



Principle of Infection

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History:

- Louis Pasteur and Robert Koch; establishing the microbiologic etiology of infectious disease.
- Pasteur;
 - * proving that microorganisms can cause disease
 - * created first attenuated vaccines; rabies vaccine for human in 1885.

- 1882, Koch; criteria for linking a specific microorganism to a disease.

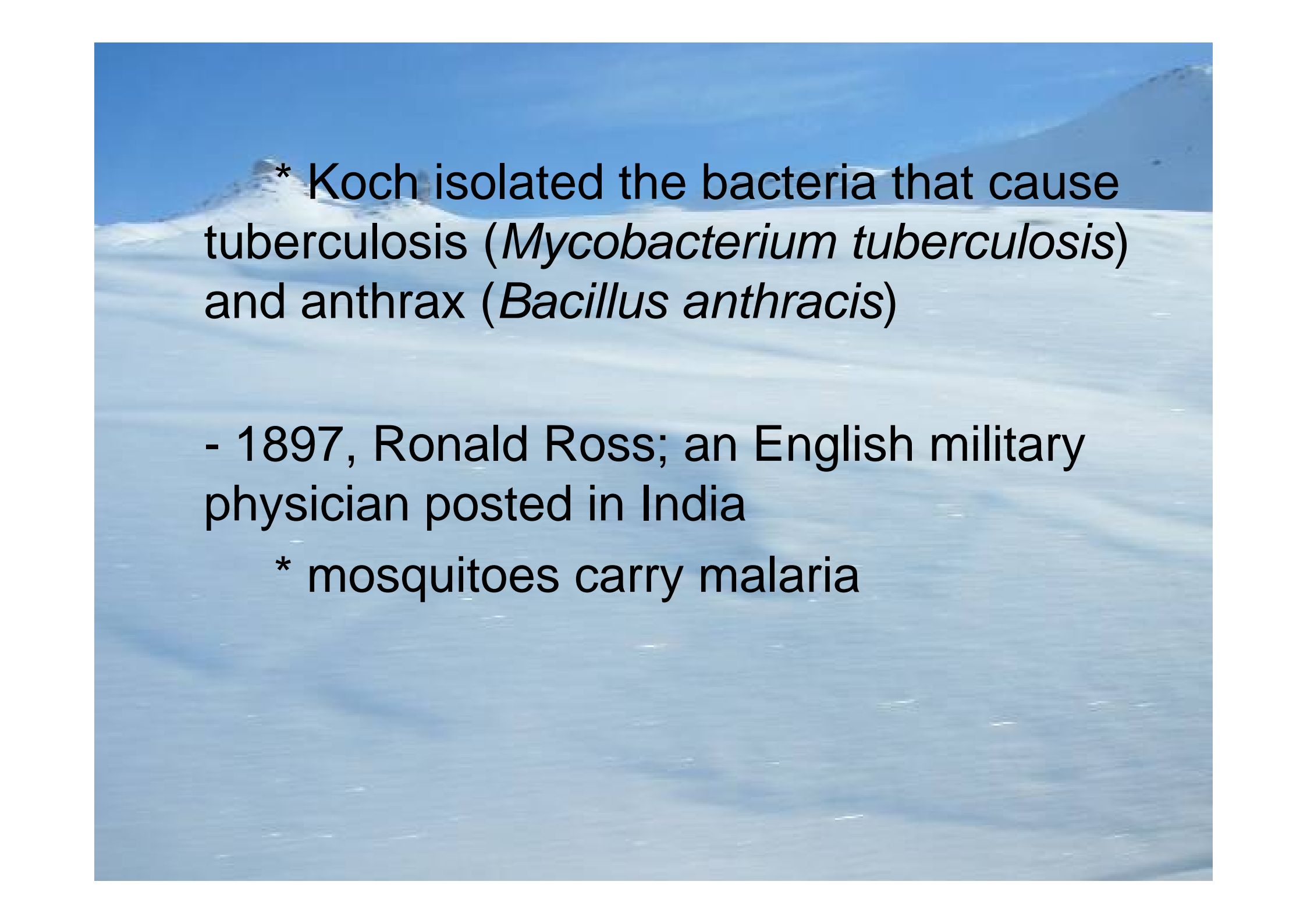
* *Koch's postulate;*

1. *the organism is found in the lesions of the disease.*

2. *the organism can be isolated as single colonies on solid media*

3. *inoculation of the organism causes lesions in experimental animals*

4. *the organism can be recovered from the experimental animal*



* Koch isolated the bacteria that cause tuberculosis (*Mycobacterium tuberculosis*) and anthrax (*Bacillus anthracis*)

- 1897, Ronald Ross; an English military physician posted in India

* mosquitoes carry malaria



- 1900, Walter Reed; an American military physician, Cuba

* yellow fever transmitted by mosquitoes.

- 1901, James Carroll showed that yellow fever caused by a virus. This was the first demonstration that a virus causes disease in human.



- 1911, Rous demonstrated that a virus causes sarcoma in chickens.

- 1944, Oswald Avery; transfer DNA from virulent to avirulent *Streptococcus pneumoniae* → explosion of research in molecular genetics.



Emerging/Reemerging infectious diseases:

Emerging diseases:

- new infectious disease or outbreaks of previously unknown disease or known disease whose incidence in human has significantly increased in the past two decades.
- SARS



Reemerging diseases:

- disease that have reappeared after a significant decline in incidence
- drug resistance, mutation
- dengue, West Nile Virus, food and waterborne infections

TABLE 8-1 Some Recently Recognized Infectious Agents and Manifestations

1977	Ebola virus	Epidemic hemorrhagic fever
	Hantaan virus	Hemorrhagic fever with renal disease
	<i>Legionella pneumophila</i>	Legionnaire's disease
	<i>Campylobacter jejuni</i>	Enteritis
1980	HTLV-I	T-cell lymphoma or leukemia
1981	<i>Staphylococcus aureus</i>	Toxic shock syndrome
1982	HTLV-II	Hairy cell leukemia
	<i>Escherichia coli</i> O157:H7	Hemolytic-uremic syndrome
	<i>Borrelia burgdorferi</i>	Lyme disease
1983	HIV	AIDS
	<i>Helicobacter pylori</i>	Gastric ulcers

1985	<i>Enterocytozoon bieneusi</i>	Chronic diarrhea
1988	HHV-6	Roseola subitum
	Hepatitis E	Enterically transmitted hepatitis
1989	Hepatitis C	Hepatitis C
	<i>Ehrlichia chaffeensis</i>	Human monocytic ehrlichiosis
1992	<i>Vibrio cholerae</i> O139	New epidemic cholera strain
	<i>Bartonella henselae</i>	Cat-scratch disease
1993	<i>Encephalitozoon cuniculi</i>	Opportunistic infections
1994	<i>Anaplasma phagocytophilum</i>	Human granulocytic ehrlichiosis (anaplasmosis)
1995	KSHV (HHV-8)	Kaposi sarcoma in AIDS
2001	Human metapneumovirus	Respiratory infections
2002	West Nile virus	Acute flaccid paralysis
2003	SARS coronavirus	Severe acute respiratory syndrome

Adapted from Lederberg J: Infectious disease as an evolutionary paradigm. *Emerg Infect Dis* 3:417, 1997.

A photograph of a snowy mountain range under a clear blue sky. The foreground is a vast, flat expanse of snow, leading up to a range of snow-capped mountains in the distance. The sky is a uniform, clear blue.

Classification of infectious agents:

- classification according to structure
- classification according to pathogenesis
- classification according to site of multiplication

A photograph of a snowy mountain range under a clear blue sky. The snow is bright white, and the mountains are in the background. The text is overlaid on the left side of the image.

Classification according to structure

- Prion
- Viruses
- Bacteria
- Rickettsia, chlamydia, mycoplasma
- Fungi
- Protozoa, metazoa
- Ectoparasite



Classification according to pathogenesis

- Infectivity
- Pathogenesis
- Pathogenic agents; high and low virulence
- Opportunistic infection

A photograph of a vast, snow-covered mountain range under a clear, bright blue sky. The snow is deep and appears to be on a high-altitude plateau or valley. The mountains in the background are partially covered in snow, with some rocky peaks visible. The overall scene is serene and cold.

Classification according to site of multiplication

- obligate intracellular organisms
- facultative intracellular organism
- extracellular organisms

A photograph of a snowy mountain landscape under a clear blue sky. The foreground is a vast, flat expanse of snow, leading up to a range of snow-capped mountains in the distance. The sky is a uniform, clear blue. The overall scene is bright and serene.

Obligate Intracellular Organisms

- Prions
- All viruses
- All rickettsiae
- All chlamydia
- Some protozoa

Facultative Intracellular Organisms

- Mycobacteria; *M. tuberculosis*
- *Brucella* spp.
- *Actinomyces*
- *Klebsiella rhinoscleromatis*
- *Francisella tularensis*
- *Pseudomonas mallei* and *P. pseudomallei*



Fungi;

- *Coccidioides immitis*
- *Histoplasma capsulatum*
- *Cryptococcus neoformans*
- *Blastomyces dermatitidis*
- *Paracoccidioides brasiliensis*
- *Sporothrix schenckii*

Some protozoa

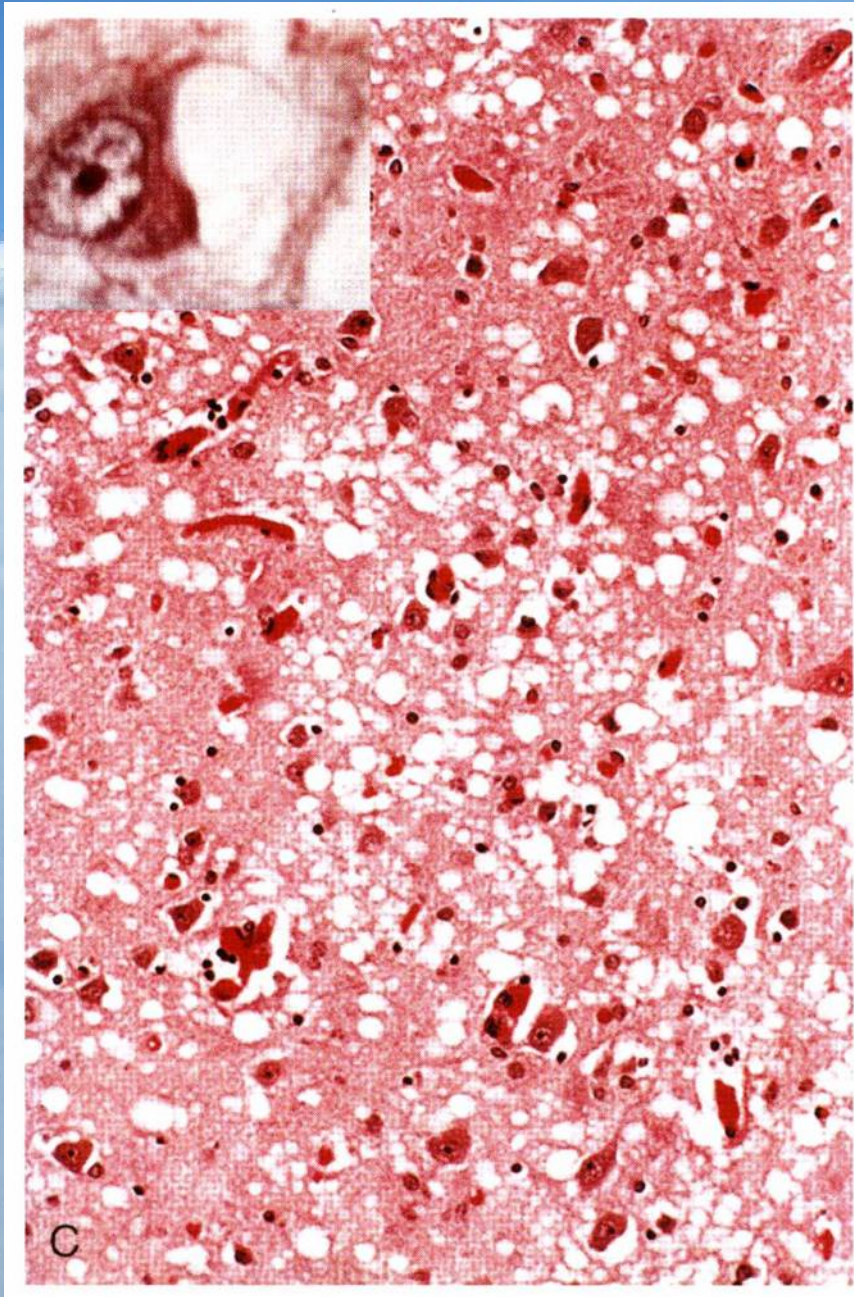
Extracellular Organisms

- Mycoplasma
- All bacteria except facultative intracellular organism
- Fungi; *Candida albicans*, *Aspergillus* spp, *Mucor* spp.
- Some protozoa except *Trypanosoma* spp, *Plasmodium* spp, *Toxoplasma* spp.
- All metazoa

Category of Infectious agents:

Prions:

- 27 kD nucleic acid-free prion
- are apparently composed of abnormal forms of host protein; prion protein
- these agents cause transmissible spongiform encephalopathies; kuru, CJD, bovine spongiform encephalopathy (mad cow)



Prion disease



Viruses:

- obligate intracellular parasites that depend on the host cell's metabolic machinery for their replication.
- consists of a nucleic acid genome surrounded by a protein coat (capsid)
- classified by their nucleic acid genome; DNA or RNA

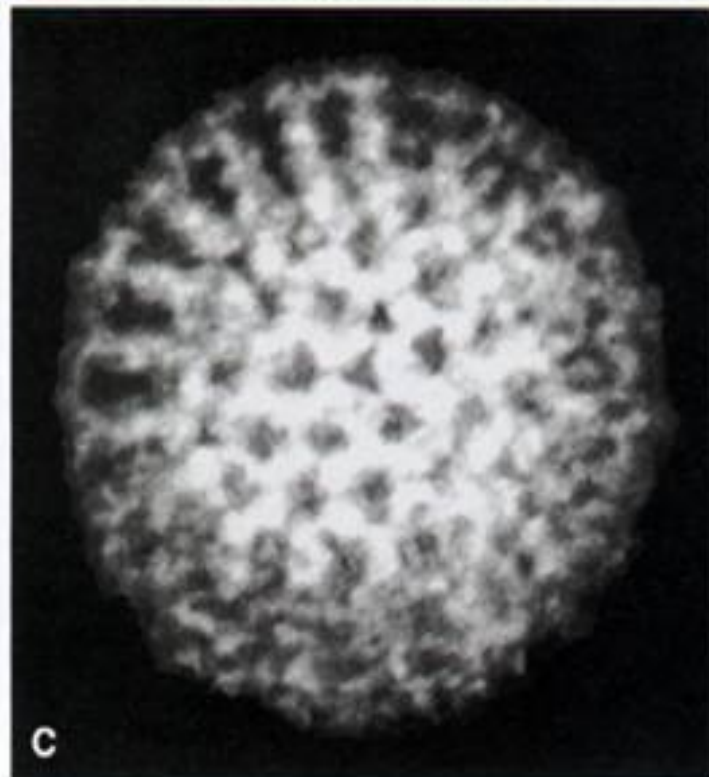
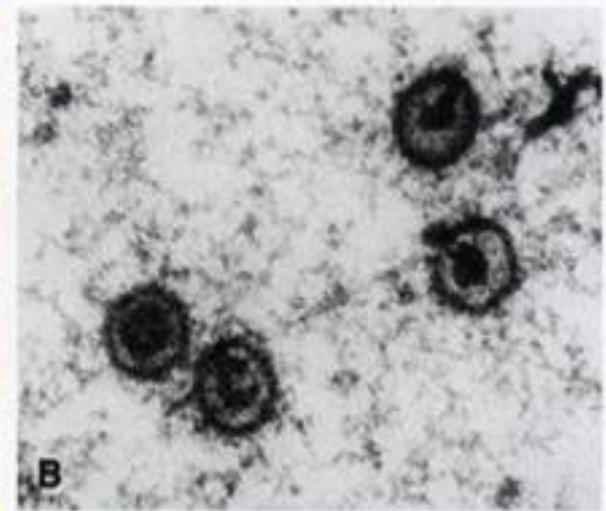
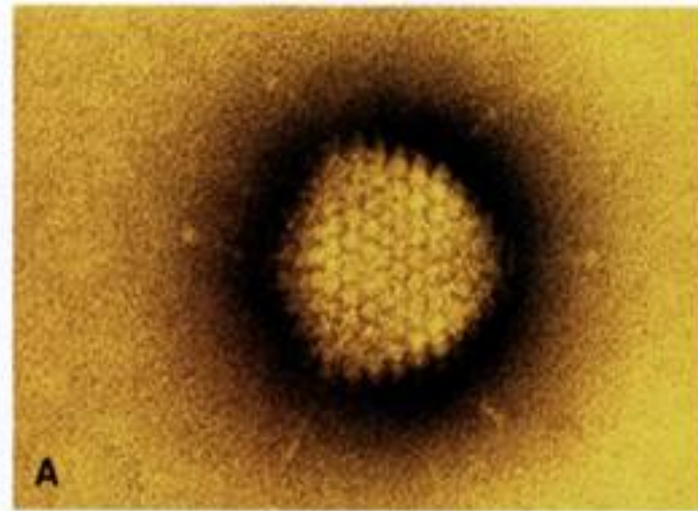


FIGURE 8-1 The variety of viral structures, as seen by electron microscopy. A, Adenovirus, an icosahedral nonenveloped DNA virus with fibers. B, Epstein Barr virus, an icosahedral enveloped DNA virus. C, Rotavirus, a nonenveloped, wheel-like, RNA virus. D, Paramyxovirus, a spherical enveloped RNA virus. RNA is seen spilling out of the disrupted virus. (Photos courtesy of Science Source; © Photo Researchers, Inc., New York, New York.)

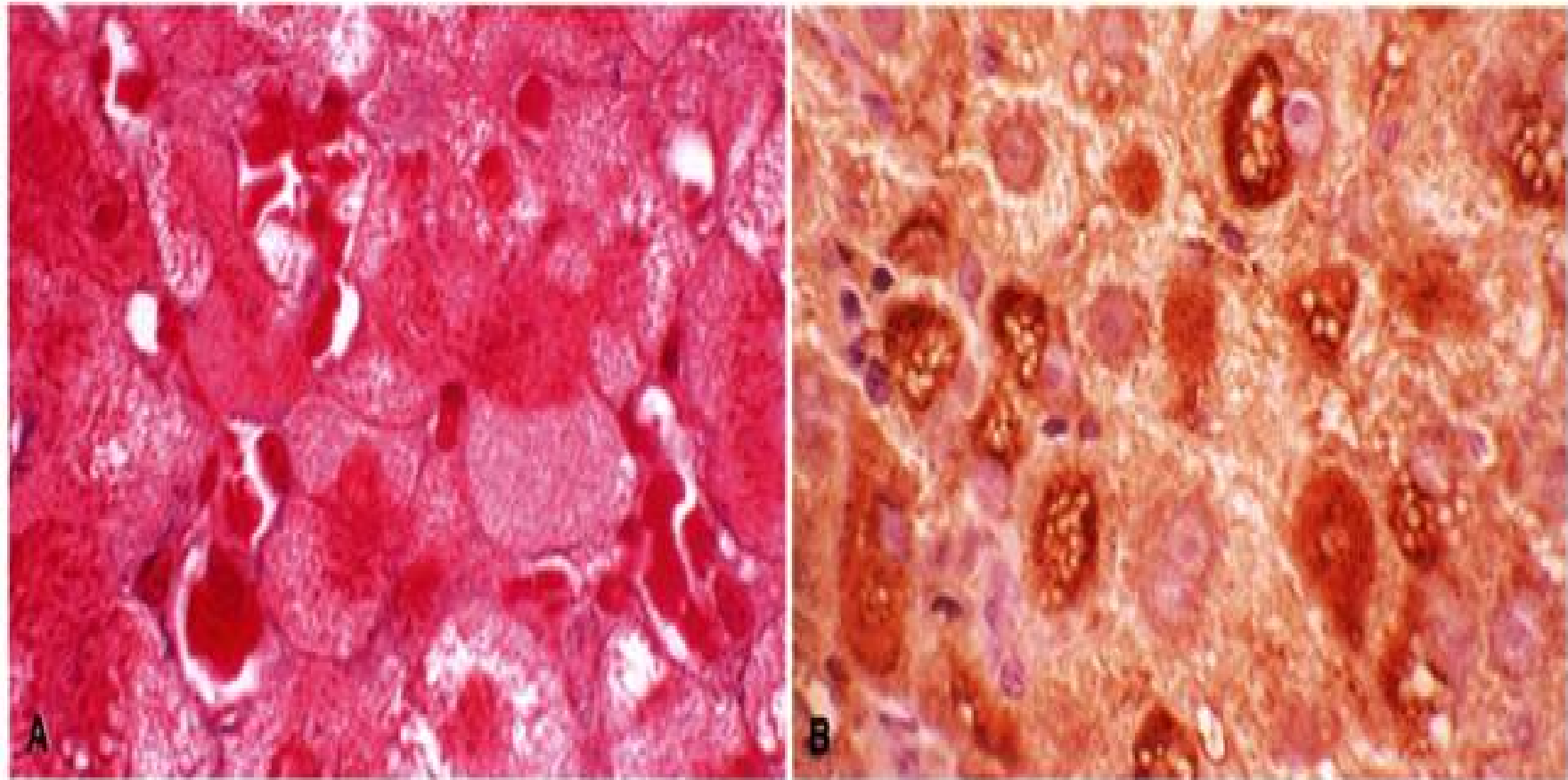


FIGURE 18-18 Hepatitis B viral infection. *A*, Liver parenchyma showing hepatocytes with diffuse granular cytoplasm, so-called ground glass hepatocytes. (H&E) *B*, Immunoperoxidase stain for HBsAg from the same case, showing cytoplasmic inclusions of viral particles.

TABLE 8-4 Selected Human Viral Diseases and Their Pathogens

Viral Pathogen	Virus Family	Genomic Type	Disease Expression
Respiratory			
Adenovirus	Adenoviridae	DS DNA	Upper and lower respiratory tract infections, conjunctivitis, diarrhea
Rhinovirus	Picornaviridae	SS RNA	Upper respiratory tract infection
Coxsackievirus	Picornaviridae	SS RNA	Pleurodynia, herpangina, hand-foot-and-mouth disease, SARS
Coronavirus	Coronaviridae	SS RNA	Upper respiratory tract infection
Influenza viruses A, B	Orthomyxoviridae	SS RNA	Influenza
Respiratory syncytial virus	Paramyxoviridae	SS RNA	Bronchiolitis, pneumonia
Digestive			
Mumps virus	Paramyxoviridae	SS RNA	Mumps, pancreatitis, orchitis
Rotavirus	Reoviridae	DS RNA	Childhood diarrhea
Norwalk agent	Caliciviridae	SS RNA	Gastroenteritis
Hepatitis A virus	Picornaviridae	SS RNA	Acute viral hepatitis
Hepatitis B virus	Hepadnaviridae	DS DNA	Acute or chronic hepatitis
Hepatitis D virus	Viroid-like	SS RNA	With HBV, acute or chronic hepatitis
Hepatitis C virus	Flaviviridae	SS RNA	Acute or chronic hepatitis
Hepatitis E virus	Norwalk-like	SS RNA	Enterically transmitted hepatitis

Systemic with Skin Eruptions

Measles virus	Paramyxoviridae	SS RNA	Measles (rubeola)
Rubella virus	Togaviridae	SS RNA	German measles (rubella)
Parvovirus	Parvoviridae	SS DNA	Erythema infectiosum, aplastic anemia
Vaccinia virus	Poxviridae	DS DNA	Smallpox vaccine
Varicella-zoster virus	Herpesviridae	DS DNA	Chickenpox, shingles
Herpes simplex virus 1	Herpesviridae	DS DNA	"Cold sore"
Herpes simplex virus 2	Herpesviridae	DS DNA	Genital herpes

Systemic with Hematopoietic Disorders

Cytomegalovirus	Herpesviridae	DS DNA	Cytomegalic inclusion disease
Epstein-Barr virus	Herpesviridae	DS DNA	Infectious mononucleosis
HTLV-I	Retroviridae	SS RNA	Adult T-cell leukemia; tropical spastic paraparesis
HIV-1 and HIV-2	Retroviridae	SS RNA	AIDS

Arboviral and Hemorrhagic Fevers

Dengue virus 1-4	Togaviridae	SS RNA	Dengue, hemorrhagic fever
Yellow fever virus	Togaviridae	SS RNA	Yellow fever
Regional hemorrhagic fever viruses	Filoviridae	SS RNA	Ebola, Marburg disease
	Hantavirus	SS RNA	Korean, U.S. pneumonia

Warty Growths

Papillomavirus	Papovaviridae	DS DNA	Condyloma; cervical carcinoma
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Central Nervous System

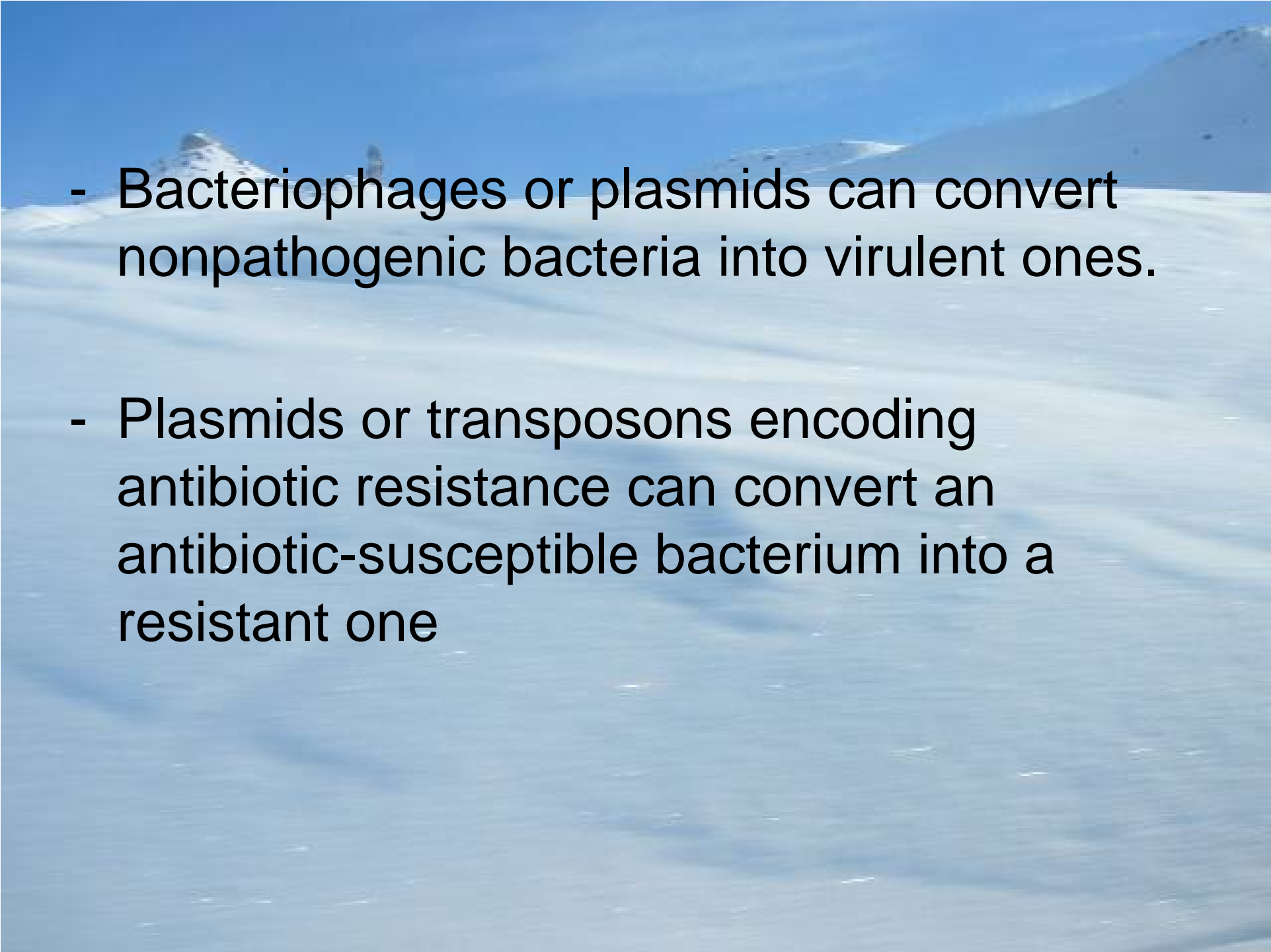
Poliovirus	Picornaviridae	SS RNA	Poliomyelitis
JC virus	Papovaviridae	DS DNA	Progressive multifocal leukoencephalopathy (opportunistic)
Arboviral encephalitis viruses	Togaviridae	SS RNA	Eastern, Western, Venezuelan, St. Louis,

DS, double-stranded; SS, single-stranded.

A photograph of a snowy mountain range under a clear blue sky. The snow is bright white, and the sky is a deep, clear blue. The mountains are in the background, with some peaks visible. The overall scene is bright and clear.

Bacteriophages, Plasmids, Transposons:

- these are mobile genetic elements that infect bacteria and can indirectly cause human diseases by encoding bacterial virulence factors (e.g. adhesins, toxins, or enzymes that confer antibiotic resistance)

- 
- Bacteriophages or plasmids can convert nonpathogenic bacteria into virulent ones.
 - Plasmids or transposons encoding antibiotic resistance can convert an antibiotic-susceptible bacterium into a resistant one



Bacteria:

- are prokaryotes, have a cell membrane but lack membrane-bound nuclei and other membrane-enclosed organelles.
- gram positive and gram negative
- most bacteria synthesize their own DNA, RNA, and proteins, but they depend on the host for favorable growth conditions.

TABLE 8-5 Examples of Bacterial, Spirochetal, and Mycobacterial Diseases

Clinical or Microbiologic Category	Species	Frequent Disease Presentations
Infections by pyogenic cocci	<i>Staphylococcus aureus</i> , <i>S. epidermidis</i> <i>Streptococcus pyogenes</i> , β -hemolytic	Abscess, cellulitis, pneumonia, septicemia Upper respiratory tract infection, erysipelas, scarlet fever, septicemia
	<i>Streptococcus pneumoniae</i> (pneumococcus) <i>Neisseria meningitidis</i> (meningococcus) <i>Neisseria gonorrhoeae</i> (gonococcus)	Lobar pneumonia, meningitis Cerebrospinal meningitis Gonorrhea
Gram-negative infections, common	* <i>Escherichia coli</i> * <i>Klebsiella pneumoniae</i> * <i>Enterobacter (Aerobacter) aerogenes</i> * <i>Proteus</i> spp. (<i>P. mirabilis</i> , <i>P. morgani</i>) * <i>Serratia marcescens</i> * <i>Pseudomonas</i> spp. (<i>P. aeruginosa</i>) <i>Bacteroides</i> spp. (<i>B. fragilis</i>) <i>Legionella</i> spp. (<i>L. pneumophila</i>)	Urinary tract infection, wound infection, abscess, pneumonia, septicemia, endotoxemia, endocarditis Anaerobic infection Legionnaires disease
Contagious childhood bacterial diseases	<i>Haemophilus influenzae</i> <i>Bordetella pertussis</i> <i>Corynebacterium diphtheriae</i>	Meningitis, upper and lower respiratory tract infections Whooping cough Diphtheria
Enteropathic infections	Enteropathogenic <i>E. coli</i> <i>Shigella</i> spp. <i>Vibrio cholerae</i> <i>Campylobacter fetus</i> , <i>C. jejuni</i> <i>Yersinia enterocolitica</i> <i>Salmonella</i> spp. (1000 strains) <i>Salmonella typhi</i>	Invasive or noninvasive gastroenterocolitis, some with septicemia Typhoid fever

Clostridial infections	<i>Clostridium tetani</i> <i>Clostridium botulinum</i> <i>Clostridium perfringens</i> , <i>C. septicum</i> * <i>Clostridium difficile</i>	Tetanus (lockjaw) Botulism (paralytic food poisoning) Gas gangrene, necrotizing cellulitis Pseudomembranous colitis
Zoonotic bacterial infections	<i>Bacillus anthracis</i> * <i>Listeria monocytogenes</i> <i>Yersinia pestis</i> <i>Francisella tularensis</i> <i>Brucella melitensis</i> , <i>B. suis</i> , <i>B. abortus</i> <i>Burkholderia mallei</i> , <i>B. pseudomallei</i> <i>Leptospira</i> spp. (many groups) <i>Borrelia recurrentis</i> <i>Borrelia burgdorferi</i> <i>Bartonella henselae</i> <i>Spirillum minus</i> , <i>Streptobacillus moniliformis</i>	Anthrax (malignant pustule) <i>Listeria</i> meningitis, listeriosis Bubonic plague Tularemia Brucellosis (undulant fever) Glanders, melioidosis Leptospirosis, Weil disease Relapsing fever Lyme borreliosis Cat-scratch disease; bacillary angiomatosis Rat-bite fever
Human treponemal infections	<i>Treponema pallidum</i> <i>Treponema pertenu</i> <i>Treponema carateum</i> (<i>T. herrejoni</i>)	Venereal, endemic syphilis (bejel) Yaws (frambesia) Pinta (carate, mal del pinto)
Mycobacterial infections	* <i>Mycobacterium tuberculosis</i> , <i>M. bovis</i> (Koch bacillus) <i>M. leprae</i> (Hansen bacillus) * <i>M. kansasii</i> , <i>M. avium</i> , <i>M. intracellulare</i> <i>M. ulcerans</i>	Tuberculosis Leprosy Atypical mycobacterial infections Buruli ulcer
Actinomycetaceae	* <i>Nocardia asteroides</i> <i>Actinomyces israelii</i>	Nocardiosis Actinomycosis

*Important opportunistic infections.

Virulence factors of bacteria

Factors

Attachment to cells and artificial surfaces

Interfere with humoral response

Mechanisms

- pili, fimbriae
- outer membrane proteins
- cell-ass. polysaccharides

- destruction of Ig on mucosal surfaces
- resistance to bactericidal effect of serum

Factors

Interfere with inflammatory response

Induction of tissue ischemia

Interfere with cellular physiology

- * destruction of cells and tissue by cytotoxin production
- * competition with host for nutrients
- * resistance to host defenses

Resistance to adverse environmental factors

Mechanisms

- destruction of leukocytes

- activation of clotting system



Chlamydiae, Rickettsiae, Mycoplasma:

- divide by binary fission but lack certain structures or metabolic capabilities.

Mycoplasma lack a cell wall

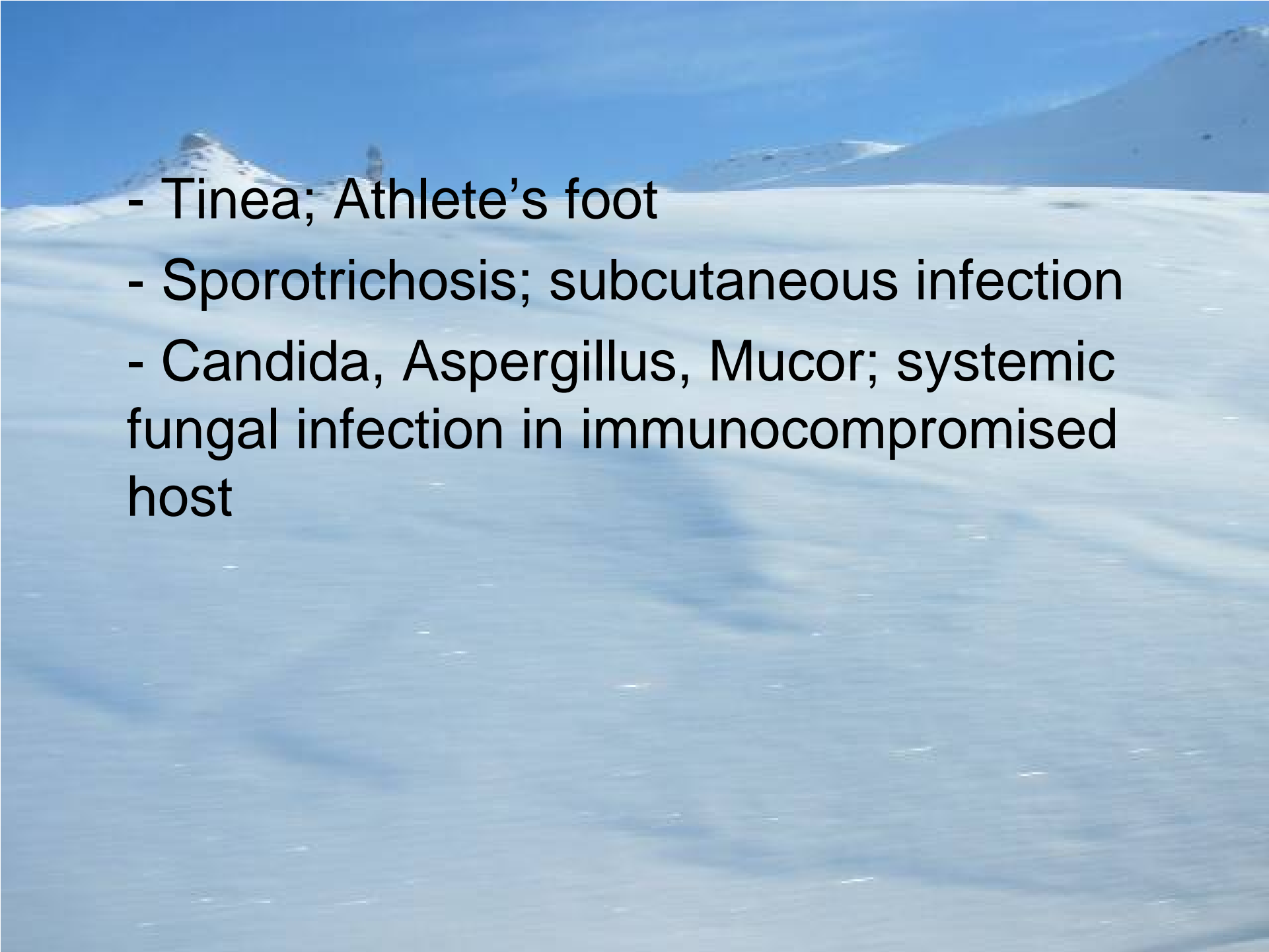
Chlamydia cannot synthesize ATP

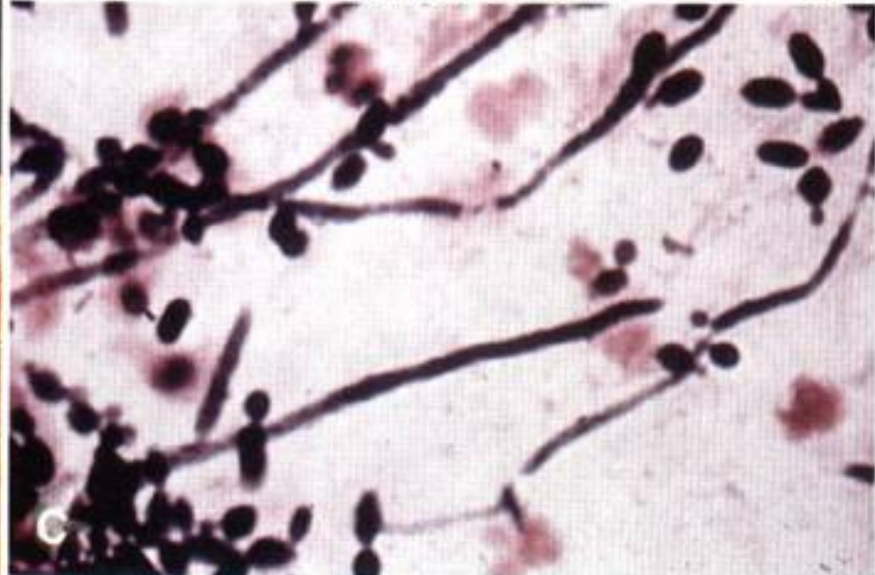
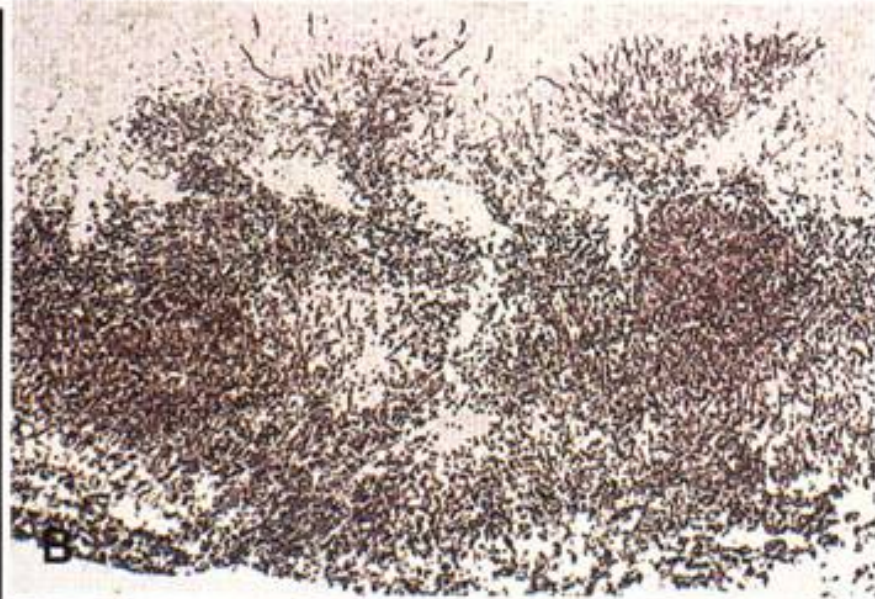
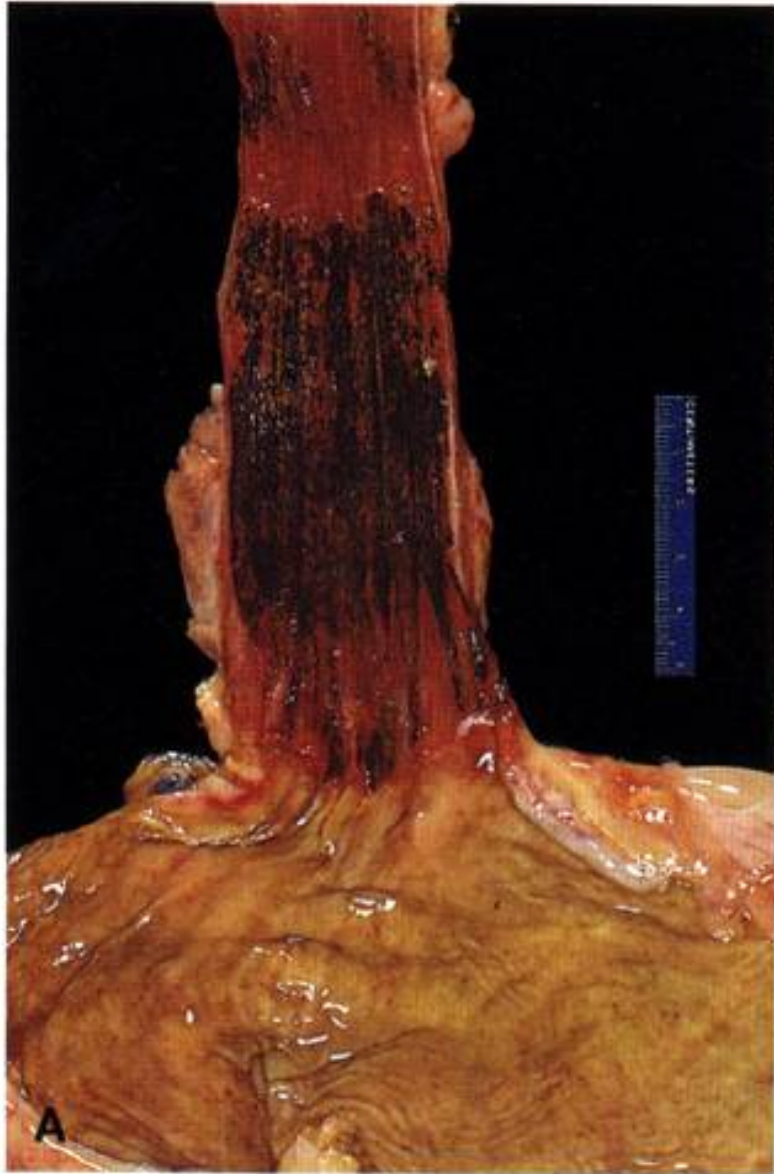
Chlamydia and Rickettsiae are obligate intracellular organisms.



Fungi:

- eukaryotes
- grow either budding yeast and hyphae (septate and aseptate)
- some of the most important pathogenic fungi exhibit thermal dimorphism; hyphal forms at room temperature but yeast forms at body temperature

- 
- Tinea; Athlete's foot
 - Sporotrichosis; subcutaneous infection
 - Candida, Aspergillus, Mucor; systemic fungal infection in immunocompromised host



Candida Infection



Protozoa:

- single-celled eukaryotes
- replicate intracellularly (*Plasmodium* in rbc, *Leishmania* in macrophages) or extracellularly in urogenital system, intestine, or blood.
- e.g. *Trichomonas vaginalis*,
Entamoeba histolytica, *Giardia lamblia*,
Toxoplasma gondii

TABLE 8-6 Protozoa Pathogenic for Humans

Species	Order	Form, Size	Disease
Luminal or Epithelial			
<i>Entamoeba histolytica</i>	Amebae	Trophozoite 15–20 μm	Amebic dysentery; liver abscess
<i>Balantidium coli</i>	Ciliates	Trophozoite 50–100 μm	Colitis
<i>Naegleria fowleri</i>	Ameboflagellates	Trophozoite 10–20 μm	Meningoencephalitis
<i>Acanthamoeba</i> sp.	Ameboflagellates	Trophozoite 15–30 μm	Meningoencephalitis or ophthalmitis
<i>Giardia lamblia</i>	Mastigophora	Trophozoite 11–18 μm	Diarrheal disease, malabsorption
<i>Isoospora belli</i>	Coccidia	Oocyst 10–20 μm	Chronic enterocolitis or malabsorption or both
<i>Cryptosporidium</i> sp.	Coccidia	Oocyst 5–6 μm	
<i>Trichomonas vaginalis</i>	Mastigophora	Trophozoite 10–30 μm	Urethritis, vaginitis
Bloodstream			
<i>Plasmodium</i> species	Hemosporidia	Trophozoites, schizonts, gametes (all small and inside red cells)	Malaria
<i>Babesia microti</i> , <i>B. bovis</i>	Hemosporidia	Trophozoites inside red cells	Babesiosis
<i>Trypanosoma</i> species	Hemoflagellates	Trypomastigote 14–33 μm	African sleeping sickness
Intracellular			
<i>Trypanosoma cruzi</i>	Hemoflagellates	Trypomastigote 20 μm	Chagas disease
<i>Leishmania donovani</i>	Hemoflagellates	Amastigote 2 μm	Kala-azar
<i>Leishmania</i> species	Hemoflagellates	Amastigote 2 μm	Cutaneous and mucocutaneous leishmaniasis
<i>Toxoplasma gondii</i>	Coccidia	Tachyzoite 4–6 μm (cyst larger)	Toxoplasmosis

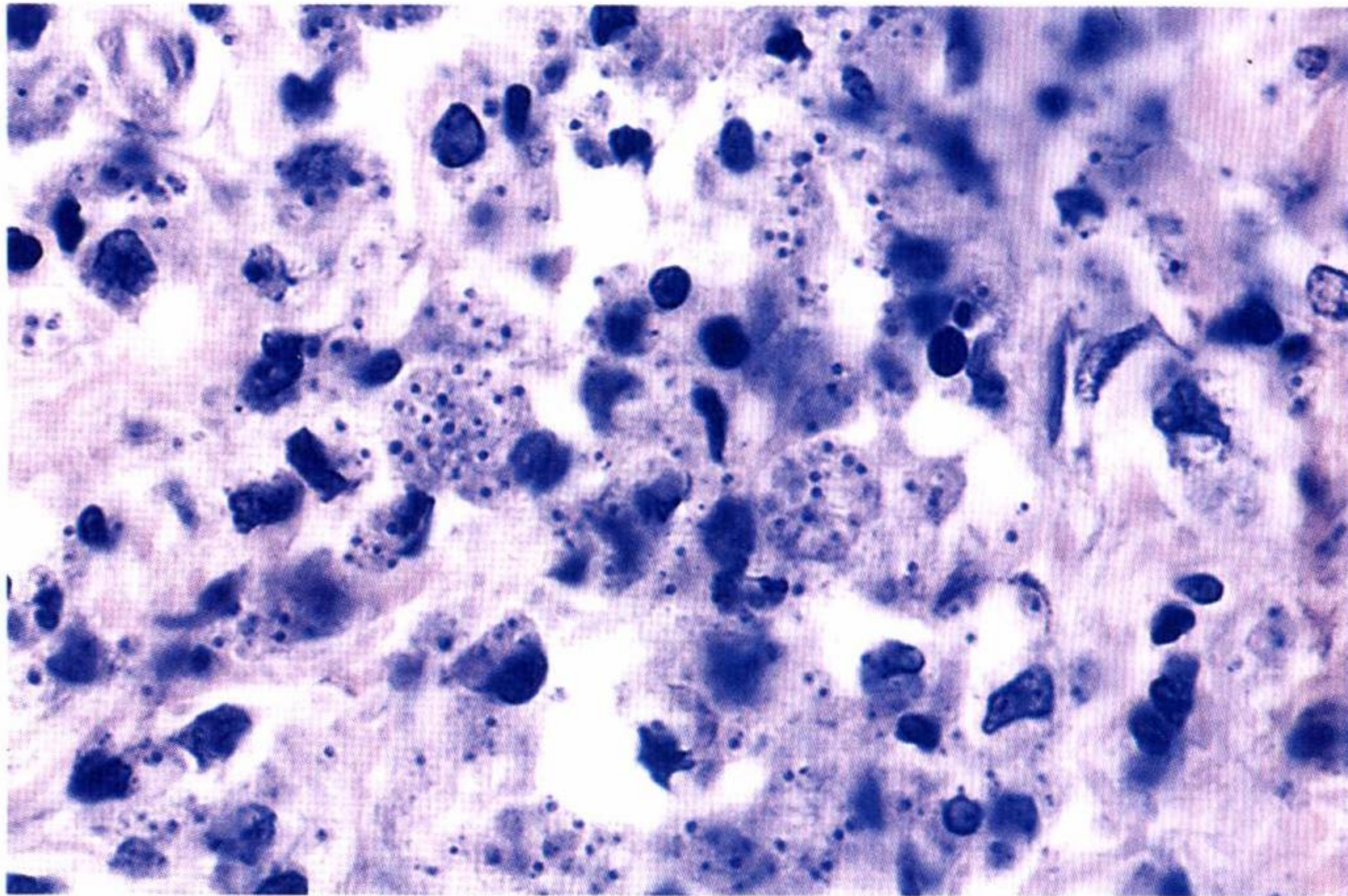


FIGURE 8-54 *Leishmania donovani* parasites within the macrophages of a lymph node in visceral leishmaniasis (kala-azar).



FIGURE 8-55 Slender bloodstream parasites of African trypanosomiasis.



Helminths:

- multicellular organisms.
- complex life cycles
- sexual reproduction in definitive host, asexual multiplication in intermediate host

Ectoparasites:

- insects (lice, fleas) and arachnids (mites, ticks, spiders)

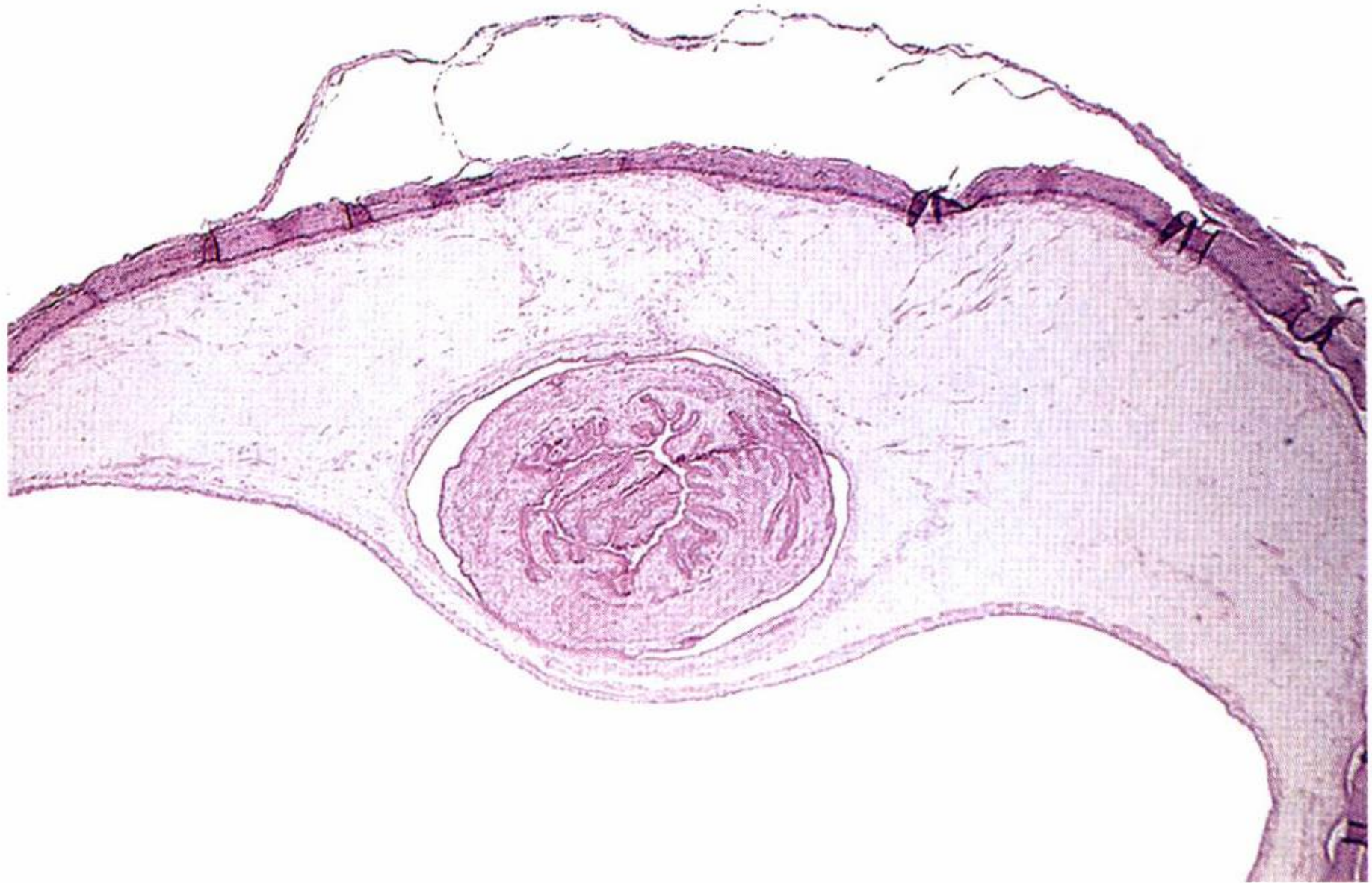
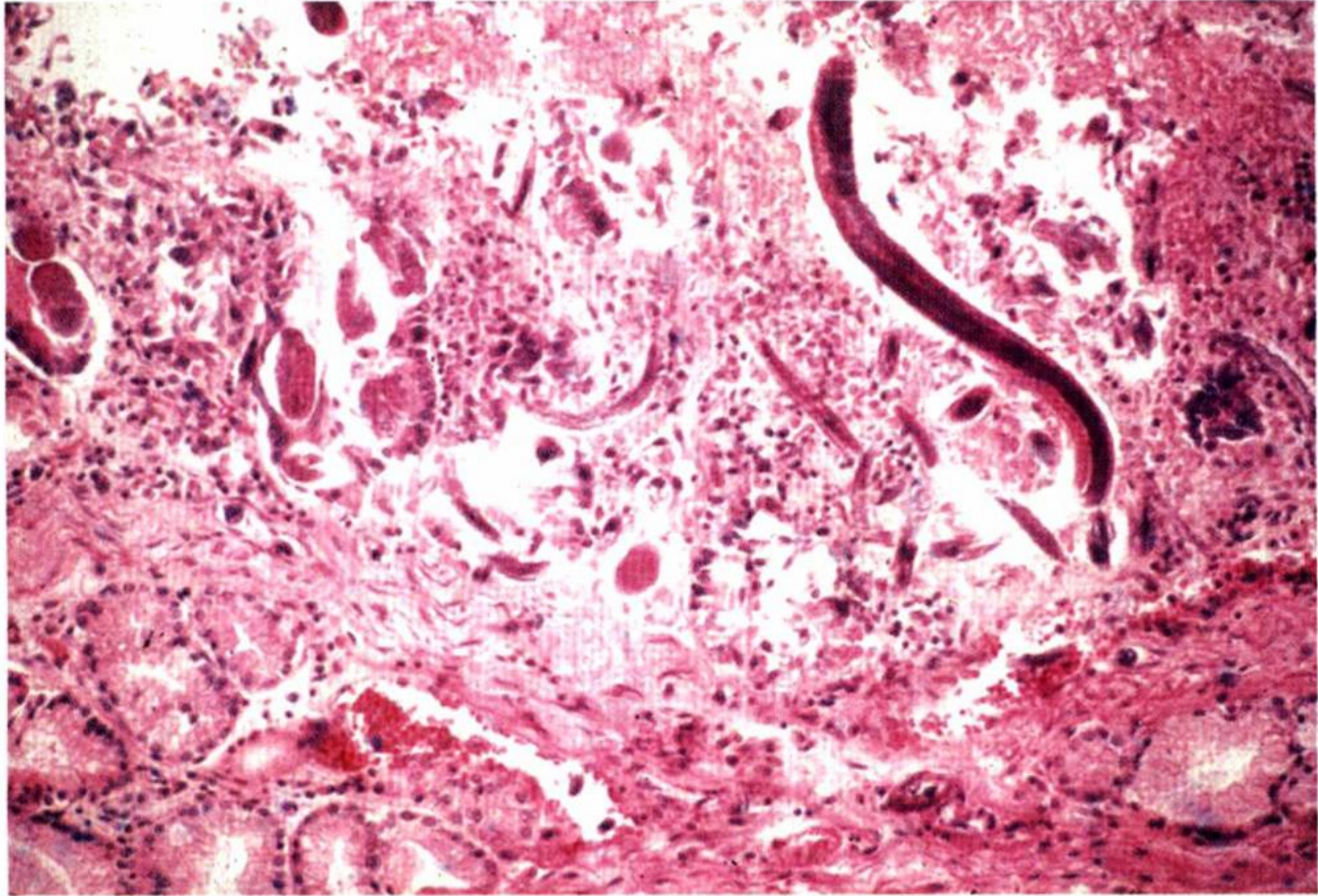


FIGURE 8-57 Portion of a cysticercus cyst.



Strongyloides hyperinfection

TABLE 8-3 Classes of Human Pathogens and Their Habitats

Taxonomic	Size	Site of Propagation	Sample Species	Disease
Viruses	20–300 nm	Obligate intracellular	Poliovirus	Polio
Chlamydiae	200–1000 nm	Obligate intracellular	<i>Chlamydia trachomatis</i>	Trachoma, urethritis
Rickettsiae	300–1200 nm	Obligate intracellular	<i>Rickettsia prowazekii</i>	Typhus fever
Mycoplasmas	125–350 nm	Extracellular	<i>Mycoplasma pneumoniae</i>	Atypical pneumonia
Bacteria	0.8–15 μ m	Cutaneous Mucosal Extracellular Facultative intracellular	<i>Staphylococcus aureus</i> <i>Vibrio cholerae</i> <i>Streptococcus pneumoniae</i> <i>Mycobacterium tuberculosis</i>	Wound Cholera Pneumonia Tuberculosis
Fungi	2–200 μ m	Cutaneous Mucosal Extracellular Facultative intracellular	<i>Trichophyton</i> sp. <i>Candida albicans</i> <i>Sporothrix schenckii</i> <i>Histoplasma capsulatum</i>	Tinea pedis (athlete's foot) Thrush Sporotrichosis Histoplasmosis
Protozoa	1–50 μ m	Mucosal Extracellular Facultative intracellular Obligate intracellular	<i>Giardia lamblia</i> <i>Trypanosoma gambiense</i> <i>Trypanosoma cruzi</i> <i>Leishmania donovani</i>	Giardiasis Sleeping sickness Chagas disease Kala-azar
Helminths	3mm–10 m	Mucosal Extracellular Intracellular	<i>Enterobius vermicularis</i> <i>Wuchereria bancrofti</i> <i>Trichinella spiralis</i>	Enterobiasis Filariasis Trichinosis

TABLE 8-7 Classification of Important Sexually Transmitted Diseases

Pathogens	Disease or Syndrome and Population Principally Affected		
	Males	Both	Females
Viruses			
Herpes simplex virus		Primary and recurrent herpes, neonatal herpes	
Hepatitis B virus		Hepatitis	
Human papillomavirus	Cancer of penis (some cases)	Condyloma acuminatum	Cervical dysplasia and cancer, vulvar cancer
Human immunodeficiency virus		Acquired immunodeficiency syndrome	
Chlamydiae			
<i>Chlamydia trachomatis</i>	Urethritis, epididymitis, proctitis	Lymphogranuloma venereum	Urethral syndrome, cervicitis, Bartholinitis, salpingitis and sequelae
Mycoplasmas			
<i>Ureaplasma urealyticum</i>	Urethritis		
Bacteria			
<i>Neisseria gonorrhoeae</i>	Epididymitis, prostatitis, urethral stricture	Urethritis, proctitis, pharyngitis, disseminated gonococcal infection	Cervicitis, endometritis, Bartholinitis, salpingitis, and sequelae (infertility, ectopic pregnancy, recurrent salpingitis)
<i>Treponema pallidum</i>		Syphilis	
<i>Haemophilus ducreyi</i>		Chancroid	
<i>Calymmatobacterium granulomatis</i>		Granuloma inguinale (donovanosis)	
<i>Shigella</i>	*Enterocolitis		
<i>Campylobacter</i>	*Enterocolitis		
Protozoa			
<i>Trichomonas vaginalis</i>	Urethritis, balanitis		Vaginitis
<i>Entamoeba histolytica</i>	*Amebiasis		
<i>Giardia lamblia</i>	*Giardiasis		

*Most important in homosexual populations.

Modified and updated from Krieger JN: Biology of sexually transmitted diseases. Urol Clin North Am 11:15, 1984.

A wide-angle photograph of a snowy mountain range under a clear blue sky. The foreground is a vast, flat expanse of snow, leading up to a range of snow-capped peaks. The sky is a uniform, bright blue. The overall scene is serene and cold.

Pathogenesis of Infectious Disease

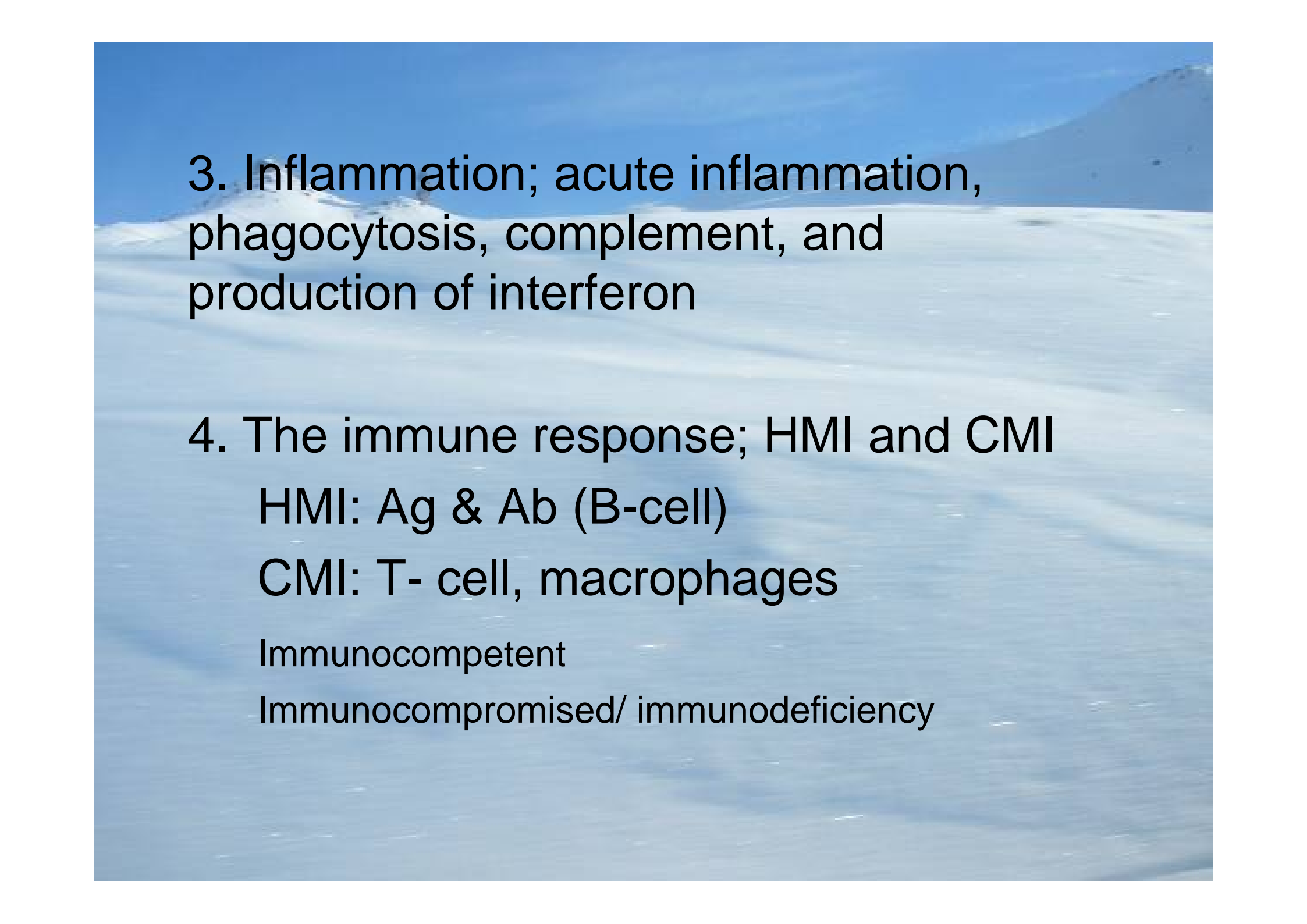
- Host

- Pathogen; organism or parasite that cause disease



Host factors:

1. General factors; socioeconomic status, behavior pattern, occupational, and internal factors
2. Natural defense mechanism; skin and normal flora, respiratory tract and mucociliary mechanism, Hcl production in stomach, or normal flushing action of urine



3. Inflammation; acute inflammation, phagocytosis, complement, and production of interferon

4. The immune response; HMI and CMI

HMI: Ag & Ab (B-cell)

CMI: T- cell, macrophages

Immunocompetent

Immunocompromised/ immunodeficiency

Organism factors:

1. Transmission; congenital transfer (Rubella, CMV, HIV, HSV), directly contact, fomite, food and water, airborne, animal, sexual

2. Spread and dissemination; localized and disseminated infection

- viremia, bacteremia, fungemia, parasitemia

- **sepsis** is a serious medical condition characterised by a whole-body inflammatory state caused by infection.

Definition of sepsis

- Sepsis is considered present if infection is highly suspected or proven and two or more of the following *systemic inflammatory response syndrome* (SIRS) criteria are met:
 - Heart rate > 90 beats per minute
 - Body temperature < 36 or > 38 °C
 - Hyperventilation (high respiratory rate) > 20 breaths per minute or, on blood gas: a PaCO₂ less than 32 mmHg.
 - White blood cell count < 4000 cells/mm³ or > 12000 cells/mm³ or greater than 10% band forms (immature white blood cells).



- ***septicemia*** (blood poisoning; bacteremia with sepsis)

is the presence of bacteria in the blood (bacteremia) and is often associated with severe disease.

is a serious, life-threatening infection that gets worse very quickly.

is considered a subset of sepsis.

It can arise from infections throughout the body.



3. Number of organism

-numerous low virulent organism
can cause severe disease

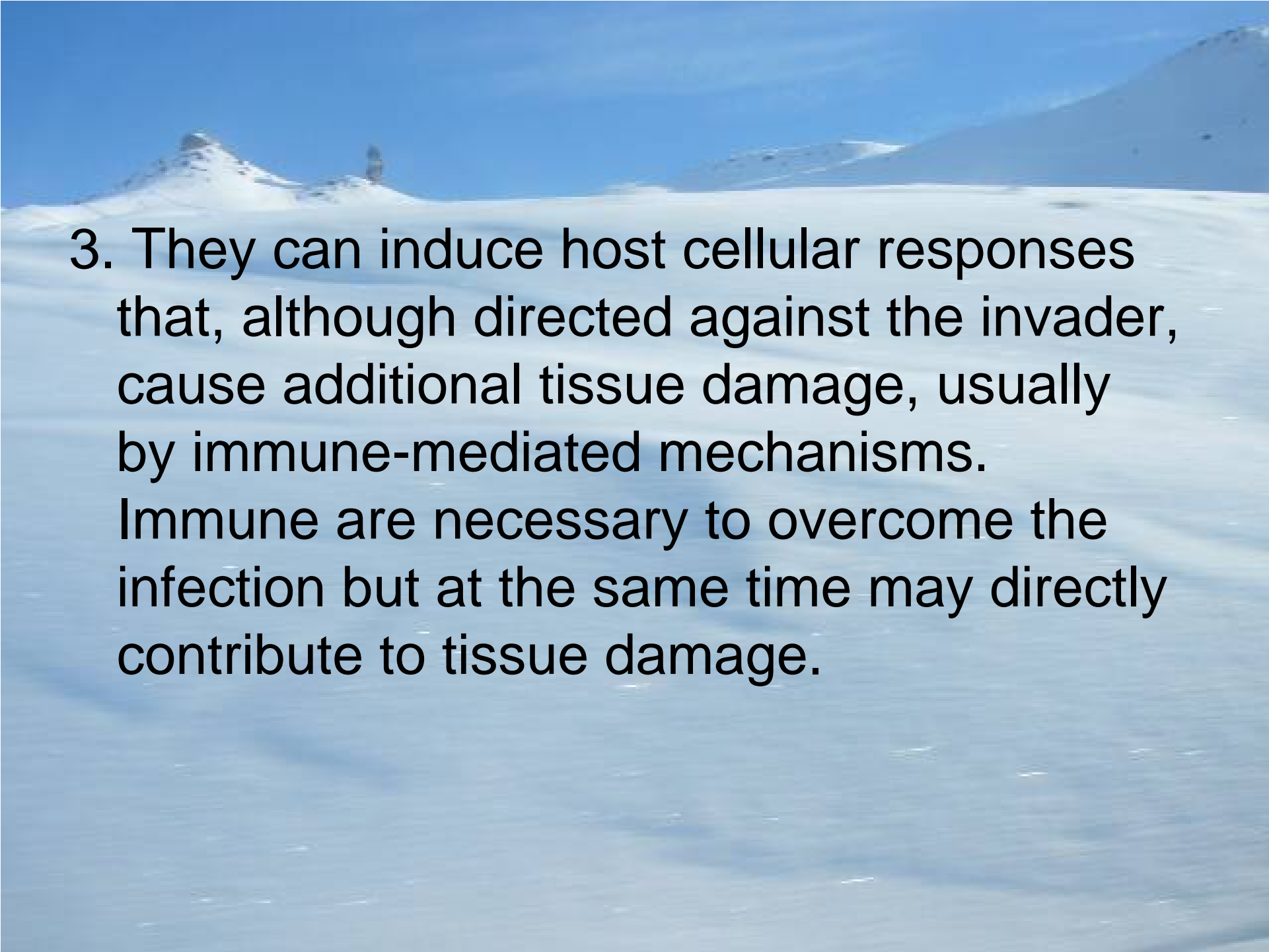
4. Pathogenicity of organism;

- ability to invade tissue; *S.pyogenase* → hyaluronidase → breakdown ground substance
- toxin production; *C. botulinum* → neurotoxin
- multiplication
- resistance to host defense mechanism
- ability to cause necrosis
- enzyme release; anthrax → enzyme → vasculitis → ischemia

How microorganisms cause disease:

Infectious agents establish infection and damage tissues in three ways:

1. They can contact or enter host cells and directly cause death
2. They may release toxins that kill cells at a distance, release enzymes that degrade tissue components, or damage blood vessels and cause ischemic necrosis



3. They can induce host cellular responses that, although directed against the invader, cause additional tissue damage, usually by immune-mediated mechanisms. Immune are necessary to overcome the infection but at the same time may directly contribute to tissue damage.



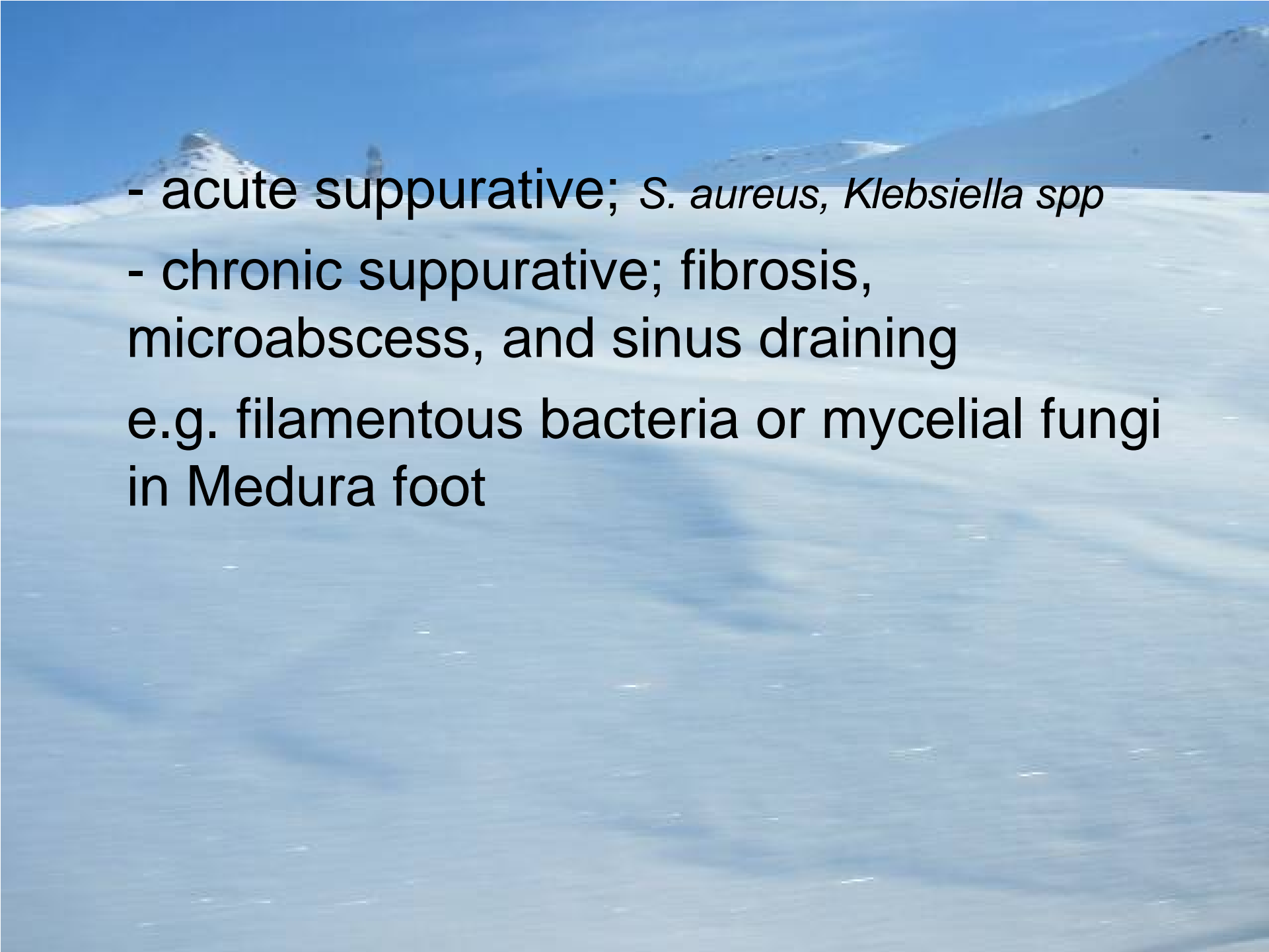
Spectrum of inflammatory responses to infection:

1. Suppurative Inflammation; ***neutrophils***

- complication of acute inflammation; liquefactive necrosis with abscess formation

- extracellular organisms; bacteria

except Salmonella typhi – neutropenia, macrophages

- 
- acute suppurative; *S. aureus*, *Klebsiella spp*
 - chronic suppurative; fibrosis, microabscess, and sinus draining
e.g. filamentous bacteria or mycelial fungi
in Madura foot

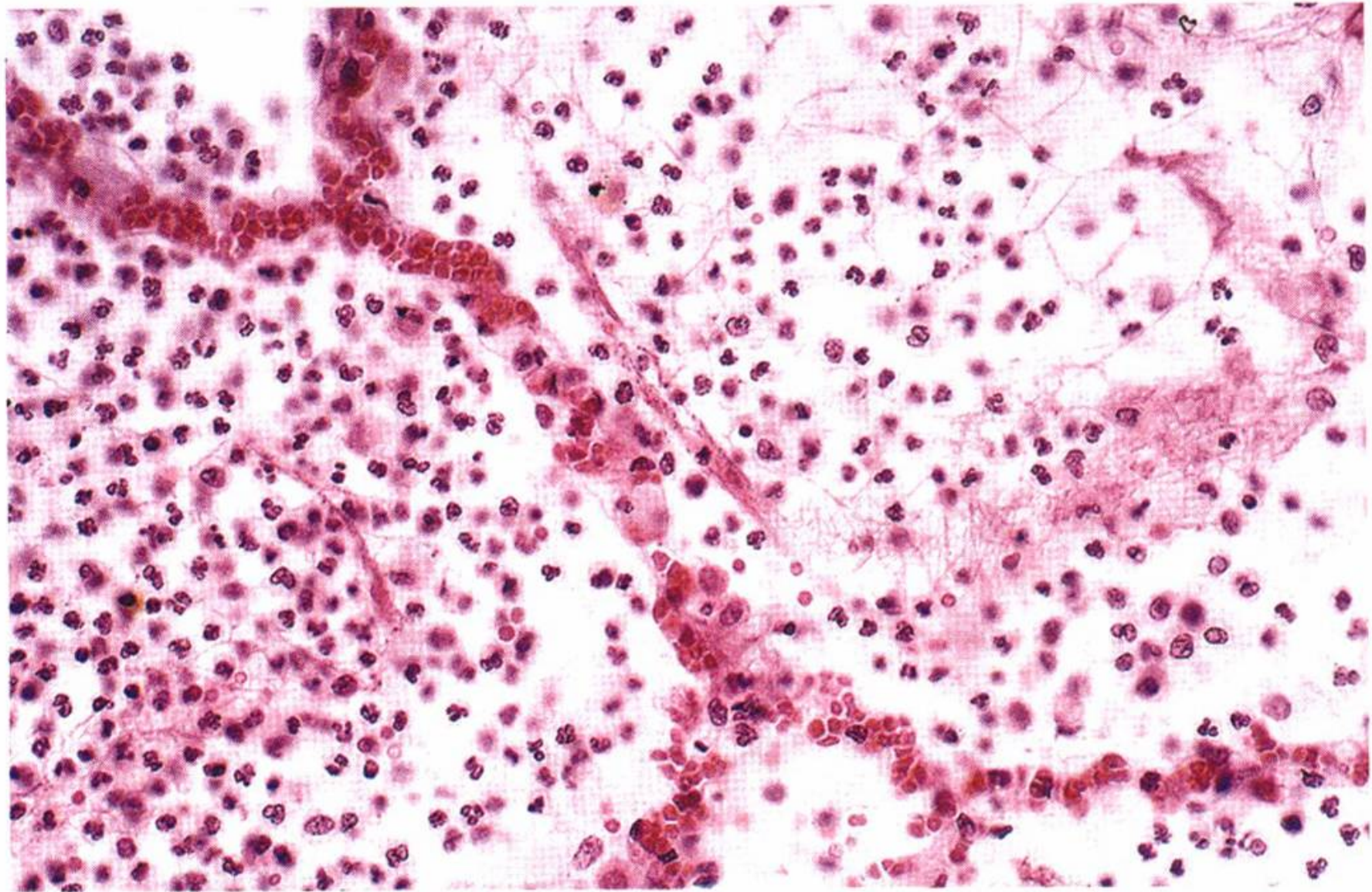


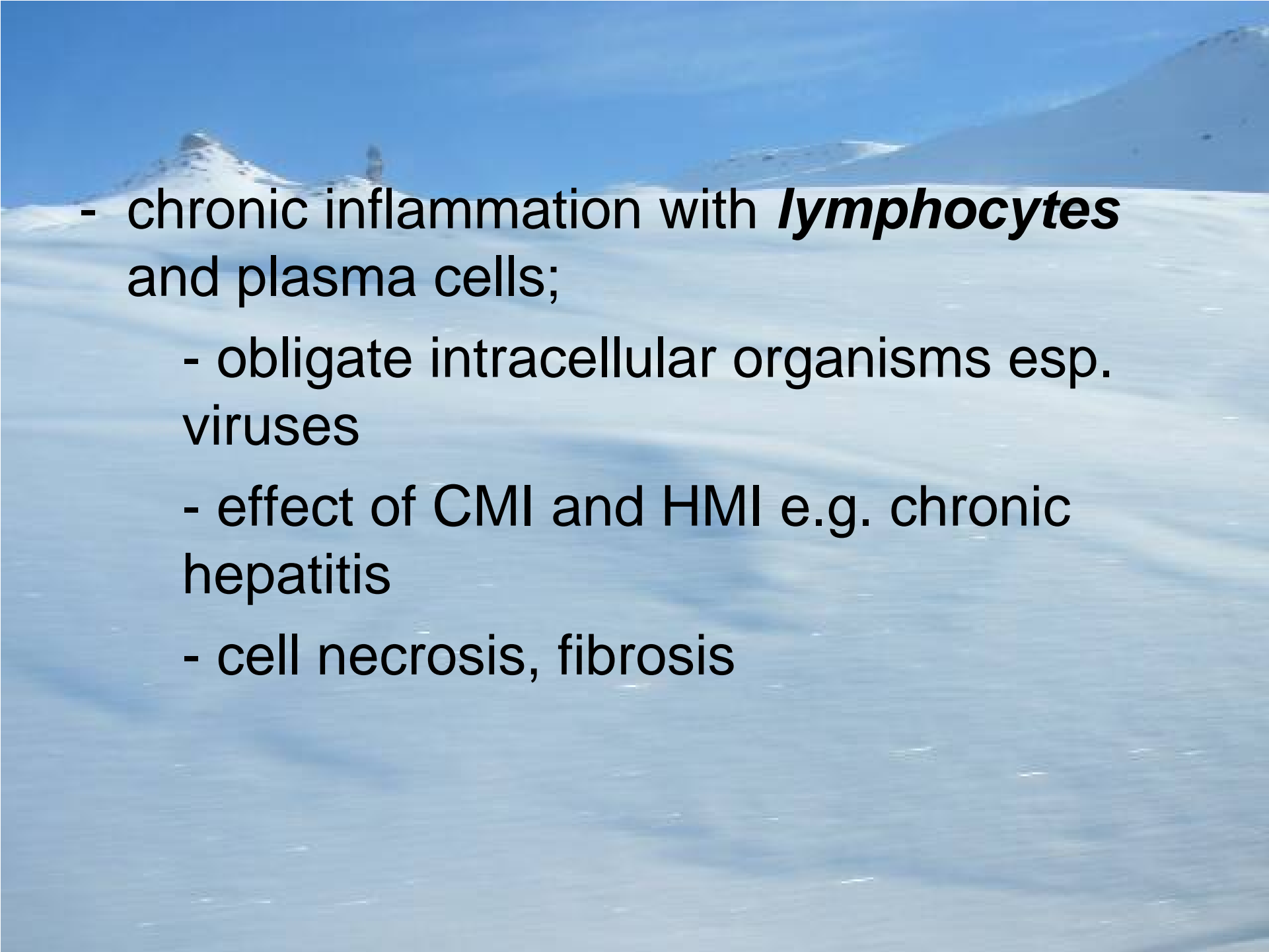
FIGURE 8-7 Pneumococcal pneumonia. Note the intra-alveolar polymorphonuclear exudate and intact alveolar septa.

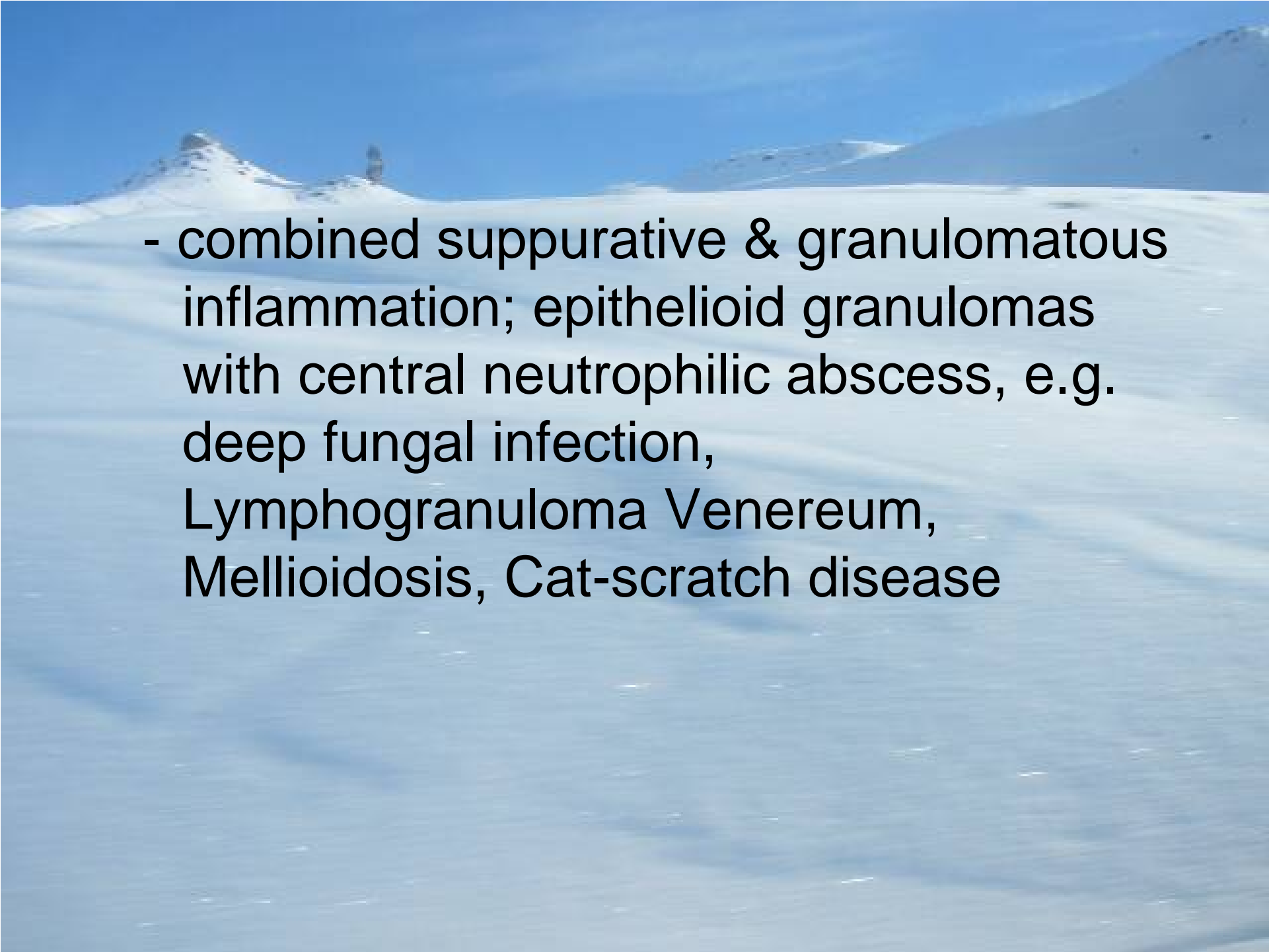
2. Chronic inflammation

- chronic granulomatous inflammation;

Mycobacteria, fungus (*Histoplasma*, *Coccidioides*)

- chronic inflammation with diffuse proliferation of macrophages; in abnormal CMI patient --- no distinct granuloma, foamy macrophages with numerous organisms

- 
- chronic inflammation with ***lymphocytes*** and plasma cells;
 - obligate intracellular organisms esp. viruses
 - effect of CMI and HMI e.g. chronic hepatitis
 - cell necrosis, fibrosis



- combined suppurative & granulomatous inflammation; epithelioid granulomas with central neutrophilic abscess, e.g. deep fungal infection, Lymphogranuloma Venereum, Melioidosis, Cat-scratch disease

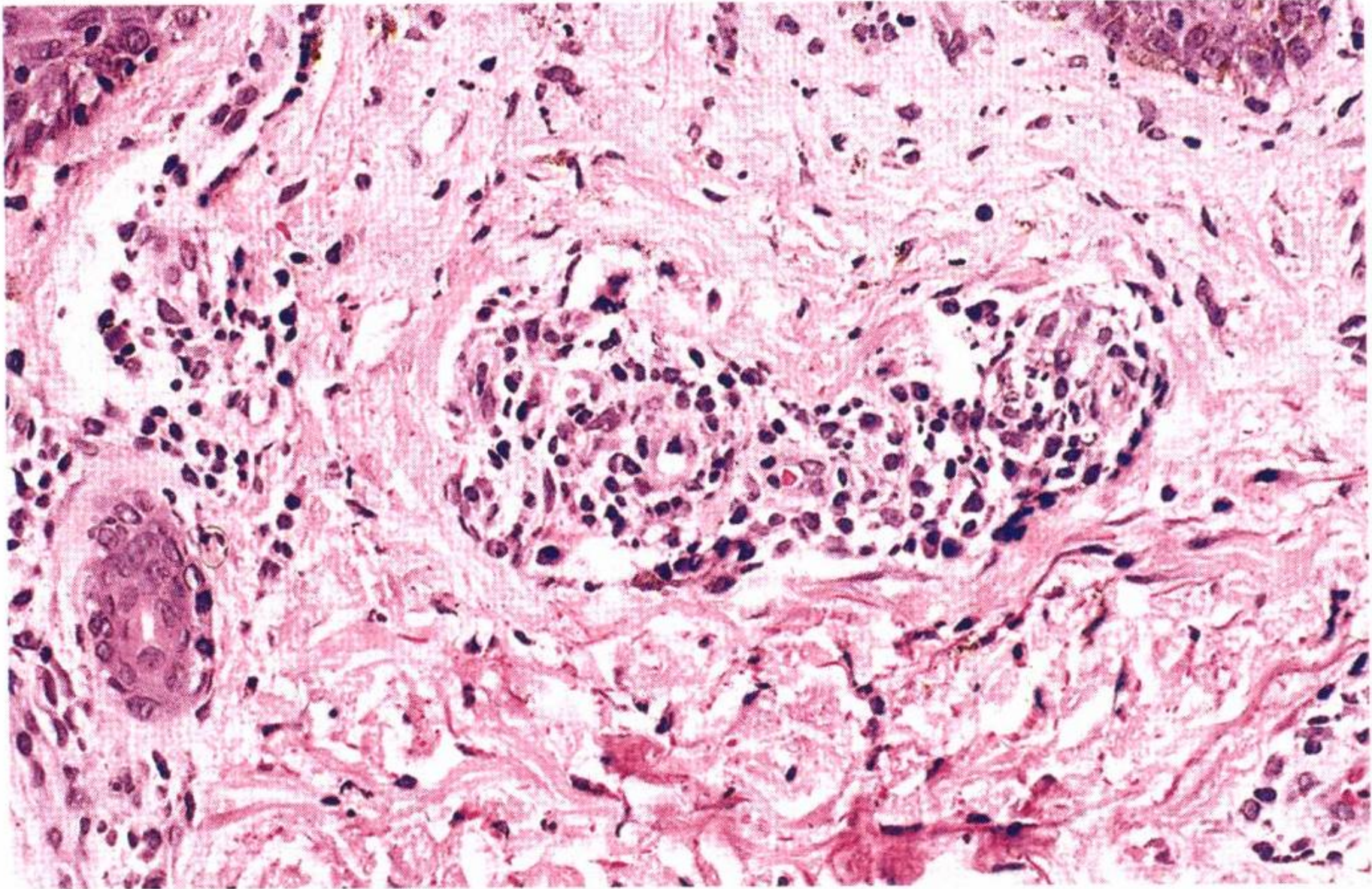


FIGURE 8–8 Secondary syphilis in the dermis with perivascular lymphoplasmacytic infiltrate and endothelial proliferation.

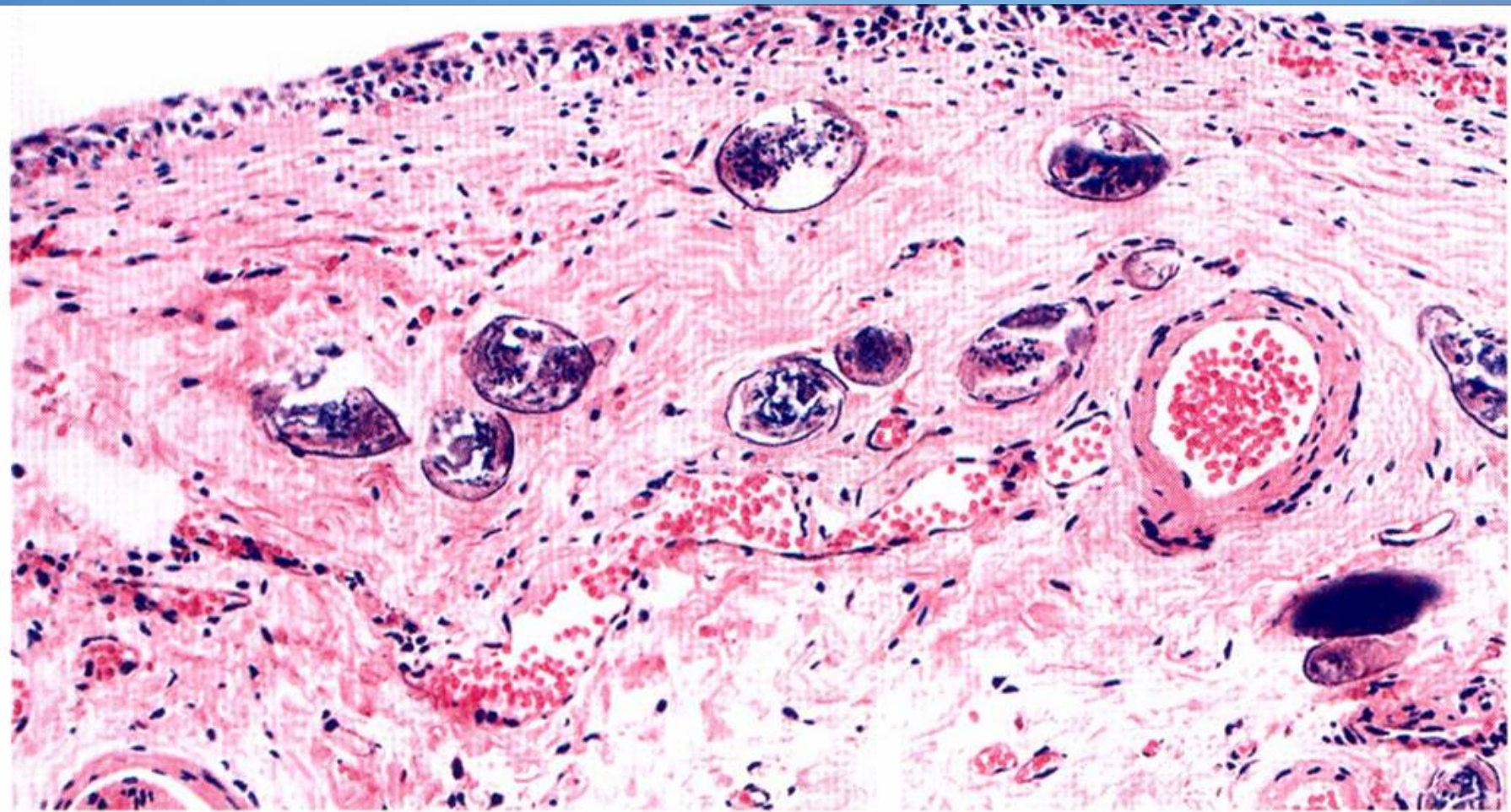
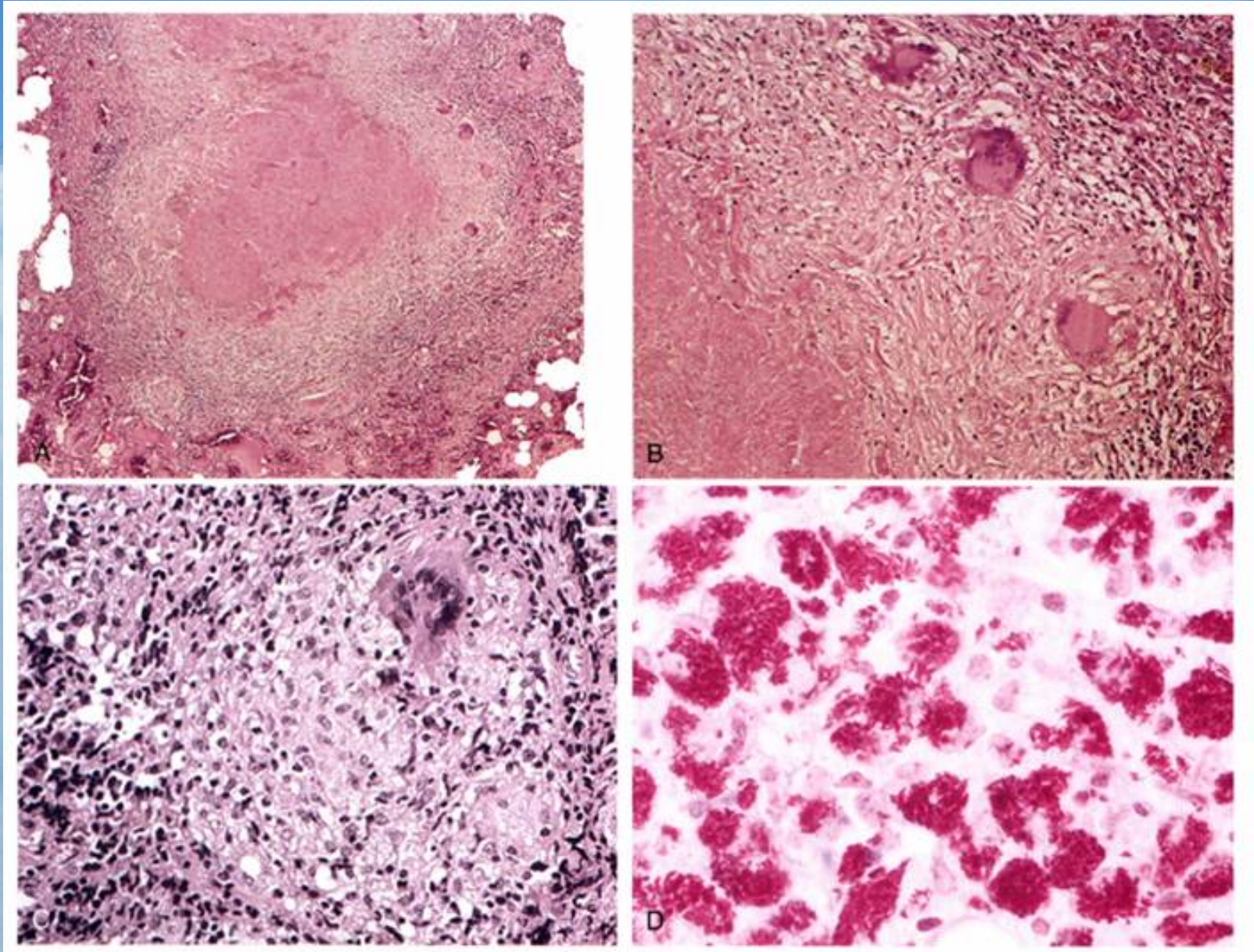


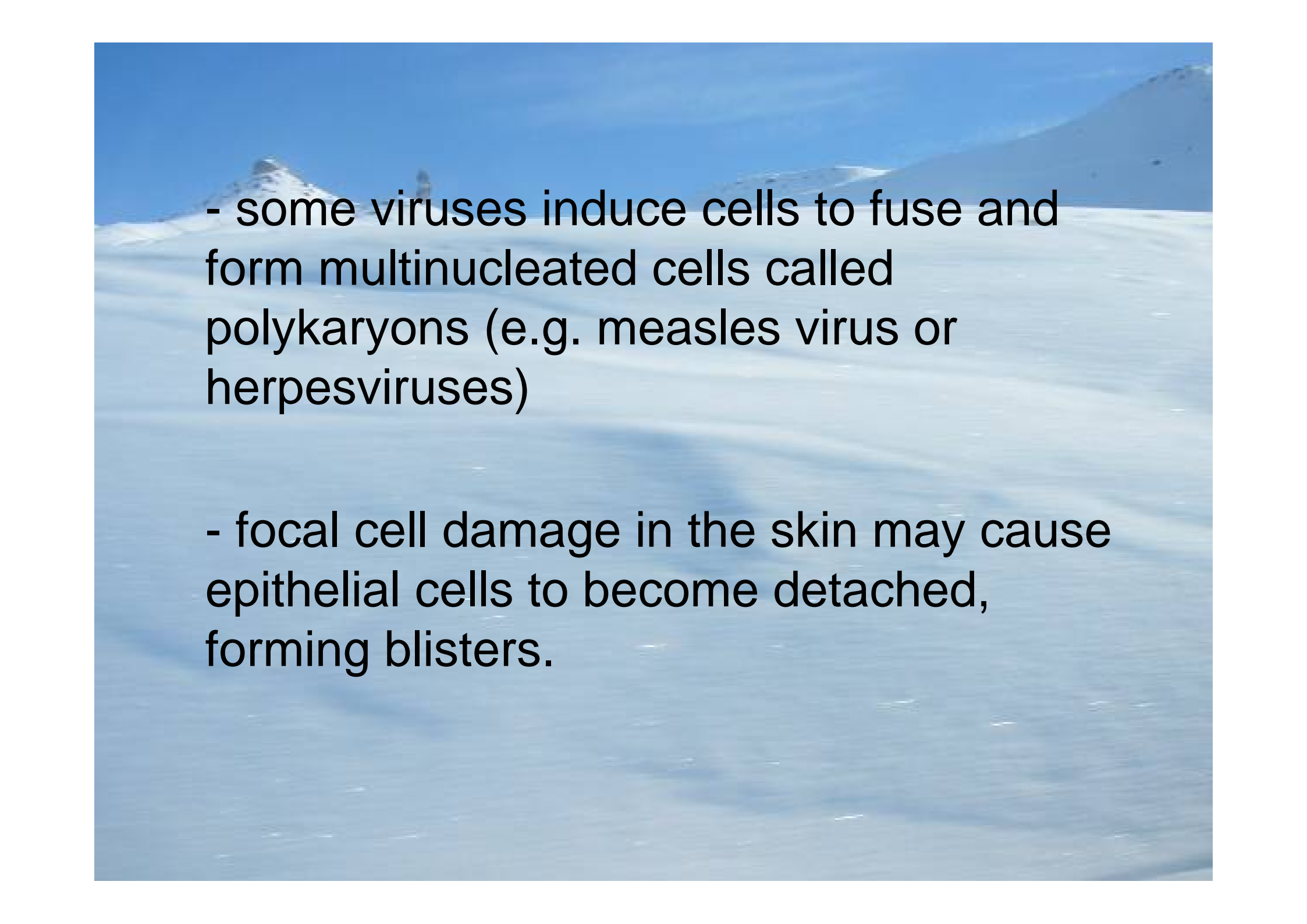
FIGURE 8-10 *Schistosoma haematobium* infection of the bladder with numerous calcified eggs and extensive scarring.



Spectrum of tuberculosis

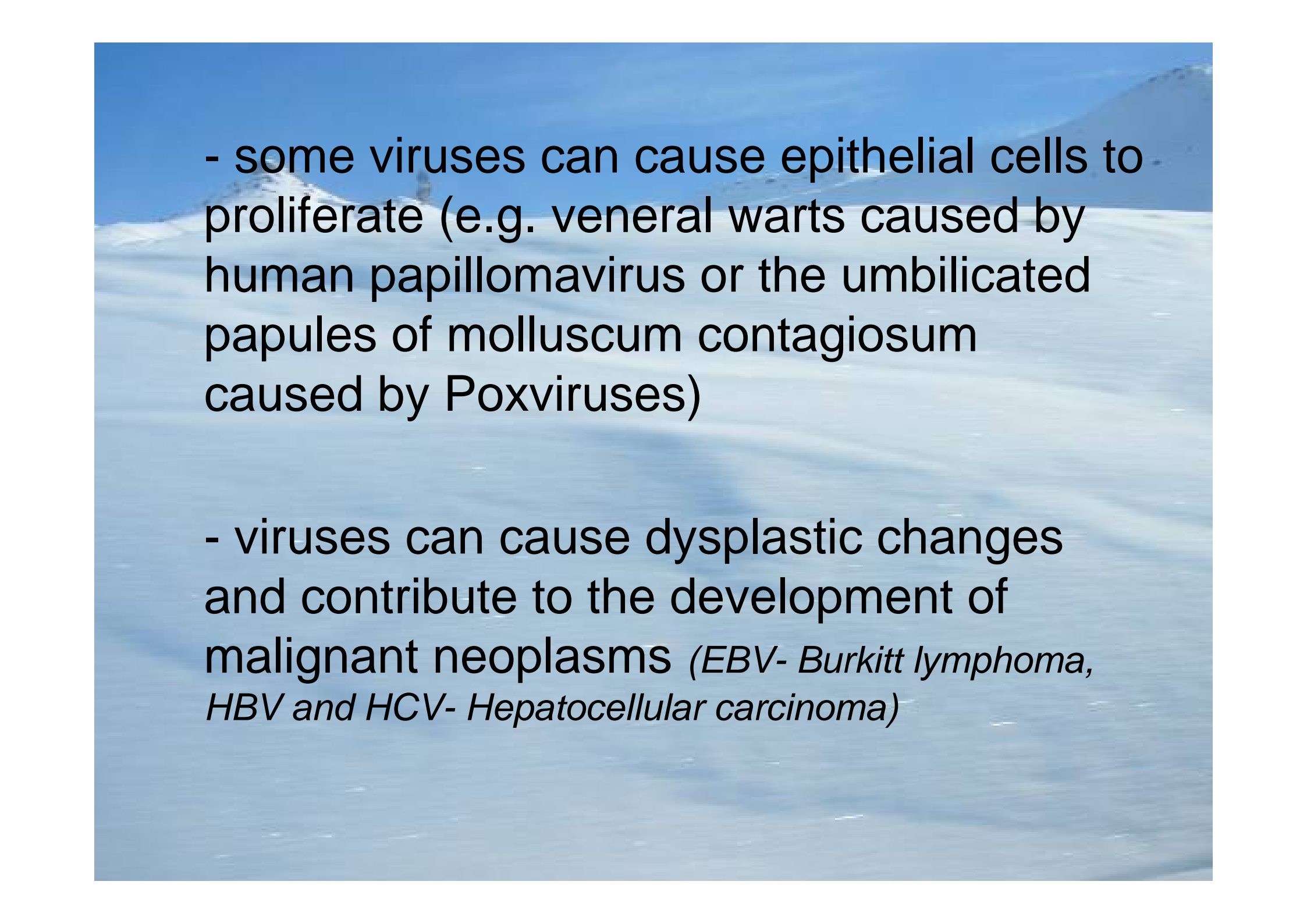
3. Cytopathic-Cytoproliferative Inflammation

- these reactions are usually produced by viruses
- cell necrosis or cellular proliferation, usually with sparse inflammatory cells
- some viruses replicate within cells and make viral aggregates that are visible as inclusion bodies (e.g. herpesviruses or adenovirus)



- some viruses induce cells to fuse and form multinucleated cells called polykaryons (e.g. measles virus or herpesviruses)

- focal cell damage in the skin may cause epithelial cells to become detached, forming blisters.



- some viruses can cause epithelial cells to proliferate (e.g. venereal warts caused by human papillomavirus or the umbilicated papules of molluscum contagiosum caused by Poxviruses)

- viruses can cause dysplastic changes and contribute to the development of malignant neoplasms (*EBV- Burkitt lymphoma, HBV and HCV- Hepatocellular carcinoma*)

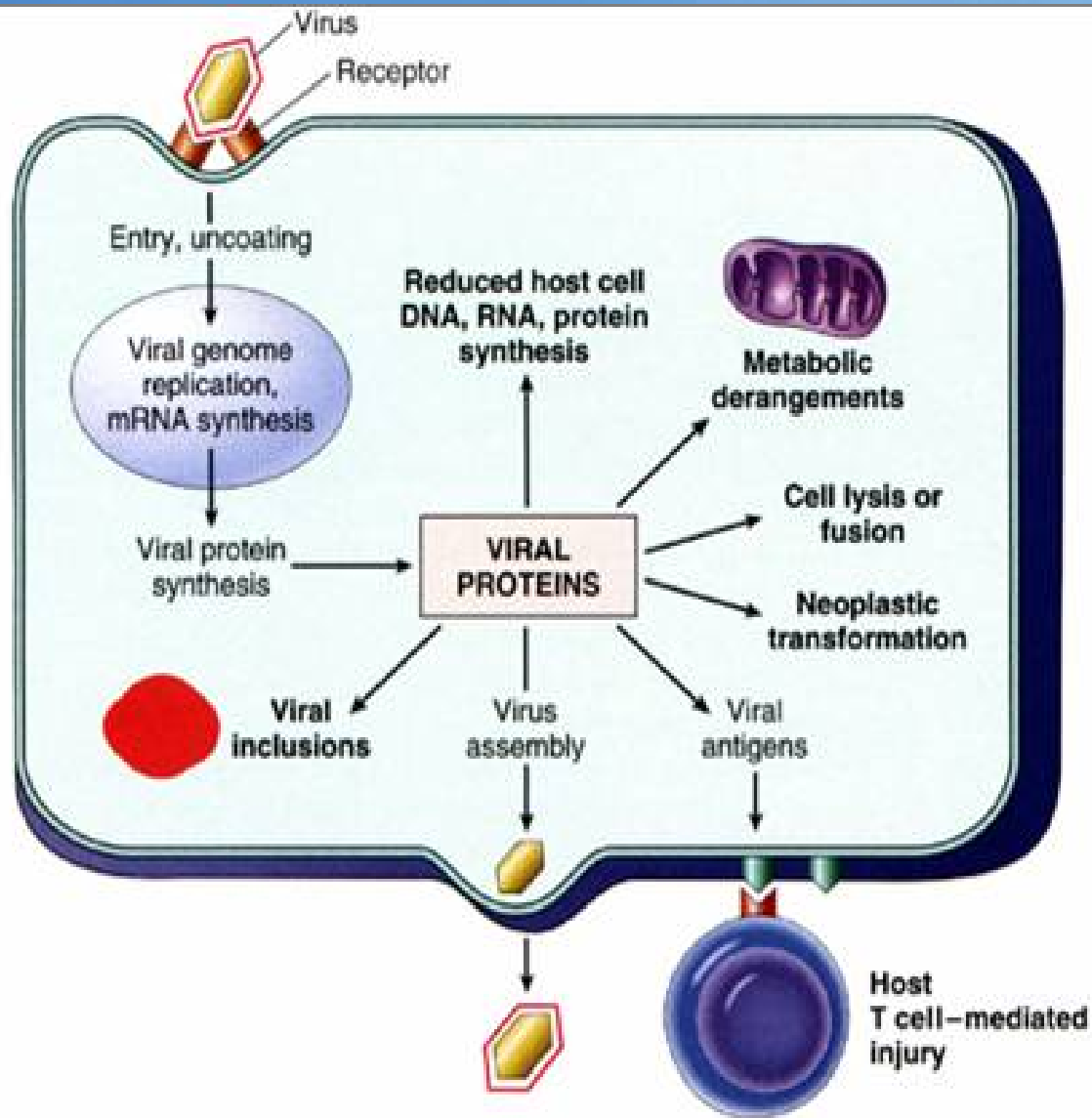


FIGURE 8-5 Mechanisms by which viruses cause injury to cells.

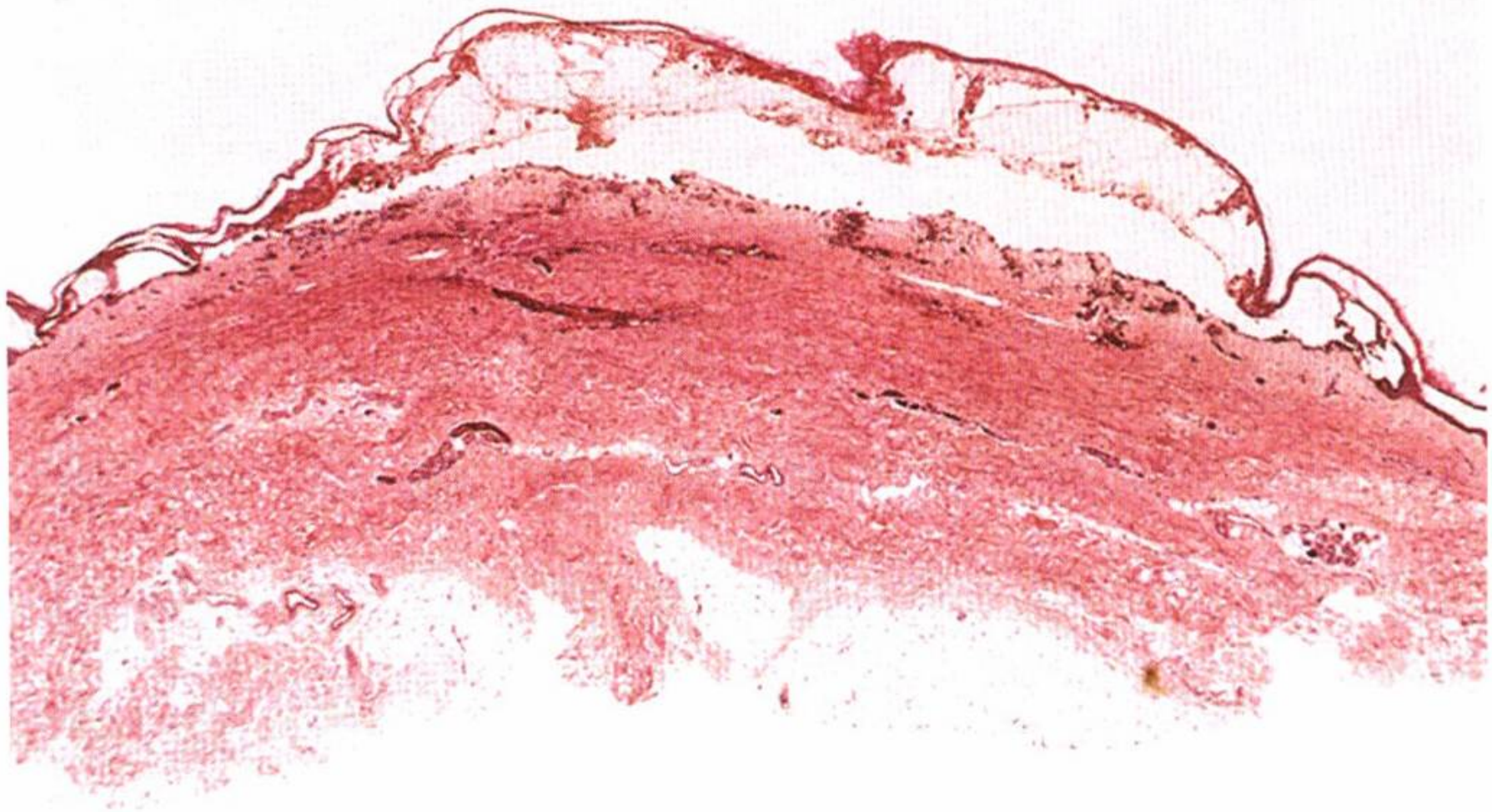


FIGURE 8-9 Herpesvirus blister in mucosa. See Figure 8-13 for viral inclusions.

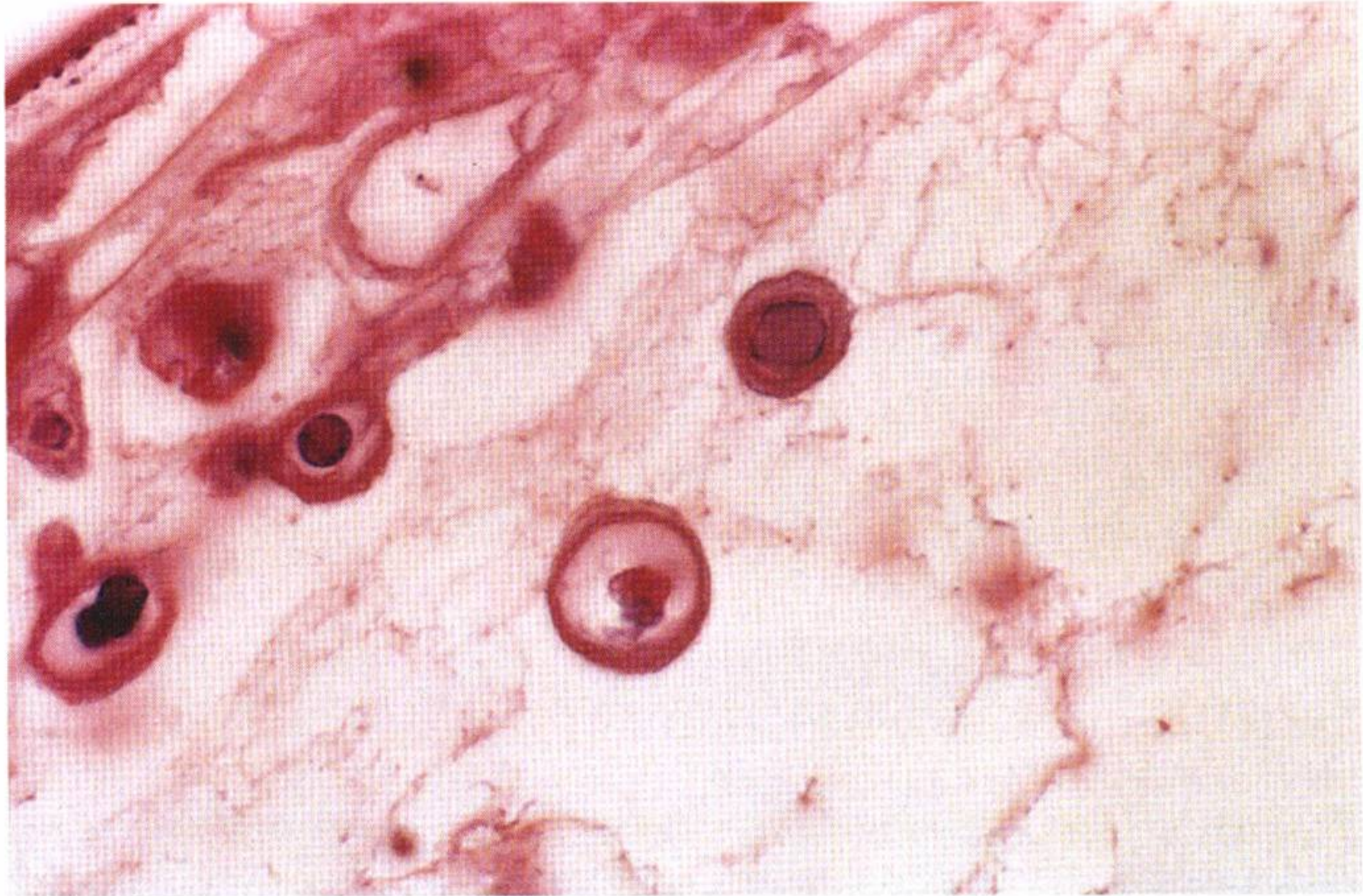


FIGURE 8-12 High-power view of cells from the blister in Figure 8-9 showing glassy intranuclear herpes simplex inclusion bodies.

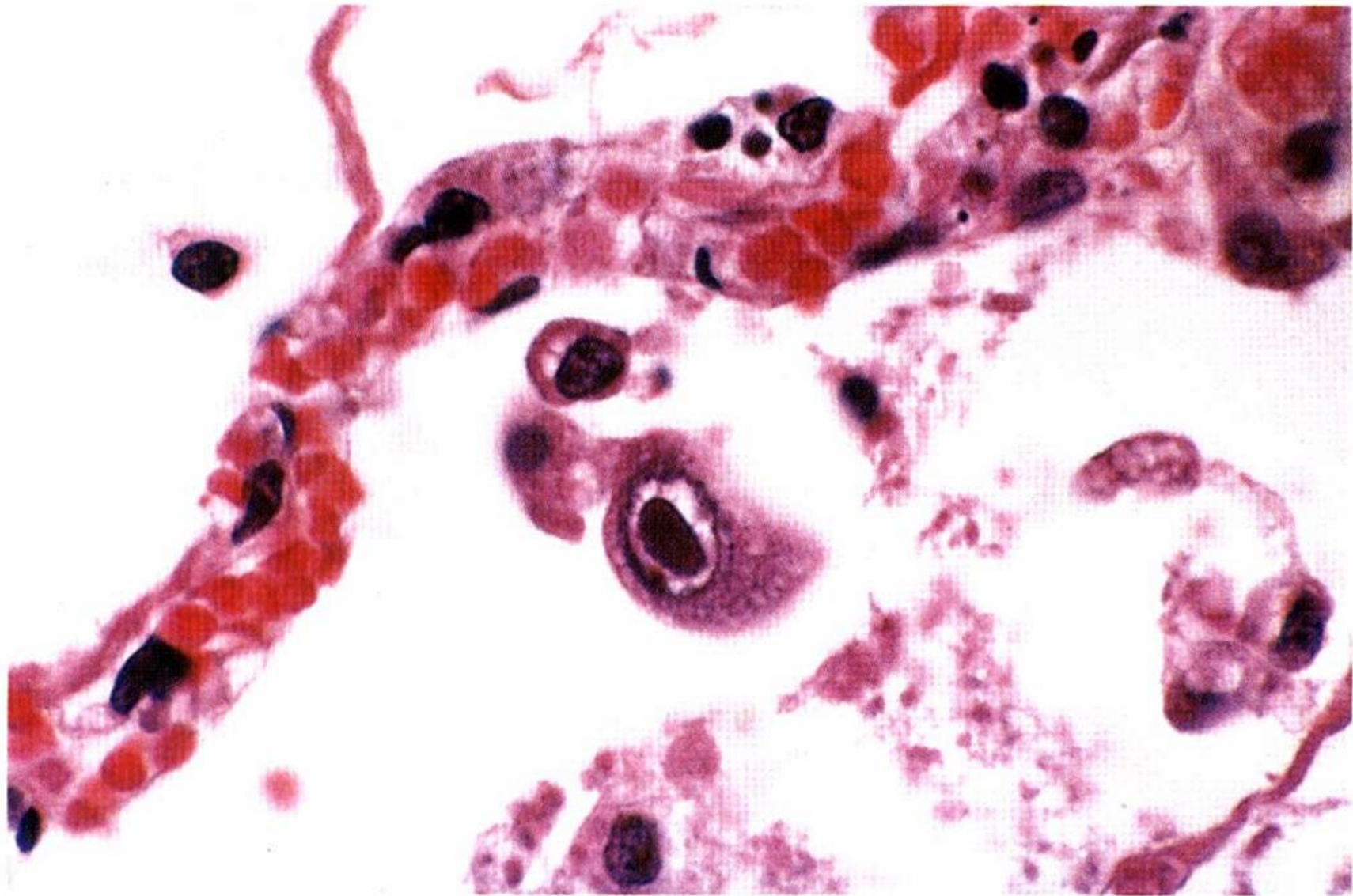


FIGURE 8-13 Cytomegalovirus: distinct nuclear and ill-defined cytoplasmic inclusions in the lung.

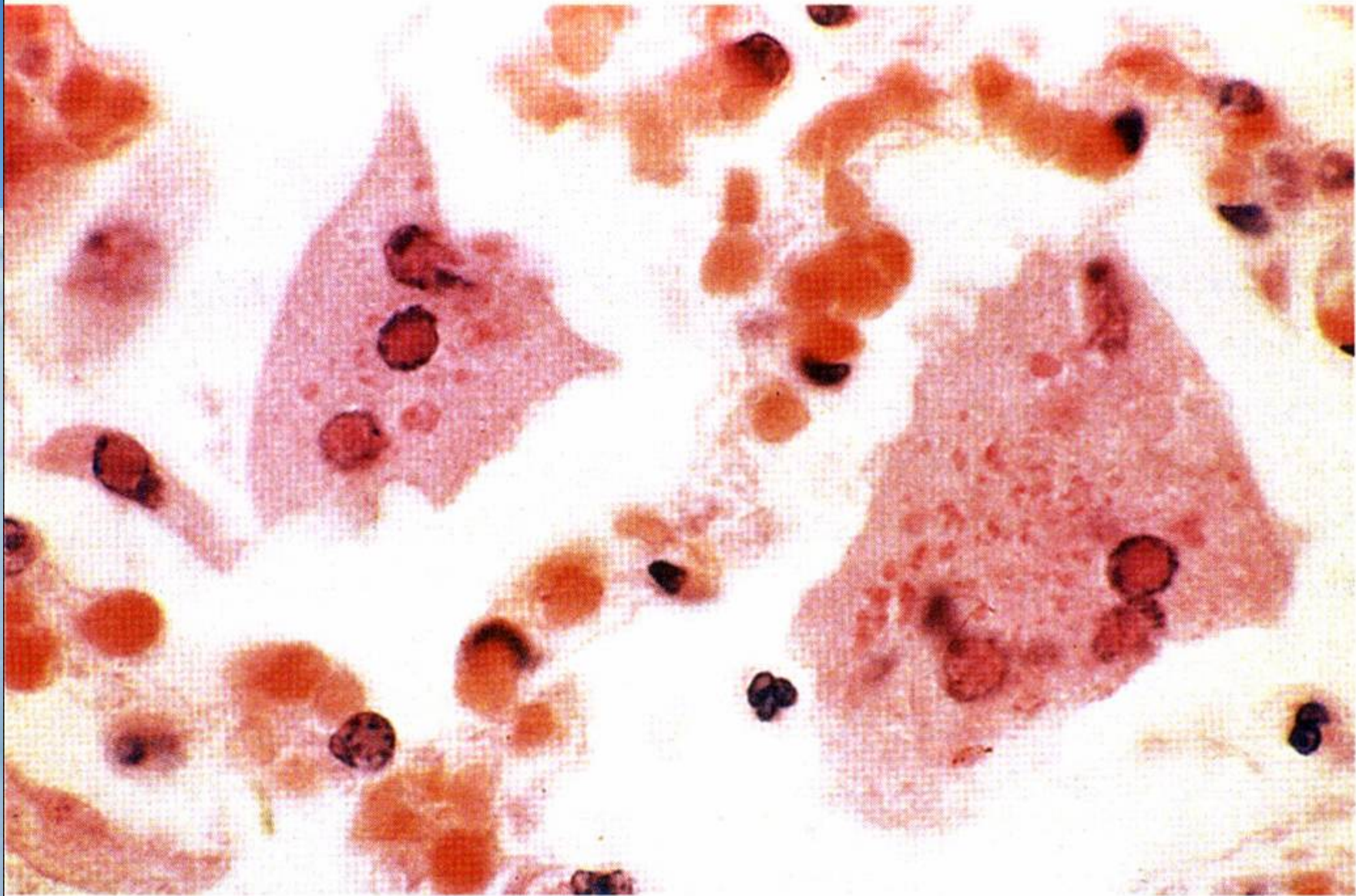
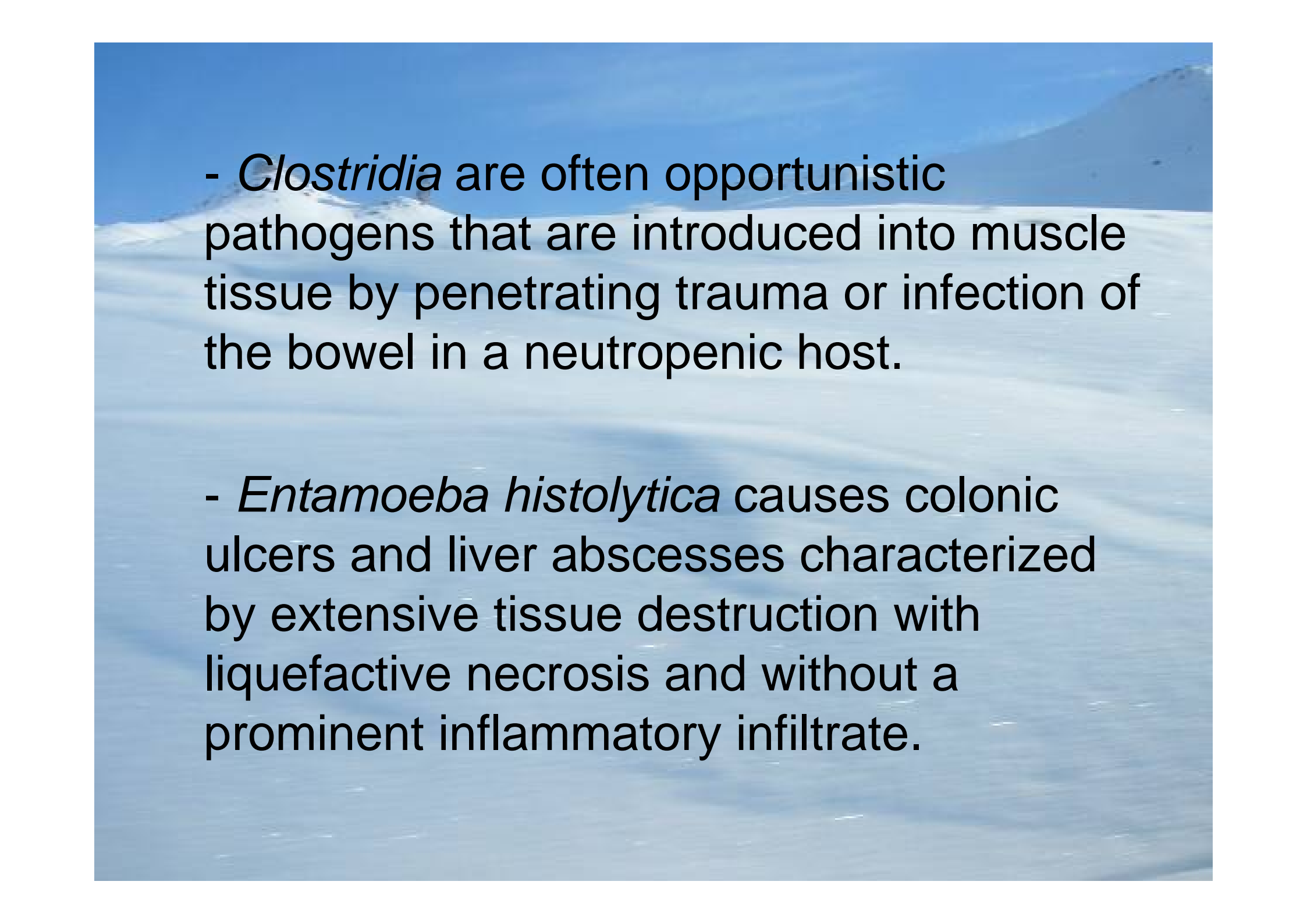


FIGURE 8-11 Measles giant cells in the lung. Note the glassy eosinophilic intranuclear inclusions.

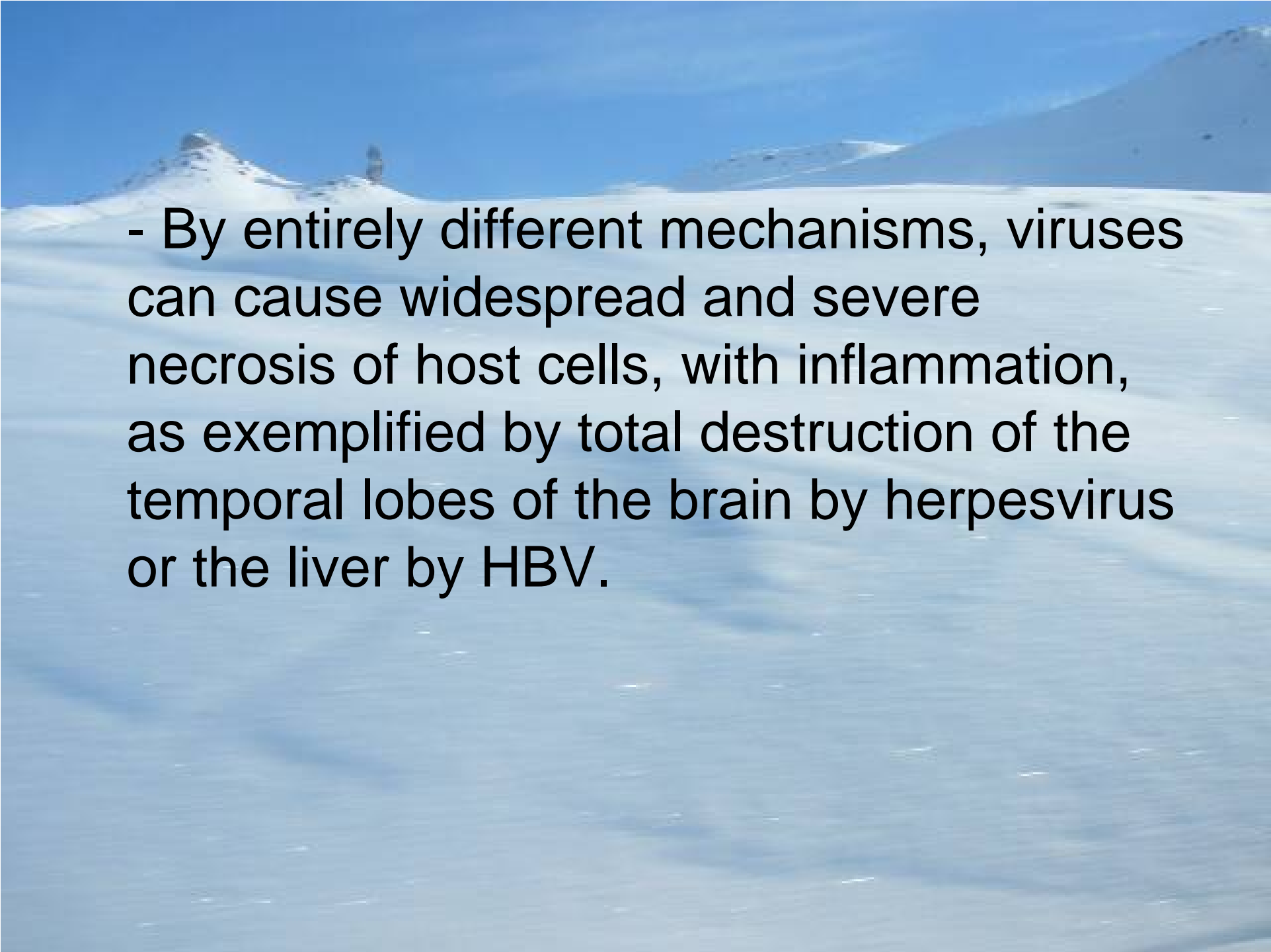
4. Necrotizing inflammation

- *Clostridium perfringens* and other organisms that secrete powerful toxins can cause rapid and severe necrosis.
- because few inflammatory cells are present, these lesions resemble infarcts with disruption or loss of basophilic nuclear staining and preservation of cellular outlines.



- *Clostridia* are often opportunistic pathogens that are introduced into muscle tissue by penetrating trauma or infection of the bowel in a neutropenic host.

- *Entamoeba histolytica* causes colonic ulcers and liver abscesses characterized by extensive tissue destruction with liquefactive necrosis and without a prominent inflammatory infiltrate.

A scenic view of a snowy mountain range under a clear blue sky. The foreground is a vast, flat expanse of snow, leading up to a range of snow-capped mountains in the distance. The sky is a uniform, clear blue. The overall atmosphere is bright and crisp.

- By entirely different mechanisms, viruses can cause widespread and severe necrosis of host cells, with inflammation, as exemplified by total destruction of the temporal lobes of the brain by herpesvirus or the liver by HBV.

5. Chronic inflammation and scarring

- chronic HBV infection; cirrhosis of liver
- sometimes the exuberant scarring response is the major cause of dysfunction (e.g., the “pipe-stem” fibrosis of the liver or fibrosis of the bladder wall caused by *schistosomal* eggs or the constrictive fibrous pericarditis in tuberculosis)

A scenic view of a snowy mountain range under a clear blue sky. The foreground is a vast, flat expanse of snow, leading up to a range of snow-capped mountains in the distance. The sky is a clear, bright blue.

Clinical evaluation:

1. Clinical history

- Prevalence of infectious disease
- Assessment of immune status
- Exposure to animals
- Travel history

Prevalence of infectious disease

- Community-acquired infection
- Hospital-acquired infection/Nosocomial infection

Increased susceptibility

Used of invasive procedure

Numerous source of infection

Use of antibiotic

- Opportunistic infections

TABLE 6-14 AIDS-Defining Opportunistic Infections and Neoplasms Found in Patients with HIV Infection

INFECTIONS

Protozoal and Helminthic Infections

Cryptosporidiosis or isosporidiosis (enteritis)
Pneumocytosis (pneumonia or disseminated infection)
Toxoplasmosis (pneumonia or CNS infection)

Fungal Infections

Candidiasis (esophageal, tracheal, or pulmonary)
Cryptococcosis (CNS infection)
Coccidioidomycosis (disseminated)
Histoplasmosis (disseminated)

Bacterial Infections

Mycobacteriosis (atypical, e.g., *M. avium-intracellulare*, disseminated or extrapulmonary; *M. tuberculosis*, pulmonary or extrapulmonary)
Nocardiosis (pneumonia, meningitis, disseminated)
Salmonella infections, disseminated

Viral Infections

Cytomegalovirus (pulmonary, intestinal, retinitis, or CNS infections)
Herpes simplex virus (localized or disseminated)
Varicella-zoster virus (localized or disseminated)
Progressive multifocal leukoencephalopathy)

NEOPLASMS

Kaposi sarcoma
B-cell non-Hodgkin lymphomas
Primary lymphoma of the brain
Invasive cancer of uterine cervix

CNS, central nervous system.



2. Physical examination

3. Investigation

- Microbiological tests
- Immunological tests
- Histological examination of tissue specimens
- Immunohistochemistry, PCR, DNA probe, DNA microarray

TABLE 8–9 Special Techniques for Diagnosing Infectious Agents

Gram stain	Most bacteria
Acid-fast stain	Mycobacteria, nocardiae (modified)
Silver stains	Fungi, legionellae, pneumocystis
Periodic acid–Schiff	Fungi, amebae
Mucicarmine	Cryptococci
Giemsa	Campylobacteria, leishmaniae, malaria parasites
Antibody probes	Viruses, rickettsiae
Culture	All classes
DNA probes	Viruses, bacteria, protozoa



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2. Cedric Mims, Hazel M Dockrell, Richard V Goering and et al. Medical Microbiology, updated third edition. Elsevier Mosby, 2004.
3. จุลินทร สำราญ, เอกสารประกอบการสอนรายวิชา พยาธิวิทยา 1 เรื่อง Principle of Infection, คณะแพทยศาสตร์ มหาวิทยาลัยนเรศวร, 2547.