**Steatosis/Steatohepatitis**

**Macrovesicular**

- Represents a change in lipid metabolism
- Predominant pattern = Nucleus pushed to the side by usually a single medium to large sized droplet
- Ok to have smaller droplets mixed in also

**Microvesicular**

- Usually represents mitochondrial injury
- Nucleus remains central with innumerable, fine fat droplets
- Only use this term if it is a diffuse change (not focal, or in a mostly macrovesicular case)

**Quantifying Fat**

Estimate the % of cells with macrovesicular steatosis

- Average over the entire specimen
- Report rounded to the nearest 10%

<table>
<thead>
<tr>
<th>Amount of Fat</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>Normal</td>
</tr>
<tr>
<td>5-33%</td>
<td>Mild</td>
</tr>
<tr>
<td>34-66%</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;67%</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Often found in zone 3 first.

**Fibrosis**

- Fatty liver disease causes pericellular, pericentral fibrosis first (where the most fat is)
  - Progresses to portal and pericentral fibrosis
  - Bridging fibrosis
  - Cirrhosis

- Once cirrhotic, there may be relatively little fat!
Alcoholic Hepatitis

Hepatocyte injury and inflammation resulting from chronic alcohol consumption

AST/ALT ratio typically >2

**Micro:** Steatosis, Findings that Favor EtOH: *More* hepatocyte ballooning, *more* neutrophilic lobular inflammation (black arrow), *More* Mallory-Denk bodies (red arrow), lobular cholestasis, and *more, diffuse* pericellular fibrosis

Mallory-Denk Bodies = pink, ropey cytoplasmic inclusions = ubiquitinated cytokeratins. Cells also loose expression of CK8/18.

*But* Histology *can* be identical to NASH!

Non-Alcoholic Steatohepatitis (NASH)

Associated with metabolic syndrome, including obesity, type 2 diabetes, dyslipidemia, hypertension

**Micro:** Steatosis, Ballooning, Lobular lymphs and Neuts (exception in pediatric patients, where inflammation is more portal), acidophil bodies, and Pericellular fibrosis.

Sometimes adults have mild portal inflammation, mostly lymphs.

Grade/Stage using NASH-CRN system:

<table>
<thead>
<tr>
<th>Fibrosis</th>
<th>Steatosis</th>
<th>Lobular Inflammation</th>
<th>Hepatocellular Ballooning</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 None</td>
<td>0: &lt;5%</td>
<td>0: None</td>
<td>0: None</td>
</tr>
<tr>
<td>1a Mild zone 3 sinusoidal fibrosis</td>
<td>1: 5-33%</td>
<td>1: &lt;2 foci/20x field</td>
<td>1: Mild, few</td>
</tr>
<tr>
<td>1b Moderate zone 3 sinusoidal fibrosis</td>
<td>2: 34-66%</td>
<td>2: 2-4 foci/20x field</td>
<td>2: Moderate-marked, many</td>
</tr>
<tr>
<td>1c Portal fibrosis only</td>
<td>3: &gt;66%</td>
<td>3: &gt;4 foci/20x field</td>
<td></td>
</tr>
<tr>
<td>2 Zone 3 sinusoidal fibrosis and portal fibrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Bridging fibrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Cirrhosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sum the individual components for a total grade  (maximum of 8)
Wilson’s Disease

Mutations of copper transport protein (ATP7B gene) results in inability to excrete copper in bile → accumulate copper in liver and other tissues

Variable presentation: Acute or chronic liver disease, neurologic/psychiatric findings, hemolytic anemia, ± Kayser-Fleischer rings

Labs: Low ceruloplasmin, Increased urine copper, AST/ALT ratio >2.2, Alk phos/T. Bili <4

Micro: Variable! Steatohepatitis, possible Malory-Denk bodies and glycogenated nuclei; Later chronic hepatitis

When considering diagnosis → send block for copper quantification

Total Parental Nutrition

Variable steatohepatitis or cholestasis depending on age

Other causes of Macrovessicular steatosis

Drugs including: Amiodarone, Glucocorticoids, methotrexate, tamoxifen, and certain chemotherapeutic agents

Other conditions, including: Malnutrition (marasmus or kwashiorkor), hormone alterations (e.g., hypothyroidism, elevated cortisol, growth hormone deficiency), cystic fibrosis, and lipodystrophies.

Microvesicular steatosis

Finely divided fat cells accumulate in cytoplasm as a result of Mitochondrial damage, which is often serious

DDX: Reye’s syndrome, inborn errors of metabolism, Drugs, Toxins, Acute fatty liver of pregnancy
Chronic Hepatitis C

~90% Develop chronic infection; Bloodborne
Antibodies (anti-HCV) indicate exposure
Detection of HCV RNA indicates virus persistence
Newer Meds: Ledipasvir/sofosbuvir (Harvoni) → highly effective
Slow, silent, progressive disease (over decades)
→ cirrhosis (risk of HCC)

Micro: Variably dense portal lymphocytic infiltrates
Periportal interface activity
Scattered lobular collections of inflammatory cells ± acidophil bodies
Portal lymphoid aggregates
Rare plasma cells allowed.

Viral Hepatitis: Distinguishing Acute vs Chronic:
Often use clinical definition = elevated liver enzymes for ≥6 months.
Fibrosis also indicates chronic damage. Diffuse moderate lobulitis means acute or acute-on-chronic.
Stage viral hepatitis using Batts-Ludwig, Ishak, Sheuer, or METAVR systems (fairly similar)

Chronic Hepatitis B

~10% Develop chronic disease; Bloodborne

Micro: Portal chronic inflammatory infiltrates
Interface activity, Lobular hepatitis
Ground glass inclusions
Sanded nuclei
IHC: HBsAg = infected, HBcAg = actively replicating

Fibrosing Cholestatic Hep B: Variant with more progressive/worse disease. Usu. Immunosuppressed state (e.g., post-transplant). Extensive cholestasis, bile ductular reaction, hepatocyte swelling, and fibrosis

Hepatitis D: Requires Hep B → acute-on-chronic hepatitis

Autoimmune Hepatitis

Strong Female Predominance
Elevated AST/ALT (often marked)
Serology: + anti-Smooth Muscle Antibody, ANA, LKM-1, Elevated IgG

Micro: Dense portal infiltrates with marked interface activity → Lymphs & Plasma Cells
Lobular injury
Regenerative rosette formation
Can have “Overlap” with PBC
See Scoring Rubric on next page.
### Criteria for Autoimmune Hepatitis:

<table>
<thead>
<tr>
<th>Finding</th>
<th>Cutoff</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autoantibodies</strong></td>
<td>(maximum 2 points!)</td>
<td></td>
</tr>
<tr>
<td>ANA or SMA</td>
<td>≥ 1:40</td>
<td>1</td>
</tr>
<tr>
<td>ANA or SMA</td>
<td>≥ 1:80</td>
<td>2</td>
</tr>
<tr>
<td>LKM</td>
<td>≥ 1:40</td>
<td>2</td>
</tr>
<tr>
<td>SLA</td>
<td>Positive</td>
<td>2</td>
</tr>
<tr>
<td><strong>Serum IgG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; Upper limit of normal</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>&gt; 1.10 times the upper limit of normal</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence of hepatitis</td>
<td></td>
<td>Disqualifying (Not AIH)</td>
</tr>
<tr>
<td>Atypical for AIH</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Compatible with AIH</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Typical of AIH</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Absence of viral hepatitis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral serology all negative</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

### Scoring:

- ≥6: Probable AIH
- ≥7: Definite AIH

### Histology:

**Typical:** 1) Lymphoplasmacytic interface hepatitis extending into the lobule, 2) Regenerative rosette formation, 3) Emperipolesis

**Compatible:** Chronic hepatitis with lymphocytic infiltration without all the features considered typical

**Atypical:** Signs of another diagnosis, such as steatohepatitis

**Graft-vs-host Disease (GVHD)**

Usually post-stem cell transplant (transplanted immunocompetent T-cells attack new host)

Involves skin, liver, GI tract → rash, ↑LFTs, diarrhea, and vomiting

**Micro:** Bile duct epithelial injury (lymphocytic inflammation, withering, drop out)

Mild portal inflammation; Possible endothelitis

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**Rejection**

Immune-mediated inflammation/damage in transplanted liver.

---

**T cell-mediated rejection**

*Formerly:* Acute Cellular Rejection

**Micro:** 1) Mixed portal tract inflammation (lymphs, including activated lymphs, Eos, etc.), 2) Bile duct damage/inflammation, 3) Endothelitis

---

**Plasma cell-rich rejection**

*Formerly:* de novo autoimmune hepatitis

**Micro:** Portal and/or central plasma cell-rich (>30%) infiltrates and lymphocytic cholangitis

Note: Original disease **MUST** not be autoimmune hepatitis (otherwise, classify as recurrent autoimmune hepatitis likely)

---

**Chronic rejection**

**Micro:** Bile duct injury → eventual loss/paucity; Also often lose hepatic arterioles.

Chronic vascular damage with foam cell arteriopathy and luminal narrowing

---

**Antibody-mediated rejection**

**Micro:** Portal vascular dilation, endothelial hypertrophy, and arteritis, Often edematous portal tract and cholestasis.

C4d IHC showing >50% staining of vein and capillaries;

Positive Serum Donor-specific Antibody (DSA)
Lobular Injury

Indicates an **acute process** (too injurious to be chronic!)
Often very high transaminases.

**Lobular disarray** (normal plate structure disrupted)
**Lobulitis** (lymphs attacking hepatocytes in lobule)
**Acidophil bodies** (apoptotic hepatocytes)

---

**Acute Viral Hepatitis**

Usu. due to Hep. A or B
*(Hep A and E are spread by fecal-oral; “the vowels hit the bowels”)*

Diagnosis confirmed with serology or serum PCR.

**Micro:**
- Lobular damage and disarray
- Diffuse lobular inflammation
- Hepatocyte ballooning/swelling
- Hepatocyte necrosis and regeneration
- May see mild portal and periportal inflammation
- **NO fibrosis**

---

**Drug reaction**

2 chief mechanisms: **Intrinsic** (predictable, dose-dependent, less inflammation, more necrosis) vs. **Idiosyncratic** (majority of cases, not dose-dependent, more inflammation)

Herbal and botanical drugs are important but often overlooked cause of hepatotoxicity

**Very Diverse findings.** Can mimic many other disorders (e.g., Autoimmune hepatitis)

[https://livertox.nih.gov/](https://livertox.nih.gov/)

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**Idiopathic Neonatal Hepatitis**

*aka Neonatal giant cell hepatitis*

Neonatal jaundice with hepatomegaly, elevated T. Bili and Conj. Bili, variable AST/ALT

**Diagnosis of exclusion** (must exclude biliary atresia)
Loose association with hypopituitarism

**Micro:**
- Lobular disarray with prominent **giant cell transformation**
- Absent to mild lobular inflammation (despite name)
- Canalicular and hepatocellular **cholestasis**
- Minimal portal tract changes and **preserved** bile ducts
Cholestasis/Biliary

**Large Duct Obstruction**

Mechanical blockage of bile ducts (by gallstones, stricture, or tumor) → usually diagnosed clinically

**Micro:** Portal tract edema, mixed inflammation with prominent neutrophils, and bile ductular reaction
Canalicular and/or ductular cholestasis

**Additional considerations:**
Lots PMNs in duct epithelium or lumen → consider ascending cholangitis
Can see prominent bile ductular reaction with extensive necrosis/hepatitis as part of liver regeneration (so look for lobular injury!)

**Primary Biliary Cholangitis**

Autoimmune disease with destruction of intrahepatic bile ducts
Usu. Older women with +AMA serology (M2 subtype)

**Micro:** Moderate portal chronic inflammation.
“Florid duct lesion” → lymphocytic cholangitis with bile duct injury, +/- Granulomas
Often causes bile ductular reaction and bile duct paucity

**Primary Sclerosing Cholangitis**

Progressive fibrosis and stricturing of bile ducts—predominantly seen extrahepatic, but also intrahepatic
Often diagnosed by cholangiography (multiple strictures) → Increased risk of cholangiocarcinoma

Frequently young to middle-age men; Strong association with UC

**Micro:** Classically, Concentric fibrosis of ducts—“Onion Skin” (but not often seen on bx)
Biliary obstruction pattern (edema, pmns, ductular reaction)
Eventual bile duct obliteration by fibrosis with ductopenia

**Labs:** Elevated Alkaline phosphatase, GGT, and serum bilirubin.
Can highlight bile ducts with CK7 and CK19. Often see increased copper deposition in periportal hepatocytes with cholestasis.
Biliary Atresia

Idiopathic prenatal destruction/fibrosis of extrahepatic bile ducts—Most common cause of pathologic infant jaundice. Usually present in first few weeks of life with jaundice and failure to thrive. Hepatobiliary (HIDA) scan demonstrates failure of excretion of radiotracer into duodenum. Surgical intervention with Kasai procedure and/or liver transplantation required.

**Micro:** Large bile duct obstruction findings—(non-specific, requires clinical/radiographic correlation)

Also consider in pediatric cholestatic liver disease: Bile salt deficiency diseases (formerly, Progressive Familial Intrahepatic Cholestasis, or, PFIC), and inherited defects in bilirubin metabolism (mostly tested for with send-out testing).

Neonatal Paucity of Intrahepatic Bile Ducts

Can by Non-syndromic or Syndromic (Alagille syndrome—JAG1 mutations; associated with other abnormalities such as cardiac and skeletal)

**Micro:** Interlobular bile ducts absent in > 50% of portal tracts. Can highlight with CK7. Ductular reaction may be present

Sepsis

Patients systemically ill, often with sepsis and/or bacteremia Often jaundiced

**Micro:** Classically, Ductular cholestasis (“cholangitis lenta”)

> However, this is challenged by some as this seems to be common in any condition with cholestasis (including during the hepatic dysfunction seen with sepsis)

Ductular reaction with inspissated bile and flattened, atrophic epithelium.

Drug Reaction

Most common histologic pattern of drug-induced liver injury is cholestasis

Can have several patterns:

**Bland/Pure cholestasis:** Cholestasis with minimal inflammation (also see with systemic illness and pregnancy)

**Cholestatic hepatitis:** Cholestasis with inflammation and hepatocellular damage

**Prolonged cholestasis/ductopenia:** > 3 months,

**Sclerosing duct injury:** Fibrosis affecting large bile ducts (similar to PSC)

https://livertox.nih.gov/
Most common causes of Neonatal Cholestasis:
1) Biliary atresia (BA)
2) Idiopathic Neonatal Hepatitis (INH)
Jaundice after 2 weeks of age

Laboratory studies (Bili, AST, ALT, ALK, GGT, INR, CBC)

Conjugated/direct hyperbilirubinemia

Clinical “red flags”

Targeted, disease-specific evaluation

Liver Ultrasound

Choledochal cyst (or other mass)

Surgery

Possible Biliary Atresia

Liver biopsy

Normal

Additional laboratory work-up (A1AT typing, etc...)

Biliary Obstructive Pattern

Intraop Cholangiogram +/- HIDA scan

Biliary Atresia

Kasai Procedure

Neonatal hepatitis Pattern

Paucity of intrahepatic bile ducts

Possible Next Gen sequencing

Modified from a presentation from Grace Kim MD at USCAP March 2020
**Altered Blood Flow**

**“Shock Liver”**
Liver hypoperfusion of any cause
Massive elevation in AST & ALT (thousands)

**Micro:** Central coagulative necrosis (zone 3)
Collapse of reticulin plates. No inflammation.

Other causes of bland Central Necrosis:
Acetaminaphen toxicity (indistinguishable histologically)

**Congestive Hepatopathy**
Caused by hepatic venous outflow obstruction
Can be due to RHF, Budd-Chiari, etc...
Grossly: Nutmeg liver

**Micro:** Central zone sinusoidal dilatation, congestion, hepatic plate atrophy, and necrosis
Chronic cases can lead to central vein and sinusoidal fibrosis → Cirrhosis

**Sinusoidal Obstruction Syndrome**  
aka Veno-Occlusive Disease
Sinusoidal endothelial injury; Often due to chemotherapy or Stem Cell Transplantation

**Micro:** Central vein obliteration (best seen on trichrome) →
Sinusoidal dilation/congestion; Sinusoidal endothelial edema

**Cirrhosis**

**Common End-Stage** for many liver disorders

Regenerative nodules surrounded by fibrosis
(want to see both for Dx)

**Special type:** “Biliary Cirrhosis” seen with long-standing cholestasis
Cholate stasis (ballooning, feathery degeneration at edges of nodules), “jigsaw” pattern of cirrhosis (instead of round nodules, biliary cirrhosis is classically irregular), copper deposition in zone 1, ductopenia, periductal fibrosis, bile infarcts.
Miscellaneous

Iron Overload  
*aka Hemosiderosis*

- With excessive transfusions or iron supplementation
- Iron accumulates in Kupffer cells (sinusoidal macrophages) first. When those are saturated, then it is deposited in hepatocytes

Hereditary Hemochromatosis

- Inherited disorder of iron metabolism
- HFE gene mutations cause increased iron absorption & storage
  - Iron accumulates first in periportal hepatocytes
  - Progressively involves all zones & bile duct epithelium
  - Less Kupffer cell involvement (relatively)

Glycogenic Hepatopathy

- Poorly-controlled diabetes → abundant glycogen stores → Hepatomegaly and elevated LFTs
- A component of Mauriac Syndrome (with delayed puberty and Cushingoid features)
  - **Micro:** Diffuse glycogenation of hepatocytes
  - Demonstrated by PAS stain (Diastase sensitive)
  - Absence of inflammation

α1-Antitrypsin Deficiency

- Genetic disorder characterized by abnormal α-1-antitrypsin protein synthesis
  - PiZZ phenotype accounts for most cases
    - Chronic liver disease and emphysema
  - **Micro:** Eosinophilic, PAS-D (+) globules within periportal hepatocytes are characteristic
  - Neonatal hepatitis features cholestasis and hepatocyte injury
    (too early for globule formation)
Almost exclusively in immunocompromised individuals.

Inclusions can be subtle (so use stain liberally).

Classically: Neutrophilic microabscesses.

“Resolving Hepatitis”
Can look “almost normal”
Minimal/no lobulitis or portal inflammation
Mild lobular disarray (somewhat disorganized plates)
Kupfer cell hypertrophy (cleaning up debris)
Highlighted with a PASd stain
Most common causes: acute self-limited viral infection or idiosyncratic drug reaction

“Resolving Hepatitis”

Adenovirus/Herpes Hepatitis
Massive, bland azonal necrosis with characteristic inclusions at edge of necrosis.
Usu. Immunocompromised. Poor prognosis.

CMV Hepatitis
Almost exclusively in immunocompromised individuals.
Inclusions can be subtle (so use stain liberally).
Classically: Neutrophilic microabscesses.

EBV Hepatitis
Often looks like a nondescript hepatitis with mild to moderate portal and lobular inflammation (so often keep in DDX, esp. if young or immunocompromised!)
Classically: Lots of activated lymphocytes in sinuses

Amyloid
Part of system illness, often plasma cell dyscrasias.
Required: Apple-green birefringence on Congo Red stain
**Embryologic ductal plate malformation** that leads to bridging fibrosis (*cirrhosis*) with prominent malformed ducts. Ducts ectatic, anastomosing, and irregularly shaped. No significant inflammation. Few/abnormal portal veins → Leads to portal hypertension.

Results from changes in hepatic blood flow from obliteration of small portal veins → leads to localized atrophy → other areas grow to compensate. Can cause portal hypertension.

**Cystic Fibrosis**

CFTR (Chloride ion channel) mutations result in exocrine gland malfunction. Autosomal recessive. Usually presents with respiratory problems, meconium ileus, or pancreatic insufficiency.

In liver, **thick abnormal secretions** are present in bile ducts (similar to in lungs and pancreas) → biliary obstruction → epithelial atrophy, bile ductular proliferation, inflammation → fibrosis → biliary *cirrhosis*.

Secretions stain with PAS-D.
Acute Hepatitis
*Marked Transaminitis (AST & ALT >5x normal)*

- Non-Hepatotropic Virus (CMV, EBV, Adeno)
- HAV & HEV: Fecal oral transmission; only acute
- HBV: Ground Glass inclusions
- AIH: Plasma cells
- Adverse drug reaction
- Massive altered hepatic blood flow (e.g., Shock)

Chronic Hepatitis
*Mild Transaminitis (AST & ALT <5x normal)*

- HBV: 5% develop chronic hepatitis
- AIH: + ANA, ASMA, Elevated IgG; Interface necroinflammatory lymphoplasmacytic infiltrate
- HCV: 80% develop chronic hepatitis; nodular aggregates of lymphocytes
- Hereditary Hemochromatosis: + HFE genetic mutation Elevated Transferrin saturation and serum ferritin
- Wilson’s: Increased liver copper quantification; + ATP7B gene; AST/ALT ratio >2.2, Alk. Phos./T. Bili <4
- A1AT Deficiency: PiZZ phenotype, Hyaline globules in hepatocytes stain with PAS with diastase stain
- Alcoholic: Clinical history of alcohol, AST:ALT > 2, more likely to show neutrophils and Mallory’s hyaline
- NASH: Diabetes or metabolic syndrome, Obesity
- Drug reaction

Cholestatic Hepatitis
*Elevated Alk Phos. & GGT; +/- Bili Jaundice*

- Large duct obstruction
- PBC: Female, + AMA, IgM, lymphocytic cholangitis and florid duct lesion
- PSC: Male, IBD, diagnosed with cholangiography, concentric fibrosis around bile ducts, risk of cholangiocarcinoma
- Drug reaction

Cirrhosis/Liver Failure
*Synthetic Dysfunction (Elevated INR, Low Albumin, Low platelets)*

*Based on a presentation from Max Smith M.D., Mayo Clinic*
Differential Diagnoses

### Acute Liver Failure

**Histologically, typically lobulitis or necrosis patterns (as they are too injurious to be chronic)**
- Acetaminophen toxicity (40 – 50%)
- Drug reaction (10 – 20%)
- Acute viral hepatitis (10 – 20%)
- Idiopathic (20 – 30%)
- Rare causes: Wilson’s disease, Autoimmune hepatitis, Budd-Chiari syndrome, Non-hepatotropic viruses

### Almost Normal Liver

**With Elevated LFTs**
- Systemic autoimmune conditions
- Vascular outflow obstruction
- Intermittent ischemia
- Metabolic syndrome (even if fat-free)
- Medication

**With Portal hypertension and/or ascites**
- Hepatoportal sclerosis
- Portal venopathy
- Peritoneal serositis (no liver disease)

### Fatty Liver

- Metabolic syndrome (NASH)
- Alcohol use
- Drug effect
- Wilson’s disease (and other genetic disorders)
- Cystic fibrosis
- Elevated cortisol

### Bland Lobular Necrosis

**Necrosis with NO (or little) associated inflammation**
**Due to direct injury/toxicity (not secondary immune damage)**

<table>
<thead>
<tr>
<th>Zone 1</th>
<th>Zone 2</th>
<th>Zone 3</th>
<th>Azonal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron Toxicity</td>
<td>Poisons</td>
<td>Acetaminophen</td>
<td>Herpes</td>
</tr>
<tr>
<td>Phosphorous Toxicity</td>
<td>Beryllium</td>
<td>Ischemia</td>
<td>Adenovirus</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Yellow fever</td>
<td>Some toxins</td>
<td>Varicella</td>
</tr>
<tr>
<td>Some industrial chemicals</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on: Atlas of Liver Pathology: A Pattern-based Approach, by Dr. Michael Torbenson*
### Granulomas
- Primary biliary cholangitis
- Sarcoidosis
- Drug effect
- Infection
- CVID and other systemic granulomatous diseases
- Paraneoplastic

### Bland Lobular Cholestasis
- Drug effect
- Severe systemic illness/sepsis
- Paraneoplastic syndrome

### Ductopenia (adult)
- Chronic obstruction
- Primary biliary cholangitis
- Chronic rejection
- GVHD
- Drug effect
- Idiopathic

### Chronic Hepatitis Pattern
- Viral Hepatitis
- Autoimmune hepatitis
- Drug effect

### Microvesicular Steatosis
- Medication (e.g., Reye’s syndrome)
- Toxin (e.g., arsenic)
- Acute fatty liver of pregnancy
- Alcohol foamy degeneration
- Genetic diseases (e.g., Alper’s syndrome)
- Infection (e.g., HDV + HBV)

### Pediatric Cholestatic Disease
- Biliary atresia (extrahepatic)
- Paucity of intrahepatic bile ducts
  - Non-syndromic vs Syndromic
- Neonatal giant cell hepatitis
- Sepsis
- TPN
- Bile salt deficiency (PFIC’s)
- Genetic diseases (e.g., alpha-1 antitrypsin, Niemann-Pick, etc…)

### Cystic Biliary Malformations
- Congenital hepatic fibrosis
- Caroli syndrome/disease
- Autosomal recessive polycystic kidney disease
- Autosomal dominant polycystic kidney disease
### Portal Hypertension

**Pre-hepatic**
- Portal vein thrombosis
- Portal vein stricture

**Hepatic**
- Cirrhosis
- Schistosomiasis

**Post-Hepatic**
- Portal vein thrombosis

- Sarcoidosis
- Nodular regenerative hyperplasia
- Hepatoportal sclerosis
- Peliosis hepatitis
- Veno-occlusive disease

---

### Veno-Occlusive Disease

- Bone marrow transplantation
- Chemotherapy medications

- Radiation therapy
- Herbal teas/remedies

---

### Congestive Hepatopathy

- Budd-Chiari syndrome
- Right-sided heart failure
- Compression of hepatic veins or IVC
- Medications (e.g., estrogen)

- Veno-occlusive disease
- Sickle cell anemia
- Hemophagocytosis syndrome
- Autoimmune diseases
- Paraneoplastic syndromes

---

### Things that are easy to overlook

- Glycogenopathy
- Alpha-1-antitrypsin deficiency
- Nodular regenerative hyperplasia

- Hepatoportal sclerosis
- Early bile duct loss
- Amyloid
- Stellate cell hyperplasia

---

*Based on: Atlas of Liver Pathology: A Pattern-based Approach, by Dr. Michael Torbenson*