MJF COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY

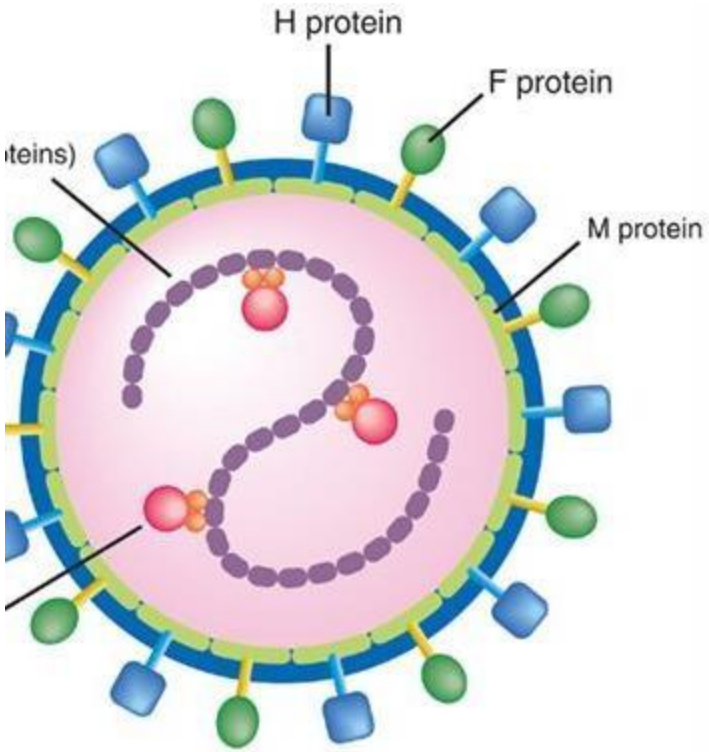
CD

Canine Distemper

- Synonym :
  - Carre's Disease
  - Hard-pad disease
  - Old dog encephalitis

- CD is a highly contagious, systemic, viral disease of dogs, characterized by a diphasic fever, leukopenia, GI and respiratory catarrh, and frequently pneumonic and neurologic complications.

- Canine distemper virus – **Pantropic** – SS RNA
- Genus: **Morbillivirus**
- Family: **Paramyxoviridae**
- Virulence factors
  - Hemagglutinin (H):
    - Attachment to host cells
  - Fusion (F) protein:
    - Cell membrane penetration
    - Syncytia formation
- Closely related to the viruses of measles, rinderpest and PPR



- Primarily a disease of **Dog / Canine**

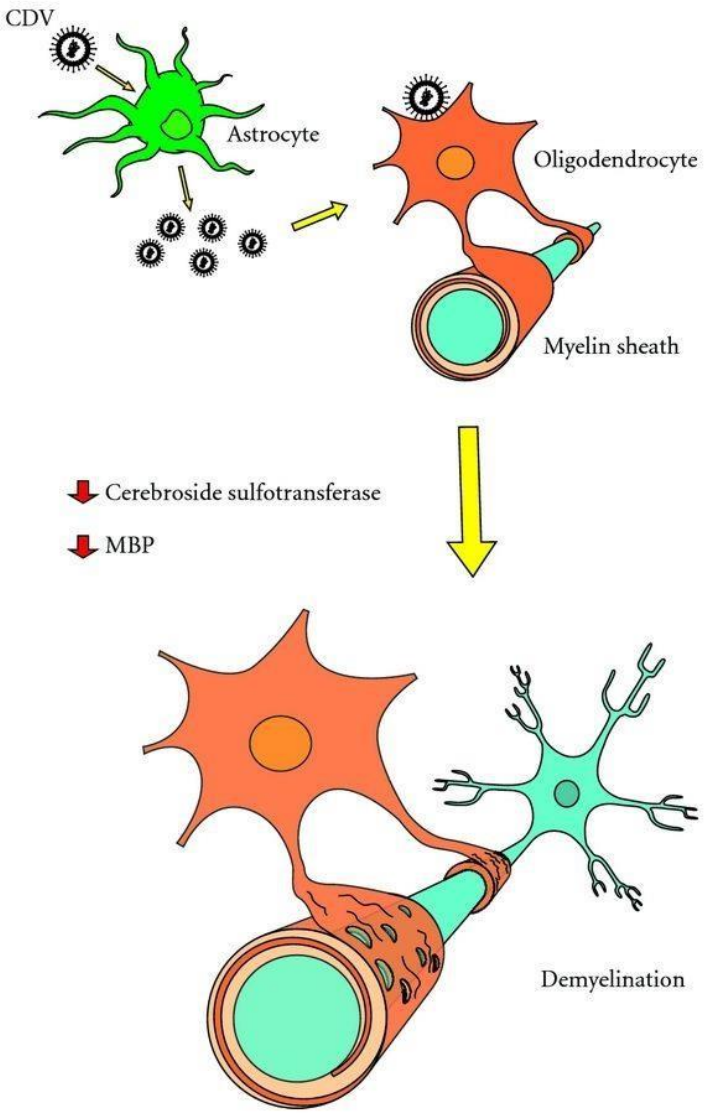
- Wide range of terrestrial carnivores
- **Canidae (dog, fox, wolf)**
- Ferrets, mink, raccoons
- Red Panda
- Bear

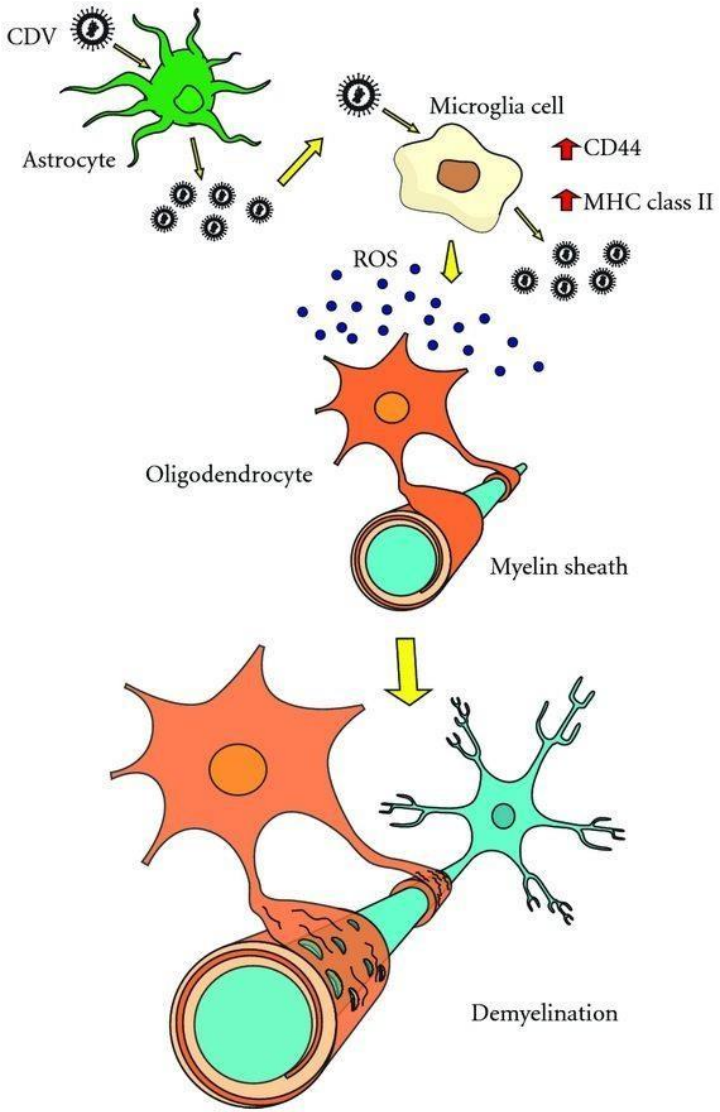
- Direct contact
  - Secretion from nasal and oral cavity
  - Aerosol
- Contaminated food, water, fomites

- Virus reach to nasopharyngeal mucosa→ binds to host CD150 on activated T cells, B cells and dendritic cells of tonsils and regional lymphnodes → Virus replication in first 24 hours → Cell-associated viremia by 2 days post infection (PI) → Spread to all lymphoid tissues and blood lymphocytes by 2-5 days PI → Virus replication in cells → Lymphocytolysis → Leukopenia → Immunosuppression
- Further development depends on immune status of the host, the age of the host, and the strain of virus

1. Adequate humoral / cellular immunity
   - Neutralize virus by 14 days PI – No clinical disease
2. Delayed / intermediate humoral / cellular immunity:
   - Viral infection / persistence in mucosal epithelium and brain → may develop neurologic disease
3. Failure to develop neutralizing antibody by 8-9 days PI
   - Virus disseminates to respiratory, GI, urogenital, and central nervous systems; integumentary, exocrine and endocrine systems also affected → virus shedding in secretion and excretion → secondary infections common

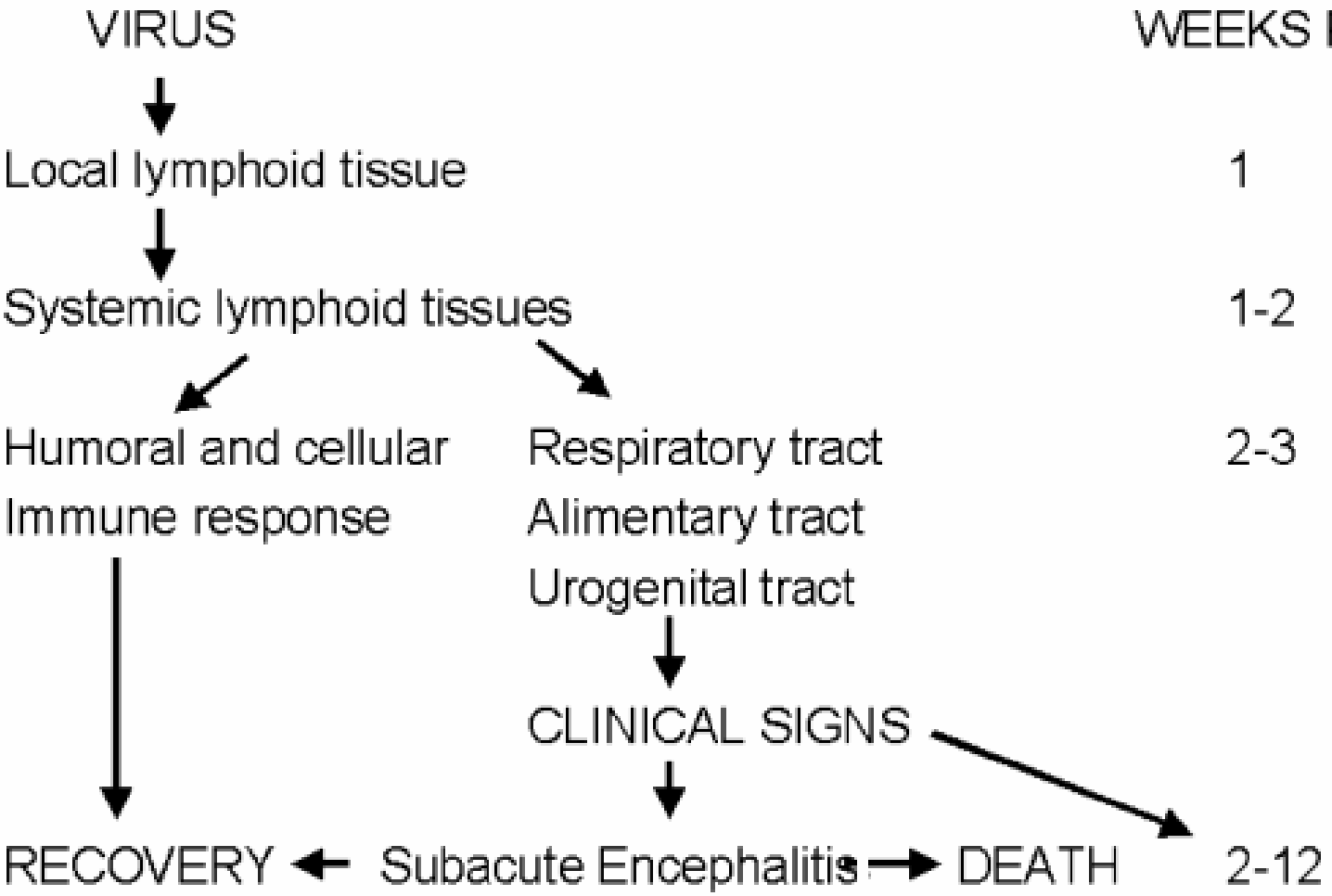
- CNS → Viral enter in CNS through infected lymphocytes / cell free virus state → Virus replication in endothelium cells → Infect Astrocytes, Microglial cells and Choroid plexus epithelium/Ependymal cells → Spread in CSF → Infect Neurons (Polioencephalomyelitis) and Oligodendrocyte (Leukoencephalomylitis)
  - Virus replication in neurons leads to neuronal necrosis
  - Direct or indirect effect of virus leads to oligodendrocyte necrosis and loss of myelin sheath (demyelination)
- Development of CNS signs


CDV
Astrocyte
Oligodendrocyte
Myelin sheath
Cerebroside sulfotransferase
MBP
Demyelination


CDV
Astrocyte
Microglia cell
CD44
MHC class II
ROS
Oligodendrocyte
Myelin sheath
Demyelination

- Respiratory → Viral replication in Pneumocyte, Bronchiolar epithelium and alveolar macrophages → Death of these cells
  → Inflammation and immunosuppression → Secondary bacterial infection → Development of bronchopneumonia
- Skin/Foot pad → Viral replication in stratum spinosum → Disfunction in cell replication and differentiation → Orthokeratotic hyperkeratosis (Hard pad disease) → Secondary bacterial infection → Impetigo
- Virus replicate in many other tissue - e.g. In ameloblasts → defective enamel production → multifocal enamel hypoplasia

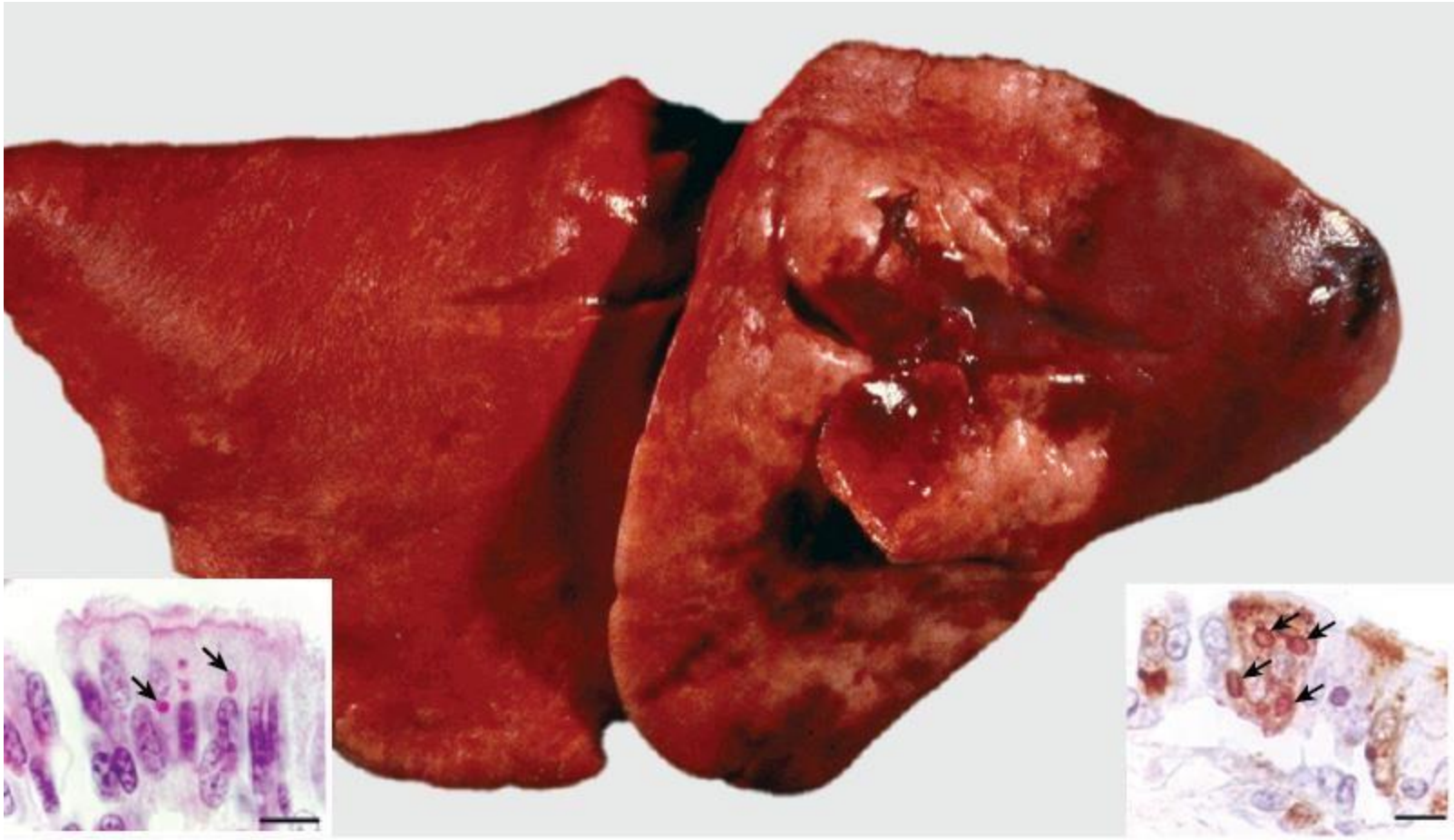
PATHOGENESIS OF CANINE DISTEMPER



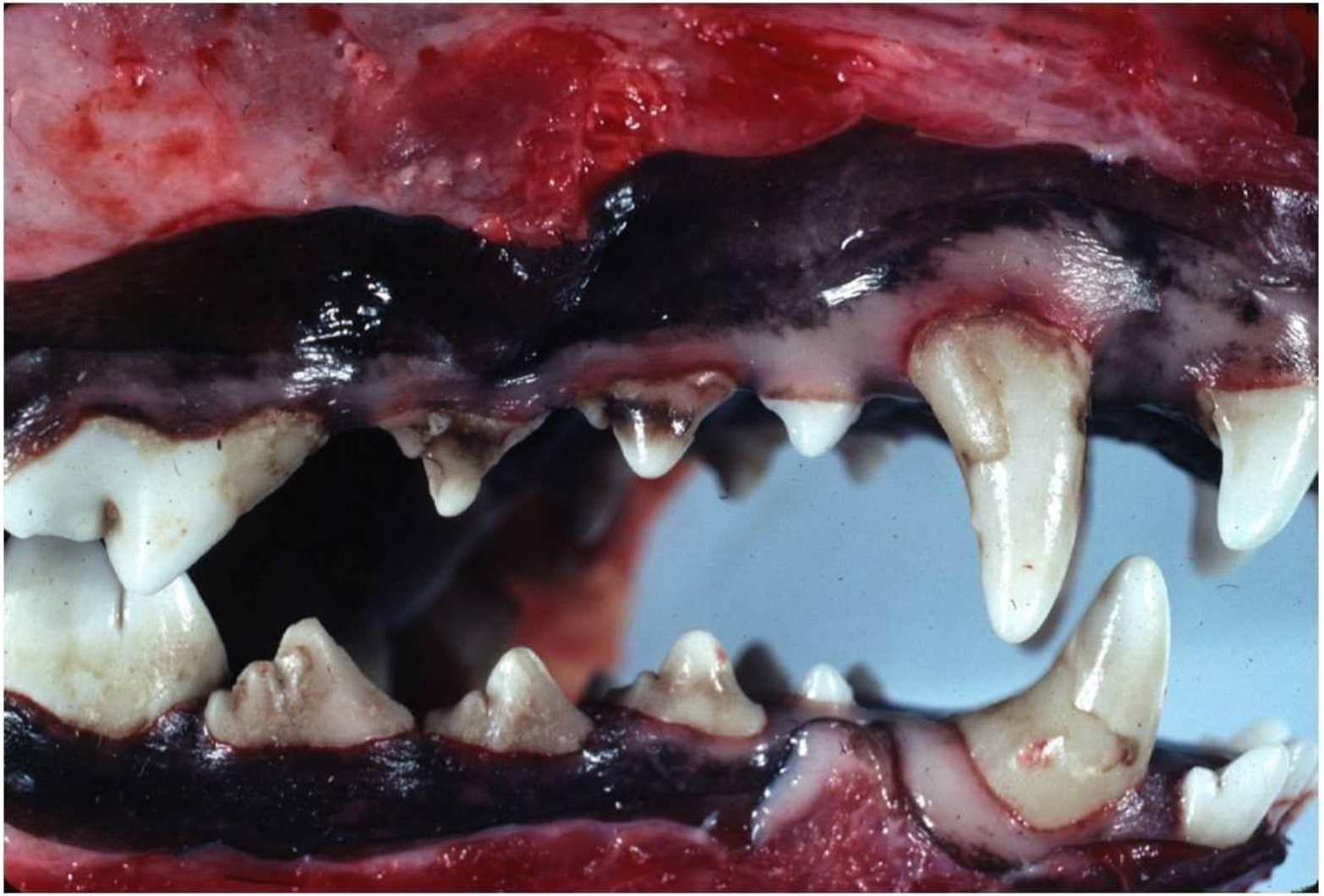
- Disease most common in 12-16 week-old puppies
- Early:
  - Transient fever after 3–6 days PI - unnoticed
  - After few days again fever (Diphasic Fever), conjunctivitis cough, vomiting, diarrhea, depression, anorexia, serous to mucopurulent oculonasal discharge
  - Signs of Pneumonia
  - Diarrhea – Dehydration / Emaciation
  - Pustules on ventral abdomen/Inner thigh
  - Hyperkeratosis of Digital pads (Hard Pad)
  - Keratitis / Retinitis – Blindness

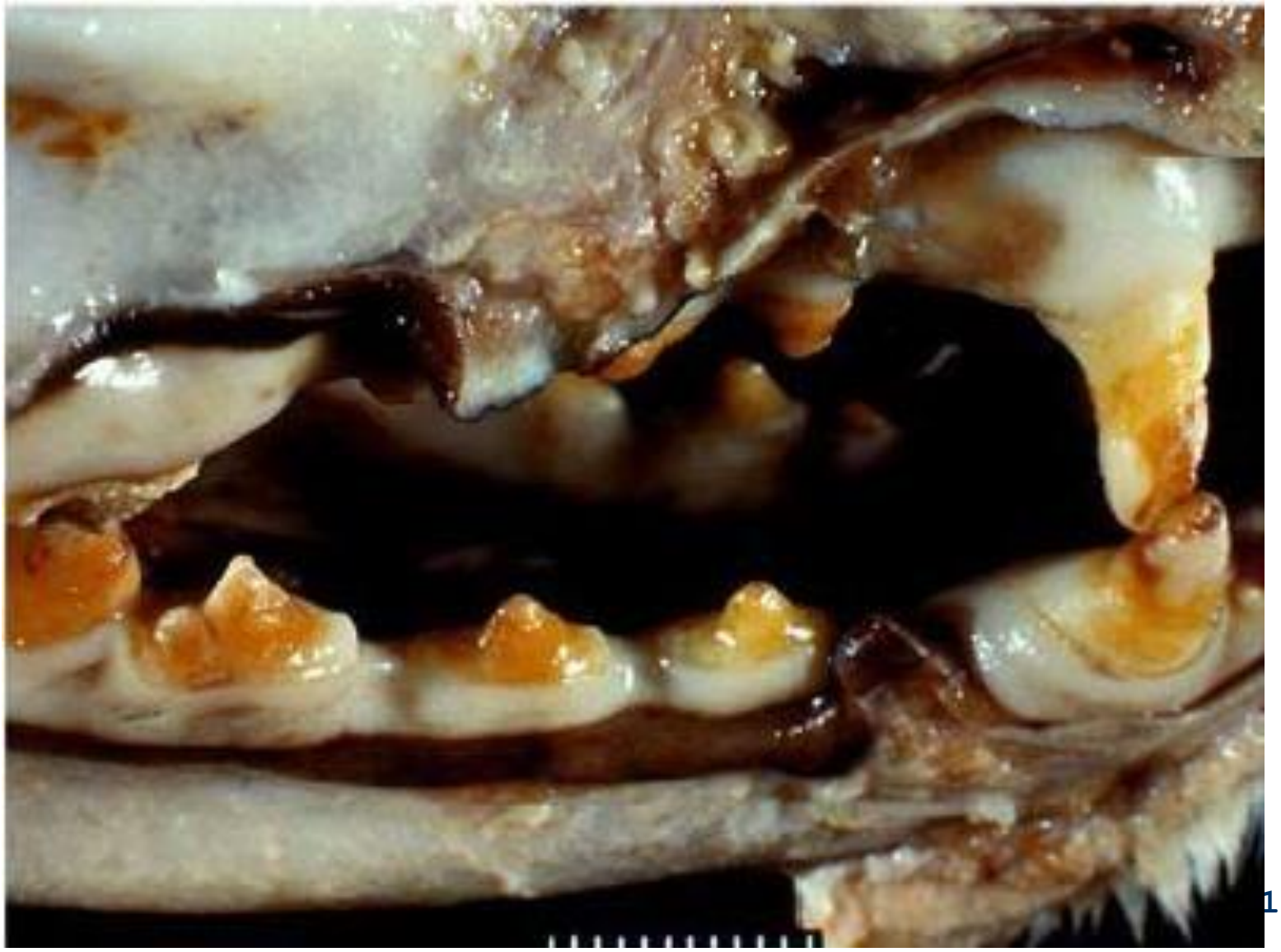
- Later (1-4 weeks): Neurologic
  - Epilepsy
  - Chewing movements
  - In coordination
  - Muscular twitching (myoclonus) in face, head, neck or shoulder muscles
- May see minimal or no signs of epithelial infection and only neurologic signs in some dogs

- Integument
  - Hyperkeratosis of footpads and nose
  - Secondary pyoderma (pustular dermatitis, especially ventral abdomen)
- Lungs
  - Patchy red-tan, rubbery subpleural and marginal lesions (bronchointerstitial pneumonia)
  - May be edematous and consolidated (secondary pneumonia)
- Eyes/conjunctiva: Conjunctivitis, keratitis
- Lymphoid tissues: Tonsillar enlargement, thymic atrophy
- Teeth: Enamel hypoplasia



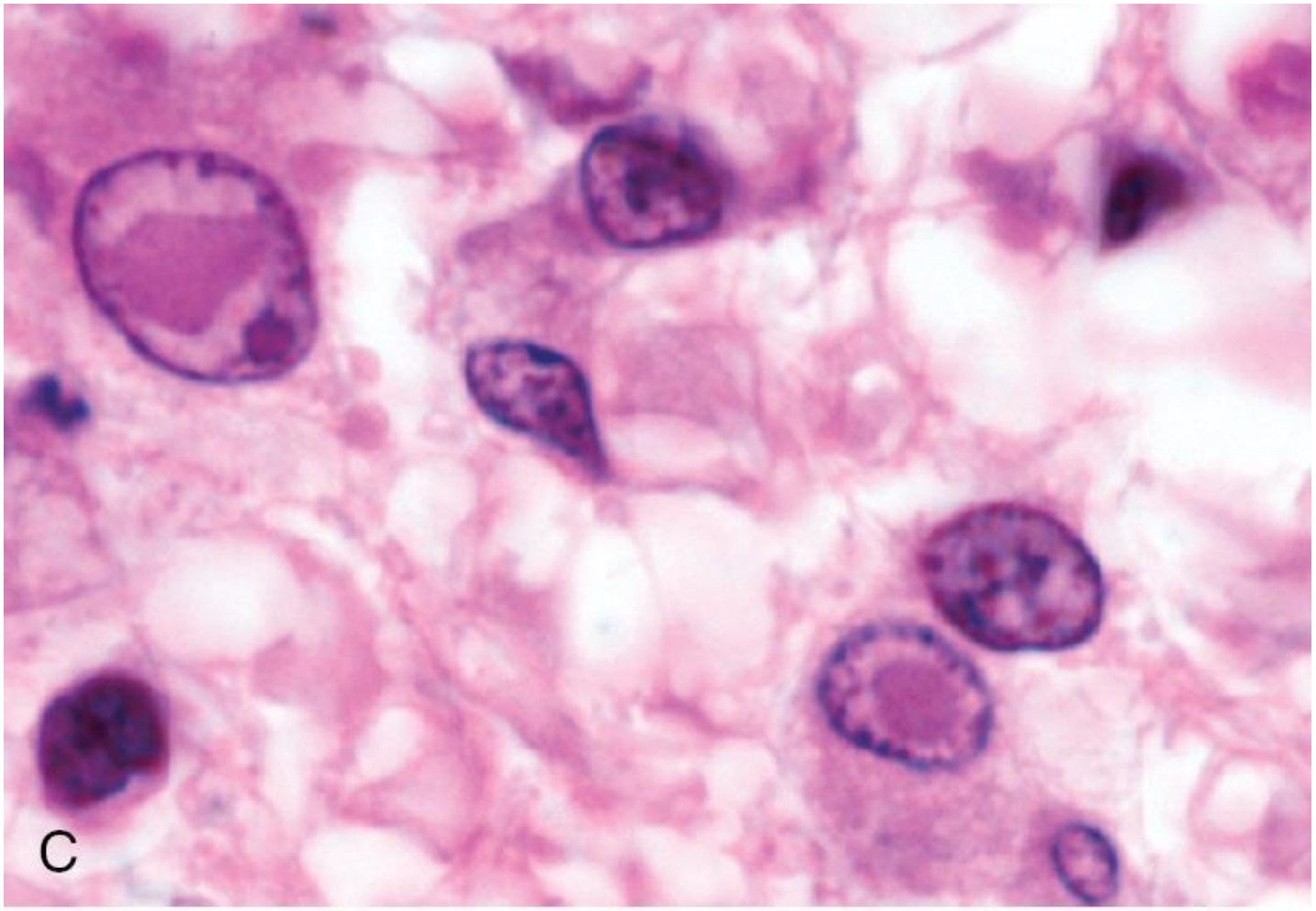
(From Berrocal A, López A: *J Vet Diagn Invest* 15:292-294, 2003.)
Zachary and McGavin: Pathologic Basis of Veterinary Disease, 5th edition.





- **Eosinophilic intracytoplasmic (IC) and/or intranuclear (IN) inclusion bodies (IB) with syncytia**
- Most numerous 10-14 days PI
- Most obvious in brain (often IN) and epithelium (usually IC), especially in urinary bladder
- **Integument:**
  - Orthokeratotic and/or parakeratotic hyperkeratosis of footpad, nose with IB
- **Lungs:**
  - Ibs in bronchial/bronchiolar epithelium
  - Alveoli: Filled with edema, fibrin, mononuclear cells, necrotic epithelium
  - Septa expanded by mononuclear cells; Syncytial cells

- **Central nervous system:**
  - White matter: Demyelination
  - Gray matter - IB in neurons, neuronal necrosis, MNC infiltrate surrounding necrotic neurons , perivascular cuffing
- Lymphoid tissues:
  - Early lymphoid depletion and lymphocytic necrosis
- Teeth
  - Cystic degeneration of ameloblastic epithelium
- Other epithelia
  - Degeneration and IB



(Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)
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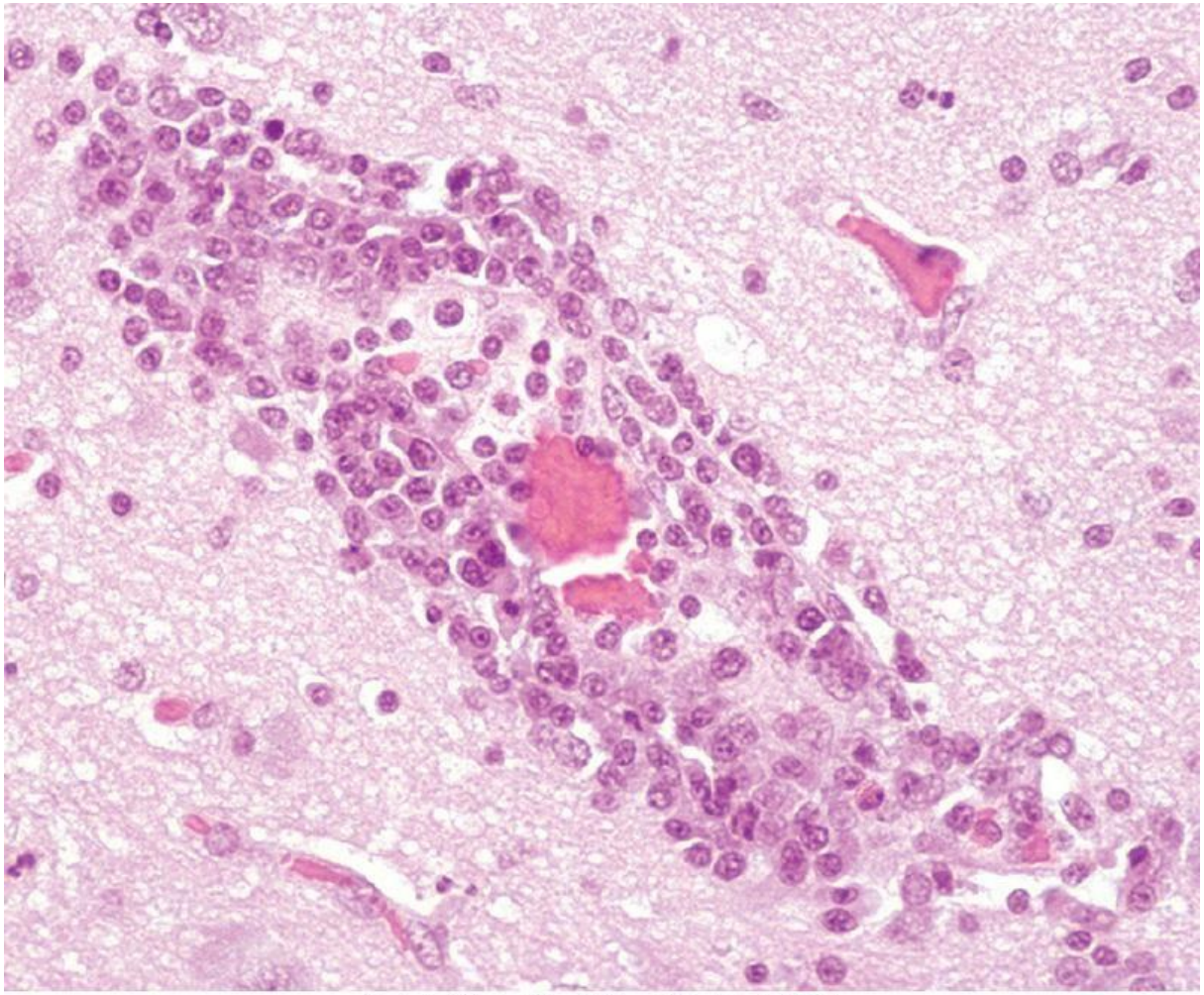

(Courtesy Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)
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- Occur in mature adult dogs
- Rare variant
- Possibly caused by infection with replication-defective virus
- Chronic progressive neurologic disease
- Nervous signs as like CD
- Pathology - CNS - similar to CD

- Clinical signs
- Histopathology
- Laboratory tests
  - Virus isolation
  - Virus neutralization tests
  - Enzyme-linked immunosorbent assay (ELISA)
  - Polymerase chain reaction
  - Serological tests

ICH

Infectious canine hepatitis

- Synonym :
  - Rubarth's disease
  - Hepatitis contagiosa canis
  - Fox encephalitis

- ICH is a contagious disease of dogs with signs that vary from a slight fever and congestion of the mucous membranes to severe depression, marked leukopenia, and coagulation disorders

- **Canine adenovirus 1 –** dS DNA virus
- Genus: **Mastadenovirus**
- Family: **Adenoviridae**
- Tropism for endothelium, mesothelium and hepatocytes

- Antigenically related only to CAV-2 (mild respiratory infection)

- Primarily a disease of young **Dog / Canine (< 2 year)**

- Also is seen in foxes, wolves, bears and other carnivores

- Direct contact
  - Urine, feces, or saliva of infected dogs
  - Aerosol
  - Recovered dogs shed virus in their urine for ≥6 mo
- Contaminated food, water, fomites

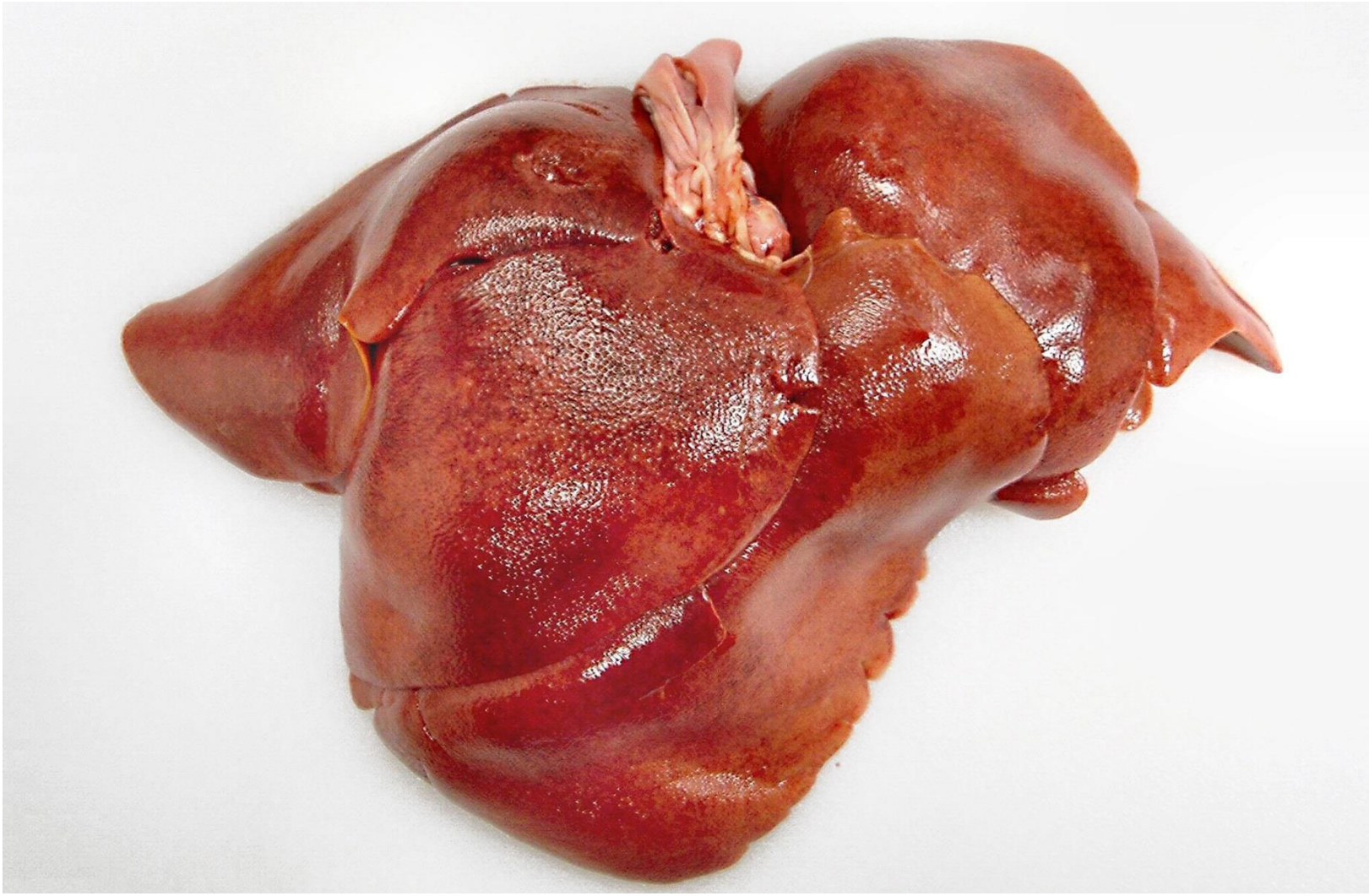
- Virus reach to nasopharyngeal mucosa → initially replicates in the tonsils → tonsillitis → cervical lymph nodes → thoracic duct → blood (viremia) → dissemination to viscera and CNS → Virus enter in to endothelial cells → virus replication in EC → necrosis
  and lysis of EC →vasculitis and thrombus formation in organs and mucosa → Ischemic necrosis (infract) edema and hemorrhages, DIC
- Virus enters the aqueous humor → virus replicates in corneal endothelial cells → degeneration and corneal edema (“**blue eye**”)

- Virus reach to liver→ replication → **centrilobular** **hepatocyte** **necrosis** → decreased production of clotting factor → Widespread endothelium damage and decreased production of clotting factor → Bleeding defects and coagulopathy
- Some recover dog - glomerulonephritis and/or anterior uveitis (type 3 hypersensitivity)

- Infection may cause no clinical signs
- Fever, Anorexia
- Serous discharge from the eyes and nose
- Occasionally vomiting
- Intense hyperemia or petechiae of the oral mucosa
- Mild tonsillitis
- Corneal edema
- CNS signs: Depression, disorientation, seizures, coma
- Epistaxis

- Early neutropenia, lymphopenia, and thrombocytopenia
- Neutrophilia and lymphocytosis during recovery
- Prolonged BT, APTT, and TT
- Elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST)
- Marked bilirubinuria, proteinuria (albumin)
- Decreased or absent megakaryocytic in bone marrow during viremic stage

- Serosal petechial and ecchymotic hemorrhages ("epicardial lesions")
- Subcutaneous edema
- Lymph nodes, tonsils: Edema and hemorrhage
- Gallbladder edema
- Hepatomegaly; liver turgid and friable with yellowish mottling
- Fibrin strands on the hepatic capsule
- Corneal edema



(Courtesy Dr. W. Crowell, College of Veterinary Medicine, The University of Georgia; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)
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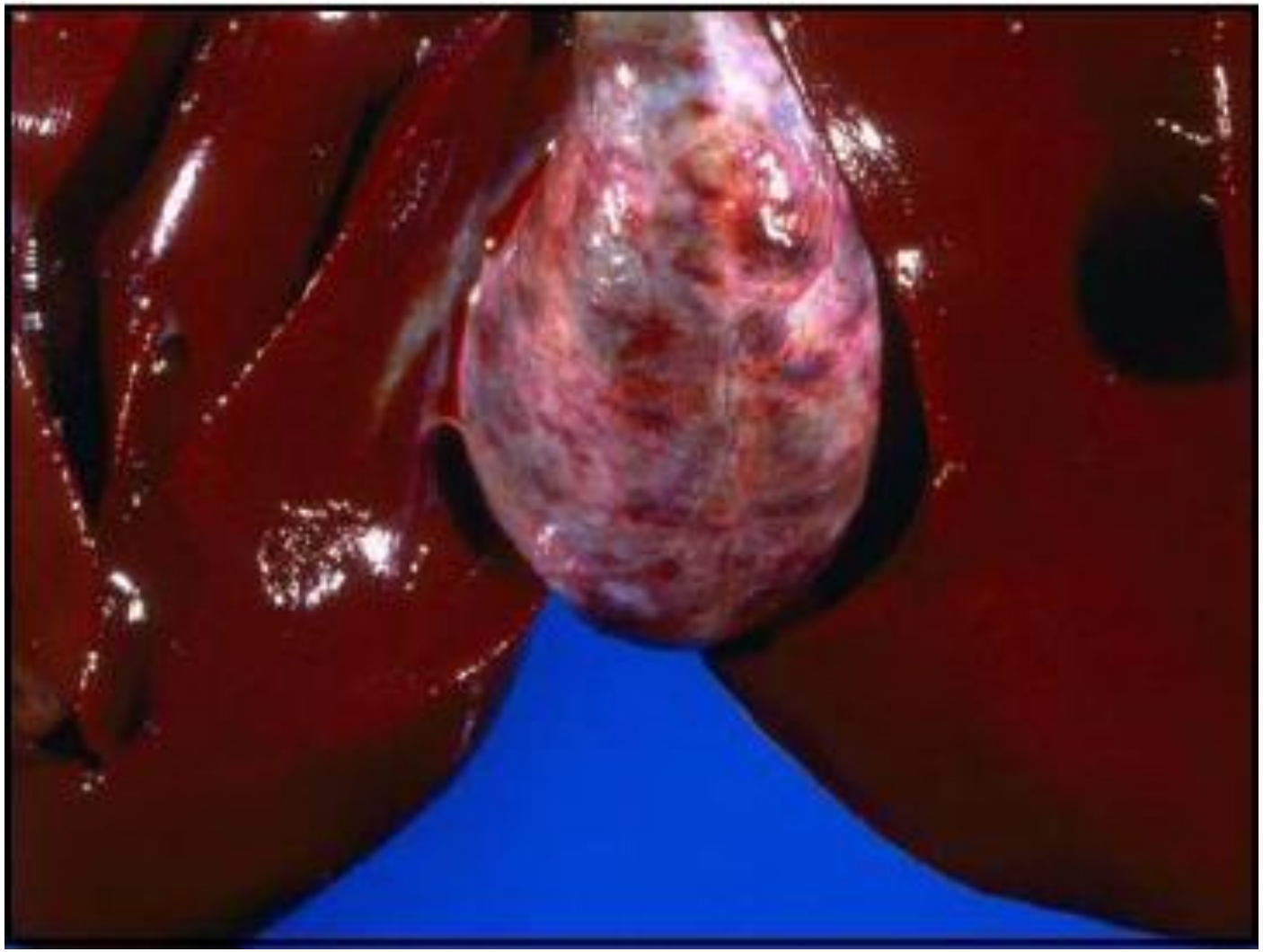

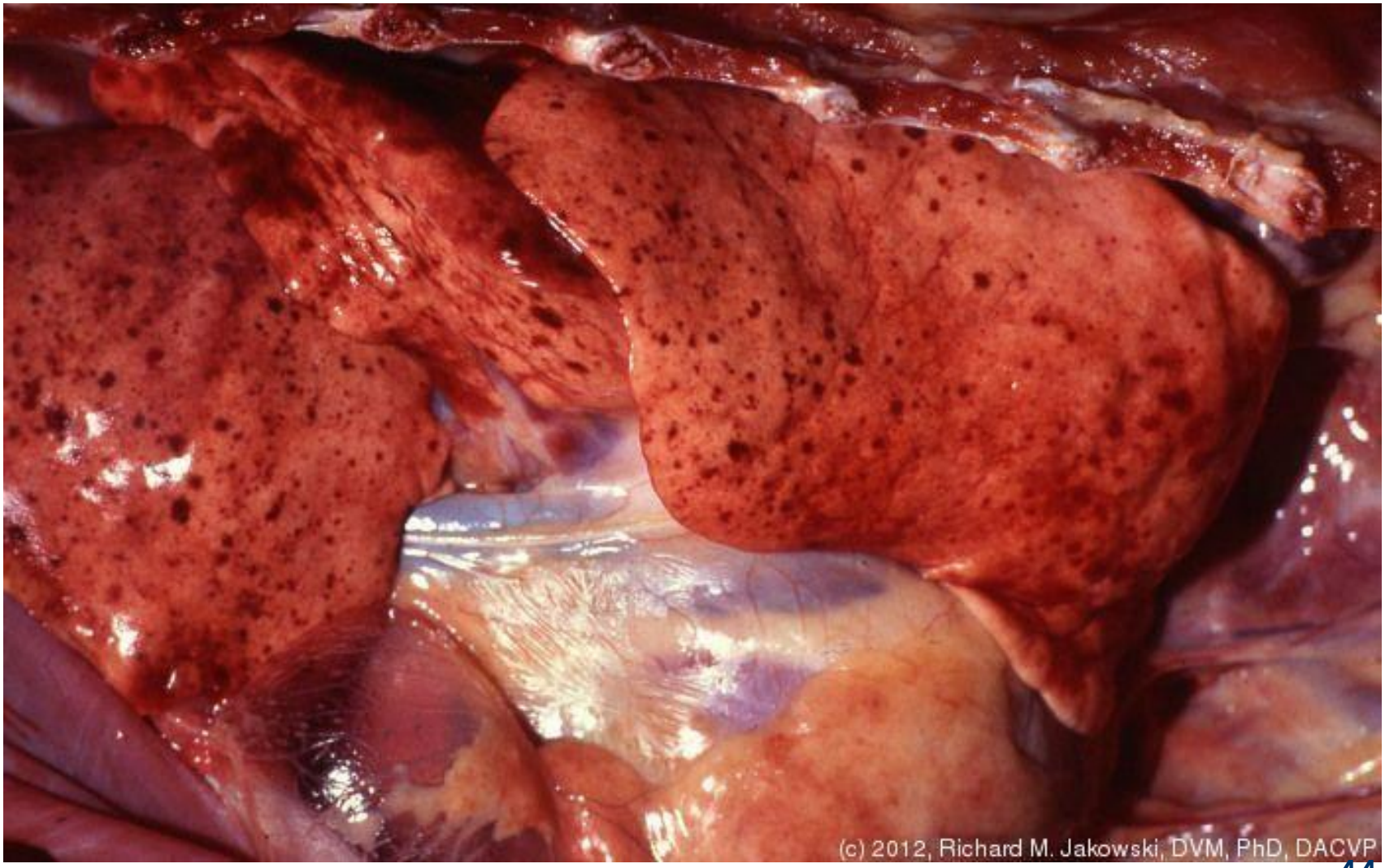
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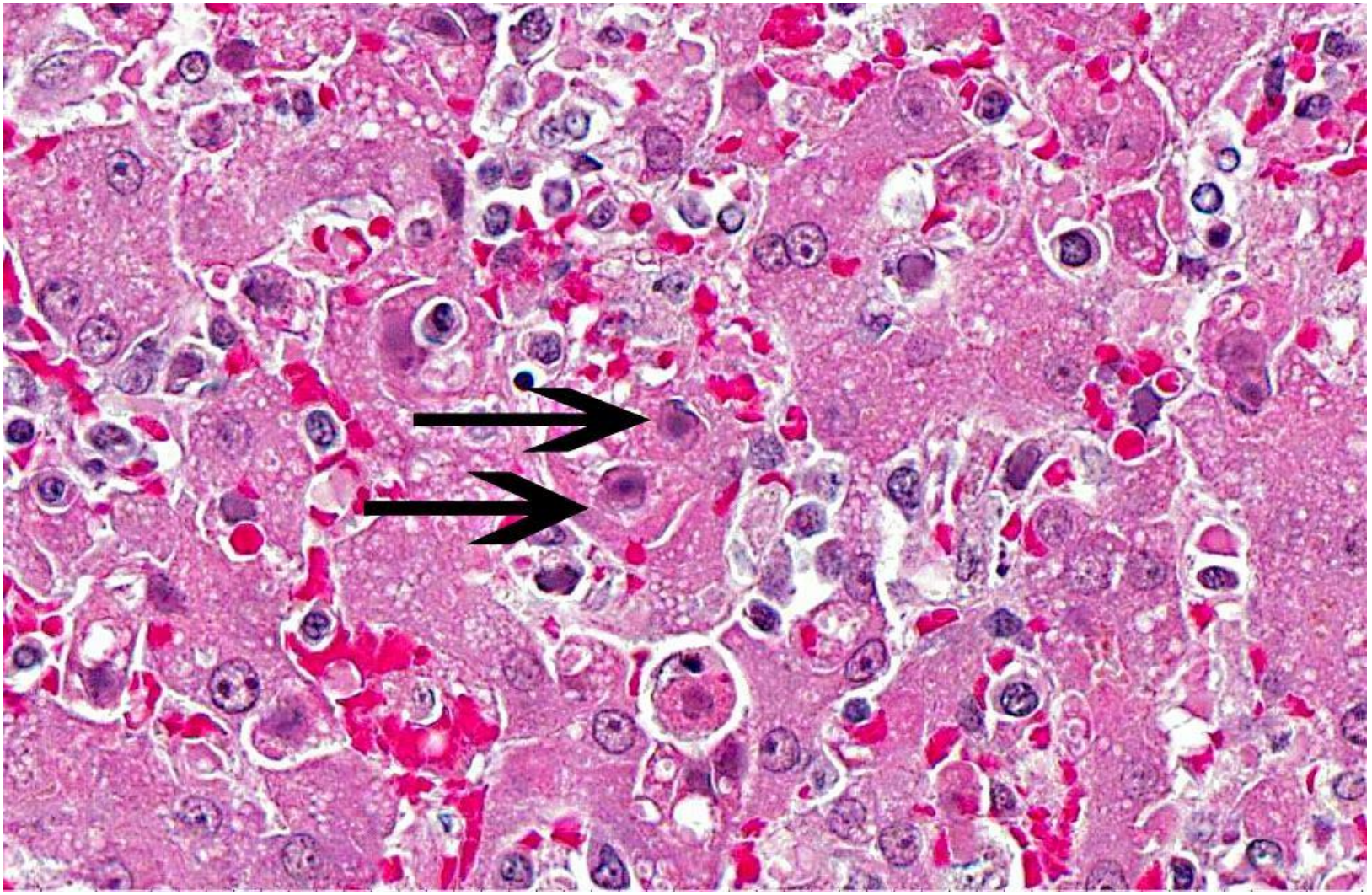
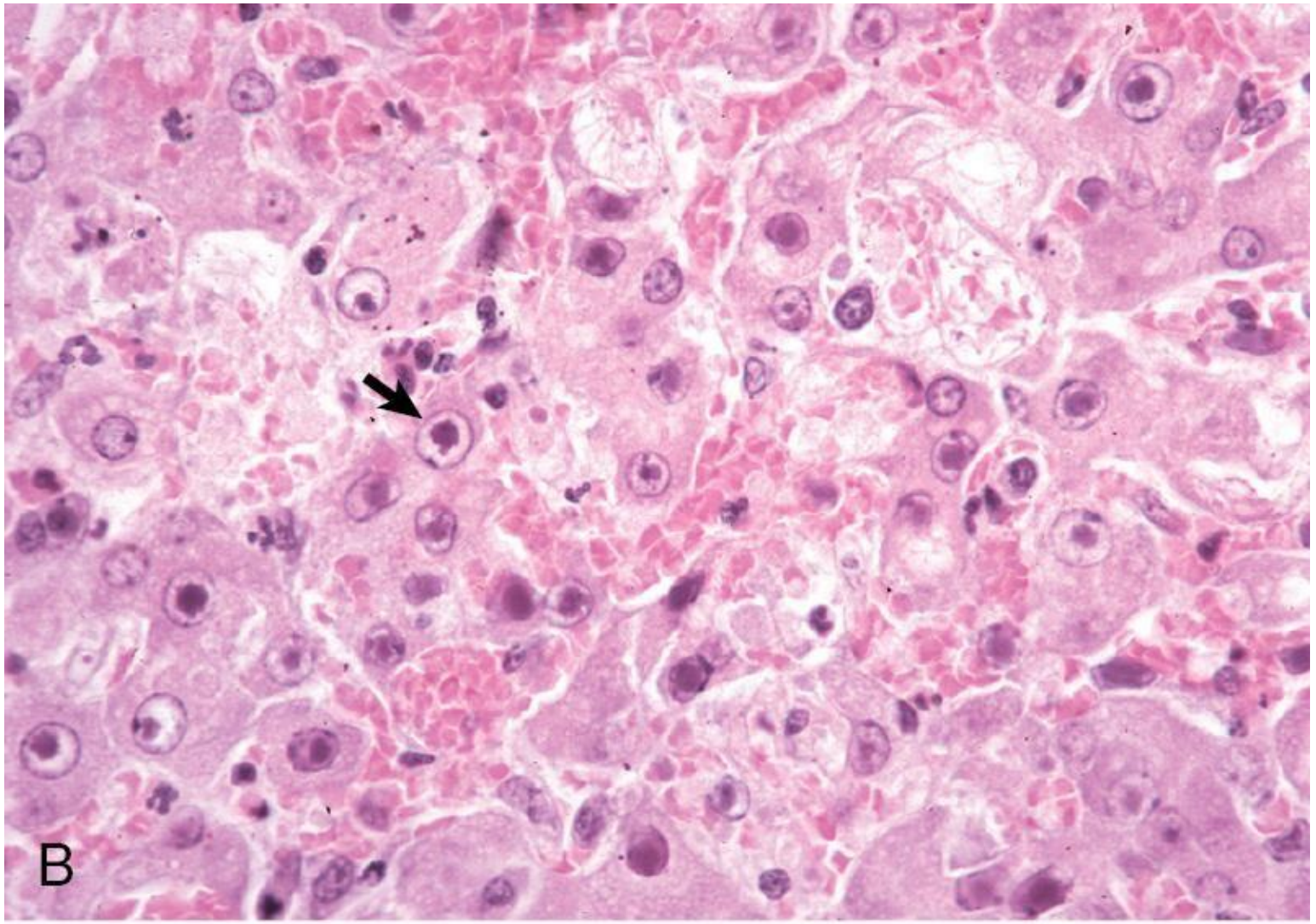
- **Liver:**
  - centrilobular to panlobular coagulative necrosis
  - **Intranuclear inclusion bodies** in Kupffer cells, hepatocytes, endothelial cells and biliary epithelium
  - Sinusoids dilated and filled with blood
- Gallbladder: Marked subserosal edema
- **Intranuclear inclusion bodies** in glomerular mesangial cells, glomerular capillary endothelium and tubular epithelium; inclusions in the urothelium of urinary bladder
- Eye: Granulomatous iridocyclitis; corneal edema
- Brain: Hemorrhages, perivascular cuffing; vasculitis; IB
- Widespread intravascular fibrin thrombi





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Thank you