

Passive Congestion and Centrilobular Necrosis

Hepatic circulation • Zonal vulnerability • Morphologic continuum

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

01 Locate centrilobular (zone 3) parenchyma and trace hepatic venous drainage.

02 Distinguish passive venous congestion from reduced hepatic perfusion.

03 Explain the morphology of nutmeg liver, pericentral necrosis, and cardiac sclerosis.

04 Interpret the findings alongside cardiac disease, shock, and related outflow disorders.

Congestion and necrosis form a continuum

- Both are hepatic consequences of systemic circulatory compromise.
- Venous stasis first changes blood distribution and hepatocyte architecture.
- Added or severe hypoxic injury may produce hemorrhagic pericentral necrosis.
- The morphologic severity depends on the hemodynamic insult and its duration.

Venous congestion



Hepatocyte atrophy



Hypoxic injury



Centrilobular necrosis

Classify liver circulatory disturbances by level

- Inflow: Hepatic artery or portal venous compromise.
- Intrahepatic passage: Impaired sinusoidal circulation.
- Outflow: Hepatic venous obstruction or systemic venous backpressure.
- The level of disturbance helps predict the morphologic pattern.

Blood inflow



Sinusoidal transit

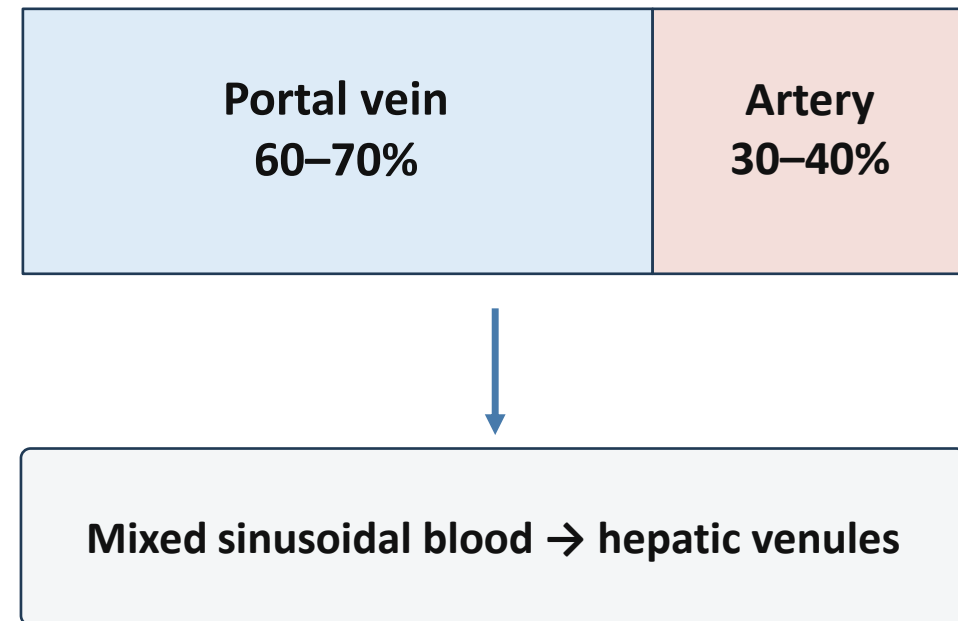


Venous outflow

The liver has a dual blood supply

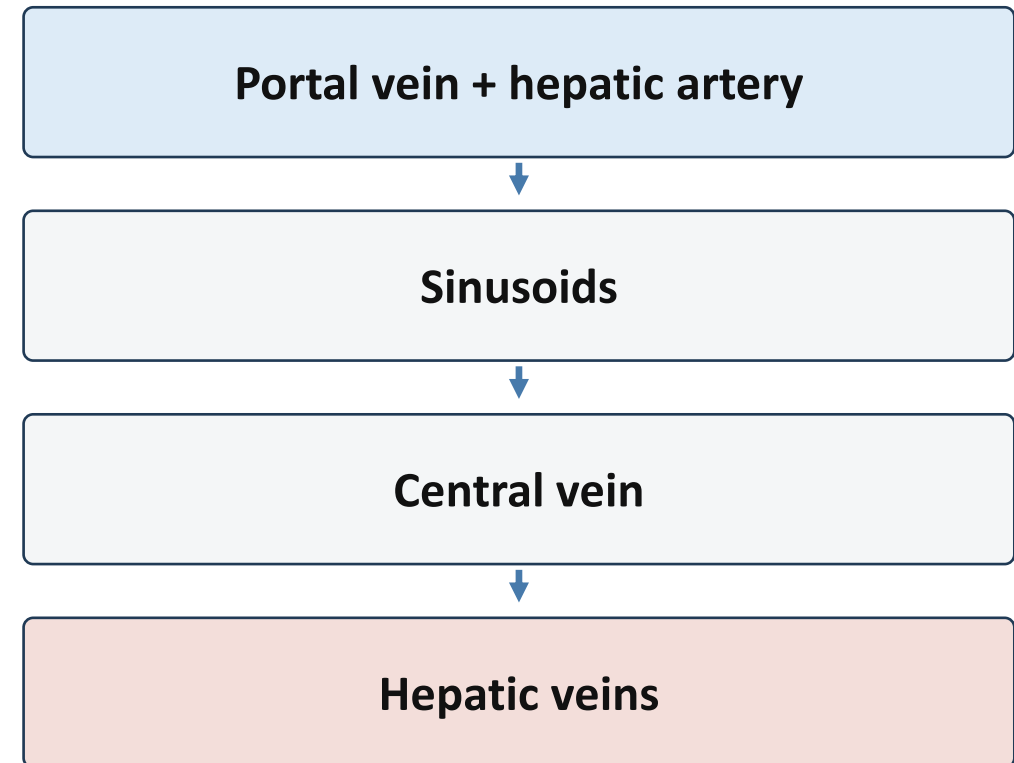
- The portal vein provides approximately 60–70% of normal hepatic blood flow.
- The hepatic artery contributes approximately 30–40%.
- The blood streams mix within sinusoids and drain into hepatic venules.
- Dual supply mitigates complete infarction but does not prevent zone 3 hypoxia.

Normal hepatic blood flow



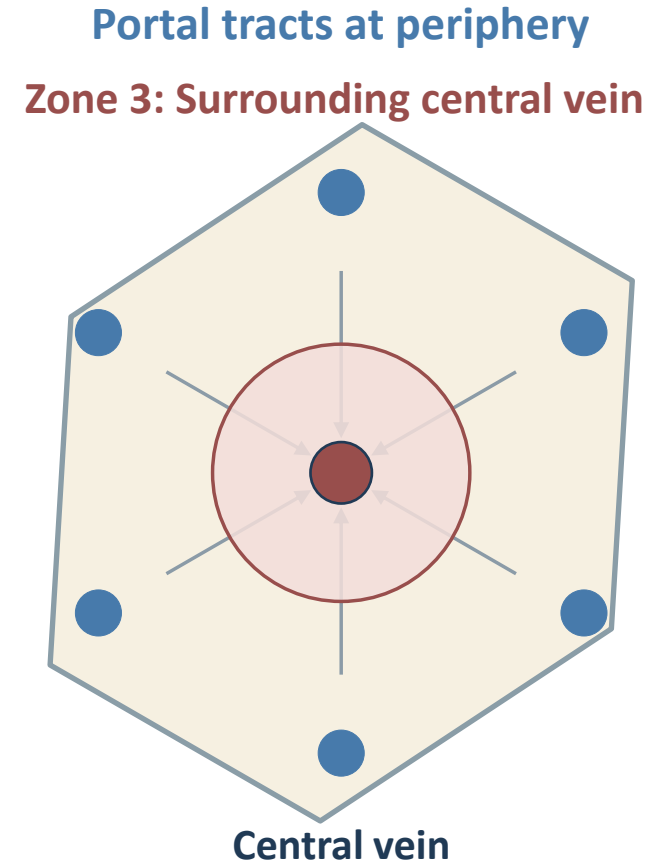
Trace blood from portal tract to central vein

- Portal venous and hepatic arterial branches accompany bile ducts in portal tracts.
- Blood traverses sinusoids between hepatocyte plates.
- It drains into terminal hepatic venules (central veins).
- Venous backpressure is transmitted toward the centrilobular sinusoidal bed.



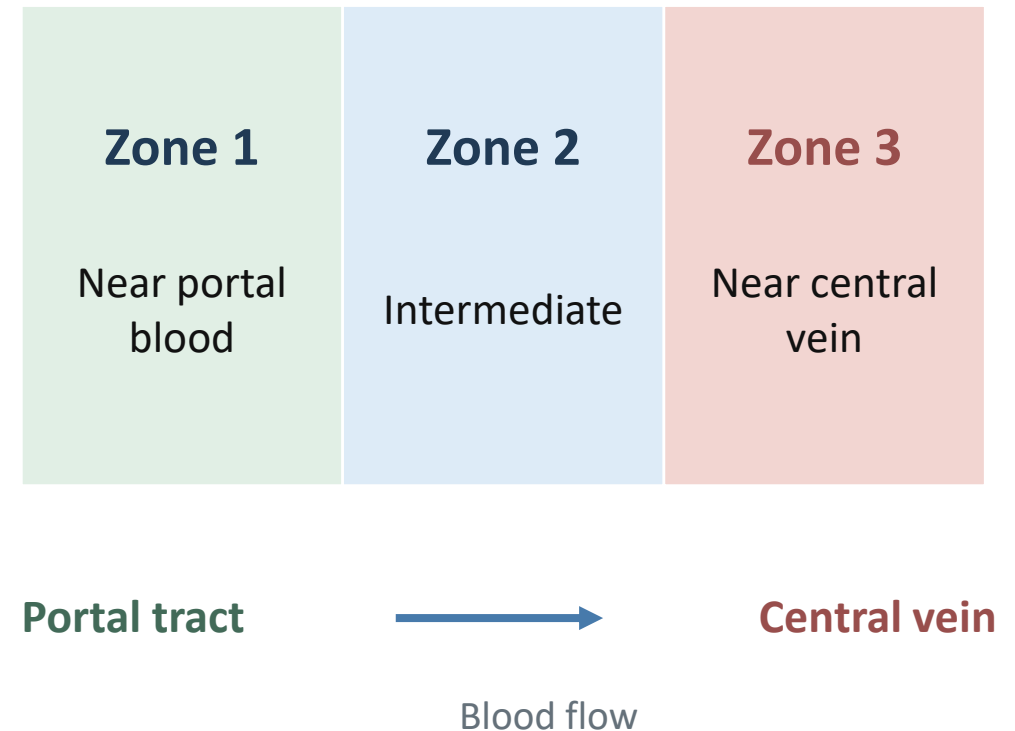
The classic hepatic lobule: Anatomic landmarks

- The central vein is located near the center of the classic lobule.
- Portal tracts lie at the polygonal periphery.
- Parenchyma near the central vein is called pericentral or centrilobular.
- A correct zonal diagnosis begins with locating these landmarks.



The hepatic acinus defines three functional zones

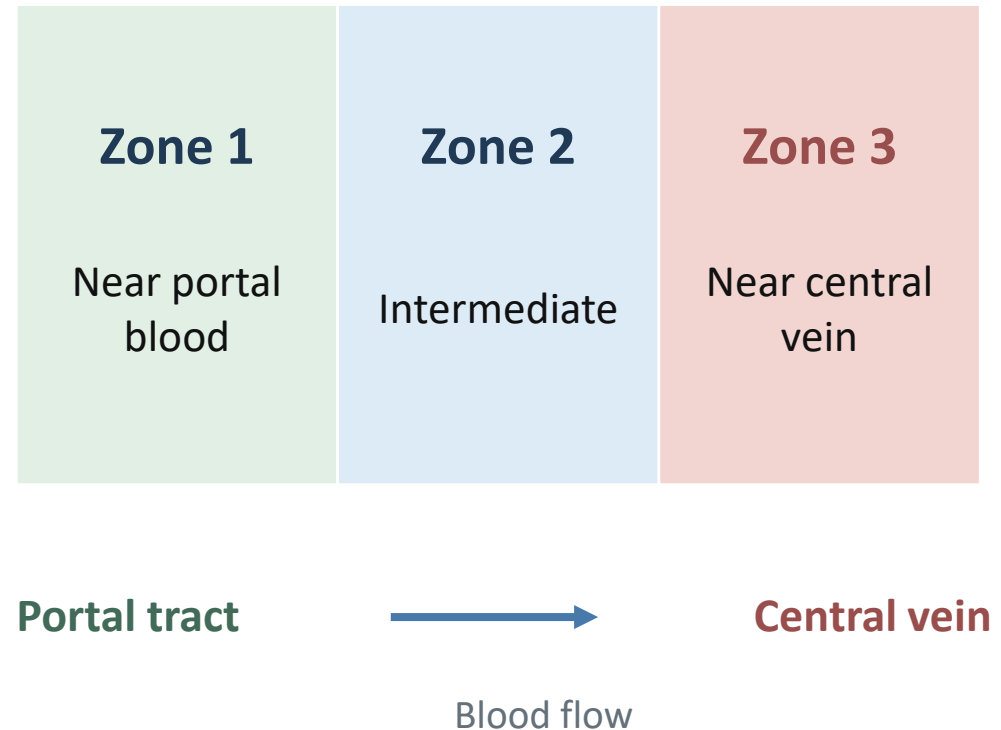
- Zone 1 is closest to portal-tract blood supply.
- Zone 2 is intermediate along the sinusoidal pathway.
- Zone 3 lies farthest downstream, adjacent to the terminal hepatic venule.
- Zonal distribution follows perfusion and hepatocyte metabolic specialization.



Zone 3 normally receives less oxygen

- Along the sinusoidal path, oxygen availability declines toward the central vein.
- Zone 1 is relatively well oxygenated; Zone 3 has the lowest oxygenation.
- Zone 3 therefore becomes particularly susceptible to reduced perfusion.
- This gradient explains selective pericentral injury in circulatory failure.

Relative oxygenation decreases downstream



Passive congestion is not active hyperemia

Property	Hyperemia	Passive congestion
Primary event	Increased arteriolar inflow	Reduced venous outflow
Hemodynamics	Active	Passive
Typical color	Red	Dusky blue-red
Late sequelae	Depend on cause	Hypoxia and scarring

Venous backpressure dilates hepatic sinusoids

- Impeded outflow increases venous and sinusoidal blood retention.
- Centrilobular sinusoids and the central-vein region become engorged.
- Congestion is most prominent near the venous drainage endpoint.
- Sinusoidal widening compresses and separates neighboring hepatocyte plates.

Impaired venous return



Raised hepatic venous pressure



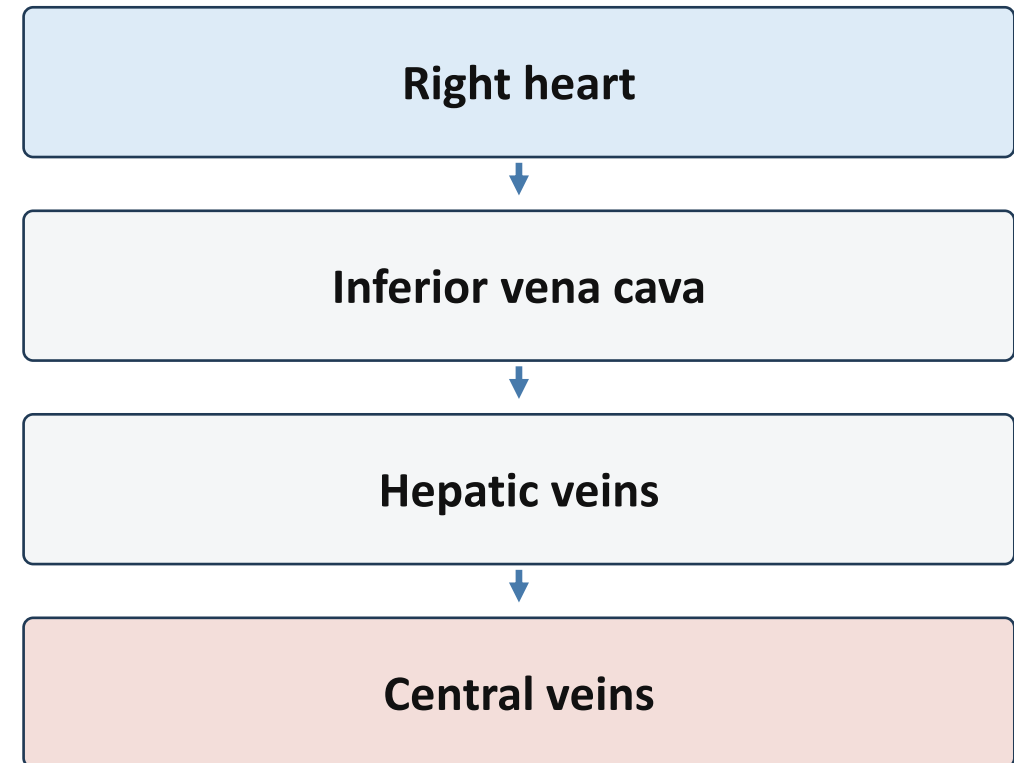
Dilated zone 3 sinusoids



Hepatocyte compression

Right-sided cardiac decompensation is the prototypic cause

- Right-sided cardiac failure raises systemic venous pressure.
- Hepatic venous drainage becomes impeded without a necessary hepatic-vein thrombus.
- Passive blood accumulation develops within centrilobular sinusoids.
- Cardiac status is therefore essential context for hepatic congestion.



Gross appearance in early passive congestion

- The liver is slightly enlarged, with a tense capsule.
- Rounded hepatic margins reflect enlargement.
- A cyanotic hue reflects accumulation of poorly oxygenated blood.
- Gross congestion does not alone establish hepatocyte necrosis.

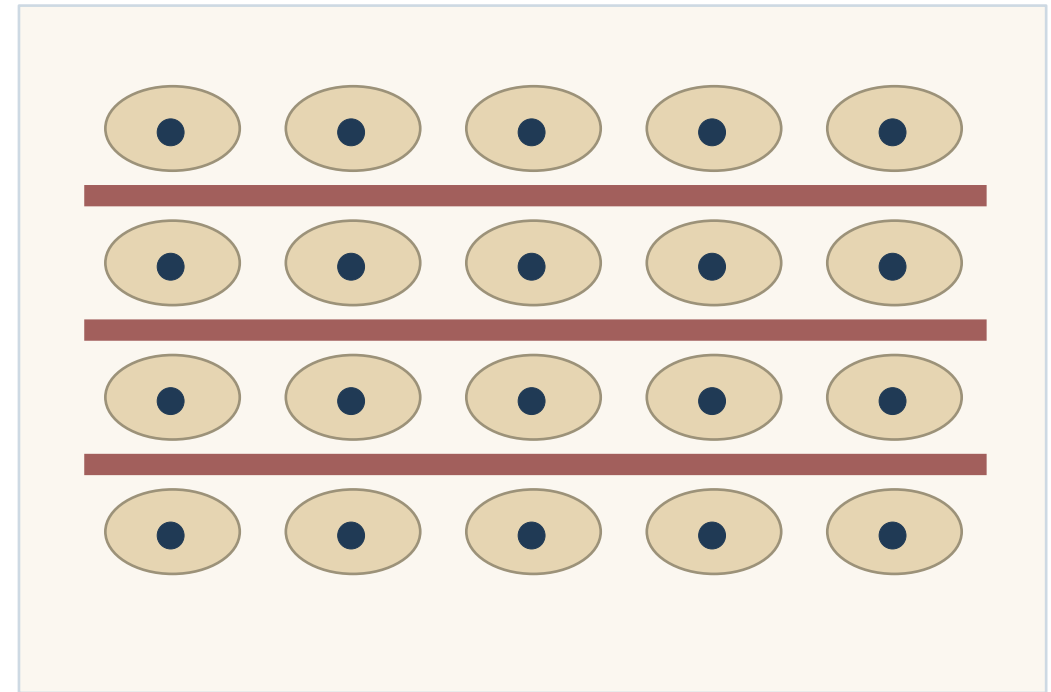
**Slight enlargement · tense capsule ·
cyanotic color**

**Passive venous
engorgement**

No required necrosis

Microscopic signature: Sinusoidal dilation

- Dilated sinusoids contain excess blood, especially in zone 3.
- The pericentral area is darker and more blood-filled than adjacent regions.
- Congestion affects vascular spaces before extensive hepatocyte destruction.
- Identify the central vein before assigning the lesion to zone 3.



Portal side

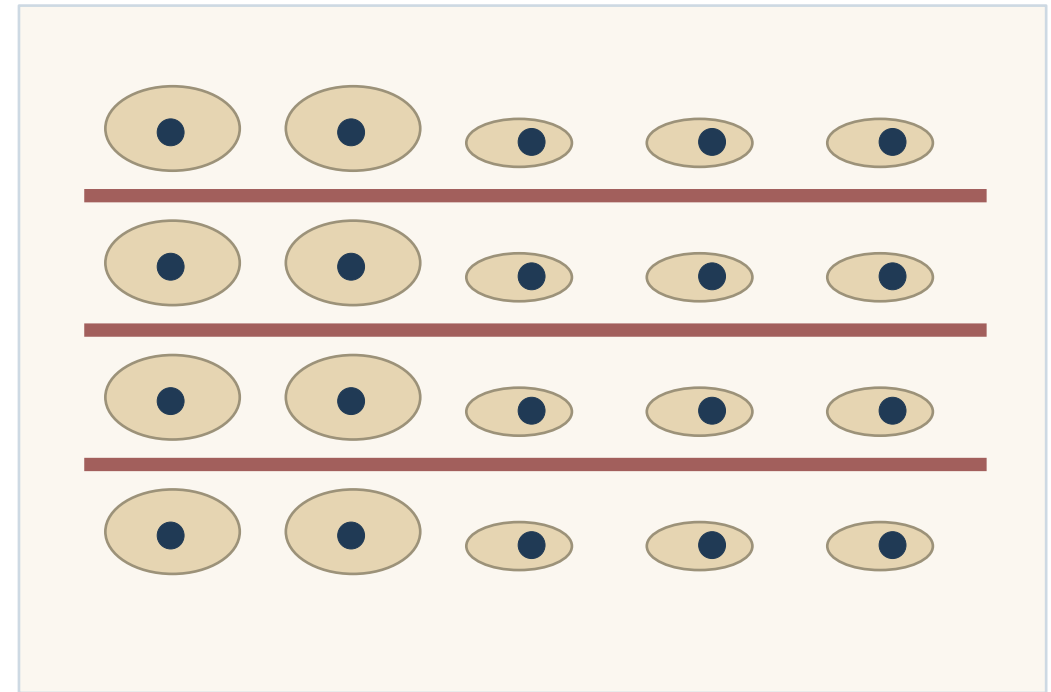


Central-vein side

Schematic hepatocyte plates and sinusoidal spaces

Sustained congestion attenuates hepatocyte plates

- Prolonged venous stasis is associated with centrilobular hepatocyte atrophy.
- Hepatocytes become thinner; Adjacent cell plates are markedly attenuated.
- An atrophic plate is not equivalent to a focus of coagulative necrosis.
- The structural finding reflects a chronic pressure and oxygenation burden.



Portal side



Central-vein side

Schematic hepatocyte plates and sinusoidal spaces

Congestion evolves with intensity and duration

- Early changes emphasize central venous and sinusoidal engorgement.
- Persistence leads to atrophy and loss of centrilobular hepatocytes.
- Superimposed perfusion failure intensifies hypoxic damage.
- Long-standing severe disease may culminate in pericellular fibrosis.

Dilation and stasis



Cell plate atrophy



Hemorrhagic injury



Fibrosis if sustained

Left-sided failure may impair hepatic perfusion

- Left-sided cardiac failure can reduce effective hepatic blood delivery.
- Systemic shock similarly decreases tissue perfusion.
- Pericentral hepatocytes lie at the downstream end of sinusoidal blood flow.
- Reduced oxygen delivery preferentially injures this vulnerable region.

Reduced cardiac output



Reduced hepatic perfusion



Zone 3 hypoxia

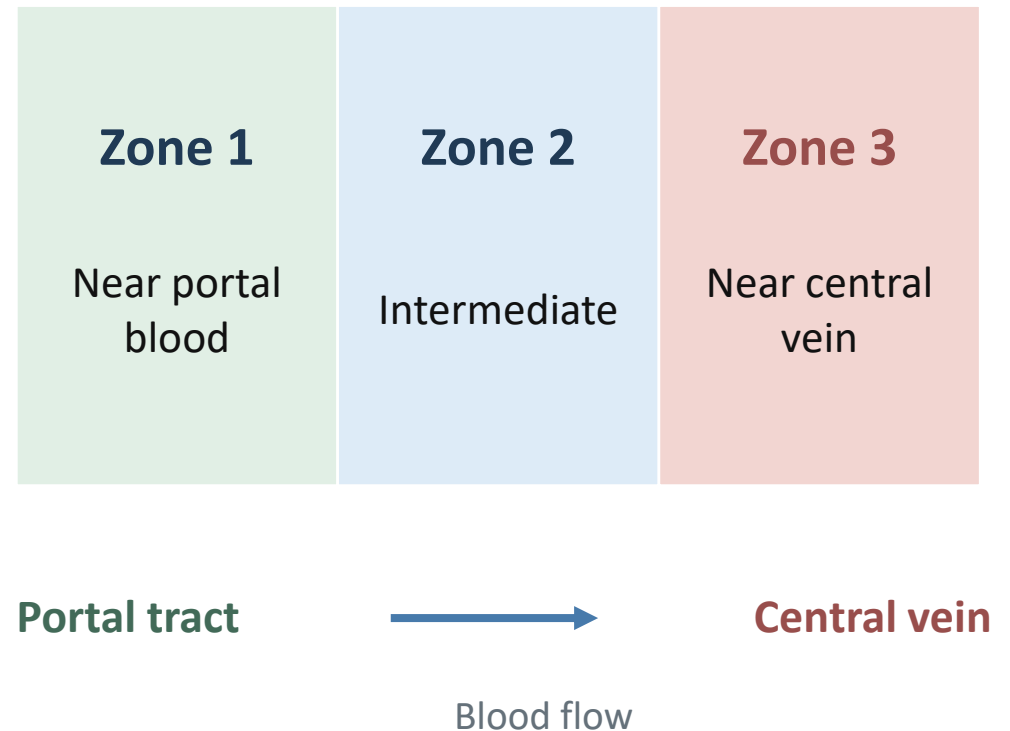


Cell injury

Shock produces a global oxygen-delivery problem

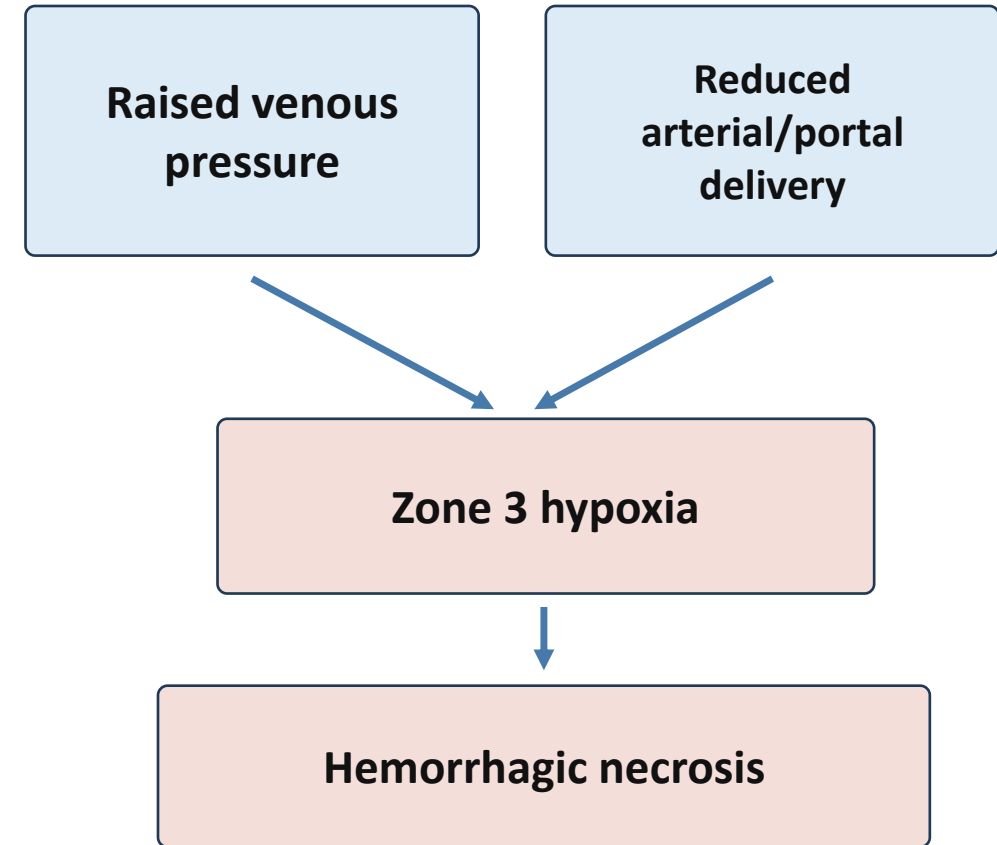
- Shock compromises circulatory perfusion beyond an isolated hepatic vein.
- Oxygen delivery declines along the entire hepatic microcirculation.
- Because zone 3 starts with the least oxygen reserve, it is injured first.
- The expected pattern is pericentral hepatocyte necrosis with periportal preservation.

Shock reduces incoming oxygen delivery



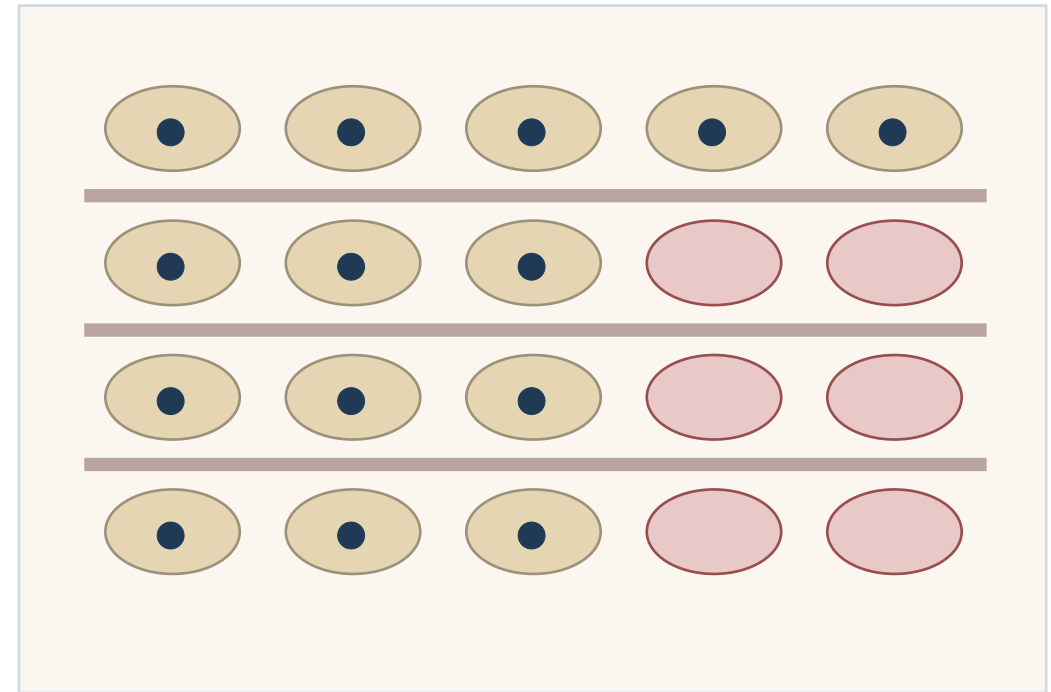
Congestion and hypoperfusion can reinforce each other

- Venous stasis impedes blood transit and sustains local deoxygenation.
- Low systemic perfusion reduces incoming oxygen delivery.
- Together, these effects increase susceptibility to cell death.
- Synergistic centrilobular hemorrhagic necrosis.



How centrilobular hepatocytes undergo necrosis

- An inadequate oxygen supply impairs energy-dependent hepatocyte function.
- Progressive ischemic injury causes pericentral cell death.
- Hepatocyte loss becomes recognizable around central veins.
- The lesion is geographically zonal rather than necessarily panlobular.



Portal side

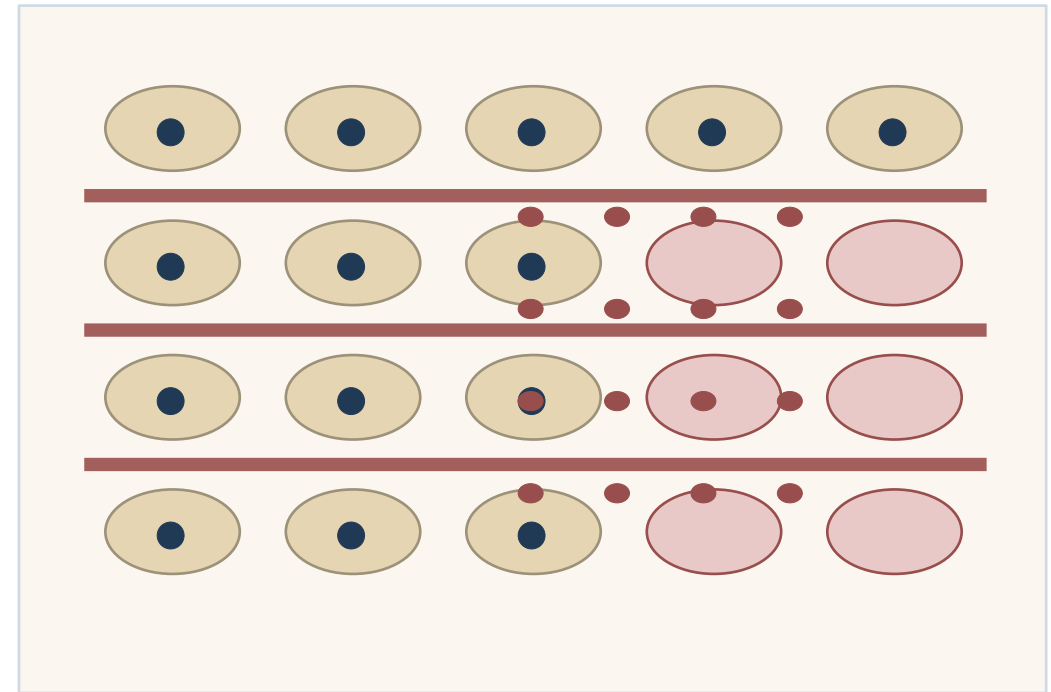


Central-vein side

Schematic hepatocyte plates and sinusoidal spaces

Why the necrotic region may be hemorrhagic

- Backed-up or damaged centrilobular sinusoids are filled with red cells.
- Hemorrhage and blood suffusion may accompany hepatocyte loss.
- The combined lesion produces dark red pericentral regions.
- Hemorrhage must be interpreted alongside hepatocyte viability.



Portal side

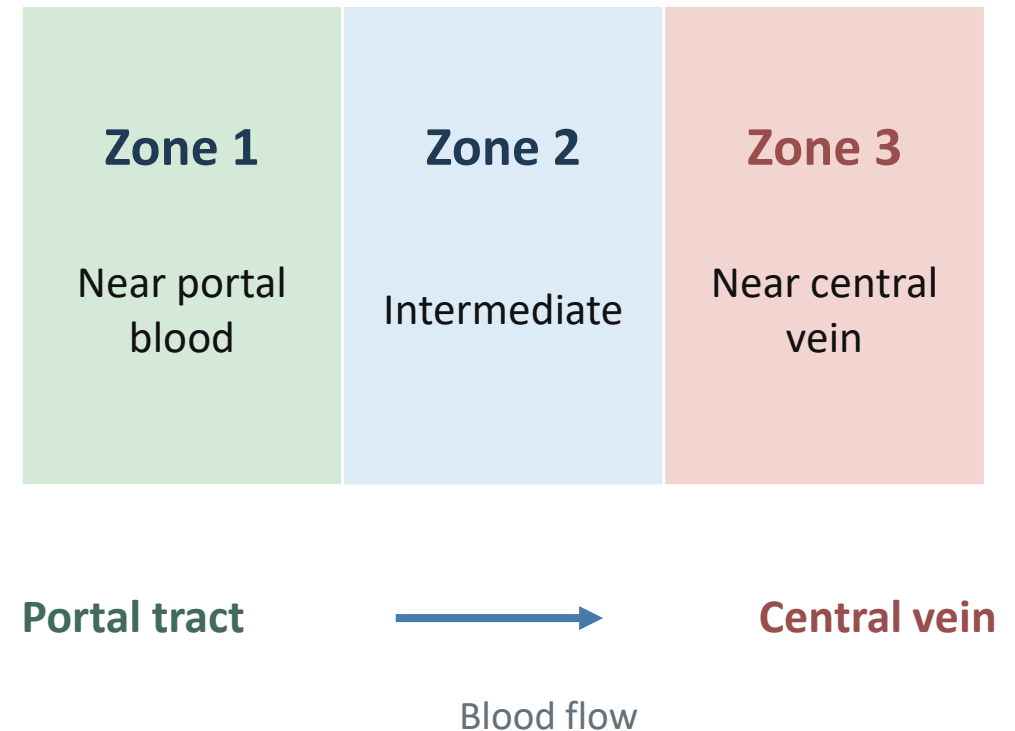


Central-vein side

Schematic hepatocyte plates and sinusoidal spaces

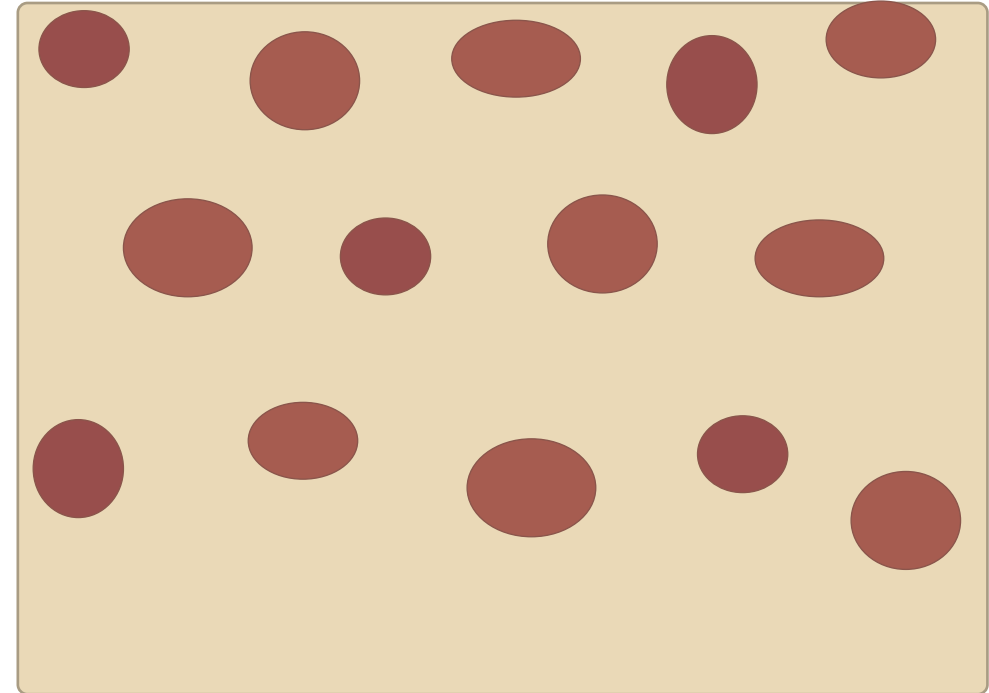
Periportal hepatocytes are relatively preserved

- Zone 1 is closest to branches of the hepatic artery and portal vein.
- Its better oxygenation confers relative resistance to hypoperfusion.
- Microscopy may show a sharp border between viable periportal cells and zone 3 loss.
- Relative preservation does not imply that periportal injury is impossible.



Nutmeg liver is a zonal macroscopic pattern

- The cut surface may appear mottled or variegated.
- Dark red-brown regions reflect centrilobular congestion, hemorrhage, and necrosis.
- Paler intervening regions represent relatively spared parenchyma.
- The name describes an appearance, not an independent etiology.



Dark: Zone 3 congestion / injury

Schematic cut-surface pattern — not a specimen

Translate the gross pattern into histology

- Dark centrilobular foci correspond to congested or hemorrhagic zone 3.
- Paler areas correspond to comparatively preserved portal-adjacent liver.
- Microscopic examination identifies whether hepatocytes are atrophic or necrotic.
- Gross appearance alone cannot grade the cellular injury.

Dark pericentral gross foci



Blood-filled zone 3 sinusoids



Atrophy or necrosis: Assess microscopy

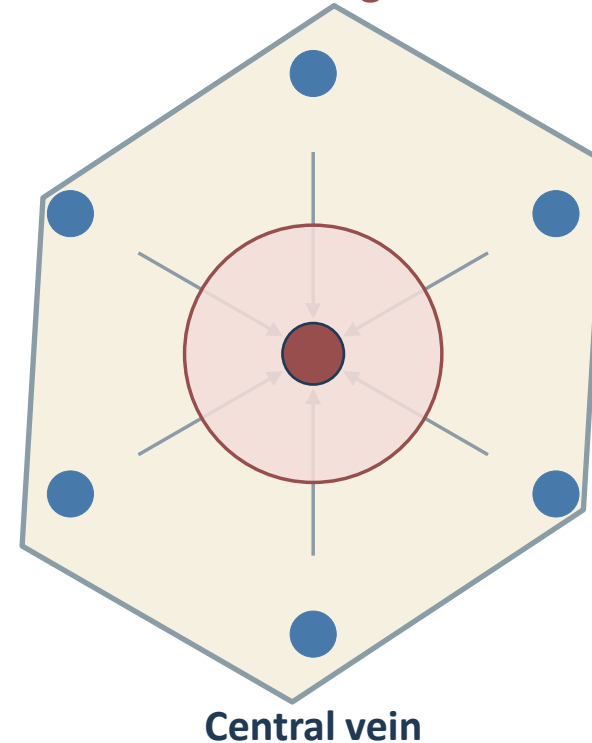
Acute congestion versus advanced injury

Pattern	Predominant lesion	Context
Early passive congestion	Central-vein / sinusoidal dilation	Raised venous pressure
Atrophic congestion	Thin pericentral cell plates	Persistence
Hemorrhagic necrosis	Zone 3 cell death + red cells	Severe hypoxia
Cardiac sclerosis	Pericellular $\pm$ bridging fibrosis	Chronic severe failure

Find the central vein on a liver section

- The central vein receives sinusoidal blood from surrounding liver plates.
- It normally lacks the full portal-tract triad grouping.
- Pericentral red-cell accumulation maps outward from this vessel.
- Misidentifying the central vein may reverse the apparent injury zone.

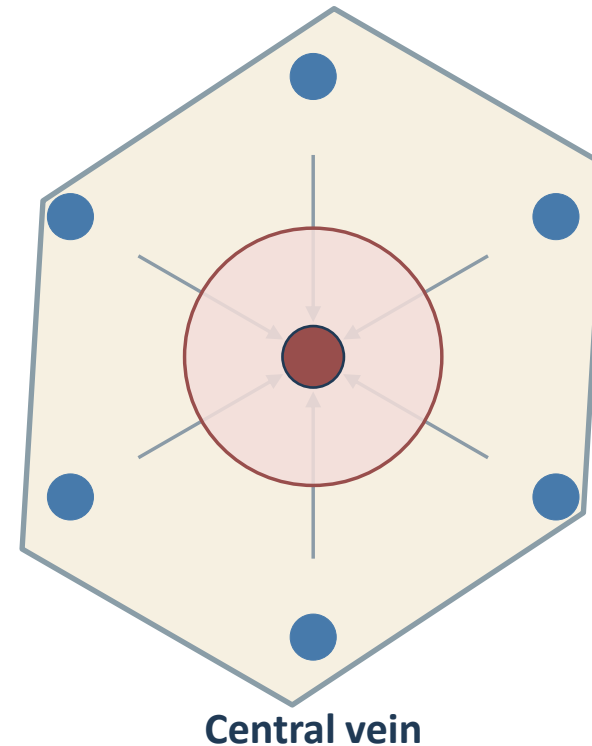
Zone 3: Surrounding central vein



Find the portal tract before labeling zone 1

- Portal tracts contain paired arterial and portal venous branches and bile ducts.
- They reside toward the classic lobule periphery.
- Periportal plates are usually relatively viable in centrilobular ischemia.
- Mapping both portal tract and central vein makes a zonal diagnosis reliable.

Portal tracts at periphery



Red-cell suffusion is not the same as necrosis

Observation	Represents	Not sufficient alone for
Sinusoids packed with RBCs	Congestion	Necrosis
RBCs between damaged plates	Hemorrhagic suffusion	Specific etiology
Hepatocyte loss / necrosis	Parenchymal damage	Cause without context

Atrophy and hepatocyte dropout differ

Feature	Atrophy	Necrosis / dropout
Hepatocytes	Present but shrunken	Lost or nonviable
Plate pattern	Attenuated	Interrupted or absent
Implication	Chronic stress	Cell death
May coexist with	Congestion	Hemorrhage

Hemosiderin-laden macrophages mark prior hemorrhage

- Chronic congestion may be accompanied by capillary injury and local hemorrhage.
- Breakdown of extravasated erythrocytes can leave hemosiderin in macrophages.
- These macrophages indicate prior red-cell extravasation, not a unique cause.
- Interpret them with the distribution of congestion and hepatocyte injury.

Red-cell leakage



Erythrocyte breakdown



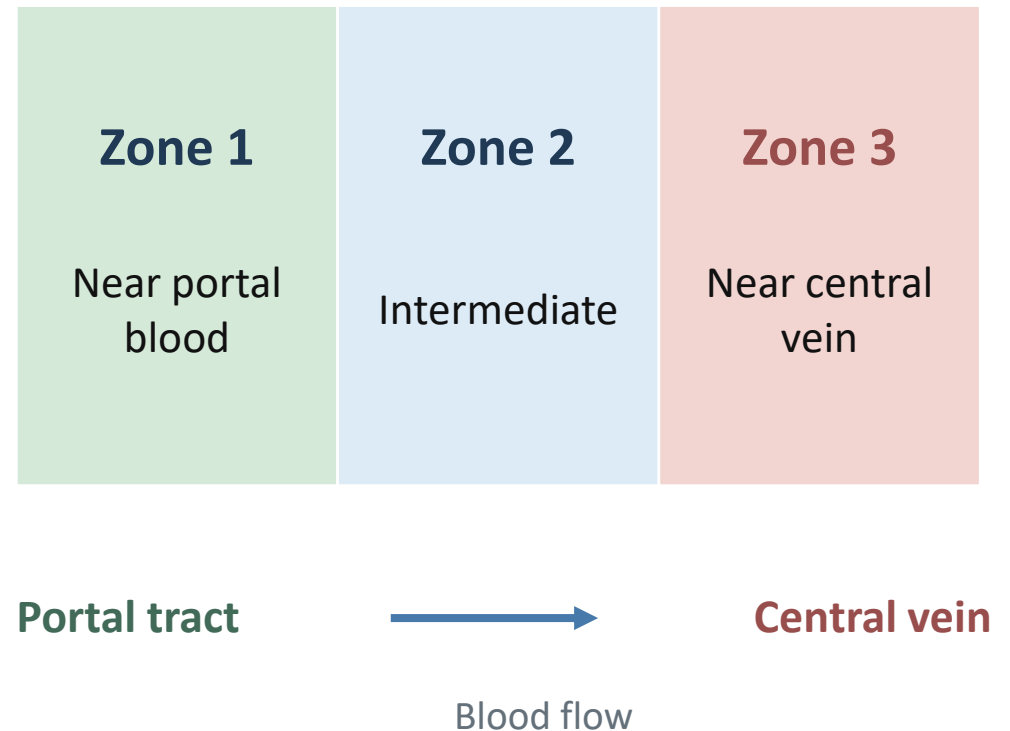
Hemosiderin accumulation



Macrophages in lesion

Periportal fatty change can accompany hypoxic injury

- Zone 1 hepatocytes may show fatty change while zone 3 undergoes ischemic necrosis.
- The pattern reflects different zonal responses to circulatory stress.
- Fat accumulation is not synonymous with necrosis.
- Use the combination of findings, rather than one component, for interpretation.



Read a congested liver section systematically

- Locate both central vein and portal tract.

- Evaluate sinusoidal dilation, red-cell accumulation, and bleeding.

- Assess pericentral hepatocyte atrophy, necrosis, or dropout.

- Look for pericellular fibrosis and extension toward other zones.

Locate landmarks



Evaluate vascular spaces



Assess hepatocytes



Inspect fibrosis

Cardiac sclerosis: Chronic severe venous injury

- Sustained severe congestive heart failure can produce hepatic fibrotic remodeling.
- The initial pattern is described as centrilobular pericellular fibrosis.
- Bridging fibrous septa may develop in advanced examples.
- Not every congested liver has cardiac sclerosis.

Chronic heart failure



Recurrent zone 3 stress



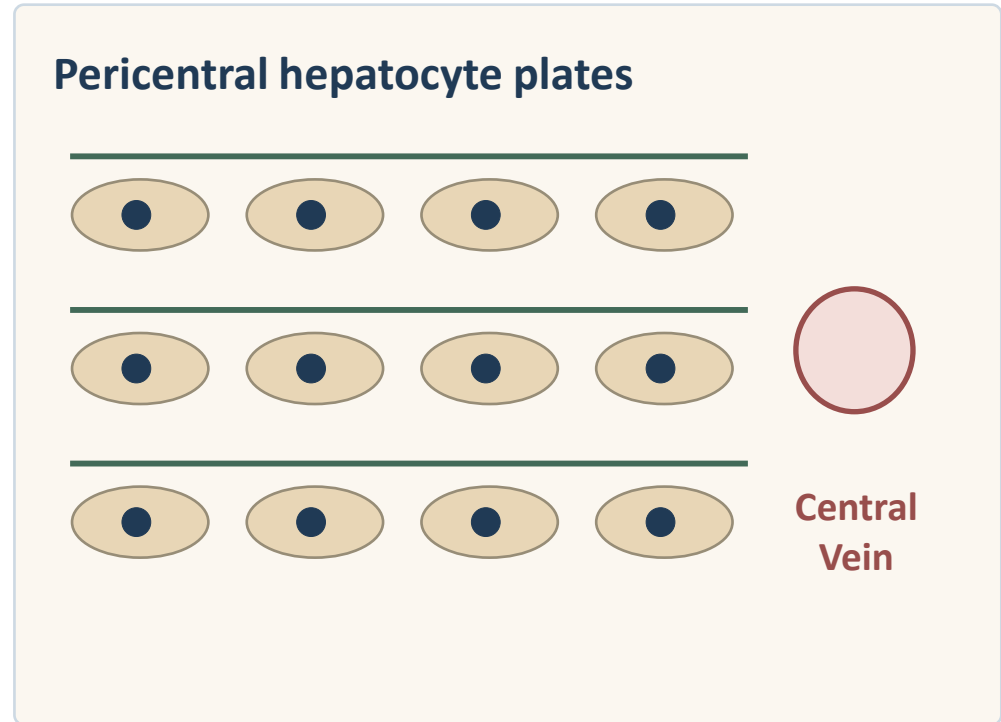
Pericellular fibrosis



Possible bridging

Pericellular fibrosis begins near central veins

- The collagen accumulates around affected centrilobular hepatocytes.
- This is distinct from beginning the diagnosis with a portal-based scar.
- Distribution reflects the vascular locus of chronic injury.
- A collagen stain can help demonstrate fibrous expansion when tissue is available.

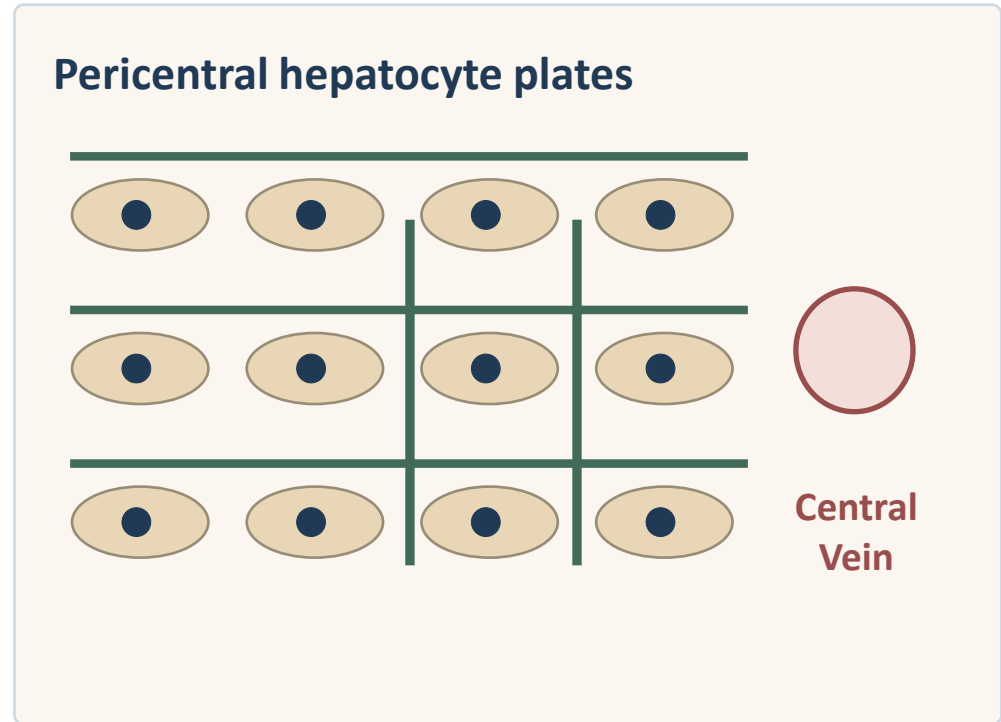


Pericellular collagen near zone 3

Schematic — not a histologic specimen

Bridging fibrosis represents more extensive remodeling

- Chronic severe congestion may progress beyond local pericellular fibrosis.
- Fibrous septa can bridge regions of injury.
- Fibrosis is an endpoint of persistent damage, not an inevitable feature of acute stasis.
- Recognize distribution before attributing scar to a specific vascular disorder.



Bridging collagen between injured areas

Schematic — not a histologic specimen

Cardiac sclerosis is a pattern, not proof of mechanism

- The zonal scar supports a chronic venous-hemodynamic contribution.
- Historical cardiac disease and contemporaneous congestion strengthen attribution.
- Fibrosis alone does not identify the exact cardiac lesion.
- Interpret associated liver diseases before assigning all scarring to congestion.

Histologic pattern



Clinical cardiac context



Competing injuries



Integrated interpretation

Outflow abnormalities occur at different levels

- Systemic right-heart failure impedes hepatic venous return.
- Budd–Chiari syndrome is associated with obstruction of major hepatic veins.
- Sinusoidal obstruction syndrome targets terminal venules and sinusoids.
- All may create centrilobular injury, but mechanisms are different.

Systemic right heart



Major hepatic veins



Terminal venules / sinusoids

Budd–Chiari syndrome can resemble congestion

Feature	Budd–Chiari syndrome	Passive cardiac congestion
Primary defect	Major hepatic-vein thrombosis	Systemic venous backpressure
Zone 3 lesion	Congestion and necrosis	Congestion ± necrosis
Distinguishing context	Hepatic venous thrombosis	Right-heart decompensation

Sinusoidal obstruction syndrome has an endothelial lesion

- Toxic endothelial injury damages sinusoidal and terminal venular lining.
- Obstructive debris and progressive venular fibrosis limit hepatic outflow.
- Acute lesions can include centrilobular congestion and necrosis.
- The cause and venular pathology differ from uncomplicated cardiac congestion.

Endothelial injury



Sinusoidal/venular obstruction



Pericentral congestion



Hepatocyte injury

Compare three causes of pericentral congestion

Condition	Dominant disturbance	Useful discriminator
Cardiac congestion	Systemic venous pressure	Right-heart dysfunction
Budd–Chiari	Major hepatic vein obstruction	Large hepatic-vein thrombi
Sinusoidal obstruction	Sinusoidal/terminal venular injury	Obliterative small-vein changes

Do not confuse inflow ischemia with venous congestion

Dimension	Inflow reduction	Outflow congestion
Hemodynamic event	Reduced delivery	Impeded drainage
Morphologic emphasis	Ischemic injury	Dilated blood-filled sinusoids
Possible overlap	Hypoxia	Secondary hypoxia / necrosis

Clinical expression may be limited

- The liver has substantial functional reserve.
- Circulatory lesions may be evident morphologically before marked clinical hepatic failure.
- Transient serum aminotransferase elevation may be the only clinical evidence.
- Assessment must consider underlying systemic hemodynamics.

Morphology can exceed clinical symptoms

Large functional reserve

Systemic context is essential

Aminotransferases reflect hepatocellular damage

- Transient aminotransferase elevation in many cases.
- Aminotransferase release signals hepatocyte injury, not its etiology.
- A circulatory history and zone 3 pattern make hypoxic-congestive injury plausible.
- No single liver enzyme result demonstrates a nutmeg pattern.

Hypoxic injury



Hepatocyte damage



Enzyme release



Transient serum elevation

Jaundice is possible with greater parenchymal injury

- Injury may be sufficient to induce mild to moderate jaundice.
- The clinical expression depends on the extent of parenchymal dysfunction.
- Jaundice alone does not establish a circulatory mechanism.
- Interpret alongside hepatic morphology and the cardiac/shock history.

Larger zone 3 injury



Impaired hepatic function



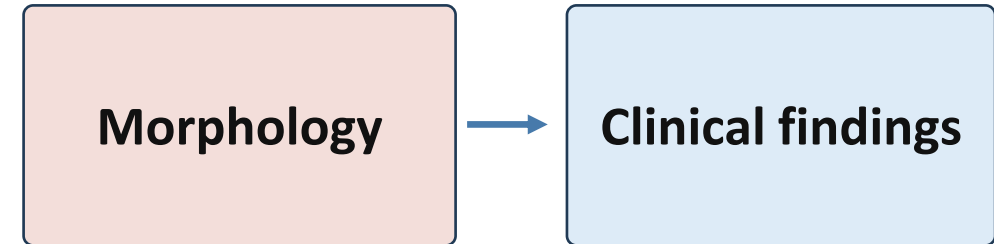
Serum bilirubin increase



Clinical jaundice

Hepatic reserve explains clinicopathologic mismatch

- The liver may tolerate modest injury without overt dysfunction.
- Gross and microscopic venous congestion may be conspicuous.
- Laboratory abnormalities can be transient or limited.
- Absence of marked jaundice does not exclude a congestive pattern.



The severity of congestion or zonal damage need not parallel obvious symptoms.

Correlate the liver with right-sided heart disease

- Venous-pressure elevation provides a mechanism for sinusoidal engorgement.
- A mildly enlarged, cyanotic liver supports congestive involvement.
- Zone 3 atrophy or chronic fibrosis suggests persistence.
- Exclude a major hepatic-vein obstruction when the clinical scenario warrants.

Right-heart state



Venous backpressure



Pericentral congestion



Assess chronicity

Correlate abrupt necrosis with systemic hypoperfusion

- Acute circulatory failure can reduce hepatic oxygen delivery.
- Zone 3 necrosis is compatible with its low baseline oxygenation.
- Coexisting venous congestion increases susceptibility.
- Interpret the lesion as part of multisystem hemodynamic compromise.

Shock / low output



Reduced oxygen delivery



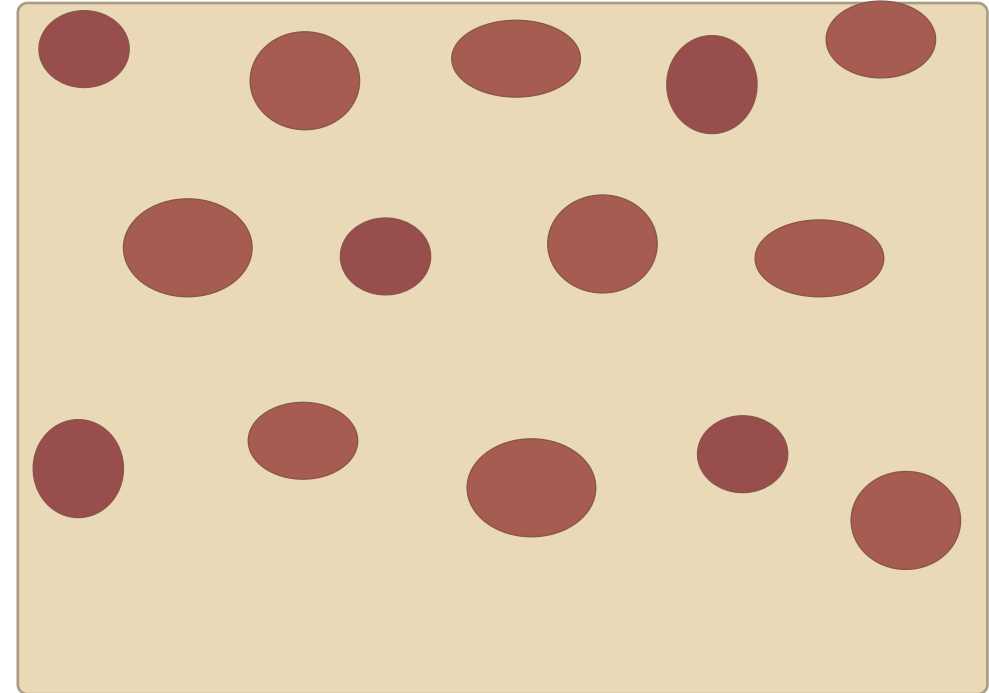
Zone 3 necrosis



Clinical correlation

Macroscopic teaching exercise: Map the colors

- A dark centrilobular region indicates a blood-rich zone in this schematic.
- The intervening pale region represents comparatively preserved parenchyma.
- Multiple repeated lobules create the mottled cut-surface pattern.
- Actual necrosis must be assessed histologically, not from the pattern alone.



Dark: Zone 3 congestion / injury

Schematic cut-surface pattern — not a specimen

A focused interpretation workflow

- Start with systemic clinical context: Failure, shock, or outflow obstruction.
- Locate the lesion relative to portal tracts and central veins.
- Classify predominant change as congestion, atrophy, necrosis, or fibrosis.
- Check for a competing vascular or parenchymal disorder before concluding.

Clinical setting



Zonal distribution



Dominant morphology



Alternative causes

Autopsy context: Avoid overstating significance

Finding	Possible interpretation	Necessary context
Engorged sinusoids	Terminal or chronic stasis	Clinical time course
Zone 3 necrosis	Recent circulatory compromise	Shock / cardiac data
Zone 3 fibrosis	Prolonged injury	Chronic hemodynamics

Three avoidable diagnostic errors

- Equating blood-filled sinusoids with hepatocellular necrosis.
- Calling any mottled liver a distinct primary hepatic disease.
- Attributing centrilobular fibrosis to heart failure without context.
- Overlooking Budd–Chiari or sinusoidal obstruction when suggested by findings.

Congestion ≠ necrosis

Nutmeg ≠ etiology

Fibrosis ≠ proof of heart failure

Case 1: Long-standing right-heart dysfunction

- A patient with chronic right-sided cardiac decompensation has an enlarged cyanotic liver.
- Histology shows dilated pericentral sinusoids and thin hepatocyte plates.
- No substantial centrilobular necrosis is apparent.
- What is the dominant lesion and why does it occur?

Dominant process?

Case 1: Explain the observed pattern

- The raised right-heart venous pressure impairs hepatic outflow.
- Central-vein and zone 3 sinusoids fill with excess blood.
- Prolonged congestion attenuates neighboring hepatocyte plates.
- The absence of conspicuous necrosis does not negate chronic congestion.

Right-heart dysfunction



Hepatic venous stasis



Dilated sinusoids



Zone 3 atrophy

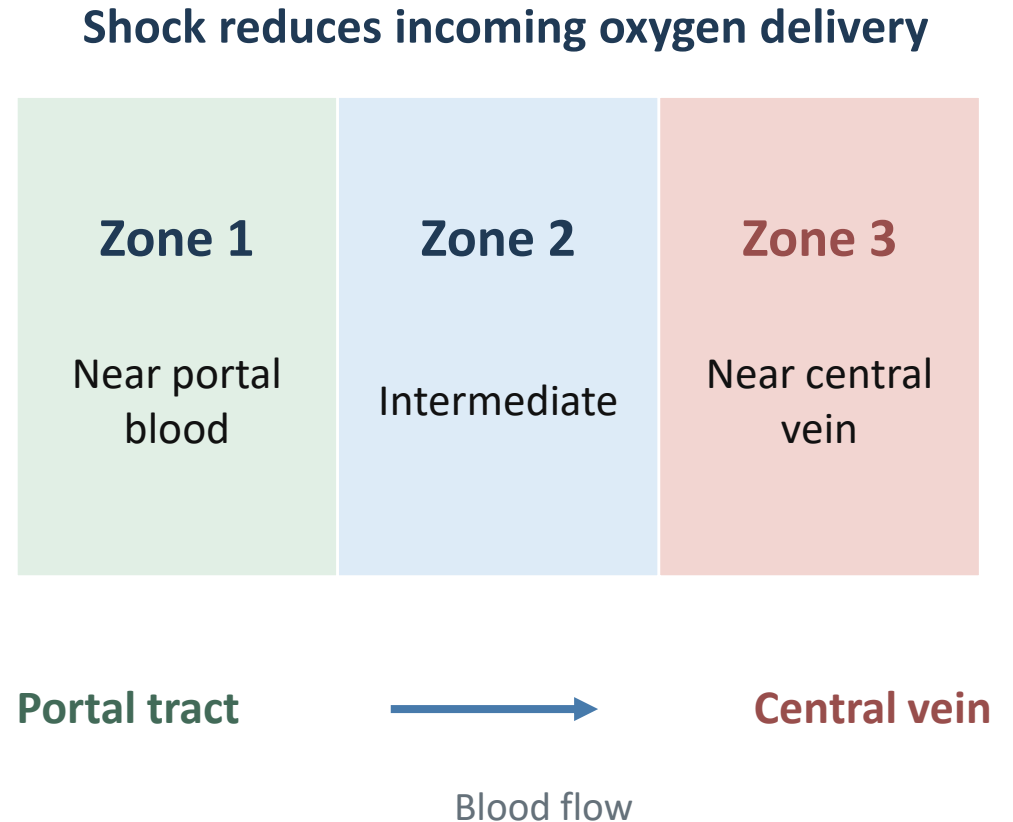
Case 2: Circulatory shock

- Following profound systemic circulatory failure, a liver section has cell loss around central veins.
- Periportal hepatocytes remain viable, with local hemorrhagic suffusion.
- The clinician asks why the pattern is selectively centrilobular.
- What zonal property explains the distribution?

Why zone 3?

Case 2: Explain selective zone 3 necrosis

- The acinar oxygen gradient places zone 3 at the lowest oxygen availability.
- Shock reduces upstream oxygen delivery.
- Pericentral cell death and hemorrhage follow severe hypoxic injury.
- Zone 1 is relatively spared because of proximity to incoming blood.



Case 3: Pericentral congestion with venular injury

- A patient after hematopoietic stem cell transplantation develops hepatic dysfunction.
- Tissue shows centrilobular congestion with obliterative terminal-venule changes.
- The microscopic findings overlap with cardiac congestive injury.
- Which vascular mechanism requires special consideration?

Competing diagnosis?

Case 3: Locate the decisive pathologic feature

- Sinusoidal obstruction syndrome begins with toxic endothelial injury.
- Terminal hepatic venules can be narrowed or obliterated.
- Pericentral congestion and necrosis are downstream consequences.
- The obstructive venular lesion distinguishes it from uncomplicated systemic backpressure.

Endothelial toxicity



Venular lumen injury



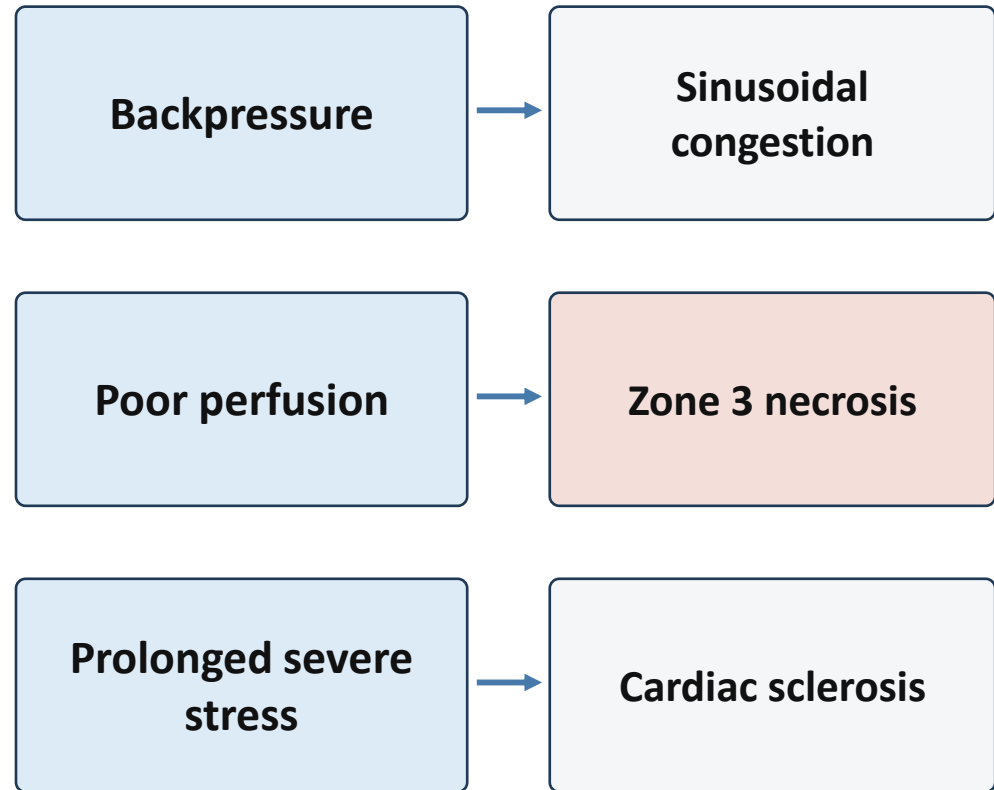
Sinusoidal obstruction



Zone 3 damage

Integrate mechanisms, morphology, and clinical setting

- Backpressure predominantly causes centrilobular sinusoidal congestion.
- Hypoperfusion preferentially produces zone 3 necrosis.
- Both together can yield hemorrhagic necrosis and a nutmeg pattern.
- Persistent severe congestion may progress to cardiac sclerosis.



References and visual provenance

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 18, pp. 749–750 and 783–786.
- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 4, p. 102.
- Diagrams in this presentation are original editable PowerPoint schematics, not patient images.
- Diagrams illustrate anatomical and pathologic relationships; they are not diagnostic tissue images.