Pediatric Liver Disease

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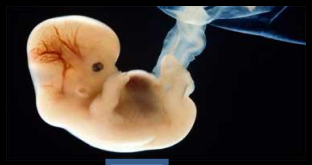
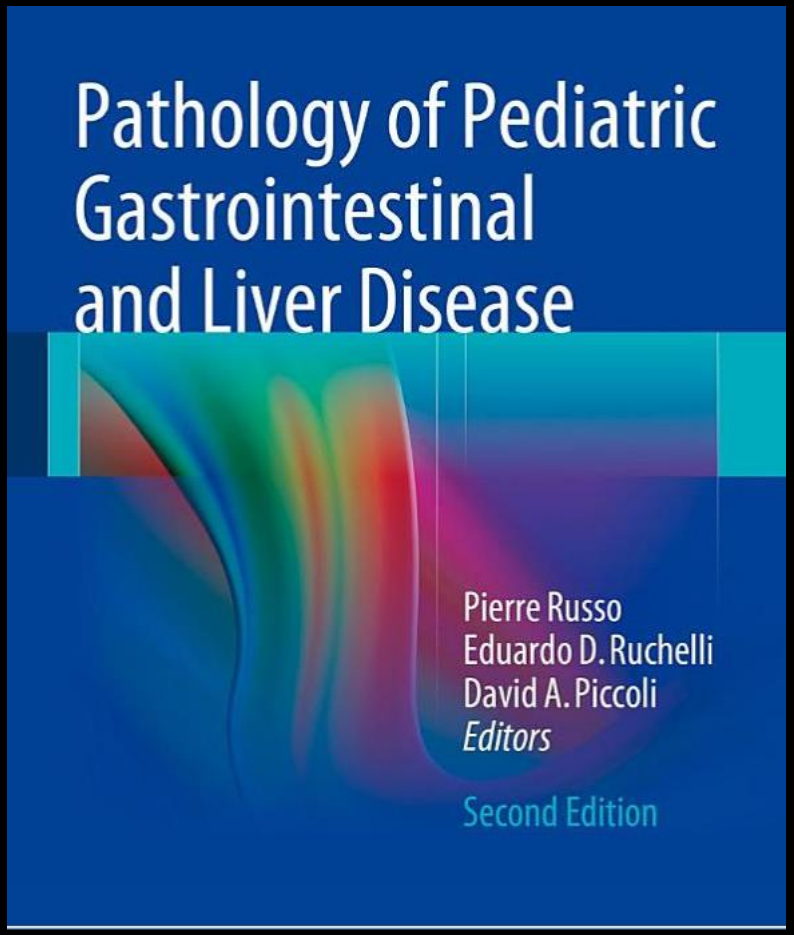
Disclaimer: I have no conflicts of interest, financial interests or affiliations with any companies that might profit from this presentation.

Scope of Pediatric Pathology



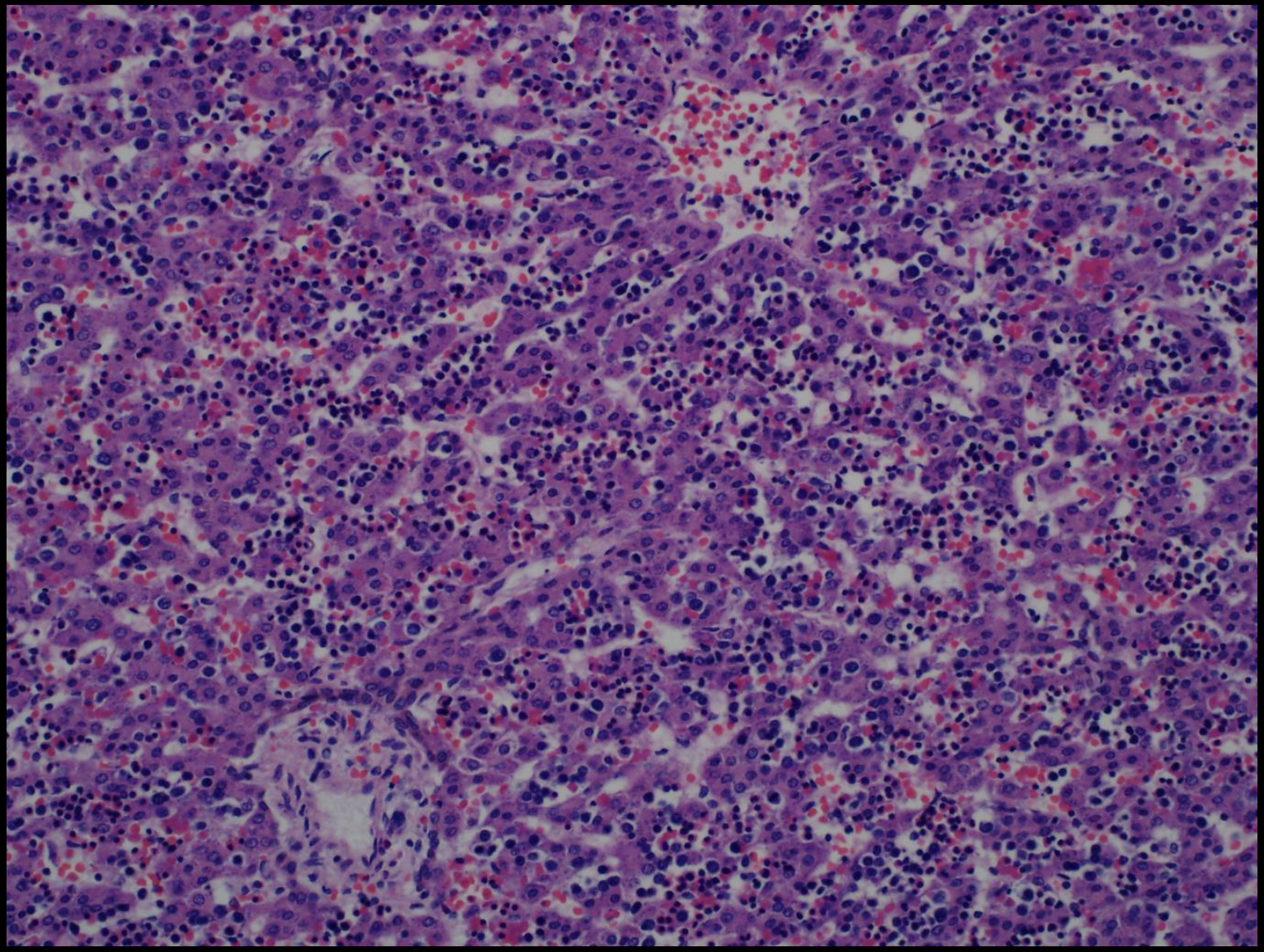


271 of 699 pages are devoted to Liver

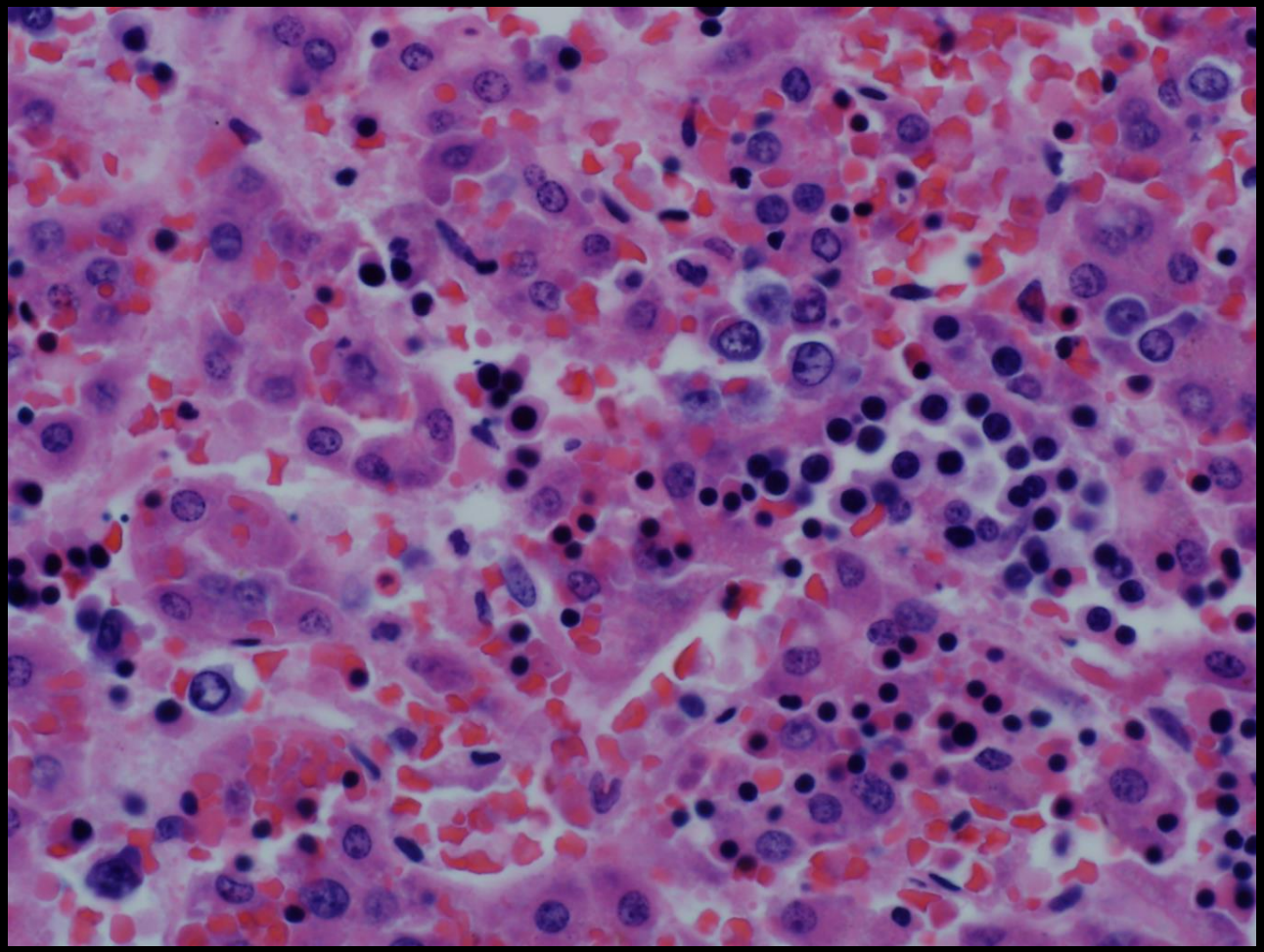
Good first stop to get an overview before consulting the literature.

Certainly not comprehensive in detail rich subjects like metabolic disease.

- Developmental
- Fulminant hepatic failure
- Cholestatic disease
- Infectious disease
- Metabolic Disease
- Neoplasia (benign and malignant)
- Others: drugs, toxins, vascular compromise, iatrogenic, idiopathic.

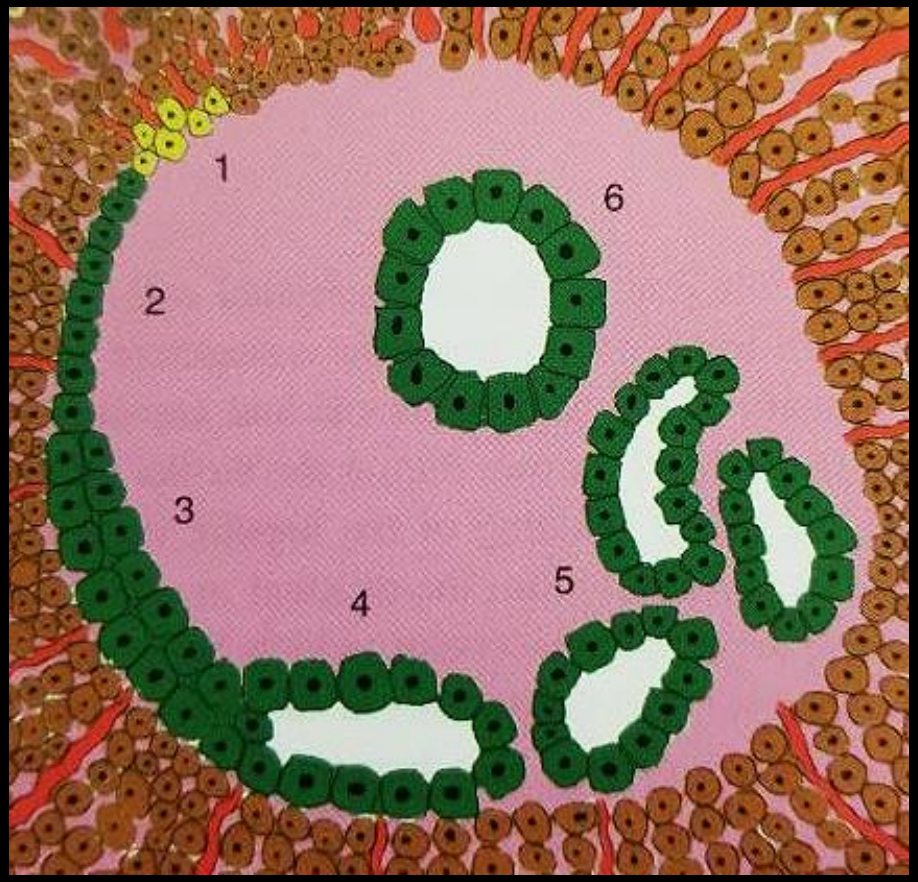


Normal Fetal Liver – Marked Erythropoiesis



Erythropoiesis – spectrum of maturation

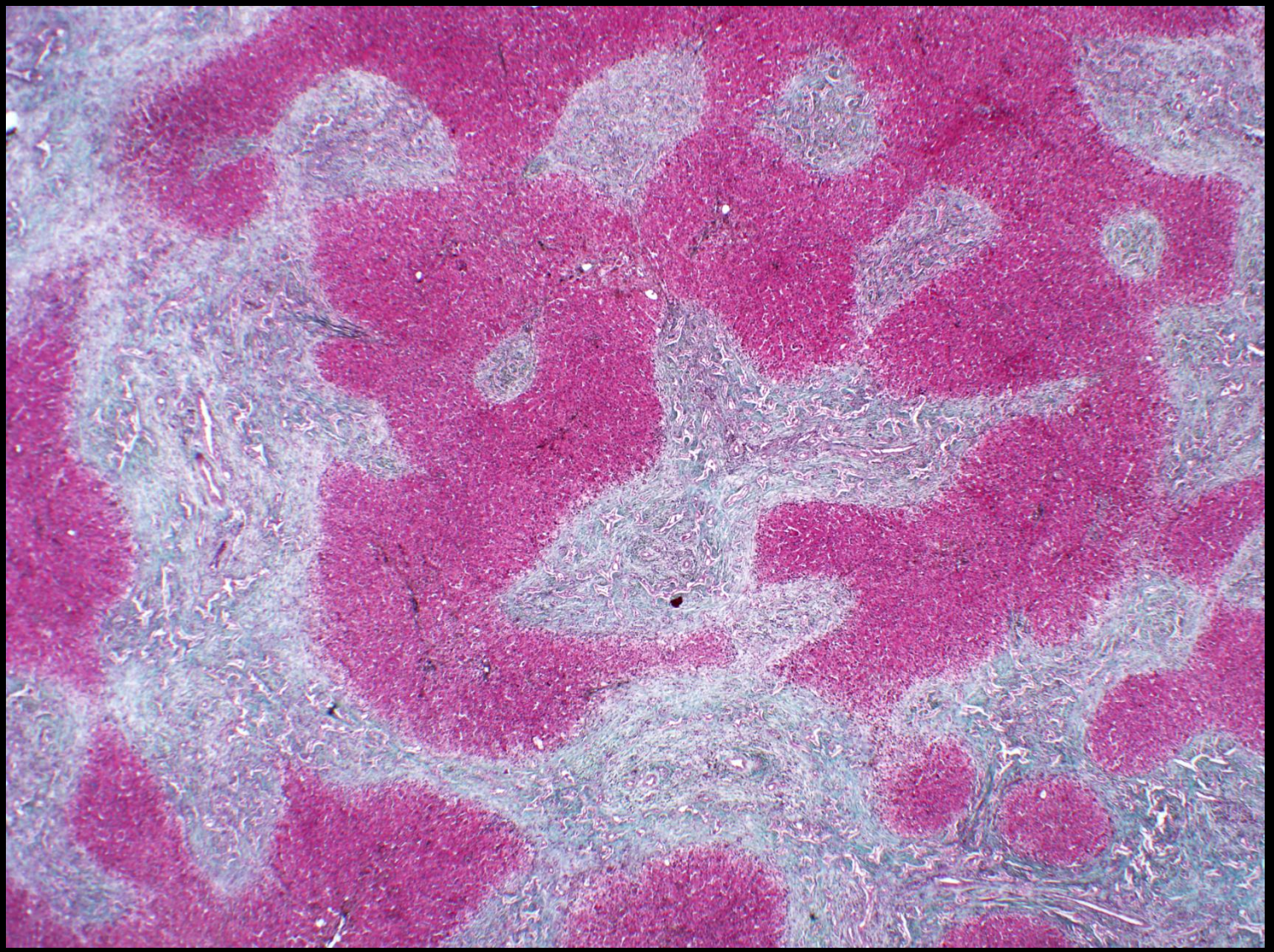
Begins around week 6-7, begins to taper in 3rd trimester of pregnancy, and very little remains at term.



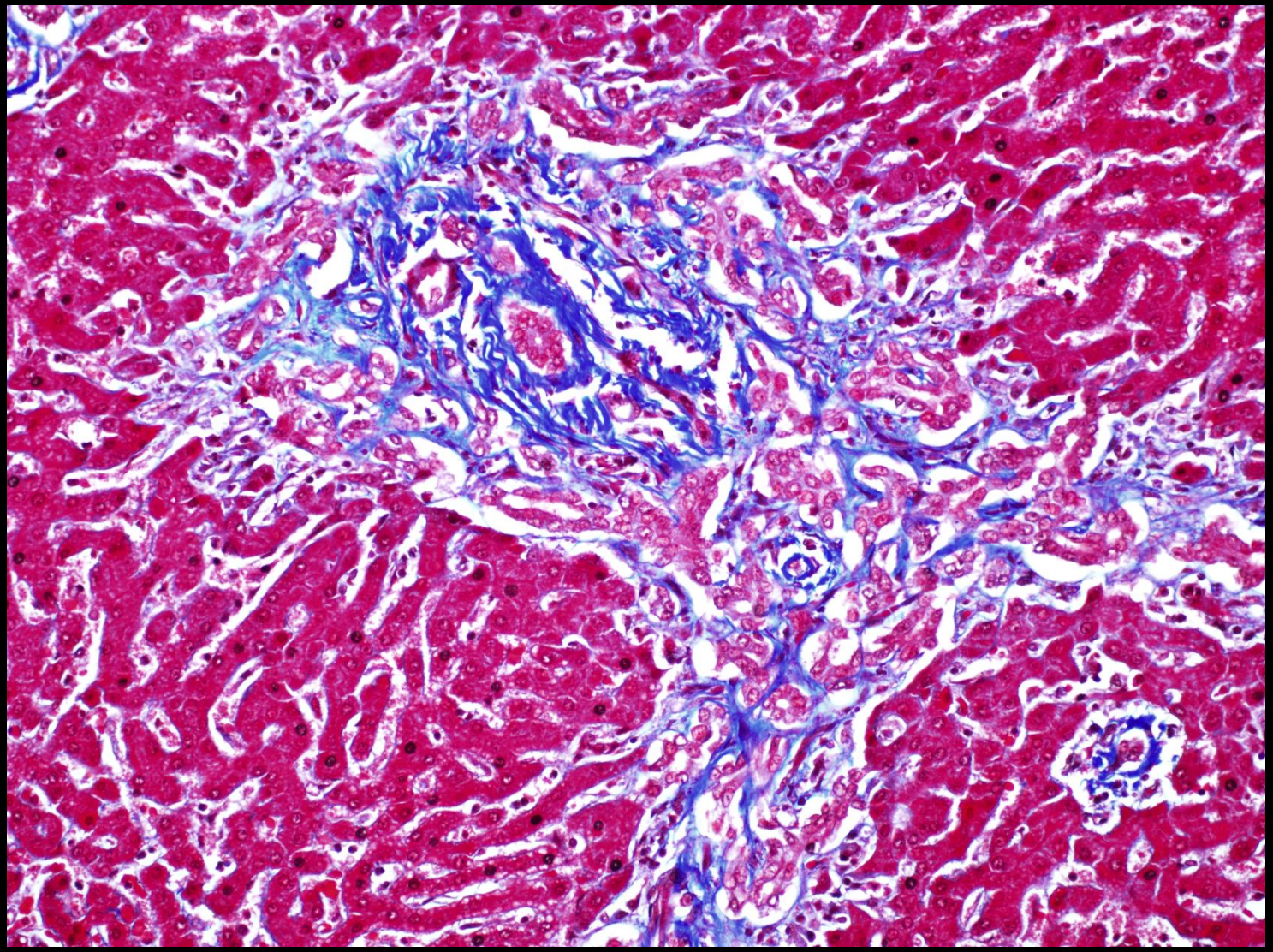
Bile Duct Development

1. Hepatoblasts differentiate into hepatocytes and ductal epithelium
2. Ductal plate forms.
3. Doubles
4. Forms lumen.
5. Migrates to center.
6. Fully mature bile duct.

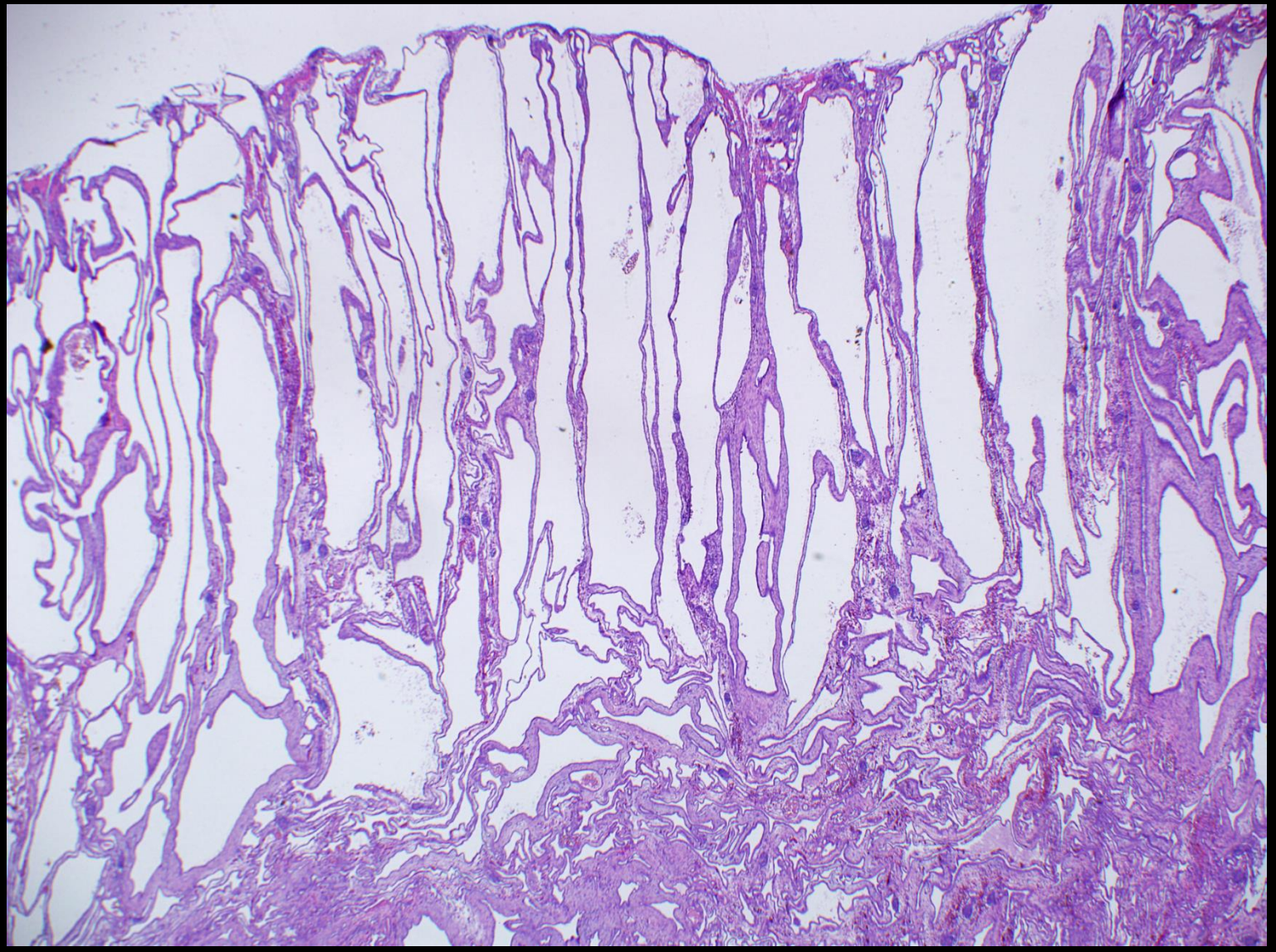
Pathology of Pediatric Gastrointestinal and Liver Disease, Russo et al, 2nd ed., pg 372.



Congenital Hepatic Fibrosis – geographic pattern



Congenital Hepatic Fibrosis – bile duct proliferation

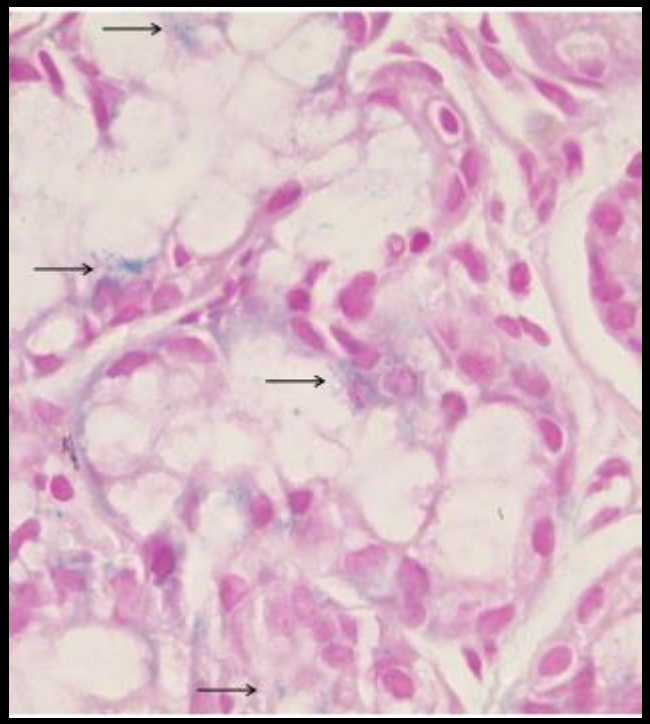


Infantile Polycystic Kidney Disease

- Fulminant hepatic failure

Neonatal hemochromatosis

- too coagulopathic to biopsy liver.
- minor salivary gland biopsy from lip.

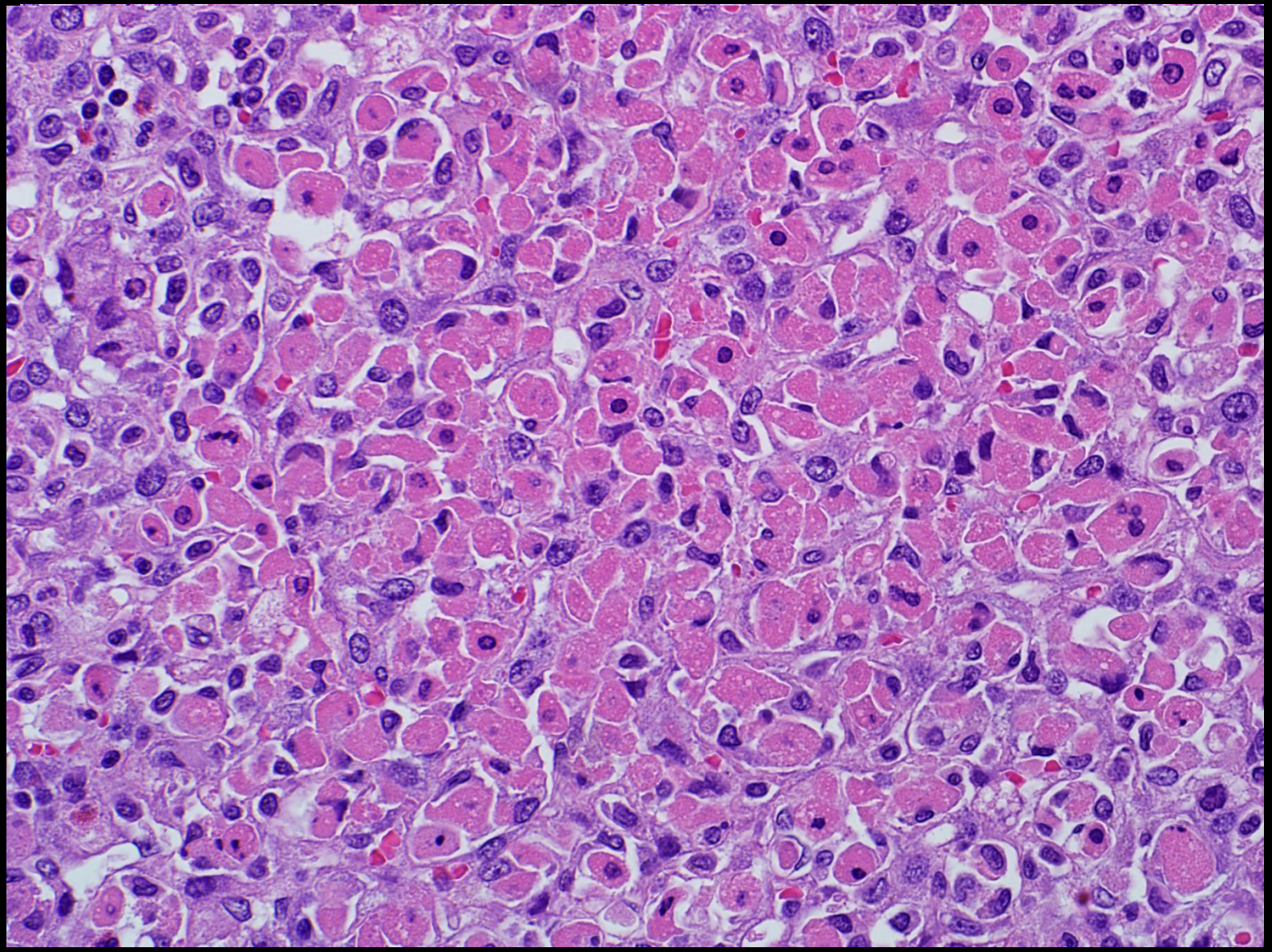


- Prussian blue iron stain shows tiny granules of iron.
- Normal is completely negative.
- Even the slightest bit of iron supports a diagnosis of neonatal iron storage disorder / hemochromatosis.

Journal of Oral and Maxillofacial Surgery, Volume 69, Issue 10, October 2011, Pages 2592-2594

- Fulminant hepatic failure
  - acute liver failure at 15 months, resolved in a week
  - acute liver failure at 16 months, resolved in a week
  - biopsy and NGS done at 16 months
    > nonspecific hepatitis.
    > 2 weeks later, mutations in NBAS gene

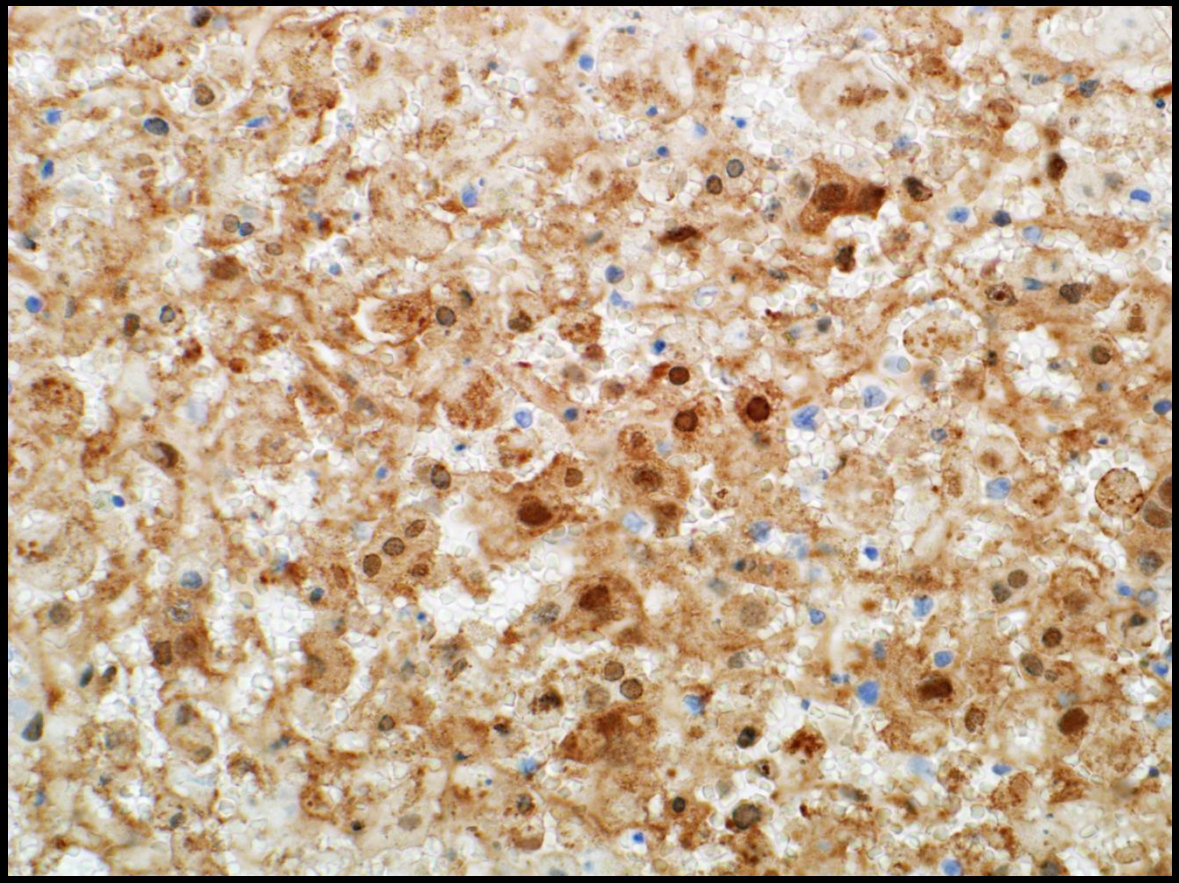
- Neuroblastoma Amplified Sequence
  - a cause of recurrent acute liver failure
  - diverse phenotype, often preceded by a fever



Global Hepatocyte Failure

- # Fulminant hepatic failure

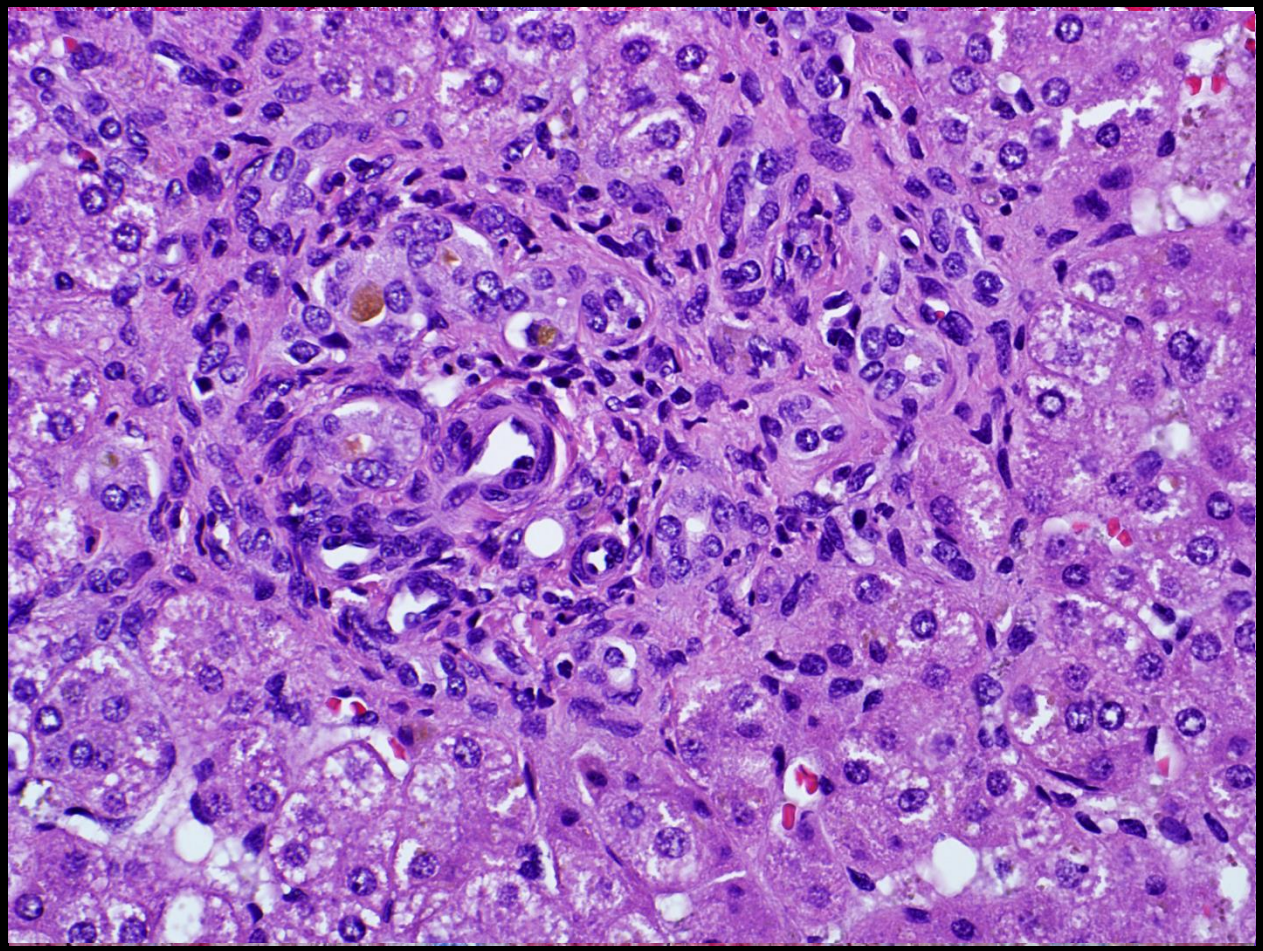
1. Teen with no prior medical history, on steroids for asthma, sudden death
2. Term infant died at 10 days of life after a week of indolent symptoms



Herpes simplex – confirmed by IHC

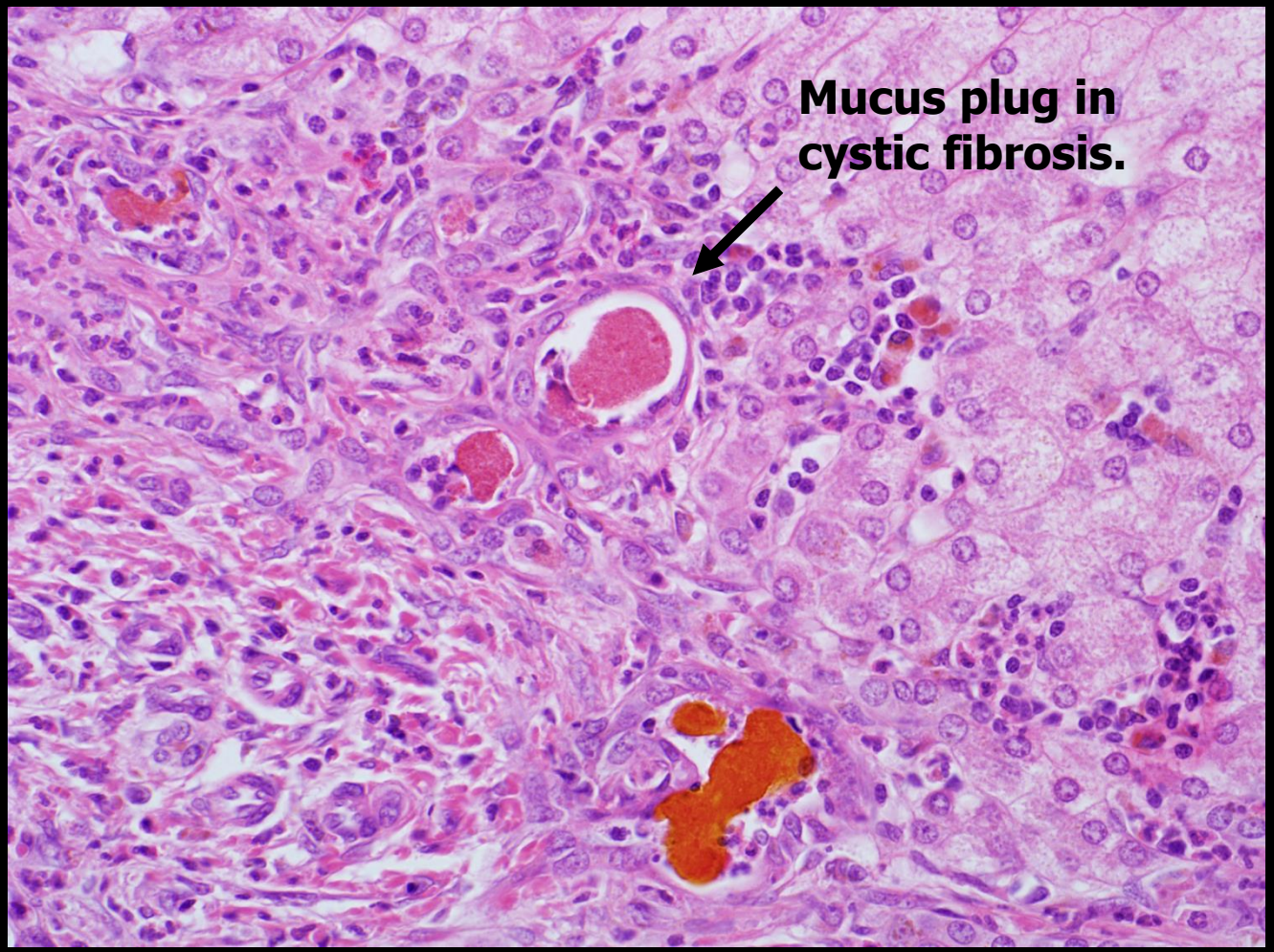
Cholestatic Disease

- broad differential diagnosis
- acholic stools, ? biliary atresia (extrahepatic biliary obstruction)



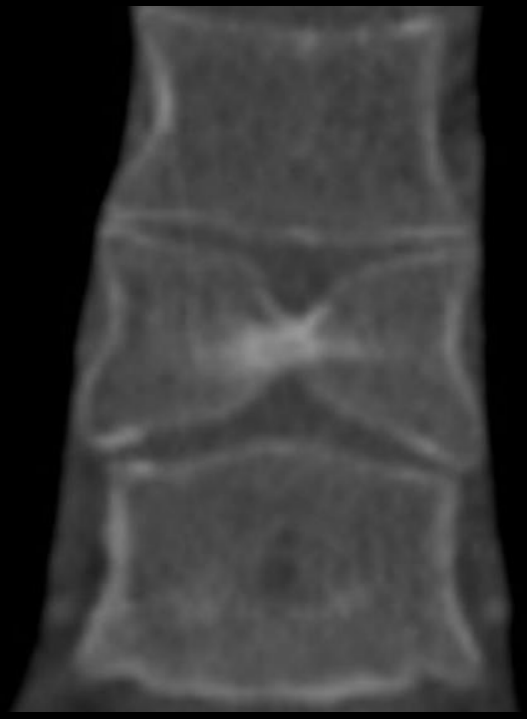
no expansion of portal areas, bile duct plugs

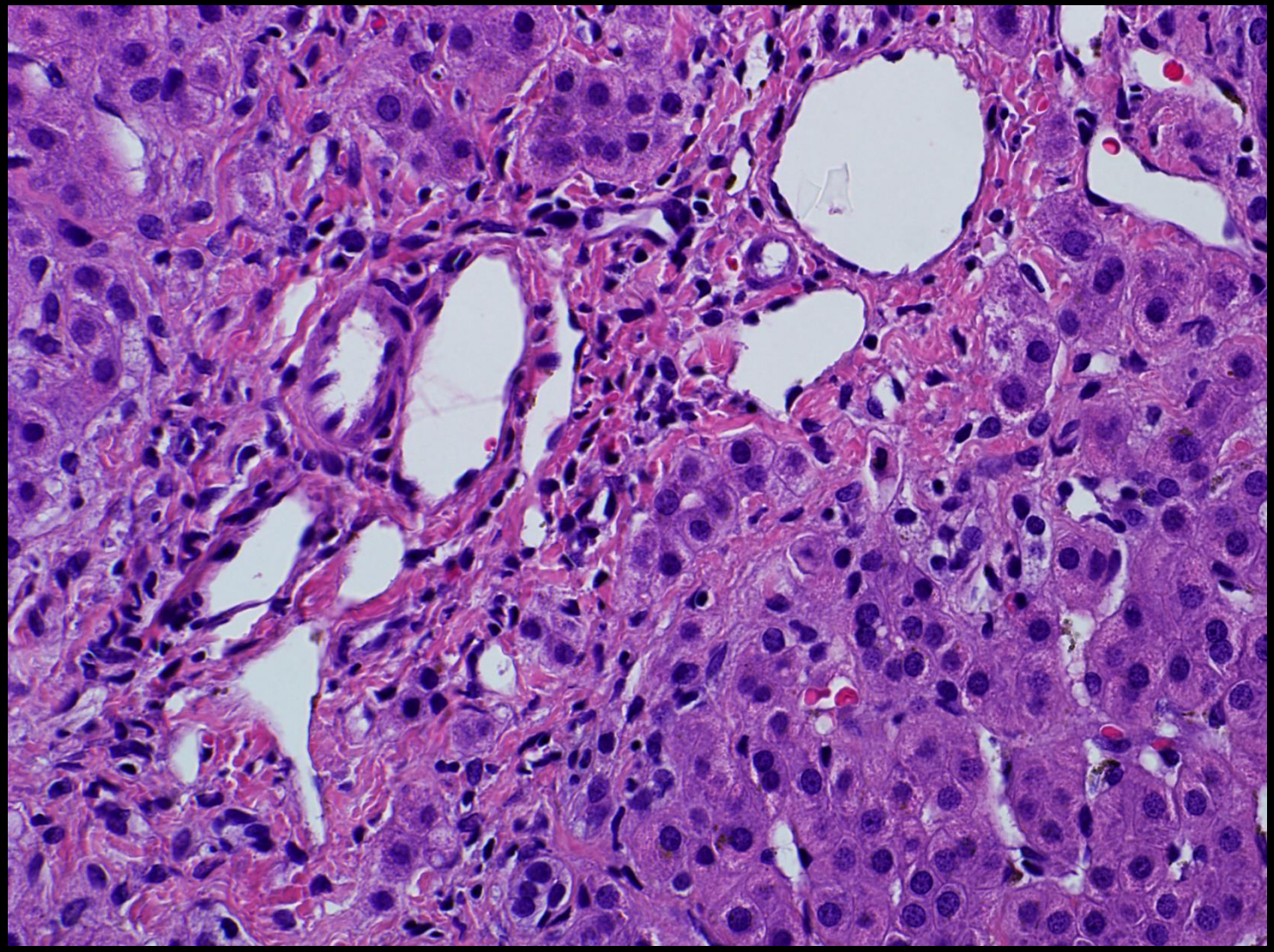
- Acholic stools not always biliary atresia
- Bile duct plugs not always biliary atresia



Bile Duct Paucity

Syndromic (Alagile Syndrome):
- autosomal dominant, JAG1 gene
- affects liver and other organs
- pulmonary artery stenosis
- heart defects (VSD, ASD, PDA, Coarc, TOF)
- butterfly vertebrae
- characteristic inverted triangle facies
- kidneys, brain, eyes





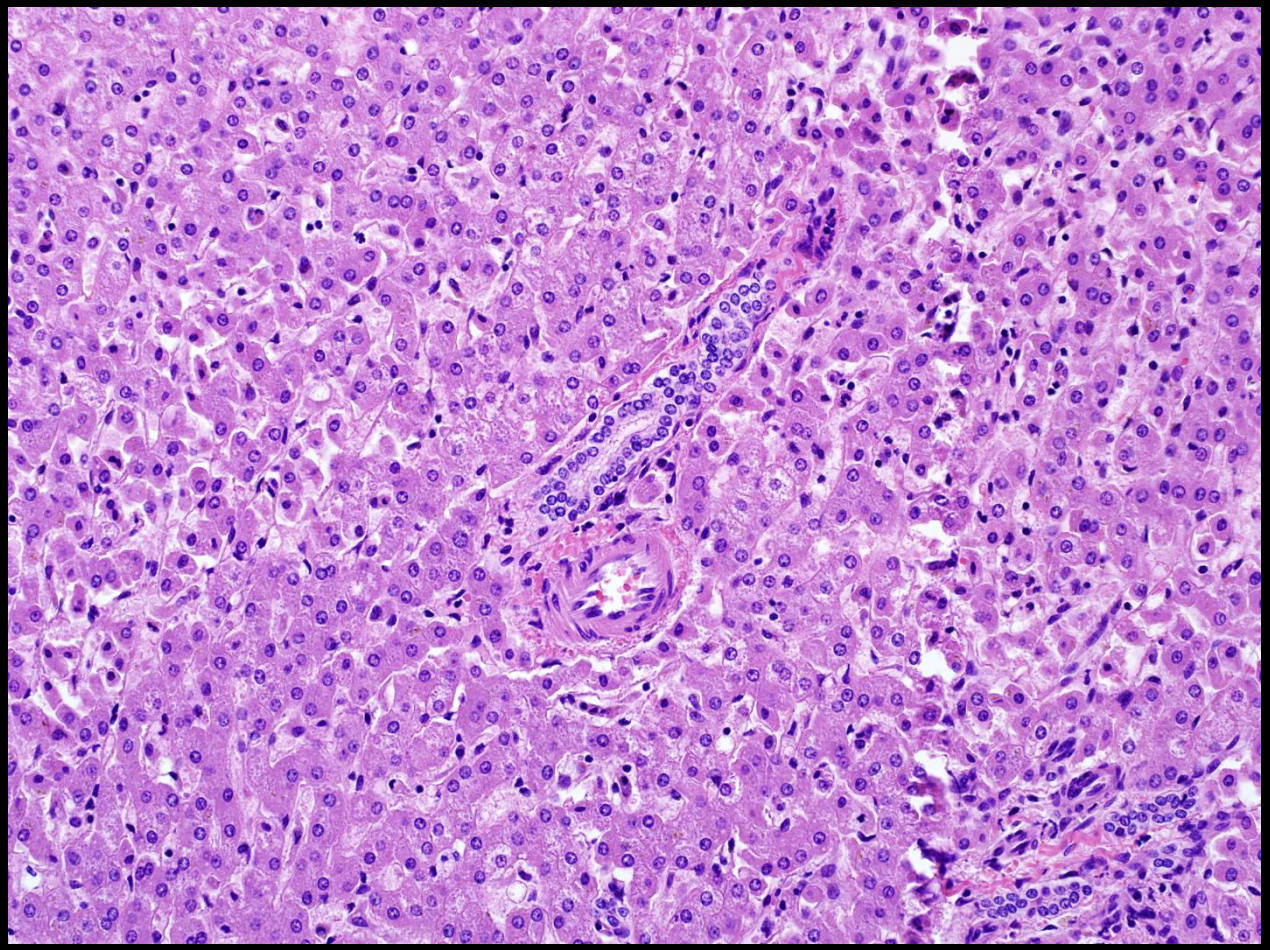
Fairly normal appearance except for absence of bile ducts and canalicular cholestasis

Nonsyndromic Paucity of Interlobular Bile Ducts

- sampling error
- post infectious (CMV)
- genetic (progressive familial intrahepatic cholestasis)
- acquired (transplanted liver and GVHD)
- many others: chronic obstruction, PBC, PSC, drugs, ischemia, cystic fibrosis, mitochondrial DNA depletion, idiopathic

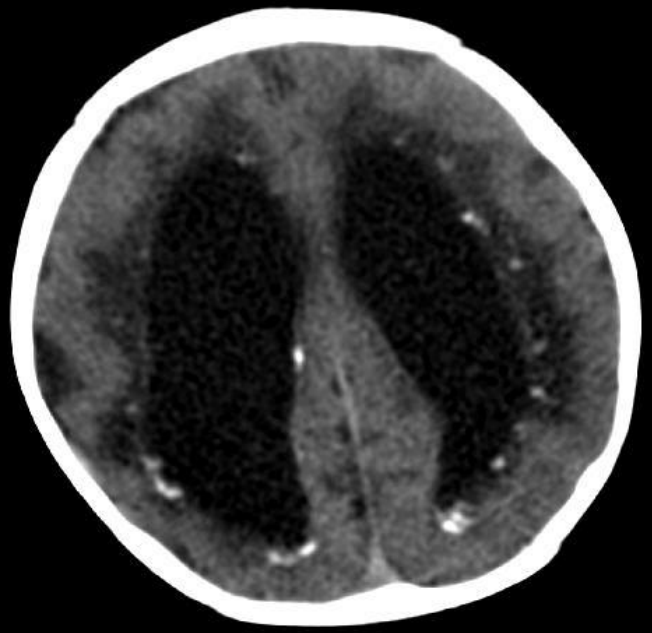
Rx: ampicillin, amoxicillin, flucloxacillin, erythromycin, tetracycline, doxycycline, cotrimoxazole

Abernathy Syndrome – congenital absence of a portal vein.



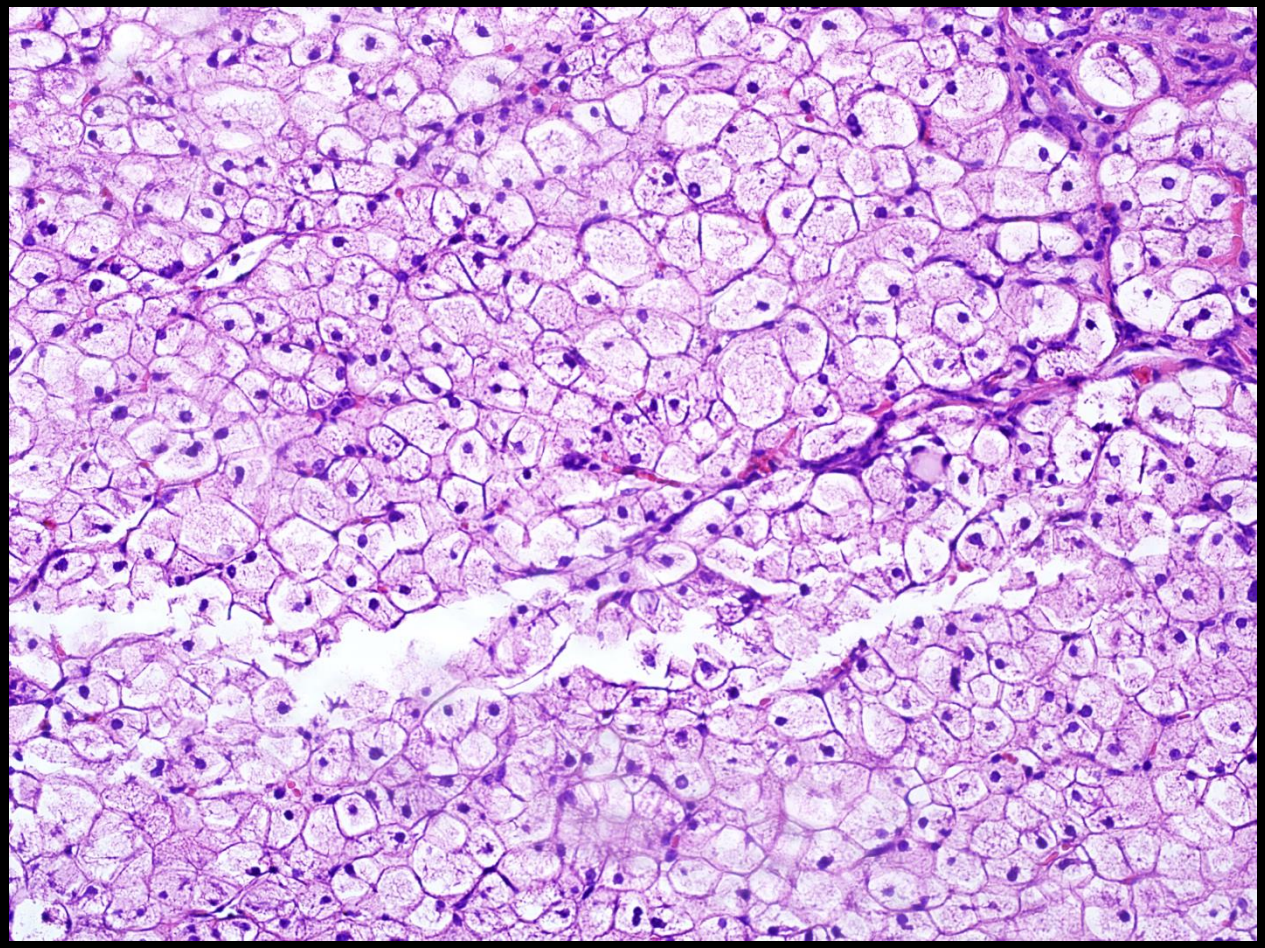
- Infectious disease (bacteria, fungus, virus, parasites|| hematogenous and ascending biliary routes).

Congenital CMV: stigmata: rash, jaundice, microcephaly, IUGR, hepatosplenomegaly, seizures, and retinitis.



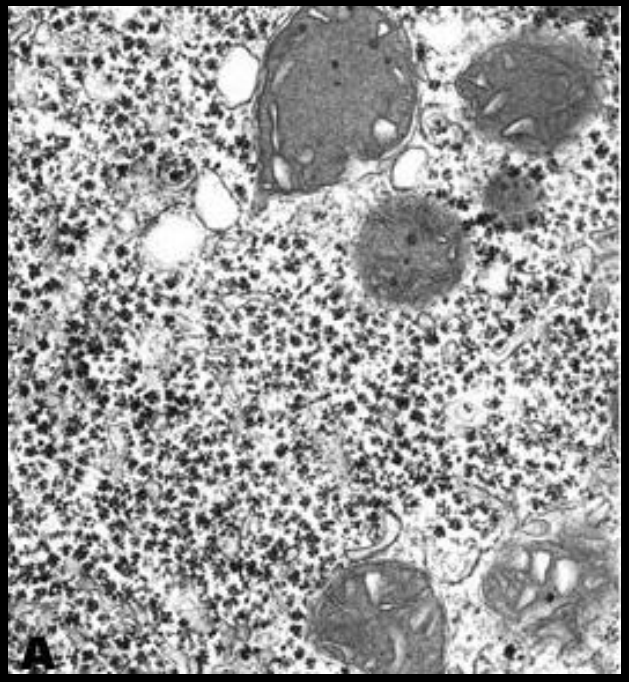
- Immunostains help
- CMV clue in a transplant liver is a microabscess filled with neutrophils (and knowing that the transplant was recent).

- Metabolic Disease
  - Glycogen storage disease (GSD)

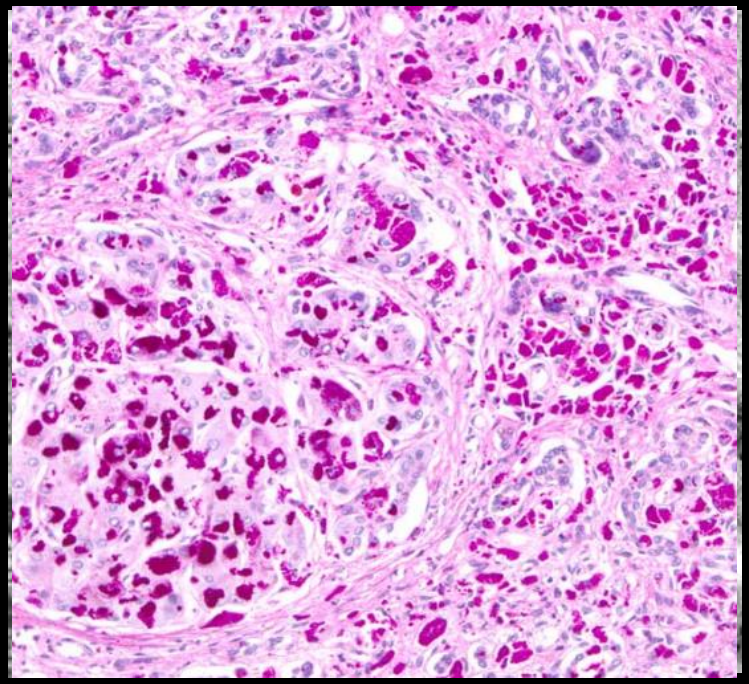


Liver typically shows a "plant like appearance"

- Metabolic Disease
  - if suspected, put a small piece in glutaraldehyde
  - type II GSD (Pompe disease), membrane bound glycogen
  - type IV GSD (Andersen disease), amylopectin bodies, PAS+, diastase resistant, cytoplasmic bodies.



Monoparticulate glycogen.



Amylopectin bodies, PASD

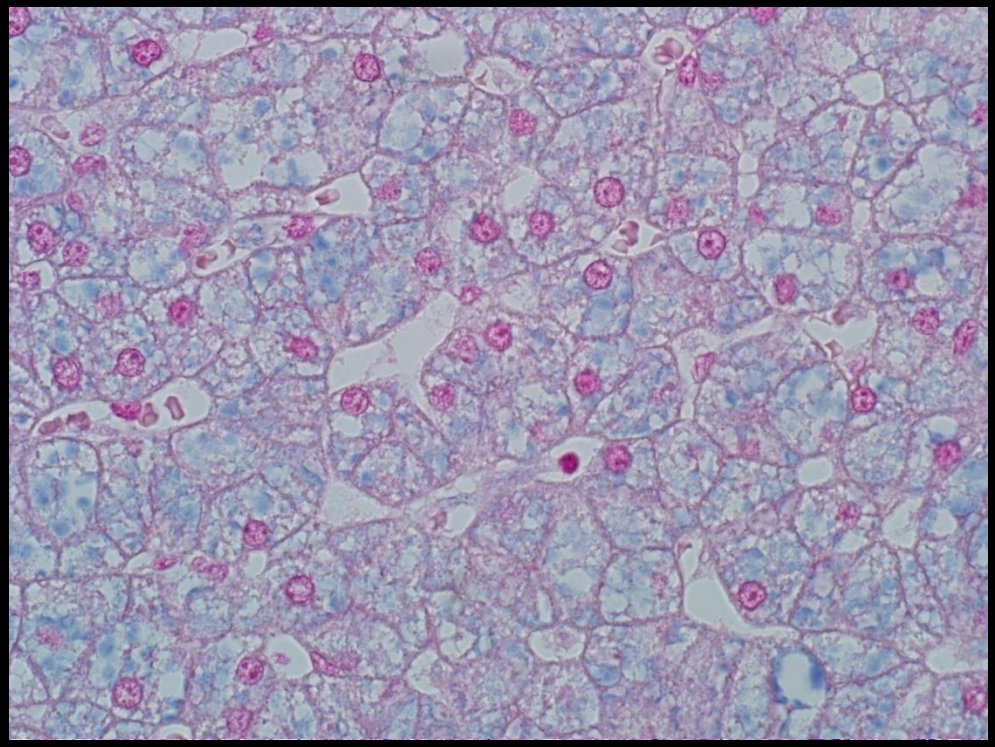
- # Metabolic Disease
  ## Glycogen storage disease

  - In past, age, serum chemistry (glucose, lactic acid), appearance on liver biopsy, wet weight glycogen, enzyme studies on liver

  - Current art, NGS panel, study on blood

AGL	ALDOA	ENO3	FBP1	G6PC	GAA
GBE1	GYG1	GYS1	GYS2	LAMP2	LDHA
PFKM	PGAM2	PHKA1	PHKA2	PHKB	PHKG2
PYGL	PYGM	RBCK1	SLC2A2	SLC37A4	

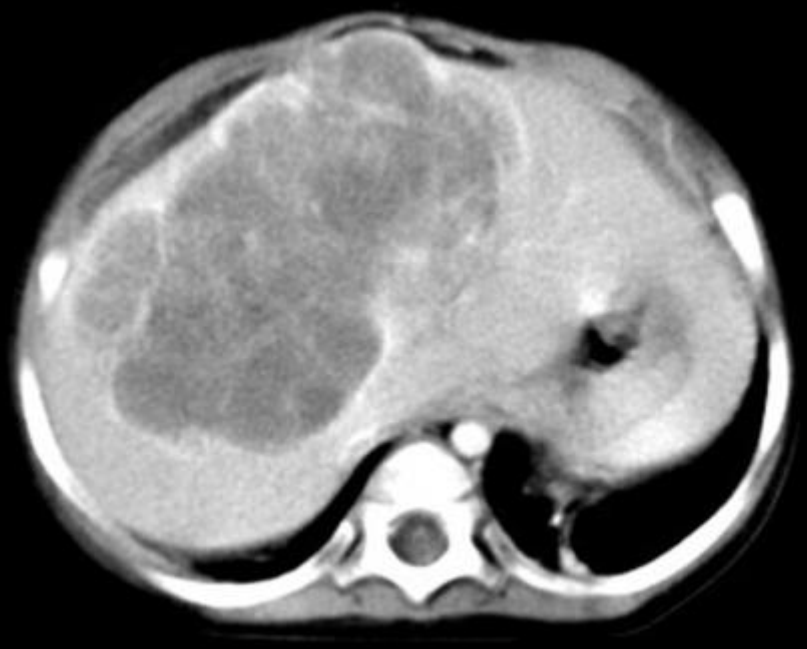
- Metabolic Disease



Colloidal Iron – Positive lysosomes

- Mucopolysaccharidosis
- Not always dysmorphic Hunter-Hurler features
- Sanfilippo may look normal, patient and biopsy
- EM (lysosomal storage) and MPS in urine

Liver Masses



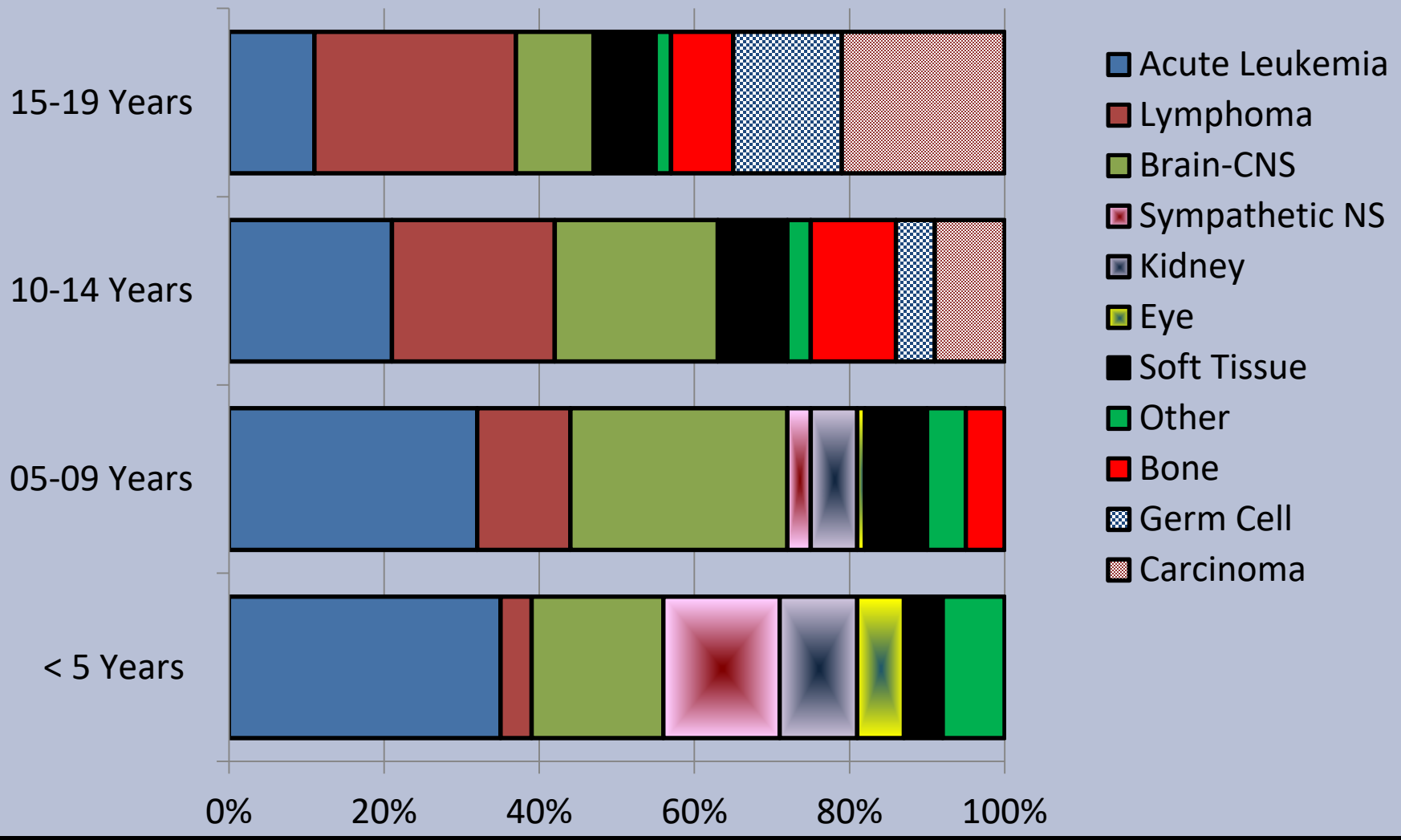
Non-Neoplastic:
- hematoma, abscess (bacteria, fungal), granulomas

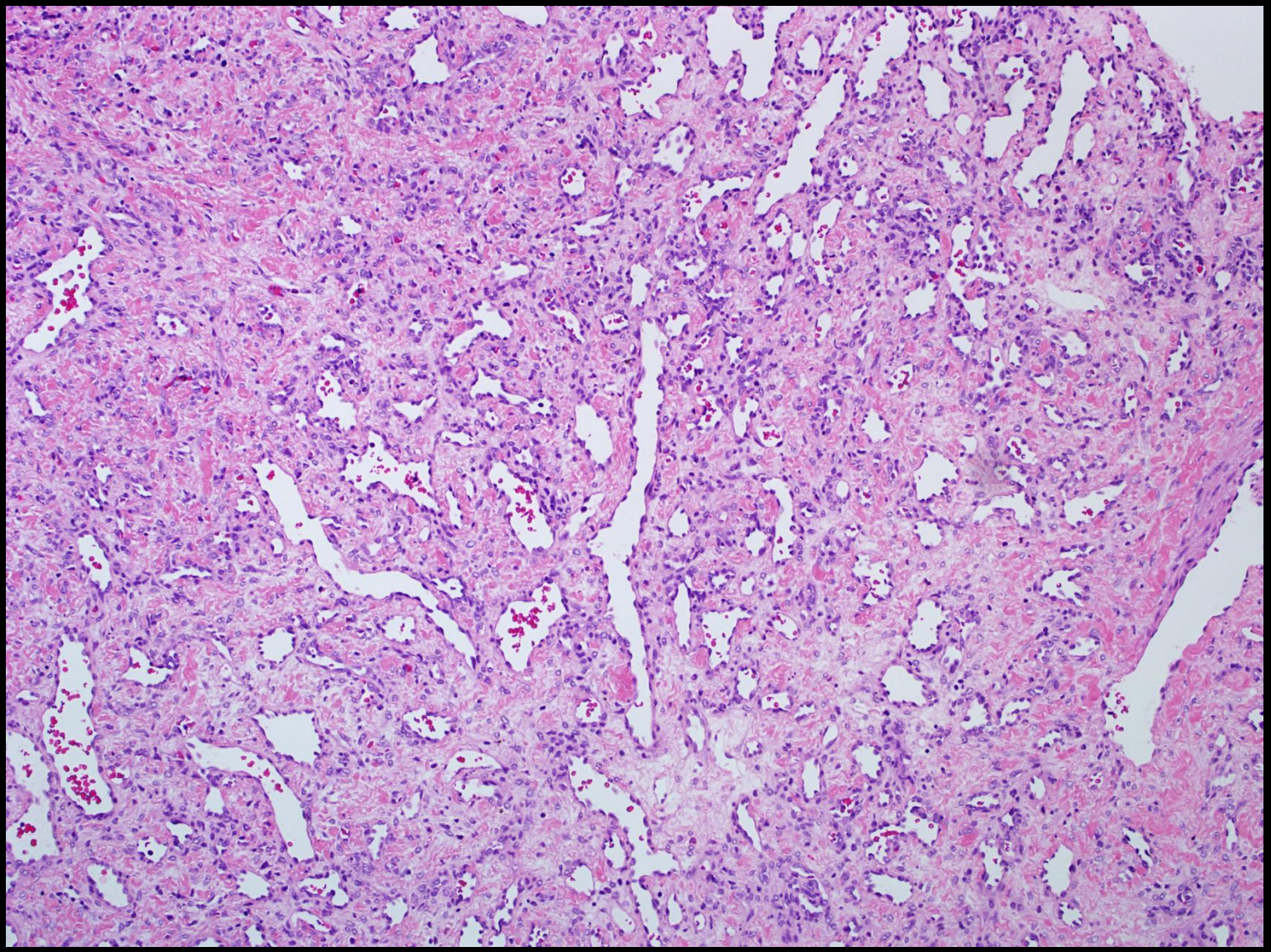
Benign Neoplasms:
- infantile hemangioendothelioma, mesenchymal hamartoma, adenomas, hemangioma, focal nodular hyperplasia, teratoma

Malignant neoplasms:
- hepatoblastoma, hepatocellular carcinoma, germ cell tumors, angiosarcoma, rhabdoid tumor.

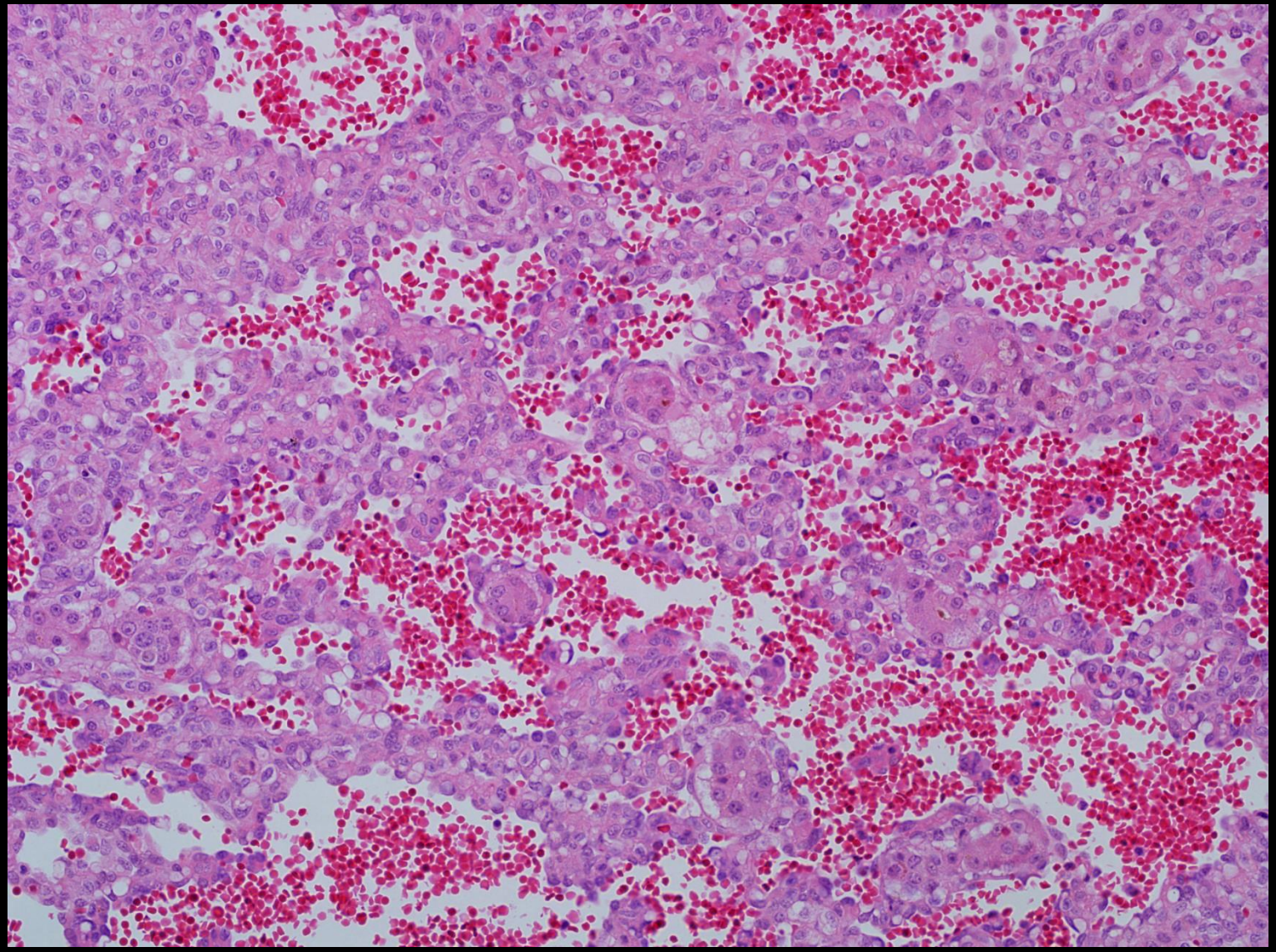
Metastatic neoplasms:
- neuroblastoma, Wilms' tumor, leukemia, lymphoproliferative disorder.

Pediatric Neoplasia (by age group)

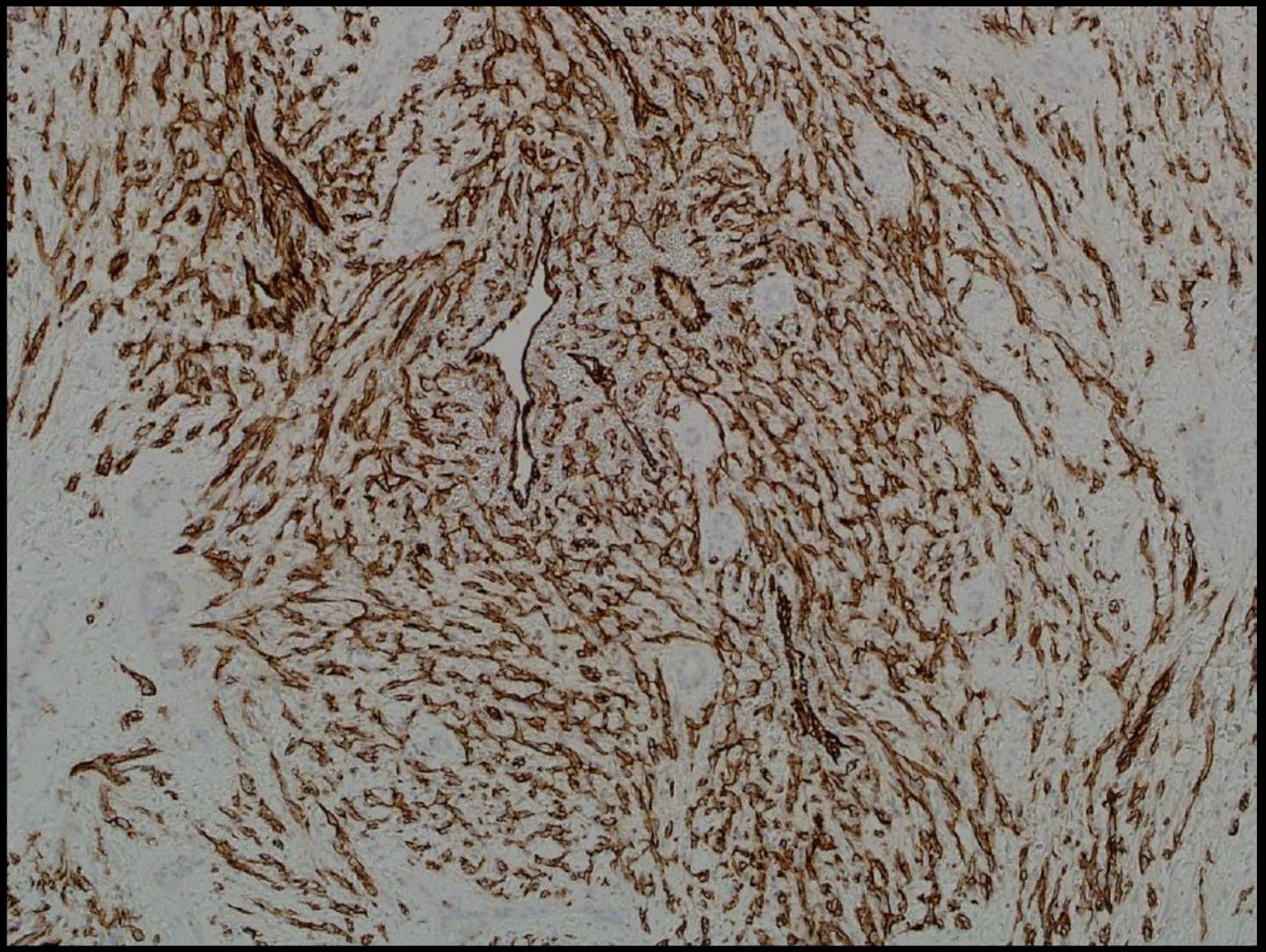




Infantile Hemangioendothelioma Type I



Infantile Hemangioendothelioma Type II



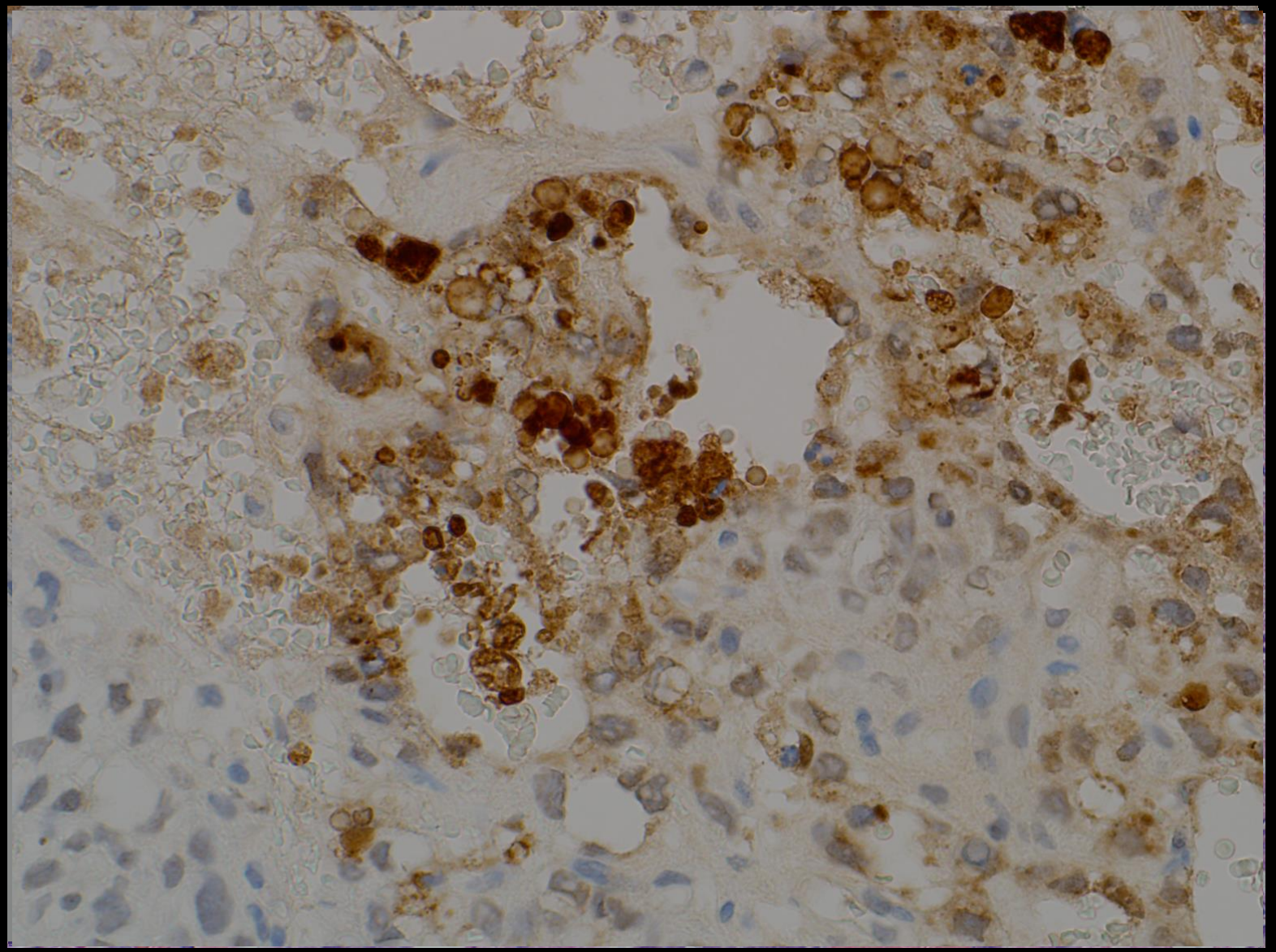
Positive for CD31 (endothelial marker).
Angiosarcoma

Hepatoblastoma:
- slide seminar

Hepatocellular carcinoma:
- vs Hepatoblastoma can be difficult.
- well differentiated vs FNH vs Adenoma (*Prof Aileen Wee*)

Rhabdoid Tumor: eccentric nucleus, prominent nucleolus, paranuclear body (cytokeratin positive) is typical, but morphology is varied. Loss of nuclear INI-1 is a key feature.

Germ Cell Tumor: Remember that Yolk Sac Tumor has many morphologies.



Positive for AFP (above) and cytokeratin. Negative for OCT4, D2-40, and CD30.

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Lecture posted at:

Ibdregistry.net