

Congenital Disorders of the Canine and Feline Biliary Tree

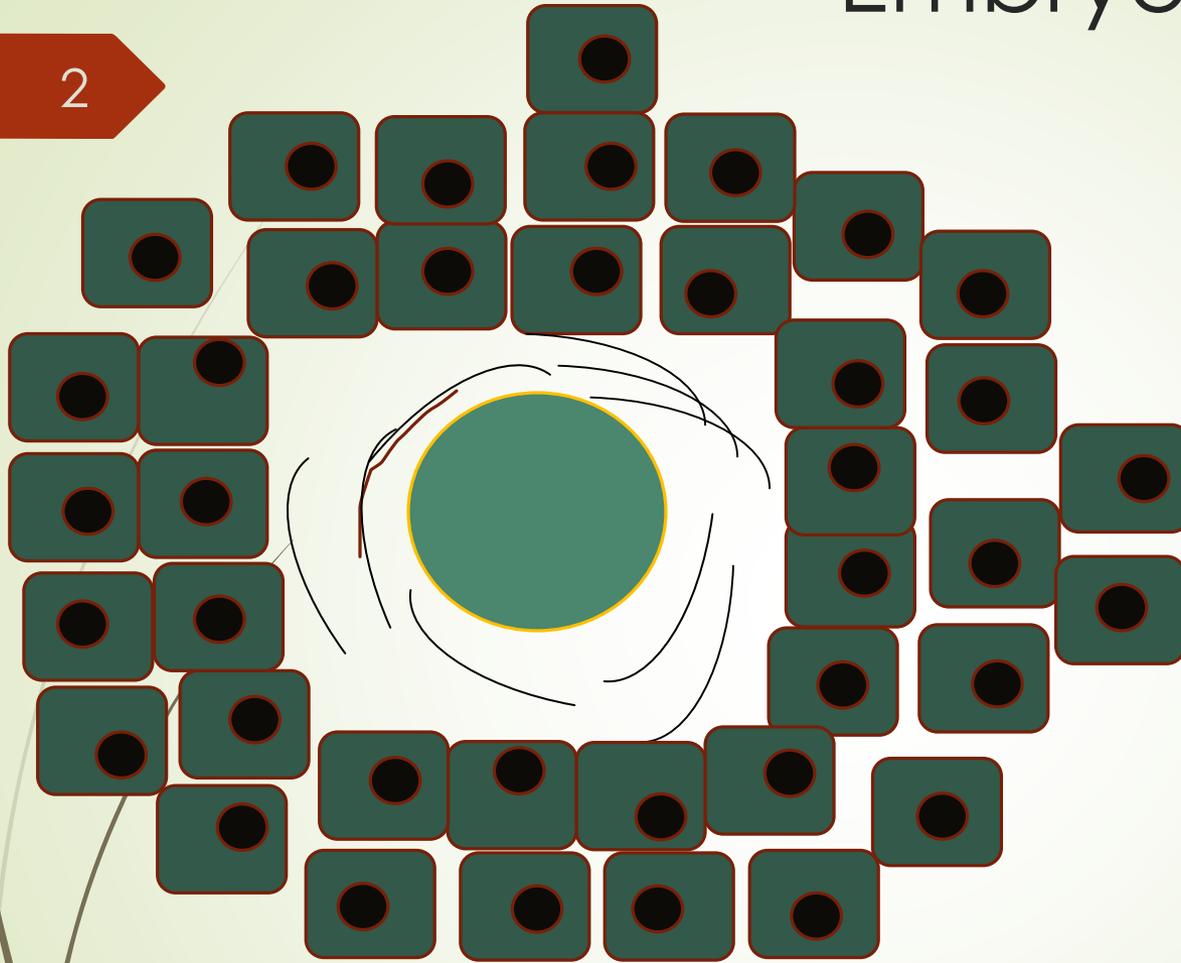
John M. Cullen VMD PhD DACVP FIATP

1

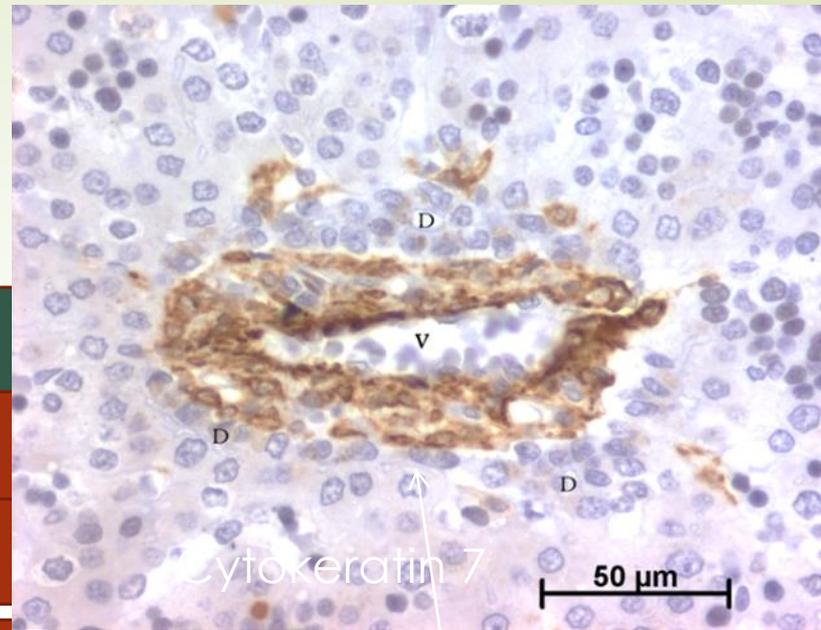
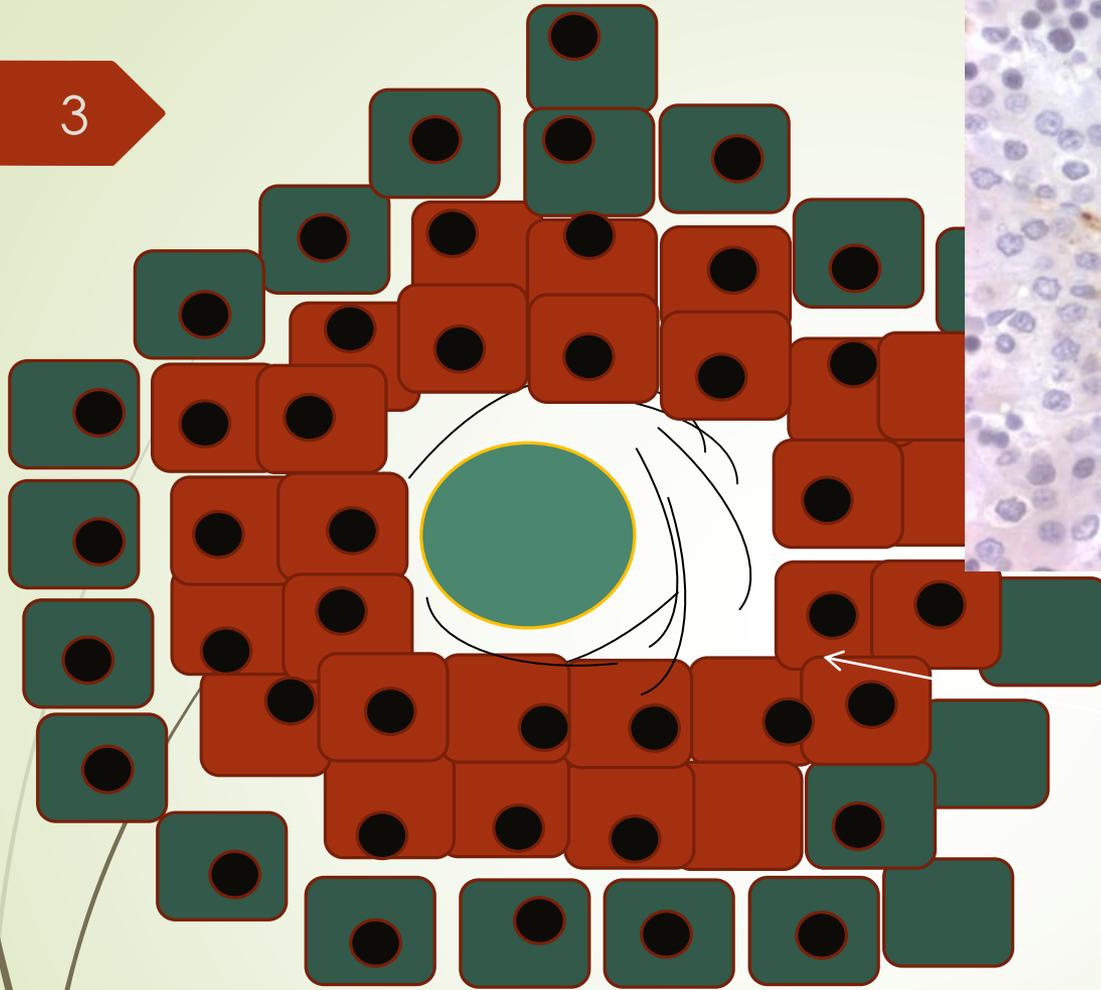
**Annual Seminar of the French
Society of Veterinary
Pathology**

Embryonic Liver

2

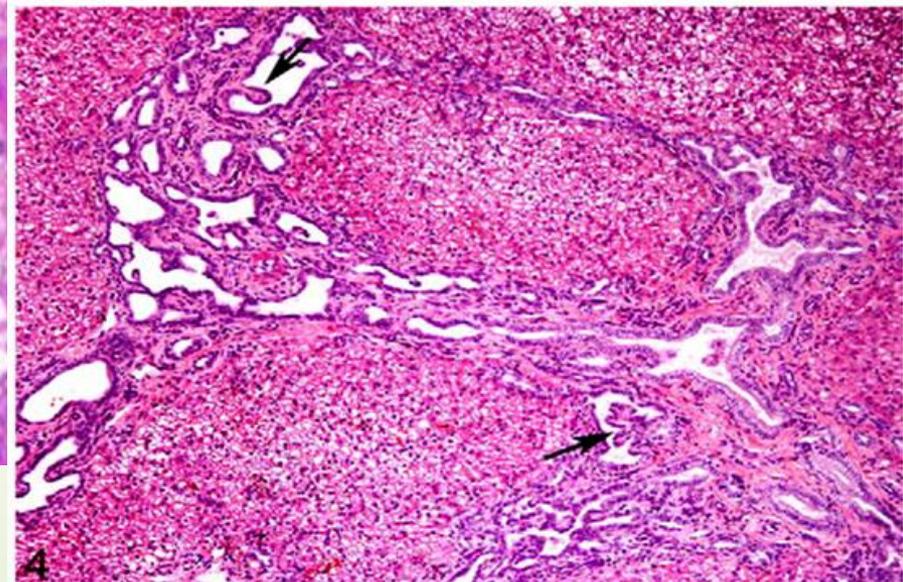
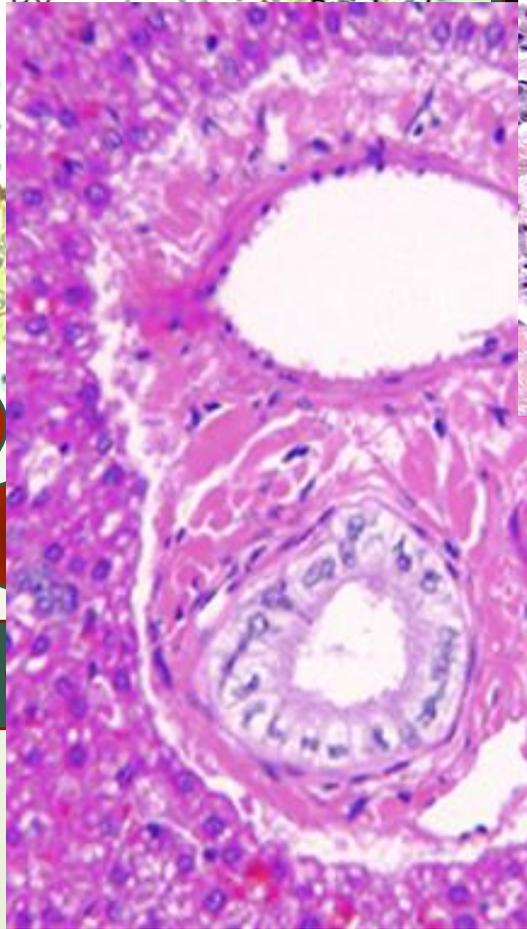
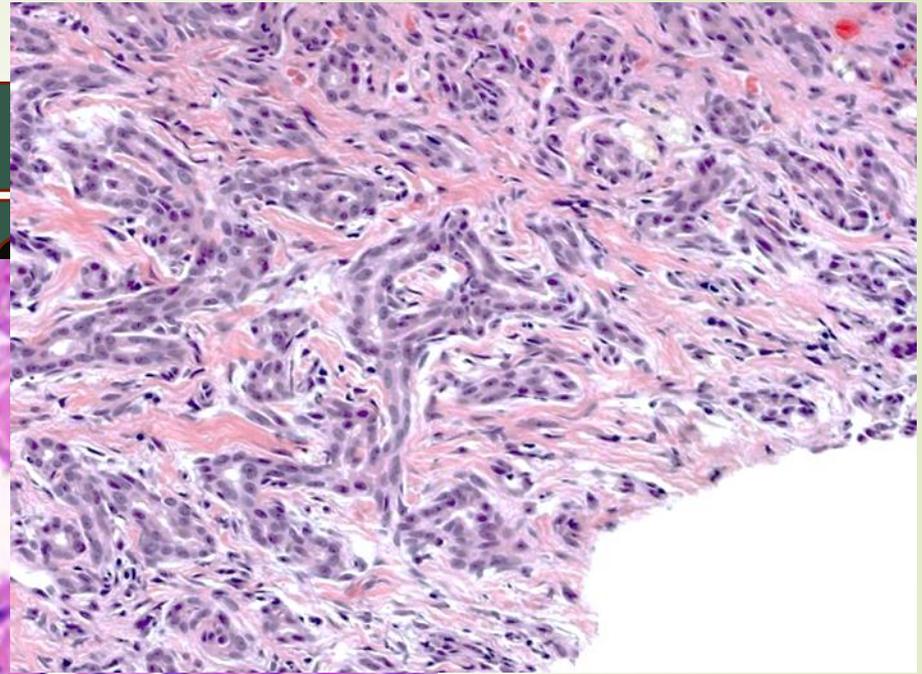
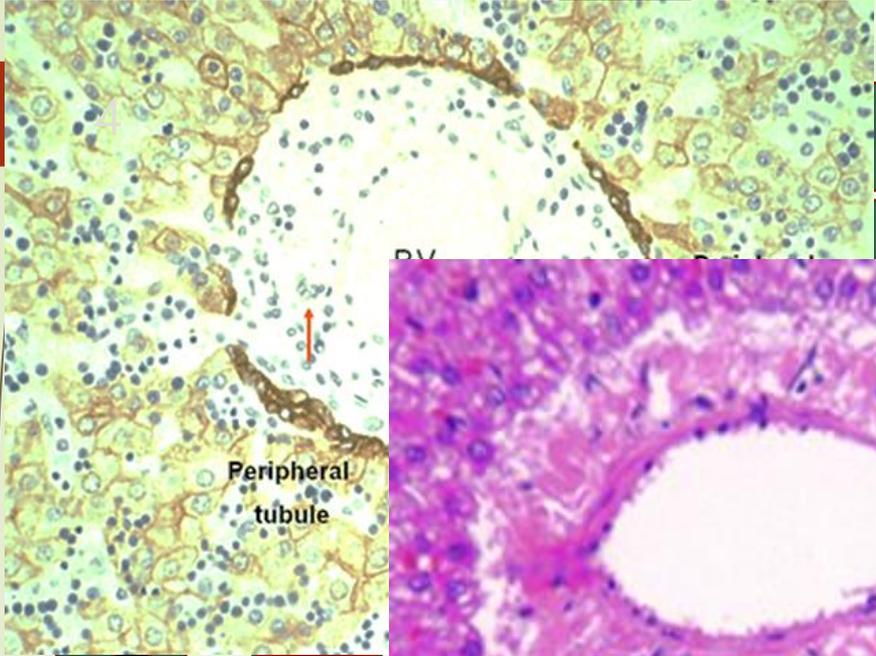


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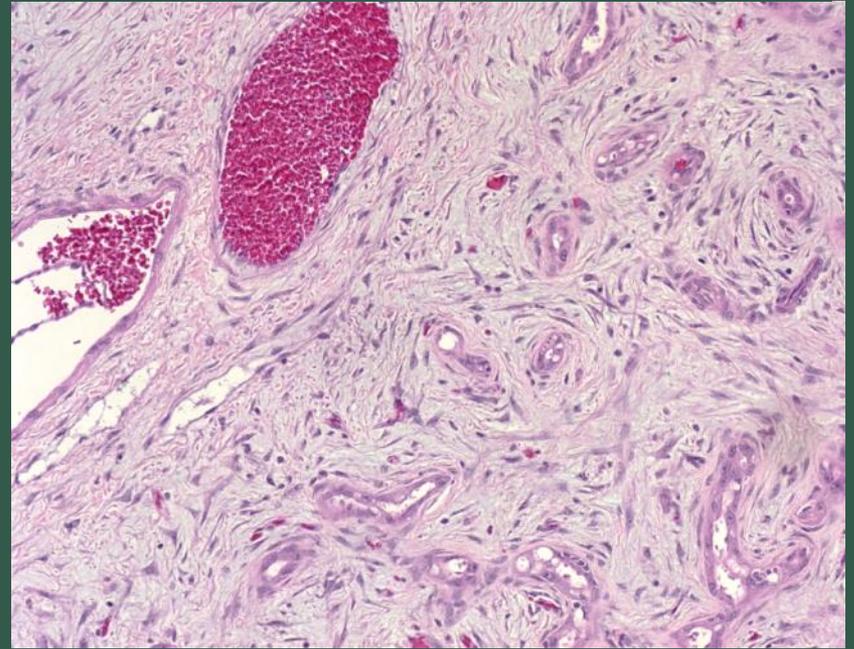
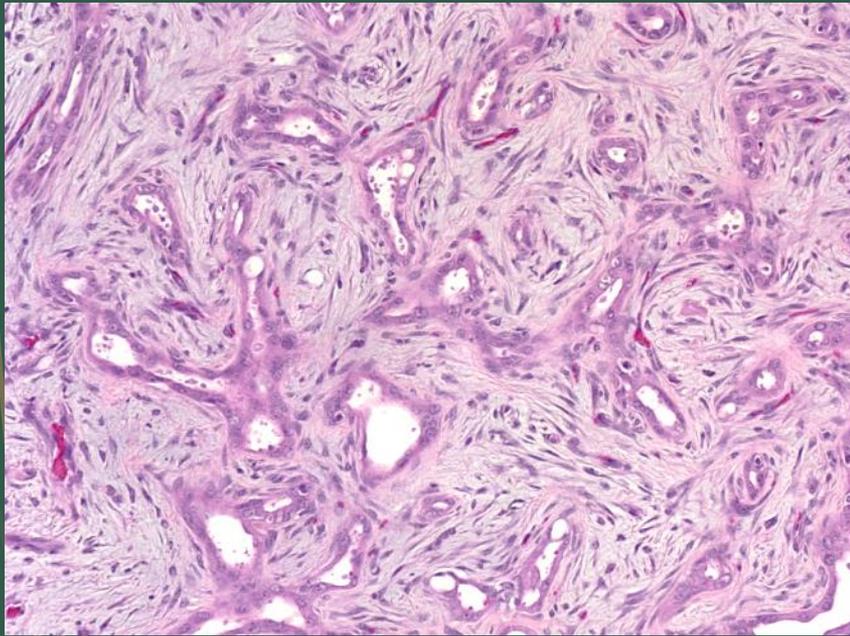
Ductal Plate

In utero AND later



Still-born Arab foal

Mesenchymal Hamartoma



Vet Pathol **44**:100–102 (2007)

Mesenchymal Hamartoma of the Liver in a Late-Term Equine Fetus

D. L. BROWN, M. ANDERSON, AND J. M. CULLEN

Human Cystic Biliary Disorders

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➤ Polycystic Liver Disease

➤ ADPKD

➤ Kidney

➤ Liver

➤ Pancreas

➤ "isolated" PCLD

➤ No kidney involvement

➤ Fibropolycystic diseases

➤ Congenital hepatic fibrosis

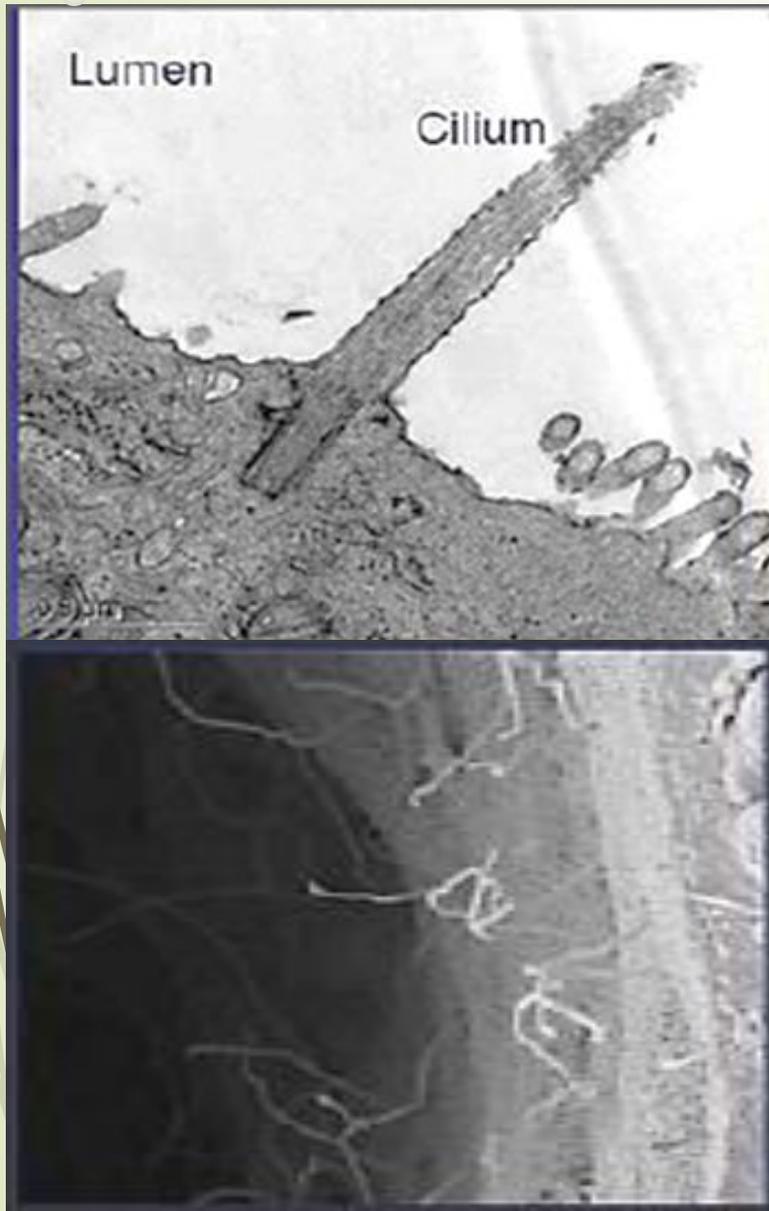
➤ Caroli's disease

➤ ARPKD

Genetics of Human Biliary Cystic Disorders

- ▶ All involve primary cilia function
 - ▶ Modulation of Ca^{++}
 - ▶ ER glycoprotein traffic
- ▶ ADPKD:
 - ▶ polycystin 1, 2
 - ▶ Isolated polycystic liver disease:
 - ▶ hepatocystin
 - ▶ Fibropolycystic diseases:
 - ▶ fibrocystin

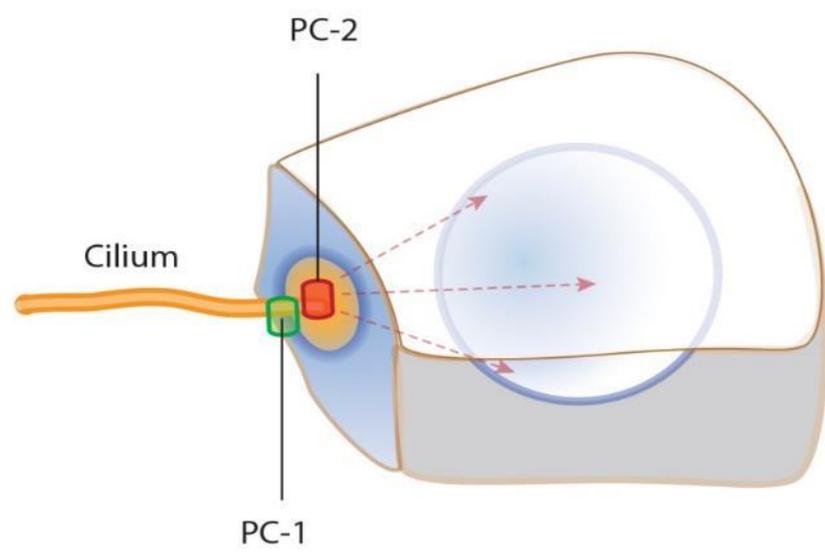
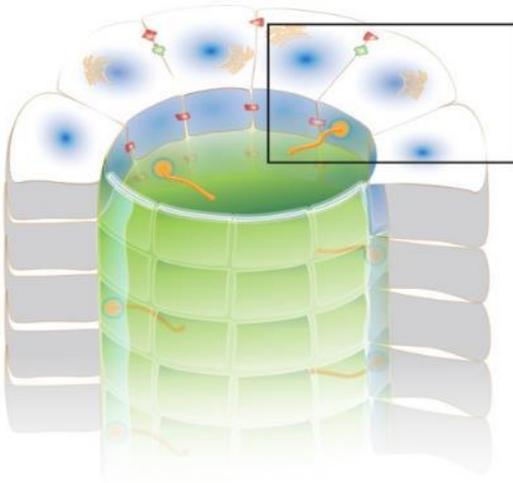
Primary Cilia in Biliary Epithelium



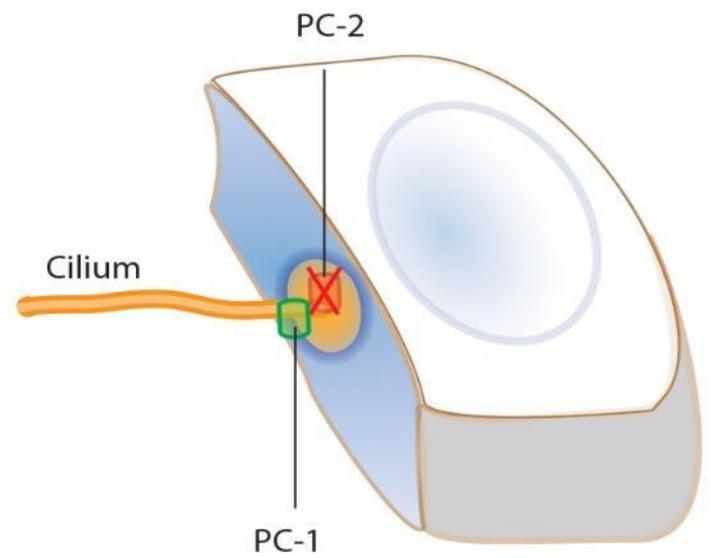
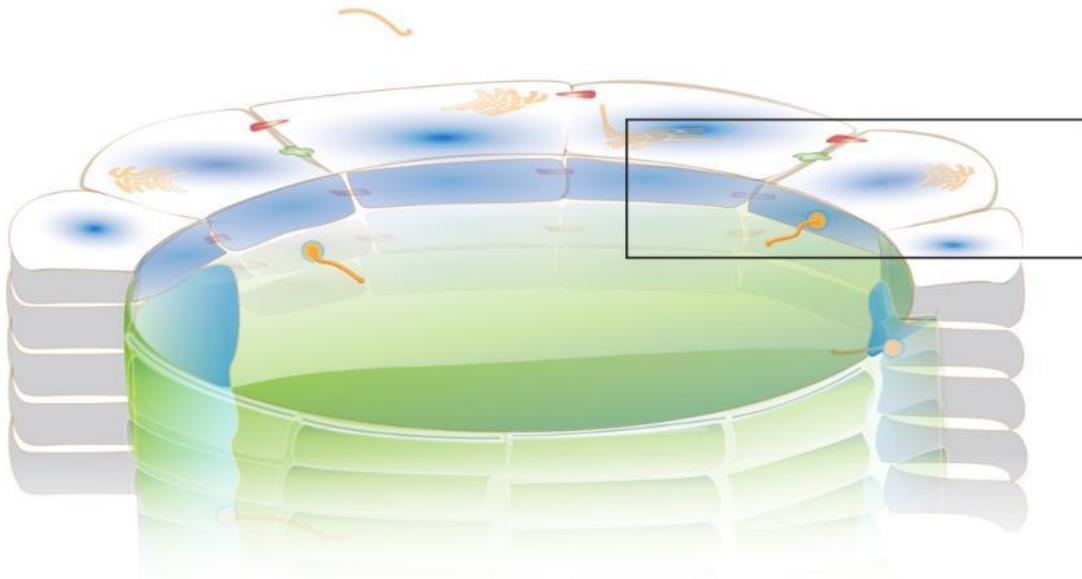
- Non motile
- Sense
 - Flow
 - Composition
 - Osmolatility

Normal Liver

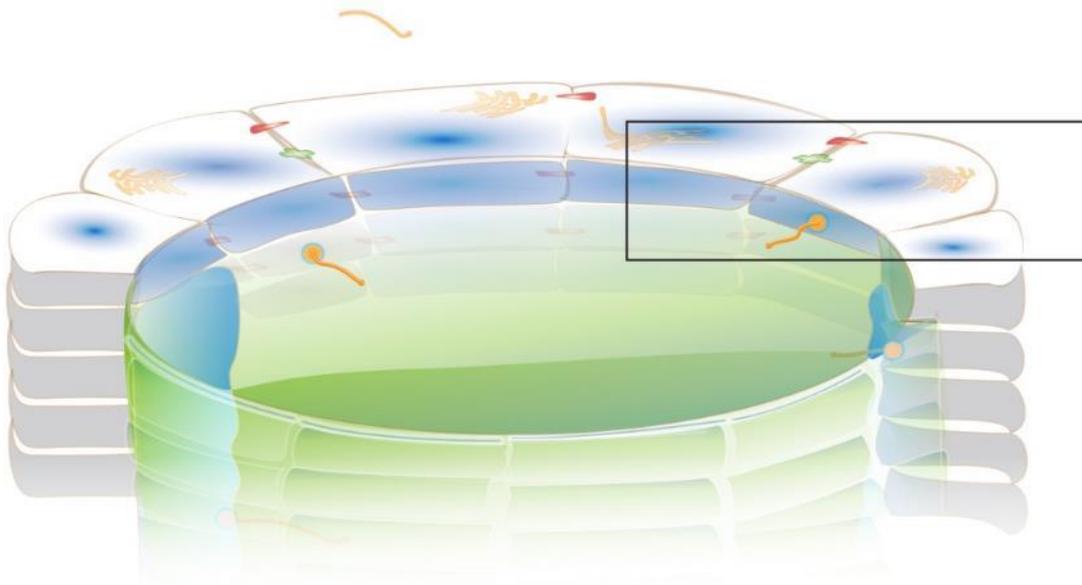
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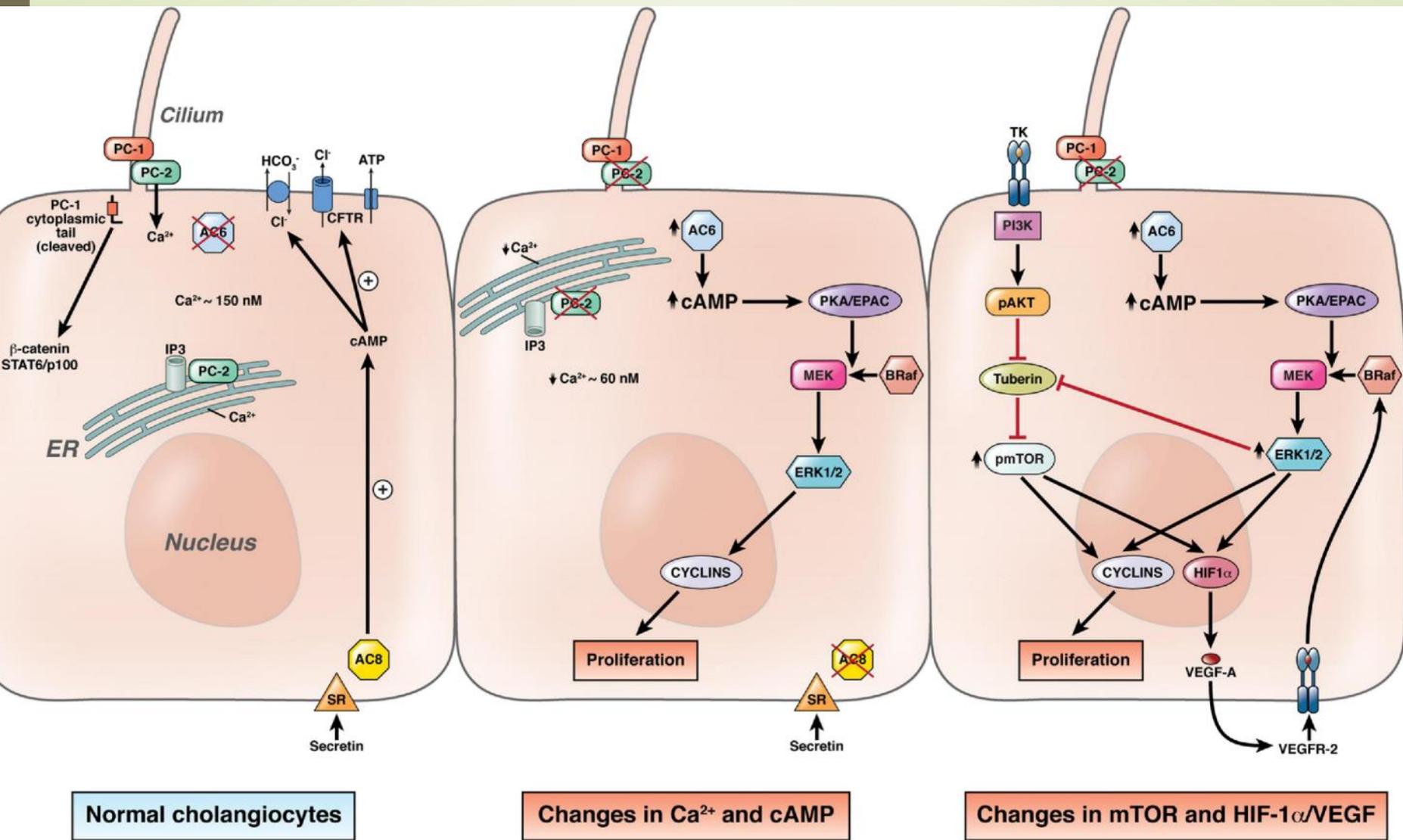


Cystic Liver



Cystic Liver





Ductal Plate Malformations

With ectasia

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ADPKD

Polycystic
Liver
Disease

ARPKD

Caroli Disease

With involution

von Meyenburg
Complexes

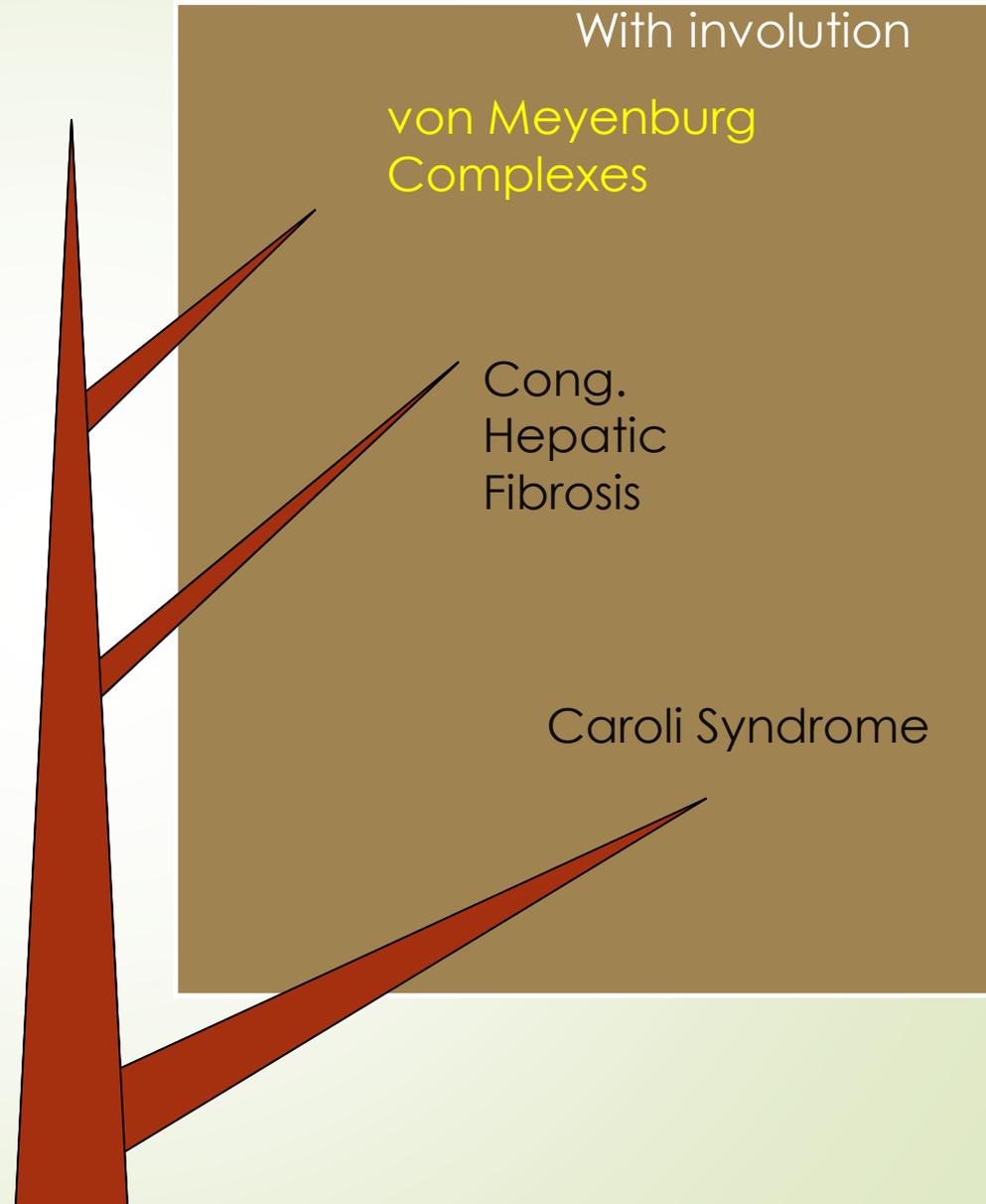
Cong.
Hepatic
Fibrosis

Caroli Syndrome

Modified from Desmet,
V. Hepatology, 2009

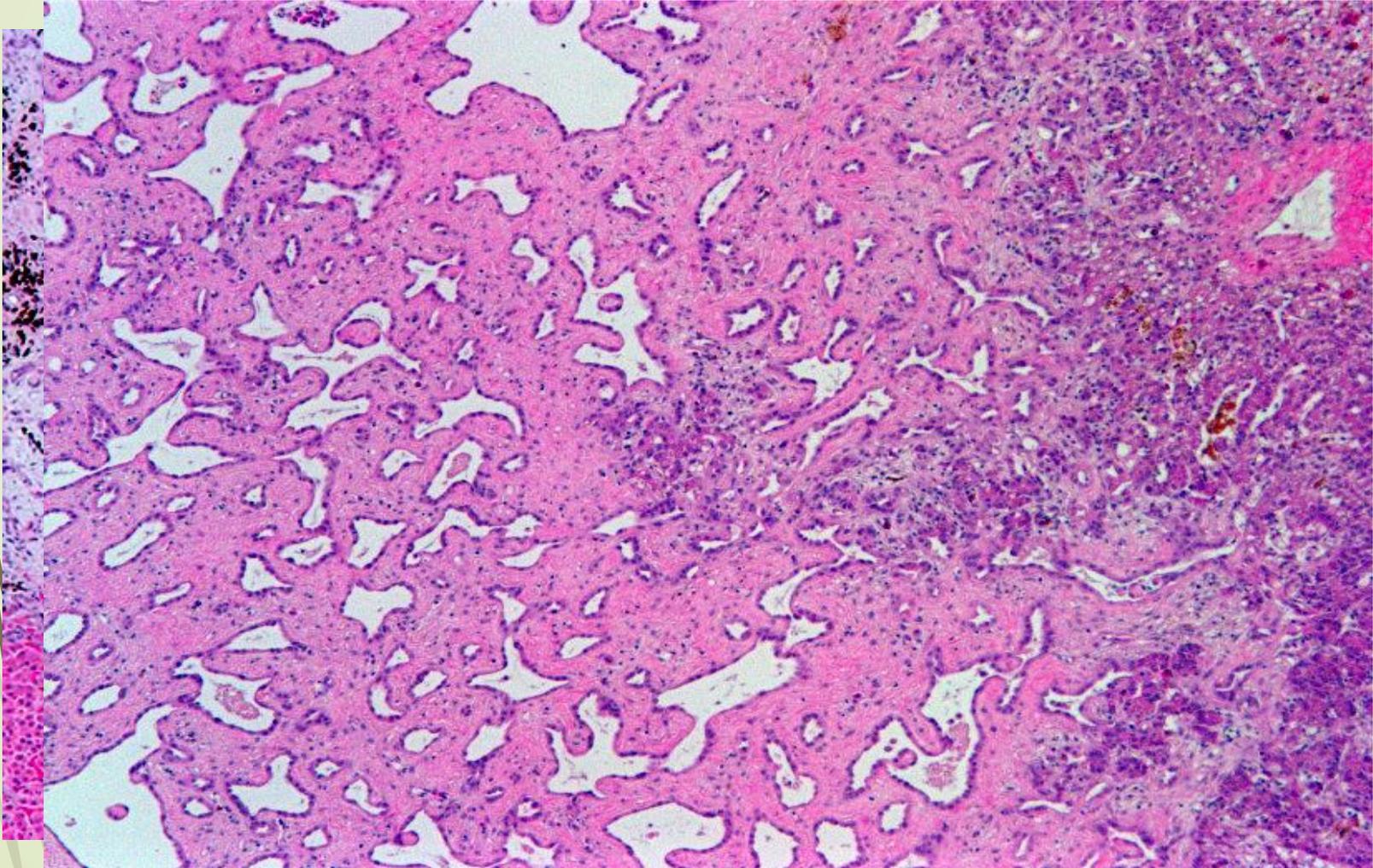
Ductal Plate Malformations

13



Modified from Desmet,
V. Hepatology, 2009

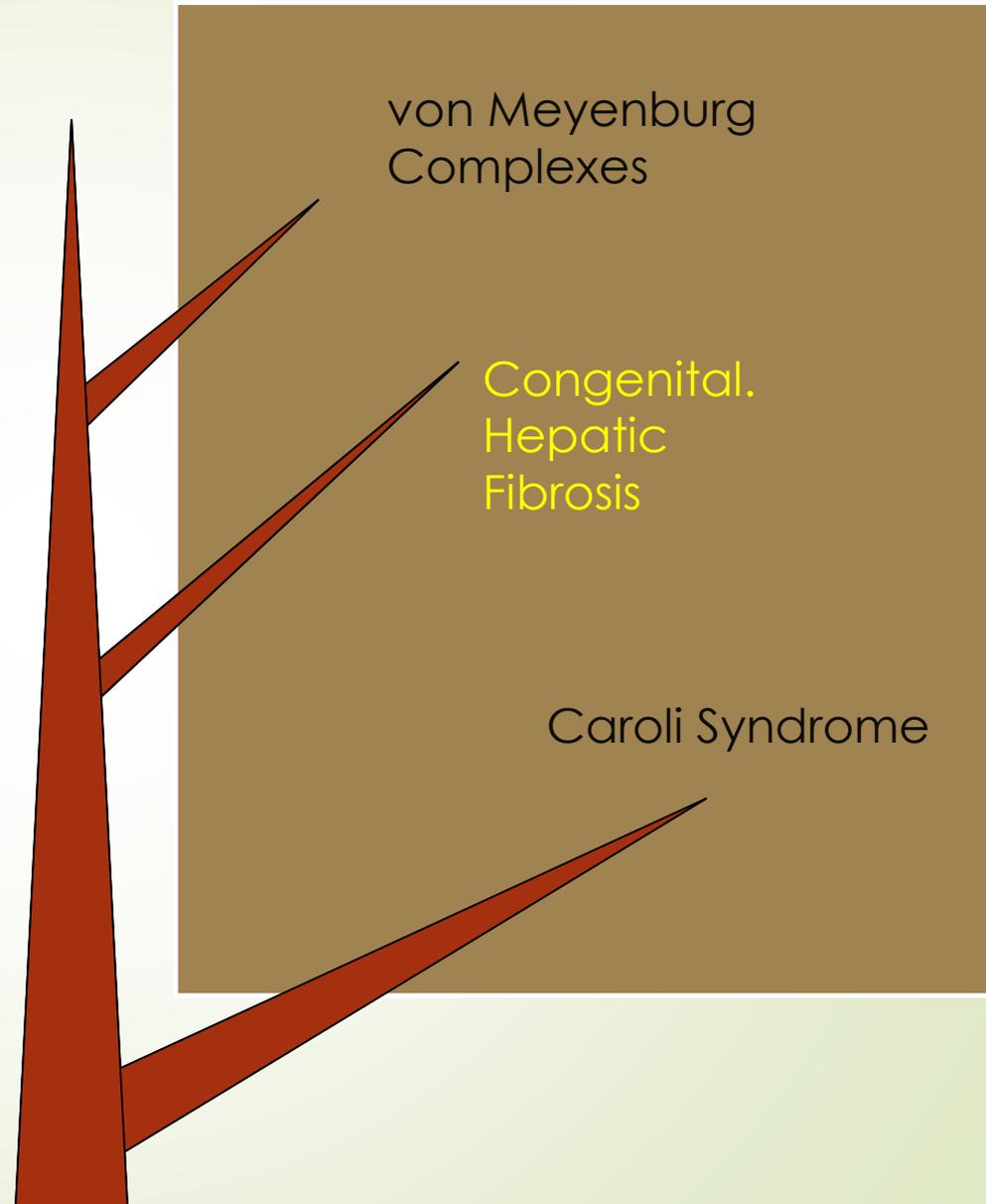
von Meyenburg Complex



jr

Ductal Plate Malformations: **With involution**

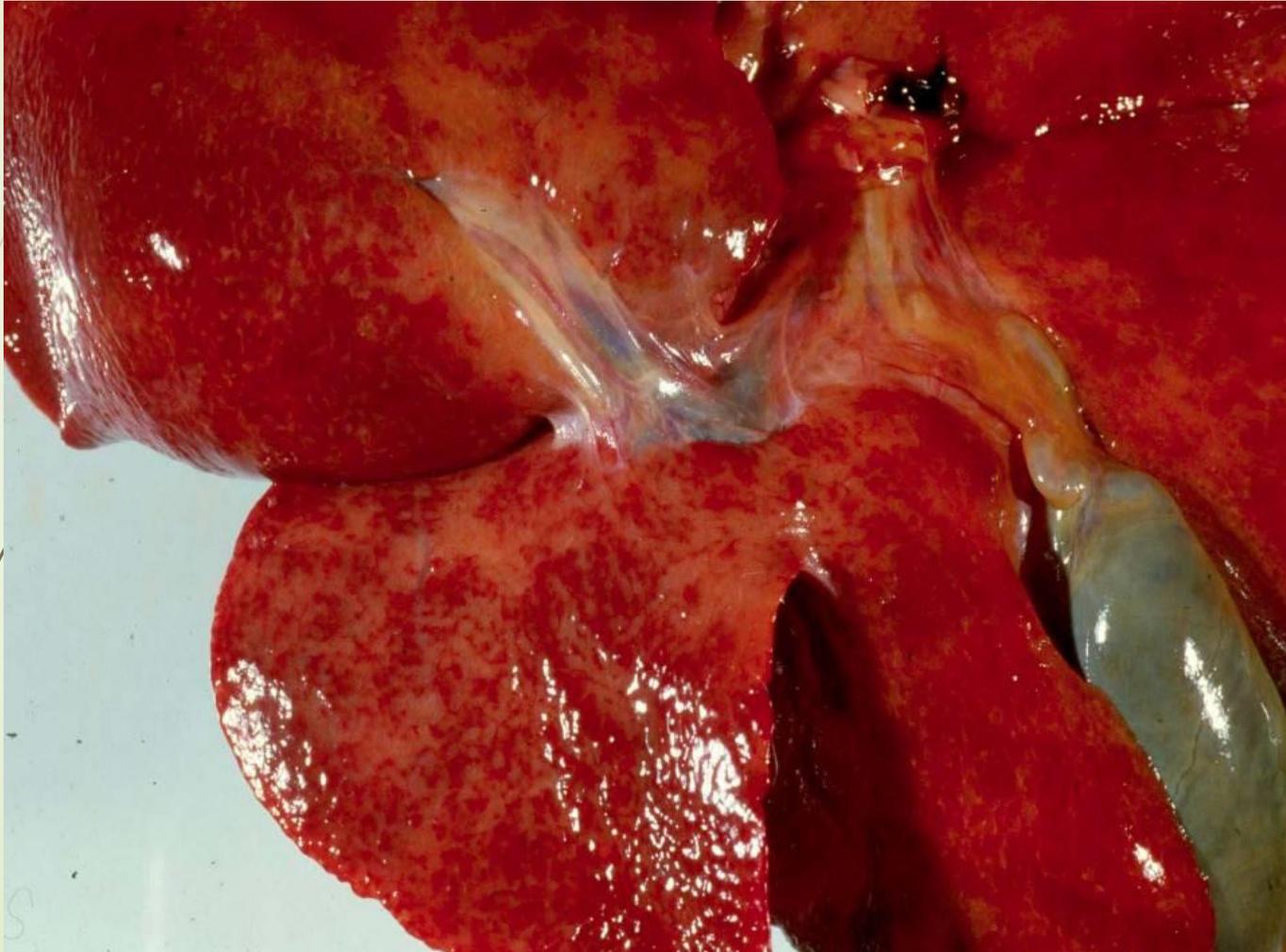
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Modified from Desmet,
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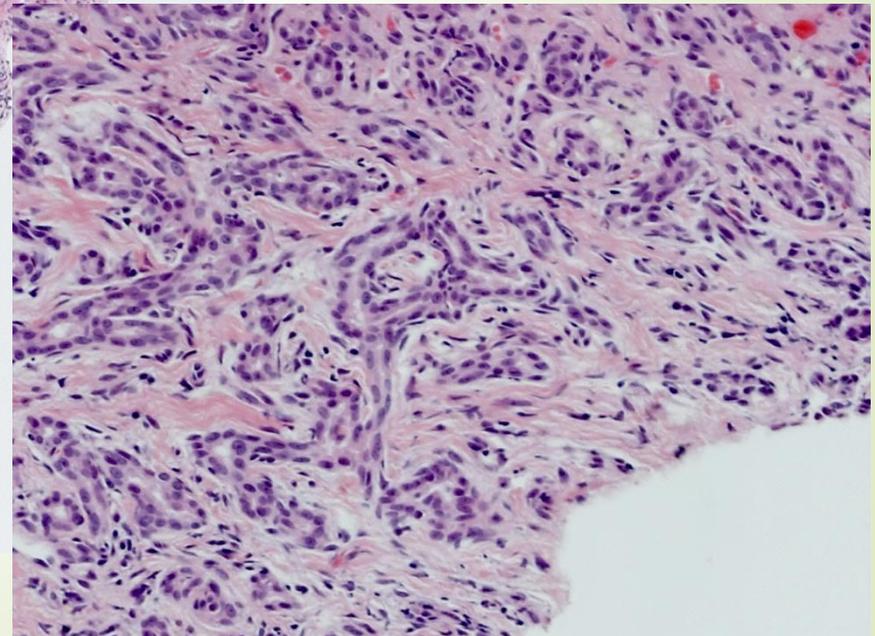
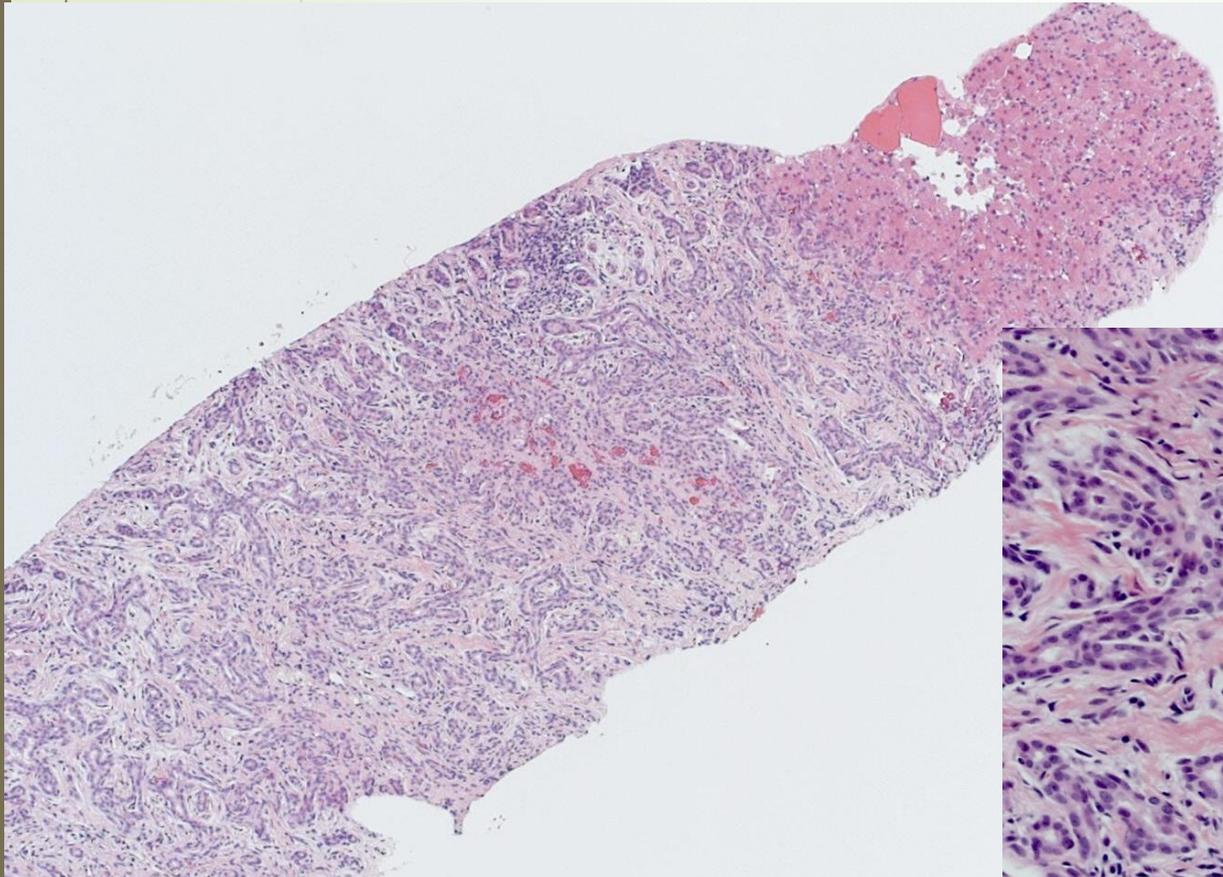
CONGENITAL HEPATIC FIBROSIS: CAT

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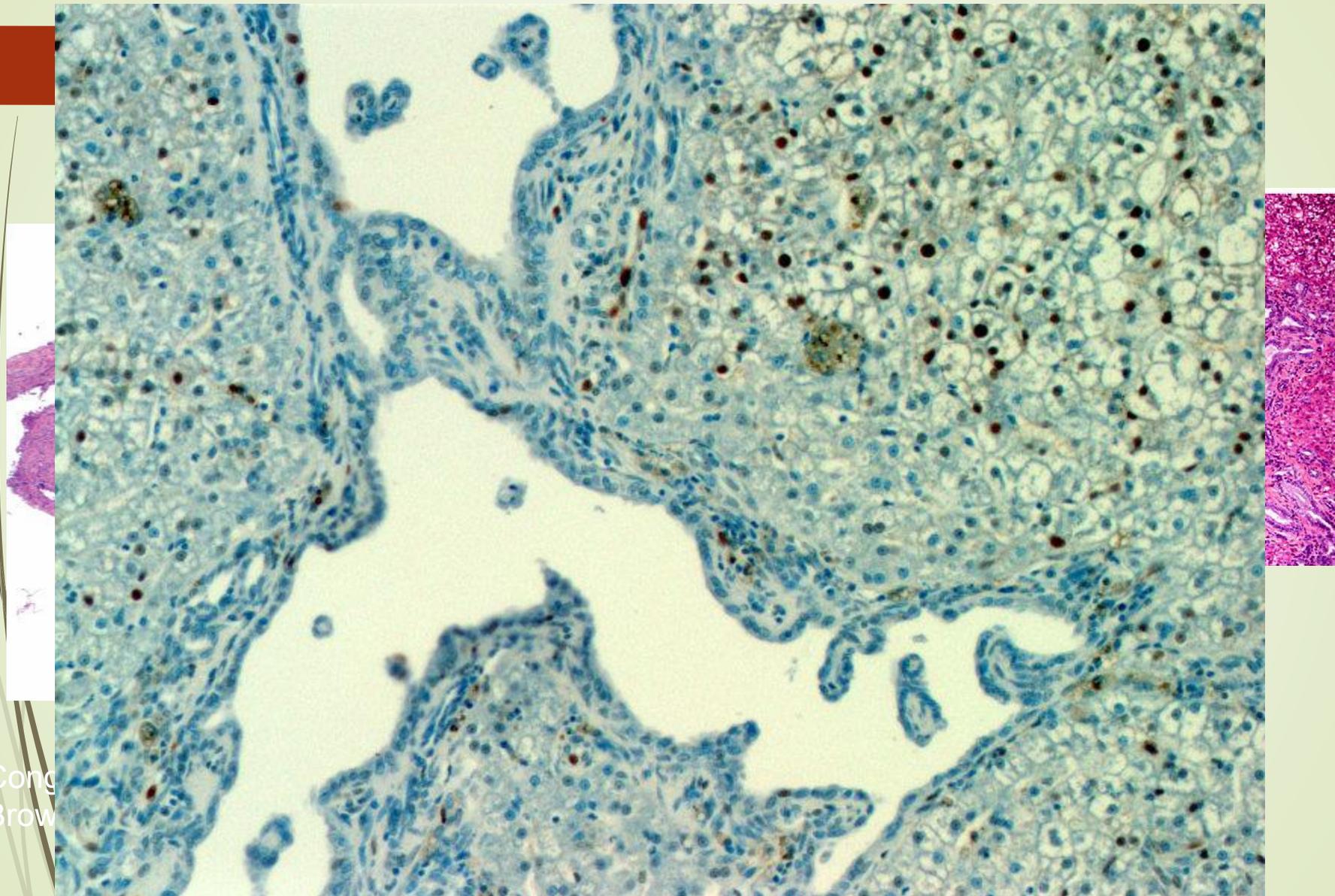


Courtesy Dr. T. van den Ingh

Congenital Hepatic Fibrosis: Feline

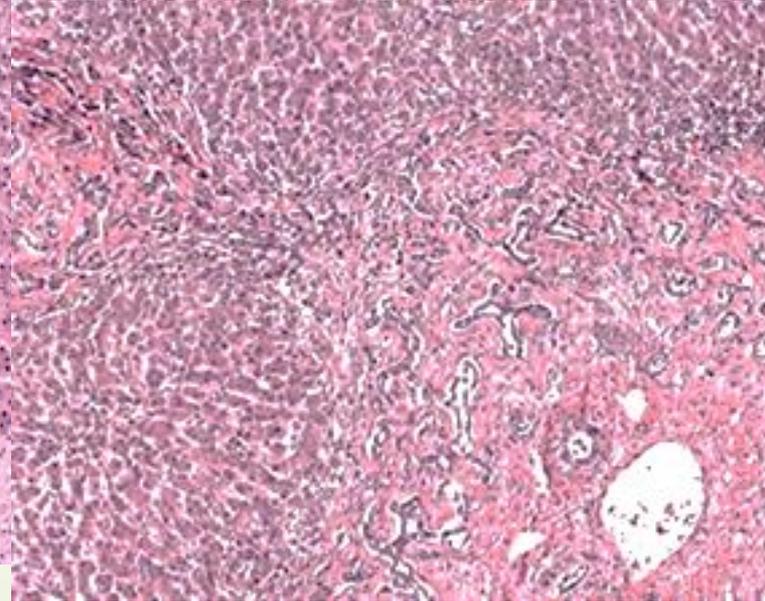
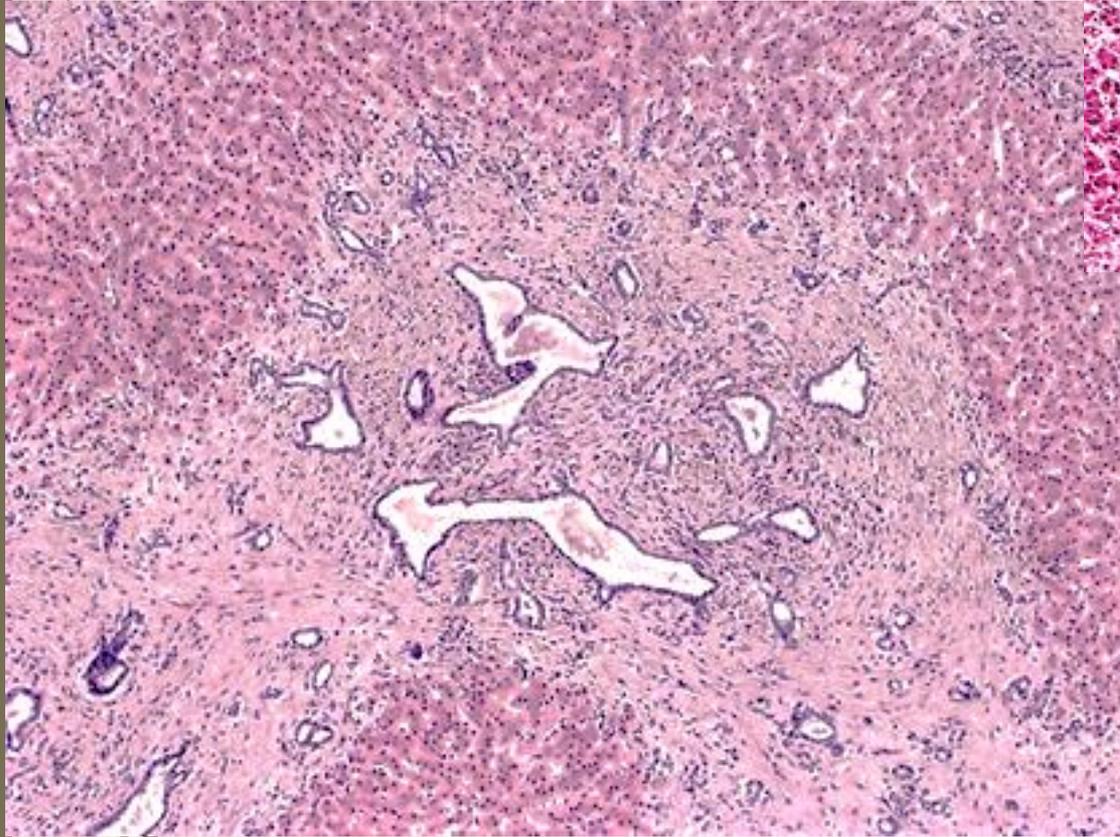
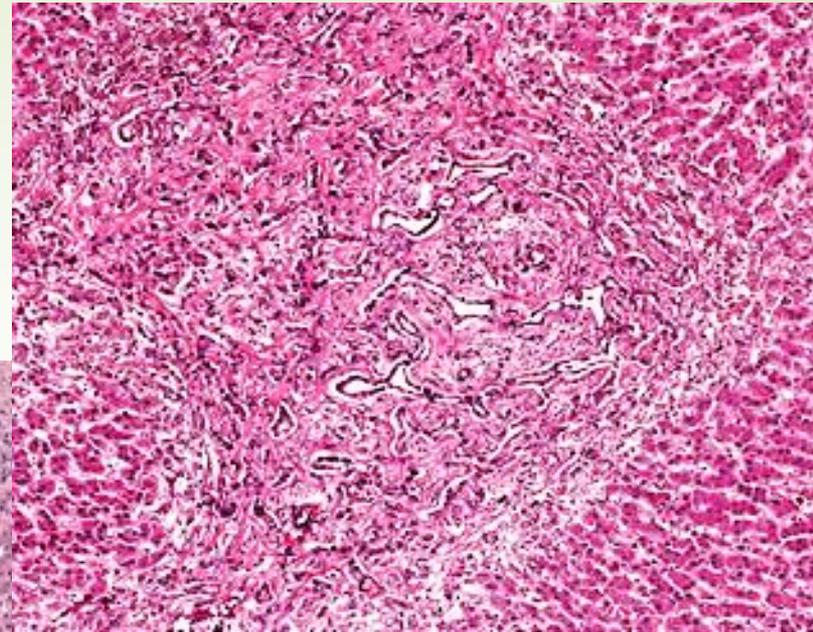


Canine Congenital Hepatic Fibrosis



Cong
Brow

Swiss Freiburger Horses



Van den Ingh et al.

Swiss Freiburger Horses

- Gender: male
- Age: 2 months
- Weight: 84 kg



- History:

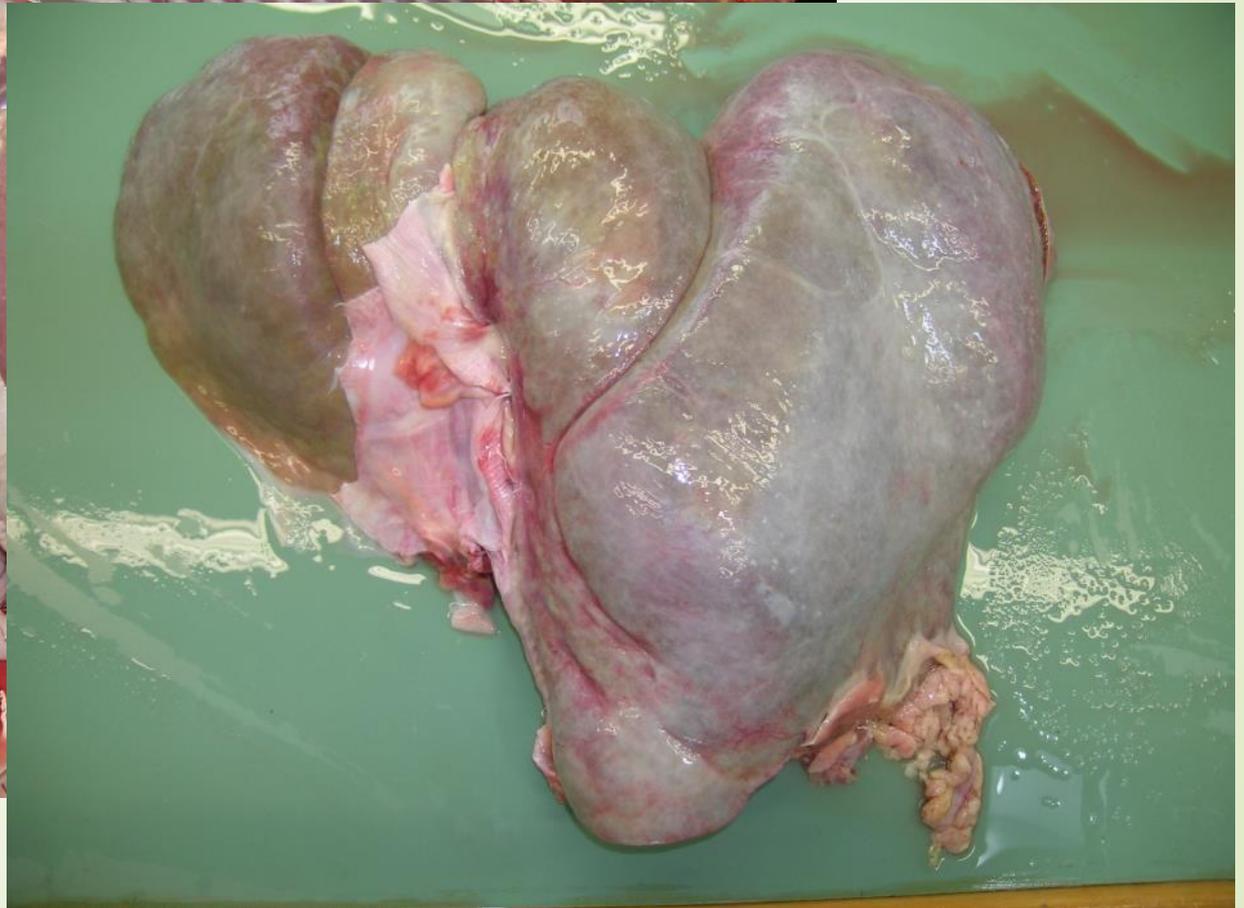
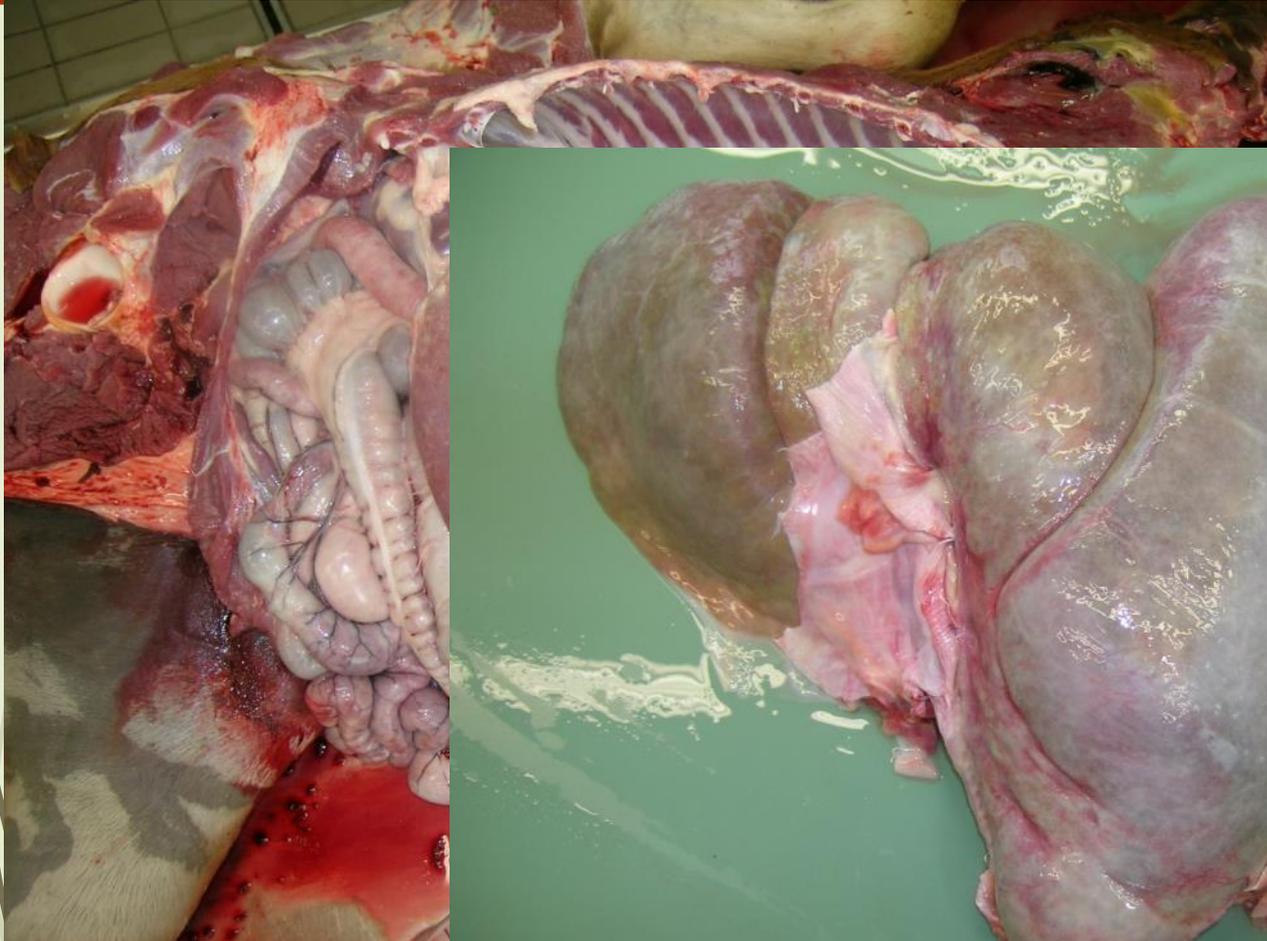
Runt, apathic, big abdomen

Ultrasound: liver with variable texture and cysts,

Blood: high numbers of leucocytes, high liver values

Christine Gopfert Inst. Swiss
Vet. Annual Meeting, Berne

Necropsy

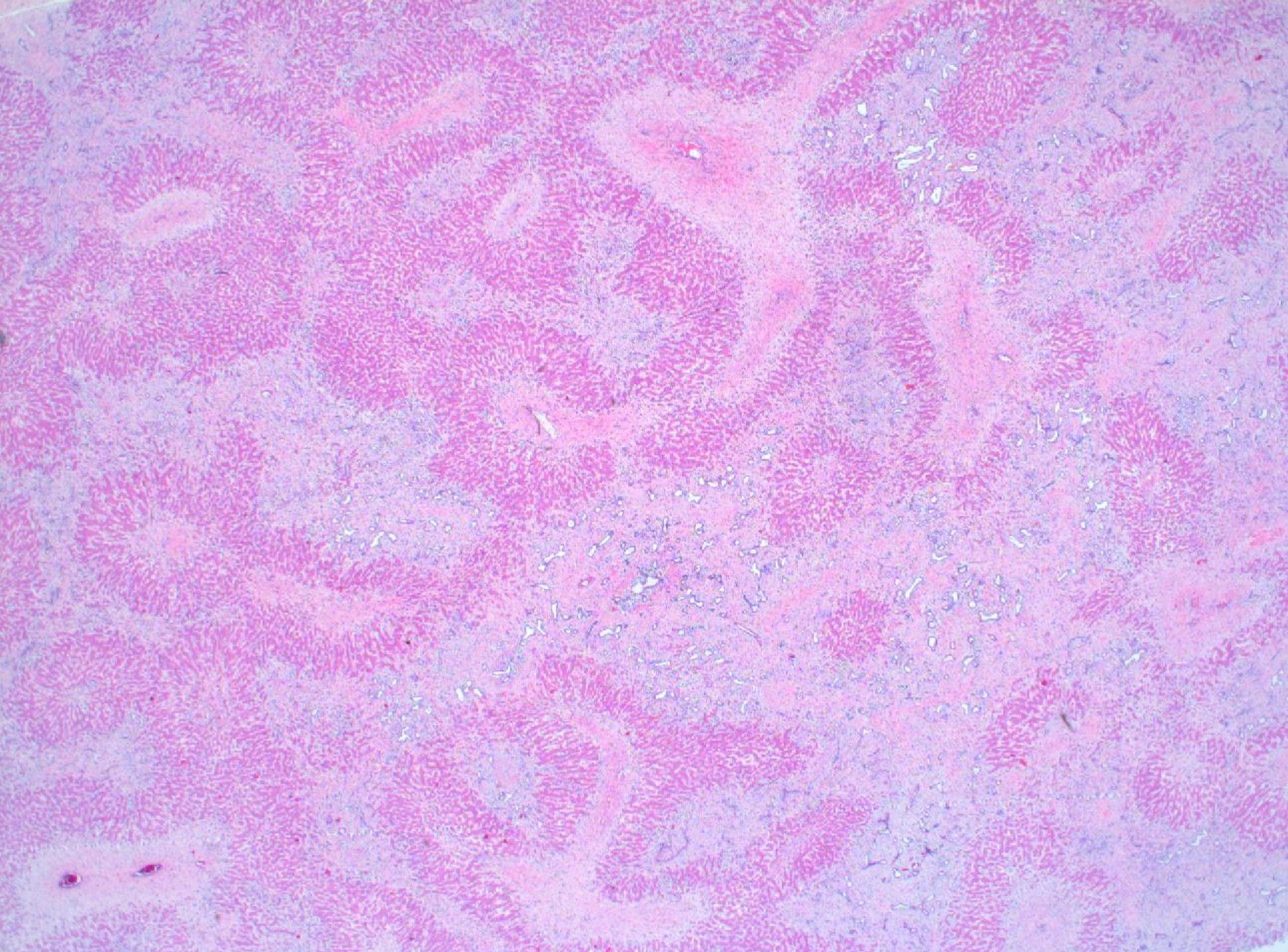


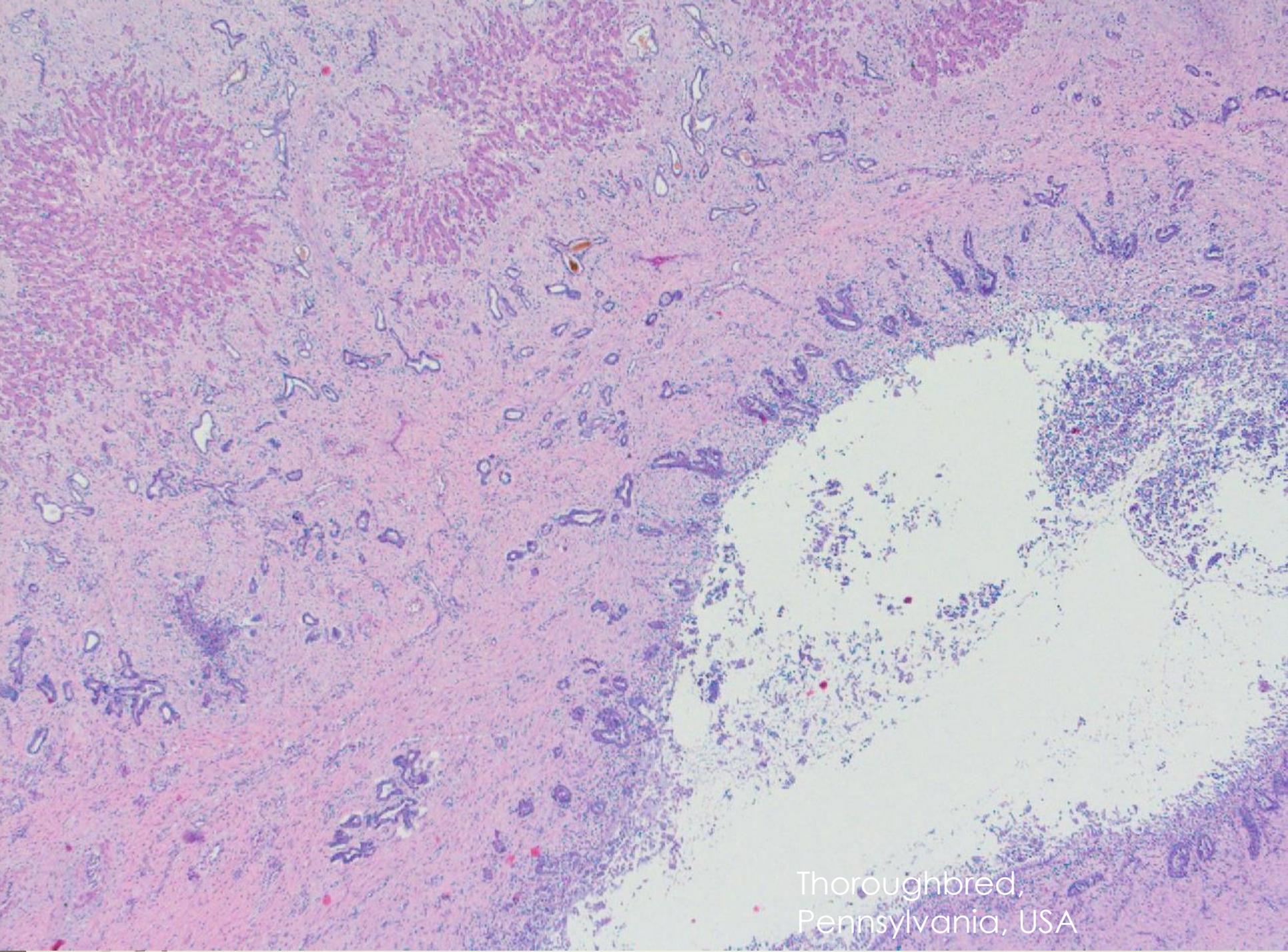
Christine Gopfert Inst. Swiss Vet. Annual Meeting, Berne

Autopsy

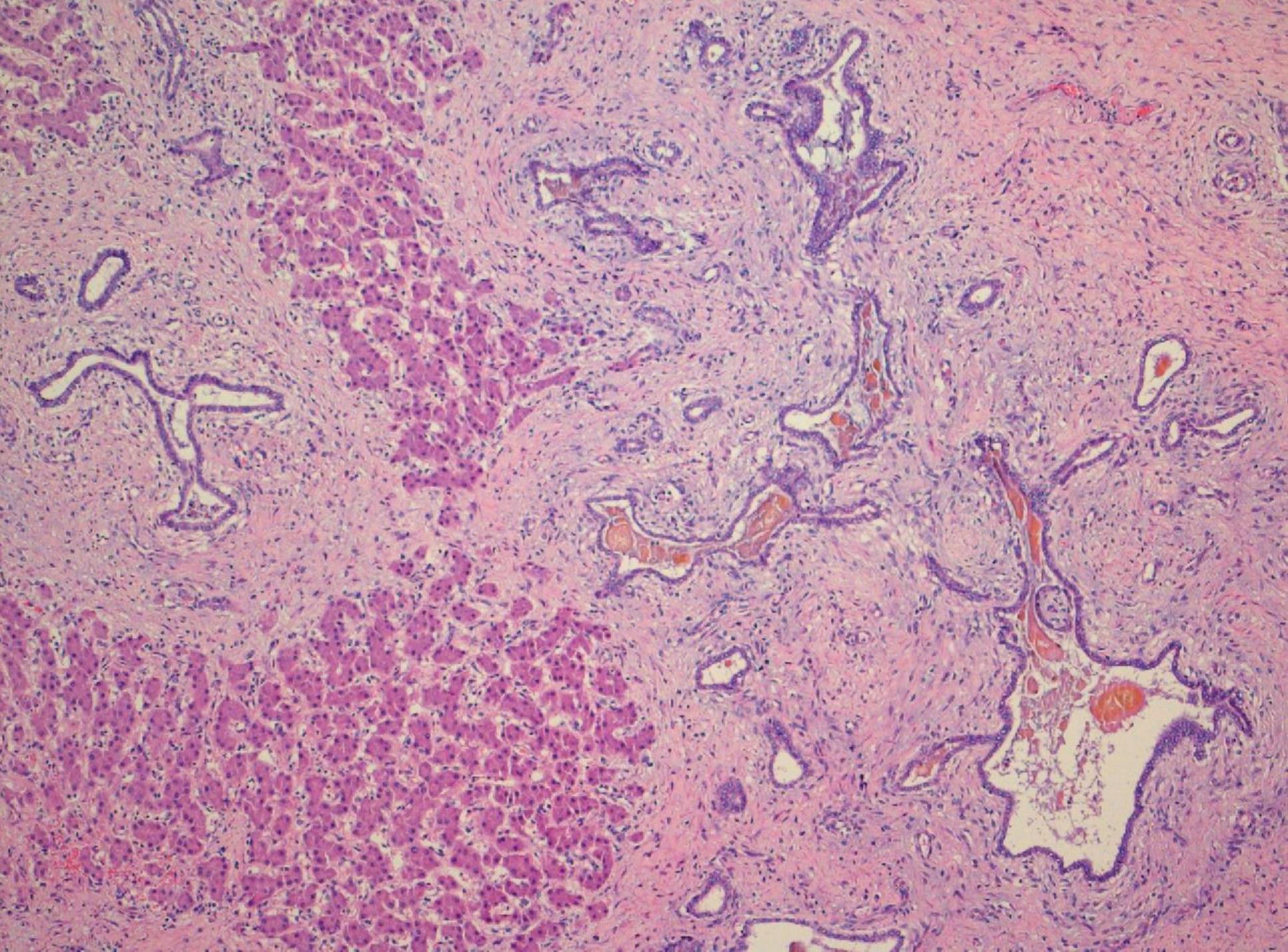


Christine Gopfert Inst. Swiss Vet. Annual Meeting, Berne





Thoroughbred,
Pennsylvania, USA

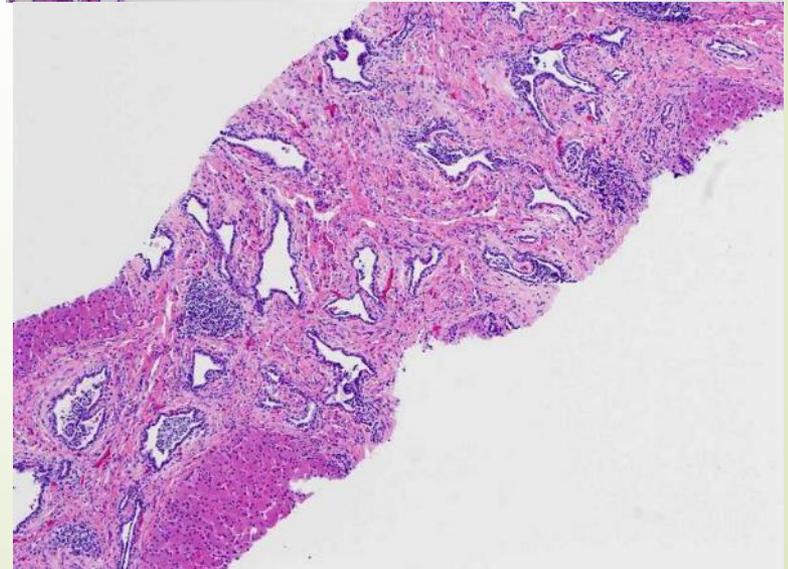
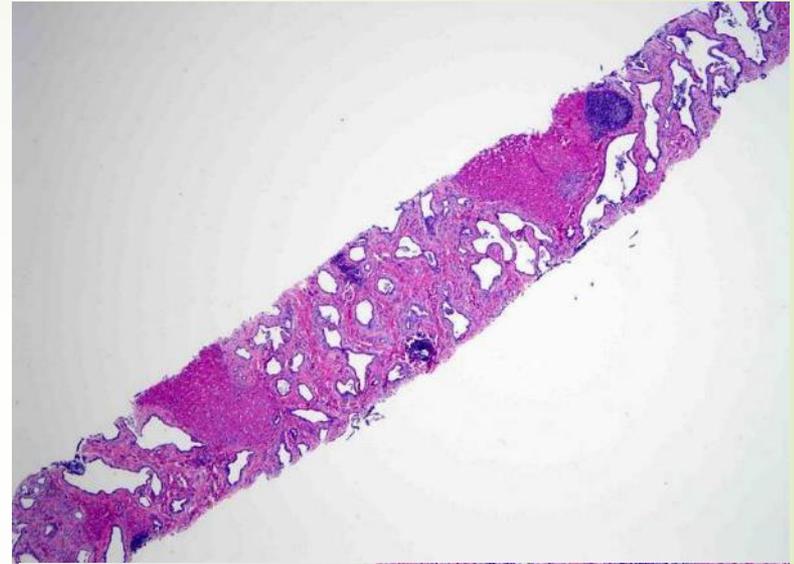
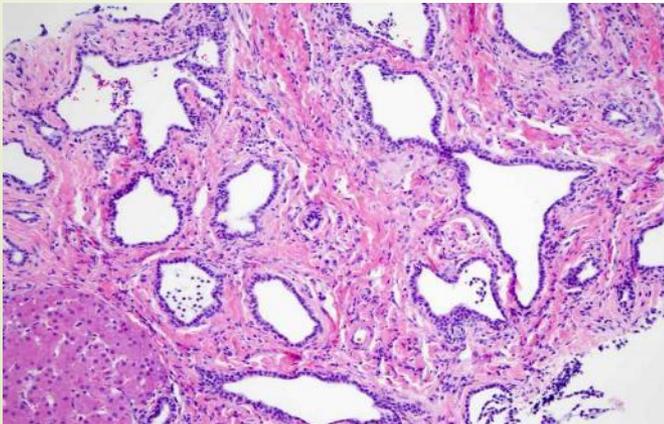


Case Example

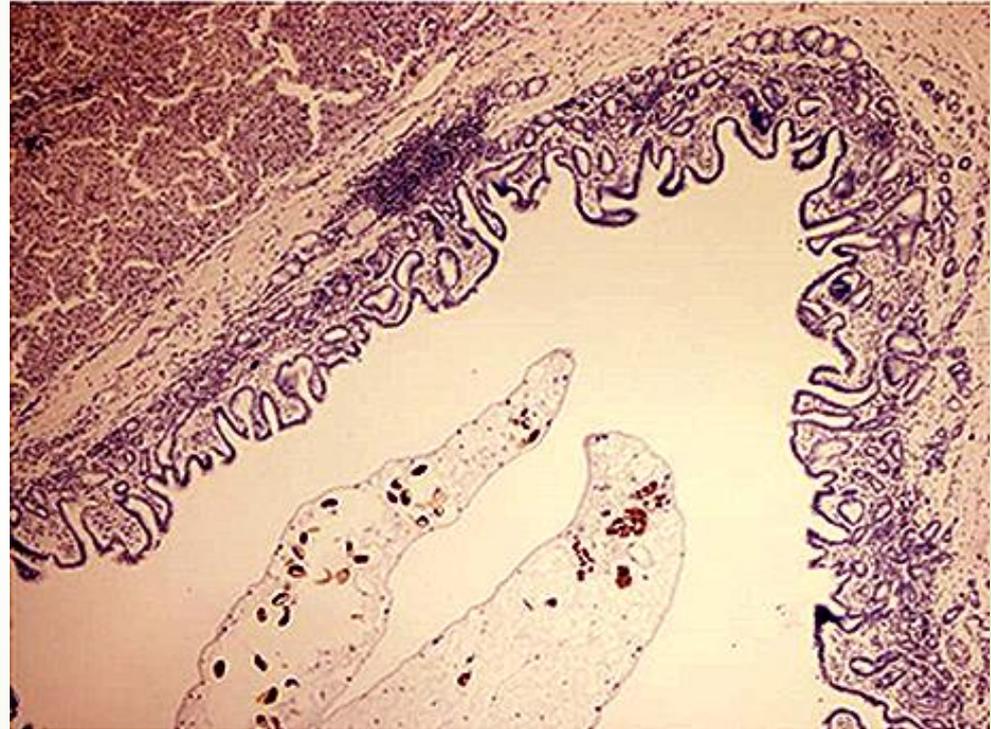
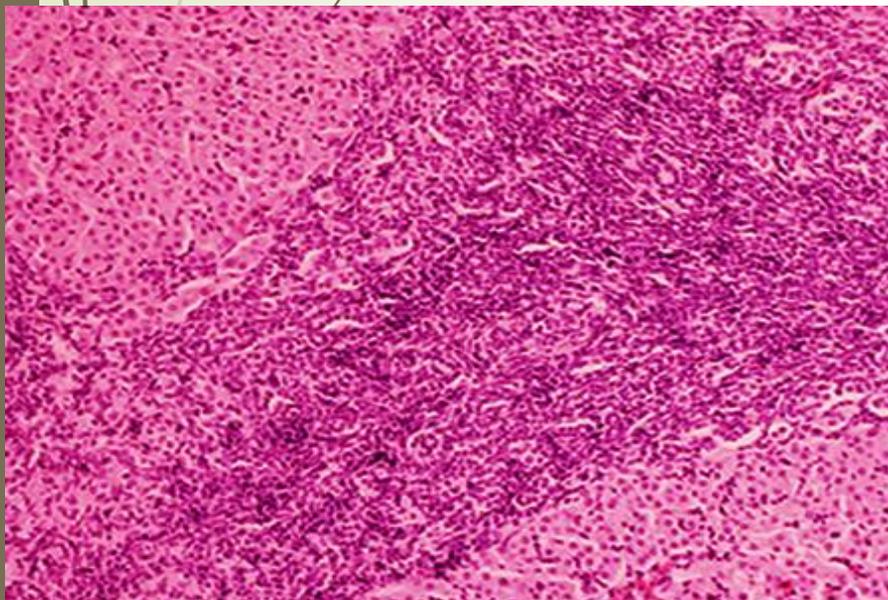
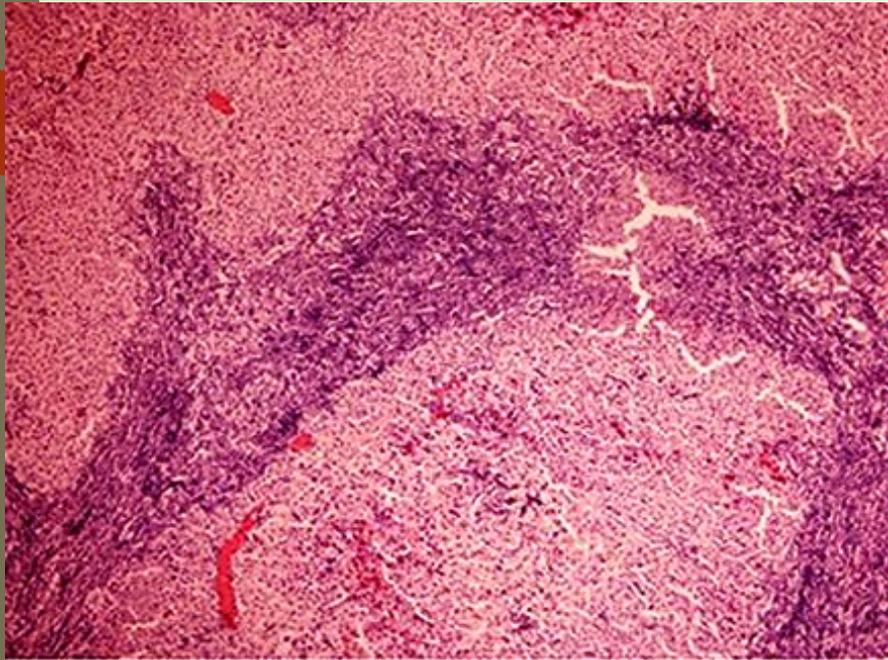
4 yo Domestic Short Hair, Male,
castrated

➤ Clinical signs

- Diffusely enlarged, inhomogenous liver on ultrasound,
- Elevated ALT/AST,
- Slightly low albumin,
- Ascites,
- Toxic neutrophilia.



Clinical Context



Differential diagnoses

- ▶ Extra-hepatic obstruction

- ▶ Vascular anomalies with biliary proliferation
 - ▶ Portosystemic shunts
 - ▶ Portal vein hypoplasia
 - ▶ Fibrous variant
 - ▶ A-V fistula

Ductal Plate Malformations

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ADPKD

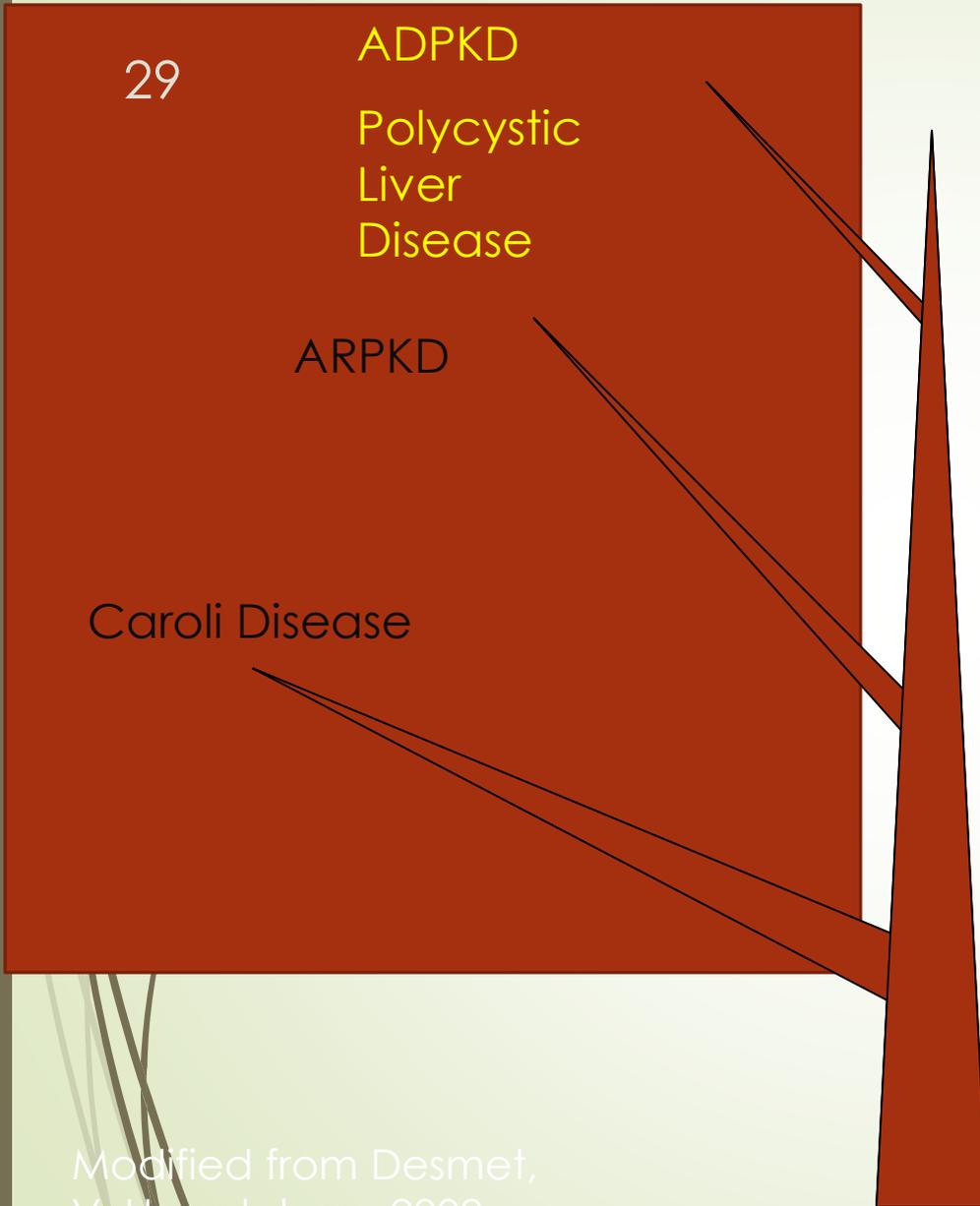
Polycystic
Liver
Disease

ARPKD

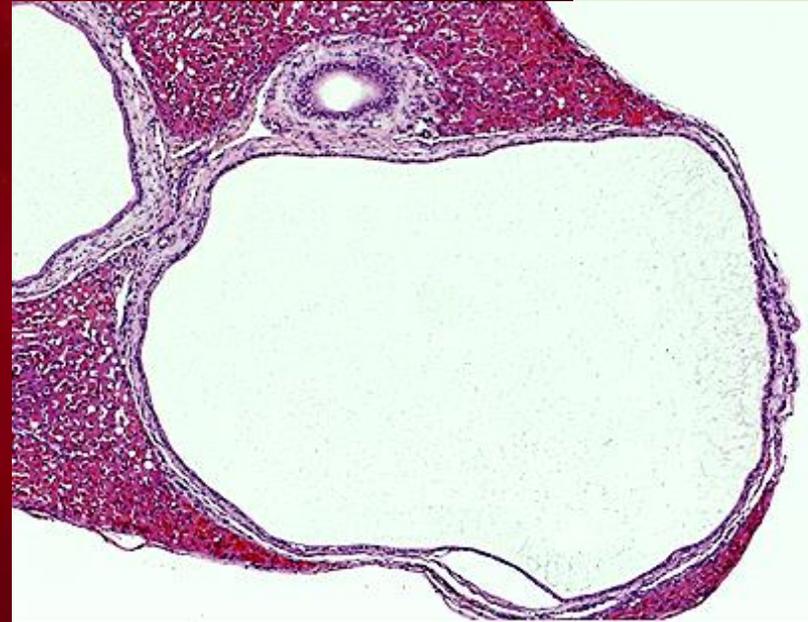
Caroli Disease

➤ With ectasia

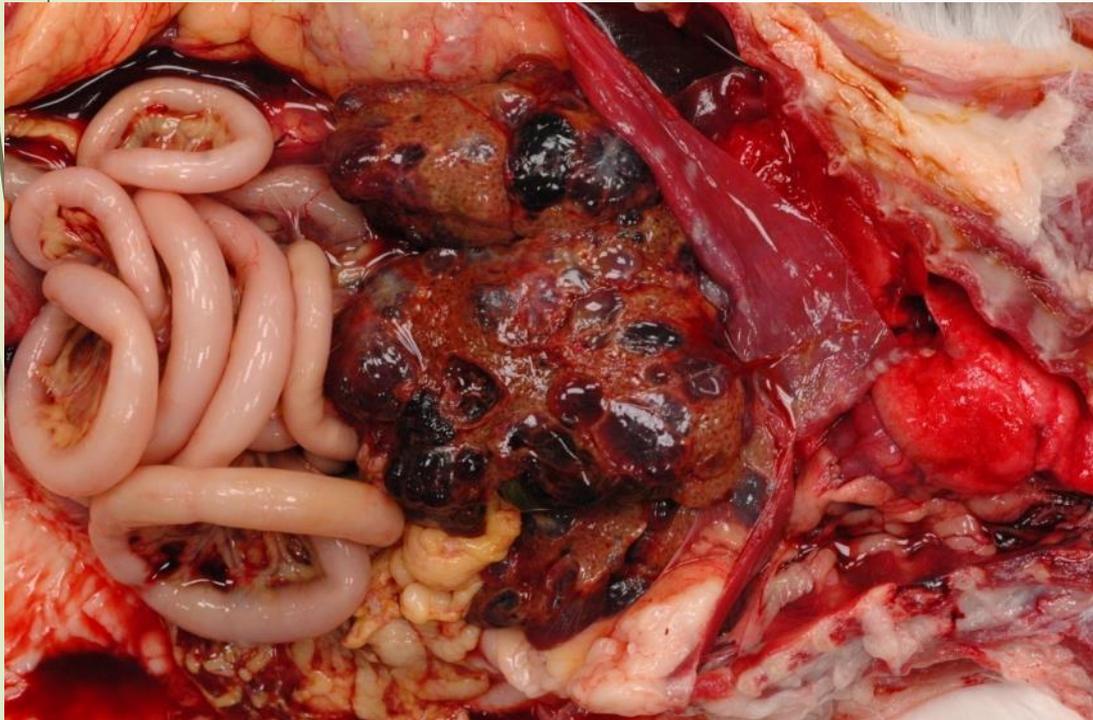
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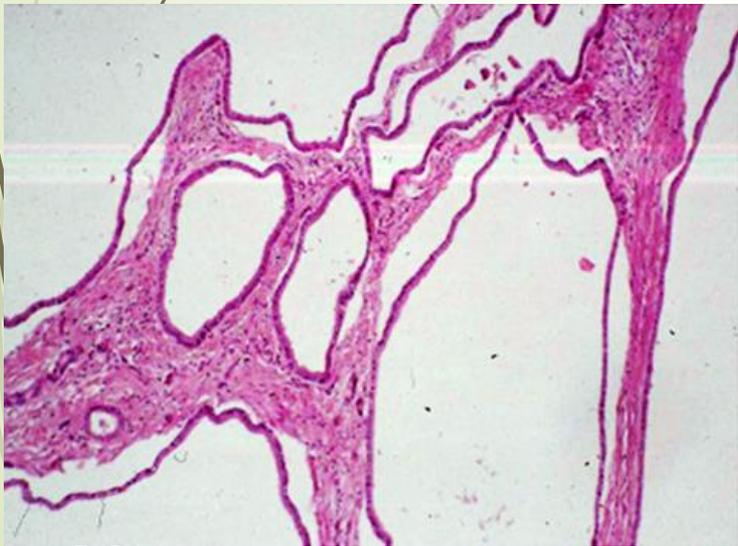
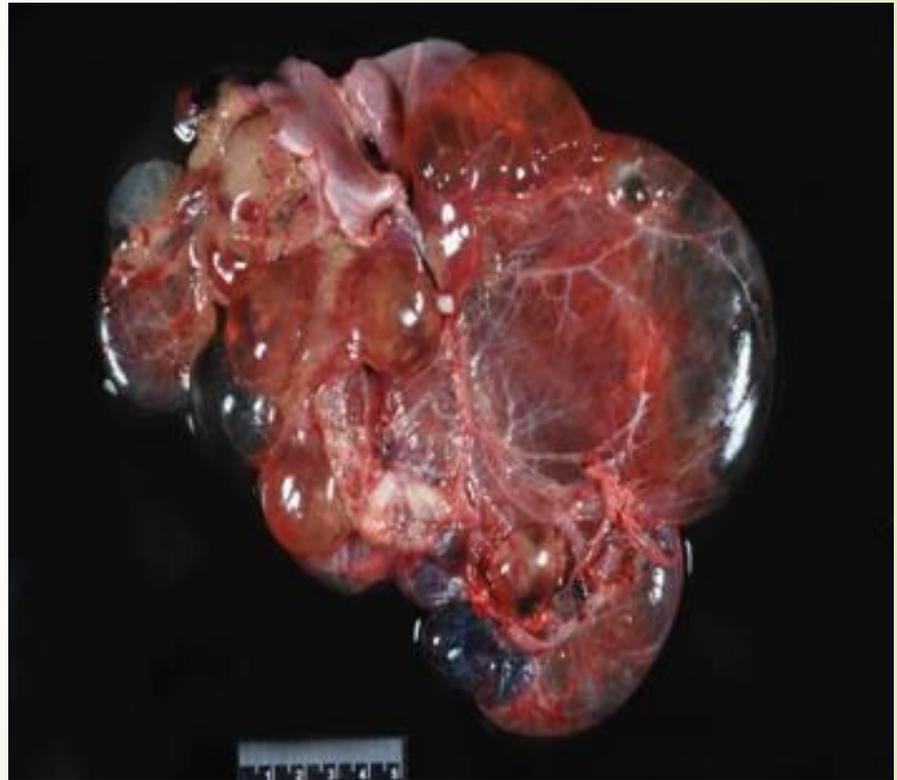
30 Solitary Biliary Cyst: Dog



Polycystic Hepatic Disease



- ▶ Cats: PDK1
- ▶ Autosomal dominant
 - ▶ Persian
 - ▶ Siamese
- ▶ Dogs
 - ▶ Cairn Terriers
 - ▶ West Highland White



Fel 08-1291 Kidneys
Polycystic Disease

When are a lion and a cat the same?

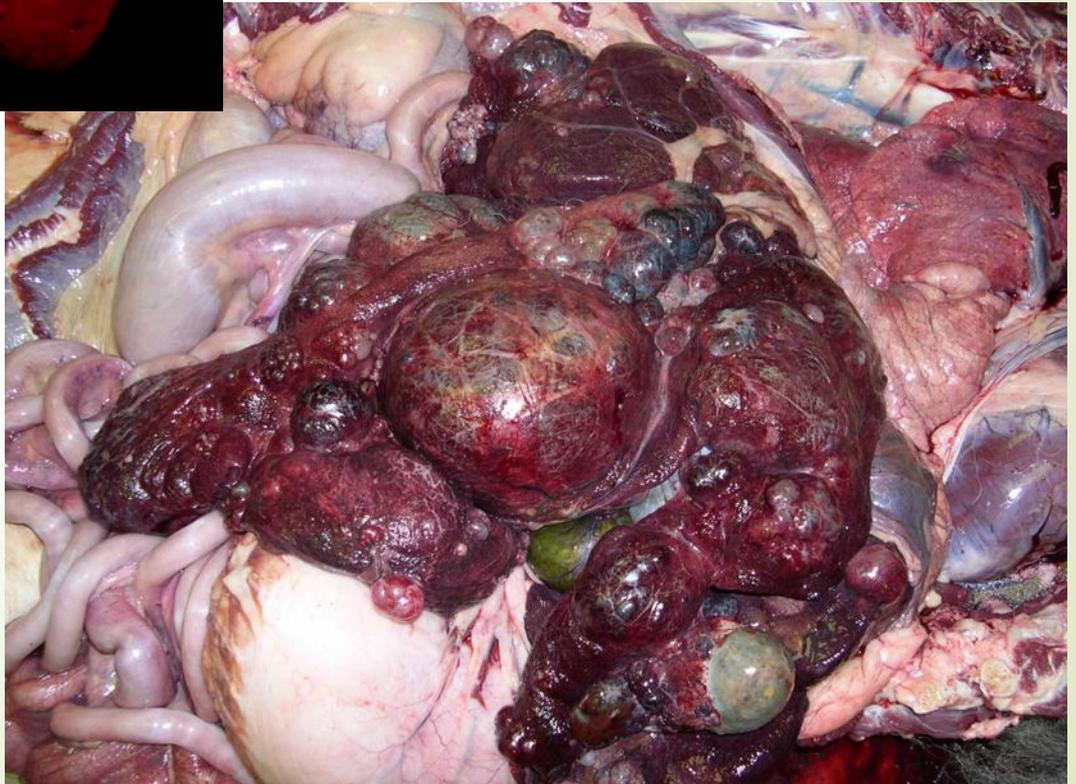
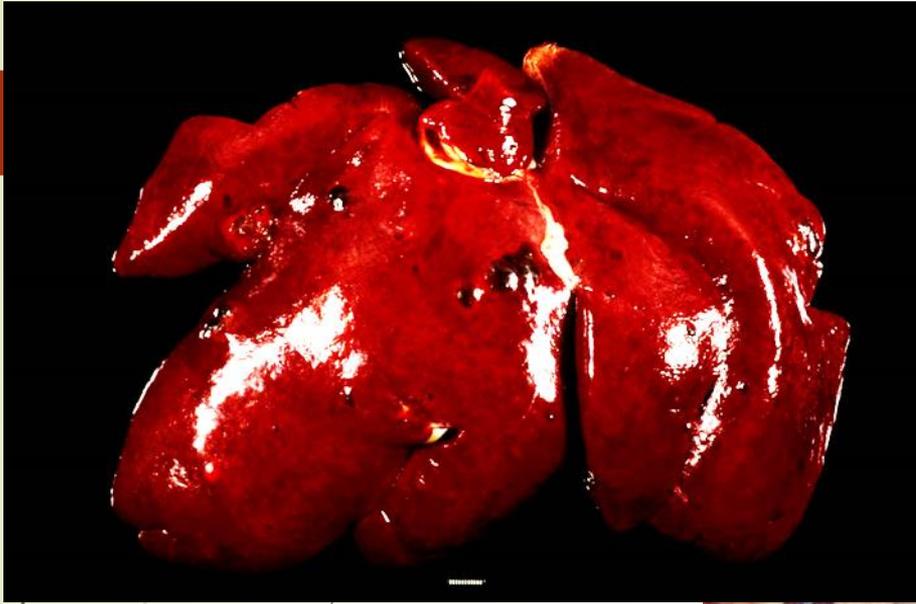
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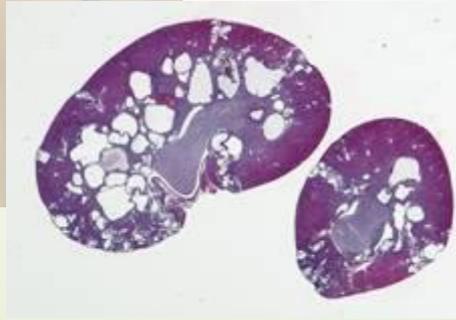
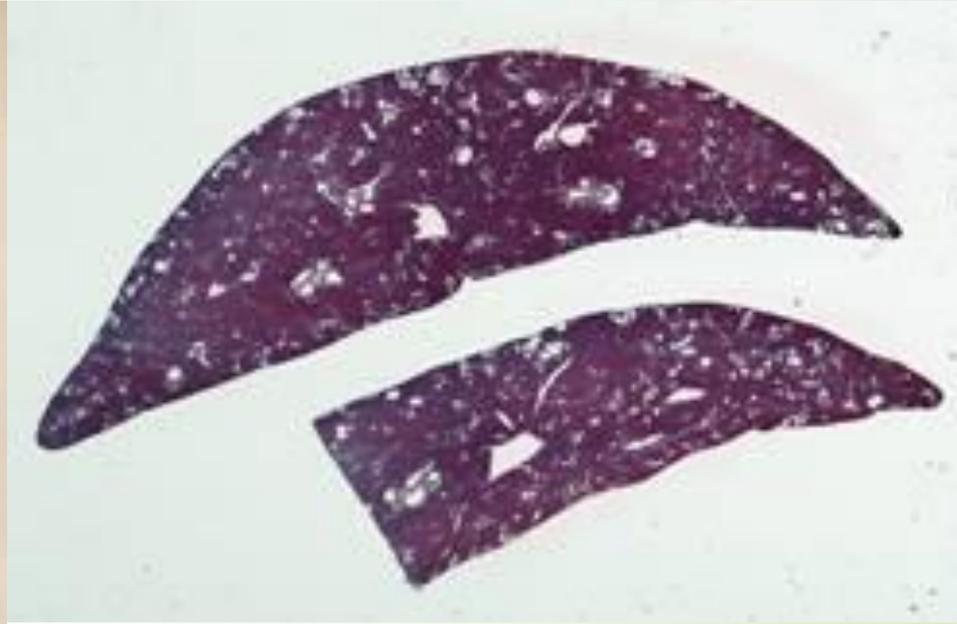
Wallpaperswide.com



Cattime.com



Polycystic Disease: PCK Rat Sprague-Dawley *Pkhd1*



Ductal Plate Malformations

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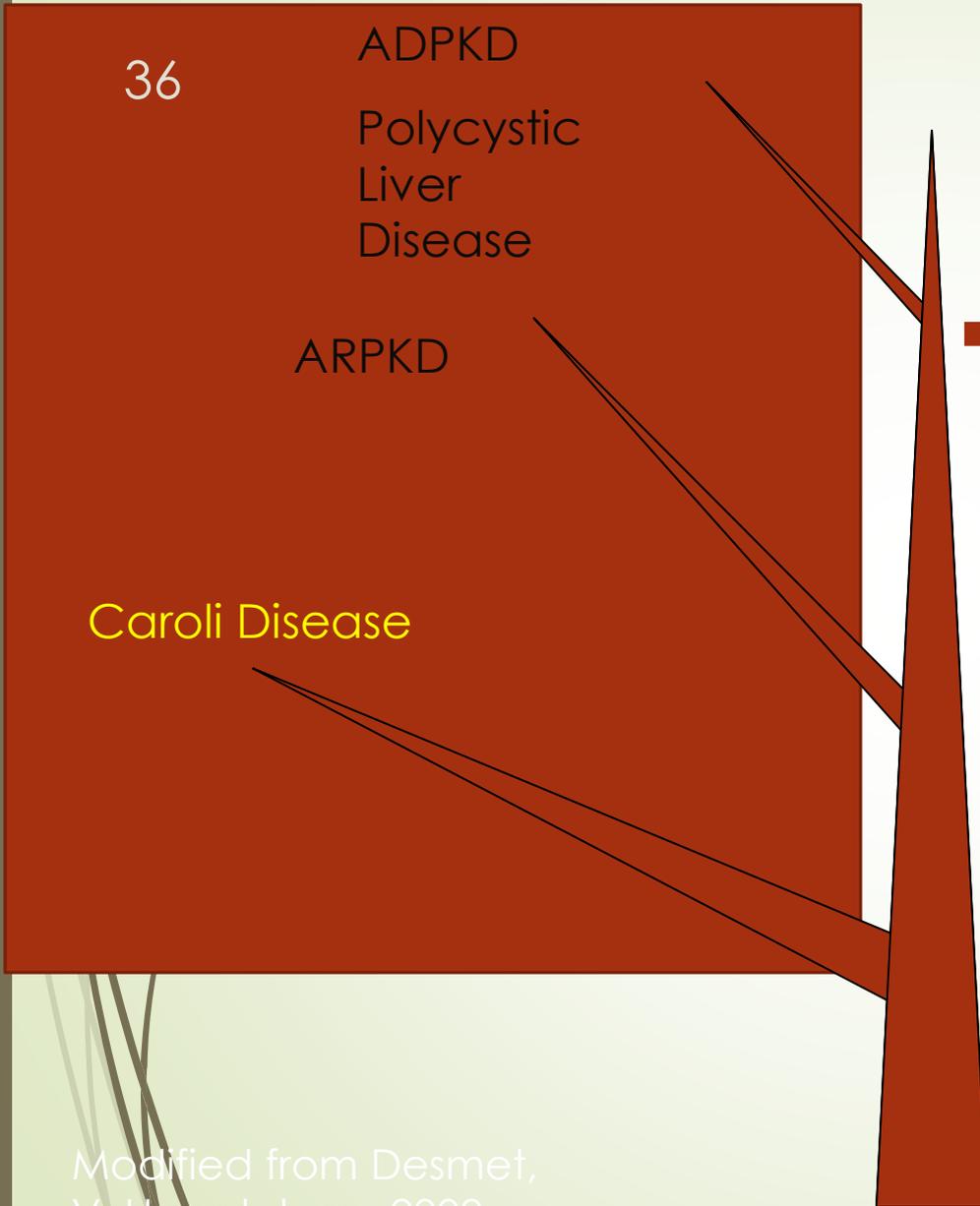
ADPKD

Polycystic
Liver
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ARPKD

Caroli Disease

➤ With ectasia



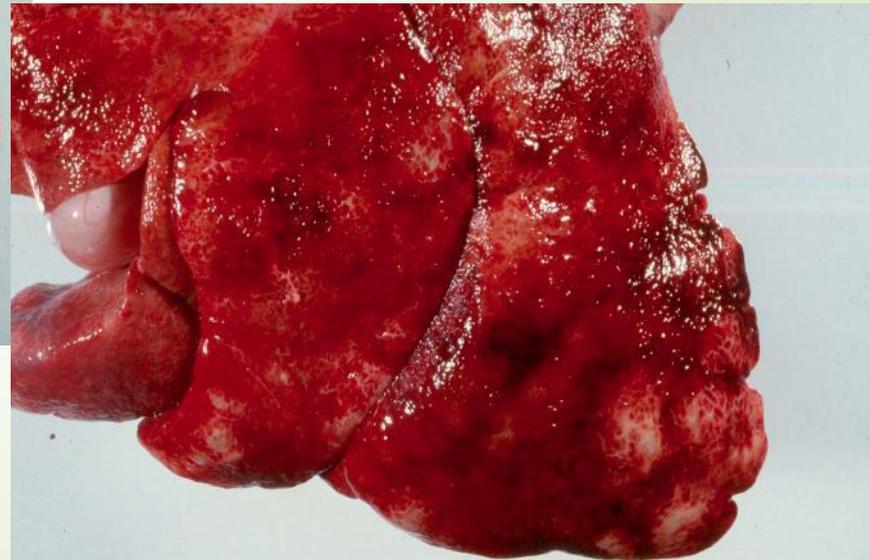
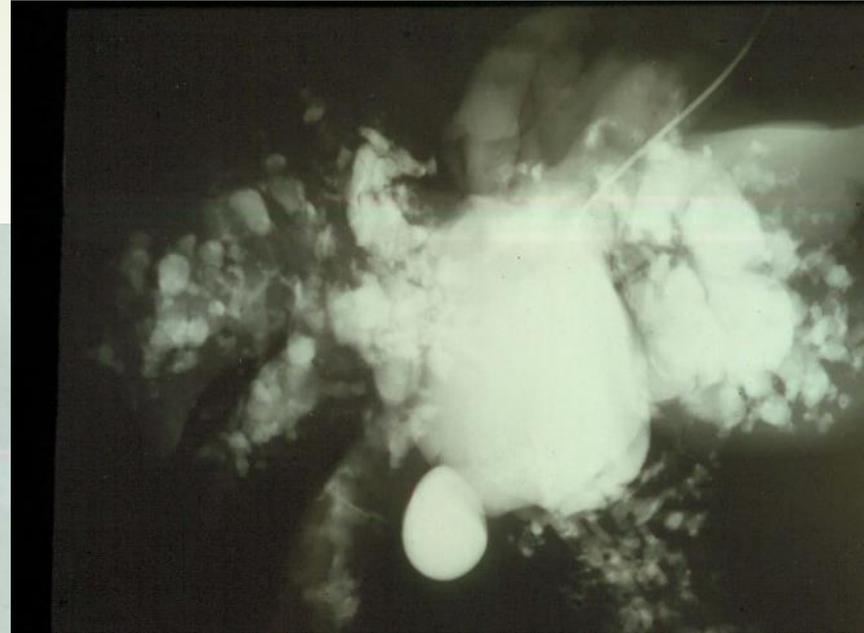
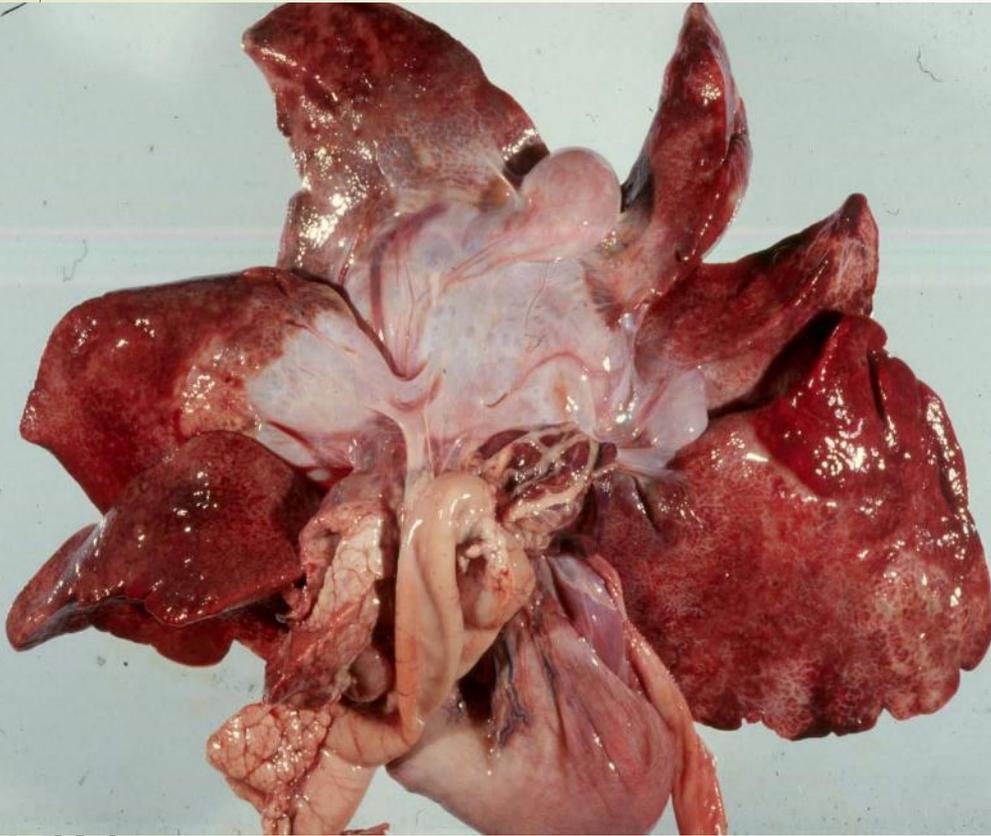
Caroli's disease

- Fusiform and saccular dilatation of the large bile ducts
- Patent Vater's papilla
- Kidneys: diffusely affected with radially arranged elongated cysts

Caroli's disease

Dog

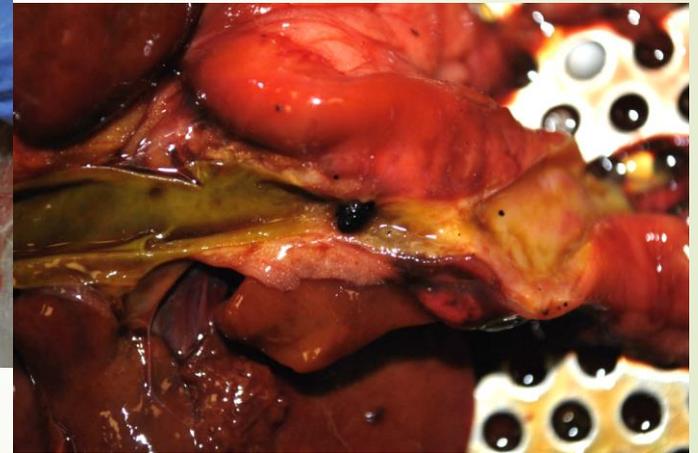
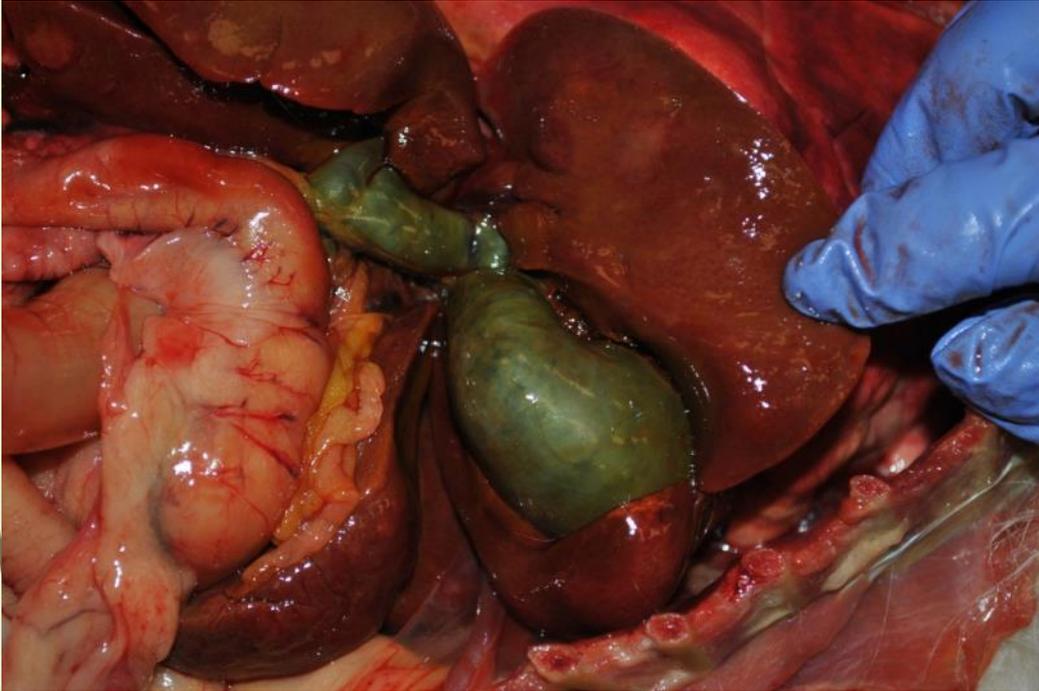
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T. van den Ingh

Last, RD, J S Afr Vet Assoc 77: 2006
Gorlinger, S et al. JVIM 17:2003

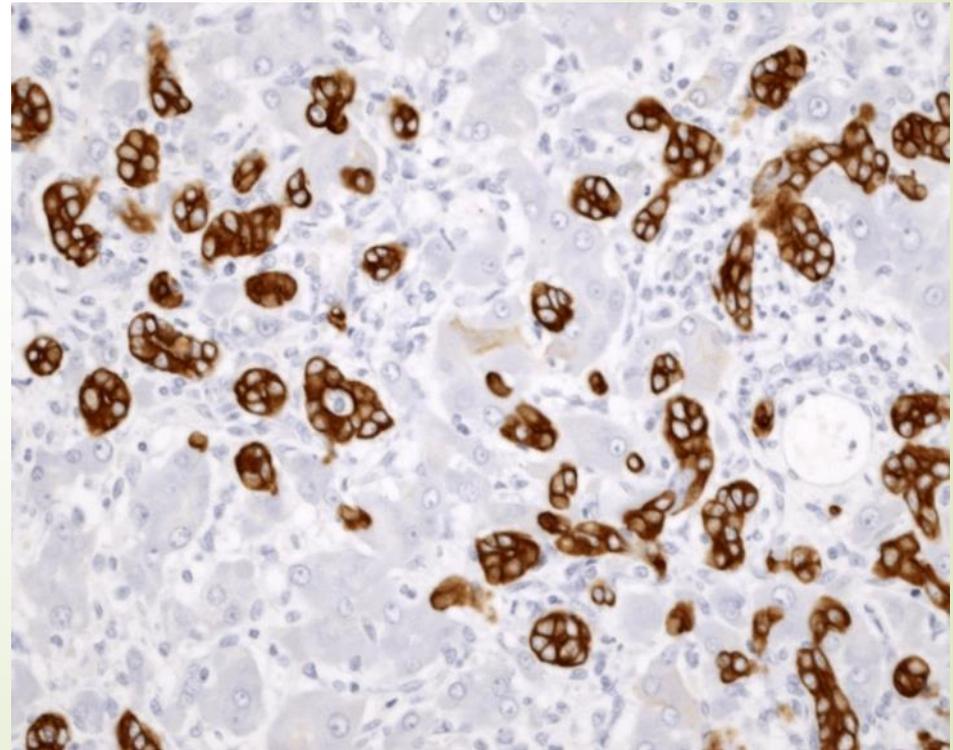
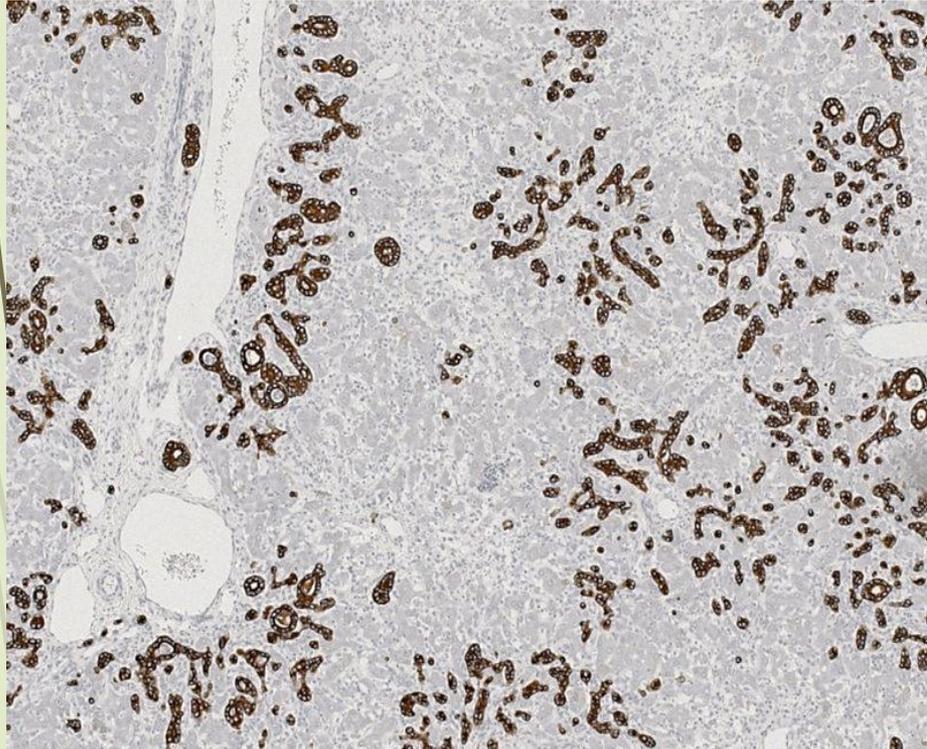
Differential: Obstruction



Differential Diagnosis: What is a Biliary Adenoma?

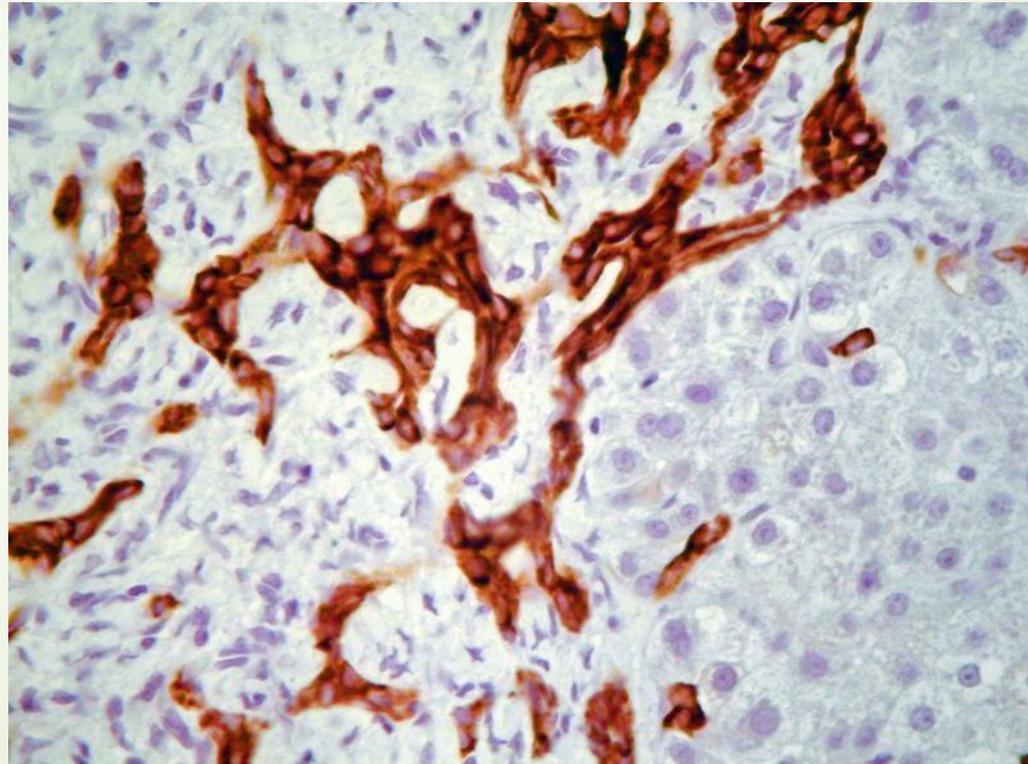
- Rare
- Localized metaplasia?
- Distended von Meyenburg complexes?
- Biliary cystadenoma
- “Benign Biliary Proliferation”

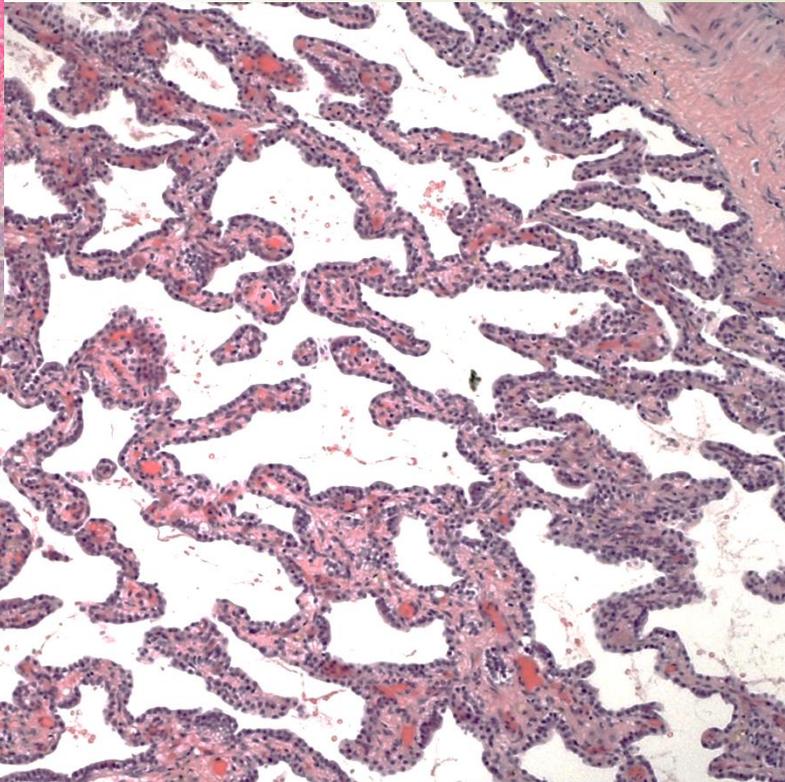
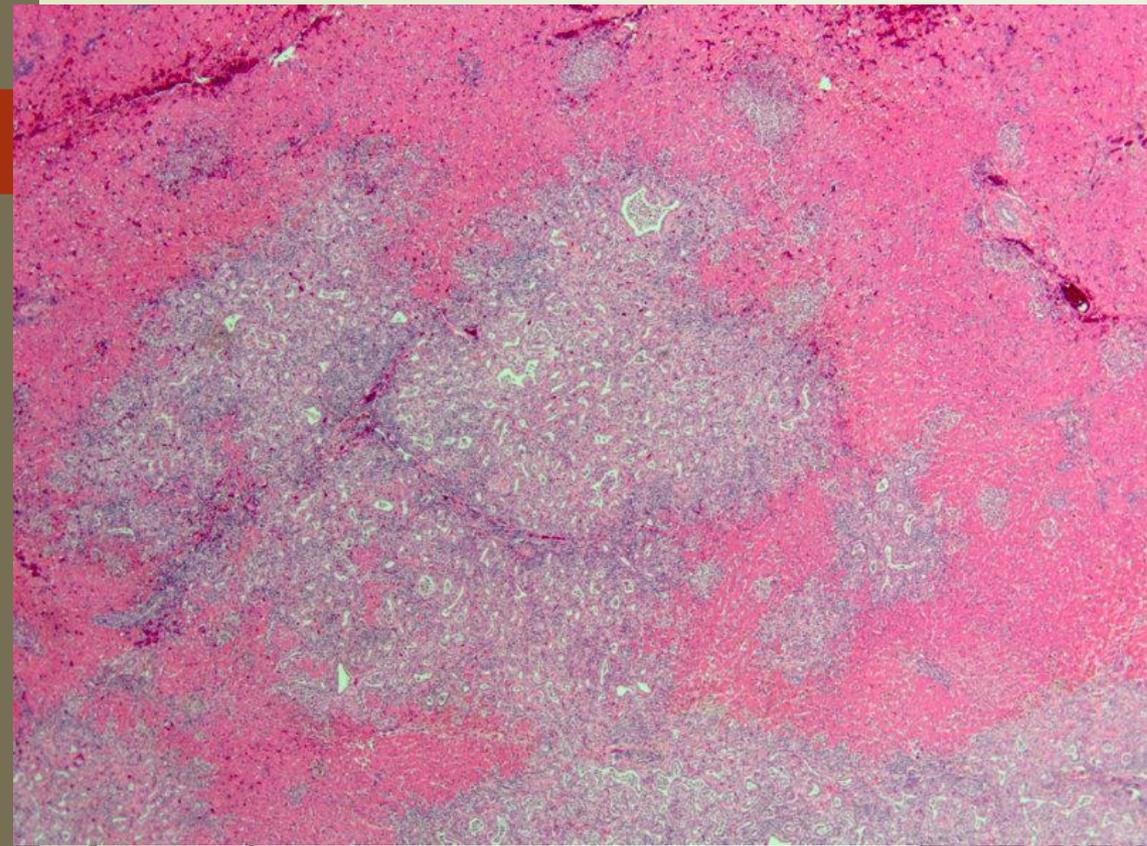
Differentiation



Metaplastic example

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Dedifferentiation and
re-differentiation?

Segmental abnormalities

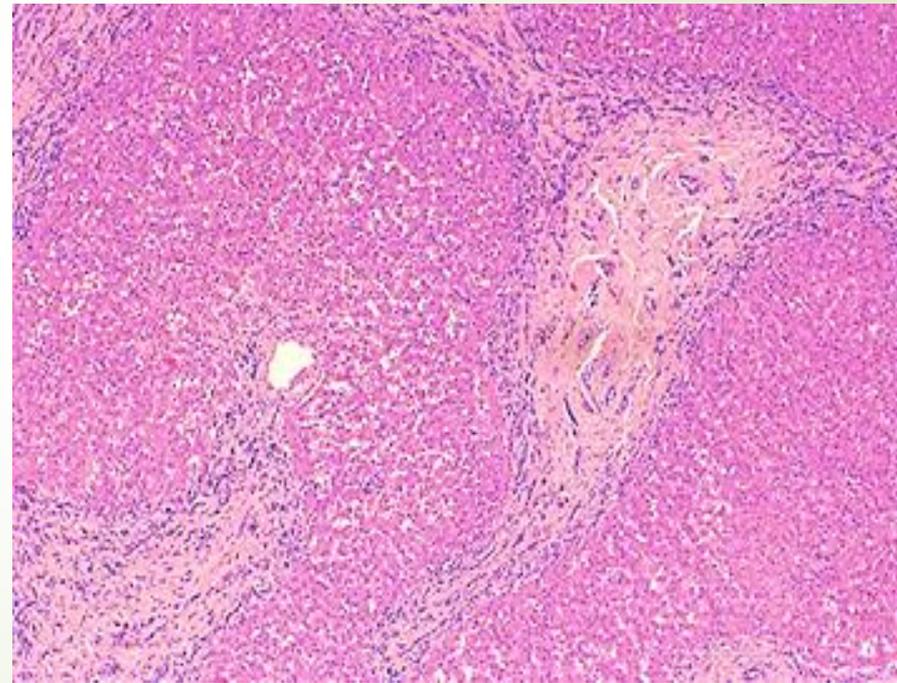
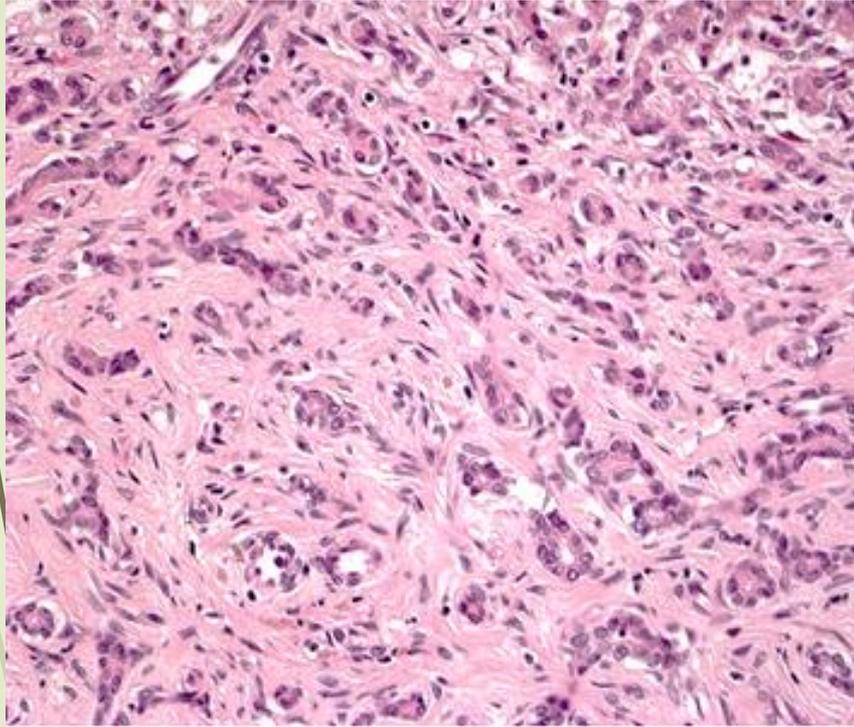
Biliary Atresia: Canine

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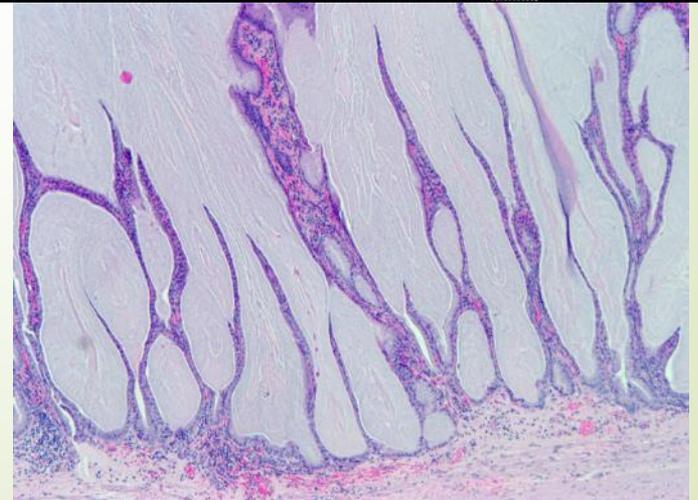
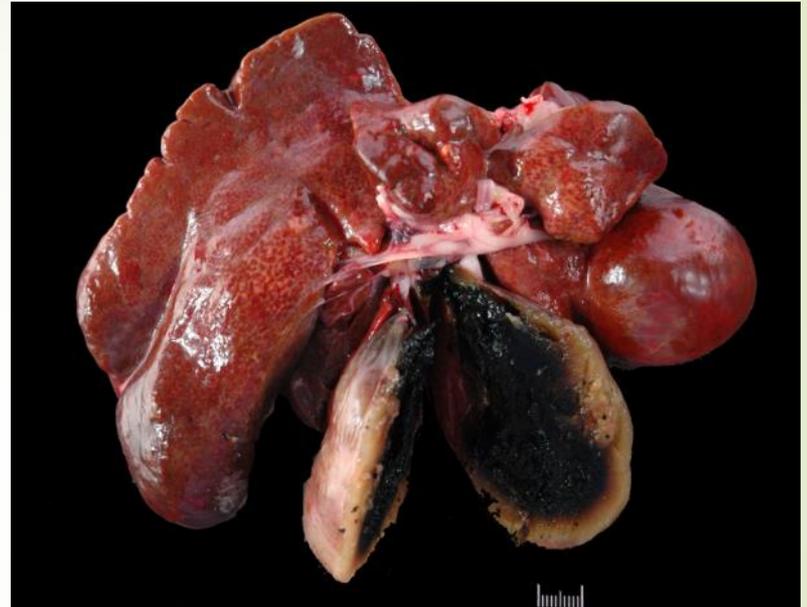


Dr. M. Stalker, U. of Guelph

Biliary Atresia

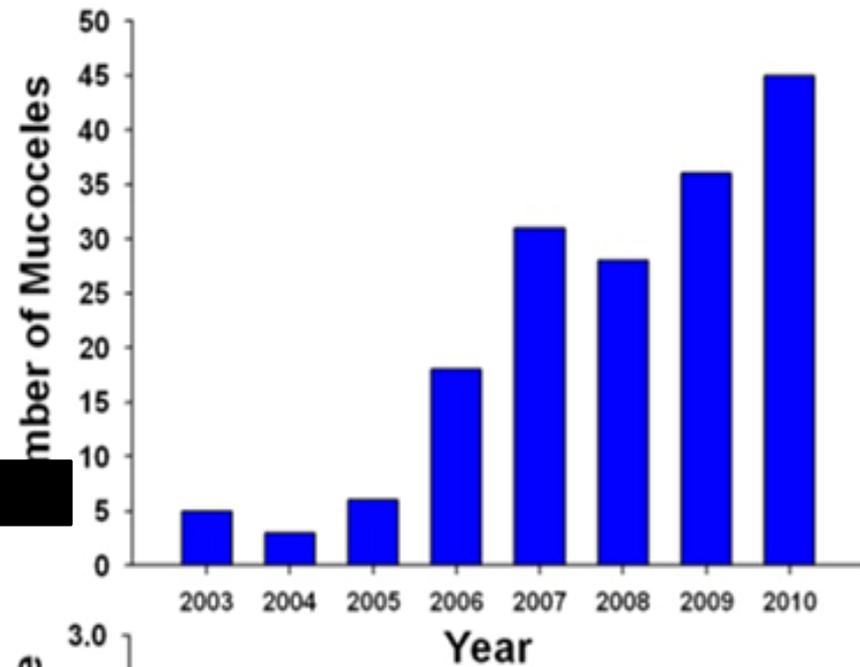


Gallbladder Mucocoele



Canine Gall Bladder Mucocoele

- Rare 10 years ago
- Common biliary disorder today
- ~20% mortality with surgery



Cause(s)

48

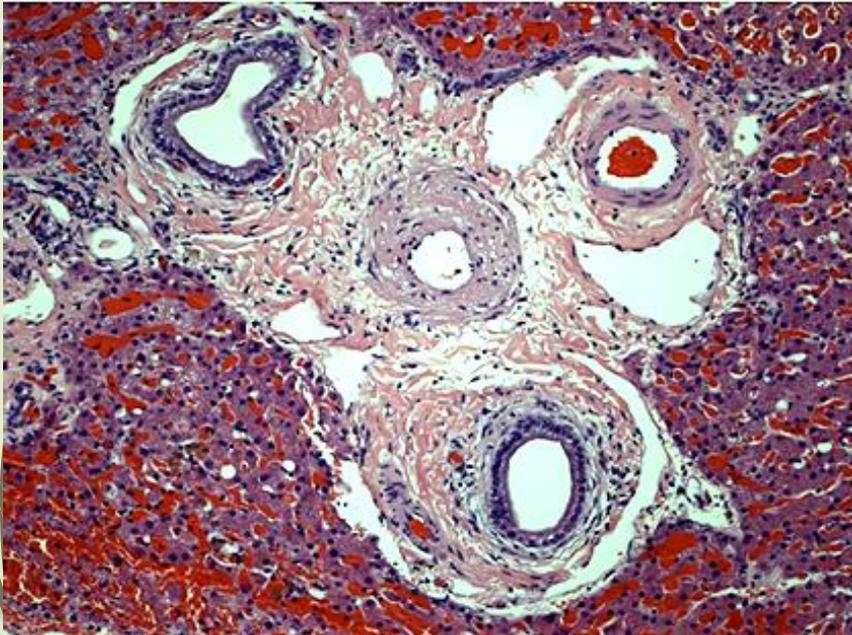
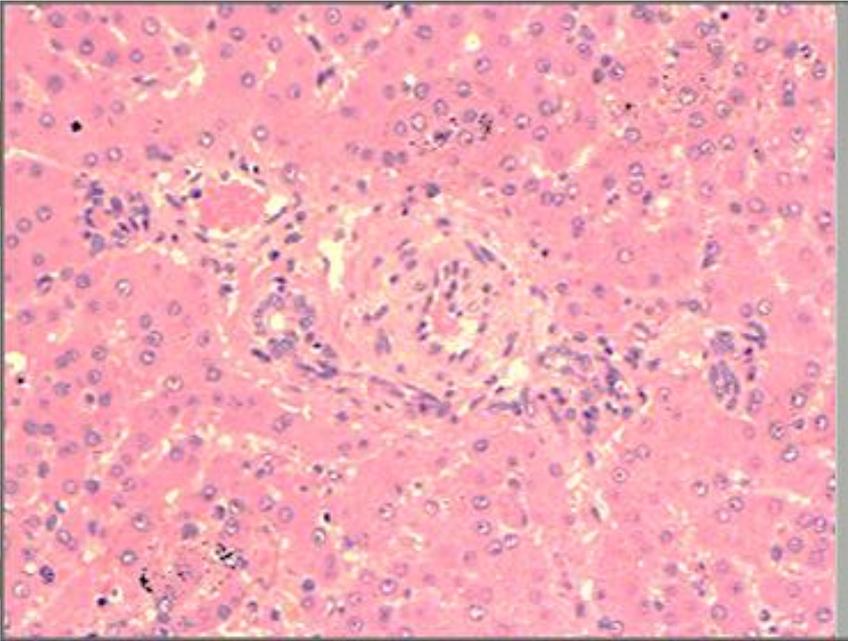
- Breed association
 - Shetland Sheepdogs
 - Miniature Schnauzers
- Transporter mutation?
 - ABCB4 (mdr-3) insertion mutation
 - No homozygous mutants
- Micelle formation
 - Phosphatidylcholine flippase
- Drug exposure?

- Evaluated 88 dogs
- Roughly equal distribution of insertion in affected and normal dogs.
- Complex pathogenesis

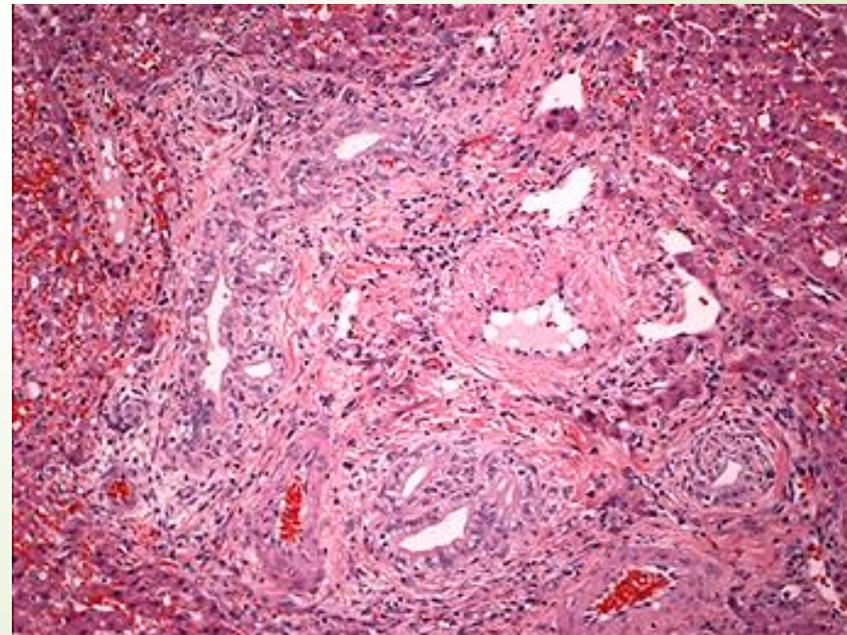
Causes

- ▶ Endocrine status?
 - ▶ Cushing's Disease
 - ▶ 29-fold increased risk
 - ▶ Other steroids
- ▶ Hyperlipidemia
- ▶ Diet?
- ▶ Therapeutic drugs?

Mucocoele: Dog



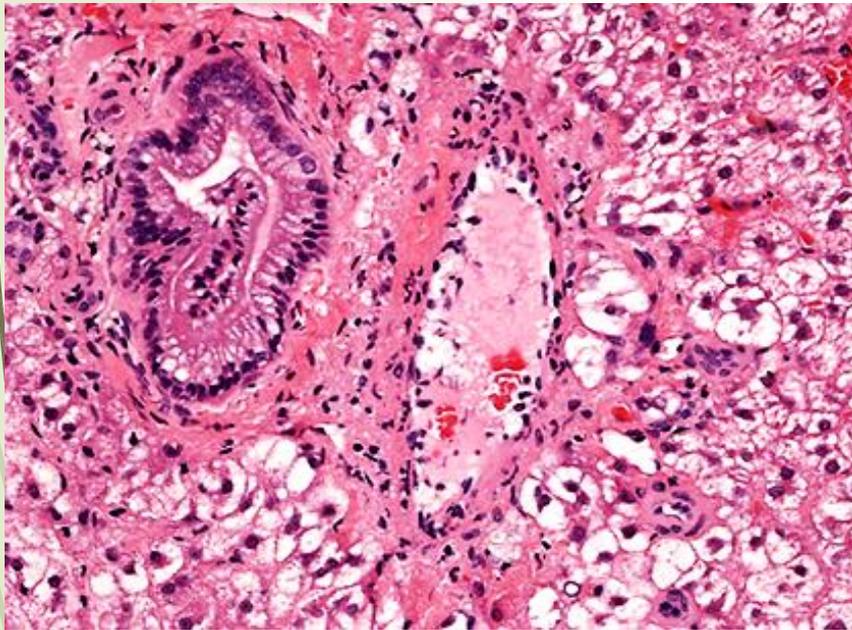
Dog 1



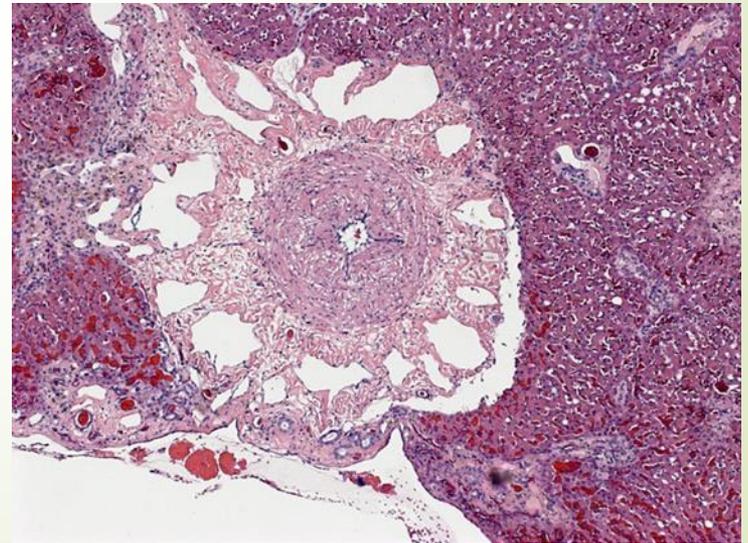
Dog 2

Histologic change

- Loss of portal vein profiles.



- “Fuzzy” Portal vein
- Ménage à foie



Veterinary Congenital Biliary Tree Diseases

➤ Congenital

➤ Ductal Plate anomalies

- Congenital cystic diseases
- Acquired metaplastic ductular changes
 - Adenomas

➤ Acquired

➤ Gall Bladder

- Mucocoele
- Parenchymal effects