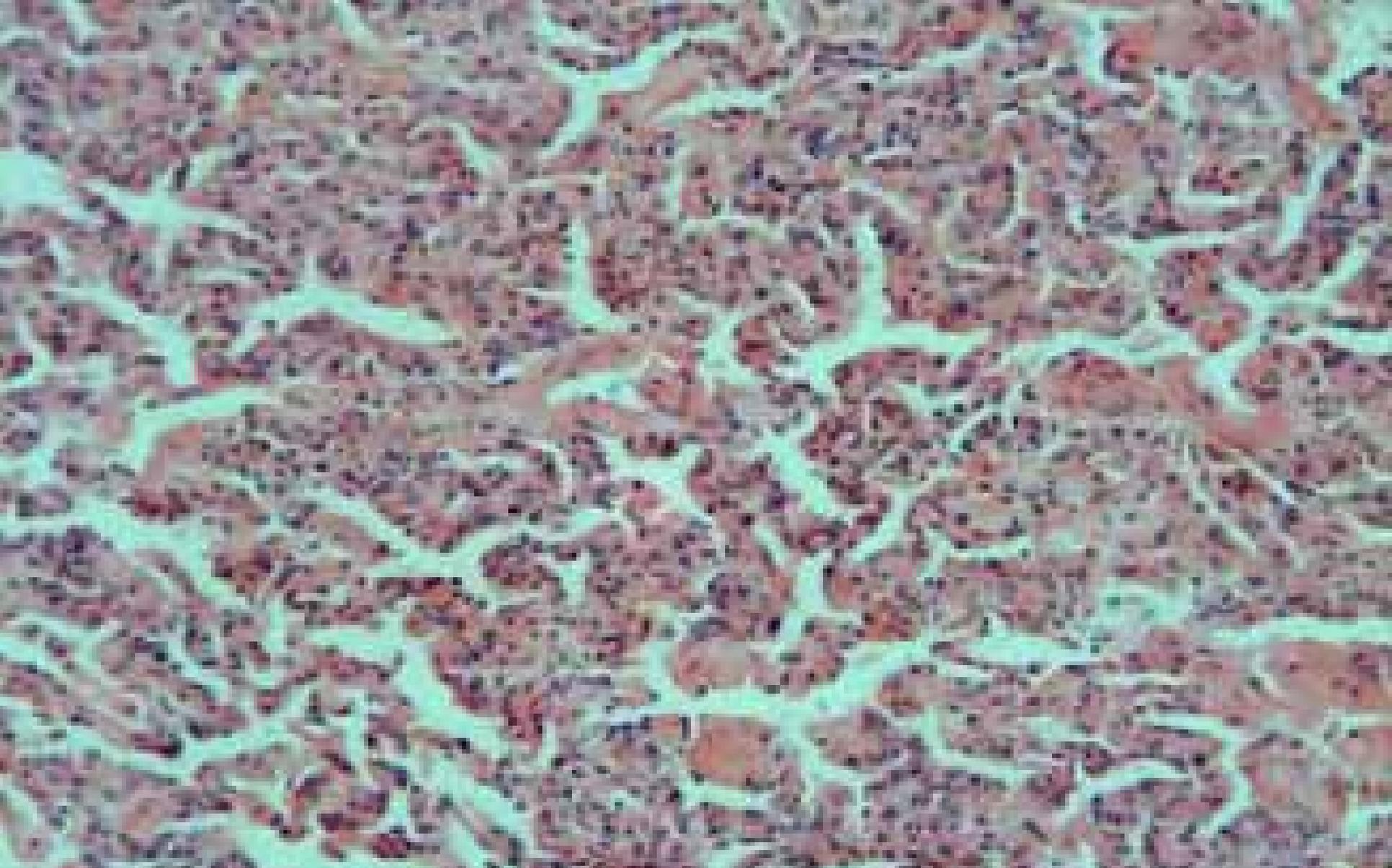


Feng et al. Emerging Infectious Diseases
Vol. 14, No. 11, November 2008

Atypical PRRS in Asia

- **Skepticism by PRRS researchers:**
 - Of 1500 "sources" sampled, 30% were PCR positive to the new PRRS variant
 - *Streptococcus suis* was isolated from 1/3 of the cases and *Haemophilus parasuis* from another third
 - Samples are negative for PRV
 - Classical Swine Fever is endemic in China's pig herds
 - Producers routinely vaccinate for CSF as well as for Foot and Mouth Disease and Pseudorabies
 - Prior to this most recent outbreak, some herds were being vaccinated against PRRS using a Chinese vaccine
 - Did not appear to prevent infection with the latest pathogen



Li et al. (The Veterinary Journal 174, 577-584, 2007) reproduced only “classical” lesions.



PCVAD

**Porcine Circovirus
Associated Diseases**

Circoviruses

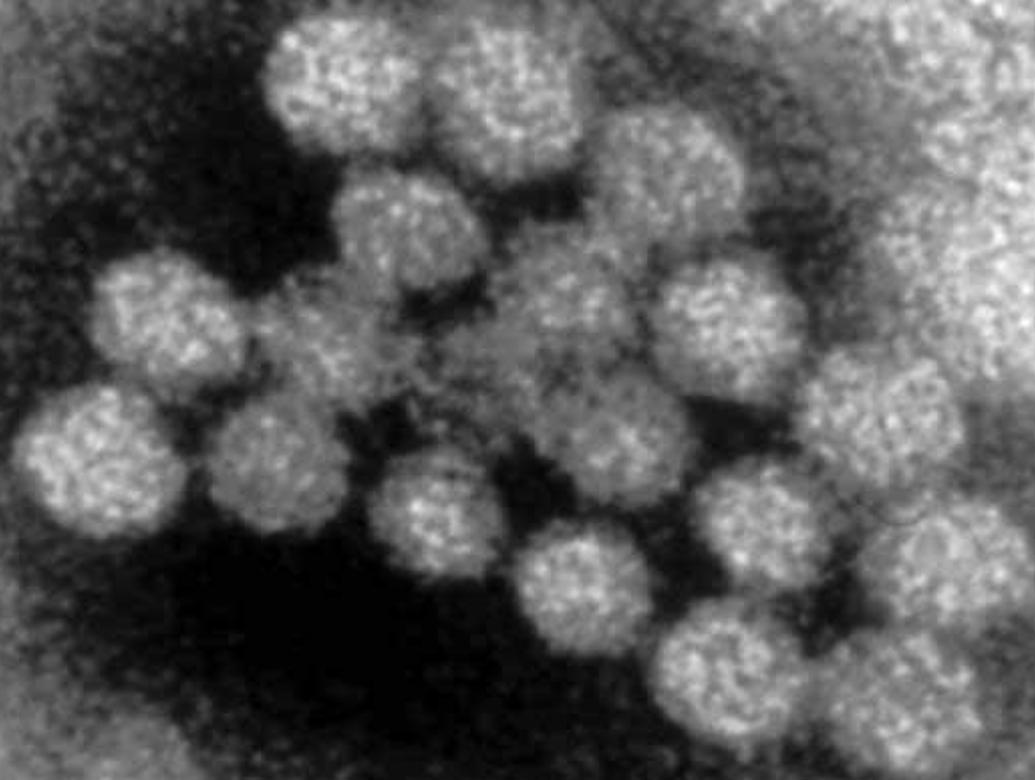
- **Chicken (Chicken Anemia Virus, CAV)**
- **Pigs (Porcine Circovirus, PCV1 and 2)**
- **Psittacines (Psittacine Beak and Feather Disease Virus, PBFDV)**
- **Racing pigeons (Pigeon Circovirus)**
- **Canary circovirus**
- **Goose circovirus**
- **Duck circovirus, finch circovirus, gull circovirus**
- **Starlings, Australian ravens, ostriches, pheasants, mute swans**

Porcine Circovirus (PCV)

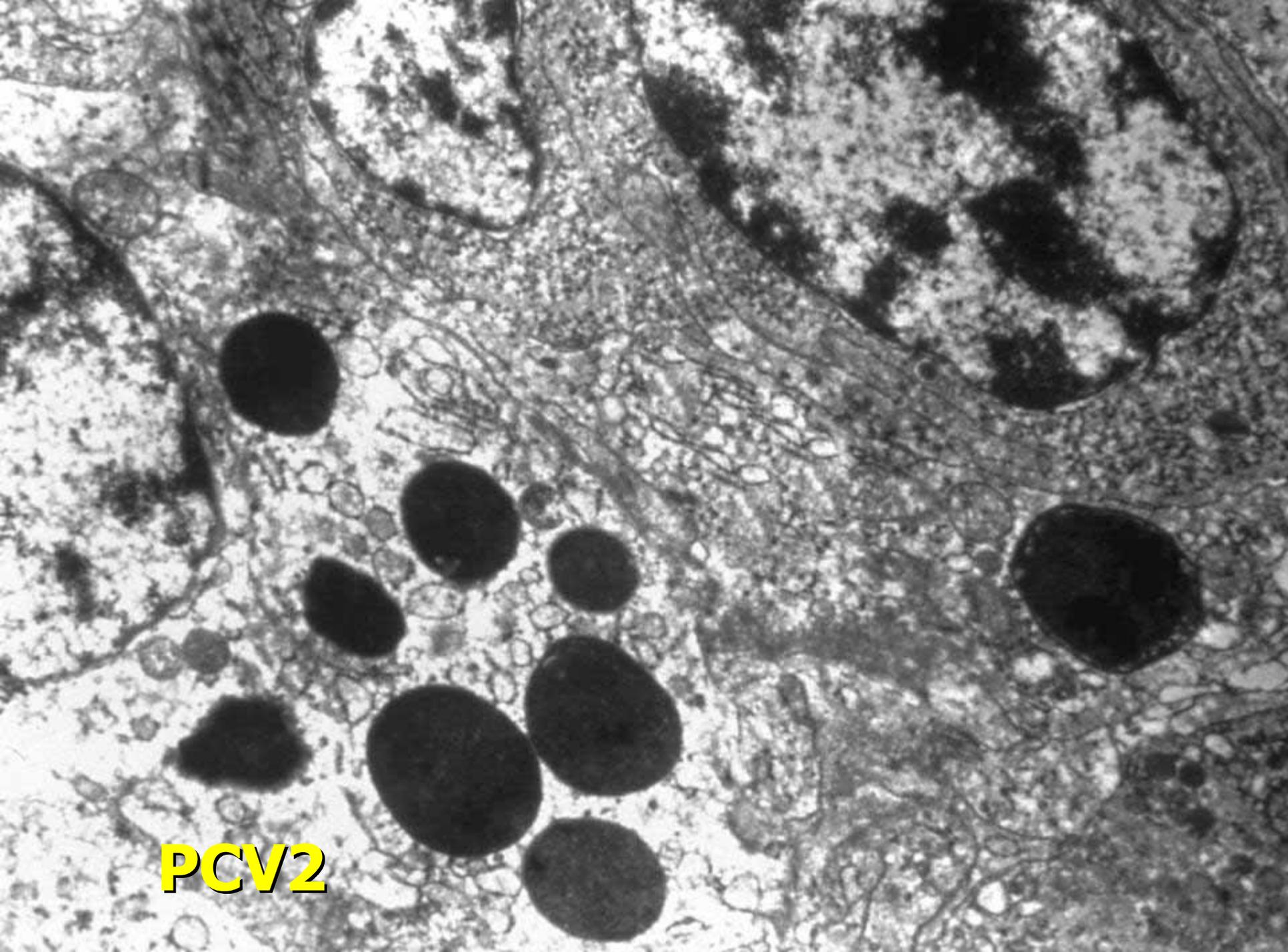
- Smallest known mammalian virus
- Single stranded DNA genome
- Rolling-circle replication
- Homologue rep protein (**Mankertz et al., 1997, 1998**)
- Named by **Tischer (1982)** in Germany*
- First isolated from persistently infected PK-15 cells
- **No cytopathic effect in PK-15 cells**

* Description of this virus: **Kanitz et al., 1972**

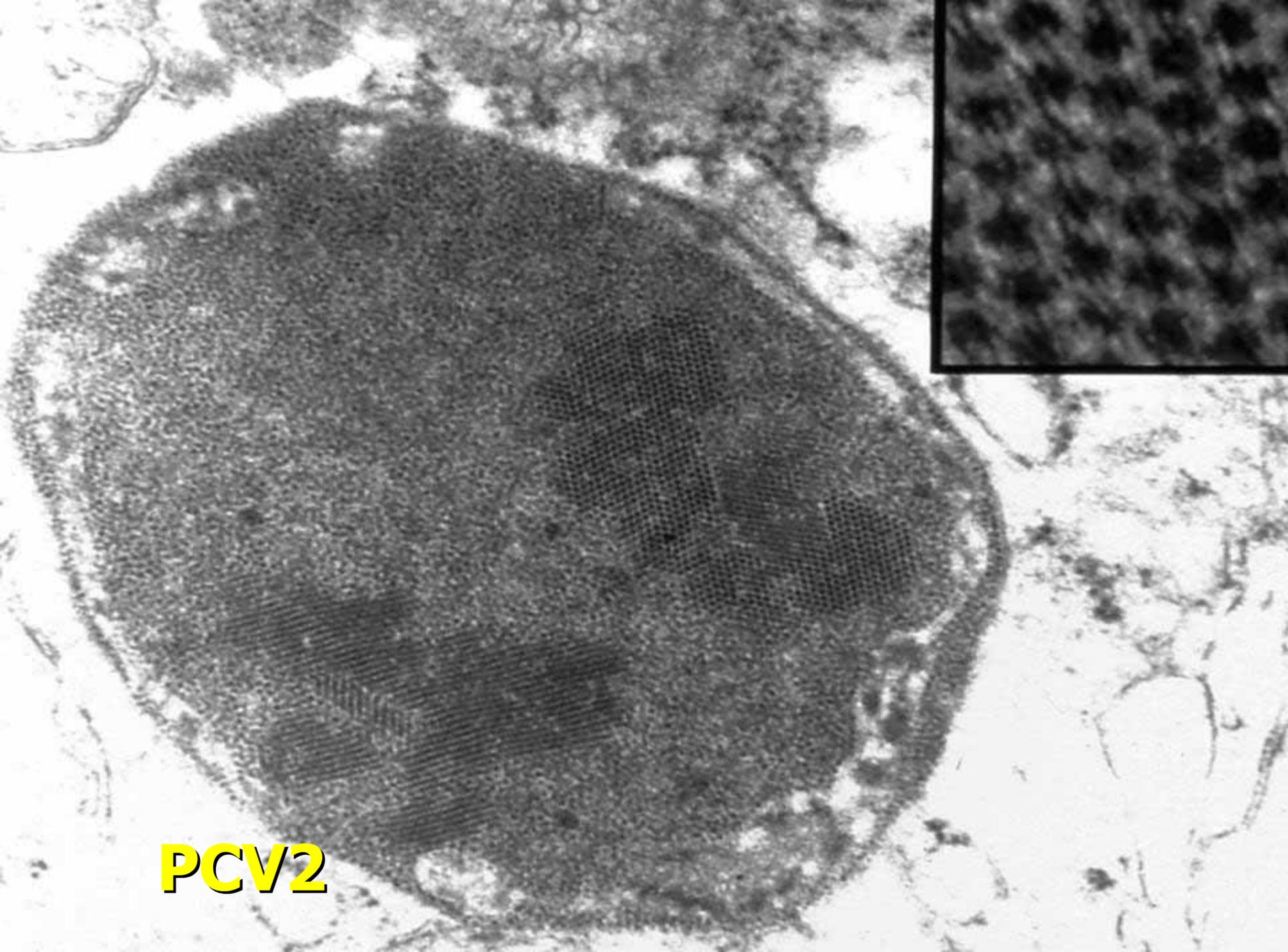
Tischer et al., 1974



PCV2



PCV2



PCV2

Epidemiology of PCV

Seroprevalence high in:

- Germany (Tischer et al., 1986)
- Great Britain (Edwards et al., 1994)
- Canada (Dulac et al., 1989)
- New Zealand (Horner, 1991)
- USA (Hines et al., 1995)

Identified by EM:

- South Africa (Gerdes, 1993)

The Role of PCV in Swine Diseases

Field isolates of PCV from pigs have been associated with:

- **Postweaning Multisystemic Wasting Syndrome (PMWS)**
- **Congenital Tremors Type A2**
- **Abortions**
- **Porcine Dermatitis Nephropathy Syndrome (PDNS)**
- **Porcine Respiratory Disease Complex (PRDC)**
- **Proliferative and Necrotizing Pneumonia (PNP)**

Two types of PCV have been identified:

- **PCV1 (similar to virus from PK-15 cells)**
- **PCV2 (isolates from pigs with PMWS)**

Wasting Disease in Pigs

- First report of circovirus associated with severe interstitial pneumonia in pigs by **Daft** in California (1996)
- Postweaning Multisystemic Wasting Syndrome in pigs in Western Canada (**Clark et al. 1997**)
- Circoviral associated disease in weaned pigs in Indiana (**Kiupel et al. 1998**)
- Similar syndrome in France and Spain (**Albina et al. 1996, Allan et al. 1998**)
- Sporadic occurrence before 1995
- Now reported worldwide: epizootic PMWS in late 90's in Asia and Europe, after 2004 in America

Postweaning Multisystemic Wasting Syndrome (PMWS)

Clinical Signs

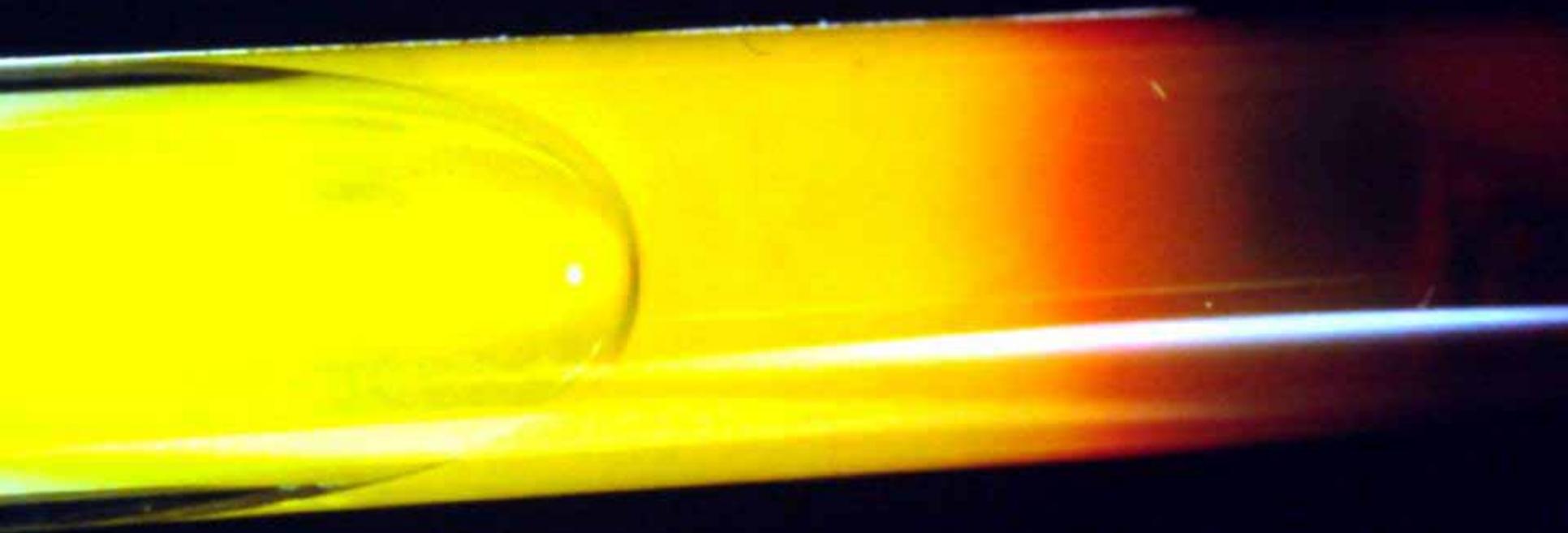
- Disease of nursery and grower pigs
- Progressive weight loss (emaciation)
- Diarrhea
- Dyspnea, tachypnea and lethargy
- Icterus and pallor (less consistent)
- Cutaneous hyperemia of extremities following exercise
- Morbidity: 5-15%



PMWS



PMWS



PMWS

Postweaning Multisystemic Wasting Syndrome (PMWS)

Gross Lesions

- **Generalized lymphadenopathy**
- **Interstitial pneumonia**
- **Icterus**
- **Hepatic necrosis and atrophy**
- **Renomegaly**
- **Splenomegaly**
- **Gastric ulcers**
- **Intestinal wall edema**



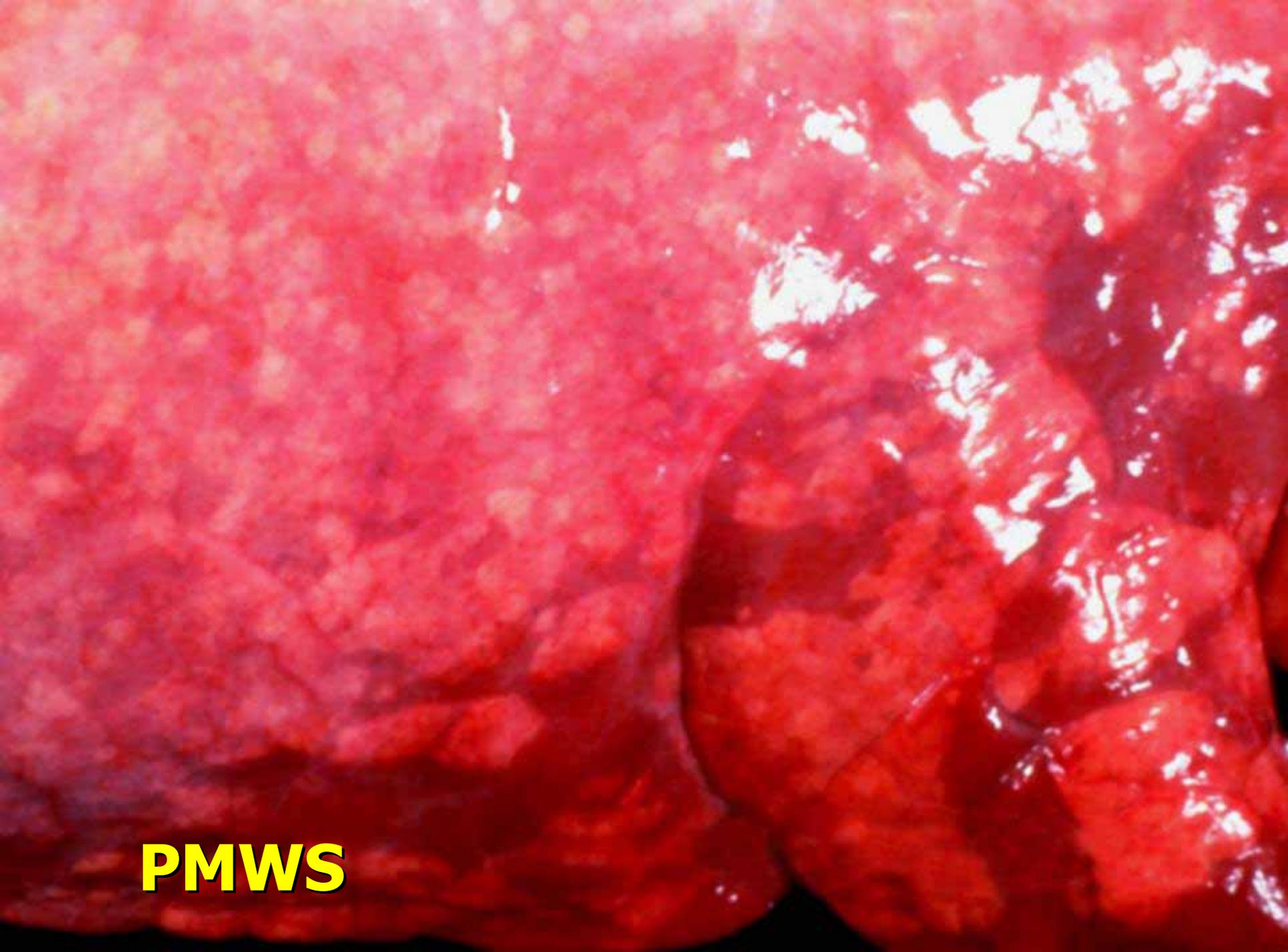
PMWS



PMWS



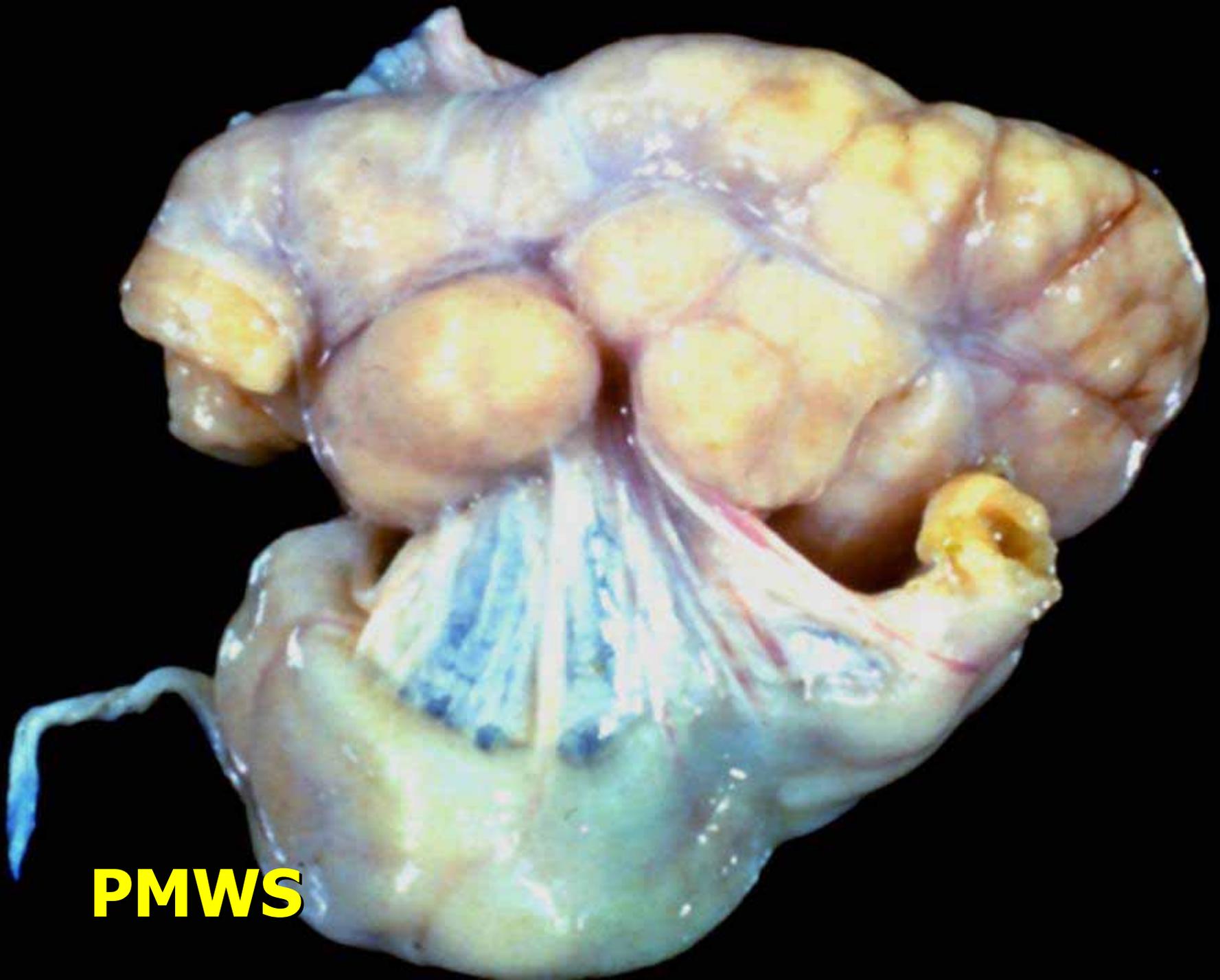
PMWS



PMWS



PMWS



PMWS



PMWS



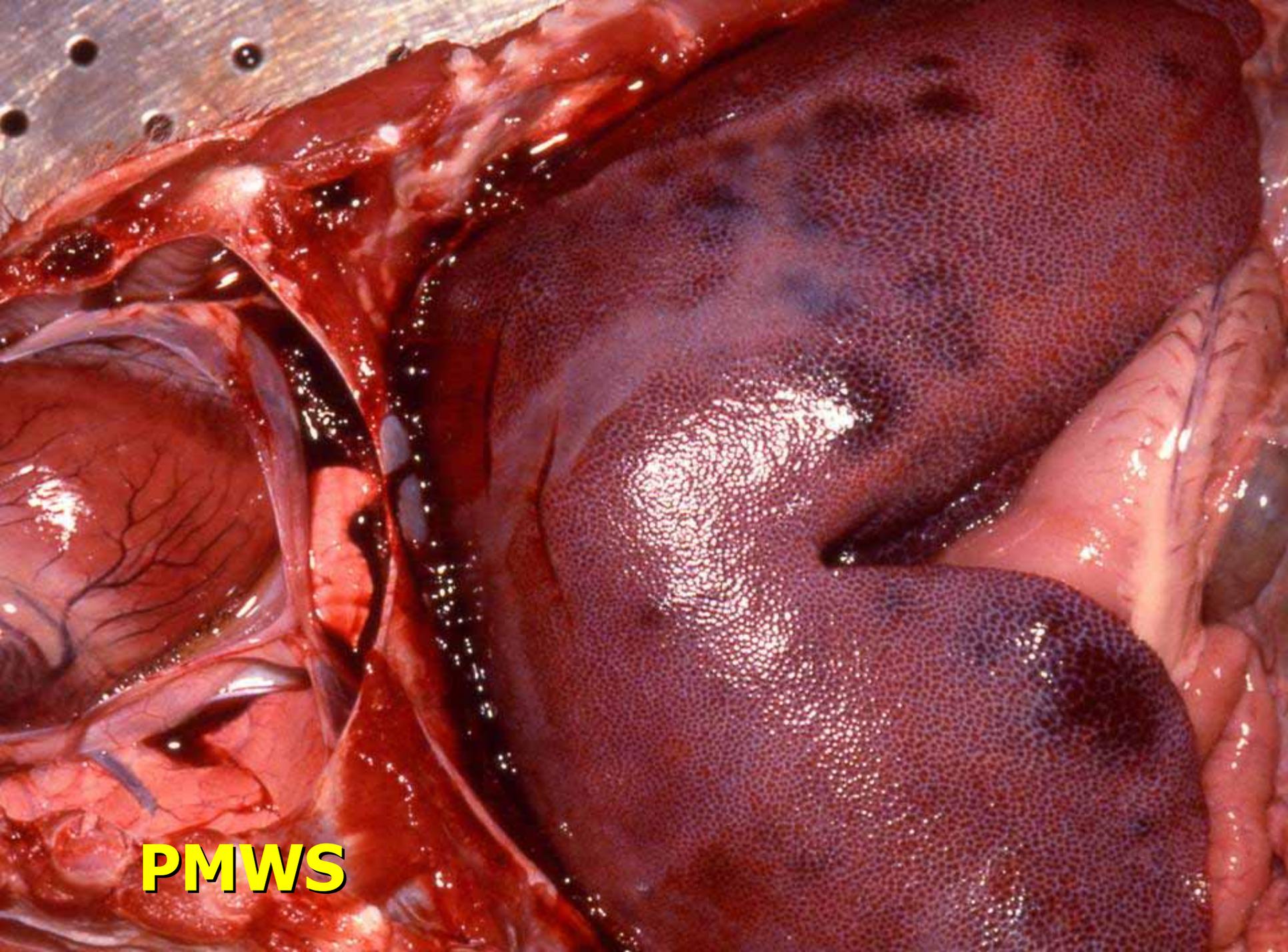
PMWS



PMWS



PMWS



PMWS



PMWS



PMWS



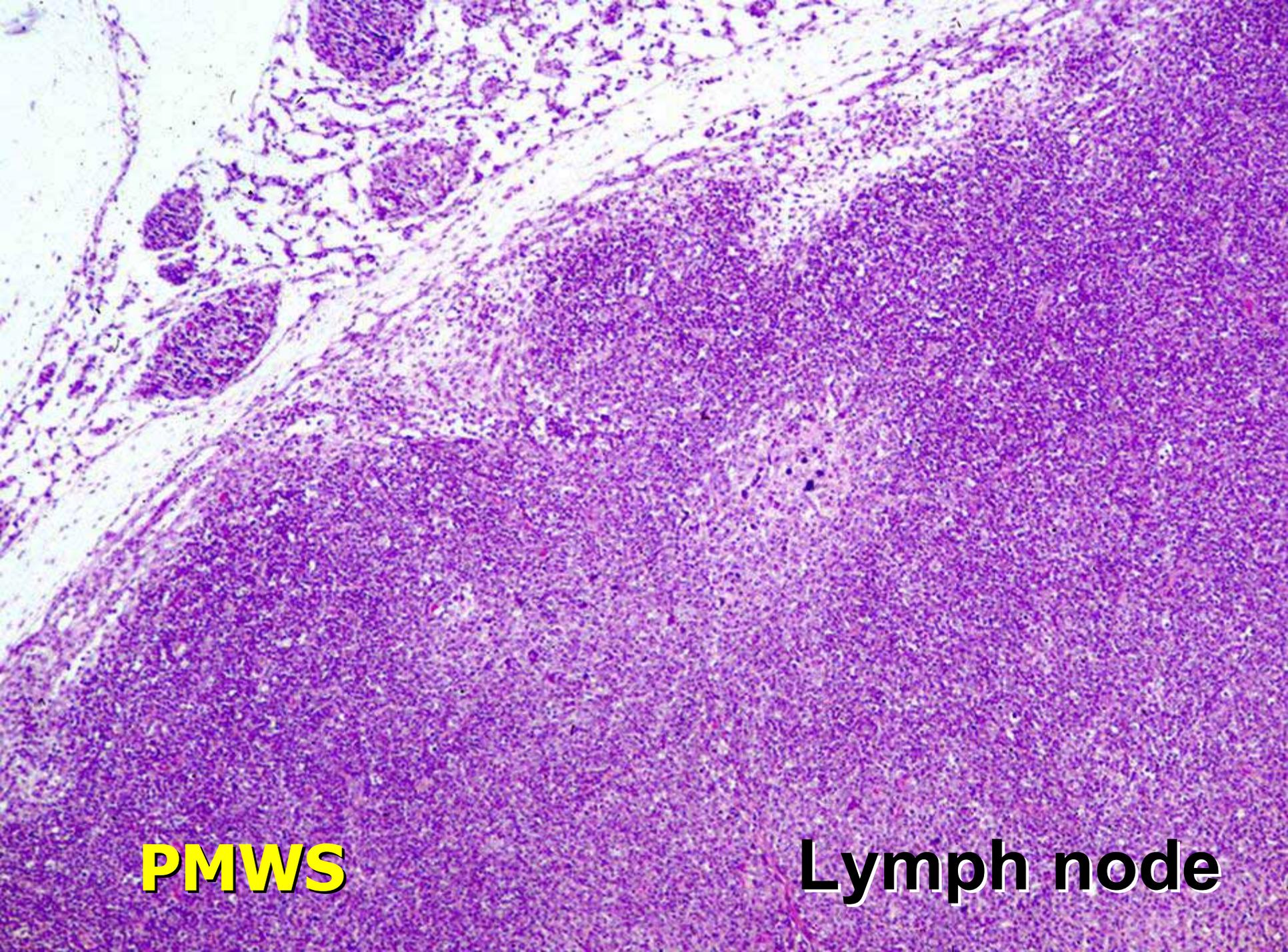
PMWS

Postweaning Multisystemic Wasting Syndrome (PMWS)

Microscopic Lesions

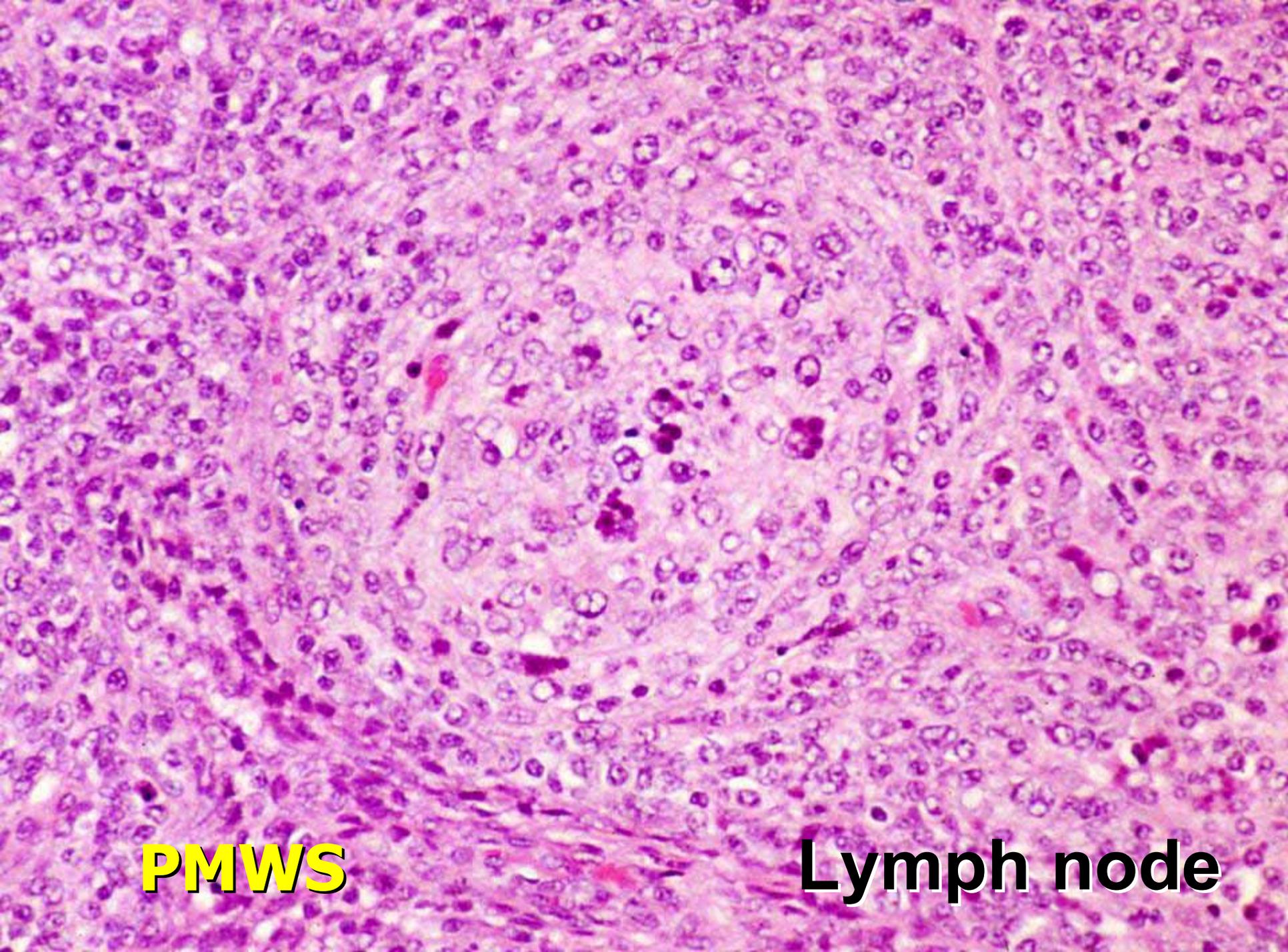
Lymphatic Tissue

- **Lymphoid cell depletion and granulomatous inflammation in lymphoid organs**
- **Characteristic intracytoplasmic inclusion bodies in epitheloid or multinucleated macrophages**



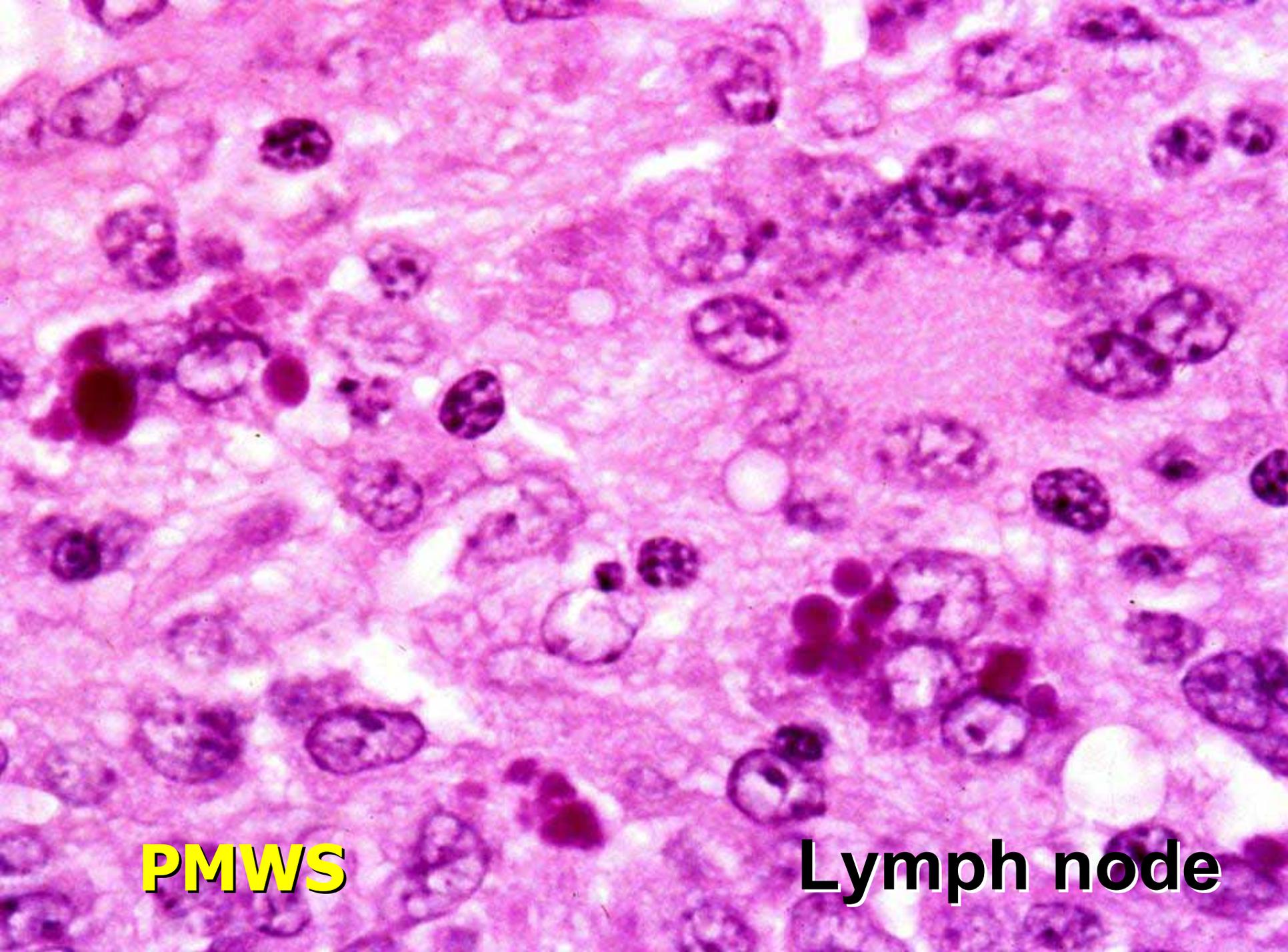
PMWS

Lymph node



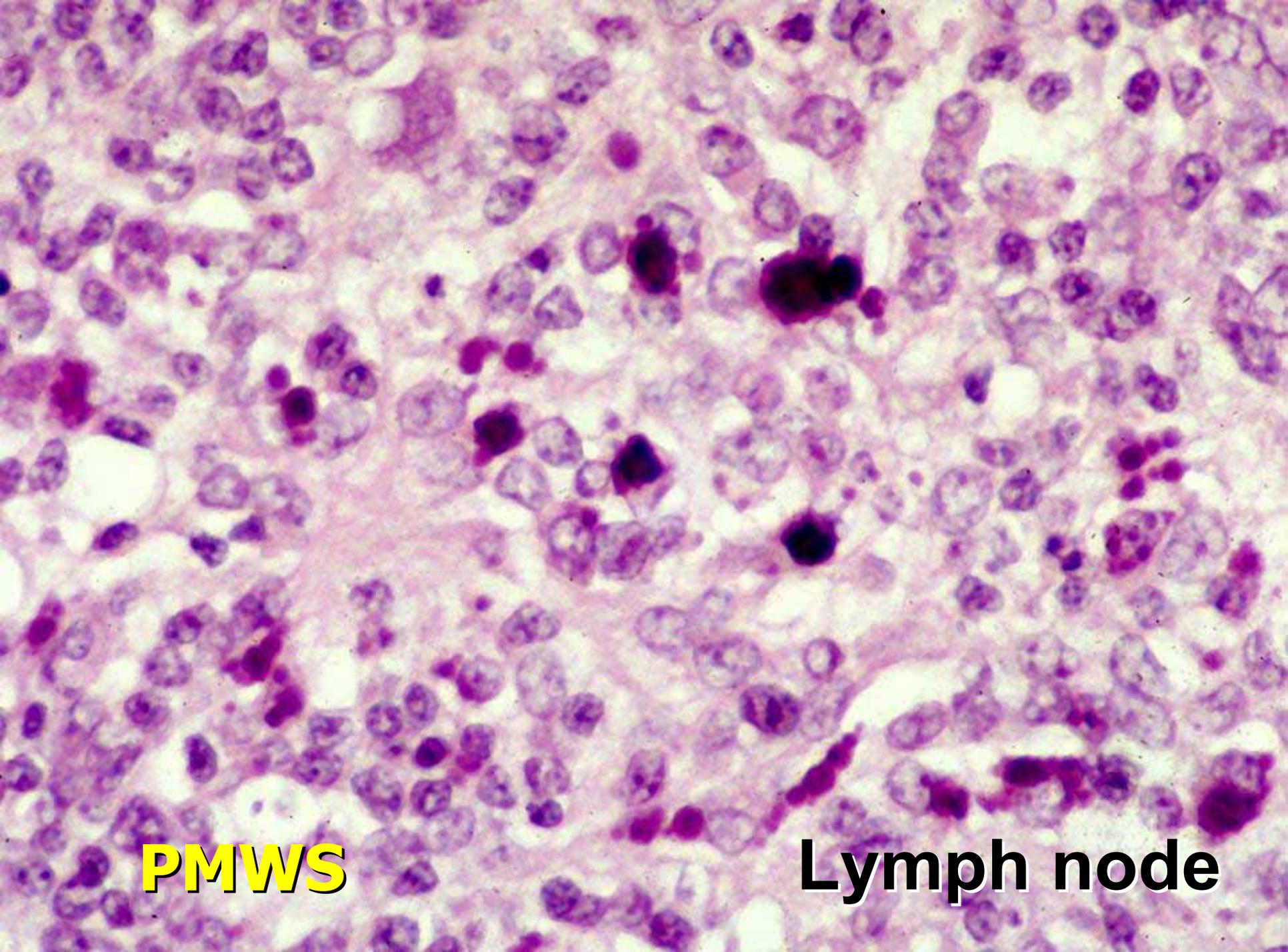
PMWS

Lymph node



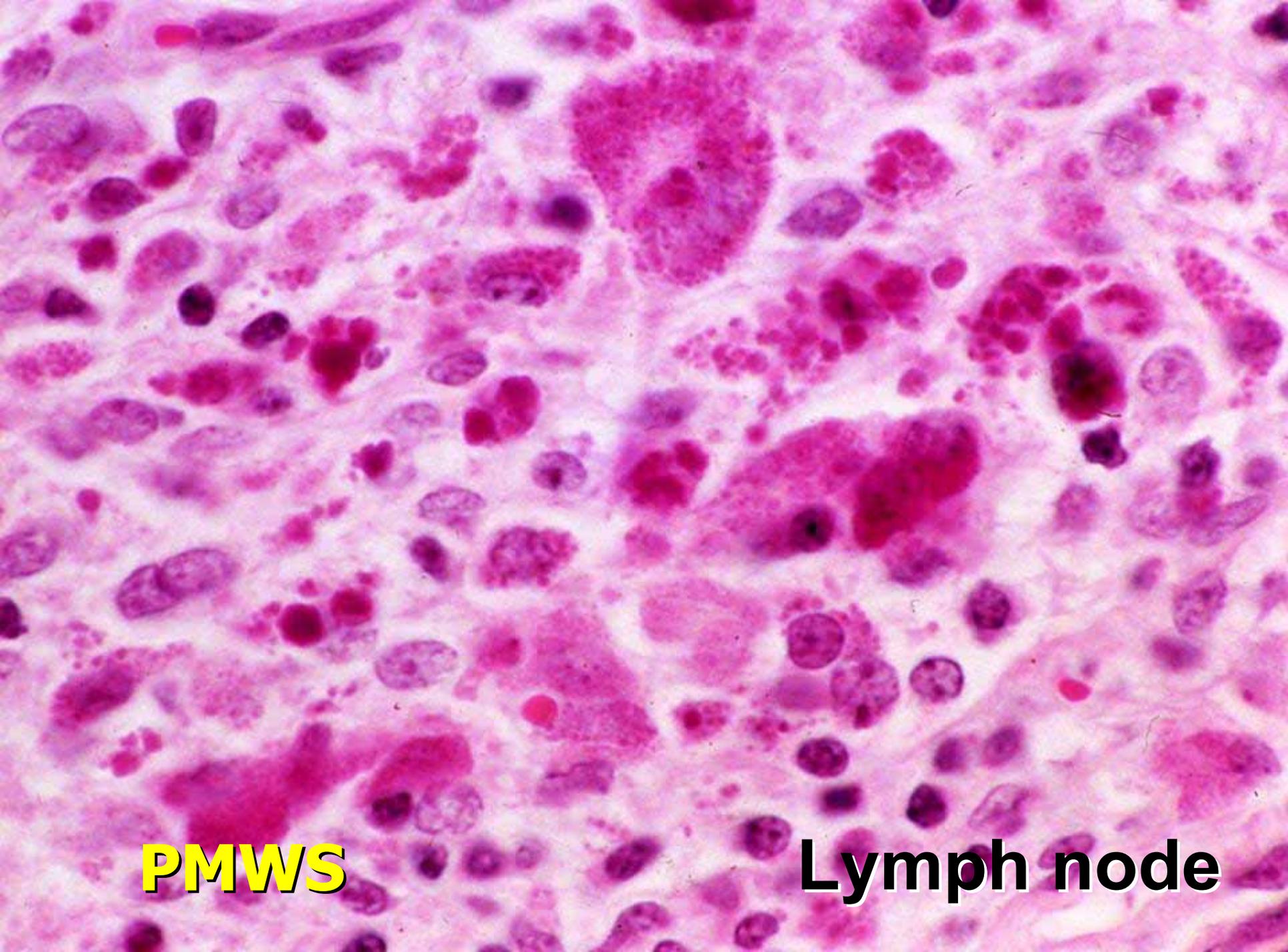
PMWS

Lymph node



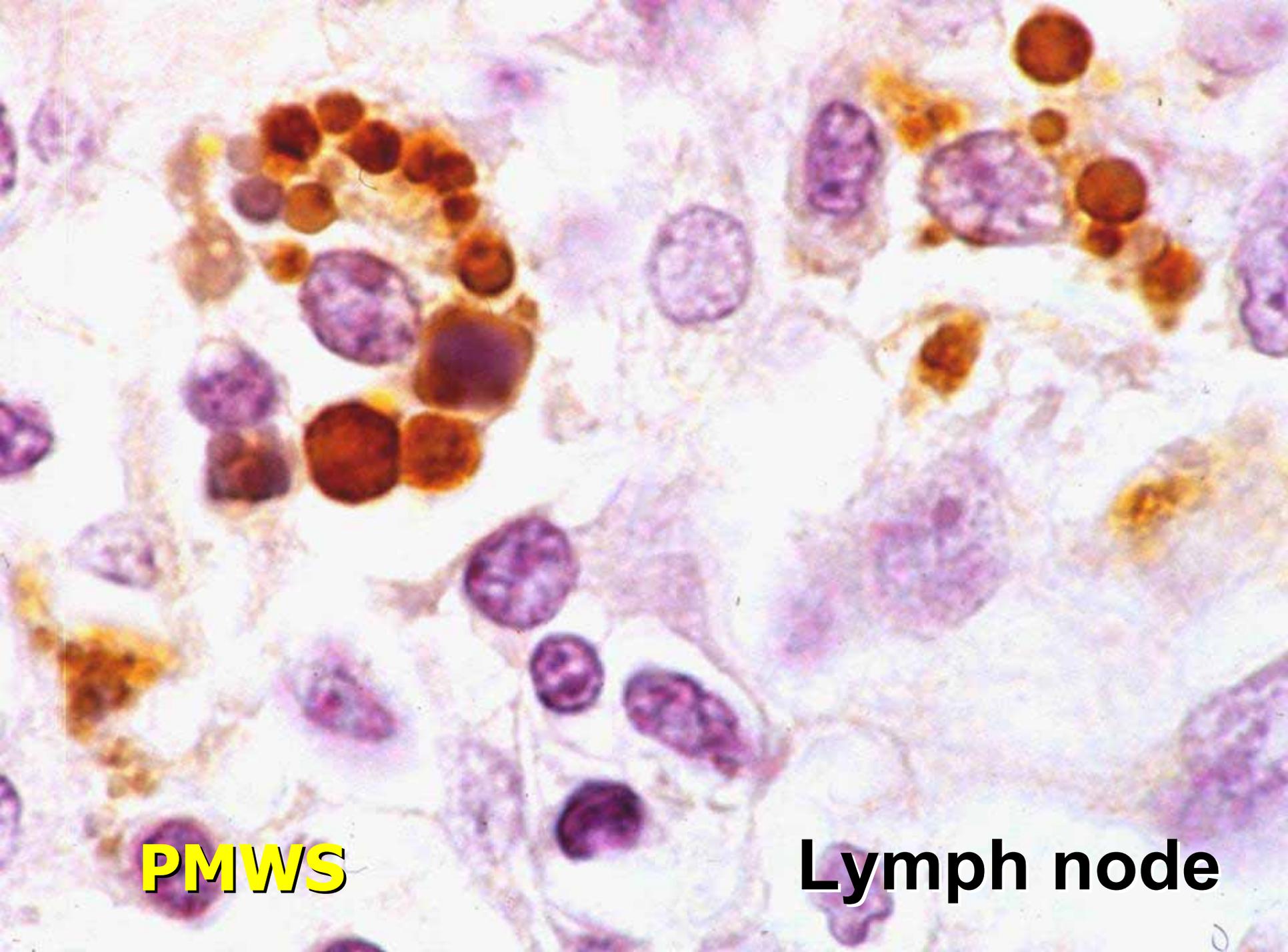
PMWS

Lymph node



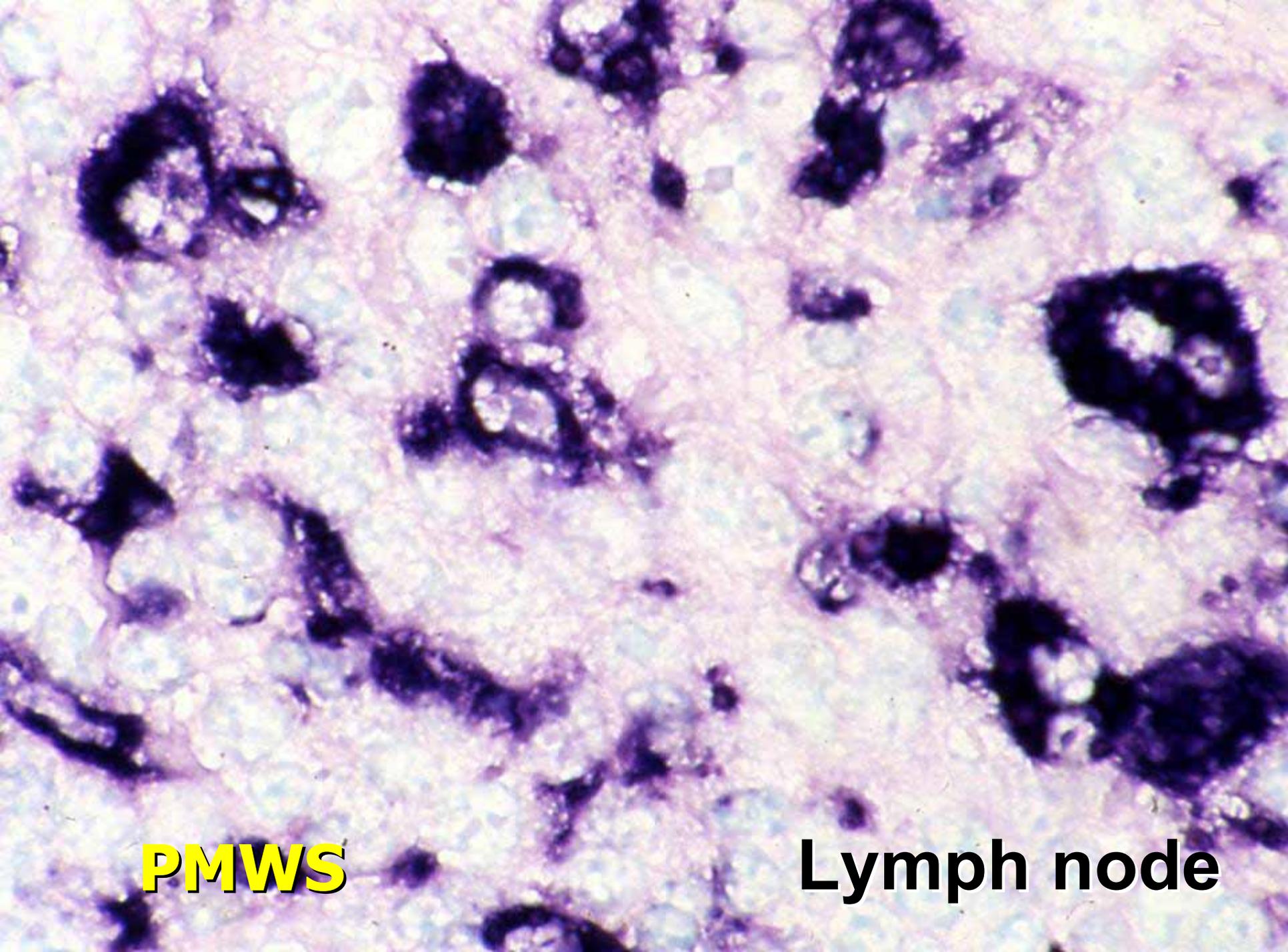
PMWS

Lymph node



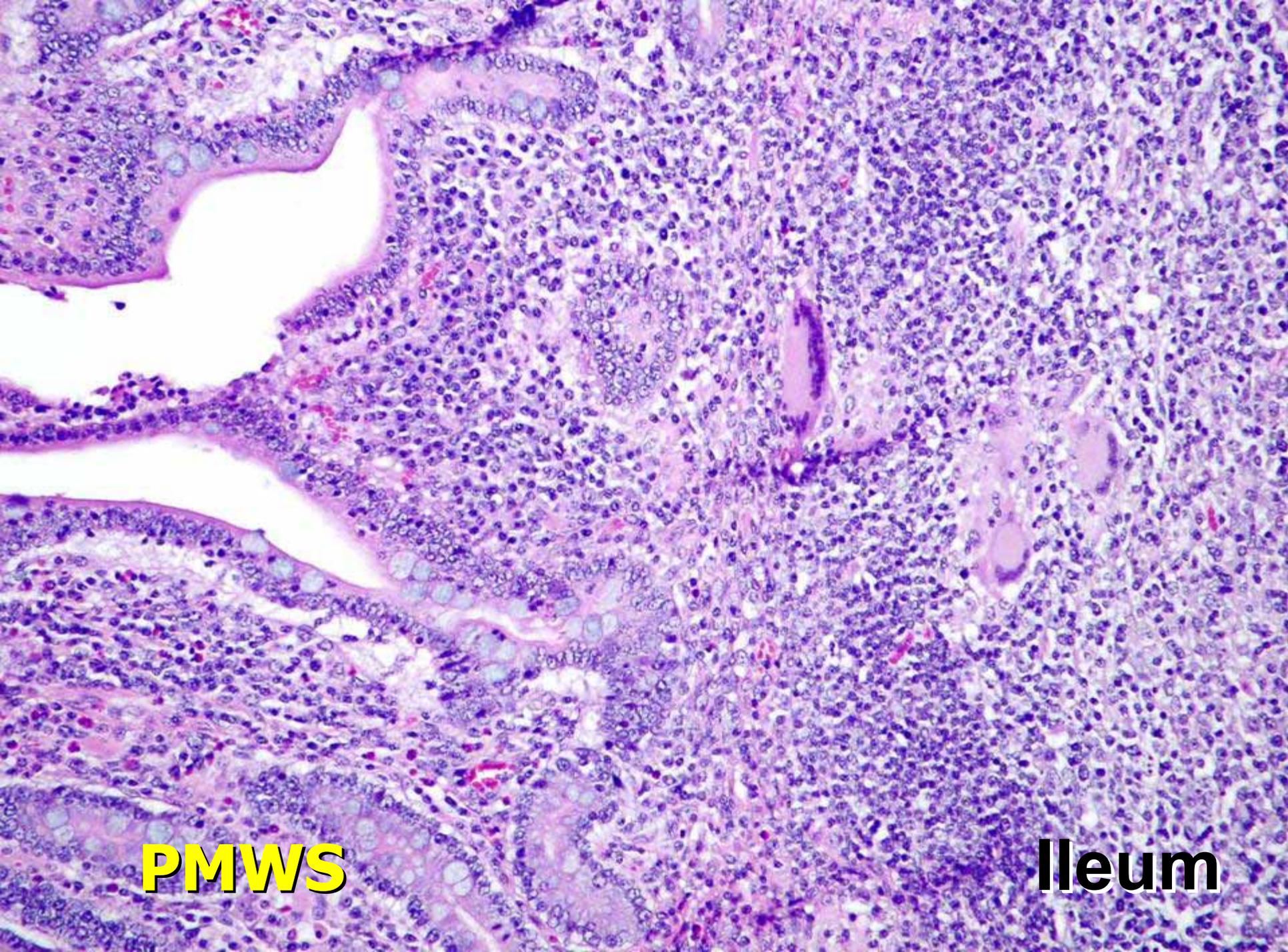
PMWS

Lymph node



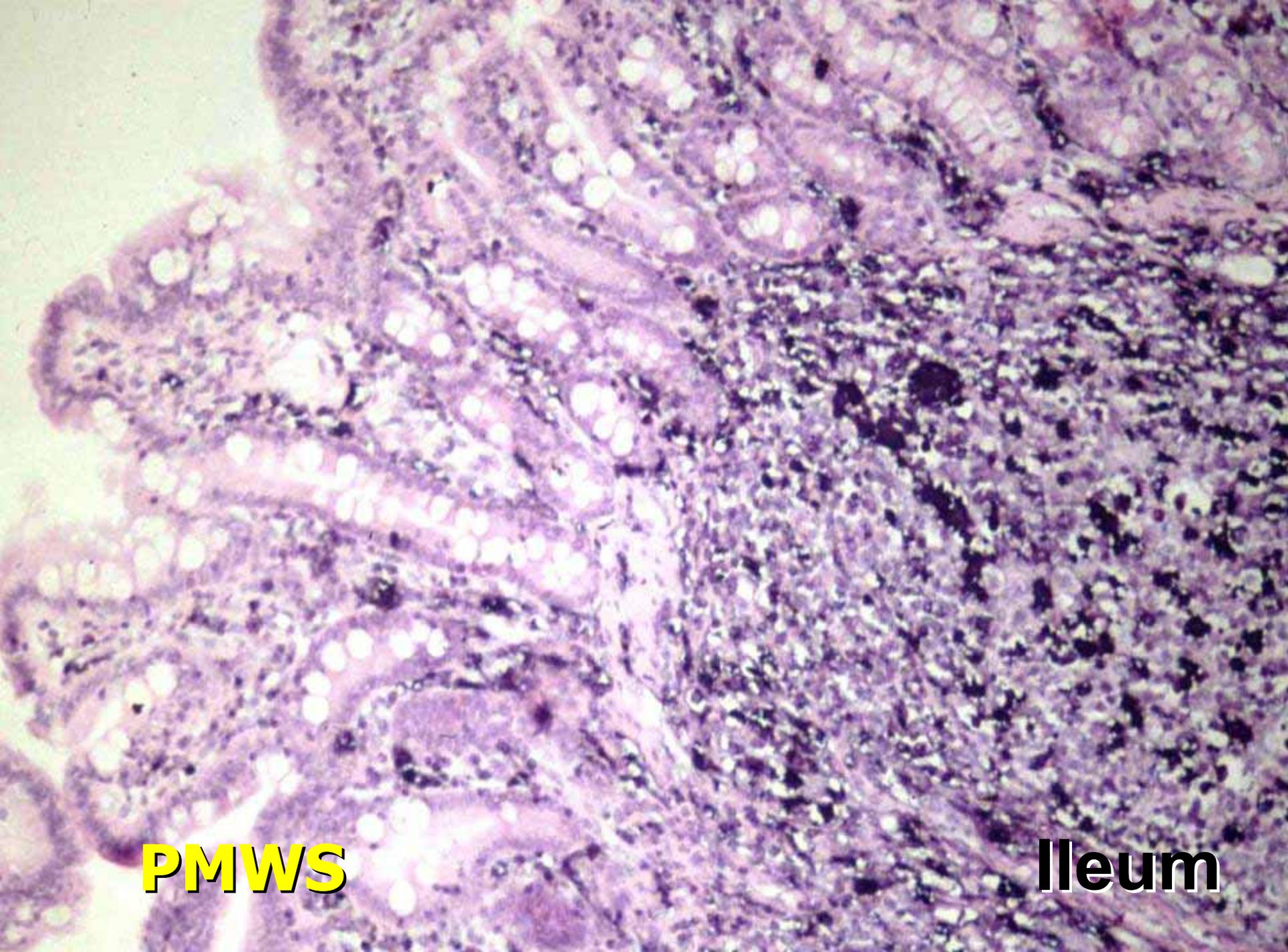
PMWS

Lymph node



PMWS

Ileum



PMWS

Ileum

Postweaning Multisystemic Wasting Syndrome (PMWS)

Microscopic Lesions

Lungs

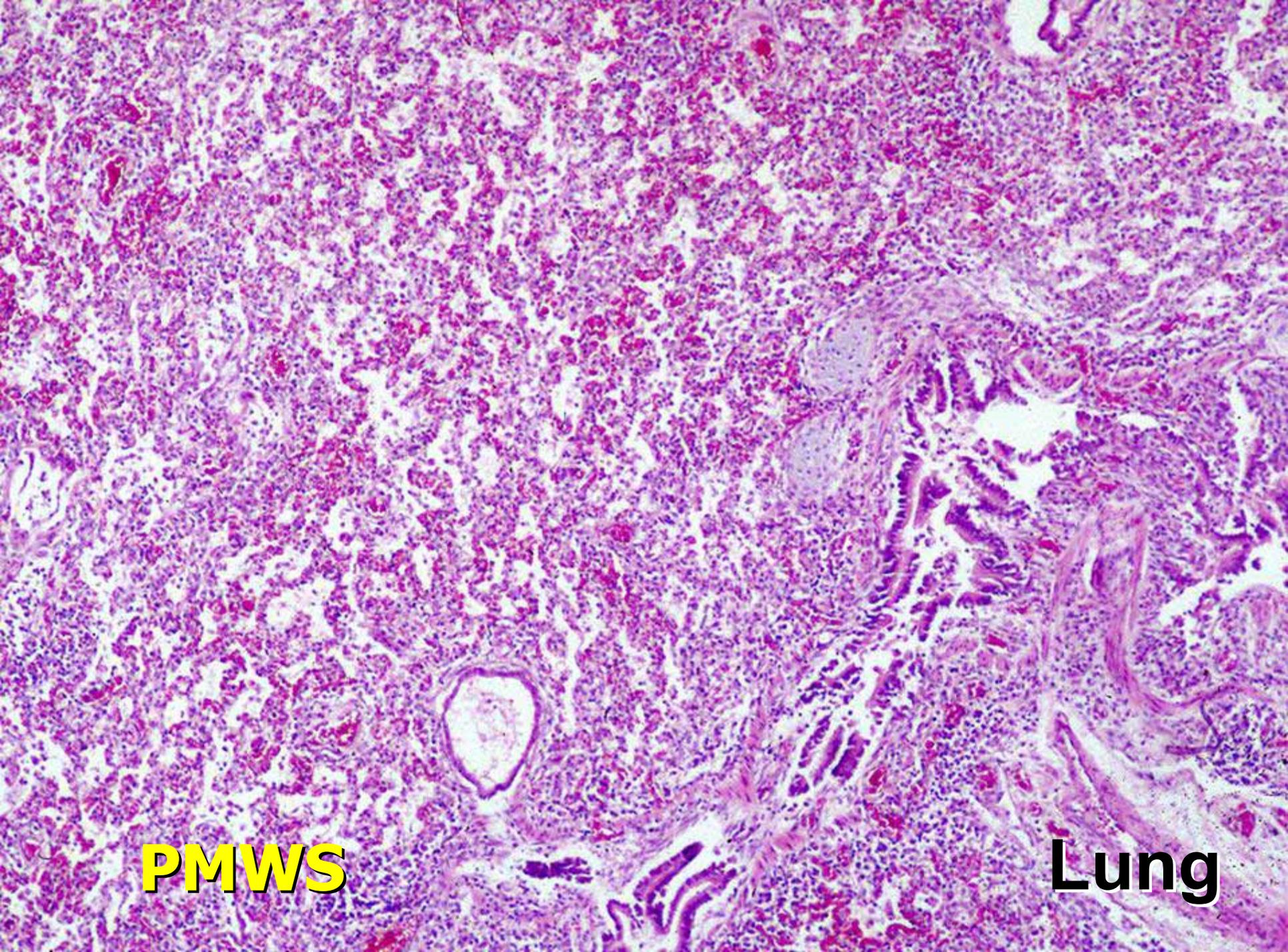
- Multifocal to diffuse interstitial pneumonia

Liver

- Periportal, lympho-histiocytic hepatitis
- Scattered piecemeal necrosis (apoptosis)

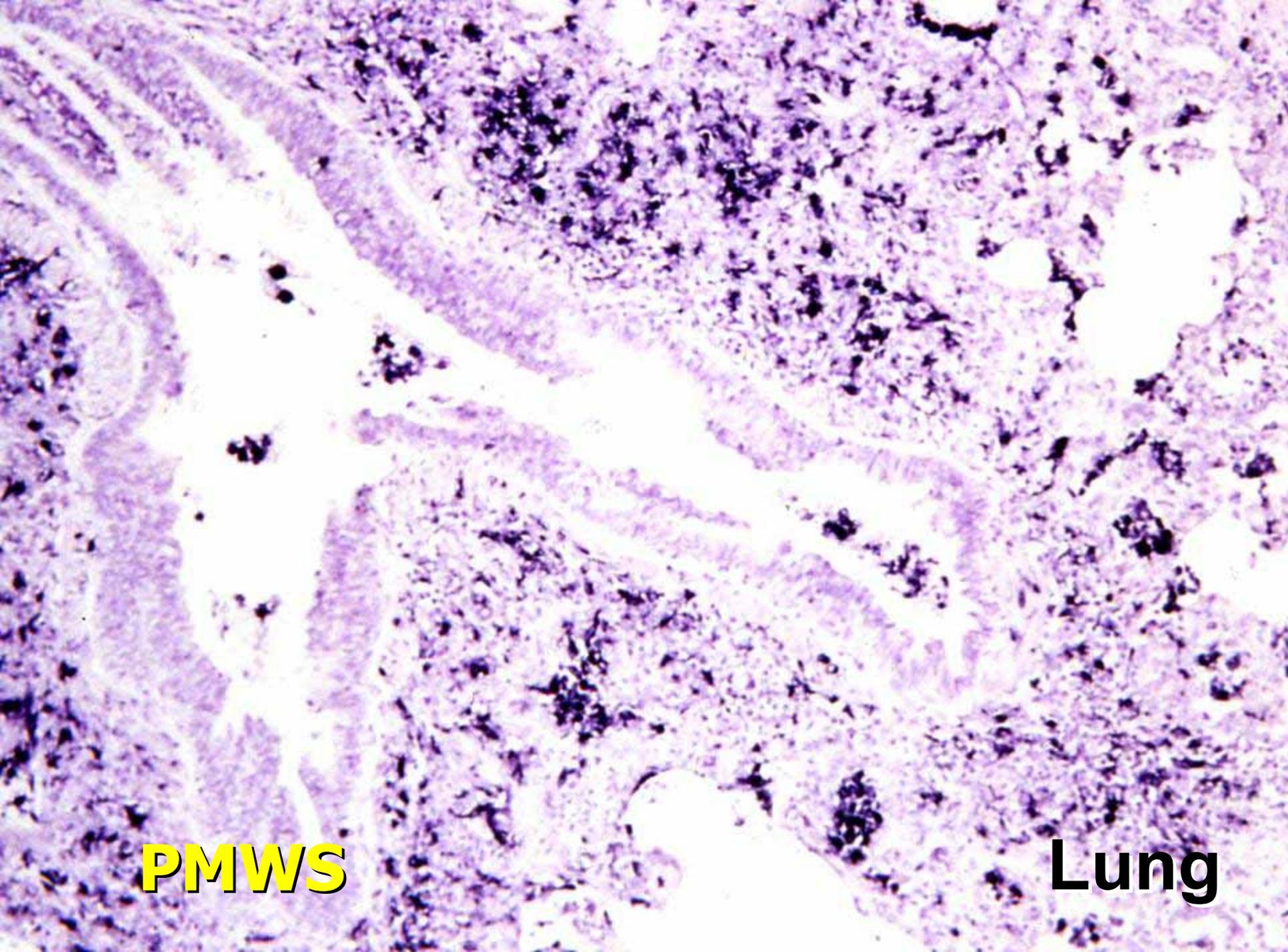
Kidneys

- Focal, lympho-histiocytic interstitial nephritis
- Peripelvic granulomatous vasculitis



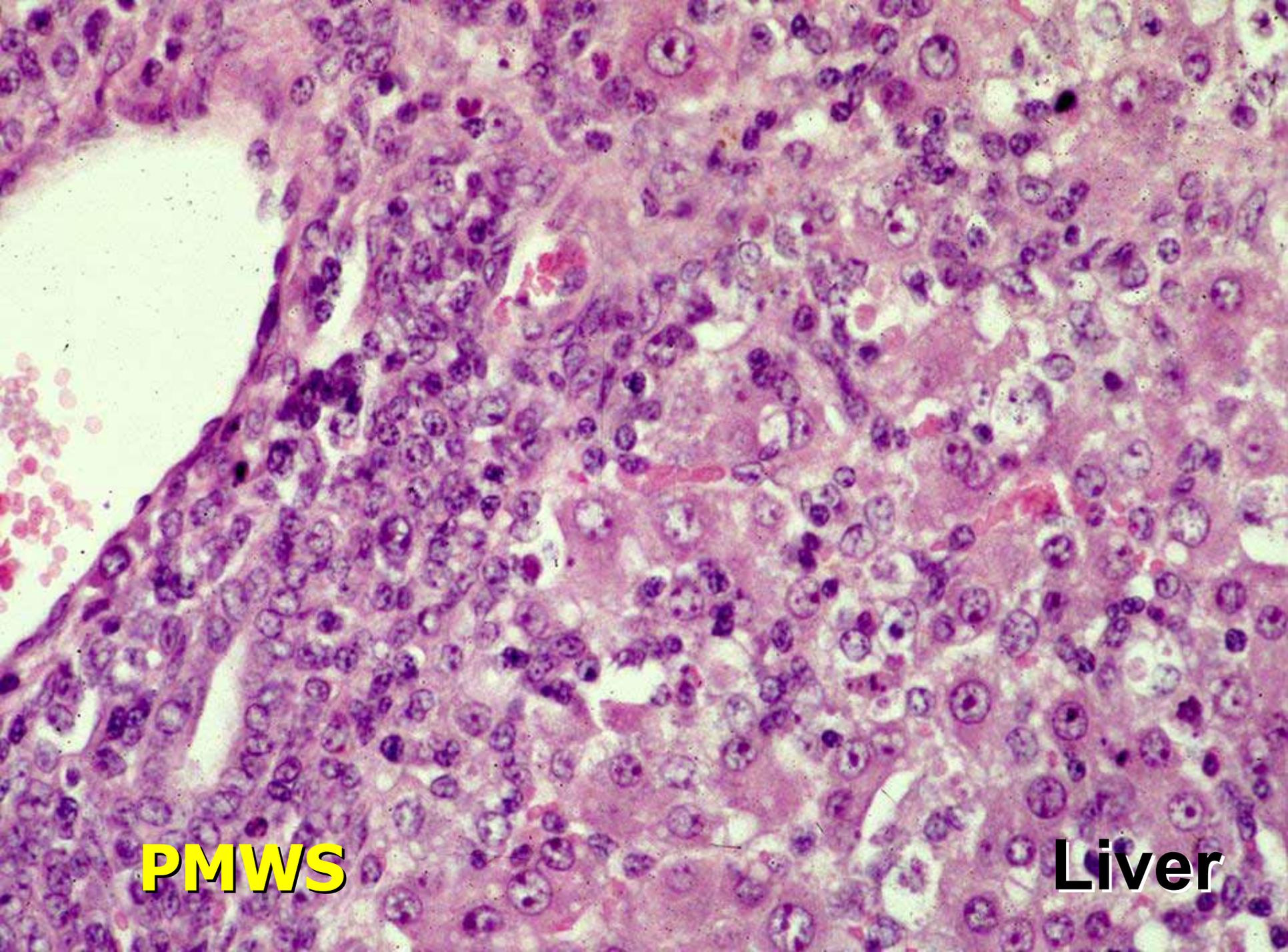
PMWS

Lung



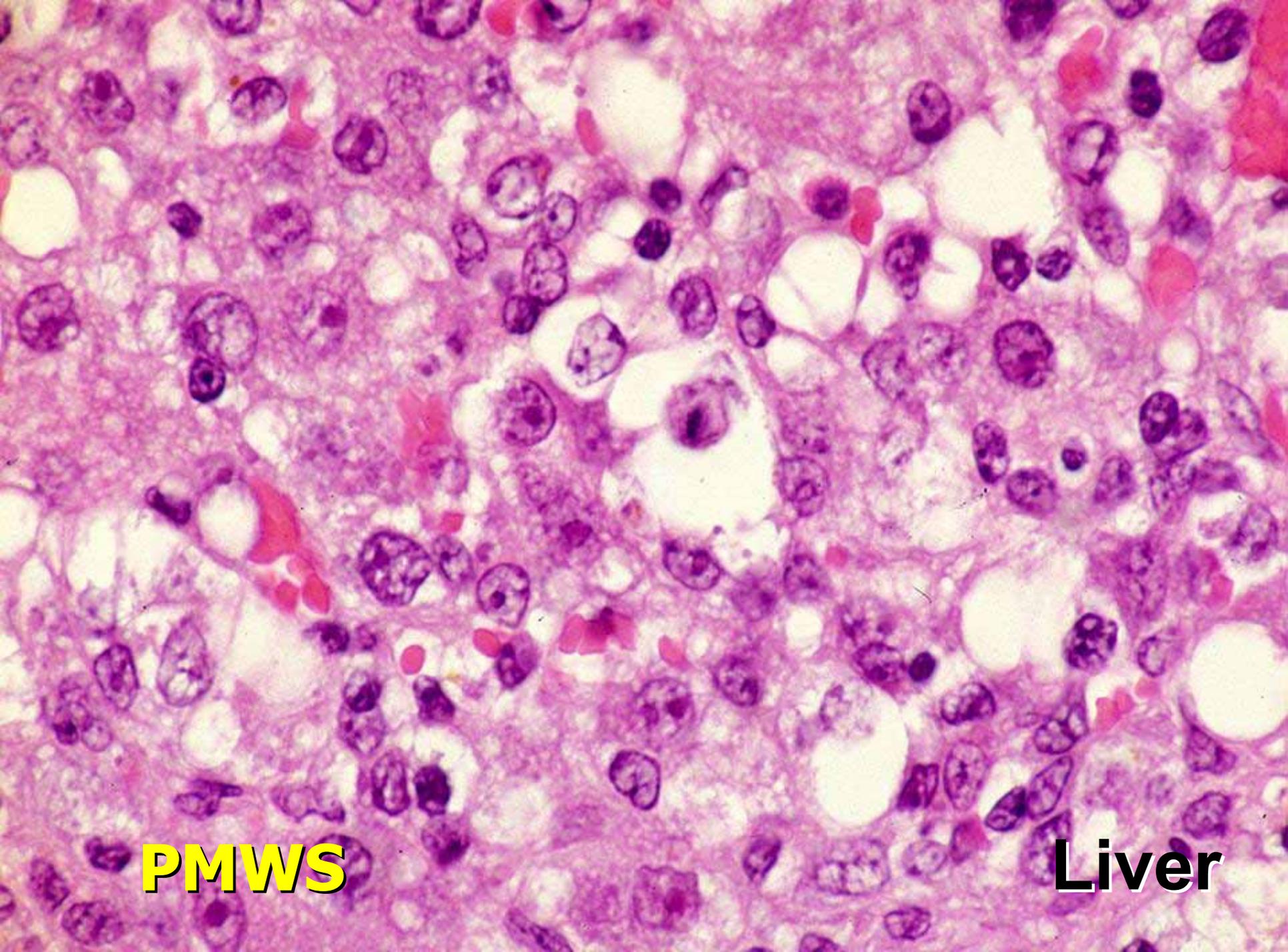
PMWS

Lung



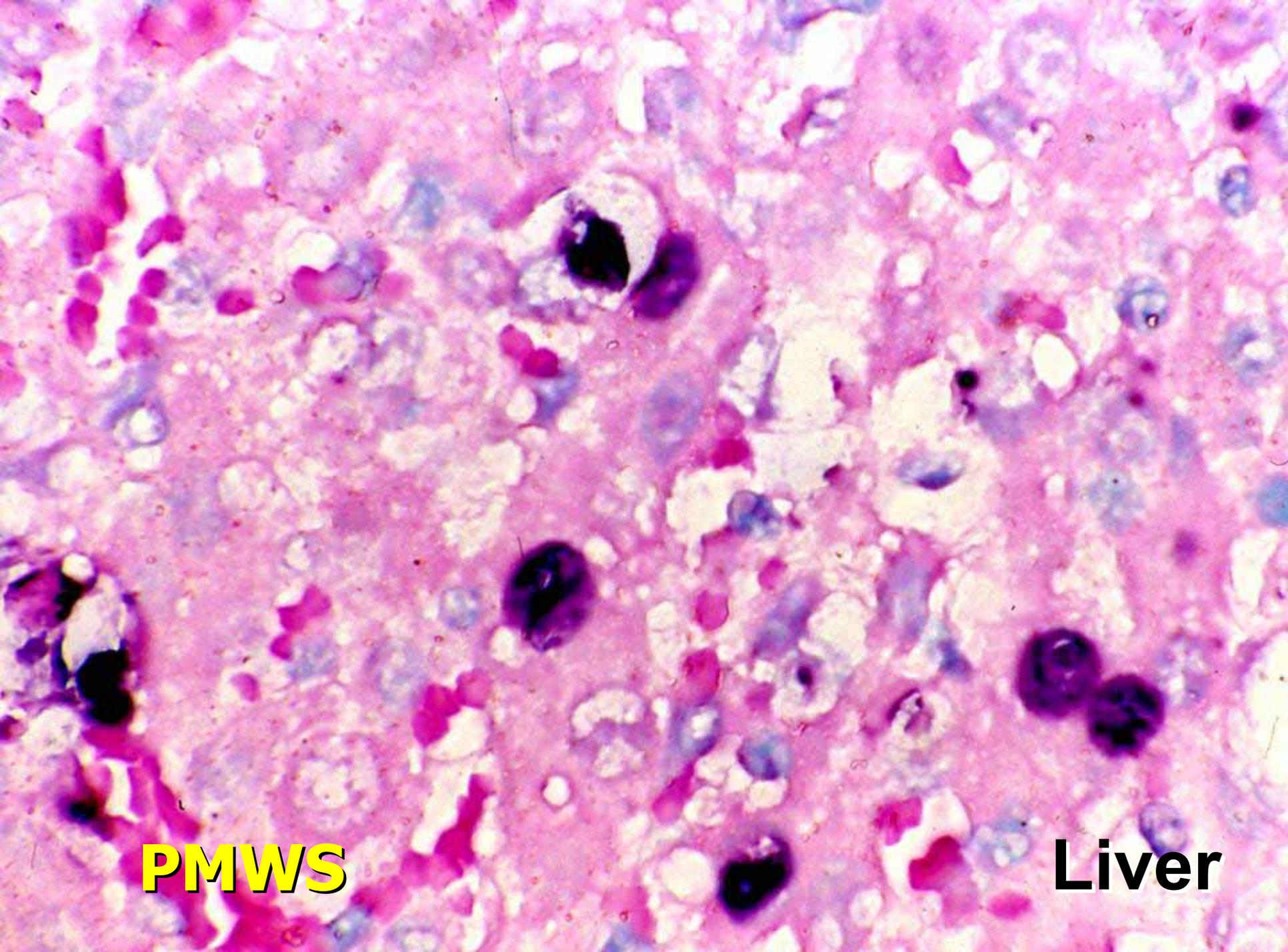
PMWS

Liver



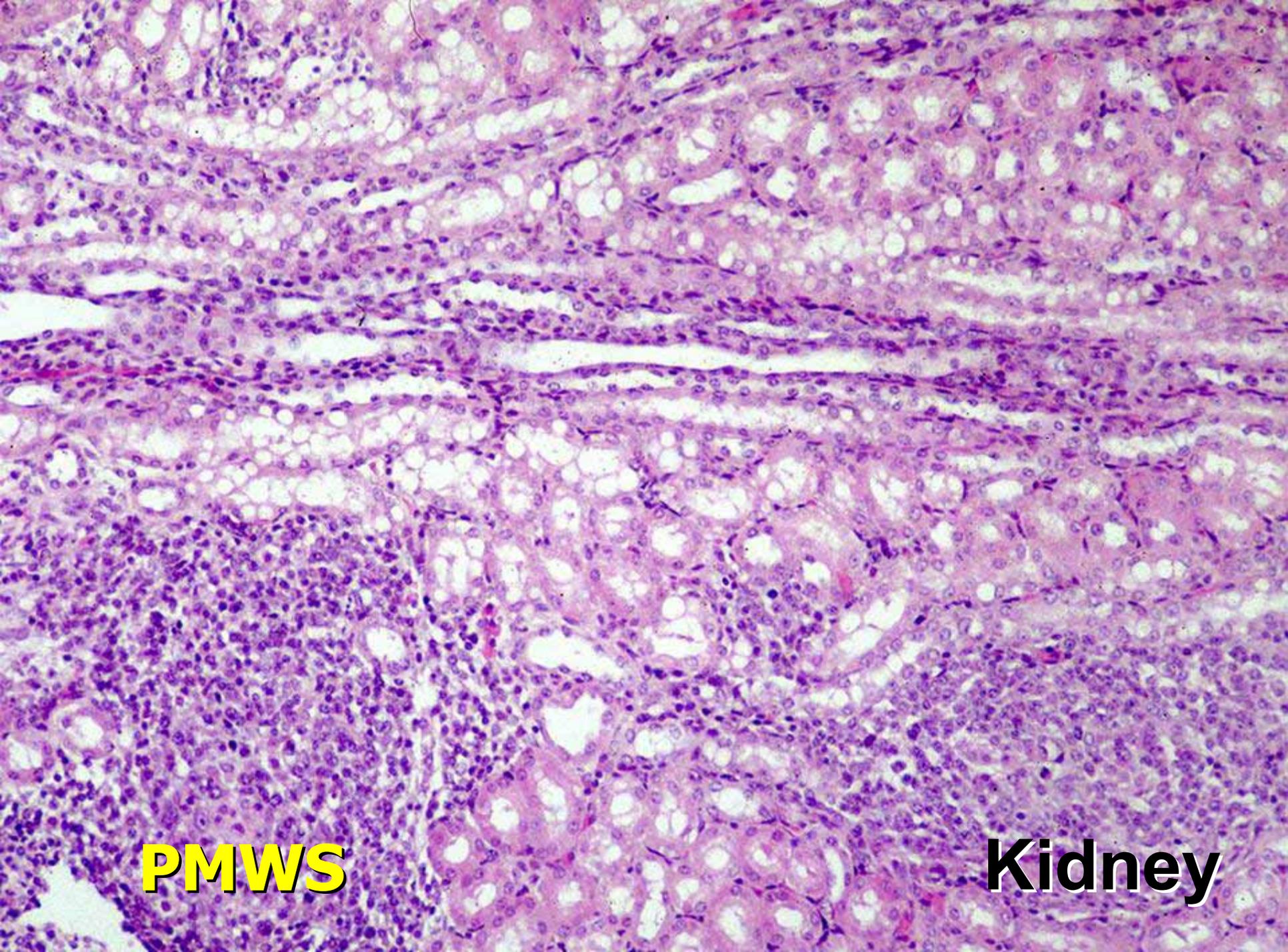
PMWS

Liver



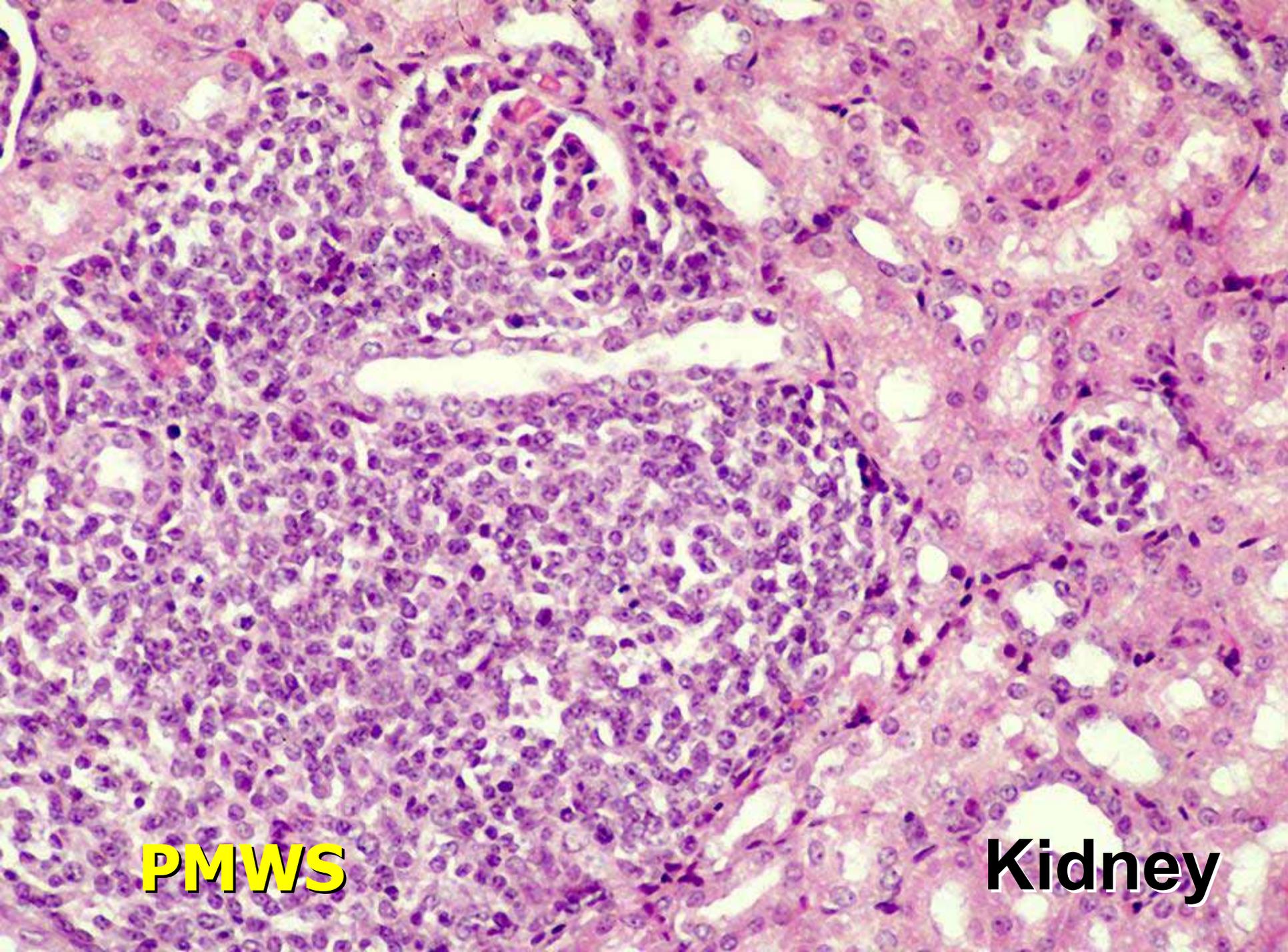
PMWS

Liver



PMWS

Kidney



PMWS

Kidney



PMWS

Kidney

Diagnosis of PMWS

1. Characteristic clinical signs:

wasting/weight loss/ill thrift with or without icterus

2. Characteristic microscopic lesions:

Depletion of lymphoid tissue

Granulomatous inflammation in any organ

3. Demonstration of PCV2 within lesions:

Immunohistochemistry

In situ hybridization

PCV2 \neq PMWS

Lesions and PCV2 must be present to diagnose PMWS in a poorly performing pig!

Pathogenicity of PCV1

Inoculation studies in pigs using PCV1 from persistently infected PK-15 cells have not demonstrated clinical disease (Tischer et al., 1986, Allan et al., 1995, Krakowka et al., 2000).

Pathogenicity of PCV2

- A certain restriction fragments length polymorphism (RFLP) pattern (321) is much more frequently associated to PMWS cases than other RFLP patterns (422 and others)
- Different pathology in lymphoid tissues were detected when comparing pigs infected by a PCV2 isolated from a PMWS case (“high virulence strain”) and pigs infected by an isolate from healthy pig (“low virulence strain”)
- 2 major phylogenetic groups: type 1 and 2
- type 1 more commonly associated with PMWS

Experimental PMWS

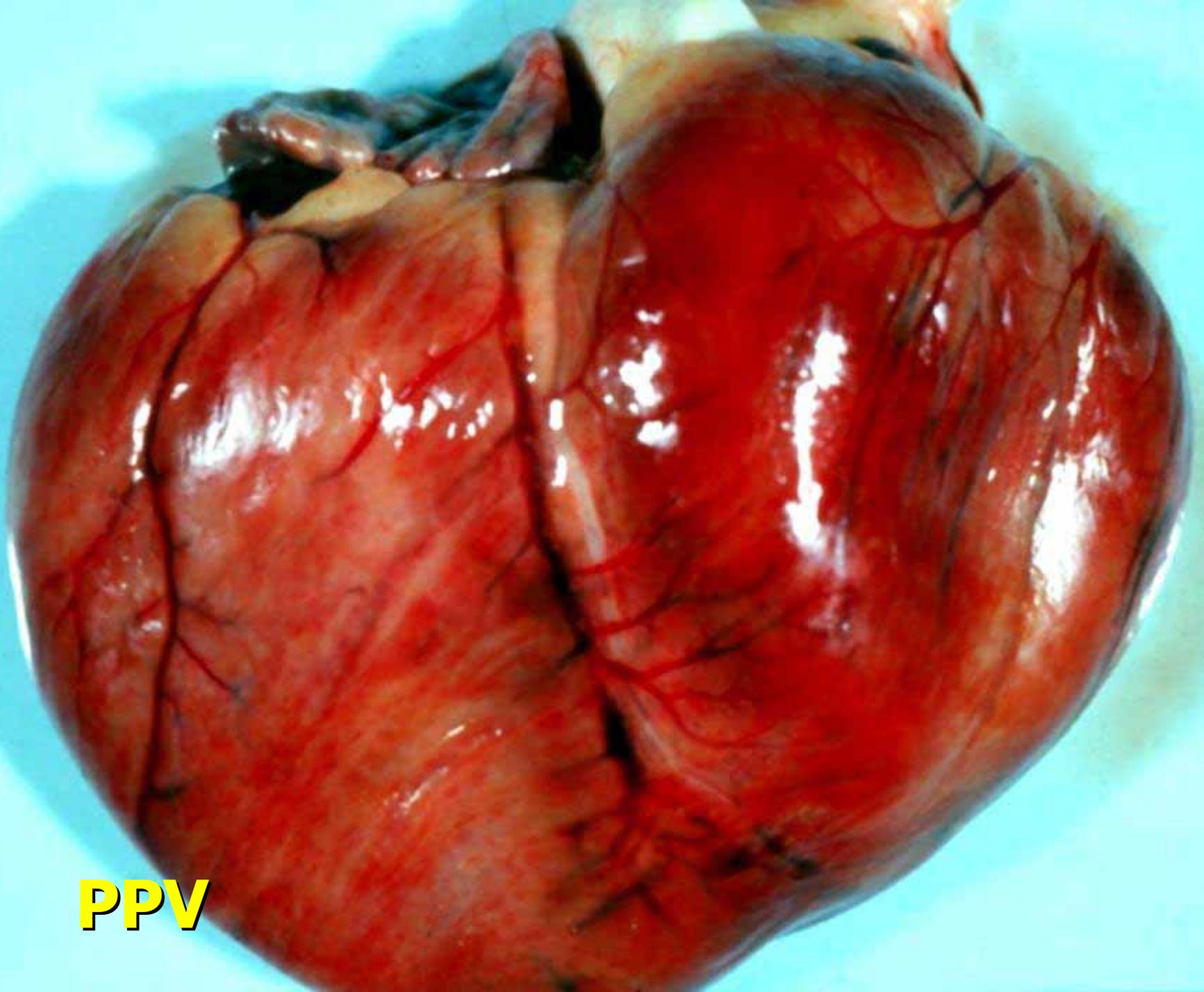
- Experimentally reproduced in cd/cd and germ-free pigs dually infected with PCV2 and porcine parvovirus (PPV), PRRSV, Mycoplasma hyopneumoniae
- Experimentally reproduced in germ-free pigs dually inoculated with PCV2 and keyhole limpet hemocyanin in incomplete Freund's adjuvant
- Experimental inoculation of germ-free pigs with PCV2 alone did not reproduce PMWS
- Experimental inoculation of cd/cd pigs with PCV2 alone produced PMWS in some studies

How to Successfully Experimentally Reproduce PMWS

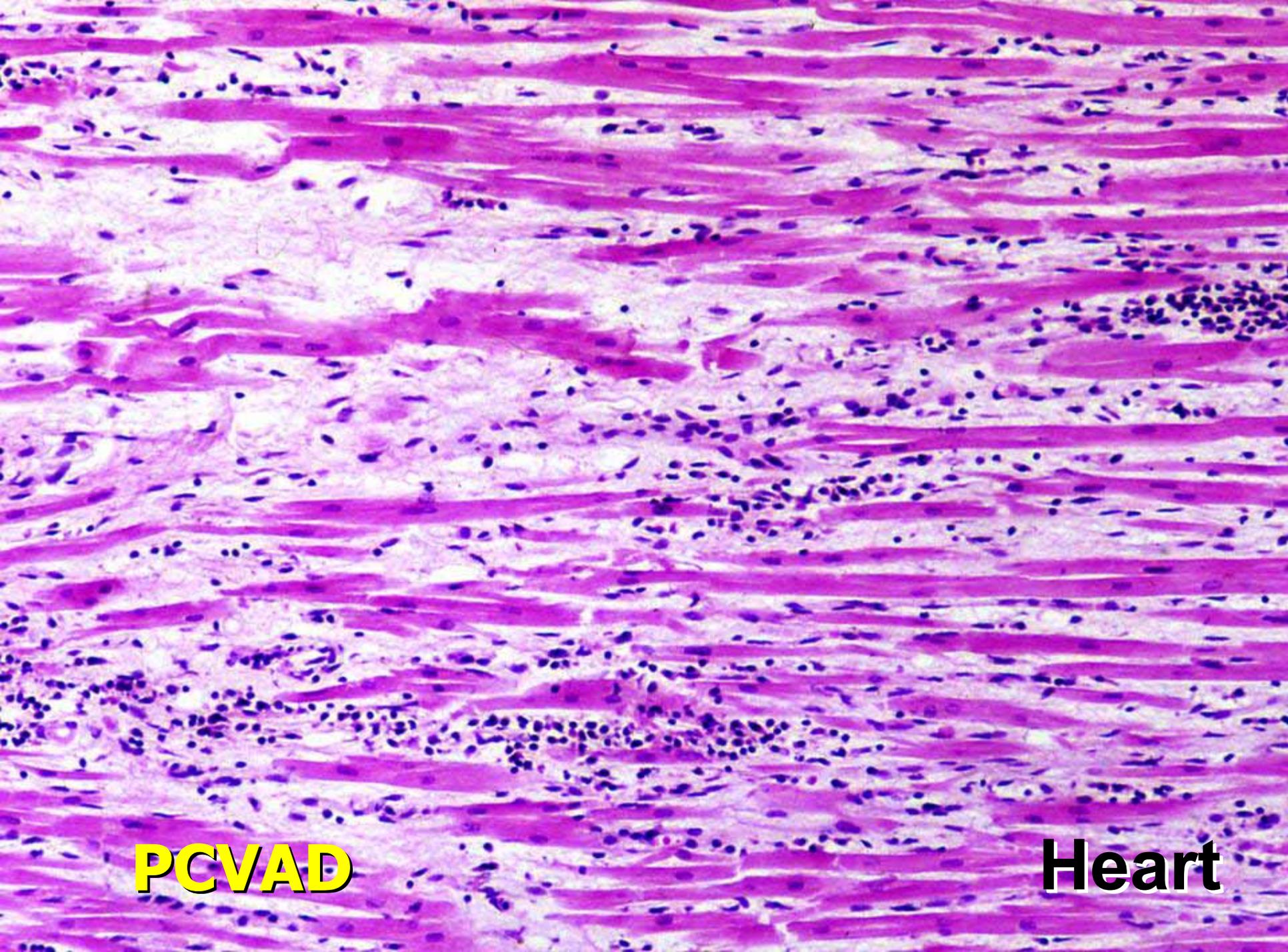
- **colostrum-deprived pigs**
- **age of inoculation below 3 weeks**
- **high doses of PCV2 inoculum**
- **PCV2 strain from genotype 1**
- **co-infection with another swine pathogen as a triggering factor**

Reproductive Failure

- PCV2 has been associated with reproductive disease since 1999
- Transplacental infection
- Late-term abortions
 - Only 1% of cases in Europe
- Stillborn and nonviable neonatal piglets
 - Chronic passive congestion, cardiac hypertrophy, and severe diffuse myocarditis

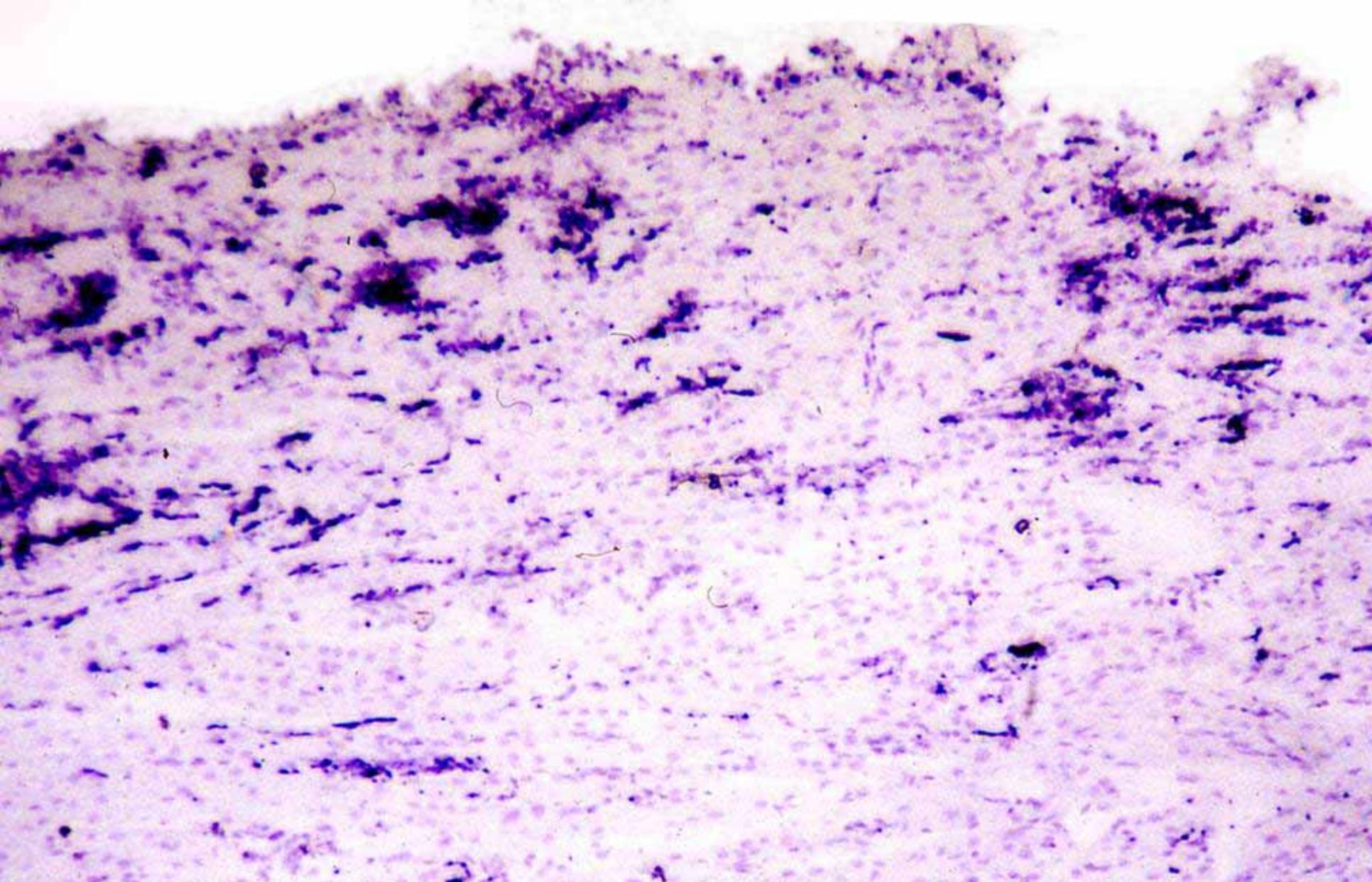


PPV



PCVAD

Heart



PCVAD

Heart

Congenital Tremor Type A2 in Newborn Pigs

- Most common form of CT in North America
- Associated with:
 - **myelin deficiency**
 - **clonic contractions of skeletal muscles in newborn pigs**
- Inoculation of pregnant sows with PCV1 (Kanitz et al., 1972) and a PCV of an unknown type (Hines et al., 1994) reproduced congenital tremors
- PCV2 was detected in large numbers of neurons in brain/spinal cord of pigs with CT (**Stevenson et al., 2001**)
- **Uncertain whether PCV2 and/or PCV1 are the cause**



CT

Spinal Cord

Porcine Dermatitis and Nephropathy Syndrome

- First described in the UK in 1993
- Clinical signs and Gross lesions:
 - +/- Fever
 - Depression
 - Multifocal dermal hemorrhage
 - Necrotizing dermatitis
 - Enlarged, pale kidneys with cortical petechiae
- Histological lesions:
 - Systemic necrotizing vasculitis including dermatitis and glomerulitis
 - Interstitial nephritis/fibrosis



PDNS



PDNS



PDNS



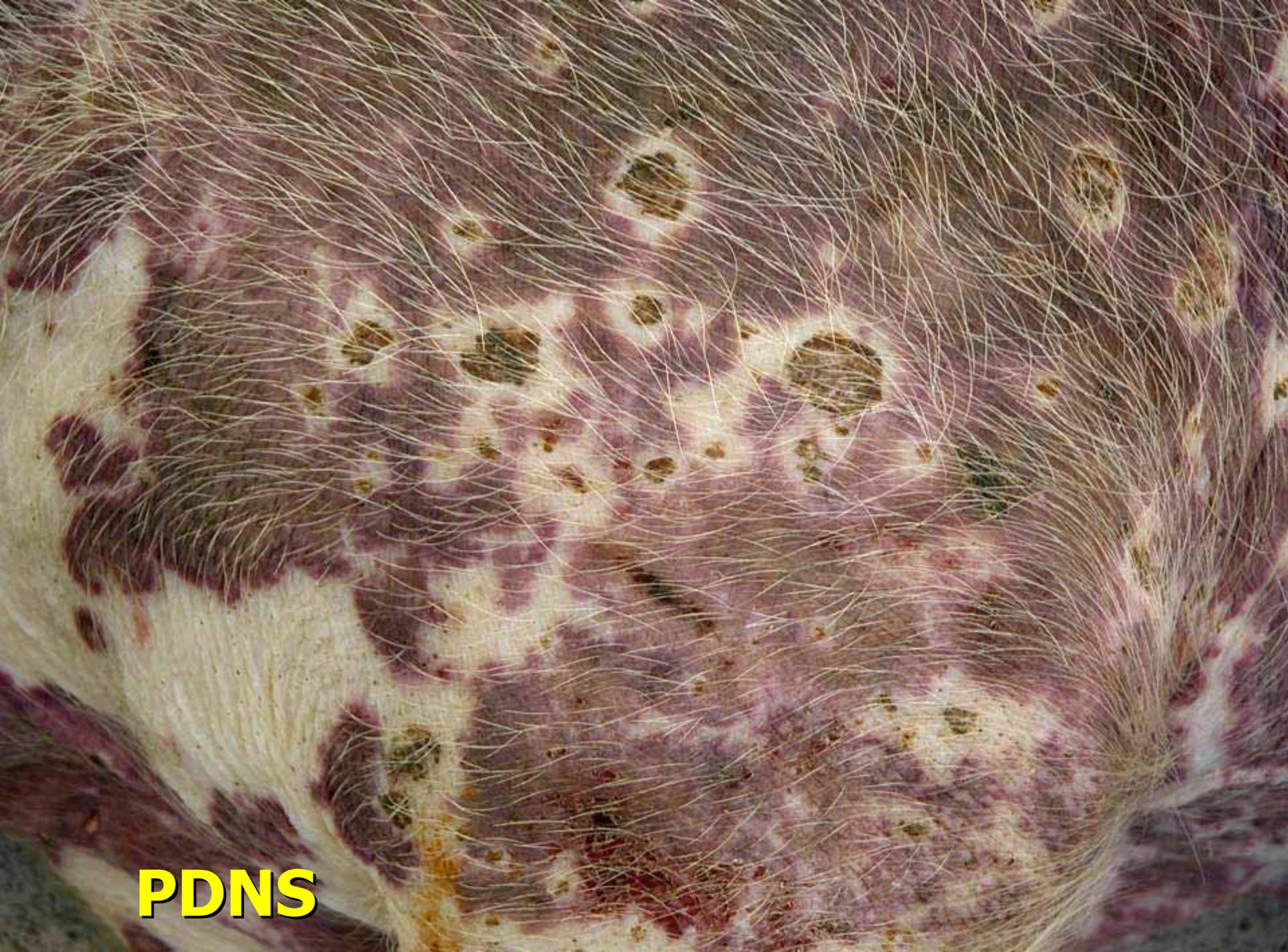
PDNS



PDNS



PDNS



PDNS



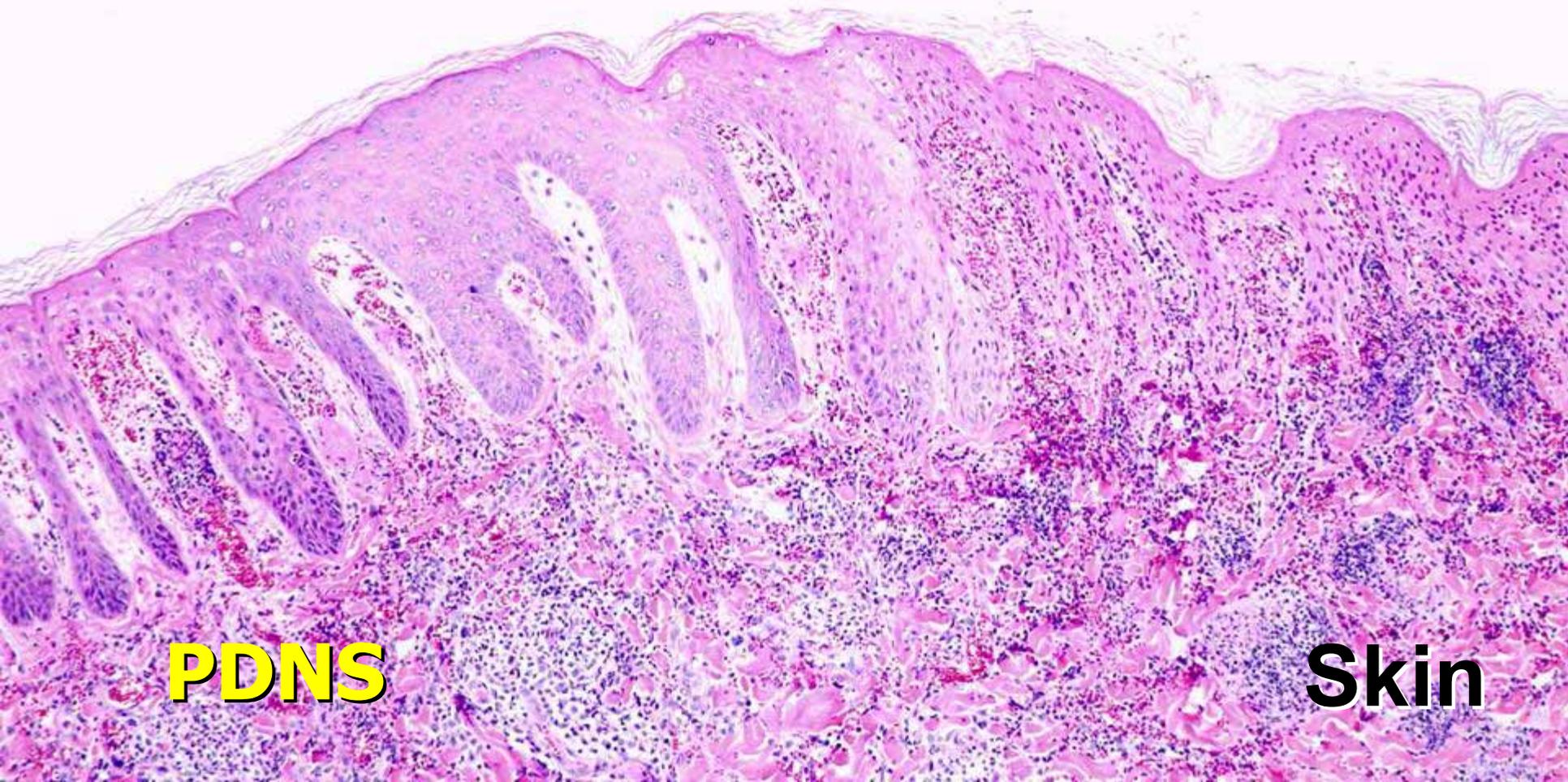
PDNS



PDNS

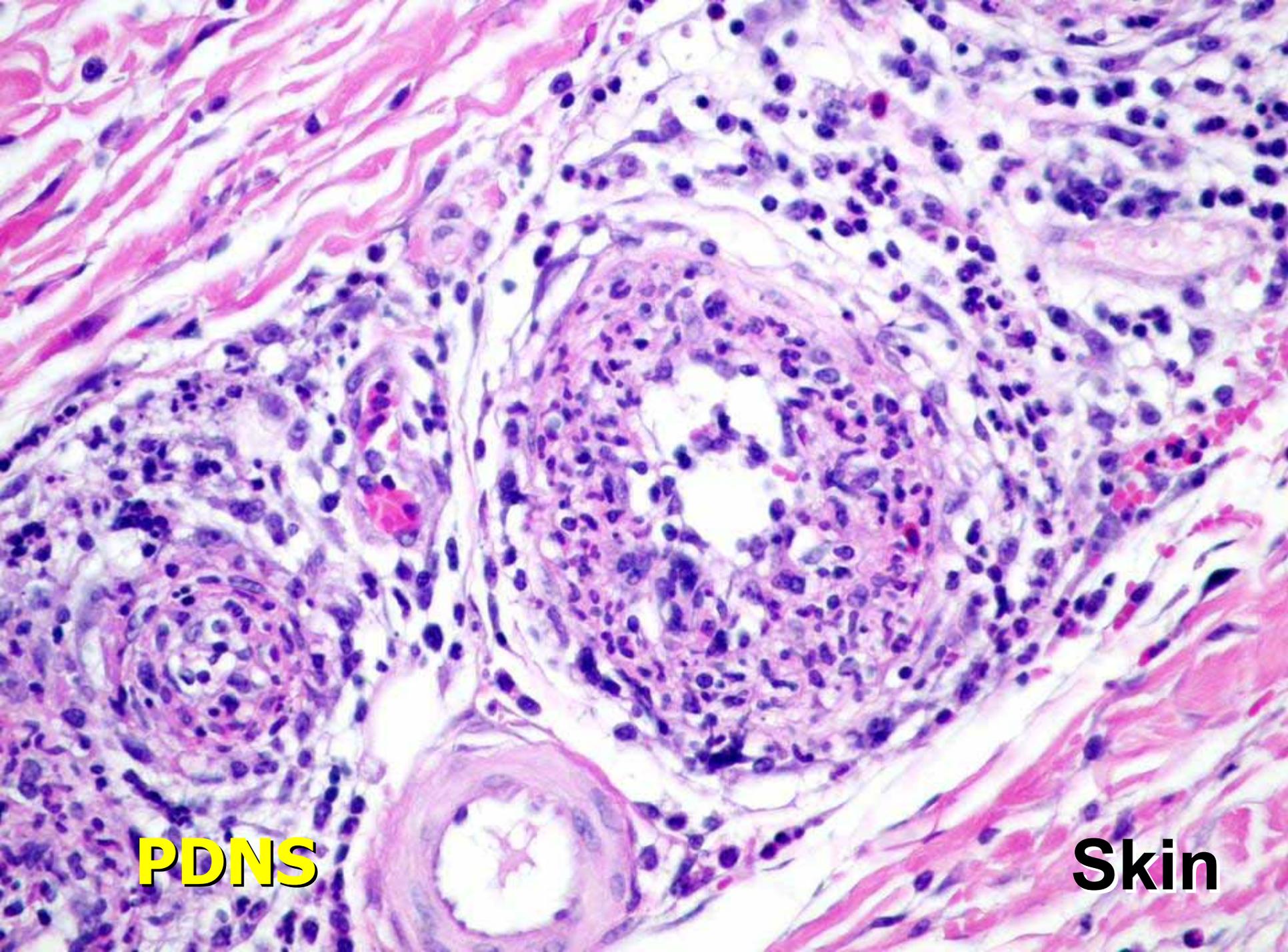


PDNS



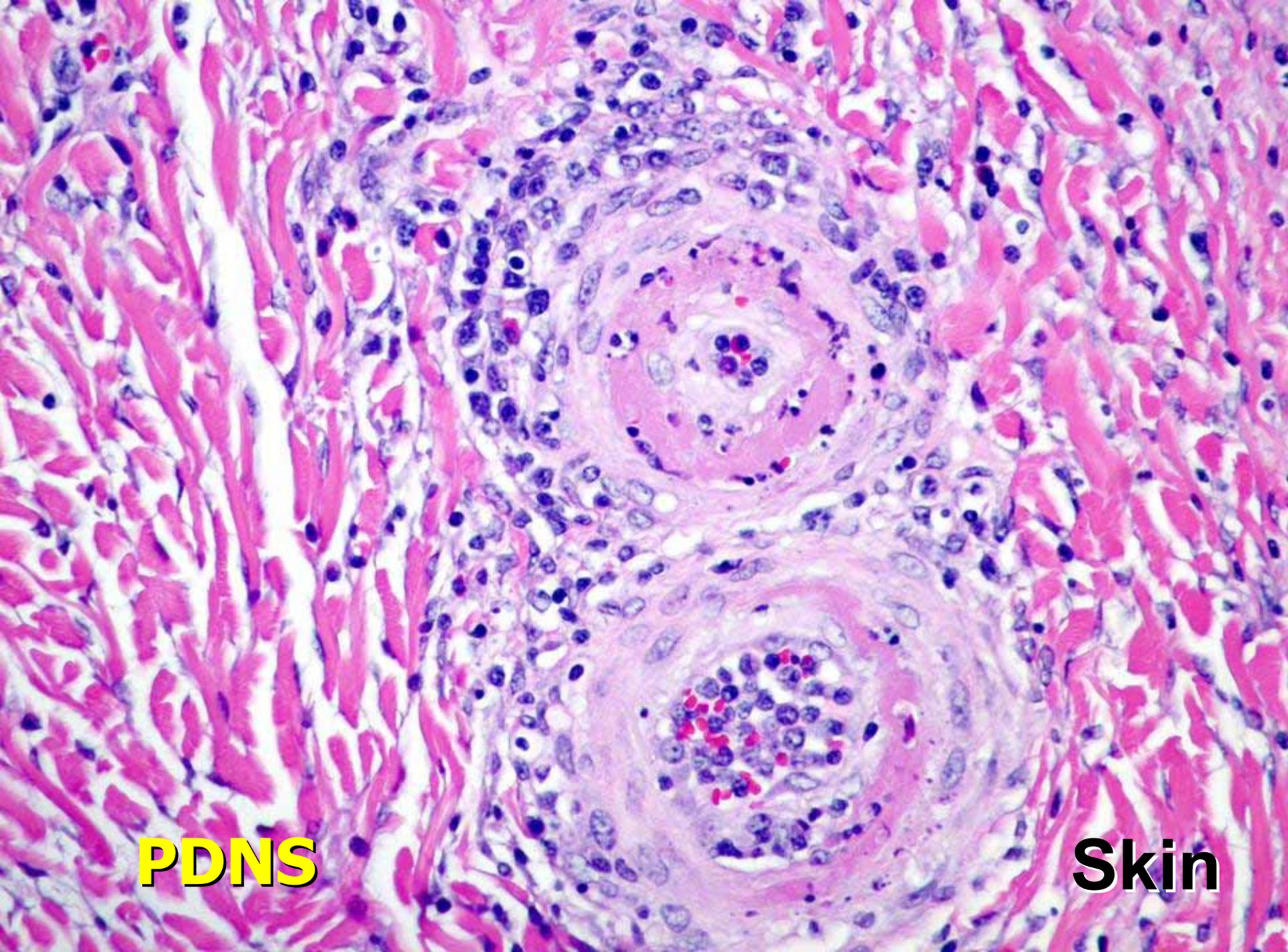
PDNS

Skin



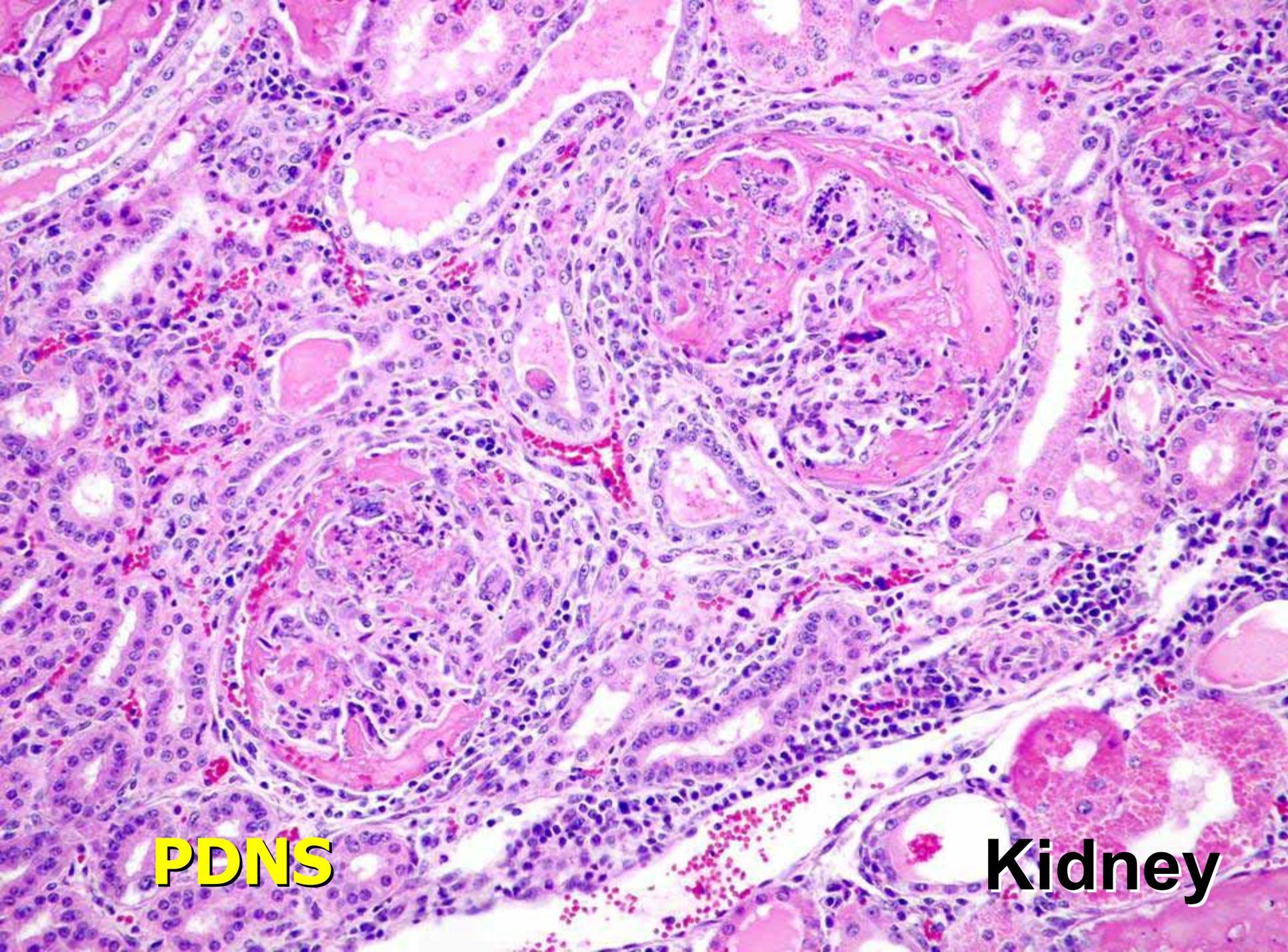
PDNS

Skin



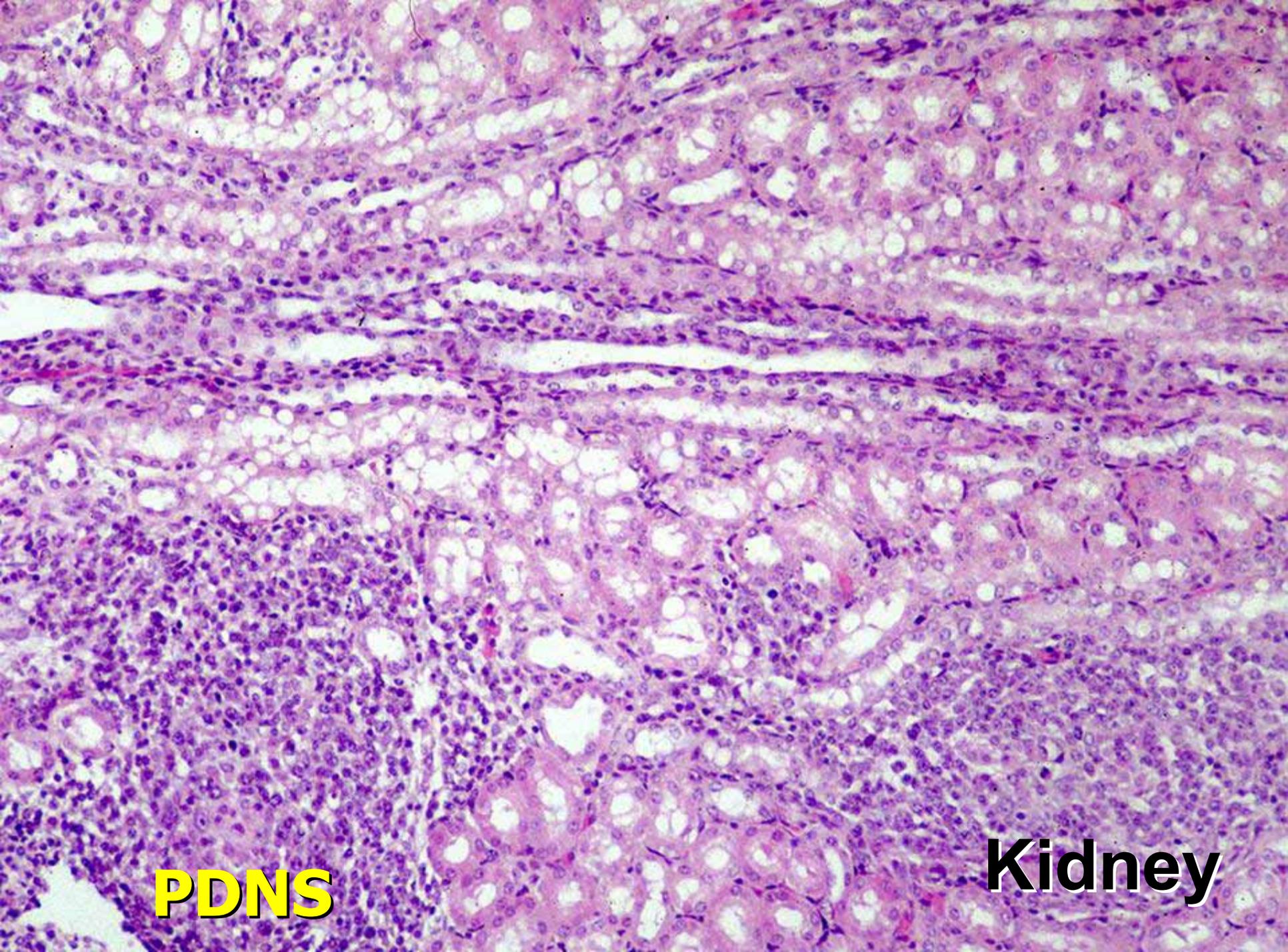
PDNS

Skin



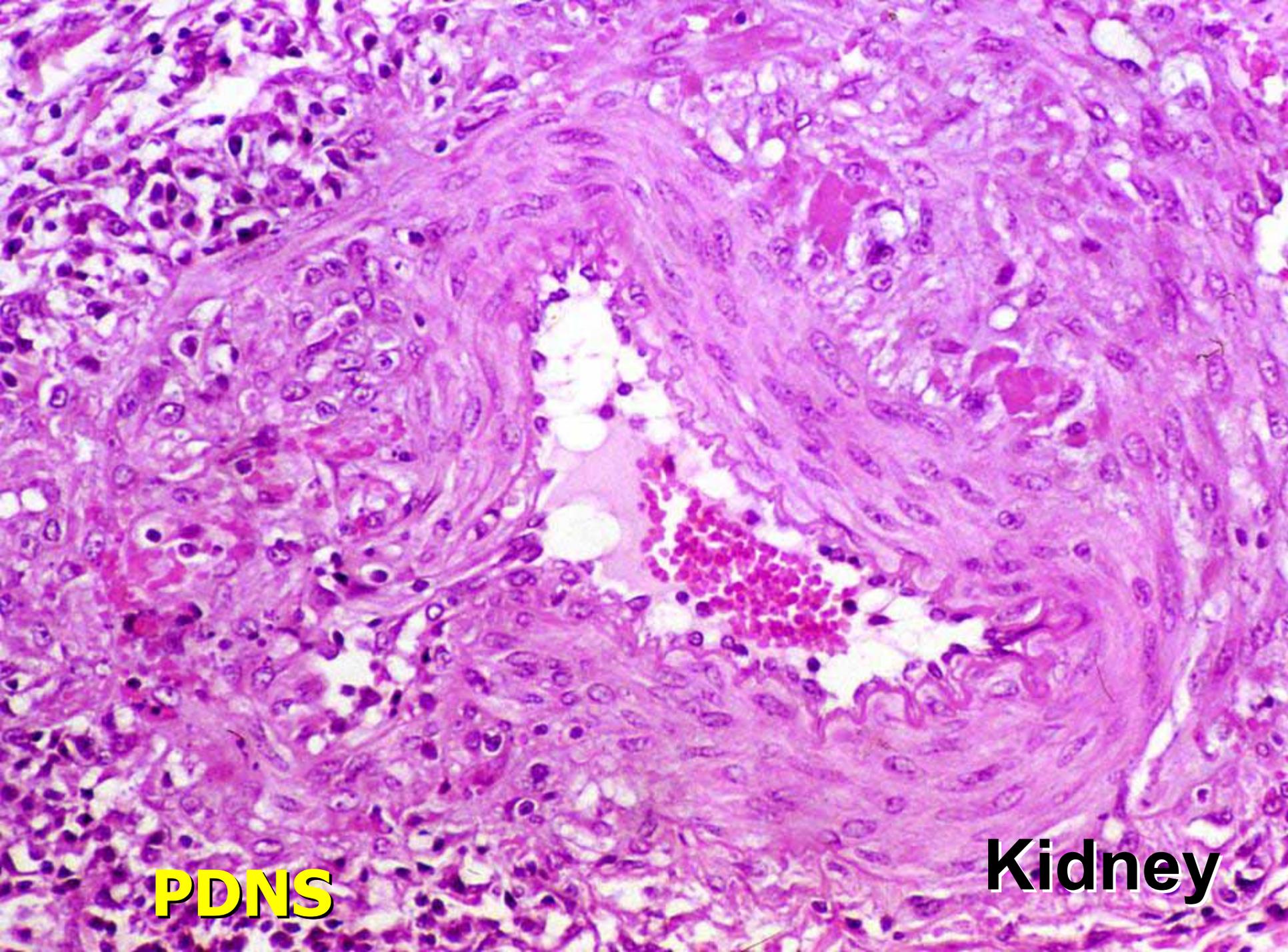
PDNS

Kidney



PDNS

Kidney



PDNS

Kidney