

Yayılıma / İşgale Karşı Sistemik Reaksiyon

Vücudun herhangi bir yerinde yangı veya doku tahribatı oluştuğu zaman, canlı- hayvan- vücudun tümünü korumaya yardım edecek reaksiyonlar oluşturarak cevap verir.

Bu sistemik cevaplar **Ateş, Neutophilia, Lethargy, Nihai kas zafiyeti** ve **Yeni Proteinlerin** sentezlenmesidir.

Bu reaksiyonlara Makrofajlardan salınan 3 cytokine tarafından aracılık yapılır.

Makrofajlardan köken alan 3 cytokine: **IL-1, IL-6, TNF- α** **Akut Faz Proteinlerinin** sentezlenmesini tetikler.

Akut Faz Proteinleri: (Akut faz cevabı/ reaksiyonu ;

1) Akut ya da kronik yangı sırasında ortaya çıkan patofizyolojik ve davranışsal değişiklikleri,

2) Yangı sırasında konsantrasyonları gerçekten değişen proteinleri tanımlamak için kullanılır.

Her iki halde de, konakçının adaptif cevabı söz konusudur ve bu cevabın teorik amacı konakçı hayvanı yaşatmak-kurtulmak ve iyileştirmek için daha iyi bir pozisyona erdirmektir.

IL-1, TNF- α ve özellikle IL-6'nın etkisiyle karaciğer epitel hücreleri protein sentezi ve salgılanmasını artırır. Hepatositlerin bu uyarımlara cevap vermesi, zedelenmeyi takiben bir iki saat içinde başlar ve 24-48 içinde sonuçlanır.

Bu proteinler

Complement component'leri

Pıhtılaşma faktörleri

Proteaz inhibitörleri

Metal Bağlayıcı proteinlerdir.

Bu proteinlerin bir kısmı azalırken (negatif) kimisi yükselme (pozitif) gösterir. Bunlar Türler arasında farklılıklar gösterir.

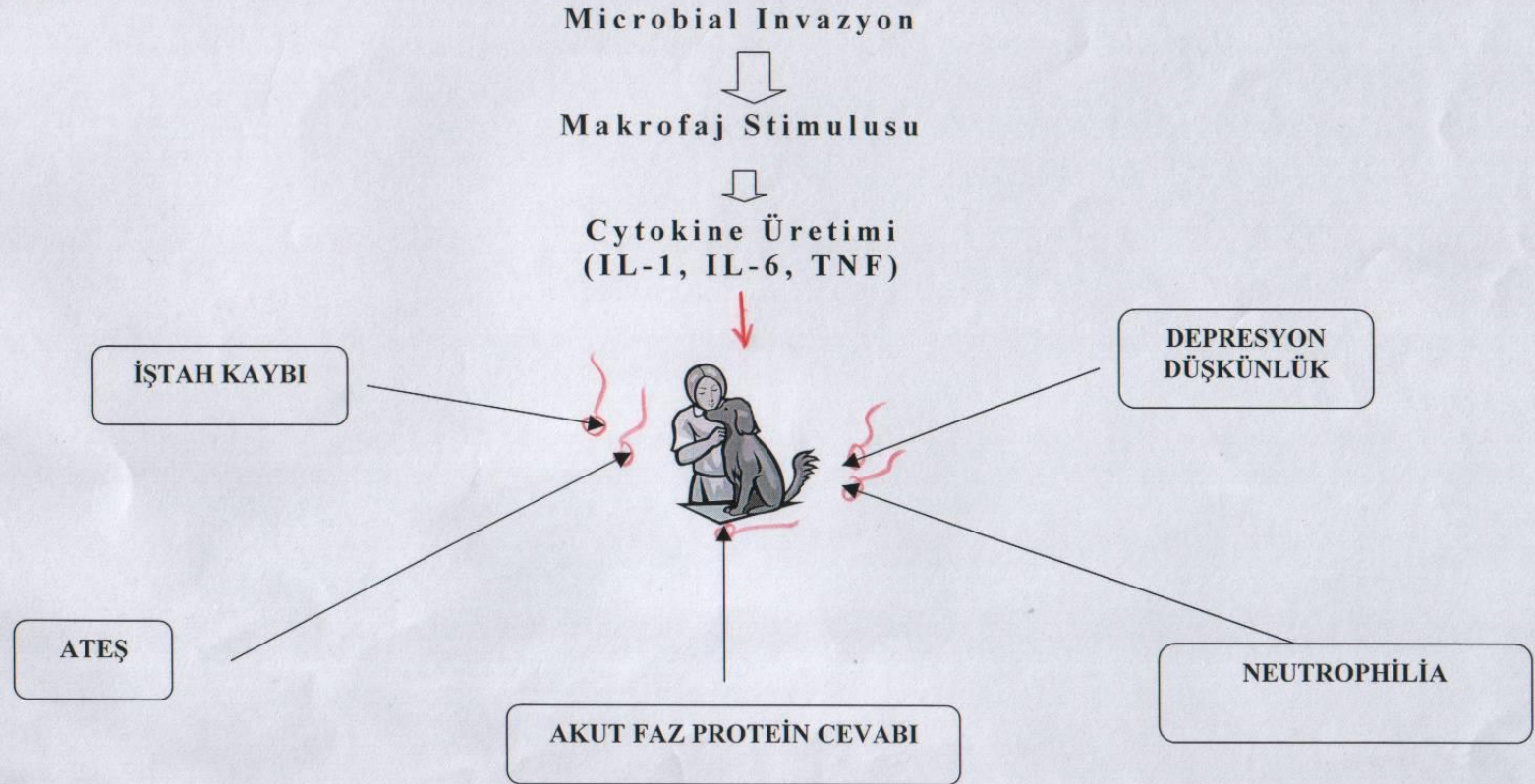
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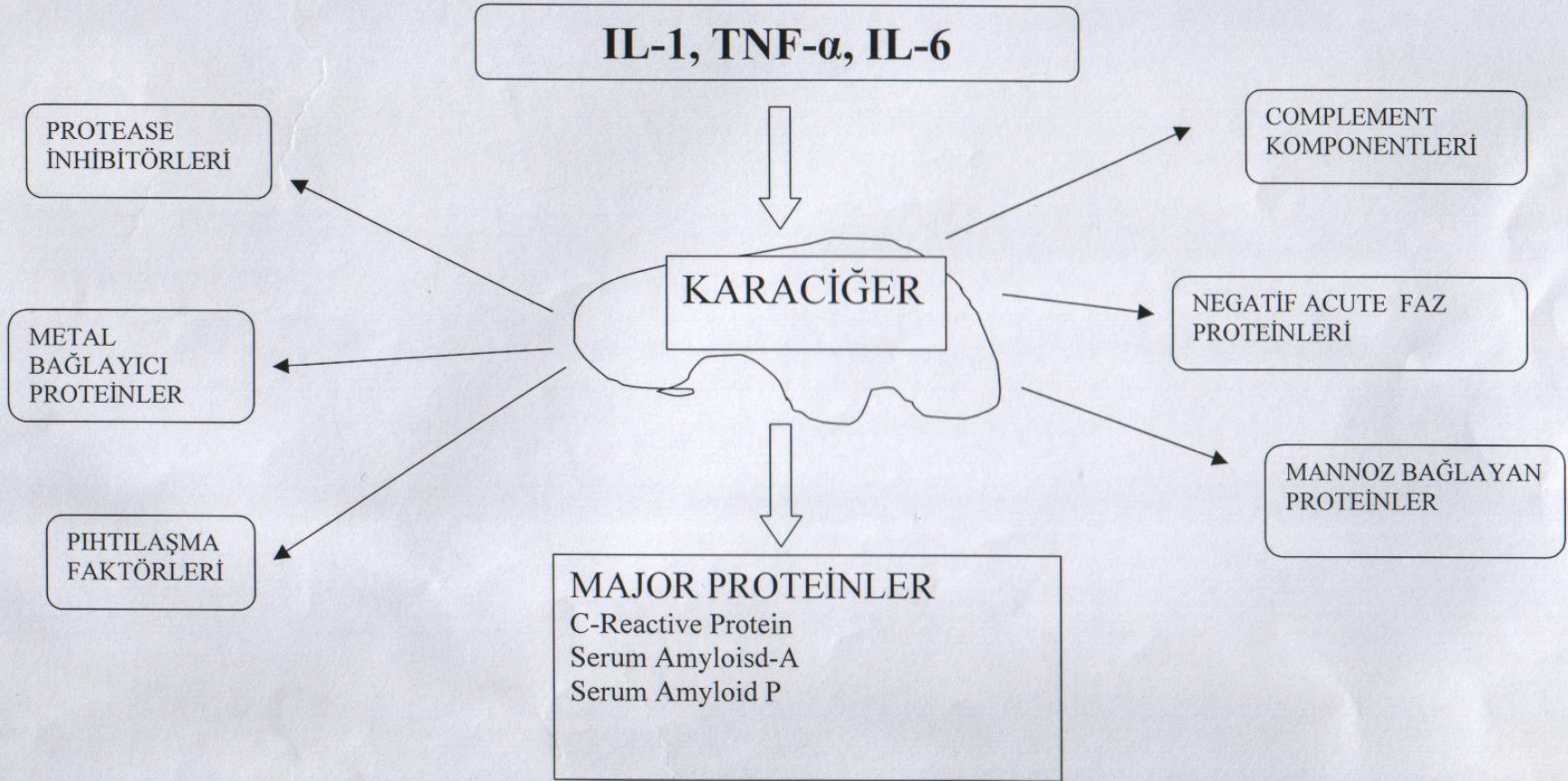
Vücutun Yangısal Uyarılara Cevabı

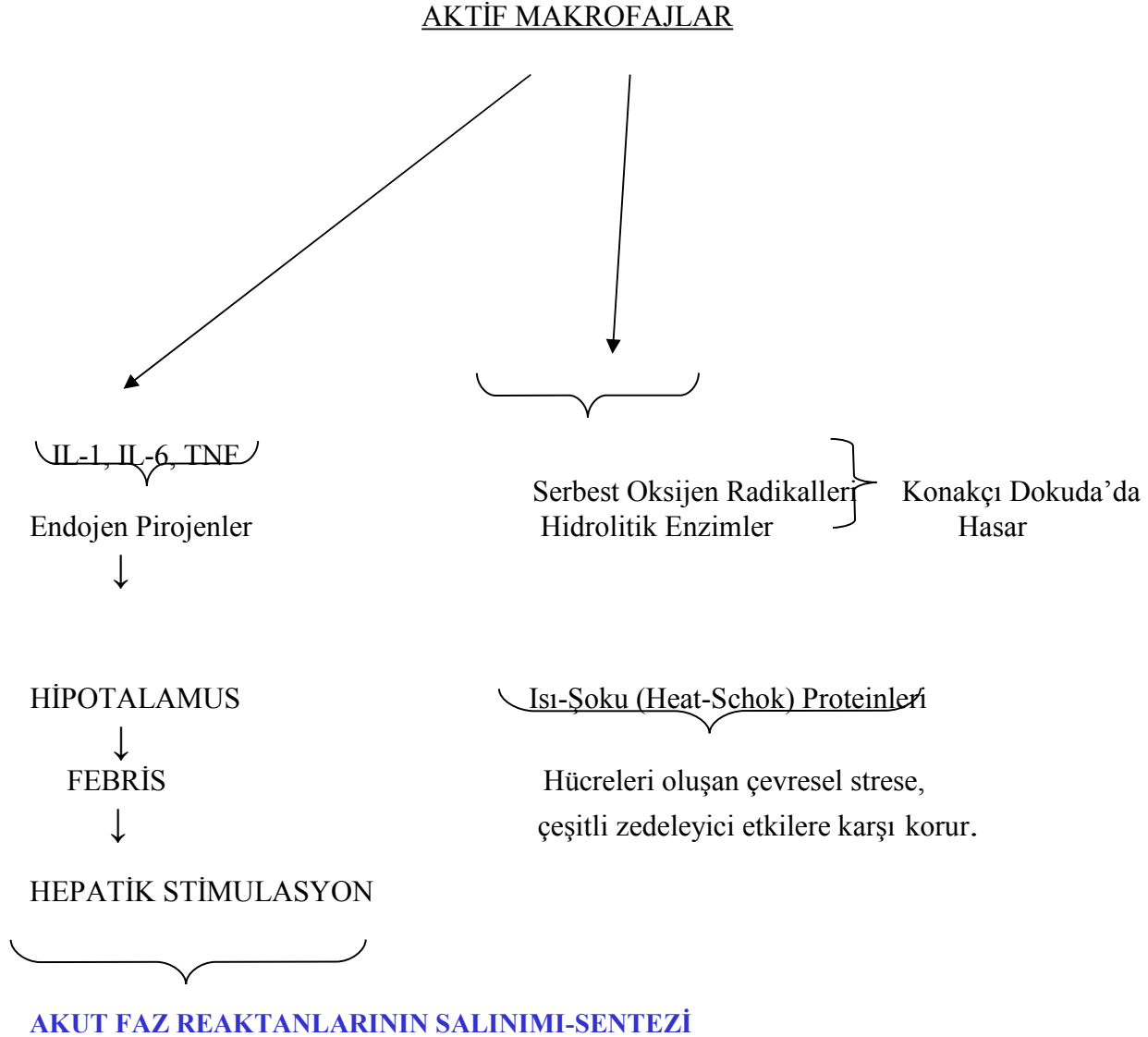
Çok sayıdaki sistemik etkiler Makrofajlar salınan üç ana CYTOKİNE bağlı olarak gelişir.



ACUTE-PHASE PROTEİN SİSTEMİ

Karaciğer IL-1, TNF- α , IL-6 etkisi altında çok sayıda protein salgılar. Bunların hemen hepsi vücudun enfeksiyonu kontrol etmesine yardım eder.





AKUT FAZ REAKTANLARININ SALINIMI-SENTEZİ

(AKUT FAZ PROTEİNİ; bir yangısal reaksiyon sonucu plazma konsantrasyonu minimum-en az %25

artan-Pozitif- veya azalan-Negatif- proteine denir.)

Complement komponentleri (C-3, -4, -9)

C-reactive Protein (CRP)

Antiproteazlar

Demir ve diğer Metal Bağlayan Proteinler

Pıhtılaşma ile ilişkili proteinler (Fibrinogen, Plasminogen)

LPS bağlayan protein

Serum Amyloid A (SAA) ailesi

Serum Amyloid P (SAP) ailesi

Konsantrasyonu Artanlar
(Pozitif Akut Faz Proteinleri)

Albümin

Trasferrin

Factor XII

Insulin benzeri büyüme faktörü I

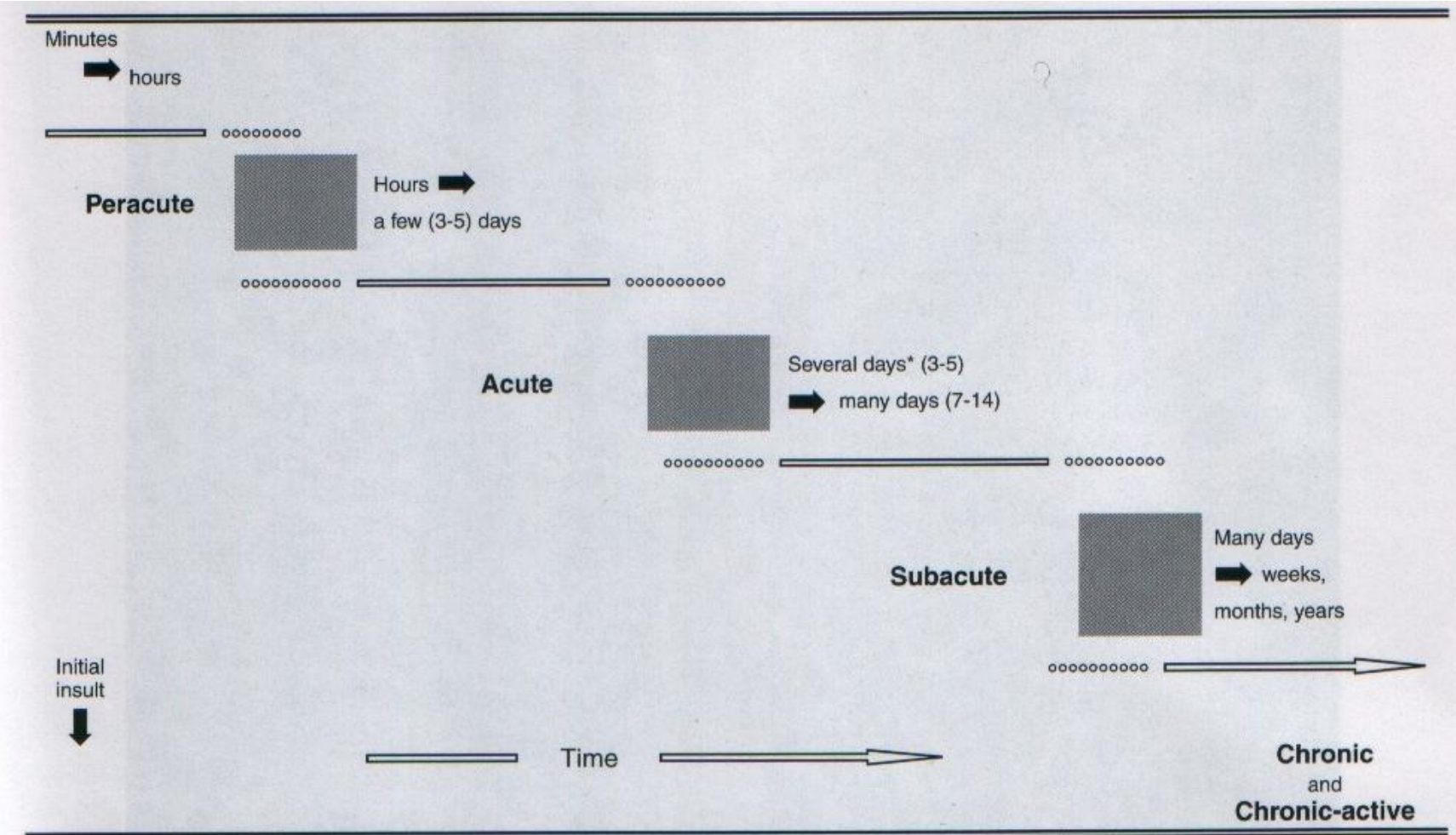
Konsantrasyonu Azalanlar
(Negatif Akut Faz Proteinleri (SandC))

Pratikte akut faz cevabını belirlemede - **Carbohydrate Reactive Protein (CRP)** ölçümüne bakılır. Doku hasarının fazla olduğu olgularda yüksektir.

C-reactive protein İNSAN, maymun, domuz, tavşan, hamster ve KÖPEKLERDE ana-temel akut faz proteinlerinden birisidir.

SİĞİR, AT ve KEDİLERDE ise değildir. Sığırlarda, CRP laktasyon ile ilişkili bir protein gibi görülmektedir. Laktasyondaki sığırlarda değerleri iki kat, beş kat artar. CRP pentraxin ailesine ait, birbirinin benzeri beş alt üiteden oluşan bir polimerdir.

CRP ilk kez *Streptococcus pneumoiae* ait C-polysaccaridi bağlama ve presipite etme yeteneği nedeniyle tanınmış- fark edilmiş ve isimlendirilmiştir.



*Opinions vary regarding the appropriate transition times when the term "subacute" is used.

Fig. 4-3 Determining the duration, or time frame, of inflammatory reactions. The time frames are general estimates for each of the categories: peracute, acute, subacute, and chronic. The transition between each category is gradual, a "gray zone."

ACUTE –CHRONİC YANGI

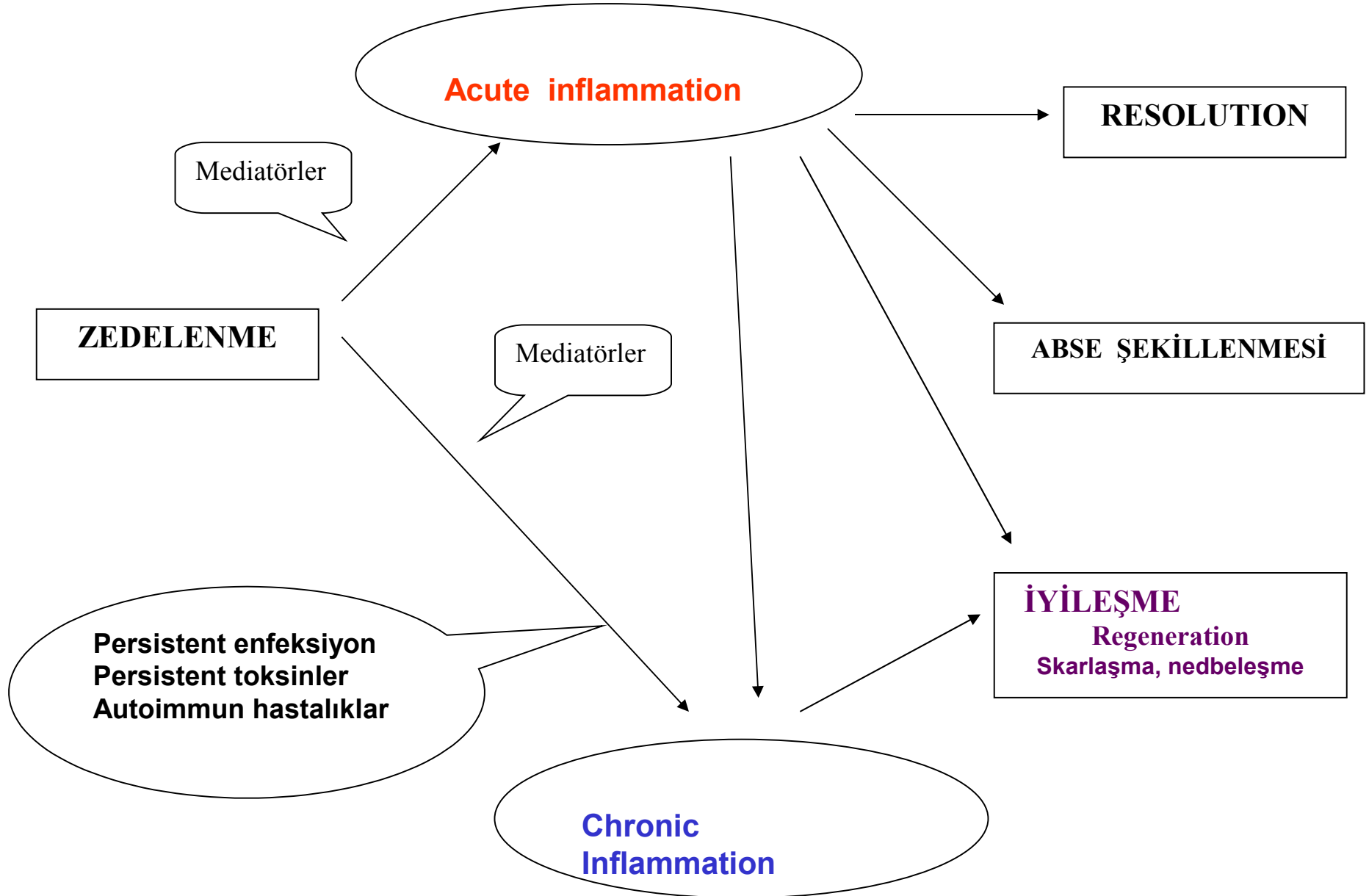
ACUTE YANGI

- VASKULER DEĞİŞİKLİKLER
- ÖDEM
- NÖTROPİL LÖKOSİT İNFİLTRASYONU FAZLA

CHRONİC YANGI

- MONONUCLEAR HÜCRE İNFİLTRASYONU FAZLADIR-
(makrofajlar, lenfositler, plasma hücreleri)
- DOKU TAHRİBATI (HEM PARANKİM HÜCRELERİNİN HEM DE STROMAL ÇATININ)-
(büyük ölçüde yangı hücreleri tarafından oluşturulur)
- BAĞ DOKU YERİNE KONULMASIYLA ONARIM ÇABALARI-
(küçük kan damarlarının çoğalması-angiogenesis ve özellikle FİBROSİS (fibroblastların göçü ve çoğalması)

ACUTE YANGININ SONLANMASI

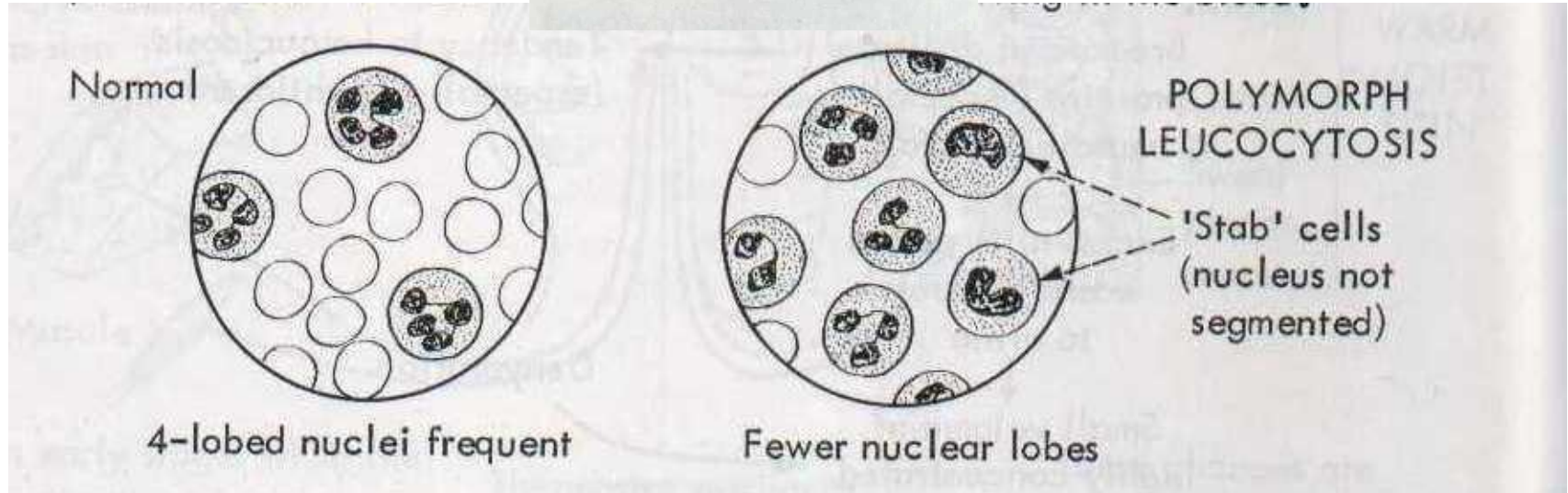
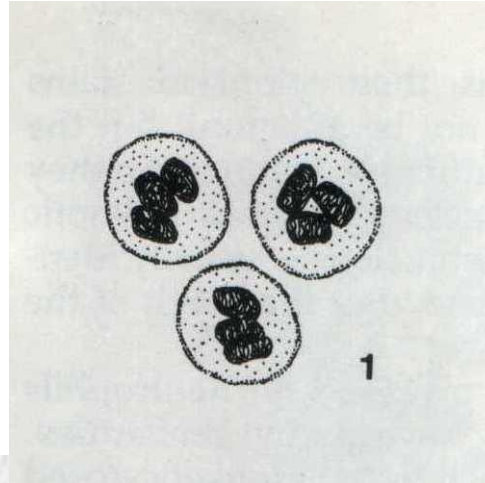


Hücreler

Nötrofiller—Neutrophil—Polymorphonuclear

Yangıda önemli görev alır. Görevi fagositoz yapmak ve yangıdaki hücre artıklarını enzimlerle lize etmektir. Opsonize edici antikorlar tarafından kaplanan mikroorganizmalar daha kolay fagosite edilirler.

10-12 μ



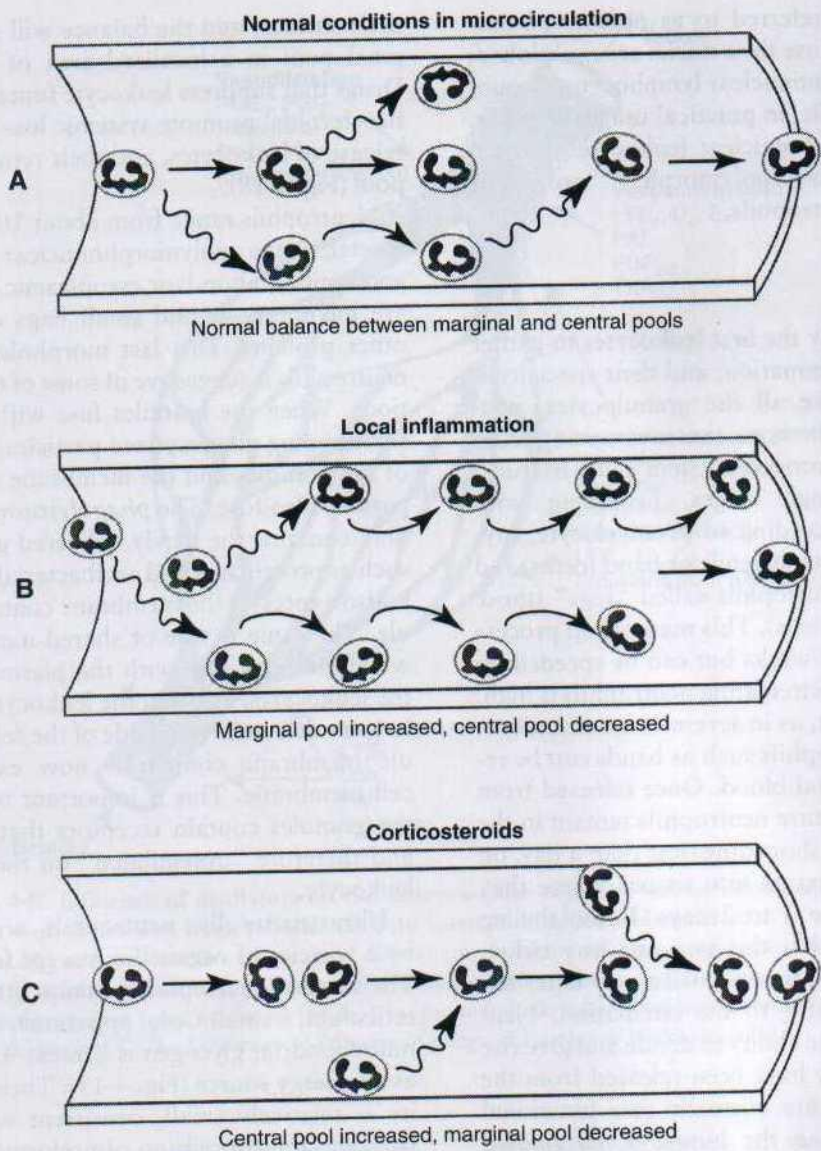


Fig. 4-18 The margined and circulating pools of neutrophils in the peripheral vasculature. **A, B,** and **C,** Local conditions in the tissue or systemic administration of some drugs may affect the balance between the margined and circulating pools. (Copyright © The University of Tennessee College of Veterinary Medicine, 2000.)

Kanda normalde iki fonksiyonel kompartmanda sirküle ederler. Marjinal kompartman—kan damarı lumeninde ama kan damarı duvarından uzakta ve sirküle eden kompartman—serbestçe hareket eden ve kan örneği alındığında örneklenen hücre grubudur.

TABLE 4-9 Some of the Neutrophil Granule Constituents

AZUROPHIL GRANULES†	SPECIFIC GRANULES	TERTIARY (GELATINASE) GRANULES
Myeloperoxidase*	Collagenase (MMP-8)	
Elastase	Gelatinase (MMP-9)	Gelatinase (MMP-9)
Lysozyme*	Lysozyme*	Lysozyme*
Cathepsin G and several other cathepsins	Histaminase	
Proteinase-3	Heparinase	
β -Glucuronidase	Cytochrome <i>b</i> *	Cytochrome <i>b</i> *
α -Mannosidase	Lactoferrin	
Defensins*	Vitamin B ₁₂ -binding protein*	
Bactericidal/permeability-increasing protein (BPI)*	TNF- α receptor	
	CD11b/CD18 β_2 -integrin (adhesion molecules)	CD11b/CD18 β_2 -integrin (adhesion molecules)
	Urokinase plasminogen activator (uPA)	
	uPA receptor	uPA receptor

This table is not intended to be a specific or complete listing of granule content applicable to all species.

*These constituents have a function more specifically directed to microbicidal activity.

†Azurophil granules can also be subdivided into two types in some species, based on the finding that some are rich in defensins and some contain little or no defensins.

Abbreviations: *MMP*, matrix metalloproteinase; *TNF*, tumor necrosis factor.

BOX 4-2 Partial List of the Array of Enzymes and Other Substances in Lysosomes of Various Leukocytes

ENZYMES ACTING ON PROTEINS

Cathepsins (B, D, G, H, L, S)
Collagenases (matrix metalloproteinases (MMP-1, -8)
Gelatinases (MMP-2, -9)
Leukocyte elastase
Metalloelastase (MMP-12)
Urokinase plasminogen activator
Trypsin
Chymase
Matrilysin (MMP-7)
Stromelysins (MMP-3, -10, -11)
Granzymes (NK cells and cytotoxic T lymphocytes)

ENZYMES ACTING ON CARBOHYDRATES

β -Acetylgalactosaminidase
 α -Acetylglucosaminidase
 α -Galactosidase
 β -Galactosidase
 α -Glucosidase
 β -Glucosidase
 β -Glucuronidase
 α -L-Fucosidase
 β -D-Fucosidase
Hyaluronidase
Lysozyme
 α -Mannosidase
Neuraminidase

ENZYMES ACTING ON LIPIDS

Acid lipase
Cholesterol esterase
Glucocerebrosidase
Galactocerebrosidase
Phospholipase A₁
Phospholipase A₂

ENZYMES ACTING ON NUCLEIC ACIDS

Acid deoxyribonuclease
Acid ribonuclease

MISCELLANY

Acid phosphatase
Anticoagulants
Arylsulfatase
Myeloperoxidase
Peroxidase
Phosphodiesterase
Phosphoprotein phosphatase
Antimicrobial peptides and proteins (bactericidal permeability-increasing protein [BPI], defensins)
Some cytokines

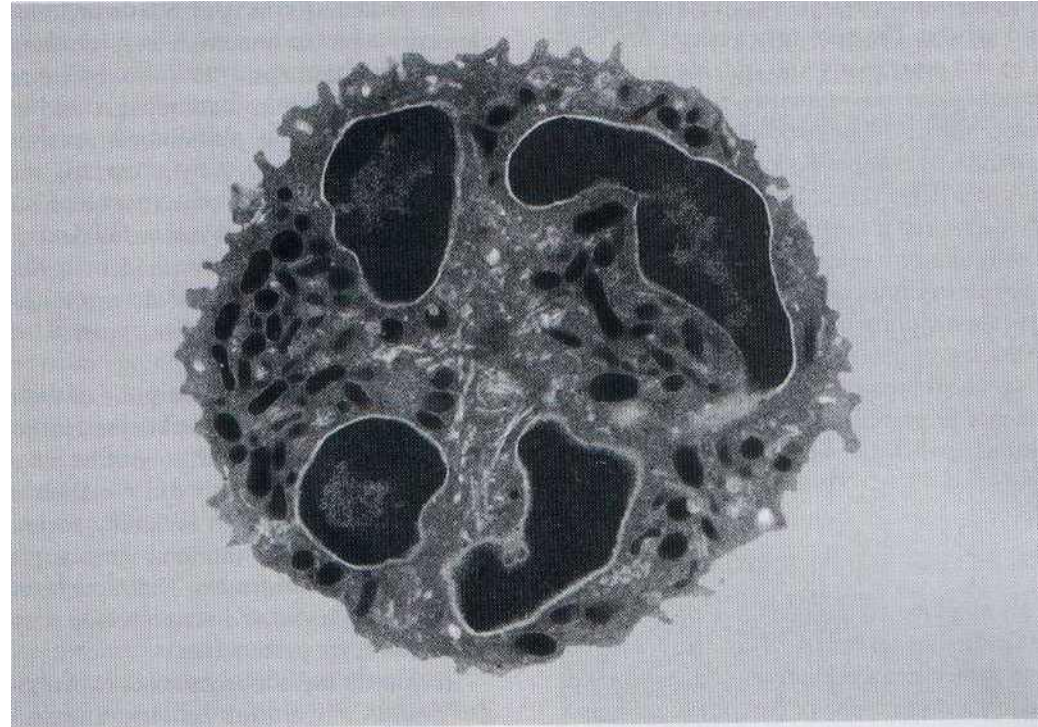
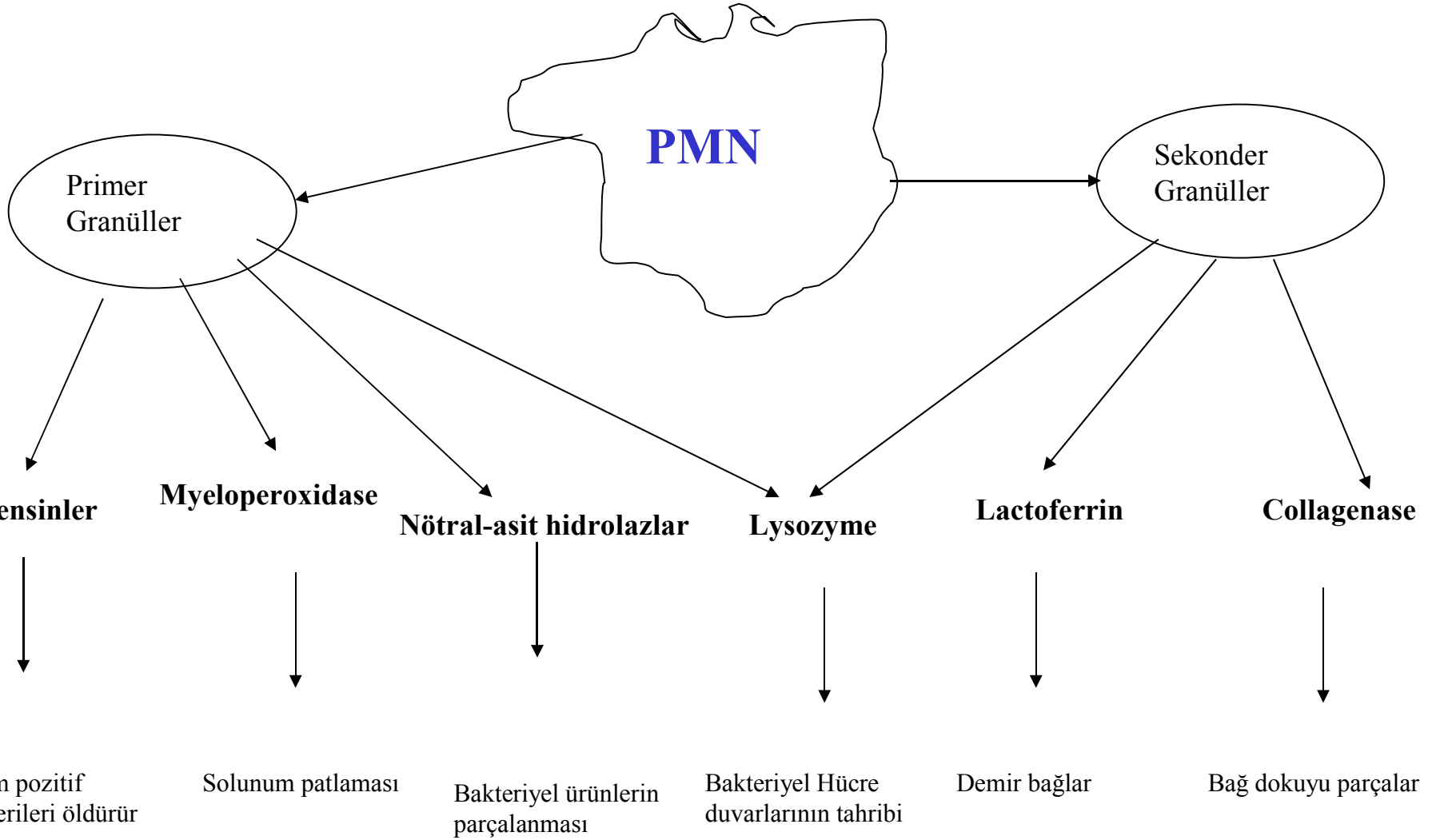


Fig. 4-19 Neutrophil. The segmented nucleus and numerous lysosomal granules in the cytoplasm of this sheep neutrophil are typical of this kind of granulocyte.

NEUTROPHİL SİTOPLAZMASINDAKİ GRANÜLLERİN İÇERİKLERİ VE FONKSİYONLARI



Eosinophil leukocyte

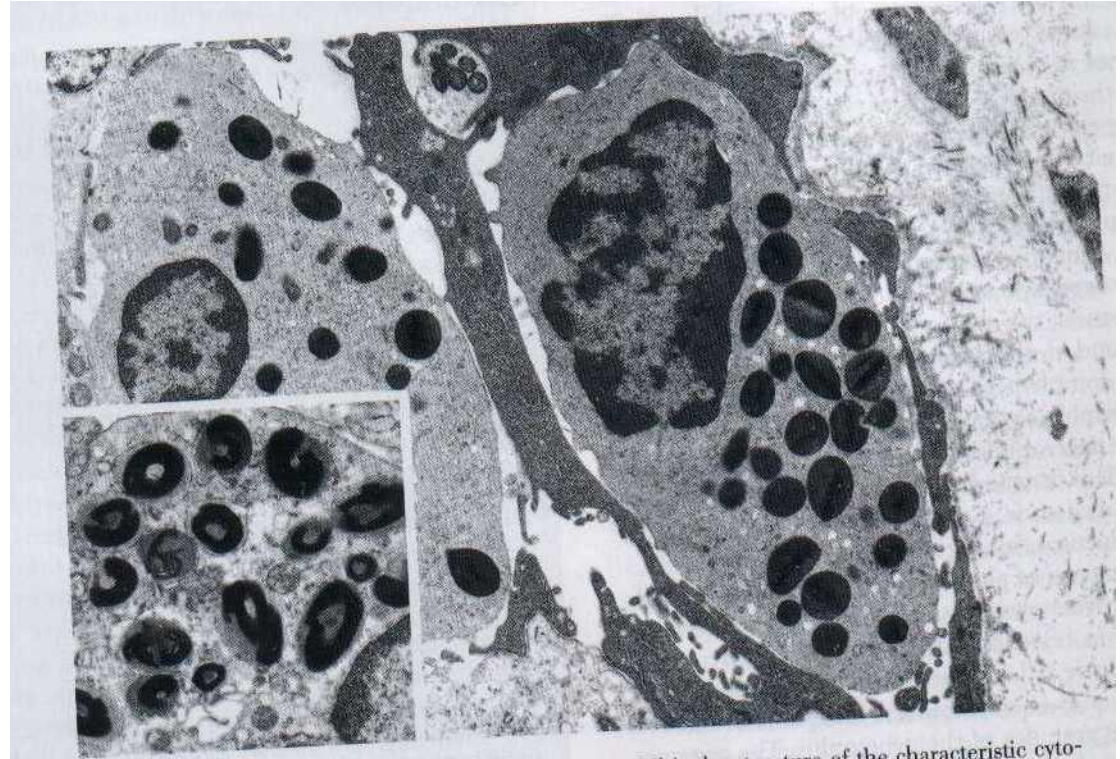
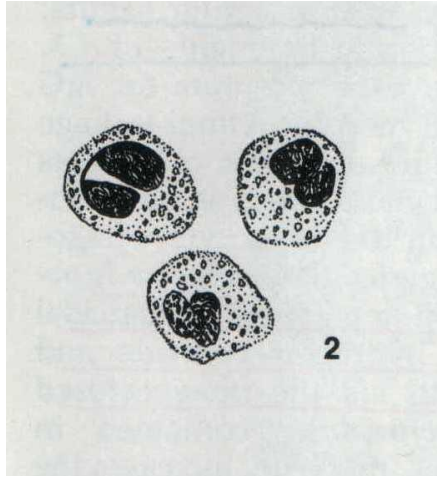


Fig. 4-20 Eosinophils. The hallmark of the eosinophil is the structure of the characteristic cytoplasmic granules, which have a dense central core. This dense core is the source of "major basic protein," an important eosinophil constituent. These eosinophils are from a rhesus monkey. To show the variation in granules between species, feline eosinophil granules are shown in the inset. (Courtesy Drs. W.L. Castleman, Gainesville, Fla., and J.M. Ward, Bethesda, Md.)

Mast Hücresi ve Basophil

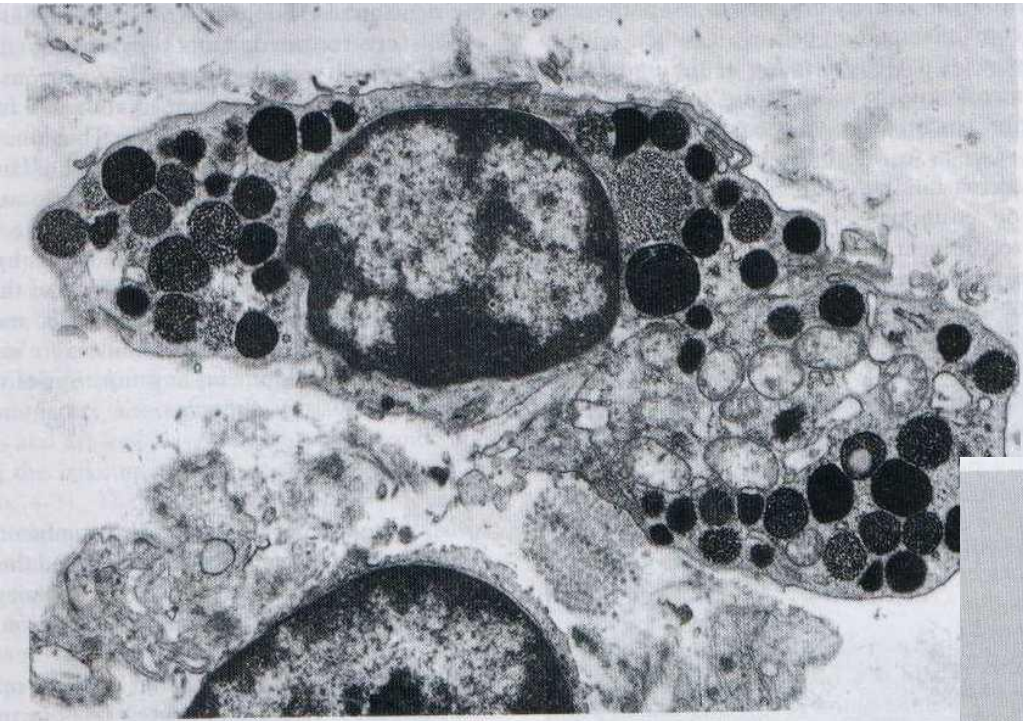


Fig. 4-22 Mast cell. Equine subcutis. The mononuclear mast cell is strikingly similar ultrastructurally to the basophil. Notice that the variation in granule morphology is similar to that of the basophil. These granules also contain potent mediators of inflammation. (Courtesy Dr. John F. Cummings, Ithaca, N.Y.)

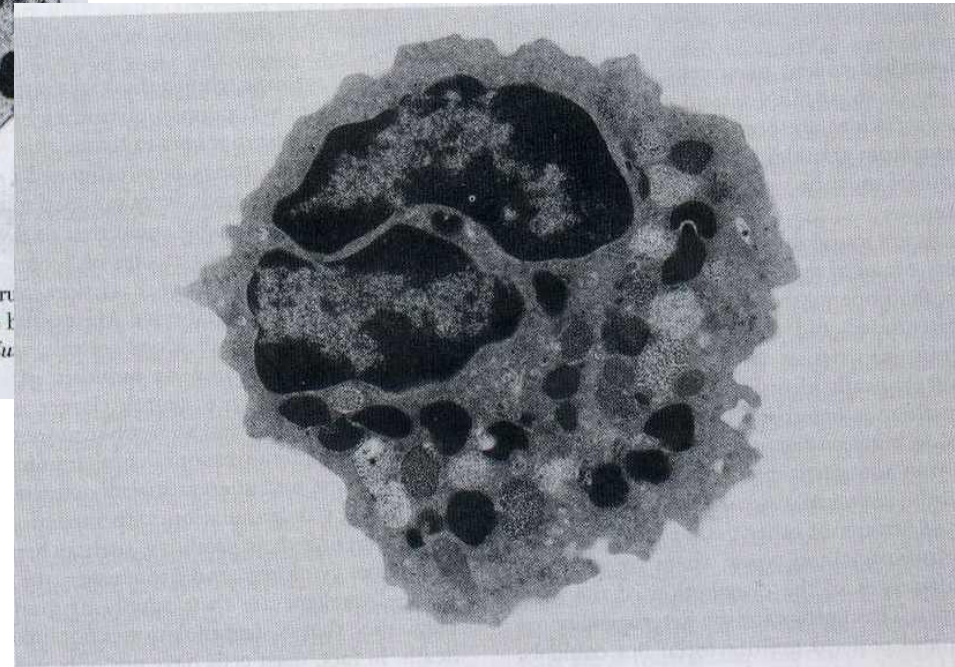


Fig. 4-23 Basophil. Sheep blood. The granules of the basophil vary from dense structures to more loosely associated aggregates of smaller, electron-dense granules sometimes organized into tubular or chainlike arrays. The granules contain potent inflammatory mediators.

Lenfosit ve plazma hücreleri

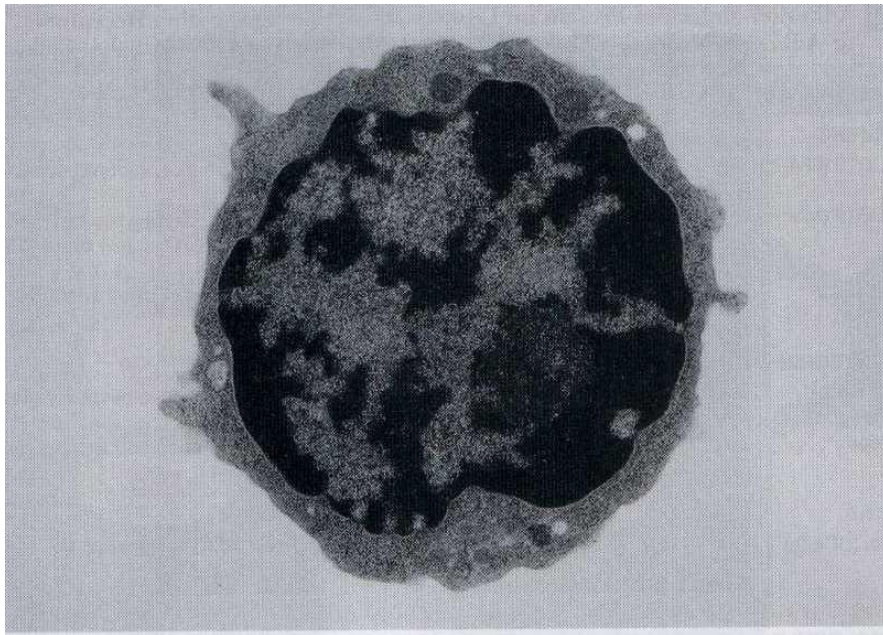
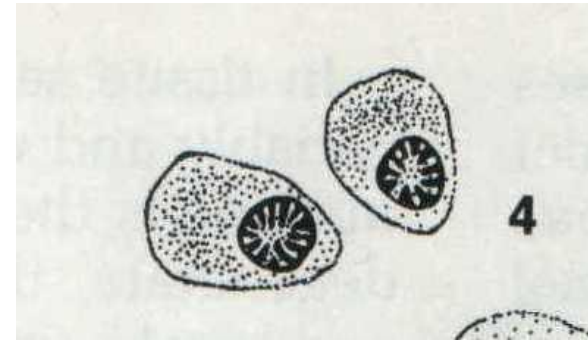
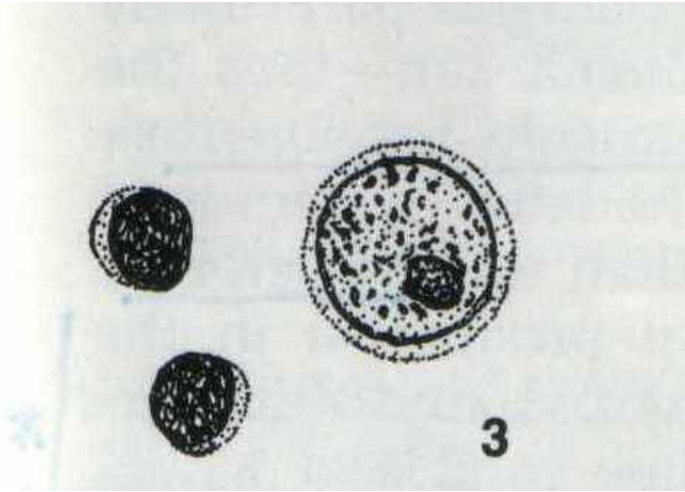


Fig. 4-26 Lymphocyte. This typical sheep lymphocyte has only scant amounts of cytoplasm con-

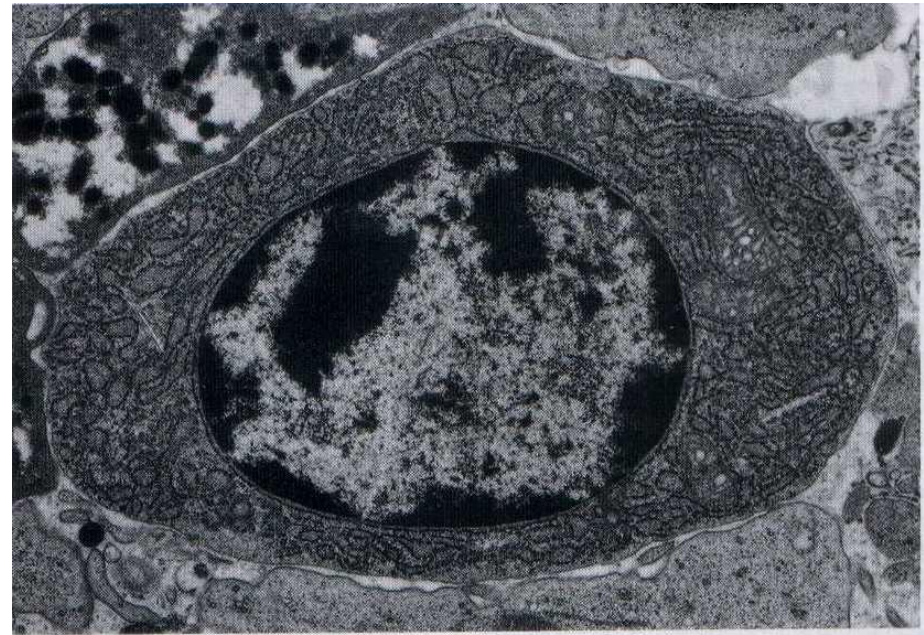


Fig. 4-27 Plasma cell. This sheep plasma cell shows the abundant, rough-surfaced endoplasmic

Monosit—Makrofaj—Histiyosit—Dev Hücre

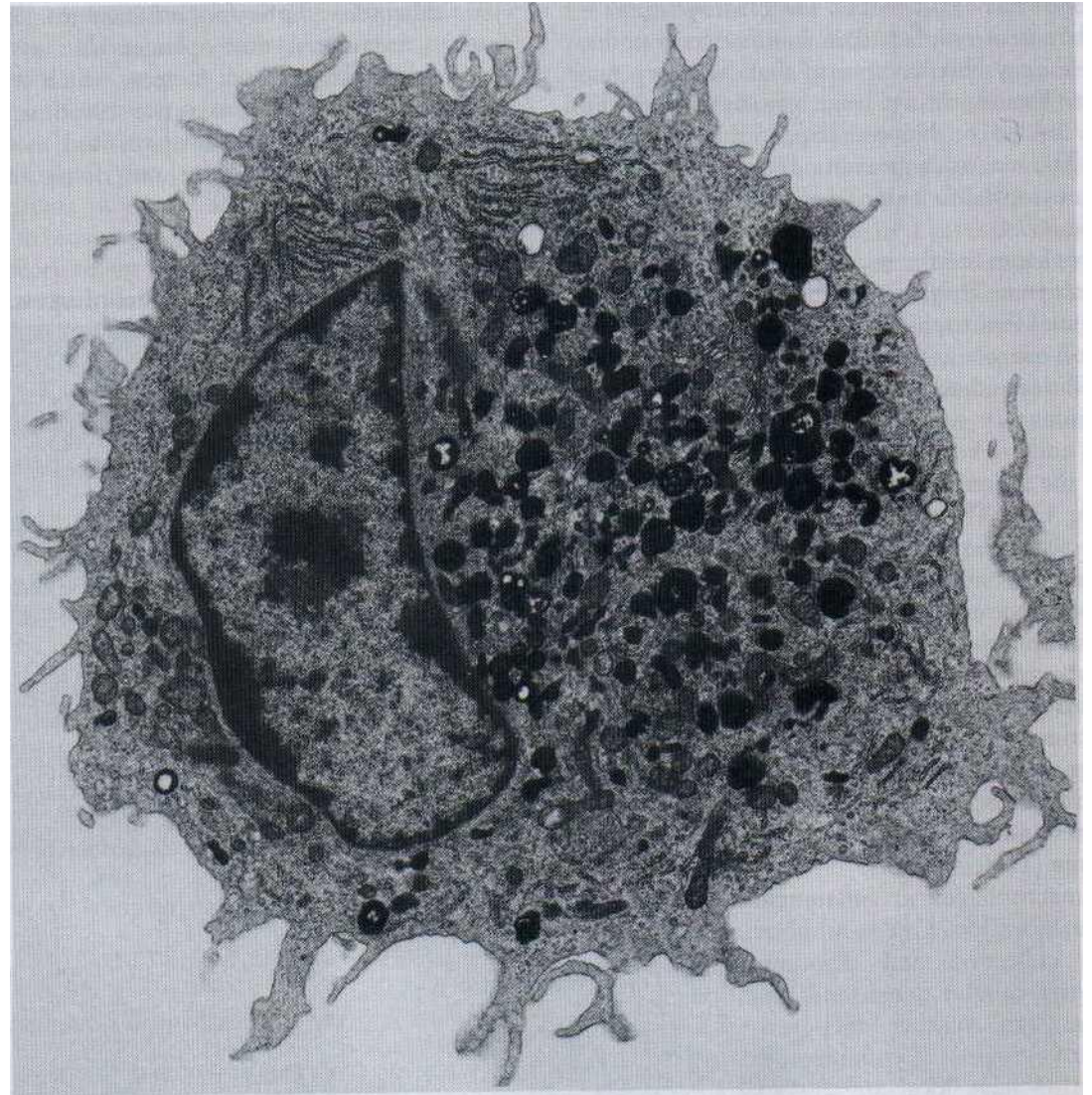
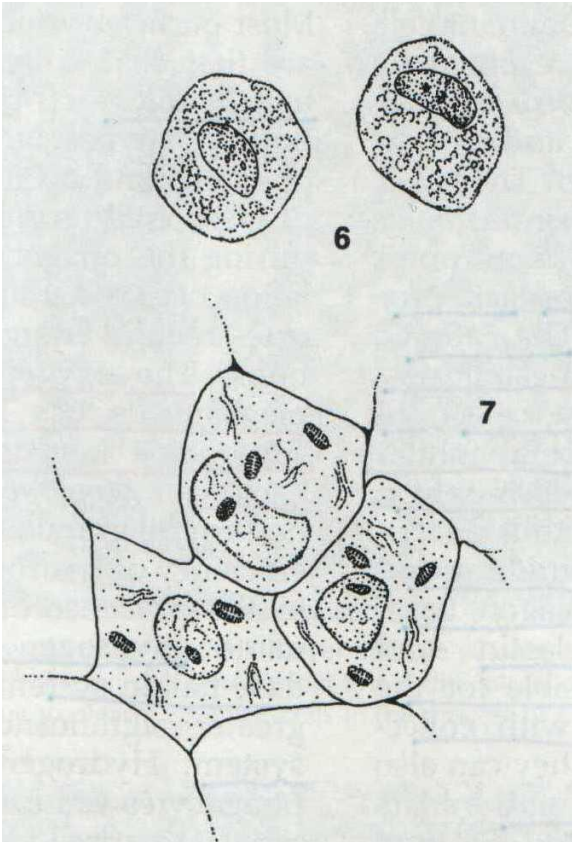


Fig. 4-24 Macrophage. This rabbit alveolar macrophage shows abundant cytoplasmic granules, which are characteristic of this cell type. Notice the numerous cytoplasmic processes at the

TABLE 4-12 Some of the Cytokines and Other Mediators Synthesized and Secreted by Stimulated Macrophages or Monocytes

SOURCE	TYPE OF MEDIATOR	EXAMPLES
Macrophages or monocytes	Interleukins and TNF: Chemokines: Interferons: Hematopoietic growth factors: Other growth factors and miscellaneous: Others:	IL-1 α , -1 β , IL-1ra, IL-4, -6, -8, -10, -12, -15, -18, TNF- α IL-8, GRO- α /MGSA, MCP-1/MCAF, MIP-1 α , MIP-1 β , interferon-inducible protein-10 (IP-10) IFN- α , IFN- β (not IFN- γ) G-CSF, GM-CSF, M-CSF TGF- β , TGF- α , PDGF, leukemia inhibitory factor (LIF), hepatocyte growth factor (HGF), oncostatin M (OSM) Some complement components, prostaglandins and leukotrienes, nitric oxide (NO), platelet-activating factor (PAF)

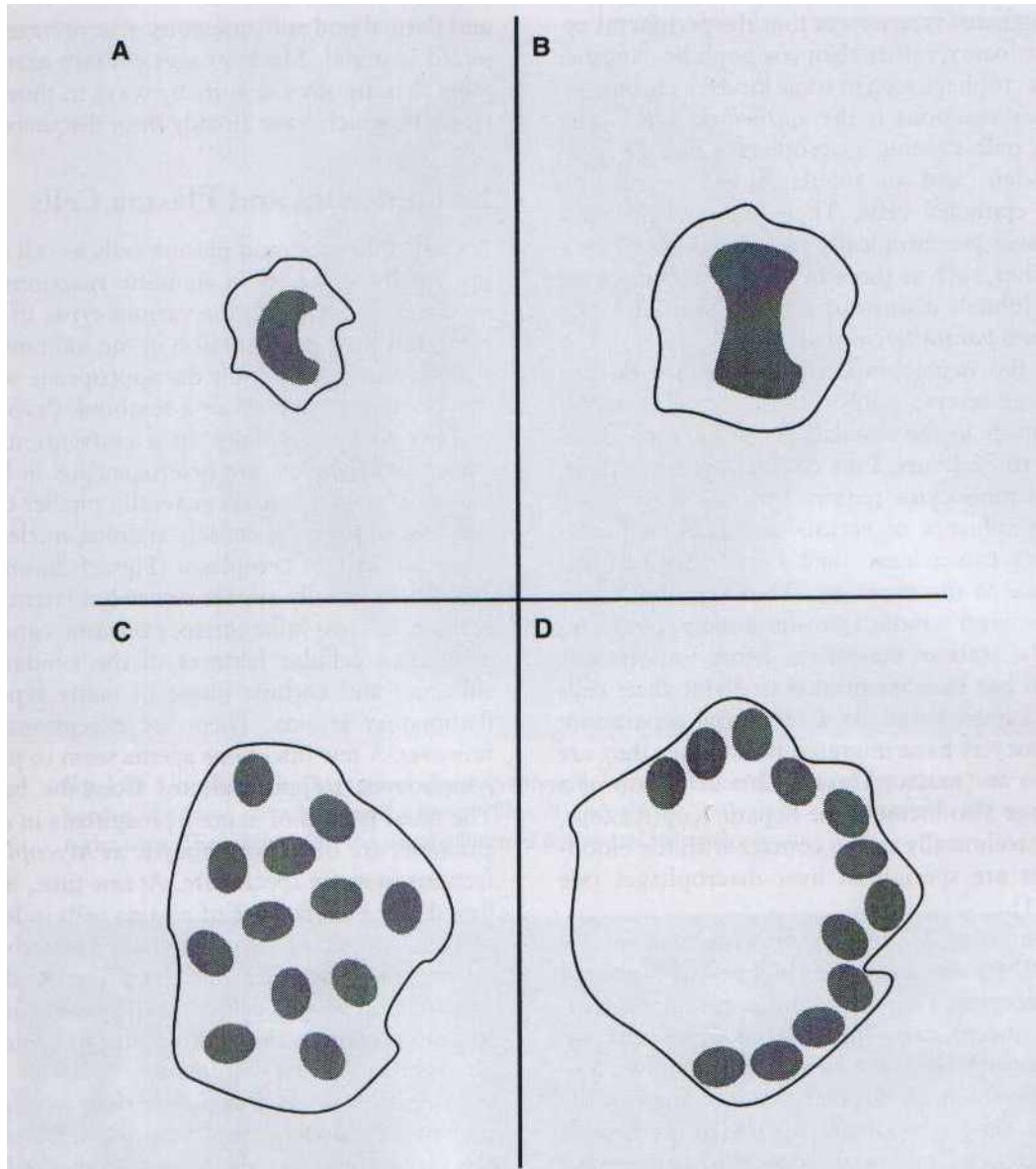
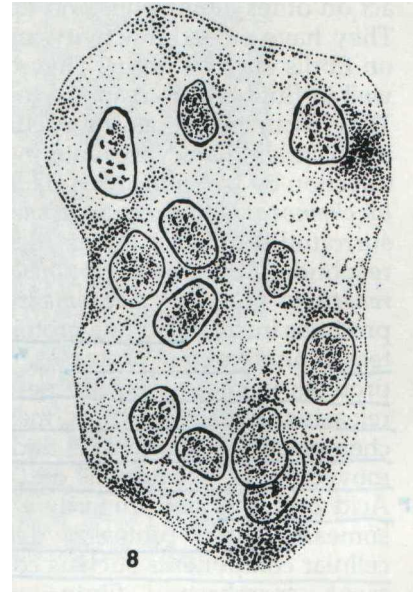
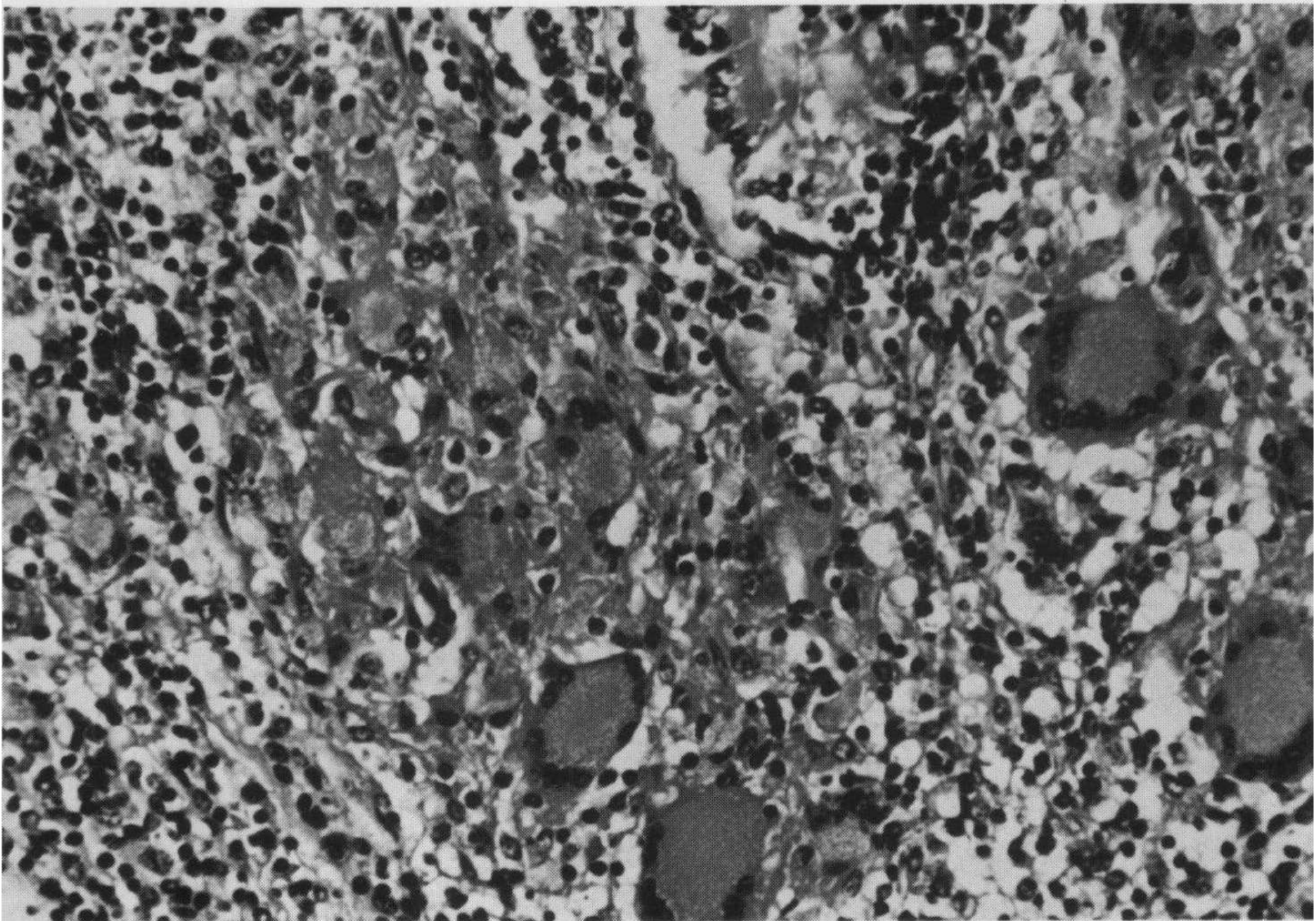
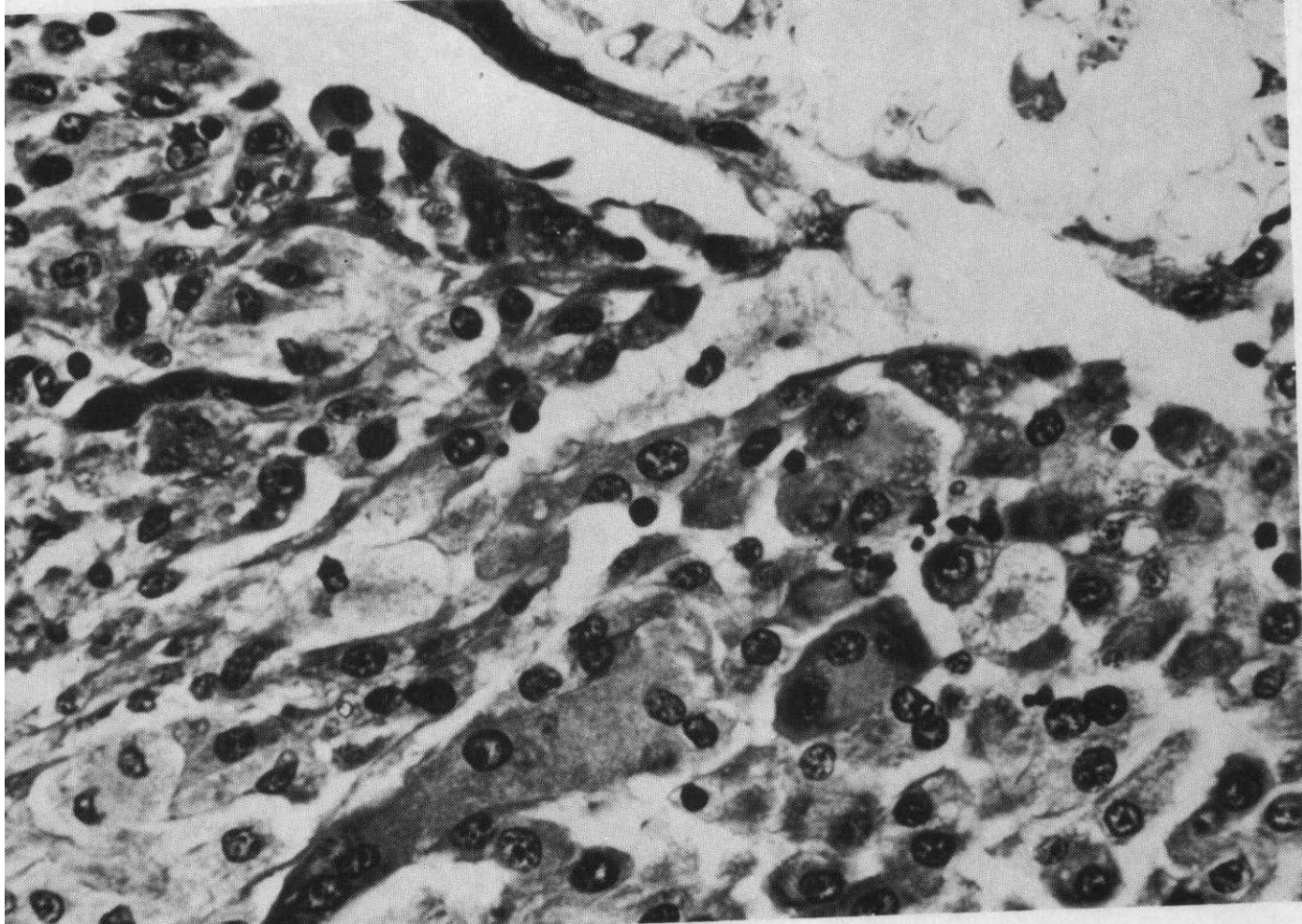


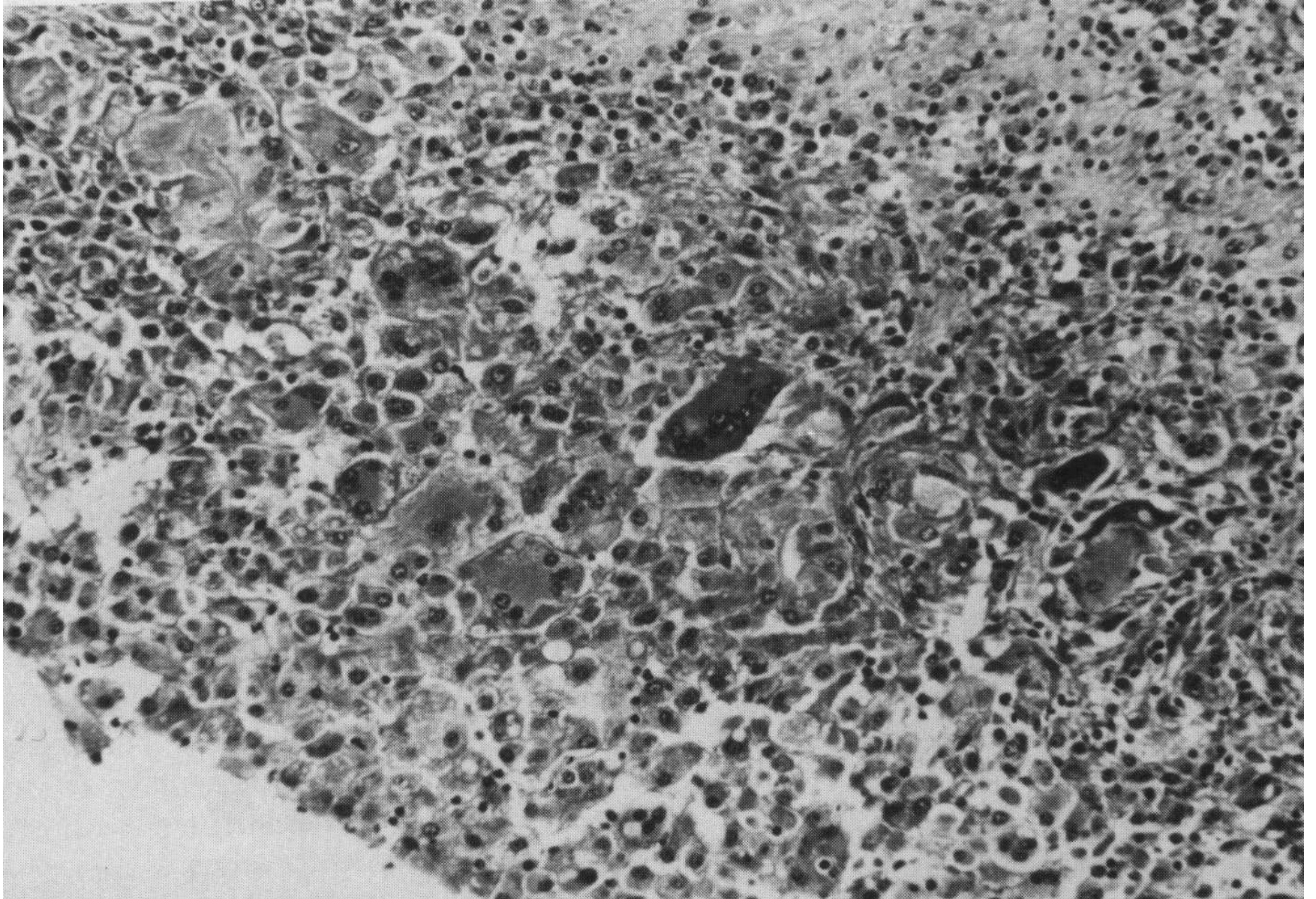
Fig. 4-25 Various morphological forms of macrophages at tissue sites of inflammation. **A**, Regular macrophage, also called a histiocyte. **B**, Epithelioid macrophage; larger with ample cytoplasm. **C**, Multinucleated giant cell, with scattered nuclei throughout. **D**, Langhans' type of giant cell, with numerous peripheral nuclei. (Copyright © The University of Tennessee College of Veterinary Medicine, 2000.)

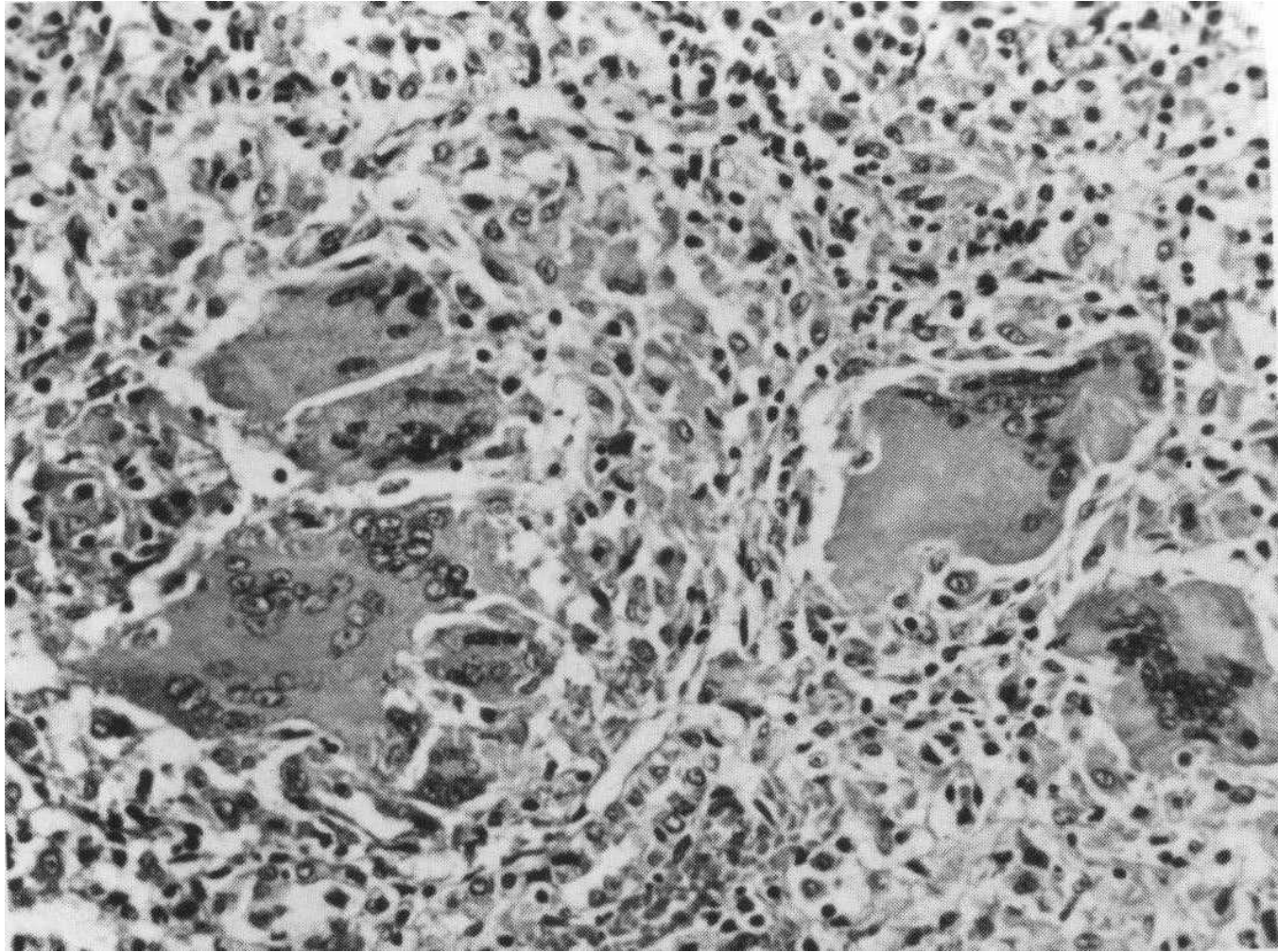




-24. Giant cells and epithelioid cells in the intestinal mucosa of a cow with Johne's disease. The epithelioid cells have indistinct boundaries, but with some imagination, their transition to giant cells may be visualized.







Platelet

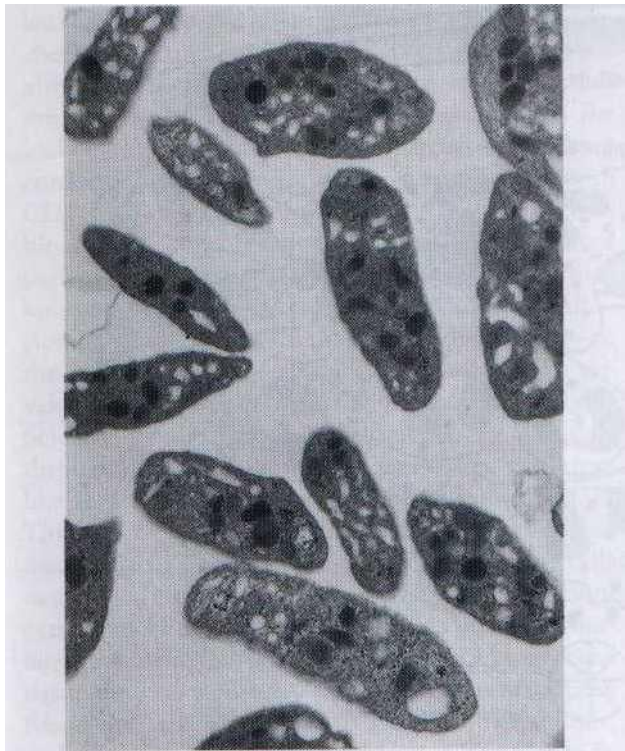


Fig. 4-30 Platelets. Rabbit blood. These typically anucleate platelets show the cytoplasmic granules and dense bodies as well as the open cytocavitary network typical of most platelets and through which granule constituents are secreted to the exterior. (Courtesy Jan Henson and Dr. Peter Henson, Denver, Colo.)

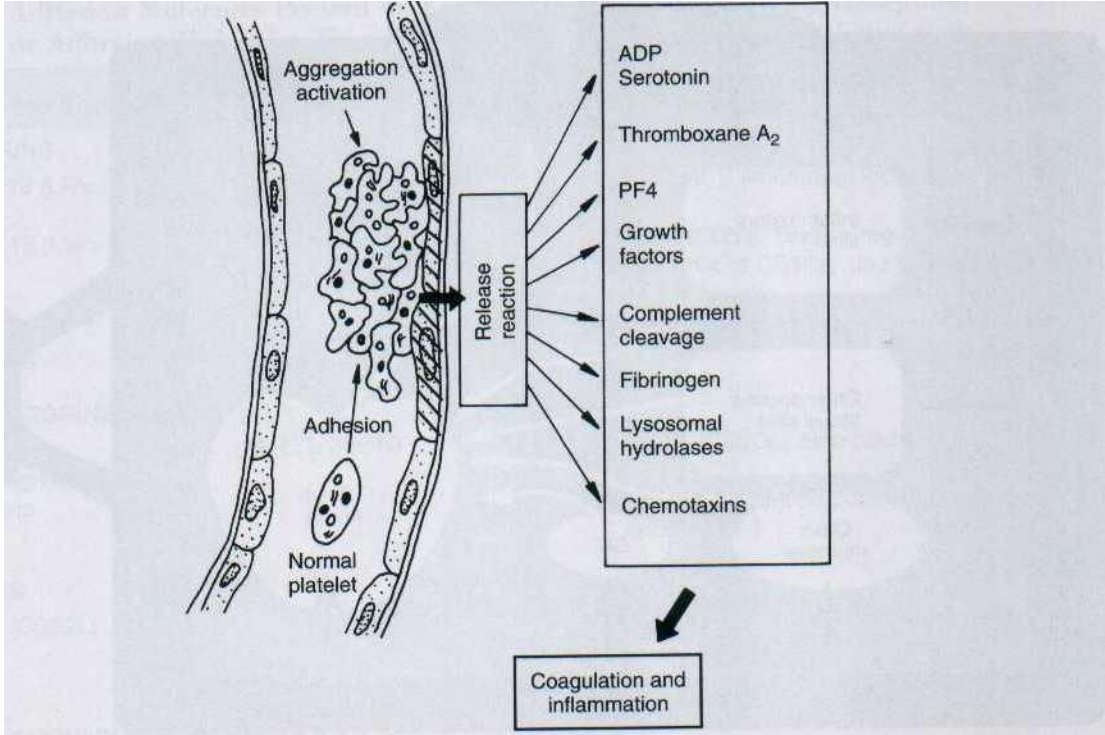


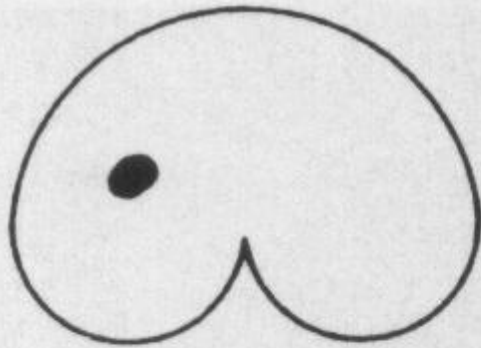
Fig. 4-29 Platelet release of inflammatory mediators. When platelets are activated and aggregated, the ensuing platelet release reaction causes the secretion of many chemical mediators of importance to inflammation and coagulation. ADP, Adenosine triphosphate; PF, platelet factor.

BOX 4-1**Some of the Products of Platelets
Related to Coagulation,
Inflammation, and Healing**

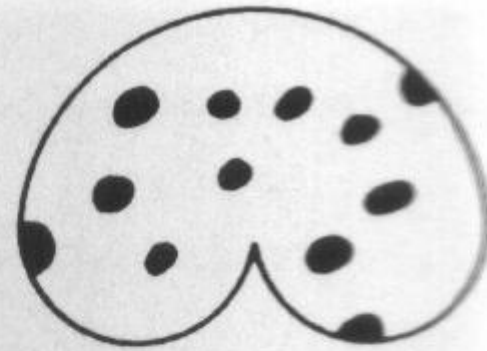
Platelet factor 4
Fibrinogen
Fibronectin
Coagulation factors VIII and V
Serotonin
Histamine
ADP, ATP
Ca⁺⁺ cations
The arachidonic acid product TXA₂
Complement-cleaving protease (resulting in C5a)
Platelet-activating factor
Growth factors: PDGF, TGF-β, FGF
P-selectin (CD62P, adhesion molecule)

ADP, Adenosine diphosphate; *ATP*, adenosine triphosphate; *FGF*, fibroblast growth factor(s); *PDGF*, platelet-derived growth factor(s); *TGF-β*, transforming growth factor-beta; *TXA₂*, thromboxane A₂.

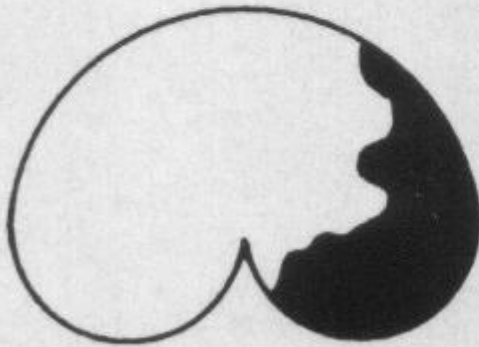
Endotel ve Fibroblast Hücreleri



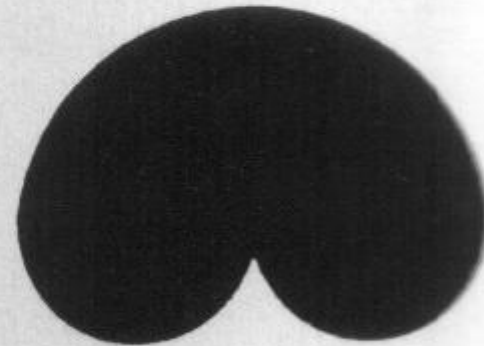
Focal



Multifocal



Locally
extensive



Diffuse

4-6 Distribution of lesions. Lesions usually are

TABLE 4-3 Classification of Inflammatory Lesions—The Morphologic Diagnosis

SEVERITY	DURATION	DISTRIBUTION	EXUDATE	ANATOMIC MODIFIERS	ORGAN
Minimal	Peracute	Focal	Serous	Interstitial	Nephritis
Mild	Acute	Multifocal	Catarrhal	Broncho-	Hepatitis
Moderate	Subacute	Locally extensive	Suppurative/purulent	Glomerulo-	Enteritis etc.
Severe or marked	Chronic	Diffuse	Fibrinous	Submandibular	
	Chronic-active		Serofibrinous	Bilateral etc.	
			Fibrinopurulent		
			Necrotizing		
			Granulomatous		
			Nonsuppurative		
			Caseous etc.		

Examples

Severe chronic focal caseous submandibular lymphadenitis

Severe acute locally extensive fibrinopurulent bronchopneumonia

ACUTE –CHRONİC YANGI

ACUTE YANGI

- VASKULER DEĞİŞİKLİKLER
- ÖDEM
- NÖTROPİL LÖKOSİT İNFİLTRASYONU FAZLA

CHRONİC YANGI

- MONONUCLEAR HÜCRE İNFİLTRASYONU FAZLADIR-
(makrofajlar, lenfositler, plasma hücreleri)
- DOKU TAHRİBATI (HEM PARANKİM HÜCRELERİNİN HEM DE
STROMAL ÇATININ)-
(büyük ölçüde yangı hücreleri tarafından oluşturulur)
- BAĞ DOKU YERİNE KONULMASIYLA ONARIM ÇABALARI-
(küçük kan damarlarının çoğalması-angiogenesis ve özellikle
FİBROSİS (fibroblastların göçü ve çoğalması)

TABLE 4-5 Types and Significance of Various Inflammatory Exudates

TYPE	COMMENTS/SIGNIFICANCE
PRIMARILY ACUTE REACTIONS	
Suppurative	Often a response to microbes, especially bacteria. Synonym: Purulent.
Purulent	See Suppurative.
Fibrinous	Often seen in combination with purulent lesions.
Fibrinopurulent	Often a response to microbes, especially certain bacteria.
Serous	Usually peracute. The protein-rich and cell-poor fluid is often a result of burns, blisters, etc.
Mucinous/mucoid	Associated with irritation of the respiratory and gastrointestinal tracts, often by microbes. Synonym: Catarrhal.
Mucopurulent	Mucoid/catarrhal and purulent. Usually caused by microbes on respiratory and intestinal surfaces.
Hemorrhagic	Synonym: Sanguineous. Serosanguineous refers to a dilute serum-blood mix.
Necrotizing	Often used in combination with suppurative, hemorrhagic. Toxins from certain microbes can cause this.
ACUTE OR CHRONIC	
Eosinophilic	May be acute, subacute, or chronic. Often a response to allergic or hypersensitivity diseases or to parasites.
USUALLY SUBACUTE, CHRONIC, OR CHRONIC-ACTIVE REACTION	
Granulomatous	Frequently a response to persistent microbes or foreign bodies.
Pyogranulomatous	Similar to granulomatous but may be a slightly "younger" lesion or a chronic-active lesion. Suggestive of certain microbes, including <i>Blastomyces</i> species and other fungi.
Lymphocytic, plasmacytic, or lymphoplasmacytic	Can be caused by persistent, nonpyrogenic microbes (such as <i>Mycoplasma</i>) or other chronic immune stimuli.
Nonsuppurative	Refers to lymphoplasmacytic, granulomatous, or a combination of both.

Yangısal Eksudat Tipleri

Serous

Catarrhal

Fibrinous

Suppurative

Fibrinous

Hemorrhagic

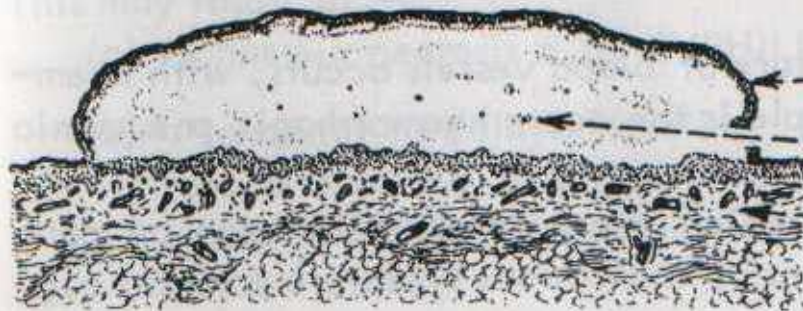
Nekroze edici

Nonsuppurative

Granulomatous

(a) SEROUS INFLAMMATIONS

In this type excessive clear watery fluid, with a variable protein content but no fibrin, is formed. Good examples are blister formation following burning (acute) and the pleural effusion associated with tuberculosis (chronic).



-----Blister containing serous fluid

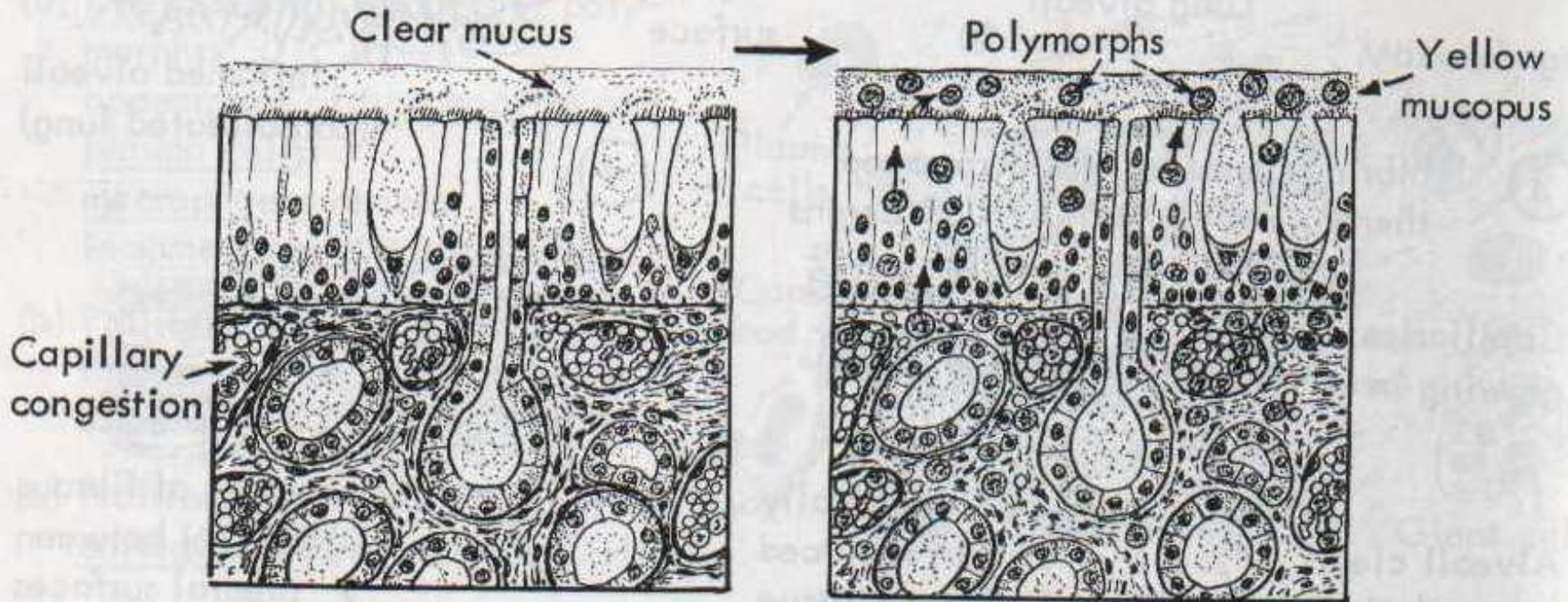
-----Relatively few cells

-----Mild capillary congestion

Note that the exudate remains fluid and resolution is not impeded.

CATARRHAL INFLAMMATION

A surface inflammation associated with greatly increased secretion of clear mucus: later, polymorphs appear.



Good examples are the common cold and some forms of colitis.

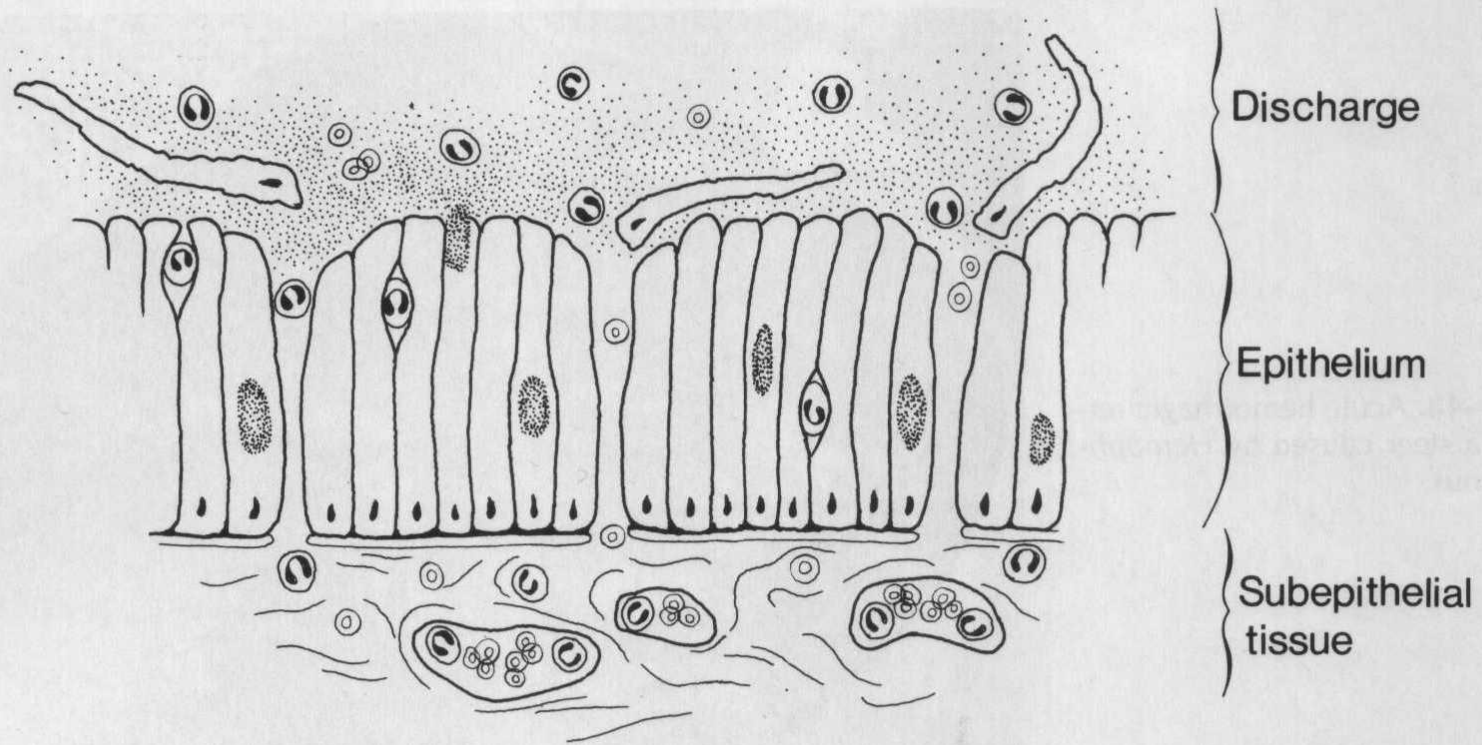


Figure 4-50. Diagrammatic representation of catarrhal exudate. The exudate contains mucus, necrotic epithelial cells, red cells and neutrophils. (Modified from Willis, R. A.: Principles of Pathology. 2nd ed. New York, Plenum Publishing Corp. [Butterworth], 1961. Reprinted by permission.)

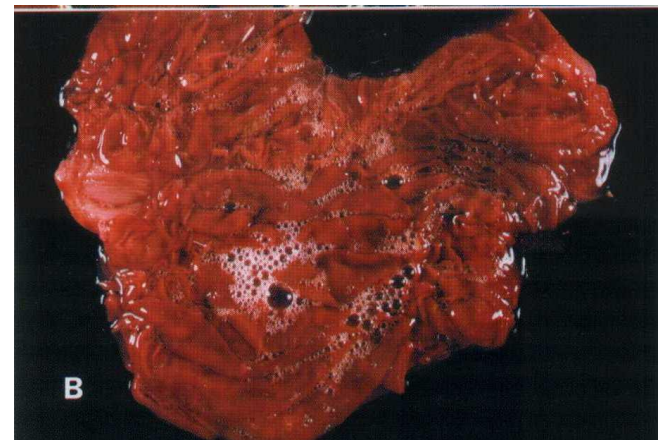




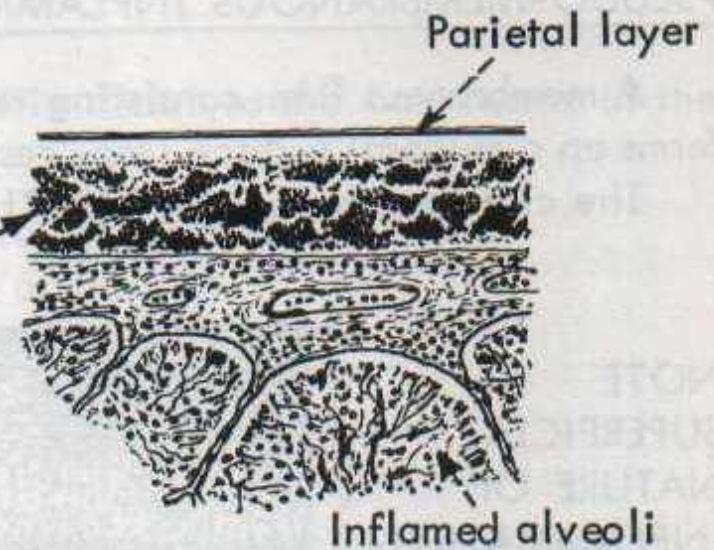


Figure 4-51. Catarrhal exudate in the colon of a pig with swine dysentery. Note the clumps of mucus and dark color of the fluid exudate.

EXUDATIVE INFLAMMATIONS (continued)

(b) FIBRINOUS EXUDATION

In this type the formation of fibrin is striking. An example is acute pleurisy complicating pneumonia where the fibrin can be seen as an amorphous dull deposit on the pleural surface. Note that the presence of solid fibrin tends to inhibit resolution, and organisation with adhesion formation often follows.



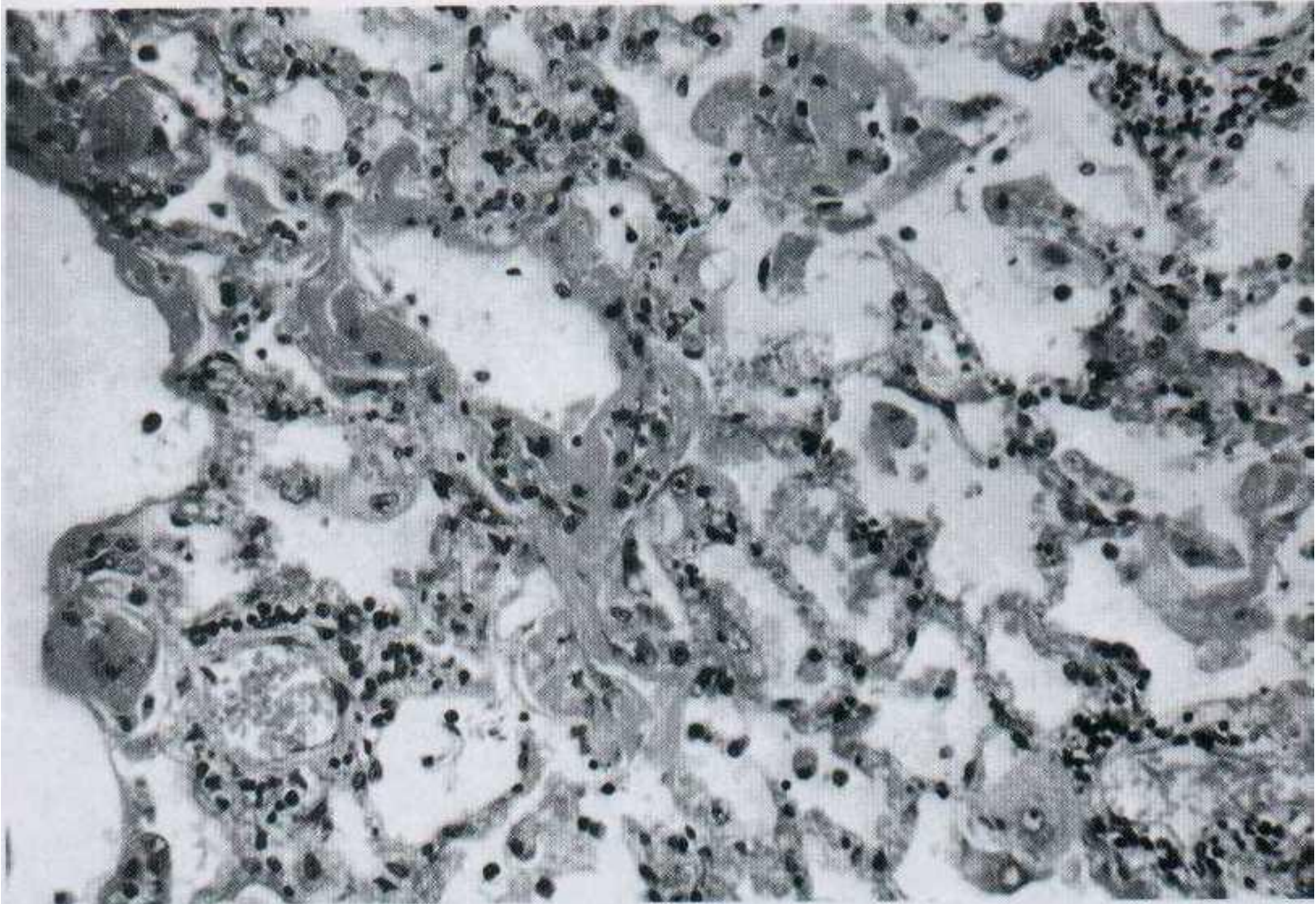


Fig. 4-8 Fibrinous exudate. The strands and accumulations of pale-staining debris here consist

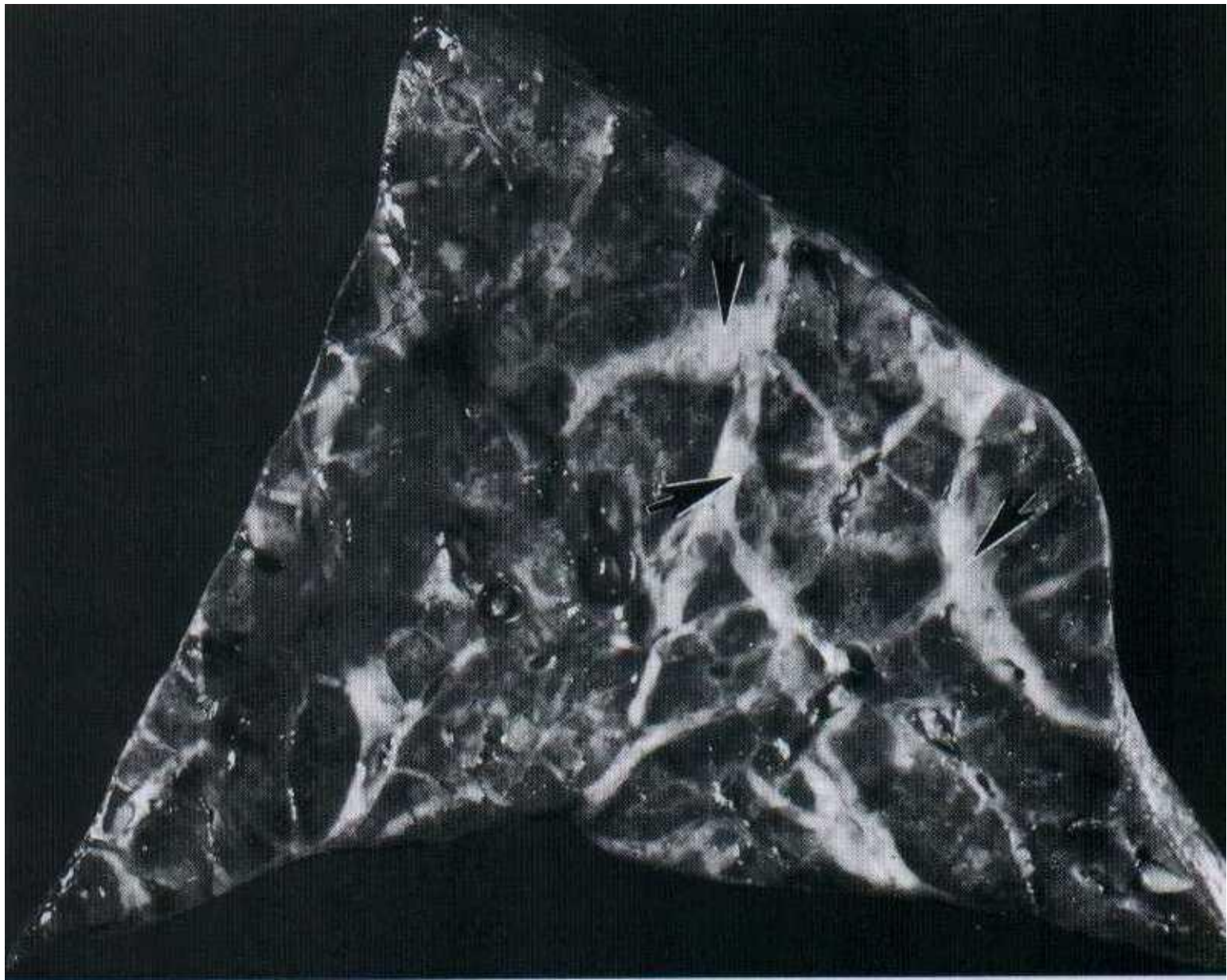
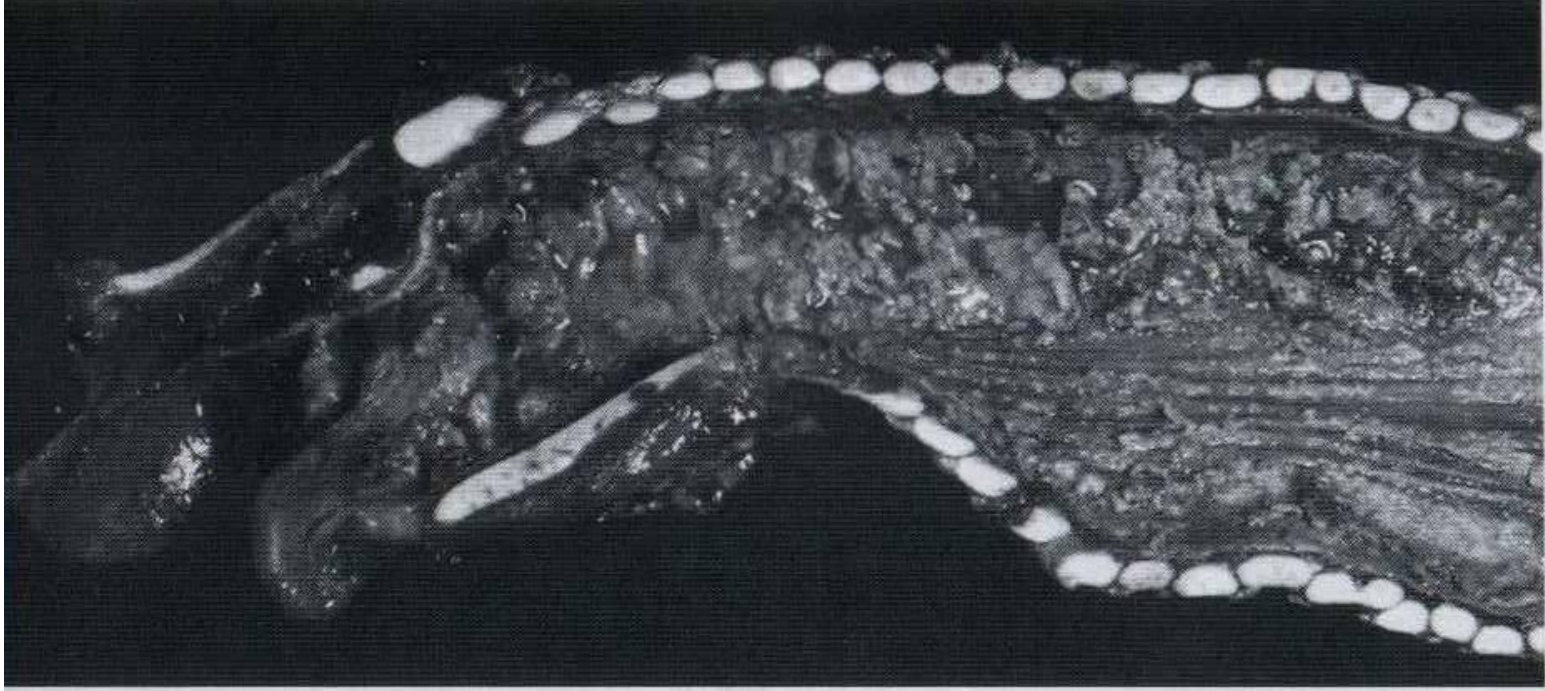


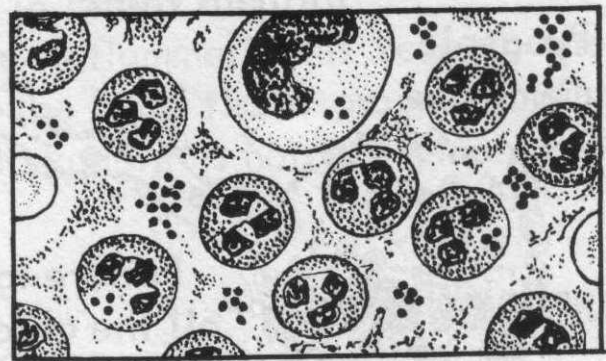
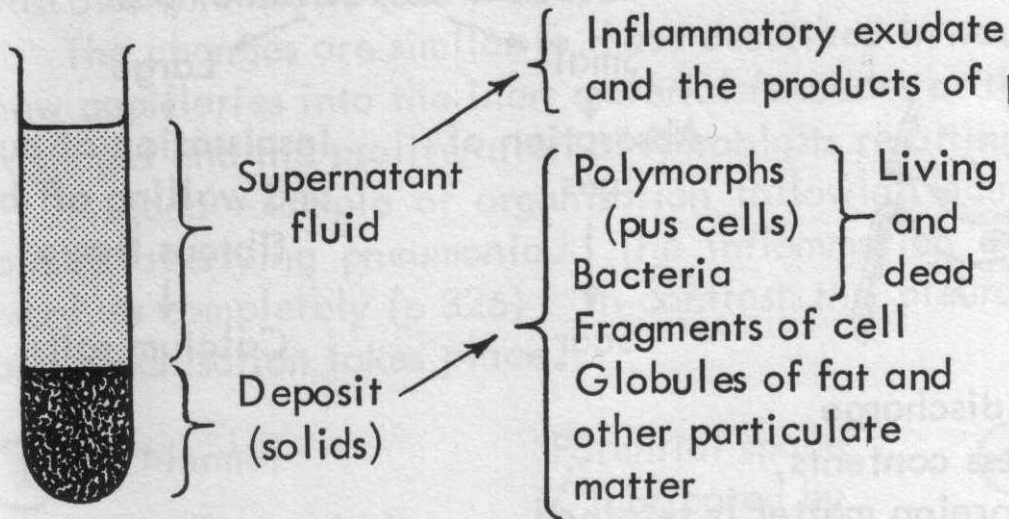
Fig. 4-9 Bovine fibrinous pneumonia. The interlobular deposition of fibrin, *arrows*, is a typical

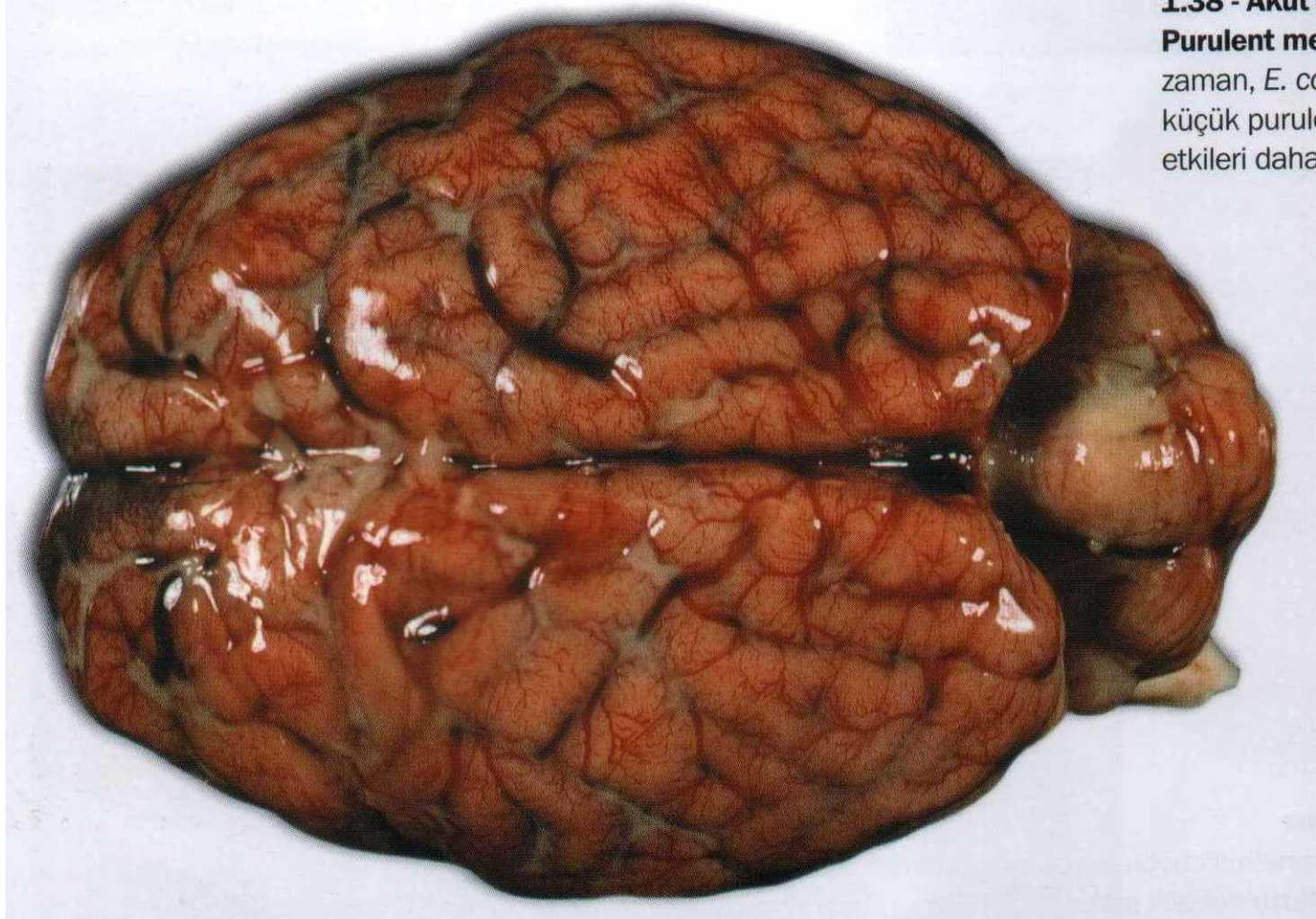


4-10 Fibrinonecrotic tracheitis. Necrosis and fib

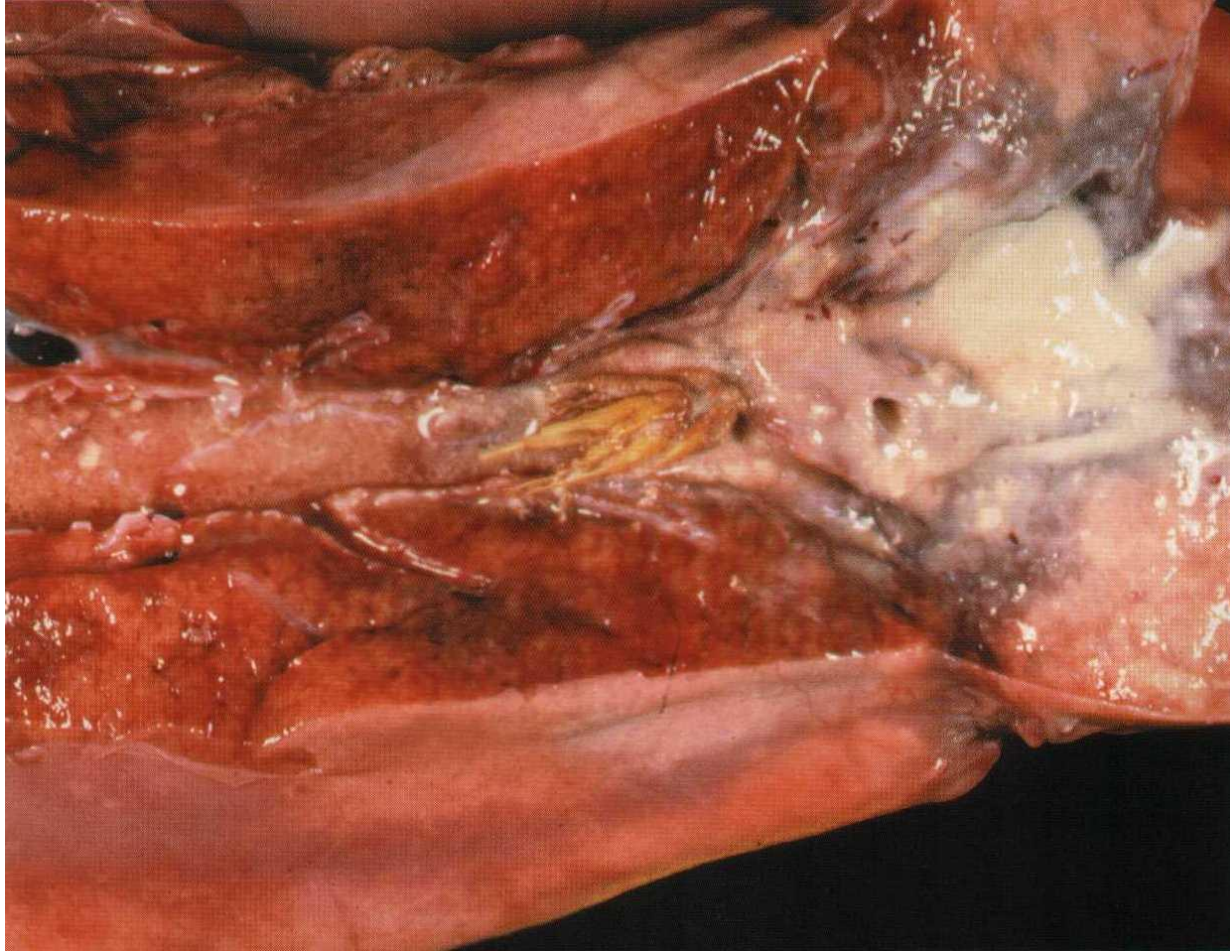
SUPPURATION means the formation of PUS: where pus accumulates an **ABSCESS** forms.

Infection by pyogenic (pus forming) bacteria is the usual cause e.g. staphylococcal abscess (or boil). The pus in this case is a thick, creamy, yellow fluid which, on centrifugation, separates thus:-





1.50 - Akut
Purulent me
zaman, *E. coli*
küçük purul
etkileri daha



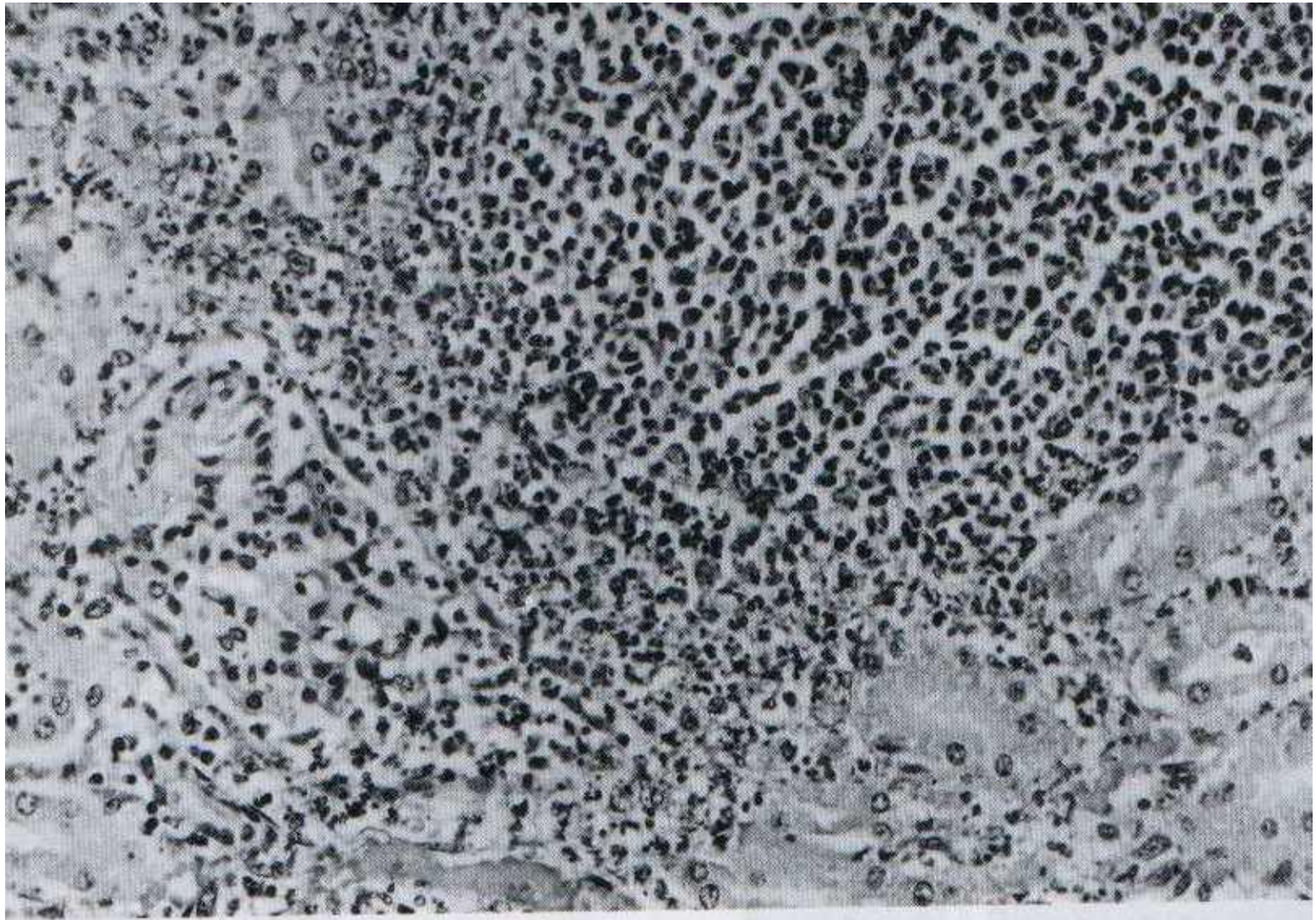


Fig. 4-7 Suppurative exudate. Almost all the inflammatory cells in this focus of inflammation are neutrophils. This makes the lesion suppurative, or purulent, and the exudate is called "pus."

The usual evolution of an abscess is as follows:-

① Skin surface



Bacteria cause tissue damage and necrosis.

Inflammation

② Swelling (oedema)



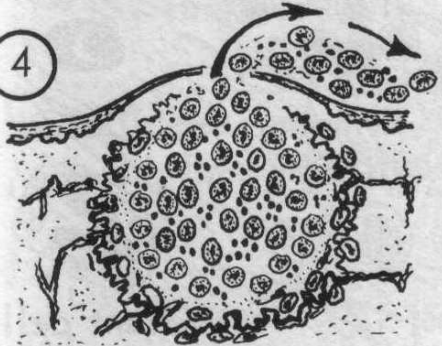
Bacteria multiply: polymorphs pack the central zone.

③ Thinning of epidermis



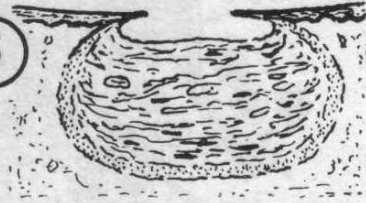
Pus forms in centre
Pus tracking towards surface
Delineation of abscess by 'pyogenic membrane' - new capillaries, polymorphs and a few fibroblasts.

④



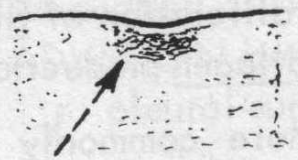
Abscess 'points' and ruptures discharging pus. Pyogenic membrane more pronounced.

⑤



Swelling subsides, cavity collapses, organisation (see p 37) and fibrosis proceed.

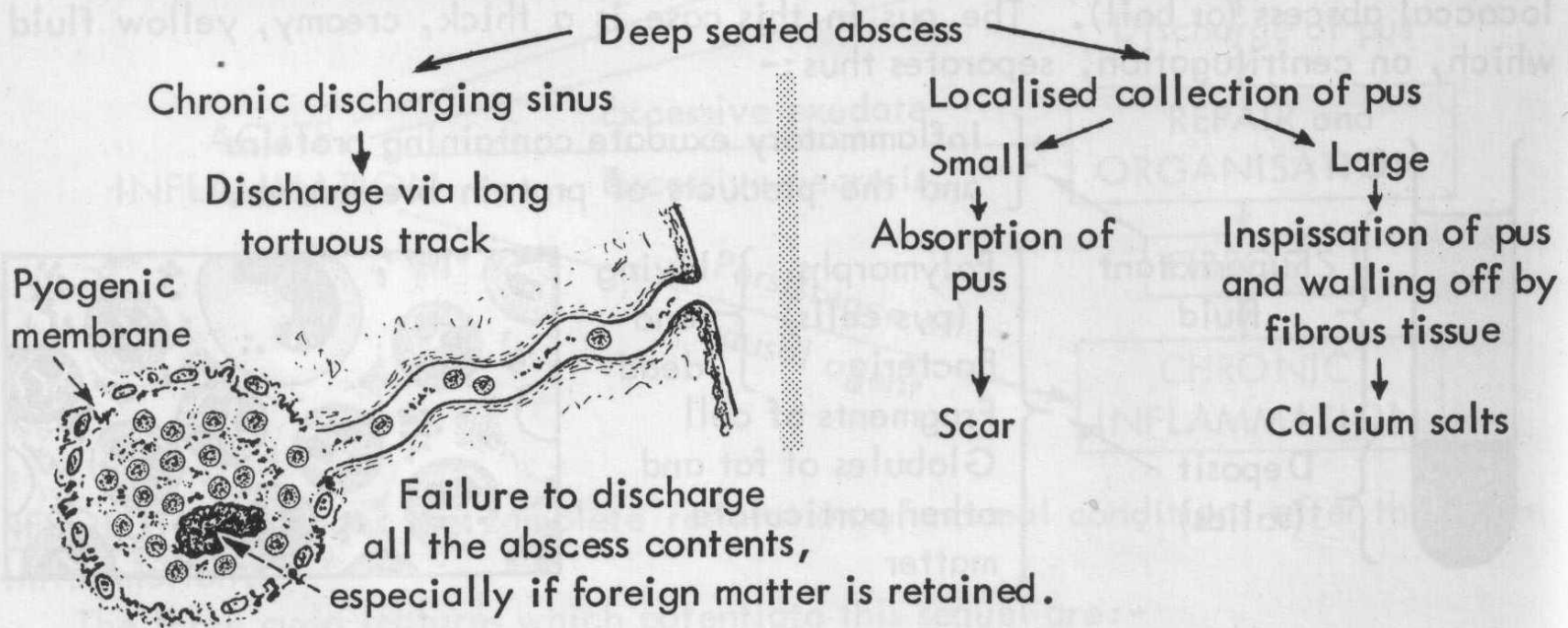
⑥



Final small scar

Evolution of an Abscess (continued)

When the abscess is deep seated the process may be modified as follows:-



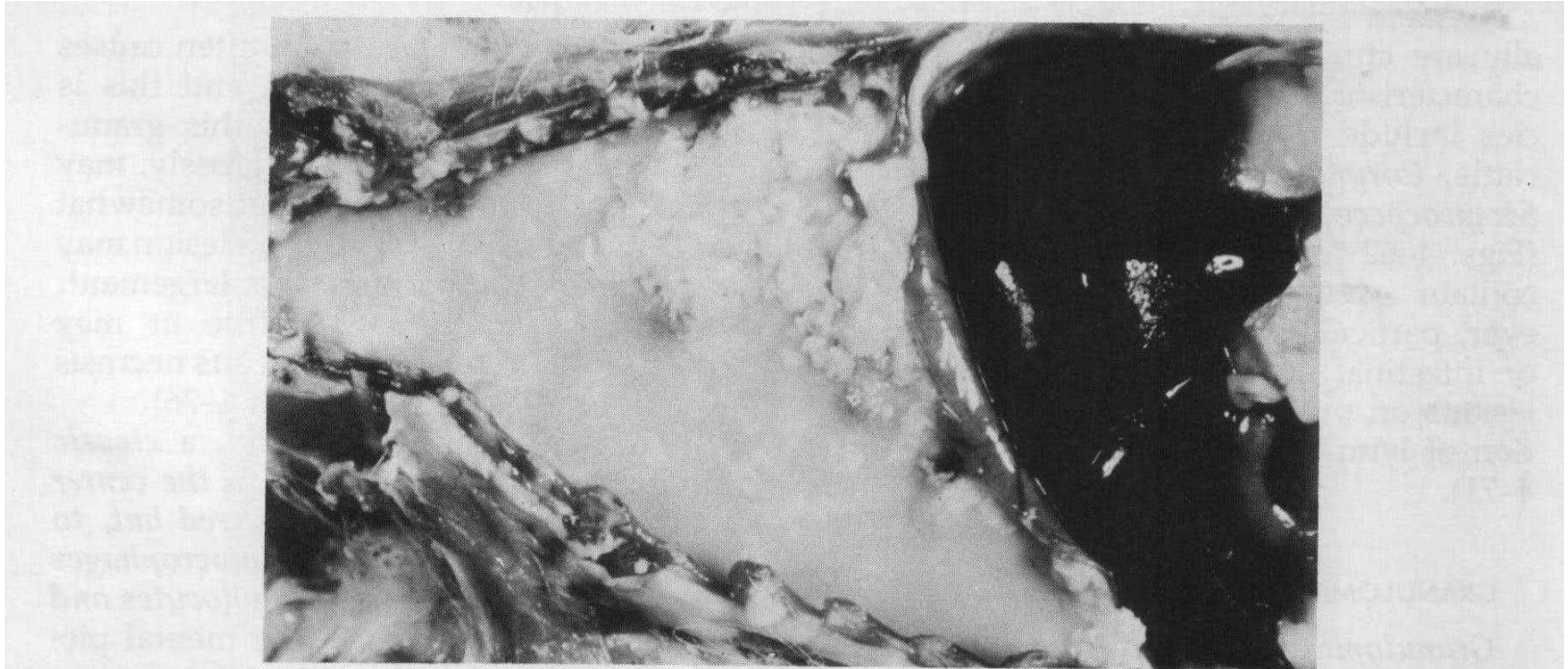
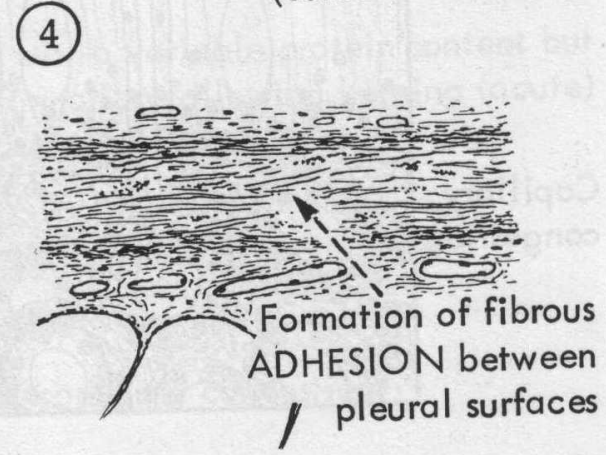
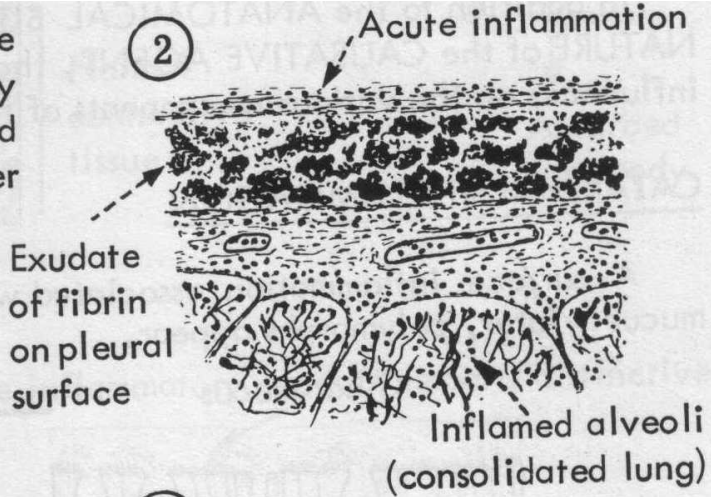
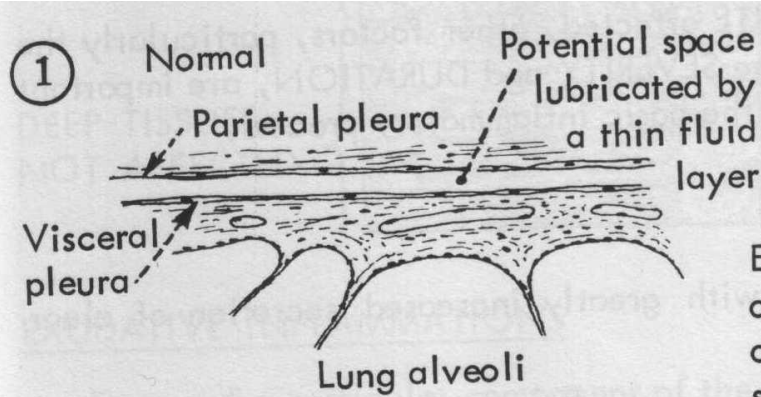
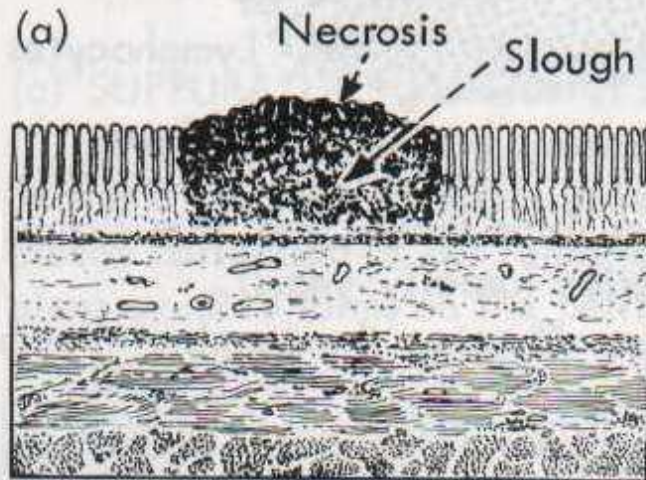


Figure 4–61. Empyema in a cat. The lungs are still in the thorax but are covered by fibrinopurulent exudate. This is a common lesion in cats.

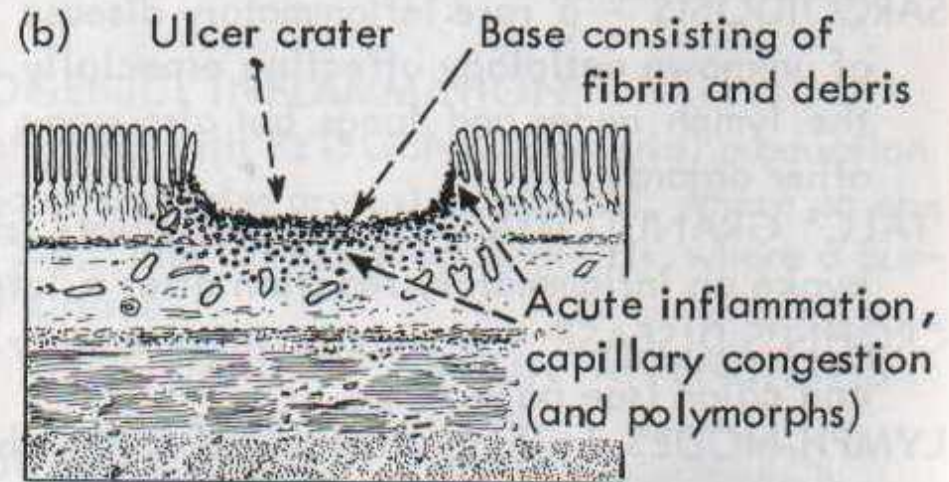


Other good examples of organisation are seen after infarction (see pp 131, 259).

Evolution of a Simple ulcer

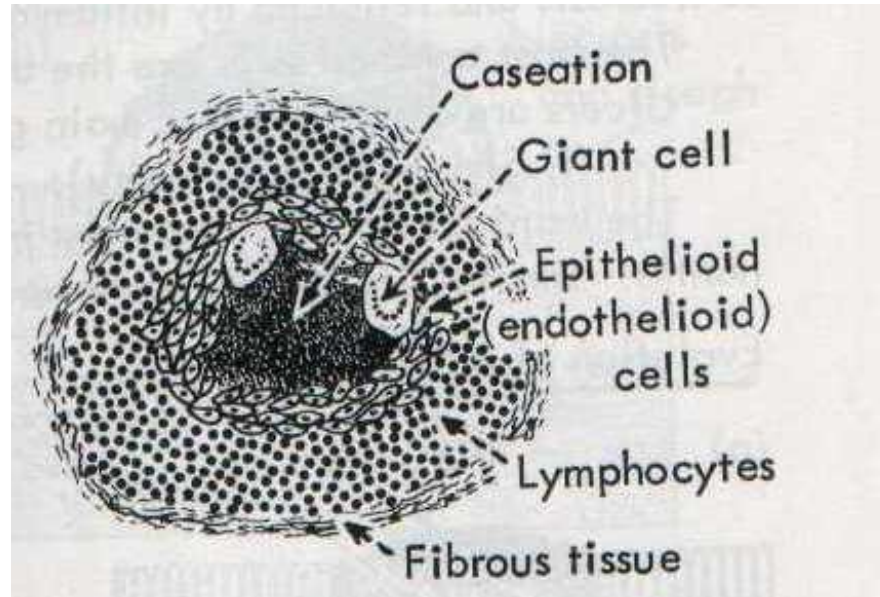


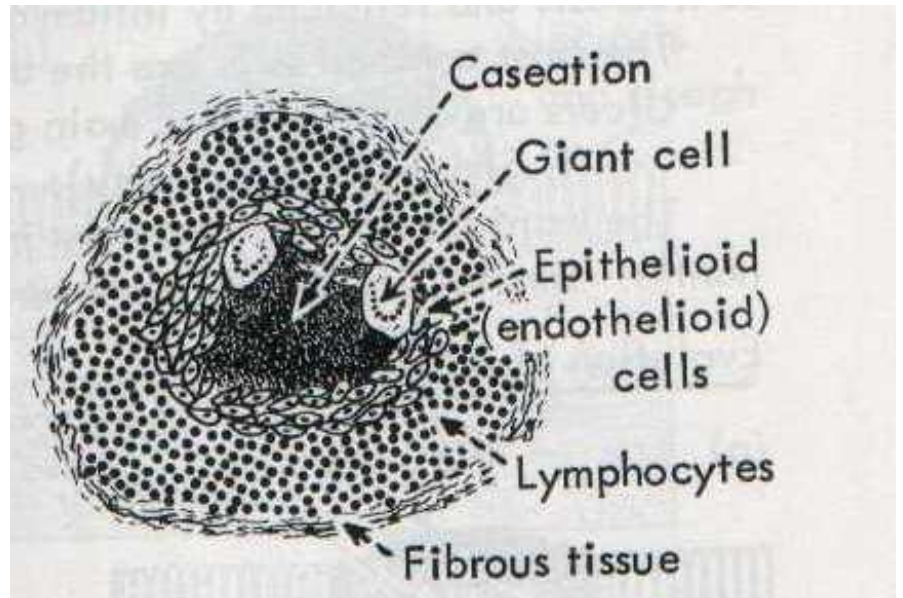
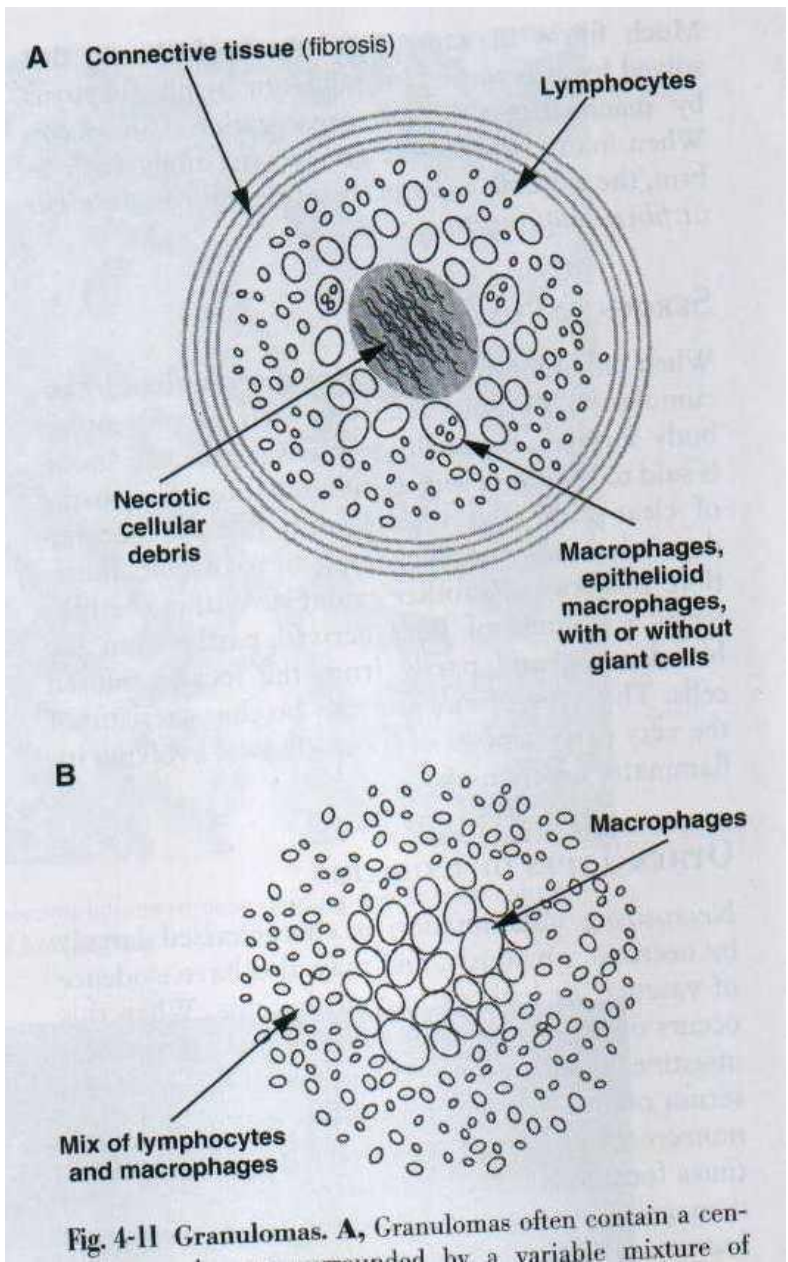
ACUTE ULCER



Healing can occur at this stage with restoration to normal BUT, if irritation (e.g. bacterial action, slight trauma, digestive juices and acid) continues, a







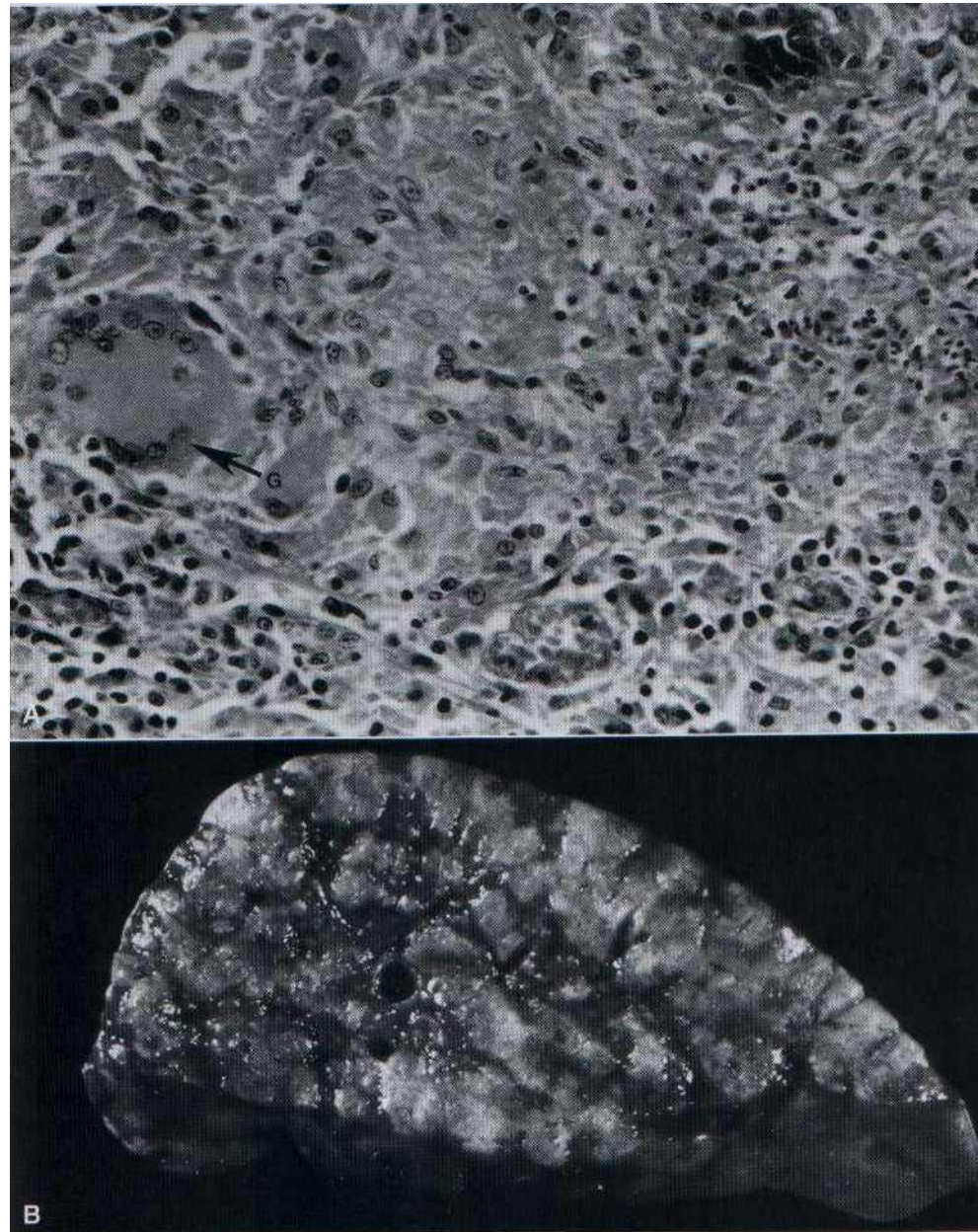


Fig. 4-12 Granulomatous inflammation. **A**, Necrosis, fibroplasia, and a mixed population of in-

