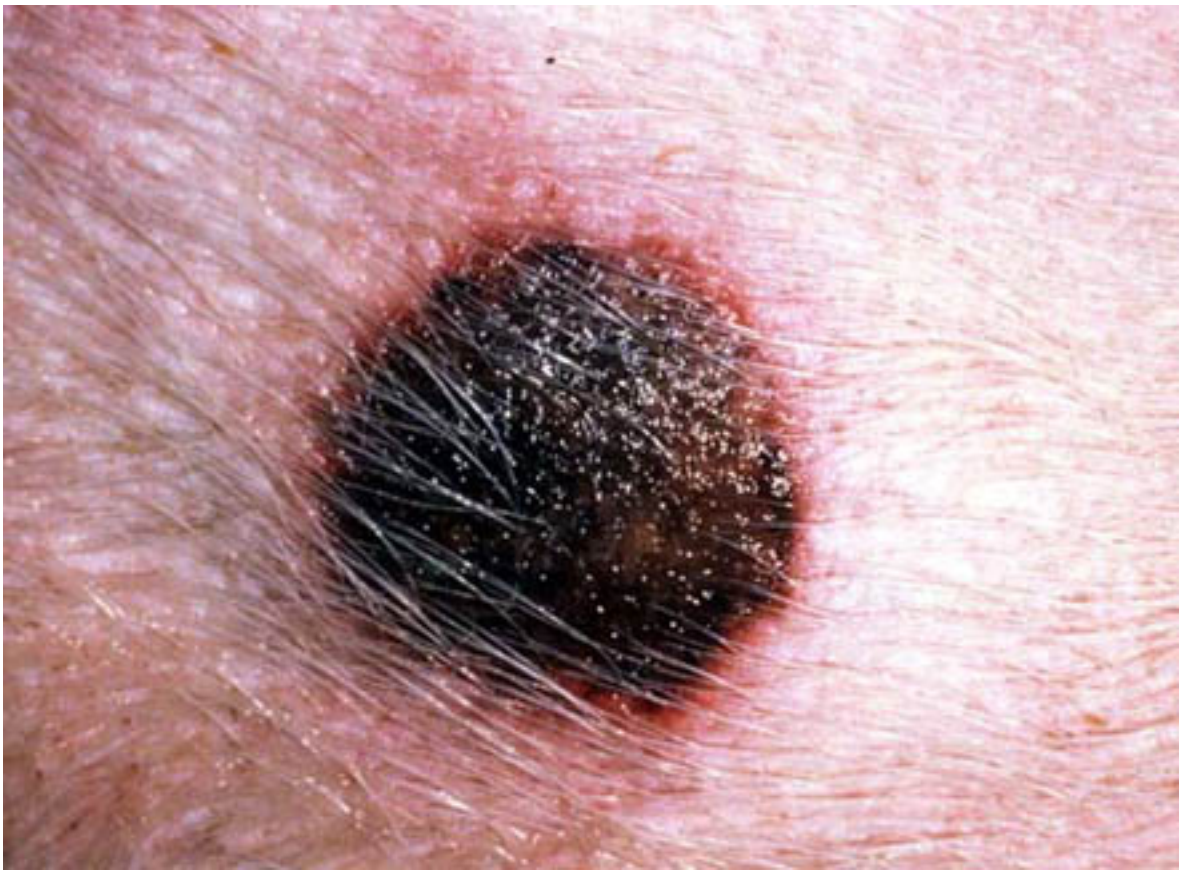

Fig. 22. ASF - Necrosis of the skin in chronic ASF can also be focal; the areas begin as raised hyperemic areas and progress to areas of necrosis.

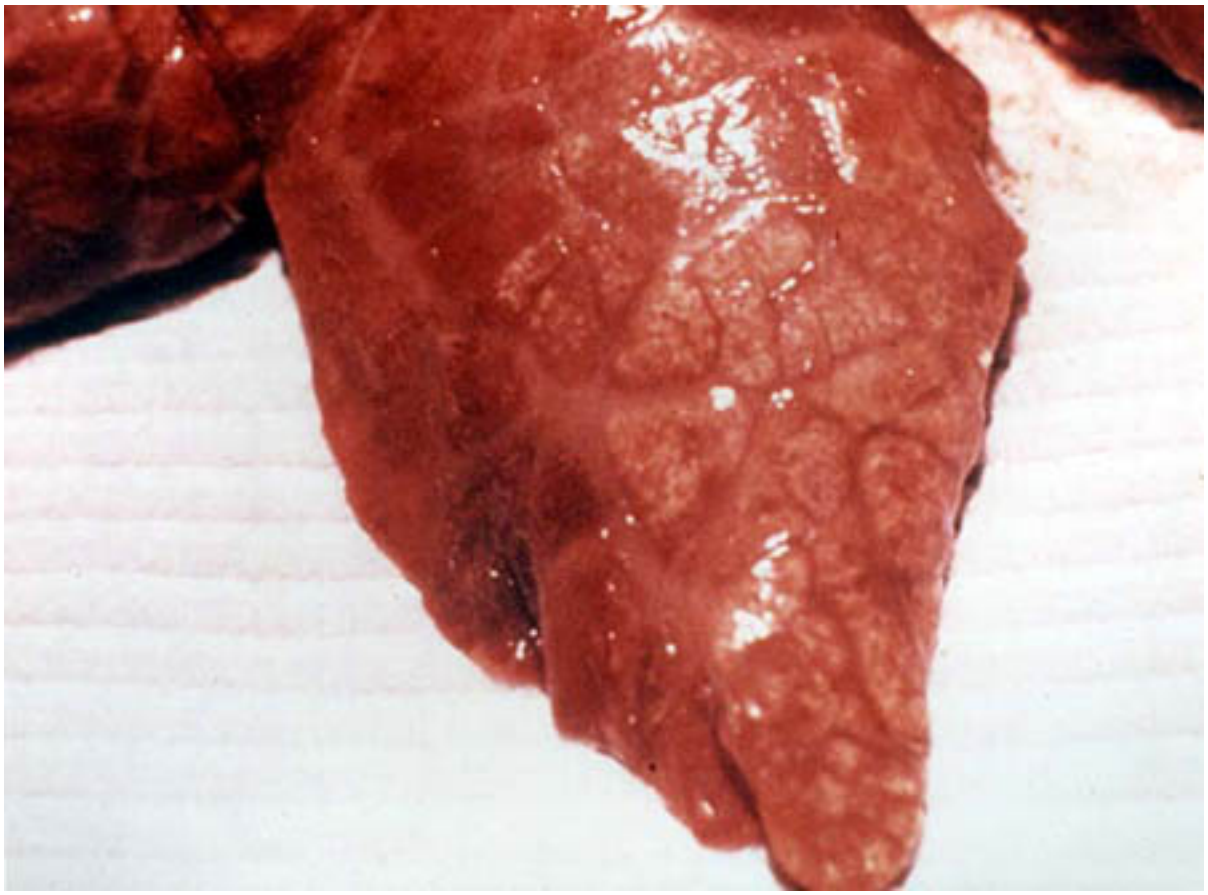

Fig. 19. ASF - Chronic ASF; consolidated lobules in the lung.

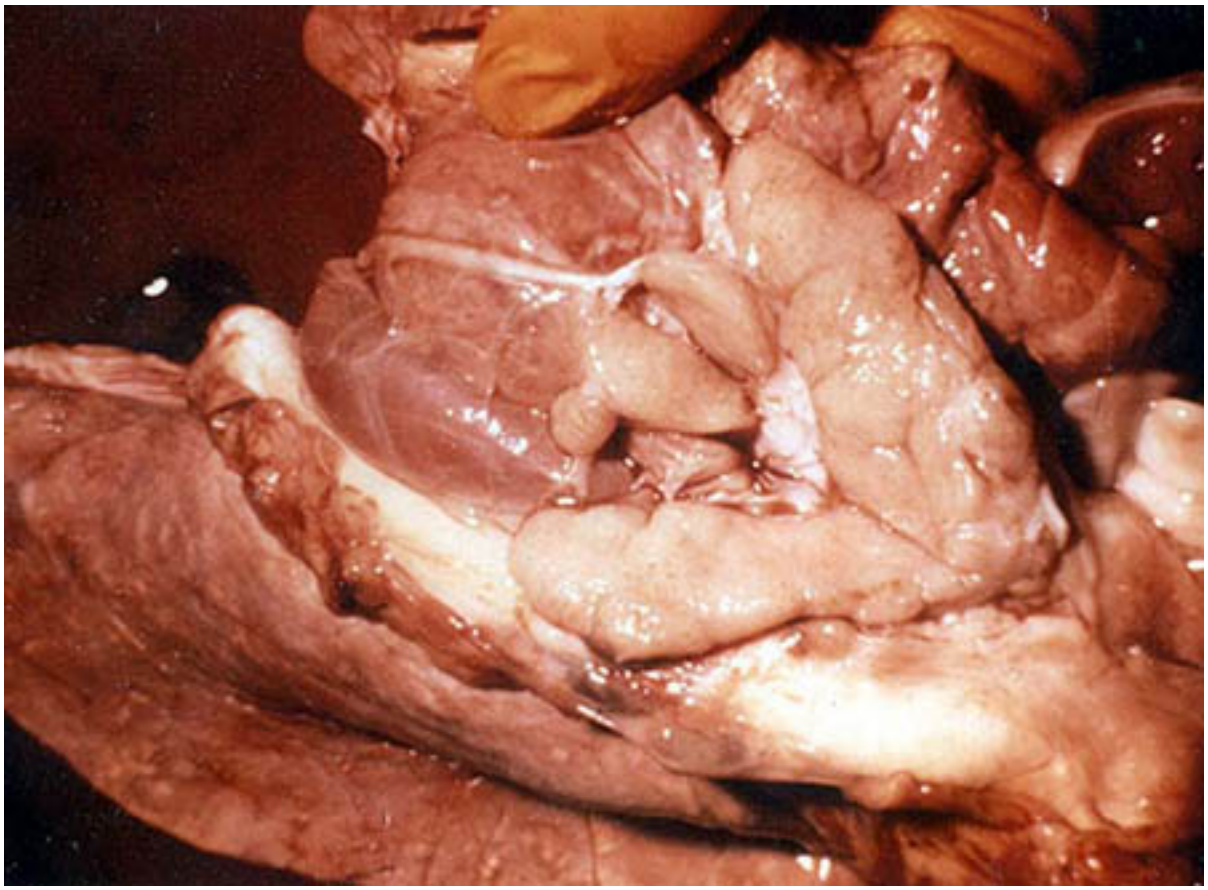

Fig. 20. ASF - Enlarged bronchial lymph nodes are part of a generalized lymphadenopathy in chronic ASF.

PART IV
FOREIGN ANIMAL DISEASES

AKABANE

(Congenital arthrogryposis-hydranencephaly syndrome, A-H syndrome, Akabane disease, congenital bovine epizootic A-H syndrome, acorn calves, silly calves, curly lamb disease, curly calf disease, dummy calf disease)

Definition

Congenital arthrogryposis-hydranencephaly (A-H) syndrome is an infectious disease of the bovine, caprine, and ovine fetus caused by intrauterine infection and interference with fetal development after transmission to the dam by biting gnat- or mosquito-transmitted Akabane virus and some other antigenically related members of the Simbu group of arboviruses (1,7). Fetal infection may cause abortions, stillbirths, premature births, mummified fetuses, and various dysfunctions or deformities of fetuses or liveborn neonates. Adult animals are not clinically affected while actively infected with virus (17).

Etiology

The etiologic agents of congenital A-H syndrome are arboviruses of the Simbu group of the family Bunyaviridae. Akabane virus was the first member of the Simbu group to be incriminated in congenital A-H syndrome, but other members (namely Aino, Peaton, and Tinaroo viruses) have the capacity to produce fetal defects (3,10,13,18). In recent years, Cache Valley virus, a mosquito-borne member of the Bunyaviridae outside the Simbu group, has been found to reproduce a similar syndrome in ruminants within the United States (2). The Simbu group of viruses are spread only by insect vectors. Spread by contact, infected tissues, exudates, or fomites does not occur.

Host Range

Congenital A-H syndrome associated with Akabane virus and other Simbu group viruses has been reported only in cattle, sheep, and goats. Although antibody against these viruses has been detected in horses, no clinical evidence of fetal infection has been reported. Infections of wild ruminants do occur, and fetal damage must be considered but has not been reported.

Geographic Distribution

In Japan, the periodic outbreaks of AH syndrome have been reported since 1949. Enzootic Akabane virus (and presumably other Simbu group virus) activity has occurred in the northern half of Australia since at least 1931 with occasional temporary epizootic incursions southward dependent on favorable seasons (18). Reports of A-H syndrome in Israel (8) and other countries in the Middle East, Cyprus (8,18,19), Korea, Zimbabwe, and South Africa have been published in the last decade. Serological surveys indicate that the virus occurs throughout Africa, Asia, and Australia but not Papua New Guinea, the Pacific Islands, or the Americas.

Transmission

The occurrence of A-H syndrome is seasonally and geographically restricted. The location and timing of the infection of the fetus during early pregnancy is consistent with the seasonality of transmission by hematophagous insects. Akabane virus has been isolated from *Aedes vexans* and *Culex triteeniorhynchus* mosquitoes in Japan; *Anopheles funestus* mosquitoes in Kenya; *Culicoides milnei* and *C. imicola* in Africa; *C. oxystoma* in Japan; and *C. brevitarsis* and *C. wadei* gnats in Australia (3,13,17,18). Confirmation of the biologic transmission by these species is lacking; however, epidemiologic evidence incriminates them. In Australia, *C. brevitarsis* is

believed to be the principal vector of Akabane virus. Cache Valley virus has been isolated from at least nine different mosquito species, and antibodies to this virus have been detected in man, as well as wild and domestic animals in the Americas.

There is no indication that Akabane virus, other Simbu group viruses or Cache Valley virus is transmitted in any other way than by a vector. Transmission happens months before disease in the fetus is evident.

Incubation Period

Infection of adult animals produces no overt clinical sign, but viremia generally occurs 1-6 days after infection. A natural viremia may last 4 to 6 days before antibodies to Akabane virus are detectable (17). However, infection of pregnant animals during the first months of gestation may result in fetal infection that is not apparent until much later in pregnancy or at term (6).

Timing of the infection relative to the stage of gestation is critical to the development of defects in the fetus. In pregnant sheep, the gestational period for the occurrence of fetal abnormalities has been shown to vary from 30-36 days to 30-50 days (6,14,15). This variation in the reported results has been ascribed to (a) differences in the virulence of virus strains used, (b) differences in the passage level of the virus strain used, or (c) differences caused after growth of the virus in the arthropod vectors. Inoculation of pregnant cattle with virus between 62 and 96 days of gestation resulted in fetal lesions; in pregnant goats, the critical period in the gestational cycle was about 40 days (10,12).

Clinical Signs

Congenital A-H syndrome is manifested as a seasonally sporadic epizootic of abortions, stillbirths, premature births, and deformed or anomalous bovine, caprine, and ovine fetuses or neonates. The pregnant dam has no clinical manifestation at the time of infection with virus. Sentinel cattle under close observation have no clinical sign during viremia induced by natural infection. If infection develops during the first third of pregnancy, gross fetal damage may occur. At the other end of the disease spectrum, damage to the central nervous system (CNS) may be minor and produce changes in behavior of the new born or young animal. Dystocia at parturition may occur owing to the deformities in the fetus. Badly deformed fetuses are usually dead at birth, and the limbs are locked in the flexed or extended position. Most live neonates have central nervous system degeneration and muscle lesions that prevent the animal from standing or suckling. Torticollis, scoliosis, brachygnathism, and kyphosis may coexist with arthrogryposis. Lesions in the central nervous system are manifested clinically as blindness, nystagmus, deafness, dullness, slow suckling, paralysis, and incoordination.

Mildly affected calves or lambs may improve their mobility with time. However, most eventually die by 6 months as a result of blindness and other neurological defects (5,7,10,12,14,15,17).

Gross Lesions

An individual fetus or newborn may have arthrogryposis and hydranecephaly or both syndromes. Lesions are associated with damage to the enervation of the musculature and to the central nervous system. Arthrogryposis is the most frequently observed lesion. Affected joints cannot be straightened even by application of force because of ankylosis of the joint in the extended or flexed position (Fig. 23). Torticollis, scoliosis, and brachygnathism are observed. There may be shallow erosions about the external nares and muzzle and between the distal digits. Hypoplasia of the lungs and skeletal muscles, fibrinous polyarticular synovitis, fibrinous navel infection, ophthalmia, cataracts, and presternal steatosis occur. Within the CNS, hydranencephaly (Fig. 24), hydrocephalus, agenesis of the brain, microencephaly, porencephaly and cerebellar cavitation, fibrinous leptomeningitis, fibrinous ependymitis, and agenesis or hypoplasia of the spinal cord are variously reported (5, 16, 20). The cerebellum appears intact. Lesions due to Akabane tend to be symmetrical. However, some asymmetry occurs when Aino virus is involved. Akabane virus was isolated from fetuses of naturally infected pregnant cows or ewes by the use of predictive serology. When the mothers

seroconverted from negative to positive in Akabane virus neutralization tests, Akabane virus was isolated from the fetus (4,11).

Morbidity and Mortality

In endemic areas, animals are exposed and become immune before becoming pregnant; thus, congenital abnormalities are seldom seen in native animals, for antibodies prevent virus from spreading from the site of the bite to the fetus. However, when the infected vector spreads (e.g., during an extended humid summer) to an area where the animals are not immune, A-H syndrome can occur months later in many animals. The disease can also appear when pregnant animals from a disease-free area are moved into an endemic area.

There is no reported damage to the dam in congenital A-H syndrome. Most live-born affected calves, lambs, or kids die shortly after birth or must be slaughtered for humane reasons. Some mildly affected calves do improve gait and learn to follow the herd.

Diagnosis

Field Diagnosis

A field diagnosis of congenital A-H syndrome can be made on the basis of the clinical condition, gross pathologic lesions, and the epidemiology. The sudden onset of aborted, mummified, premature, or stillborn fetuses with arthrogryposis and hydranencephaly should be suggestive. The dam will have had no clinical history of disease. A retrospective study would indicate that the first third of pregnancy occurred during a time of biting insect activity.

Specimens for Laboratory

The following specimens should collected for virus isolation: placenta, fetal muscle, cerebrospinal fluid, and fetal nervous tissue; for serology: fetal or precolostral serum, and serum from the dam. For histopatholgy send pieces of spleen, liver, lung, kidney, heart, lymph nodes, affected muscle, spinal cord and brain in 10 percent buffered formalin.

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quickfreeze the specimens and do not allow them to thaw during transit

Laboratory Diagnosis

Virus isolation should be attempted from placenta, fetal muscle, or fetal nervous tissue. The chances of success are very low except with a fetus and placenta aborted before antibodies are generated within an immunocompetent fetus. In the absence of viral isolations, a serologic diagnosis is usually made by demonstrating antibodies in precolostral or fetal serum samples. In adult animals, seroconversion or a demonstrable rise in antibody titer indicates that there was infection. A microtiter neutralization test and an immunofluorescence test are available for detecting and assaying antibodies (18). Tissues of the dam are free of virus by the time the damage is observed in the fetus or newborn. Low titers (<10) in unpaired serum samples should not be taken as diagnostic because of cross-reaction problems.

Differential Diagnosis

The demonstration that Cache Valley virus, a Bunyavirus that is ubiquitous within the United States, can cause the A-H syndrome means that serological tests are essential to distinguish exotic from enzootic etiologies (2). It is a reasonable assumption that other Bunyaviridae will be proven to be teratogenic in livestock in the Americas. A variety of nutritional, genetic, toxic, and infectious diseases will produce fetal wastage and deformities. Fetal brain lesions resulting from bluetongue vaccine virus infections of pregnant ewes are similar to those produced within the congenital A-H syndrome. Bluetongue presents the greatest difficulty in the initial differential diagnosis of hydranencephaly. Bovine virus diarrhea infection can cause cerebellar dysplasia in calves. Border disease virus infection can cause undersized, excessively hairy lambs with

muscular tremors and skeletal defects. Wesselsbron virus infection can cause congenital porencephaly and cerebral hypoplasia in calves. Serology of the dam and fetus will resolve any confusion.

Vaccination

A formalin-inactivated, aluminum phosphate, gel-absorbed vaccine and an attenuated vaccine have been developed in Japan for Akabane virus. An effective killed vaccine for Akabane virus has been developed but not marketed in Australia (7,9). These vaccines induce immunity in the cow or ewe, and the circulating antibodies prevent the virus from reaching the fetus. The vaccines are used prior to exposure to infected vectors. Vaccine is no longer available for economic reasons. Immunizing agents for other Simbu group viruses are not currently available and are not expected to be developed.

Control and Eradication

Techniques for the control of the viral agents that cause congenital A-H syndrome are those typically recommended for other vector-transmitted agents. Control of the vector depends upon disruption of breeding sites, reduction of vector populations with pesticides, and protection of host animals from feeding by the vectors. In addition to these procedures, animals should be vaccinated before breeding.

Public Health

There is no evidence that humans can be infected by Akabane virus.

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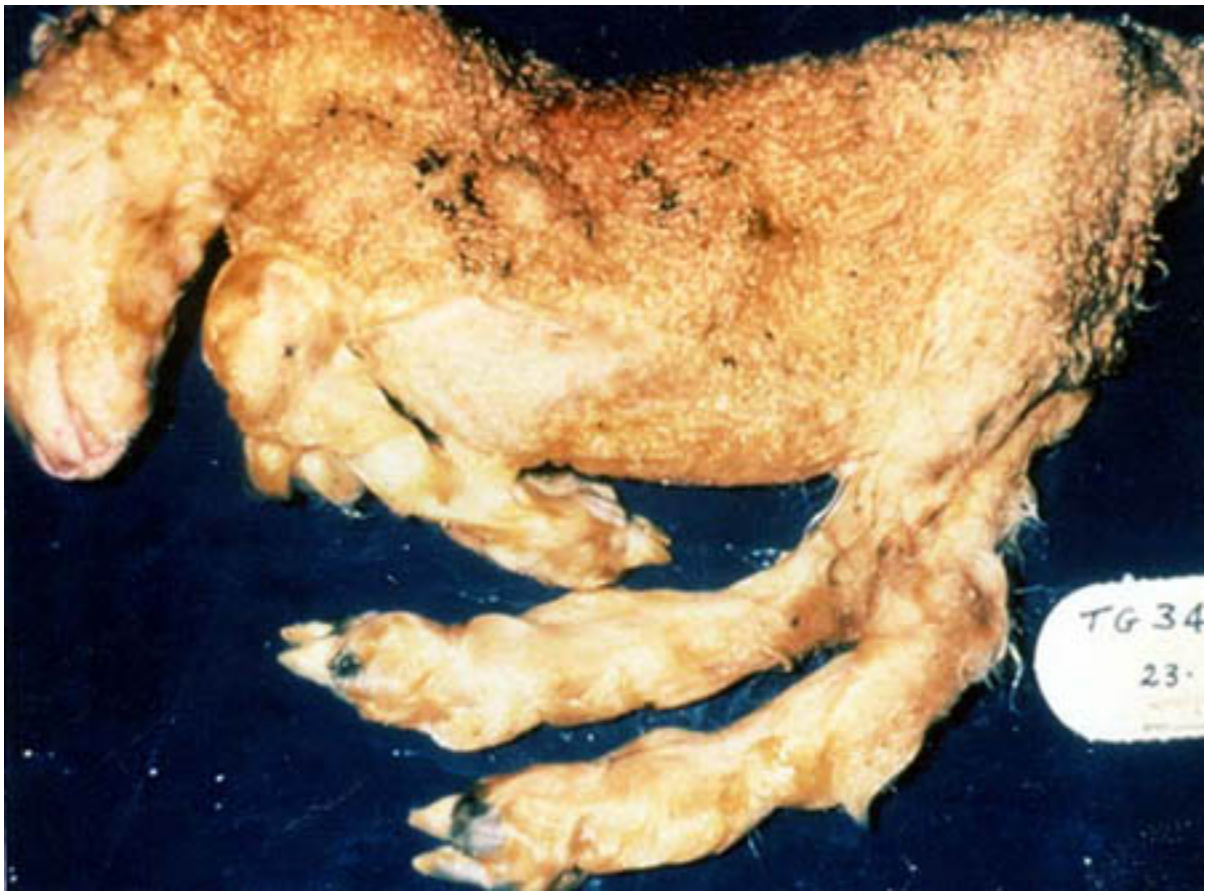

Fig. 23. Akabane - Arthrogryposis is the most frequently observed lesion.

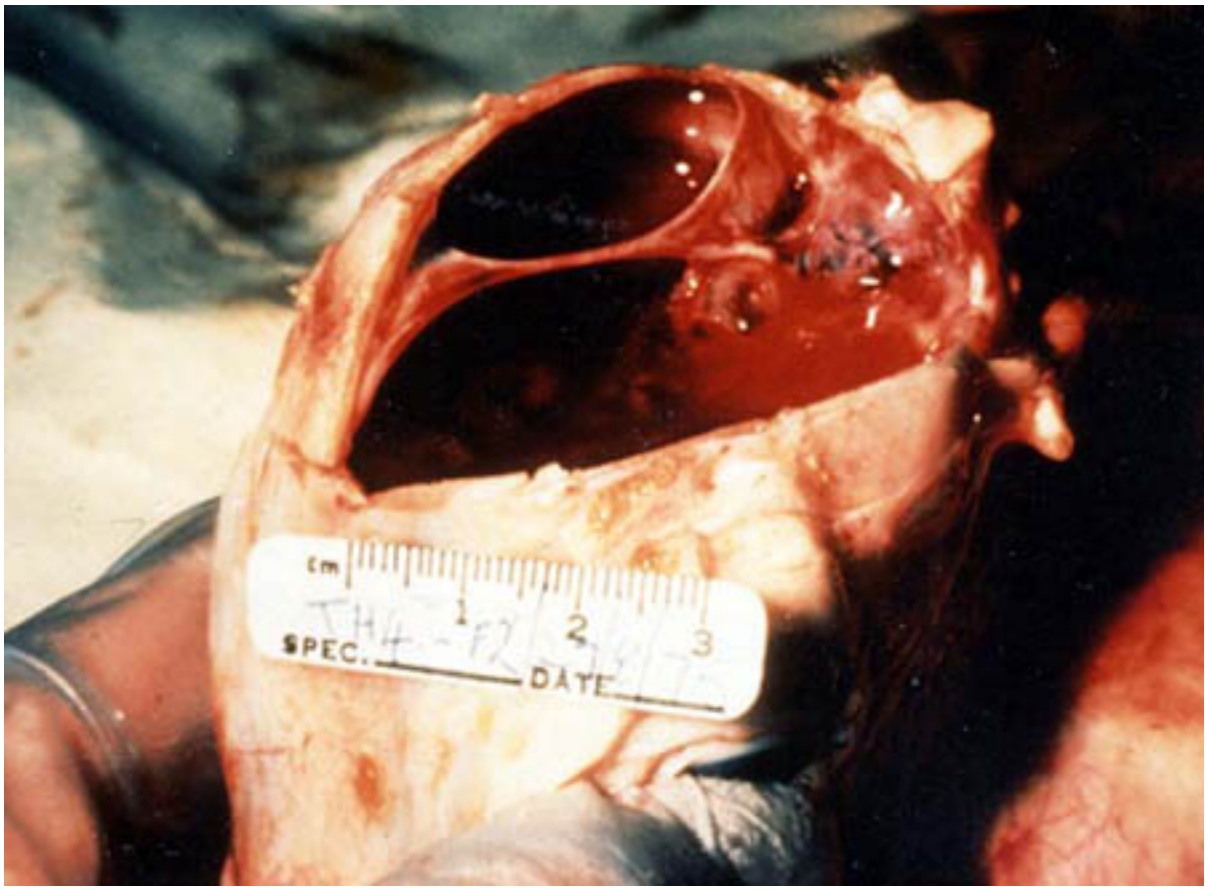

Fig. 24. Akabane - Hydranencephaly.

PART IV
FOREIGN ANIMAL DISEASES

AVIAN INFLUENZA

(Fowl Plague)

Definition

Avian influenza (AI) is a disease of viral etiology that ranges from a mild or even asymptomatic infection to an acute, fatal disease of chickens, turkeys, guinea fowls, and other avian species, especially migratory waterfowl (1,2,3,4,8,9,10,11).

Etiology

Fowl plague was described in 1878 as a serious disease of chickens in Italy. It was determined in 1955 that fowl plague (FP) virus is actually one of the influenza viruses. The AI viruses, along with the other influenza viruses, make up the virus family Orthomyxoviridae. The virus particle has an envelope with glycoprotein projections with hemagglutinating and neuraminidase activity. These two surface antigens, hemagglutinin (HA) and neuraminidase (NA), are the basis of describing the serologic identity of the influenza viruses using the letters H and N with the appropriate numbers in the virus designation e.g., H7N2. There are now 15 hemagglutinin and 9 neuraminidase antigens described among the Type A influenza viruses. The type designation (A, B, or C) is based upon the antigenic character of the M protein of the virus envelope and the nucleoprotein within the virus particle. All influenza viruses affecting domestic animals (equine, swine, avian) belong to Type A, and Type A influenza virus is the most common type producing serious epidemics in humans. Types B and C do not affect domestic animals.

Classical fowl plague viruses have H7 as one of the surface antigens but can have different N antigens. It was once believed that all H7 viruses are highly pathogenic fowl plague viruses and that no other avian influenza viruses could produce a fowl-plague-like disease. When avirulent AI viruses with the H7 antigens were demonstrated in turkeys in 1971 and highly virulent AI viruses with the H5 antigen were first found in chickens in 1959, the necessity for redefining the term fowl plague or using other terminology became apparent. Because there are highly virulent AI viruses that possess H antigen other than the H7 and H7 AI viruses that do not produce clinical fowl plague, an international assembly of avian influenza specialists proposed that the term fowl plague no longer be used. They suggested that any AI virus, regardless of its HA designation, meeting specified virulence requirements in the laboratory be designated highly pathogenic avian influenza (HPAI). The criteria that serve as the basis for classifying an AI virus as HPAI has more recently been modified to include molecular considerations such as the type of amino acids at the cleavage site of its HA. This chapter will be limited to describing the HPAI and not the AI viruses of less virulence and pathogenicity.

Host Range

Most avian species appear to be susceptible to at least some of the AI viruses. A particular isolate may produce severe disease in turkeys but not in chickens or any other avian species. Therefore, it would be impossible to generalize on the host range for HPAI, for it will likely vary with the isolate. This assumption is supported by reports of farm outbreaks where only a single avian species of several species present on the farm became infected. Swine appear to be important in the epidemiology of infection of turkeys with swine influenza virus when they are in close proximity. Other mammals do not appear to be involved in the epidemiology of HPAI. The infection of humans with an H5 avian influenza virus in Hong Hong in 1997 has resulted in a reconsideration of the role of the avian species in the epidemiology of human influenza.

Geographic Distribution

Highy pathogenic avian influenza viruses have periodically occurred in recent years in Australia (H7), England (H7), South Africa (H5), Scotland (H5), Ireland (H5), Mexico (H5), Pakistan (H7), and the United States (H5). Because laboratory facilities are not readily available in some parts of the world to differentiate Newcastle disease and HPAI, the actual incidence of HPAI in the world's poultry flocks is difficult to define. It can occur in any country, regardless of disease control measures, probably because of its prevalence in wild migratory waterfowl, sea birds and shore birds.

Avian influenza has produced losses of variable severity, primarily in turkeys in the United States, since the mid-1960's. The disease outbreaks in turkeys in the United States have been caused by AI viruses with many of the HA designations. It was in the fall of 1983 that a highly virulent H5 virus produced severe clinical disease and high mortality in chickens, turkeys, and guinea fowl in Pennsylvania. This severe disease, clinically indistinguishable from classical fowl plague, occurred after a serologically identical but apparently mild virus had been circulating in poultry in the area for 6 months.

Outbreaks of less virulent AI have frequently been described in domestic ducks in many areas of the world. The AI viruses are often recovered from apparently healthy migratory waterfowl, shore birds, and sea birds worldwide. The epidemiologic significance of these isolations relative to outbreaks in domestic poultry has led to the generally accepted belief that waterfowl serve as the reservoir of influenza viruses.

Transmissions

There is a considerable body of circumstantial evidence to support the hypothesis that migratory waterfowl, sea birds, or shore birds are generally responsible for introducing the virus into poultry. Once introduced into a flock, the virus is spread from flock to flock by the usual methods involving the movement of infected birds, contaminated equipment, egg flats, feed trucks, and service crews, to mention a few. Preliminary trapping evidence indicates that garbage flies in the Pennsylvania outbreak were sources of virus on the premises of the diseased flocks. Virus may readily be isolated in large quantities from the feces and respiratory secretions of infected birds. It is logical to assume, therefore, that because virus is present in body secretions, transmission of the disease can take place through shared and contaminated drinking water. Airborne transmission may occur if birds are in close proximity and with appropriate air movement. Birds are readily infected via instillation of virus into the conjunctival sac, nares, or the trachea. Preliminary field and laboratory evidence indicates that virus can be recovered from the yolk and albumen of eggs laid by hens at the height of the disease. The possibility of vertical transmission is unresolved; however, it is unlikely infected embryos could survive and hatch. Attempts to hatch eggs in disease isolation cabinets from a broiler breeder flock at the height of disease failed to result in any AI-infected chickens. This does not mean that broken contaminated eggs could not be the source of virus to infect chicks after they hatch in the same incubator. The hatching of eggs from a diseased flock would likely be associated with considerable risk.

Incubation Period

The incubation period is usually 3 to 7 days, depending upon the isolate, the dose of inoculum, the species, and age of the bird.

Clinical Signs

Infections of HPAI result in marked depression with ruffled feathers, inappetence, excessive thirst, cessation of egg production, and watery diarrhea. Mature chickens frequently have swollen combs, wattles (Fig. 25), and edema surrounding the eyes. The combs are often cyanotic at the tips and may have plasma or blood vesicles on the surface with dark areas of ecchymotic hemorrhage and necrotic foci (Fig. 26). The last eggs laid, after the onset of illness, are frequently without shells. The diarrhea begins as watery bright green and progresses to almost totally white. Edema of the head, if present, is often accompanied by edema of the neck.

The conjunctivae are congested and swollen with occasional hemorrhage. The legs, between the hocks and feet, may have areas of diffuse hemorrhage (Fig. 27). Respiratory signs can be a significant feature of the disease, depending on the extent of tracheal involvement. Mucus accumulation can vary. It is not unusual in caged layers for the disease to begin in a localized area of the house and severely affect birds in only a few cages before it spreads to neighboring cages.

Death may occur within 24 hours of first signs of disease, frequently within 48 hours, or be delayed for as long as a week. Some severely affected hens may occasionally recover.

In broilers, the signs of disease are frequently less obvious with severe depression, inappetence, and a marked increase in mortality being the first abnormalities observed. Edema of the face and neck and neurologic signs such as torticollis and ataxia may also be seen.

The disease in turkeys is similar to that seen in layers, but it lasts 2 or 3 days longer and is occasionally accompanied by swollen sinuses.

In domestic ducks and geese the signs of depression, inappetence, and diarrhea are similar to those in layers, though frequently with swollen sinuses. Younger birds may exhibit neurologic signs.

Gross Lesions

Birds that die with the peracute disease and young birds may not have significant gross lesions other than severe congestion of the musculature and dehydration. In the less acute form, and in mature birds, significant gross lesions are frequently observed. They may consist of subcutaneous edema of the head and neck area, which is evident as the skin is reflected (Fig. 28). Fluid may exit the nares and oral cavity as the bird is positioned for postmortem examination. The conjunctivae are severely congested— occasionally with petechiation. The trachea may appear relatively normal except that the lumen contains excessive mucous exudate. It may also be severely involved with hemorrhagic tracheitis similar to that seen with infectious laryngotracheitis. When the bird is opened, pinpoint petechial hemorrhages are frequently observed on the inside of the keel as it is bent back. Very small petechia may cover the abdominal fat, serosal surfaces, and peritoneum, which appears as if it were finely splattered with red paint. Kidneys are severely congested and may occasionally be grossly plugged with white urate deposits in the tubules.

In layers, the ovary may be hemorrhagic or degenerated with darkened areas of necrosis. The peritoneal cavity is frequently filled with yolk from ruptured ova, causing severe airsacculitis and peritonitis in birds that survive for 7 to 10 days.

Hemorrhages may be present on the mucosal surface of the proventriculus — particularly at the juncture with the gizzard. The lining of the gizzard peels easily and frequently reveals hemorrhages and erosions underneath. The intestinal muscosa may have hemorrhagic areas — especially in the lymphoid foci such as the cecal tonsils. The gross lesions are not distinctly different from those observed with velogenic viscerotropic Newcastle disease (VVND). The lesions in turkeys and domestic ducks are similar to those in chickens but may not be as marked.

Morbidity and Mortality

The prognosis for flocks infected with HPAI is poor. Morbidity and mortality rates may be near 100 percent within 2 to 12 days after the first signs of illness. Birds that survive are usually in poor condition and resume laying only after a period of several weeks.

Diagnosis

Field Diagnosis

Highly pathogenic avian influenza is suspected with any flock where sudden deaths follow severe depression, inappetence, and a drastic decline in egg production. The presence of facial edema, swollen and cyanotic combs and wattles, and petechial hemorrhages on internal membrane surfaces increases the likelihood that the disease is HPAI. However, an absolute diagnosis is dependent upon the isolation and identification of the causative virus. Commercially available type A influenza antigen-capture enzyme linked immunosorbent assay kits designed for use in human influenza have recently shown promise as a possible rapid diagnositic test for poultry.

Specimens for Laboratory

Specimens sent to the laboratory should be accompanied by a history of clinical and gross lesions, including any information on recent additions to the flock. Diagnosis depends upon the isolation and identification of the virus from tracheal or cloacal swabs, feces, or from internal organs (5). Specimens should be collected from several birds. It is not unusual for many of the submitted specimens to fail to yield virus. Swabs are the most convenient way to transfer AI virus from tissues or secretions of the suspect bird to brain and heart infusion broth or other cell culture maintenance medium containing high levels of antibiotics. Dry swabs should be inserted deeply to ensure obtaining ample epithelial tissue. Trachea, lung, spleen, cloaca, and brain should be sampled. If large numbers of dead or live birds are to be sampled, cloacal swabs from up to five birds can be pooled in the same tube of broth. An alternative technique is to place 0.5 cm^3 of each tissue into the broth. Blood for serum should be collected from several birds. If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quickfreeze the specimens and do not allow them to thaw during transit.

Laboratory Diagnosis

Nine to 11-day-old embryonated chicken eggs are inoculated with swab or tissue specimens. Avian influenza virus will usually kill embryos within 48-72 hours. If the virus isolated is identified as a Type A influenza virus, through the AGP or ELISA tests, it is then tested using a battery of specific antigens to identify its serologic identity (HA and NA type).

Sera from infected chickens usually yield positive antibody tests as early as 3 or 4 days after first signs of disease.

Differential Diagnosis

Highly pathogenic avian influenza is easily confused with VVND, because the disease signs and postmortem lesions are similar, and may also be confused with infectious laryngotracheitis and acute bacterial diseases such as fowl cholera and *Escherichia coli.* However, in an area where AI is prevalent, such as during an outbreak, sound presumptive diagnoses can be made by flock history, signs, and gross lesions.

Treatment

Amantadine hydrochloride has been licensed for use in humans to treat influenza since 1966. The medication is effective in reducing the severity of influenza Type A in humans. Experimental evidence indicated possible efficaciousness in poultry when the drug was administered in drinking water to reduce disease losses, but drug-resistant viruses quickly emerged, negating the initial beneficial effects. Thus, the drug is not recommended for use in poultry.

Vaccination

Inactivated oil-emulsion vaccines, although fairly expensive, have been demonstrated to be effective in reducing mortality, preventing disease, or both, in chickens and turkeys (7). These vaccines may not, however, prevent infection in some individual birds, which go on to shed virulent virus. More economical viable vaccines prepared using naturally avirulent or attenuated strains have the disadvantage of the possible creation of reassortant influenza viruses with

unpredictable characteristics. These reassortants could result when a single host bird is simultaneously infected with both the vaccine and another AI virus. Owing to the segmented nature of the influenza virus genome, a reassortment of genetic material can readily occur, creating new influenza viruses. The basic drawback to any vaccine approach for the control of HPAI is the large number of HA subtypes that can cause the disease. Because there is no cross-protection among the 15 known HA subtypes, either a multivalent vaccine will be needed or vaccination postponed until the prevalent disease-causing subtype in the area is identified. A recombinant fowl pox virus vaccine containing the gene that codes for the production of the H5 antigen has recently been licensed. The use of a recombinant insect virus containing the gene for either the H5 or H7 antigen has been used to make these vaccine proteins in insect cell cultures.

Control and Eradication

The practice of accepted sanitation and biosecurity procedures in the rearing of poultry is of utmost importance. In areas where waterfowl, shore birds, or sea birds are prevalent, the rearing of poultry on open range is incompatible with a sound AI prevention program (12). Appropriate biosecurity practices should be applied, including the control of human traffic and introduction of birds of unknown disease status into the flock. Cleaning and disinfection procedures are the same as those recommended in the chapter on velogenic Newcastle disease.

Public Health

The AI viruses are Type A influenza viruses, and the possibility exists that they could be involved in the development, through genetic reassortment, of new mammalian strains. An influenza virus isolated from harbor seals that died of pneumonia had the HA and NA surface antigens of an influenza virus isolated from turkeys a decade earlier. The infection and deaths of 6 of 18 humans infected with an H5 avian influenza virus in Hong Hong in 1997 has resulted in a reconsideration of the portentous role that the avian species have on the epidemiology of human influezna. Previously there was only one report of a human becoming infected with an H7 AI virus. Is is impossible to predict the importance of AI virus in determining the strains of virus that infect humans. There was no evidence to indicate that humans coming in contact with large quantities of the H5N2 virus during depopulation efforts in the HPAI outbreak of 1983 in Pennsylvania became infected with the virus.

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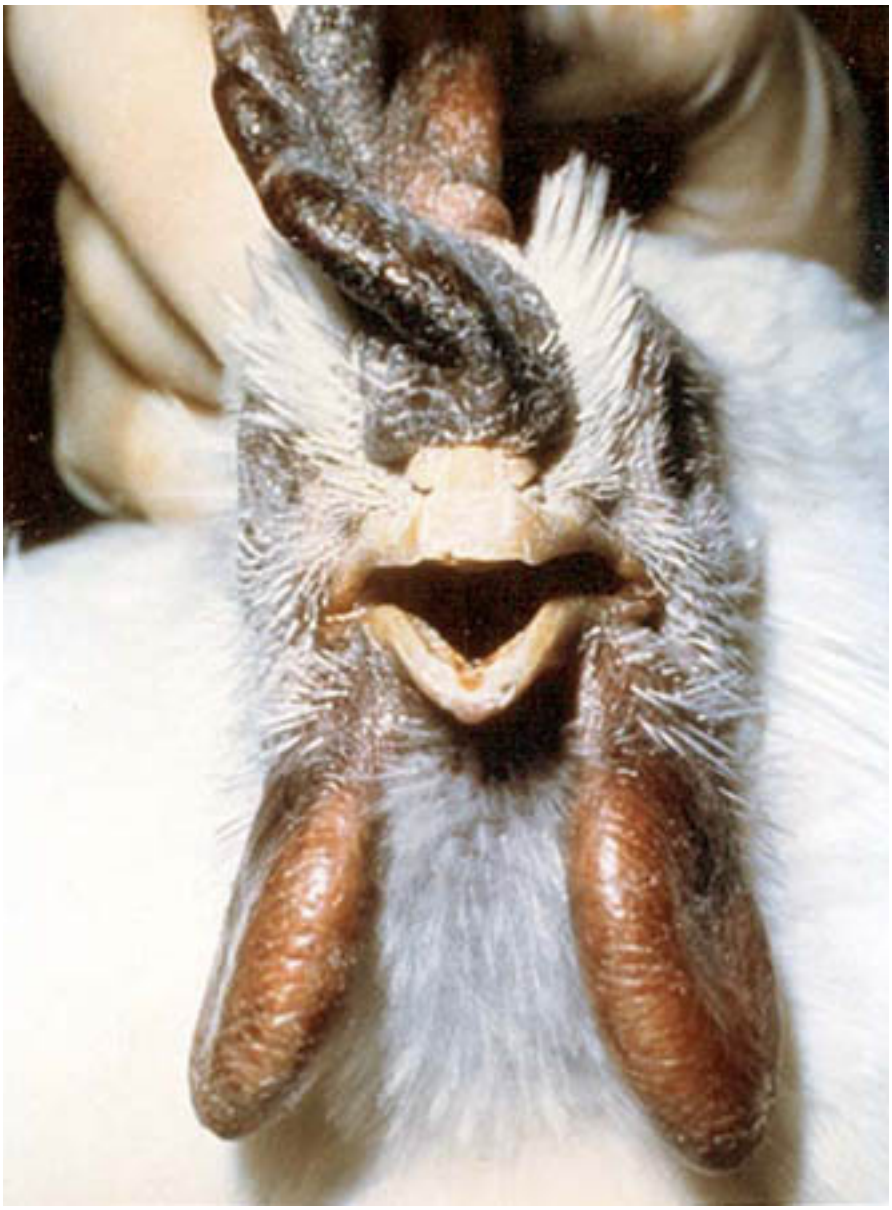

Fig. 25. HPAI - Edema of the wattles.

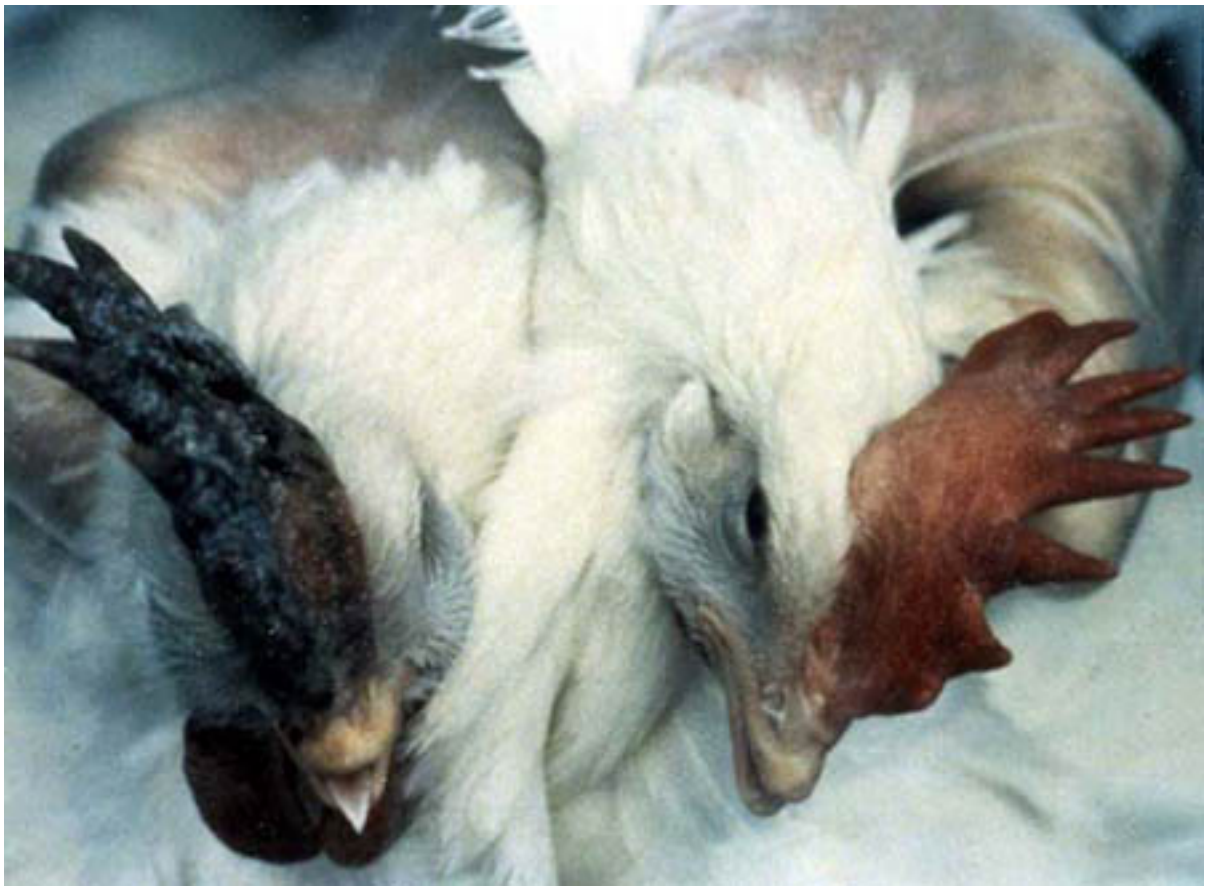

Fig. 26. HPAI - Cyanotic comb of an infected chicken on the left compared to a normal chicken on the right.

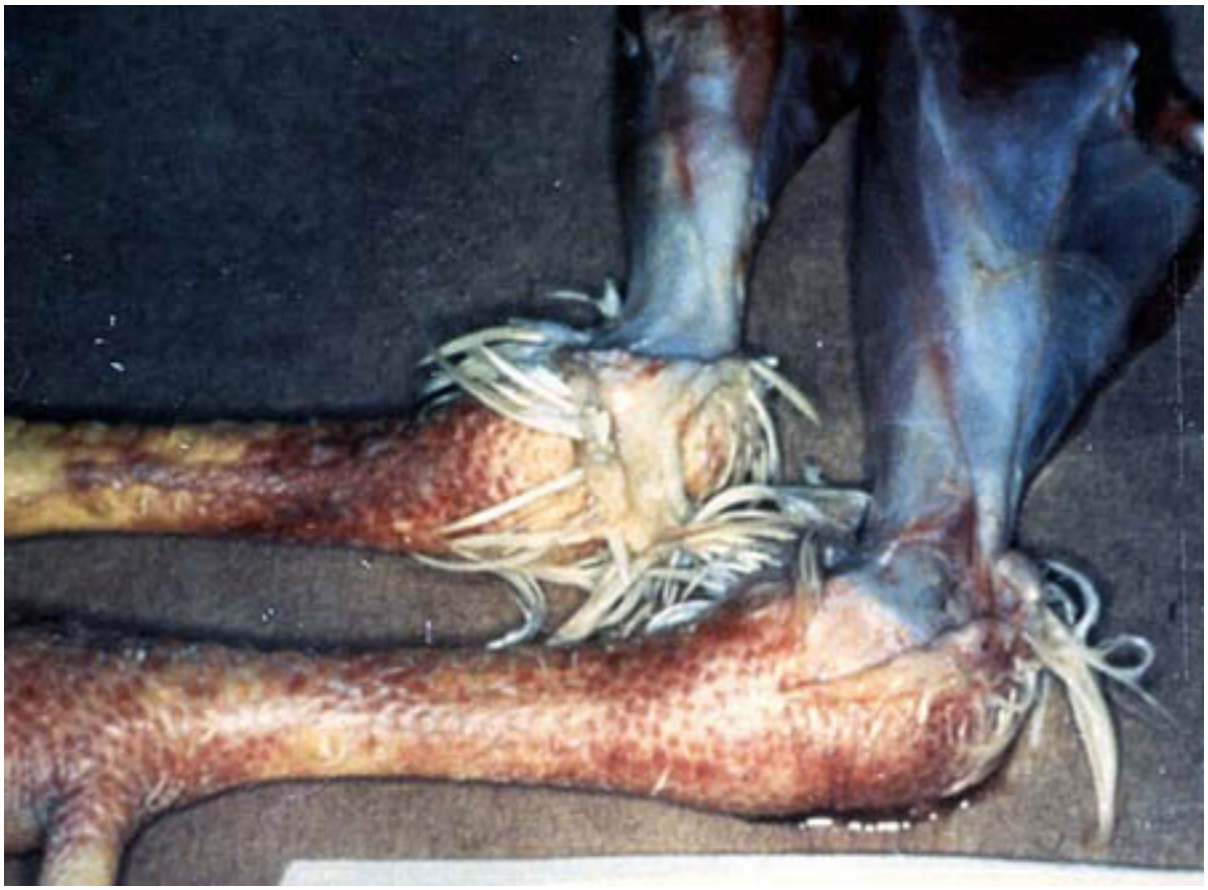

Fig. 27. HPAI - Congestion and petechiae in the skin on the hocks and shanks.

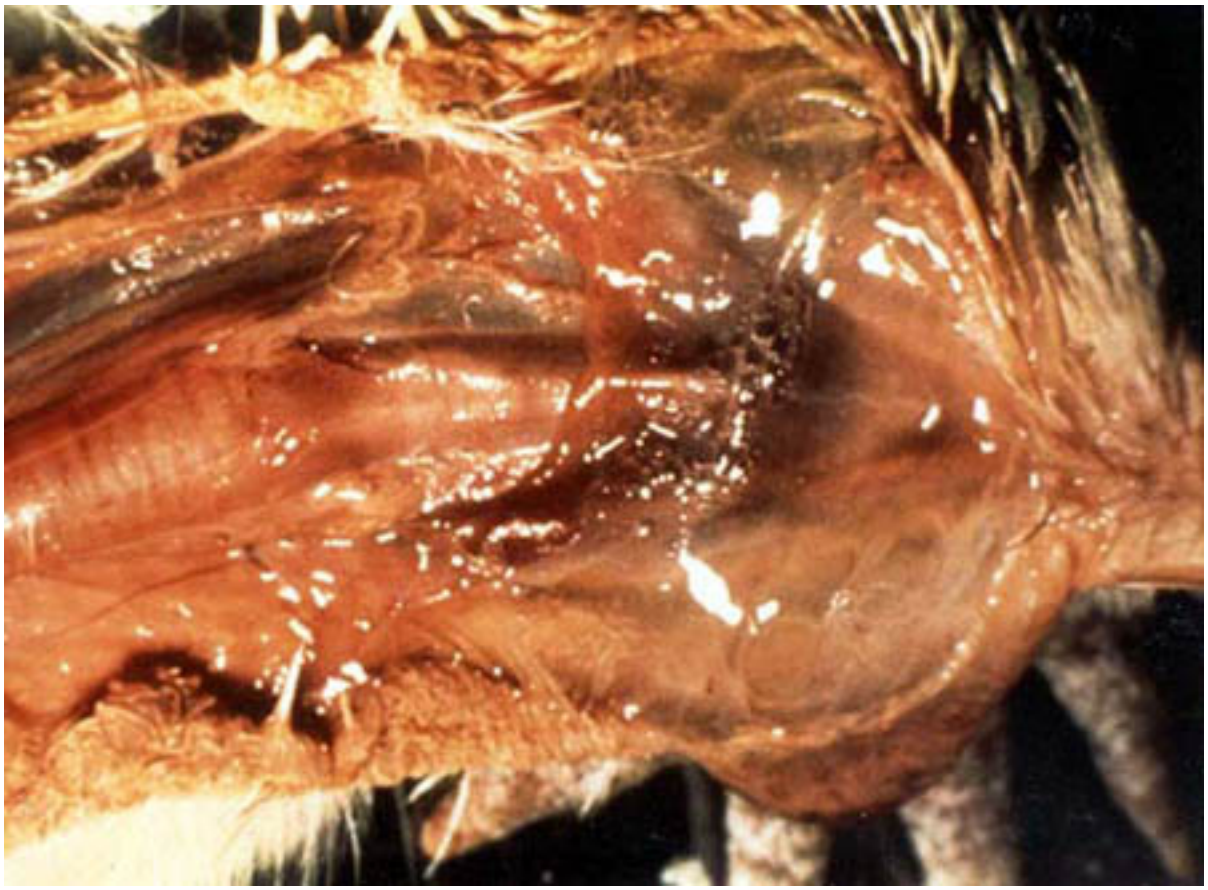

Fig. 28. HPAI - Opened edematous wattle.

PART IV
FOREIGN ANIMAL DISEASES

BABESIOSIS

Introduction

Babesiosis is caused by any one of many *Babesia* species that infect a wide variety of vertebrate hosts, including domestic and wild animals, as well as man. In nature, babesias typically are transmitted biologically by ixodid ticks, but other means, such as biting flies and fomites that transfer blood from the infected carrier to a susceptible animal, may be involved in the mechanical transmission of these intraerythrocytic parasites. A list of commonly encountered babesias is presented in Table 1. Although it is possible for a single *Babesia* species to infect more than one vertebrate host, as seen in *B. microti* (rodents and man) and *B. divergens* (cattle, man, and gerbils), the general pattern is that the *Babesia* species are reasonably host specific.

This review will deal primarily with those babesias afflicting cattle. It is thought that these animals are, from an economic point of view, the most severely affected by babesial infections. Equine babesiosis and babesiosis of other animals are discussed briefly in this chapter.

Bovine Babesiosis

(Piroplasmosis, Texas fever, redwater, tick fever)

Definition

Bovine babesiosis is a febrile, tick-borne disease of cattle, caused by one or more protozoan parasites of the genus *Babesia* and generally characterized by extensive erythrocytic lysis leading to anemia, icterus, hemoglobinuria,and death.

There are probably at least six *Babesia* species (Table 1) responsible for bovine babesiosis. Most can be categorized as being small or large babesia. Morphological and serological differences are used to distinguish the different species. The two that are of most concern in the United States are *B. bigemina* and *B. bovis*, which are transmitted primarily by *Boophilus* ticks. These species and their vector ticks once occurred in large areas of the United States, and still occur in Mexico and throughout the tropical and subtropical areas of the Western Hemisphere.

Babesia bigemina

Etiology

B. bigemina (Fig. 29) is a large babesia that is pleomorphic but characteristically is seen and identified by the pear-shaped bodies joined at an acute angle within the mature erythrocyte. Round forms measure 2 µm and the pear-shaped, elongated ones are 4-5 µm (1).

History

One of the early accounts in the United States of babesiosis dates from 1868, when a disastrous epizootic broke out among native cattle in Illinois and Indiana with the loss of 15,000 head after the importation of apparently healthy cattle from Texas (2). The mortality rate among affected cattle approached 90 percent. The fear and respect for Texas or southern cattle fever was wellfounded. Even then it was not a new disease, having been described as early as 1814. It was not, however, until much later that the cause and mode of transmission became apparent.

The classical investigations of Smith and Kilborne (1893) were the first to establish that a pathogenic protozoan (*B. bigemina*) could be transmitted by an intermediate arthropod host (*Boophilus annulatus*) (3). At that time, *Boophilus* ticks, and presumably babesiosis, occurred in the United States throughout the South, from Texas to the Atlantic States, as well as in southern California (Illustration 1) (4). In 1906, it was estimated that economic losses associated with the tick, and *B. bigemina* (probably *B. bovis* also) amounted to $130.5 million annually. In terms of present dollars, and considering the larger number of cattle now present in the South, these losses would easily exceed a billion dollars annually if ticks and babesias were left uncontrolled. A tick eradication program was essentially completed by 1943, and bovine babesiosis ceased to exist in the United States except in the quarantine buffer zone adjacent to the Mexican border (4). Babesiosis is now considered an exotic disease of cattle for the United States. This impressive accomplishment of tick eradication has never been duplicated in an area of comparable size, notwithstanding similar efforts in various parts of the world. As a result of those failures, both ticks and babesia are widely prevalent elsewhere and constitute a continuing threat to U.S. livestock.

Host Range

Cattle are the principal hosts, but it is reported that the water buffalo and African buffalo may also become infected (11). It is possible that other ungulates are infected, but from a practical point of view, these infections are nominal and, except under unusual conditions, rare. Such hosts are probably not significant reservoirs of infection.

Babesia bigemina is widespread in cattle and occurs wherever *Boophilus* ticks are encountered, which includes North and South America, Southern Europe, Africa, Asia, and Australia (10). Babesiosis also occurs on the Caribbean and South Pacific islands. Cattle and the invertebrate tick hosts provide the major reservoir of infection. Wildlife and nonbovine hosts generally have not been incriminated.

Transmission

Ticks acquire babesia infection during their feeding on infected animals. The infection is then passed to the ovaries, and thus the emerging larvae carry the infection. The babesias continue to develop within the larvae, and transmission usually occurs in the new host during the nymphal and adult stages. *Boophilus annulatus*, *B. microplus*, and *B. decoloratus* are the principal vectors of *B. bigemina* (5,6). Mechanical transmission is possible, but it is not efficient enough to maintain infection in the absence of specific tick vectors.

Incubation Period

Natural transmission occurs by the feeding of infected nymphal and adult ticks, and evidence of infection occurs 2-3 weeks after tick infestation. Following blood inoculation, the incubation time may be 4-5 days or less, depending on the size of the exposing inoculum.

Clinical Signs

Infection with *B. bigemina* is usually accompanied by the presence of *Boophilus* ticks. Calves normally are reasonably resistant to babesia, for the infection does not usually result in clinical disease (5). In older animals, clinical signs can be very severe; however, differences in pathogenicity may occur with various *B. bigemina* isolates associated with different geographic areas. Mahoney observed that the Australian *B. bigemina* rarely causes disease, whereas *B. bigemina* in Africa is highly pathogenic (6). Personal experience by the author suggests that *B. bigemina* as seen in the Western Hemisphere is highly pathogenic; however, it is probably less so than *B. bovis*.

The first sign is usually a high fever with rectal temperatures reaching 41.5º C (106.7º F). There is anorexia, and ruminal atony. Often the first visible appearance of infection is that the animal isolates itself from the herd, becomes uneasy, seeks shade, and may lie down. Cattle may stand with an arched back, have a roughened hair coat, and show evidence of dyspnea and

tachycardia. The mucous membranes are first injected and reddened, but as erythrocytic lysis occurs, the color changes to the pallor of anemia. Anemia is a contributory factor to the weakness and loss of condition seen in cattle that survive the acute phase of the disease. The anemia may occur very rapidly, with 75 percent or more of the erythrocytes being destroyed in just a few days. This is usually associated with severe hemoglobinemia and hemoglobinuria. After onset of fever, the crisis will usually pass within a week, and if the animal survives, there is usually severe weight loss, drop in milk production, possible abortion, and a protracted recovery. Mortality is extremely variable and may reach 50 percent or higher, but in the absence of undue stress most animals will survive (5,6).

Gross Lesions

The lungs may be edematous and congested in cattle that have died early in the course of infection. The pericardial sac may contain serosanguineous fluid and subepicardial and subendocardial petechial hemorrhages. The liver is enlarged and icteric, and the gallbladder, which may have hemorrhage on the mucous surface, is distended with thick, dark green bile. The spleen is markedly enlarged, and has a dark pulpy consistency. The abomasal and intestinal mucosa may be icteric with patches of subserosal hemorrhages. The blood is thin and watery. The urinary bladder is frequently distended, with dark, reddish-brown urine. Jaundice is commonly distributed in the connective tissue. The lymph nodes are edematous and often have petechiation.

In cattle that have suffered a more prolonged illness, acute lesions are much less conspicuous. Subepicardial petechial hemorrhages may be present, the carcass is usually emaciated and icteric, the blood is thin and watery, the intermuscular fascia is edematous, the liver yellowish-brown, and the bile may contain flakes of semisolid material. The kidneys are pale and often edematous, and the bladder may contain normal urine, depending on how long past the hemolytic crisis the necropsy is performed. Although the spleen is enlarged, the pulp is firmer than in acute babesiosis (5,6,7).

Diagnosis

Field Diagnosis

Fever, anemia, jaundice, and hemoglobinuria are suggestive clinical signs of babesiosis in cattle located in enzootic areas where *Boophilus* ticks occur. If these signs are also associated with erythrocytic destruction, the diagnosis of babesiosis is strengthened. A positive diagnosis requires the identification of the babesia on blood smears or either positive serologic tests or transmission experiments, or both.

Specimens for the Laboratory

From each animal six blood smears should be made, air-dried and fixed in methanol and/or a sample of whole blood in an anticoagulant and serum should be collected.

In acute infection, *B. bigemina* can usually be detected on Giemsa-stained thin blood smears. Thick smears (8) increase the likelihood of detecting the causative organism, but the characteristic morphology is more difficult to identify with this technique. In cases of chronic infection, diagnosis is usually made using a variety of serologic tests for the detection of specific antibodies, since the organism disappears or is present in extremely low numbers soon after the acute infection.

Differential Diagnosis

Other conditions that should be considered and may resemble babesiosis are anaplasmosis, trypanosomiasis, theileriosis, leptospirosis, bacillary hemoglobinuria, hemobartonellosis, and eperythrozoonosis.

Prognosis

After the onset of hemoglobinuria, the prognosis is guarded. Among fully susceptible older cattle, the mortality may reach 50 percent without treatment. Among cattle raised in an area where babesiosis is endemic, few, if any, losses occur even though infection takes place (6). This phenomenon usually reflects early exposure of the neonates, when they are more resistant, resulting in varying levels of protection. Once having the infection, the bovine experiences a high level of resistance to reexposure.

Treatment

Successful treatment of *B. bigemina* depends on early diagnosis and the prompt administration of effective drugs. There is less likelihood of success if treatment is delayed until the animal has been weakened by fever and anemia. If medication is administered early, however, success is the rule, for there are several effective compounds (Table 2) (14).

One of the first successful treatments was trypan blue. This treatment may be used to determine the type of infection present. *B. bigemina* is susceptible to trypan blue treatment, whereas *B. bovis*, is not. Generally, the small babesias are more resistant to chemotherapy. The most commonly used compounds for the treatment of babesiosis are diminazene diaceturate (3-5 mg/kg), imidocarb (1-3 mg/kg), and amicarbalide (5-10 mg/kg); however, the quinuronium and acridine derivatives are also effective (Table 2). Treatment of *B. bigemina* is so effective in some instances that radical cures occur that will eventually leave the animal susceptible to reinfection. For this reason, reduced drug levels are sometimes indicated. Imidocarb has been successfully used as a chemoprophylactic, that will prevent clinical infection for as long as 2 months but allow mild subclinical infection to occur as the drug level wanes, resulting in premunition and immunity (15,16). The relative efficacy of some the more common compounds used is shown in Table 3.

Vaccination

The most common form of immunization against *B. bigemina* entails inoculating live organism (attenuated or virulent) into susceptible young cattle followed by chemotherapy, as needed, to modify the clinical effects; thus, coinfectious immunity or a state of premunition is induced (6). If older animals are to be so vaccinated, care may be necessary to prevent serious reactions (17,18). An attenuated organism has successfully been used in Australia (19). Such a premunition approach, although useful in endemic areas, would be less desirable in areas where the infection rate is low because this approach, in essence, establishes a large reservoir of infection.

Experimental trials with nonviable vaccines have been successfully conducted, but no commercial vaccine of this type is available at this time (6,9). After having recovered from a premunizing parasitemia cattle will have a degree of sterile immunity for a short time (20). Carrier infections, if accompanied by reexposure, as is common in endemic areas, will result in immunity that may persist for the lifetime of the animal (18). There are instances when antigen variations may occur that might challenge the immunity of a vaccinated animal. Usually, however, when animals are premunized, even variants will not produce a clinically detectable reaction (6,9).

Control and Eradication

Preventive Measures

The oldest and probably the most effective procedure for the control of babesiosis is to control and eradicate its vector, the *Boophilus* tick (4). The eradication campaign in the United States conducted in the 1920's and 1930's relied largely on dipping all cattle every 2-3 weeks in vats charged with arsenical acaricides (4). These acaricides have been replaced by a wide variety of improved compounds, including the chlorinated hydrocarbons, carbamates, organophosphates, and natural and synthetic pyrethrins (4). In some tropical countries, tick control rather than eradication is the goal. This approach attempts to establish an equilibrium in which the tick numbers are sufficient to maintain low-level infection in the cattle and hence immunity to acute

babesiosis. Care must be taken, however, to prevent the development of excessive ticks that could be responsible for livestock losses (12,13). In the absence of reinfection, the babesias gradually disappear, and the cattle become susceptible; hence, a desire exists to sustain low levels of exposure to maintain immunizing infections. Tick control in some areas has been complicated by the development of tick resistance to many of the common acaricides (4).

Sanitation and Disinfection

Aside from efforts involved in the control and elimination of the tick vector, sanitation and disinfection do not contribute to an abatement of the disease incidence in enzootic areas. As with most blood diseases, however, care is recommended in routine surgery (dehorning, castration, etc.) and needle vaccination procedures to prevent the accidental transfer of blood from one animal to another, thereby transmitting infection.

"Babesia bovis"

Etiology

Babesia bovis (Fig. 30) is a small pleomorphic babesia typically identified as a single body, as small round bodies, or as paired, pear-shaped bodies joined at an obtuse angle within the mature erythrocyte. The round forms measure 1-1.5 µm, and the pear-shaped bodies 1.5 by 2.4 µm in size (5,6).

History

Soon after Smith and Kilborne's work, the presence of a second morphologically distinct small babesia of cattle occurring in Argentina was identified as *B. argentina*. This was later determined to be synonymous with *B. bovis* (21). Rees in 1930 described a small babesia in Louisiana that he determined to be *B. bovis* (21). If one studies the early drawings of Smith and Kilborne, it is evident that both *B. bigemina* and *B. bovis* were present even then. The history of this organism closely follows that of *B. bigemina*, and it is sometimes difficult to distinguish one from the other in the early literature.

Host Range

Although cattle are the principal hosts, it is probable that infections can be maintained in other ungulates such as buffalo (11). There are reports in the literature of human cases due to *B. bovis* (24).

Geographic Distribution

Babesia bovis usually occurs in the same areas a *B. bigemina* and in association with *Boophilus* ticks but has been described in some parts of Europe where *Boophilus* does not occur, which suggests other vectors.

Transmission

The same ticks (*B. annulatus*, *B. microplus*) that transmit *B. bigemina* are usually capable of transmitting *B. bovis*. The tick *B. decoloratus*, which is widely distributed in Africa, does not appear to transmit *B. bovis* even though it readily transmits *B. bigemina* (9). There are reports from Europe of B. bovis, for which the vector is thought to be *Ixodes ricinus* (11,23).

Incubation Period

B. bovis has a longer incubation time than does *B. bigemina*, but since *B. bovis* is transmitted by the larval stage of the vector rather than by the nymphal and adult stages, *B. bovis* prepatency (measured from the time of tick infestation) is only slightly longer than that of *B. bigemina*. With blood inoculation, the incubation time is usually 10-14 days; however, this can be shortened by large inoculums.

Clinical Signs

Infections of *B. bovis* resemble, in many respects, those seen with *B. bigemina*, but there are some characteristic differences. Hemoglobinuria and hemoglobinemia are not as consistently seen in infections with *B. bovis*, although they may occur (5,6). The level of anemia is frequently less severe, but central nervous system involvement is more common. It is generally conceded that *B. bovis* is the more virulent of the two organisms. This is particularly so in Australia and to a lesser extent in Africa and the Western Hemisphere (6).

Animals commonly develop incoordination and depression and go down with the head extended but later thrown back and have involuntary movement of the legs. These signs are followed by death. Whereas the packed cell volume (PCV) in most fatal infections with *B. bigemina* will be well below 10 percent, death commonly occurs with *B. bovis* when the PCV is 12 percent or higher. When hemoglobinuria is seen, the color is not nearly so dark, nor is the plasma following PCV determination so red. The observed parasitemias in peripheral blood are usually much lower with *B. bovis* than with *B. bigemina*.

Gross Lesions

Changes similar to those described for *B. bigemina* are apparent.

Diagnosis

Field Diagnosis

Fever, anemia, jaundice, and hemoglobinuria are suggestive clinical signs of babesiosis in cattle located in enzootic areas where *Boophilus* ticks occur. If these signs are also associated with erythrocytic destruction, the diagnosis of babesiosis is strengthened. A positive diagnosis requires the identification of the babesia on blood smears or either positive serologic tests, or transmission experiments, or both. In addition, a technique of brain biopsies has been described that has proven very useful in detecting and diagnosing *B. bovis* infections (9,22). The characteristic low parasitemias in the circulating blood make this technique very useful in improving the chances of seeing the organism. There is a marked concentration of infected erythrocytes in the capillaries of the brain.

Specimens for the Laboratory

From each animal six blood smears should be made, air-dried and fixed in methanol and/or a sample of whole blood in an anticoagulant and serum should be collected. Serologic diagnostic techniques are similar to those described for *B. bigemina*. Presently, immunofluorescence assay is the test of choice in the serologic diagnosis of *B. bovis* (9).

Differential Diagnosis

In addition to those conditions mentioned for *B. bigemina*, a differential diagnosis of *B. bovis* infection must include diseases producing central nervous system (CNS) involvement such as rabies, other encephalitides, or toxic effects that would produce similar CNS changes.

Prognosis

Once CNS signs become pronounced, the prognosis is poor. Generally, *B. bovis* produces a somewhat more severe clinical response than does *B. bigemina*.

Treatment

Chemotherapy is generally effective, with essentially the same drugs as used for *B. bigemina*. *B. bovis* is usually somewhat more difficult to treat, and a second treatment, or slightly increased dose rates, may be desirable. Trypan blue is not effective against *B. bovis* (14). Imidocarb has been reported to induce radical cures in vertebrate hosts. *Babesia bovis*-infected *B. annulatus* ticks, when placed on animals recently treated with imidocarb, apparently lost their

infectivity, for their progeny failed to transmit infection (15). Tick infection remained following imidocarb treatment in a similar experiment with *B. bigemina* in *B. decoloratus* (25).

Vaccination

Vaccines are used in a number of places where babesiosis is endemic. Repeated passage of *B. bovis* in splenectomized calves results in the attenuation of the organism (9,26). For many years, this attenuated vaccine has been produced and successfully used in Australia for the prevention of *B. bovis* (6). In some cattle (older, and producing dairy cows), chemotherapy may be indicated, but usually the vaccine may be used without treatment.

The development of in vitro techniques for the cultivation of *B. bovis* on bovine erythrocytes has led to the isolation of soluble antigens, which, when combined with adjuvants, have proven immunogenic (27,28). These noninfectious vaccines, although they do not prevent infection, appear to be responsible for moderating the effects of infection. They do not produce as high a level of protection as is seen with premunizing vaccines but are safe and do not yield carriers. In some instances, these vaccines, although protective against homologous challenge, may not protect against immunologic variants.

The continuous in vitro passage of *B. bovis* has been shown to induce a level of attenuation similar to that seen with the passage of the organism in splenectomized calves. Infection with this attenuated organism has been reported to prevent clinical infection following a challenge with virulent *B. bovis* (29,30).

Control and Eradication

Eradication of the *Boophilus* vectors would eliminate transmission of *B. bovis* which, over a period of time, would lead to its eradication.

Sanitation and Disinfection

Aside from the efforts involved in the control and elimination of the tick vector, sanitation and disinfection do not contribute to an abatement of the disease incidence in enzootic areas. As with most blood diseases, however, care is recommended in routine surgery (dehorning, castration, etc.) and needle vaccination procedures to prevent the accidental transfer of blood from one animal to another, thereby transmitting infection.

Other Bovine Babesias

Babesia divergens appears to be a serious pathogen for cattle in the United Kingdom and northern Europe (11). It is a small species that morphologically resembles *B. bovis* but is slightly smaller and tends to be located at the periphery or margins of the infected erythrocyte. It is transmitted by *Ixodes ricinus*, which becomes infected when the adult feeds on either a carrier or an acutely infected host. All stages of the F1 and sometime F2 generation are infective and capable of transmission (11).

Babesia divergens produces a disease syndrome similar to *B. bigemina* and *B. bovis*; however, the cerebral form is rarely seen. Treatment with those babesiacides previously discussed is effective.

The presence of *Ixodes* ticks (*I. scapularis*, *I. pacificus*, and *I. dammini*) in the United States suggests the potential for this babesia to become established here. Consequently, *B. divergens* is a pathogen that should not be ignored.

Babesia jakimovi (a large species) is the causal agent of Siberian piroplasmosis in cattle. It can also infect the Tartarean roe deer, Asian elk, and reindeer. It appears to be transmitted transovarially by *I. ricinus*, but mechanical transmission by gadflies is also suggested. Signs of infection and response to treatment closely resemble *B. bigemina* (11).

Babesia major is a large species only slightly smaller than *B. bigemina*. This babesia is

transmitted by *Haemaphysalis punctata* and occurs in the United Kingdom, and northern Europe (11). It is essentially nonpathogenic but can be induced to produce clinical effects and even death by serial passage in splenectomized calves.

Babesia ovate, a large species, has been described in Japan. It is apparently serologically distinct from *B. bigemina*. It is only mildly pathogenic and responds to the same therapy used against *B. bigemina* (31). Transmission in Japan is by the larvae of *Haemaphysalis longicornis*. No immunity or cross-protection occurs with *B. bigemina*, *B. bovis*, or *B. major*. Serologically it appears to be a distinct species.

Equine Babesiosis

(Equine Piroplasmosis)

Definition

Equine babesiosis is a febrile tick-borne disease of horses caused by either *Babesia caballi* (Fig. 31), *B. equi* (Fig. 32) or both and is generally characterized by erythrocytolysis leading to anemia, icterus, hemoglobinuria, and death.

Geographic Distribution

Equine babesiosis is widely distributed throughout the tropics and subtropics and to a lesser extent is known to occur in temperate regions.

Transmission

Babesia caballi is transmitted by ticks of the genera *Dermacentor*, *Hyalomma*, and *Rhipicephalus* and is passed transovarially from one tick generation to the next. Experimental transmission of *B. caballi* under laboratory conditions has been reported using *Dermacentor nitens*, *D. albipictus*, and *D. variabilis* (9). The widespread prevalence of these ticks (*D. albipictus* and *D. variabilis*), plus the presence or past presence of *B. caballi* in the United States (32), creates an unanswered question of why *B. caballi* has not become more widespread in the United States. Transmission of *B. equi* appears only to occur transstadially (33). The vector or vectors of *B. equi* have not been identified in the Western Hemisphere. Elsewhere, ticks of the genera *Dermacentor*, *Hyalomma*, and *Rhipicephalus* appear to be involved.

Clinical Signs

The severity of clinical response is variable, and in many cases spontaneous recovery may occur following a febrile response with no marked hemoglobinuria or anemia (11). Other reports describe the response as more like that seen in cattle babesiosis.

Diagnosis

A positive diagnosis requires the identification of the babesia on blood smears, or positive serologic tests.

Specimens for the Laboratory

From each animal six blood smears should be made, air-dried and fixed in methanol and/or a sample of whole blood in an anticoagulant and serum should be collected.

Treatment

Both *B. caballi* and *B. equi* respond to the babesiacidal drugs (Table 2), but *B. equi* is more refractory to treatment than *B. caballi* (14). Imidocarb appears to be the drug of choice for eliminating carrier status of infected horses. In the case of *B. caballi*, .2 mg/kg given two times at a 24-hour interval appears effective. For the same effect in *B. equi*-infected horses, 4 mg/kg is given four times at 72-hour intervals (14). This amount of drug approaches the lethal dose for

50 percent of the inoculated group (LD_{50}) of 32 mg/kg when given in two 16 mg/kg doses at 24-hour intervals (36). Side effects characterized by restlessness, abdominal pain, sweating, rolling, heavy breathing, etc., are not uncommon following imidocarb treatment at these higher levels.

Vaccination

No efficacious vaccine for equine babesiosis is available.

Control and Eradication

Preventive Measures

Once a horse is infected, the carrier status may persist for an extended period during which the carrier horse may act as reservoirs of infection. To prevent the introduction of equine babesiosis into areas free of infection, restrictive measures are sometimes imposed on imported horses.

Sanitation and Disinfection

Aside from measures involved in the control and elimination of the tick vector, sanitation and disinfection do not contribute to an abatement of the disease incidence in enzootic areas. As with most blood diseases, however, care is recommended in routine surgery (castration, etc.) and needle vaccination procedures to prevent the accidental transfer of blood from one animal to another, thereby transmitting infection.

Babesiosis of Other Domestic Animals

Sheep and Goats

Babesia motasi, a large species resembling *B. bigemina* morphologically, is infective for sheep and is transmitted by ticks of the genera *Haemaphysalis* and *Rhipicephalus*. This organism is widespread in the Old World, having been identified in Europe, the Middle East, the former Soviet Union, Southeast Asia, and Africa (11). *B. motasi* produces a mild clinical response characterized by fever and anemia but alone is rarely responsible for significant death losses. Some strains are transmissible to goats, but this is not a consistent observation.

Babesia ovis is a small species observed in sheep and goats and occurs as a pathogenic entity in southern Europe and the Middle East (11). *Rhipicephalus* bursa has been shown to be a vector for this parasite, and *I. ricinus* and *D. reticulatus* are suspected vectors. The signs of infection may resemble those described for cattle with a febrile response, anemia, icterus, edema, and hemoglobinuria. Infections are usually mild and often are inapparent.

Both *B. motasi* and *B. ovis* respond to one or more those babesiacidal drugs referred to in Table 2 (14). Information on these babesias is limited, and few serological and cross-immunological studies have been made to clarify the identity of these intraerythrocytic parasites of sheep and goats.

Swine

Both *Babesia trautmanni* (large) and *B. perroncitol* (small) occur in swine and, on occasion, are responsible for serious losses following infections, producing signs not unlike those described for cattle (11). Swine babesiosis has been described in the former Soviet Union, southern Europe, and Africa. In Africa, the wild pigs (warthogs and bush pigs) are thought to be reservoirs. Several ticks (species of the genera, *Boophilus*, *Hyalomma*, and *Rhipicephalus*) are suspected as possible vectors. These infections generally respond to chemotherapy with those drugs referred to in Table 2 (14).

Other Species

An array of other babesia species exist, and a great number of vertebrate species are infected

by one or more of these intraerythrocytic parasites. Wildlife are also involved, but because these babesias are often relatively nonpathogenic, they frequently go unnoticed.

Public Health

Of recent interest has been the occurrence of babesiosis in man. At one time these human infections were thought to occur only in splenectomized individuals, or those who were otherwise immunosuppressed. This is not, however, the case where *B. microti.*, transmitted by *I. dammini* (24), is involved.

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Table 1. **Recognized babesia species of domestic animals**

Organism	Animals affected	Morphology of organism	Vectors
B. bigemina[1]	Cattle	4.5 by 2.5 µm (Large, round and pryiform, acute angle)	*Boophilus annulatus, B. decoratus, B. microplus*
B. bovis[2]	Cattle	2.4 by 1.5 µm (small, more rounded obtuse angle)	*B. annulatus*, *B.microplus, Ixodes* spp. (?)
B. divergens	Cattle	1.5 by 0.4 µm (small, narrow and obtuse angle)	*Ixodes ricinus*
B. major	Cattle	2.6 by1.5 µm (large round & pyriform)	*Haemaphysalis punctata*
B. jakimovi	Cattle and wild ruminants	Similar to *B. major*	*I. ricinus*
B. ovata	Cattle	Similar to *B.bigemina*	*H. longicornis*

B. caballi	Horses	Similar to *B. bigemina*	*Dermacentor, Hyalomma*, and *Rhipicephalus* spp
B. equi	Horses	1.0-2.0 µm (small and rounded, Maltese cross is common)	*Dermacentor*, *Hyalomma*
B. motasi	Sheep and goats	Simlar to *B. bigemina*	*D. silvarum* (?), *R. bursa, Haemaphysalis* spp
B. ovis	Sheep and goats	1.5 by 1.0 µm (small, rounded, obtuse)	*I. ricinus* (?), *D. reticulatus* (?). *R bursa*
B. trautmanni	Swine	3.5x2.0 µm (large, narrow and long, acute angle)	*R. sanguineus* (?), *Boophilus, Hyalomma*, *Dermacentor* spp, (?)
B. perroncitoi	Swine	0.7-2.0 µm (small and more rounded)	Vectors unknown

(?) Suspected vectors

1.The American bison has been artificially infected with *B. bigemina*, producing detectable parasitemias.

2. Synonyms *B. berbera*, and *B. argendna*

Table 2**. Products used to treat babesiosis successfully**

Compound or compound group	Proprietary name

Acridine derivatives	
Acriflavine hydrochloride (Euflavine, Trypaflavine)	Gonacrine[1]
Blue Azo-Naphthalene dyes	
Trypan blue	Congo Blue, Niagara Blue
Qiamidine derivative	
Aromatic:	
Diminazene diaceturate	Berenil[2] , Ganaseg[3]
Pentamidine diisethionate	Lomidine[1]
Phenamidine diisethionate	Lomidine[1]
Carbanilide:	
Amicarbalide diisethionate	Diampron[1]
Imidocarb dipropionate	Imizol[4]
Quinoline derivatives	
Quinuronium sulfate	Acaprin[5]
	Akiron
	Pirevan
	Piroplasmin
	Babesan[6]

1. May and Baker Ud., Dagenham, England
2. Farbwerke-Hoechst AG, Frankfurt, Germany
3. Squibb Mathieson, E. R. Squibb and Sons de Mexico, Mexico City, Mexico
4. Pitman-Moore, Europe, Middlesex, England
5. Ludabel Farbenfabriken, Bayer, Leverkusen, Germany
6. Imperial Chemical Industries Ud., Macclesfield, Cheshire, England

Table 3. **Relative efficacy of the more commonly used babesiacidal compounds**

	B. bigemina	*B. bovis*	*B. divergens*	*B. caballi*	*B. equi*
Diminazene	++++	+++	++	+++	++
Imidocarb	++++	+++	+++	++++	++
Amicarbalide	++++	++	++	+++	+
Phenamidine	++	++	+++	++	
Quinuronium	+++	++	+	++	—
Trypan Blue	++	—	—	++	—
Pentamidine	++				

—: not effective.

Information provided in Tables 2 and 3 does not constitute an endorsement by the USAHA. State and Federal authorities should be contacted before use.

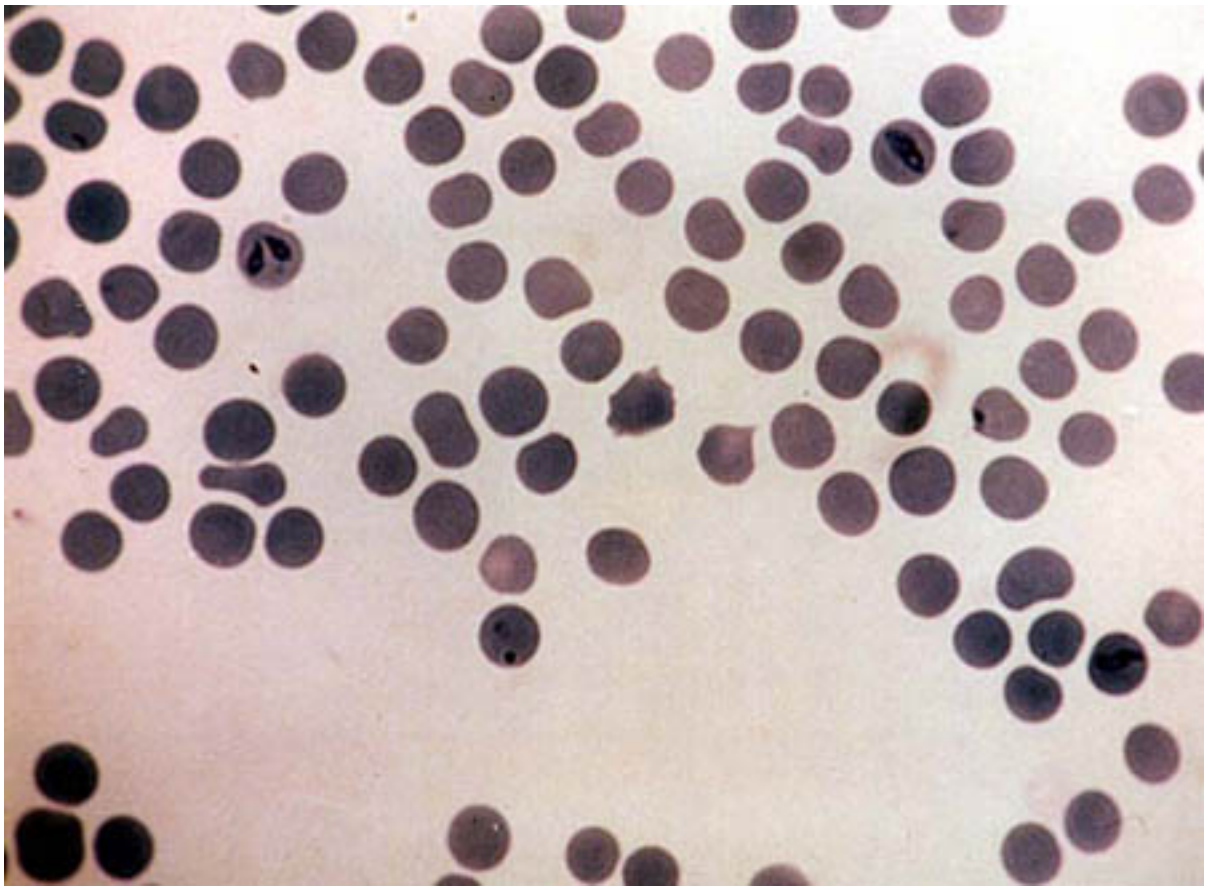

Fig. 29. Babesiosis - *B. bigemina* in erythrocytes.

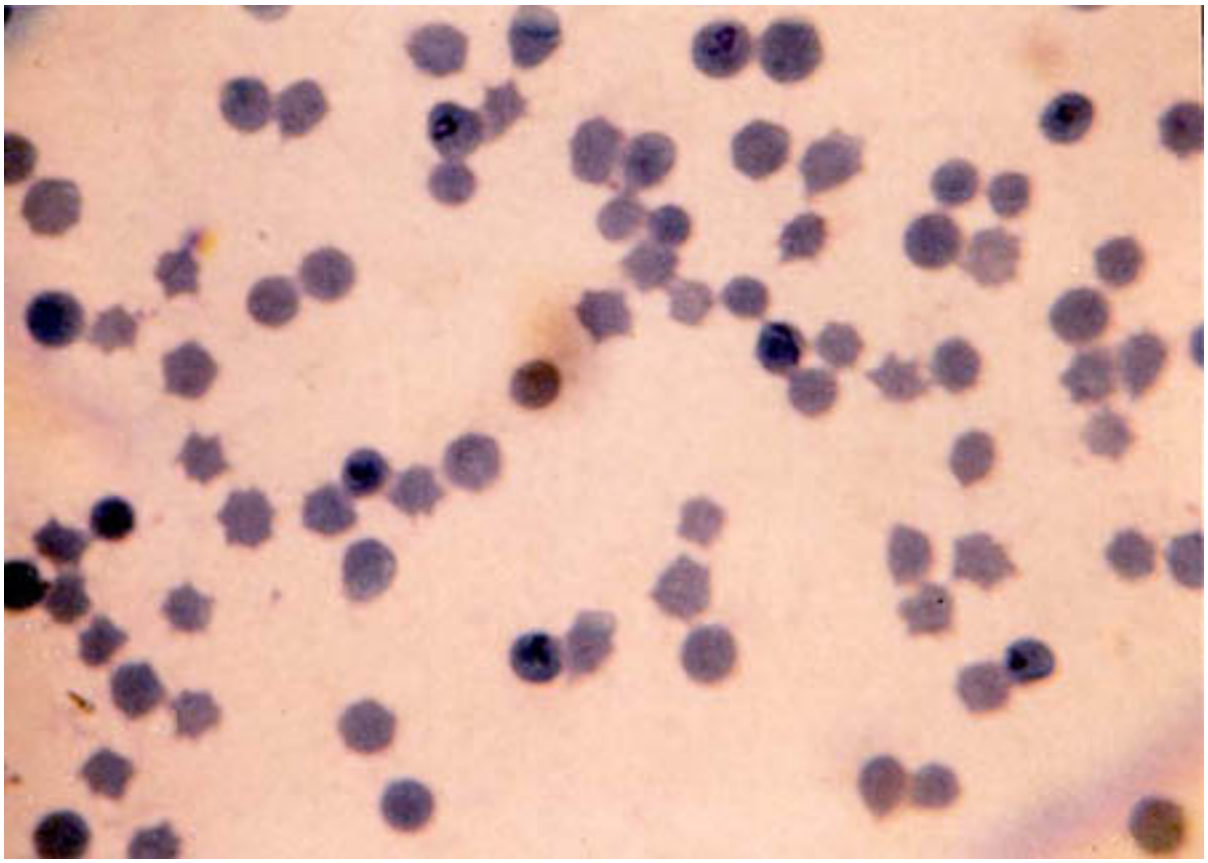

Fig. 30. Babesiosis - *B. bovis* in erythrocytes.

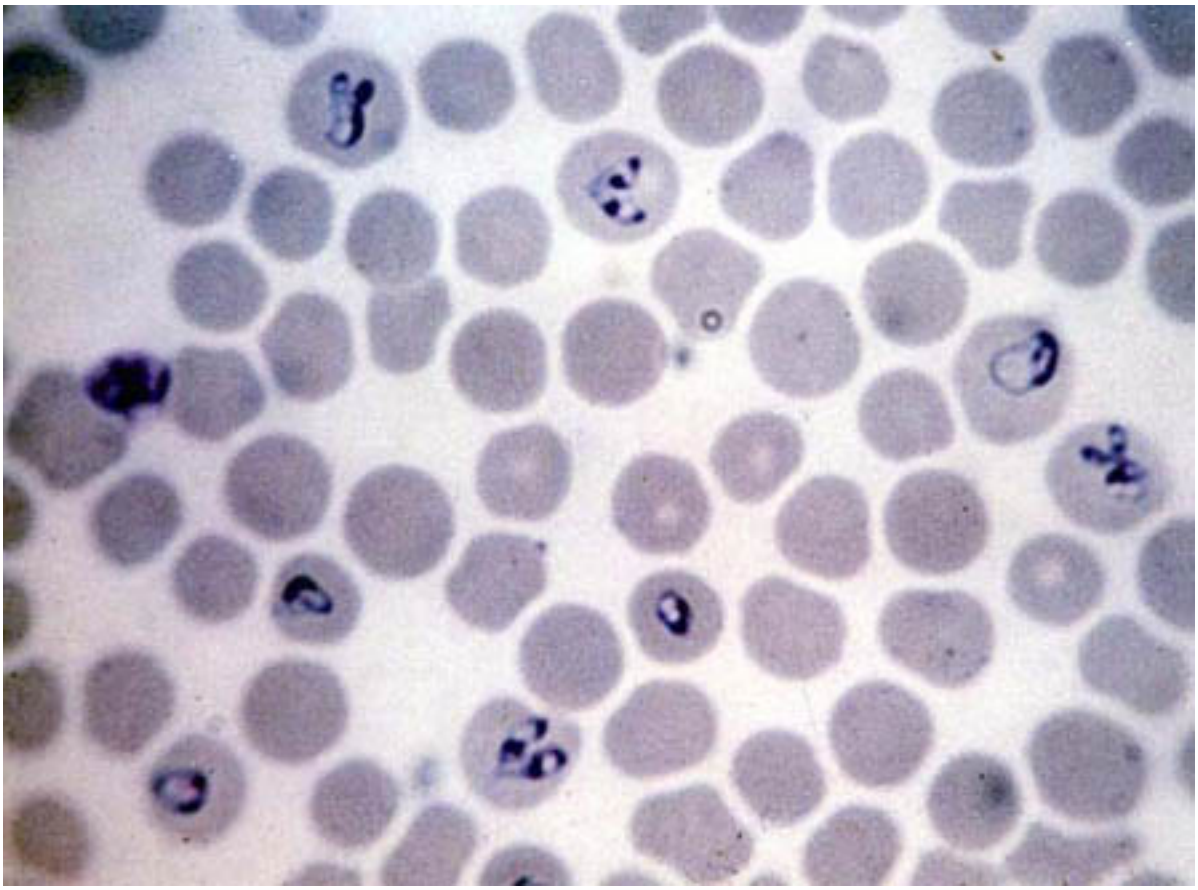

Fig. 31. Babesiosis - *B. caballi* in erythrocytes.

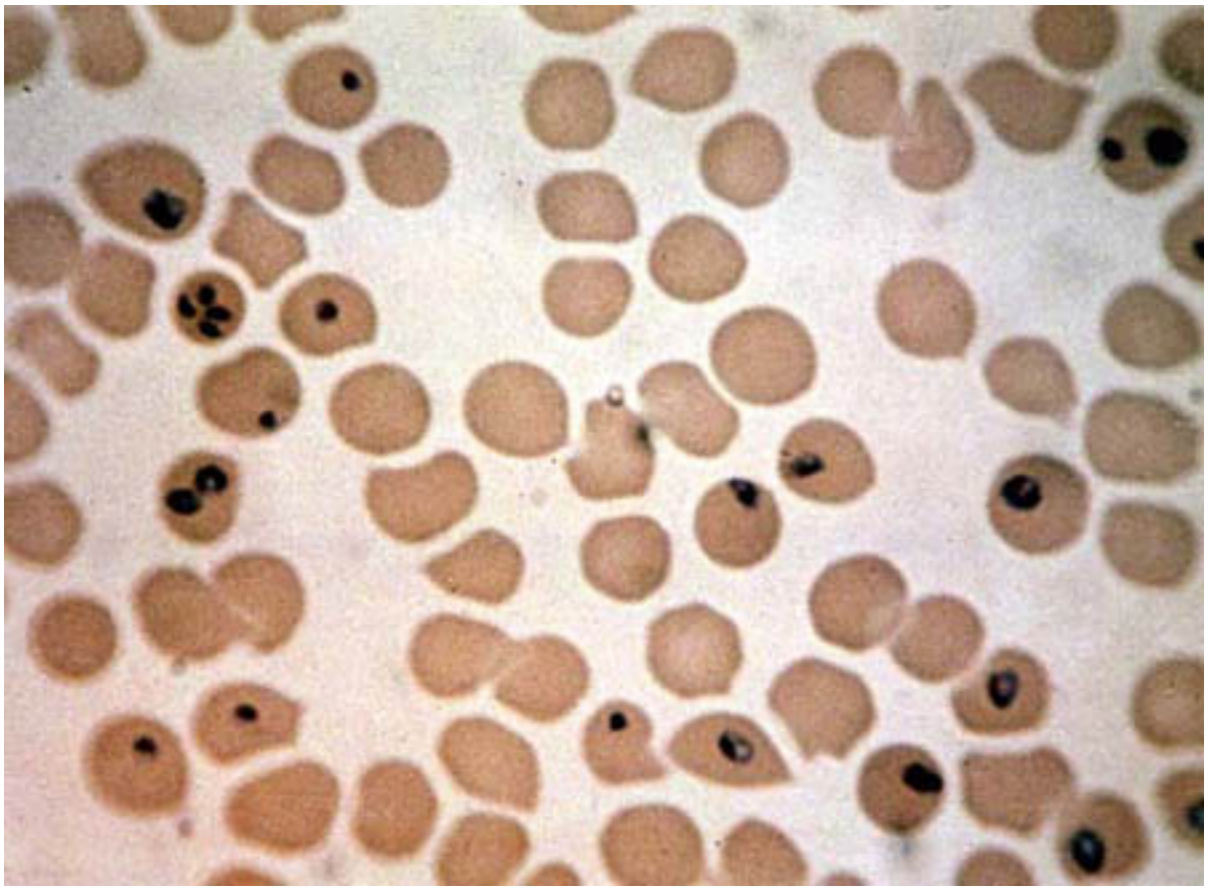

Fig. 32. Babesiosis - *B. equi* in erythrocytes.

PART IV
FOREIGN ANIMAL DISEASES

BLUETONGUE AND EPIZOOTIC HEMORRHAGIC DISEASE

(Sore muzzle, pseudo foot-and-mouth disease, muzzle disease)

Definition

Bluetongue (BT) and epizootic hemorrhagic disease (EHD) are insect-borne viral diseases of ruminants characterized by acute or subacute clinical courses in susceptible ruminants. The BT virus (BTV) and EHD virus (EHDV) have also been associated with congenital disease in sheep and cattle.

Etiology

Bluetongue and epizootic hemorrhagic disease are caused by orbiviruses in the family *Reoviridae*. Other orbiviruses include Ibaraki, Palyam, Eubenangee, and Tilligerry. The viruses are resistant to lipid solvents, which is typical of nonenveloped viruses. The viruses are relatively acid-labile, and slow freezing at -10 to -20 oC (14 - 4o F) is deleterious to the virus.

Worldwide, 24 serotypes of BTV and 9 serotypes of EHDV have been identified. Five serotypes of BTV and two serotypes of EHDV have been isolated in the United States. However, only BTV serotypes 10, 11, 13, and 17 and EHDV serotypes 1 and 2 are currently active. BTV serotype 2, originally isolated from animals imported into Florida, may not have established itself in the United States; however, epidemiologic studies will be required to resolve this issue.

Acetic acid is an effective disinfectant.

Host Range

The host range of BTV is very broad and includes all ruminant species tested to date. However, the expression of clinical disease varies in different species. Sheep are fully susceptible to BTV. EHDV typically also infects most ruminant species; however, sheep appear to be a poor host and rarely develop signs of EHDV infection.

Geographic Distribution

The geographic distribution of the orbiviruses is extensive, but current knowledge is still incomplete. Virus distribution is based on the presence of certain *Culicoides* species, including *C. variipennis*, *C. imicola*, *C. brevitaris*, and others. Orbivirus infections are common in tropical, subtropical, and temperate climates. Areas with year- round vector activity could easily maintain the virus by a continuous vector-host cycle. Virus persistence in areas with severe winters is not understood. Reintroduction of virus into the area in the warm months by transportation of infected animals or infected *Culicoides* being carried on the wind is probably common. Some research reports suggest that overwintering of the virus in these areas occurs by mechanisms such as (1) prolonged viremias (up to 3 months) in certain animals, (2) transplacental transmission of BTV in the late fall and early winter to the late-term developing fetus with subsequent birth of a viremic calf, and (3) overwintering of the virus in *Culicoides* that may survive through the winter at very low population densities. Virological and serological testing has suggested that BTV exists in North, Central, and South America; Africa; and parts of Asia; Europe; the Middle East; and the South Pacific; EHDV is probably similarly distributed.

Transmission

Transmission of orbiviruses is primarily by *Culicoides* species, which are biological vectors.

Limited experimental studies have also demonstrated that ticks are capable of mechanically or biologically transmitting BTV; however, their role in the epidemiology of BTV is probably minimal. Virus can also be transferred from viremic dams (sheep and cattle) to the developing fetus. Although BTV can be found in the semen of certain rams and bull, it is only isolated at the time of peak viremia; this presence of virus would appear to be the result of blood cells in the semen. Extensive field and experimental studies suggest that transmission of BTV via semen is of not importance in the epidemiology of BTV. The potential for BTV transmission also exists owing to poor management practices such as using the same needle or infected surgical equipment on several animals (mechanical transmission).

Incubation Period

The incubation period of BT in sheep is usually 7-10 days; however, viremia may appear as early as 3 to 4 days after infection. In cattle, viremia occurs as early as 4 days postinfection, but clinical signs are uncommon. Development of clinical BT in cattle may be the result of hypersensitization. Under laboratory conditions such animals develop clinical signs 10 to 12 days following reexposure to the virus. The incubation of BTV infection in deer is 7 to 12 days. No information is available on the incubation periods for EHDV.

Clinical Signs of Bluetongue

BT in Sheep

The classic signs of BT in sheep are those of an acute to subacute infection by a virulent strain of virus in fully susceptible animals belonging to the fine wool or mutton breeds. However, the signs of BT are variable. Not all strains of BTV that infect sheep cause clinical disease. In some flocks, no clinical sign is apparent, whereas in other flocks infected by the same virus up to 30 percent may develop signs of disease.

The first sign of illness which begins 7 to 8 days after infection, is a rise in temperature to 106-107º F (41.6-41.7º C). Temperatures may be elevated for 4 to 12 days following the initial rise. Within 24 hours of the initial rise in temperature, excessive salivation and frothing at the mouth develop and are associated with hyperemia and swelling of the buccal and nasal mucosa (Fig. 33). If forced to move, sheep may pant like a dog. During the next 2 to 3 days, erosions and ulcerations may develop in the buccal mucosa. By 4 to 7 days in severe cases, extensive ulcerations may be covered by gray necrotic tissue on the dental pad and dorsal surface of the tongue. In addition, affected animals being fed rough feed (stemmy alfalfa) may have more severe lesions of the oral mucosa.

Hyperemia is often observed around the coronary bands of the hooves. Often the hooves are tender and varying degrees of lameness are apparent. In more severe cases, the animals stand with an arched back (Fig. 34). If the animals are driven during this time, they may slough their hooves. Animals that recover may have a dark line in the wall of the hoof.

The lesions in the mouth, the reluctance to move, and the necrosis of striated musculature lead to weakness, depression, and rapid weight loss. These can result in prostration and eventual death in severely affected animals. Sheep that recover from severe infections may have a break in the wool 3 to 4 weeks after the fever has subsided. This can lead to partial or complete shedding of wool.

Bluetongue virus infection of pregnant ewes in the first trimester can cause fetal death and resorption, abortion, or birth of "dummy" lambs. Attenuated BTV vaccines can also cause reproductive failure.

BT in Cattle

Bluetongue virus infection in cattle usually does not cause any clinical sign of disease. Subclincal disease is only evidenced by changes in the leukocyte and lymphocyte subpopulation counts in the peripheral blood and a mild acute eosinophilic dermatitis. A

consistent fluctuation in rectal temperature is indicative of viremia and a mild disease. Occasionally, field outbreaks of BT disease occur in which as many as 30 percent of the cattle have clinical signs. Experimental data support the contention that clinical BT in cattle occurs as result of prior sensitization to a related orbivirus followed by a later second exposure. After secondary exposure, clinical signs become apparent in 10-12 days. Clinical signs consist of mild hyperemia in the buccal cavity and around the coronary band; vesicular lesions, which lead to ulcerations, in the buccal mucosa; erect hair over the cervical and dorsal thoracic areas; and a definite hyperesthesia. In addition, the dermis becomes thickened with prominent folds apparent in the cervical areas, and a dry crusty exudate leads to matting of hair in affected areas. These lesions may persist for 10 to 20 days. Similar lesions have been reported on teats of cattle with clinical BT. Hoof lesions may be associated with lameness. In some instances severe breaks in the hooves occur 40 to 60 days after infection and are usually followed by foot rot.

Bluetongue virus infection can cause reproductive failure in cattle. Some infected bulls will become temporarily sterile following acute infections. After recovery, production of sperm resumes, and the bulls are capable of settling cows.

Certain strains of BTV are capable of causing fetal death, resorption and or abortion; cell-culture-adapted live virus may be more effective than field virus in establishing fetal infection. Teratogenic effects of BTV in the bovine fetus include hydranencephaly and cerebral cysts that result in "dummy" calves.

Critical factors for fetal infection include the stage of embryonic or fetal development when infection occurs, the immune status of the dam, and the strain(s) of BTV causing infection. The most susceptible period for fetal infections occurs between 60 and 140 days gestation in nonimmune dams. Experimental studies suggest 15 to 20 percent of viremic dams will transmit virus to their fetuses. In areas where strains of BTV are endemic, there is little evidence that BTV has adverse affects on reproduction.

BT in Goats

Bluetongue infection of goats is typically an inapparent infection similar to that described for cattle.

Clinical Signs of EHDV Infection

EHD in Sheep

The EHD virus does not appear to cause significant clinical disease in sheep.

EHD in Cattle

The EHD virus rarely causes disease in cattle. However, Ibaraki virus (an EHDV serotype) has been associated with sporadic outbreaks of severe disease in cattle in Japan. Mortality rates have been as high as 10 percent. Clinical signs consist of fever, erosive and ulcerative lesions of the oral and esophageal mucosa, stiffness, lameness, and thickened, edematous skin. In addition, there has been a report of a combined EHDV and BTV disease of cattle. In pregnant cows, EHDV infection can result in fetal resorption or hydranencephaly if infection occurs between days 70 and 120 of gestation.

EHD in Deer

An EHD virus infection in white-tailed deer usually follows a peracute course leading to death. Often, deer are found dead around waterholes which suggests that they had a high fever and were dehydrated.

Gross Lesions

BT in Sheep

The lesions of BT in sheep vary greatly depending on (1) the strain of virus, (2) individual animal and breed susceptibility and (3) environmental (stress) factors. Prominent lesions include facial edema, edematous ears, and dry, crusty exudate over the nostrils (Fig. 33). Lesions in the oral cavity include focal petechial (pinhead-size) hemorrhages that progress to gray necrotized debris over erosions and ulcerations on the lips; on the dorsal, lateral, and ventral surfaces of the tongue; and on the dental pad. The buccal mucosa may be cyanotic. Hyperemia and occasional erosions can occur on papillae and laminae in the reticulum and omasum.

Lesions in the respiratory system include cyanosis and edema of the nasal mucosa and pharynx, and there may be tracheal hyperemia and congestion. Froth in the trachea is present only when there is pulmonary congestion and edema.

Lesions in the vascular system cause hyperemia, edema, and hemorrhages. A characteristic lesion is hemorrhage at the base of the pulmonary artery. Petechial and ecchymotic (larger than pinhead-size) hemorrhages may be observed at times in the endocardium. Focal gray-white areas of necrosis are often found in the papillary muscles and less frequently in other areas of the myocardium.

The most prominent changes in the skin include dermal and subcutaneous edema of the head and ears. Sometimes an irregular rash (exanthematous eruptions) may progress into serous and crusty exudates on the skin. Hyperemia is prominent at the coronet of the hoof. Often, this reddening is accompanied by petechial or ecchymotic hemorrhages that extend down the horn.

A yellow gelatinous exudate is common in the fascia (connective tissue) along and between skeletal muscles. On the cut surface of the heavy muscle there may be focal hemorrhages and areas that appear dry and gray-white.

Newborn lambs with congenital BT have hydranencephaly or porencephaly. These lesions are characterized by fluid-filled cavities, either occupying the whole of the cranial vault or as cystic cavities in the gray and white matter of the cerebral cortex. Cerebellar dysplasia (abnormal development) (Fig. 35) with rudimentary medial and lateral lobes may be present. The spinal cord may be dysplastic (abnormal development) and lack white matter. Skeletal deformities may consist of scoliosis (lateral curvature of the spine) and torticollis (twisted neck).

BT in Cattle

Gross lesions in cattle differ in some respects from those observed in sheep. The most prominent lesions involve the skin, mouth, and hooves. Skin lesions are characterized by marked edema that leads to thick folds — particularly in the cervical areas. Lesions may form in the folds as serous exudate accumulates and dries. Dry, crusty exudate is present on the skin over the cervical and thoracic areas. The crusty material results from vesicular eruptions and ulcerations.

The external nares may have erosions covered by crusty exudate that sloughs. Lesions in the mouth start as vesicles and proceed to ulcers covered with grayish necrotic debris. These lesions are more common on the buccal mucosa and dental pad and rarely the tongue. Hyperemia occurs at the coronary band. In some instances, fissures occur 6 to 8 weeks following infection.

In utero BTV infection may lead to fetal death and resorption, abortion, hydranencephaly, or cerebral cysts.

BT in Deer

Bluetongue in susceptible deer causes widespread hemorrhages throughout the body. These lesions are associated with intravascular thromboses and hemorrhages varying in size from petechial to ecchymotic. In chronic BT, deer may develop severe fissures and even sloughing of hooves. Ulcers covered with gray necrotic debris are found in the buccal mucosa, dental pad, and tongue.

EHD in Deer

In susceptible deer EHDV causes lesions very similar to those caused by BTV. The widespread hemorrhages in mucous membranes, skin, and viscera are the result of disseminated intravascular clotting. The Ibaraki strain of EHDV can cause widespread vascular lesions similar to those described for BTV in cattle. Degenerative changes (focal hemorrhage or dry and gray-white appearance, or both) in striated musculature are prominent in the esophagus, larynx, tongue, and skeletal muscles.

Morbidity and Mortality

In sheep, BT can range from inapparent to severe, depending on the breed, strain of virus, and environmental stress on the animals. Morbidity can reach 100 percent; mortality can vary from 0 to 50 percent. Many animals will recover within a few days to 2 weeks.

In cattle, BTV and EHDV infection is usually subclinical. Although morbidity can approach 5 percent, cattle typically recover within a few weeks. However, lameness and unthriftiness may persist for prolonged period.

The morbidity and mortality for BTV infection in other species are as follows:

Goats - - minimal clinical signs

White-tailed deer - - morbidity approaching 100 percent and a mortality of 80-90 pecent

Pronghorn antelope - - morbidity approaching 100 percent and a mortality of 80-90 percent

Bighorn sheep - - morbidity approaching 100 percent and a mortality of 0 to 50 percent

North American elk - - similar to cattle; the disease is usually subclinical.

Diagnosis

Field Diagnosis

Tentative diagnosis of BT can be made when (1) clinical signs appear in populations known to be susceptible, (2) the occurrence of disease coincides with a prevalence of insect vectors, (3) necropsy of sheep reveals characteristic gross lesions, and (4) a flock history of recent wasting (loss of weight) and pododermatitis (foot rot).

Specimens for Laboratory

Preferred samples for confirmatory diagnosis include sterile heparinized blood samples from animals with clinical signs or spleen or bone marrow, or both, from dead animals. Samples from aborted and congenitally infected newborn animals should include heparinized blood and, if possible, spleen, lung, brain, and serum. If possible, the heparinized whole blood (erythrocytes and white cells) should be washed in saline containing antibiotics and resuspended in saline prior to shipping. This procedure will reduce the antibody that may neutralize the virus if blood-cell lysis occurs.

Specimens should be shipped refrigerated, not frozen. Freezing makes virus isolation difficult.

Laboratory Diagnosis

Confirmatory diagnosis is based on isolation and identification of virus from blood or tissues. Diagnosis for lambs and calves infected in utero is based on serology (if no colostrum has been

ingested) or virus isolation, or both.

Differential Diagnosis

Differential diagnoses include plant photosensitization, foot-and-mouth disease, vesicular stomatitis, bovine virus diarrhea, malignant catarrhal fever, infectious bovine rhinotracheitis, parainfluenza-3, contagious ecthyma, and actinobacillosis.

Vaccination

Vaccination has been the primary means of controlling BT disease in sheep. To date, only modified-live (attenuated) virus vaccines have been used. Because of the multiplicity of BTV serotypes and variable cross-protection between serotypes, vaccination has resulted in varying degrees of success. The serotypes incorporated into the vaccine must be the same as those causing infection in the field. The practice of administering multiple virus serotypes in a single vaccination is argued against by some scientists because (1) an immune response (virus neutralizing antibody) is typically only induced to one, or at best two of the serotypes incorporated in the vaccine and (2) reassortment between the genome segments of the multiple vaccine viruses may occur in the host of a vector feeding on such a vaccinated animal. Although simultaneous infection of sheep, cattle, or *Culicoides* can result in creation of reassortant viruses, there is no evidence that this process has resulted in generation of new serotypes. However, such reassortant events may result in altered virulence and biological transmissibility.

No inactivated or subunit vaccines are currently available, though several experimental vaccine preparations have been studied, including inactivated virus vaccines, subunit vaccines prepared by purification of natural VP2 (viral protein responsible for inducing virus neutralizing antibody), and recombinant VP2 expressed in a baculovirus system.

No vaccine is available for EHDV.

Control and Eradication

Vaccination can be used in endemic areas.

Vector control measures to impede the spread of BTV infection are not commonly used. However, certain measures have potential effectiveness such as water management (reduction of *Culicoides* breeding sites), use of insecticides and larvacides (spraying breeding areas), and insect repellents in which animals are dipped.

The only applicable treatment available is to minimize animal stress and administer broad-spectrum antibiotics to combat secondary infection.

Public Health

There is only one documented human infection, and that was in a laboratory worker

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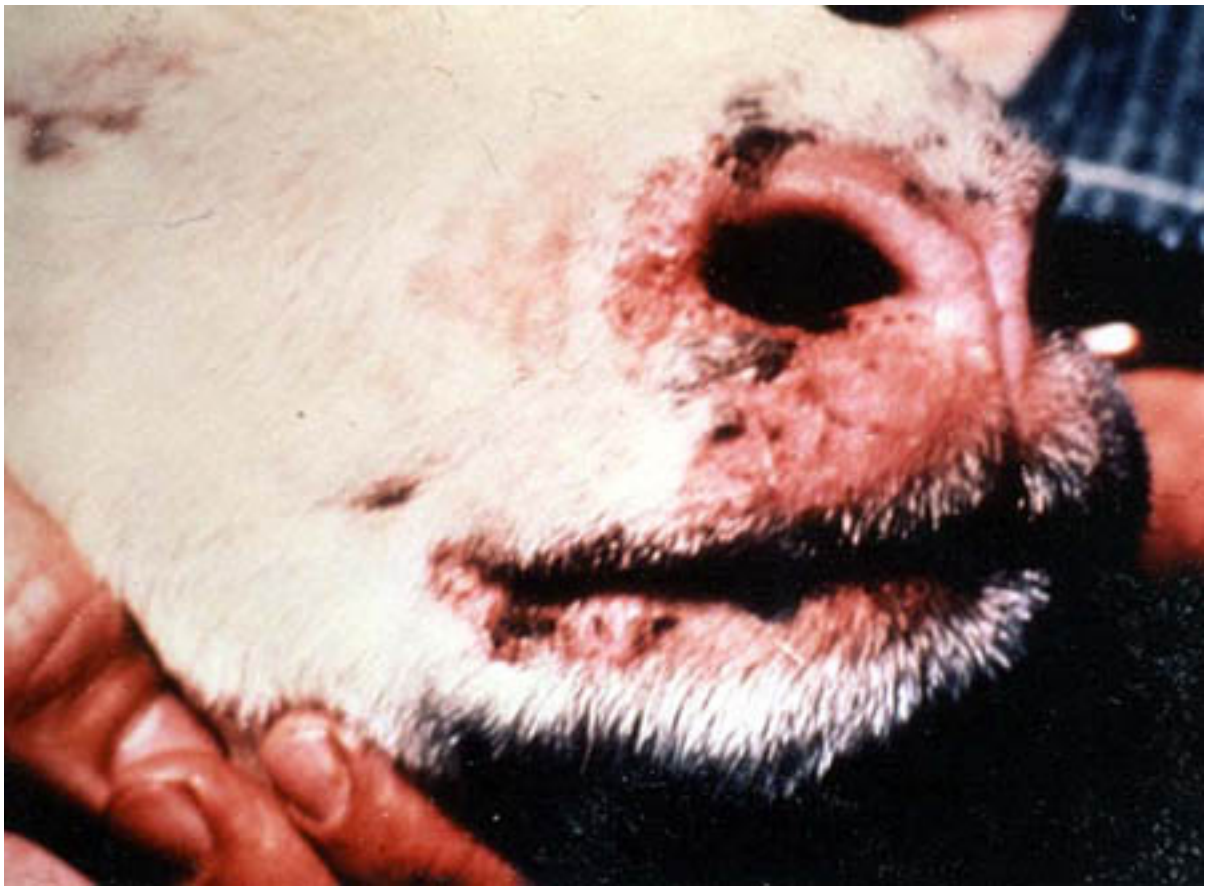

Fig. 33. BT - Swelling of and exudate on the nostrils and lips.

Fig. 34. BT - Animals with severe coronitis stand with an arched back.

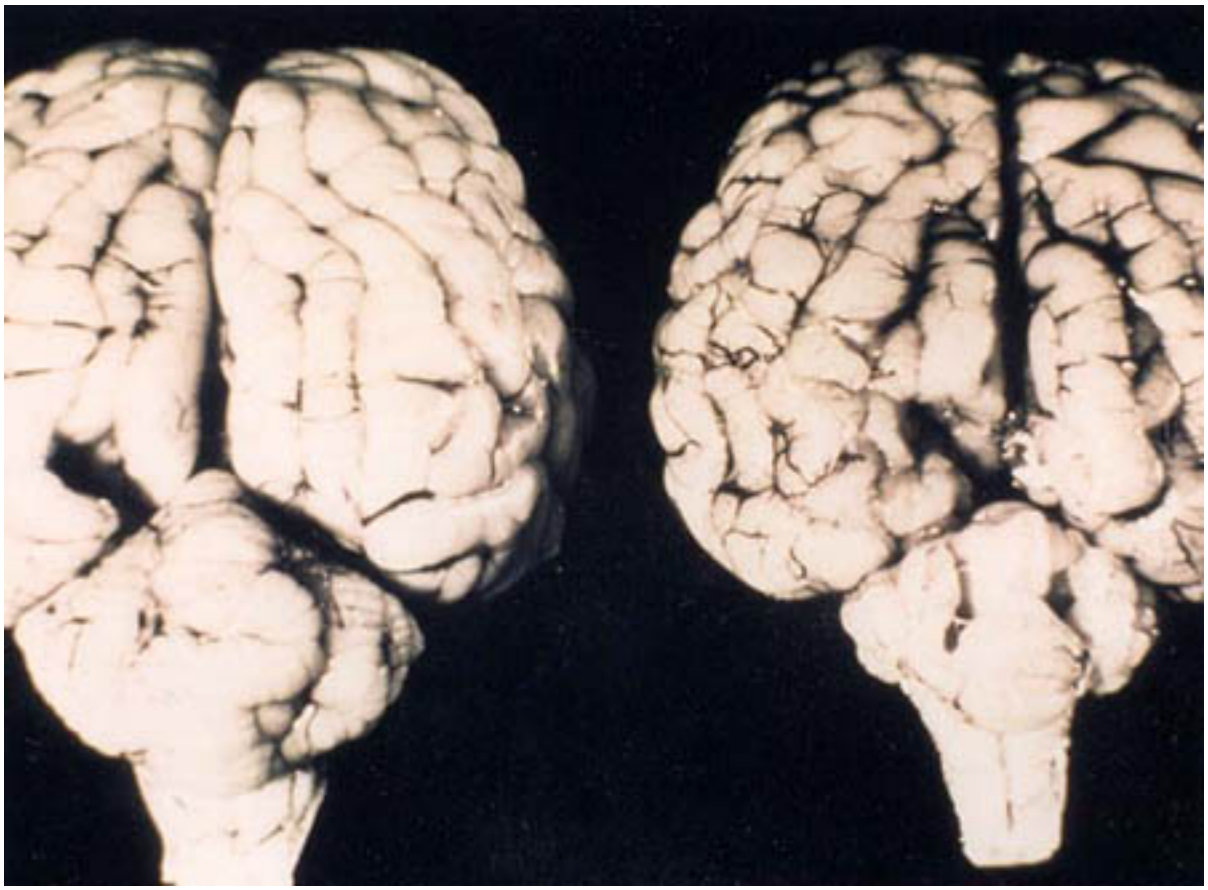

Fig. 35. BT - The brain on the right has cerebellar hypoplasia resulting from a congenital BT infection. The brain on the left is normal.

PART IV
FOREIGN ANIMAL DISEASES

BOVINE EPHEMERAL FEVER

(Three-day sickness, Bovine epizootic fever, Three-day stiffsickness, Dragon boat disease)

Definition

Bovine ephemeral fever (BEF) is a noncontagious epizootic arthropod-borne viral disease of cattle and water buffaloes characterized by sudden onset of fever, depression, stiffness, and lameness. The clinical severity of the disease is inconsistent with the subsequent rapid recovery of most of the affected animals.

Etiology

The BEF virus is a single-stranded RNA, ether-sensitive rhabdovirus with five structural proteins. This virus is antigenically related to at least three other viruses nonpathogenic for cattle: Kimberley virus, Berrimah virus, and Adelaide River virus and two that produce an ephemeral fever-like disease in cattle, Kotonkan and Puchong viruses in Africa and Malaysia, respectively (3). The antigenic relationships with other rhabdoviruses infecting cattle have more than academic significance because prior infections with related viruses, though not providing cross-protection, can enhance the antibody response of cattle subsequent to clinical ephemeral fever.

Host Range

Clinical disease has been observed only in cattle and water buffaloes. However, neutralizing antibodies to BEF virus have been found in Cape buffalo, and species of deer and antelope in Africa (4) and deer in Australia. Antibodies can be produced in various small laboratory animals by the intravenous or subcutaneous injection of BEF virus.

Geographic Distribution

Ephemeral fever was first described in South Africa in 1906, though the disease was known to have occurred previously and was referred to briefly by Schweinfurth in 1867. It was clearly recognized in Egypt in 1895 and 1924. The disease is now known to exist in a broad belt of tropical, subtropical, and temperate countries in Africa, Asia, and Australia and to be the same disease as bovine epizootic fever of Japan (14,16).

The countries where ephemeral fever occurs lie on both sides of the Equator and include all the countries of Africa and those of Asia south of the general line encompassing Israel, Syria, Iraq, Iran, Pakistan, India, Bangladesh, southern and central China, and southern Japan through Southeast Asia to Australia. There is serological evidence to support the absence of BEF virus from Papua New Guinea (since 1956), the Pacific Islands, New Zealand, and the United States. There has been no report of ephemeral fever from Europe or North or South America.

Transmission

The disease can be reproduced experimentally in cattle only by the intravenous inoculation of BEF virus. Subcutaneous or intramuscular injection is ineffective. Epizootiological evidence indicates that BEF virus is spread in nature only by an insect bite. The disease will not spread from cow to cow by close contact, droplet infection, bodily excretions, or by the transfer or injection of exudates (10). There is experimental evidence that BEF virus is not spread by semen. Meat does not represent even a theoretical risk for transmission because the virus is rapidly inactivated at pH levels below 5 (7). Such acidic levels are attained rapidly in bovine

muscle after death. Disinfection plays no part whatsoever in control of spread.

Epizootics of ephemeral fever occur in the summer in temperate climates of Australia, South Africa, China, and Japan and disappear with the first frosts. In Africa, China, and Australia the disease has moved rapidly over long distances but always in a general direction away from the Equator (14,15). In Kenya, epizootics are associated with recent rainfall. The BEF virus has been isolated from *Culicine* and *Anopheline* mosquitoes in Australia (12) and from biting midges of the genus *Culicoides* in Africa and Australia (16). The necessity for the BEF virus to be delivered intravenously to reproduce disease experimentally, plus the absence of the virus from in the lymph during early viremia, strongly supports mosquitoes as the major vectors.

They are vessel feeders. *Culicoides* species lacerate the skin and are pool feeders. A close study of the epidemiology in Australia also favors mosquitoes as the important vectors (8). It is not known whether suitable vectors exist in the Americas.

Incubation Period

The incubation period following experimental intravenous inoculation of BEF virus varies between 2 and 4 days, and 9 days is the rare extreme. The time is probably influenced by the strain and dose used. The natural incubation period can only be inferred but is probably similar. An index case or cases occur under epizootic conditions approximately 1 week ahead of the main wave of cases in a herd. The peak of viremia occurs 24 hours before the onset of fever (10).

Clincial Signs

The name ephemeral fever was applied very early in the disease's recorded history. The disease is not ephemeral in the sense of being hard to see. The clinical signs are very obvious and can be quite severe (2). The fever of ephemeral fever is generally biphasic, sometimes triphasic, with peaks of 40-41.5° C (104-107° F) spaced 12-18 hours apart. Thus, the actual height of the rectal temperature measured during an initial examination varies with the stage of the febrile cycle. The physical signs during the first febrile phase tend to be mild except for the dramatic fall in milk production of lactating cows. The characteristic signs associated with BEF are those of the second febrile phase (5,10,18,22). These signs include accelerated heart and respiratory rates, anorexia, ruminal atony, depression, serous or mucoid nasal and ocular discharges, salivation, muscle twitching or waves of shivering, a generalized stiffness or a shifting lameness. There may be submandibular edema or patchy edema elsewhere on the head. Many animals become recumbent for 12-24 hours but are able to rise if sufficiently stimulated. Others are completely unable to rise and remain in sternal recumbency for hours or days with the head turned to the flank, or in lateral recumbency with or without loss of most reflexes. Recovery begins 1-2 days after the overt clinical signs are first noticed and is usually complete and without sequelae in a further 1- 2 days after the overt clinical signs are first noticed. The early signs of improvement develop in a few hours after fever disappears in most cattle. Most cases, especially those in young cattle, are mild to moderately severe, and recovery is well advanced by the third day after clinical signs are first observed. Lactating cows, bulls in good condition, and fat steers are the worst affected, and their recovery may take up to a week even without complications.

A range of complications can occur in a minority of cases. Death can occur suddenly in the febrile or in the recovery phase. Paralysis of the limbs may persist for days, weeks, or permanently. Recovery from the longer-term paralysis can be complete, or some disablement of gait may remain. A temporary infertility may occur in bulls that show structural defects in spermatozoa persisting for up to 6 months, but infertility may be a nonspecific effect of the inflammatory nature of the illness. The loss of fertility of bulls can be minimized with nursing care and treatment. There is no effect on the long- term fertility of the female, though abortions do occur if the cow suffers ephemeral fever in the eighth or ninth month of pregnancy. Earlier reports on the teratogenic effects of BEF virus in Australia have since been correctly attributed to the Simbu group viruses— particularly Akabane and Aino viruses.

Emphysema and the subcutaneous accumulation of air along the backline is an uncommon complication (19). Aspiration pneumonia can occur from inhaled ingesta or from oral medication in those animals in which the swallowing reflex has been lost.

Except for those cows that abort in late term, the milk production of most cows returns to 85-90 percent of the predisease levels within 10 days of disease. The 10-15 percent loss of production (5,18) persists in affected animals for the balance of the lactation period. Subsequent lactations are normal except in those cows that develop a secondary bacterial mastitis.

The full spectrum of clinical signs is not seen in any one animal nor usually in one herd. The signs are exacerbated by forced exercise or severe climatic stress. Mortality varies from 1-2 percent on average. In focal outbreaks in very fat cattle, mortality can exceed 30 percent. The other economic effects of the disease are due to lost production and trade restrictions.

Gross Lesions

The pathology of experimental disease is well described. Personal observation suggests it is consistent with that of the natural disease for which few descriptions have appeared. The sporadic mortality is responsible for this gap in published information. The most obvious gross lesions are the small amounts of fibrin-rich fluid in the pleural, peritoneal, and pericardial cavities and variable amounts in the joint capsules. The joint capsules of the limbs are the most consistently involved, but even the synovial surfaces of the spine may have fibrin plaques. The lungs may have patchy edema. Lymphadenitis is consistent, but petechial hemorrhages of the lymph nodes are less frequent. Focal necrosis can be found in major muscle groups in some cases.

The hematological changes are very characteristic. There is an absolute rise in leukocyte numbers with a reversal of neutrophil and lymphocyte proportions. With the onset of fever, there is a rapid fall in circulating lymphocytes, and a return to normal levels after 3-4 days. This fall is followed some hours later by a rapid rise in neutrophil numbers and the concurrent appearance of immature forms. The leukocyte counts return to normal on clinical recovery. Eosinopenia is constant. The serum fibrinogen level rises to 3-4 times the normal level and returns to normal 1-2 weeks after recovery. The total serum calcium level falls to 1.8 $mmol^{-1}$ during the febrile phases and returns to normal on recovery. This is the biochemical event that causes the reversible early paralysis. However, the biochemical dyscrasias are far more extensive. These biochemical changes are similar to those of milk fever. Collectively, these changes are typical of a systemic inflammatory disease (1,11,16,20,22).

Morbidity and Morality

Morbidity is partly influenced by the number of susceptible cattle in the herd and partly by the intensity of the epidemic. The course of the disease in the herd may range from 3 to 6 weeks. Quite often, the main wave of clinical cases occurs a week or more after a single case or a small cluster of cases.

High mortality may occasionally occur (13,14). Cattle of all breeds have similar signs, and the clinical course in buffaloes, though milder, seems to be much the same as in cattle.

Diagnosis

Field Diagnosis

Single cases are difficult to diagnose, but with a herd outbreak, when cattle at various stages of disease can be examined, diagnosis is made from clinical observations and the history of the outbreak.

Specimens for Laboratory

A sample of blood should be taken during the period of fever and a second 1-2 weeks later. Part

of the first sample of blood is allowed to clot, and another portion is mixed with anticoagulant. From the uncoagulated blood, a smear is made on a glass slide and allowed to dry in air. The balance is used for virus isolation (22).When blood taken during illness is allowed to clot, it usually fails to contract on standing, even over several days. It may be streaked with fibrin. Samples should be taken from animals in various stages of the disease to facilitate a rapid laboratory confirmation.

Laboratory Diagnosis

The most efficient means of proving the identity of the disease is the transmission to susceptible cattle by the intravenous injection of uncoagulated whole blood. These cattle are closely observed for the development of fever and the characteristic signs. Virus isolation can be attempted (from the leukocyte fraction of the blood) in tissue cultures but is not very efficient (22). A differential leukocyte count on the blood smear provides the most rapid supporting evidence for the field diagnosis. A high percentage of neutrophils with many immature forms is not pathognomonic of ephemeral fever, but if not present the field diagnosis is likely to be wrong. Eosinopenia also occurs. Testing of antibody (virus-serum neutralization test) is the most generally available laboratory test. However, false positives do occur. The enzyme-linked immunosorbent assay test is specific and rapid and distinguishes between antibodies induced by BEF and those from infections with antigenically related viruses (26).

Differential Diagnosis

Various diseases may be confused with ephemeral fever when a diagnosis in the field has to be made on a single animal (for example, early Rift Valley fever, heartwater, bluetongue, botulism, babesiosis, or blackleg). The salivation may suggest foot-and-mouth disease; however, there is no vesicular lesion in the mouth or on the feet. It is very simple to have a blood smear stained and examined at any veterinary or human laboratory to check for the characteristic neutrophilia and to obtain supporting, though not definitive, evidence to exclude most other viral diseases. When many cattle are involved, different stages of the disease will be observed — some with the characteristicly rapid resolution of severe clinical signs.

Treatment

Ephemeral fever is one of the rare virus diseases for which treatment is effective (21). The inflammatory nature of the disease process means it is responsive to anti-inflammatory drugs. These drugs must be given for the expected course of the clinical disease. During fever, the paresis or paralysis responds to injected calcium borogluconate in the same manner as parturient paresis (milk fever) (15). In both syndromes, low levels of ionized calcium in the plasma induce the signs. Early treatment is more effective than late. Also, relapses occur in ephemeral fever if anti-inflammatory treatment is discontinued too early. Viremias and subsequent immunity are not significantly affected by treatment. An underlying paralysis of the Guillain-Barré type persists in a small proportion of cattle after the fever has gone.

Vaccination

Almost all animals that undergo a single bout of ephemeral fever are immune to natural or artificial challenge. Although antigenic variation has been demonstrated by panels of monoclonal antibodies, challenge with BEF strains of a different origin does not cause disease in immune animals. The immunity is sterile, for no evidence of carrier animals has been found experimentally or been suspected from epizootiological evidence (9,15). Where double bouts of disease have been reported, they have been within a single epizootic season. Various vaccines have been produced in South Africa, Japan, and Australia because the virus is easy to attenuate (7,22). These vaccines appear to protect against severe laboratory challenge, but evidence of their effectiveness in the field in the face of an epizootic is variable. A subunit vaccine has been developed and protects against laboratory and field challenge (25). The vaccine has not yet been manufactured.

Control and Eradication

Prevention

The species of insect vector involved in the spread of BEF virus are not yet defined. Therefore, no large-scale specific control can be recommended. Housing may protect small numbers of susceptible cattle. In Australia, clinical cases are seldom seen in housed animals, but this may be related to local vector biology and not apply generally throughout the world. Vaccination is the only useful preventive measure.

Containment and Eradication

Unless very special circumstances apply, containment is not possible. A particular circumstance would be when the disease is recognized in a quarantine area in recently imported stock. Useful steps are to place the cattle in an insect-proof area, spray with insecticides, or suppress insects in the local environment. No country has attempted to eradicate BEF, although it did die out naturally in New Guinea.

Public Health

There is no evidence that humans can be infected, although many thousands of people have been in contact with infected cattle and potentially exposed in the same environment to the vectors of the virus. A limited amount of serology on farmers handling infected cattle and on laboratory workers handling the BEF virus has given negative results.

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PART IV
FOREIGN ANIMAL DISEASES

BOVINE SPONGIFORM ENCEPHALOPATHY

Definition

Bovine spongiform encephalopathy (BSE), widely known as "mad cow disease," is a chronic, afebrile, degenerative disease affecting the central nervous system (CNS) of cattle.

Bovine spongiform encephalopathy belongs to the family of diseases known as the transmissible spongiform encephalopathies (TSE's). These diseases are caused by a transmissible agent that is yet to be fully characterized. They share the following common characteristics:

a. A prolonged incubation period of months or years;

b. A progressive debilitating neurological illness that is always fatal;

c. When examined by electron microscopy, detergent-treated extracts of brain tissue from animals or humans affected by these diseases reveal the presence of scrapie-associated fibrils (SAF's);

d. Pathological changes appear to be confined to the CNS and include vacuolation and astrocytosis;

e. The transmissible agent elicits no detectable specific immune response in the host.

Specific types of TSE's include scrapie, which affects sheep and goats; transmissible mink encephalopathy; feline spongiform encephalopathy; chronic wasting disease of deer and elk; and five rare diseases in humans: kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia (FFI), and new variant Creutzfeldt-Jakob disease (nvCJD).

Etiology

The clinical, pathological, and molecular genetic features of BSE, as well as other transmissible spongiform encephalopathies, have led to speculation on the nature of the etiologic agent and the pathogenic mechanisms of the disease. There are three main theories on the nature of the scrapie agent:

1. The virus theory, in which the virus would have to have unusual biochemical and biophysical characteristics that would help explain the remarkable physicochemical properties (12, 24, 39, 40).

2. The prion theory, in which the agent is conceived of being composed exclusively of a host-coded normal cellular protein (PrP^{c}) that becomes partially protease resistant (PrP^{BSE}) — most likely through a post-translational conformation change after infection. In this theory there is no nonhost component of the agent. That is, a specific informational molecule (nucleic acid e.g., RNA or DNA) is not present (5, 36).

3. The virino theory, which states that the agent consists of a host-derived protein coat, (PrP being one of the candidates for this protective protein) and a small noncoding regulatory nucleic acid (14, 21).

All of the proposed theories have some degree of validity. Proponents of the virus and virino theories have concluded that the existence of different scrapie strains unequivocally proves the presence of a nucleic acid component of the infectious agent which, as in conventional viruses, may undergo mutations responsible for phenotypic variations. The problem with these theories is that no agent-specific nucleic acid has been convincingly identified to copurify with infectivity (15, 25, 28, 32, 42). Moreover, chemical, enzymatic, or physical treatments that usually inactivate or degrade nucleic acids have no effect on the transmissible properties of the infectious agent (3, 4, 27, 31). Possible reasons for this are that the amount of nucleic acid of the putative agent is too small to be detected with available techniques and that its tight bond to the protein protects it from chemical or physical inactivation. Also weakening the virus and virino theories is the inability to identify any virus particles under the electron microscope (6, 10), and the failure of an infected host to generate an immune response. Recently small particles resembling virus structures have been observed by electron microscopy (33).

The prion model involves propagation of a protein-only agent (PrP^{BSE}) whereby PrP^{c} can assume various tertiary structures caused by a combination of host genetics and the introduction of altered (infectious) PrP (PrP^{BSE}). More simply stated, the structure of the infecting PrP^{BSE} imprints upon the normal cellular precursor (PrP^{c}) and results in a conformation change to the protease-resistant form. It is suspected that "strain" differences result from mutations in the PrP gene that may cause proteins "flip" and change shape. Several explanations for scrapie strain genetics in the context of the prion theory have been suggested but none have been proven (35, 41, 46).

It should be pointed out that the prion theory fails to explain a) how the PrP of the infecting agent originally assumed the aberrant structure associated with infectivity, and b) how the different structures originated as a function of the different strains. Although numerous scrapie strains can be differentiated in a single host (i.e., sheep), the PrP agents associated with these strains have not shown any biochemical and molecular differences; thus, BSE seems to be caused by a single strain type. This BSE strain is different from historical or contemporary isolates from sheep or goats with natural scrapie, as determined by study of incubation periods and brain "lesion profiles" in mice.

Regardless of whether the prion (PrP^{BSE}) is or is not the etiologic agent, the partially protease-resistant form of the prion protein is a marker of infection.

Host Range

Bovine spongiform encephalopathy has been experimentally transmitted to the following species via intracerebral (IC) inoculation: cattle, sheep, and goats (17), mink (38), pigs (13), marmosets (1), macaques (22), and mice (16). Intracerebral transmission was attempted in hamsters but was not successful. Via the oral route, BSE has been successfully transmitted to cattle, sheep, and goats (17); mice (2); and mink (38). Oral transmission has not been successful in swine. Parenteral and oral transmission has also been attempted in chickens with no evidence of disease thus far.

A transmissible spongiform encephalopathy has been diagnosed in eight species of captive wild ruminants as well as exotic (cheetahs, pumas, a tiger, and an ocelot) and domestic cats. There have been about 81 domestic cat cases of feline spongiform encephalopathy (FSE) in Great Britain and in 1 domestic cat each in Norway, Northern Ireland, and Liechtenstein. The agent isolated from several of these cases using strain typing in mice is indistinguishable from BSE in cattle, which suggests that FSE is actually BSE in exotic and domestic cats. This also appears to be true for the other ruminants. Epidemiological evidence suggests BSE-contaminated feed to be the primary source of infection in these species (30).

Other cases of spongiform encephalopathy have been reported in kudu, eland, nyala, gemsbok, and a few exotic cats. These too are thought to be linked to contaminated feed.

It has also been suggested that 23 cases (as of January 31, 1998) of a variant form of CJD (nvCJD) (a human disease) in Great Britain (U.K. Department of Health, March 2, 1998) and 1

case in France may be linked to exposure to BSE before the introduction of a specified bovine offal (SBO) ban at slaughter in 1989. The SBO ban excludes from human consumption brain, spinal cord, and other tissues with potential BSE infectivity.

Geographic Distribution

Worldwide there have been more than 170,000 cases since the disease was first diagnosed in 1986 in Great Britain. Over 95 percent of these cases have occurred in the United Kingdom. The disease has also been confirmed in native-born cattle in Belgium, France, Ireland, Luxembourg, the Netherlands, Northern Ireland, Portugal, and Switzerland but is not known to exist in the United States.

Transmission

Different scientific hypotheses have been advanced concerning the origins of BSE. The epidemiologic data suggest that BSE in Great Britain is an extended common source epidemic involving feed containing TSE-contaminated meat and bone meal as a protein source. The causative agent is suspected to be from either scrapie-affected sheep or cattle with a previously unidentified TSE.

Changes in rendering operations in the early 1980's — particularly the removal of a solvent-extraction process that included a steam-heat treatment — may have played a part in the appearance of the disease and the subsequent amplification of the agent in the food chain. A ban on feeding animal protein of ruminant origin to ruminants was enacted in Great Britain in July 1988(50).

In Great Britain the epidemic peaked in 1992-93, when approximately 1,000 cases were being reported per week. In 1998 it remains on the decline with approximately 100 cases reported per week. Cases that have been detected in other countries appear be a result of importations of live cattle or, more significantly, contaminated feed from Great Britain.

There is no evidence that BSE spreads horizontally; that is, by contact between unrelated adult cattle or from cattle to other species.

New evidence suggests that maternal transmission may occur at an extremely low level. Results of British research show low levels of transmission of BSE from affected cows to their offspring. These results demonstrated that there is approximately a 9 percent increase in the occurrence of BSE in offspring of BSE-affected dams as compared with calves born to dams where BSE was not detected. The study did not ascertain if this was the result of genetic factors or true transmission. The research did, however, point out that, at this level, if maternal transmission does occur, it alone will not sustain the epidemic (51).

In the naturally infected animals, the agent has been identified by mouse bioassay in the brain, spinal cord, and retina. The route of inoculation into the mice was intracranial. The naturally infected animals were adult cattle exhibiting clinical signs of disease (16).

Mice fed milk, mammary gland, placenta, lymph nodes, or spleen have failed to develop the disease or to establish subclinical infection of the lymphoreticular system within their natural lifespan (29).

Another study was conducted to examine the pathogenesis of BSE in cattle; that is the replication (tissue distribution) of the agent during the incubation period. This study, which has not yet been completed, has identified the agent via mouse bioassay in the distal ileum of the experimentally infected calves. It is thought that the agent may be associated with the lymphoid tissue of the intestines. The calves were 4 months of age at the time of oral dosing. First isolation of the agent in the distal ileum was made at 6 months after oral dosing. Subsequent isolations from the distal ileum were made at 10, 14, and 18 months after dosing (47). Recently this study has also identified infectivity in bone marrow, trigeminal ganglion, dorsal root ganglion, brain, and spinal cord (48).

No infectivity has been found by parenteral or oral challenge, or both, in over 40 other tissues from clinically ill cattle using the mouse bioassay. It appears as if the distribution of the BSE agent is not as diverse as the scrapie agent in sheep. However, there is a possibility that the agent is present but is at such low levels that the bioassay is not sensitive enough to detect it (30).

Incubation Period

The incubation period usually ranges from 2 to 8 years. Following the onset of clinical signs, the animal's condition gradually deteriorates until the animal becomes recumbent, dies, or is destroyed. This usually takes from 2 weeks to 6 months. Most cases in Great Britain have occurred in dairy cows (Friesians) between 3 and 6 years of age (50). The youngest confirmed case occurred in a 20-month-old heifer, and the oldest case was found in a cow 18 years of age.

Clincial Signs

Cattle affected by BSE develop a progressive degeneration of the nervous system. Affected animals may display changes in temperament, abnormalities of posture and movement, and changes in sensation. More specifically, the signs include apprehension, nervousness or aggression, incoordination, especially hind-limb ataxia, tremor, difficulty in rising, and hyperaesthesia to sound and touch. In addition, many animals have decreased milk production or loss of body condition, or both, despite continued appetite.

Gross Lesions

There is no gross lesion associated with BSE.

Morbidity and Mortality

In Great Britain, 19 percent of the dairy herds and 1.6 percent of the beef herds have had one or more cases of BSE. This difference is believed to result from the fact that dairy calves were fed a higher level of protein supplement. The average incidence in herds in Great Britian has been 1.75 cases. However, there have been a few herds with over 30 cases. Affected animals die.

Diagnosis

Field Diagnosis

A field diagnosis of BSE is based on the occurrence of clinical signs of the disease. A bovine animal that has signs of a CNS disturbance should be observed over time (at least 2 weeks) to determine whether the signs become progressively more severe. If, after this interval, improvement or recovery has not taken place, BSE should be suspected and the animal humanely euthanized.

Specimens for Laboratory

Because the BSE agent is considered a human pathogen, protective clothing, gloves, and face protection should be worn when performing the necropsy. The entire brain should be removed intact with a portion of the cranial cervical spinal cord attached. Portions should be placed in a plastic bag and submitted unfixed. The remainder of the brain should be fixed in 10 percent buffered formalin solution. One cerebral hemisphere is removed by cutting the brain stem through the space between the cerebellum and cerebrum with a longitudinal cut between the cerebral hemispheres.

Laboratory Diagnosis

Bovine spongiform encephalopathy currently must be confirmed by histopathological examination of brain tissue. Bilaterally symmetrical degenerative changes are usually seen in the gray matter of the brain stem. These changes are characterized by vacuolation or

microcavitation of nerve cells in the brain stem nuclei. The neural perikarya and axons of certain brain stem nuclei contain intracytoplasmic vacuoles of various sizes, that give the impression of a spongy brain. Hypertrophy of astrocytes often accompanies the vacuolation (49). A diagnosis may also be made by the detection of SAF's using electron microscopy.

Two supplemental tests are available to enhance the diagnostic capabilities for BSE. These are immunohistochemistry and the Western blot technique. In the past, if the brain tissue was not harvested shortly after the animal's death, autolysis often made it very difficult to confirm a diagnosis by histopathology. These tests allow for the possibility of confirming a diagnosis of BSE by detecting PrP^{BSE} even if the brain has been frozen or autolytozed .

Differential Diagnosis

Differentials for BSE include rabies, listeriosis, nervous ketosis, milk fever, grass tetany, lead poisoning, and other toxicities or etiological agents affecting the nervous or musculoskeletal system of adult cattle.

Treatment

There is no known treatment for BSE or any of the TSE's.

Vaccination

There is no preventative vaccine.

Control and Eradication

Bovine spongiform encephalopathy from foreign sources may be prevented by the implementation of import regulations prohibiting live ruminants and ruminant products (especially meat, bone meal, and offal) from countries where BSE may exist. Because the origin of BSE remains unknown, preventing an epidemic of BSE would involve, at a minimum, the prohibition of feeding ruminant proteins to ruminants. The prevention program of any country should also include an active surveillance effort focused on high-risk cattle for the early detection of BSE. Most countries of the world have prohibited the importation of cattle and bovine products from countries known to have BSE. In addition many countries have taken steps to enact regulations prohibiting the feeding of ruminant proteins to ruminants. This is true even in countries such as Australia and New Zealand with no known animal TSE's.

Agricultural officials in countries known to have BSE have taken a series of actions to control and, it is to be hoped, eradicate BSE. These include making BSE a notifiable disease, prohibiting the inclusion of certain animal proteins in ruminants' rations (the feed bans vary depending on the amount of BSE detected), and depopulating certain populations of cattle thought to be of higher risk because of epidemiological findings.

To prevent human exposure to the BSE agent numerous countries have established prohibitions on the inclusion of high risk material in foods, pharmaceuticals, cosmetics, and so forth.

U.S. Actions

With an active surveillance program in place for 8 years, BSE has not been detected in the United States. The United States Department of Agriculture (USDA), Food and Drug Administration (FDA), and industry groups are actively working to maintain this status. The measures USDA, Animal and Plant Health Inspection Service (APHIS), has taken in this regard include prohibitions or restrictions, or both, on certain animal and product imports, ongoing surveillance for the disease in the United States, preparation of an emergency response plan in the unlikely event an introduction were to occur, and continuing educational efforts. The Animal and Plant Health Inspection Service actively shares information and coordinates closely with other Federal agencies, as well as the States, livestock and affiliated industries, veterinary and

research communities, and consumer groups, to ensure that the United States has a uniform approach to transmissible spongiform encephalopathies based on sound scientific information.

A comprehensive surveillance program has been implemented by APHIS in the United States to ensure timely detection and swift response in the unlikely event that an introduction of BSE were to occur. This surveillance program entails the location of imports from countries known to have BSE and targeted active and passive surveillance for either BSE or any other TSE in cattle.

To locate each of the 496 British cattle that were imported into this country between January 1, 1981, and July 1989, APHIS has conducted a traceback effort. In July 1989, the United States prohibited the importation of ruminants from countries affected with BSE. As of March 1998, only 17 of these animals are known to be alive in the United States, and these are being carefully monitored by APHIS personnel on an ongoing basis. In addition, five head of cattle imported from Belgium in 1996 are now under quarantine. In cooperation with the states and industry, APHIS continues to purchase these animals for diagnostic purposes. No evidence of BSE has been found in any of these imported animals.

The United States has had an aggressive, active surveillance program for BSE since May 1990. Bovine spongiform encephalopathy is a notifiable disease, and there are more than 250 Federal and State regulatory veterinarians specially trained to diagnose foreign animal diseases, including BSE. The Animal and Plant Health Inspection Service leads an interagency surveillance program, which includes the Food Safety Inspection Service (FSIS) and the Centers for Disease Control (CDC). The surveillance samples include field cases of cattle exhibiting signs of neurological disease, cattle condemned at slaughter for neurological reasons, rabies-negative cattle submitted to public health laboratories, neurological cases submitted to veterinary diagnostic laboratories and teaching hospitals, and random sampling of cattle that are nonambulatory at slaughter. As of February 21, 1998, over 6,600 brains had been examined for BSE or another form of a transmissible spongiform encephalopathy in cattle. No evidence of either condition has been detected by histopathology or immunohistochemistry.

As of December 12, 1997, APHIS has prohibited the importation of live ruminants and most ruminant products from all of Europe until a thorough assessment of the risks can be made. The new restrictions apply to Albania, Austria, Bosnia-Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Federal Republic of Yugoslavia, Finland, Germany, Greece, Hungary, Italy, Former Yugoslav Republic of Macedonia, Norway, Poland, Romania, Slovak Republic, Slovenia, Spain, and Sweden.

This action was taken because, in the past year, the Netherlands, Belgium, and Luxembourg have reported their first cases of BSE in native-born cattle. There is evidence that European countries may have had high BSE risk factors for several years and less than adequate surveillance. Additionally, Belgium reported that the cow diagnosed with BSE was processed into the animal food chain.

The Food and Drug Administration (FDA) has recently established regulations that prohibit the feeding of most mammalian proteins to ruminants. The effective date of this regulation was August 4, 1997.

Public Health

BSE and CJD — Human Health Concerns

On March 20, 1996, the U.K.'s Spongiform Encephalopathy Advisory Committee (SEAC) announced the identification of 10 cases of a new variant form of CJD (nvCJD). All of the patients developed onset of illness in 1994 or 1995. The following features describe how these 10 cases differed from the sporadic form of CJD:

· The affected individuals were much younger than the sporadic CJD patient. Typically, sporadic CJD patients are over 63 years old. The average patient age

for the variant form of CJD is 27.5 (range of 16 to 42) years.

· The course of the disease in the nvCJD averaged 13 months. Sporadic CJD cases average a 6-month duration.

· In the variant cases, electroencephalographic (EEG) electrical activity was not typical of sporadic CJD.

· Although brain pathology was recognizable as CJD, the pattern was different from normal CJD, and evidenced large aggregates of prion protein plaques.

Epidemiologic and case studies have not revealed a common risk factor among the cases of nvCJD. According to the SEAC, all victims were reported to have eaten beef or beef products in the last 10 years, but none had knowingly eaten brain material. One of the affected individuals had been a vegetarian since 1991 (52).

The SEAC concluded that, although there was no direct scientific evidence of a link between BSE and nvCJD, on the basis of current data and in the absence of any credible alternative, the most likely explanation was that the cases were linked to exposure to BSE before the introduction of control measures; namely, the specified bovine offal (SBO) ban in 1989.

Research reported in later 1996 and 1997 has presented further evidence to support a causal association between nvCJD and BSE. Two significant studies published in the October 2, 1997, edition of Nature led the SEAC to conclude that the BSE agent is very likely to be the cause of nvCJD. Dr. Moira Bruce and colleagues at the Institute for Animal Health in Edinburgh, Scotland, inoculated three panels of inbred mice and one panel of crossbred mice with BSE, nvCJD, and sporadic CJD. Interim results indicate that mice inoculated with BSE show the same pattern of incubation time, clinical signs, and brain lesions as mice inoculated with tissues from patients with nvCJD. This provides evidence that BSE and nvCJD have the same signature or are the same "strain." In addition classical CJD and known scrapie strains were not similar to nvCJD or BSE (9).

Results from another study published by Dr. John Collinge and colleagues of Imperial College School of Medicine, London, United Kingdom, strongly support Bruce's results. Collinge's paper reports experimental transmission of BSE to transgenic mice expressing only human PrP (20).

The Health and Safety Executive in the United Kingdom now advises that BSE must be considered a biological agent (human pathogen) within the meaning of the Control of Substances Hazardous to Health Regulations 1994 (45).

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PART IV
FOREIGN ANIMAL DISEASES

CONTAGIOUS AGALACTIA OF SHEEP AND GOATS

Definition

Contagious agalactia (CA) of sheep and goats is an infectious disease of males and females of these species characterized by fever, malaise, and septicemia followed by arthritis, keratoconjunctivitis, and in the females, mastitis and agalactia.

Etiology

The etiologic agent of the classical disease is *Mycoplasma agalactiae*, which, since its isolation in 1923, has been considered to be the main cause of the disease. However, it has become evident that the "contagious agalactia" syndrome (especially in goats) can also be caused by several other mycoplasmas, notably *M. capricolum capricolum* and *M. putrefasciens* (5), *M. mycoides capri* (10), and the "large colony" or LC type of *M. mycoides mycoides* (1). Some have questioned limiting the term "contagious agalactia" to the disease caused by *M. agalactiae* (6). This discussion will focus on CA as caused by *M. agalactiae*.

Many of the routinely used disinfectants will effectively inactivate the organism. Effective disinfectants are sodium hypochlorite (30 ml of household bleach in 1 gallon of water), cresol, 2 percent sodium hydroxide (lye) (pH 12.4), formalin (1 percent), sodium carbonate (4 percent anhydrous or 10 percent crystalline with 1 percent detergent), and ionic and nonionic detergents.

Host Range

Goats seem to be more susceptible to the natural disease than are sheep, but *M. agalactiae* is an important pathogen of both species. Most outbreaks occur in the summer months and coincide with the time of births and peak lactation.

Geographic Distribution

Contagious agalactia is an important disease in the Mediterranean countries of Europe, Asia, and North Africa, in the former Soviet Union, in India and Pakistan, and in countries of the Near East. It has also been reported from Australia, South Africa, and South America. Although three isolations of *M. agalactiae* have been reported from the United States, it appears that North American strains are of low virulence and do not cause classical CA.

Transmission

The disease spreads by ingestion of feed, water, or milk contaminated with infected milk, urine, feces, or nasal and ocular discharges. Transmission may also be by direct entry to the teat opening at milking or by inhalation of contaminated dust. Animals with subclinical or chronic infections can carry and shed the mycoplasmas for months, and the organisms can survive in the supramammary lymph nodes from one lactation to the next. Contaminated fomites can transmit the organisms between premises. The disease appears to be less contagious than it was formerly thought to be (6).

Incubation Period

The incubation period in the natural disease varies between 7 and 56 days.

Clincial Signs

Infection with *M. agalactiae* occurs in male and female sheep and goats and can be inapparent or can cause mild, acute, or chronic disease. Freshening female goats at the beginning of lactation are especially susceptible and often display the acute form of the disease After an incubation period of from 1 to 8 weeks, transient fever followed by malaise and inappetance are observed. This is followed by mastitis, polyarthritis, and keratoconjunctivitis.

The mastitis is characterized by a change in the color of the milk to greenish-yellow or grayish-blue, and in the texture of the milk to a watery and later lumpy consistency as lactation decreases and eventually ceases. The udder eventually becomes flabby, fibrosed, and atrophic.

The polyarthritis, first seen as swelling of the periarticular tissues, especially of the carpal and tarsal joints, later develops into painful chronic infection, resulting in lameness and inability to stand or walk. In male goats this may be the main manifestation of the disease.

The keratoconjunctivitis is usually of short duration and is seen in about 50 percent of infected animals. It may occasionally develop into a chronic infection, occasionally resulting in unilateral or bilateral blindness.

Abortion has been described in chronically infected animals, but its pathogenesis is not understood. *Mycoplasma agalactiae* has also been associated with granular vulvovaginitis in goats (13).

Gross Lesions

The principal lesion in female animals is catarrhal mastitis with primary inflammation of the interstitial tissues followed by secondary acinar involvement. If the mastitis becomes chronic, progressive fibrosis and eventually parenchymatous atrophy will be seen.

In males and females dying of the acute disease, congestion of the musculature and of the spleen and liver may be seen as a result of the septicemia. In both acute and more chronically affected animals, arthritis with periarticular edema is common and especially affects the carpal joints. Synovial membranes may be hyperemic, and joint cavities may be filled with turbid or hemorrhagic fluid. The early eye lesion is usually a serous and later a mucopurulent conjunctivitis followed by keratitis and occasionally corneal ulceration.

Morbidity and Mortality

The economic impact of the disease lies in its high morbidity and resultant loss of milk and meat production rather than in its mortality. The greatest number of cases develops during those periods when the young are being born and the dams are in full lactation. In most outbreaks of CA, the mortality is low, seldom exceeding 20 percent, but occasionally secondary bacterial pneumonia may cause a higher mortality.

Diagnosis

Field Diagnosis

The characteristic clinical signs of the disease, namely mastitis with loss of milk production, keratoconjunctivitis, and arthritis, all occurring at or soon after parturition, warrant a clinical diagnosis of contagious agalactia. Because there are several look-alike mycoplasmal and bacterial infections, laboratory confirmation of field diagnosis is essential.

Specimens for Laboratory

From a live animal, milk, swabs from the eyes, joint fluid, blood, urine, and feces, all provide good samples for isolation attempts. From a dead animal that has had severe clinical disease, the best specimens to submit are blood, urine, and tissues from liver, spleen, and other organs, and joint fluid from those animals with arthritis. All samples should be collected aseptically and, if possible, placed in transport medium (heart infusion broth, 20 percent serum, 10 percent yeast extract, benzylpenicillin at 250 to 1000 IU/ml). Samples should be kept cool and shipped on wet

ice as soon as possible. If transport to the laboratory is delayed (more than a few days), samples may be frozen (1). Blood should be collected for serum.

Laboratory Diagnosis

Diagnosis of CA must be confirmed by isolation and serological identification of the causative agent. Serology, (the complement fixation [CF] test, indirect hemagglutination test, enzyme-linked immunosorbent assay [ELISA][11]) for the detection of antibodies is useful on a herd basis after the presence of the disease has been confirmed by isolation of the organism.

Differential Diagnosis

As stated in the section on etiology, several other mycoplasmas (especially of goats) can cause syndromes resembling contagious agalactia. Pneumonia, mastitis, and arthritis can also be caused by *Pasturella haemolytica*; mastitis can also be caused by streptococci, staphylococci, or other bacteria; and arthritis can also be caused by both caprine arthritis encephalitis virus and the bacteria *Erysipelothrix rhusiopathiae*.

Treatment

With early antibiotic (tetracyclines, tylosin, erythomycin, and tiamulin fumarate) treatment the prognosis is good, and only in those animals developing chronic arthritis or keratoconjunctivitis is recovery unlikely. Oxyteracycline does not prevent subsequent shedding of the organisms, and with the other drugs this still needs to be determined.

Vaccination

Both live and inactivated vaccines have been used in the prevention of CA. A live-attenuated vaccine for goats (7) and vaccine prepared from a naturally avirulent strain of mycoplasma are effective in goats. Formalin-inactivated aluminum hydroxide precipitated vaccines have been extensively used in Eastern Europe. Because there seems to be some strain variation, the use of autogenous vaccines incorporating local strains of mycoplasma is recommended. The efficacy of inactivated vaccines is low. Two concerns about the use of live vaccines are that the vaccine organism may be shed in the milk and that although the vaccines may prevent the development of clinical disease, they do not prevent infection and shedding of virulent organisms.

Control and Eradication

Prevention

Because CA is a chronic disease that may exist subclinically in carrier animals, it is important to maintain sufficient regulatory restrictions to prevent its introduction in apparently healthy animals.

Control and Eradication

In endemic areas, normal sanitary precautions of separating affected animals from healthy animals, separating milking animals from younger animals, cleaning and disinfection of milking utensils, practicing good hygienic principles when milking, cleaning and disinfection of stalls, and eliminating litter will reduce the incidence of disease in a flock. If possible, newborn animals should be removed from the dam immediately after birth and fed only pasteurized colostrum and then pasteurized milk.

Eradication can be accomplished by slaughter of all infected and contact flocks.

Public Health

There is no evidence that humans are susceptible to M. agalactiae.

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PART IV
FOREIGN ANIMAL DISEASES

CONTAGIOUS BOVINE PLEUROPNEUMONIA

Definition

Contagious bovine pleuropneumonia (CBPP) is a highly infectious acute, subacute, or chronic disease, primarily of cattle, affecting the lungs and occasionally the joints, and caused by *Mycoplasma mycoides mycoides*.

Etiology

Contagious bovine pleuropneumonia is caused by *M. mycoides mycoides* small-colony type (SC type). *M. mycoides mycoides* large-colony type is pathogenic for sheep and goats but not for cattle. *M. mycoides mycoides* (SC type) survives well only in vivo and is quickly inactivated when exposed to normal external environmental conditions. *M. mycoides mycoides* does not survive in meat or meat products and does not survive outside the animal in nature for more than a few days. Many of the routinely used disinfectants will effectively inactivate the organism.

Host Range

Contagious bovine pleuropneumonia is predominantly a disease of the genus *Bos*; both bovine and zebu cattle are naturally infected. There are many reported breed differences with respect to susceptibility. In general, European breeds tend to be more susceptible than indigenous African breeds (8). There does seem to be some age resistance, for animals less than 3 years of age are less resistant to experimental challenge (5). In zoos the infection has been recorded in bison and yak. Although it has been reported that the domestic buffalo (*Bubalus bubalis*) is susceptible, the disease is difficult to produce experimentally in this species (7).

Geographic Distribution

Contagious bovine pleuropneumonia is endemic in most of Africa. It is a problem in parts of Asia, especially India and China. Periodically, CBPP occurs in Europe, and outbreaks within the last decade have occurred in Spain, Portugal, and Italy. Contagious bovine pleuropneumonia was eradicated from the United States in the nineteenth century. It is of historical interest that the Bureau of Animal Industries, which is the forerunner of the USDA's Animal and Plant Health Inspection Service, was formed in 1884 specifically to eradicate CBPP. The United States was declared free of CBPP only 9 years later in 1893. Currently, CBPP is not present in the Western hemisphere.

Transmission

Contagious bovine pleuropneumonia is spread by inhalation of droplets from an infected, coughing animal. Consequently, relatively close contact is required for transmission to occur. Outbreaks usually begin as the result of movement of an infected animal into a naive herd. It is widely believed that recovered animals harboring infectious organisms within a pulmonary sequestrum, may become active shedders when stressed. Although this may be a factor in some outbreaks, it has not been substantiated experimentally (9). There are limited anecdotal reports of fomite transmission, but this means of transmission is not generally thought to be a problem.

Incubation Period

The time from natural exposure to overt signs of disease is variable but generally quite long. It has been shown that healthy animals placed in a CBPP-infected herd may begin showing signs

of disease 20 to 123 days later (7). Experimentally, subsequent to instillation of large quantities of infective material at the tracheal bifurcation, the incubation period is 2 to 3 weeks.

Clinical Signs

Usually the first abnormality noticed is a depressed, inappetent animal with fever. Coughing may be the next sign (Fig. 36) followed by evidence of thoracic pain and an increased respiratory rate. As pneumonia progresses and animals become increasingly dyspneic, animals are inclined to stand with elbows abducted in an attempt to decrease thoracic pain and increase chest capacity. Auscultation of the lungs reveals any of a wide variety of sounds, depending on how severely the subjacent pulmonary parenchyma is affected.

Crepitations, rales, and pleuritic friction rubs are all possible. Percussion over affected areas reveals dullness. When pulmonary involvement is extensive and severe, there will be very labored respiration and, sometimes, open-mouthed breathing. Occasionally in calves, pneumonia may be accompanied by a polyarthritis. Animals affected in this manner may be very reluctant to move and stand stiffly with a distinctly arched back. Getting up and down may cause obvious discomfort. Large joints (Fig. 37) may be distended and warm on palpation. If joint pain is severe, animals may be so reluctant to bend the joints that they lie in lateral recumbency with legs outstretched. Contagious bovine pleuropneumonia often evolves into a chronic disease. This form, characterized by ill thrift and recurrent low-grade fever, may be difficult to recognize as pneumonia. Forced exercise may precipitate coughing.

Gross Lesions

The gross pathologic features of CBPP are quite characteristic (3). If the animal dies, there is usually extensive and marked inflammation of the lung and associated pleurae (Fig. 38). In severe cases there can be abundant fluid in the thoracic cavity. The inflammation is not uncommonly unilateral (Fig. 39). The initial focus can be in any part of the lung and, in fatal cases, usually has spread locally and extensively to include a sizable segment. The affected pulmonary parenchyma is odorless and often has all stages of lesions with both acute and chronic inflammatory changes adjacent to one another. The predominant gross change is consolidation, or thickening, of individual lobules, which become encased in markedly widened interlobular septa, resulting in the very characteristic marbled appearance (Figs. 40, 41). Interlobular septa become distended first by edema, then by fibrin, and finally by fibrosis. The overlying pleura may be very thickened by an irregular layering of yellow fibrin which, with time, becomes fibrosed, often resulting in adhesions between parietal and visceral pleurae. Not uncommonly, within an affected lung will be found a sequestrum - a focus that has undergone coagulative necrosis (Fig. 42) and is effectively sealed off from the rest of the lung. Such sequestra may even be found in recovered. animals. It has been shown that *M. mycoides mycoides* (SC-type) can survive within these sequestra for months or possibly longer (9).

Morbidity and Mortality

The attack rate with CBPP is variable. It is not thought to be a highly contagious disease. With increased confinement of animals, morbidity rises. The mortality rate with CBPP is quite varied and ranges from 10 to 70 percent in various outbreaks. As with many subacute and chronic infectious diseases, mortality may depend on other intercurrent factors such as plane of nutrition, level of parasitism, and general body condition

Diagnosis

Field Diagnosis

Clinical diagnosis of CBPP is difficult. At postmortem the gross lesions of CBPP are somewhat distinct. Often there is an extensive deposition of fibrin and a large quantity of straw-colored fluid in the thoracic cavity with a prominent marbling of pulmonary parenchyma. Generally, all stages of pathologic changes, from acute through to chronic, are present in one animal. In some

chronic cases the nodules of inflammation may not be readily apparent from the pleural surface but can be palpated within the parenchyma. Unlike many other pneumonias, CBPP is often unilateral.

Specimens for Laboratory

From a live animal, nasal swabs, transtracheal washes, or pleural fluid obtained by thoracic puncture all provide good samples for isolation attempts. From a dead animal that has had severe clinical disease, the best specimens to submit are affected lung, swabs of major bronchi, tracheo-bronchial or mediastinal lymph nodes, and joint fluid from those animals with arthritis. All samples should be collected aseptically and, if possible, placed in transport medium (heart infusion broth, 20 percent serum, 10 percent yeast extract, benzylpenicillin at 250 to 1000 IU/ml). Samples should be kept cool and shipped on wet ice as soon as possible. If transport to the laboratory is delayed (more than a few days), samples may be frozen (1). Blood should be collected for serum.

Laboratory Diagnosis

A definitive diagnosis is made by isolating and identifying the organism. Serology is helpful in the diagnosis of CBPP. Because CBPP is a subacute to chronic disease, most animals will have developed antibodies by the time of clinical disease.

Differential Diagnosis

Clinically, CBPP may be confused with other pneumonic conditions, most especially bovine pasteurellosis. However, bovine pasteurellosis would likely spread much more rapidly and consequently the epidemiologic picture may be distinct.

Treatment

Mycoplasma mycoides mycoides (SC-type) is susceptible to a variety of antimicrobials, including streptomycin, oxytetracycline, and chloramphenicol. However, antimicrobial therapy may only serve to slow the progression of the disease or may even in some cases favor the formation of sequestra. In the case of chronically affected animals or subclinically affected carriers, the organisms may be in an inaccessible location within an area of coagulative necrosis, which by definition is not served by a blood supply.

Vaccination

A modified live vaccine is available for use in enzootic areas. A major drawback of this vaccine is that it generates an unpredictable local reaction. For this reason it is often given in the tail tip, which may become necrotic and slough. Immunity subsequent to vaccination is generally good and lasts at least 12 months. The CBPP vaccine is often given in combination with the vaccine for rinderpest.

Control and Eradication

Prevention

Because CBPP is a chronic disease that may exist subclinically in carrier animals, it is important to maintain sufficient regulatory restrictions to prevent its introduction in apparently healthy animals. Serologic testing of susceptible animals for importation is a recommended safeguard.

Control and Eradication

Successful control of the spread of CBPP rests on removing susceptible animals from any possible contact with CBPP-infected animals, whether they are clinically affected or subclinical carriers only. On-farm quarantine of suspicious and contact animals would be very advantageous in stemming the spread of the disease. In an outbreak situation, testing, slaughter, and quarantine would be the methods of choice.

Public Health

There is no evidence to indicate that humans are susceptible to this disease.

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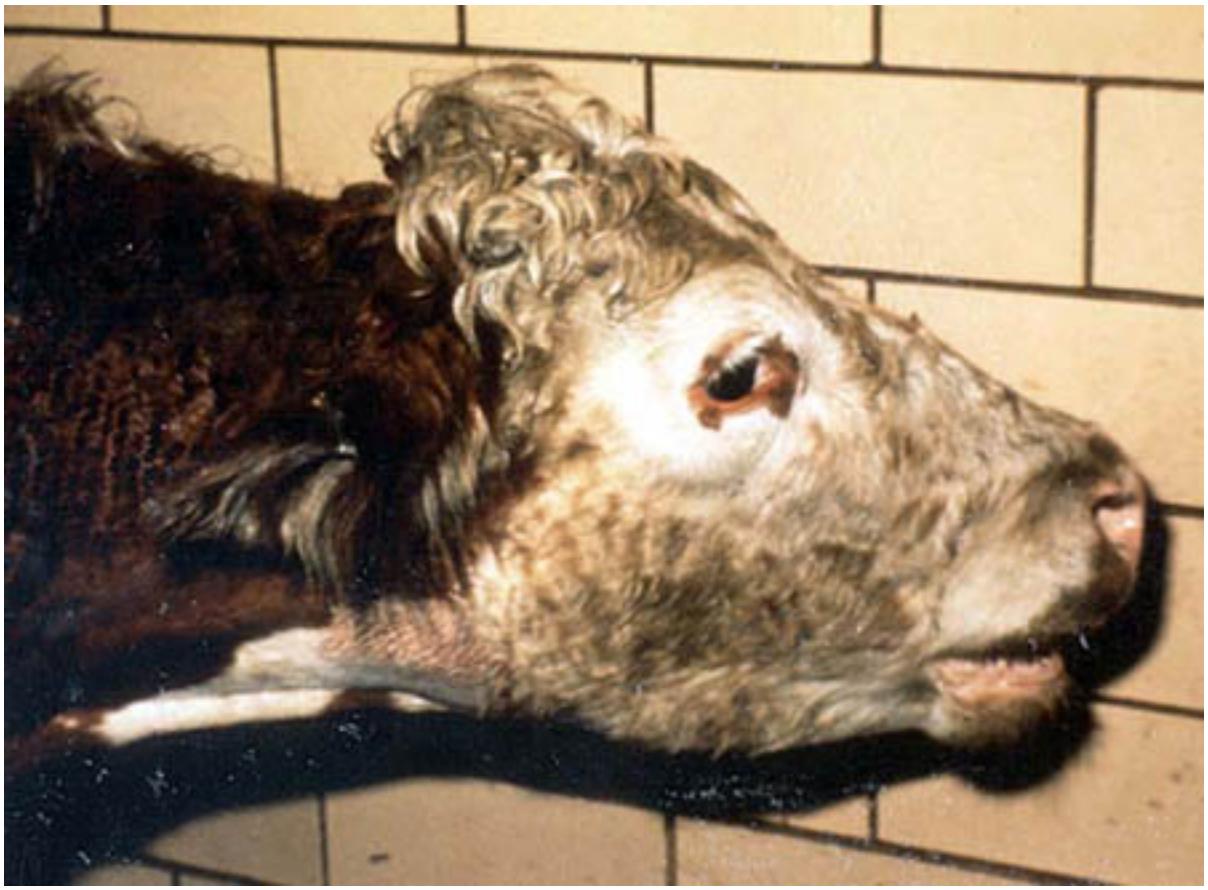

Fig. 36. CBPP - The extended neck and head is due to respiratory distress and coughing.

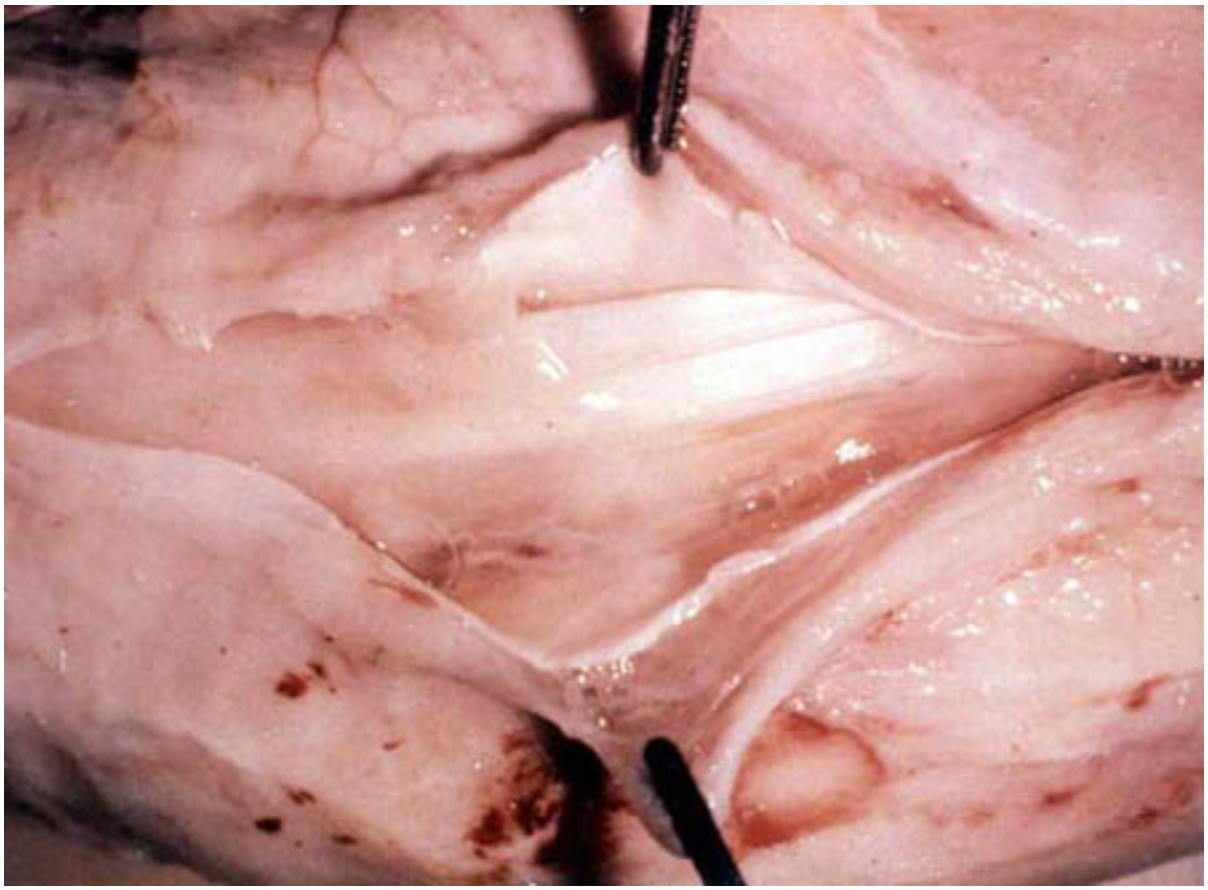

Fig. 37. CBPP - Enlarged joint is due to tendosynovitis and arthritis resulting from a mycoplasma.

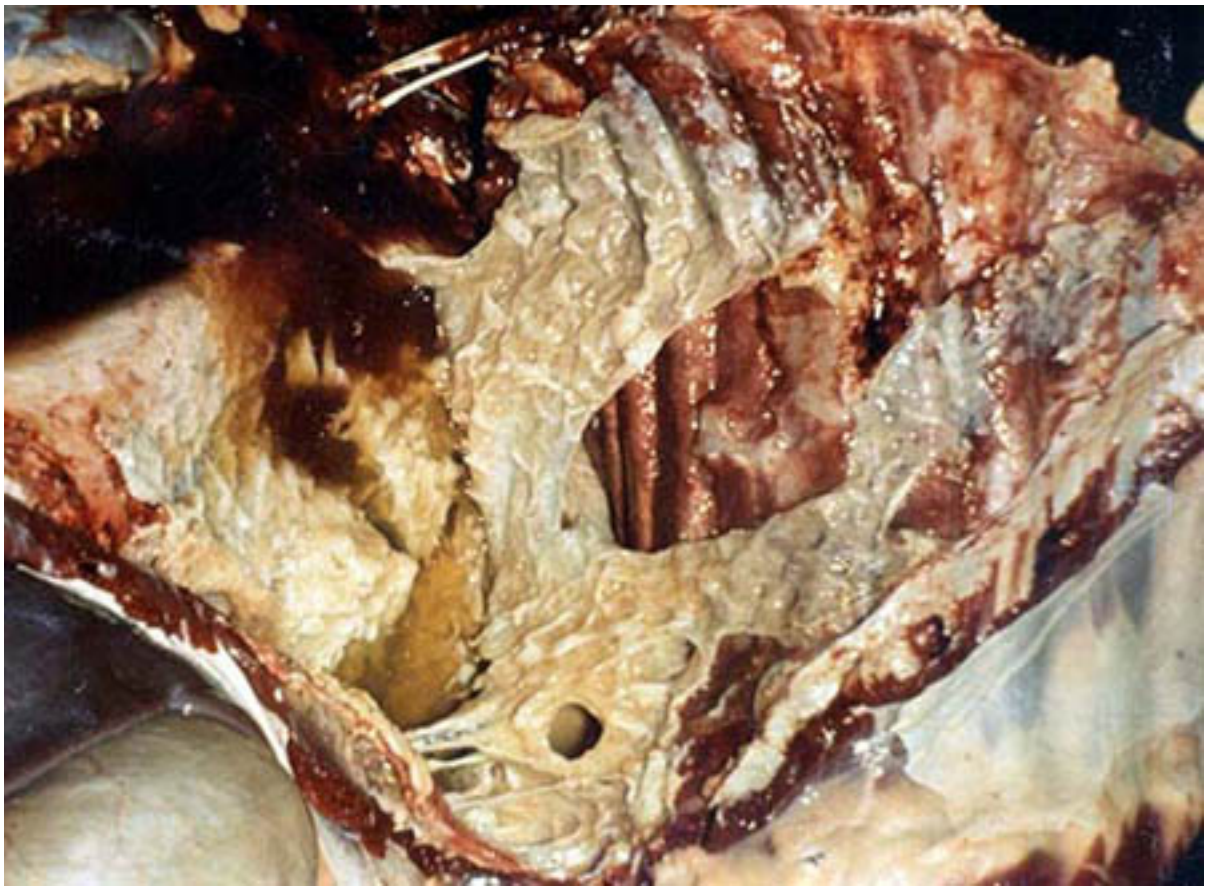

Fig. 38. CBPP - The thoracic wall is reflected; there is excessive fibrin on the parietal and visceral pleurae and a cloudy fluid in the thoracic cavity.

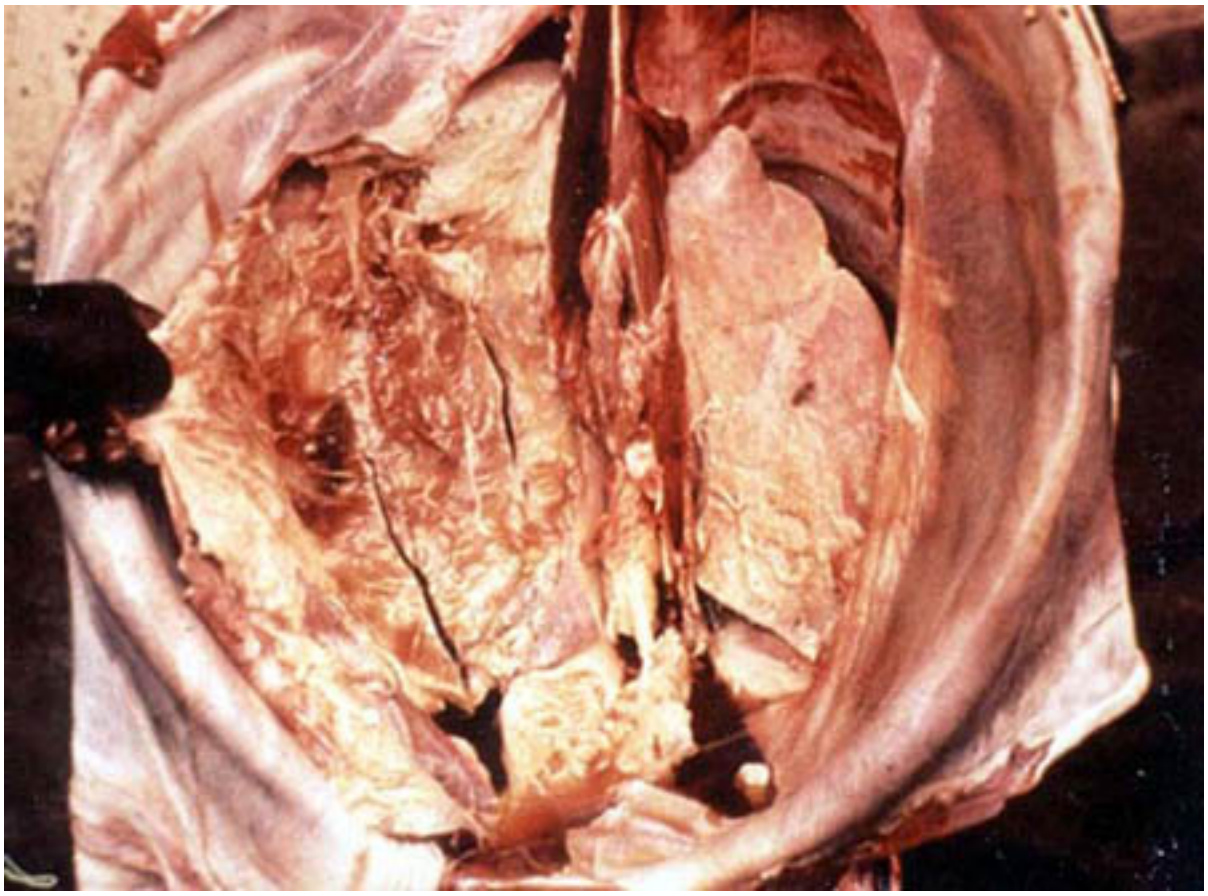

Fig. 39. CBPP - The pneumonic lesion in CBPP is not uncommonly unilateral.

Fig. 40. CBPP - Classical prominent interlobular septal thickening or "marbling" in a section of lung affected with CBPP.

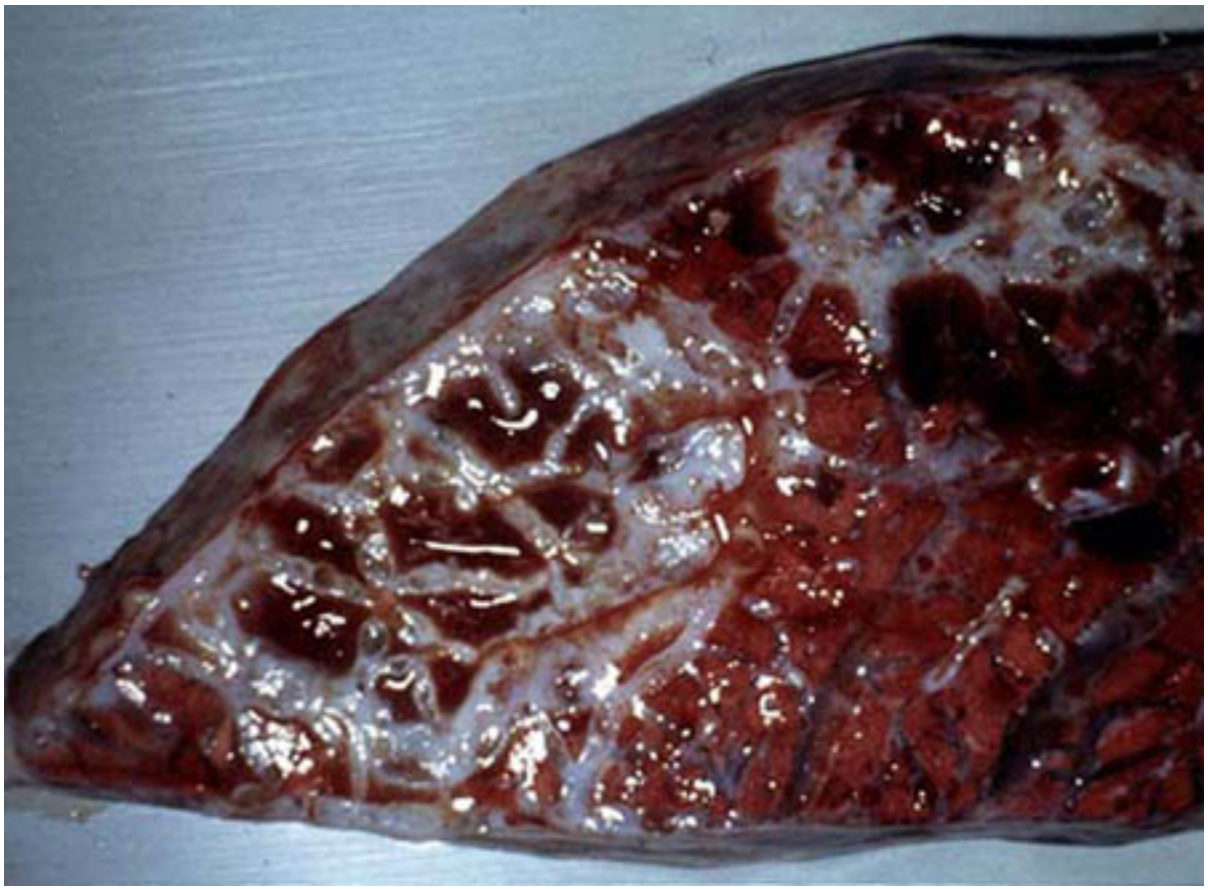

Fig. 41. CBPP - Classical prominent interlobular septal thickening or "marbling" in a section of lung affected with CBPP.

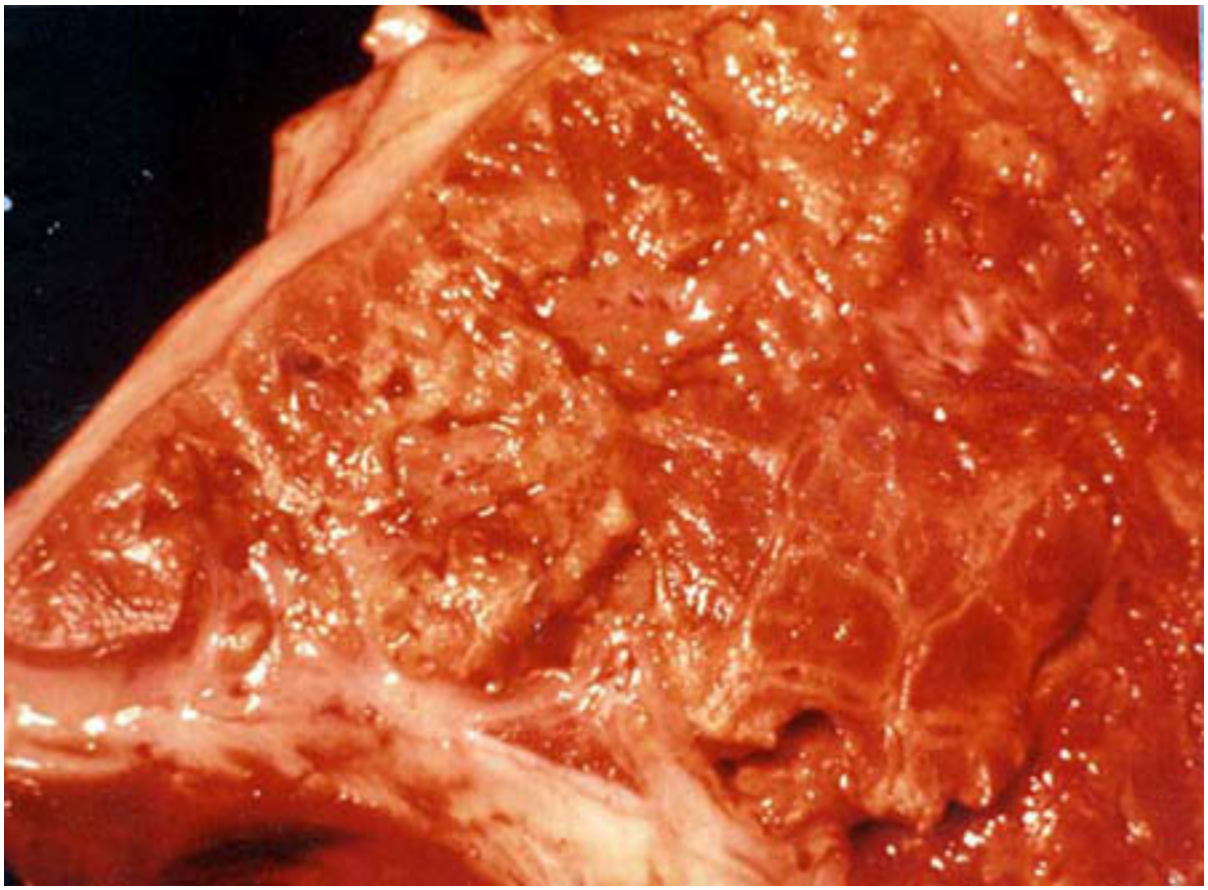

Fig. 42. CBPP - Area of coagulation necrosis in a section of lung affected with CBPP.

PART IV
FOREIGN ANIMAL DISEASES

CONTAGIOUS CAPRINE PLEUROPNEUMONIA

Definition

Contagious caprine pleuropneumonia (CCPP) is an acute highly contagious disease of goats caused by a mycoplasma and characterized by fever, coughing, severe respiratory distress, and high mortality. The principal lesion at necropsy is fibrinous pleuropneumonia.

Etiology

For many years the causative agent of CCPP was considered to be *M. mycoides capri* (type strain PG-3) because this was the agent most commonly isolated from goats with CCPP. In 1976, however, MacOwan and Minette (13) reported isolating a new mycoplasma (designated F-38) from a CCPP outbreak in Kenya and demonstrated it to be the cause of a highly contagious form of pneumonia resembling the original description of CCPP by Hutcheon in 1881. McMartin et al. (11) presented very convincing arguments supporting this agent as the cause of the classical disease, at least in Africa. Both of these mycoplasmas are now considered to cause CCPP, although the infrequency with which *M. mycoides capri* has been isolated from CCPP in recent years (19) suggests that it may be a minor cause of the disease. Neither of these agents occurs in North America. The name *M. capricolum capripneumoniae* proposed for mycoplasma F-38 by Leach et al. (10) is not in common usage. *Mycoplasma mycoides capri* is easily propagated on standard mycoplasma media, but F-38 is much more fastidious and can easily be missed at diagnosis, which may explain its late recognition as the major cause of CCPP.

M. mycoides mycoides has also been isolated from goats with pneumonia. This agent (the so-called large colony or LC variant of *M. mycoides mycoides*) usually produces septicemia, polyarthritis, mastitis, encephalitis, conjunctivitis, hepatitis, or pneumonia in goats. Some strains of this agent will cause pneumonia closely resembling CCPP (15), but the agent is not highly contagious and is not considered to cause CCPP. It does occur in North America. *M. capricolum capricolum*, a goat pathogen commonly associated with mastitis and polyarthritis in goats, can also produce pneumonia resembling CCPP, but it usually causes severe septicemia and polyarthritis. This agent (which does occur in the United States) is closely related to mycoplasma F-38 but can be differentiated from it using monoclonal antibodies (22).

Host Range

Contagious caprine pleuropneumonia is a disease of goats, and where the classical disease has been described, only goats were involved in spite of the presence of sheep and cattle. Mycoplasma F-38, the probable cause of the classic disease, does not cause disease in sheep or cattle.

M. mycoides capri, the other agent considered a cause of CCPP, will result in a fatal disease in experimentally inoculated sheep and can spread from goats to sheep. It is however, not recognized as a cause of natural disease in sheep.

Geographic Distribution

Contagious caprine pleuropneumonia has been described in many countries of Africa, the Middle East, Eastern Europe, the former Soviet Union, and the Far East. It is a major scourge in many of the most important goat-producing countries in the world and is considered by many to be the world's most devastating goat disease.

The classical disease, as caused by mycoplasma F-38, has not been described in North America. The reports of CCPP occurring in the United States (23) and in Mexico (1) were erroneous in that, although similar syndromes were described, the agents isolated were misidentified as *M. mycoides capri* and were subsequently shown to be *M. mycoides mycoides* (LC type). Neither mycoplasma F-38 nor *M. mycoides capri* has been isolated in North America

Transmission

Contagious caprine pleuropneumonia is transmitted by direct contact through inhalation of infective aerosols. Of the two known causative agents, F-38 is far more contagious. Outbreaks of the disease often occur after heavy rains (e.g., after the monsoons in India) and after cold spells. This is probably because recovered carrier animals start shedding the mycoplasmas after the stress of sudden climatic change. It is believed that a long-term carrier state may exist.

Incubation Period

The incubation period can be as short as 6 to 10 days but may be very prolonged (3-4 weeks) under natural conditions

Clinical Signs

The clinical signs described for CCPP from different parts of the world have varied enormously. This is not surprising because at least two different mycoplasmas have been regarded as causative agents of the disease. In many field outbreaks, the clinical picture has probably been further complicated by the presence of viruses and other bacteria (e.g., pasteurella) as part of the etiologic picture.

The classical disease as caused by mycoplasma F-38 is a purely respiratory illness. It is characterized by a fever- of 106º F (41º C), coughing, and a distinct loss of vigor. Affected goats have labored breathing; later they may grunt or bleat in obvious pain. Frothy nasal discharges and stringy salivation are often seen shortly before death. In the acute disease, which occurs in fully susceptible populations of goats, death occurs within 7 to 10 days of the onset of clinical signs. A more chronic form of the disease is often seen in endemic areas and may lead to recovery of a higher percentage of infected animals, many of them carriers of the mycoplasmas.

M. mycoides capri tends to cause a more generalized infection in which septicemia is frequently seen. An acute or peracute septicemic form of the disease involving the reproductive, respiratory and alimentary tracts has been described. In addition, thoracic and reproductive formes of the disease have been attributed to this agent. The disease is considerably less contagious than F-38-induced disease, and the mortality and morbidity rates are also lower.

Gross Lesions

The gross lesions in classical CCPP are confined to the thoracic cavity (11). Pea-sized yellowish nodules are seen in the lungs in early cases, whereas in more established cases there is marked congestion around the nodules. The lesions may be confined to one lung or involve both, and an entire lobe may become solidified. The pulmonary pleura becomes thickened, and there may be adhesions to the chest wall. Hutcheon emphasized that the lesions of CCPP do not resemble those of contagious bovine pleuropneumonia (CBPP) in that "no thickening of the interlobular tissue" occurrs, a classical lesion of CBPP. He described a CCPP-diseased lung as resembling a "somewhat granular looking liver", which is his description of the massive hepatization seen in CCPP lungs.

In sharp contrast, *M. mycoides capri* has been reported to cause lesions in a wide variety of organ systems and to produce lung lesions closely resembling those seen in CBPP. The generalized lesions described include encephalitis, meningitis, lymphadenitis, splenitis, genitourinary tract inflammations, and intestinal lesions, none of which are a feature of classical CCPP. The lung lesions, which resemble those seen in CBPP, are usually confined to one lung and reflect various stages of fibrinous pneumonia. Extensive pleuritis is usually present, and

various stages of hepatization and marked dilation of interlobular septa is commonly seen (Fig. 43). The cardiac and diaphragmatic lobes are the ones most commonly involved. Some describe this as a mild form of CCPP; others argue that it is not CCPP.

Morbidity and Mortality

Morbidity can be 100 PERCENT and mortality may be in the range of 70 percent to 100 percent (19). Gathering or increased confinement of animals facilitates the spread of the disease.

Diagnosis

Field Diagnosis

A highly contagious disease occurring in goats and characterized by severe respiratory distress, high mortality, and postmortem lesions of fibrinous pleuropneumonia with pronounced hepatization and pleural adhesions warrants a field diagnosis of CCPP.

Specimens for Laboratory

From a dead animal that has had severe clinical disease, the best specimens to submit are affected lung, swabs of major bronchi, and tracheobronchial or mediastinal lymph nodes. All samples should be collected aseptically and if possible, placed in transport medium (heart infusion broth, 20 percent serum, 10 percent yeast extract, benzylpenicillin at 250 to 1000 IU/ml). Samples should be kept cool and shipped on wet ice as soon as possible. If transport to the laboratory is delayed (more than a few days), samples may be frozen (1). Blood should be collected for serum.

Laboratory Diagnosis

Diagnosis must be confirmed by isolation of the agent (F-38). The causative agent, once isolated, can be identified by immunofluorescence or by growth or metabolic inhibition tests. Several serological tests can be used in the laboratory for the detection of antibodies to mycoplasma F-38. These include complement fixation (CF), passive hemagglutination (PH), and enzyme-inked immunosorbent assay (ELISA). The latex agglutination test (20) is a very convenient field test for detecting antibodies in whole blood or in serum.

Differential Diagnosis

Clinically, CCPP may be confused with other pneumonic conditions such as pasteurellosis and peste des petits ruminants.

Treatment

The mycoplasmas are sensitive to several broad-spectrum antibiotics (notably the tetracyclines, tylosin, and tiamulin). Although early treatment can be effective, chemotherapy and chemoprophylaxis have not played important roles in CCPP control programs.

Vaccination

A crude vaccine prepared from goat lung was used to vaccinate goats in South Africa after the original outbreak of CCPP in the late 1800's. A combination of this vaccine and other control methods eliminated the disease from the country.

Vaccines to *M. mycoides capri* have been used with little success. This is probably because the disease is usually caused by mycoplasma F-38, first recognized in 1976. Since that time both live attenuated and inactivated F-38 vaccines have been tested with varying degrees of success. The most promising of the experimental vaccines is the lyophilized saponin-inactivated F-38 vaccine shown in field tests to confer 100 percent protection to contact exposure (21). This vaccine could be of inestimable value in many countries of Africa.

Control and Eradication

Sufficient regulatory restrictions should be maintained to prevent introduction of CCPP into apparently healthy animals. Serologic testing of susceptible animals for importation is a recommended safeguard.

Successful control of the spread of CCPP rests on removing susceptible animals from any possible contact with CCPP-infected animals, whether they are clinically affected or subclinical carriers only. On-farm quarantine of suspicious and contact animals would be very advantageous in stemming the spread of the disease. In an outbreak situation, testing, slaughter, and quarantine would be the methods of choice.

Public Health

Human infection with these mycoplasmas has not been reported.

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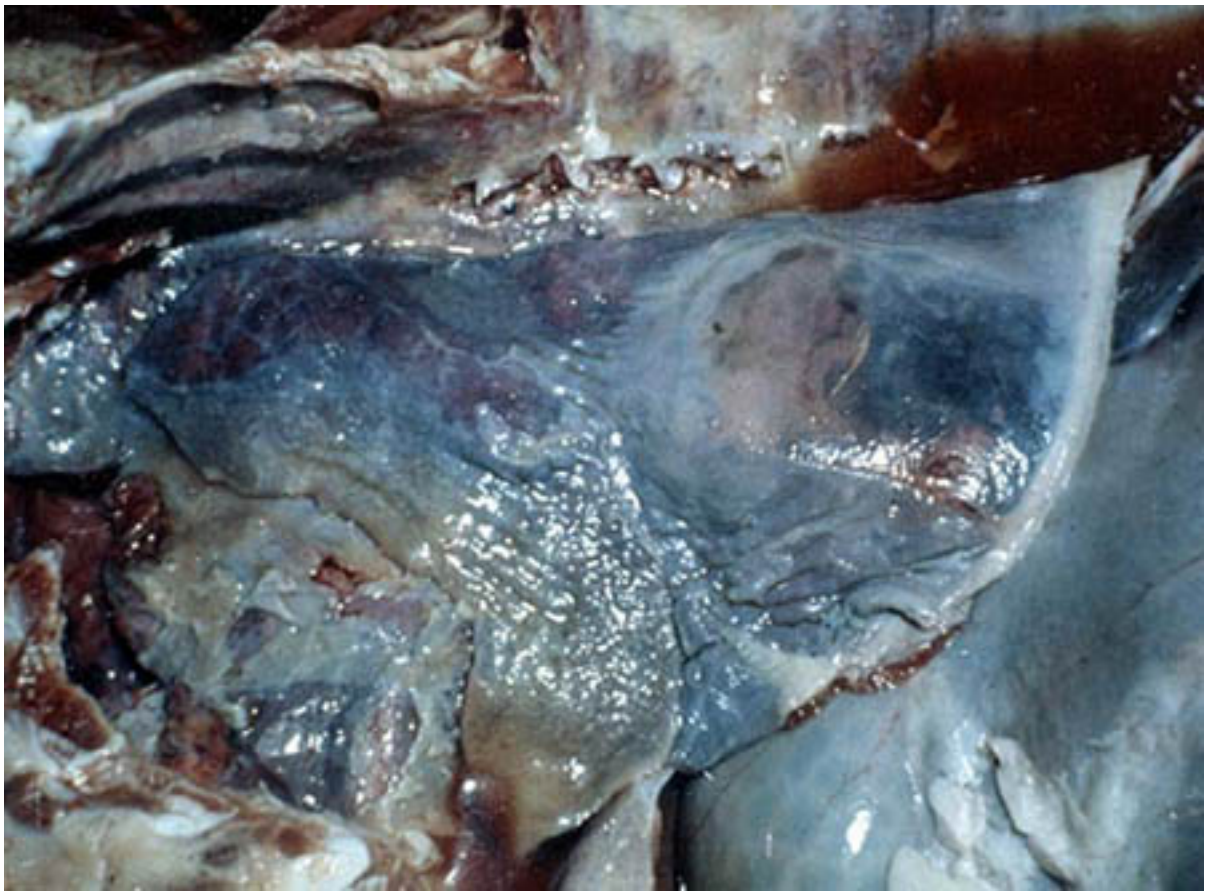

Fig. 43. CCPP - Lung is covered with fibrin and there is excessive fluid in the thoracic cavity.

PART IV
FOREIGN ANIMAL DISEASES

CONTAGIOUS EQUINE METRITIS

Definition

Contagious equine metritis (CEM) is a highly contagious venereal disease of horses that causes an acute purulent metritis and a copious mucopurulent vaginal discharge 10 to 14 days postbreeding to an infected stallion. The first exposure to the disease usually results in temporary infertility in the mare. Mares may become chronically infected and remain carriers of the causal organism for several months or longer. Stallions carry the contagious equine metritis organism (CEMO) on their external genitalia, and the primary site of localization is the urethral fossa. The stallions may carry the CEMO on their external genitalia for years. Newborn foals may become infected at birth and remain infected until they are mature.

Etiology

The CEMO is a microaerophilic gram-negative coccobacillus (17). There are two important strains of the CEMO, one being streptomycin sensitive and the other streptomycin resistant (14). A suggested name, *Taylorella equigenitalis*, has recently been accepted by the International Committee on Systemic Bacteriology.

The organism is susceptible to most commonly used disinfectants such as sodium hypochlorite (30 ml of household bleach in 1 gal of water), chlorhexidine, and ionic and nonionic detergents.

Host Range

Only the equine species appear to be natural hosts for the disease. Thoroughbred horses appear to be more severely affected by the disease than other breeds (14).

Geographic Distribution

Although the disease was first described as an entity in England in 1978 (4), the causal organism was likely present in horse populations in different countries for several years before that time.

The CEMO has since been detected in several countries, including Australia, Czechoslovakia, Ireland, France, Germany, Japan, Belgium, Denmark, Italy, Netherlands, Norway, Sweden, Switzerland, and Luxembourg. The disease has been eradicated from the United States.

Transmission

The disease is naturally transmitted by coitus. Also, the CEMO can be transmitted indirectly to mares and stallions with contaminated instruments and equipment (3). Undetected carrier mares and stallions are the source of infection for acute outbreaks of the disease. During the breeding season, an infected stallion may infect several mares before the disease is suspected and diagnosed. Also, the CEMO may be transmitted through the use of artificial insemination.

Incubation Period

In field cases, the disease does not become evident until 10 to 14 days postbreeding when the mare short-cycles and shows signs of estrus. The inflammatory reaction starts 24 hours after exposure to CEMO and reaches maximum intensity 10 days to 2 weeks postbreeding.

Clinical Signs

In the mare, a copious mucopurulent vaginal discharge occurs 10 to 14 days postbreeding to an infected stallion (Fig. 44). The first indication of infection is short-cycling of infected mares and a return to estrus. At this time, a mucopurulent vaginal discharge or a dried vaginal discharge can be found on the tail and inside the thighs (Fig. 45). The discharge subsides after a few days, but the mare may remain chronically infected for several months. In experimental infections in ponies (9,18,19) and horses (1), there was evidence of a mucopurulent vaginal discharge 24 to 48 hours postinfection, which lasted for 2 to 3 weeks. Most mares will not conceive when infected at the time of breeding. If infected mares do conceive, they may abort the fetus or carry an infected foal to term. The newborn foal may then become a carrier of the causal organism.

Gross Lesions

The lesions of contagious equine metritis are not pathognomonic for the disease. The most severe lesions are present in the uterus, but salpingitis, cervicitis, and vaginitis also occur (1,9). The most severe lesions occur at about day 14 postinfection. The changes gradually decrease in severity over the next several weeks as the disease becomes chronic. On the uterine mucosal surface, the endometrial folds may be edematous and swollen with a mucopurulent exudate evident between the folds at the height of the infection (Fig. 46). The cervix is edematous and hyperemic, and the surface is covered with a mucopurulent exudate (Fig. 47) (1).

Morbidity and Mortality

Morbidity is high in animals exposed venereally to the organism. Death to CEM has not been observed.

Diagnosis

Field Diagnosis

Mares that have a copious mucopurulent vaginal discharge 10 to 14 days postbreeding are suspect cases of CEM. Chronically infected mares and stallions do not have any clinical evidence of the disease.

Specimens for Laboratory

In both the acute and chronic stages of the disease, isolation of the bacterium is necessary for a diagnosis of CEM (14). Mares suspected of being carriers of the CEMO should be cultured during estrus, preferably during the first part of the heat cycle. Culture sites in the mare are the uterus, clitoral fossa, and clitoral sinuses (11). In the stallion, the culture sites are the urethra, urethral fossa and diverticulum, and the sheath (14). Culture swabs should be placed immediately in Amies transport media and maintained at 4^{o} C or lower to prevent the organism from dying and to prevent overgrowth by contaminating bacteria. If the culture swabs are not cultured within a few hours, the specimens in the transport media should be frozen. The organism appears to remain viable when frozen, for it has remained viable in Amies transport media for 18 Years at -20^{o} C (16).

Laboratory Diagnosis

Smears of the uterine exudate during the acute stages of the disease are helpful in making a presumptive diagnosis of CEM (12). Examination of Gram- and Giemsa-stained smears of the uterine exudate may reveal large numbers of inflammatory cells, mainly neutrophils. Numerous gram-negative coccobacillary bacteria can be demonstrated in the mucus and in the cytoplasm of the neutrophils. The organisms are usually seen individually or in pairs arranged end to end.

In both the acute and chronic stages of the disease, isolation of the bacterium is necessary for a diagnosis of CEM (14).

Various serologic tests may be used to detect antibodies to the CEMO (2,3,5,10). Evaluation of

the rapid plate agglutination (RPA), antiglobulin, enzyme-linked immunosorbent assay (ELISA), passive hemagglutination (PHA), complement fixation (CF), and agar-gel diffuse tests in ponies and Thoroughbreds provided varied results (10). Antibodies to CEMO were detected in the sera of Thoroughbred mares by the ELISA, RPA, CF, and PHA tests. The CF test was unreliable during the chronic stages of the disease owing to anticomplementary activity and low or undetectable CF titers. Most acute and chronic CEM infections are detected with the RPA, ELISA, and PHA tests. The rapid plate agglutination test (RPT) is very simple and rapid. The RPT detected 100 percent of the culture positive mares in the 1978 outbreak of the disease in Kentucky (14). The test also detected mares in the chronic stages of the disease — in many cases over a year after exposure to the CEMO. The CF test is only reliable between 15 and 45 days postinfection. A seropositive mare may or may not be infected with the CEMO (14). Stallions do not develop detectable antibodies to the CEMO.

Differential Diagnosis

Contagious equine metritis is the most contagious bacterial venereal infection of horses and should be suspected when several mares develop characteristic clinical signs after being covered by the same stallion. Typically, an uncomplicated CEM-infected mare produces a mucoid, gray purulent exudate from the uterus. However, mixed bacterial infections may occur, and the discharge may vary from gray to yellow. Other bacterial venereal diseases in the mare may produce a similar purulent, gray to yellow vaginal discharge, but they tend to be less contagious. As with other bacterial infections, CEM infections may be very mild to inapparent, or they may be severe. Although a tentative diagnosis of CEM may be suspected, laboratory tests are necessary to confirm a case or outbreak of CEM.

Treatment

The uterine infection can be treated with antibiotics, but it is questionable whether treatment effectively eliminates or facilitates elimination of the CEMO. The mare cannot be successfully treated until the CEMO clears from the uterus, which may take several months. The external genitalia of the mare and stallion can be treated with disinfectants and antibiotics. A standard treatment currently used is thorough washing of the external genitalia with soap and water and then with chlorhexidine surgical scrub once a day for 5 days. After cleaning with chlorhexidine, the external genitalia are rinsed with warm water to remove the chlorhexidine because it may irritate the sensitive mucous membranes. Then, the external genitalia are coated with nitrofurazone-containing ointment. A disadvantage of this treatment is the destruction of the normal flora and the potential overgrowth by opportunistic pathogens such as pseudomonas and klebsiella (13). The clitoral sinuses are common sites of persistence in carrier mares, and these sinuses are difficult to expose for cleaning and treatment. Surgical excision of the clitoral sinuses will aid in the treatment of the disease, and will usually rid the mare of infection (15).

Vaccination

Natural infection does confer some immunity in the mare, for the first exposure to the CEMO causes a very severe metritis, which usually results in temporary infertility. Subsequent exposure to the CEMO is less severe, and the infection may not prevent conception. However, the carrier state may result. Because of the nature of the disease and the carrier state, artificial immunization is a not practical or recommended procedure for preventing transmission of infection.

Control and Eradication

Preventive Measures

Inapparent infections in carrier mares (19) and carrier stallions make the disease difficult to control. To prevent the spread of the disease, it is necessary to detect and treat the infection in mares and the stallion. Suspect carrier mares should be tested bacteriologically to ensure they are not carrying the CEMO when bred to stallions because one stallion may infect several mares. Stallions suspected of being carriers should be cultured and bred to susceptible test

mares free of the disease and the test mares cultured for CEMO.

The small-colony types are less virulent and may be responsible for the gradual decrease in the number of naturally infected horses showing typical clinical signs of CEM in the field (7). These variants present unique problems, both clinically and in laboratory testing, for the small variants have no distinguishing cultural characteristics except that colonies are transparent and small. In addition, the slow growth of these variants, possible contaminating bacteria, and occurrence of streptomycin-sensitive strains of the organism make bacteriologic testing for the disease rather difficult.

Because of the difficulty of bacterial isolation of the streptomycin-sensitive strains, serologic testing is a valuable aid in detecting mares that have previously been exposed to the CEMO. Currently, the CF test is the only serologic test used to detect the disease in the field, but it will only detect the infection during the acute phase when the organism is easy to culture. Other serologic tests are available, and they will detect mares that have previously been exposed to the CEMO. If other serologic tests were utilized, the disease could easily be detected in carrier mares and steps taken for quarantine and treatment. Such testing would also aid in the prevention of reintroducing the disease into the United States from CEM-infected countries. Serologic testing is of no value in stallions because the latter do not produce detectable antibodies to the CEMO.

Public Health

There is no evidence that man is affected by the CEMO.

Contagious Equine Metritis Regulations

All horses must have been in the country of export for 60 days immediately preceding exportation. If not, the horse is to be accompanied by a health certificate issued by a full-time salaried veterinary officer of the national government of each country in which the horse has been during the 60 days immediately preceding shipment to the United States.

Preembarkation Requirements in Country of Origin

Stallions

> Collect one set of specimens from the surface of the prepuce, urethral sinus, fossa glandis (including the diverticulum of the fossa glandis) within 30 days of export but not less than 21 days following treatment if treated.

Mares

> The importer has the options to have the clitoral sinusectomy performed on the mare in the country of origin prior to export or performed in the United States after arrival.

Mares (Option for Clitoral Sinusectomy in the United States)

> Collect one set of specimens from the clitoral sinuses within 30 days prior to export, but not less than 21 days following treatment if treated.

Mares (Option for Clitoral Sinusectomy in the Country of Origin)

> Surgically remove clitoral sinuses no less than 30 days prior to export. Two hours prior to surgery collect a specimen from the clitoral sinuses and submit with removed clitoral sinuses to approved laboratory.

After surgery, collect a specimen from the clitoral fossa within 30 days prior to export but not less than 21 days following treatment if treated.

U.S. Entry Requirements

Horses imported into the United States are required to be detained at the port of entry while tests for dourine, glanders, equine piroplasmosis, and equine infectious anemia (EIA) are conducted. Horses that are positive to tests for any of these diseases will be refused entry.

Upon completion of USDA import quarantine and testing requirements, the mare or stallion must be consigned to a State approved to receive mares and stallions from CEM-affected countries to undergo the prescribed CEM treatment and testing requirements.

Mares

Mares with an Incomplete Sinusectomy or Option for Surgery in the United States

Surgery must be performed at The College of Veterinary Medicine, University of California, Davis, California, or The School of Veterinary Medicine, Cornell University, Ithaca, New York.

Two hours prior to surgery, collect a specimen from the clitoral sinuses and submit with removed clitoral sinuses (or portion) to the National Veterinary Services Laboratories, (NVSL), Ames, IA or to a laboratory approved by APHIS.

Within 2 hours prior to treatment, collect a specimen from the clitoral fossa and clitoral sinuses if present and submit with the clitoral sinuses (or portion) to NVSL or a laboratory approved by APHIS. For 5 consecutive days, clean, wash (2 percent chlorhexidine) and coat the external genitalia and vaginal vestibule with not less than 0.20 percent nitrofurozone ointment. Wait 7 days after cleaning and washing. Collect three separate sets of specimens not less than 7 days apart from the clitoral fossa. Collect one additional specimen from the endometrium of the uterus during estrus.

Pregnant mares are treated the same as above. except 7 days after foaling collect three specimens from the endometrium of the uterus and one specimen from the foal. Collect specimens from the vaginal vestibule of the female foal and the prepuce of the male foal.

Stallions

One specimen each shall be taken from the prepuce, the fossa glandis, and urethral sinus of the stallion and be cultured for CEM. After the specimens have been cultured for CEM, for at least 5 consecutive days the prepuce, penis (including the fossa glandis) and urethral sinus of the stallion shall be thoroughly cleaned and washed while in full erection with a solution of not less than 0.2% nitrofurazone by an accredited veterinarian under the monitoring of a State or Federal veterinarian.

The stallions must be tested for CEM by being bred to two mares. The test breeding shall be performed in not less than 7 days after treatment is completed. Mares selected for test breeding must be permanently identified before the mares are used for testing with the letter T (hot iron, freezemarking, or lip tatoo).

Before breeding, the mares must be to qualified as free from CEM by negative culture of two sets of specimens (bacteriological swabs) collected at intervals of not less than 7 days and a negative complement fixation (CF) test.

The two mares are to be bred by the stallion. The mares are then cultured for CEM by collecting three sets of specimens from each of the mucosal surfaces of the cervix, the clitoral fossa, and the clitoral sinuses on the second, forth, and seventh days after being bred.

Another set of specimens, the fourth set, must be collected from the endometrium of the uterus, the clitoral sinuses, and clitoral fossa during the next estrus. If natural estrus does not occur within 28 days of the date of the breeding, hormonal precipitation of estrus shall be carried out. The test mares are required to have two negative CF tests after they are bred. Serum samples are to be collected between the 15th and 40th days after breeding. The intervals between

collection of serum samples should not be less than 7 days.

NOTE: The clitoral sinusectomy is not required for thoroughbred mares from England, France, Ireland, and Germany.

Thoroughbred mares and stallions from England, France, and Ireland shall be treated as follows:

Mares

Collect one set of specimens during estrus from the endometrium and the mucosal surfaces of urethra, clitoral fossa, and cervix. Collect two sets of specimens from the mucosal surfaces of the urethra, clitoral fossa, and cervix. The samples should be collected at intervals of not less than 7 days apart, and the last of the sets shall be collected within 30 days of export.

Stallions

Collect three 3 sets of specimens from the prepuce, urethral sinus, and fossa glandis (including the diverticulum of the fossa glandis) at intervals of not less than 7 days and with the last of the sets collected within 30 days of export.

Upon completion of the USDA import quarantine in the United States, the horses are free to compete without any further restrictions.

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Fig. 44. CEM - Infected mares may have a copious mucopurulent vaginal discharge in the acute stage of the disease.

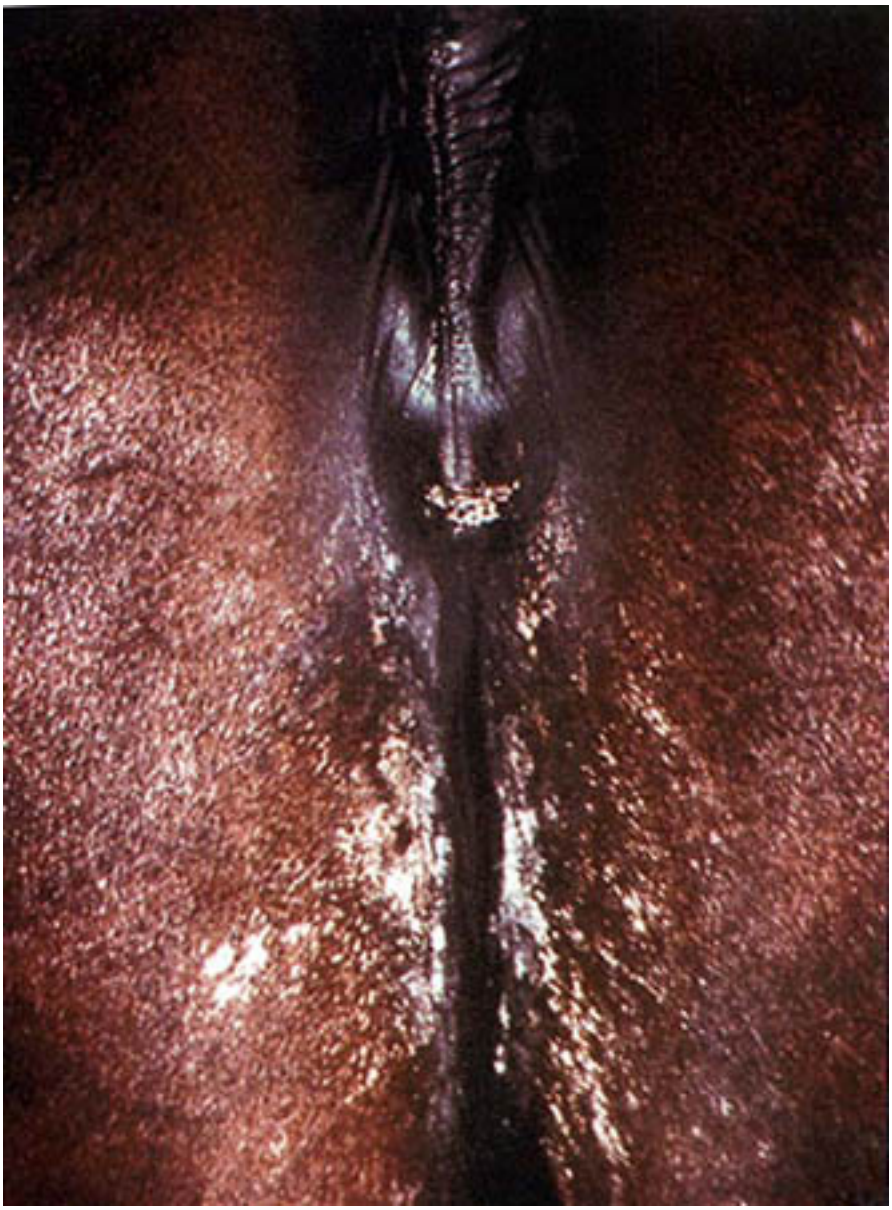

Fig. 45. CEM - Dried vaginal discharge on the inside of the thighs.

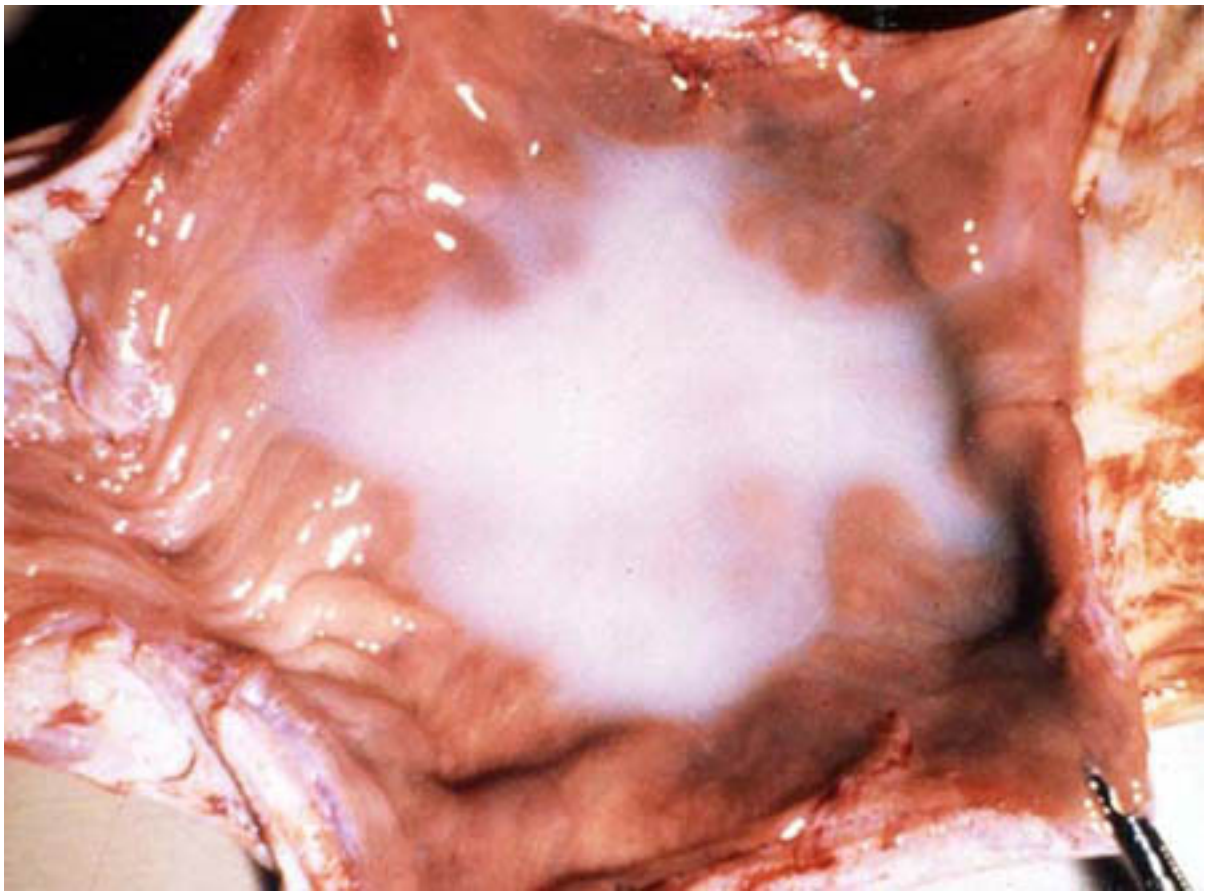

Fig. 46. CEM - There is a mucopurulent exudate in the lumen of the uterus in the acute stage of the disease.

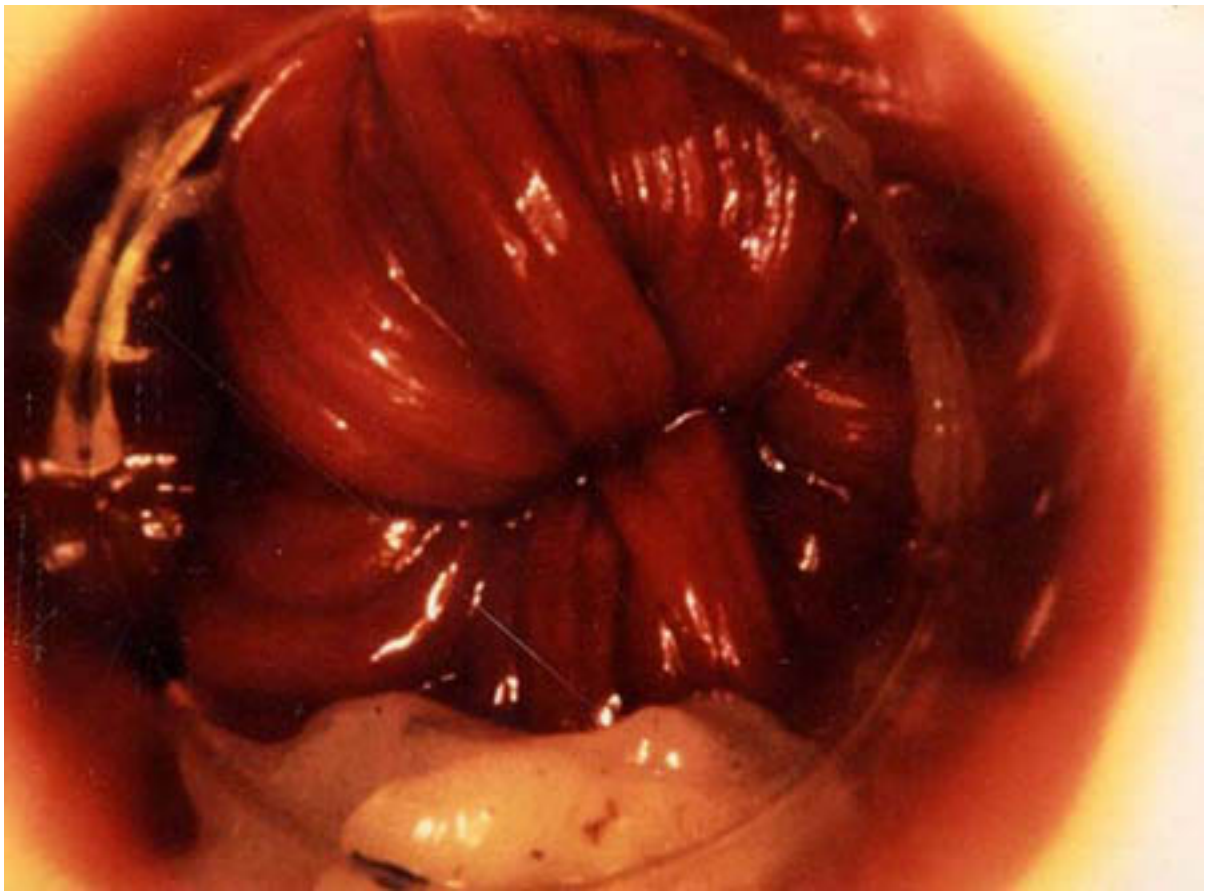

Fig. 47. CEM - There is a mucopurulent cerviitis in the acute stage of the disease.

PART IV
FOREIGN ANIMAL DISEASES

DOURINE

(Slapsiekte, el Dourin, Mal de Coit, Beschalseuche, Covering Disease)

Definition

Dourine is a chronic trypanosomal disease of Equidae. The disease is transmitted almost exclusively by coitus and is characterized by edematous lesions of the genitalia, nervous system involvement, and progressive emaciation.

Etiology

Dourine is caused by *Trypanosoma equiperdum* (Fig. 48) (Doflein, 1901), a protozoan parasite related morphologically and serologically to *T. brucei*, *T. rhodesiense*, and *T. gambiense* (of the subgenus *Trypanozoon* of the *Salivarian* section of organisms of the pathogenic genus *Trypanosoma*). Different strains of the parasite vary in pathogenicity (5).

Host Range

Dourine is typically a disease of horses and donkeys. Positive CF tests have been obtained from zebras, although it has not been shown that zebras can be infected with *T. equiperdum* or transmit the disease. The organism has been adapted to a variety of laboratory animals (5,6,9).

Improved breeds of horses seem to be more susceptible to the disease. The disease in these animals often progresses rapidly and involves the nervous system. In contrast, native ponies and donkeys often exhibit only mild signs of the disease. Infected male donkeys, which may be asymptomatic, are particularly dangerous in the epidemiology of the disease, for they may escape detection as carriers.

Geographic Distribution

Once widespread, this disease has been eradicated from many countries. It is currently present in most of Asia, southeastern Europe, South America, and in northern and southern Africa (3)

Transmission

This venereal disease is spread almost exclusively by coitus. Organisms are present in the urethra of infected stallions and in vaginal discharges of infected mares. The organism may pass through intact mucous membranes to infect the new host. Infected animals do not transmit the infection with every sexual encounter, however. As the disease progresses, trypanosomes periodically disappear from the urethra or vagina; during these periods, the animals are noninfective. Noninfective periods may last for weeks or months and are more likely to occur in the later stages of the disease. Thus, transmission is most likely early in the disease process.

It is possible for mares to become infected and pregnant after mating with an infected stallion. Foals born to infected mares may be infected. It is unclear if this occurs in utero or during birth. Because trypanosomes may occur in the milk of infected mares, these foals may be infected per os during birth or by ingestion of infected milk. Foals infected in this way may transmit the disease when mature and develop a lifelong positive CF titer. This method of disease transmission is rare, however. Some foals may acquire passive immunity from colostrum of infected mares without becoming actively infected; in such foals, the CF titer declines, and the animal becomes seronegative by 4 to 7 months of age. Although the possibility of noncoital transmission remains uncertain, it is supported by sporadic infections in sexually immature

equids (1,3,5).

Incubation Period

The incubation period is highly variable. Clinical signs usually appear within a few weeks of infection but may not be evident until after several years (1,5,7).

Clinical Signs

Clinical signs vary considerably, depending on the virulence of the infecting strain, the nutritional status of the infected animal, and the presence of other stress factors. The strain prevalent in southern Africa (and formerly in the Americas) is apparently less virulent than the European, Asian, or north African strains and produces an insidious, chronic disease. In some animals, clinical signs may not be apparent for up to several years (so-called latent infection). Clinical signs may be precipitated by stress in these animals.

In mares, the first sign of infection is usually a small amount of vaginal discharge, which may remain on the tail and hindquarters. Swelling and edema of the vulva develop later and extend along the perineum to the udder and ventral abdomen. There may be vulvitis and vaginitis with polyuria and other signs of discomfort such as an elevated tail. Abortion is not a feature of infection with mild strains, but significant abortion losses may accompany infection with a more virulent strain.

In stallions, the initial signs are variable edema of the prepuce and glans penis (Fig. 49), spreading to the scrotum and perineum and to the ventral abdomen and thorax. Paraphimosis may be observed. The swelling may resolve and reappear periodically. Vesicles or ulcers on the genitalia may heal and leave permanent white scars (leukodermic patches). Transient cutaneous plaques are a feature of the disease in some locations and strains but not others. When they occur, they are pathognomonic. Conjunctivitis and keratitis are often observed in outbreaks of dourine and may be the first signs noted in some infected herds.

Nervous disorders may be seen soon after the genital edema or may follow by weeks or months. Initially these signs consist of restlessness and the tendency to shift weight from one leg to another followed by progressive weakness and incoordination and ultimately by paralysis and recumbency. Anemia and emaciation sometimes accompany development of clinical signs even though the appetite remains unaffected.

Dourine is characterized by stages of exacerbation, tolerance, or relapse that may vary in duration and occur several times before death or recovery. The course of the disease may last several years after infection with a mild strain. Experimentally, horses have survived for up to 10 years after infection. The course is apparently more acute in the European and Asian forms of the disease in which the mortality rate is higher (1,5).

Gross Lesions

Anemia and cachexia are consistent findings in animals that have succumbed to dourine. Edema of the genitalia and ventral abdomen become indurated later in the course of the disease. Chronic lymphadenitis of most lymph nodes may be evident. Perineural connective tissue becomes infiltrated with edematous fluid in animals with nervous signs, and a serous infiltrate may surround the spinal cord, especially in the lumbar or sacral regions (1,5,7).

Mortality

Although the course of the disease may be long, it is usually fatal. Uncomplicated dourine does not appear to be fatal unless the nervous system is involved. The progressive debilitation associated with the neurological manifestation of the disease predisposes infected animals to a variety of other conditions. Because of the long survival time in some experimental cases, reports of recovery from dourine should be regarded with skepticism.

Diagnosis

Field Diagnosis

Diagnosis on physical signs is unreliable because many animals develop no sign. When signs are present, however, they are suggestive of a diagnosis of dourine. If "silver dollar plaques" occur, they are pathognomonic for dourine.

Specimens for Laboratory

Detection of trypanosomes is highly variable and is not a reliable means for diagnosis of dourine. The following specimens should be submitted: serum, whole blood in EDTA, and blood smears.

Laboratory Diagnosis

A reliable complement-fixation test (CFT) has been the basis for the successful eradication of dourine from many parts of the world. The antigen used in the CFT is group-specific, leading to cross-reactions with sera of horses infected with *T. brucei*, *T. rhodesiense*, or *T. gambiense*. The test is therefore most useful in areas where these parasites do not occur. Indirect fluorescent antibody, card agglutination, and enzyme-linked immunosorbent assay test (ELISA) have also been developed for dourine but have not replaced the CFT (1,3,4,5,6,10,11).

Differential Diagnosis

The perineal and ventral abdominal edema characteristic of dourine may also be seen in horses with anthrax. These signs may also resemble infection with equine infectious anemia or equine viral arteritis. Coital exanthema and purulent endometritis (as occurs in contagious equine metritis) should also be considered.

Treatment

Although there are reports of successful treatment with trypanocidal drugs (e.g., suramin at 10 mg/kg IV, quinapyramine dimethylsulfate at 3-5 mg/kg SC), treatment is more successful when the disease is caused by the more virulent (European) strains of the parasite. In general, treatment is not recommended for fear of continued dissemination of the disease by treated animals (1,6). Treatment may result in inapparent disease carriers and is not recommended in a dourine-free territory.

Vaccination

Immunity to trypanosomiasis is complicated. *T. equiperdum* has the ability periodically to replace major surface glycoprotein antigens, which is a strategy supporting chronic infections (2). No method of immunization against dourine exists at present.

Control and Eradication

The most successful prevention and eradication programs have focused on serologic identification of infected animals. Infected animals should be humanely destroyed or castrated to prevent further transmission of the disease. Some geldings may still show service behavior and constitute a risk. All equids in an area where dourine is found should be quarantined and breeding should be stopped for 1 to 2 months while testing continues.

Sanitation and disinfection are ineffective means of controlling the spread of dourine because the disease is normally spread by coitus.

Public Health

Humans are not susceptible to infection with *T. equiperdum*.

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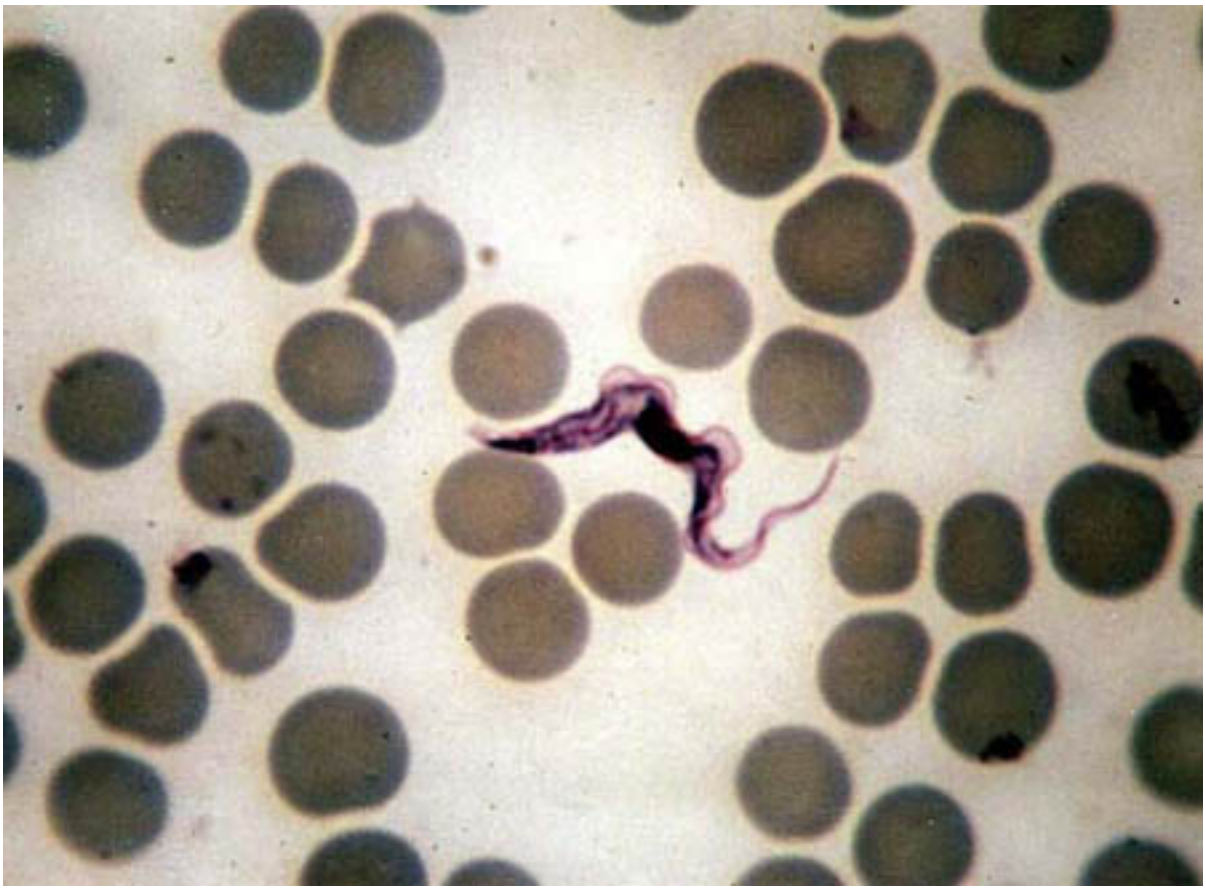

Fig. 48. Dourine - Organism in a blood smear.

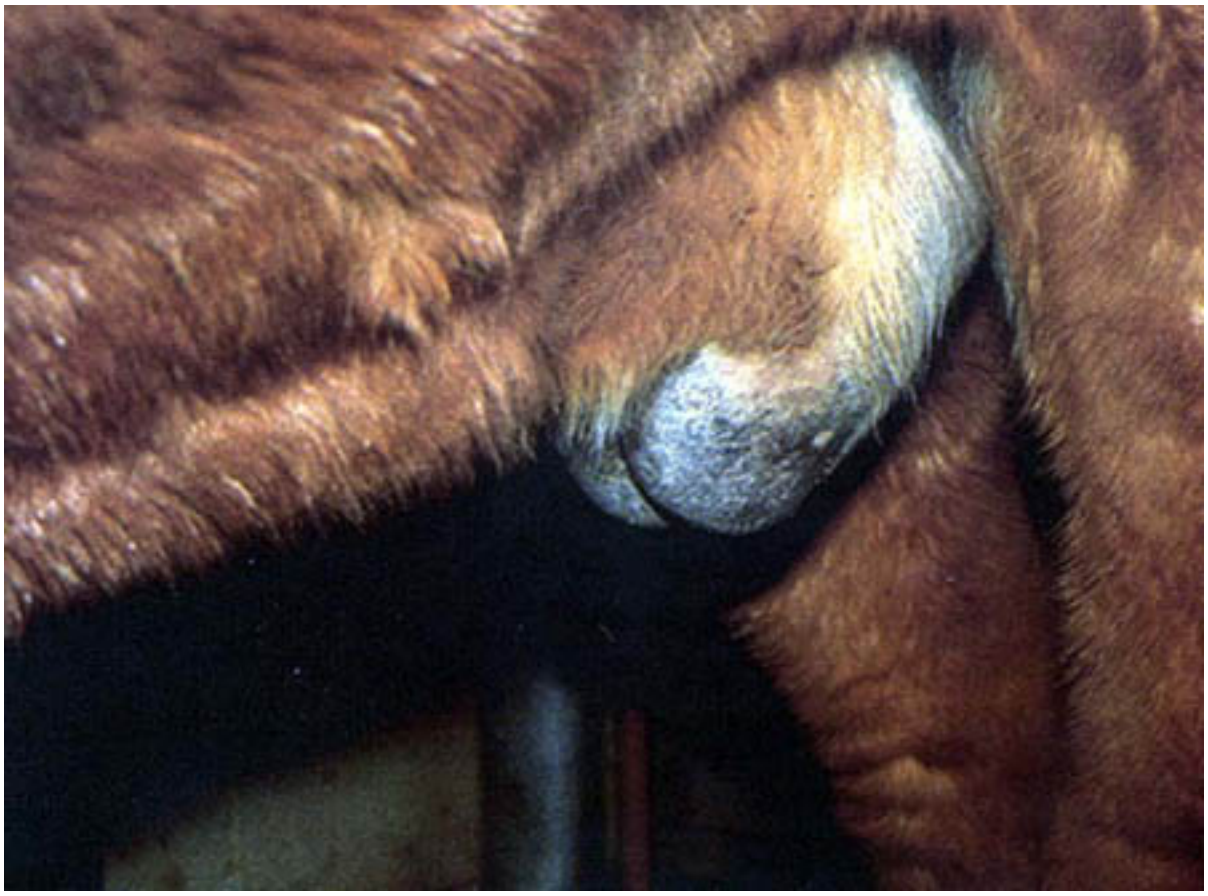

Fig. 49. Dourine - Swollen sheath.

PART IV
FOREIGN ANIMAL DISEASES

EAST COAST FEVER

(Theileriasis, Theileriosis, Zimbabwean tick fever, African Coast fever, Corridor disease, January disease)

Definition

East Coast fever (ECF), a form of bovine theileriosis, is a tick-transmitted protozoal disease of cattle characterized by high fever and lymphadenopathy. The disease causes high mortalities in breeds nonindigenous to the endemic areas, and is confined to eastern, central, and parts of southern Africa.

Etiology

The causative agent of classical ECF is *Theileria parva*. Some previously recognized separate species and subspecies have been combined with *T. parva* as a result of recent studies on their DNA (1,2).

The life cycle of *T. parva* is complex in its tick and mammalian hosts (2). Sporozoite stages, produced in large numbers in the acinar cells of the salivary glands of the infected tick vector, are inoculated along with saliva during feeding and rapidly enter target lymphocytes, which become transformed after the Theileria schizont is formed. The infected lymphocyte is transformed into a lymphoblast and divides in conjunction with the schizont, giving rise to two infected daughter cells. This process has been termed "parasite-induced reversible transformation" because, if the cells are treated with antitheileria drugs, the transformed cells revert to quiescent lymphocytes (3).

Within the infected lymphocytes, schizonts are associated with microtubules involved in spindle formation during host cell division (2). Clonal expansion of infected cells occurs with an approximate tenfold increase of schizonts every 3 days. Schizonts, traditionally called macroschizonts or Koch's blue bodies vary in size and in the number of nuclei. Early detectable forms are small with nuclei that, when Giemsa-stained, appear as chromatic granules.

From day 14 after tick infection of cattle, individual schizonts undergo merogony to produce merozoites (traditionally called microschizonts). Merozoites invade the erythrocytes to become piroplasms, which may subsequently undergo limited division also by merogony (4), Piroplasm-infected erythrocytes are ingested by ticks of the larval or nymphal stages and undergo a sexual cycle in the gut of the replete tick to produce zygotes, which in turn develop into motile kinete stages that infect the salivary glands of the next instar, the nymph or adult (5,6).

Host Range

Cattle in endemic areas, particularly the zebu type (*Bos indicus*), appear less susceptible to ECF, as do young animals. In addition, introduced cattle, whether of a taurine, zebu, or sanga breed, are much more susceptible to theileriosis than cattle from endemic areas. The Indian water buffalo (*Bulbalis bulbalis*) is as susceptible to *T. parva* infection as cattle. The African buffaloes (*Syncerus caffer*) are reservoirs of *T. parva* infection, and it has recently been proved that waterbucks (*Kobus* spp.) are also reservoirs (2). Buffaloes may suffer clinical disease from *T. parva* infection, but its effects on waterbuck are unknown. Organisms isolated from buffalo, on repeated passage in cattle, result in a parasite that produces disease characteristics indistinguishable from those associated with ECF (2). Hence, the organism causing ECF is assumed to be a cattle-adapted form of the buffalo parasite causing Corridor disease.

Piroplasms can be demonstrated in most wild antelopes in east Africa, but the relationship of most of them to *T. parva* is unclear.

Geographic Distribution

The distribution of ECF is strictly associated with the distribution of the vector tick species. In the case of *Rhipicephalus appendiculatus*, the area extends from southern Sudan to South Africa and as far west as Zaire. The range of *T. parva* is less than the tick vector for *T. parva*-free populations of R. appendiculatus occur in Zambia, Kenya, and South Africa. *R. appendiculatus* is found from sea level to over 8,000 feet in areas where there is annual rainfall of over 20 inches (500 mm). Up to three generations of the tick vector can occur per year in favorable areas of east Africa (Lake Victoria Basin), but there is only one generation a year in southern and central Africa because of a behavioral diapause, controlled by photoperiod, in the adult tick (2). This results in a strict seasonal occurrence of the different tick stages on cattle and a seasonal occurrence of ECF. This behavioral diapause allows the tick to survive during the long hot dry seasons occurring in the southern parts of Africa. Tropical theileriosis caused by *T. annulata* infection does not overlap in distribution with *T. parva* and is transmitted by ticks of the genus *Hyalomma*. It is distributed in north Africa, down the Nile Valley to Sudan, southern Europe, the Middle East, and parts of Asia, including the Indian subcontinent and China.

Transmission

Rhipicephalus appendiculatus is the main field vector of ECF, although in certain areas other field vectors occur, such as *R. zembeziensis* in drier areas of southern Africa and *R. duttoni* in Angola. East coast fever is not maintained in the absence of these field vectors. The rhipicephalid vectors are three-host ticks, and transmission occurs from stage to stage; transovarian transmission does not occur. Ticks can remain infected on the pasture for up to 2 years depending on the climatic conditions and the stage of infection, for adults survive longer than nymphs (2). The parasite dies out faster in hot climates and in nymphs compared with adults (2). Normally, for transmission to occur, the infected tick has to attach for several days to enable sporozoites to mature and be emitted in the saliva of the feeding tick. However, under high ambient temperatures, ticks on the ground may develop infective Theileria sporozoites, which can be transmitted to cattle within a few hours after attachment (2).

Unlike other Theileria species and Babesia species, *T. parva* is not easily transmitted experimentally by blood. Schizont-infected lymphoid tissues have been used to initiate infection with variable results.

Incubation Period

Under experimental conditions, using either ticks of known infection or sporozoite stabilate, the incubation period has a medium range of 8 to 12 days. The incubation period may be much more variable in the field owing to differences in challenges experienced by the cattle and may extend to beyond 3 weeks after attachment of infected ticks.

Clinical Signs

The first clinical sign of ECF in cattle appears 7 to 15 days after attachment of infected ticks. This is seen as a swelling of the draining lymph node, usually the parotid, for the ear is the preferred feeding site of the vector. This is followed by a generalized lymphadenopathy in which superficial subcutaneous lymph nodes such as the parotid, prescapular, and prefemoral lymph nodes, can easily be seen and palpated (Fig. 50). Fever ensues and continues throughout the course of infection. This rise in temperature is rapid and is usually in excess of 103° F (39.5° C) but may reach 106° F (42° C). Anorexia develops, and loss of condition follows. Other clinical signs may include lacrimation, corneal opacity, nasal discharge, terminal dyspnea, and diarrhea. Before death the animal is usually recumbent, the temperature falls, and there is a severe dyspnea due to pulmonary edema that is frequently seen as a frothy nasal discharge. Death usually occurs 18 to 30 days after infestation of susceptible cattle by infected ticks. Mortality in fully susceptible cattle can be nearly 100 percent. The severity and time course of the disease

depend on, among other factors, the magnitude of the infected tick challenge, for ECF is a dose- dependent disease, and on the strain of parasites. Some stocks of parasites cause a chronic wasting disease. A fatal condition called "turning sickness" is associated with the blocking of brain capillaries by infected cells and results in neurological signs.

In recovered cattle, chronic disease problems can occur that result in stunted growth in calves and lack of productivity in adult cattle (17). However, this syndrome tends to be in the minority of recovered clinical cases; in a majority of cases, asymptomatic carriers can be recognized with apparently little or no effect on their productivity (17). A review of the clinical disease is given by Irvin and Mwanachi (11).

Gross Lesions

A frothy exudate is frequently seen around the nostrils of an ECF-infected animal. Signs of diarrhea, emaciation, and dehydration may be seen. Lymph nodes are greatly enlarged and may be hyperplastic, hemorrhagic, and edematous (Fig. 51). In acute cases of ECF, lymph nodes are edematous and hyperemic but often become necrotic and shrunken in more chronic disease. Generally, muscles and fat appear normal but, depending on relative acuteness of infection, fat may become greatly depleted; serosal surfaces have petechial and ecchymotic hemorrhages, and serous fluids may be present in body cavities. Hemorrhages and ulceration may be seen throughout the gastrointestinal tract — particularly in the abomasum and small intestine, where necrosis of Peyer's patches can be observed. Lymphoid cellular infiltration appear in the liver and kidney as white foci that have been referred to as pseudoinfarcts. The most striking changes are seen in the lungs. In most cases of ECF, interlobular emphysema and severe pulmonary edema appear, the lungs are reddened and filled with fluid, and the trachea and bronchi are filled with fluid and froth.

Morbidity and Mortality

Morbidity and mortality depend on, among other factors, the magnitude of the infected tick challenge and susceptibility of the host and strain of parasite. East Coast fever in susceptible cattle, which are not indigenous to the enzootic area, is very severe with a mortality approaching 100 percent. Animals that recover are often unthrifty and sickly. Zebu cattle residing for many generations in endemic areas become infected (100 percent morbidity), but only a minor proportion succumb; however, many become carriers, and early infection with *T. parva* can affect their growth and productivity (17).

Diagnosis

Field Diagnosis

East coast fever is only found in association with its known tick vectors, *Rhipicephalus appendiculatus*, *R. zembeziensis* and possibly *R. duttoni* and *R. nitens* (2). A febrile disease with signs of enlarged lymph nodes associated with infestation by tick vectors is suggestive of ECF. An acute disease with high mortality on farms, where tick control is not effectively applied, also is suggestive of ECF. In many epidemiological situations, high mortality occurs only in calves; the adult cattle represent immune survivors.

In the field, diagnosis is usually achieved by finding Theileria parasites in Giemsa-stained blood smears and lymph node needle biopsy smears (Fig. 52).

Specimens for Laboratory

Specimens consisting of buffy coat smears air-dried and fixed in methanol; lymph node impressions air-dried and fixed in methanol; lymph nodes, spleen, lung, liver, and kidney samples for histopathology; and serum should be collected.

Laboratory Diagnosis

The demonstration of schizont-infected cells in lymph node samples is diagnostic of ECF. Small piroplasms in erythrocytes are suggestive of ECF, but diagnosis must be confirmed by the detection of schizonts. Schizonts can be detected in sections but are best seen in smears

Antibody in the mammals can be detected by a variety of serological tests of which the most widely used is the indirect fluorescent antibody test employing cell culture schizont antigen. Enzyme-linked assays have been developed using whole parasite lysates or specific antigens isolated by monoclonal antibodies (14). Because of the often acute nature of the disease, serological tests are useful in detecting a changed immune status of recovered animals within an exposed herd. Now DNA technologies can be applied to material from cattle and ticks, including the use of probes and the polymerase chain reaction (1,2,15,16).

Differential Diagnosis

Identification of schizonts in lymphoid cells is considered to be pathognomonic of ECF. However, it must be realized that in an area such as Kenya, five species of *Theileria* have been recognized in cattle (*T. parva*, *T. mutans*, *T. velifera*, *T. taurotragi* and *T. buffeli*) and it is possible for an individual animal to harbor all these parasites at once (2). Also, all these species produce schizonts which, except for those of *T. mutans*, are not morphologically distinct (2). Piroplasms of *Theileria* spp. have similar morphology and thus are difficult to differentiate on blood slides. In addition, recovered animals, particularly in areas with endemic stability, become carriers of parasites and may show both *T. parva* schizont and piroplasm stages without clinical ECF (2).

Theileria parva derived from African buffalo (*Syncerus caffer*), which causes Corridor disease in cattle, is characterized by production of low parasitosis and parasitaemia in cattle although it can result in high fatality rates (2). Because enzyme-linked immunosorbant assay antibody and antigen tests and DNA probes are being developed for this range of *Theiletia* species, it will become easier to differentiate them in the field. Other species tend to either be of low pathogenicity (*T. mutans*, *T. taurotragi*, *T. buffeli*) or avirulent (*T. velifera*) in cattle.

T. annulata is the cause of Mediterranean or tropical theileriosis, which is also a severe disease of cattle; although it is endemic in northern Africa, there is no evidence that its distribution overlaps with that of *T. parva* (2).

Gross postmortem lesions of ECF may be confused with those of a variety of diseases such as the following:

1. Heartwater because of pulmonary edema and hydrothrax. Examination of brain smears and lymph node or spleen impression smears can differentiate between the two diseases.

2. Trypanosomiasis because of edema, lymphadenopathy, and anemia. Blood and lymph node smear examination will normally differentiate between the two diseases.

3. Babesiosis and anaplasmosis because of anemia. These diseases can easily be differentiated from ECF on examination of blood smears.

4. Malignant catarrhal fever because of lymphadenopathy and corneal opacity. Examination of blood and lymph node smears will clearly differentiate between the two diseases.

Treatment

There are currently three effective drugs for the treatment of ECF: parvaquone (Clexon), buparvaquone (Butalex), and halofuginone lactate (Terit). Each of these drugs has been introduced to the market within the last 15 years (2). The availability of a therapeutic means of controlling ECF is a significant development. However, there are two constraints to widespread use of medication: the drugs are too expensive for most African farmers, and rapid, accurate diagnosis is required for effective therapy (2).

Vaccination

Methods of immunization using live parasites have been summarized by Cunningham (19). The most successful involves an "infection and treatment method" initially using oxytetracycline and more recently the newer drugs mentioned above. Animals are inoculated with a potentially lethal dose of infective sporozoite stabilate prepared from ticks and treated either simultaneously (tetracyclines, buparvaquone) or subsequently (parvaquone and halofuginone) with a drug. Sporozoite stabilates are produced from adult ticks fed as nymphs on infected cattle; the adult ticks are ground up in a medium after prefeeding on rabbits for 4 days, and the sporozoite suspension is prepared by centrifugation and cryopreserved as a stabilate. Extensive trials have been carried out using infection and treatment immunization in the ECF zones, and this method is now approved for field use by several countries in Africa (2). Problems do occur in the recognition of suitable antigenic stocks for immunization (2), and any vaccination scheme can only follow after a careful assessment of the local complex of *T. parva* parasites. In any population of *T. parva* parasites in the field, an isolate may constitute several strains. This method of immunization requires a reliable cold chain and extensive monitoring. Recovery from ECF usually results in an excellent immunity to homologous or related stocks of the parasite, lasting for over 3 1/2 years in the absence of reinfection.

The nature of the immunity has been studied in some detail (2,20). Neutralizing antibodies to sporozoites have been recognized and related to a 67Kda antigen on the surface of the sporozoites. This has been synthesized by recombinant technology and has been shown to provide a degree of protection to cattle immunized with it (21). Other potential protective antigens have been recognized associated with the surfaces of sporozoites and schizont-infected cells (2).

Control

Preventive Measures

The current primary method of controlling ECF in cattle is immunization (see vaccination) and treatment of cattle with chemical acaricides. A number of acaricides, mainly organochlorides and organophosphorus compounds but recently synthetic pyrethroids and amidens, are applied in dips, spray races, or by handspraying. More recently, "pour on" or "spot on" formulations have been introduced. The application is usually on a weekly basis, but this rate has to be increased when the challenge is high. The cost of this control measure is becoming exorbitant, and the farming economies in many countries in Africa are not able to afford it. This may well be an advantage because this level of acaricide exposure leads to resistance of vectors, unacceptable residues in milk and meat, and, where successful, the creation of an epidemic instability with a large proportion of the cattle population becoming susceptible. A more rational approach using integrated control has been suggested by Young et al (18). These measures include effective fencing, pasture management, rotational grazing to reduce the level of challenge, selection of tick resistant cattle, and new methods of immunization; with strategic acaricide application, this approach offers a more satisfactory method of ECF control (18).

Sanitation and disinfection measures other than those associated with tick control are not applicable to ECF .

Public Health

Theilertia spp. show a high degree of host specificity for both the vector and the mammalian host. *Theileria parva* does not infect man.

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Fig. 50. ECF - In ECF there is generalized lymphadenopathy; note the prescapular lymph node.

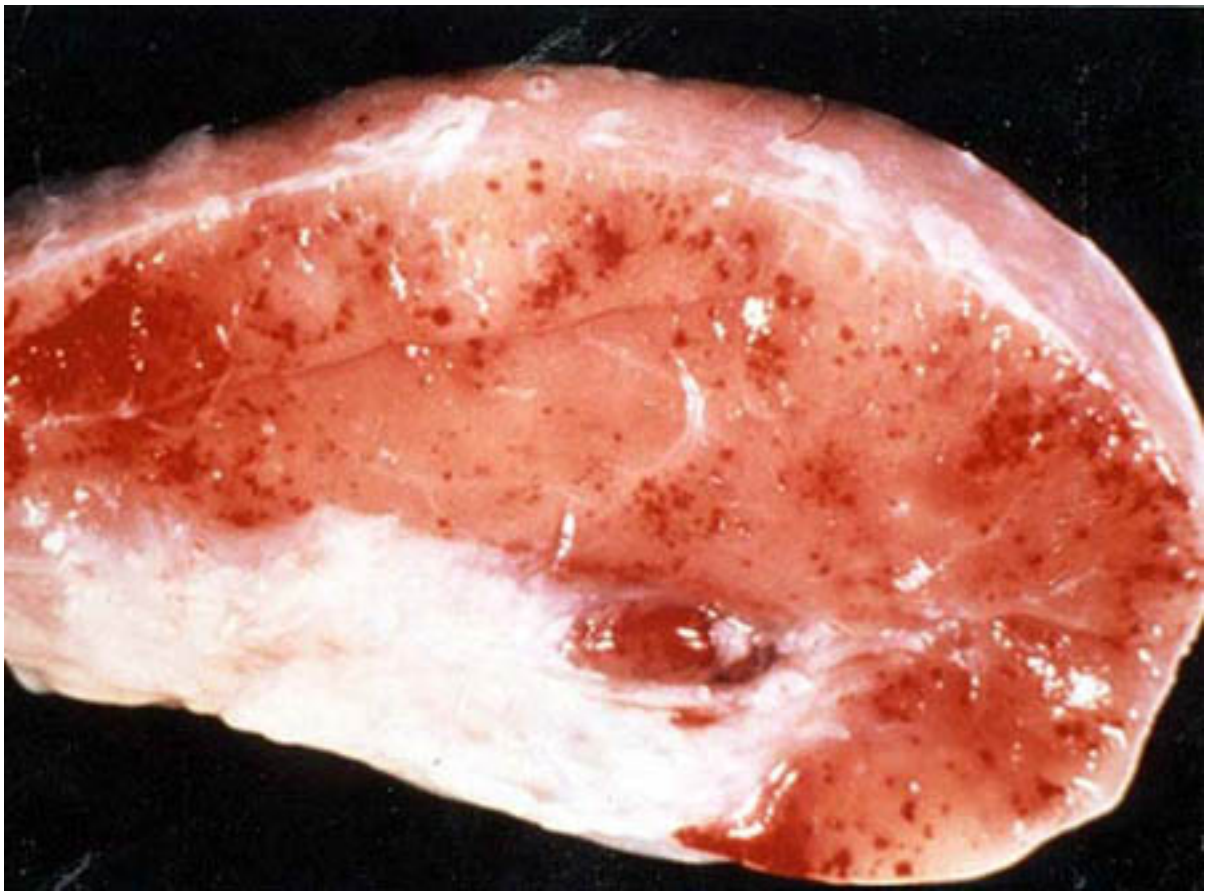

Fig. 51. ECF - Lymph nodes in ECF are enlarged, hemorrhagic, and edematous.

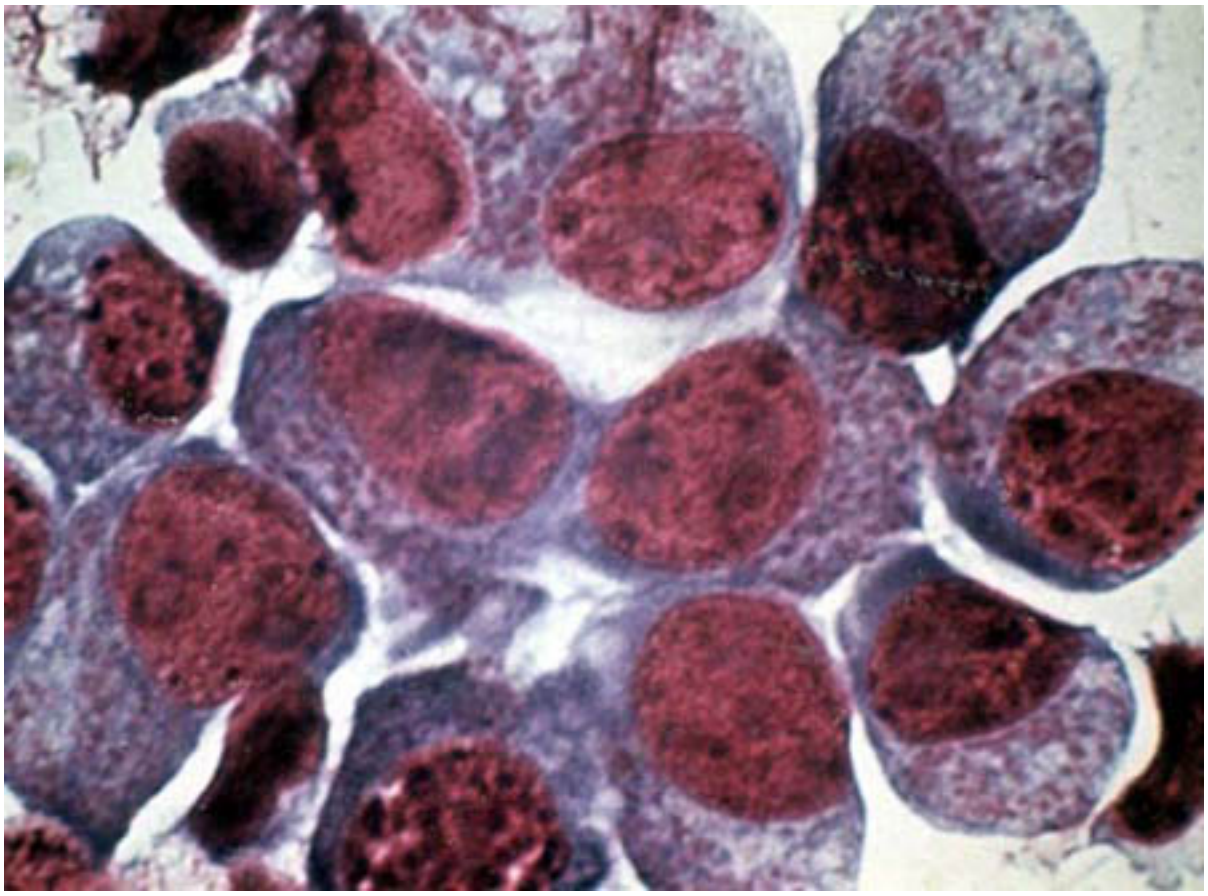

Fig. 52. ECF - Lymphoblasts containing *Theileria* parasites.

PART IV
FOREIGN ANIMAL DISEASES

EPIZOOTIC LYMPHANGITIS

(Pseudoglanders, Histoplasmosis farciminosi, Equine Blastomycosis, Equine Histoplasmosis, Equine Cryptococcosis, African Farcy)

Definition

Epizootic lymphangitis is a chronic infectious granulomatous disease of the skin, lymph vessels, and lymph nodes of the neck and legs of horses caused by *Histoplasma farciminosum*.

Etiology

Epizootic lymphangitis is caused by a dimorphic fungus, *Histoplasma farciminosum*, formerly known as *Cryptococcus farciminosis*, *Zymonema farciminosa*, *Saccharomyces farciminosus*, or *H. capsulatum* var. *farciminosum*. In tissue, the organism is present in a yeast form; it forms mycelia in the environment, has a saprophytic phase in the soil, and is relatively resistant to ambient conditions, which allows it to persist many months in warm, moist conditions (3).

Host Range

The natural host range seems to be limited to horses, donkeys, and occasionally mules. Rare cases of human infection have been reported, but identification of the causative organism has not been substantiated.

Geographic Distribution

Currently the disease is endemic in west, north, and north-east Africa, the Middle East, India, and the Far East. The disease earned its designation of epizootic during the international conflicts of the first half of the twentieth century in which large numbers of horses were congregated and moved. Many outbreaks occurred in military animals.

Transmission

H. farciminosum is introduced via open wounds. Transmission generally involves infection of wounds by flies contaminated by feeding on the open wounds of infected animals (1,7). (The organism has been isolated from the gastrointestinal tract of flies [1]).

Incubation Period

The incubation period is variable and is usually several weeks.

Clinical Signs

There is no breed, sex, or age predilection in epizootic lymphangitis. This disease most typically involves the skin and associated lymph vessels and nodes. In addition, the conjunctiva and nictitating membrane may be involved. Occasionally there is involvement of the respiratory tract (1,3,7,8). The body temperature and general demeanor of the animal are not changed. The initial lesion is a painless cutaneous nodule about 2 cm in diameter. This nodule is intradermal and is freely moveable over the subcutis. Lesions are most commonly found on the skin of the face, forelimbs, thorax, and neck or the (less often) medial aspect of the rear limbs. The subcutaneous tissue surrounding the nodule becomes diffusely edematous. The nodule gradually enlarges and ultimately bursts. Some cases do not progress beyond small, inconspicuous lesions that heal spontaneously. More typically, resultant ulcers increase in size and undergo cycles of granulation and partial healing followed by renewed eruption. The

surrounding tissues become hard, variably painful, and swollen. The infection spreads along lymph vessels and causes cord-like lesions, leading to diffuse and irregular involvement of an area of skin. After, a lesion initially increases in size, additional cycles of eruption and granulation lead to progressively smaller areas of ulceration until eventually only a (usually stellate) scar remains. The development and regression of a lesion takes about 3 months (1,3,7,8). Where lesions overlie joints, involvement may extend to synovial structures and produce severe arthritis.

Conjunctivitis or keratoconjunctivitis may occur — usually in conjunction with skin lesions (1). A serous or purulent nasal discharge containing abundant organisms may be observed. Although respiratory lesions are described as common in older literature (3), this form of the disease appears to be rare in more recent outbreaks (1)

Gross Lesions

The affected skin and subcutaneous tissue is thickened, fibrous, and firm. Several purulent foci may be apparent on cut section. Lymphatic vessels are distended with pus. Regional lymph nodes are swollen, soft, and reddened and may contain purulent foci. Arthritis, periarthritis, and periostitis have been described. The nasal mucosa may have multiple, small gray-white nodules or ulcers with raised borders and granulating bases. Nodules and abscess may occur in internal organs, including the lungs, spleen, liver, and testes (3).

Morbidity and Mortality

The incidence of disease is high only when large numbers of animals are collected together (as in military situations, for racing, or on village commonages). Mortality is low.

Diagnosis

Field Diagnosis

Although the clinical presentation of the disease may lead to a presumptive diagnosis of epizootic lymphangitis, the similarity of this disease to glanders makes laboratory confirmation essential.

Specimens for Laboratory

A whole or section of a lesion and a serum sample should be collected aseptically. The samples should be kept cool and shipped on wet ice as soon as possible. Sections of lesions in 10 percent buffered formalin and air-dried smears of exudate on glass slides should be submitted for microscopic examination.

Laboratory Diagnosis

Demonstration of the yeast in tissue sections or smears of lesions is considered the most reliable means of diagnosis. Attempts to culture the organism fail in up to half of cases (1,2,8). The organism in the tissues is in its yeast form. It may be stained with Giemsa, Diff-Quik, or Gomori methenamine silver (2,8). In addition, an indirect fluorescent antibody technique for demonstration of the organism has been developed (4).

Affected animals do mount a humoral immune response to the infection, and an enzyme-linked immunosorbent assay (ELISA) for the diagnosis of epizootic lymphangitis has been developed (5,6). Attempts have also been made to utilize intradermal skin testing (with histoplasmin or histofarcin) with encouraging results (5,10).

Differential Diagnosis

Epizootic lymphangitis must be differentiated from glanders (mallein test and serology, absence of yeasts in the pus), strangles (which usually occurs in outbreak form, affects mainly young animals, is always acute and febrile, and is not associated with cutaneous nodules, buds and

ulcers), and ulcerative lymphangitis (which is more acute and caused by Corynebacterium pseudotuberculosis).

Treatment

Successful treatment with intravenous administration or sodium iodide, oral administration of potassium iodide, and surgical excision of lesions where possible has been reported, but recurrences of clinical signs months later is possible (3,7). In vitro sensitivity of the organism to amphotericin B, nystatin, and clotrimazole has been reported (7,8). In most areas, epizootic lymphangitis is a reportable disease, and treatment is not allowed. Affected animals must be destroyed (1).

Vaccination

Horses that recover from clinical infection are immune to reinfection. Although promising results have been obtained with experimental vaccines, a vaccine is not commercially available.

Control and Eradication

Strict hygienic precautions are essential to prevent spread of epizootic lymphangitis. Great care should be taken to prevent spread by grooming or harness equipment. Contaminated bedding should be burned. The organism may persist in the environment for many months.

Epizootic lymphangitis is a chronic disease. Many mildly affected horses recover. Those that do are reputedly immune for life — a belief that has led to a premium being placed in endemic areas on horses with characteristic scars (3). In most areas of the world, however, this is a reportable disease; treatment of clinical cases is not permitted, and destruction of affected horses is usually mandatory. In most areas, epizootic lymphangitis has been eradicated by a strict policy of slaughter of infected animals.

Public Health

Although rare cases of human infection have been reported, they have not been substantiated by unequivocal identification of the causative organism.

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PART IV
FOREIGN ANIMAL DISEASES

EQUINE MORBILLIVIRUS PNEUMONIA
(Since publication of this volume, equine morbillivirus pneumonia has been renamed "Hendra virus disease")

(Acute respiratory syndrome)

Definition

Equine morbillivirus pneumonia (EMP) is an acute febrile respiratory infection of horses characterized by fever, increased respiratory and heart rates, respiratory distress, and death.

Etiology

The cause of EMP is a newly recognized virus in the genus *Morbillivirus* and was named equine morbillivirus (EMV). When EMV was tested against antisera to a range of paramyxoviruses, morbilliviruses, and pneumoviruses there was a very weak reaction with only rinderpest virus (4).

History

Equine morbillivirus pneumonia has been reported only in Australia. The disease was first recognized on one property in Hendra, Australia, in September 1994. In this outbreak, 20 horses were sick and 13 died, and 2 humans were infected and 1 died (4). A retrospective diagnosis of EMP was made for horses that died in August 1994 on a property in Mackay about 1,100 km from the first reported case of EMP. In this outbreak four horses were infected and two died; the farmer became ill, recovered, had a relapse, and died of EMV infection 13 months later. There was no evidence of epidemiological association between these outbreaks (5,6).

Host Range

Equine morbillivirus has naturally caused disease in horses and humans. Experimentally, cats and guinea pigs have been infected (3). The disease in cats is very similar to the disease in horses (8). The recent detection of neutralizing antibody to EMV in the native Australian fruit-bats suggests a possible resevoir for EMV (10).

Geographic Distribution

Equine morbillivirus pneumonia has been reported only in Australia.

Transmission

On the basis of epidemiologic findings and experimental results with cats, EMV is not readily transmissible. In the field, very few horses in contact with infected horses became ill, and even horses placed in uncleaned stalls previously occupied by an infected horse did not become ill (8). For both animals and humans, EMV seems to require direct contact with respiratory secretions of infected animals (6). If a fruit-bat is the reservoir, the mechanism for spread to the horse is not known.

Incubation Period

The incubation period in horses is 8 to 14 days (2).

Clinical Signs

The initial case of EMP in both outbreaks was a pregnant mare on pasture. Clinical signs in field cases at Hendra were fever up to 105.8º F (41º C), severe respiratory distress, and death. Two horses that recovered had mild myoclonic twitching (5). In the Mackay outbreak, the pregnant mare had "severe respiratory distress, ataxia, and marked swelling of the head — particularly of the infraorbital fossa and cheeks. The second horse, a stallion (horse B), reportedly showed aimless pacing, muscle trembling and a haemorrhagic nasal discharge" and died (5).

In experimentally infected horses, the first sign of disease was fever that ranged from 102.2 to106º F (39 to 41.2º C). In some animals, as the disease progressed, heart and respiratory rates increased up to 72 and 60 per minute, respectively, breathing became labored, and the animal's demeanor varied from somnolence to mild agitation (2).

Gross Lesions

The most distinctive gross lesion in EMP is a bilateral "pulmonary edema characterized by gelatinous distention of subpleural lymphatics." The lungs are heavy and congested; the edema is more prominent in the ventral parts and the lungs vary from a mottled yellowish-brown to dark blue. The major air passages are essentially normal. In one experimental horse, there was also a bilateral dilation of the pulmonary lymphatics and a very enlarged dark spleen (2).

Morbidity and Mortality

The number of animals that have been infected naturally and experimentally is small, but using these numbers, mortality is high in animals infected. Owing to the low transmissibility of EMV, morbidity has been low.

Diagnosis

Field Diagnosis

Equine morbillivirus pneumonia should be suspected when a horse that dies has been febrile and the necropsy findings include a pulmonary edema characterized by gelatinous distention of subpleural lymphatics.

Specimens for Laboratory

Specimens sent to the laboratory for culture should consist of pieces of lung, liver, spleen, kidney, lymph nodes, brain, and heparinized blood. For serology, serum samples from acute and convalescent animals should be submitted. For histopathologic examination, send a complete set of tissues in 10 percent formalin.

Laboratory Diagnosis

To confirm a suspected diagnosis of EMP, the virus has to be isolated and identified. The disease can tentatively be diagnosed by histopathology as well as histochemical and molecular biological techniques.

Differential diagnosis

Because of the pulmonary edema, African horse sickness is a primary consideration in a differential diagnosis.

Other causes of acute death are poisons, intoxications (botulism), and acute bacterial diseases such as anthrax.

Treatment

There is no treatment for the primary disease.

Vaccination

There is no vaccine.

Control and Eradication

In Australia, disease control and eradication procedures consisted of slaughter of known infected horses and extensive serological surveillance. No antibody to EMV was detected in sera from 98 horses remaining on the Hendra property, in sera from horses on adjacent properties, nor in sera from horses on trace-back and trace-forward properties. No EMV antibody was detected in sera collected from the Queensland population of nonracing horses selected using a stratified proportional approach (7).

Public Health

If one considers that there have been three human infections and two human deaths in only two outbreaks of this disease, maximum precautions should be used if this disease is suspected. The three individuals infected had extensive contact with the infected horses and "assisted in their necropsies without gloves, mask, or protective eyeware"(6). It should be noted, however, that others also had contact with the animals and conducted or participated in necropsies and did not get infected; thus it is suspected that "direct contact with respiratory secretions of infected animals seems to be necessary for transmission"(6).

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PART IV
FOREIGN ANIMAL DISEASES

FOOT-AND-MOUTH DISEASE

(Afta epizootica, Bek-en-klouseer, Fiebra aftosa, Fievre aphteuse, Maul-und-Klauenseuche)

Definition

Foot-and-mouth disease (FMD) is a highly contagious viral infection primarily of cloven-hoofed domestic animals (cattle, pigs, sheep, goats, and water buffalo) and cloven-hoofed wild animals. The disease is characterized by fever and vesicles with subsequent erosions in the mouth, nares, muzzle, feet, or teats.

Etiology

The FMD virus (FMDV) is a member of the genus *Aphthovirus* in the family Picornaviridae. There are seven serotypes of FMDV: A, O, C, Asia 1, and Southern African Territories (SAT) 1, 2 and 3. Within these serotypes, over 60 subtypes have been described, and new subtypes occasionally arise spontaneously. However, at a specific time, there are only a few subtypes causing disease throughout FMD endemic areas. The importance of subtypes is that a vaccine may have to be tailored to the subtype present in the area in which the vaccine is being used.

The FMD virus is pH sensitive; the virion is inactivated when exposed to pH below 6.5 or above 11. However, in milk and milk products, the virion is protected and can survive at 70º C for 15 seconds and pH 4.6. Between pH 6.7 and 9, stability increases with decreasing temperature; the virus in cell culture medium will remain viable for a year at 4º C. The virus in serum or other organic material will survive drying and can be carried on inanimate objects. In meat, the virus can survive for long periods in chilled or frozen bone marrow and lymph nodes.

Host Range

Cloven-footed domestic and wild animals are primarily affected. Examples of other susceptible species are hedgehogs, armadillos, nutrias, elephants, capybaras, rats, and mice.

Geographic Distribution

Foot-and-mouth disease, after World War II, was widely distributed throughout the world. In 1996, endemic areas were Asia, Africa, and parts of South America. In South America, Chile is free, and Uruguay and Argentina have not had an outbreak since April 1994. Most European countries have been recognized as free. Countries belonging to the European Union have stopped FMD vaccination. North and Central America, Australia, New Zealand, Japan, and the British Isles have been free of FMD for many years.

Geographic Serotype Prevalence of FMD

It is interesting how certain serotypes tend to be restricted to certain areas of the world.

Some examples are as follows:

Europe (historically)	A (5) O (1) C (1)
Asia	
Near East	A (22) O (1)

Middle East	A (22) O (1) C Asia (1)
Far East	A O (1) C Asia (1)
Africa	
Central East to West	A O
Northeast Central and South	SAT 1 and 2
South	SAT 3
Serotype C is uncommon in Africa	
South America	A (24), (27) O (1) C (3)

Transmission

The FMD virus can be introduced into a free area by the following means:

1. Direct or indirect contact with infected animals.

2. Spread of aerosol from infected animals (requires proper humidity and temperature). Aerosol from bulk milk trucks spread FMD in England. A person in contact with infected animals can have sufficient FMDV in his or her respiratory tract for 24 hours to serve as a source of infection for susceptible animals.

3. Feeding contaminated garbage (meat, milk, blood, glands, bones, cheese, etc.)

4. Contact with contaminated objects (hands, footwear, clothing).

5. Artificial insemination.

6. Contaminated biologicals such as hormones (extraction procedure may not inactivate the virus).

After an animal becomes infected by any means, the primary mode of spread is then via respiratory aerosols. Other important means of spread are direct and indirect contact. In an outbreak of FMD, the roles of the three primary hosts in transmission are as follows:

Sheep act as maintenance hosts,

Pigs act as amplifiers,

Cattle act as indicators.

When sheep or goats become infected with FMDV, the disease may not be diagnosed for a considerable time because signs and lesions can be very mild. However, during this time, the animals will be producing infectious aerosols, contaminating fomites, and spreading the virus by contact.

Foot-and-mouth disease in pigs spreads very rapidly, for they produce 30 to 100 times more virus in aerosols than sheep or cattle. An infected pig can produce a hundred million infectious doses per day.

When cattle are infected with FMDV, signs and lesions usually develop more rapidly and are more severe than in pigs, sheep, or goats. If cattle, sheep, and pigs are exposed together, cattle will usually get sick first. This may result from increased exposure due to a greater pulmonary tidal volume.

Some animals can be carriers of FMDV. Most ruminant species can harbor the virus in their pharyngeal tissues for a long period. Recovered cattle or vaccinated cattle exposed to diseased animals can become healthy carriers for 6-24 months. Sheep can be carriers for 4-6 months. Although under experimental conditions it has been difficult to demonstrate transmission of FMD from carriers to susceptible livestock, there is strong circumstantial field evidence that carriers may have been the occasional cause of outbreaks. Also it has been shown that the virus was maintained for many years in a relatively small, isolated group of African buffaloes without the appearance of clinical signs.

Some strains of FMDV seem to have a predilection for certain species. There have been strains that affect pigs but not cattle. In South America, mature cattle have had clinical signs of FMD, when sheep in an adjacent pasture were normal.

Incubation Period

After experimental exposure, signs may develop as early as 12 hours. The usual interval is 24 to 48 hours.

When susceptible animals are in contact with clinically infected animals (peak time of transmission is generally when vesicles rupture), clinical signs usually develop in 3 to 5 days.

Pigs fed infected garbage usually develop signs in 1 to 3 days. Intact oral epithelium is resistant to infection, but during the process of ingesting food there may be injury, and the virus may also enter through the tonsils.

Clinical Signs

Cattle

Initial signs are fever of 103-105º F (39.4-40.6º C), dullness, anorexia, and fall in milk production. These signs are followed by excessive salivation; drooling (Fig. 111), serous nasal discharge; shaking, kicking of the feet or lameness; and vesicle (blister) formation. Sites of predilection for vesicles are the tongue (Figs. 115, 117), dental pad, gums, soft palate, nostrils, muzzle, interdigital space (Fig.112), coronary band, and teats (Fig.116.). Vesicles may be difficult to see. The animal may need to be tranquilized to facilitate a thorough examination.

After vesicle formation, drooling may be more marked, and nasal discharge, lameness or both may increase. Pregnant cows may abort, and young calves may die without developing any vesicle.

The course of an FMD infection is 2 to 3 weeks. Secondary infection may delay recovery. A lactating animal may not recover to preinfection production because of damage to the secretory tissue.

Sequelae to FMD in Cattle

Secondary infection — mouth, nose, feet

Hoof deformation

Low milk production

Mastitis

Unthriftiness — failure to gain weight

Breeding problems

Panting — associated with pituitary gland damage

Diabetes mellitus

Swine

Initial signs are fever of 104-105º F (40-40.6º C), anorexia, reluctance to move (Fig. 113), and squeal when forced to move. These signs are followed by vesicles on the coronary band (Figs. 114, 119), vesicles on the heals, vesicles in the interdigital space (foot involvement is usually severe), and vesicles on the snout (Fig. 114). Mouth lesions are not too common and when they occur are smaller and of shorter duration than in cattle and tend to be a "dry"-type lesion (Fig. 118). There is no drooling. Sows may abort. Piglets may die without showing any clinical sign.

Sheep and Goats

Clinical signs, if they occur, tend to be very mild, and may include dullness; fever; and small vesicles or erosions on the dental pad, lips, gums, and tongue. Mild lameness may be the only sign. In lame animals there may be vesicles or erosion on the coronary band or in the interdigital space. Infected animals may abort. Nursing lambs may die without showing any clinical sign.

Gross Lesions

Cattle

The diagnostic lesions are single or multiple vesicles ranging from 2 mm to 10 cm. These can occur at all sites of predilection. Gross lesions on the tongue usually progress in the following manner:

1. A small blanched whitish area develops in the epithelium.

2. Fluid fills the area, and a vesicle (blister) is formed.

3. Vesicle enlarges and may coalesce with adjacent ones.

4. Vesicle ruptures.

5. Vesicular covering sloughs leaving an eroded (red) area (Figs. 117, 120).

6. Gray fibrinous coating forms over the eroded area.

7. Coating becomes yellow, brown or green.

8. Epithelium is restored, but line of demarcation remains; line then gradually fades.

Occasionally "dry" FMD lesions develop. Instead of forming a vesicle, the fluid is apparently lost as it forms and the upper layers of the epithelium become necrotic and discolored. The lesion therefore appears necrotic rather than vesicular.

Gross Lesions on the Feet:

The vesicle in the interdigital space is usually large because of the stress on the epithelium caused by movement and weight. The lesion at the coronary band at first appears blanched; then there is separation of the skin and horn. When healing occurs, new horn is formed, but a line resulting from the coronitis is seen on the wall of the hoof.

Gross Cardiac and Skeletal Lesions:

Animals that die may have grayish or yellowish streaking in the myocardium - degeneration and necrosis. These findings are known as "tiger heart" (Fig. 121). Skeletal muscle lesions occur but

are rare.

Swine

Vesicles on the snout can be large and filled with clear or bloody fluid. Mouth lesions are usually the "dry" type and appear as necrotic epithelium. Feet lesions are usually severe, and the hoof can become detached. Animals that die may have grayish or yellowish streaking in the myocardium with degeneration and necrosis ("tiger heart").

Sheep

Lesions in the mouth and vesicles on the coronary band may be few, small, and difficult to find. Animals that die may have grayish or yellowish streaking in the myocardium with degeneration and necrosis ("tiger heart").

Morbidity and Mortality

The morbidity rate is essentially 100 percent in a susceptible population of domestic animals. Mortality is usually less than 1 percent, but in young animals and with certain isolates mortality can be high. In an FMD outbreak in Israel, there was a high mortality (at least 50 percent) in wild mountain gazelles. The same virus caused typical low mortality in cattle. In the gazelles, there was a severe viral pancreatitis that accounted for the high mortality.

Diagnosis

Field Diagnosis

In cattle, FMD should be considered whenever salivation and lameness occur simultaneously and a vesicular lesion is seen or suspected. Fever often precedes other clinical signs; therefore, febrile animals should be carefully examined. Early diagnostic lesions may be found before animals start to salivate, have a nasal discharge, or become lame. To avoid missing a diagnosis, examine the mouth of a lame animal and the feet of any animal with signs or lesions involving the mouth or nostrils. Typically, FMD spreads rapidly and there is a high clinical attack rate; however, this cannot be counted upon, for a relatively avirulent strain could appear, or more resistant animals (sheep) could be affected.

In pigs, sheep, and goats, FMD should be considered when animals have sore feet, vesicular lesion is suspected, or both.

Specimens for Laboratory Diagnosis

Because the various vesicular diseases have similar clinical signs, a laboratory diagnosis is mandatory. Oral, nasal, foot, or mammary lesions are good sources of specimens. The following should be collected from each of two or three animals:

1. Vesicular fluid (as much as possible).

2. Epithelium covering a vesicle.

3. Flaps of epithelial tissue still attached.

(For 2 and 3 above, try to collect about 0.5 gm.)

Old necrotic or fibrinous material that is difficult to remove is undesirable and often is highly contaminated with bacteria.

4. About 5 ml of blood with anticoagulant (viremia ends about 5 days after the onset of disease).

5. Esophageal—pharyngeal (OP) fluid from convalescent cattle, sheep, or goats.

This should immediately be diluted with an equal volume of cell culture fluid (e.g., Hanks balanced salt solution with lactalbumin hydolysate) and shaken vigorously for about 1 minute. If the solution turns yellow, the pH is low and the virus could be inactivated; discard and collect another sample.

6. Blood for serum (10 ml of serum).

7. From dead animals, collect samples of epithelial lesions, lymph nodes, thyroid, adrenal gland, kidney, and heart (about 10 gm).

8. Full set of tissues in formalin.

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quickfreeze the specimens, and do not allow them to thaw during transit. If dry ice is used, be sure that the vials are tightly sealed with stopper and tape so that no carbon dioxide enters the vial. The carbon dioxide will lower the pH and inactivate FMDV. Epithelium can also be placed in buffered glycerin and kept at 39º F (4º C) or -4º F (-20º C). Ratio of epithelium to glycerin should not exceed 1:10.

Laboratory Diagnosis

To confirm the initial case of FMD, the virus has to be isolated and identified. After confirmation of the initial case, diagnosis can be made by antigen or nucleic acid detection, or both.

Serological tests are available to detect antibody and differentiate infected and vaccinated animals.

Differential Diagnosis

Differential diagnosis for FMD should include vesicular stomatitis, swine vesicular disease, vesicular exanthema of swine, foot rot, and chemical and thermal burns. In cattle, oral lesions caused by rinderpest, infectious bovine rhinopneumonitis, bovine virus diarrhea, malignant catarrhal fever, and bluetongue can be similar to the later lesions in FMD. In sheep, lesions caused by bluetongue, contagious ecthyma, and lip and leg ulceration can be similar to the later lesions of FMD.

Vaccination

Starting about 1951, FMD vaccine was produced by the Frenkel method. Normal tongue epithelium was removed, minced, placed in a nutrient broth, and inoculated with FMDV. After replication of

FMDV, the virus was inactivated with formalin, and aluminum hydroxide was added as an adjuvant. This method as well as virus propagation in cell culture is being used today to produce FMD vaccine.

Outbreaks of FMD have been traced to use of formalin-inactivated vaccine. Apparently, in some cases, vaccine contained viable virus. Today (1996) the classical FMD vaccines are prepared using binary-ethyleneimine (BEI) inactivated virus and aluminum hydroxide-saponin or oil as an adjuvant. Double emulsion oil vaccines have been shown to produce an immunity of longer duration than aluminum hydroxide-saponin vaccine.

To date, molecular-engineered vaccines have not been as effective or as economical as the cell culture vaccines.

When vaccinating animals, it is important that the vaccine contain the same subtype of virus as is in the area. This necessitates frequent checking of the serotype and subtype during an outbreak because FMD virus frequently changes during natural passage through various species.

Protection induced by a good aluminum hydroxide vaccine decreases rapidly in 4-6 months. A double emulsion oil vaccine can protect for up to 1 year.

Vaccinated animals that are not completely protected can be a source of infection. The virus may replicate and be shed, but the animals may not show any clinical sign of infection.

Control and Eradication

The official attitude of a country regarding control of a disease depends on how seriously the disease affects the country, the financial and technical ability of the country, and what its neighbors are doing. The degree of control of FMD varies as follows:

1. Virtually no control in some Asian and African countries where FMD is enzootic.

2. Protection of valuable or accessible animals or vaccination along a border to provide a buffer zone. (May vaccinate cattle because of severity of the disease but not sheep and goats.)

3. Large-scale vaccination and quarantine with or without slaughter of infected animals.

4. Regulatory measures to prevent entry of FMD virus and quarantine and implementation of an eradication program.

A country where FMD is endemic should be as concerned about introduction of FMD virus as a country that is free of FMD because the introduced virus may be a serotype to which the native animals have no immunity.

The following are the essential features of a control and eradication program:

1. Stop movement of animals and animal products in the area affected.

2. Slaughter infected animals (and known contact animals).

3. Destroy carcasses.

4. Disinfect vehicles leaving the infected area.

5. Perform vaccination.

If eradication by slaughter fails, vaccination may be used to control the outbreak. There are experimental results indicating that potent vaccine may induce significant immunity in 4 days to protect exposed cattle to FMD.

6. Inform and educate the community.

Most developed countries have detailed plans to deal with an outbreak of FMD.

Public Health

In a review of the zoonotic aspects of FMD by K. Bauer in 1997, he reported that, since 1921, FMD virus has been isolated and typed from slightly over 40 human cases (4). The cases occurred on three continents: Europe, Africa, and South America. Type O predominated, followed by C, and rarely A. Because infection is uncommon, FMD is not considered to be a public health problem.

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Fig. 111. FMD - Excessive salivation and drooling in acute FMD.

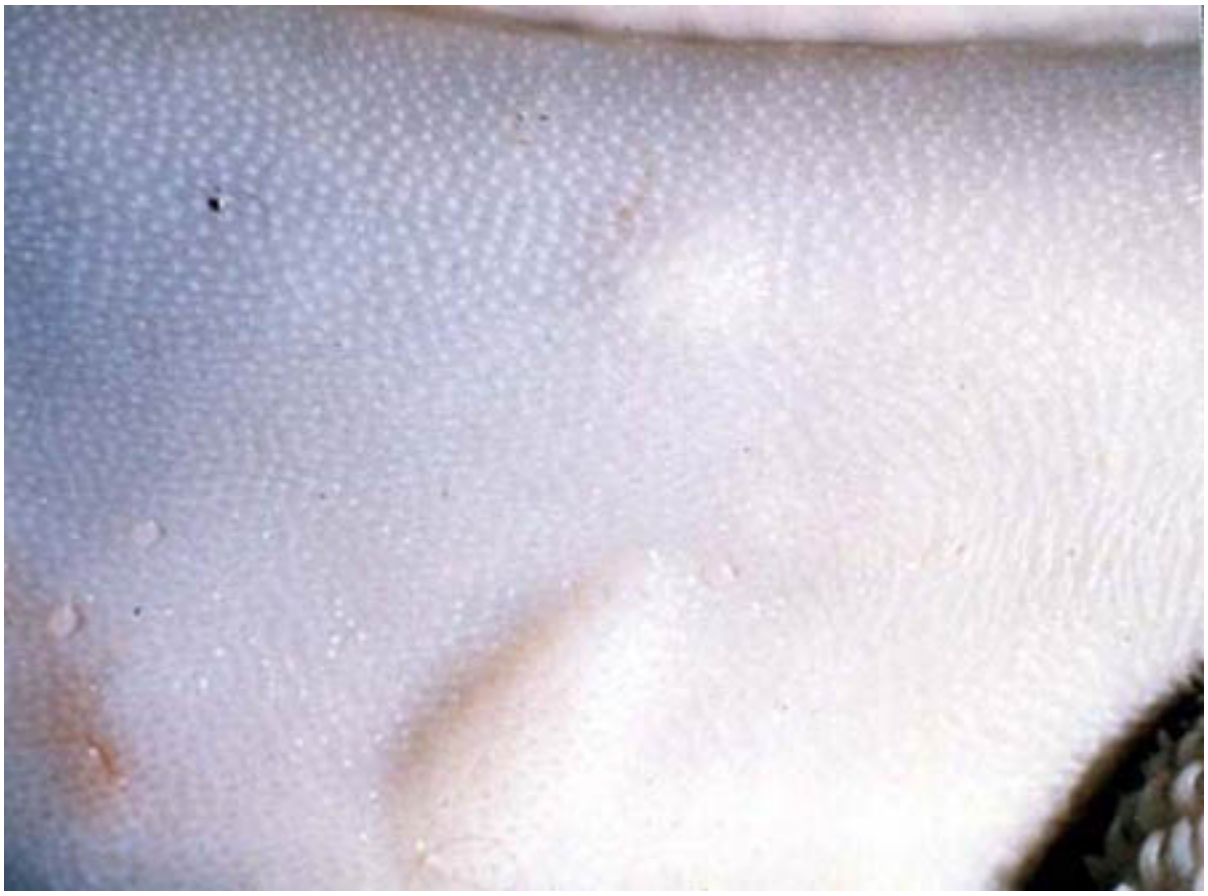

Fig. 115. FMD - Two unruptured vesicles on a bovine tongue.

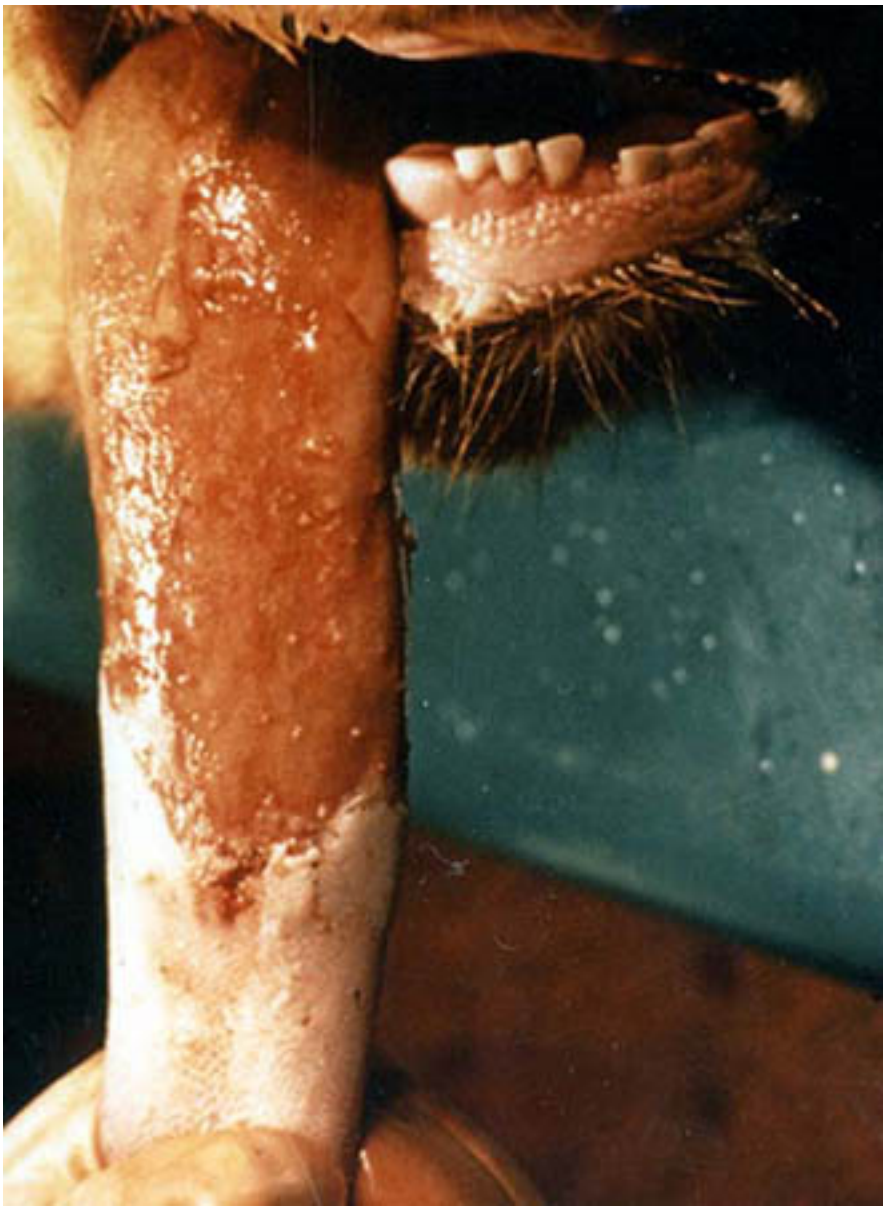

Fig. 117. FMD - Large erosion on the tongue of a steer.

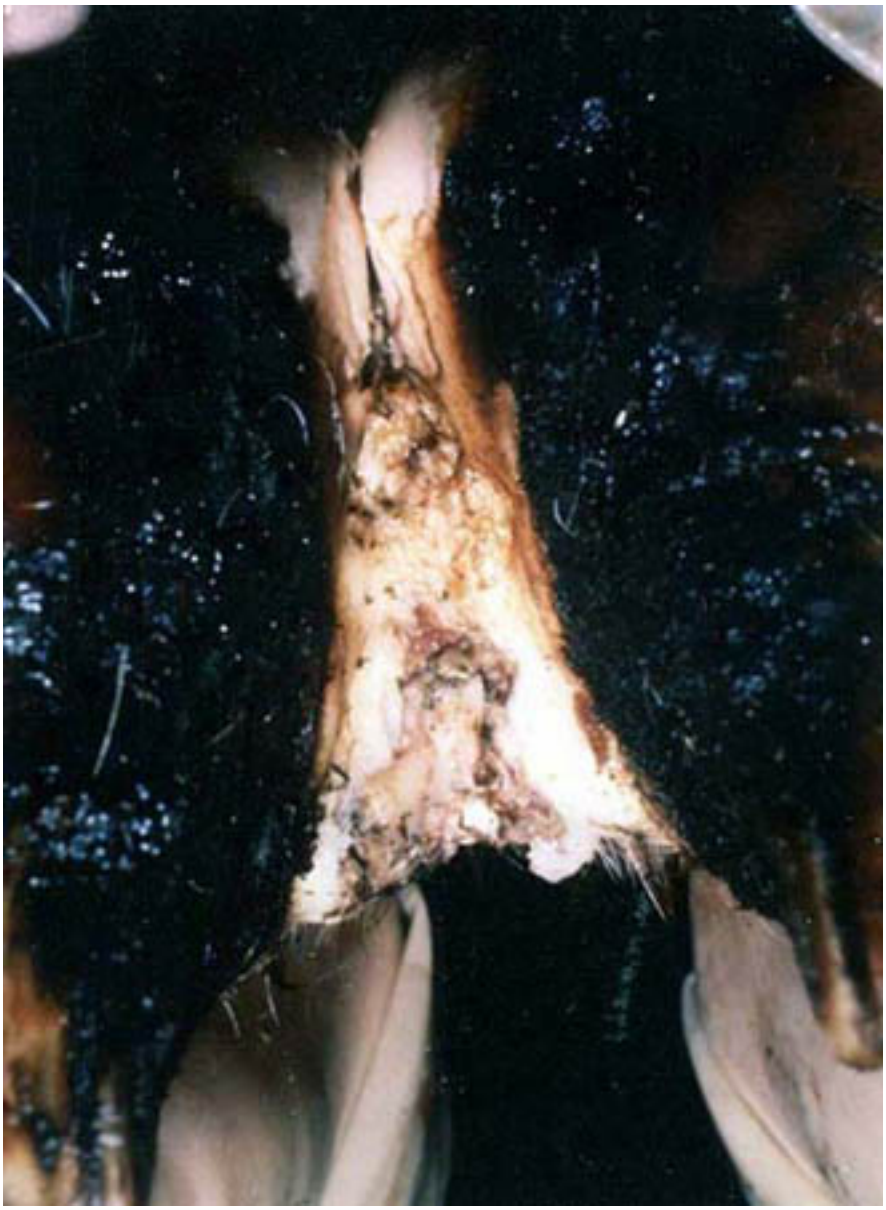

Fig. 112. FMD - Ruptured vesicles in the interdigital cleft of a steer.

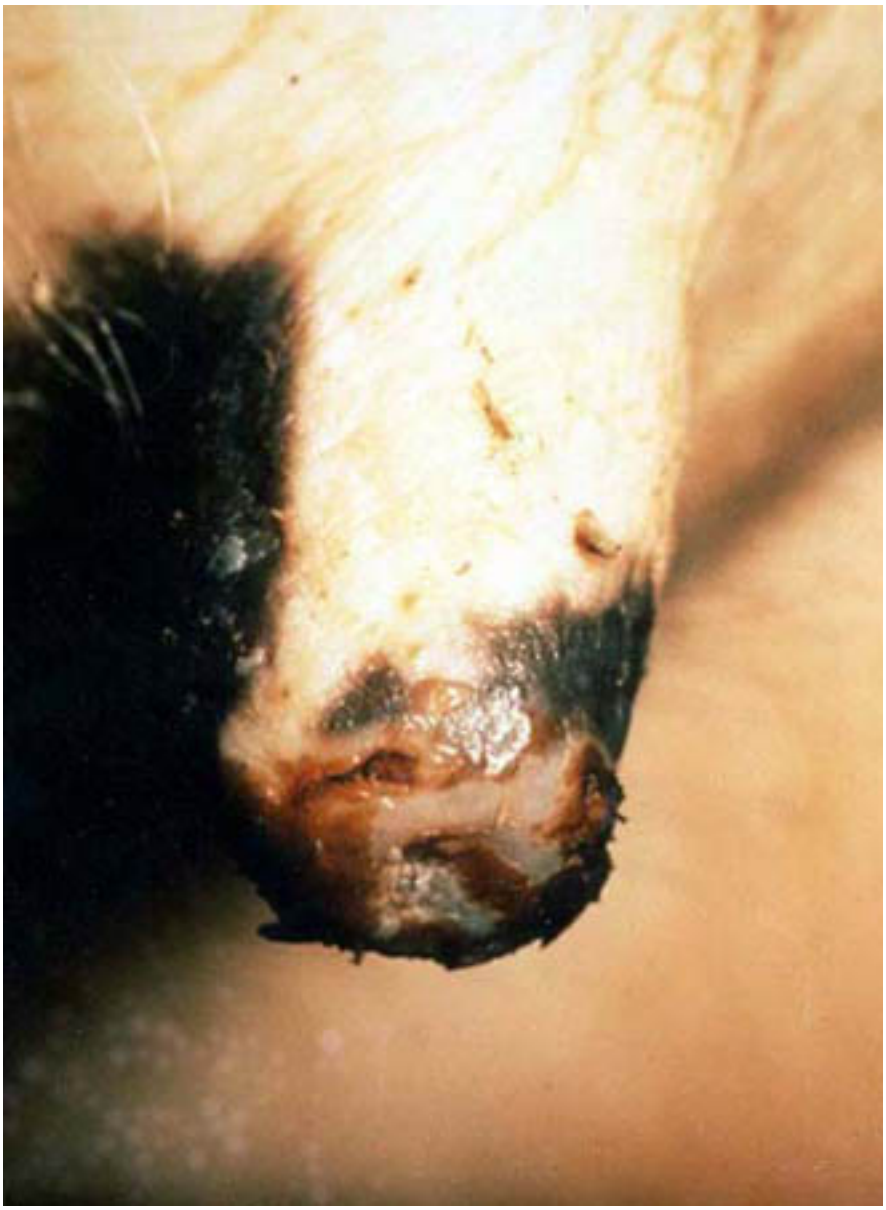

Fig. 116. FMD - Ruptured vesicles on the end of a bovine teat.

Fig. 113. FMD - Pigs with sore feet - note the position of the feet.

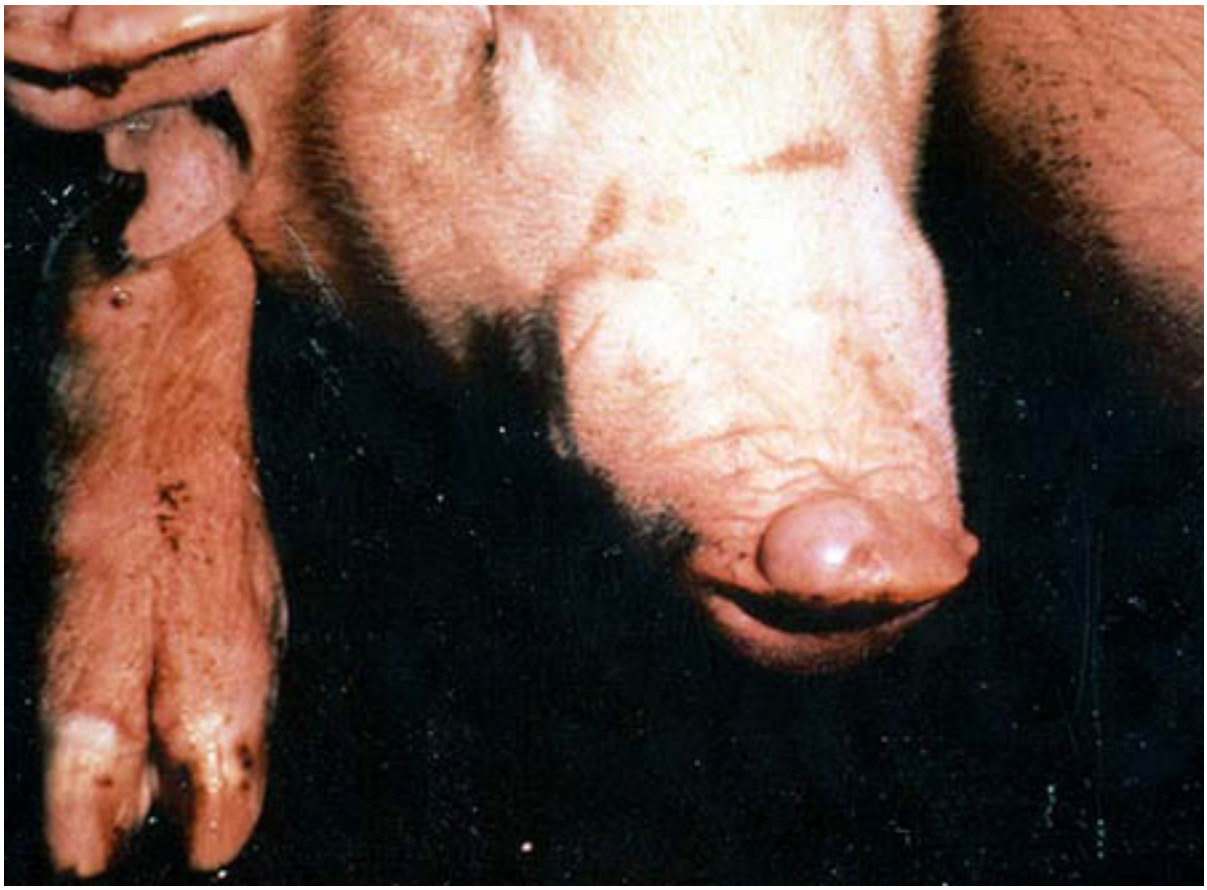

Fig. 114. FMD - Unruptured vesicle on the snout and blanching of the coronary bands.

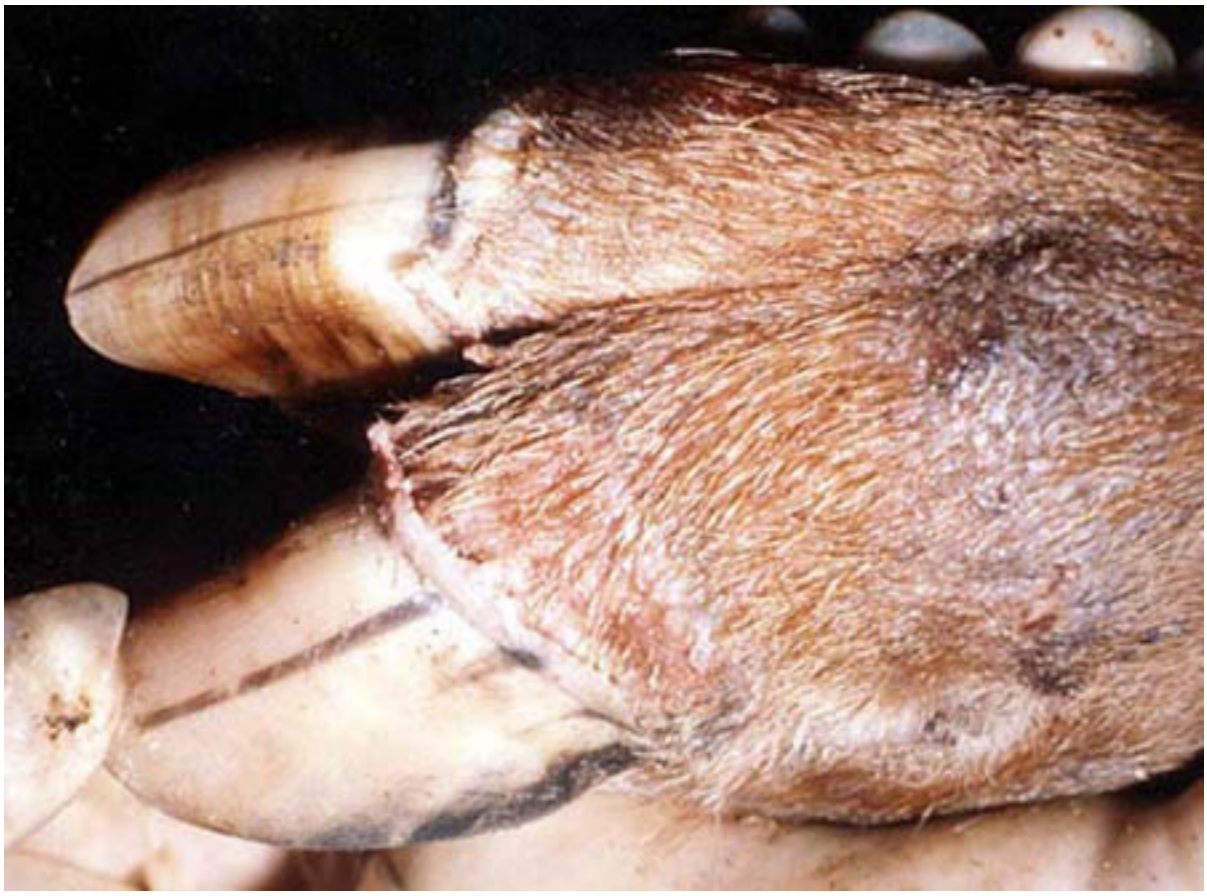

Fig. 119. FMD - Vesiculation and necrosis of the coronary band in a pig.

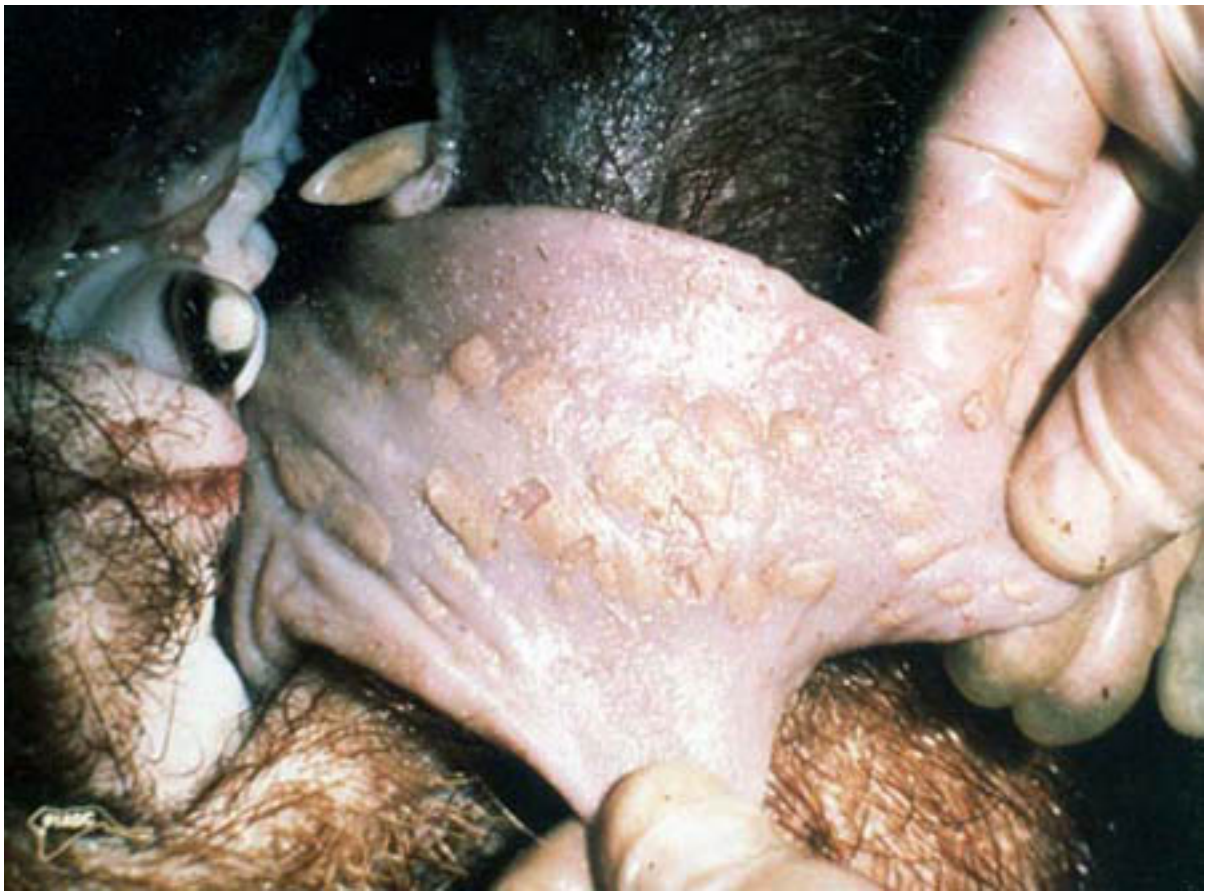

Fig. 118. FMD - Oral lesions in the pig are usually areas of epithelial necrosis.

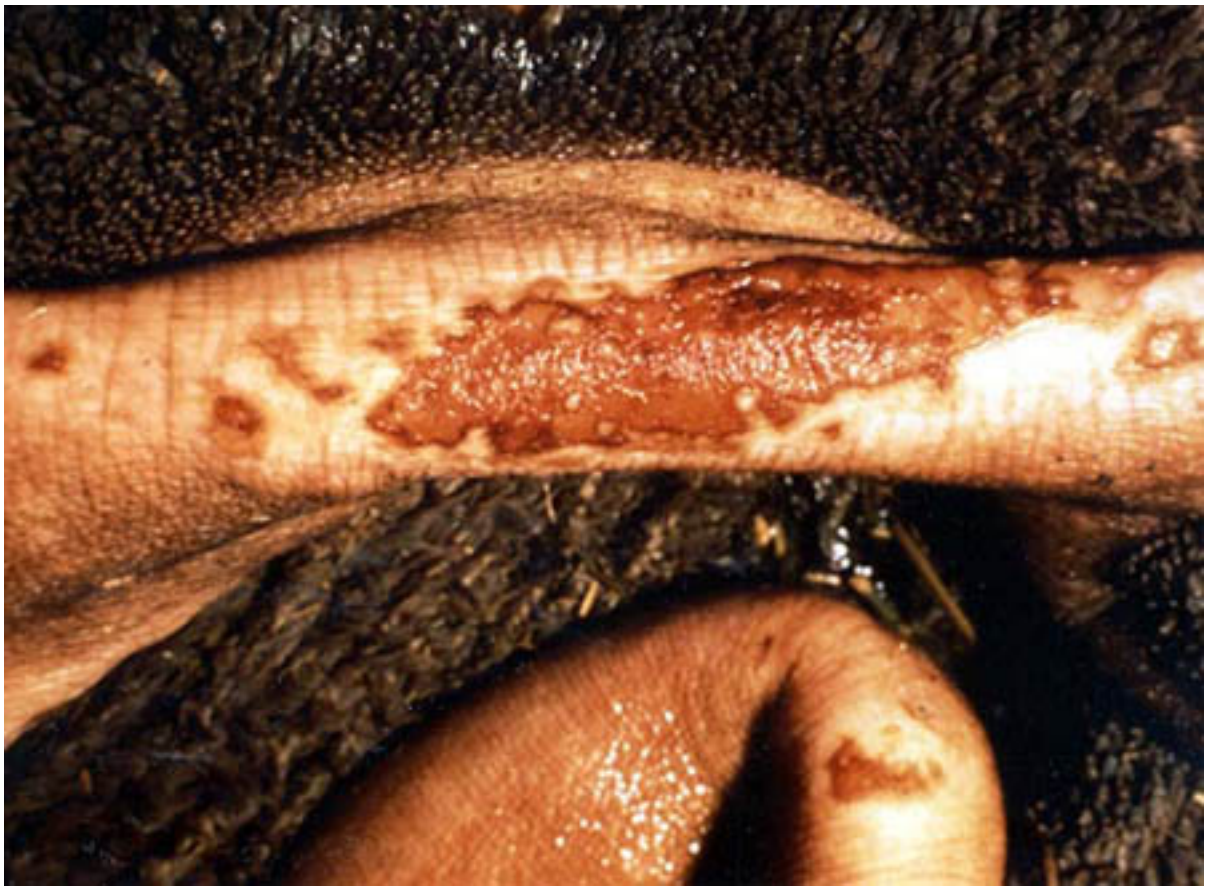

Fig. 120. FMD - Erosion of the epithelium on a rumen pillar.

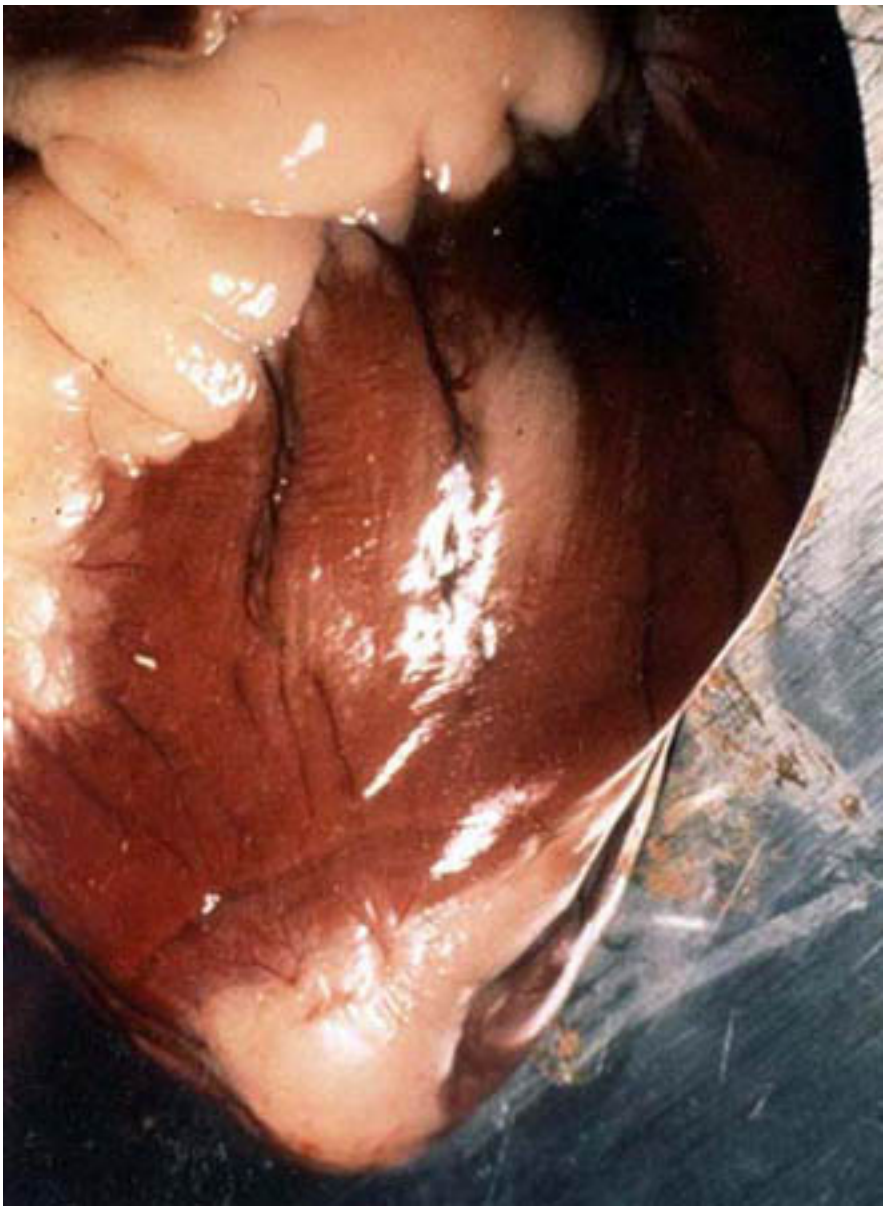

Fig. 121. FMD - Pale area in the myocardium is an area of myocardial necrosis.

PART IV
FOREIGN ANIMAL DISEASES

FOREIGN PESTS AND VECTORS OF ARTHROPOD-BORNE DISEASES

(Vector-borne Diseases and Arthropod Vectors)

In many areas of the world, particularly the tropics, arthropod-borne diseases are among the major limiting factors to the efficient production of livestock and poultry. These diseases result in debilitation, lameness, blindness, wasting, congenital defects, abortions, sterility, and death. Some exotic arthropod-borne diseases of livestock are zoonotic and affect humans as well as animals.

All of the major groups of pathogenic organisms have representatives that are transmitted by arthropod vectors and cause disease in domestic livestock or poultry. For example, over 400 arthropod-borne viruses (arboviruses) have been recognized, including the etiologic agents of such major livestock diseases as African swine fever, Akabane disease, bovine ephemeral fever, the equine encephalitides, bluetongue, and epizootic hemorrhagic fever (16). Rickettsial agents that are primarily tick-borne cause several extremely important livestock disease problems, including bovine and ovine anaplasmosis, heartwater, tick-borne fever, bovine infectious petechial fever, epizootic bovine abortion, Jembrana disease, and Q fever. Arthropod-borne bacteria cause such well-known diseases as borreliosis of cattle and horses, spirochetosis of poultry, tularemia, and Lyme disease.

Some of the most devastating of all animals diseases are caused by arthropod-borne blood protozoa, including babesiosis of cattle, sheep, goats, horses, and swine; theileriosis, the East Coast fever syndrome, and Mediterranean fever; the trypanosomiases causing illness in cattle, sheep and goats, camels, pigs, dogs, and many wild game species; as well as several arthropod-borne protozoa that cause diseases of birds. Bovine filariasis is a prime example of an exotic helminthic disease that is arthropod-borne. In fact, over half of all exotic diseases of livestock and poultry of critical concern to the United States are arthropod-borne.

The most prominent groups of arthropods that transmit etiological agents pathogenic to livestock are those that are blood-feeding (hematophagous) and are biologically involved in transmission cycles. Ticks, tsetse flies, mosquitoes, and biting midges, for example, have leading roles in the biological transmission of agents causing significant livestock and poultry diseases. Of somewhat lesser general importance are those hematophagous arthropod groups that mechanically transmit pathogens. Horse flies, deer flies, stable flies, horn flies, and others have been incriminated in disease transmission through interrupted feeding.

There are also those arthropod groups in which the many species are not blood sucking — such as muscoid flies, beetles, or grasshoppers — but which mechanically transport pathogens or serve as intermediate hosts of helminths. Of course, examples can also be found for any variety of transmission methods and cycles within each of the major vector groups.

As a whole, ticks are the most versatile vectors, for they parasitize all vertebrate groups except fish. The tick-borne diseases that they transmit are among the most significant animal health deterrents to efficient livestock production. The methods of pathogen transmission employed by ticks are both mechanical and biological. In the case of soft ticks belonging to the family Argasidae, the ability of some individuals to survive for 3 years or more between blood meals permits them to assume the dual role of vector and reservoir, which is particularly important in the transmission of African swine fever virus (16).

Mosquitoes are notorious as proven vectors of some of the most devastating human diseases. There is little need to document the impact on human public health of malaria, yellow fever, filariasis, and several mosquito-borne diseases of arboviral etiology. Rift Valley fever and the equine encephalitides are important livestock diseases transmitted by mosquitoes. Although over 2,500 species of mosquitoes have been described worldwide in 18 genera and subgenera, those species of greatest importance as vectors of pathogenic agents are found in the genera Aedes, Culex, Anopheles, and Mansonia.

Biting midges, particularly species of the genus Culicoides, have been incriminated in the transmission of viral, protozoal, and filarial agents pathogenic to livestock and poultry. Owing to their small size and difficulties encountered in colonization, scientific progress on their role as animal disease vectors has been delayed. However, considering the fact that biting midges are frequently among those species of biting flies in greatest abundance that attack livestock, increased attention should be given to them as animal disease vectors.

Although tsetse flies are limited in their distribution to sub-Saharan Africa, the importance of the animal trypanosomiases (nagana of cattle) on that continent ranks tsetse as one of the world's major arthropod-vector groups. The very complex developmental cycle of the trypanosome within the tsetse vector is further complicated by several of other factors related to the biology of the vector, pathogen, and host. Not only are the various species of tsetse flies characterized by differences in their distribution, biology, and host preferences, but even within the same species environmental factors (especially humidity, temperature, and vegetation), densities and composition of mammalian hosts, and vector population densities affect their epidemiological role. In addition, there are wide intraspecific variations in both morphology and pathogenicity of trypanosomes. Certain parasite antigens that stimulate production of protective antibodies by the host change before the parasites are completely eliminated; new antibodies are then produced by the host, and the parasites change their antigenic constitution again to maintain themselves.

The key to the success of arthropod-borne disease transmission lies in the competence of vector efficiency (6). Whereas one vector species may be extremely efficient in the transmission of a particular pathogen, a closely related species may be totally incompetent as a vector. Even within a single vector species, individuals and populations vary dramatically in their competence to transmit a particular pathogenic agent. The expression of vector competence appears to be controlled, in part, by genetic factors involving multiple genes. For example, although the biting midge species, Culicoides varipennis, is incompetent to transmit bluetongue virus in the Northeastern United States, populations of the same species from the Southwest and Western States are extremely efficient vectors of the virus. Genetic crosses between families of the insect vector species showed results consistent with the theory that a single genetic locus controls insect vector competence for infection with the bluetongue virus (12, 15).

Foreign Arthropod Pests and Arthropod-Borne Disease Factors

Although the introduction and establishment of any exotic arthropod pest of livestock or poultry, or any arthropod-borne disease vector, could have devastating results to affected industries, certain foreign species are of considerably greater importance than others. On the basis of potential for introduction, establishment, and economic impact, three categories of foreign arthropod pests and arthropod-borne disease vectors have been established (Appendix 2).

Category A. These species have the highest potential for introduction, establishment, and economic impact. They consist of five tick species, one parasitic mite, one blowfly, and one muscoid fly. The southern cattle tick, *Boophilus microplus*, is a vector of bovine babesiosis, bovine anaplasmosis, and benign bovine theileriosis. This tick is found is the hotter, more humid parts of the West Indies, Mexico, Central America, South American, Africa, Australia, the Orient, and Micronesia. At one time it was also established in southern Florida, in several counties in southern Texas, and is found in Puerto Rico and St. Croix, U. S. Virgin Islands. A closely related species, *B. annulatus*, the cattle tick, was once the most important external parasite of cattle in the Southern United States. It is a principal vector of bovine babesiosis and has also been incriminated in the transmission of bovine anaplasmosis, benign bovine theileriosis, and spirochetosis of cattle, sheep, goats, and horses. The cattle fever tick has been eradicated from the continental United States, but periodic

introductions from Mexico continue to occur. It is also found in western and central Africa, the Mediterranean basin, and the Near East.

Another exotic tick species of great concern to this hemisphere is the tropical bont tick, *Amblyomma variegatum* (Fig. 53). A native of Africa south of the Sahara Desert, the tropical bont tick was introduced into the Caribbean island of Guadeloupe around 1830 on cattle imported from Senegal. This tick is a common vector of *Cowdria ruminantium*, which is the etiological agent of heartwater that affects cattle, sheep and goats. The bont tick is also associated with the spread of dermatophilosis and has been incriminated in the transmission of Nairobi sheep disease. An international effort is under way to eradicate the tropical bont tick from the Western Hemisphere. *A. hebraeum* (Fig. 54), the bont tick, is also of African origin and is a common vector of heartwater. The exceptionally long mouthparts enable it to produce deep- seated painful wounds that often become infected and lead to abscess formation.

The brown ear tick, *Rhipicephalus appendiculatus*, is widely distributed in the wetter areas of Africa. Although primarily a cattle tick, there are numerous secondary host species. Because the most important predilection site of this species is the inside of the earflap, it is the most important species involved in transmitting the etiological agent of East Coast fever. *Rhipicephalus appendiculatus* has also been incriminated in the transmission of bovine babesiosis, other pathogens of the East Coast fever syndrome, louping ill, Nairobi sheep disease, and Kisenly sheep disease.

Another tick species of high vector potential is the European castor bean tick, *Ixodes ricinus*. This tick is common throughout most of Europe, including the British Isles, and is found in North Africa and limited areas of Asia. It has never been established in North America, although closely related species of the genus *Ixodes* do exist in this hemisphere. The European castor bean tick is responsible for transmitting the causative agents of bovine babesiosis, bovine anaplasmosis, louping ill, and tick-borne fever of cattle, sheep, and goats. Completion of the life cycle can require as long as 3 years.

The sheep scab mite, *Psoroptes ovis,* is recognized as an exotic arthropod pest having highest potential for introduction because it has been eradicated from the United States and could easily be reintroduced from other countries of this hemisphere. Interceptions at port of entry have been made from sheep, goats, llamas, and alpacas.

Another exotic arthropod pest of highest importance is the New World screwworm, *Cochliomyia hominivorax*. This species has been eradicated from the United States and Mexico through the classic application of the sterile male technique, and the program continues to approach its goal of eradication throughout Panama. Screwworms were introduced into Libya from South America and subsequently eradicated through an international effort utilizing the sterile male technique. Until a barrier is established in Panama, there is a persistent threat for the reintroduction of screwworms on infested mammalian hosts from areas that have not yet been eradicated.

The louse fly, *Hippobosca longipennis* (Fig. 55), which inflicts a painful bite, is an ectoparasite of all hairy animals, including livestock, dogs, cats, and wild game. The louse fly has been introduced into the United States on a shipment of cheetahs destined for zoological parks and subsequently eradicated from six states. This species has also been introduced on bat-eared foxes.

The final species in Category A is a licking fly, *Musca vitripennis*. This species has been reported as being a tenacious feeder on the facial secretions of cattle, a mechanical vector of the etiological agent of infectious keratoconjunctivitis, and a biological vector of bovine filariasis. Adults of this fly have been intercepted on several occasions in aircraft originating from the Azores, but this species has not yet become established in North America (13).

Category B. Exotic arthropod pests and arthropod-borne disease vectors in Category B merit particular concern with respect to introduction, establishment, and economic impact. So many arthropod species could be assigned to this category that they are listed by genera rather than by individual species. As before, the lead is taken by hard ticks of the genera *Amblyomma*, *Dermacentor*, *Hyalomma*, *Ixodes*, and *Rhipicephalus*, followed by soft ticks of the genera *Argas* and *Ornithodoros*. Mosquitoes of the genera *Aedes*, *Anopheles*, and *Culex* are a continual concern for introduction and establishment, as

has recently occurred with the Asian tiger mosquito, *Aedes albopictus*. Muscoid flies (*Musca*) could be introduced in bedding material of animal importations. The numerous species of tsetse flies, *Glossina* spp., are listed within Category B because they are all limited to the African continent and, in view of their biological cycle and naturally low reproductive efficiency and population density, are less likely to be a threat to introduction. However, should a tsetse species become established in a tropical or semitropical area of this hemisphere, eradication would undoubtedly be a formidable task.

Category C. Species of foreign arthropod pests and arthropod-borne disease vectors assigned to Category C are those with some potential for introduction, establishment, and economic impact. They originate from all areas of the globe and are too numerous to characterize even at the generic level. Thus, species of particular concern are found in the families Ceratopogonidae (biting midges), Simuliidae (black flies), Oestridae (bot flies), Chloropidae (eye gnats), Sarcophagidae (flesh flies), Ixodidae (hard ticks), Tabanidae (horse flies and deer flies), Culicidae (mosquitoes), Muscidae (muscoid flies), and Cuterebridae (robust bot flies).

Examples of Interceptions and Introductions

Historically, some of the most economically important arthropod pests of livestock found in the United States were introduced from Europe (2). There is evidence to suggest that the house fly and stable fly were introduced when the first settlers brought livestock with them from their home countries. The horn fly, a pest of cattle throughout the United States, was first discovered near Camden, New Jersey, in 1887. By 1990, it had spread to all states of the United States and all provinces in Canada. More recently, the face fly, a livestock pest and carrier of parasites, entered Nova Scotia in 1952 on cargo transported by air from England. Face flies now infest cattle in all but the southernmost states.

Examples of arthropod vectors that have been intercepted at ports of entry or that have been detected on premises and subsequently eradicated are numerous and alarming (3,8,11,17). Records on exotic arthropod pests found on animals and products have systematically been compiled for over 35 years. Since that time, over 70 species of exotic ectoparasites, primarily ixodid ticks, have been collected from a wide variety of both domestic and zoological animals at ports of entry into the United States. Many of the species intercepted are known vectors of some of the most economically important livestock diseases in the world, including bovine babesiosis, heartwater, East Coast fever, corridor disease, Nairobi sheep disease, louping ill, and tropical disease (Table 1). Other species intercepted, such as the sheep scab mite, New World screwworm, and louse flies, although not disease vectors, could become serious pests of our nation's livestock population if they were to become established in the United States. Most of the exotic pests intercepted were found on animals while in quarantine at a USDA import center. Examination and precautionary treatment routinely provided to these animals ensure that they are free of ectoparasites before being released from quarantine. When exotic animal pests are found on animal or plant products, baggage, cargo, etc., at ports of entry other than USDA quarantine stations, treatment of the infested material is provided to eliminate the pest before further movement into commerce.

The greatest threat to the livestock industry comes from those animals that may enter the United States without being held in quarantine or undergoing a precautionary treatment before entering. Such animals are those zoological specimens not regulated by the USDA. Table 2 summarizes those arthropod pests of livestock that have been introduced into the United States. In some cases, lengthy and expensive eradication programs had to be conducted to ensure that these pests did not become established. Specific examples of some of these introductions are briefly discussed below.

In 1960, the red tick, *Rhipicephalus evertsi*, was discovered at a wild animal compound in Florida (3). This was the first time that this tick had been identified in North America. It was never determined when and how the red tick was introduced into the United States; however, it was probably brought in on eland or zebra imported from Africa. The tick was found as a result of an intensive surveillance campaign by the USDA and the State of Florida during an eradication program of the southern cattle tick, *B. microplus*, in Florida. Many of the wild animals representative of the various species at the compound were inspected to determine the relative abundance of the red ticks. Systematic application of pesticide to the entire compound, lasting for 9 months, was implemented and the tick eradicated.

In 1972, the louse fly, *H. longipennis* (Fig. 55), was identified in California on cheetahs that had been imported from Africa in 1970 (7). Subsequent investigations revealed that the louse fly had also become established at zoological compounds in Georgia, Texas, and Oregon. Although primarily an ectoparasite of wild carnivores, there was concern that *H. longipennis* would become an endemic pest of pet animals, native wildlife, or livestock. As a result, treatments began at the various parks in 1972. However, because of the louse fly's adaptability and the relative ineffectiveness of the pesticides used early in the treatment program, the eradication effort was not successfully completed until 1975. The louse fly was reintroduced in 1983 when bat-eared foxes imported from Africa were found infested with this species at a zoological park in North Carolina. Systematic treatment of the foxes and the area in which they were housed was conducted and the infestation eliminated.

The New World screwworm, *C. hominivorax*, was successfully eradicated from the United States in 1966. Since that time, it has been introduced on five occasions, twice in 1987, once in 1990, and twice in 1997 (in 1988, screwworm larvae were collected from 1 of 45 Argentine polo ponies during quarantine at a USDA quarantine facility; the larvae were removed and both the wound and the quarantine facility were treated with an appropriate pesticide). The 1987 introductions occurred when screwworm larvae were collected from dogs returning to the United States from either South or Central America. In both cases, sterile screwworm flies from Mexico were released around the area where the dogs were located in the United States. In 1990, screwworm larvae were removed from a head wound of a paratrooper who had jumped from a plane into Panama, was injured, and subsequently evacuated to Ft. Sam Houston Military Hospital, San Antonio, TX. Even though climatic conditions were not conducive for establishment, surveillance activities were conducted in the area to ensure that screwworms were not present. The 1997 introductions occurred when dogs returning from Panama were found with infestations of screwworm larvae. In both instances, the infestations were discovered early enough to preclude the release of sterile screwworm flies. However, in both cases, the infested wounds were treated for screwworms, and all conveyances used to transport the dogs and the premises where the dogs were housed were cleaned and disinfected.

In 1997, the African tortoise tick, *Amblyomma marmoreum,* an experimental vector of heartwater, was discovered on the premises of a reptile breeder in central Florida (1). Surveillance data indicated that the infestation was restricted to the one premises. Appropriate actions to eradicate the tick, including treatment of the infested animals and the premises, are under way.

The recent trend towards placing zoological animals in situations that directly expose them to susceptible domestic and native wildlife greatly increases the risk of introducing exotic arthropod pests of livestock. Two introductions of hard ticks serve to emphasize this risk. The first, in 1984, occurred when the bont tick, *A. hebraeum*, a vector of heartwater, was collected from black rhinoceroses imported into the United States from South Africa (17). Some of the infested rhinoceroses were placed on a working cattle ranch in south Texas. The rhinoceroses and premises were systematically treated. After an intensive 6-month surveillance program, it was determined that this tick had not become established in the United States. In the second introduction, other vectors of heartwater, including *A. gemma*, *A. lepidum*, and *A. variegatum*, were introduced into the United States on ostriches imported from Africa in 1989 (10). Like the black rhinoceroses, some of the ostriches were placed in ecological settings favorable for the establishment of exotic ticks, whereas others were placed in situations that directly exposed them to domestic livestock. Premises with the ostriches were placed under quarantine, and the ostriches and premises systematically treated with an acaricide to eliminate the ticks.

Principles of Exclusion and Eradication

Historically, arthropod pests and their associated diseases have migrated with humanity and their animals. When travel was slow and difficult, and trading in animals and animal products was limited, pests of livestock moved slowly. Moreover, many of these pests were excluded from many parts of the world by natural environmental barriers such as mountains, oceans, deserts, rivers, and unfavorable climates (9). These barriers served to limit the distribution of both the pests and their hosts. Today, however, because of the volume and rapidity of international commerce, these natural barriers are not nearly effective in limiting the distribution of pests as in the past. As a result, strategies have been developed to prevent pests from entering the United States on

animals, animal products, or other articles of commerce. Guidelines for eradication of arthropod pests and their associated diseases have also been formulated.

Effective strategies for exclusion or eradication of livestock pests must be based upon detailed knowledge of the pest's biology, host preference, and susceptibility to pesticides. In addition, those factors that limit the pest's distribution and methodologies for its surveillance must also be known. For exclusion efforts to be most effective, knowledge of the avenues by which the pests might enter the United States and become established is also needed. For example, a knowledge of the host preference(s) of ectoparasites such as ticks, helps alert animal health officials in determining the potential for introduction, whereas knowledge that some species of ticks have preferred attachment sites on the host helps focus the attention of the inspector during an examination of animals for ectoparasites.

International cooperation also plays an important role in the exclusion of many pests of livestock. For example, in some situations, inspection of certain animals (including zoo animals) destined for export to the United States and certification that they are free of ectoparasites are two of the requirements that must be met prior to export. In other situations, it may be a requirement of the exporting country to certify that the animals have been treated for ectoparasites within a specified time prior to export. Cooperation of neighboring countries with mutual interests can also play a role in the exclusion or eradication of certain livestock pests. The joint effort by the United States and Mexico in eradicating the New World screwworm from Mexico and Central America is a recent example of such cooperation.

Regulating the import of certain animals, particularly domestic livestock, is the principal means by which livestock pests and their associated diseases are prevented from entering the United States. Livestock and certain zoological animals are required to remain in quarantine before entering into commerce in the United States. During quarantine, which is usually for a 30-day period, the animals are carefully examined for ectoparasites. The ears, flanks, escutcheon, and other less accessible areas of the host's body as well as the more obvious sites of attachment are carefully examined. With horses and other equines, particular attention is given to the careful examination of the nasal diverticula (false nostrils). If an ectoparasite is found, the animals are treated with an appropriate pesticide. An additional treatment is provided if warranted. Animals are not released from quarantine until they are free of ectoparasites.

When nonregulated animals, particularly zoological specimens, enter the United States without being held in quarantine or given a precautionary treatment with a pesticide before entering, the risk of introducing an arthropod pest of livestock is greatly increased. The risk is minimized for those zoological specimens destined for well-established and well-run zoos or zoological parks or gardens where animals are thoroughly examined and treated, if necessary, for ectoparasites. However, in situations where nonregulated zoological specimens are imported by private individuals and are subsequently sold or traded to others, many of the animals end up being exposed to domestic livestock or native wildlife. The deleteriousness of this practice is exacerbated by the ignorance of the animal owners who are not aware of the potential danger that these animals present to our Nation's livestock industry. When an arthropod pest of livestock is identified from these animals, States cooperate with Federal animal health officials to eradicate the pest. The first action taken by State animal health authorities is to quarantine the premises where the animals are located to prevent further spread of the pest. If the arthropod pest is a known or potential vector of a foreign animal disease, infested animals are observed for clinical signs of the disease. Tracebacks, conducted by Federal authorities, are made of other animals that may have come into contact with the infested animals since their entry into the United States. In some situations, because of the extensive movements of the infested animals from the time they enter the United States and the time the pest is found, tracebacks may become extremely complex and time consuming. If, through the traceback procedure, other premises are found with infested animals, these too are quarantined. Surveillance activities are undertaken on the infested premises and, if appropriate, on adjacent premises as well. Once the extent of infestation is determined, the infested animals and the premises where they are located are systematically treated with pesticides known to be effective against the pest on and off the host. Surveillance activities are continued throughout the quarantine and treatment procedures to ensure the pest is eradicated.

To date, introductions of exotic arthropod pests of livestock have been relatively localized or have involved pests whose spread has primarily been related to the movement of their hosts (e.g., ticks and louse flies). As a result, activities to eradicate these pests have been relatively inexpensive and of short duration. However, if broad-area introductions were to be made, or if highly mobile pests such as mosquitoes or flies were to be introduced into the United States, eradication could be exceedingly costly and lengthy. In addition, because of increasing environmental concerns, eradication activities involving the widespread use of pesticides may not be sociologically acceptable and may therefore not be feasible.

Summary

Several economically important arthropod pests of livestock in the United States have been introduced. For the most part, these introductions occurred during the time when livestock entered the country without restriction. Now, however, extensive efforts are made to preclude the introduction of exotic arthropod pests of livestock and poultry and arthropod-borne disease vectors. Regulating the import of live animals, particularly domestic livestock, is the principal means by which arthropod pests are prevented from entering the United States. These animals are required to remain in quarantine until it can be determined that they are free of pests and disease.

The greatest risk of introducing pests of livestock and poultry comes from the importation of nonregulated animals — particularly zoological specimens. Such animals can enter the United States without being held in quarantine to ensure that they are free of exotic pests and diseases. When an arthropod pest of livestock or an arthropod-borne disease vector is identified from these animals, State and Federal animal health officials cooperate to eradicate the pest. Depending on the circumstances, these eradication efforts may be expensive and time consuming.

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TABLE 1. **Exotic arthropod pests of livestock intercepted at U. S. ports of entry**[1]

Year	Arthropod species	Animal or product	Suspected or confirmed disease relationship(s)[2]
1958	*Rhipicephalus pulchellus*	Giraffe	NSD
1960	*Rhipicephalus evertsi*	Zebra	ECF, BB
	R. pulchellus	Zebra	NSD

1961	*Dermacentor reticulatus*	Oryx	BB
	Rhipicephalus evertsi	Oryx, zebra	ECF, BB
	R. e. mimeticus	Zebra, oryx, hartebeest	ECF
	R. pulchellus	Zebra	NSD
1965	*Boophilus decoloratus*	Giraffe, hartebeest	BB
	Rhipicephalus evertsi	Eland	ECF, BB
1966	*Hyalomma marginatus*	Equine	TD
	Rhipicephalus appendiculatus	Zebra	ECF, BB, CD, LI
	R. bursa	Equine	BB. NSD
	R. e. evertsi	Zebra, antelope	ECF, BB
	R. e. mimeticus	Giraffe, zebra, eland	ECF
	R. pulchellus	Zebra	NSD
1967	*Rhipicephalus e. evertsi*	Zebra	ECF, BB
	R. pulchellus	Zebra	NSD, BB
1968	*R. e. evertsi*	Zebra	ECF
1969	*Amblyomma gemma*	Zebra	HW, NSD
	Haemaphysalis longicornis	Equine	BBT
	Hyalomma detritum	Equine	TD
	Rhipicephalus e. evertsi	Zebra	ECF, BB
	R. pulchellus	Zebra	NSD
1970	*Amblyomma gemma*	Zebra	HW, NSD
	Rhipicephalus evertsi	Zebra	ECF, BB
	R. pulchellus	Zebra	NSD
1971	*Rhipicephalus evertsi*	Zebra	ECF, BB
	R. e. mimeticus	Zebra	ECF
	R. pulchellus	Zebra	NSD

1972	*Rhipicephalus pulchellus*	Zebra	NSD
	R. e. mimetcus	Zebra	ECF
	R. evertsi	Zebra	ECF, BB
1973	*Boophilus decoloratus*	Zebra	BB
	Ixodes ricinus	Donkey	BB, LI
	Rhipicephalus appendiculat	Zebra	ECF, BB, CD, LI
	R. evertsi	Zebra	ECF, BB
	R. pulchellus	Zebra	NSD
1974	*Boophilus decoloratus*	Zebra	BB
	Rhipichephalus e. evertsi	Gnu, zebra	ECF, BB
	R. e. mimeticus	Gnu	ECF
	R. pulchellus	Zebra	NSD
1975	*Rhipicephalus evertsi*	Zebra	ECF, BB
1976	*Boophilus decoloratus*	Zebra	BB
	Rhipicephalus evertsi	Zebra	ECF, BB
1981	*Hyalomma margintaum*	Cork[3]	TD
1982	*Haemaphysalis longicornis*	Horse	BBT
	Musca vitripennis	Military cargo [4]	BP
1983	*Rhipicephalus compositus*	Plant material[5]	ECF
	R. e. evertsi	Zebra	ECF, BB
	R. e. mimeticus	Zebra	ECF
1984	*Hyalomma excavatum*	Baggage[6]	TD
	Rhipicephalus kochi	Cut flowers[5]	ECF
985	*Musca vitripennis*	Military cargo[4]	BP
	Rhipicephalus capensis	Cut flowers[5]	ECF
1986	*Musca vitripennis*	Military cargo[4]	BP
	Hippobosca equine	Horse	NP

1988	*Haemaphysalis longicornis*	Horse	BBT
	Ixodes ricinus	Horse	BB, LI
	Cochliomyia hominivorax	Horse	M
1989	*Amblyomma gemma*	Ostrich	HW, NSD
	A. lepidum	Ostrich	HW
	A. sparsum	Tortoise, rhinoceros	HW
	A. variegatum	Ostrich	HW, NSD, BBT, DT
	Haemaphysalis punctata	Ostrich	BB, BBT
	Hyalomma marginatum rufipes	Ostrich, rhinoceros	TD
	H. truncatum	Ostrich	BB, SS
	Ixodes ricinus	Horse	BB, LI
1990	*Rhipicephalus e. evertisi*	Horse	ECF, BB
1992	*Haemaphysalis longicornis*	Horse	BBT
1993	*Amblyomma variegatum*	Cattle	HW, NSD, BBT, DT
1994	*Amblyomma hebraeum*	Giraffe	HW
	A. marmoreum	Leopard tortoise	HW
	A. sparsum	Monitor lizard	HW
	A. variegatum	Horse, sheep	HW, NSD, BBT, DT
1995	*Haemaphysalis longicornis*	Horse	BBT
	Ixodes ricinus	Leopard tortoise	BB, LI
	Amblyomma marmoreum		HW
1996	*Amblyomma marmoreum*	Leopard tortoise	HW
1997	*Amblyomma marmoreum*	Bell's hingeback tortoise	HW
		Leopard tortoise	
		Karoo Cape tortoise	
	A. variegatum	Savanna monitor lizard	HW, NSD, BBT, DT
	Haemaphysalis longicornis	Horse	BBT

[1] Unless otherwise indicated, all collections were from USDA quarantine facilities.

[2] Abbreviatons:
BB=bovine babesiosis
BBT=benign bovine theleriosis
CD=Corridor disease
DT=dermatophilosis
ECF=East Coast fever
HW=heartwater
LI=louping ill
M=myiasis
ND=nuisance pest
NSD=Nairobi sheep disease
SS=sweating sickness
TD=Tropical disease.

[3] Collected at Baltimore, MD.

[4] Two interceptions in 1982; all interceptions of *M. vitripennis* made at McGuire Air Force Base, NJ.

[5] Collected at JFK airport.

[6] Collected at Dover, DE.

Table 2. **Exotic arthropod pests of livestock detected on premises**

Year	Arthropod species	Animal	Locality disease collected	Suspected or confirmed relationship(s)[1]
1960	*Rhipicephalus evertsi*	Zebra	Florida	ECF, BB
1961	*Rhipicephalus evertsi*	Zebra	New York	ECF, BB

1962	*Amblyomma hebraeum*	Rhinoceros	New York	HW
1963	*Amblyoma hebraeum*	Rhinoceros	New York Oklahoma	HW
1965	*Amblyomma gemma*	Rhinoceros	Michigan	HW, NSD
	A. tholloni	Elephant	Texas	HW
	A. variegatum	Rhinoceros	Michigan	HW, NSD, BBT, DT
	Rhipicephalus pulchellus	Rhinoceros	Michigan	NSD
	R. simus simus	Rhinoceros	Michigan	ECF
1966	*Amblyomma hebraeum*	Elephant Rhinoceros Rhinoceros	Florida California Texas	HW
1969	*Amblyomma sparsum*	Boa constrictor	Washington	HW
1970	*Amblyomma hebraeum*	Rhinoceros	Texas	HW
1971	*Amblyomma sparsum*	Tortoise	Oregon	HW
1972	*Hippobosca longipennis*	Cheetah	California Texas Oregon Georgia	NP
1973	*Amblyomma hebraeum*	Rhinoceros	Virginia	HW
1974	*Amblyomma gemma*	Rhinoceros	North Carolina	HW, NSD
	A. tholloni	Elephant	Tennessee	HW
	A. variegatum	Rhinoceros	North Carolina	HW, NSD, BBT, DT
	Hyalomma truncatum	Rhinoceros	North Carolina	
	Rhipicephalus pulchellus	Rhinoceros	North Carolina	NSD
1977	*Boophilus microplus*	Sloth	New York	BB
1979	*Amblyomma variegatum*	Kudu	Colorado	HW, NSD, BBT, DT
1980	*Amblyomma variegatum*	Eland	Colorado	HW, NSD, BBT, DT

1983	*Hippobosca longipennis*	Bat-eared foxes	North Carolina	NP
1984	*Amblyomma hebraeum*	Rhinoceros	Texas	HW
1987	*Cochliomyia hominivorax*	Dog	Colorado	M
		Dog	Florida	
			Louisiana	
1989	*Amblyomma gemma*	Ostrich	Texas	HW, NSD
	A. lepidum	Ostrich	Texas	HW
	A. sparsum	Tortoise	California	HW
	A. variegatum	Ostrich	Texas	HW, NSD, BBT, DT
	Haemaphysalis punctata	Ostrich	California	BB
		Pig	Florida	
	Hyalomma albiparmatum	Ostrich	Texas	TD
	H. marginatum rufipes	Ostrich	Texas	TD
		Ostrich	California	
		Ostrich	Indiana	
	Ixodes ricinus	Horse	California	BB, LI
1990	*Ornithodoros moubata*	Tortoise	Florida	ASF
	Cochliomyia hominivorax	Man	Texas	M
1991	*Amblyomma sparsum*	Tortoise	South Carolina	HW
	Amblyomma marmoreum	Leopard tortoise	Florida	HW
	Cochkiomyia hominivorax	Dog	Utah	M
		Dog	Texas	

[1] Abbreviations:
ASF=African swine fever
BB=bovine babesiosis
BBT=benign bovine theileriosis
DT=dermatophilosis
ECF=East Coast fever
HW=heartwater
LI=louping ill
M=myiasis
NP=nuisance pest
NSD=Nairobi sheep disease
TD=tropical disease

Fig. 53. Vectors - Male tropical bont tick, *Amblyomma variegatum.*

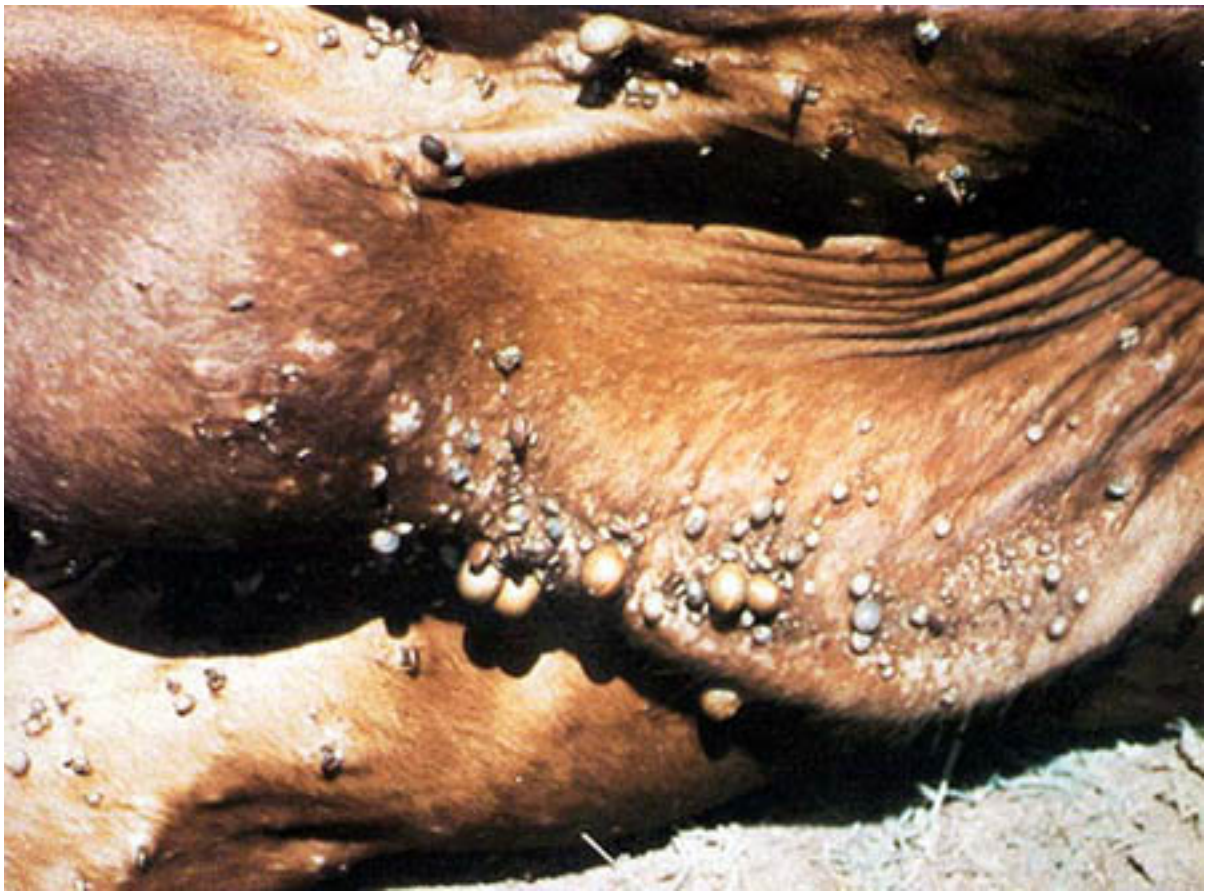

Fig. 54. Vectors - A heavy infestation of the bont tick (*Amblyomma variegatum*) on the dewlap of a cow.

Fig. 55. Vectors - Adult louse fly, *Hippobosca longipennis*.

PART IV
FOREIGN ANIMAL DISEASES

GLANDERS

(Droes, Farcy, Malleus)

Definition

Glanders is a highly contagious disease of solipeds caused by *Pseudomonas mallei* and characterized by nodular lesions of the lungs and other organs as well as ulcerative lesions of the skin and mucous membranes of the nasal cavity and respiratory passages. The disease typically has a progressive course and poses a significant human health risk.

Etiology

Glanders is caused by the bacteria *Pseudomonas mallei*. Former names of this pathogen include *Loefflerella mallei*, *Pfeifferella mallei*, *Malleomyces mallei*, *Actinobacillus mallei*, *Corynebacterium mallei*, *Mycobacterium mallei*, and *Bacillus mallei*. In experimental infection of guinea pigs *Ps. mallei* produces a tenacious capsule that may serve to protect it from phagocytosis (6). The organism is closely related to *Ps. pseudomallei*, the cause of melioidosis, and is serologically indistinguishable in some cases (3,8). Genetic homology between *Ps. mallei* and *Ps. pseudomallei* approaches 70 percent. Because of this many consider them to be biotypes or isotypes.

The organism is destroyed by direct sunlight and is sensitive to desiccation. It is readily killed by common disinfectants. It may survive for up to 6 weeks in infected stables (3).

Host Range

Glanders is primarily a disease of solipeds — particularly horses, donkeys, and mules. Traditionally, donkeys have been regarded as most likely to experience the acute form of the disease and horses a more chronic form, with mules intermediate in susceptibility (3,8). Recent reports suggest that chronic and even latent infections are equally likely in mules (10). Carnivores are susceptible to disease if they consume glandered meat; felids appear to more susceptible than canids, and outbreaks of glanders in captive wild felids have been reported (1,3,8). Several laboratory animals are susceptible to infection including, hamsters and guinea pigs. The susceptibility of the latter species formed the basis of the Strauss reaction in the diagnosis of the disease. Humans also are susceptible to infection with glanders, which is an important occupational disease of veterinarians, farriers, and other animal workers (8). Swine and cattle are resistant to infection with *Ps. mallei*, but goats can be infected.

Geographic Distribution

Glanders is currently limited to parts of Asia, Africa, the Middle East, and Asia (specifically Turkey, Syria, Iraq, Iran, Pakistan, India, Burma, Indonesia, the Philippines, China, and Mongolia) and possibly the Balkan states, former Soviet republics, Mexico, and South America (7,8,9,10). Cross-reactions with serological tests for *Ps. pseudomallei* may confound estimates of worldwide distribution. Although glanders was once widespread throughout the world, it has been eradicated from many countries by diligent test and slaughter programs.

Transmission

The disease is introduced into horse populations by diseased or latently infected animals. Ingestion of the pathogen, present in secretions from infected animals, constitutes the major route of infection in glanders. Experimental evidence suggests that inhalation of the organism is

less likely to result in typical cases of the disease. Although invasion by way of skin lesions is possible, it is regarded as being of minor importance in the natural spread of the disease. Close proximity alone does not usually result in transmission of glanders; transmission is facilitated if the animals share feeding troughs or watering facilities or if they nuzzle each other (3,8,10).

Incubation Period

After artificial infection, a fever, 106º F (41º C), develops in about 3 days and clinical signs within a week. After natural infection, weeks or months may elapse before manifestations of the disease are apparent. Such latent infections are a feature of the epidemiology of glanders.

Clincial Signs

Classical descriptions of glanders distinguish between cutaneous, nasal, and pulmonary forms of the disease, but in most outbreaks these forms are not clearly distinct and may occur simultaneously in an animal. Chronic infections with slow progression of an insidious disease are more common than the acute form of glanders. The acute form (more common in donkeys and mules than in horses) typically progresses to death within about a week.

The nasal form of glanders is characterized by unilateral or bilateral nasal discharge. The yellowish-green exudate is highly infectious. The nasal mucosa has nodules and ulcers. These ulcers may coalesce to form large ulcerated areas, or they may heal as stellate scars of the mucosa. In some cases the septum may even be perforated. Nasal lesions are accompanied by enlargement and induration, or sometimes rupture and suppuration, of regional lymph nodes.

In the cutaneous form of glanders, multiple nodules may develop in the skin of the legs or other parts of the body (Fig. 56). These nodules may rupture, leaving ulcers that discharge a yellow exudate to the skin surface and heal slowly. Cutaneous lymphatic vessels in the region become involved. They become distended and firm by being filled with a tenacious, purulent exudate (3,8). (These may be referred to as "Farcy pipes.") In the pulmonary form of glanders, lesions in the lungs develop in concert with nasal and cutaneous lesions or may be the sole manifestation of the disease (typical of latent cases). The lung lesions begin as firm nodules or as a diffuse pneumonic process (Fig. 57). The nodules are gray or white and firm, surrounded by a hemorrhagic zone, and may become caseous or calcified. Clinical signs in animals with lung lesions may only range from inapparent infection to mild dyspnea, or severe coughing and obvious lower respiratory tract involvement (3,8).

Lesions may also occur in the liver or spleen and, in male animals, glanderous orchitis is a common lesion (5,8).

Gross Lesions

Nodular lesions of glanders are most consistently found beneath the pleura of the lung. In some acute cases, however, a more diffuse form of lobular pneumonia may be present. The nodular lesions, typically about 1 cm in diameter, consist of a gray or white core of necrotic material that may become calcified and are surrounded by a zone of hyperemia and edema. Similar lesions may be found in other viscera. Glanderous orchitis may be seen in intact males.

Nasal lesions consist of submucosal nodules surrounded by a small zone of hyperemia. These nodules may rupture, leaving exudative ulcers. As new lesions develop it is not unusual to find small nodules, ulcers, and scars side by side. Lymphadenitis of associated lymph nodes is a consistent finding. In some cases laryngeal lesions similar to the nasal lesions may be found.

Cutaneous lesions consist of cord-like thickening of subcutaneous lymphatics along which are distributed chains of nodules, some of which are ulcerated.

Morbidity and Mortality

When horses, donkeys, and mules are concentrated, the morbidity can be high.

Diagnosis

Field Diagnosis

Typical nodules, ulcers, scars, and a debilitated condition can be sufficient to diagnose glanders. Unfortunately, many cases of glanders are latent and clinically inapparent. Therefore, systematic testing is essential to identify all infected animals in an outbreak (3,5,8,9). The mallein test has been the mainstay of field diagnosis. Mallein is a lysate of *Ps. mallei* containing both endotoxins and exotoxins elaborated by the organism. Infected animals are allergic to mallein and exhibit local and systemic hypersensitivity after mallein inoculation similar to that exhibited in tuberculin testing. Inoculation with mallein may trigger a humoral serologic reaction to the complement fixation test. This seroconversion is thought to be transient but may be permanent if the animal undergoes repeated mallein testing. This is extremely important to consider if animals are destined for export to countries that depend on the complement fixation test.

The preferred method of application of mallein is intrapalpebral. The mallein (0.1 ml) is injected into the dermis of the lower eyelid. In positive cases marked edema of the eyelid, purulent conjunctivitis, photophobia, pain, and depression may be observed within 12 to 72 hours. The test is usually read 48 hours after injection.

The ophthalmic mallein test consists of the instillation of mallein into the conjunctival sac. A positive reaction is characterized by development of severe purulent conjunctivitis within 6 to 12 hours. A larger volume of dilute mallein (2.5 MI) may be injected subcutaneously, causing fever, local swelling, and pain in positive animals.

Specimens for Laboratory

A whole or section of a lesion and a serum sample should be collected aseptically. The samples should be kept cool and shipped on wet ice as soon as possible. Sections of lesions in 10 percent buffered formalin and air-dried smears of exudate on glass slides should be submitted for microscopic examination.

Laboratory Diagnosis

The causative organism may be cultured from fresh lesions or lymph nodes. It may also be demonstrated micoscopically in films made from this material.

The Strauss reaction is observed when infectious material from glanders patients is injected intraperitoneally into male guinea pigs. In positive cases, the guinea pig develops localized peritonitis involving the scrotal sac. Glanderous orchitis follows with painful enlargement of the testes. The testis becomes enlarged and painful and ultimately necrotic and is discharged through the scrotal skin.

A variety of serologic tests for glanders have been developed. They are superior to mallein testing in sensitivity and specificity. The complement fixation test is widely used and is reported to have an overall accuracy of 95 pecent. A counter-immunoelectrophoresis test has been described (4). Recently a dot enzyme-linked immunosorbent assay has been developed and found to be superior to all previously described tests in its sensitivity. This test is inexpensive, rapid, and easy to perform and is not influenced by anticomplement activity (11).
Cross-reactions with *Ps. pseudomallei,* the cause of melioidosis, are features of all of the serological tests for glanders. Therefore, these tests will result in false positive reactions in animals from areas where melioidosis is endemic.

Differential Diagnosis

Signs of glanders must be distinguished from strangles, epizootic lymphangitis, ulcerative lymphangitis, melioidosis, and other forms of pneumonia. Purulent sinusitis, guttural pouch empyema, and other causes of nasal catarrh should also be considered. Skin lesions may be

similar to those of dermatophilosis or dermatomycoses such as sporotrichosis. Knowledge of the progressive debilitating nature of glanders and application of serological or mallein tests will serve to distinguish glanders from other similar diseases.

Strangles is caused by *Streptococcus equi*. It is characterized by fever, anorexia, and depression with swollen submandibular lymph nodes and mucopurulent nasal discharge. The nasal discharge is usually bilateral, whereas it is most often unilateral in cases of glanders. Skin nodules and typical lung lesions are absent. Animals with strangles will not react to mallein testing or serological tests for glanders. *S. equi* is readily demonstrable. Strangles does not develop into a chronic, debilitating condition, and most infected horses recover within a few weeks.

Epizootic lymphangitis (caused by *Histoplasma farciminosum*) is characterized by cutaneous nodules originating from superficial lymph vessels. In epizootic lymphangitis, conjunctivitis is a common lesion. Demonstration of the infectious agent and application of the mallein test and serological testing will help distinguish between these diseases.

Ulcerative lymphangitis (caused by *Corynebacterium pseudotuberculosis*) is characterized by dermatitis and abscess formation predominantly in the pectoral and ventral abdominal regions. Standard diagnostic tests are again valuable in distinguishing this disease from glanders.

Melioidosis (caused by *Ps. pseudomallei*) is characterized by multiple abscesses in a variety of tissues and organs. Unlike glanders, it is not specifically a disease of equids and occurs most often in sheep, goats, and swine. It is characterized by dyspnea and lameness, but a wide array of clinical signs may be elicited. Diagnosis is confirmed by isolation of the causative organism. Serological cross-reactions occur with *Ps. mallei*.

Treatment

Ps. mallei is sensitive to many antimicrobials (2,5), but the risk of spreading infection to other equids or to people dictates that infected animals be destroyed. This policy has successfully eradicated glanders from most parts of the world. Sulfonamides have traditionally been used for the treatment of human infection (8).

Vaccination

Protective vaccines have not been developed.

Control and Eradication

In endemic areas, routine testing and destruction of positive animals have proven successful in the eradication of the disease. Particular care is required where animals are congregated — most often for military purposes. In endemic areas, communal feeding and watering sites should be avoided.

Ps. mallei is quite sensitive to heat, desiccation, and common disinfectants. In warm, moist environments, however, it may remain viable for several months. In outbreaks it is important to bury or burn all contaminated bedding and foodstuffs to prevent infection of susceptible animals. Stalls and harness equipment should be thoroughly disinfected. Removal of susceptible species from contaminated premises for a period of months is advisable.

Public Health

People are susceptible to glanders. The human form of the disease is painful and frequently fatal. Laboratory workers and animal attendants are most at risk. Symptoms of glanders in people include nodular eruption on the face, legs, and arms; involvement of the nasal mucosa; and later pyemia and metastatic pneumonia. Human glanders may be confused with a variety of other diseases, including typhoid fever, tuberculosis, syphilis, erysipelas, lymphangitis, pyemia, yaws, and melioidosis. The diagnosis can be confirmed by serology and by isolation of the

causative organism.

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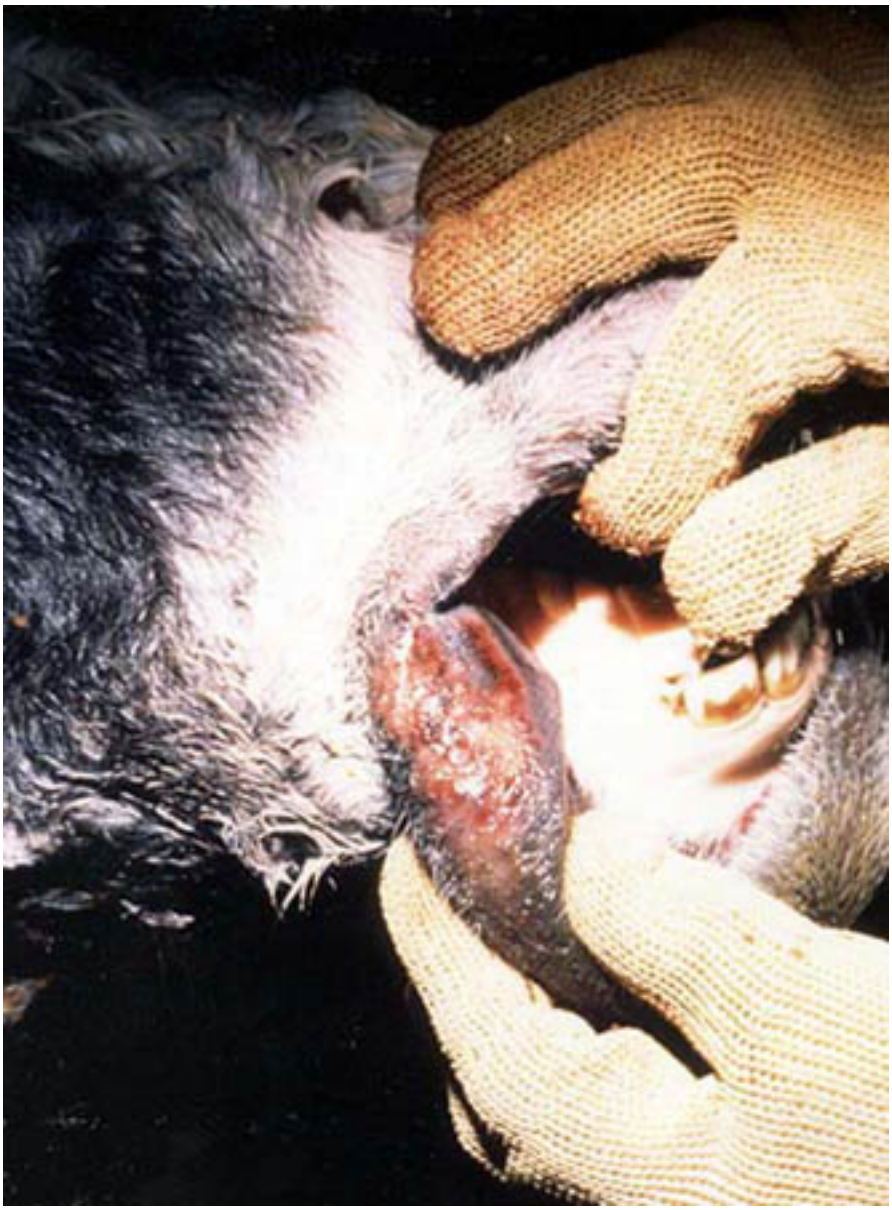

Fig. 56. Glanders - A granulomatous lesion in the lip of a donkey.

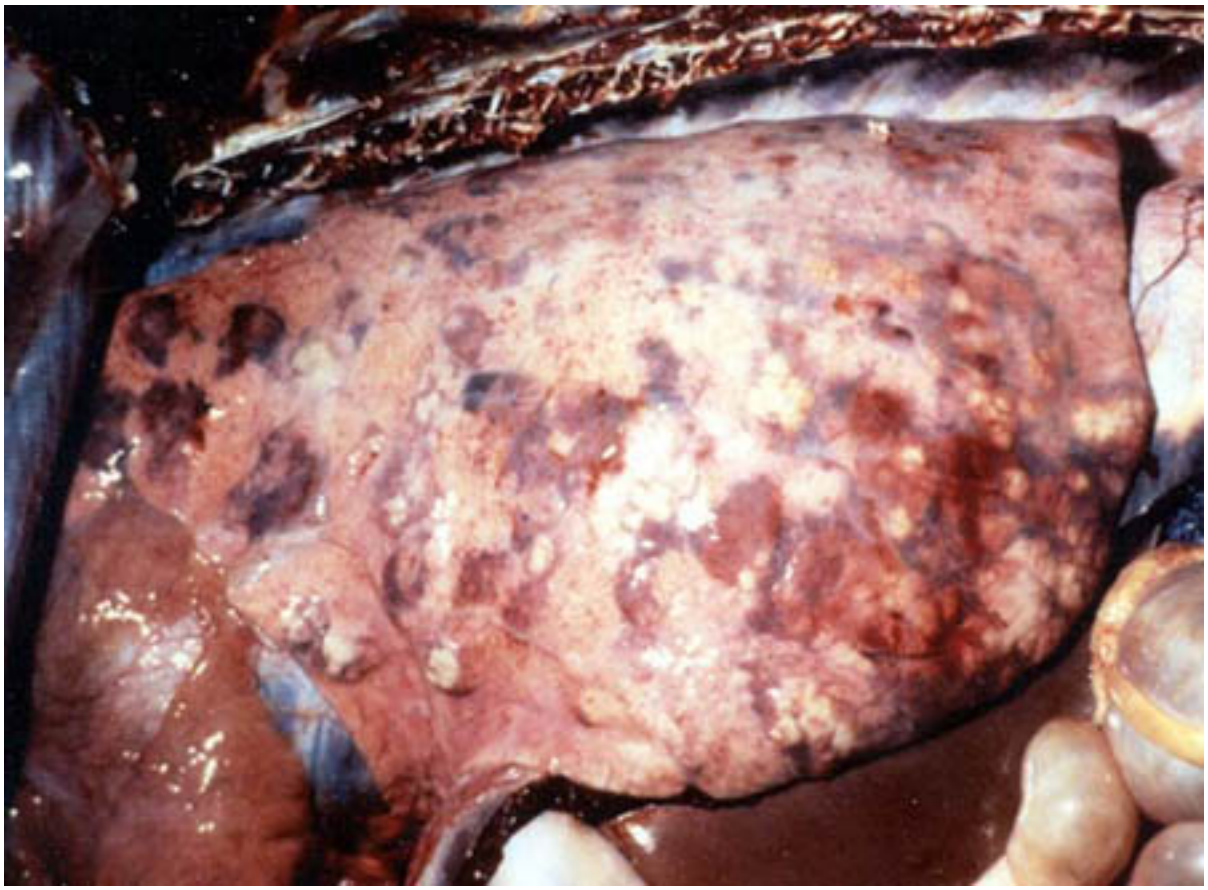

Fig. 57. Glanders - An extensive pyogenic granulomatous pneumonia in a donkey.

PART IV
FOREIGN ANIMAL DISEASES

HEARTWATER

(Cowdriosis)

Definition

Heartwater (HW) is an acute noncontagious infectious disease of ruminants affecting cattle, sheep, goats, and antelope and is caused by the rickettsial organism *Cowdria ruminantium*, which is transmitted by ticks of the genus *Amblyomma*. The disease is characterized by fever, nervous signs, hydropericardium, hydrothorax, ascites, edema of the lungs, and high mortality. In some wild ruminants the agent causes subclinical infection. The name "heartwater" is derived from the hydropericardium, which is commonly seen with this disease (Fig. 59).

Etiology

The disease is caused by *Cowdria ruminantium*, a rickettsial agent. It is the only species of the genus *Cowdria*, in the tribe Ehrlichia, family Rickettsiaceae, order Rickettsiales. The organism multiplies in vascular endothelial cells throughout the body and in the reticulum cells of the lymph nodes. The agent is pleomorphic, usually coccoid, occasionally ring-formed, and measures from 400 to over 1,000 nm in diameter. It usually occurs in clumps of from less than five to several thousand organisms within the cytoplasm of infected capillary endothelial cells, especially in the brain. The HW organism is extremely fragile and cannot persist outside of a host for more than a few hours. Because of its fragility, the organism must be stored in dry ice or liquid nitrogen to preserve its infectivity.

Heartwater strains vary in virulence, and although all are apparently pathogenic for sheep and goats, at least one strain is nonpathogenic for cattle.

Host Range

Heartwater causes severe disease in cattle, sheep, goats, and water buffalo; mild disease in some indigenous African breeds of sheep and goats; and inapparent disease in several species of antelope indigenous to Africa. The blesbok (*Damaliscus albifrons*), the black wildebeest (*Connochaetes gnu*), the eland (*Taurotragus oryx oryx*) and the springbok (*Antidorcas marsupialis*) have experimentally been shown to be susceptible to HW, and although the natural disease in these animals is usually mild, deaths in springbok have been attributed to HW. The blesbok and wildebeest are known carriers of *C. ruminantium* and are believed to play a role in the maintenance of the disease in nature.

Nonruminant hosts of *C. ruminantium*, such as guinea-fowl, leopard tortoises, and scrub hare, may also be important in the maintenance of the organism in nature because they are all known carriers of the agent. Although the striped mouse and the multimammate mouse have been shown to be susceptible to *C. ruminantium*, they are not hosts of the vector ticks and are not believed to play a role in the epizootiology of HW.

In the United States the most common deer species, *Odocoileus virginianus* (the white-tailed deer), has been shown by experimental inoculation to be susceptible to *C. ruminantium*. Severe clinical signs were noted along with typical postmortem lesions (Fig. 62). The mortality rate was high. *Amblyomma maculatum*, an experimentally proven vector of HW, is a common parasite of white-tailed deer in the southern United States.

The ferret and the albino mouse are susceptible to *C. ruminantium* under experimental conditions, and a mouse agent resembling C. ruminantium has been isolated in South Africa.

Geographic Distribution

Heartwater occurs only where vector ticks of the genus *Amblyomma* are active. For decades, the disease has been known to occur in most countries of Africa south of the Sahara Desert and on the island of Madagascar. The disease has also been reported from Tunisia and the former Yugoslavia; however, the Yugoslavian report is probably erroneous. For the last half century or more, the disease has been considered one of the most important livestock diseases in Africa and has been surpassed only by trypanosomiasis and East Coast fever.

Heartwater is now known to occur in the Caribbean, where the vector tick *A. variegatum* (tropical bont tick) has been recognized for many years. This tick, now known to occur on numerous Caribbean islands (e.g., Puerto Rico, Antigua, Guadeloupe, Martinique, St. Lucia, Nevis, St. Kitts) was probably introduced to the French Antilles with a shipment of cattle from Senegal in the 1830's. A fatal disease of cattle with neurologic and hemorrhagic signs, which in retrospect could have been HW, was described from Guadeloupe in 1932. Rapid spread of the tropical bont tick in the West Indies is believed to have occurred only after the introduction of the cattle egret from Africa in the early 1960's. Egrets are now known to be efficient porters of the tick. Heartwater has been diagnosed on the islands of Antigua, Guadeloupe, and Marie Galante. A disease closely resembling HW has also been reported from other Caribbean islands (e.g., Cuba and Antigua), but the diagnoses have not been confirmed. *Cowdria ruminantium* is far more widespread in the Caribbean than was formerly believed. Recent serological surveys (13) have demonstrated HW antibodies in cattle from 10 Caribbean islands (Antigua, Dominica, Granada, Guadeloupe, Martinique, Montserrat, St. Kitts, St. Lucia, St. Martin, and St. Vincent).

Transmission

Heartwater is transmitted only by ticks of the genus *Amblyomma*. Of the 12 species known to transmit the disease, *A. variegatum* (tropical bont tick) is by far the most important, for it is widely distributed in Africa and has extended its range to include Yemen, Reunion, the Cape Verde islands, and several islands of the West Indies (26). Other major vector species are the bont tick *A. hebraeum* (in southern Africa), and *A. lepidum* (in East Africa and the Sudan). *Amblyomma astrion* (mainly on buffalo) and *A. pomposum* are also natural vectors of the disease, and five other African ticks — *A. sparsum*, *A. gemma*, *A. cohaerans*, *A. marmoreum* and *A. tholloni* (the elephant tick) — have experimentally been shown to be capable of transmitting HW.

Two North American species of *Amblyomma* ticks have been shown by Uilenberg (1982) to be capable of transmitting the disease. They are *A. maculatum* (the Gulf Coast tick) and *A. cajennense*, but neither of these ticks has been incriminated as natural vectors of HW. The former tick is widely distributed in the eastern, southern, and western United States, and was shown by Uilenberg to be as good a vector as one of the principal African vectors, *A. hebraeum*.

Amblyomma ticks are three-host ticks whose life cycles may take from 5 months to 4 years to complete. Because the ticks may pick up the infection as larvae or nymphs and transmit it as nymphs or as adults, the infection can persist in the tick for a very long time. The infection does not pass transovarially. *Amblyomma* ticks are multihost and will feed on a wide variety of livestock, wild ungulates, ground birds, small mammals, reptiles, and amphibians.

Incubation Period

The incubation period is generally shorter in sheep and goats than in cattle. Experimental intravenous inoculation usually results in a febrile response between the 7th and 10th day after inoculation in sheep and goats, and between the 10th and 16th day after inoculation in cattle. Under field conditions, susceptible animals can be expected to show signs of the disease 14 to 28 days after introduction into an HW-infected area.

Clincial Signs

Heartwater occurs in four different clinical forms determined by variations in susceptibility of the

hosts and the virulence of various strains of the HW agent.

The relatively rare peracute form of the disease is usually seen in Africa in nonnative breeds of cattle, sheep, and goats introduced to an HW enzootic area. Heavily pregnant cows are especially prone to develop the peracute disease. Sudden death occurs, usually preceded only by a fever, severe respiratory distress, and terminal convulsions. Severe diarrhea may be seen in some breeds of cattle (e.g., Jersey, Guernsey).

The acute form of the disease, by far the most commonly observed syndrome, is seen in nonnative and indigenous domestic ruminants. A sudden fever of up to 107° F (42° C) is followed by inappetance, depression, listlessness, and rapid breathing. Nervous signs then develop, the most prominent being chewing movements, twitching of the eyelids, protrusion of the tongue (Fig. 58) and circling, often with highstepping gait. The animal may stand with its legs apart and head lowered. The nervous signs increase in severity, and the animal goes down in convulsions. Galloping movements and opisthotonos are commonly seen before death. Hyperesthesia is often observed in the terminal stages of the disease, as is nystagmus and frothing at the mouth. Diarrhea is occasionally seen, especially in younger animals. The acute disease is usually fatal within a week of the onset of signs.

Rarely, the disease may run a subacute course characterized by prolonged fever, coughing (a result of lung edema), and mild incoordination; recovery or death occurs in 1 to 2 weeks. A mild or subclinical form of the disease, known as "heartwater fever," is seen in partially immune cattle or sheep, in calves less than 3 weeks old, in antelope, and in some indigenous breeds of sheep and cattle with high natural resistance to the disease. The only clinical sign in this form of the disease is a transient febrile response.

Gross Lesions

The gross lesions in cattle, sheep, and goats are very similar. Heartwater derives its name from one of the prominent lesions observed in the disease, namely pronounced hydropericardium (Fig. 59). The accumulation of straw-colored to reddish fluid in the pericardium is more consistently observed in sheep and goats than in cattle. Ascites, hydrothorax, mediastinal edema, and edema of the lungs (Fig. 60), all resulting from increased vascular permeability with consequent transudation, are frequently encountered. Subendocardial petechial hemorrhages are usually seen, and submucosal and subserosal hemorrhages may occur elsewhere in the body. Degeneration of the myocardium and liver parenchyma, splenomegaly, edema of lymph nodes, nephrosis, and catarrhal and hemorrhagic abomasitis and enteritis are all commonly encountered. Meningeal congestion and edema are often present. Brain congestion may occur, but brain lesions can be remarkably few when one considers the severity of the nervous signs observed in this disease.

Morbidity and Mortality

Once signs of the disease have developed, the prognosis is poor for nonnative sheep, goats, and cattle infected with the more virulent strains of the HW organism. The mortality rate in merino sheep may be 80 percent in contrast to 6 percent mortality observed in Persian or Afrikander sheep. Angora goats are extremely susceptible to HW. In cattle, mortality of about 60 percent is not uncommon.

Diagnosis

Field Diagnosis

The presence of *Amblyomma* ticks plus the rather characteristic signs and lesions of heartwater allows tentative field diagnosis of the disease, which must then be confirmed by demonstration of the causative organism, its antigens, or its DNA.

Specimens for Laboratory

From live animals, collect 10 ml of blood using heparin as an anticoagulant and add sufficent DSMO to make a 10 percent concentration; freeze on dry ice. Collect an additional 50 ml of heparinized blood and 10 ml of serum. From a dead animal, submit smears of cerebral cortex or half of the brain unpreserved and a set of tissues in 10 percent buffered formalin.

Laboratory Diagnosis

1. Demonstration of the Organism: The HW organism stains purplish-blue with Giemsa stain and can be seen by microscopic examination of brain smears prepared as follows: A small piece of cerebrum, cerebellum, hippocampus, or other well-vascularized portion of the brain is macerated between two microscope slides. The resultant pulp is then drawn across a slide with varying pressure, which results in "ridges and valleys" on the slide. The slide is then air-dried, fixed with methanol, and stained with Giemsa. Under low magnification, the capillaries will be found extending from the "thick" areas of the slide. Examination of the capillary endothelial cells under oil immersion will reveal the blue to reddish-purple clumps of organisms (Fig. 61). A rapid method for obtaining brain tissue for examination is to drive a large nail through the unopened skull and make a smear from the tissue adhering to the nail. The HW organisms can also be observed in smears prepared from the intima of large blood vessels or in stained sections of kidney glomeruli and lymph nodes.

Although microscopic examination of Giemsa-stained brain smears is still widely employed in HW diagnosis, newer and more sensitive techniques such as the use of DNA probes (25) have been applied to detect *Cowdria* nucleic acids in tissues of infected livestock and ticks. These newer techniques should supplant the older methods of diagnosis as facilities and equipment become more available in HW-enzootic areas.

2. Antibody Detection: The indirect fluorescent antibody (IFA) test has extensively been used for HW antibody detection, and the newer competitive enzyme-linked immunosorbent assay (CELISA) (10, 14) promises to be a useful addition to the meager array of tests available for the detection of HW antibodies. The cross-reactions described with several *Ehrlichia* spp. can now be eliminated with the use of more specific antigens and monoclonal antibodies.

Differential Diagnosis

The peracute form of HW can be confused with anthrax. The acute nervous form of HW can be confused with rabies, tetanus, chlamydiosis, bacterial meningitis or encephalitis, cerebral trypanosomiasis, piroplasmosis or theileriosis, and various intoxications such as with strychnine, lead, organophosphates, or chlorinated hydrocarbons. Heavy helminth infestations may produce accumulations of fluid similar to those seen in HW. Arsenical poisoning may resemble the enteric form of the disease, and certain poisonous plants (e.g., Cestrum laevigatum, Pachystigma spp., Pavetta spp.) may produce signs and lesions similar to those seen in HW.

Treatment

Tetracycline antibiotics (especially oxytetracycline) are very effective in the treatment of HW, especially when animals are treated early in the course of the disease. Tetracycline antibiotics administered before signs appear will suppress the disease entirely, but will allow immunity to develop. Doxycycline and rifamycin are both very effective, and a wide variety of sulfonamides have successfully been used in HW treatment. Treatment for ruminal atony, a commonly observed sequel to this disease, may be indicated, and diuretics may be useful to control fluid accumulations in body cavities.

Vaccination

Animals recovering from the natural disease or from artificial exposure to the organism are solidly immune for a variable period ranging from 6 months to 18 months. Animals exposed to reinfection during this period of resistance will have their immunity reinforced and will remain immune as long as they are periodically reinfected. There is now conclusive evidence that immunity to HW is T-cell mediated (6) and that circulating antibodies play a minor role in

immunity.

Calves and lambs are very resistant to *C. ruminantium* in the first 4 weeks of life. This resistance seems to be a true age resistance and has successfully been used in the immunization of cattle and sheep. Calves of less than 4 weeks of age, and lambs in the first week of life can be immunized by intravenous inoculation of HW-infected blood. The infection that follows is usually mild, and upon recovery animals are immune to reinfection because immunity is continuously stimulated by natural exposure to the organism. Older animals or very valuable calves should be examined daily after immunization and should be treated with antibiotics as soon as the febrile response commences. A subcutaneous implant of doxycycline at the time of immunization will eliminate the labor-intensive tetracycline treatment method. The immunity will not be affected by the antibiotic treatment. Flock immunization of sheep and goats can be accomplished by inoculation followed by mass treatment at the end of the incubation period.

Immunologically different strains of the organism do exist, but present evidence indicates that there is considerable cross-protection between different strains (9), thus allowing successful immunization. However, there are some stains between which there is little cross-protection.

A strain of *C. ruminantium*, attenuated by serial passage in bovine umbilical endothelium cells has been shown to confer solid HW immunity to sheep and goats (9). This finding suggests that a live-attenuated vaccine to HW may soon be available, but because other strains of the organism have not become attenuated by cell-culture passage, the degree of cross-protection between strains still needs clarification. A universally effective vaccine is probably not imminent.

Control and Eradication

Tick Control

The HW organism is extremely fragile and cannot persist outside of a host for more than a few hours. The principal mode of bringing the disease into an area is thus through introduction of infected ticks or carrier animals. It is not known for how long wild or domestic ruminants can be a source of infection for ticks in nature, but Andrew and Norval (1989) have shown that experimentally infected sheep, cattle, and African buffalo can be a source of infection for nymphs of the bont tick (*A. hebraeum*) for 223, 246, and 161 days, respectively. After molting to adults, the ticks transmit the disease to susceptible sheep. This prolonged carrier state needs to be considered when animals are moved from HW-enzootic to HW-free areas. It is also not known for how long a tick can remain a carrier of the organism. Careful dipping and hand-dressing followed by inspection to ensure the absence of ticks is recommended for animals in transit to HW free areas.

Vector control measures aimed at eradication of *Amblyomma* ticks by dipping of cattle have failed principally because the vector is a multihost tick with a high rate of reproduction. The development of acaricide resistance has further complicated attempts at tick control. In enzootic areas, tick levels are now allowed to remain at levels high enough to permit reinfection of immune animals to booster the immunity.

Chemoprophylaxis

Cattle, sheep, and goats moving into an HW-enzootic area can be protected from HW by prophylactic treatment with tetracycline (short or long-acting) either by feeding (15) or by inoculation (22). However, they should be kept under surveillance and individually treated if clinical signs are seen.

Public Health

Humans are not known to be susceptible to Cowdria ruminantium.

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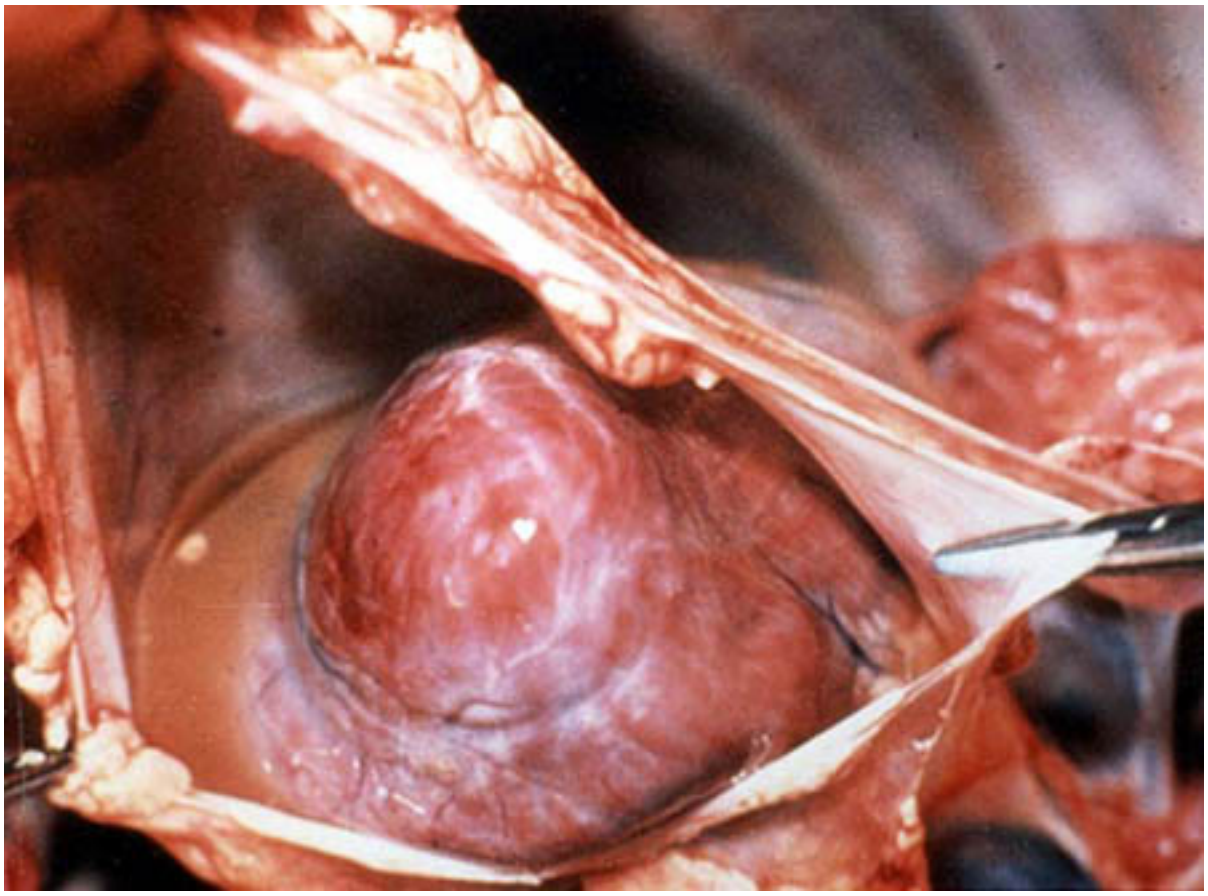

Fig. 59. HW - Hydopericardium.

Fig. 62. HW - Deer with signs of a central nervous system disturbance.

Fig. 58. HW - Cow with signs of a central nervous system disturbance.

Fig. 60. HW - Excessive fluid in the thoracic cavity and pulmonary edema; note the distended interlobular septa.

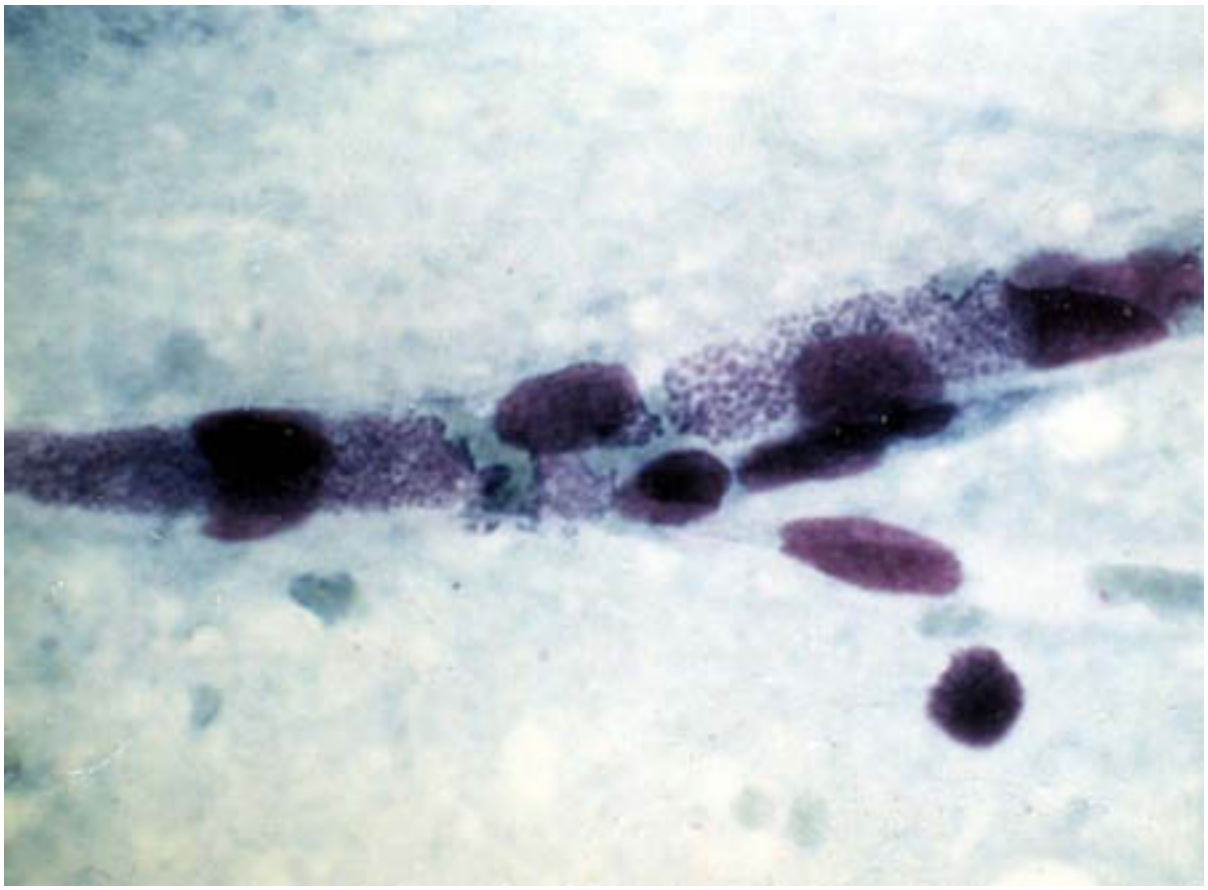

Fig. 61. HW - Brain smear from a goat. Colonies of *Cowdria ruminantium* are the granular blue areas in the cytoplasm of the capillary endothelial cells.

PART IV
FOREIGN ANIMAL DISEASES

HEMORRHAGIC SEPTICEMIA

Definition

Classical hemorrhagic septicemia is a particular form of pasteurellosis caused by *Pasteurella multocida* and manifested by an acute and highly fatal septicemia mainly in susceptible cattle and water buffaloes.

The name hemorrhagic septicemia is used rather loosely in some countries to include pneumonic pasteurellosis (shipping or transport fever), a disease caused mainly by *P. haemolytica*, although various serotypes of *P. multocida* are occasionally involved. Although the morbidity of pneumonic pasteurellosis of cattle can be high, the mortality rate is much less than that of hemorrhagic septicemia.

Etiology

Hemorrhagic septicemia is caused by two serotypes of *P. multocida*; namely, B:2 and E:2. The letter denotes the capsular antigen as determined originally by the indirect hemagglutination test of Carter (5), and the numeral 2 stands for the somatic or O antigen as determined by the agar gel diffusion precipitin test developed by Heddelston and associates (17). This somatic antigen 2 is the equivalent to the 6 in the classification of Namioka and associates. In a new classification, *Pasteurella multocida* strains causing most pasteurella infections, including hemorrhagic septicemia, are called *P. multocida* subspecies *multocida*.

Host Range

Cattle and water buffaloes are the principal hosts of hemorrhagic septicemia, and it is widely considered that buffaloes are the more susceptible. The disease is thought to be endemic in one large herd of North American range bison; however, epidemics appear to be rare. In the United States, the disease has been confirmed only in American bison in 1912, 1922, and 1965. The *P. multocida* isolant from the 1922 outbreak, a serotype B:2, is maintained in the USDA culture collection as a reference strain. Although outbreaks of hemorrhagic septicemia have been reported in sheep and swine, it is not a frequent or significant disease. Cases have been reported in deer, elephants and yaks. There is as yet no evidence of a reservoir of infection outside the principal hosts: cattle, water buffaloes, and bison.

Geographic Distribution

Hemorrhagic septicemia in epidemic form is a disease mainly of cattle and water buffaloes either maintained separately or together. Radical changes in weather, including the advent of monsoons, debility caused by seasonal levels of low nutrition, and the pressure of work (draft animals) are related to the explosive occurrences of the disease in certain parts of the world. Southeast Asia, where such conditions often coincide, is the area of highest incidence. The disease occurs in the Middle East and Africa where the environmental circumstances and predisposing conditions are not as clearly defined as in Southeast Asia. As in Asia, the disease is frequently associated with the rainy season and poor physical condition.

Hemorrhagic septicemia was recognized in Japan as a specific disease of cattle caused by particular strains of *Pasteurelia* as early as 1923. Since 1926, the disease has been controlled, and the last recorded case in cattle in Japan occurred in 1952.

The B:2 serotype has been recovered from hemorrhagic septicemia in countries of Southern Europe, the Middle East, and Southeast Asia, including China. This same serotype has been

reported from Egypt and the Sudan. The E:2 serotype has been recovered from hemorrhagic septicemia occurring in Egypt, the Sudan, the Republic of South Africa, and several other African countries. There is no report of either serotype being recovered from Australia, New Zealand, and countries of South and Central America.

There is no evidence that the disease has spread from carrier bison in the Western United States to neighboring cattle. Given the conditions in which hemorrhagic septicemia occurs in endemic areas (e.g., primitive husbandry practices, low country plains, and well-defined dry and wet seasons), it seems unlikely that the disease will reach epidemic proportions in the United States.

Transmission

The disease is spread by direct and indirect contact (fomites). The source of the infection is infected animals or carriers. The carrier state may be greater than 20 percent shortly after an outbreak, but within 6 weeks the rate is usually less than 5 percent. The causal agent does not survive for more than 2 to 3 weeks in the soil or on pastures. Close herding and wetness, as occurs during the rainy season, appear to contribute to spread. There is no evidence that biting arthropods are significant vectors.

Incubation Period

The influence of extrinsic factors in the development of the clinical pasteurelloses, and particularly in hemorrhagic septicemia, has been noted by many workers. When favorable circumstances for the growth and multiplication of *P. multocida* in the animal body occur, severe septicemia develops within a few hours. However, the organisms may be harbored for varying periods in a small percentage of carrier animals without any clinical sign. The perpetuation of the disease from year to year or season to season is generally attributed to the carrier state. The immune status of the animal is thought to influence the severity of the disease.

Cattle or buffalo artificially inoculated subcutaneously with lethal doses (approximately 20,000 bacilli) show clinical signs within a few hours and succumb within 18 to 30 hours.

Clinical Signs

The majority of cases in cattle and buffalo are acute or peracute with death occurring from 6 to 24 hours after the first recognized signs. In a few outbreaks, animals may survive as long as 72 hours. Dullness, reluctance to move, and elevated temperature are the first signs. Following these signs, salivation and nasal discharge appear, and edematous swellings are seen in the pharyngeal region and then spread to the ventral cervical region and brisket. Visible mucous membranes are congested, and respiratory distress is soon followed by collapse and death. Recovery, particularly in buffaloes, is rare. Chronic manifestations of hemorrhagic septicemia do not appear to occur.

Gross Lesions

Widely distributed hemorrhages, edema, and general hyperemia are the most obvious tissue changes observed in infected animals. In almost all cases there is an edematous swelling of the head, neck, and brisket region (Fig. 63). Incision of the edematous swellings reveals a coagulated serofibrinous mass with straw-colored or blood-stained fluid. This edema, which distends tissue spaces, is also found in the musculature (Fig. 64). There are subserosal petechial hemorrhages throughout the animal, and blood-tinged fluid is frequently found in the thoracic and abdominal cavities. Petechiae may be found scattered throughout some tissues and lymph nodes, particularly the pharyngeal and cervical nodes, which are also swollen and often hemorrhagic. Pneumonia is not usually extensive nor is gastroenteritis. Cases that are atypical in regard to throat swelling (absent) and pneumonia (extensive) are occasionally seen.

Morbidity and Mortality

Husbandry, weather and immunity affect morbidity. In endemic areas, from 10 to 50 percent of the cattle or buffalo populations acquire solid immunity through exposure or subclinical infection. Close herding and wetness predispose to an increased morbidity. Most animals that develop clinical signs die.

Diagnosis

Field Diagnosis

In countries where hemorrhagic septicemia is endemic, it is usually readily diagnosed — particularly if there is a history of previous outbreaks and a failure to vaccinate. When a small number of animals are affected, diagnosis may be more difficult. This could be the case if hemorrhagic septicemia were to occur in the United States. In endemic areas, the rapid course, usual high herd incidence, and the appearance of edematous swellings in the throat, cervical, and parotid regions is highly suggestive.

Specimen for Laboratory

From an animal with typical signs, the organism can be isolated from heparinized blood, affected tissue, liver, lung, kidney, and spleen. All samples should be collected aseptically. Samples should be kept cool and shipped on wet ice as soon as possible. Swabs in transport media, ribs, and tips of ears are sometimes submitted from remote areas in developing countries.

Laboratory Diagnosis

Isolation of a small gram-negative rod or coccobacillus in pure or nearly pure culture with the general colonial appearance of a *Pasteurella* species from an animal with typical signs is grounds to suspect hemorrhagic septicemia. If there has been postmortem decomposition with the presence of extraneous bacteria, the inoculation of mice and rabbits with blood or suspensions of tissues will facilitate recovery of the pasteurellae of hemorrhagic septicemia in pure or nearly pure culture. Both mice and rabbits are highly susceptible to the two serotypes B:2 and E:2. Definitive diagnosis depends upon the identification of the cultures as *P. multocida* and the subsequent identification of serotype B:2 or E:2. Because several different serotypes of *P. multocida* that do not produce classical hemorrhagic septicemia occur in cattle, it is necessary to serotype the isolate. The National Veterinary Services Laboratories, Ames, IA should be contacted regarding the serotyping of suspected hemorrhagic septicemia strains of *P. multocida*.

Serologic procedures for the detection of specific antibody are not used in diagnosis.

Differential Diagnosis

The sudden death seen with peracute and acute hemorrhagic septicemia must be differentiated from that due to lightning, snakebites, blackleg, rinderpest, and anthrax.

Treatment

The onset and course of the disease are generally rapid and leave little time for antimicrobial therapy. However, several of the sulfonamides and antibiotics such as penicillin and the tetracyclines can be used successfully in the early stages. In some outbreaks in Southeast Asia, animals with elevated temperatures are isolated and treated intravenously with a soluble sulfonamide.

Vaccination

The most efficacious immunizing agent has been the oil-adjuvant vaccine prepared from the appropriate serotype. Vaccine of this type is more slowly absorbed and produces a longer-lasting immunity than do regular and alum-precipitated-type bacterins. The oil-adjuvant bacterin has the advantage of requiring only one dose annually, but it has the disadvantages of

being difficult to syringe and occasionally produces a marked local reaction. A live vaccine prepared from a fallow deer strain of *P. multocida* has shown considerable promise with protection for as long as a year. This strain, serotype B:3,4, is closely related immunologically to serotype B:2 but is less virulent.

Control and Eradication

In endemic areas the only practical ways to protect animals are by an organized program of vaccination and maintenance of animals in as good a condition as possible. When favorable conditions for outbreaks are known to recur periodically, such preventive measures can be carried out in advance, and the potential consequences of the disease will thus be lessened.

Public Health

There is as yet no authenticated report of human infections due to serotypes B:2 and E:2. However, because other serotypes of *P. multocida* can cause a variety of human infections, precautions should be taken to minimize exposure to the hemorrhagic septicemia varieties of *P. multocida*.

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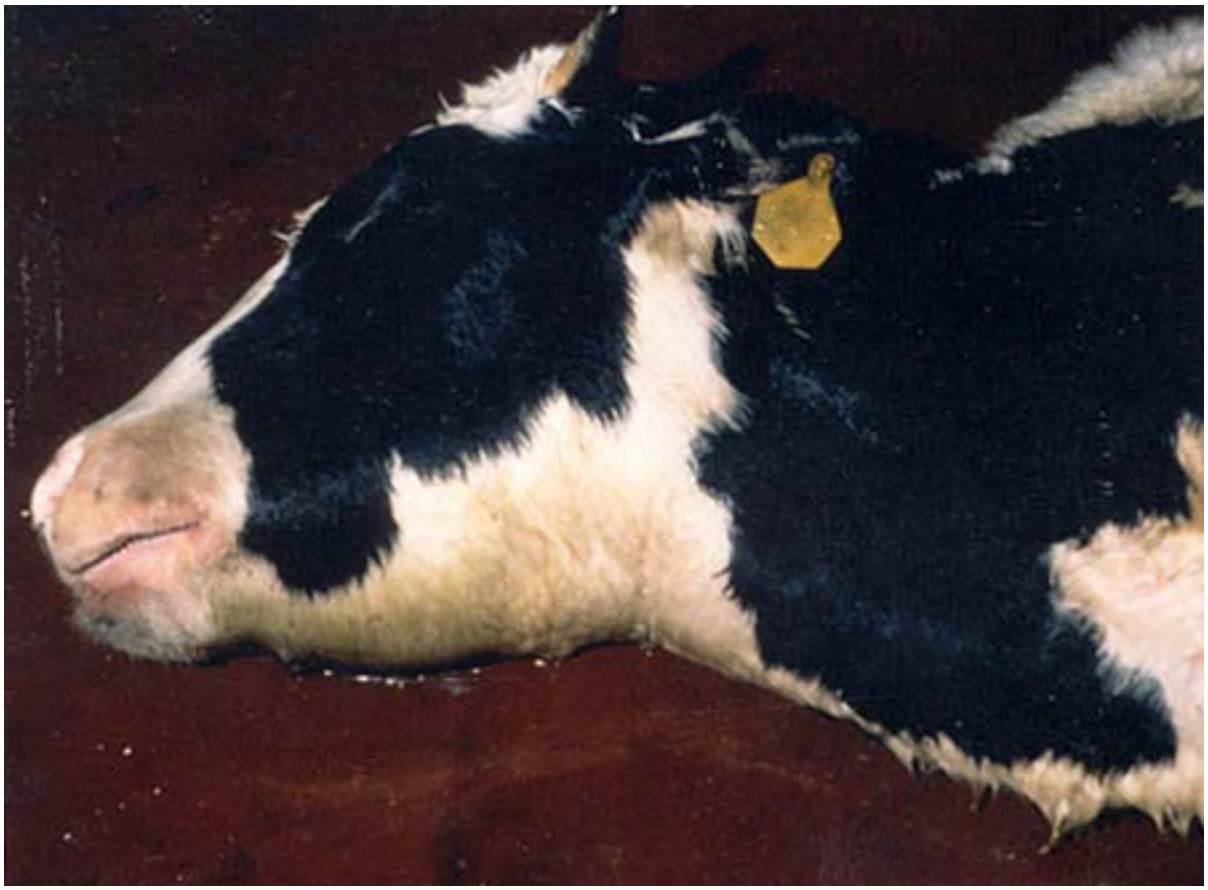

Fig. 63. HS - Extensive edematous swelling of the head and neck.

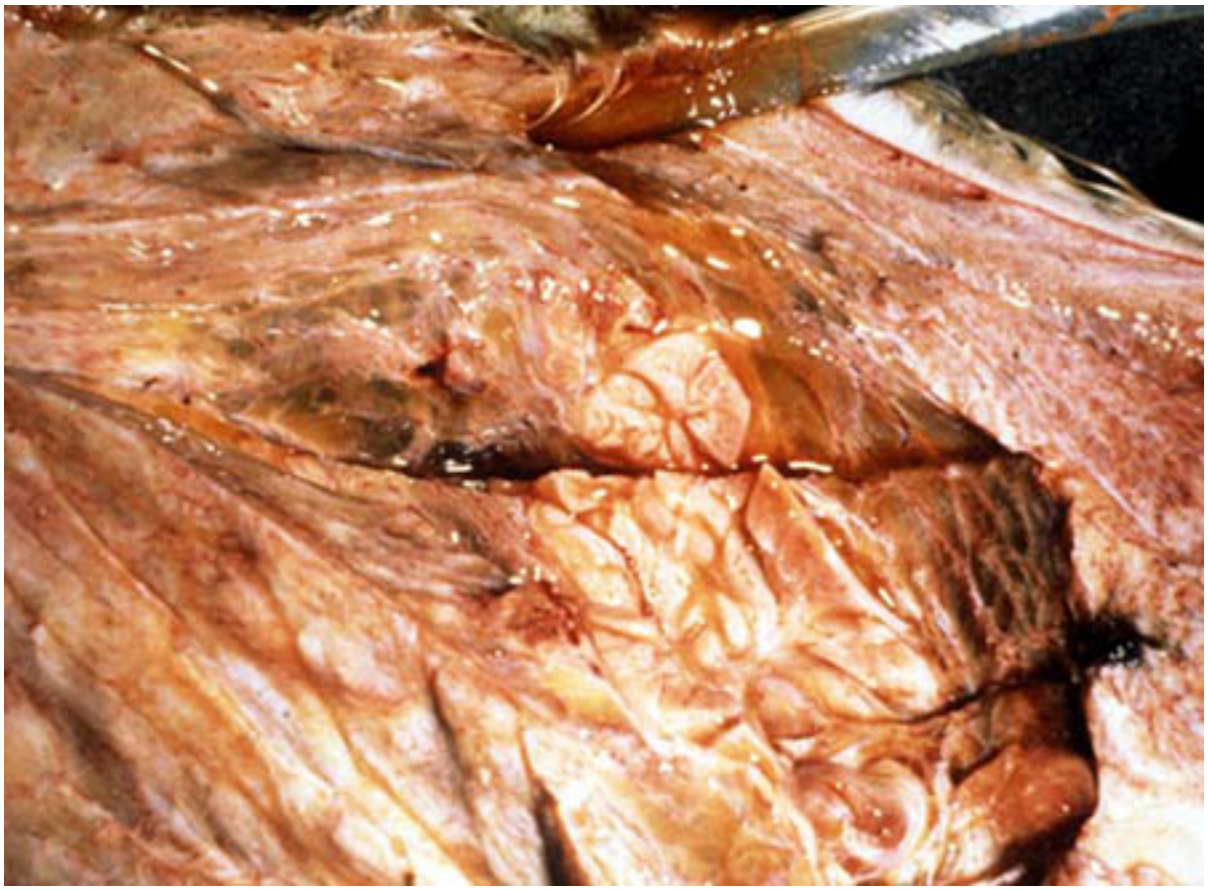

Fig. 64. HS - Extensive serofibrinous exudation and necrosis in the musculature of the neck.

PART IV
FOREIGN ANIMAL DISEASES

HOG CHOLERA
(Note: The preferred term for this disease is now classical swine fever.)

(Classical swine fever, peste du porc, colera porcina, Virusschweinepest)

Definition

Hog cholera (HC) is a highly contagious viral disease of swine that occurs in an acute, a subacute, a chronic, or a persistent form. In the acute form, the disease is characterized by high fever, severe depression, multiple superficial and internal hemorrhages, and high morbidity and mortality. In the chronic form, the signs of depression, anorexia, and fever are less severe than in the acute form, and recovery is occasionally seen in mature animals. Transplacental infection with viral strains of low virulence often results in persistently infected piglets, which constitute a major cause of virus dissemination to noninfected farms.

Etiology

Although minor antigenic variants of hog cholera virus (HCV) have been reported, there is only one serotype. Hog cholera virus is a lipid-enveloped pathogen belonging to the family Flaviviridae, genus *Pestivirus*. The organism has a close antigenic relationship with the bovine viral diarrhea virus (BVDV) and the border disease virus (BDV), as demonstrated in the immunodiffusion and immunofluorescence tests. The serum neutralization test can, however, differentiate between HCV and BVDV. In a protein-rich environment, HCV is very stable and can survive for months in refrigerated meat and for years in frozen meat. The virus is sensitive to drying (desiccation) and is rapidly inactivated by a pH of less than 3 and greater than 11.

Host Range

The hosts of HCV are the pig and wild boar.

Geographic Distribution

According to the FAO—WHO—OIE Animal Health Yearbook 1989, HC is recognized in 36 countries and is suspected of being present in another 2. The disease has been eradicated in Australia, Canada, and the United States. Constant progress toward eradication has been made in the countries of the European Economic Community since the guidelines for HC control in individual member states were accepted in 1980.

Transmission

The pig is the only natural reservoir of HCV. Blood, tissues, secretions and excretions from an infected animal contain HCV. Transmission occurs mostly by the oral route, though infection can occur through the conjunctiva, mucous membrane, skin abrasion, insemination, and percutaneous blood transfer (e.g., common needle, contaminated instruments). Airborne transmission is not thought to be important in the epizootiology of HC, but such transmission could occur between mechanically ventilated units within close proximity to each other.

Introduction of infected pigs is the principal source of infection in HC-free herds. Farming activities such as auction sales, livestock shows, visits by feed dealers, and rendering trucks are also potential sources of contagion. Feeding of raw or insufficiently cooked garbage is a potent source of HCV. During the warm season, HCV may be carried mechanically by insect vectors that are common to the farm environment. There is no evidence, however, that HCV replicates in invertebrate vectors. Husbandry methods also play an important role in HC transmission.

Large breeding units (100 sows) have a higher risk of recycling infection than small herds. In large breeding units where continuous farrowing is practiced, strains of low virulence may be perpetuated indefinitely until the cycle is interrupted by stamping-out procedures and a thorough cleaning and disinfection are carried out.

Incubation Period

The incubation period is usually 3 to 4 days but can range from 2 to 14 days.

Clinical Signs

The clinical signs of HC are determined by the virulence of the strain and the susceptibility of the host pigs. Virulent strains cause the acute form of the disease, whereas strains of low virulence induce a relatively high proportion of chronic infections that may be inapparent or atypical. These strains are also responsible for the "carrier-sow" syndrome from which persistently infected piglets are produced.

Acute Hog Cholera

In acute HC, the pigs look and act sick. Their disease progresses to death within 10 to 15 days, and remissions are rare. In an affected herd, some pigs will become drowsy and inactive and will stand with arched backs. Other pigs will stand with drooping heads and straight tails. Some pigs may vomit a yellow fluid containing bile. The sick pigs will huddle and pile up on each other in the warmest corner of the enclosure and will rise only if prompted vigorously. Anorexia and constipation will accompany a high fever that may reach 108° F (42.2° C) with an average of 106° F (41.1° C). Pigs may continue to drink and may have diarrhea toward the end of the disease process. Conjunctivitis (Fig. 65) is frequent and is manifested by encrustation of the eyelids and the presence of dirty streaks below the eyes caused by the accumulation of dust and feed particles. Sick pigs become gaunt and have a weak, staggering gait related to posterior weakness. In terminal stages, pigs will become recumbent, and convulsions may occur shortly before death. In the terminal stage, a purplish discoloration of the skin may be seen; if present, the lesions are most numerous on the abdomen and the inner aspects of the thighs.

Chronic Hog Cholera

Chronic HC is characterized by prolonged and intermittent disease periods with anorexia, fever, alternating diarrhea and constipation, and alopecia. A chronically infected pig may have a disproportionately large head relative to the small trunk. These runt pigs may stand with arched backs and their hind legs placed under the body. Eventually, all chronically infected pigs will die.

Congenital Hog Cholera

Congenital HCV infection by virulent strains will likely result in abortions or in the birth of diseased pigs that will die shortly after birth. Transplacental transmission with low-virulence strains may result in mummification, stillbirth, or the birth of weak and "shaker" pigs. Malformation of the visceral organs and of the central nervous system occurs frequently. Some pigs may be born virtually healthy but persistently infected with HCV. Such infection usually follows exposure of fetuses to HCV of low virulence in the first trimester of fetal life. Pigs thus infected do not produce neutralizing antibodies to HVC and have a lifelong viremia. The pigs may be virtually free of disease for several months before developing mild anorexia, depression, conjunctivitis, dermatitis, diarrhea, runting, and locomotive disturbance leading to paresis and death. In breeding herds affected with lowvirulence strains of HCV, poor reproductive performance may be the only sign of disease.

Gross Lesions

Acute Hog Cholera

The most common lesion observed in pigs dying of acute HC is hemorrhage. Externally, a purplish discoloration of the skin is the first observation. There may be necrotic foci in the tonsils (Fig. 66). Internally, the submandibular and pharyngeal lymph nodes are the first to be affected and become swollen owing to edema and hemorrhage. Because of the structure of the pig lymph node, hemorrhages are located at the periphery of the node (Fig. 67). As the disease progresses, the hemorrhage and edema will spread to other lymph nodes. The surface of the spleen, and particularly the edge of the organ, may have raised, dark wedge-shaped areas. These are called splenic infarcts. Infarcts are frequently observed in pigs infected experimentally with older strains of HCV but are less commonly seen with the contemporary strains (Fig. 68).

Pinpoint to ecchymotic hemorrhages on the surface of the kidney are very common in HC (Fig. 69). Such lesions are easier to see in the decapsulated kidney. Hemorrhages are also found on the surface of the small and large intestine (Fig. 70), the larynx, the heart, the epiglottis, and the fascia lata of the back muscles. All serous and mucosal surfaces may have petechial or ecchymotic hemorrhages.

Accumulation of straw-colored fluids in the peritoneal and thoracic cavities and in the pericardial sac may be present.

The lungs are congested and hemorrhagic and have zones of bronchopneumonia.

Chronic Hog Cholera

In chronic HC, the lesions are less severe and are often complicated by secondary bacterial infections. In the large intestine, button ulcers are an expression of such a secondary bacterial infection. In growing pigs surviving for more than 30 days, lesions may be seen at the costochondral junction of the ribs and at the growth plates of long bones.

Congenital Hog Cholera

In pigs infected transplacentally with HCV strains of low virulence, the most commonly seen lesions are hypoplasia of the cerebellum, thymus atrophy, ascites, and deformities of the head and of the limbs. Edema and petechial hemorrhages of the skin and of the internal organs are seen at the terminal stage of the disease.

Morbidity and Mortality

In acute HC, the morbidity and mortality are high.

Diagnosis

Field Diagnosis

Septicemic conditions in which pigs have high fever should be investigated carefully. A thorough history from the herd owner should be obtained to determine if raw garbage was fed, if unusual biological products were used, or if recent additions were made to the herd. Careful observation of the clinical signs and of the necropsy lesions should be recorded. In acute HC, it is helpful to necropsy four or five pigs to increase the probability of observing the representative lesions.

A marked leukopenia is detectable at the time of initial rise in body temperature and persists throughout the course of the acute and chronic disease. This feature was once widely used in the field diagnosis of HC. Nowadays, with the development of more specific laboratory diagnostic methods, which are aimed at demonstrating the virus or its structural antigens in tissues or at detecting specific antibodies in the serum, the white blood count is not as widely used. In endemic areas it could be helpful.

Specimens for Laboratory

For virus isolation and antigen detection, the tonsils are considered essential. In addition, submandibular and mesenteric lymph nodes, spleen, kidneys, and the distal part of the ileum should be collected. In live pigs, tonsil biopsies and whole blood collected with anticoagulants are useful to diagnose HC. Sample collection should be targeted to pigs having fever or showing other signs of the disease. Each sample of tissue should be placed in a separate plastic bag and identified. The samples should not be frozen (interference with fluorescent antibody tissue section test) but kept at refrigeration temperature. The material should be transported and stored in leak-proof containers in accordance with national regulations for transportation of diagnostic biologic samples.

Serum samples for antibody detection should be collected from animals that have recovered from suspected infection or from sows known to have been in contact with infected or suspected cases. A sufficient number of samples should be collected to ensure a high probability of detecting infection.

A complete set of tissues, including the whole brain, should be submitted in 10 percent buffered formalin.

Laboratory Diagnosis

Any clinical diagnosis of HC must be confirmed by the submission of specimens to a specialized diagnostic laboratory that should also have the capability to distinguish between HC and African swine fever.

The laboratory diagnostic procedures for HC have evolved in parallel with the emergence of new technologies. Until the 1960's, laboratory diagnosis was restricted to recognition of gross lesions and confirmation by histopathology. Inoculation of susceptible pigs was often used as final confirmatory test and to determine the virulence of the viruses. Numerous laboratory techniques have been described to diagnose HC, but only a few have gained international acceptance and have been integrated into national HC control programs. Only these will be discussed in this presentation.

In the fluorescent antibody tissue section test (FATST), direct fluorescent antibody technique is applied to detect HC viral antigens in frozen tissues of organs from dead pigs, in biopsy material, or in impression smears. Theoretically, a diagnosis can be confirmed within hours from the reception of the specimen. In countries where the disease has been eradicated, the diagnosis of the "index case" by the FATST alone may be difficult, and confirmation in cell culture may be needed. The FATST may not differentiate HC from BVDV infection; an accurate distinction between the two viruses has to be made before releasing a final diagnosis. Differentiation between HCV and BVDV can readily be made with the immunoperoxidase test using monoclonal antibodies or the serum neutralization test.

The isolation of HCV in cell culture and the identification using fluorescein-labeled hog cholera antibody (fluorescent antibody cell culture test) can provide confirmation in cases where the results of investigation of frozen tissue sections are inconclusive.

As control measures for HC are implemented in a country, virulent strains of HCV will be reduced, and there will be a relative increase of low-virulence strains. As the proportion of subclinical cases in a national herd increases, it will become increasingly difficult to recognize the disease. The antigen detection systems previously described become less effective; thus, serological tests are essential for a successful control and eventual eradication program.

Approximately 75 percent of pigs infected with acute HC have microscopic lesions of an encephalitis characterized by perivascular cuffing, endothelial proliferation, and microgliosis. This feature is easily recognized in a nonspecialized diagnostic laboratory and may constitute the most important single factor that will cause the pathologist to suspect HC.

Differential Diagnosis

Differential diagnosis of HC should include African swine fever, erysipelas, salmonellosis, eperythrozoonosis, and salt poisoning.

Vaccination

Over the years, numerous regimens of vaccination have been advocated with a variable degree of success. In the past two decades, modified live vaccines (MLV) with no residual virulence for pigs have become available. The lapinized Chinese (C) strain, the Japanese guinea pig cell culture-adapted strain, and the French Thiverval strain have been widely used. All three strains are considered innocuous for pregnant sows and piglets over 2 weeks old.

Control and Eradication

In countries where HC is enzootic, a systematic vaccination program is effective in preventing losses. Experience in the United States and in some countries of the European Union has proven that a strict regimen of vaccination will reduce the number of outbreaks to a level at which complete eradication by sanitary measure alone will be feasible. At that point, vaccination must be stopped. A successful eradication program requires a massive input of funds from a central government and cooperation from the government, the swine industry, and the veterinary profession. Eradication measures will be assisted by strictly enforcing the garbage cooking laws, having an effective swine identification system, and using serological surveys targeted primarily to breeding sows to detect subclinical infections.

In countries where HC has been eradicated and in which the threat of reintroduction is significant, it is essential to initiate an effective serological monitoring system. Sampling may be limited to strategic locations such as the border of an infected neighbor country or be intensified to target populations such as the garbage-fed herds. Such a system has been in effect in the United States since successful eradication in 1976; several thousand samples have been accessed annually.

Public Health

Human beings are not susceptible to HCV infection.

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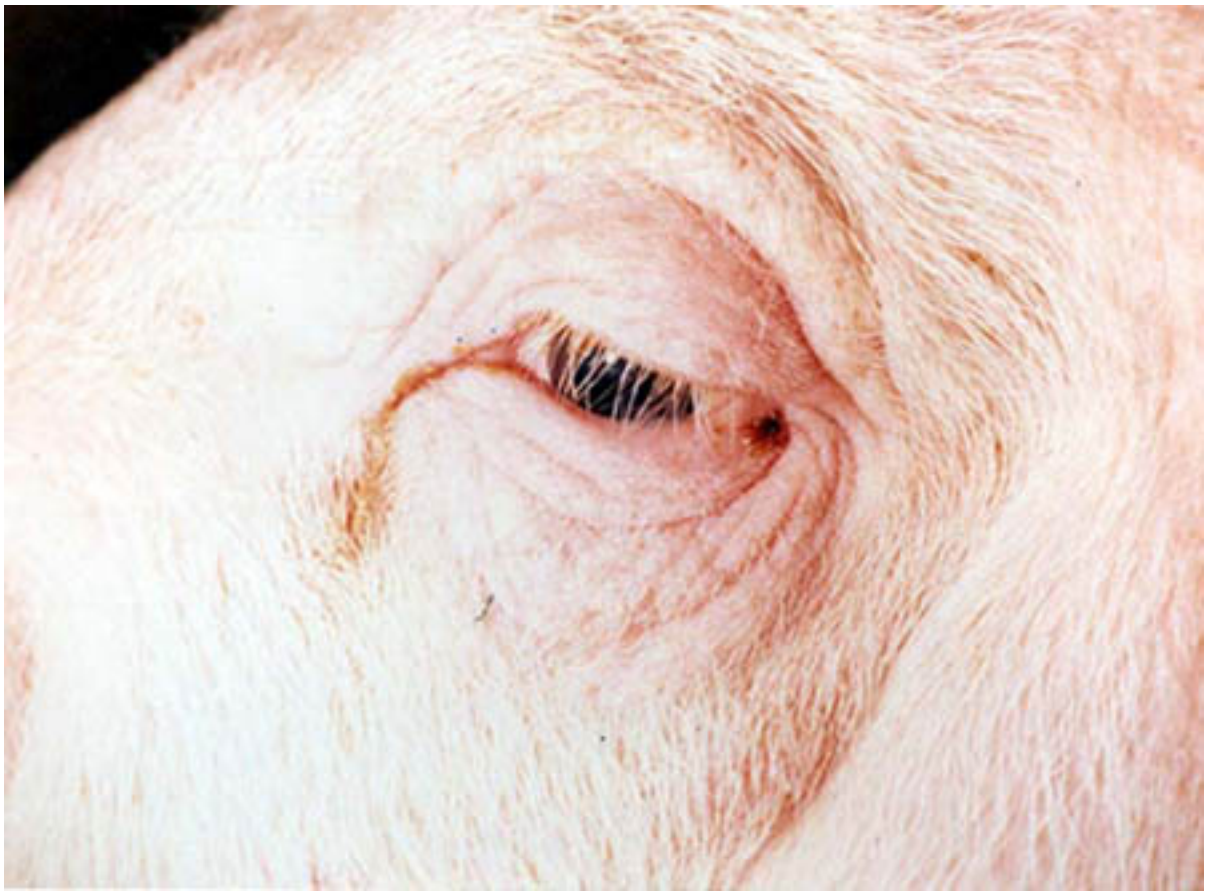

Fig. 65. HC - Conjunctivitis and exudate in the medial canthus.

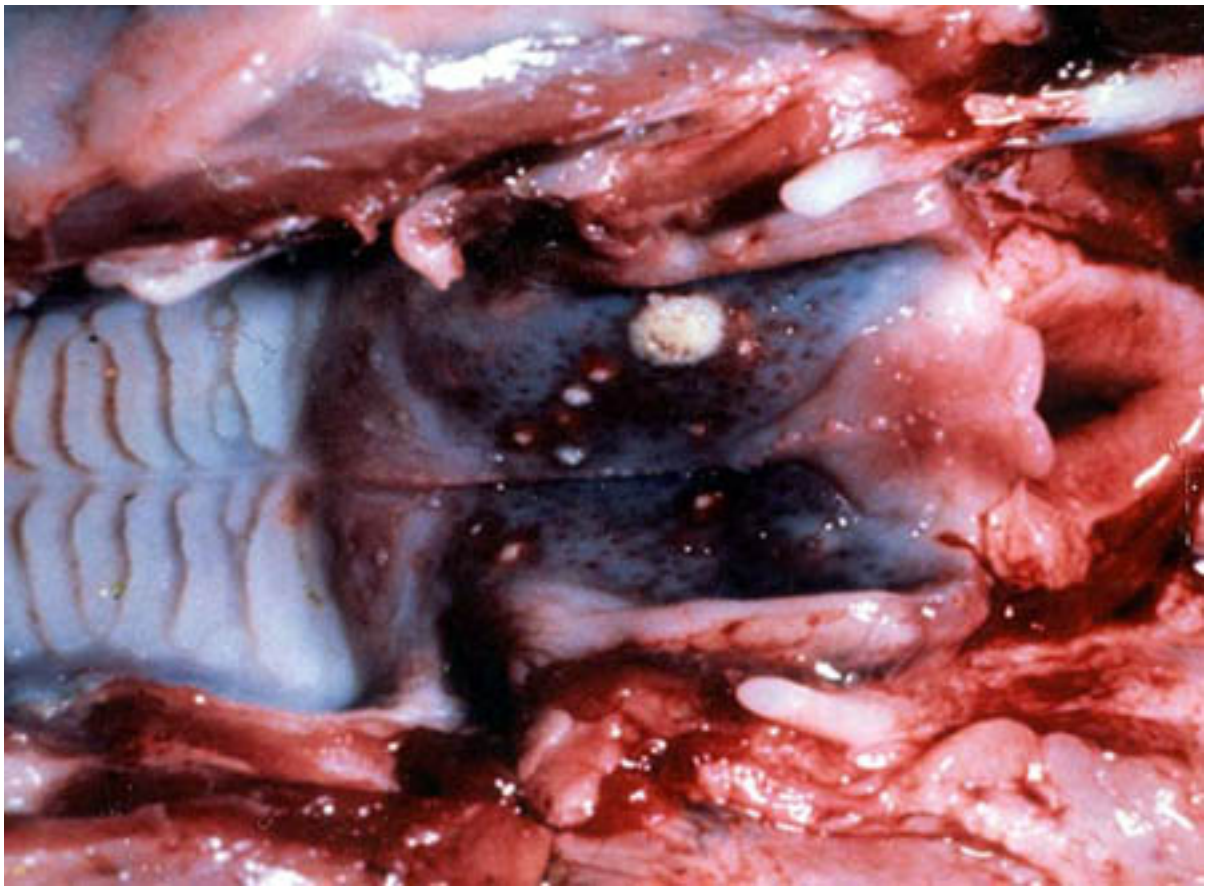

Fig. 66. HC - Multiple necrotic foci in the tonsils.

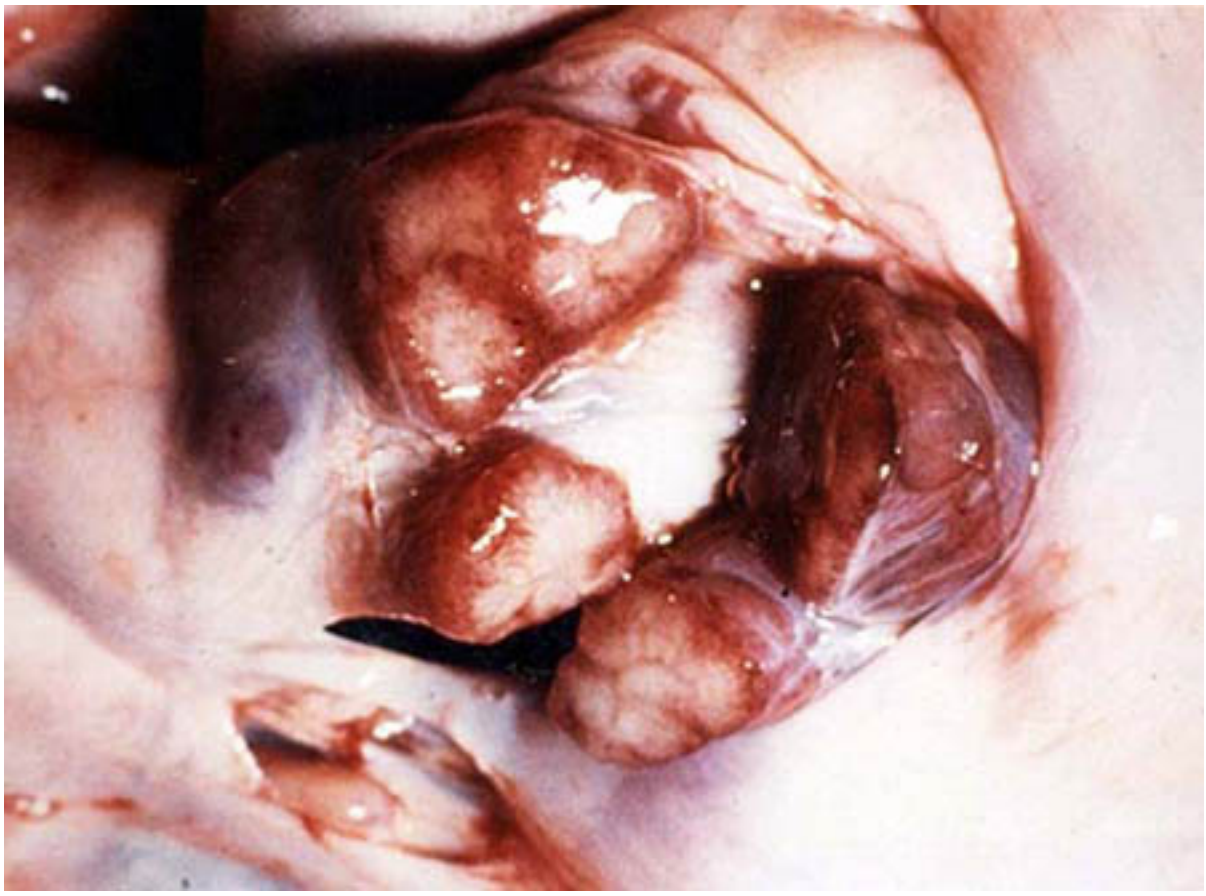

Fig. 67. HC - Peripheral hemorrhages in the lymph nodes.

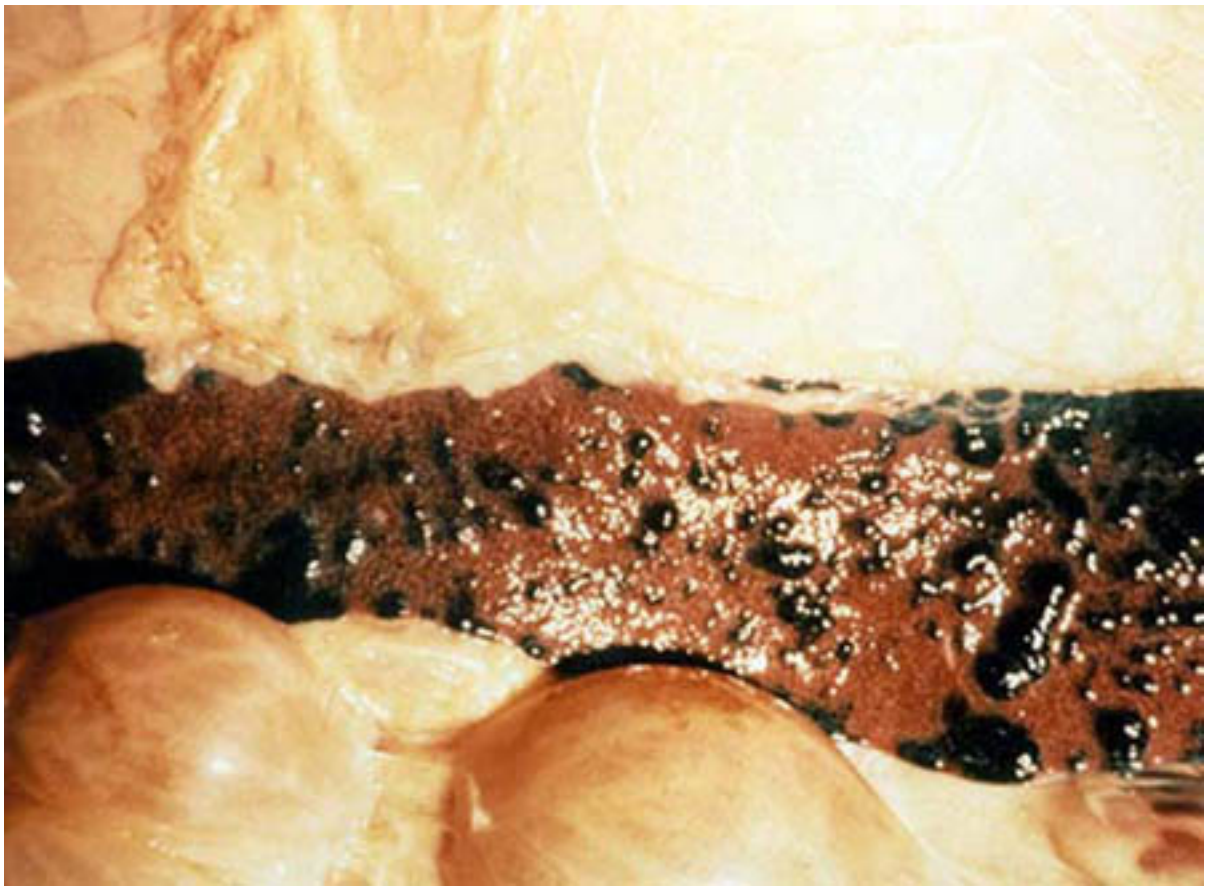

Fig. 68. HC - The dark raised areas are splenic infarcts.

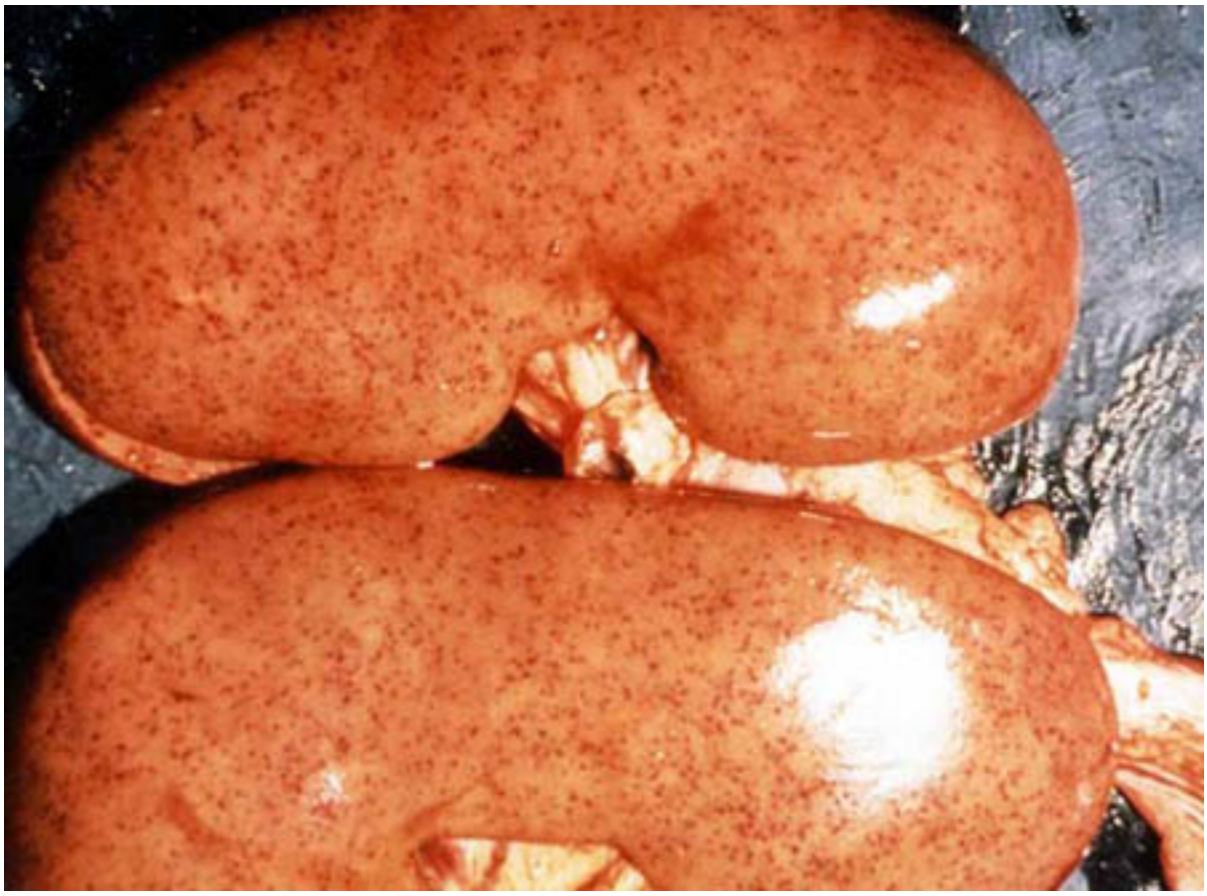

Fig. 69. HC - Petechial hemorrhages in the renal cortex.

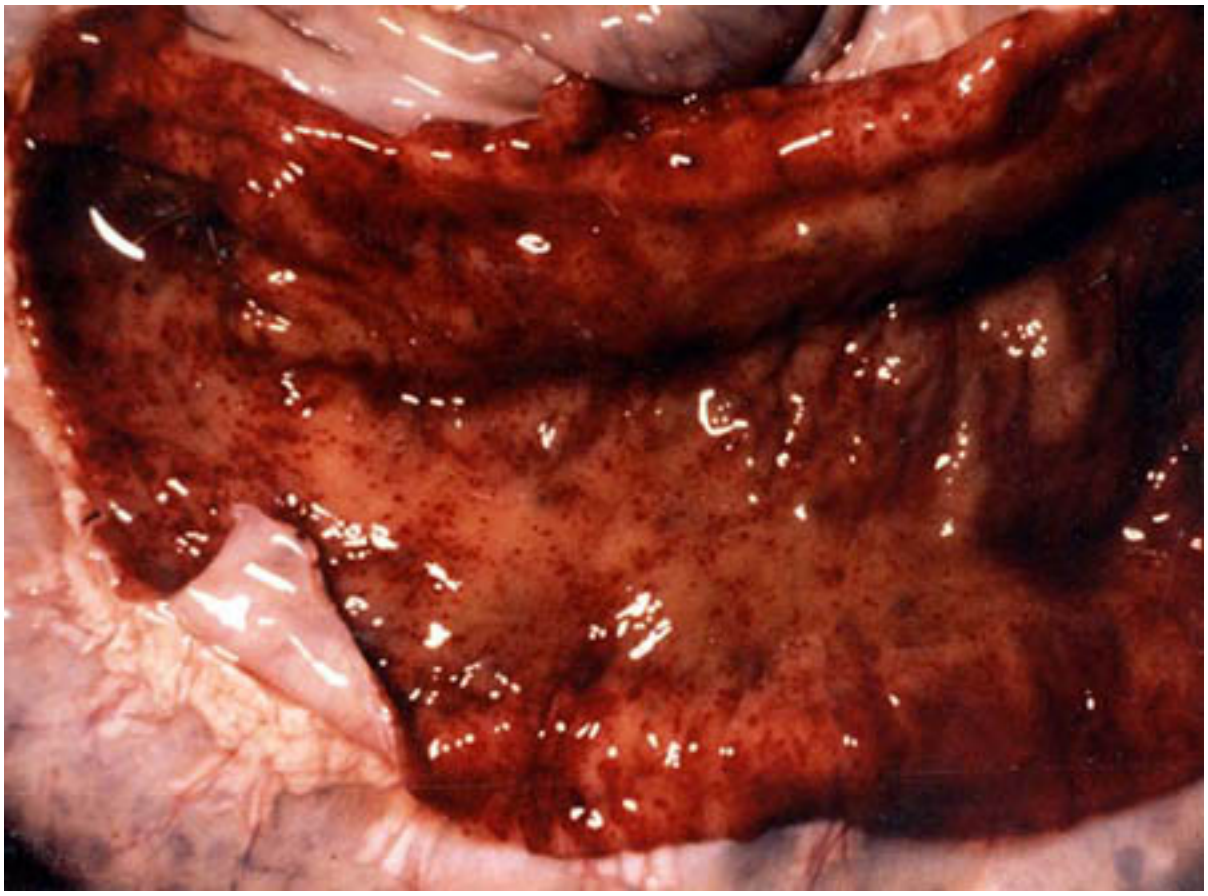

Fig. 70. HC - Colitis: the contents of the spiral colon are liquid and there are petechial hemorrhages in the mucosa.

PART IV
FOREIGN ANIMAL DISEASES

JAPANESE ENCEPHALITIS

(Japanese B encephalitis)

Definition

Japanese encephalitis (JE) is an arthropod-borne virus disease affecting the central nervous system (CNS) of human beings and, less frequently, horses. The infection also results in the birth of litters of pigs with a high percentage of stillbirths or pigs affected with encephalitis.

Etiology

The JE virus is a member of the family Flaviviridae and is in the genus *Flavivirus*. Host range and other characteristics are described in detail in the International Catalogue of Arboviruses (1).

Host Range

People and horses are victims of the JE virus infection but appear to be dead-end hosts from an epidemiologic standpoint. Viremia levels in infected human beings and equine species are generally too low to provide potential mosquito vectors with an infective blood meal. Under experimental conditions, however, Gould et al. (9) demonstrated horse to horse transmission by *Culex tritaeniorhynchus*. Cattle are frequently infected in enzootic areas (24) but do not develop sickness or viremia (14).

Swine in Japan and Taiwan are both victims of disease as well as amplifiers of infection in nature. This is particularly true when swine are bred to farrow at a time when infected mosquitoes make their first appearance. This type of breeding program is practiced in Japan where, because of immunity or natural seasonal lows in transmission, gilts resist infection during pregnancy, and thus losses due to abnormal litters resulting from JE infection are reduced. However, normal newborn piglets soon lose maternally acquired antibody and are fully susceptible to infection from arthropod vectors.

Although JE infection in shoats is subclinical, viremias are sufficiently high to provide emerging broods of *Cu. tritaeniorhynchus*, which feed readily on swine, with a plentiful source of virus-containing blood. Following a period of extrinsic incubation of virus, the mosquitoes are able to transmit the infection to susceptible vertebrate hosts.

In Japan, herons and egrets play a role in the spread of infection to man and other vertebrates and may be responsible for carrying the virus from rural to urban areas. *Cu. tritaeniorhynchus* feeds readily on herons and egrets and ranges sufficiently high off the ground to feed on the young nesting birds.

Geographic Distribution

Human encephalitis in Japan was recognized as early as 1871, and Japanese encephalitis in epidemic form has been known since 1924 when 4,000 human deaths were recorded in Japan. The epidemiology of the disease was studied extensively after World War II in Japan by scientists of the U.S. Army's 406th Medical General Laboratory (2). Concurrent with vaccination of people and extensive use of agricultural pesticides in the last three decades, the disease has practically disappeared from Japan.

Japanese encephalitis virus infection is widespread throughout temperate and tropical Asia;

increasing numbers of human and equine cases have appeared in India, Nepal, China, Philippines, Sri Lanka, and northern Thailand. The disease in humans is sporadic in Indonesia and northern Australia but is not known in the rest of the world.

Transmission

The virus is maintained in nature in a cycle involving *Culex mosquitoes* of the genera *tritaeniorhynchus*, *annulus*, *fuscocephala*, *gelidus*, and *vishnui* complex. Mosquitoes transmit the virus to many species of birds and to swine (2,25).

The sequence of events in temperate Asia is initiated by appearance of virus in mosquitoes in late spring followed by the infection and disease in susceptible horses and swine. This is followed by the appearance of disease in man in August and September. In tropical and semitropical areas of Asia, the seasonal nature of the disease is less marked.

Basically, however, it appears the *Culex* mosquitoes and birds are common factors in the epidemiology of JE, regardless of the region of occurrence, and that swine are involved where they are numerous in Asia (15).

The mechanism of maintaining the virus over the winter in temperate areas has not been elucidated. Overwintering in mosquitoes is a possibility either in infected hibernating mosquitoes or by transovarial passage (23). It is also possible that bats may carry the virus for prolonged periods (18,6).

Incubation Period

In horses, the incubation period is 8 to 10 days. The time between exposure of pregnant swine to an infectious dose of JE virus and delivery of abnormal litters does not seem to be clearly established, although exposure early in gestation appears more likely to result in abnormal litters than later exposure.

Clinical Signs

In horses, initial signs are fever, impaired locomotion, stupor, and grinding of teeth. Blindness, coma, and death follow in more severe cases. Although the clinical signs resemble those seen in horses with Western equine encephalomyelitis and Eastern equine encephalomyelitis, mortality is relatively low. Inapparent or subclinical infections in horses are far more common than cases of recognizable encephalitis.

The principal manifestation of disease in swine is the expulsion of litters of stillborn or mummified fetuses, usually at term. Viable piglets frequently die shortly after birth and exhibit tremor and convulsions before expiring. Experimental infection of boars leads to diminished sperm count and decreased mobility of sperm. Virus has been transmitted to gilts by way of infected semen (11).

Gross Lesions

In horses, gross lesions are similar to those observed in animals dying from Eastern equine encephalomyelitis and Western equine encephalomyelitis virus infections and are not specific enough to establish an etiologic diagnosis. Litters from infected pigs contain fetuses that are mummified and dark in appearance (24,4). Hydrocephalus, cerebellar hypoplasia, and spinal hypomyelinogenesis have been noted (20).

Morbidity and Mortality

The equine mortality caused by JE has been reported at about 5 percent in Japan and may actually be less than this in Southeast Asia. Mortality in adult pigs is close to zero. Litters of pigs from infected sows may be dead at delivery or, if living, may be quite weak and apt to succumb to encephalitis shortly after birth.

Diagnosis

Field Diagnosis

Presumptive diagnosis can be made in horses that manifest CNS disease accompanied by fever, particularly in an epizootic period. It has been observed that illness in horses at race tracks in Malaysia is frequently due to JE infection. The infection is manifested only by fever and a short period of lethargy (16,12,22). In temperate zones, the disease appears during late summer and early fall.

A presumptive diagnosis in swine is based on the birth of litters with a high percentage of stillborn or weak piglets.

Specimens for Laboratory

One half of a brain from animals having signs of encephalitis should be submitted unfixed and the other half fixed in 10 percent formalin. Paired serum samples collected at least 14 days apart should be submitted from animals that survive. Cerebrospinal fluid from horses with CNS signs should be submitted for detection of JE-specific IgM.

Laboratory Diagnosis

Confirmation of JE can be accomplished by demonstrating seroconversion in animals that survive long enough to yield properly spaced blood samples. Neutralization, complement fixation, hemagglutination inhibition, immunofluorescence, and enzyme-linked immonosorbent assay tests are used to show a rise in titer from the acute stage to death or recovery. Reliance on seroconversion or IgM as a means of diagnosis in horses is not definitive because seroconversion may have resulted from exposure to another nonpathogenic *Flavivirus*.

Demonstration of JE-specific IgM in serum of an encephalitic equine is presumptive evidence of the diagnosis.

Further confirmation of JE in horses can be obtained by examination of the cerebrospinal fluid and the brain. Specific IgM in the spinal fluid is excellent evidence of CNS infection. Although microscopic lesions of the brain are of value, definitive confirmation is based on isolation and identification of the virus from the brain. Virus isolations are more likely to be successful from brains of animals that died after a short course of the disease.

Confirmation of JE in diseased litters of pigs is accomplished by isolation of the virus from fetal brains or brains of piglets that die after manifesting signs of encephalitis. Demonstration of antibody increase in dams bearing affected litters is probably not a reliable measure because seroconversion in such animals would probably have occurred earlier in infection.

Differential Diagnosis

The disease in horses must be differentiated from other viral encephalitides. In Asia, JE is the only recognized arboviral infection causing encephalitis in horses. Because there are many mild or subclinical infections, laboratory confirmation is essential.

Various forms of toxic encephalitis must be considered in differential diagnosis. In temperate-zone Asia, the midsummer seasonal occurrence of JE in horses aids in differential diagnosis.

Japanese encephalitis in pigs must be differentiated from a hemagglutinating DNA virus infection that appears to be as commonplace in Japan as JE (21) and causes the same pattern of disease. There is evidence that the DNA virus infection is established in gilts in the middle or last trimester of pregnancy. Seasonal patterns of DNA virus infection need more complete study, but the disease does appear concurrently with Japanese encephalitis and therefore requires laboratory tests for differentiation.

Another hemagglutinating virus, myxovirus parainfluenza 1 (Sendai), has been shown capable of producing stillbirth in swine under experimental conditions (20). Encephalitis in neonatal pigs is also associated with a coronavirus infection. This agent is known to cause encephalitis in piglets in at least North America and Europe (19).

Vaccination

A live attenuated vaccine produced in hamster kidney tissue culture is in widespread use in horses in China (13). This vaccine reduced disease by about 85 percent. An inactivated vaccine prepared in mouse brain is licensed in Japan, Korea, Taiwan, India, and Thailand for use in humans. A similar inactivated product made in hamster kidney tissue culture has been used to immunize children annually in China since 1965. Live attenuated vaccines are used to immunize pigs in Japan and Taiwan (8) and humans in China (13A).

Control and Eradication

Options for control include elimination of the vectors, prevention of amplification of the infection cycle in birds and pigs, or immunization of horses, pigs, and people. Although some success in vector control was achieved by modification of irrigation methods to minimize breeding of *Cu. tritaeniorhynchus* in Southeast Asia and coincidentally by the use of agricultural pesticides, vector control has never been more than marginally successful. Reduction of the avian reservoir hosts does not appear feasible.

The most promising approach to reducing livestock losses and at the same time reducing the totality of infection in nature is widespread immunization of swine. Live attenuated vaccines are in use in Japan and Taiwan (8). Immunization of shoats prevents infection in vaccinees and neutralizes their role as amplifiers of infection in nature. It is anticipated that those animals retained for breeding will remain immune, and, because of immunity or natural seasonal lows in transmission resist infection during pregnancy and therefore bear normal litters. Although controlling the disease in swine dampens the spread of infection in nature, there is a continued threat to horses and human beings from other sources.

The introduction of JE virus into the United States is always a possibility, but whether the infection, once introduced, would become established in nature is difficult to assess. Animal health authorities must continue to be alert to detecting and identifying agents associated with encephalitis in horses and with abnormal litters of pigs. The means for rapid diagnosis and identification of JE are available, although it is doubtful that control of the disease in Asia will be achieved in the near future.

Public Health

Japanese encephalitis can cause an explosive, highly fatal form of human encephalitis.

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PART IV
FOREIGN ANIMAL DISEASES

LOUPING-ILL

(Ovine Encephalomyelitis, Infectious Encephalomyelitis of Sheep, Trembling-ill)

Definition

Louping-ill (LI) is an acute viral disease primarily of sheep that is characterized by a biphasic fever, depression, ataxia, muscular incoordination, tremors, posterior paralysis, coma, and death. Louping-ill is a tick-transmitted disease whose occurrence is closely related to the distribution of the primary vector, the sheep tick *Ixodes ricinus*.

Etiology

Louping-ill is caused by a neurotropic single-strand RNA virus of 40-50 nm that has been classified in the Flaviviridae family, *Flavivirus* genus (20). It belongs to a subgroup of antigenically related viruses known as the tick-borne encephalitis complex whose members also include tick-borne encephalitis virus of Europe, the Omsk haemorrhagic fever virus of Russia, the Kyasanur forest disease virus of India, Langat virus of Malaysia, Negishi virus of Japan, and Powassan virus of North America (2). This complex of viruses is found throughout the northern temperate latitudes. The LI virus has been shown to be most closely related antigenically to strains of the Western European subtype of tick-borne encephalitis virus (17). Although there is no evidence of any significant variation in pathogenicity between strains of LI virus from a variety of vertebrate species and from ticks (11), monoclonal antibody analysis has revealed antigenic heterogenicity among isolates of the virus (8).

In tissue suspensions, LI virus will remain viable for at least 82 days when stored in 50 percent glycerol or at temperatures of -20° C or lower. It is rapidly inactivated in saline or broth — especially in dilute or acid suspensions.

Host Range

Louping-ill is of greatest veterinary medical signifcance as a disease of sheep. All ages of sheep can be affected with LI, depending on their immune status and the severity of virus challenge.

Infecion with LI virus has been demonstrated in other domestic species and wildlife; namely, cattle, horses, pigs, dogs, deer, and humans as well as in a range of species of small mammals such as shrews, woodmice, voles, and hares. Because none of these species develop a high-titered viremia, they are regarded as unlikely to play a significant role in the maintenance of LI virus in nature (11). Most recently, the influence of low or nonviremic hosts such as hares, both in the multiplication of vectors and the amplification of virus through nonviremic transmission, is now considered significant for virus persistence (9). Humans, though susceptible to infection with LI virus, are considered an accidental or tangential host of the virus.

Investigation of European grouse species has revealed marked variation in susceptibility to experimental infection with LI virus. Whereas two woodland or forest species, pheasant and capercaillie, were found to be resistant to disease, both of the mountain or tundra species of birds studied, red grouse and ptarmigan, were highly susceptible and developed high viremias and succumbed rapidly to the infection. If available, both red grouse and ptarmigan may act as amplifing hosts of the virus in endemic areas.

Geographic Distribution

Louping-ill is endemic in rough upland areas in Scotland, Northern England, Wales and Ireland.

A disease of sheep very closely related to LI has been reported in Bulgaria (10), Turkey (17), the Basque region in Spain (6) and Norway (4).

Transmission

Although many ixodid ticks have been shown to be capable of transmitting LI virus, including *Rhipicephalus appendiculatus*, *Ixodes persulcatus*, and *Haemaphysalis anatolicum*, *I. ricinus* is considered the natural vector of this disease. *I. ricinus* is a three-host tick with a life cycle from egg to engorged adult of 3 years. Occurrence of LI in those countries in which it is endemic can be correlated closely with the distribution of the tick vector, which requires an environment with a high relative humidity. All stages of ticks, larva, nymph, and adult, acquire the virus by feeding on a viremic host . Because transovarial transmission of the virus has never been established, transmission appears to be entirely transstadial (11). None of the known vectors of LI virus currently occur in the United States.

A significant feature of the bionomics of *I. ricinus* that has a major impact on the epidemiology of LI is the annual periodicity of tick activity. Peak tick activity occurs in the spring (the "spring rise"), and a minor resurgence of activity is experienced in some areas in the fall. Although cases of LI can occur at any time of the year, the disease is most prevalent during the periods of maximal tick activity between April and June and again in September.

On the basis of the level and duration of viremia that develops in sheep following infection with LI virus, this species appears to be the essential maintenance host for the virus (11). Irrespective of clinical outcome, sheep consistently develop viremias of sufficient magnitude to transmit the virus to the tick vector.

Experimentally, LI virus has been shown to be shed in the milk of goats and ewes following infection with the virus. Although titers of virus in the milk of both species were similar, virus was shed for a longer period in goats (13). Transmission of virus, presumably through the ingestion of infective milk, was demonstrated in kids that suckled infected goats. Similar attempts to transmit the infection in sheep were unsuccessful.

Louping-ill virus has been transmitted experimentally to various animal species by several parenteral routes of inoculation and following exposure to infective aerosols. Accidental infection of humans has occurred following tickbite, penetration of the virus through skin wounds, or by aerosol exposure in the laboratory.

Incubation Period

Under conditions of natural exposure to the virus, the incubation period of LI ranges from 6 to 18 days. This is shortened in sheep experimentally infected by certain unnatural routes of challenge such as intracerebral inoculation.

Clinical Signs

Exposure to LI virus may result in subclinical or clinical infection, depending on a range of host-related and environmental factors. Initial clinical signs in naturally infected sheep are nonspecific and include fever, which may reach 42° C (107.6° F), depression, anorexia, and possibly constipation. The fever is biphasic, with the second rise occurring about the fifth day after the appearance of clinical signs, at which point the virus may invade the central nervous system. If it does not, the animal will recover rapidly and develop a durable protective immunity. Involvement of the central nervous system is associated initially with evidence of cerebellar dysfunction characterized by muscular tremors and incoordination, ataxia, hyperaesthesia, and development of the characteristic louping gait. At this stage of the disease, sheep are often hypersensitive to noise and touch and will go into convulsive spasms if disturbed. Progression of the disease leads to cerebrocortical involvement. Affected animals exhibit head-pressing, paraplegia, convulsions, opisthotonos and coma. In many cases, death supervenes after a clinical course ranging from 7 to 12 days. Animals that survive never regain full health and display residual central nervous system deficits of variable severity.

Intercurrent infection of sheep with *Cytoecetes phagocytophila* or *Toxoplasma gondii* can influence the clinical outcome of infection with LI virus. Concurrent infection with either of these agents can enhance the pathogenicity of the virus — apparently by exerting a profound immunosuppressive effect on the animal's defense system. Viremias are markedly greater and more prolonged in such animals compared with those in sheep exposed to LI virus alone (14, 15).

Although no differences in susceptibility to LI virus have been demonstrated between a variety of breeds of sheep, the clinical course of the disease may vary in very young lambs versus older sheep. Lambs born to nonimmune ewes that are exposed to the virus may develop a peracute terminal illness with death supervening within 48 hours after the onset of clinical signs.

Naturally occurring cases of LI in cattle, horses (18) and pigs (1) present clinical features broadly similar to those observed in sheep. Evidence of neuromuscular dysfunction is seen. Affected cattle frequently have a staggering gait, hyperexcitability, head-pressing, recumbency, and convulsions and then die. Young piglets infected with LI virus can have a range of nervous signs, including aimless movement, head-pressing, ataxia, muscular spasms, and convulsions. Natural cases or outbreaks of LI in horses are very uncommon, and most cases of infection with the virus are apparently subclinical.

Gross Lesions

Wth the exception of possible congestion of meningeal vessels, there is no pathognomonic gross lesion.

Morbidity and Mortality

All ages of sheep can be affected with LI, depending on their immune status and the severity of virus challenge. Typically, however, lambs born of immune dams are passively protected in their first year of life but then become susceptible. Replacement breeding stock are vulnerable to infection at 1 year of age (hoggets), and it is in this age group that losses from the disease are most frequently observed. Mortality rates as high as 60 percent can occur, however, in lambs whose passively acquired immunity has declined and which are introduced onto heavily tick-infested pastures for the first time. The incidence of LI in mature sheep is usually low unless they have recently been moved from a non-LI endemic area into an area in which the disease is endemic. Whereas the prevalence of infection may be as high as 60 percent, the case fatality rate is low and uncommonly exceeds 15 percent. Intercurrent tick-borne fever or toxoplasma infection or a range of environmental stress factors can predispose to the development of encephalitis and a higher mortality.

Diagnosis

Field Diagnosis

A diagnosis of LI must remain tentative or provisional until corroborated by confirmatory laboratory evidence. The disease should be strongly suspected, however, in sheep having signs of central nervous system disturbance consistent with those seen in typical cases of LI virus infection and where there is a flock history of recent introduction onto tick-infested pastures in an endemic area. Diagnosis of LI in other domestic species similarly cannot be based on clinical grounds alone.

Specimens for Laboratory

Heparinized blood should be collected during the acute viremic phase of the disease and preferably during the first 3 to 4 days after the onset of fever, which is best for virus isolation. In the majority of cases, virus isolation is attempted on the brain and spinal cord of animals that died. Although this is frequently successful in sheep, results in cattle have been variable. Unfixed portions of brain and spinal cord are best transported to the laboratory in 50 percent glycerol and normal saline or frozen on dry ice and dispatched in a closed, insulated container

using an overnight delivery service. Paired serum samples, acute and convalescent, should be submitted for serologic examination. Half of the brain and portions of spinal cord should be submited in 10 percent formalin.

Laboratory Diagnosis

A definitive diagnosis of LI is based on isolation and identification of the virus, virus detection by a reverse transcriptase polymerase chain reaction assay (RT-PCR), and confirmatory serological evidence. Where LI is suspected, isolation of virus can be attempted from the blood during the acute viremic phase of the disease. Virus isolation from the blood is not feasible, however, after the onset of central nervous system signs, for at this point the viremia has ceased because of the appearance of neutralizing and hemagglutinating-inhibiting antibodies in the blood. In the majority of cases, virus isolation is attempted on the brain and spinal cord from animals that died. Although this is frequently successful in sheep, results in cattle have been variable.

Although not yet widely in use, an automated RT-PCR assay followed by nucleotide sequencing of the cDNA product has been used successfully in the rapid detection and indentification of LI virus in field specimens (5).

Serological confirmation of a diagnosis of LI virus infection is based on the demonstration of seroconversion or a significant (fourfold or greater) rise in antibody titer to the virus between acute and convalescent sera. Hemagglutination-inhibition antibodies appear 5 to 10 days after infection and decline after 6 to 12 months; serum neutralizing antibodies persist for years. The complement fixation test is of very limited value in the diagnosis of this disease in sheep because these antibodies appear late in the course of infection and are transient. A standardized tick-borne encephalitis virus antigen is now commercially available for use in an enzyme-linked immumosorbent assay (ELISA) test for this disease, which obviates the need to prepare in-house antigen reagents. Demonstration of specific IgM antibody in serum is also confirmatory of infection.

An avidin-biotin-complex (ABC) immunoperoxidase technique has successfully been applied to the detection of LI virus in formalin-fixed brain material from experimental and natural cases of infection.

Differential Diagnosis

Louping-ill in sheep may be confused clinically with a range of other infectious and noninfectious diseases, including scrapie, pregnancy toxemia, hypocalcemia, tetanus, listeriosis, tick pyemia, hypocuprosis ("swayback"), rabies, hydatid disease, and various plant poisons. Cases of the disease in cattle must be differentiated from malignant catarrhal fever, listeriosis, pseudorabies, bovine spongiform encephalopathy, rabies, hypomagnesemia, hypocalcemia, acute lead poisoning, and certain plant poisons. With the exception of the need to distinguish LI from other viral encephalomyelitides, a differential diagnosis for LI is not provided for the other domestic animals because of the infrequency of reported occurrences of the disease in those species. In humans, LI virus infection may be confused with a range of other agents that can cause septic or aseptic meningitis and meningoencephalitis.

Treatment

There is no specific treatment for encephalitic cases of LI virus infection. Unlike sheep, cattle affected with LI may respond favorably to good nursing and symptomatic treatment.

Vaccination

A formalin-inactivated commercial vaccine is available that has been used successfully for many years in endemic areas (16). Two doses of vaccine with an interval of 2 to 8 weeks between injections are recommended to achieve optimal protection to natural infection. Vaccination of pregnant ewes during the last trimester is advocated to ensure that lambs receive maximal

levels of passively acquired antibodies and are protected during the initial critical months of life. Vaccination of lambs after weaning when maternal immunity has waned may be advisable in areas where there is a secondary "fall rise" in tick activity (19). The same LI vaccine has been used in cattle with reasonable success based on annual revaccination against the disease.

Control and Eradication

Preventive Measures

It is very doubtful whether measures aimed at reducing the tick population on infected pastures are a practical approach to controlling LI in areas endemic for the disease. Certainly, such measures are out of the question where rough upland or mountainous terrain is involved. Frequent acaricidal dipping or spraying of sheep, and where appropriate, cattle, during the period(s) of maximal tick activity is a valuable means of controlling the level of tick infestation and transmission of the virus.

The single most important means of controlling LI in areas endemic for the disease is vaccination. This should be applied initially to all stock and subsequently to all replacement animals introduced from an area in which the disease is nonendemic. Vaccination should take place at least 1 month before exposure to infection. Because LI virus is likely to be maintained in a tick/sheep cycle, systematic vaccination of a flock over a period of years may result eventually in elimination of the virus. This should not, however, prompt discontinuation of vaccination because the potential for further outbreaks of LI remains as long as the tick vector is present.

Public Health

Louping-ill virus is transmissible to humans. Humans can develop any one of four clinical syndromes: either an influenza-type illness, a biphasic encephalitis, a poliomyelitis-like illness or a hemorrhagic fever following infection with LI virus (3). Transmission can take place by tick bite, exposure to aerosolized infective material, or through skin abrasions or wounds. Nonlaboratory-acquired infections most frequently result from handling infected carcasses in abattoirs. The potential for oral transmission of LI virus to humans also exists where milk for human consumption is obtained from goats or sheep that are in the acute phase of the infection (12).

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PART IV
FOREIGN ANIMAL DISEASES

LUMPY SKIN DISEASE

(Pseudo-urticaria, Neethling virus disease, exanthema nodularis bovis, knopvelsiekte)

Definition

Lumpy skin disease (LSD) is an acu:te to chronic viral disease of cattle characterized by skin nodules that may have inverted conical necrosis (sitfast) with lymphadenitis accompanied by a persistent fever.

Etiology

The causative agent of LSD is a capripoxvirus. The prototype strain of LSD is the Neethling virus (1). The LSD virus (LSDV) is one of the largest viruses (170-260 by 300-450 nm) (16). There is only one serotype of LSDV. The LSDV is very closely related serologically to the virus of sheep and goat pox (SGP) from which it cannot be distinguished by routine virus neutralization or other serological tests (3). Restriction endonuclease studies of capripoxviruses indicate that LSDV strains are essentially identical with each other and with a Kenyan strain (O 240/KSGP) of sheep and goat pox virus (SGPV). Other strains of SGPV from Kenya were different from the O 240/KSGP strain but similar to each other and resembled strains of SGPV from the Arabian Peninsula. The Kenyan group of SGPV strains showed differences when compared with ones from India, Iraq, and Nigeria (13).

The LSDV is very resistant to physical and chemical agents. The virus persists in necrotic skin for at least 33 days and remains viable in lesions in air-dried hides for at least 18 days at ambient temperature (22).

Host Range

Lumpy skin disease is a disorder of cattle. There is inconclusive evidence regarding the infection of water buffalo (*Bubalus*) with LSDV. The African Cape buffalo (*Synercus caffer*) and other wild ungulates have not been infected during epizootics of LSD in Africa. Experimental infection of some species is possible (7).

Geographic Distribution

Lumpy skin disease was first described in Northern Rhodesia in 1929 (17). Since then, the disease has spread over most of Africa in a series of epizootics (7, 11). The most recently affected countries include Kuwait in 1986-88 (2) and Egypt in 1988 (20). An outbreak of LSD occurred in Israel in 1989 (21). For the first time, the disease was eradicated by slaughter and vaccination.

Transmission

Biting insects play the major role in the transmission of LSDV (5,15). Epidemics of LSD are associated with rainy seasons. The disease spreads in river basins and areas conducive to insect multiplication (6,10,15,22). *Stomoxys calcitrans* experimentally transmitted LSDV, but biting lice (*Mallophaga* spp.), sucking lice (*Damalinia* spp.), or *Culicoides nubeculosus* did not (14). In Kenya, *Culex mirificus* but also *Aedes natronius* were in heavy concentration during an LSD epizootic and were associated with transmission (15). Direct contact seems to play a minor role in the spread of LSD.

Incubation Period

In the field the incubation period is 2 to 5 weeks (10). Following experimental infection by intradermal inoculation, a lesion usually develops at the inoculation site within 6 to 20 days.

Clinical Signs

Lumpy skin disease virus causes inapparent to severe disease in cattle. All ages of cattle can be affected, but young calves are usually more severely affected (Fig. 72). The severity of the disease depends on the dose of the inoculum as well as the susceptibility of the host (*Bos taura* is more susceptible than B*os indicus*) and the route of exposure. A fever 104 to 107º F (40-41.5º C) can occur and can be transitory or last up to 4 weeks. Generally within 2 days after the appearance of the fever, swellings or nodules 1 to 5 cm in diameter appear in the skin and generalization occurs. Depression, anorexia, excessive salivation, oculonasal discharge, agalactia, and emaciation are presented. Nodules 1 to 7 cm in diameter may occur anywhere on the body but especially in the skin of the muzzle, nares, back, legs, scrotum, perineum, eyelids, lower ear, nasal and oral mucosa, and tail. The hair stands erect over early skin lesions. The nodules are painful and involve the epidermis, dermis, and subcutaneous tissue and may even involve the musculature. As the disease progresses, the nodules become necrotic, and eventually a deep scab forms; this lesion is called a sitfast (Fig. 71). Secondary bacterial infection can complicate healing and recovery. Lesions on the teats can result in severe secondary bacterial infection with loss of the quarter owing to mastitis.

Where extensive generalization occurs, animals can become lame and reluctant to move because of edema. Lameness also may result from inflammation of the tendons, tendon sheaths (tendosynovitis), joints (synovitis), and laminae (laminitis). Severe edema in the brisket and legs can occur. If secondary bacterial infection develops in the tendon sheaths and joints, pemmanent lameness may result. Superficial lymph nodes such as the mandibular, parotid, prescapular, and prefemoral nodes, draining affected areas of skin become enlarged 4 to l0 times normal size.

Abortion may occur as the result of prolonged fever. Davies (7) has reported intrauterine infection of late-term fetuses in which calves are born with LSD lesions. Temporary or pemmanent sterility in bulls can result from the fever or lesions of the reproductive organs. Cows may not come into estrus for several months after LSD (7).

The lesions may persist in various stages over a course of 4 to 6 weeks. Final resolution of lesions may take 2 to 6 months, and nodules can remain visible 1 to 2 years. Permanent damage to the hide is inevitable in clinical cases.

Gross Lesions

The gross lesions of LSD are well described (3,10,19,22). Skin nodules have congestion, hemorrhage, edema, and vasculitis with consequent necrosis and involve all layers of the epidermis, dermis, subcutaneous tissue, and often adjacent musculature. Lymph nodes draining affected areas are enlarged up to 10 times normal size with extensive lymphoid proliferation, edema, congestion, and hemorrhage.

Mucous membranes of the oral and nasal cavities can have pox lesions that coalesce in severe cases. Pox lesions may occur in the pharynx, epiglottis, and trachea (Fig. 73). Pox lesions are not easily visualized in the lungs but appear as focal areas of atelectasis and edema (Fig. 74). In severe cases, pleuritis can occur with enlargement of the mediastinal lymph nodes.

Synovitis and tendosynovitis with fibrin in the synovial fluid can occur. Pox lesions can be present in the testicles and urinary bladder.

Morbidity and Mortality

Morbidity for LSD varies from 3 to 85 percent (10,15,22) and likely depends on prevalence of the mechanical insect vector and the susceptibility of the cattle. Mortality is generally low (1 to 3

percent). In one outbreak in South Africa, mortality was about 20 percent when an anaplasmosis vaccine was prepared from bovine blood contaminated with LSDV (9,10). Unusually high mortality (75 to 85 percent) in other outbreaks of LSD was not explained (9,10).

Diagnosis

Field Diagnosis

A tentative diagnosis of LSD can be made based upon clinical signs. A contagious disease with generalized skin nodules having a characteristic inverted conical necrosis of skin nodules (sitfast), persistent fever, emaciation, and low mortality suggests LSD.

Specimens for Laboratory

Skin biopsies of early lesions (ones where necrosis has not occurred) provide samples that can be used for virus isolation, histopathology, and electron microscopy. Samples should be taken from at least three animals. Samples aspirated from enlarged lymph nodes can be used for virus isolation. Samples for virus isolation should be shipped to the laboratory under wet ice if they will arrive in 2 days and be shipped under dry ice if more time will be required. Samples for histopathology should be preserved in 10 percent buffered formalin (DO NOT FREEZE). Serum samples should be taken from acute and chronic cases. Followup serum samples (convalescent samples) should be taken 2 to 3 weeks after the first appearance of skin lesions.

Laboratory Diagnosis

To confirm an initial diagnosis in an LSD-free area, the virus has to be isolated and identified. The laboratory procedures for the diagnosis of LSD include virus isolation in lamb testicle or fetal bovine lung cell cultures or both. Virions may be detected by electron microscopy (7). Herpesviruses may be present in bovine skin samples (1,12) and cause confusion in cell culture studies. Serological tests include virus neutralization and indirect fluorescent antibody (IFA) (8). The IFA test may measure group-reactive antibody that may be elicited by other pox viruses.

Differential Diagnosis

Listed below are several diseases that should be considered in the differential diagnosis of LSD:

Bovine herpes mammillitis (also called Allerton virus infection caused by Bovid Herpesvirus-2) — The lesions are superficial (involving only the epidermis) and occur predominantly on the cooler parts of the body such as teats and muzzle. Generalized skin lesions can occur accompanied by a transient fever (1 to 3 days). Resolution of the lesion is rapid and results in focal alopecia but no hide damage.

Streptotrichosis (Dermatophilus congolensis infection) — lesions are superficial (often moist and appear as crusts) scabs or 0.5- to 2-cm diameter accumulations of keratinized material. Lesions are common in the skin of the neck, axillary region, inguinal region, and perineum. The organism can be demonstrated by Giemsa staining.

Ringworm — The lesions of ringworm in cattle are grayish, raised, plaque-like, and often pruritic. The organism can be demonstrated with a silver stain.

Hypoderma bovis infection —The parasitic fly larvae of this parasite have a predilection to migrate to the dorsal skin of the back. They cause a nodule with a small central hole through which the larva exits the body, which results in significant hide damage.

Photosensitization — Dry, flaky, inflamed areas are confined to the nonpigmented parts of the skin.

Bovine papular stomatitis — Pox-like lesions occur in the skin of the muzzle, oral cavity, and esophagus. There is no generalized disease.

Insect bites — The trauma from insect bites causes local inflammation, edema, and pruritus. Insects seldom bite mucous membranes.

Urticaria — Delayed hypersensitivity reactions can be confused with LSD. Such lesions generally resolve within 3 to 5 days. An example of this was described by Shimshony (1989) where allergic reactions occurred after vaccination with a foot-and-mouth disease vaccine.

Besnoitiosis (Globidiosis) — Thick-walled cysts in the skin are caused by sporozoan parasites of the genus *Besnoitia*, which are transmitted mechanically by certain biting flies. Histologic sections will reveal the parasites.

Treatment

Treatment is directed at preventing or controlling secondary infection. Animals infected with LSDV generally recover (mortality is usually less than 3 percent). Complete recovery may take several months and may be prolonged where secondary bacterial infection occurs. Loss of production results from severe emaciation, lowered milk production, extensive damage to hides, and loss of draft from lameness. It may take up to 6 months for animals severely affected by LSDV to recover fully (9).

Vaccination

In endemic areas, vaccination against LSD has been successfully practiced. In the Union of South Africa, an attenuated LSD vaccine is used. In Kenya, sheep and goat pox virus is used (4). In Egypt, the Romanian strain of sheep and goat pox vaccine has been used successfully for prophylaxis against LSD.

Control and Eradication

The most likely way for LSD to enter a new area is by introduction of infected animals. Biting insects that have fed on infected cattle may travel and be blown for substantial distances. It is likely that LSD spread to Israel via contaminated insects blown across the Sinai Desert (21). The movement of contaminated hides represents another potential means for this resistant virus to move.

If LSD is confirmed in a new area before extensive spread occurs, the area should be quarantined, infected and exposed animals slaughtered, and the premises cleaned and disinfected. Vaccination of susceptible animals within the quarantine should be considered.

If the disease has spread over a large area, the most effective means of controlling losses from LSD is vaccination. However, even with vaccination, consideration still should be given to eliminating infected and exposed herds by slaughter, proper disposal of animals and contaminated material, and by cleaning and disinfecting contaminated premises, equipment, and facilities.

In the Union of South Africa, the control of insects was not effective in preventing the spread of LSD, but current insecticides together with repellents aid in the prevention of the spread of LSD.

Public Health

There is no evidence that LSDV infects humans.

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Fig. 72. LSD - A Balidy calf in Egypt affected with LSD; note the large skin nodules.

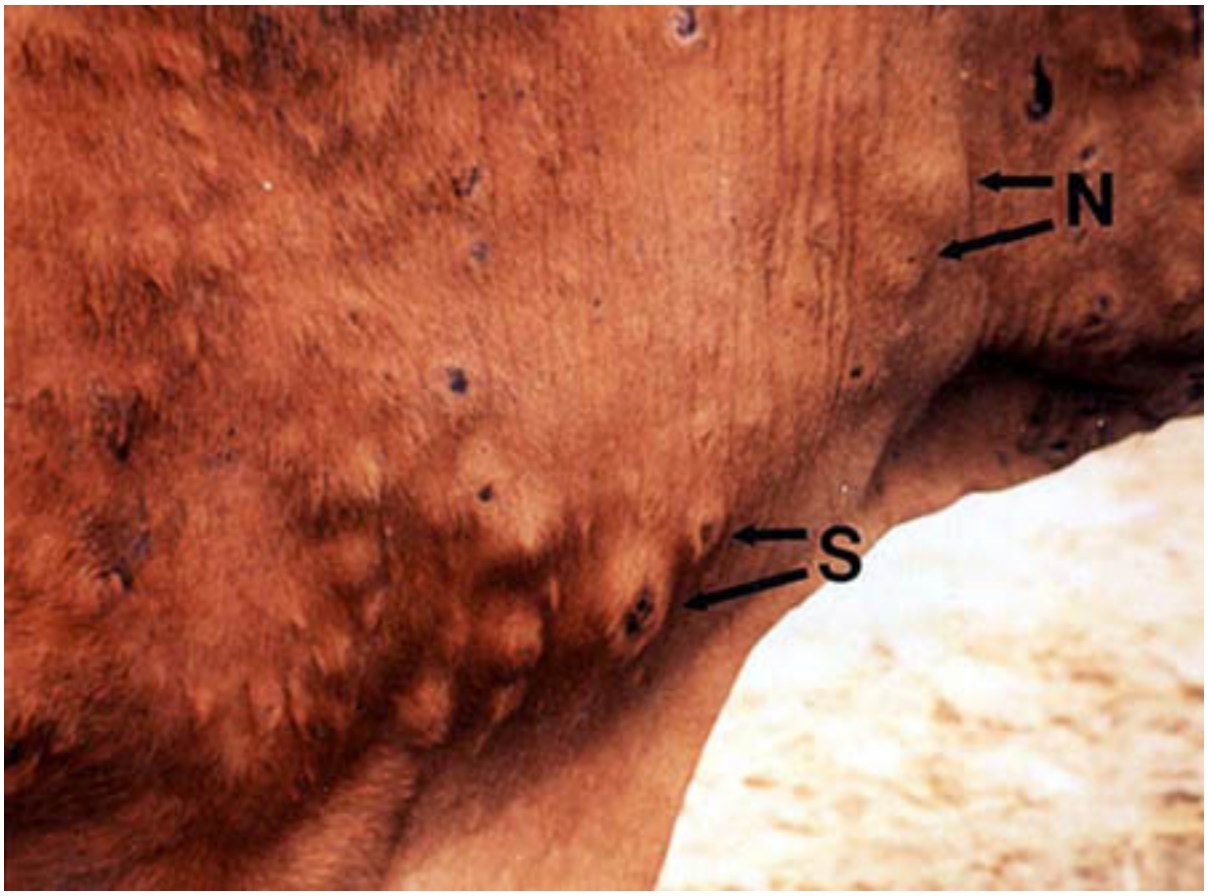

Fig. 71. LSD - Nodules (N) and sittasts (S) in a Balidy cow in Egypt affected with LSD.

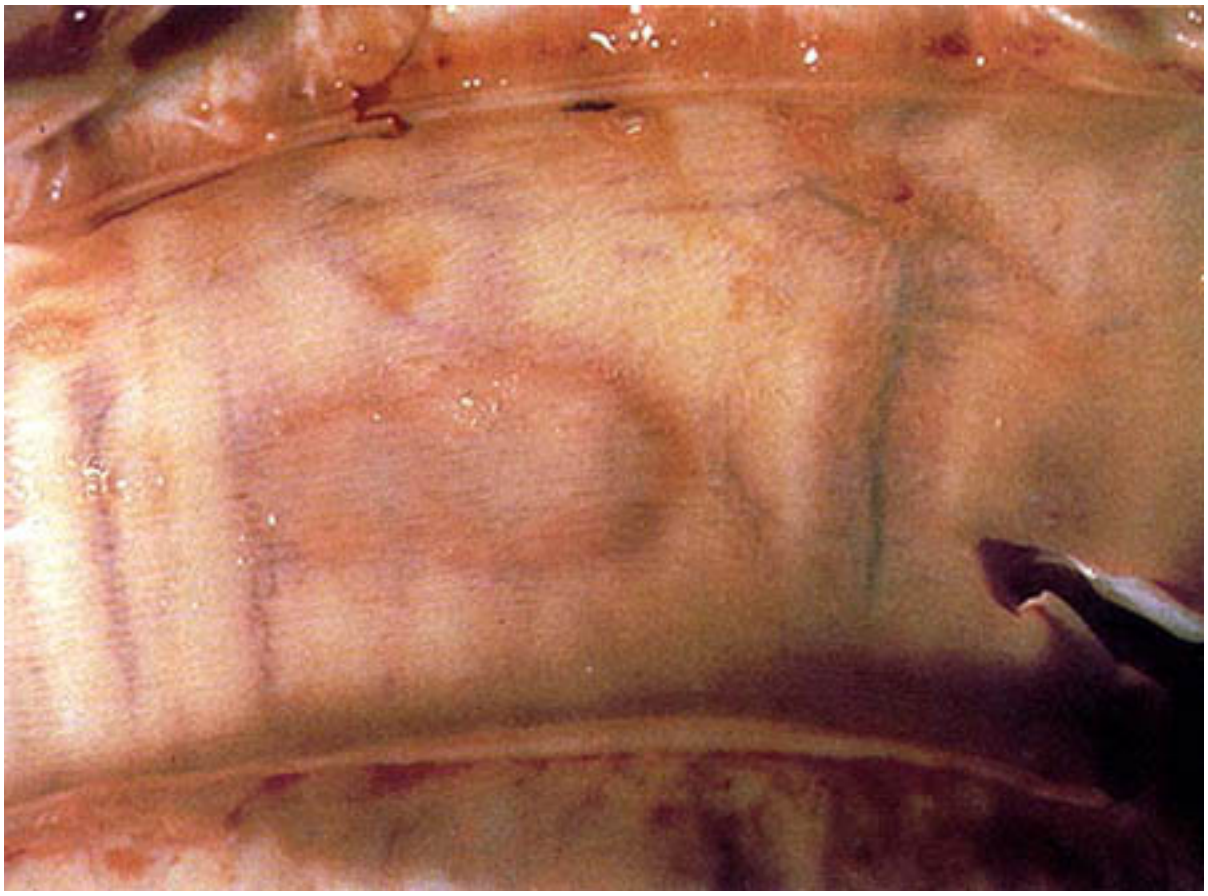

Fig. 73. LSD - An LSD (pox) lesion in the trachael mucosa.

Fig. 74. LSD - LSD lesions in the lung are areas of atelectasis and interlobular edema.

PART IV
FOREIGN ANIMAL DISEASES

MALIGNANT CATARRHAL FEVER

(Malignant head catarrh, malignant catarrh, snotsiekte)

Definition

Malignant catarrhal fever (MCF) is a generalized viral disease of domestic cattle and buffaloes and many species of wild ruminants characterized by high fever, profuse nasal discharge, corneal opacity, ophthalmia, generalized lymphadenopathy, leukopenia, and severe inflammation of the conjunctival, oral, and nasal mucosas with necrosis in the oral and nasal cavities sometimes extending into the esophagus and trachea. Occasionally central nervous system (CNS) signs, diarrhea, skin lesions, and nonsuppurative arthritis are observed.

Etiology

The etiologic agent of MCF in Africa is a highly cell-associated lymphotropic herpesvirus of the subfamily *Gamma herpesvirinae*. Two viral strains have recently been designated: alcelaphine herpesvirus-1 (AHV-1) and alcelaphine herpesvirus-2 (AHV-2), although some continue to designate this agent as bovid herpesvirus-3. This agent is carried as a latent infection by African antelope of the family Bovidae, subfamily Alcelaphinae which includes wildebeest (*Connochaetes* sp.), hartebeest (*Alcelaphus* sp.), and topi (*Damaliscus* sp.). The wildebeest herpesvirus of MCF (AHV-1) was first isolated by Plowright from a blue wildebeest (*Connochaetes taurinus taurinus*) in 1960.

Epidemiologic evidence suggests that domestic and wild sheep and goats may be additional major reservoirs of a virus causing MCF. Serologic evidence also suggests this virus may be related but not identical to the alcelaphine herpesvirus-l.

Sheep-associated MCF herpesviruses were isolated from domestic cattle in Minnesota in 1977 and from domestic cattle in Austria in 1990. On the basis of morphology and molecular DNA mapping, both isolates appear similar to AHV-1.

Viruses identical or closely related to AHV-1 and AHV-2 have been isolated from several captive wild ruminant species in two U.S. zoos located in Oklahoma City and San Diego. Animals infected with AHV-1 were white-tailed gnu, white-bearded gnu, gaur, greater kudu, Formosan sika deer, axis deer, and nilgai. The AHV-2 was isolated from a topi and a hartebeest at the San Diego Wild Animal Park.

The agent of MCF on deer farms in Scotland and New Zealand has not yet been demonstrated by electron microscopy or isolation of cell-free virus in a cell culture system. However, it has been passaged in lymphocyte cultures, rabbits, and deer.

Host Range

All species of wildebeest, hartebeest, and topi are considered carriers of alcelaphine MCF virus. There is serologic evidence that several other African wild ruminants, such as various species of oryx and addax, may also be reservoir hosts, although MCF virus has not been isolated from these species.

Domestic and wild sheep and goats are also considered reservoir hosts for MCF virus.

Many exotic ruminant species in zoos have been reported affected with MCF, including several wild bovines such as bison, water buffalo, gaur and banteng, and several deer (including

white-tailed deer) and antelope species. Interestingly, no cases of MCF have been reported from antelope species that normally cohabitate wildebeest grazing areas in Africa.

In cattle and susceptible wild ruminants, MCF affects all ages, breeds, and sexes.

Geographic Distribution

Sheep-associated MCF occurs worldwide. The alcelaphine antelope-associated form in cattle occurs chiefly in Africa in the natural habitat of wildebeest, hartebeest, and topi. This form of MCF has, however, occurred in zoos and wild animal parks that also kept wildebeest. The increasing popularity in North America and other areas of the world of wild game animal ranches, often in association with domestic cattle raising, increases the possibility that MCF will become a more prevalent disease in cattle and ranched exotic ruminants. There is increasing serologic evidence that cattle may develop low levels of neutralizing antibodies following exposure to MCF, especially of sheep or goat origin, without manifesting clinical disease. There is evidence that stress or some other immunosuppressive effector may be necessary as a precursor of clinical sheep-associated MCF.

Transmission

The MCF virus in wildebeest, hartebeest, and topi is largely cell-associated in adult animals and hence rarely transmissible. However, neonatal wildebeests have been found to shed cell-free MCF virus in nasal and ocular secretions and in feces. Cell-free MCFV has also been demonstrated in nasal secretions of captive adult wildebeests after stress or administration of corticosteroids. Transmission to cattle or other susceptible species may occur by inhalation of cell-free virus in infectious aerosol droplets, ingestion of feed or water contaminated with infectious secretions or feces, or possibly mechanically by arthropods. Masai herdsmen believed cattle acquire MCF by contact with wildebeest placentas or birth hair of neonates. Recent studies have failed to demonstrate infective MCFV in fetal fluids or placentas of wildebeest probably owing to the rapid inactivation of virus by sunlight. The mode of transmission of sheep-associated MCF remains unknown, although relatively close contact between cattle and sheep, especially lambing ewes, is believed necessary. MCF-affected cattle appear to shed only cell-associated virus, and thus cattle-to-cattle transmission is thought to be rare or nonexistent, although there are documented instances where this has occurred.

Incubation Period

The incubation period in natural cases is not known, but epidemiologic evidence indicates it may be as long as 200 days. Experimentally, the incubation period has varied from 9 to 77 days.

Clinical Signs

Clinical MCF in cattle has arbitrarily been divided into four forms as follows:

1. Peracute form: Fever, severe inflammation of the oral and nasal mucosas and hemorrhagic gastroenteritis with a course of 1 to 3 days.

2. Intestinal form: Fever, diarrhea, hyperemia of oral and nasal mucosas with accompanying discharges, and lymphadenopathy with a course of 4 to 9 days (Fig. 75).

3. Head and eye form: This is the typical syndrome of MCF with fever, nasal, and ocular discharges progressing from serous (Fig. 76) to mucopurulent and purulent. Encrustation of the muzzle and nares occurs in later stages, causing obstruction to the nostrils and dyspnea, open-mouthed breathing, and drooling (Fig. 77). There is intense hyperemia and multifocal or diffuse necrosis of the oral mucosa (usually on the lips, gums, and hard and soft palate) and buccal mucosa. Erosion of the tips of buccal papillae, leaving them reddened and blunted, is often encountered (Fig. 78).

Ocular signs referable to ophthalmia include lacrimation progressing to purulent exudation,

photophobia, hyperemia, and edema of the palpebral conjunctiva and injection of scleral vessels. Corneal opacity, starting peripherally and progressing centripetally, results in partial to complete blindness (Fig. 79). Hypopyon may also be seen. Corneal opacity is usually bilateral but occasionally is unilateral. Fever is common and usually high (104-107° F [40-41.6° C]) until the animal becomes moribund, at which time it is hypothermic. Clinical features at early onset have included reddening of the skin of the udder, the coronary bands and interdigital spaces, and marked hyperemia of the oral cavity. Increased thirst accompanies the fever, and anorexia is seen in late stages. Constipation is common in this form of MCF, but terminal diarrhea is sometimes observed.

Nervous signs are not frequently seen but may be manifested by trembling or shivering, uncoordinated gait, and terminal nystagmus.

Necrotic skin lesions occasionally are seen, and horn and hoof coverings may be loosened or sloughed in some cases. The course of the head and eye form, which is invariably fatal, is usually 7 to 18 days.

4. Mild forms: These are syndromes caused by experimental infection of cattle with attenuated viruses and are usually nonfatal.

There is considerable variation and overlap among these artificial categories, and their use has little value.

Although the manifestations of the "head and eye" form of MCF are considered the typical syndrome in cattle, clinical signs in exotic ruminants are often less dramatic and not usually specifically diagnostic, except in members of the subfamily *Bovinae* (i.e., wild cattle). In deer and antelope species MCF tends to be more subtle clinically and usually is manifested by conjunctivitis, photophobia, moderate corneal clouding (often unilateral), fever, depression, variable lymphadenopathy, occasionally diarrhea, and usually a mild serous nasal discharge. Death may be sudden following a brief course of hemorrhagic diarrhea. Inflammation of the oral and nasal cavity is usually less severe than in cattle and only occasionally progresses to mucosal erosions.

There is some suggestion from studying cases of MCF among exotic ruminants of a host-dependent modification with respect to the clinical and pathologic manifestations of MCF virus infection.

Gross Lesions

Gross lesions vary considerably, depending on the form or severity and course of the disease. Animals that die of the peracute disease may have few lesions other than a hemorrhagic enterocolitis.

In the more protracted acute to subacute disease (intestinal and head and eye forms), the carcass may be normal, dehydrated, or emaciated. The muzzle is often encrusted and raw. Cutaneous lesions sometimes occur as a generalized exanthema with exudation of lymph causing crusting and matting of the hair. Where skin is unpigmented, hyperemia is apparent. These lesions are frequently seen in the ventral thorax and abdomen, inguinal region, perineum and loins, and sometimes on the head.

Enlarged lymph nodes are characteristic findings in MCF. All nodes may be involved, but those in the head and neck and periphery are the most consistently prominent (Fig. 75). Affected nodes are grossly enlarged and edematous and sometimes have patchy reddened or beige-brown areas on cut surfaces. Hemolymph nodes are also enlarged and prominent. The spleen is slightly enlarged, and Malpighian corpuscles are prominent. Pale areas may be seen in the heart muscle.

Lesions in the respiratory system range from mild to severe. When the clinical course is short, there is slight serous nasal discharge and hyperemia of the nasal mucosa. Later the discharge

becomes more copious and mucopurulent to purulent and is accompanied by intense nasal mucosal hyperemia, edema, and small focal erosions.

Occasionally a croupous pseudomembrane formation is seen. Lesions in the nasal passages and turbinates may extend to the frontal sinuses. The pharyngeal and laryngeal mucosas are hyperemic and edematous and later develop multiple erosions, often covered with gray-yellow pseudomembranes (Fig. 80). Inflammation and sometimes petechiation and ulceration are seen in the tracheobronchial mucosa. The lungs are often edematous and sometimes emphysematous but in some cases may appear normal. A bronchopneumonia may complicate chronic cases.

The alimentary tract mucosa may have no gross lesion in peracute cases. When the course is longer, alimentary lesions are commensurately more severe and include mild to severe mucosal inflammation (hyperemia and edema), erosions, and ulcerations— especially on the dental pad and gingival surfaces, the palate (Fig. 81), tongue, and buccal papillae. Mucosal inflammation, hemorrhage, and erosions may also be found in the rest of the digestive tract including the esophagus, rumen, omasum, abomasum, small intestines, colon, and rectum. Petechiation may be seen. Feces are usually scant, dry, pasty, or blood stained.

Urinary tract lesions include hyperemia and sometimes marked distention and prominence of bladder mucosal vessels and mucosal edema, perhaps with petechial to severe hemorrhage and occasionally epithelial erosion and ulceration. Kidneys may appear normal or mottled with patches of beige, discolored raised areas. Petechiae or ecchymoses may occur in the renal pelvis and ureters.

The liver is usually slightly enlarged, and, upon close examination, has a prominent reticular pattern. There may be hemorrhages and erosions in the gallbladder mucosa.

In most cases, small arterioles are very prominent and tortuous and have thickened walls. This is usually seen in subcutaneous vessels and those in the thorax, abdomen, and CNS.

Fibrinous polyarthritis is seen in many cases of MCF.

Morbidity and Mortality

Clinical MCF in cattle in the United States is usually sporadic. However, in an outbreak in a Colorado feedlot, morbidity was 37 percent. Morbidity in nonalcelaphine MCF outbreaks in Malaysia ranged from 28 percent to 45 percent. The prognosis in MCF is poor. Once clinical signs are observed, mortality is usually greater than 95 percent (90-100 percent). In some parts of New Zealand, MCF is, along with tuberculosis, the most important cause of mortality in the deer-farming industry.

Diagnosis

Field Diagnosis

A history indicating contact with sheep, goats, or alcelaphine antelope, especially around the period of parturition, associated with typical clinical features of MCF, provides grounds for a tentative diagnosis of MCF.

Gross necropsy lesions consisting of corneal opacity; enlarged lymph nodes; inflammation and erosions in nasal passages, alimentary tract mucosa, and urinary bladder; and prominent tortuous small arteries in the subcutaneous tissue, thorax, and abdomen, provide further evidence for a presumptive diagnosis of MCF.

Specimens for Laboratory

1. For animal transmission and inoculation at least 300 to 500 ml blood in EDTA (1 mg/ml blood), heparin, or ACD solution should be collected and carried or shipped iced, not frozen. For

virus isolation in cell culture, 10 to 20 ml of blood in EDTA is preferred. This should also be shipped cold but not frozen.

2. Tissues for virus isolation, FA, or immunoperoxidase examination should also be refrigerated (iced) but NOT FROZEN and should include pieces of spleen, lung, lymph nodes, adrenals, and thyroids as well as unclotted blood. These should be collected as soon after death as possible, for the virus becomes inactivated rapidly in an animal dead more than 1 hour. The most useful specimens for animal inoculation or virus isolation attempts are those collected from a moribund animal immediately after euthanasia.

3. Tissues for histopathology, fixed as thin pieces in 10 percent neutral buffered formalin, should include lung, kidney, liver, adrenals, lymph nodes, eyes, oral epithelium, esophagus, Peyer's patches, urinary bladder, carotid rete, thyroid, heart muscle, skin (if lesions are present), and whole brain.

4. Serum for serology should consist of paired samples taken 3 to 4 weeks apart (i.e., the first during the acute phase of disease and the second during convalescence or at death). Serologic methods currently preferred include virus neutralization and competitive inhibition enzyme-linked immuosorbent assay for MCF antibody.

Laboratory Diagnosis

Microscopic lesions of an extensive fibrinoid necrotizing vasculitis, perivasculitis, and lymphoreticular proliferation in lymphoid organs with mononuclear infiltrations in kidney, liver, adrenals, CNS, etc., are pathognomonic for MCF and are a sound, practical basis for a confirmed diagnosis.

Virologic and serologic examinations provide additional information that may also ultimately lead to a better understanding of the epizootiology and differences between viral strains and the clinical manifestations. Methods used consist of virus isolation, identification of viral isolates, demonstration of the appearance, or rising titers of MCF antibodies and molecular techniques using viral DNA probes, or target DNA amplifying methods such as the polymerase chain reaction (PCR). Because of the presence of MCF antibodies in asymptomatic U.S. cattle, a single antibody positive serologic sample is of limited value in establishing an etiologic diagnosis. The PCR method for demonstrating MCF DNA segments is proving to be useful for identifying MCF carriers as well as diagnosing overtly diseased animals.

Differential Diagnosis

Clinical MCF must be distinguished from other diseases and factors that produce inflammation and erosions and ulcerations of the nasal and alimentary tract mucosas such as BVD mucosal disease, bluetongue, rinderpest, vesicular diseases (FMD, VS), ingested caustics, and some poisonous plants and mycotoxins. The inability to differentiate the alcelaphine clearly from the sheep-associated MCF by clinical observations, lesions, or laboratory means presents an enigma in evaluating the possibility of a foreign animal disease. With our current knowledge, history of association with sheep, goats, or with alcelaphine antelope remains the only practical means of differentiating one form from the other.

Vaccination

Cattle and experimentally infected rabbits recovered from MCF have a solid immunity against all strains of MCF virus.

An effective vaccine is not available for MCF. Some viral strains have undergone limited attenuation after serial passage in cell cultures and offer hope for a future modified live virus vaccine. Experimental killed virus vaccines have been inconsistent in inducing protection against virulent virus challenge, although some have induced significant titers of serum virus neutralizing antibodies

Control and Eradication

Cattle should be kept separated from potential reservoir hosts such as sheep, goats, and wildebeest — especially during lambing, kidding, or calving seasons, respectively.

The stocking of cattle ranches with alcelaphine antelope, wild sheep, or goats should be discouraged or should require a negative MCF serologic test, preferably by the serum-virus neutralization method, or a negative PCR test for any wild ruminants destined for such a facility. Similar testing of such wild ruminants before being placed in, or transferred between, zoos is also recommended as a means to prevent the introduction of potential carriers of MCF virus.

Containment of an outbreak usually means the immediate separation of cattle or the susceptible host from sheep and goats in the case of the domestic disease and the susceptible host from alcelaphine or wild ruminants in the case of alcelaphine MCF.

Public Health

There is no evidence that MCF is infectious for humans.

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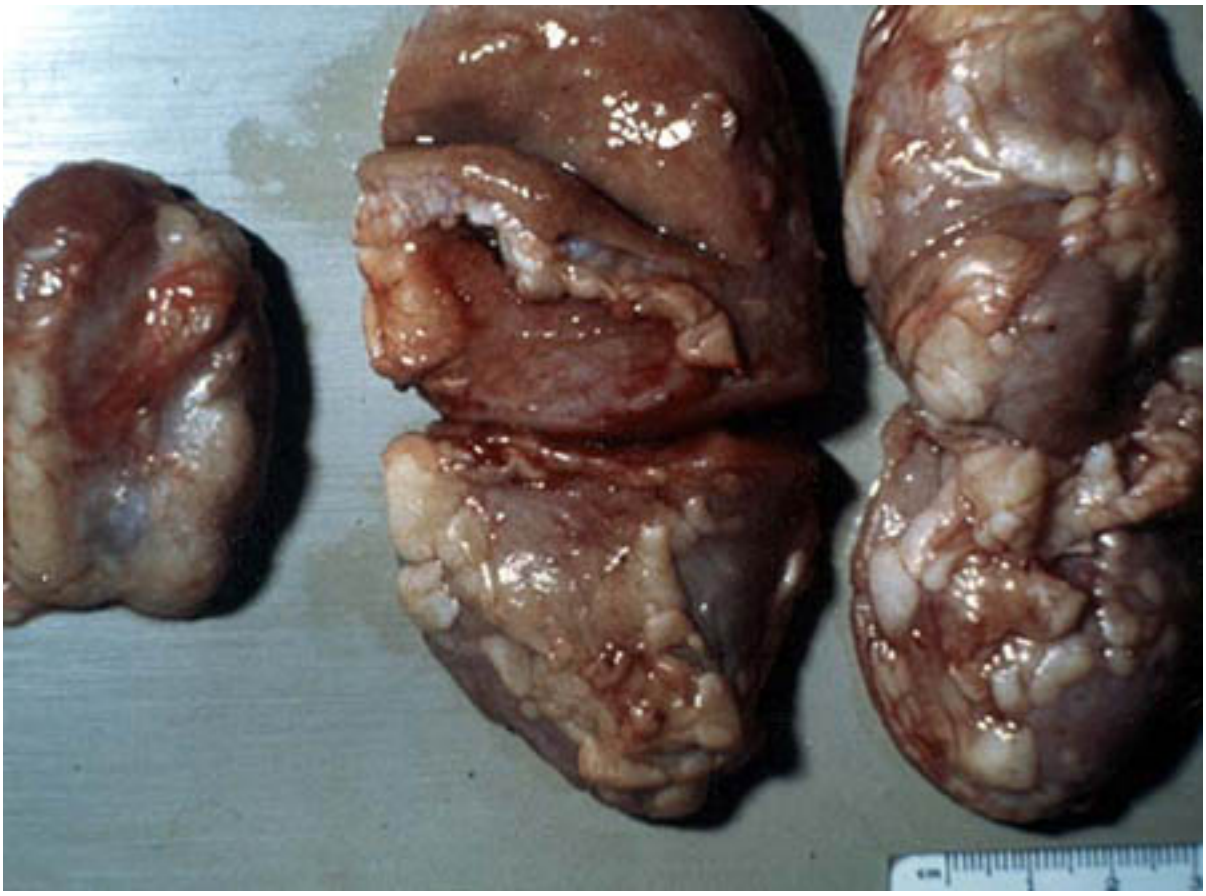

Fig. 75. MCF - Enlarged prescapular lymph node from an MCF infected steer on the right compared to a normal prescapular lymph node on the left.

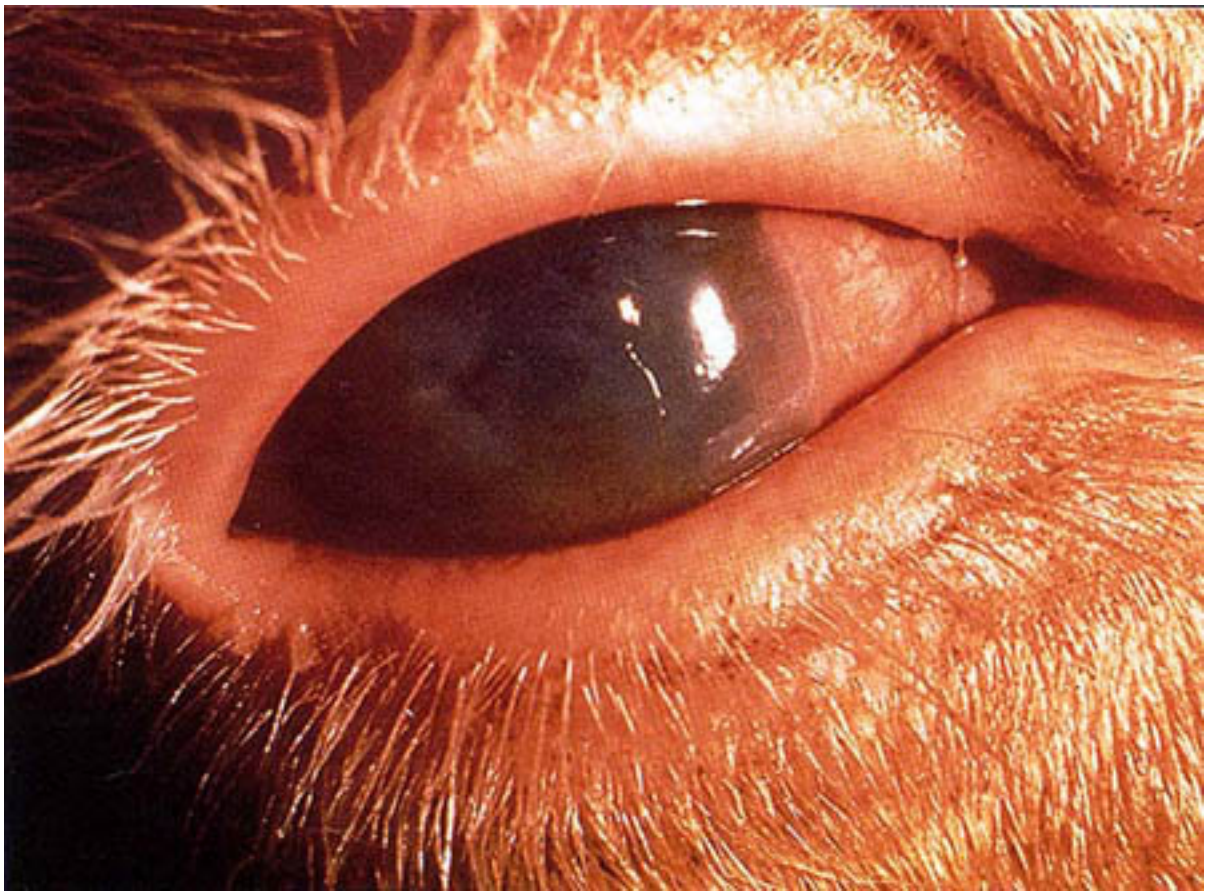

Fig. 76. MCF - Conjunctival hyperemia, lacrimation, and early corneal edema in the early course of MCF.

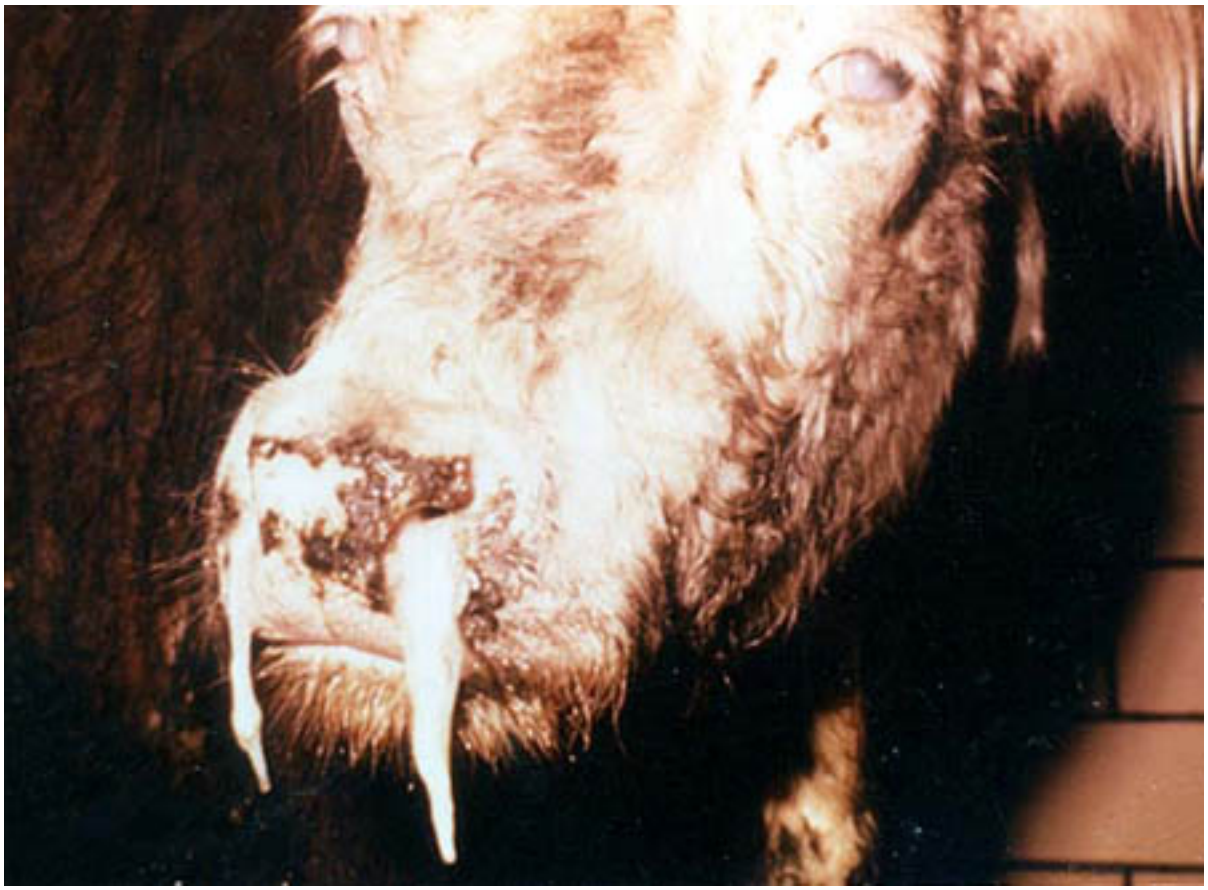

Fig. 77. MCF - Typical head and eye form of MCF. Encrustation on the muzzle, nasal exudate, lacrimation, and corneal opacity.

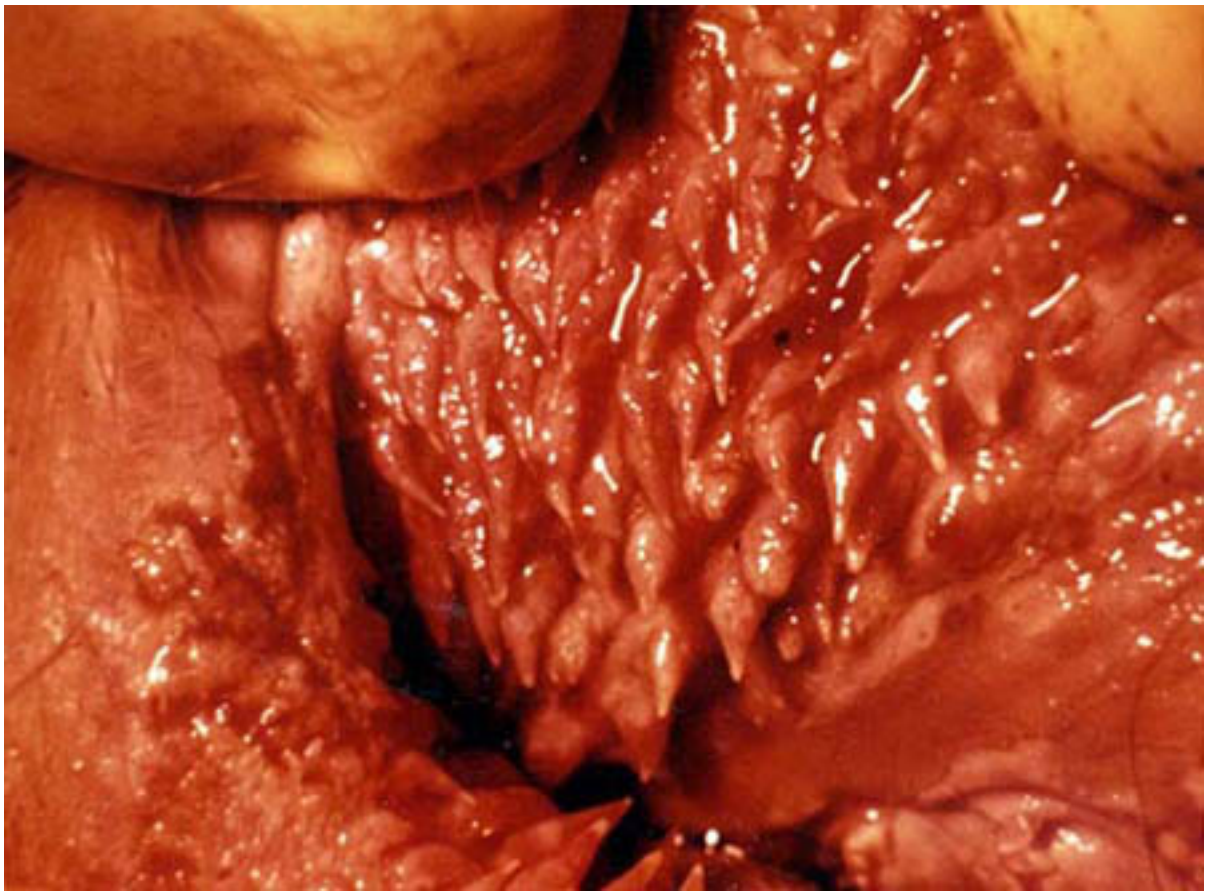

Fig. 78. MCF - Hyperemia, necrosis (white tips), and erosions of the buccal papillae.

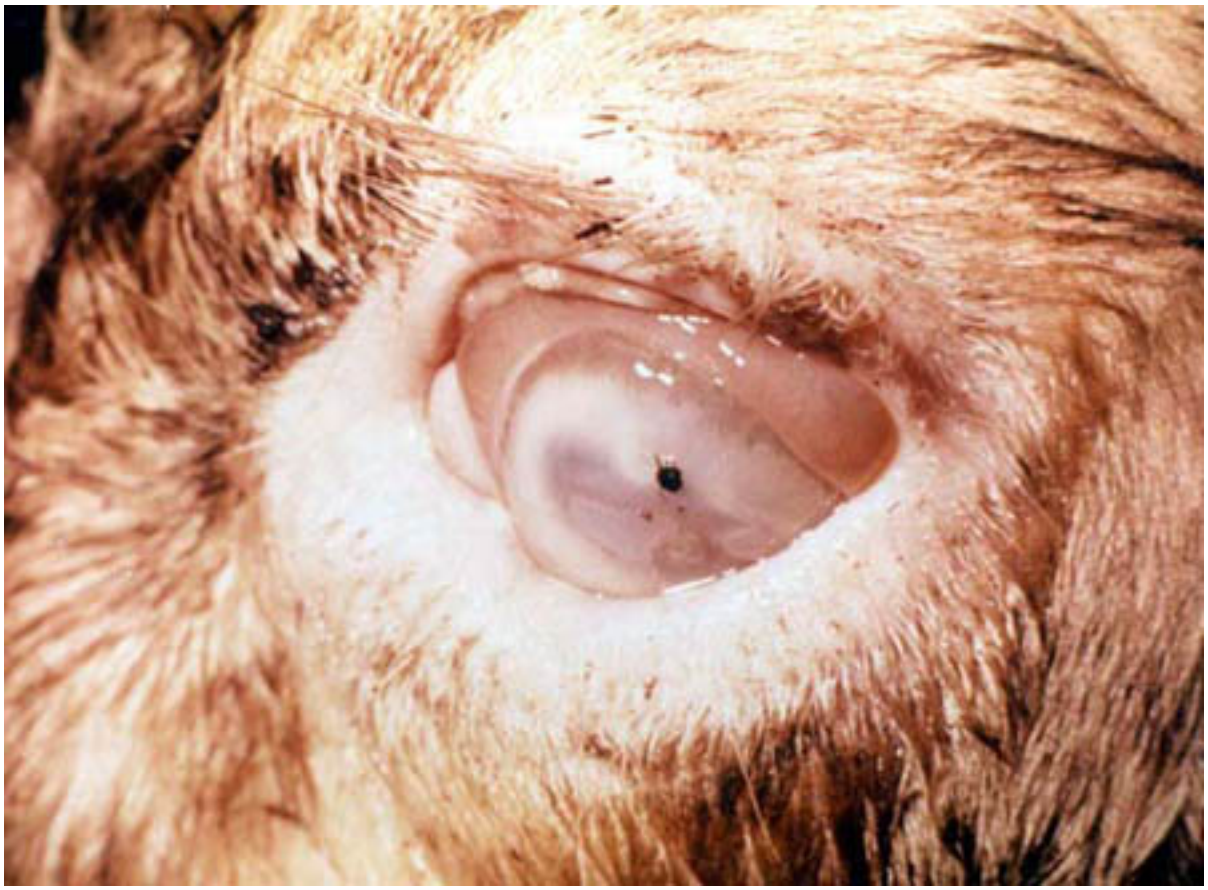

Fig. 79. MCF - Corneal opacity and conjunctival exudate.

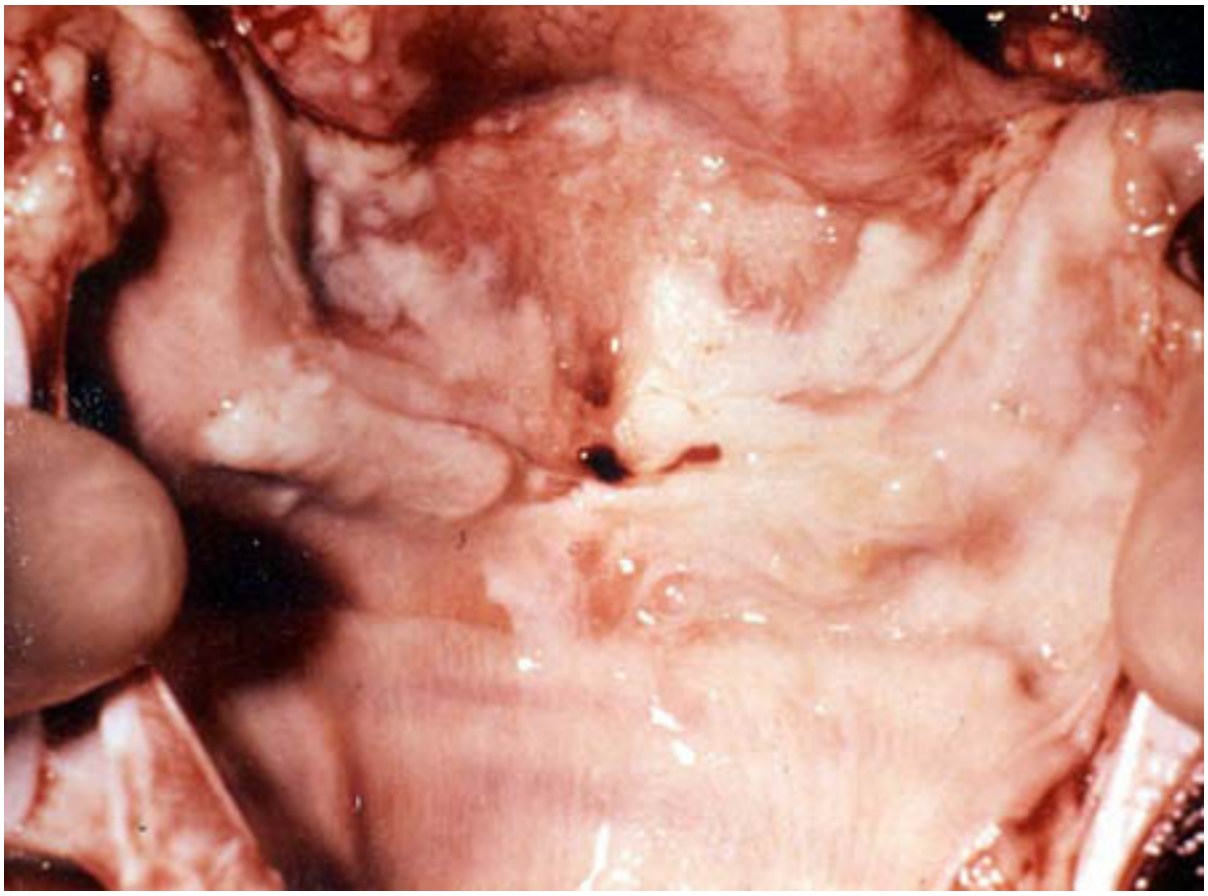

Fig. 80. MCF - Laryngeal necrosis - whitish areas in the mucosa.

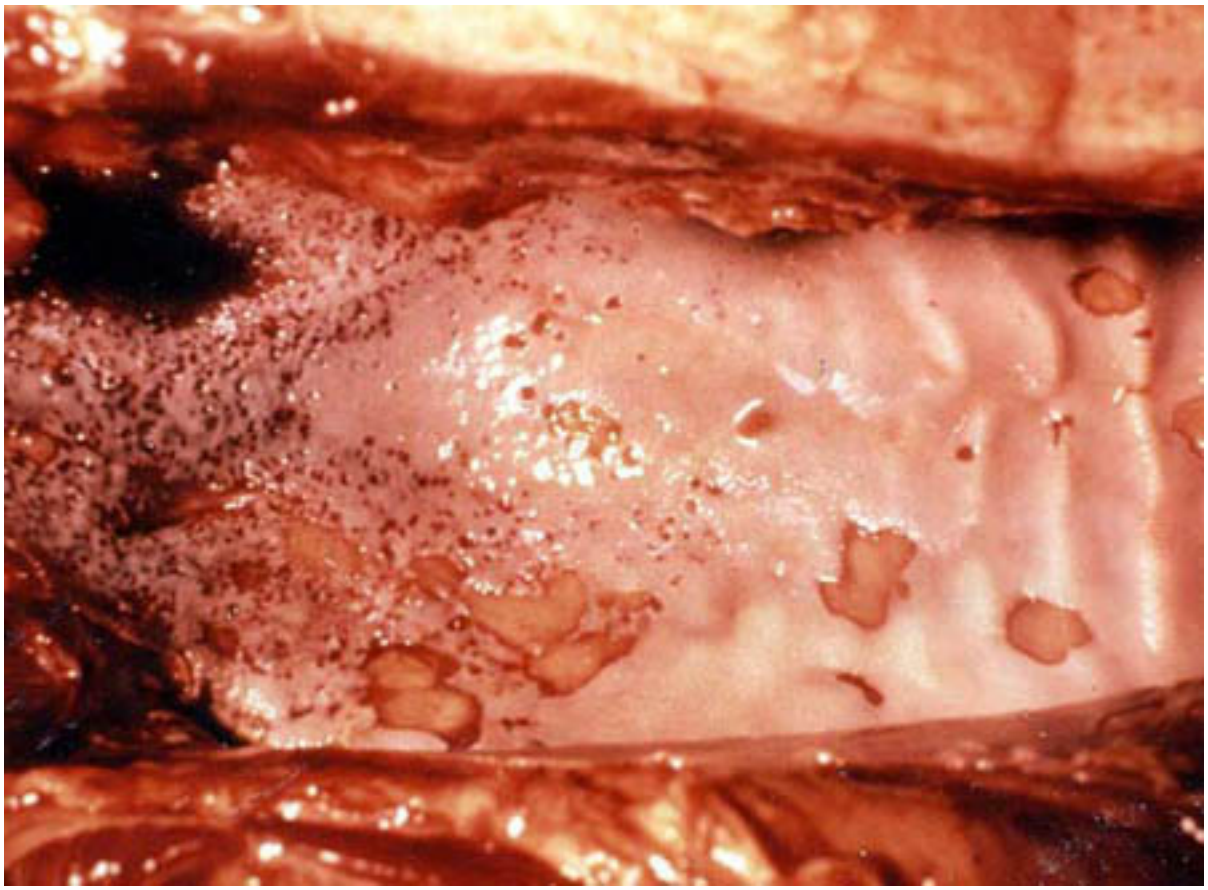

Fig. 81. MCF - Erosions on the hard and soft palate.

PART IV
FOREIGN ANIMAL DISEASES

NAIROBI SHEEP DISEASE

Definition

Nairobi sheep disease (NSD) is a noncontagious, tick-borne, viral infection of sheep and goats characterized by hemorrhagic gastroenteritis and high mortality.

Etiology

Nairobi sheep disease virus (NSDV) is transmitted primarily by the brown tick, *Rhipicephalus appendiculatus*. The causative agent is an RNA-containing virus having structural and chemical characteristics common within the *Bunyaviridae* viruses (16). However, it is antigenically independent of this group but is closely related to the Ganjam virus of goats in India (7). Ganjam virus is antigenically related to Dugbe virus isolated from cattle in west Africa. A new genus, *Nairovirus*, has been proposed for these three viruses (19).

Host Range

Laboratory and domesticated animals other than sheep and goats are resistant to infection with NSDV (17). Davies (5) was unable to isolate NSDV from blood or tissues of a wide range of wild ruminants and rodents. However, it has been suggested (4) that the African field rat (*Arvicathus abysinicus nubilans*) might be a reservoir host.

Geographic Distribution

Nairobi sheep disease is usually confined to countries in east Africa, where the principal vector, *R. appendiculatus*, is endemic. The disease has been reported most frequently in Kenya in Kikuyu country between Nairobi and Mount Kenya as well as in Uganda, Tanzania, and Somalia (1). A disease similar to NSD called Kisenyi sheep disease has been described in the Republic of the Congo (3). Sera positive for NSDV antibody were confirmed in an outbreak in haired sheep in Harar Province of Ethiopia.

Transmission

Nairobi sheep disease is not contagious and is only transmitted by ticks. Transmission by contact does not occur. Experimentally, NSD can be transmitted by the inoculation of infectious blood, serum, or organ suspensions into susceptible animals. Large doses (50 cc) of virulent blood or serum given to sheep by mouth may also cause infection.

The major vector of NSD is *R. appendiculatus* and is generally thought to be the only species of tick in which transovarial transmission of NSD is known to occur; however, there is firm evidence that a population of *R. pulchellus* in Somalia also transovarially transmits the virus. The African bont tick (*Amblyomma variegatum*) is believed to have been responsible for one large outbreak of NSD in Kenya (3). However, in a laboratory investigation, *A. variegatum* was found to be a less efficient vector than *R. appendiculatus* (4). More recently in Kenya, a closer correlation has been shown to exist between the presence of NSD antibody in sheep and goats and infestations with *R. appendiculatus* than with *A. variegatum* (14). Of eight species of ticks representing three genera (*Amblyomma*, *Hyalomma*, and *Rhipicephalus*) collected in Kenya, NSDV was isolated only from *R. appendiculatus* (5). Unfed adult ticks are infective for over 2 years. It has previously been stated by Daubney and Hudson (3) that infected *R. appendiculatus* lose their infectivity when allowed to feed on immune sheep or on nonsusceptible animals; however, this was later shown not to be the case (11).

Incubation Period

The incubation period in natural infections is 4 to 15 days. Experimental inoculation of sheep and goats with virus results in a shorter incubation period of 1 to 3 days (19).

Clinical Signs

Nairobi sheep disease is characterized by an acute hemorrhagic gastroenteritis (17). Clinical signs of NSD begin with a temperature rise to 40 to 41° C (104 to 106° F) and, during this stage, a prominent clinical depression develops followed by a temperature decline and diarrhea. There is an abundant mucopurulent nasal discharge, and breathing may become rapid and painful. Leukopenia is prominent during the period of hyperthermia (18). Initially the feces are thin and watery but later they may contain mucus and blood. In less acute cases the course of the disease is slower, and sheep become anorexic, weak, and recumbent with signs of diarrhea. There may be abortions. In hyperacute infections there is a sudden rise in body temperature that abruptly declines on the third to the sixth day followed by collapse and death within a few hours.

Gross Lesions

The most obvious lesions are those associated with hemorrhagic gastroenteritis. The abomasal mucosa is hyperemic and may be covered with petechial hemorrhages. Intestinal lesions are most severe in the cecum and the anterior part of the colon. Hemorrhages in the mucosa of the large intestine are numerous, and the intestinal contents are blood stained.

There is nonspecific congestion and petechial and ecchymotic hemorrhages in most organs and tissues.

Generalized hyperplasia of lymphoid tissue is a prominent lesion. Lymph nodes are enlarged and edematous. The spleen may be several times its normal size and engorged with blood.

In pregnant ewes, the genital tract may be very hyperemic, which is indicative of inflammation, and fetal membranes may be swollen and edematous, and contain hemorrhages. The aborted fetus has numerous hemorrhages in its tissues and organs.

Morbidity and Mortality

Early studies (17) revealed that sheep and goats resident in endemic areas were generally immune, whereas severe outbreaks occurred in susceptible animals moved into these region. Davies (5) in a 9-year study discovered that NSD outbreaks were mainly associated with the trading of livestock in the vicinity of Kenya's major cities. Sporadic outbreaks in nonendemic regions were usually preceded by excessive amounts of rainfall and the appearance of the tick vector.

Prognosis in susceptible sheep and goats is poor, although mild infection may occur. Mortality in Merino and Merino crossbreds is about 40 percent, but mortality in Masai sheep is much higher.

Diagnosis

Field Diagnosis

An outbreak of NSD is nearly always associated with movement of susceptible animals into an endemic area where *R. appendiculatus* is abundant. When recently introduced small ruminants become ill with signs of severe enteritis and nasal discharge within an NSD endemic area and sheep native to the area do not, it is a likely assumption that NSD is the current problem. This is particularly true if the incidence of illness in sheep is high, is low in goats, and is absent in cattle and other animals. Susceptibility of goats may depend on breed (6).

Specimens for Laboratory

Heparinized blood is the best source of NSDV during the febrile stage. During later stages of illness, when body temperature has declined or is normal and the amount of virus in the blood stream is low or absent, spleen and mesenteric lymph nodes are the best tissues for virus isolation (2,17). Also submit serum, preferably paired specimens, for serology.

Laboratory Diagnosis

Laboratory confirmation is necessary for a definitive diagnosis. Inoculation of cell culture with suspensions of infected organs or plasma and subsequent staining of the cell culture by the direct (FAT) or indirect fluorescein conjugated antibody test (IFAT) provide the most reliable means of identifying NSDV. The use of a fluorescein conjugated antibody test allows detection virus in 24 to 48 hours after inoculation of cell cultures and thus is not dependent on cytopathogenic effects in tissue culture cells (10).

Intracerebral inoculation of suckling mice is an excellent method of isolating NSDV. The brain material from infected mice can be used as a source of viral antigen, and its identity can be determined by FAT or a complement fixation test (10).

Differential Diagnosis

The disease must be differentiated from heartwater, Rift Valley fever, anthrax, some types of plant and heavy metal poisoning, peste des petits ruminants, and coccidiosis.

Differentiation from other viral or rickettsial diseases is based on geographic location of the outbreak, species of animal affected, cross-immunity studies, serologic investigations, and viral isolation.

The following criteria may be of assistance in arriving at a diagnosis:

1. Nairobi sheep disease

    a. Nairobi sheep disease causes severe illness in sheep — an affliction that is characterized by diarrhea, often hemorrhagic.

    b. There is high mortality in Masai sheep, low mortality in Merino or Merino crosses, low mortality in goats, and no mortality in other ruminants, including wildlife.

    c. *R. appendiculatus* ticks are abundant in the region.

    d. Intracerebral inoculation of mice with blood or tissue suspensions causes rodent death.

    e. The Nairobi sheep disease virus can be isolated and propagated in tissue culture.

    f. The fluorescein antibody test and serum neutralization and complement fixation tests will identify the causative agent.

2. Heartwater

    a. Heartwater causes severe illness in sheep and is characterized by CNS signs followed by death. Pulmonary edema and an abundance of fluid in the pericardial sac and pleural cavities may be seen in the more prolonged cases. Gastroenteritis is rare.

    b. There is a high incidence of illness and mortality in exotic breeds of sheep, goats, and cattle in contrast to a lower incidence and mortality in indigenous breeds.

c. *Amblyomma hebraeum* or *A. variegatum* ticks are abundant in the affected area.

d. The rickettsia may be passaged in mice, often without any evidence of illness in the affected mice.

e. *Cowdria ruminantium*, a rickettsia, can be demonstrated in endothelial cells of capillaries found in brain smears and endothelial cells of large blood vessels stained with Giemsa.

f. The rickettsia cannot be isolated easily in tissue culture.

3. Rift Valley Fever (RVF)

a. In cattle, sheep, goats, and man, RVF is a very acute disease.

b. Rift Valley fever is characterized by a rapid course of infection, severe depression, diarrhea, massive liver necrosis, and widespread abortion.

c. The illness appears after periods of heavy rainfall when there is an abundance of mosquitoes, the arthropod vectors of the virus.

d. Ticks are not vectors of RVF and may be absent from the area of infection.

e. Mice, tissue cultures, and embryonated hen's eggs can be infected, and the isolated virus can be identified by serologic and immunologic methods.

4. Anthrax

a. Many species of mammals may be affected.

b. The most prominent lesions are multiple hemorrhages, hemorrhagic enteritis, and prominent swelling of the spleen with failure of blood to clot.

c. Blood or tissue smears stained with Giemsa reveal numerous encapsulated rod-shaped bacteria arranged in chains.

d. Inoculated laboratory animals die, have numerous hemorrhages, and have an abundance of encapsulated bacteria in their tissues.

e. *Bacillus anthracis* can be grown and identified on laboratory media.

5. Arsenic poisoning (from dips)

a. Many species of animals may be affected.

b. Signs: Profuse watery diarrhea, sometimes blood tinged, severe colic, dehydration, depression, weakness, and CNS signs; high fatality rates.

c. Lesions: Edema and necrosis of gastric and intestinal epithelium and subepithelium. Diffuse degeneration of liver and other abdominal viscera.

d. Arsenic detected in tissues.

6. Coccidiosis

a Signs: Diarrhea (sometimes bloody), dehydration, fever, anorexia, and anemia.

The diseasecan be fatal — especially in lambs.

b. Lesions: Edema, inflammation, and mucosal hemorrhage predominantly in the ileum, cecum, and upper colon.

c. Thick white patches of oocysts may develop in small intestine. These oocysts can be demonstrated microscopically.

Treatment

There is no specific treatment for NSD. Supportive treatment, protection from climatic adversities, and availability of good quality feed may reduce the mortality rate.

Vaccination

Recovery from NSD leads to lifelong immunity. Because sheep and goats in endemic areas are constantly exposed to ticks carrying virus, they maintain good immunity and have no clinical signs of illness. It has been suggested (14) that lambs and kids are protected by colosteral antibody until they can acquire an active immunity through infection.

The Nairobi sheep disease virus can be propagated in cell culture (goat testes, goat kidneys, and hamster kidneys). When cell culture virus is attenuated, it is capable of protecting sheep and goats from NSD (9). The Entebbe strain of NSDV passaged 140 to 150 times through mouse brain is also used as vaccine. However, because of variability of breed responses to modified live virus vaccines and their adverse effects, they are generally not recommended.

Control and Eradication

Susceptible sheep and goats must be protected from the vector by weekly acaricide dipping and spraying. Movement of animals into endemic areas must be controlled unless sheep and goats are naturally immune or have been vaccinated.

Because the infection is not transmitted by contact, there is little need for strict quarantine procedures. Dead sheep should be buried or incinerated. Livestock on the premises should be dipped or sprayed with acaricides to reduce the existing tick population.

Public Health

Antibodies against NSDV have been detected in human blood serum, but it is not known if these antibodies are the result of NSDV infection or have been caused by a yet unidentified agent. An apparently naturally acquired clinical case was reported from Uganda in which a young man from whom virus was isolated experienced transient clinical signs (15). However no serological conversion has been demonstrated in investigators working with the virus (6).

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PART IV
FOREIGN ANIMAL DISEASES

PARAFILARIASIS IN CATTLE

Definition

Parafilariasis is a vector-borne parasitic infection of cattle and buffalo caused by the filaroid nematode *Parafilaria bovicola*. The disease is characterized by hemorrhagic nodules on the skin of cattle and subsequent bruise-like lesions in subcutaneous and intramuscular tissues of affected carcasses (1,2,3,4).

Etiology

The parasite species *P. bovicola* belongs to the family Filariidae, subfamily Filariinae, genus *Parafilaria* (1). The parasite female is 5 to 6 cm long and 500 mm wide, and the male is half that size.

Host Range

No age, sex, or breed preference of cattle and buffalo has been noted in cases exposed to *P. bovicola*. Bleeding points are more easily recognized in light-colored breeds like the Charolais, and therefore positive cases are reported more often in these breeds.

Geographic Distribution

Parafilaria bovicola was first described in 1934 by M. A. Tubangui from the Philippines (6) and has since been identified on all the major continents except Australia and South America. Parafilariasis in cattle has also been reported from India (1934); U.S.S.R. (1941); Tunisia and Morocco (1935) (7); French-speaking west Africa, Nigeria, and east Africa (8); Rwanda (1949); Burundi, South Africa (1964); Romania (1949); Bulgaria and France (9); Sweden (5,10); and most recently from Pakistan (20). The source of introduction in Sweden was probably Charolais cattle imported from France in 1969 and 1970, for the parasite was earlier recovered from Charolais cattle imported from France into Canada in 1966 (5,21,22). The parasite was not transmitted from the imported cattle to indigenous cattle in Canada (21,22). *P. bovicola* has not been reported in the United States.

Transmission

Vector-borne diseases, such as parafilariasis in cattle, are restricted to certain geographical regions that coincide with those of their vectors. Although the parasite is not presently known in the United States, a real threat exists to the beef industry, because of the presence of the face fly, *Musca autumnalis*. Experimental transmission studies carried out in Sweden demonstrated that face flies obtained from the United States are capable of serving as biological vectors of *P. bovicola*, as is the European face fly (15).

Investigations in South Africa have shown that the licking flies, *Musca xanthomela*, *M. lusoria*, and *M. nevilli* species are vectors of *P. bovicola* (7,11,12,13). A preliminary research note from India suggests another licking fly, *M. vitripennis*, may also act as a vector for *P. bovicola* (14).

Results of experimental transmission in calves indicated that positive cases were observed following inoculation by the intraconjunctival route, whereas calves exposed by the subcutaneous route did not develop lesions (15). This correlates with reported findings that *M. autumnalis* feeds primarily on eye secretions (11,18). However, experimental infections and intraconjunctival routes have been reported by others (9,11).

The spread of *P. bovicola* to new localities may occur in several ways. Infected vectors may move actively or passively (livestock trade) to new sites, or the infected bovine may be moved to virginal geographic areas (16,17,29).

The developmental period of the parasite extends from the time vector flies feed on bleeding points of parafilaria-affected cattle during the pasture season to the time bleeding points first appear in February (3,15). Later in the year, only sterile or calcified nematodes, or both have been found in healing or healed lesions (3). Also, forth-stage larvae from new infections are found (5). These observations indicate that adult parasites seem to die off after oviposition and do not survive into the next season and that affected animals are newly infected every year (5,28). This is an important fact when considering parasite control (Fig. 85).

Life Cycle

The life cycle of *P. bovicola* begins when flies feed on the bleeding points of parafilariasis-affected cattle and ingest infective microfilariae (first-stage larvae). These flies then become the intermediate host.

After 11 days in South Africa (11) and 20 days in Sweden (15), the microfilariae develop in the fly into infective third-stage larvae (12). These larvae are infective for cattle on which the vector flies subsequently feed. The developmental period in cattle from the infective third stage larvae to mature adult *Parafilaria* is 9 to 10 months under Swedish conditions. This is comparable to the 7 to 10-month period reported from South Africa (7), which suggests that the prepatent period of the parasite under Swedish conditions might be longer than in South Africa owing to differences in climate (5,15,19) (Fig. 82).

Viljoen (9) has subsequently shown that the third molt takes place about 7 days after infection and the fourth molt at approximately 65 days after infection. After 135, days the fifth-stage larva is adult; oviposition starts about 240 days after infection (9). The parasites produce subcutaneous nodules in the superior parts of the body, particularly the head and neck, the withers, the shoulders, and the sides of the body. Several hours after the appearance of the nodule, the female makes an opening about 0.5 to 1 mm in diameter on the summit. Generally, the nodules develop rapidly and within a few hours exude blood that coagulates, matting the hair in the region. The bleeding stops within 24 to 48 hours, and another nodule may develop in the vicinity of the first one and produce the same sequence of events (Fig. 83). Later in the year, only sterile or calcified nematodes, or both are found in healing or healed lesions (3). These observations indicate that adult parasites seem to die off after oviposition and do not survive into the next season, and that affected animals are newly infected every year (5,28).

The reservoir of infection in Sweden is the infected cow herd, where the presence of infection does not present an economic problem for the farmer, because there are few condemnation losses of cows at slaughter owing to the minimal lesions caused by the parasite in adult cattle (5,26). Direct economic losses exist for beef producers who have limited their production to raising young bulls and steers for market. These become infected on initial pasture exposure to flies containing *P. bovicola* infective larvae. At this time the cattle weigh from 300 to 400 kg and are 1 to 2 years of age. Three to nine months later (December through July) the infections result in a high percentage of condemnations and substantial economic losses. However, these animals are not important as reservoirs of infection under the present Swedish meat production system, for they do not normally survive through two subsequent pasture seasons (29).

Clinical Signs

Clinical signs are mild and rather characteristic. Female *P. bovicola*, which live in the subcutaneous tissue, lay eggs on the surface of the skin, reaching this position by penetrating the dermis and epidermis. As the female pierces the skin at the neck and back of the bovine, a trickle of bleeding becomes visible for some minutes or even hours. In the live animal the condition is characterized by the appearance of swollen, painful hemorrhagic nodules on the skin (40 mm in diameter and 10 mm in depth) as a result of the female penetrating the skin. Before penetration by the female, the nodules are 12 to15 mm in diameter and 5 to7 mm in

height (9) (Fig. 84).

Lesions and cutaneous bleeding points caused by the parasite appear in a seasonal pattern in the Northern Hemisphere, starting in December and February, respectively, and lasting through the first half of the calendar year. After this they gradually disappear (3,5). In the Southern Hemisphere, on the African continent, this reportedly occurs in a similar but reversed seasonal pattern in the period from June to January (23). The developmental period of the parasite to sexual maturity coincides with vector fly activity during the pasture season (May to September) in Sweden, and results in this seasonal occurrence of bleeding points and lesions detected at slaughter.

Gross Lesions

Subcutaneous lesions on the carcasses of affected cattle look remarkably like bruises caused by handling and transport before slaughter (Fig. 85). Acute lesions have an opaque yellow-green appearance. Edematous areas are intermingled by clearer areas with petechiae in the subcutaneous tissue, on the fascia, and in the superficial muscle layers (Fig. 86). Chronic lesions have a greenish, dirty brown appearance because of eosinophilic infiltration of the inflammatory tissue (2,5,15,24,25).

Morbidity and Mortality

Retrospective studies in Sweden revealed parafilarial lesions at slaughter in 35 percent of the young cattle from herds exposed to face flies on pasture during the year preceding slaughter. However, parafilarial lesions were not found in cattle from herds managed indoors and not exposed to face flies (15).

Diagnosis

Field Diagnosis

A provisional diagnosis is usually made by clinical examination (cutaneous bleeding points) in endemic areas. However, many bleeding foci remain undetected, and therefore, many of infected animals are not diagnosed (Fig. 87).

Specimens for Laboratory

To help confirm a diagnosis of parafilariasis in cattle, collect blood for serum and blood (fresh or dried) from a cutaneous bleeding point of a suspicious case into a suitable container holding 1 ml of 0.85 percent saline solution. The specimens should be kept cool during transport to the laboratory. In addition, a biopsy of a skin lesion can be submitted in 10 percent formalin.

Laboratory Diagnosis

The blood collected from the cutaneous bleeding point should be transferred to a centrifuge tube and centrifuged at 400 gravities for 10 minutes. The pellet should then be examined microscopically for the characteristic eggs containing microfilariae or free microfilariae, or both, which are 200 to 300 mm wide.

A serologic enzyme-linked immunosorbent assay (ELISA) test has been developed (26) and evaluated (27) to diagnose *P. bovicola* infection reliably in living animals. Significant diagnostic titers appear approximately 3 months after exposure.

Differential Diagnosis

In live cattle, the focal cutaneous hemorrhages resemble injury by thorns, wire, biting flies, or ticks. Identification of microfilariae in cutaneous bleeding lesions establishes the diagnosis of parafilariasis. Subcutaneous lesions on carcasses of affected cattle resemble bruises due to trauma. Parafilaria-induced lesions can easily be differentiated from bruises by the presence of

an eosinophilic infiltrate and by isolating the nematode.

There are other nematodes belonging to the *Filarioidea* superfamily that cause tissue lesions in cattle, namely the *Onchocerca* species. However, in contrast to *Parafilaria*, the *Onchocerca* species cause neither extensive edema and discoloration of subcutaneous tissues nor intermuscular and intramuscular lesions (5). *O. gutturosa* causes a green-colored inflammation, but this is mainly restricted to the nuchal ligament and knee-joint tendon (5).

Treatment

Ivermectin has been used successfully in the Union of South Africa to reduce the number and surface area of *Parafilaria* lesions and the weight of tissue trimmed from affected carcasses (31-34). Similar results have been reported from Pakistan (11) as well as from Burundi (35) and Sweden (30,34). A single dose of 200 µg/kg reduced the number of subcutaneous lesions by 88.2 percent, the total lesion area by 98.7 percent and the mass of tissue trimmed from carcasses by 98.8 percent at slaughter 83 days posttreatment (30).

Nitroxynil is an effective anthelmintic at a dose of 20 mg/kg repeated 3 days later. Lesion area was reduced by 95 percent and visible carcass lesions by 90 percent. High doses of levamisole and fenbendazole given daily for 4 to 5 days have also been used (23,24,36).

Control and Eradication

Elimination of infective *P. bovicola* from cattle before they leave the exporting country would be the method of choice in preventing the entry of parafilariasis into free areas such as the United States. Availability of the diagnostic serologic ELISA test makes possible testing of cattle in *P. bovicola* endemic areas (26,27). Cattle on pasture should be tested about 3 months after the pasture season ends. If tested earlier, a retest should be done at least 3 months after the pasture season ends. Seropositive animals should be considered to have been infected with *P. bovicola* during the previous pasture season. The following recommendations are offered for buyers and sellers of livestock in Sweden (30):

1. Calves should be sold during the period October 1 to April 30 if they are born between October and March.

2. The trade of young livestock and older cattle can take place according to the following alternatives:

> a. Serological control.
>
> The animal can he sold during the period December 1 to April 30 if the animal tests negative on serology. If the animal tests positive, the animal can be sold if treated according to alternative b.
>
> b. Treatment with Ivermectin.
>
> During the period May 1 to November 30, the animal can be sold if it is treated with ivermectin in the herd of origin (seller) in conjunction with the sale and is treated in the herd of destination (buyer) 1 month before being released onto pasture. This later treatment can be abolished if serologic testing of a sample taken between December 1 and April 30 is negative.
>
> c. Animals kept stabled for the entire pasture season.

Animals can be traded during the period October 1 to April 30 if it can be guaranteed that the animal has not been on pasture during the previous pasture season.

Experience from South Africa indicated that treatment with ivermectin reduces bleeding points 14 days after a single treatment using 200 µg/kg. These trials indicated that ivermectin has a substantial effect on the reduction of *Parafilaria* lesions — most probably as the result of activity

against the adult worm. Further work is required to ascertain whether this activity includes the preadult stages (31).

For import into a *P. bovicola*-free area such as the United States, where the vector fly *M. autumnalis* is abundant, it is highly recommended that animals be serotested in the country of origin before export. Specific guidelines regarding live animal trade between endemic and *P. bovicola*-free areas have been developed in Sweden (30). Guidelines are constantly being updated as changes in the disease situation occur.

Vector control measures against *M. autumnalis* as a method to control *P. bovicola* have had limited success in breaking the infection cycle in endemic areas. Because this fly occupies vast areas and remains for only a short time at the host, control has been inadequate with conventional methods of repeated application of insecticidal sprays as well as the use of self-application devices such as dust bags and oilers. Good vector control over the entire period of *P. bovicola* transmission will lead to control of the parasite, as reported by Nevill et al. (34). They used weekly to fortnightly dipping of all cattle with a pyrethroid spray-wash containing 2.5 percent m/v delmethrin. All cattle were sprayed with 50 ppm delmethrin in a spray race weekly from August to April (9 months). Another approach of using pyrethroid-impregnated eartags or spot treatments with pyrethroids aimed at control of the face flies found around the head has been reported from Sweden (34), where *Parafilaria bovicola* control was achieved in a 260 km2 area by treating all 2,600 cattle with a fenvalerate-impregnated eartag in each ear. The use of insecticide-impregnated cattle eartags reportedly reduces the number of face flies around tagged livestock (18,37-39).

Public Health

Humans are not known to be susceptible to *P. bovicola*.

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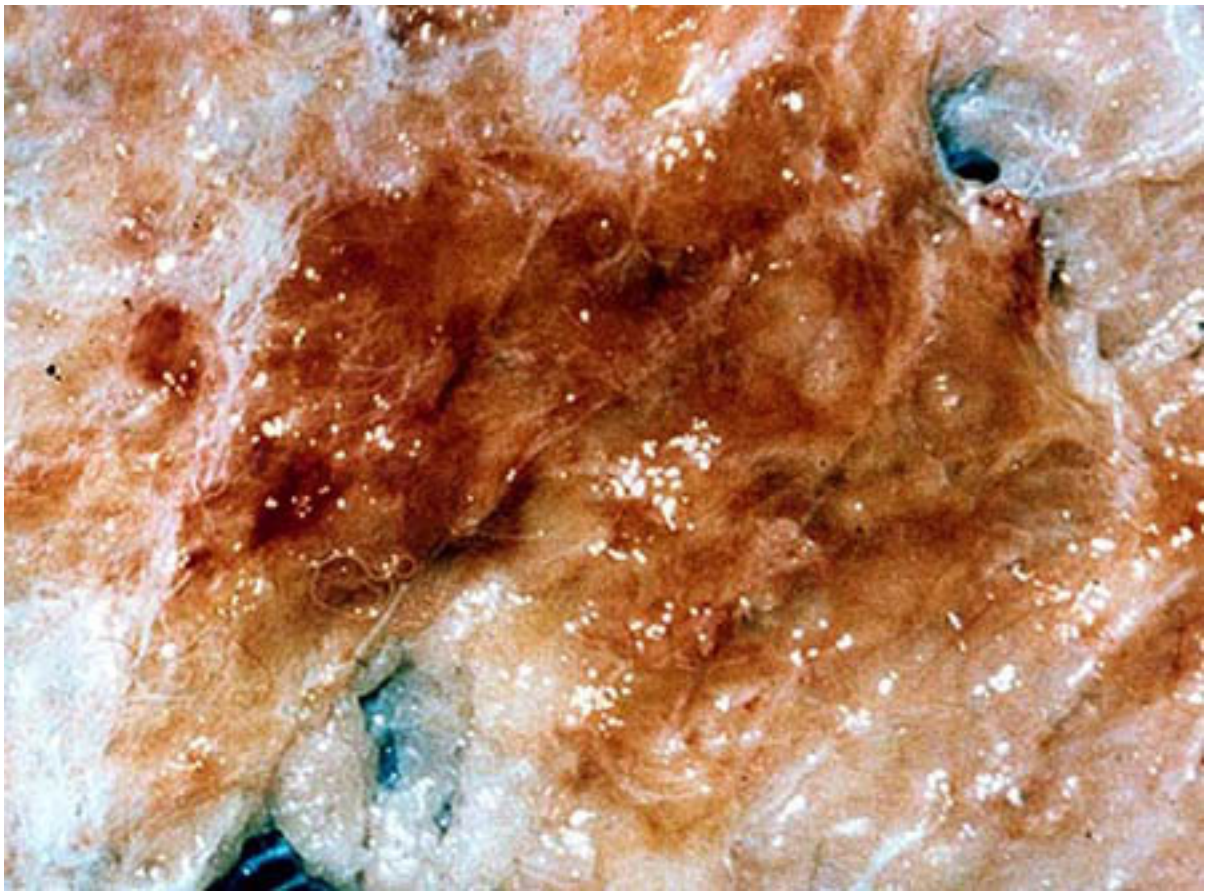

Fig. 85. Parafilariasis - Edema and hemorrhages in the subcutaneous tissue caused by the parasite.

Fig. 82. Parafilariasis - Two adult *Parafilaria bovicola* females in the subcutaneous tissue of a *Parafilaria* induced lesion. X 1.5.

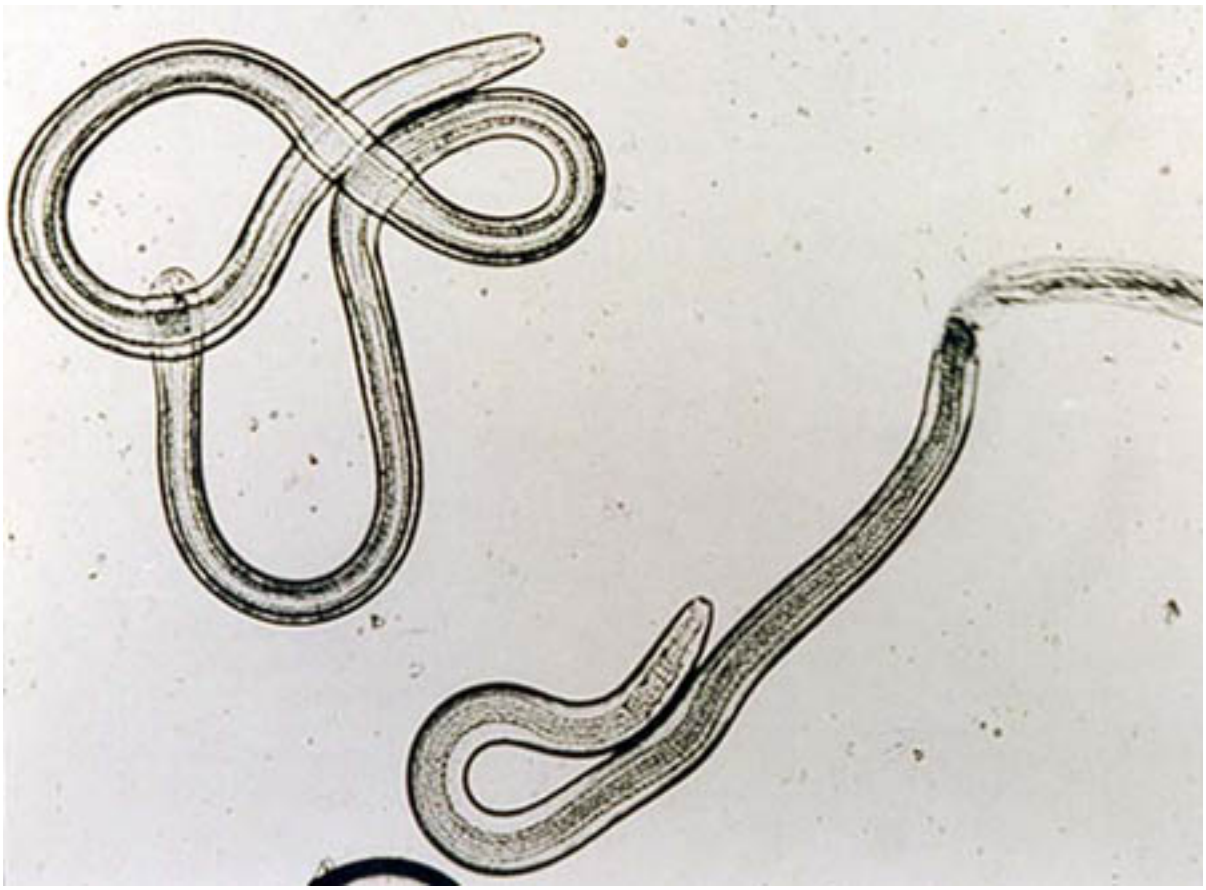

Fig. 83. Parafilariasis - *Parafilaria bovicola*. Infective third stage larvae.

Fig. 84. Parafilariasis - Vector *Musca autumnalis*.

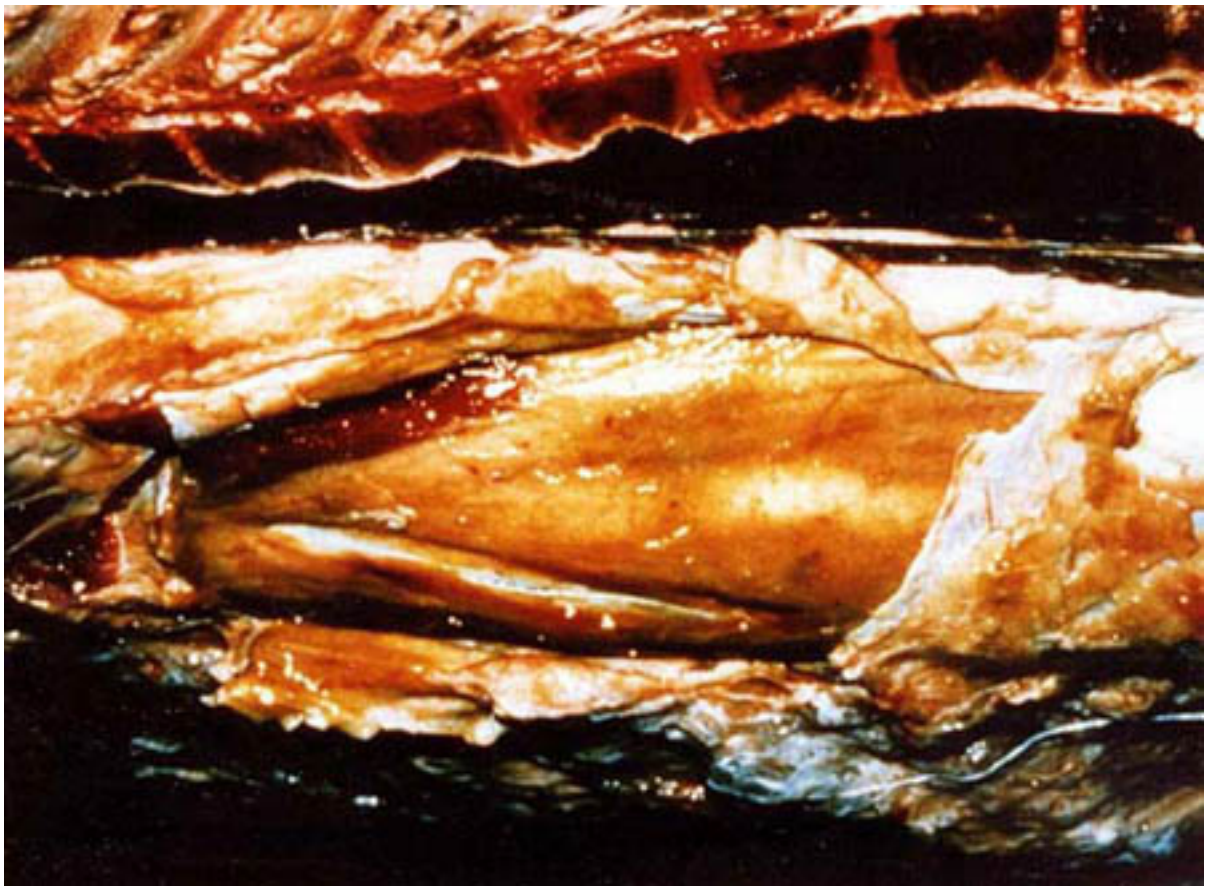

Fig. 86. Parafilariasis - Chronic muscular lesions (inflamed fascia).

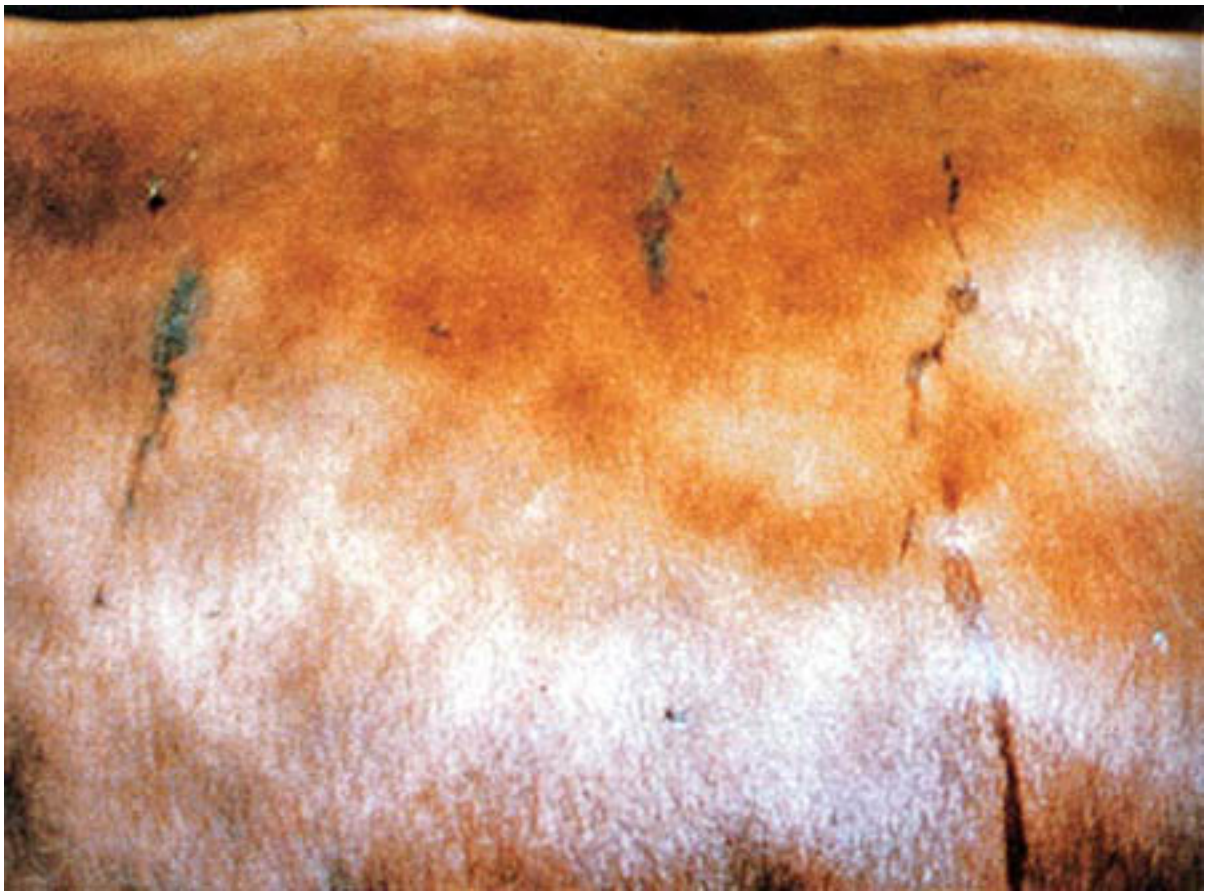

Fig. 87. Parafilariasis - Bleeding from the skin.

PART IV
FOREIGN ANIMAL DISEASES

PESTE DES PETITS RUMINANTS

(Pest of Small Ruminants, stomatitis-pneumoenteritis complex or syndrome pseudorinderpest of small ruminants and kata [Pidgin English for catarrh])

Definition

Peste des petits ruminants (PPR) is an acute or subacute viral disease of goats and sheep characterized by fever, erosive stomatitis, conjunctivitis, gastroenteritis, and pneumonia. Goats are usually more severely affected than sheep.

Etiology (1,2,9,16)

Peste des petits ruminants is caused by a paramyxovirus of the *Morbillivirus* genus. Other members of the genus include rinderpest virus (RPV), measles virus (MV), canine distemper virus (CDV), and phocid distemper virus (PDV) of sea mammals (seals). For many years, PPR virus was considered a variant of RPV, specifically adapted for goats and sheep, that had lost its virulence for cattle. It is now known that the two viruses are distinct though closely related antigenically.

Host Range (8)

Peste des petits ruminants is primarily a disease of goats and sheep. However, there is one report of naturally occurring PPR in captive wild ungulates from three families: *Gazellinae* (*dorcas gazelle*), *Caprinae* (Nubian ibex and Laristan sheep), and *Hippotraginae* (gemsbok). Experimentally, the American white-tailed deer (*Odocoileus virginianus*) is fully susceptible. The role of wildlife on the epizootiology of PPR in Africa remains to be investigated. Cattle and pigs are susceptible to infection with PPRV, but they do not exhibit clinical signs. Such subclinical infections result in seroconversion, and cattle are protected from challenge with virulent RPV. Cattle and pigs do not, however, play a role in the epizootidogy of PPR because they are apparently unable to transmit the disease to other animals.

Geographic Distribution (7,12,13,21)

Presently, PPR occurs in most African countries situated in a wide belt between the Sahara and Equator, the Middle East (Arabian Peninsula, Israel, Syria, Iraq, Jordan), and the Indian subcontinent.

Transmission

Peste des petits ruminants is not very contagious and transmission requires close contact. Ocular, nasal, and oral secretions and feces are the sources of virus. Contact infection occurs mainly through inhalation of aerosols produced by sneezing and coughing. Fomites such as bedding may also contribute to the onset of an outbreak. As in rinderpest (RP), there is no known carrier state. Infected animals may transmit the disease during the incubation period.

Incubation Period

Peste des petits ruminants has an incubation period of 4 to 5 days.

Clinical Signs (11,12,14,15,21)

The disease usually appears in the acute form, with an incubation period of 4 to 5 days followed by a sudden rise in body temperature to 104-106° F (40-41° C). The temperature usually

remains high for about 5 to 8 days before slowly returning to normal preceeding recovery or dropping below normal before death. Affected animals appear ill and restless and have a dull coat, dry muzzle, and depressed appetite. Accompanying these nonspecific signs are a series of changes that make up a highly characteristic syndrome. From the onset of fever, most animals have a serous nasal discharge, which progressively becomes mucopurulent. The discharge may remain slight or may progress, resulting in a profuse catarrhal exudate, which crusts over and occludes the nostrils. At this stage, animals have respiratory distress, and there is much sneezing in an attempt to clear the nose. Small areas of necrosis may be seen on the visible nasal mucous membranes. The conjunctiva usually becomes congested, and the medial canthus may have some crusting. As with the nose, there may be profuse catarrhal conjunctivitis resulting in matting of the eyelids (Fig. 88).

Necrotic stomatitis is common. It starts as small, roughened, red, superficial necrotic foci on the gum below the incisor teeth. These areas may resolve within 48 hours or progressively increase to involve the dental pad, the hard palate, cheeks and their papillae, and the dorsum of the anterior part of the tongue. Necrosis may result in shallow irregular nonhemorrhagic erosions in the affected areas of the mouth and deep fissures on the tongue. Necrotic debris may collect at the oral commissures, and scabs may form along the mucocutaneous junction of the lips. There may be excessive salivation but not to the extent of drooling.

At the height of development of oral lesions, most animals manifest severe diarrhea, often profuse but not hemorrhagic. As it progresses, there is severe dehydration, emaciation, and dyspnea followed by hypothermia, and death usually occurs after a course of 5 to 10 days. Bronchopneumonia, evidenced by coughing, is a common feature in the later stages of PPR. Pregnant animals may abort.

Secondary latent infections may be activated and complicate the clinical picture.

Gross Lesions (4,5,11,17)

The pathology caused by PPR is dominated by inflammatory and necrotic lesions in the mouth and the gastrointestinal tract. Unlike RP, there is also a definite, albeit inconstant, respiratory system component; hence, the synonym stomatitis-pneumoenteritis complex.

Emaciation, conjunctivitis, erosive stomatitis involving the inside of the lower lip and adjacent gum, cheeks near the commissures, and the free portion of the tongue are frequent lesions. In severe cases, lesions may also be found on the hard palate, pharynx, and upper third of the esophagus (Fig. 89). The necrotic lesions do not evolve into ulcers because the basal layer of the squamous epithelium is rarely penetrated.

The rumen, reticulum, and omasum rarely have lesions. Sometimes, there may be erosions on the pillars of the rumen. The abomasum is a common site of regularly outlined erosions and often oozes blood.

Lesions in the small intestine are generally moderate, being limited to small streaks of hemorrhages and, sometimes, erosions in the first portion of the duodenum and the terminal ileum. Peyer's patches are the site of extensive necrosis, which may result in severe ulceration. The large intestine is usually more severely affected with congestion around the ileocecal valve, at the ceco-colic junction, and in the rectum. In the posterior part of the colon and the rectum, discontinuous streaks of congestion ("zebra stripes") form on the crests of the mucosal folds.

In the respiratory system, small erosions and petechiae may be visible on the nasal mucosa, turbinates, larynx, and trachea. Bronchopneumonia may be present, usually confined to the anteroventral areas and is characterized by consolidation and atelectasis. There may be pleuritis, which may become exudative and results in hydrothorax.

The spleen may be slightly enlarged and congested. Most lymph nodes throughout the body are enlarged, congested, and edematous. Erosive vulvovaginitis similar to the lesions in the oral mucocutaneous junction may be present.

Morbidity and Mortality (13,21)

The incidence of PPR in an enzootic area may be similar to that of rinderpest (RP) in that a low rate of infection exists continuously. When the susceptible population builds up, periodic epizootics (outbreaks) occur, that receive more attention than usual. Such epizootics may be characterized by almost 100 percent mortality among affected goat and sheep populations.

The prognosis of acute PPR is usually poor. The severity of the disease and outcome in the individual is correlated with the extent of mouth lesions. Prognosis is good in cases where the lesions resolve within 2 to 3 days. It is poor when extensive necrosis and secondary bacterial infections result in an unpleasant, fetid odor from the animal's breath. Respiratory involvement is also a poor prognostic sign. A morbidity rate of 80-90 percent and a casefatality rate of 50-80 percent are not uncommon — particularly in goats.

Young animals (4 to 8 months) have more severe disease, and morbidity and mortality are higher. Both field and laboratory observations indicate that PPR is less severe in sheep than in goats. Nevertheless, field outbreaks have been reported in the humid zones of west Africa in which no distinction could be made between the mortality rates in sheep and in goats. Poor nutritional status, stress of movement, and concurrent parasitic and bacterial infections enhance the severity of clinical signs.

Diagnosis (7,9,13,19-22)

Field Diagnosis

In the field, a presumptive diagnosis can be made on the basis of clinical, pathological, and epizootiological findings.

Laboratory confirmation is an absolute requirement — particularly in areas or countries where PPR has not previously been reported.

Specimens for Laboratory

Specimens to submit include blood in EDTA anticoagulant, clotted blood or serum (if possible, paired sera), mesenteric lymph nodes, spleen, lung, tonsils, and sections of the ileum and large intestine.

Swabs of serous nasal and lachrymal discharges may also be useful. All samples should be shipped fresh (not frozen) on ice within 12 hours after collection.

Laboratory Diagnosis

A wide range of laboratory procedures have been described for detecting virus or viral antigen, viral nucleic acid, and antibody.

Differential Diagnosis (1)

Rinderpest. Clinical RP is rare in goats and sheep in Africa. In India, these species are quite often involved in RP outbreaks. Clinically, RP and PPR are similar, but the former should be the prime suspect if the disease involves both cattle and small ruminants.

Confirmation requires virus isolation and cross-neutralization.

Pasteurellosis. Enzootic pneumonia or the septicemic form of pasteurellosis is characterized by obvious respiratory signs, infrequent diarrhea, and a fatality rate rarely exceeding 10 percent.

Contagious caprine pleuropneumonia. There is no digestive system involvement, and the clinical signs and lesions are confined to the respiratory system and pericardium.

Bluetongue. Swelling of the lips, muzzle, and oral mucosa, together with edema of the head region, should serve to differentiate bluetongue from PPR. Coronitis, common in bluetongue, is not a feature of PPR. Also, sheep are more affected than goats.

Heartwater. There is often central nervous system involvement, including convulsions. There is no diarrhea.

Contagious ecthyma (contagious pustular dermatitis, orf). The orf virus causes proliferative, not necrotic lesions, that involve the lips rather than the whole oral cavity. The absence of nasal discharges and diarrhea also distinguish orf from PPR.

Foot-and-mouth disease. This condition is comparatively mild, and the most characteristic clinical sign, lameness, is not a feature of PPR.

Nairobi sheep disease. Sheep are more severely affected than goats. It is limited geographically to parts of east and central Africa (Kenya, Uganda, Tanzania, Ethiopia, Somalia and Congo [formerly Zaire]). Diagnosis requires isolation and serologic identification of the virus.

Coccidiosis. There is no upper digestive tract and respiratory system involvement.

Plant or mineral poisoning. Several plants and minerals may cause severe intestinal lesions. Case history and absence of fever should distinguish poisoning from PPR.

Treatment

There is no specific treatment for PPR. However, drugs that control bacterial and parasitic complications may decrease mortality.

Vaccination

The tissue culture rinderpest vaccine at a dose of 102.5 $TCID_{50}$ protects goats for at least 12 months against PPR. The vaccine is currently used in many African countries for vaccination against PPR. The efficacy notwithstanding, its wide use is disadvantageous for the ongoing Pan-African rinderpest campaign (PARC) because it is impossible to determine if seropositive small ruminants have been vaccinated or naturally infected with RPV. A homologous attenuated PPR vaccine is being tested and may soon be commercially available.

Control and Eradication (3,6,13,21)

Eradication is recommended when PPR appears in new areas. Methods that have been successfully applied for RP eradication in many areas would be appropriate for PPR. These should include quarantine, slaughter, and proper disposal of carcasses and contact fomites, decontamination, and restrictions on importation of sheep and goats from affected areas.

Public Health

Peste des petits ruminants is not infectious for humans.

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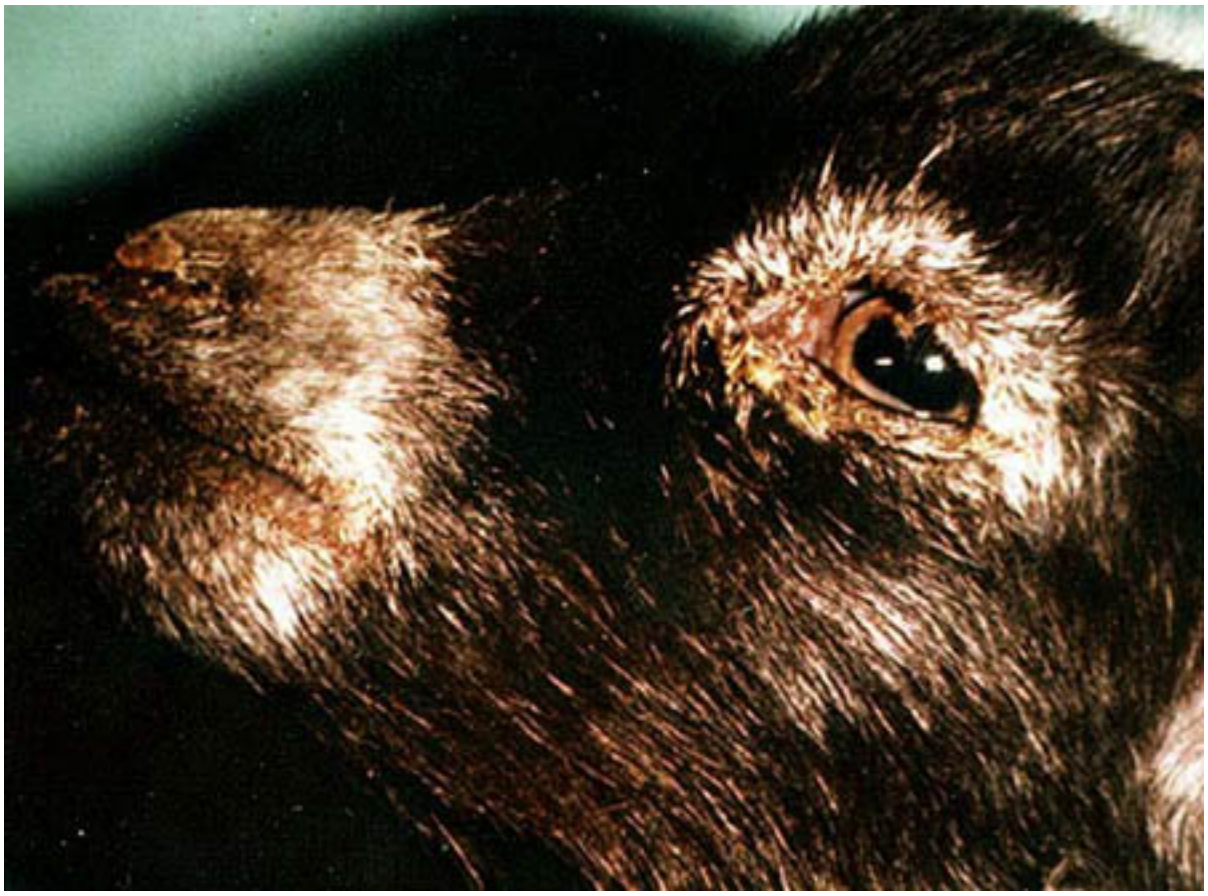

Fig. 88. PPR - Dried exudate on the muzzle and around the eye resulting from rhinitis and conjunctivitis.

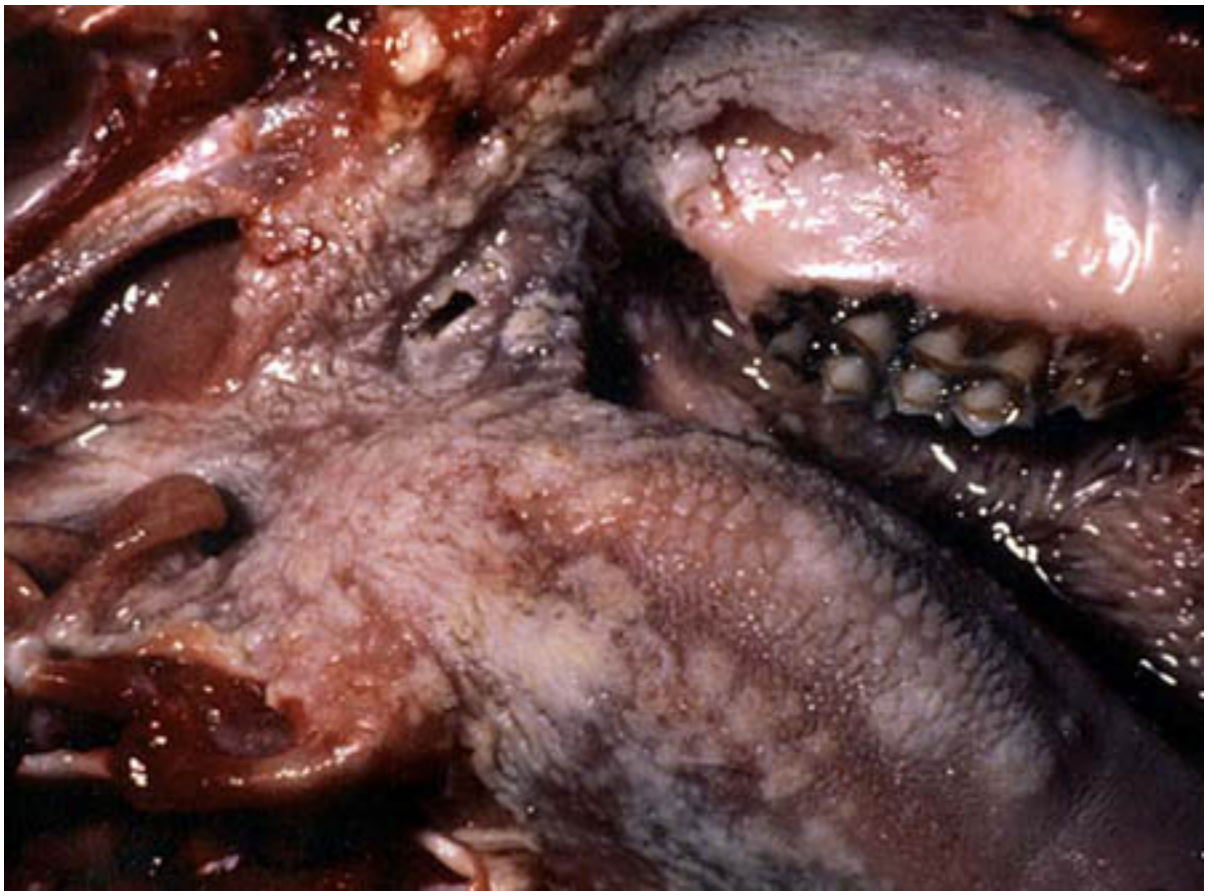

Fig. 89. PPR - Necrosis (whitish areas) of the epithelium on the tongue and pharynx.

PART IV
FOREIGN ANIMAL DISEASES

RIFT VALLEY FEVER

(Infectious enzootic hepatitis of sheep and cattle)

Definition

Rift Valley fever (RVF) is an arthropod-borne (primarily mosquito), acute, febrile, viral disease of sheep, cattle, and goats (4). The disease in these species is characterized by high abortion rates, high mortality in neonates, and hepatic necrosis (6). Humans are highly susceptible. Symptoms in humans in most cases are those of an acute undifferentiated febrile disease; severe cases (about 1 percent) resemble a dengue-like disease (18) accompanied by hemorrhage, meningoencephalitis, retinopathy, and sometimes death (10).

Etiology

Rift Valley fever is caused by a three-stranded RNA virus in the *Phlebovirus* genus of the family Bunyaviridae (11). All isolates are serologically similar. Detection of differences between isolates requires RNA fingerprinting.

Rift Valley fever virus is inactivated by lipid solvents, detergents, and low pH. At neutral or alkaline pH in the presence of protein such as serum, the virus can remain viable for up to 4 months at 4º C. Specimens stored below 0º C will retain infectivity for 8 years (6). Rift Valley fever virus in aerosols has a half-life in excess of 77 minutes at 25º C and 30 percent relative humidity (9). Humans have been infected by aerosols generated during the slaughtering procedure, by handling aborted fetuses, performing necropsies, and conducting laboratory procedures.

Contaminated surfaces should be washed to remove large amounts of organic matter and disinfected using strong solutions of sodium or calcium hypochlorite; residual chorine should exceed 5,000 ppm. Solutions having a pH of 6.2 (acetic acid) or lower are also effective.

Host Range

Rift Valley fever virus infects many species of animals and humans (table 1). Neonatal lambs, kids, calves, and puppies are highly susceptible and have a high mortality. Sheep and cattle are the primary species affected and the primary amplifiers of the virus. Humans are highly susceptible to RVF virus infection and are readily infected by mosquitoes and aerosols. Humans develop a sufficient viremia to be a source of infection for mosquitoes and thus could introduce the disease into uninfected areas.

TABLE 1. **Rift Valley fever host range and disease severity (6, modified)**

Mortality ~100%	Severe illness Abortion Mortality	Severe illness Viremia Abortion	Infection Viremia	Refractive to infection
Lambs	Sheep	Monkeys	Horses	Guinea pigs

Calves	Cattle	Camels	Cats	Rabbits
Kids	Goats	Rats	Dogs	Pigs
Puppies	Water buffalo	Gray squirrels	Monkeys	Hedgehogs
Kittens	Humans			Tortoises
White mice				Frogs
Hamster				Chickens
Field mice				Canaries
Door mice				Pigeons
Field voles				Parakeets

Geographic Distribution

Rift Valley fever has been found to occur in most of Africa.

Transmission

Historically, explosive outbreaks of the disease have occurred simultaneously over a wide area of Africa at 5 to 15 year intervals. The outbreaks have generally occurred in otherwise dry areas following periods of heavy rainfall. The long interval between outbreaks in animals allows for the development of a susceptible population. For many years, the reservoir during the interepidemic periods was unknown. Then researchers found RVF virus to be present in dormant eggs of the mosquito *Aedes lineatopinnis* located in the soil of grassland depressions known as dambos (5). When these depressions become full of water, the eggs hatch, and infected mosquitoes develop. These mosquitoes infect an amplifying host (ruminant), which serves as a source of infection for many other genera of mosquitos that rapidly spread the disease. If the area of infected mosquitoes extends into areas of susceptible animals, there are many clinical cases. In contrast, in most areas of Africa the disease is enzootic and best monitored by the use of sentinel animals.

In Africa, many of the species of mosquitoes in the genera *Aedes*, *Anopheles*, *Culex*, *Eretmapoites*, and *Mansonia* can transmit RFV. In North America, mosquitoes in the genera *Aedes*, *Anopheles*, and *Culex* experimentally are capable vectors of RFV (8). Experimentally, *Culex pipiens*, an important vector in Egypt, was shown to feed preferentially on febrile rather than normal sheep. Experimentally, vector competence of *Culex pipiens* also increased with increasing holding temperature (17).

Incubation Period

Experimentally, the incubation period in newborn lambs, kids, calves, and puppies, is about 12 hours. In adult sheep, cattle, goats, and dogs the incubation period may be as long as 3 days. In humans, the incubation period is 4 to 6 days.

Clincial Signs

Clinical signs depend on the species affected and physiologic conditions such as age and pregnancy. Lambs develop a fever of 104-107º F (40-42º C) accompanied by anorexia and

become weak and die about 36 hours after inoculation. Mortality in lambs under 1 week of age exceeds 90 percent. Mortality in lambs over a week old is greater than 20 percent. Adult sheep develop a fever of 104-106º F (40-41º C), along with a mucopurulent nasal discharge, and they may vomit. If animals are pregnant, abortion will be the most prominent sign. Mortality, particularly in ewes that abort, may reach 20 to 30 percent. Calves develop a fever of 104-106º F (40-41.1º C)

and become depressed. Mortality can range from 10 to 70 percent. Adult cattle develop a fever of 104-106º F (40-41.1º C), have excessive salivation, anorexia, and weakness; some may develop a fetid diarrhea. If animals are pregnant, abortion will be the most prominent sign (Fig. 90). Mortality is usually less than 10 percent.

Humans develop influenza-like symptoms with fever of 100-104º F (37.8-40º C), headache, muscular pain, weakness, and nausea plus epigastric discomfort and photophobia. Most people recover in 4 to 7 days; however, a small percentage of infected individuals will develop complications. Some may develop a hemorrhagic syndrome of jaundice, hematemesis, melena, and petechiae 2 to 4 days after becoming febrile and die. Others will develop a meningoencephalitis, and a third group a retinopathy 5 to 15 days after becoming febrile.

Gross Lesions

The primary lesion in RVF is hepatic necrosis. In aborted fetuses and in neonatal animals, particularly lambs and calves, hepatic necrosis can be massive. The liver may be enlarged and yellowish, have petechial hemorrhages, and be friable (Fig. 91). Older animals may have a focal hepatic necrosis; this may be visible as small pale foci in the parenchyma or be seen only by histopathologic examination. In both neonatal and older animals that die, there may be widespread cutaneous hemorrhages, petechial to ecchymotic hemorrhages on parietal and visceral serosal membranes, and a hemorrhagic enteritis.

Morbidity and Mortality

Rift Valley fever causes a high mortality in young lambs, calves, and kids. Mortality in adult sheep is about 20 percent and in adult cattle about 10 percent. A high percentage of pregnant animals may abort.

Diagnosis

Field Diagnosis

Rift Valley fever should be considered in the differential diagnosis whenever the following observations are made in a disease outbreak:

1. High abortion rates (possibly approaching 100 percent) in ewes, cows, and bitches but lower rates in goats and in other ruminants,

2. High mortality (possibly approaching 100 percent) in lambs and calves less than 7 days of age and lower rates of disease and mortality in older animals,

3. Extensive liver lesions in aborted fetuses and neonatal animals,

4. An influenza-like disease in man — particularly in individuals associated with livestock,

5. Occurrence of the disease during a period of high insect activity, and

6. Rapid spread.

Although this scenario may appear to make the suspicion of RVF rather obvious, unfortunately, a lack of communication may result in a delay in recognizing the pattern.

Specimens for Laboratory

If RVF is suspected, extra precautions should be taken in the collection and shipment of specimens because of the potential for human infection. Samples for virus isolation should be collected from aborted fetuses or febrile animals, or both. Specimens for virus isolation should include liver, spleen, heparinized blood, serum, and brain. For serologic confirmation of the disease, febrile animals should be permanently identified, a serum sample collected, and a second serum sample collected a minimum of 30 days later.

Differential Diagnosis

In animals, RVF could be misdiagnosed as bluetongue, Wesselsbron, ephemeral fever, enterotoxemia of sheep, brucellosis, vibriosis, trichomoniasis, Nairobi sheep disease, heartwater, or ovine enzootic abortion.

Vaccination

Several vaccines have been used to protect against RVF infection. Rift Valley fever virus was first attenuated by serial intracerebral inoculation of mice (Smithburn strain) (18). One inoculation of this vaccine produced protection in 6 to 7 days and immunity that lasted at least 3 years. However, when administered to pregnant ewes, it caused abortion, and the vaccine was pathogenic for man. Because of these problems with the attenuated vaccine, inactivated vaccines produced from cell-culture-propagated virus were developed. These vaccines protected; however, they had the disadvantages of requiring two inoculations for protection, annual vaccination, and large amounts of antigen (17). When the epizootic occurred in Egypt, enough inactivated vaccine could be produced to vaccinate only the more valuable breeding stock. Recently a mutagen-attenuated Vero-cell-propagated vaccine has been developed for use in people (2). The vaccine has also been tested in sheep and cattle. The vaccine causes no adverse effect in neonatal lambs, calves, or pregnant sheep or cattle. Bovine fetuses inoculated with the vaccine via a laparotomy continued a normal development and were seropositive when born. This vaccine also has the advantage that one inoculation induces rapid immunity, and as few as 10 plaque-forming units of the virus induce protection (12,13). Thus, many doses of vaccine can be produced quickly.

Attenuated vaccines induce a higher and more persistent serum antibody neutralizing titer than inactivated vaccines. Animals and people vaccinated with inactivated vaccine should have their RVF neutralizing antibody titer determined annually or be revaccinated. A serum neutralization titer of 20 or greater is protective (18). Lambs and calves that receive colostrum from a convalescent dam or dam vaccinated with an attenuated virus are passively protected for about 3 months.

Control and Eradication

In RVF enzootic areas, vaccination is the only practical method of preventing low-level losses. Movement of animals from an enzootic area to RVF-free areas during the period of virus activity should be discouraged to prevent an epizootic. Mosquito control during an epizootic is logical but not practical for large areas; it could be used to reduce human exposure in limited areas. Slaughter of sick animals is not recommended because of the risk of human infection from aerosols of blood and body fluids. In an epizootic, widespread vaccination of all susceptible animals to prevent infection of amplifying hosts and thus infection of vectors is the only way to prevent infection of animals and man.

Public Health

Humans are highly susceptible to infection. In an enzootic or epizootic area, protective measures should be taken to prevent infection by mosquitoes. Of even more importance, protective measures should be taken to prevent infection by aerosols produced during the handling of infected fetuses and tissues and in laboratory procedures. People who could be exposed to the virus should be vaccinated.

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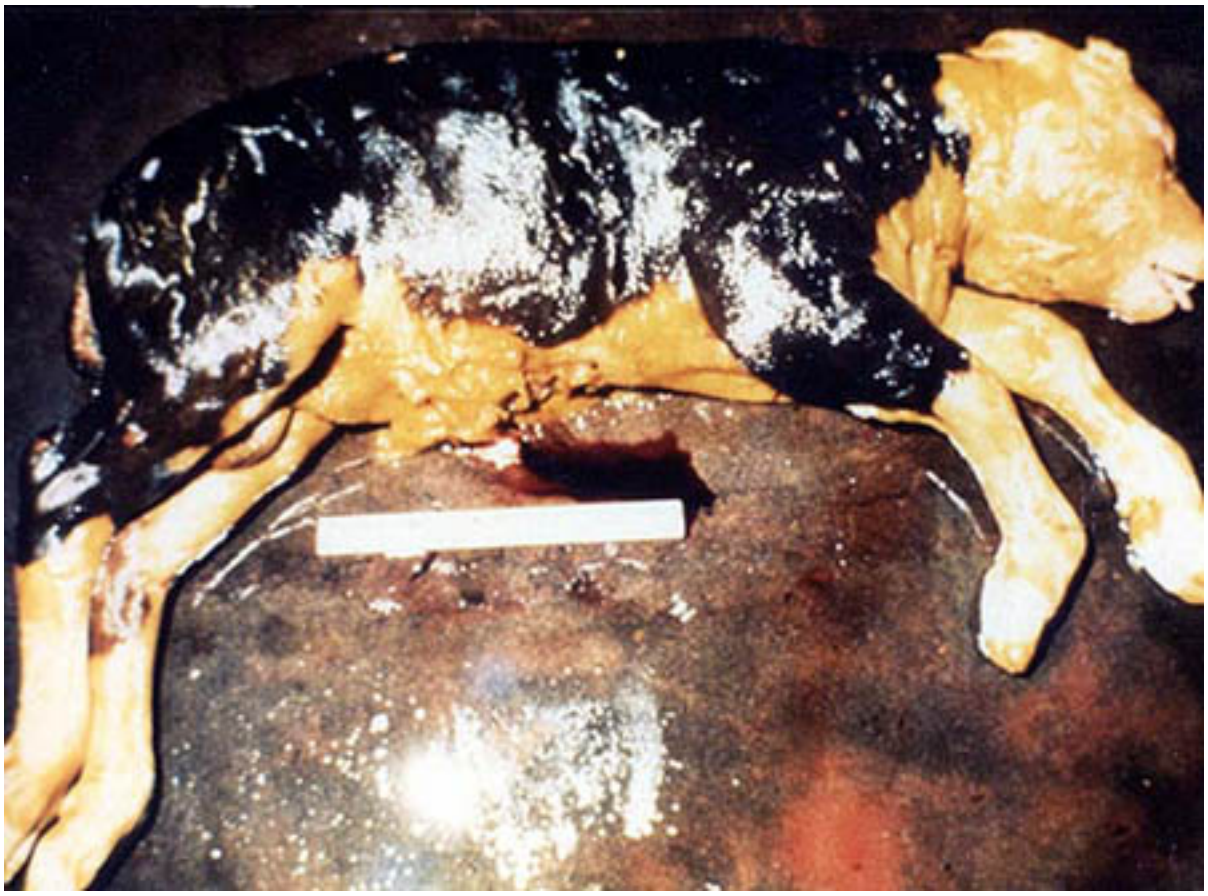

Fig. 90. RVF - Fetuses can be aborted at any stage of gestation.

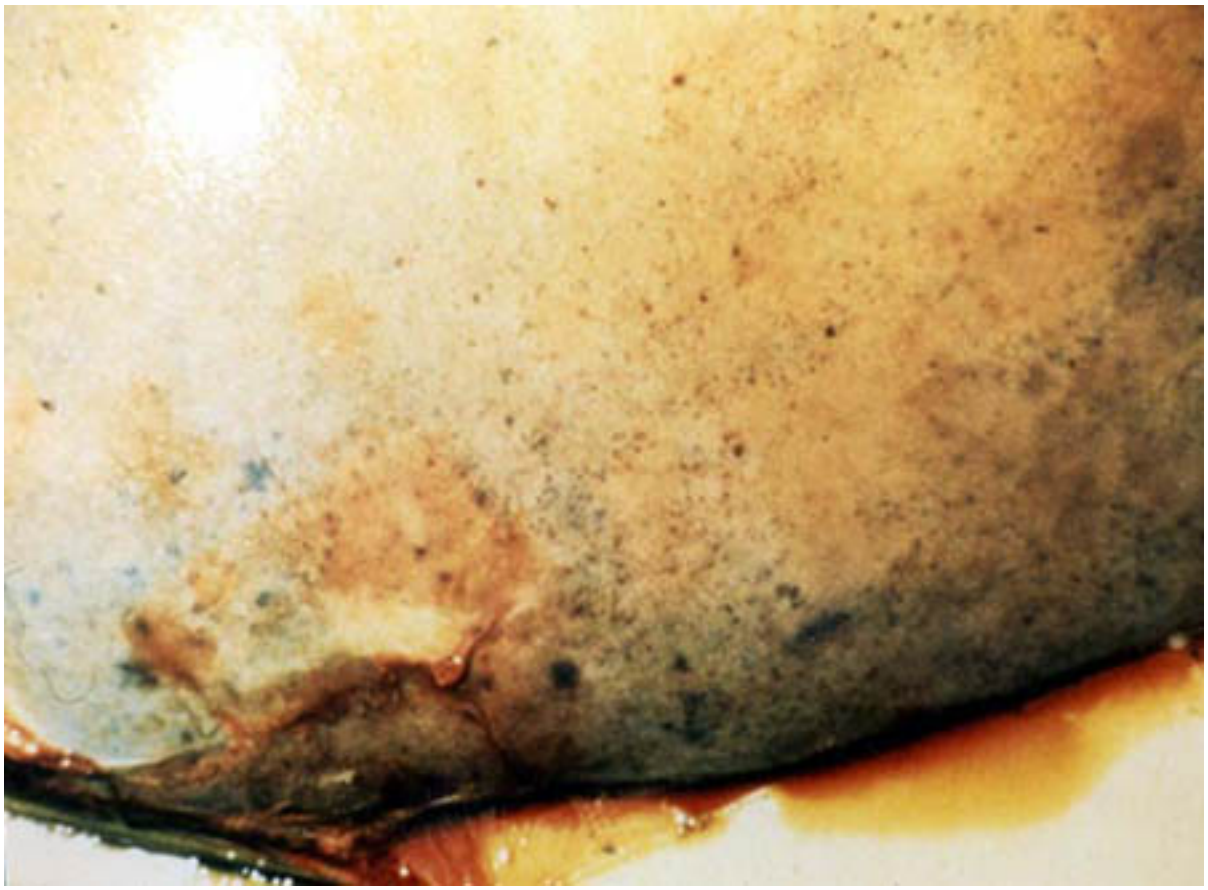

Fig. 91. RVF - The yellow appearance and petechial hemorrhages are characteristic of hepatic necrosis.

PART IV
FOREIGN ANIMAL DISEASES

RINDERPEST

Definition

Rinderpest (RP) is a contagious viral disease of cattle, domestic buffalo, and some species of wildlife. It is characterized by fever, oral erosions, diarrhea, lymphoid necrosis, and high mortality.

Etiology

Rinderpest virus (RPV) is a single-stranded RNA virus in the family Paramyxoviridae, genus *Morbillivirus*. It is immunologically related to canine distemper virus, human measles virus, peste des petits ruminants virus, and marine mammal morbilliviruses. There is only one serotype of rinderpest virus, but field strains vary widely in virulence, ease of transmission, and host affinity.

Rinderpest virus is a relatively fragile virus. Sunlight is lethal, and the vaccine must therefore be kept in a brown bottle and protected from light; virus in a thin layer of blood is inactivated in 2 hours. Moderate relative humidity inactivates the virus more quickly than either high or low humidity. The virus is very sensitive to heat, and both lyophilized and reconstituted virus should therefore be kept cold; lyophilized virus stored at -20º C is viable for years. Vaccine reconstituted in pure water quickly loses potency. Vaccine is more stable in a saline solution; reconstitution in a molar concentration of sulfate ions greatly increases resistance to heat.

Rinderpest virus is rapidly inactivated at pH 2 and 12 (10 minutes); optimal for survival is a pH of 6.5-7. The virus is inactivated by glycerol and lipid solvents.

Transmission

Rinderpest was established as an infectious disease in 1754 when susceptible animals were infected by placing bits of material previously dipped in morbid discharge into an incision made in the dewlap. In 1899, cattle were infected with a bacteria-free filtrate.

Secretions and excretions, particularly nasal-ocular discharges and feces, 1 to 2 days before clinical signs to 8 to 9 days after onset of clinical signs contain large quantities of virus. Spread of RP is by direct and indirect (contaminated ground, waters, equipment, clothing) contact with infected animals; aerosol transmission is not a significant means of transmission (it occurs only in a confined area and over a short distance). A major reason RP spreads in Africa is that the herds are nomadic. Cattle follow the grass and thus move great distances, and during the dry season, many herds will use the same well or watering area, and thus there is ample opportunity for cross-infection. It is said that a good fence will control RP.

There is only one serotype of RPV; recovered or properly vaccinated animals are immune for life, and there is no vertical transmission, arthropod vector, or carrier state. For these reasons, RPV is an ideal virus to be targeted for eradication.

Highly virulent strains of RPV are responsible for epizootics in susceptible animals and tend to die out. Milder strains tend to persist in an area, and the disease is not recognized as RP unless serology is performed.

The roles the various hosts can play in the disease are as follows:

Cattle and domestic buffalo — highly susceptible

Sheep and goats in Africa — subclinical infection and seroconversion, but there is no transmission to other animals.

Sheep and goats in India — when infected by low-passage goat RP vaccine will transmit to domestic buffalo.

Pigs — Swayback pigs in Thailand and the Malay peninsula can be naturally infected and may die. European pigs can be infected by ingestion of RPV-infected meat and will transmit to cattle and other pigs.

Host Range

Most wild and domestic cloven-footed animals can be infected.

Geographic Distribution

Rinderpest is present in the Indian subcontinent, Near East, and sub-Saharan Africa.

Wild ungulates

Highly susceptible — African buffalo, wildebeest, kudu, eland, giraffe, warthog

Fairly susceptible — Thompson gazelle, hippopotamus

Wild ungulates are infected by contact with cattle and can transmit to cattle. In the absence of RP in cattle, the disease dies out in wildlife.

Incubation Period

The incubation period varies with the strain of virus, dosage, and route of exposure. Following natural exposure, the incubation period ranges from 3 to 15 days but is usually 4 to 5 days.

Clinical Signs

Depending on the strain of virus, resistance of the animal affected, and concurrent infection, RP can appear as a peracute, acute, or mild infection.

Peracute Form

This form is seen in highly susceptible and young animals. The only signs of illness are a fever of 104-107º F (40-41.7º C), congested mucous membranes, and death within 2 to 3 days after the onset of fever.

Acute or Classic Form

This form of the disease progresses as follows:

Small amounts of virus may be in nasal and ocular secretions before the onset of fever

Fever of 104-106º F (40-41.1º C)

Serous to mucopurulent ocular discharge (Fig. 92)

Serous to mucopurulent nasal discharge.

Leukopenia

Depression

Anorexia

Constipation

Oral erosions — Salivation may be abundant and frothy (Fig. 93).

Fever decreases and viral titer drops.

Diarrhea — May be very watery or hemorrhagic, or both.

Dehydration, emaciation

Prostration and death 6 to 12 days after onset of illness.

Gross Lesions

Oral lesions are variable; some isolates cause good oral lesions and with others there is no oral lesion. Oral lesions start as small grey foci that may coalesce. The grey (necrotic) epithelium then sloughs off and leaves a red erosion.

Mouth — Lesions occur on the gums, lips, hard and soft palate, cheeks, and base of the tongue. Early lesions are grey, necrotic, pinhead-sized areas that later coalesce and erode and leave red areas (Fig. 94).

Esophagus — Brownish necrotic or eroded areas.

Rumen and reticulum — Lesions are rare.

Omasum — Erosions and hemorrhage are rare.

Abomasum — Congestion and edema.

Small intestine — Necrosis or erosion of Peyer's patches in the jejunum (Fig. 95); necrosis or erosions over the lymphoid area in the ileum (ingesta adhering to the intestinal mucosa indicates areas of necrotic epithelium).

Cecum and colon — The wall may be edematous, and there may be blood in the lumen and blood clots on the mucosa. Lesions are usually more severe in the upper colon (edema of the wall, erosions in the mucosa, and congestion) (Fig. 96). The lesions may be accentuated at the cecocolic junction (Fig. 97). Further down the colon, the colonic ridges may be congested; this is referred to as "tiger striping" (Fig. 98). Tiger striping can occur in other diarrheas and probably results from tenesmus.

Severity of intestinal lesions varies between isolates.

Lymph nodes — Generally swollen and edematous.

Liver — There may be petechial to ecchymotic hemorrhages in the gall bladder (Fig. 99).

Lung — There may be emphysema, congestion, and areas of pneumonia.

Diagnosis

Field Diagnosis

Rinderpest should be considered in all ages of cattle whenever there is a rapidly spreading acute febrile disease accompanied by the preceeding clinical signs and lesions of RP. The all ages stipulation is important because this will be one of the major differences between bovine virus diarrhea-mucosal disease, which predominately affects animals between 4 and 24 months of age.

Specimens for Laboratory

Because the viral titer drops when the fever falls and diarrhea starts, specimens should preferably be collected from animals with a high fever and oral lesions. The following samples should be collected from live animals:

Blood in EDTA or heparin

Blood for serum

Swabs containing lacrimal fluid

Necrotic tissue from the oral cavity

Aspiration biopsies of superficial lymph nodes

For the best specimens, a febrile animal should be slaughtered and specimens collected. If this cannot be done, then collect specimens from moribund animals. Collect the blood samples listed above and sections of

Spleen

Lymph nodes

Tonsil

The preceeding samples should be transported to the laboratory on wet ice — NOT FROZEN.

A complete set of tissues, including sections of all lesions, should be collected in 10 percent formalin.

Laboratory Diagnosis

To confirm the initial diagnosis in a free area, the virus has to isolated and identified.

Differential Diagnosis

The differential diagnosis for RP should include bovine virus diarrhea (mucosal disease), infectious bovine rhinotracheitis, malignant catarrhal fever, foot-and-mouth disease, vesicular stomatitis, salmonellosis, paratuberculosis, and arsenic poisoning.

Vaccination

The following types of RP vaccine have been used:

Lapinized in China and Korea

Avianized-lapinized in Korea

Goat-adapted in India

cell-culture-adapted in Africa, Middle East, and India.

An experimental vaccinia-vectored vaccine containing the F and H genes of RPV has protected against challenge inoculation of virulent virus

The two most commonly used vaccines today (1996) are the goat-adapted and cell-culture-adapted vaccines. The goat-adapted vaccine is only partially attenuated; it will cause disease in animals with low innate resistance or concurrent latent disease and kills sheep and goats. The cell-culture-attenuated vaccine was developed by Plowright in Kenya in the 1960's. This is a safe vaccine for many species and produces life-long immunity in cattle (animals challenge-inoculated 7 years after vaccination were protected). In endemic areas where cattle have been vaccinated, colostral immunity will interfere with the vaccination of calves up to 11 to 12 months of age. Because the duration of colostral immunity is variable, the recommendation is to vaccinate calves annually for 3 years.

One of the biggest problems with the cell-culture-adapted vaccine has been stability. The lyophilized virus has to be kept cold (cold chain) until used. The combination of maintenance of the cold chain and remoteness of vaccination sites made RP vaccination very expensive. Because of the uncertainty that the vaccine being used was viable, in areas of Africa it is and was the policy to vaccinate animals every year in the hope that one of the vaccinations would immunize the animal. Researchers at Plum Island in the early 1990's greatly increased the stability of the lyophilized vaccine by modifying the stabilizers and lyophilization process. This change in production is now being used in some production facilities in Africa.

Experimentally, the vaccinia-vectored RP vaccine protected cattle against challenge inoculation with RPV. This vaccine is undergoing field testing. This vaccine could be particularly useful in an eradication program because vaccinia-vectored-RP-vaccine immunized animals can be differentiated serologically from animals having antibody induced by live virus. The vaccinia-vectored vaccine would enable a country toward the end of an eradication program to maintain herd immunity to RP without using a live RP virus.

Control and Eradication

Countries and areas free of RP should prohibit unrestricted movement of RP-susceptible animals and uncooked meat products from areas infected by RP or practicing RP vaccination. Because recovered animals are not carriers, and there are good serological techniques, zoological ruminants and swine can be imported with proper quarantine and testing. If an outbreak occurs, the area should be quarantined, infected and exposed animals slaughtered and buried or burned, and ring vaccination considered.

Experimentally it has been shown that RPV will not be transmitted by bovine embryo transfer if the embryos have been processed by the technique recommended by the International Embryo Transfer Society and the OIE.

High-risk countries (those trading with, or geographically close to, infected countries) can protect themselves by having all susceptible animals vaccinated before they enter the country or vaccinating the national herd, or both. If an outbreak occurs, the area should be quarantined and ring vaccinated.

Endemic countries should vaccinate the national herd. Owing to the uncertainty of vaccine potency, the recommendation is to vaccinate annually for at least 4 years, followed by annual vaccination of calves. Foci of infection should be quarantined and stamped out. Wildlife, sheep, and goats should be monitored serologically. Serological monitoring of sheep and goats could be complicated by using RP vaccine to protect against peste des petits ruminants.

Public Health

There is no report of RPV infection in a human.

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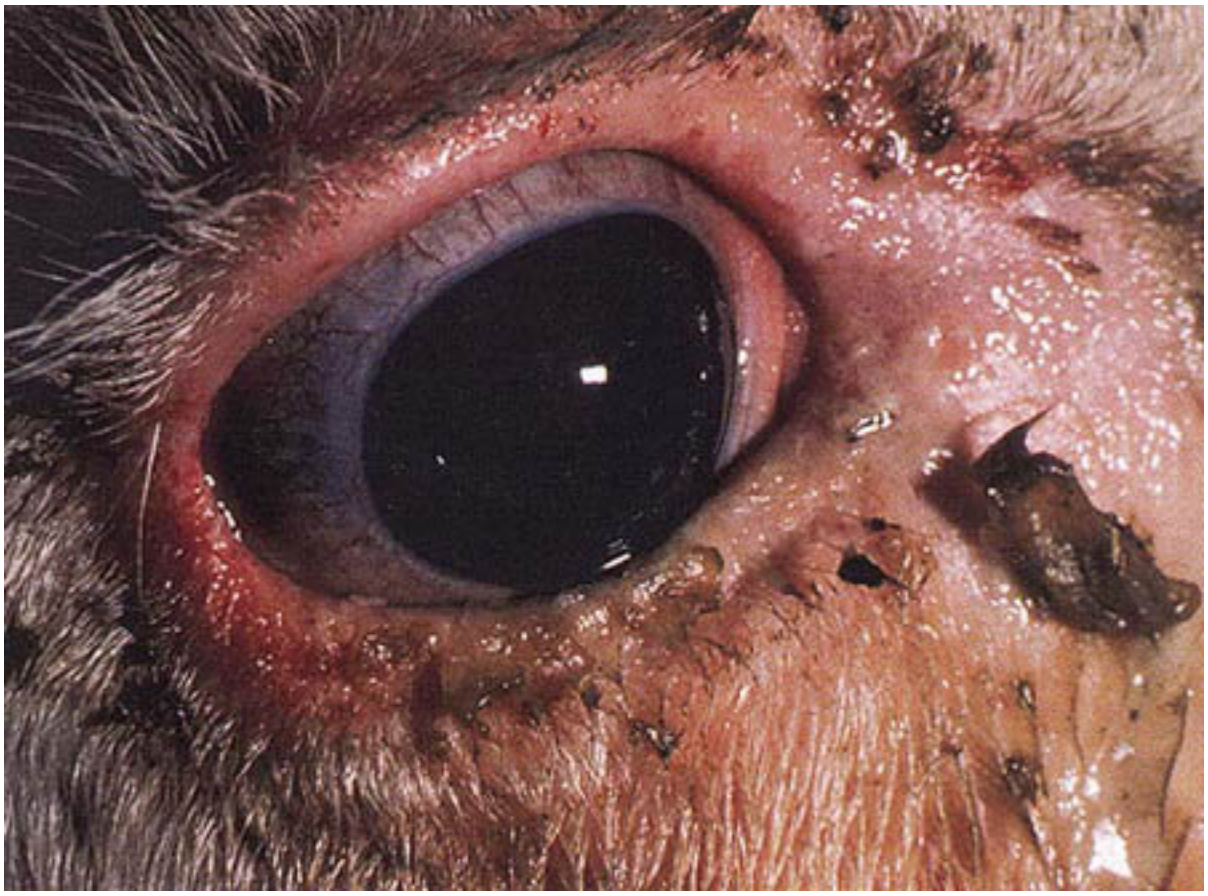

Fig. 92. RP - Conjunctivitis and mucopurulent exudate in the early stage of RP infection.

Fig. 93. RP - Excessive salivation in the early stage of RP infection.

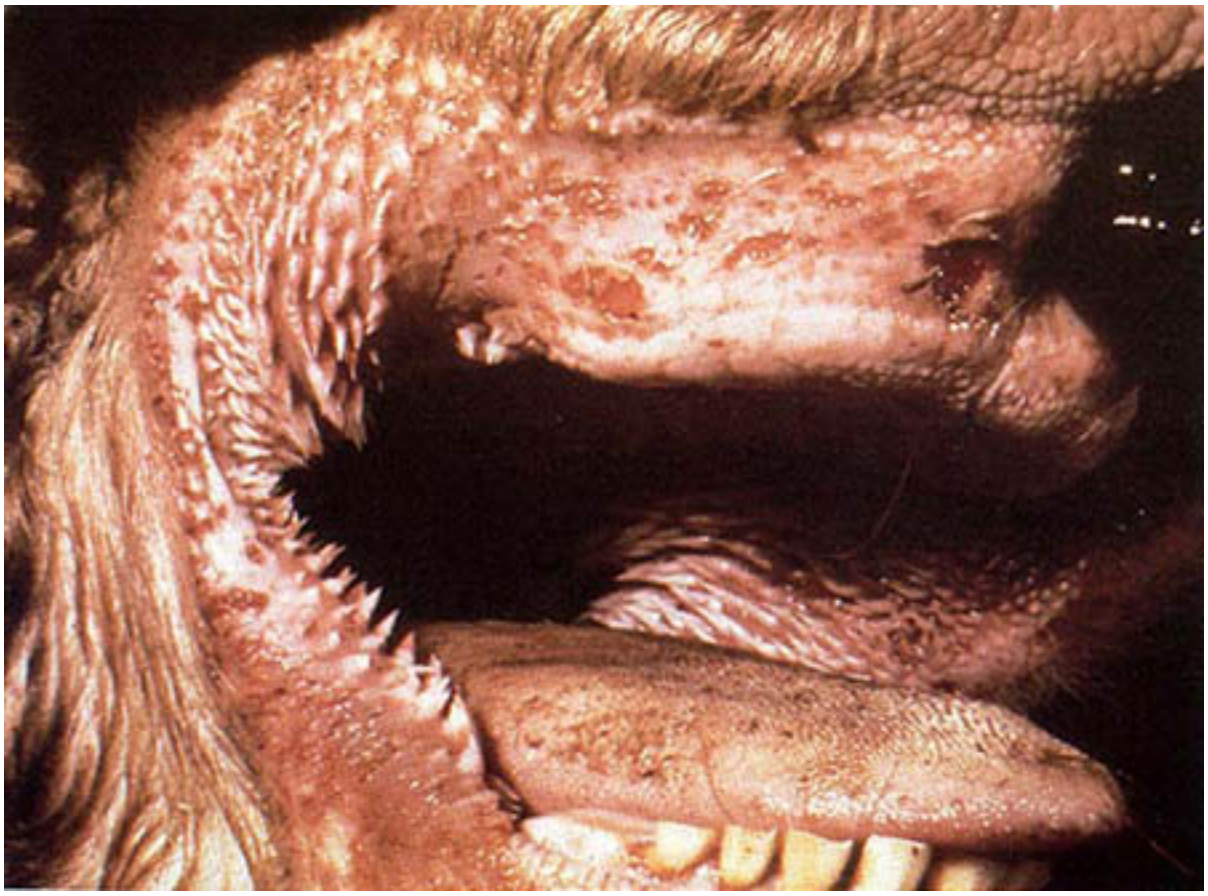

Fig. 94. RP - Oral erosions.

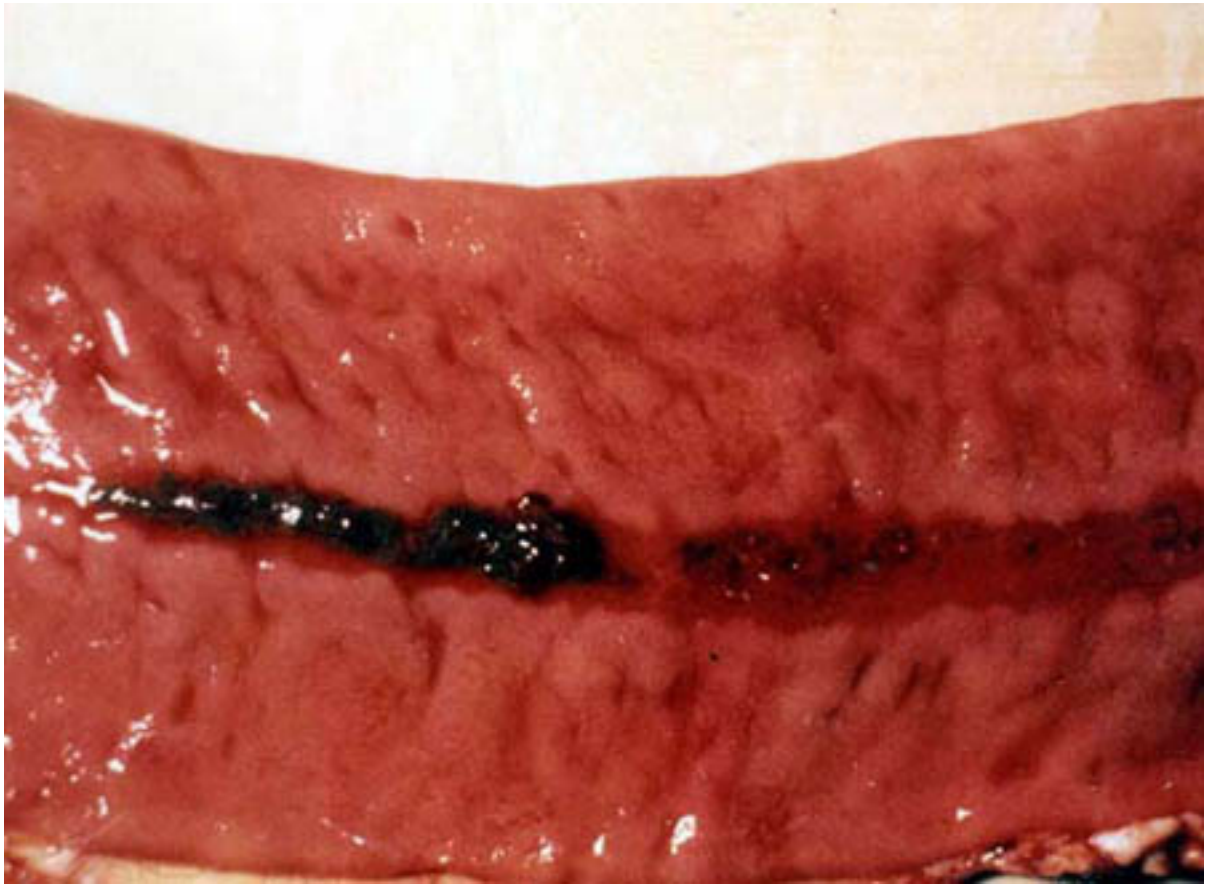

Fig. 95. RP - Sloughing of the epithelium over a necrotic Peyer's patch.

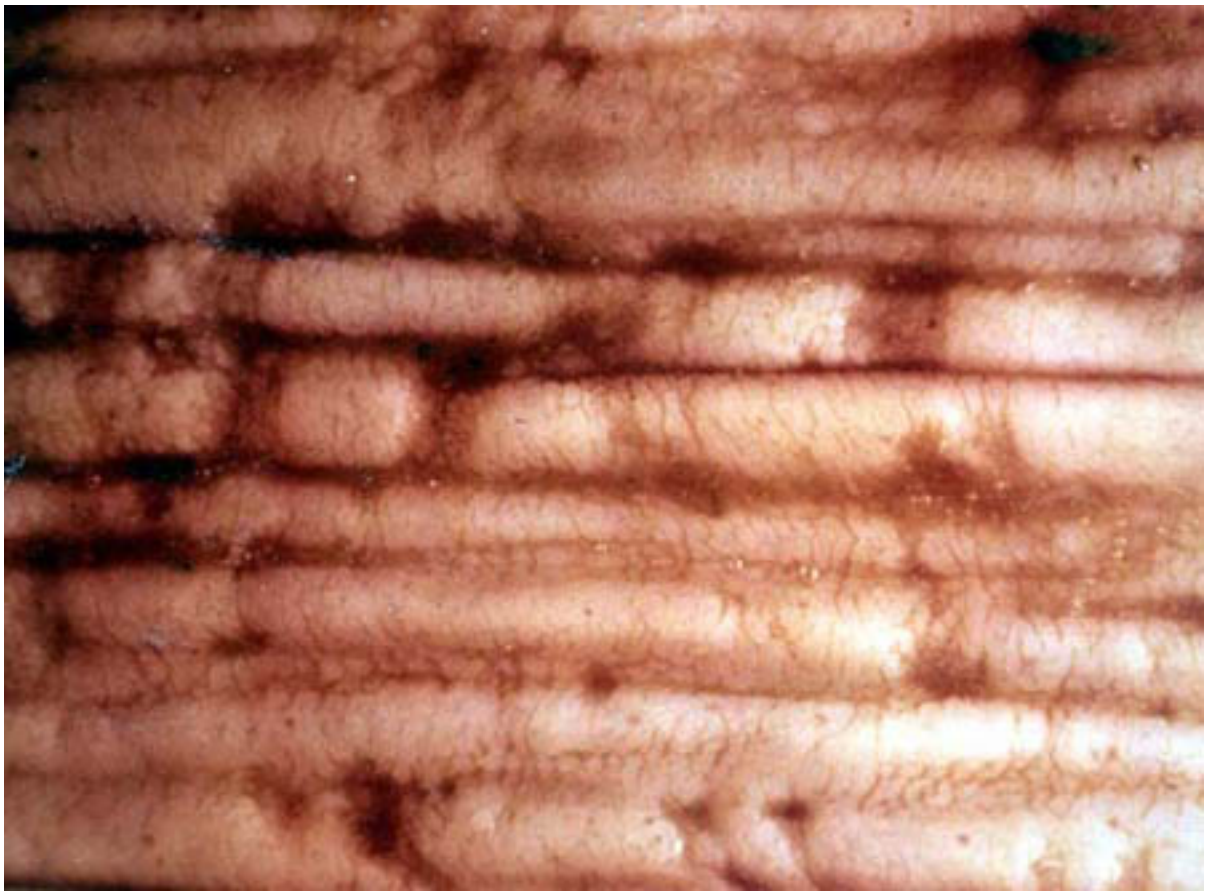

Fig. 96. RP - Ulcerations in the mucosa of the upper colon.

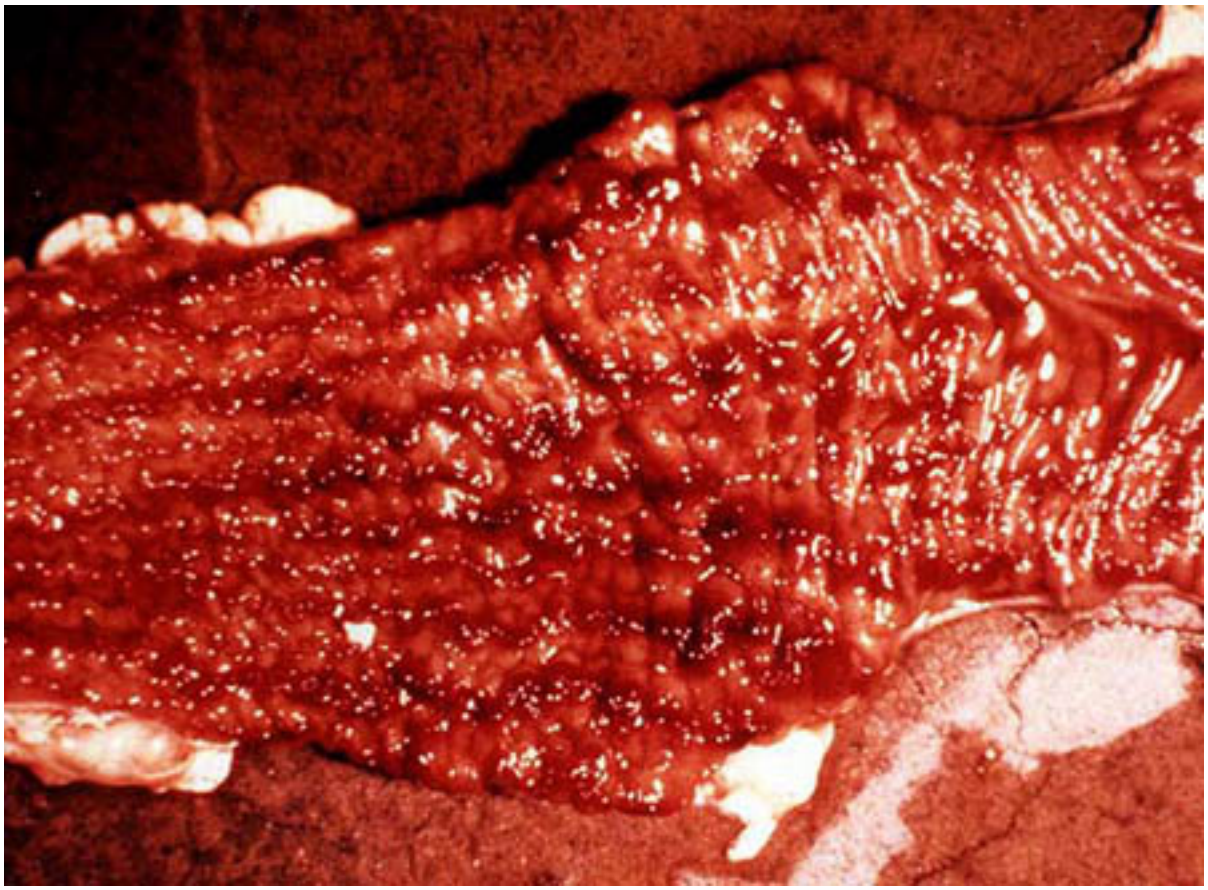

Fig. 97. RP - Hyperemia of the cecum and colon with accentuation of lesions (hemorrhage) at the ceco-colic junction.

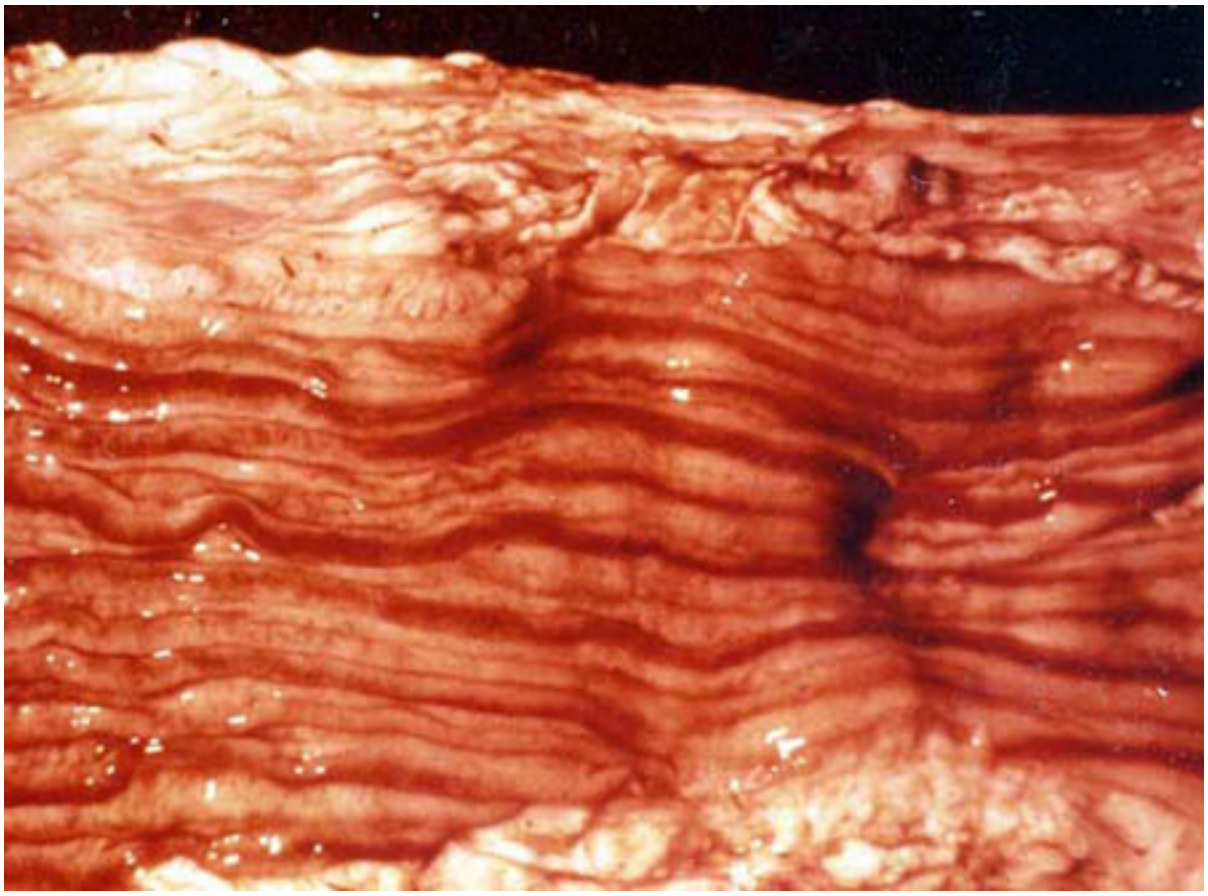

Fig. 98. RP - Hyperemia and hemorrhages in the longitudinal folds of the colon - Zebra striping.

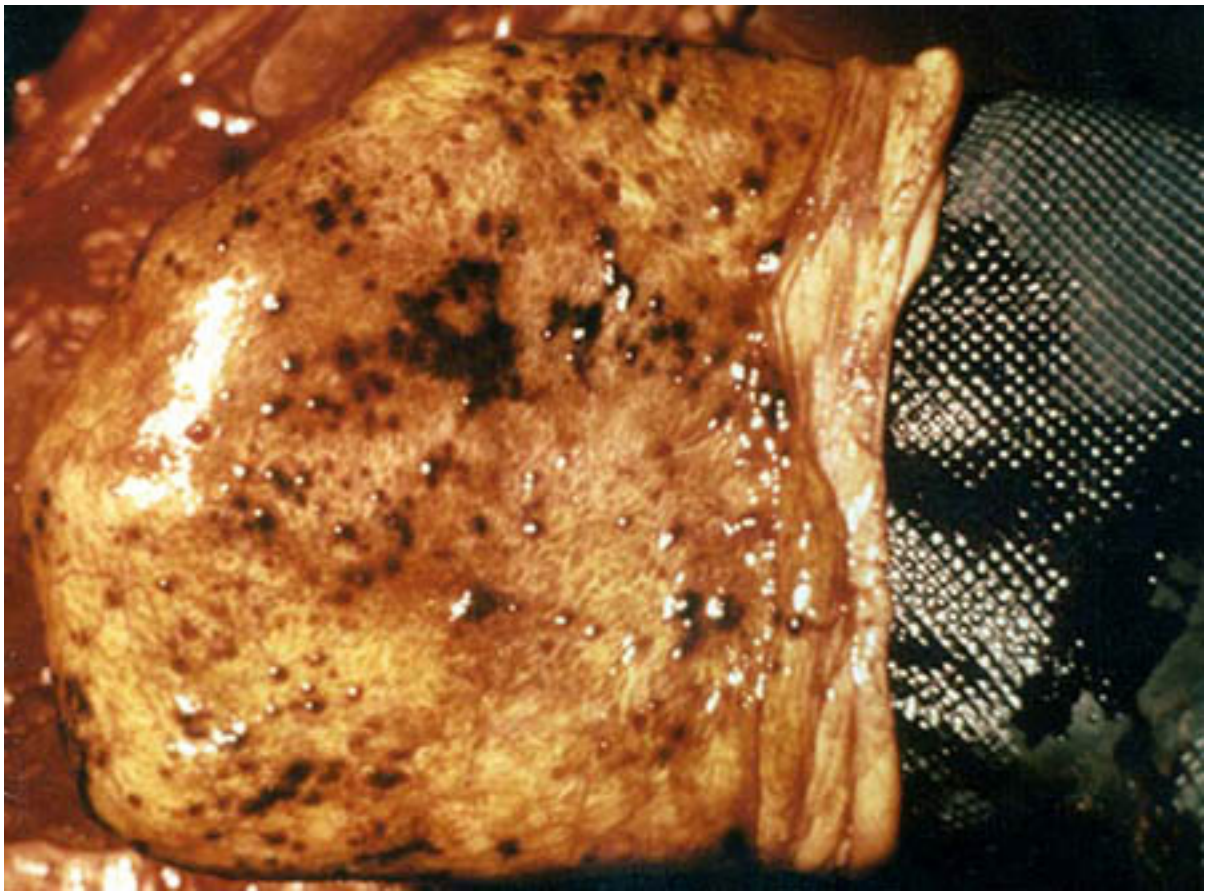

Fig. 99. RP - Hemorrhage in the mucosa of the gall bladder.

PART IV
FOREIGN ANIMAL DISEASES

SCREWWORM MYIASIS

(Gusanos, Mosca Verde, Gusano barrendor, Gusaneras)

Definition

Myiasis is the infestation of live vertebrate animals with dipterous larvae, which for at least a certain period feed on the host's dead or living tissue, liquid body substances, or ingested food (27). Depending on their reliance on the host, such larvae are classified as obligatory or facultative. Screwworms are classified as obligatory because they feed on live tissue. Screwworm larvae penetrate deeply into a wound of a warmblooded animal and feed on living tissue and body fluid. Facultative larvae, which feed on dead tissue and decaying matter, may be present in wounds — even simultaneously with screwworm larvae.

Etiology

Screwworm myiasis is caused by two species of diptera larvae in the family Calliphoridae, subfamily Chrysomyinae: *Chrysomya bezziana* (Villeneuve), Old World Screwworm, and *Cochliomyia hominivorax* (Coquerel), New World Screwworm (15).

Host Range

Any warmblooded animal, including human, is subject to screwworm myiasis, but infestation in poultry or fowl is rare.

Geographic Distribution

Screwworms survive from year to year in tropical and semitropical regions. The insect is killed by freezing temperatures or long periods of near-freezing temperatures. Because of susceptibility to low temperatures, occurrence of screwworms may be seasonal, and rarely are they found more than 7,000 feet above sea level.

New World Screwworm was first reported in the southeastern part of the United States in 1933 and probably had been introduced through the importation of animals with screwworm myiasis from the southwestern United States (3). New World Screwworm survived winters in the United States in Florida and Texas and occasionally in southern Arizona and California. During the spring and summer, screwworms spread north to the central United States, creating a seasonal problem for livestock and wildlife.

Eradication of the New World Screwworm from the southeastern United States was initiated in early 1959. This effort was aided by a colder than normal winter that limited survival of the insect to the southern half of the Florida peninsula. Near the end of 1961, the southeastern United States was declared free of this pest. Then, in early 1962, a similar eradication program was initiated in the southwestern United States. Again the program was aided by a colder than normal winter that limited survival of the insect to the southernmost part of Texas. Near the end of 1964, the screwworm was declared eradicated from all of the contiguous states of the United States. From 1965 to 1981, a buffer zone was maintained, with varying degrees of success, along the entire expanse of the United States-Mexican border region. The objective of the buffer zone was to control the migration of the screwworm from Mexico into the Untied States and to minimize the incidence of cases of screwworm in the region.

In August 1972, an agreement between the United States and Mexico was signed establishing a joint commission to eradicate screwworm from Mexico. Such an action was considered

necessary to prevent screwworm infestation in the United States totally. Eradication of the screwworm from Mexico was initiated near the end of 1976, and progressed from north to south (17). The last local case of screwworm in the United States was reported from Star County, Texas, in August 1982. Mexico and the United States signed agreements with Guatemala in 1986, and Belize in 1988, to extend the joint eradication program into those countries. Mexico was declared free of the screwworm in February 1991.

Cattle movements from Central America north into Mexico continued to present a threat of reinfestation. Such activity was probably responsible for outbreaks discovered in central and southern Mexico in 1992 and 1993. These outbreaks were rapidly contained and eliminated.

The United States signed agreements with Honduras, El Salvador, and Nicaragua in 1991, with Costa Rica in 1993; and with Panama in 1994. To maintain the North American continent free of the screwworm, it was considered necessary to extend the eradication program to Central America and Panama. A permanent barrier will be established at the Isthmus of Panama to prevent reinfestation of regions to the north.

Guatemala and Belize were declared free of the screwworm in 1993. Then El Salvador and Honduras were declared free of the pest in 1995 and 1996, respectively. The last local case of screwworm in Nicaragua was reported in February 1997. Eradication of the screwworm was initiated in Costa Rica in early 1996 and is scheduled to be initiated in Panama in 1998.

Other regions of the Western Hemisphere that have been freed of the New World Screwworm are Puerto Rico, the Virgin Islands, and the island of Curacao of the Netherlands Antilles. New World Screwworm is present on several of the islands in the Caribbean Sea and in the tropical and semitropical regions of South America. There is a seasonal spread of the screwworm into the temperate regions of Argentina, Uruguay, and Paraguay in the spring and summer (12). Rarely is screwworm reported in Chile or southern Argentinia, and then only from imported animals.

The only recorded establishment of New World Screwworm in the Eastern Hemisphere was in a 20,000-square kilometer area around Tripoli, Libya, in north Africa. Introduction of the screwworms is thought to have occurred with animals imported from South America during or before 1988. The outbreak was eradicated in 1991.

Old World Screwworm has never become established in Europe, North Africa, the Middle East, Australia or the Western Hemisphere. It is found in most of the remainder of the tropical and semitropical regions of the Eastern Hemisphere: the Indian subcontinent, Southeast Asia, the main island of Papua New Guinea, tropical and sub-Saharan Africa , Oman, Muscat, Fujaira, and Kuwait (24).

Life Cycle

Screwworm larvae feeding in a wound are closely packed. As the larvae feed, they destroy tissue, thus continually making the wound larger. Within 5 to 7 days the larvae reach maturity. At this stage of development (third instar), the larvae will exit the wound and drop to the ground. Mature larvae are negatively phototrophic (i.e., they move away from light and usually burrow 2 to 5 cm deep in the soil, where they develop into pupae. Many larvae do not survive owing to desiccation and predation (2). Transformation into the fly occurs during the pupal stage and may take about 7 days at 28° C (82.4° F) or may take as long as 60 days at temperatures of 10-15° C (13,21).

Flies that survive during this stage of development emerge from the pupal casing, taking about 2 hours to dry, spread their wings and then seek food such as water and nectar. Survival of the flies is dependent on temperatures, humidity, food sources, host availability, and other ecological factors (21). Ambient air temperatures of 25-30° C (77-86° F) with a relative humidity of 30-70 percent are ideal parameters for screwworm fly activity and survival. Adult screwworm flies find superficial wounds on warmblooded animals and feed on fluids in the wound.

After 3-5 days the flies are ready to mate. Male screwworm flies will mate several times. Females usually mate once. About 3-4 days after mating, the female fly seeks a superficial wound on a warmblooded animal to oviposit eggs along the edge of the wound in a shinglelike manner. Larvae up to 2 mm in length emerge from the eggs in 8 to 12 hours, enter the wound, and begin feeding.

Female New World Screwworm flies oviposit up to 400 eggs in a single egg mass and one fly may oviposit 6 to 8 batches of eggs in her life (25). An egg mass from the Old World Screwworm contains about 100 to 250 eggs (15). Male screwworm flies usually survive about 14 days; females often survive 30 days.

Transmission

The distance that female screwworm flies travel depends on the ecological conditions, food supply, and availability of hosts with suitable wounds. The female flies tend to range only 10-20 km in tropical environments when there is a high density of animals. In arid environments with lower densities of animals, screwworm flies have traveled as far as 300 km (12). Often in more arid areas, screwworm flies will travel along water courses. In mountainous areas, screwworm flies will travel the course of valleys, where the climate is warmer, moisture is high, and animal density is high. Vehicles, especially those transporting animals, may contribute to dispersing screwworm flies in some areas. Wind may also be a factor.

Transmission of screwworms into nonendemic areas and over long distances is often the result of transporting animals with screwworm myiasis or carrying screwworm adults on transport vehicles. When new infestations are not treated and larvae mature and exit the wounds, there is the potential for screwworms to become established in a new area.

Clinical Signs

Wounds that may become infested by screwworms include those caused by engorged ticks, bites of vampire bats, castration, dehorning, branding, wire cuts, sore mouth in sheep, shedding of the velvet in deer, and a multitude of other causes. Navels of newborn mammals are a common site for screwworm infestation. Early stages of the larvae feeding in a wound are very difficult to see; only slight movement may be observed. As the larvae feed, the wound is gradually enlarged, becoming wider and deeper. By the third day, as many as 100 to 200 tightly packed, vertically oriented larvae can easily be observed embedded deep in the wound. Screwworm larvae tend to burrow deeper in a wound when disturbed and will generally not be seen crawling on the surface (Fig. 100).

After 5 to 7 days, a wound may be expanded to 3 cm or more in diameter and 5 to 20 cm deep with larvae from a single screwworm egg mass. Usually by this stage, additional screwworm flies have deposited eggs, resulting in a multiple infestation. A serosanguineous discharge often exudes from the infested wounds, and a distinct odor may be detected. In some cases, the openings in the skin may be small with extensive pockets of screwworm larvae beneath. In dogs, screwworm larvae commonly tunnel under the skin. Screwworm infestations in anal, vaginal, and nasal orifices may be difficult to detect, even in the later stages.

Animals with screwworm infestation usually display discomfort, may go off feed, and produce less milk. Typically animals with screwworm myiasis will separate themselves from the rest of the flock or herd and seek dark or shady areas to lie down. Goats frequently hide in caves. Fawns have often been observed standing in streams with water up to the abdomen when they have screwworm myiasis in the navel. Brahman-type cows will often lick the screwworm-infested navel wounds of calves — a process that cleans most larvae from the wound and reduces losses in this breed of cattle. Animals with screwworm myiasis may die in 7 to 14 days if wounds are not treated to kill the larvae — especially in cases of multiple infestation. As many as 3,000 larvae may be found in a single wound (17). Death probably results from toxicity, a secondary infections, or both. Smaller animals usually die of screwworm myiasis in a shorter time than larger animals. Location of the wound infestation is also a determining factor in the time of death.

Morbidity and Mortality

In some areas of the Western Hemisphere where screwworm populations are high and climatic and ecological conditions are ideal, livestock owners report that every newborn animal will get a screwworm infestation in the navel wound if it is not treated soon after birth. A study on the King Ranch in south Texas in the United States during the 1950's showed that screwworm seriously affected the deer population. In some years, up to 80 percent of the fawns died due to screwworm whereas in other years the death rate was around 20 percent (9). Mature larvae exiting untreated wounds may contribute to increasing the screwworm fly population in the immediate area, and, as the screwworm population increases, the percentage of animals with superficial wounds that become infested also increases.

Screwworm infestations that are treated and those that result from one oviposition are usually not lethal to the animal; however, death is always a possibility, especially in very small animals. Secondary infection is also common.

Animals with untreated screwworm infestations will often have more than one screwworm fly oviposit at the wound site, or the same fly may oviposit more than once. Left untreated, these multiple infestations often result in death of the animal, within 7 to 10 days, depending on the size and condition of the animal, the location of the infestation, and whether there are other complications such as infection or toxicity. Animal deaths due to the Old World Screwworm appear to be less common than with the New World Screwworm.

Diagnosis

Field Diagnosis

Screwworm myiasis should be suspected when the described clinical manifestations are seen. New World screwworm may be observed as creamy white eggs deposited in shinglelike fashion on the border of a superficial wound. Small screwworm larvae up to 2 mm in length hatch from the eggs in 8 to 12 hours. Egg masses of Old World Screwworm are indistinguishable except individual eggs are larger. Eggs in the masses deposited by other species of blow flies are not well organized. *C. macellaria* deposit eggs on the margin or in the hair close to a wound. Microscopic examination is required to distinguish individual eggs of this species from those of the screwworm. *Sarcophagidae* species. deposit live larvae into a wound or in soiled wool or hair. Larvae of these species are facultative and may be seen in wounds, usually near the surface, feeding on necrotic tissue or organic matter.

Larvae can be removed from a wound with tweezers. Second and third instar screwworm larvae are cylindrical, are pointed at one end and blunt at the other, and have complete rings of dark brown spines circling the body. The shape and characteristics of the second or third instar larvae (Fig. 101) resemble a wood screw, thus giving rise to the common name of the pest. Field diagnosis is difficult — even for trained individuals. A magnifying glass or microscope is usually necessary to see the distinguishing characteristics of the various insect stages. A diagnosis in the field should always be considered presumptive.

Female screwworm flies may be observed visiting a wound. They are about two and a half times the size of the common house fly. New World screwworm flies have a darkblue to blue-green thorax with a reddish-orange head and have three longitudinal dark stripes on the back of the thorax with an incomplete center stripe (Fig. 102). Old World Screwworm flies have bodies that are green to bluish-black and have two transverse stripes on the thorax. *C. macellaria* flies are similar but have a green thorax with three complete dorsal stripes.

Specimens for Laboratory

Before treatment, a sample of larvae should be removed from the wound using tweezers for submission to the laboratory. Eggs should be carefully removed from the edge of the wound using a scalpel. For laboratory diagnosis, specimens of eggs, larvae, or flies should be placed in

70 percent alcohol and sent to a recognized diagnostic laboratory (do not use formalin as a preservative). Because screwworm larvae penetrate deep into a wound, and other facultative larvae may exist more superficially in the same wound, specimens of larvae for laboratory diagnosis should be collected from the deepest part of the wound. In the United States, send specimens to the National Veterinary Services Laboratories, P.O. Box 844, Ames, IA, 50010. Experienced professional personnel will identify the specimens.

Differential Diagnosis

Scewworm larvae must be differentiated from larvae of other species of blow flies that may be present in a wound on any warmblooded animal.

Treatment

Before treatment, a sample of the larvae should be removed from the wound for submission to a laboratory using tweezers. Screwworm myiasis is treated with topical application of an approved larvacide directly into the infested wound. Wounds should be retreated two to three times on successive days to ensure that all of the larvae have been killed and removed. With this treatment, the wound will heal rapidly and will not become reinfested with screwworm larvae

Vaccination

There is no vaccine.

Control and Eradication

Prevention

Where screwworm is endemic, animals must be inspected at least every 3 to 4 days to discover and treat cases of screwworm myiasis. Open wounds on animals not infested with screwworm larvae should be treated to prevent infestation. In areas where screwworm myiasis is a seasonal occurrence, animal breeding can be regulated so births occur during the season when screwworm myiasis is rarely encountered. Similarly, management practices that create wounds, such as branding, castrating, dehorning, docking, or other operations, can be programmed for the season when screwworm myiasis is rare.

Treating wounds and spraying or dipping animals with an approved organophosphate insecticide will provide protection against screwworm infestation for 7 to 10 days. Should a screwworm egg mass be deposited on the edge of a wound on an animal treated with this insecticide, the newly hatched larvae will encounter the residual insecticide as they crawl into the wound and will be killed. This usually gives wounds sufficient time to heal. If wounds are already infested with screwworm second-or-third instar larvae when an animal is sprayed or dipped with the organophosphate insecticide, the treatment usually does not kill all larvae present. Therefore, this form of treatment should be used only as a preventive measure and not as a cure.

Preventing the introduction of screwworm into areas that have the ecological environment for screwworm propagation but are currently without the pest is an important aspect of control. Blocking such introductions is accomplished through voluntary and regulatory actions. Immediately before being transported from where screwworm is endemic, animals, this includes pets, should be thoroughly inspected for the presence of a superficial wound subject to screwworm infestation. All wounds should be treated with an approved organophosphate insecticide followed by a precautionary spraying or dipping of the animals before they are moved. An animal having wounds suspected of being infected with screwworm should not be moved until the wounds have been properly treated and have healed.

Conveyances should be sprayed with insecticide to kill any adult or immature screwworm flies. Upon arrival at the destination or port of entry, these animals should again be inspected and undergo treatment of all wounds or suspected screwworm myiasis.

Eradication

Eradication of the screwworm has been successful only when the sterile-male technique has been applied to an area. After the lab-reared insects are in the pupal stage for about 5.5 days, or 24 hours before the adult flies emerge, they are exposed to 5,000 to 7,000 rads of gamma radiation. This exposure to radiation renders the insects sexually sterile without adversely affecting them in any other way (4). Once released, sexually sterile male screwworm flies mate with native females. These females then deposit unfertilized eggs that, of course, do not hatch, thus breaking the life cycle.

Eradication areas are blanketed weekly with an equal proportion of sterile male and sterile female flies at the usual dosage rate of 3,000 per square mile. There is currently no practical method of separating the mass-produced, lab-reared males and females. Although eradication of the screwworm from an area may be enhanced by releasing a higher proportion of sterile males, the benefit of releasing sterile females needs further investigation. Nonetheless, use of the current technology has been successful. The actual dosage of sterile screwworm flies released over an area will vary according to the estimated local screwworm population, host density, and the local ecology The dosage should be sufficient to release 300 sterile male screwworm flies or more for one native male screwworm fly (14). Using this technology together with larvacide treatment of wounds and control of transport of screwworms through animal movements usually results in eradication of the insect from that area in 2 years or less. This dosage of sterile males will usually outnumber the native male screwworm fly population by 300 or more to 1 (16).

Public Health

Humans are susceptible to screwworm myiasis.

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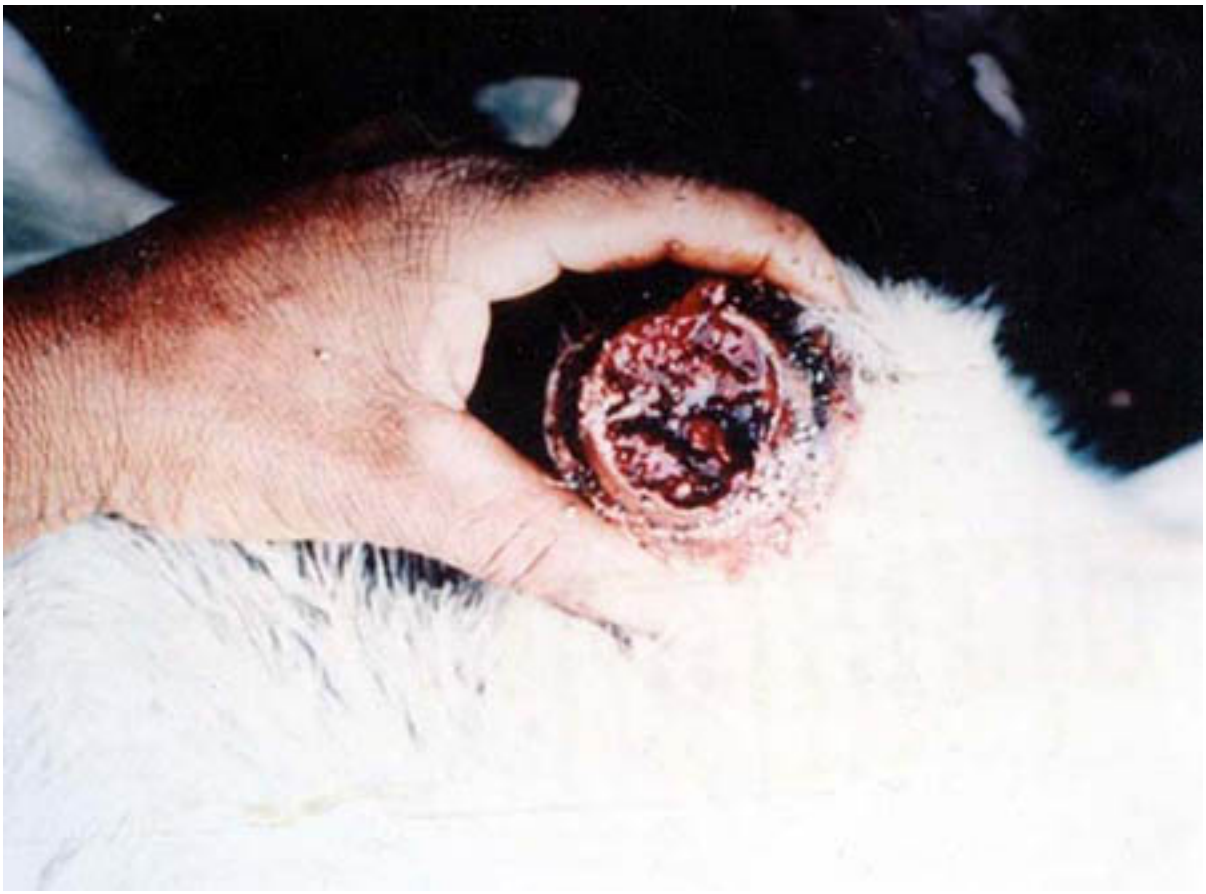

Fig. 100. Screwworm - Screwworm myiasis in a calf navel.

Fig. 101. Screwworm - Third instar larvae, *Cochliomyia hominivorax*.

Fig. 102. Screwworm - Female fly.

PART IV
FOREIGN ANIMAL DISEASES

SHEEP AND GOAT POX

Definition

Sheep and goat pox (SGP) is an acute to chronic disease of sheep and goats characterized by generalized pox lesions throughout the skin and mucous membranes, a persistent fever, lymphadenitis, and often a focal viral pneumonia with lesions distributed uniformly throughout the lungs. Subclinical cases may occur.

Etiology

The virus that causes SGP is a capripoxvirus, one of the largest viruses (170-260 nm by 300-450 nm) (10). It is closely related to the virus that causes lumpy skin disease; SGP virus and lumpy skin disease virus cannot be distinguished serologically. There is only one serotype of SGP virus (SGPV). Various strains of SGPV cause disease only in sheep, others only in goats, and some in both sheep and goats (2,3,9).

The SGPV is very resistant to physical and chemical agents.

Host Range

Sheep and goat pox virus causes clinical disease in sheep and goats. The virus replicates in cattle but does not cause clinical disease. The disease has not been detected in wild ungulate populations.

Geographic Distribution

The disease is endemic in Africa, the Middle East, the Indian subcontinent, and much of Asia.

A goat-pox-like disease was reported in the western United States (15), but no attempt was made to indentify the agent with a reference serum against SGPV. Serum samples from animals representing the affected group of goats were submitted to the Foreign Animal Disease Diagnostic Laboratory (FADDL) at Plum Island, NY, and tested for antibody to SGPV; no antibodies were found against SGPV. The serums were not tested for antibodies to bovid herpesvirus 2 or contagious ecthyma at the FADDL. Unfortunately, the viral isolate was not available for study. It is conclusive that what was reported in the literature was not goat pox.

Transmission

Contact is the main means of transmission of SGPV. Inhalation of aerosols from acutely affected animals, aerosols generated from dust contaminated from pox scabs in barns and night holding areas, and contact through skin abrasions either by fomites or by direct contact are the natural means of transmitting SGPV. Insect transmission is possible. The virus can cause infection experimentally by intravenous, intradermal, intranasal, or subcutaneous inoculation.

Incubation Period

Under field conditions, the incubation of SGP is between 4 and 8 days. Experimentally, the first sign (fever) may appear within 3 to 5 days after inoculation. The course of the disease is 4 to 6 weeks with various stages of pox lesions present at the same time. Full recovery may take up to 3 months.

Clinical Signs

Sheep and goat pox virus may cause subclinical infection; clinical cases vary from mild to severe (3). The course of the disease in sheep and goats is similar. The first signs may include fever, depression, conjunctivitis, lacrimation, and rhinitis. Within a few days of the prodromal signs, pox lesions develop in the skin. These are more easily observed on the wool-free or hair-free parts of the body such as the perineum, inguinal area, scrotum, udder, axilla, and muzzle. Lesions do occur in wooled or haired skin. Generally, more severe (extensive) skin lesions correlate with more severe illness. The skin lesion first appears as an erythematous area (macula). This lesion progress to a raised, slightly blanched lesion that presents erythema with edema in the central part of the lesion (papule) (Fig. 103). Pox lesions with a transudate, representing the vesicular stage of the lesion, may be noted, but rarely is there any gross vesicle in the skin. The center of the lesion then becomes depressed and gray (necrotic) and is surrounded by an area of hyperemia (Fig. 104). Late in the course of the disease (2 to 4 weeks after the first signs), the lesion become dry, and a scab forms (Fig. 105). A characteristic feature of a pox lesion is that lesions involve the entire epidermis and dermis and penetrate into the subcutaneous tissue; it feels like a nodule. Depending on the severity of the skin lesion, there may be a scar, an area devoid of wool or hair, after the lesion heals. Secondary bacterial infection may complicate the healing process. The muzzle may be swollen, and the nares and oral mucosa may have extensive lesions. In many cases, pneumonia may occur with labored breathing and a respiratory rate approaching 90 per minute. Depression, anorexia, and emaciation are common and may persist. Nervous signs may occur, but how these are related to the SGPV infection is not clear.

Lambs and kids under 1 month of age may suffer a very severe generalized form of SGP. The signs described above for older animals are exaggerated, and there is an increased mortality.

Gross Lesions

At necropsy, skin lesions have congestion, hemorrhage, edema, vasculitis, and necrosis and will be seen to involve all layers of the epidermis, dermis, and, in severe cases, extend into the adjacent musculature. Lymph nodes draining affected areas are enlarged up to eight times their normal size owing to extensive lymphoid proliferation, edema, congestion, and hemorrhage.

Mucous membranes of the eye, mouth, and nose have pox lesions that, in severe cases, may coalesce. In severe cases of SGP, the eyelids may be so seriously affected that the proliferative lesions and inflammation cause the eyes to close. Lesions on the muzzle and nares may coalesce, and proliferative changes and inflammation may be extensive. Pox lesions may occur in the pharynx, epiglottis, and trachea. These usually appear as rounded blanched areas surrounded by an area of hyperemia. Occasionally there may be lesions in the epithelium of the rumen and omasum.

Pox lesions in the lungs may be severe and extensive; the lesions are focal and uniformly distributed throughout the lungs as the result of hematogenous infection (Fig. 106). Early lesions are congested areas; these then progress to discrete areas of congestion and edema and finally to white nodules. Areas distal to the pox lesions have lobular atelectasis. Mediastinal lymph nodes are often enlarged up to five times their normal size and may be congested, hemorrhagic, and edematous.

Pox lesions also may be present on the vulva, prepuce, testicles, udder, and teats.

Morbidity and Mortality

The severity of SGP varies depending on the strain of the virus and the age and breed of the animals affected (5). In adult sheep and goats, morbidity may range to 80 percent with some subclinical infections. Mortality can approach 50 percent. In susceptible lambs and kids under 1 month of age, morbidity may approach 100 percent, and mortality may be as high as 95 perent. Factors that may complicate the course of the disease and increase the mortality are poor nutrition, heavy parasitism, and severe climatic conditions.

Diagnosis

Field Diagnosis

A tentative diagnosis of SGP can be made on the basis of clinical signs consisting of skin lesions, which on, palpation involve the whole thickness of the skin, a persistent fever, lymphadenitis, and often pneumonia; mortality may approach 50 percent in adults and 95 percent in lambs and kids under 1 month of age.

Specimens for Laboratory

For laboratory diagnosis of SGP, skin biopsies of early lesions can be used for virus isolation and histopathologic and electron microscopic studies. Samples aspirated from enlarged lymph nodes can be used for virus isolation. Necropsy samples should include a full set of tissues, but samples of the lungs, trachea, and rumen containing gross lesions are especially valuable for histopathology. Samples for virus isolation should be shipped to the laboratory under wet ice if they will arrive in 2 days and shipped under dry ice if delivery will take longer (send in screw-capped vials with the caps secured with electrical tape). Samples for histopathology should be preserved in 10 percent buffered formalin (DO NOT FREEZE). Serum samples should be taken from acute and chronic cases. Followup serum samples from acute cases may be taken 2 to 3 weeks after the first sample.

Laboratory Diagnosis

The laboratory procedures for the diagnosis of SGP include virus isolation; observation of the virus by electron microscopy; detection of antibody by virus neutralization, the indirect fluorescent antibody test (4), or both; and characteristic histopathologic lesions (3).

Differential Diagnosis

Following are several diseases to consider in the differential diagnosis for SGP:

Bluetongue — Animals are depressed and have a nonpurulent conjunctivitis. The muzzle is swollen, congested, and edematous, and there may be a coronitis. Deformed aborted fetuses and deformed newborn sheep and goats may be encountered.

Peste des Petits Ruminants — Conjunctivitis, rhinitis, and oral lesions that are white, raised, and necrotic are common. Pneumonia, diarrhea, and mortality approaching 90 percent in lambs and kids under 1 month of age are characteristic signs.

Contagious Ecthyma (contagious pustular dermatitis, ORF) — This disease is most severe in lambs and kids. The proliferative pox lesions are common on the muzzle and eyes of affected neonates; mortality may approach 50 percent. Nursing females may have proliferative pox lesions on the teats and muzzle. This is a zoonotic disease; lesions in attendants are not uncommon.

Photosensitization — Dry, flaky, inflamed areas are confined to the nonpigmented parts of the skin.

Insect bites — The trauma from insect bites may cause local inflammation, edema, and pruritus. Insects seldom bite mucous membranes.

Parasitic pneumonia — Severe signs of respiratory distress may occur with extensive parasitic lesions; in these cases, there is no pox lesion in the skin.

Caseous lymphadenitis — Focal, raised lesions in the skin represent caseous abscesses; abscesses are not seen in SGP.

Streptothricosis (*Dermatophilus congolensis* infection) — Lesions are superficial and often moist. Lesions are common in the skin of the neck, axillary region, inguinal region, and perineum. The organism may be demonstrated by Giemsa staining.

Mange - Scab-like skin lesions are seen in psoroptic mange. Itching and scratching are not seen in SGP.

Vaccination

In endemic areas, vaccination is an effective means of controlling losses from SGP. Killed vaccines have not proven to be practical under field conditions because they do not provide solid lasting immunity. Several modified live virus vaccines have been used for protection against SGP. The most widely employed vaccine is probably the Romanian strain that has been used effectively for many years (14,16). The Kenya O 180 strain (6) is possibly the vaccine with the best safety and efficacy.

Control and Eradication

Prevention

The most likely manner for SGP to enter a new area is by introduction of infected animals. Restrictions on the movement of animals and animal products (meat, hair, wool, and hides) are essential to prevent introduction of SGP. Wool, hair, and hides must be subjected to suitable decontamination procedures before entry into nonendemic areas.

Control

If a new case is confirmed in a new area before extensive spread occurs, the area should be quarantined, infected and exposed animals should be slaughtered, and the premises cleaned and disinfected. Vaccination of susceptible animals on premises surrounding the infected flock(s) should be considered.

If the disease has spread over a large area, the most effective means of controlling losses from SGP is vaccination; however, consideration should be given to eliminating infected and exposed flocks by slaughter; properly disposing of animals and contaminated material; and cleaning and disinfecting contaminated premises, equipment, and facilities.

Eradication

A carrier state has not been shown for SGPV. However, the virus may persist for many months on contaminated premises. The imposition of quarantines on areas and premises containing infected or exposed animals is required to prevent disease spread. Depopulation of infected and exposed flocks should be used if limited spread has occurred. If the disease has spread extensively, massive vaccination followed by cessation of vaccination and control of animal movements from the area represent a strong strategy to control and then eradicate SGP.

Public Health

There is no conclusive evidence that SGPV infects humans. A report from India (17) that implied that goat pox caused human infection was merely based on clinical signs. There was no attempt to isolate the causative virus or perform serology on the convalescent serums of the three patients to differentiate the infection from contagious ecthyma, which is a known zoonotic agent that occurs worldwide. A report from Sweden (1) indicated that human infection occurred during an outbreak of goat pox. Although serological studies seemed to indicate that the apparent causative agent of the outbreak was not vaccinia or contagious ecthyma, no virus was isolated. Therefore, it cannot be said that goat pox virus caused human infection.

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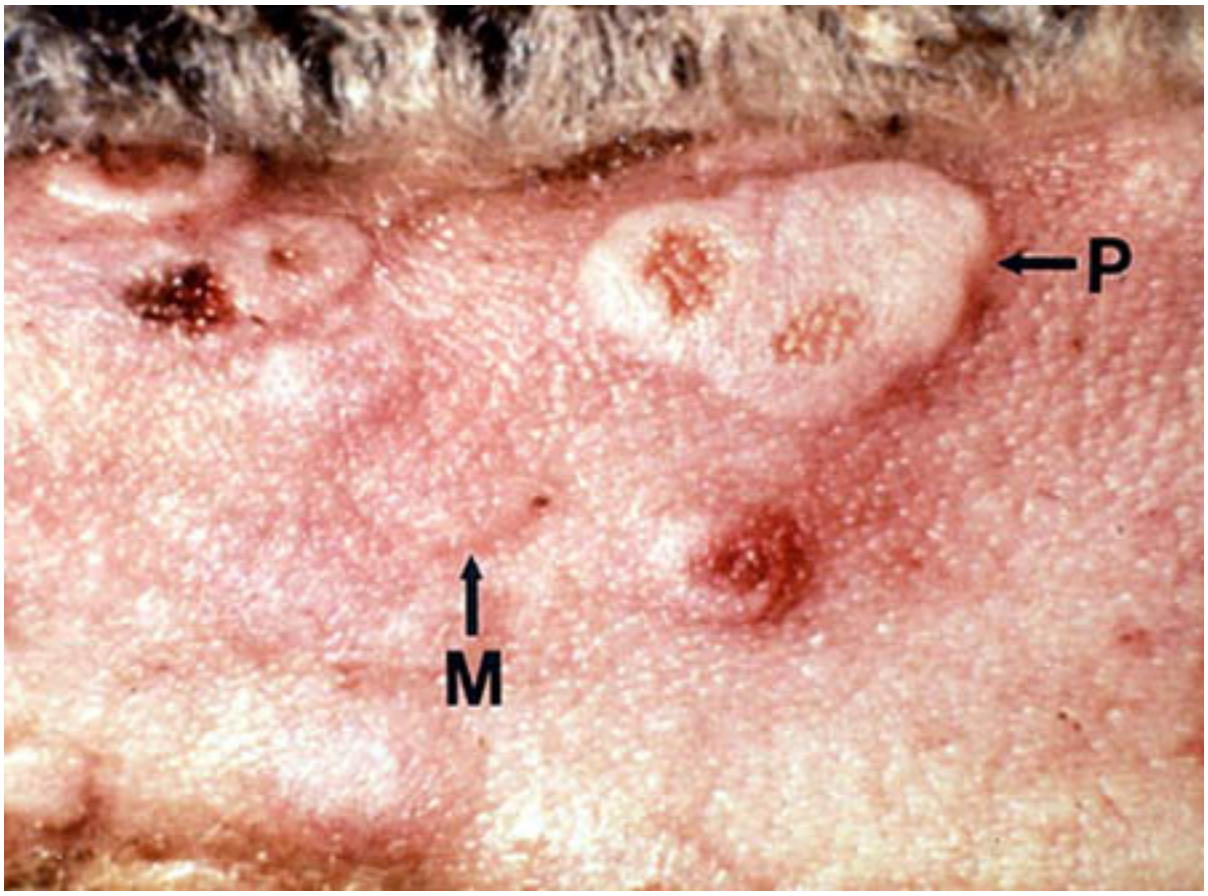

Fig. 103. SP - Sheep pox lesions on the tail of a sheep. The macular stage (M) progresses to the papular stage (P) which is erythematous, edematous, and has central necrosis.

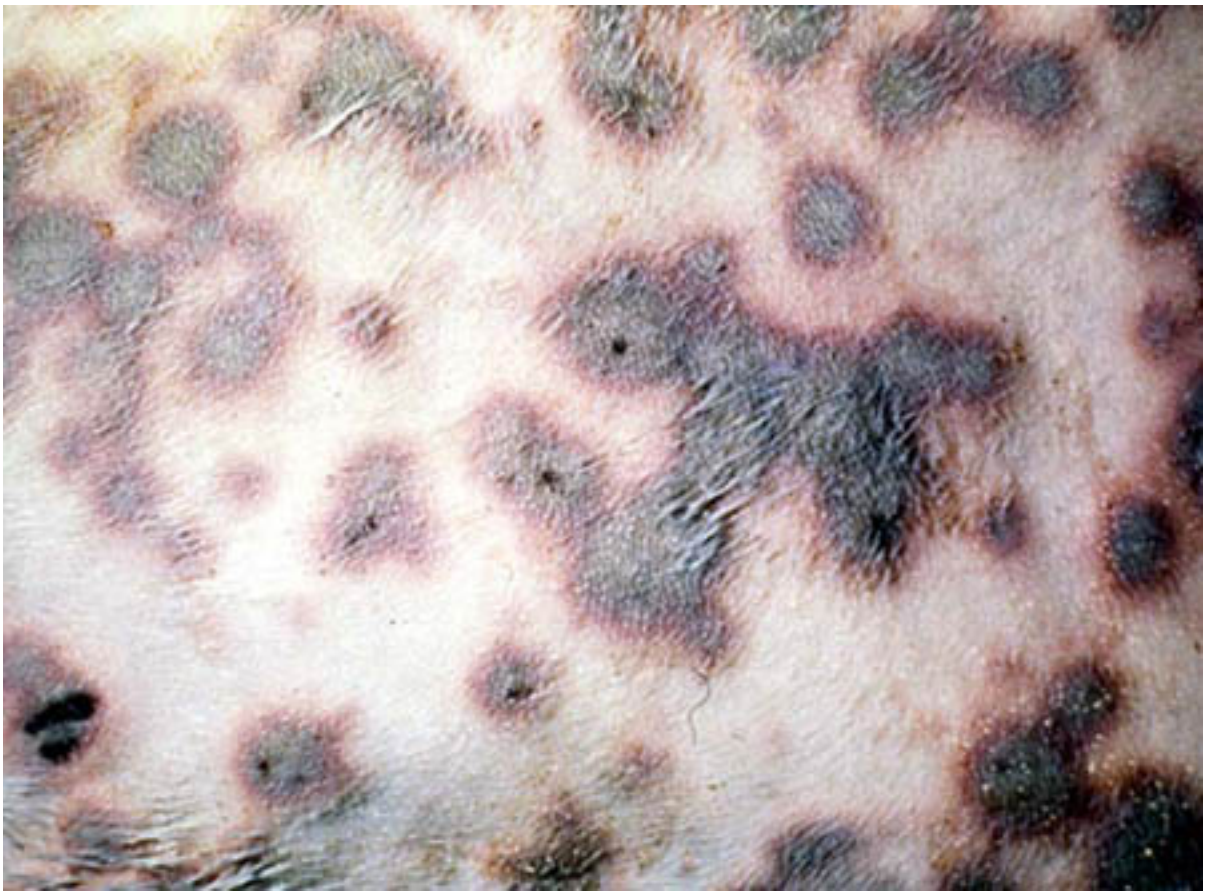

Fig. 104. GP - Necrotic (gray) lesions in the skin of a goat.

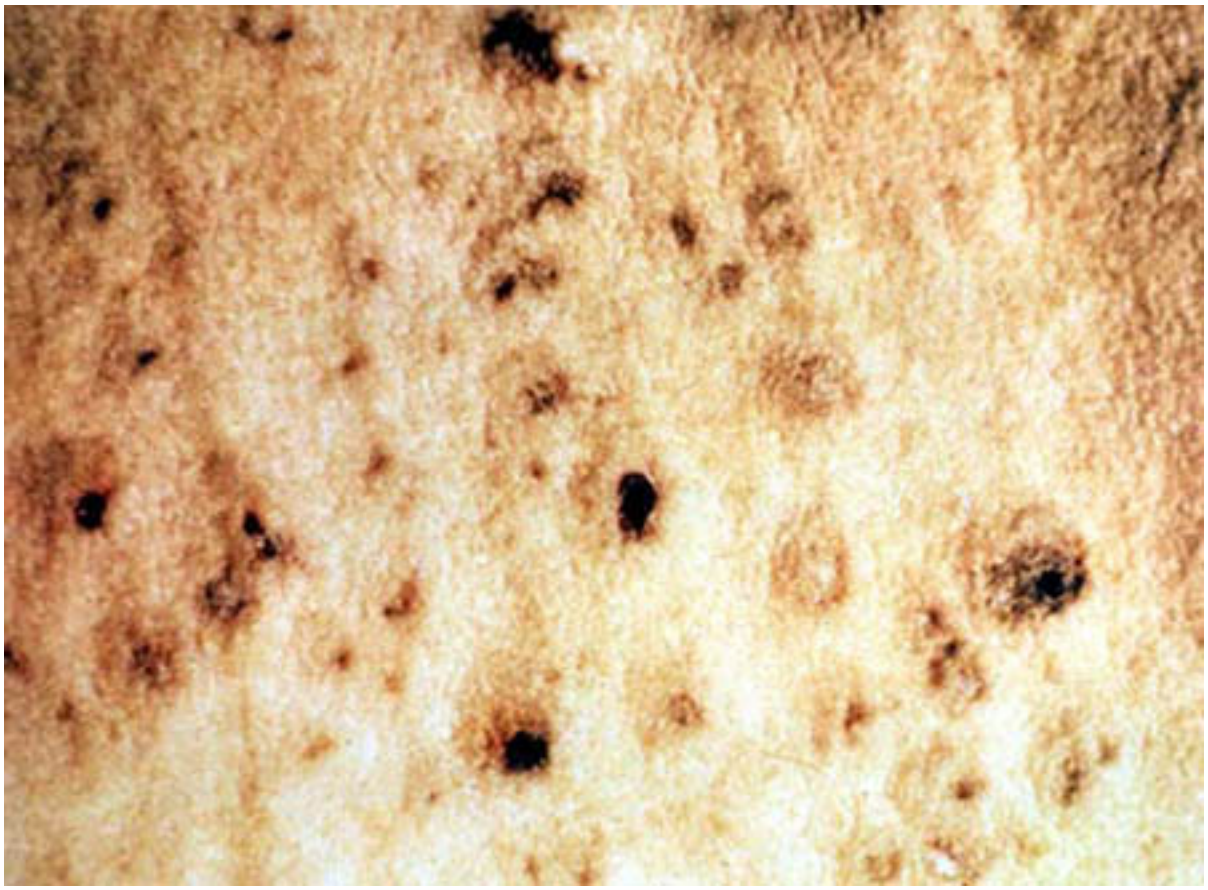

Fig. 105. SP - The black areas are dried necrotic sheep pox lesions.

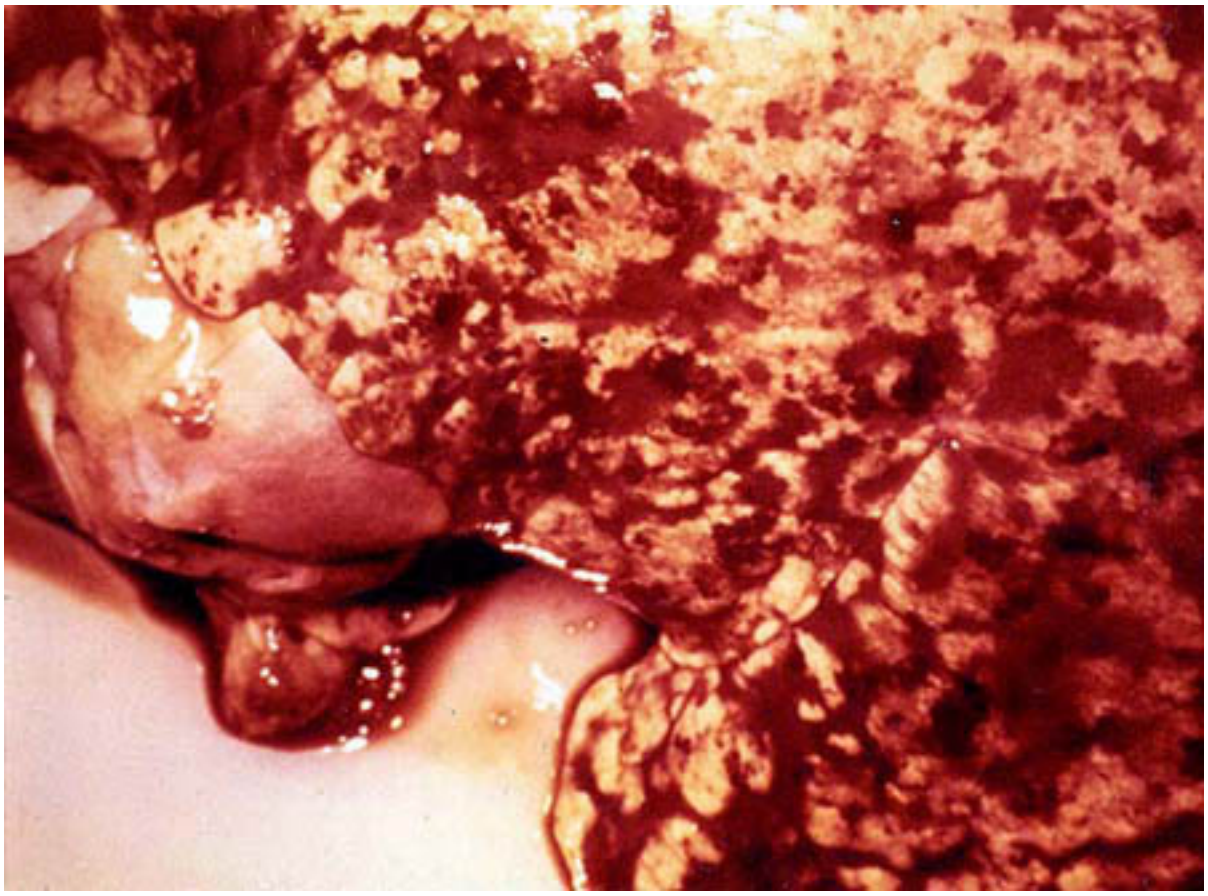

Fig. 106. SP - The diffusely distributed atelectatic areas in lung from a sheep with acute SP are the result of SP virus replication.

PART IV
FOREIGN ANIMAL DISEASES

SWINE VESICULAR DISEASE

Definition

Swine vesicular disease (SVD) is an acute, contagious viral disease of swine caused by an enterovirus and characterized by fever and vesicles with subsequent erosions in the mouth and on the snout, feet, and teats.

Etiology

Swine vesicular disease virus is in the enterovirus group of picornaviruses and is closely related to the human enterovirus Coxsackie B-5 and unrelated to known porcine enteroviruses. Some researchers believe this is a case where a human pathogen transferred to pigs through the eating of human feces. The virion is a roughly spherical 28 nm single-stranded RNA virus. This pathogen is resistant over a wide pH range (2.5-12), relatively resistant to heat (inactivated at 157º F [69º C]), and persists for a long time (up to 2 years) in salted, dried, and smoked meat products.

Host Range

Pigs are the only natural host. Baby mice can be experimentally infected, and there has been accidental laboratory infection of humans.

Geographic Distribution

Swine vesicular disease first occurred in Italy and was subsequently recognized in Hong Kong, England, Scotland, Wales, Japan, Malta, Austria, Belgium, France, the Netherlands, Germany, Poland, Switzerland, Greece, and Spain. Outbreaks in the 1990's were reported in Italy, Spain, and Portugal.

Transmission

The disease can be introduced into a herd by feeding garbage containing infected meat scraps, by introducing infected animals, or by contacting infected feces (e.g., an improperly cleaned truck).

Recent outbreaks in Europe appeared after the introduction of animals that had no clinical sign of SVD, which indicates that there is a subclinical form of the disease. After the initial infection, the disease spreads through contact of susceptible pigs with infected pigs and infected feces.

Incubation Period

Signs of SVD develop in 2 to 3 days after eating contaminated feed and in 2 to 7 days after contact with infected pigs.

Clinical Signs

Clinical signs are very similar to those of foot-and-mouth disease and other vesicular diseases. There is a fever, vesicles in the mouth and on the snout and feet, and lameness, all of which are grossly indistinguishable from FMD. More suggestive of SVD is an unsteady gait, shivering, and chorea — (jerking) — type leg movements due to an encephalitis.

Gross Lesions

Vesicles are indistinguishable from those of foot-and-mouth disease, vesicular stomatitis, and vesicular exanthema of swine (Fig.124, 125). See the foot-and-mouth disease chapter.

Morbidity and Mortality

Morbidity in SVD is lower, and lesions are less severe, than in foot-and-mouth disease. There is essentially no mortality in SVD.

Diagnosis

See chapter on foot-and-mouth disease.

Serology is complicated by cross reactions with other undefined porcine enteroviruses.

Differential Diagnosis

Differential diagnosis for SVD should include foot-and-mouth disease, vesicular stomatitis, vesicular exanthema of swine, and chemical and thermal burns.

Vaccination

There is no vaccine.

Control and Eradication

Prevention measures are similar to those for FMD: control of animals imported from infected areas, and sanitary disposal of garbage from international aircraft and ships

Eradication measures consist of quarantining infected farms and areas, slaughtering and disposing of infected and contact pigs, and cleaning and disinfecting infected premises.

Public Health

Human infection has been reported in laboratory personnel working with the virus. Caution should be taken when working with infected material.

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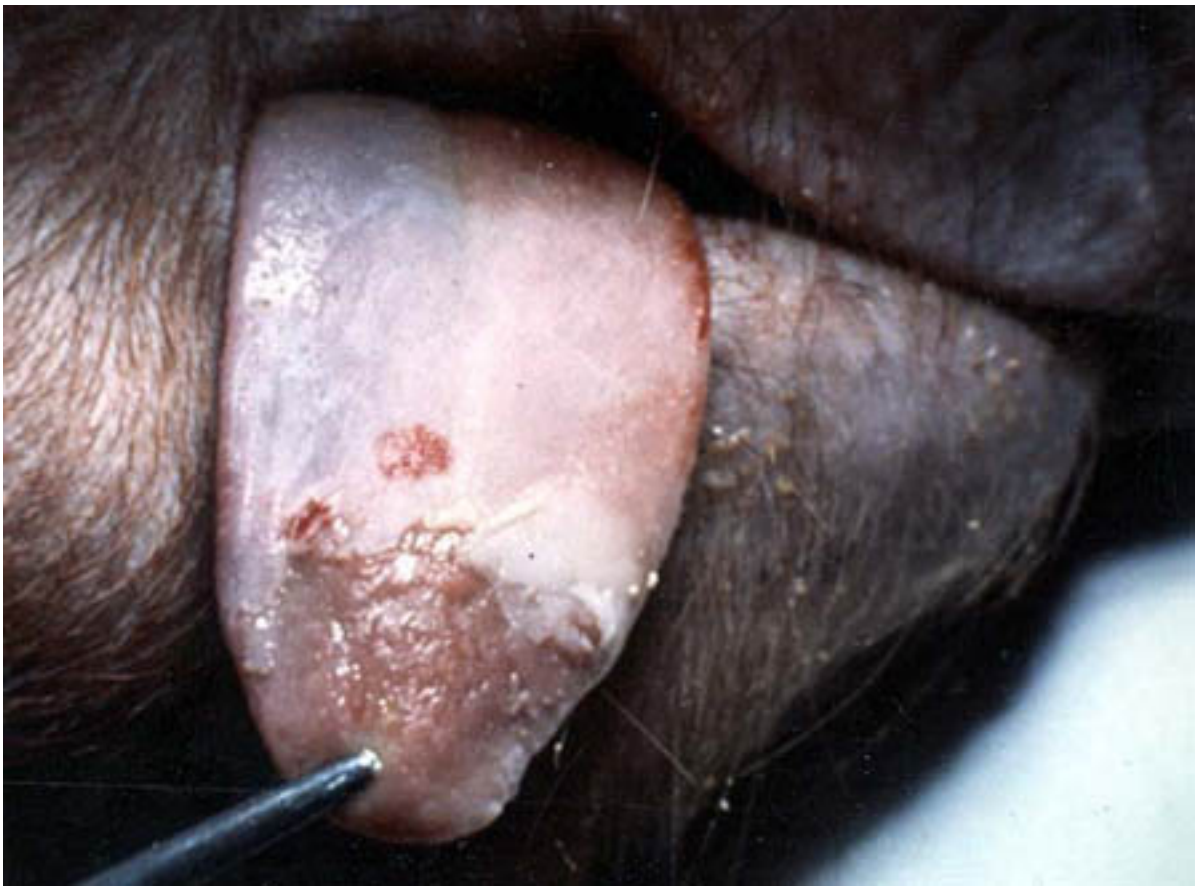

Fig. 124. SVD - Erosions on the tongue are similar to those that can occur in FMD.

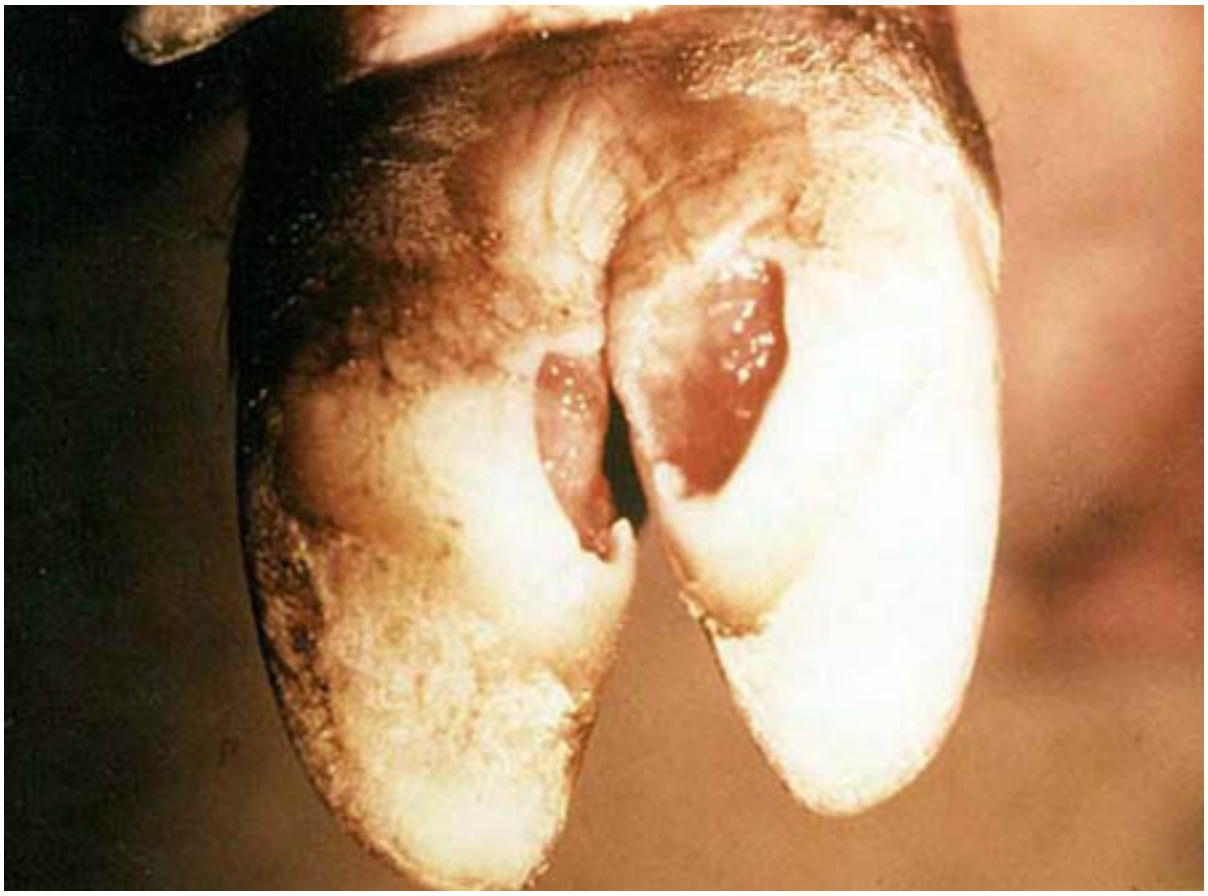

Fig. 125. SVD - Ruptured vesicles on the heel are indistinguishable from FMD.

PART IV
FOREIGN ANIMAL DISEASES

VELOGENIC NEWCASTLE DISEASE

(Exotic Newcastle disease, Asiatic Newcastle disease)

Definition

Velogenic Newcastle disease (VND) is the most severe form of Newcastle disease and is likely the most serious disease of poultry throughout the world (2,4,13). In chickens it is characterized by lesions in the brain or gastrointestinal tract, morbidity rates near 100 percent, and mortality rates as high as 90 percent in susceptible chickens. Neurologic signs or severe depression are the most obvious clinical sign, and some nonvaccinated birds may be found dead with no detected sign of prior illness.

Etiology

Newcastle disease viruses (NDV's) occur as three pathotypes: lentogenic, mesogenic, and velogenic, reflecting increasing levels of virulence. The most virulent (velogenic) isolates are further subdivided into neurotropic and viscerotropic types. The velogenic isolates are considered exotic to the United States, and the disease caused by these VND isolates is the subject of this chapter.

The Newcastle disease viruses belong to the *Paramyxoviridae* virus family and, like other members of this group, possess two surface proteins that are important to the identification and behavior of the virus. The first, hemagglutinin/neuraminidase (HN) is important in the attachment and release of the virus from the host cells in addition to its serologic identification. The other very important surface protein is the fusion (F) protein, which has a critical role in the pathogenesis of the disease. There are at least nine known types of avian paramyxoviruses based on the antigenic makeup of the hemagglutinin. NDV is the prototype virus for Type 1 avian paramyxoviruses.

Host Range

Inapparently infected carriers that are the most likely source for introduction of VND include numerous species of exotic pet and exposition birds, waterfowl, and domestic poultry (18). A persistent carrier state has been demonstrated in psittacine (8) and in certain other wild birds (19) whereas virus can be recovered from chickens for shorter periods of time, usually 14 days or less.

Geographic Distribution

Velogenic Newcastle disease is endemic in many countries of Asia, the Middle East, Africa, and Central and South America. Some European countries are considered free of VND. VND has caused high mortality in wild cormorants in Canada and the United States.

Transmission

In many parts of the tropics VND is recurrent in the poultry populations. One possibility is that they are infected from a wild bird reservoir. Additional studies will be required before it can be established which species, if any, are true carriers and which are only transiently infected. It is not known whether the occurrence of VND in wild birds moving in international trade can be reduced by avoiding the capture of certain species or their collection at certain time periods or

places. Once introduced into poultry, the virus spreads farm-to-farm by the movement of inapparently infected poultry species; on contaminated objects such as boots, sacks, egg trays, and crates; or by flies (5) or mice. Reports from England (11) that the virus can be wind-borne under certain conditions should be considered even though there was no evidence of airborne transmission between premises with the virus that caused the 1971 outbreak in California. Free-flying wild birds apparently had no role in the spread of VND during that outbreak (16).

Incubation Period

The incubation period for Newcastle disease after natural exposure varies from 2 to 15 days. For VND in chickens, an incubation period of 2 to 6 days is common. The incubation period in other species of birds may be longer.

Clinical Signs

Velogenic Newcastle disease is a devastating malady in unvaccinated chickens of any age. The first sign in laying chickens is usually a marked drop in egg production followed within 24 to 43 hours by high death losses. At the onset, 10-15 percent of a flock may be lost in 24 hours. After 7 to 10 days, deaths usually subside, and birds surviving 12 to 14 days generally do not die but may display permanent paralysis and other neurologic signs. The reproductive system may be permanently impaired, and thus egg production does not return to previous levels. In vaccinated chickens, or chicks protected by parental antibodies, the clinical signs are less severe and are proportional to the level of protective antibodies.

With viscerotropic strains (VVND), edema of the head, especially around the eyes (Fig. 107) may become apparent after birds have been sick for 2 or 3 days (9). This edema usually does not involve the comb and wattle to the extent of highly pathogenic avian influenza (HPAI). A dark ring sometimes forms around the eye, probably due to cyanosis and poor blood circulation in the edematous tissue. This "black eye" appearance is especially visible in white chickens.

Bile-stained, greenish-dark diarrhea may be noted 2 to 3 days after onset of illness. Some birds in an affected flock usually have diarrhea throughout the course of the disease.

The most noteworthy clinical sign in unvaccinated flocks is sudden death without prior indications of illness. The peracute onset often causes the owner to suspect poisoning.

Respiratory distress and signs of neurological disturbances, such as drooping wings, torticollis, and ataxia. may not be as marked as they are with the neurotropic forms of the disease. However, these neurologic signs are frequently observed in chickens that survive infection with the viscerotopic strains for 2 or 3 weeks. Because of lack of experience with viscerotropic strains, poultry owners throughout the United States and Canada may not consider Newcastle disease as a possible diagnosis unless they see the neurologic signs they have seen with the domestic neurotropic viruses.

Neurotropic strains cause respiratory signs soon followed by neurologic signs, including muscular tremors, paralysis of legs or wings, torticollis, and opisthotonos. There is a marked decline in egg production but ususally no diarrhea. Disease signs may differ markedly, depending on the host species. Psittacines or pigeons infected with the viscerotropic strains of virus may display neurologic signs typical of the disease caused by the strains of neurotropic ND in chickens (7). These same viscerotropic viruses may cause typical signs and lesions of VVND when inoculated into chickens (6). In some species, such as finches and canaries, clinical disease may not be observed.

Gross Lesions

No gross lesion may be observed in many of the first birds dying in a commercial poultry operation. Peracute deaths are generally due to collapse or dysfunction of the reticuloendothelial system before discernible gross lesions have developed. There is no pathognomonic gross lesion for VVND, but, generally, sufficient lesions can be found to make a

tentative diagnosis if enough birds are examined (14). Because of the marked similarities between the gross lesions of VVND and higly pathogenic avian influenza, a final diagnosis in the first flocks must await virus isolation and identification. In a continuing outbreak where numerous flocks are involved, gross observations may eventually be all that is necessary when typical lesions are present.

Edema of the interstitial tissue of the neck, especially near the thoracic inlet, may be marked. After the trachea and esophagus are exposed during necropsy examination, straw colored fluid may drip from these tissues. Congestion and occasionally hemorrhage may be seen in the trachea generally corresponding to the rings of cartilage.

Proventriculus

Petechial and small ecchymotic hemorrhages may be present on the mucosa of the proventriculus (Fig. 108). These small hemorrhagic foci tend to be found near the base of the papillae and concentrated around the posterior and anterior orifices.

Intestine

Peyer's patches (Fig. 109), cecal tonsils (Fig.110), and other focal aggregations of lymphoid tissue in the gut wall usually are markedly involved and are responsible for the term viscerotropic applied to this form of Newcastle disease. These areas progressively become edematous, hemorrhagic, necrotic, and ulcerative. In chickens that have died from VVND, these involved lymphoid areas can often be observed without opening the gut.

Reproductive System

Ovaries may be edematous, hemorrhagic, or degenerated. Yolk peritonitis can frequently be observed in layers as a result of VVND, and rough, misshapen eggs are frequently laid by recovering hens.

Neurotropic strains of VND may cause few gross lesions other than in the trachea and lungs. There will be no gross lesion in the brain of diseased birds. Gross lesion patterns usually differ markedly between the disease caused by the viscerotropic and neurotropic velogenic viruses.

Morbidity and Mortality

Clinical VND is most severe in chickens, peafowl, guineas, pheasant, quail and pigeons. Turkeys may develop a milder form of the disease. Severity of disease in psittacine and passerine birds is variable. In susceptible chickens, the morbidity and mortality rates can be as high as 100 percent and 90 percent, respectively. In some species such as finches and canaries, clinical disease may not be observed.

Diagnosis

Field Diagnosis

A tentative diagnosis of VND may be made on the basis of history, clinical signs, and gross lesions, but because of similarities to other diseases such as fowl cholera and highly pathogenic avian influenza, confirmation requires virus isolation and identification.

Specimens for Laboratory

Virus can readily be recovered from sick or recently dead birds. Swabs are the most convenient way to transfer VND virus from tissues or secretions of the suspect bird to brain and heart infusion broth or other cell culture maintenance medium containing high levels of antibiotics (1). Trachea, lung, spleen, cloaca, and brain should be sampled. Swabs should be inserted deeply to ensure obtaining ample epithelial tissue. If large numbers of dead or live birds are to be sampled, cloacal swabs from up to five birds can be pooled in the same tube of broth. An

alternate technique is to place 0.5 cm^3 of each tissue into the broth. If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quick-freeze the specimens and do not allow them to thaw during transit.

Laboratory Diagnosis

In the laboratory, virus isolation is attempted by inoculating 9- to 11-day-old embryonating chicken eggs. Chorioallantoic fluid (CAF) is collected from all embryos dying after 24 hours postinoculation and tested for hemagglutination (HA) activity. If positive, the hemagglutination-inhibition (HI) test is used with known NDV-positive serum to confirm the presence of NDV in the CAF (3). If NDV is found, it is characterized by inoculating 4- to 6-week-old chickens free of ND antibodies with the suspect CAF by swabbing the cloaca, instilling into the nares or conjuctival sac, or injecting into the thoracic air sac. If VVND virus is present, the inoculated chicks usually die in 3 to 7 days, revealing typical visceral lesions on postmortem examination. Neurotropic VVD viruses will cause severe neurologic and respiratory signs in inoculated chickens but no visceral lesions. If no bird dies in 10 days, the NDV is not considered to be the velogenic, viscerotropic type but is either a lentogen or mesogen.

Differential Diagnosis

The viscerotropic, velogenic Newcastle disease in poultry can be confused with highly pathogenic avian influenza, infectious laryngotracheitis, fowl cholera, and coryza.

Vaccination

Vaccination with viable or inactivated oil emulsion vaccines, or both, can markedly reduce the losses from VND in poultry flocks. If eradication of the virus is not the goal of the control program, vaccines can be used to lessen the impact of the disease. Their use, however, can make the complete eradication of the virus much more problematic by increasing the difficulty of identifying infected flocks. There is little doubt, however, that vaccination makes the flock more refractive to infection when exposed and reduces the quantity of virus shed by infected flocks.

Control and Eradication

Before 1972, VND was introduced into the United States on several occasions by unrestricted introduction of exotic pet birds, especially psittacine birds. Because pet birds are not usually associated with domestic poultry, VND outbreaks were rare (20). Since 1973, restrictions on the importation of exotic birds requiring the quarantining and testing of imported birds in approved quarantine facilities have reduced but not eliminated the threat of VND in the United States. Illegally imported exotic bird species remain the source of frequent outbreaks of VND in private or commercial aviaries.

The establishment of a strict quarantine and destruction of all infected and exposed birds with financial indemnification for losses followed by thorough cleaning and disinfection of premises were the main features necessary for eradication of VND virus from the poultry producing area of southern California. Flocks may be safely and humanely destroyed using carbon dioxide in air-tight chambers and the carcasses disposed of by burying, composting, or rendering, depending upon the geographic area and the numbers involved. The VND virus has been recovered from effluent water for as long as 21 days and from carcasses for 7 days when the daytime temperatures were over 90o F. It is recommended that premises be kept free of domestic poultry for an additional 30 days after cleaning and disinfection are completed.

Insects and mice associated with the poultry should be destroyed before depopulation of a flock begins (5,12). Usually 48 hours is sufficient to control these vectors. As soon as all birds are killed and the manure and feed removed, all equipment and structural surfaces should be thoroughly cleaned using high-pressure spray equipment. The entire premises should then be sprayed with an approved residual disinfectant such as the cresylics or phenolics. Preliminary disinfection will probably inactivate most of the viruses on the surface of floors, equipment, cages, etc., but no disinfectant is effective unless it is applied to scrupulously cleaned surfaces

free of all organic material.

Cleaning and disinfecting commercial poultry premises are time-consuming and expensive operations. All manure must be removed down to a bare concrete floor. If the floor is earthen, at least the top inch of soil should be removed with the manure. Manure can be safely disposed of by burying it at least 5 feet deep or by composting. If composting is used, the manure piles should be tightly covered with black polyethylene sheets in a manner to prevent access by birds, insects, and rodents during composting. These piles of manure should remain tightly covered and undisturbed at least 90 days during warm weather and for longer periods during cold weather. Recent studies indicate that proper composting can decompose carcasses and manure, and thus inactivate viruses in only a few weeks.

Feathers, usually numerous around commercial poultry premises, can be burned outside the buildings, and in some cases inside, with the careful use of a flame thrower, or they can be removed and the area wet down with disinfectant. The hot sun and high daytime temperatures will assist in destroying the virus in the area of the houses. Extremely cold temperatures will make the cleaning and decontamination process much more difficult, and the results more uncertain.

In 1997, because neither the neurotropic or viscertropic strain of velogenic Newcastle disease was known to exist in the United States, USDA-APHIS declared both types to be exotic and therefore indistinguishable as to the response of disease control officials should they occur in the United States.

Surveillance

The most difficult part of the VND eradication program is locating inapparently infected and exposed birds.

Repeated vaccination at 30 to 50 day intervals protects most chickens against clinical manifestation of VND. However, vaccine does not prevent all chickens in a flock from becoming infected, showing no disease sign, or shedding virulent virus. As individual chickens become susceptible and get exposed to the virus, they become infected and also shed the virus for a time. Thus, the virulent virus continues to be present in apparently healthy, vaccinated flocks. The advantages of using vaccines as part of a VND eradication program must be weighed against the difficulty created in finding asymptomatic but infected and virus-shedding flocks. In such instances owners should be encouraged to observe strict biosecurity measures to reduce the chances of their flocks being exposed to VND virus.

Infected carriers in vaccinated flocks can be detected using one of two systems. In the first, all birds dying during a 24-hour period are collected twice a week, and cloacal swabs and brains are collected and cultured for the presence of VND virus using the diagnostic sampling procedures described earlier. Birds in VND-infected flocks that die from Marek's disease, leukosis, gout, and numerous other disease conditions may yield VND virus—especially if their immune system was impaired by those diseases before death. In the second virus detection system, susceptible sentinel birds are placed in vaccinated flocks (18). The sentinel birds must be unvaccinated and obtained from a specific pathogen-free source to be certain that they do not inadvertently serve as a source of diseases for the suspect flock. In most instances the sentinel birds die from VND within a week or so after placement if there is VND virus present in the flock; however, in some cases it is sometimes difficult to place sentinel birds so they are adequately exposed to any VND virus that may be in the flock — especially in caged-layer flocks.

Public Health

Although people may become infected with VND virus, the resulting disease is typically limited to a conjunctivitis. Recovery is usually rapid, and the virus is no longer present in eye fluids after 4 to 7 days. Infections have occurred mostly in laboratory workers and vaccinating crews with rare cases in poultry handlers. No instance of transmission to humans through handling or

consuming of poultry products is known. Individuals with conjunctivitis from VND virus should not enter poultry premises or come in contact with live avian species.

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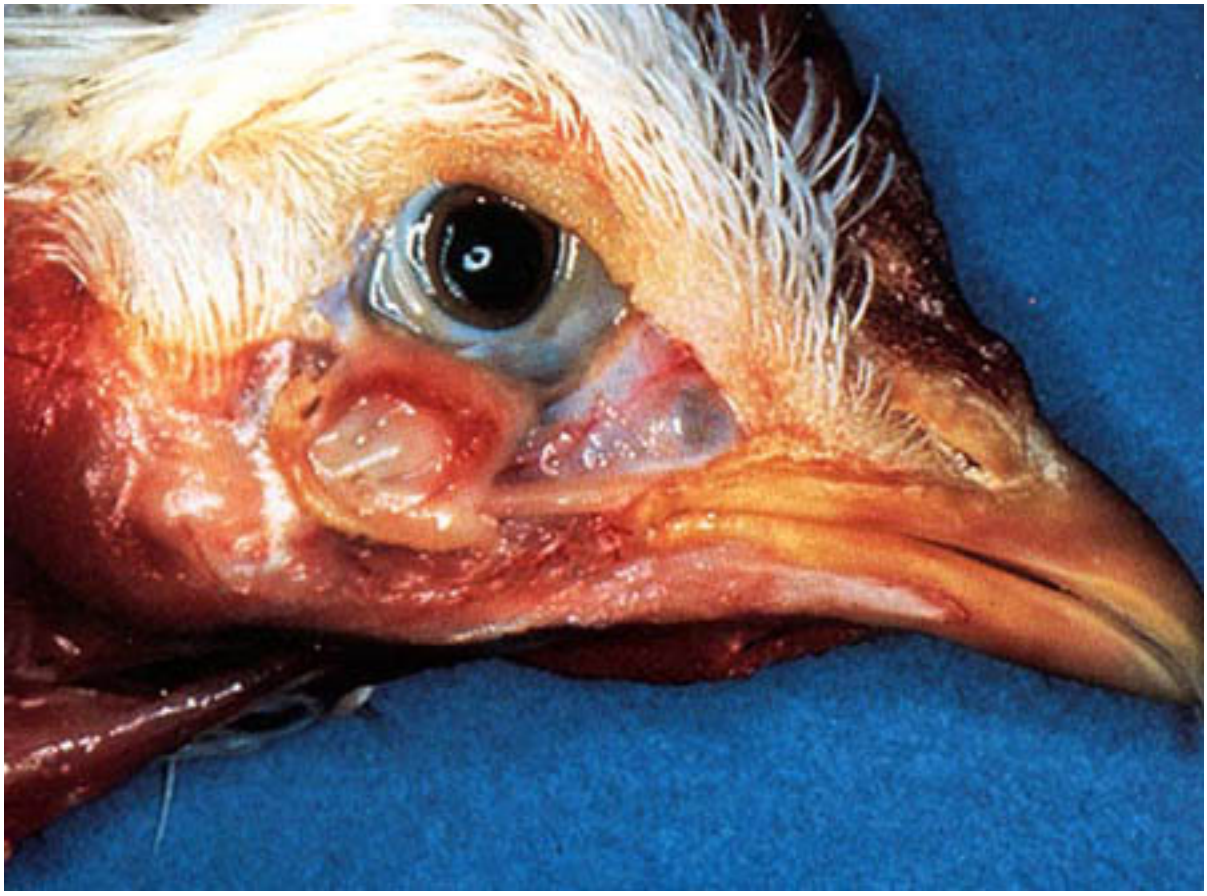

Fig. 107. VVND - Edema and hemorrhage in the reflected lower eyelid.

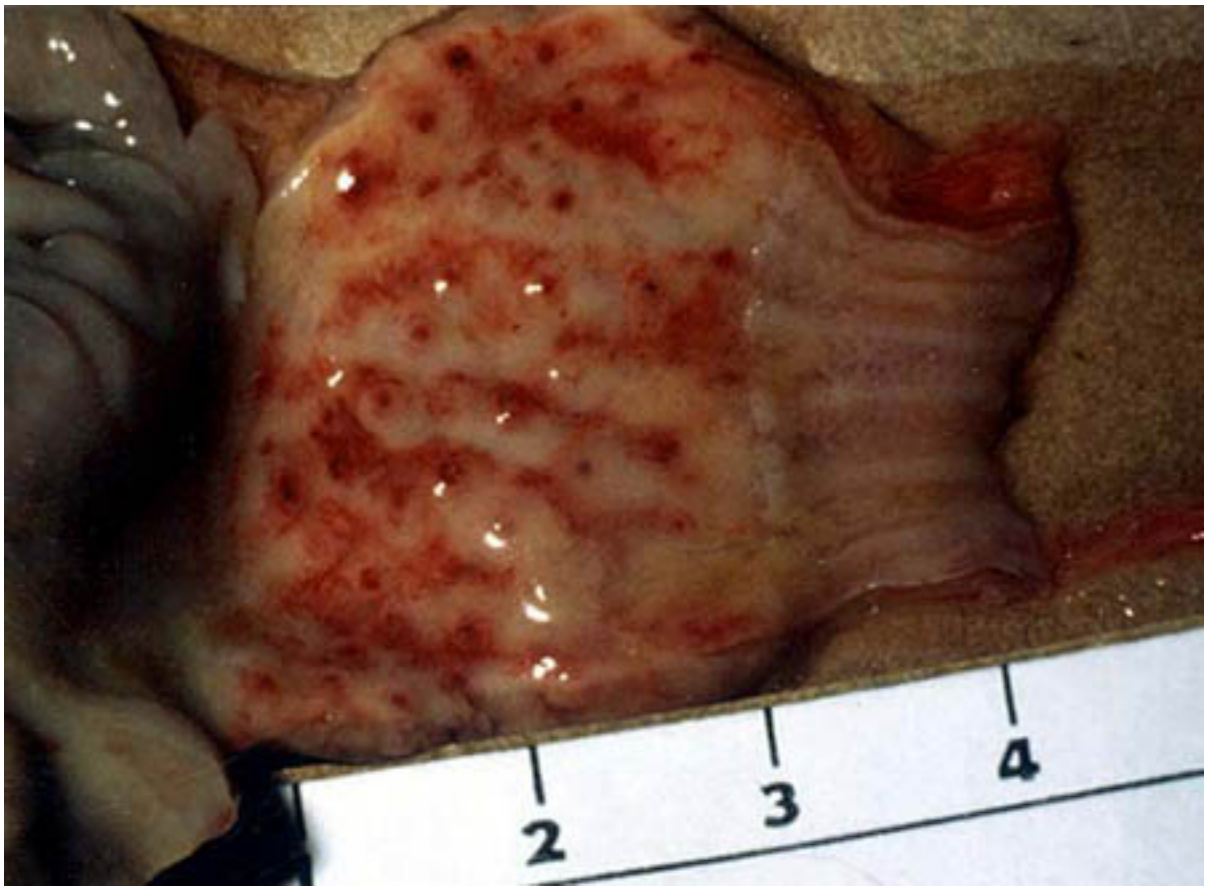

Fig. 108. VVND - Petechiae in the mucosa of the proventriculus.

Fig. 109. VVND - Necrosis of a lymphoid area in the lower small intestine.

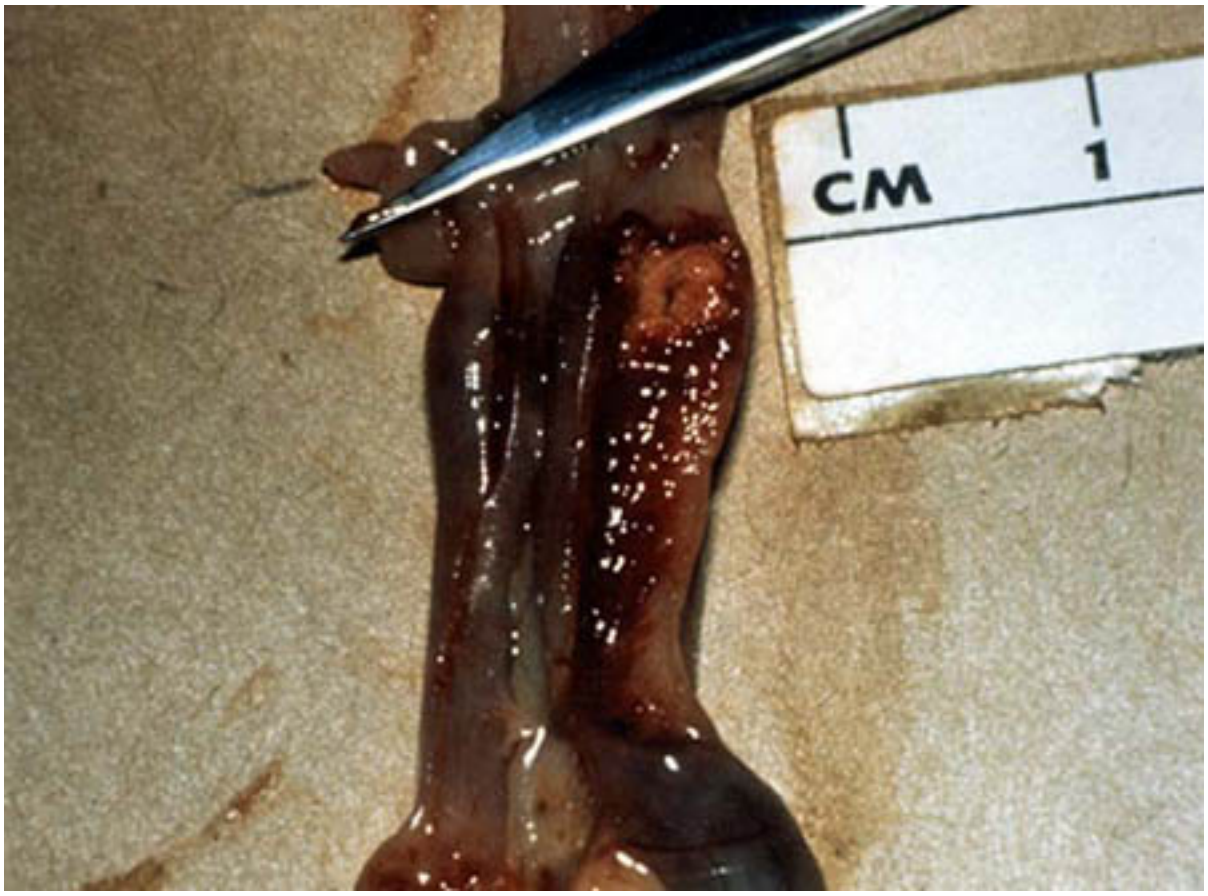

Fig. 110. VVND - Necrosis of the cecal tonsils.

PART IV
FOREIGN ANIMAL DISEASES

VENEZUELAN EQUINE ENCEPHALOMYELITIS

(Peste loca, Venezuelan encephalitis, VEE, VE)

Definition

Venezuelan equine encephalomyelitis (VEE) is a zoonotic, mosquito-borne, viral disease affecting both Equidae and humans (6,8). In Equidae, infection may produce an acute, fulminating disease that terminates in death or recovery without development of encephalitic signs, or the more classical disease with progressive clinical encephalitis. In human beings, a flulike syndrome predominates with an accompanying high fever and frontal headache. Human deaths may occur in the young or the aged. A wide variety of hosts and vectors may be infected (5,10,13,15).

Etiology

The etiologic agent of VEE is an alphavirus of the family Togaviridae (formerly the group A arboviruses). . The virions are 60-75 nm in diameter and have an essential lipid membrane.

Only minor antigenic variations exist among different VEE virus isolates (10,16). Six subtypes (I, II, III, IV, V, and VI) have been identified within the VEE complex. Within subtype I, only two (A/B and C) of the five variants (A/B through F) have been associated with epizootic activity in equines (5,10,13-15). The other variants (I-D through I-F) and subtypes (II through VI) have been associated with nonequine, sylvatic, or enzootic activity. Infection with one variant or vaccination with attenuated virus generally results in production of neutralizing antibodies and cross-protection of variable duration to infection with the other subtypes and variants (13-15).

Host Range

A wide variety of laboratory animals are susceptible in varying degrees to both enzootic and epizootic variants of VEE virus (5,10,13,15). In addition, several domestic animals, including cattle, swine, and dogs have serologic and virologic evidence of infection, but generally no clinical sign, during epizootics of VEE. However, with the possible exception of human beings, no evidence exists to date to incriminate any animal species other than Equidae as prime amplifiers of VEE epizootics (5,10,13,15).

Geographic Distribution

Venezuelan equine encephalomyelitis was first recognized as a separate disease entity following a major epizootic of encephalitis in Venezuela in 1936 (8,10). From 1936 to 1968, devastating epizootics and epidemics occurred in equines and human beings in Colombia, Ecuador, Peru, and Venezuela (5,10,13,15). In January, 1969 another major epizootic and epidemic of VEE erupted in Ecuador and spread into Peru. In June, 1969, the virus was transported by undetermined means from Ecuador to Guatemala (3). This large scale epizootic and epidemic spread into El Salvador, Honduras, and Nicaragua. In 1970, the epizootic extended into Costa Rica and Mexico and, by 1971, into the United States (5,10,13,15).

Epizootic VEE has not been diagnosed, and epizootic VEE virus variants have not been isolated in the United States since 1971. Twenty years after the last activity in the Western Hemisphere, VEE was reported in 1992-3 and 1995 in outbreaks in horses in Venezuela and in 1993 and 1996 in limited, focal outbreaks in horses in Mexico.

Transmission

Sylvatic or Enzootic Cycle

As indicated earlier, variants I-D through I-F and subtypes II through VI of VEE virus are invariably associated with a sylvatic or enzootic cycle in which rodent-mosquito transmission occurs; human beings and horses are only incidentally involved in this cycle. Although sylvatic variants and subtypes are pathogenic for human beings and have caused occasional epidemics with a few deaths, these variants and subtypes are normally nonpathogenic for horses. However, in 1993 and 1996, VEE virus variant I-E was isolated from horses during a focal, limited outbreak in Mexico in areas of sylvatic virus activity. This occasional activity is consistent with previously reported VEE during the mid-1960's in Mexico in which VEE virus variant I-E isolations were made. It is clear that under certain ideal but undefined conditions, sylvatic I-E variant viruses are pathogenic to horses.

Generally, the sylvatic virus tends to cycle in rodents in areas where a highly efficient vector such as *Culex* (*Melanoconion*) spp. is found (5,10,13-15). Foci of sylvatic virus activity have been identified in Colombia and Panama (subtype I-D); Mexico, Central America, and Panama (subtype I-E); Brazil (subtype I-F); Florida Everglades (subtype II); Brazil and Trinidad (subtype III-A); some Northern Plains states and Surinam (subtype III-B); Brazil (subtype IV); French Guiana (subtype V); and Argentina (subtype VI) (5,10,13,15,16).

Epizootic Cycle

No known epizootic virus variant (I-AB or I-C) has ever been shown to cycle enzootically in rodents. Historically, naturally occurring epizootics of VEE in Equidae have been reported in northern South America since at least the 1920's (10). The original epizootic VEE viral isolate made in Venezuela in 1937 was caused by a strain of variant I-A/B, which was also responsible for the 1969-72 epizootics in Ecuador, Central America, Mexico, and Texas. Epizootics during the 1960's and 1970's and in 1992-3 and 1995 in Colombia and Venezuela were caused by variant I-C. Recent molecular genetic studies of VEE virus isolates indicate very close phylogenetic relationships between epizootic variant I-C isolates and sylvatic variant I-D isolates (11). The results support the hypothesis that epizootic VEE virus variants emerge from sylvatic variant I-D viruses. During epizootics of VEE, many species of mosquitoes and possibly other hematophagous insects are involved in the explosive movement of the outbreak. Horses are the most important amplifiers of VEE virus during epizootics owing to the extremely high viremias that they develop and the large numbers of hematophagous insects that can feed on an animal of such size. Human infections occur tangentially to equine infections, but in spite of moderately high viremia levels, human beings probably do not contribute significantly to the maintenance and movement of an epizootic wave. The maintenance cycle of equine virulent (epizootic) VEE virus during the interepizootic period and the origin of epizootic VEE virus variants are unknown. Efficient vectors of epizootic VEE include mosquitoes of the genera *Aedes*, *Anopheles*, *Culex*, *Deinocerites*, *Mansonia*, and *Psorophora* (5,10,13,15).

Incubation Period

The incubation period from the inoculation of the virus until the febrile response generally is 0.5 to 2 days but may be as long as 5 days, depending on the virus strain or quantity of virus in the inoculum. Typically, detectable viremia occurs concurrently with the onset of fever and persists for 2 to 4 days. Onset of encephalitic signs occurs 4.5 to 5 days after infection at a time when circulating virus is disappearing, neutralizing antibody is first detectable, and body temperature is returning to a normal range (10,14,15)

Clinical Signs

In Equidae, VEE virus infection may be expressed as (a) subclinical with no overt signs; (b) moderate and characterized primarily by anorexia, high fever, and depression; (c) severe, but nonfatal, and characterized by anorexia, high fever, stupor, weakness, staggering, blindness, and, occasionally, permanent neurologic sequelae; or (d) fatal, with the same clinical signs

(5,7,10,13-15). Not all fatal cases of VEE in Equidae are accompanied by definite neurologic signs. In general, two forms of the disease exist: (a) the fulminating form in which signs of generalized, acute, febrile disease predominate, and (b) the encephalitic form in which the more impressive signs of central nervous system (CNS) involvement usually dominate. An incubation period of 0.5 to 5 days precedes a rise in body temperature to 39-41° C (103-105° F) which is accompanied by a hard, rapid pulse and depression. The onset of VEE virus infection is insidious, with fever, inappetence, and mild excitability being among the earliest clinical signs of disease. Frequently, a rapid progression ensues with depression, weakness, and ataxia followed by overt signs of encephalitis such as muscle spasms, chewing movements, incoordination, and convulsions. Early encephalitic signs include loss of both cutaneous neck reflexes and visual responsiveness; diarrhea and colic may also develop. Some animals may stand quietly in their surroundings whereas others may wander aimlessly or press their heads against solid objects. A braced stance or circling may occur late in the disease. A characteristic paddling motion of the limbs may be observed with lateral recumbency. The course of the disease may be interrupted at any point by recovery or prostration and death. The course of the disease may be rapid with death ensuing within hours after the observation of the first clinical manifestations of encephalitis (during epizootics, reports of sudden death are not uncommon), or more protracted with dehydration and extreme loss of weight occurring before an encephalitic death or recovery.

Gross Lesions

The macroscopic appearance of the CNS of horses inoculated with VEE virus varies from no visible lesion to extensive necrosis and hemorrhages. Lesions reported in other tissues have been too variable to be of any diagnostic significance (7,9,10,12,14,15).

Morbidity and Mortality

Epizootic VEE due to virus variants I-A/B and I-C may be highly fatal. Estimated case morbidity rates vary from 50 to 100 percent in some areas to 10 to 40 percent in other areas. Mortality rates vary from 50 to 90 percent; infection rates with or without clinical signs may be as high as 90 percent. In most cases, infection with sylvatic or enzootic VEE virus variants I-D, I-E, or I-F, or subtypes II, III, IV, V, and VI is considered to be nonlethal for Equidae. Occasional limited outbreaks of clinical encephalomyelitis in horses from infection with sylvatic variant I-E viruses have been documented and VEE attenuated virus, strain TC-83, has been used effectively to stop recent outbreaks (14,15).

Diagnosis

Field Diagnosis

A field diagnosis of VEE can rarely be made unless an epizootic of encephalitic disease is in progress and a prior etiologic diagnosis of VEE has been made. Seasonality of the disease and association with large populations of mosquitoes would suggest a diagnosis of arboviral encephalomyelitis. The initial signs of VEE may go undetected. When signs of encephalitis predominate, the disease in equines is indistinguishable from other arboviral equine encephalomyelitides, such as Eastern equine encephalomyelitis (EEE) and Western equine encephalomyelitis (WEE) (3,6,8,13,15). In contrast to EEE or WEE, herd morbidity and mortality with VEE are high (1,5).

Specimens for Laboratory

Specimens for diagnosis are heparinized blood, serum (paired [acute and convalescent] sera if animal survives), and half the brain and piece of pancreas unfixed and a completed set of tissues in 10 percent formalin, if the animal dies.

Laboratory Diagnosis

A specific diagnosis can be made only by laboratory procedures, namely, virus isolation or

demonstration of a specific rise in hemagglutination-inhibiting or neutralizing antibody with paired (acute and convalescent) sera. Frequently, animals die before a convalescent serum can be obtained. Experimental studies and field experiences have shown that viremia terminates before signs of clinical encephalitis are exhibited by VEE virus-infected equines. In this case, the highest probability of successful viral isolation is obtained by taking sera from other horses with marked elevations of body temperature that are in the vicinity of the encephalitic horse (5,13-15). Virus may also be isolated from brain, pancreas, or whole blood of dead or dying horses, but with a lower frequency of success (7,13,15). Virus is isolated by the intracranial inoculation of suckling mice or in various cell culture systems.

Histopathologic lesions consistent with a diagnosis of VEE are a diffuse necrotizing meningoencephalitis that ranges from a slight perivascular mixed cellular reaction to marked vascular necrosis with hemorrhages, gliosis, and frank neuronal necrosis (9,11). Lesions are usually most severe in the cerebral cortex and become progressively less severe toward the cauda equina. The degree and severity of the CNS lesions vary with the progression and duration of the clinical signs. Necrotic lesions may involve the adrenal cortex, liver, myocardium, and the walls of small and medium blood vessels (7,9-11,14,15).

Differential Diagnosis

A variety of diseases may produce signs that resemble one or more of the clinical signs of VEE infection, but since no clinical sign (including encephalitis) is pathognomonic for VEE, an all-inclusive list of differential diagnoses is virtually impossible to provide. A list of the more obvious diseases includes EEE, WEE, and other arboviral encephalomyelitides; African horse sickness; rabies; intoxications; botulism; hepatoencephalopathy; and trauma. During the Texas epizootic, VEE (confirmed) was presumptively diagnosed as equine infectious anemia, colic, or shock, and so any condition that would produce fever and depression, with or without signs of CNS involvement, would need to be considered in the differential diagnosis.

Vaccination

An attenuated VEE virus vaccine has been used in many areas of the Americas, both to combat the disease during an epizootic and to administer preventive vaccination in nonepizootic zones where a high risk of infection is present (5,10,12,13,15). Although preexisting neutralizing antibodies to EEE and WEE viruses may interfere with the neutralizing antibody response to VEE virus vaccination, the interference is not sufficient to affect immunity (4). Simultaneous vaccination with VEE attenuated virus and EEE-WEE inactivated virus produces a VEE neutralizing antibody response equivalent to that produced with the administration of attenuated VEE vaccine alone (4). An inactivated trivalent EEE-VEE-WEE virus vaccine has been shown to immunize equine recipients effectively (2).

Control and Eradication

During epizootics, restriction of horse movement between the epizootic zone and noninfected areas is important to control the spread of VEE. Because of the high levels of VEE viremia in Equidae (>$10^{5.5}$ infectious virions/ml of blood), introduction of infected animals into noninfected areas readily establishes new foci of infection. However, control of movement of the equine population is not sufficient to curb the spread of VEE (5,10,13,15).

Mosquito control measures such as aerial spraying with ultralow volumes of insecticides have been instituted during epizootics. Vector control in the absence of other control measures can do little more than slow the spread of VEE and decrease its severity in the human population (5,10,13,15). Physical disruption or insecticide treatment of the aqueous larval habitats also can reduce adult mosquito populations.

For adequate epizootic control, the preceeding measures must be accompanied by a large-scale equine immunization program (5,10,13,15).

Owing to the absence of clinical VEE in the United States as well as concerns about

seropositivity in vaccinated equines involved in international movement, it has been suggested by veterinary researchers and regulatory personnel that routine vaccination with VEE virus vaccines should be discontinued. However, vaccines should be made available and used during a VEE emergency.

Public Health

Human infections resulting from bites of infected mosquitoes occur tangentially to equine infections. Transmission can also occur by exposure to aerosolized infective material. In human beings, a flulike syndrome predominates accompanied by high fever and frontal headache. Human deaths may occur in the young or the aged.

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PART IV
FOREIGN ANIMAL DISEASES

VESICULAR EXANTHEMA OF SWINE

Definition

Vesicular exanthema of swine (VES) is an acute febrile disease of swine caused by caliciviruses and characterized by fever and vesicles with subsequent erosions in the mouth and on the snout, feet, and teats.

Etiology

The cause of VES is calicivirus, of which there are 13 serotypes. The VES viruses are closely related to at least 14 other serotypes of caliciviruses found in the San Miquel sea lion virus group.

History

1932	A vesicular disease in swine near Buena Park, CA, was thought to be FMD; 19,000 pigs were killed and buried.
1933	A vesicular disease in swine in San Diego County was shown not to be FMD, and the disease was named vesicular exanthema of swine.
1932-36	Ten more outbreaks of VES occurred in California; each was eradicated.
1936-39	There was no outbreak.
1939-52	Vesicular exanthema of swine spread to all the major swine producing areas in the United States. It appears to have spread from California through feeding of garbage from a train running between California and Chicago and subsequently through hog cholera antiserum from a production plant in North Platt, NE (on the train route).
1954	National eradication program started.
1954	Law requiring that garbage fed to pigs be cooked.
1956	Last case of VES recorded.
1959	United States declared free of VES, and VES declared a foreign disease.
1972	Existence of marine caliciviruses recognized.
1972-95	At least 14 marine caliciviruses have been recognized; it is likely that experimentally, they all can produce vesicles in pigs.

People have speculated that VES may have resulted from feeding of marine mammal (seal) meat and fish as a protein supplement during the Great Depression. Thus, some are concerned

that a VES-like disease could reappear in the United States because of the large number of marine mammals on the west coast. Marine calicivirus antibody has not yet been found in marine mammals in the Atlantic Ocean.

Host Range

Vesicular exanthema of swine occurred only in the pig. Related caliciviruses occur in marine mammals, fish in the Pacific Ocean, and in other mammals.

Geographic Distribution

Vesicular exanthema of swine occurred only in the United States and has been eradicated.

Transmission

The outbreaks up to 1939 may have been due to separate introductions of the virus. Starting in the 1939 outbreak, there was rapid pig-to-pig spread and spread from feeding infected pork scraps in uncooked garbage.

Incubation Period

The incubation period after natural exposure is 18 to 72 hours.

Clinical Signs

Clinical signs are very similar to those of foot-and-mouth disease and other vesicular diseases. There is a fever; vesicles in the mouth, on the snout (Fig. 122), and, on the feet (Fig. 123); and lameness. These signs are all grossly indistinguishable from FMD. Lesions in VES seem to be deeper, and granulation tissue commonly forms especially on the feet.

Morbidity and Mortality

Morbidity is quite variable but may be near 100 percent. Mortality is low.

Diagnosis

See chapter on foot-and-mouth disease.

Differential Diagnosis

Differential diagnosis for SVD should include foot-and-mouth disease, vesicular stomatitis, swine vesicular disease, and chemical and thermal burns.

Control and Eradication

Slaughter and disposal of infected and contact animals and disinfection of the premises.

Public Health

There has been no report of human infection by VES virus.

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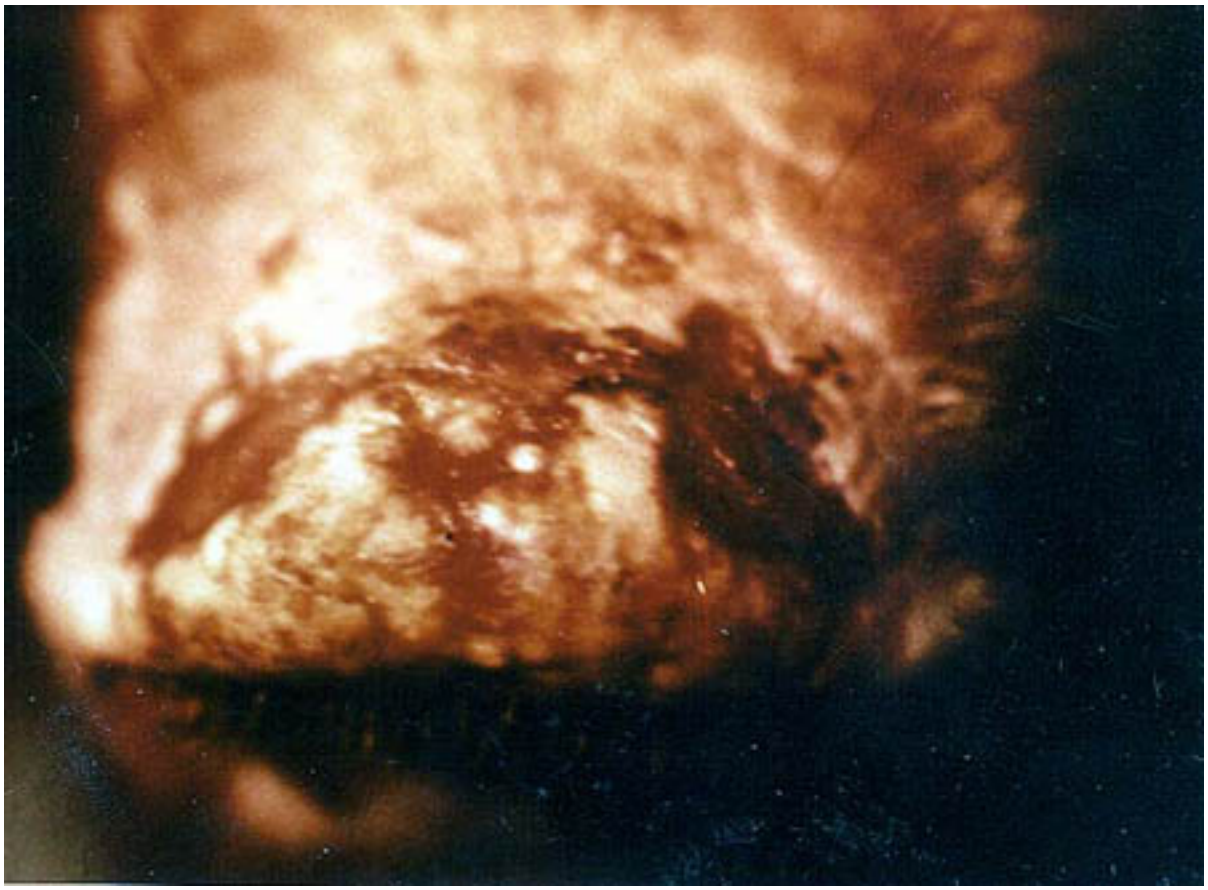

Fig. 122. VES - Ruptured vesicles on the snout are indistinguishable from FMD.

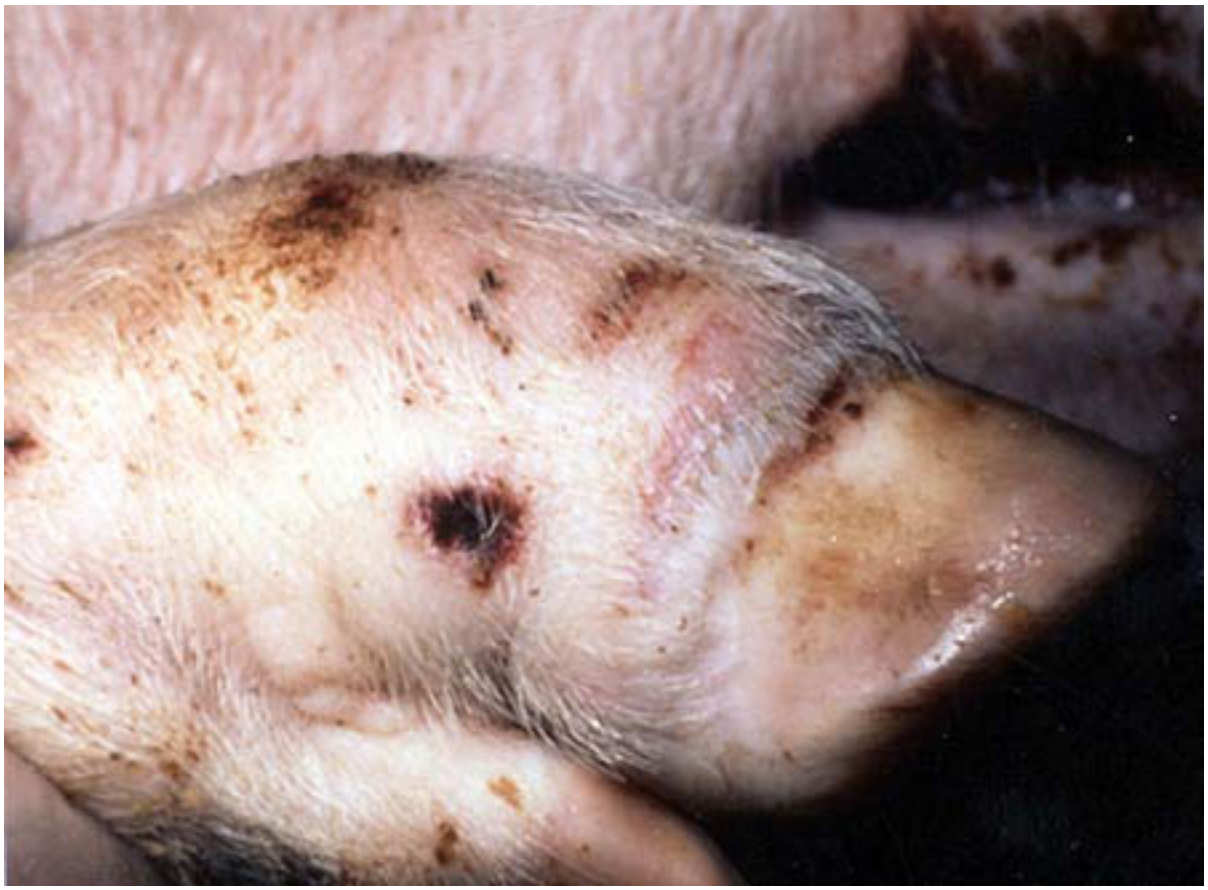

Fig. 123. VES - Severe coronary band necrosis is indistinguishable from FMD.

PART IV
FOREIGN ANIMAL DISEASES

VESICULAR STOMATITIS

Definition

Vesicular stomatitis (VS) is a viral disease characterized by fever, vesicles, and subsequent erosions in the mouth and epithelium on the teats and feet. Horses, cattle, and pigs are naturally susceptible; sheep and goats are rarely affected.

Etiology

The viscular stomatitis virus is a *Vesiculovirus* in the family *Rhaboviridae*. The virion is a large bullet-shaped (65-185 nm) RNA virus. There are two serotypes of VSV: New Jersey and Indiana 1. In the serotype Indiana 1, there are two subtypes: Indiana 2 (Cocal) and Indiana 3 (Alagoas). In addition to these two serotypes of VSV, there are other viruses within the genus *Vesiculovirus* that can experimentally cause vesicular lesions in domestic animals and infect humans; these are as follows:

Piry — first isolated from an opossum in Brazil.

Chandipura — first isolated from a person in India.

Isfahan — isolated from sandflies and humans in Iran.

Effective disinfectants are 2 percent, sodium carbonate - 4 percent, sodium hydroxide - 2 percent, iodophore disinfectants and chlorine dioxide disinfectants.

Host Range

The host range in decreasing order of severity of infection are horses, donkeys, mules, cattle, swine, and man.

South American camelids develop clinical infection.

Sheep and goats are quite resistant and rarely become affected.

Vesicular stomatitis virus has also be shown experimentally to infect a wide host range, including deer, raccoons, bobcats, and monkeys.

Geographic Distribution

Classical VS occurs only in North and Central America and the northern part of South America. Serotypes New Jersey and Indiana I occur in the United States and Central America. Serotypes New Jersey and Indiana 1, 2, and 3 occur in South America.

Transmission

The vesicular stomatitis virus has been shown to be transmitted by the sand fly (*Lutzomyia shannoni*) and the black fly (*Simuliidae*). Transovarial transmission has been shown to occur in both flies. The VS-NJ serotype was isolated from a variety of field-collected hematophagous insects such as *Culicoides* (biting midges), *Simuliidae* (black flies), *Aedes* (mosquitoes) and nonbiting insects such as *Chloropidae* (eye gnats), *Anthomyiidae*, and *Musca* (house flies) during the 1982 epizootic in the southwestern United States (1). Except for *Lutzomyia* and *Simulidae*, the role of these other insects in the transmission of VSV is unknown. Before the

1982 outbreak in the United States, people, on the basis of past experience, expected an outbreak to stop about 2 weeks after a killing frost. In the 1982 outbreak, cases and spread occurred through the winter. The winter spread of the disease is believed to have resulted from movement of infected animals and the resulting exposure of uninfected animals to contaminated waterers and feed bunks as well as contact with infected animals. It is known that VSV can be spread by a contaminated milking machine. Overwintering did not occur in the 1995 outbreak in the United States.

Humans may be infected by contact and by aerosol.

Epidemology

The disease occurs throughout the year in subtropical and tropical areas of the Americas. The disease occurs sporadically during the warm months in southern and western United States. Epidemics have occurred irregularly at 10 to 15 year intervals. The virus is spread by insect vectors, movement of infected animals, and contaminated objects. Researchers have shown transovarial transmission in the sand fly and black fly; this may be a way the virus can overwinter.

Incubation Period

A vesicle appears in about 24 hours after intradermal lingual inoculation of VSV. This similar to the incubation period for foot-and-mouth disease.

In humans, the incubation period is 24 to 48 hours.

Clincial Signs

Animals develop a fever ranging to 104-106º F (40-41º C).

Horse

Vesicles in the mouth may cause the animal to chomp its jaws, drool, and rub its mouth on the manger or other objects. Lesions on the coronary band can cause lameness.

Cattle and pigs

See the clinical signs section in the FMD chapter. The signs are very similar.

Humans

In humans, VSV causes an influenza-like illness; there is fever, headache, muscular aches, and blisters in the mouth similar to those caused by herpesvirus. The disease course is 4 to 7 days.

Morbidity and Mortality

Interesting data on the economic effect of VS in cattle were collected by Alderink during the 1982 outbreak of VS in Colorado. In 13 of the dairy herds studied. there were 2,404 cows and 378 cases of VS. Lesion distribution in these 378 was as follows:

Oral lesions only	263 animals (69.3%)
Teat lesions only	87 animals (23%)
Oral and teat lesions	22 animals (5.8%)
Foot lesions only	7 animals (1.9%)

Herds experiencing primarily oral lesions had an attack rate of 19.8 percent The attack rate in two of four herds with teat lesions was 55.8 percent and in the other two herds 1.6 percent. The clinical course in cases with oral lesions was 23.8 days. Mastitis complicated 72% of the cases with teat lesions.

The total cost to the 13 dairymen was $95,752, which came to an average cost of $253 per case. The approximate cost of a case with only oral lesions was $174 in contrast to an average cost of $568 for cases with teat lesions. Of the total $95,752 loss, 46 percent was for cows culled; 30 percent was for decreased production; 11 percent for deaths; and 11 percent for drugs, labor, weight loss, and veterinary charges.

Differences Between VS and FMD

The characteristics of VS are as follows:

Horses affected.

Sporadic incidence in the herd (see preceeding).

Distribution of lesions in an animal (small percentage of animals have lesions at more than one site of predilection; see preceeding).

No rumen lesions observed at necropsy.

No heart lesions observed at necropsy.

Vesicular stomatitis is less severe in young animals.

Stabled animals usually not affected.

In spite of these differences, do not attempt to make a final differential diagnosis in the field; get laboratory confirmation of the diagnosis.

Diagnosis

See FMD chapter.

Differential Diagnosis

Differential diagnosis for VS in cattle should include foot-and-mouth disease, foot rot, and chemical and thermal burns. In cattle, oral lesions caused by rinderpest, infectious bovine rhinopneumonitis, bovine virus diarrhea, malignant catarrhal fever, and bluetongue can be similar to the later lesions in FMD. In pigs, the differential diagnosis for VS should include foot-and-mouth disease, swine vesicular disease, vesicular exanthema of swine, foot rot, and chemical and thermal burns. In sheep, the differential diagnosis for VS lesions should include bluetongue, contagious ecthyma, lip and leg ulceration, and footrot.

Control and Eradication

Control movement of animals — no movement from an infected premise, except for slaughter, for 30 days after last lesion has healed.

Separate infected and healthy animals.

Stable animals if possible.

Disinfect milking machines between cows.

Milk infected cows last.

Control insects.

Commercial vaccines are available, but efficacy has not been field tested.

Public Health

Vesicular stomatitis (New Jersey and Indiana) infection frequently occurs in man and causes influenza-like symptoms but rarely results in vesicles. Other vesicular stomatitis viruses (Piry, Isfahan, and Chandipura) are much more infectious for man.

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PART IV
FOREIGN ANIMAL DISEASES

VIRAL HEMORRHAGIC DISEASE OF RABBITS

(Necrotic hepatitis of rabbits, rabbit hemorrhagic disease syndrome, X disease)

Definition

Viral hemorrhagic disease of rabbits (VHD) is a peracute viral disease of rabbits (*Oryctolagus cuniculus*) causing hepatic, intestinal, and lymphoid necrosis and massive terminal intravascular coagulation.

Etiology

The causative agent has not yet been fully characterized. Following initial reports from the People's Republic of China (13) that the agent was a picornavirus (22), later studies identified a parvovirus (27). Though a caliciviral etiology has been suggested by various European workers (18,19,20), studies comparing isolates from Mexico, Korea, Spain, and Italy indicate that there is little or no serologic difference between isolates (M. Beringer, personal communication).

The virus is very resistant to physical and chemical agents. It can persist in blood from an infected rabbit for more than 9 months at 4° C (39° F.). Organ homogenates are stable for more than 3 months at 20° C (68° F.) when dried on cloth (24). Virus can be shed in urine or feces of infected and recovered rabbits for up to 4 weeks (9,10). The virus is ether and chloroform resistant but is inactivated in 1 hour in 1 percent NaOH or 1 percent formalin at 37° C (98.6° F.) (26). Solutions of 2 percent One-stroke Environ (Vestal Lab Inc., St. Louis, MO) and 0.5 percent sodium hypochlorite (10 percent household bleach) have also been recommended (9).

Host Range

Only the domestic rabbit and the European rabbit (both *Oryctolagus cuniculus*) appear to be susceptible to VHD. Other lagomorphs that have been experimentally exposed but did not show clinical signs of disease include the Eastern cottontail (*Sylvilagus floridanus*), black-tailed jackrabbit (*Lepus californicus*), and volcano rabbit (*Romerolagus diazi*). The European brown hare (*Lepus europaeus*) and the varying hare (*Lepus timidus*) appear not to be natural hosts for VHD but are susceptible to a very closely related virus that causes European brown hare syndrome. No other laboratory animal is susceptible to VHD.

Geographic Distribution

The disease is enzootic in the People's Republic of China, Korea (1), most of continental Europe, Morocco, Cuba, Australia, and New Zealand. In Europe, the disease is also epizootic in the wild rabbit population with more cases occurring in the fall. An outbreak occurred in the Mexico City area in December 1988 (15,16). In February 1989, the Mexican government began a control and eradication program to eliminate the disease using test and slaughter methods. The campaign was successful; there were few reported cases in 1990 and none in 1992. Mexico is the first country to succeed in eradicating this disease.

A disease similar to VHD called European brown hare syndrome (6,7) has been reported from Sweden. European brown hare syndrome was first suspected to be caused by a severe hepatotoxin but has since been demonstrated to be caused by a virus closely related to VHD that seems to affect only hares (3,7). Both of these viruses are now widespread in continental Europe in its wild populations of rabbits and hares respectively.

Transmission

Transmission of the virus is by direct contact with infected animals or, indirectly, by contact with objects contaminated with virus. Aerosol is generally not an important means of transmission. Natural infection is more likely through oral exposure. Experimental transmission can be accomplished through inoculation by oral, nasal, subcutaneous, intramuscular, or intravenous routes.

Incubation Period

Experimentally, following oral exposure, the incubation period is about 24 hours to the onset of fever. This may vary up to 48 hours under field conditions.

Clinical Signs

The most prominent sign is that young adult and adult rabbits die suddenly after 6 to 24 hours of fever with few clinical signs. Fever may be high (up to 105° F or 40.5° C) but often is not detected until rabbits show terminal clinical signs. Most rabbits appear depressed in the final hours and may have a variety of neurologic signs including excitement, incoordination, opisthotonos, and paddling. They sometimes emit a terminal squeal. A few rabbits may have a terminal serosanguineous, foamy, nasal discharge (Fig. 126).

Gross Lesions

Many gross and histopathologic lesions have been attributed to VHD, including hemorrhages and necrosis in many organs. The primary and most consistent lesion of VHD is hepatic necrosis of the portal zone of each lobule (Fig. 127), which causes the liver to appear pale. On close examination, the liver has a fine reticular pattern of necrosis outlining each liver lobule. In some cases, necrosis is so extensive that the liver is diffusely pale. Hemorrhages are the most obvious postmortem lesion but are often variable or absent — especially in rabbits that are euthanized. Hemorrhages are the result of massive terminal intravascular coagulation in many organs and are likely the cause of death in most cases of VHD. Hemorrhages are common in the lung, (Fig. 128) trachea, and thymus whereas infarction is common in the kidneys and spleen. The spleen is usually thickened and black and has distinctly rounded edges. Infarcted kidneys may appear black. A more subtle lesion is a catarrhal enteritis due to small intestine crypt necrosis, but diarrhea usually is not present because rabbits commonly die peracutely before digestive alterations develop.

Morbidity and Mortality

Morbidity with VHD is very high. Mortality is usually 90 percent in conventionally raised rabbits, and often only suckling rabbits are spared. Suckling rabbits may be spared because of maternal immunity to a closely related virus or owing to reduced susceptibility of the immature liver. In isolated and well-managed research colonies, mortality may be 50 percent or less. The reason for this difference is not well understood, but immunologic priming seems to predispose rabbits to the massive terminal intravascular coagulation (massive coagulopathy) that is responsible for the sudden death. Experimental priming has raised the mortality rate in research rabbits from 50 percent to 100 percent. Both minute virus of mice and porcine parvovirus have produced this priming effect.

Diagnosis

Field Diagnosis

A presumptive diagnosis can be made in a rabbitry when there are multiple cases of sudden death following a short period of lethargy and fever, and characteristic hepatic necrosis and hemorrhages occur. A field diagnosis is more difficult when there are few rabbits on the premise or rabbits are relatively isolated, as in research colonies.

Specimens for Laboratory

Unfixed liver, heparinized blood and serum, and fixed liver, spleen, kidney, lung, small intestine, and brain should be sent to the laboratory to confirm suspected cases.

Laboratory Diagnosis

Ideally, several tests should be used in the laboratory. Virus can easily be concentrated from liver homogenate and visualized by electron microscopy using negative stains. Liver homogenate can also be used in a hemagglutination test (21). This virus agglutinates human type O and guinea pig erythrocytes at pH 6.3 to7.4 at 4 to 25° C. Antibody from recovered rabbits can also be detected with this test by its inhibition of erythocyte agglutination. Tissue sections can be immunostained using the avidin-biotin alkaline phosphatase staining system on either fresh or freshly fixed liver and spleen (8). Where VHD has become endemic, several different enzyme-linked immounosorbent asssay (ELISA) systems have been developed (3).

Rabbits can be inoculated to confirm the first diagnosis of this disease in a new region. No other laboratory animals are susceptible. The virus cannot easily be propagated in cell culture.

Histologically, diffuse hepatic necrosis with a periportal pattern accompanied by microthrombi in multiple organs is characteristic of this disease in rabbits.

Differential Diagnosis

There are few diseases of rabbits that would be confused with this disease. Pulmonary pasteurellosis (snuffles) causes a severe pneumonia in rabbits and is one of the most common diseases of rabbits (4). However, this disease causes an obvious pneumonia, consolidation of the lungs, and abscesses, which are not features of VHD. A severe bacteremia or septicemia with secondary disseminated intravascular coagulation (DIC) is more likely to be confused with VHD. This may cause hemorrhages in multiple organs and multifocal liver necrosis (rather than diffuse). Enterotoxemia due to *E. coli* or *Clostridium perfringens* Type E can cause such a hemorrhagic syndrome (23,25). This is often associated with oral administration of antibiotics to rabbits.

Treatment

There is no treatment for this disease. Most rabbits have a peracute disease course and are found dead.

Vaccination

Several vaccines have been developed and are used where VHD is endemic (2,11,24) . All of these vaccines are made from inactivated virus prepared from infected rabbit liver extracts. Vaccinated rabbits develop protective antibody in 5-10 days and must be revaccinated after 6 months. Owing to the short incubation time and rapid death, vaccination in the face of an outbreak is problematic. Many rabbits are likely to be exposed before they are fully protected by the vaccine. Many may survive, but it is uncertain whether some will shed virus as recovered rabbits have been shown to do experimentally.

Control and Eradication

Countries free of this disease should restrict the importation of rabbits, frozen rabbit carcasses, raw rabbit pelts, and angora wool from countries where VHD is endemic. Vaccination should be considered only if eradication is not possible or if the disease becomes endemic in susceptible wild populations.

Blood and liver of infected rabbits may contain more than a million viral particles per gram. The virus is stable in blood for at least 9 months at 4° C and much longer frozen. Therefore, frozen rabbit meat imported from countries where the disease is endemic is a particularly likely source of virus introduction. Rabbit producers are often consumers of rabbit meat, thus raising the

likelihood of contact with contaminated meat and transmission to susceptible rabbits. The disease could also inadvertently be introduced by purchasing breeding stock or raw angora wool from an endemic area. Rabbits are known to shed virus for at least 4 weeks after clinical recovery from this disease. Because clinically normal rabbits may be imported from any country into the United States without restriction, testing or quarantine, imported rabbits could easily be a source of an outbreak.

In Europe, where VHD has become endemic in both the domestic and wild populations of rabbits, control is based on strict sanitation, maintenance of closed rabbit colonies, and vaccination of breeding stock. Fecal contamination of forage by wild rabbits before it is harvested and used as feed for domestic rabbits remains a continuing source of viral exposure (17).

In countries where wild rabbits are not susceptible, eradication is feasible and should be attempted. Mexico chose to eradicate VHD because rabbits were recognized as an important source of animal protein that was produced with limited amounts of forage. The epizootic was controlled by depopulating the rabbits from affected areas, disinfection, inspection of facilities, introduction of sentinel rabbits after 30 days, and repopulation with government-raised rabbits. Continued serologic surveillance aided in the elimination of new outbreaks and possible carrier rabbits. A vaccine was not used in Mexico because it would have masked the disease and made serologic surveillance impossible.

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Fig. 126. VHD - VHD-infected rabbit with terminal serosanguinous nasal discharge.

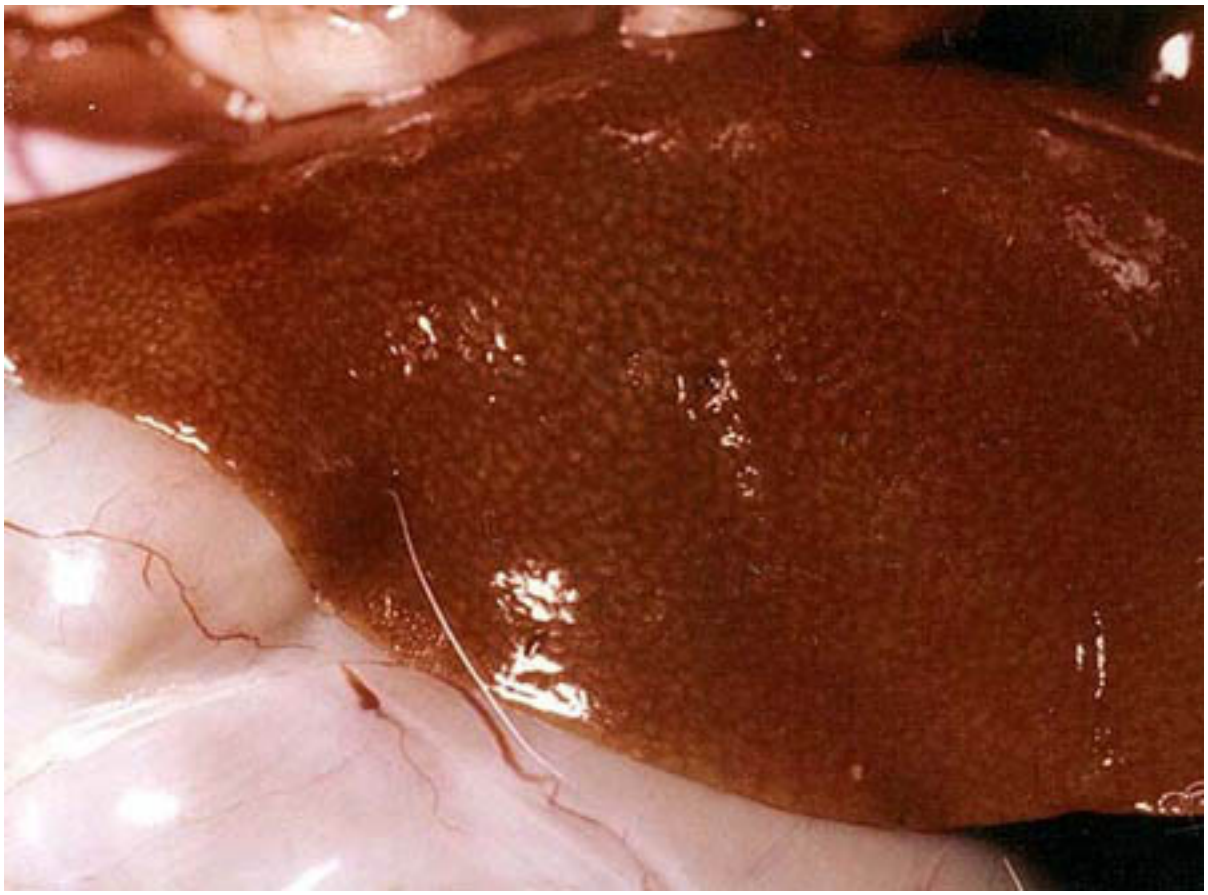

Fig. 127. VHD – Liver from a VHD-infected rabbit. Note the diffuse fine reticular pattern of hepatic necrosis.

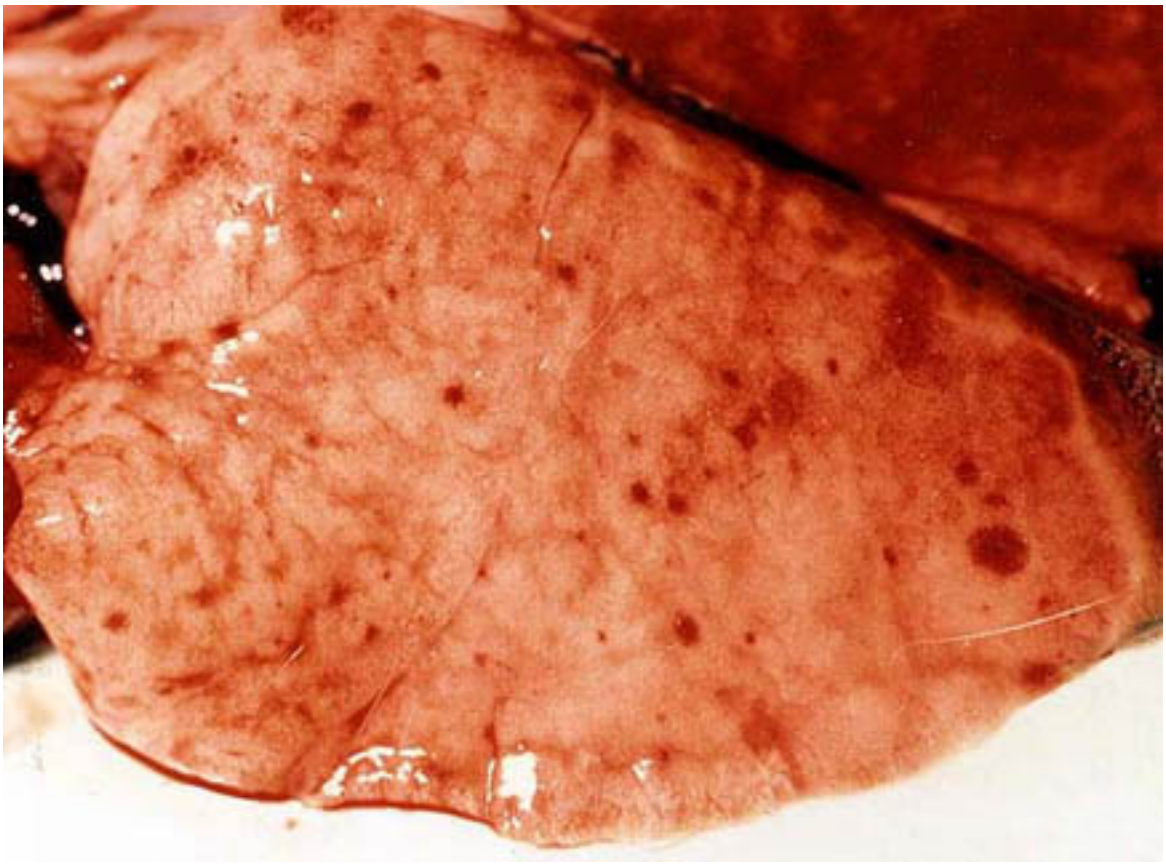

Fig. 128. VHD - Lungs from a VHD-infected rabbit. The lungs are edematous, congested, and have multiple hemorrhages.

PART V
APPENDIXES

APPENDIX 1

FOREIGN ARTHROPOD PESTS OF LIVESTOCK

Groups and species of foreign arthropod pests of livestock are listed below. Certain species of some of the groups occur in the United States.

CATEGORY A - Highest potential for introduction, establishment, and economic impact

COMMON NAME	SCIENTIFIC NAME
Brown Ear Tick	*Rhipicephalus appendiculatus*
Cattle Tick	*Boophilus annulatus*
Southern Cattle Tick	*Boophilus microplus*
New World Screwworm	*Cochliomyia hominivorax*
Sheep Scab Mite	*Psoroptes ovis*
Tropical Bont Tick	*Amblyomma variegatum*
Bont Tick	*Amblyomma hebraeum*
European Castor Bean Tick	*Ixodes ricinus*
Licking Fly	*Musca vitripennis*
Louse Fly	*Hippobosca longipennis*

CATEGORY B - Of particular concern for introduction, establishment, and economic impact.

COMMON NAME	SCIENTIFIC NAME
Hard Ticks	*Amblyomma* spp.
	Dermacentor spp.
	Hyalomma spp.
	Ixodes spp.
Soft Ticks	*Argas* spp.

	Ornithodoros spp.
Louse Flies	*Hippabosca* spp.
Mosquitoes	*Aedes* spp.
	Anolpheles spp.
	Culex spp.
Muscoid Flies	*Musca* spp.
Tsetse Flies	*Glossina* spp.

CATEGORY C - Some potential for introduction, establishment, and economic impact.

COMMON NAME	**SCIENTIFIC NAME**
Biting Midges	*Ceratopogonidae*
Black Flies	*Simulidae*
Bot Flies	*Oestridae*
Eye Gnats	*Chloropidae*
Flesh Flies	*Sarcophagidae*
Hard Ticks	*Ixodidae*
Horse Flies	*Tabanidae*
Mosquitoes	*Culicidae*
Muscoid Flies	*Muscidae*
Robust Bot Flies	*Cuterebridae*

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PART V
APPENDIXES

APPENDIX 2

PREPARATION AND SUBMISSION OF SPECIMENS FOR LABORATORY EXAMINATION

Confronting a Suspicious Foreign Animal Disease Case

The capability of a laboratory to confirm the diagnosis of a suspected exotic animal disease is directly related to the types, amounts, and conditions of the specimens submitted. The field diagnostician must select, aseptically procure, and properly preserve specimens for the isolation or demonstration of a causative agent. In addition, an adequate number of specimens must be taken from the appropriate tissues, at the proper stage of the disease, to maximize the chances of isolating the pathogen. The herd or flock owner, private practitioner, and diagnostic laboratory comprise a front-line defense and will, most likely, be confronted with the initial case of an exotic disease. It is vitally important that these people contact the State Veterinarian or Federal Veterinarian in Charge (FVIC) as soon as possible if a foreign animal disease (FAD) is suspected. The State or Federal official will, in turn, assign the suspicious case to a FAD diagnostician for immediate investigation.

A cadre of trained FAD diagnosticians exists throughout the country. These diagnosticians are on call at all times and are trained to investigate suspicious cases of exotic diseases of livestock and poultry. The FAD diagnostician is responsible for collecting and couriering specimens to a reference laboratory such as the National Veterinary Services Laboratories on Plum Island in New York or in Ames, Iowa, for a laboratory assessment.

Speed and efficiency in detecting, reporting, and diagnosing a newly introduced livestock or poultry disease are essential in preventing the disease from becoming widespread in the United States.

When the existence of a FAD is suspected, no animal or specimen should be removed from the premises of origin unless in the custody of an officially designated FAD diagnostician. Animals should not be moved from the premise until a diagnosis is obtained.

Specimen Preparation

The following general suggestions are presented as a guide for preparing diagnostic specimens for submission to a diagnostic laboratory. Developmental studies on new diagnostic procedures are in progress for certain diseases; therefore, it is wise to contact the diagnostic laboratory (see address at end of the appendix) in addition to the State Veterinarian or Federal Veterinarian for information on special handling that may be necessary.

An initial incursion of an exotic disease will, in most cases, only be confirmed in a reference laboratory through the isolation and identification of the etiologic agent. Thus, specimens to be submitted for agent identification should be collected as aseptically and completely as possible.

Disease investigation and specimen collection must be done thoroughly and properly to avoid a return visit and a need to repeat specimen collection and submission, which would only delay the laboratory diagnosis.

Prenecropsy Procedures

1. Obtain and record a complete herd history. Information should be submitted on proper forms (VS 12-27 or APHIS Form 8004) when possible; the following information should be included:

(a) Name and address of owner.

(b) Name, address, and phone number of submitter.

(c) A description of animal: breed, sex, peculiarities, etc.

(d) Suspected disease or examinations requested, or both.

(e) Number of animals showing signs and their ages.

(f) Number of animals dead.

(g) Vaccines administered to the animal(s) from which specimens were collected-especially important when examinations for antibodies will be conducted.

(h) Dates of the first losses and of subsequent losses.

(i) The disease signs and their duration.

(j) Ration fed.

(k) The condition of the animal.

(1) A description of the spread of the infection, if in a flock or herd. A diagram of the area is often useful.

(m) Treatment, if any.

(n) Type of housing.

(o) Accessory information; the type of preservative used for specimens.

(p) An epidemiological assessment, including recent movements into and out of the flock or herd.

(q) Any exposures of the affected poultry or livestock to persons having traveled abroad or foreign visitors.

2. Be objective and approach the investigation without a preconceived diagnosis.

3. Be alert to safety hazards in handling livestock and consider zoonotic potentials. As an example, the possibility of rabies as a differential diagnosis should be considered where appropriate.

4. Ensure that prelabeled specimen containers and tubes are available for collection and are scrupulously clean and sterile. The label must include proper identification of the animal and type of specimen.

5. Examine and collect specimens from live animals or poultry in various stages of clinical disease. Serum, vesicular fluid or tissue, or both, swabs of exudates or lesions, or both, can be secured from live animals. Serum from apparently healthy exposed animals or poultry can also be helpful. Animals sampled should be permanently identified because it is possible that convalescent serums or samples will be taken in the future for comparative purposes.

6. Blood smears should be prepared on clean glass slides. A thin blood film should be made, rapidly dried, and fixed in absolute methanol for 5 minutes. Slides having a frosted end should be used and should be identified using a lead pencil.

Unstained films should be protected from dust, insects, and abrasion and should not be refrigerated.

Obtaining Specimens at Necropsy

1. Necropsy and collect specimens from animals that have died and have undergone minimal putrefaction.

2. If it is possible to select several live animals for necropsy, try to select animals in various stages of clinical disease.

3. Be aware of any safety or biological hazards that necropsy might impose on you and the owner. Availability of a proper and safe disposal site should be considered before beginning necropsies.

4. Do not conduct necropsies while wearing street clothes. Wear rubber boots, gloves, overalls, etc., that can be disinfected or that are disposable. A mask and goggles may be used at the discretion of the diagnostician.

5. Prelabeled specimen containers will help ensure that recommended specimens will be collected.

(a) Use a label that cannot be easily destroyed. For instance, surgical tape should go entirely around the vial so that it will not be dislodged by moisture.

(b) Writing should be with pencil or ink that will not smudge or blur when wet.

(c) Use plastic screw-capped containers instead of glass containers where practical.

(d) Tape the lids of containers. Tape should be wound around the cap in the same direction as the screw-cap is applied.

(e) Use disposable equipment such as cardboard trays, disposable syringes, etc.

6. Have a systematic plan for the necropsy and know what specimens are to be collected before starting the proceedure. Be certain to include all lesions for laboratory examination. Body fluids and contents of cysts, abscesses, or skin lesions can be collected using a sterile swab. If an animal is presented for euthanasia, collect all blood samples before euthanizing. If the animal or bird is presented dead, collect blood from the heart. Make blood smears as previously discussed. Ectoparasites should be noted and collected, if pertinent.

The collection of specimens based on species rather than a specific disease will be most useful in providing a diagnosis. The specimens listed in the Table of Specimen Collection are the minimum recommended and are not intended to replace the field diagnostician's judgment concerning the collection of additional specimens. In addition to the listed specimens, samples of all lesions should be collected for histologic examination. Toxicology-related problems have not been given consideration in these recommendations.

7. Fluid from any enlarged joints should be aspirated aseptically.

8. Any excess body cavity fluids should be collected aseptically via a syringe.

Other Considerations in Specimen Collection

1. Two sets of tissues are to be collected.

a. Fresh tissue for microbiological examination: Any tissue that is to be preserved in a refrigerated or frozen state should be placed in a separate container.

b. Preserved tissue for histological examination: The recommended preservative is 10 percent neutral buffered formalin. All tissues can be placed in one container, but allow no more than 1 volume of tissue to 10 volumes of formalin. Tissues from organs should be cut perpendicularly to the surface to expose their anatomic structure. The specimen should include affected and surrounding normal tissue. To provide adequate fixation, tissues except for the brain, should be sliced no more than 3 to 6 mm thick. Any lymph nodes collected should be incised.

Specimens should not be folded or bent by the container in which they are fixed. Only wide-mouthed containers should be used in this procedure.

2. The initial piece of each organ or lesion should be collected aseptically for microbiology. Tissues for formalin fixation can be collected during the necropsy.

3. Swabs should be sent in appropriate transport medium (e.g., Tris-buffered typtose broth). The laboratory can assist in the proceedure for obtaining this media.

4. Materials submitted for possible virus isolation should be obtained from animals that died and have minimal putrefaction and from animals in the early, acute, febrile phase of illness. A reliable overnight delivery service should be used (the laboratory can recommend a service that has been effective in providing this service). Specimens shipped for virology and bacteriology should be shipped refrigerated. If at all possible, the use of dry ice should be avoided because the CO2 will produce acid conditions that will inactivate many viruses. If there is no way to get the specimens to the laboratory within 48 hours, dry ice must be used. In this case, the specimens must be completely sealed so that there is no contact of the gas emitted by the dry ice with the specimens.

Postnecropsy Considerations

1. Clean and decontaminate instruments.

2. Clean and disinfect all work surfaces and dispose of, or clean and disinfect, personal effects.

3. Record necropsy findings.

4. Dispose of carcasses and body parts so as to avoid exposure of other animals and contamination of environment.

Considerations for Shipping Diagnostic Specimens

Regulations require that diagnostic specimens transported in interstate traffic must be packaged and labeled properly. Improper packaging and labeling of diagnostic specimens and other hazardous materials can result in unnecessary exposure to postal, shipping, and laboratory personnel.

1. The specimens must be in securely closed, watertight primary enclosures such as a screw-cap container or sealed vial. Be certain that exterior surfaces of the primary containers are decontaminated before shipment.

2. Each primary container should be wrapped in sufficient dry absorbent cotton or paper towels to absorb the material in case of breakage. Ideally, the wrapped container should be placed in sealed plastic bags.

3. Pint-, quart-, or half- gallon-sized paint cans should be used as secondary containers. These cans should have friction-type lids and be watertight when hammered closed. The primary container should be padded with more cotton or paper to prevent jarring. A tertiary container, such as a larger-sized version of the secondary container, should be considered if a zoonotic or highly infectious FAD is suspected.

4. The sealed secondary or tertiary container should be placed in a shipping container and again packed with material such as paper. The shipping container should be an insulated box with a lid that can be taped shut. A corrugated shipping box, affixed with the proper labels and shipper's certification, is the final enclosure and contains all other containers.

5. If specimens can be in transit for less than 48 hours, ice packs may be used for cold storage. Frozen "foam ice," "blue ice" picnic packs, or water frozen in sealed containers may be used. Wet ice, even when wrapped in plastic bags, should be avoided to eliminate the possibility of leakage.

6. Dry ice is the only suitable refrigerant to keep specimens frozen. Shippers must be aware of dry ice restrictions imposed by certain airlines and plan according.

7. Regular mail or airmail shipment should not be used when a FAD is suspected. Courier service is the appropriate method of shipment. If FMD is considered as a possible diagnosis, a responsible individual should handcarry the specimen to the reference laboratory.

8. It is not desirable to have the submission form, with the history and other information, within the container. It is preferable to enclose the submission form between the shipping container and the cover of the outside corrugated box.

9. The shipper is responsible for notifying the intended recipient of all information relative to transportation arrangements in order to expedite package pickup and delivery to the laboratory.

10. Care must be taken to ensure that a FAD-suspicious package is only opened within the confines of a biosecure facility.

Reference Laboratory Contacts

1. Foreign Animal Disease Diagnostic Laboratory, P.O. Box 848, Greenport, LI, NY 11944-0848, Phone: (516) 323-2500, Ext. 256.

2. National Veterinary Services Laboratories, P.O. Box 844, Ames, IA 50010, Phone: (515) 239-8266.

L.M. Siegfried, D.V.M., USDA, APHIS, VS. Area Veterinarian in Charge. 2301 N. Cameron St. Rm. #412, Harrisburg, PA 17110

TABLE OF SPECIMEN COLLECTION

SPECIES	TISSUES FOR MICROBIOLOGICAL AND HISTOLOGICAL EXAMINATION	BLOOD SAMPLES	OTHER
Bovine	Skin and nasal swabs, prescapular lymph node (LN), body cavity fluids, joint fluid, liver, kidney, mesenteric LN, lung, heart, tracheal swab, 3" tied-off section of small intestine and ileum (affected area if present),1/2 brain, any specific lesion	Serum, 20 ml Whole blood, 20 ml (hepanized), 6 Blood smears - air dried, fix in methanol	External parasites (alcohol)
Porcine	Skin swab, fluid from any affected joint, body cavity fluid, spleen, liver, kidney, gastrohepatic and mesenteric LN, lung, tonsil, 3" tied off section of small intestine and colon, 1/2 brain, and any specific lesion	Serum, 10 ml Whole blood, 20 ml (hepanized), 6 blood smears - air dry, fix in methanol	External parasites (alcohol)

Equine	Prescapular LN, mandibular LN, body cavity fluids, spleen, liver, kidney, mesenteric LN, 1/2 brain and any specific lesion. Swabs if contagious equine metritis suspected. Mares - cervical, urethral, clitoral Stallions - penile, sheath, urethral fossa, urethra	Serum, 20 ml Whole blood 20 ml (hepanized), 6 blood smears air dry, fixed in methanol	External parasites (alcohol)
Ovine	Skin and nasal swab, prescapular LN, mammary tissue, body cavity fluids, spleen, liver, kidney, mesenteric LN, lung, mediastinal LN, tracheal and bronchial swabs, 1/2 brain and any specific lesion	Serum, 10 ml Whole blood 10 ml (hepanized), 6 blood smears air dry and fix in methanol	External parasites (alcohol)
Avian	Tracheal and Nasal swabs, liver, spleen, liver, lung, trachea, bone marrow, heart, ovary, brain, intestine, and any specific lesion	Serum, 2 ml, Hepanized terminal blood	External parasites (alcohol)
Vesicular	Vesicular fluid (all that is obtainable), vesicular lesion epithelium, flaps of epithelial tissue, esophageal-pharyngeal fluid (10 ml before dilution with Tris Buffered Tryptose Broth). In addition, if dead—prescapular LN, adrenal, kidney, thyroid, heart, tonsil, mandibular LN	Serum, 10 m	

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APPENDIXES

APPENDIX 3

CLEANING AND DISINFECTION

Thorough cleaning and disinfection of premises, buildings, pens, enclosures, equipment, personal protective clothing and vehicles that have been contaminated with manure, urine, and other discharges from infected animals are accomplished in the following order: removal and decontamination of bulky material by composting, burning, burying or chemical treatment; washing with water and detergent and finally the application of a disinfectant. The above procedures in some cases may not be relied upon to destroy all of the disease- causing organism under all conditions. An appropriate interval may be necessary after disinfection to permit the natural destruction of any surviving organisms before susceptible animals can again safely come in contact with the premise or items in question.

Vector control and eradication is an integral part of the disease eradication process in those instances where vectors are the sole or contributing factors in disease transmission.

The effective virucidal concentration of many disinfectant formulations has been demonstrated previously in successful decontamination programs and in laboratory studies. One need not commit the names of these compounds to memory, for representatives of three core disinfectant formulations can be used with confidence in an emergency situation against those disease agents of concern.

Examples of these are sodium hypochlorite (Compound No. 1), sodium hydroxide (Compound No. 2), and substituted phenolic compounds (Compound No. 3). The field veterinarian must be prepared for emergencies by having a combination of either Compound No. 1 or 2 plus Compound No. 3.

There are citations in the literature regarding the corrosiveness of Compounds Nos. 1 and 2; however, the immediate goal of a cleaning and disinfection program is to stop the spread of disease.

Compound No. 1

Sodium hypochlorite (NaOCL) or household bleach (stock concentration 5.25 percent available chlorine). This compound is effective against microbial agents of diseases, including ASF, FMD, HC, SVD, and VND at a concentration of 0.1 percent. It can be prepared at the time of use by adding approximately 30 cc (ml) of household bleach 10 a gallon of water. OR 1 gallon of bleach plus 50 gallons of water.

In areas heavily contaminated with secretions, excretions, and soil, there is a considerable organic demand for available chlorine. Therefore, the procedure must be repeated at least once. In fact, under such conditions a 3 percent solution of NaOCL should probably be used. To prepare this concentration, add 3 gallons of bleach to 2 gallons of water. This concentration is effective against a variety of agents of viral diseases such as the following:

African Swine Fever	Pest of Small Ruminants
African Horsesickness	Rift Valley Fever
Avian Influenza	Rinderpest

Bluetongue	Sheep and Goat Pox
Bovine Ephemeral Fever	Swine Vesicular Disease
Contagious Bovine Pleuropneumonia	Velogenic Newcastle Disease
Contagious Caprine Pleuropneumonia	Venezuelan Equine Encephalomyelitis
Foot-and-Mouth Disease	Vesicular Exanthema of Swine
Hog Cholera	Japanese Encephalitis
Lumpy Skin Disease	Malignant Catarrhal Fever

Compound No. 2

Sodium hydroxide (NaOH), or lye, is available as crystals and can be obtained from pharmacies, grocery stores, agricultural supply stores, and often from a residence on the premises. It can be prepared as a 2 percent solution by mixing 1/3 cup of NaOH pellets per gallon of water.

Lye has a wide viral spectrum when used at this concentration (see the above list). However, it has limited effect against the viruses of ASF and HC. A considerably higher concentration is required to be effective (1).

Compound No. 3

Substituted phenolic compound. These compounds, such as One-Stroke Environ,* have potent virucidal activity against the viruses of ASF and HC when prepared as a 1 percent solution of stock disinfectant. A 1 percent concentration of the disinfectant must provide the following minimum concentrations of active ingredients:

Active Ingredient Percentage

o-benzy-p-chlorophenol 0.085 percent

o-phenylphenol 0.1 percent

p-tertiary amphylphenol 0 .02 percent

It can be prepared as a 1 percent solution by adding 38 cc(ml) or about 1 1/2 oz. of stock disinfectant per each gallon of water.

These types of compounds are effective against the viruses of African swine fever, avian influenza, hog cholera, and Newcastle disease.

These types of compounds are not effective against the viruses of FMD and SVD.

Other Disinfectant Compounds of Importance

We should mention the extremely effective virucidal activity of certain acidified iodophor compounds containing a generic formulation of polyethoxy-substituted polypropoxy-ethane complex. The active ingredient must provide a minimum use concentration of 0.02 percent titratable iodine. Some of these products are sold under the brand names of Vanodine,* FAM 30,* and Biocid.* At this time, however, these compounds are not available in the United States.

Two newer disinfectants are Oxine,* a chlorine dioxide disinfectant, and VerKonS,* a strong oxidizing disinfectant. These disinfectants are effective against viruses, bacteria, fungi, and

spores, are essentially nonirritating, and are biodegradable.

Regarding the decontamination of aircraft, USDA, Animal and Plant Health Inspection Service, on the basis of research done by the aircraft industry, has shown that a 4 percent solution of sodium carbonate containing 0.1 percent sodium silicate has significant virucidal activity. Such a solution can be prepared by adding crystals of the chemicals to water in the following ratios:

Sodium carbonate Sodium silicate Water

1 lb (453g) 1 tablespoon (4.0 g) 3 gallons

6 lb (2.5 kg) 1 cup (24g) 19 gallons

GUIDE TO THE LITERATURE

1. STONE, S.S., and HESS, W.R. 1972. Effects of some disinfectants on African swine fever virus. Appl. Microbiol., 24:115122.

* Oxine — Bio-Cide Int., Inc., Norman, OK; VirKon S, Antec Int., distributor — DURVET, Bluesprings, MO.

* Disclaimer: Trade names are used in this publication solely to provide specific information. Mention of a trade name does not constitute a guarantee or warranty of the product by the U.S. Animal Health Association or an endorsement by the Association over other products not mentioned.

J. H. Blackwell, Ph.D., USDA. APHIS, VS, retired

PART V
APPENDIXES

APPENDIX 4

VETERINARY MEDICAL TRAINING FILMS AND VIDEOS

This appendix lists U.S. Department of Agriculture films (16 mm) and videos (VHS) that are available from several sources, including, in some instances, cooperating extension libraries of the land grant universities (a list of their addresses follows the listing of films and videos).

"APHIS-First Line of Defense" (20 min. -1980)

> In a nontechnical manner describes how APHIS agricultural quarantine inspection activities protect American agriculture from exotic pests and diseases.
>
> Contact: Regional APHIS Plant Protection and Quarantine offices
>
> or
>
> United States Department of Agriculture
>
> Animal and Plant Health Inspection Service
>
> Legislative and Public Affairs
>
> 4700 River Road, Unit 51
>
> Riverdale, MD 20737-1231

"BAI; A Century of Service" (VHS -22.5 min -1984)

> Describes advances in the health of the Nation's livestock since the founding of the Bureau of Animal Industry in 1984.
>
> Contact: Area APHIS Veterinary Services Offices
>
> or
>
> United States Department of Agriculture
>
> Animal and Plant Health Inspection Service
>
> Veterinary Services, Operational Support
>
> 4700 River Road, Unit 33
>
> Riverdale, MD 20737-1231

Biosecurtiy and the Poultry Industry Series (VHS varying lengths 1989)

> Shows how the different segments of the poultry industry can protect their operations from the introduction of diseases:
>
> "What Is Biosecurity?" (15 min)
>
> "Broiler Operations" (11 min)
>
> "Live Poultry Markets" (11 min)
>
> "Egg-Laying Operations" (11.5 min)
>
> "Hatcheries" (12 min)

Foreign Animal Disease Series (varying lengths -1970's)

This series discusses the clinical aspects -signs and lesions- of the following foreign animal diseases:

"African Horse Sickness" (11 min)

"African Swine Fever/Hog Cholera" (13 min)

"Contagious Bovine Pleuropneumonia" (9 min)

"Ephemeral Fever" (13 min)

"Exotic Newcastle Disease" (11 min)

"Foot-and-Mouth Disease" (15 min)

"Malignant Catarrhal Fever" (12 min)

"Rinderpest" (11 min)

"Sheep Pox/Goat Pox" (10 min)

"Swine Vesicular Disease" (8 min)

Contact: Area APHIS Veterinary Services Offices

or

United States Department of Agriculture

Animal and Plant Health InspeWction Service

Veterinary Services, Operational Support

4700 River Road

Riverdale, MD 20737-1231

"Pseudorabies in Swine" (22 min -1980)

Describes the disease in swine and other animals with emphasis on its signs, how it spreads, and how it affects hog production.

Contact: Area APHIS Veterinary Services Offices

or

United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services, Operational Support

4700 River Road

Riverdale, MD 20737-1231

"Task Force: Exotic Newcastle Disease" (28 min -1973)

Presents the story of how exotic Newcastle disease was eradicated from poultry in southern California in 1971-73.

Contact: Area APHIS Veterinary Services Offices

or

United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services, Operational Support

4700 River Road

Riverdale, MD 20737-1231

For videos on biosecurity for swine production, salmonella training, or on feral swine contact:

United States Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services, Operational Support
4700 River Road, Unit 33
Riverdale, MD 20737-1231

Instructional packages on FAD recognition

These instructional sets consist of a video of clinical signs and necropsy lesions, 2 by 2 slides, and a narrative.

Program Aid 1576 African horsesickness
Program Aid 1577 African swine fever
Program Aid 1578 Contagious bovine pleuropneumonia
Program Aid 1579 Lumpy skin disease, sheep pox, goat pox
Program Aid 1580 Malignant catarrhal fever
Program Aid 1581 Rinderpest, Peste des petites ruminants
Program Aid 1582 Vesicular diseases

Contact: Area APHIS Veterinary Services Offices
or
United States Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services, Emergency Programs
4700 River Road, Unit 41
Riverdale, MD 20737-1231

LEARNING AND REFERENCE CD-ROM's

These interactive CD-ROM's are exercises that allow an individual to perform a field investigation of specific exotic diseases from the initial phone contact through the diagnosis. Also included is information on the industry and a library containing chapters on the diseases of concern.

Hog cholera (Classical swine fever) and African swine fever
Vesicular diseases of swine
Vesicular diseases of cattle
Exotic Newcastle disease and avian influenza

Contact: Area APHIS Veterinary Services Offices
or
United States Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services, Emergency Programs
4700 River Road, Unit 41
Riverdale, MD 20737-1231

LAND GRANT UNIVERSITY FILM LIBRARIES

Cooperative Extension Film Library
Auburn University
Auburn, Alabama 36830
Division of Libraries
Pouch G
Juneau, Alaska 99801

Film Library
University of Arizona
Media & Instructional Services Bldg.
Tucson, Arizona 85721

Cooperative Extension Film Library
University of Arkansas
P.O. Box 391
Little Rock Arkansas 72203

Visual Aids
Cooperative Extension Bldg-Lobby
University of California
Riverside, California 92521

Film Library
Office of Educational Media
Colorado State University
Fort Collins, Colorado 80521

Audiovisual Center
University of Connecticut
Storrs, Connecticut 06268

Cooperative Extension Film Library
University of Delaware
Agricultural Hall
Newark, Delaware 19711

Motion Picture Service
Florida Cooperative Extension
University of Florida
Gainesville, Florida 32601

Film Library
Cooperative Extension Service
College of Tropical Agriculture
University of Hawaii
2500 Dole Street
Room 108
Honolulu, Hawaii 96822

Audiovisual Center
University of Idaho
Moscow, Idaho 83843

Visual Aids Service
University of Illinois
Division of University Extension
1325 South Oak
Champaign, Illinois 61820

Audiovisual Center
Purdue University
Stewart Center
West Lafayette, Indiana 47907

Media Resources Center
Iowa State University
Pearson Hall
Ames, Iowa 50010

Cooperative Extension Service
Film Library
Kansas State University
Umberger Hall
Manhattan, Kansas 66502
Audiovisual Center
University of Kentucky
Scott Street Building
Lexington, Kentucky 40506

Film Library

Cooperative Extension Service
Film Library
University of Georgia
Athens, Georgia 30601
Instructional Systems Center
University of Maine
Orono, Maine 04473

DC and Maryland borrowers, please
inquire at the nearest library or
the National Audiovisual Center,
GSA Archives Washington, DC 20409
Tel: (301) 763-1896
Krasker Film Library
School of Education
Boston University
765 Commonwealth Avenue
Boston, Massachusetts 02215

Instructional Media Center
Michigan State University
East Lansing, Michigan 48823
Agricultural Extension Service
Film Library
University of Minnesota
St. Paul, Minnesota 55101
Cooperative Extension Service
Film Library
Mississippi State University
Mississippi State, Mississippi 39762

Campus Film Library for Cooperative Extension Service
Montana State University
Bozeman, Montana 59715

University of Nebraska
Instructional Media Center
901 North 17th
Room 421
Lincoln, Nebraska 68508

Cooperative Extension Service
Louisiana State University
Knapp Hall
University Station
Baton Rouge, Louisiana 70803

Audio Visual Center
University of New Hampshire
Hewitt Hall
Durham, New Hampshire 30824

Communications Center
College of Agriculture and Environmental Science
Rutgers University
New Brunswick, New Jersey 08903

Cooperative Extension Service
Film Library
New Mexico State University
Drawer 3A1
Las Cruces, New Mexico 88003
Cornell University Film Library
55 Judd Falls Road
Ithaca, New York 14853

Department of Agricultural Information
North Carolina State University
P.O. Box 5037
Raleigh, North Carolina 27607

Cooperative Extension Service
Film Library
North Dakota State University
State University Station
Fargo, North Dakota 58102

Audio Visual & Comn. Services
University of Missouri
203 Whitten Hall
Columbia, Missouri 65201

Audio Visual Center
University of Nevada
Reno, Nevada 89507

Audiovisual Instruction
DCE Building
P.O. Box 1383
Portland, Oregon 97207

Extension Service Film Library
Ohio State University
2021 Coffey Road
Columbus, Ohio 43210
Tel: (614)422-2011

Audiovisual Center
Oklahoma State University
Stillwater, Oklahoma 7407

Agricultural Extension Service
Pennsylvania State University
104 Agricultural Adm. Bldg.
University Park, PA 16802

VETERINARY MEDICAL FILMS

Agricultural Extension Service
University of Puerto Rico
Mayaguez Campus
Rio Piedras, Puerto Rico 09928

Audiovisual Center
University of Rhode Island
Kingston, Rhode Island 02881

Agricultural Communications Dept.
Clemson University Extension Service
Room 92, Plant Animal Science Bldg.
Clemson, South Carolina 29631

Cooperative Extension Service
Film Library
South Dakota State University
Brookings, South Dakota 57006

Agricultural Communications
Texas A&M University
Room 201, Services Building
College Station, Texas 77843

Cooperative Extension Service
West Virginia University
215 Coliseum
Morgantown, WV 26506

University of Wisconsin
Bureau of Audio Visual Instruction
P.O. Box 2093
Madison, Wisconsin 53701

Audio Visual Services
The University of Wyoming
Laramie, Wyoming 82070

Teaching Materials Center
Division of Continuing Education
University of Tennessee
Knoxville, Tennessee 37916

The Audio Visual Center
University of Vermont
Ira Alen Chapel
Burlington, Vermont 05401

Audio Visual Services
Utah State University
Logan, Utah 84321

Audio Visual Center
Washington State University
Pullman, Washington 99163

Media Services
Virginia Polytechnic Institute
Patton Hall
Blacksburg, Virginia 24061

L.D. Mark, USDA, APHIS, LPA, Washington, DC

PART V
APPENDIXES

APPENDIX 5

GLOSSARY

AGENESIS - Incomplete or imperfect development.

ALOPECIA - Partial or complete loss of hair.

ANOREXIA - Absence of appetite.

ANTIGEN - Any substance that stimulates the production of antibody or reacts with antibody.

ARBOVIRUS - A virus transmitted by blood-sucking arthopods (e.g., mosquitoes and ticks).

ARTHROGRYPOSIS - Rigid fixation of the joints; usually in flexion but occasionally in extension.

ASCITES - An abnormal accumulation of serous (watery) fluid in the abdominal cavity.

ATROPHY - Reduction in size of a previously normal-sized organ.

BRACHYGNATHISM - An abnormally shortened lower jaw.

CROUPOUS MEMBRANE (synonym— diptheric membrane) - A fibrinous exudate that is readily loosened from the underlying tissue.

DERMIS - Layer of connective tissue between the epidermis and the subcutaneous tissue.

DIPTEROUS - Denotes an insect having two wings.

DYSCRASIA - A morbid condition, especially involving imbalances of essential bodily fluid components.

DYSPNEA - Difficult or labored breathing.

ECCHYMOTIC HEMORRHAGE - An area of hemorrhage somewhat larger than a petechia.

EMPHYSEMATOUS - Denotes accumulation of air in tissues or organs — especially applied to abnormal accumulations of air in the lungs.

ENDEMIC - Denotes a disease that occurs more or less constantly in any locality.

ENTEROCOLITIS - Inflammation of the small and large intestine.

ENZOOTIC - Denotes a disease present in a community at all times but that affects only a small number of animals.

EOSINOPENIA - A state of having a subnormal number of eosinophilic leukocytes in the blood.

EPENDYMA - The lining membrane of the cerebral ventricles and central canal of the spinal cord.

EPENDYMITIS - Inflammation of the ependyma.

EPIDEMIC - An unusual prevalence of a disease affecting large numbers over a wide area.

EPIDEMIOLOGY(epizootiology) - The study of epidemics; the science of dealing with the various factors that determine the frequencies and distribution of an infectious disease.

EPIDERMIS - The protective outer layer of the skin.

EPIGASTRIC - Pertaining to the upper middle part of the abdomen, including the area over and in front of the stomach.

EPIZOOTIC - Attacking many animals of one kind in any region simultaneously; widely diffused and rapidly spreading.

EROSION - Loss of a surface area by inflammation or trauma; does not involve deeper tissues.

ERYTHROCYTE - A red blood cell.

EXANTHEMA - An eruption on the skin.

FASCIA LATA - The connective tissue surrounding the muscles of the thigh.

FETID - Having a foul odor.

FOMITES - Substances that absorb, hold, and transport infectious disease agents.

HEMATEMESIS - The vomiting of blood.

HEMATOPHAGOUS - Denotes a bloodsucking insect.

HEMOGLOBINURIA - The presence of hemoglobin in the urine.

HYDRANENCEPHALY - Complete or almost complete absence of the cerebral hemispheres. The space is filled with cerebrospinal fluid.

HYDROPERICARDIUM - Excessive collection of serous fluid in the pericardial sac.

HYDROTHORAX - Excessive collection of serous fluid in the thoracic cavity.

HYPEREMIA - An increased amount of blood in a part with distention of blood vessels.

HYPOPLASIA - Defective development of any tissue, organ, limb, etc.

HYPOPYON - A collection of pus in the anterior chamber of the eye.

HYPOTHERMIC - Denotes a subnormal temperature of the body.

INFARCT - A region of dead tissue due to a complete interference with blood flow.

INTRACEREBRAL - In the cerebral hemisphere of the brain.

INTRAERYTHROCYTIC - In the red blood cell.

KYPHOSIS - Convex curvature of the spine.

LAPAROTOMY - An operation opening the abdomen by an incision through the abdominal wall.

LEPTOMENINGITIS - An inflammation of the membranes covering the brain and spinal cord.

LESION - An alteration in structure or function resulting from injury or disease.

LEUKOPENIA - A state of having a subnormal number of white blood cells in the blood.

LYMPHADENOPATHY- An enlargement of the lymph nodes.

MELENA - Black stools caused by bleeding in the stomach or small intestine.

MENINGOENCEPHALITIS - Inflammation of the brain and its membranes.

MICROENCEPHALY - A condition of having a smaller than normal brain.

MORBIDITY - The ratio of the number of sick animals to the total number of animals in the herd or flock.

MORTALITY - The ratio of the number of dead animals to the total number of animals in the herd or flock.

MUCOPURULENT - A creamy exudate consisting of mucus and cells (pus).

MUTAGEN - A substance that can cause a genetic change.

NECROTIC - Denotes a dead cell or group of cells in contact with living cells.

NYSTAGMUS - An oscillatory movement of the eyeballs.

OPHTHALMIA - An inflammation of the eye, especially one in which the conjunctiva is involved.

ORCHITIS - Inflammation of the testis.

PARENCHYMA - The essential or specialized part of an organ as distinguished from the supporting tissue.

PARESIS - A slight paralysis; weakness of a limb.

PARIETAL - Forming or situated on the wall.

PATHOGNOMONIC - Characteristic of a disease; denotes a factor distinguishing it from other diseases.

PERCUTANEOUS - Performed through the skin.

PETECHIAL HEMORRHAGES - Tiny hemorrhages not much larger than a point of a pin.

PHOTOPHOBIA - Intolerance or fear of light; hypersensitivity to light.

POLYARTICULAR - Affecting many joints.

PORENCEPHALY - Congenitally deficient development of the cerebral cortex and gray matter so that cystic cavities communicate with the brain surface.

PSEUDOMEMBRANE - A layer of fibrin that at times is dense and tough and forms a white or yellowish sheet over a surface.

PURULENT - Containing, consisting of, or forming pus.

RETINOPATHY - Any disease condition of the retina.

SCOLIOSIS - Lateral curvature of the spine.

SENTINEL - An animal used to detect the presence of a disease.

SEPTICEMIC - A systemic disease produced when a microorganism and its products are in the blood.

SEROSANGUINEOUS - Containing both serum and blood.

SPLENOMEGALY - Enlargement of the spleen.

STEATOSIS - Fatty degeneration.

SYNOVITIS - Inflamation of the lining of the joints.

THROMBOCYTOPENIA - A state of having a subnormal number of platelets in the blood.

TORTICOLLIS - Wryneck; a contraction of muscles in the neck resulting in an abnormal position of the head.

TRANSOVARIAL - Denotes passage through the egg to the next generation.

TRANSPLACENTAL - Passes through the placenta to the fetus.

TRANSSTADIAL - Passes from one stage of development to the next (e.g., nymphal to adult stage of the tick).

ULCERATION - A break in the continuity of the surface with exposure of the underlying tissue.

VASCULITIS - Inflammation of blood or lymph vessels.

VESICLE - A circumscribed cavity in the epidermis filled with serum, plasma, or blood and covered by a thin layer of epidermis that is greatly elevated above the surface.

VIREMIA - Presence of virus in the blood.

VIRULENCE - The disease producing power of a microorganism.

VISCERA - The internal organs of the body; especially those in the thoracic and abdominal cavities.

PART VI - PHOTOGRAPHS

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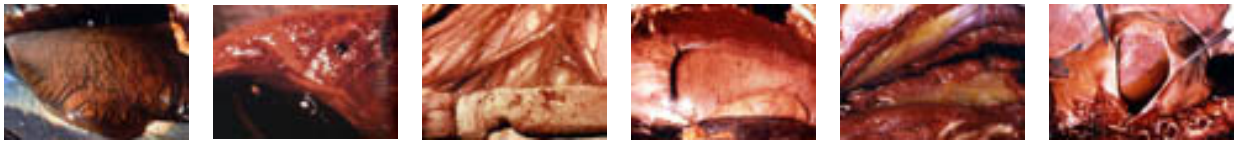

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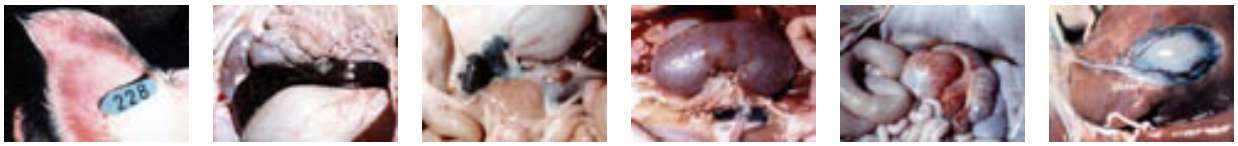

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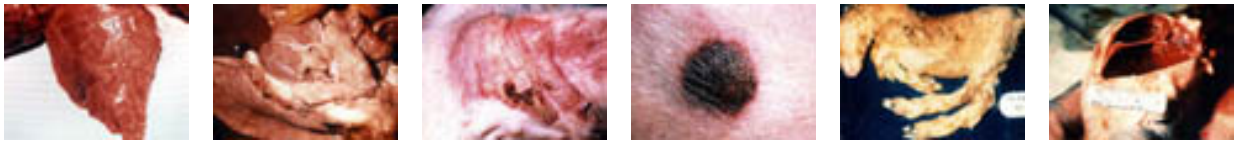

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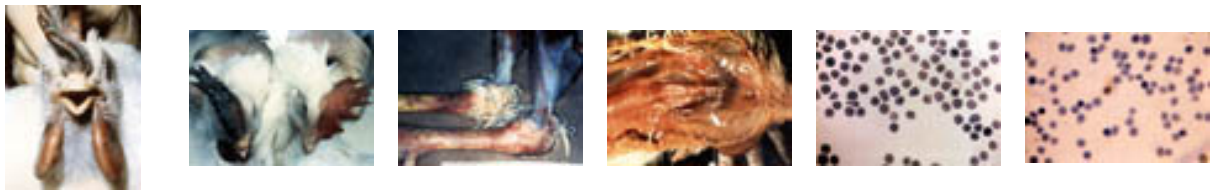

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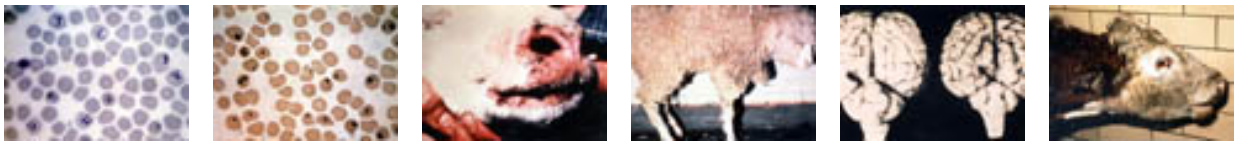

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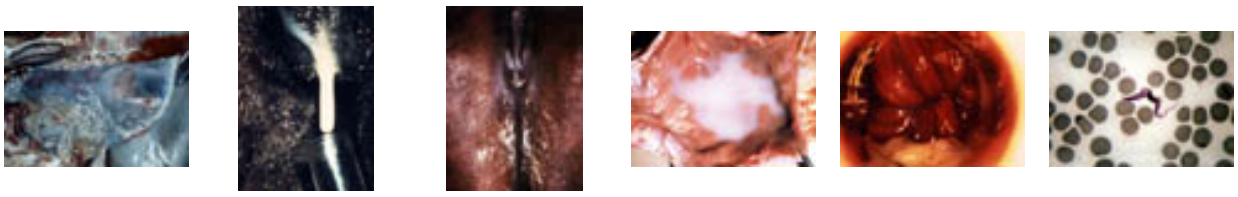

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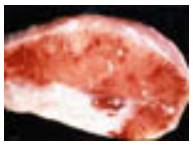
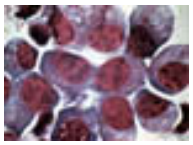
045.jpg 

046.jpg 

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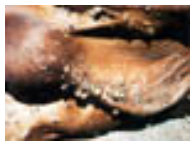
048.jpg 

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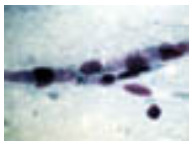
055.jpg 

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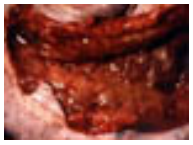
070.jpg 

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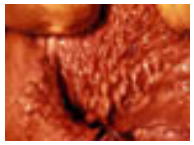
078.jpg 

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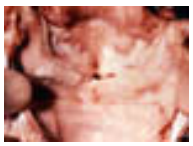
080.jpg 

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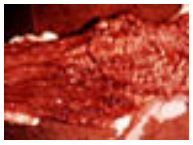
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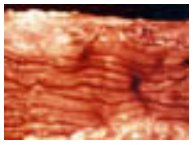
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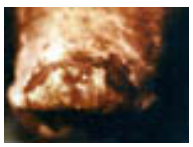
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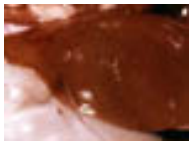
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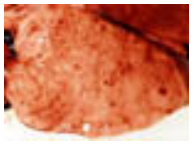
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