

Hepatic Disease Associated With Pregnancy

Clinicopathologic mechanisms, morphology and syndromic distinctions

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Learning objectives

- Classify pregnancy-associated hepatic dysfunction into infections and pregnancy-specific syndromes.
- Link characteristic hepatic lesions to preeclampsia/eclampsia, HELLP syndrome and acute fatty liver.
- Contrast the clinical patterns of acute fatty liver and intrahepatic cholestasis.
- Recognize signals of severe maternal disease and pregnancy-related fetal risk.

Two pathways to hepatic disease in pregnancy

Concurrent or exacerbated disease

Viral hepatitis; Opportunistic or systemic infections involving the liver.

Pregnancy-specific disorders

Preeclampsia/eclampsia with HELLP; Acute fatty liver; Intrahepatic cholestasis.

The gestational context changes both the differential diagnosis and the clinical consequences.

Frequency does not equal severity

3%–5%

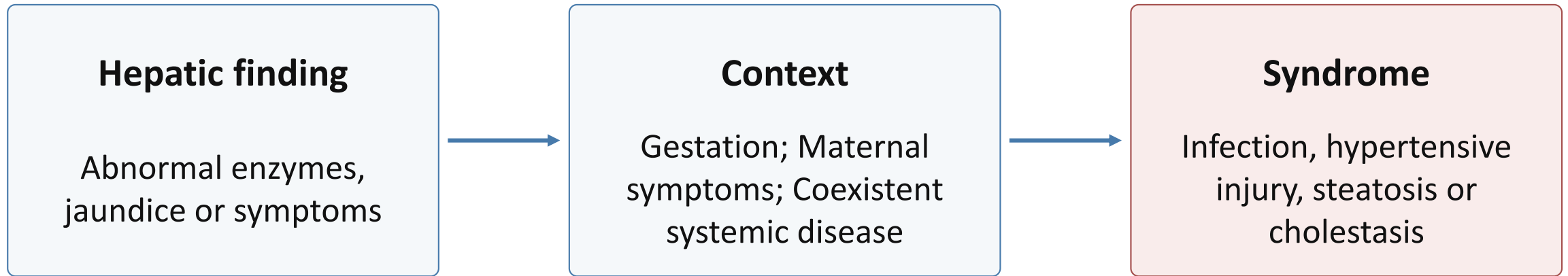
Pregnancies with abnormal liver tests; Most findings have little clinical importance.

~0.1%

Pregnancies with serious hepatic complications in the Robbins overview.

Use these textbook estimates as context, not as stand-alone diagnostic probabilities.

Clinical reasoning begins with the phenotype



The same laboratory abnormality may result from distinct pathologic processes.

Liver injury mechanisms are heterogeneous

Infectious mechanisms

- Hepatotropic viruses may produce jaundice.
- HSV may cause acute hepatic failure.
- Listeria may disseminate from infected placental tissue.

Pregnancy-associated mechanisms

- Sinusoidal fibrin and hemorrhagic injury in preeclampsia.
- Fetoplacental metabolites associated with microvesicular steatosis.
- Canalicular bile retention in cholestasis.

Abnormal liver tests require context

- Abnormal testing in pregnancy is not synonymous with severe hepatopathy.
- Severe disorders constitute a much smaller subgroup than all biochemical abnormalities.
- Symptoms, timing, liver injury mechanism and systemic manifestations help frame interpretation.
- A severe clinical syndrome cannot be excluded merely because an initial abnormality appears modest.

Infections in the maternal hepatic differential

Viral hepatitis

HAV, HBV, HCV and HDV are named in the Robbins overview.

Hepatitis E

The viral infection singled out for pregnancy-related severity.

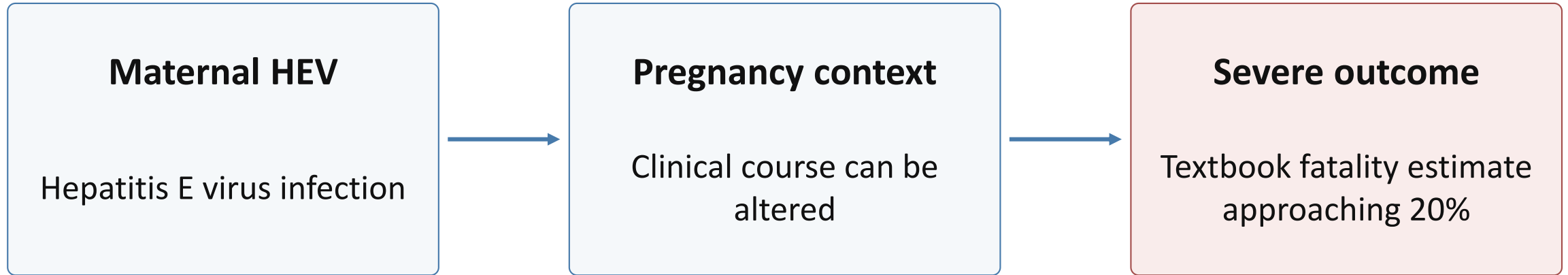
Other infections

HSV hepatitis and placentally associated Listeria infection.

Viral hepatitis: Leading infectious context

- Viral hepatitis as the most common cause of jaundice during pregnancy.
- The listed infections include hepatitis A, B and C and HBV with HDV coinfection.
- Pregnancy does not uniformly worsen the course of each viral hepatitis.
- Hepatitis E is distinguished by substantially increased maternal fatality risk.

Hepatitis E is the high-risk exception



The source states that the reason for this pregnancy-specific severity remains unknown.

Interpreting the HEV risk statement

What Robbins supports

- HEV is singled out as pregnancy-sensitive.
- A fatality estimate approaching 20% is cited.
- Mechanistic explanation is described as unknown.

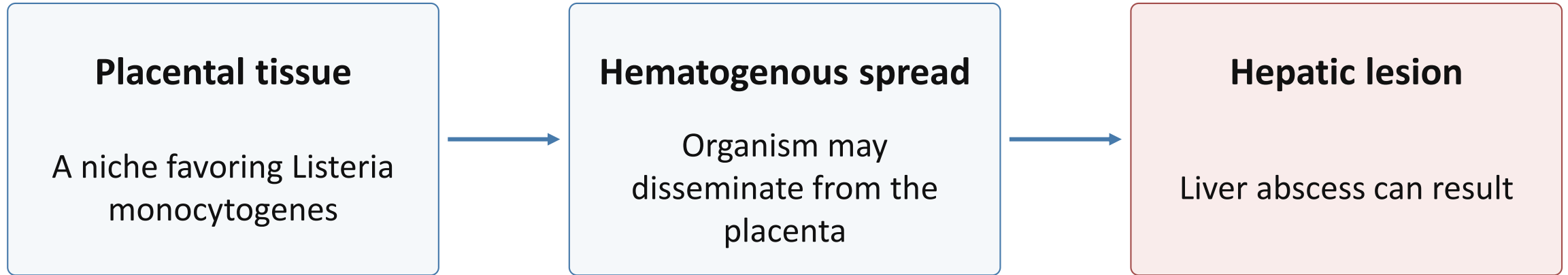
What the source does not establish

- A universal risk for every population or outbreak.
- A verified molecular explanation for maternal susceptibility.
- A patient-specific prediction from pregnancy status alone.

HSV hepatitis: An uncommon catastrophic presentation

- Herpes simplex virus can involve the liver during pregnancy.
- The source characterizes HSV hepatitis as a rare cause of acute liver failure.
- Its clinical significance derives from the potential severity, not its prevalence.
- Infectious causes remain relevant even when pregnancy-specific disorders are suspected.

Listeria: An infection with a placental route



The maternal liver lesion reflects systemic/placental infection, not a primary pregnancy metabolic syndrome.

Infectious etiologies: Discriminating emphasis

Viral hepatitis

- Principal infectious setting for gestational jaundice.
- HEV deserves specific attention to increased severity.
- HSV is rare but can produce acute liver failure.

Listerial disease

- The placenta provides a favorable tissue environment.
- Dissemination may seed the maternal liver.
- A hepatic abscess differs morphologically from diffuse hepatocyte injury.

Case: Infectious liver involvement

A pregnant patient presents with jaundice and suspected acute infectious hepatitis.

Observed findings

- Hepatotropic viruses remain a leading category.
- One viral infection is specifically associated with worse maternal outcomes.
- Pregnancy alone does not explain the exact viral etiology.

Diagnostic task

Which infectious diagnosis must be singled out for pregnancy-associated severity?

Case interpretation: Prioritize HEV as a concern

- The case cannot establish an infectious diagnosis without etiologic evaluation.
- Robbins specifically singles out HEV among hepatitis viruses for a pregnancy-altered course.
- HSV and Listeria are distinct, less common causes of potentially serious hepatic involvement.
- Risk recognition and etiologic confirmation are separate clinical tasks.

Hypertensive pregnancy disorders and the liver

Preeclampsia

Maternal hypertension with systemic and hepatic manifestations.

Eclampsia

Convulsions occur in the hypertensive disorder, potentially with severe hepatic injury.

HELLP

Hemolysis, elevated liver enzymes and low platelets.

Preeclampsia: The multisystem setting

- The Robbins description includes maternal hypertension, proteinuria and peripheral edema.
- Coagulation abnormalities can accompany the disorder.
- A frequency of up to 10% of pregnancies.
- Hepatic injury can be clinically overt or comparatively subclinical.

Eclampsia denotes neurologic escalation

- Hyperreflexia and convulsions distinguish eclampsia description.
- The condition may be life-threatening.
- Hepatic involvement may add hemorrhagic and vascular complications.
- Neurologic and hepatic severity need not appear in an identical sequence.

HELLP makes liver injury part of the syndrome

H — Hemolysis

Red-cell destruction is the hematologic component.

EL — Elevated liver enzymes

Biochemical manifestation of hepatic injury.

LP — Low platelets

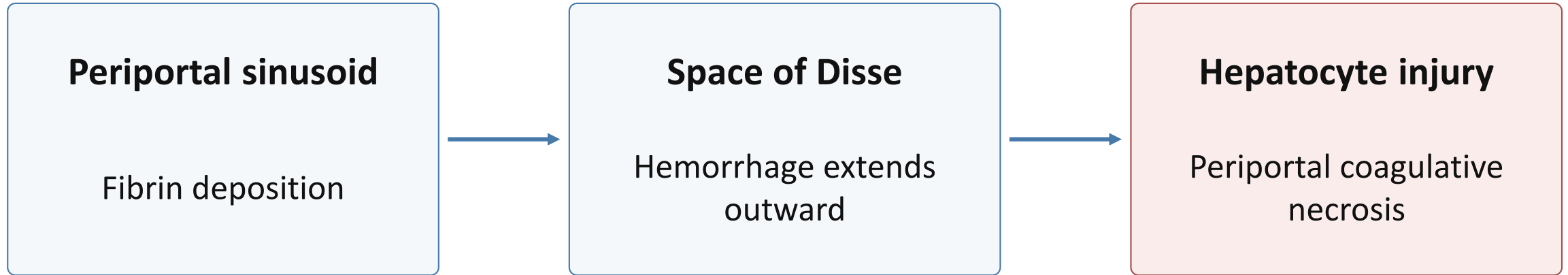
Thrombocytopenia accompanying the syndrome.

Hepatic abnormalities may be the predominant manifestation of preeclampsia.

Why hepatic preeclampsia may be overlooked

- The maternal liver may be involved before striking clinical liver symptoms appear.
- Biochemical changes can be modest or marked.
- HELLP combines hepatic injury with hematologic abnormalities.
- Serious hepatic complications can evolve despite initially subtle findings.

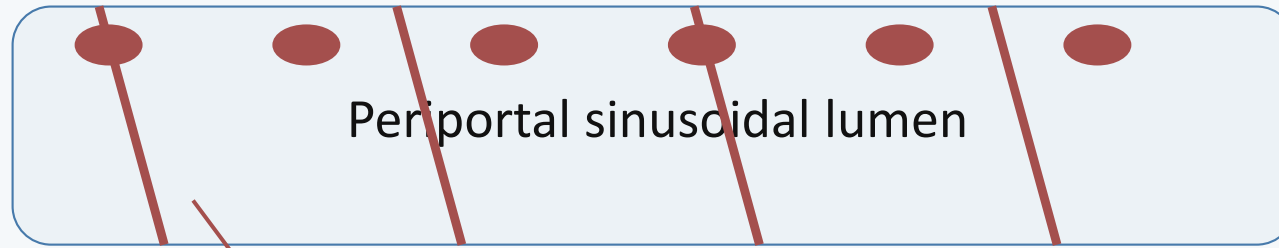
The periportal lesion: Vascular injury to necrosis



This is a periportal microvascular injury pattern in the source, not the centrilobular congestion pattern of cardiac failure.

Periportal fibrin deposition: Morphology

Simplified schematic — not histologic tissue



Fibrin deposits

What it means

Microvascular fibrin and hemorrhage precede periportal hepatocyte necrosis.

Space of Disse hemorrhage: An injury bridge

Sinusoidal blood compartment

Fibrin-containing sinusoid



Blood in space of Disse



Adjacent periportal hepatocyte injury

Morphologic sequence

- Sinusoidal fibrin is intravascular.
- Hemorrhage extends beyond the lumen.
- Hepatocytes develop coagulative necrosis.

Periportal coagulative necrosis

- Hepatocyte necrosis follows fibrin deposition and perisinusoidal hemorrhage.
- The anatomic emphasis is periportal, surrounding portal regions of the lobule.
- Coagulative necrosis denotes cell death with temporary retention of tissue architecture.
- The vascular distribution helps explain the hepatic injury pattern.

Periportal injury versus passive congestion

Preeclampsia-associated change

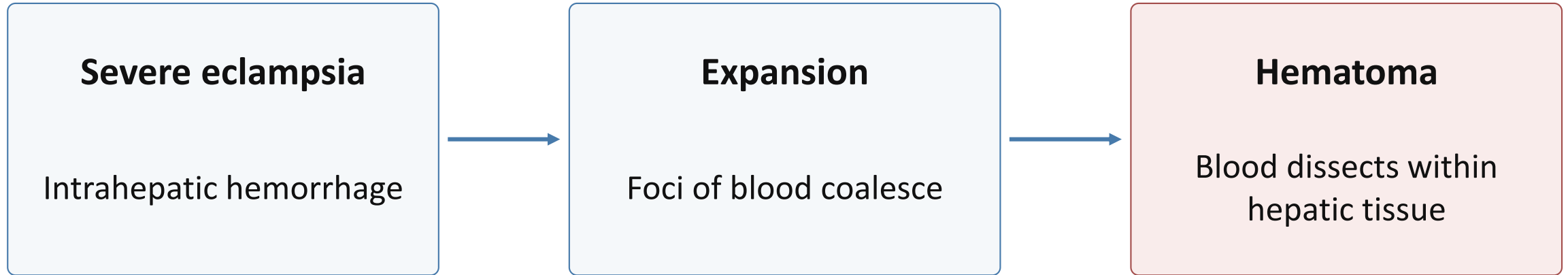
- Periportal sinusoidal fibrin.
- Hemorrhage into the space of Disse.
- Periportal coagulative necrosis.

Passive hepatic congestion

- Dilated centrilobular sinusoids.
- Congestion and atrophy of pericentral hepatocytes.
- A distinct hemodynamic cause and zonal pattern.

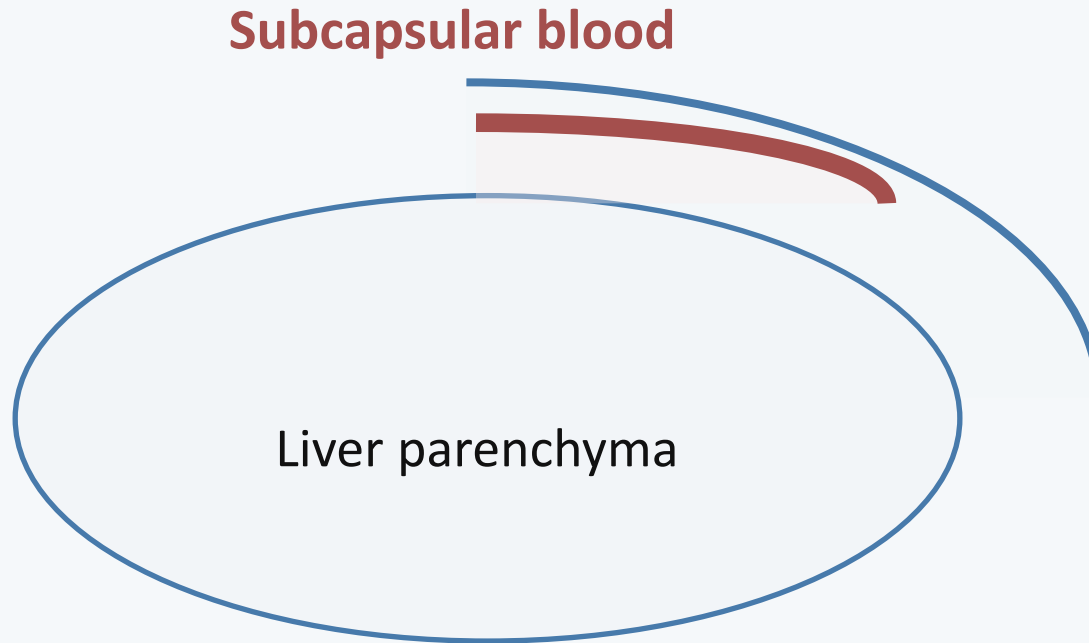
These are different vascular mechanisms discussed in the same Robbins chapter.

Progression to a hepatic hematoma



Progressive hemorrhage can be clinically catastrophic rather than simply biochemical.

Glisson capsule: The danger of subcapsular blood



Conceptual cutaway — not a specimen

Pathologic consequence

- Blood tracks beneath Glisson capsule.
- Tension may culminate in hepatic rupture.
- Rupture represents a potentially fatal event.

Hepatic rupture is a vascular emergency

- The source describes subcapsular hematoma dissecting under Glisson capsule.
- Rupture is a possible endpoint of severe hemorrhagic hepatic injury.
- The pathology is not equivalent to uncomplicated elevation of aminotransferases.
- A severe clinical presentation warrants immediate specialist obstetric assessment.

Severity distinction

Hepatic rupture is a complication of severe disease, not a routine finding.

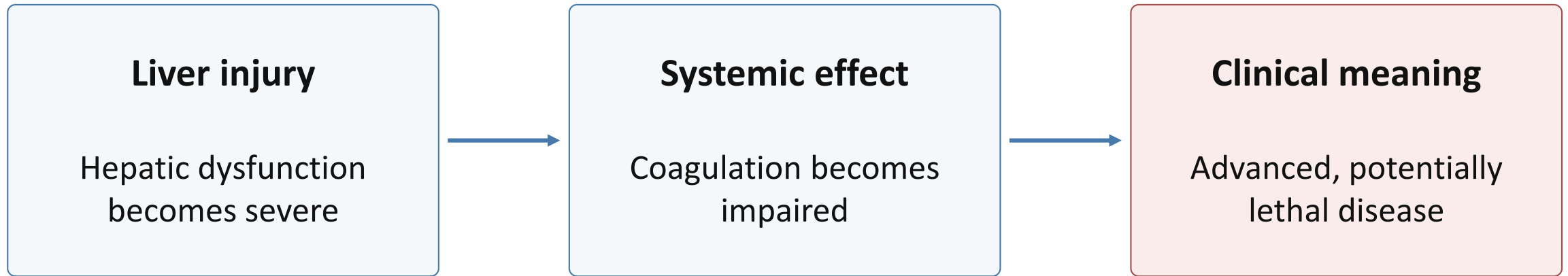
Aminotransferases indicate hepatocellular injury

- Preeclampsia-related hepatic involvement may elevate serum aminotransferases.
- A range from modest to severe elevation.
- Enzyme release reflects hepatocyte injury but does not by itself define its cause.
- Interpret biochemistry alongside hypertensive and hematologic manifestations.

Bilirubin changes may be comparatively mild

- Mild serum bilirubin elevation in hepatic preeclampsia.
- Severe aminotransferase elevation does not require proportionately severe jaundice.
- The vascular and hemorrhagic mechanisms remain clinically important.
- Bilirubin and aminotransferases report different dimensions of hepatic dysfunction.

Coagulopathy marks advanced hepatic involvement



The textbook explicitly flags hepatic dysfunction sufficient to cause coagulopathy as ominous.

Preeclampsia: Severity determines intervention

Milder hepatic involvement

- Conservative management as possible.
- Biochemical severity and symptoms require monitoring.
- Maternal and fetal status determine the actual clinical plan.

Severe hepatic involvement

- The source specifies pregnancy termination in severe cases.
- Hemorrhage, hematoma and coagulopathy indicate high risk.
- Requires coordinated clinical management.

These are pathology teaching principles; No obstetric management protocol is specified in the source.

Maternal course after surviving preeclampsia

- According to the textbook, survivors of mild or severe preeclampsia recover without hepatic sequelae.
- That recovery statement does not minimize risk during acute severe illness.
- Resolution of the pregnancy-associated process differs from irreversible chronic liver disease.
- The immediate hazard is the potentially life-threatening complication phase.

Acute fatty liver of pregnancy: Core features

Uncommon

Approximately 1 in 16,000 pregnancies in the Robbins estimate.

Late pregnancy

Usually arises during the third trimester.

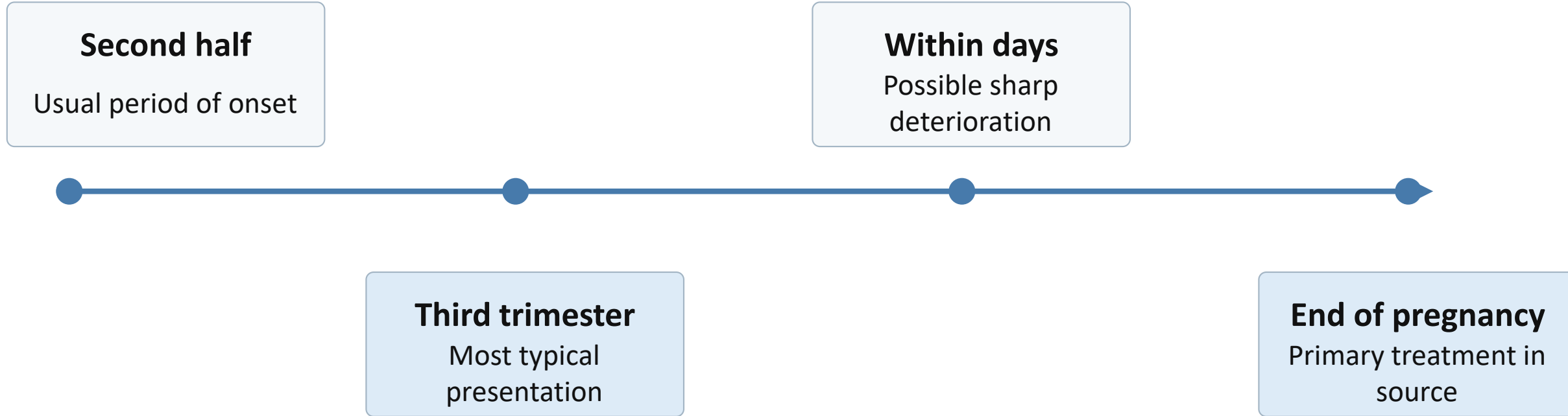
Potentially severe

May progress rapidly to liver failure, coma and death.

AFLP spans a spectrum of severity

- Acute fatty liver of pregnancy may be subclinical or initially modest.
- Aminotransferase elevation may be the first biochemical signal.
- At the severe end are hepatic failure, coma and death.
- Rapid progression over days makes initial apparent mildness potentially deceptive.

AFLP: Gestational timing and progression

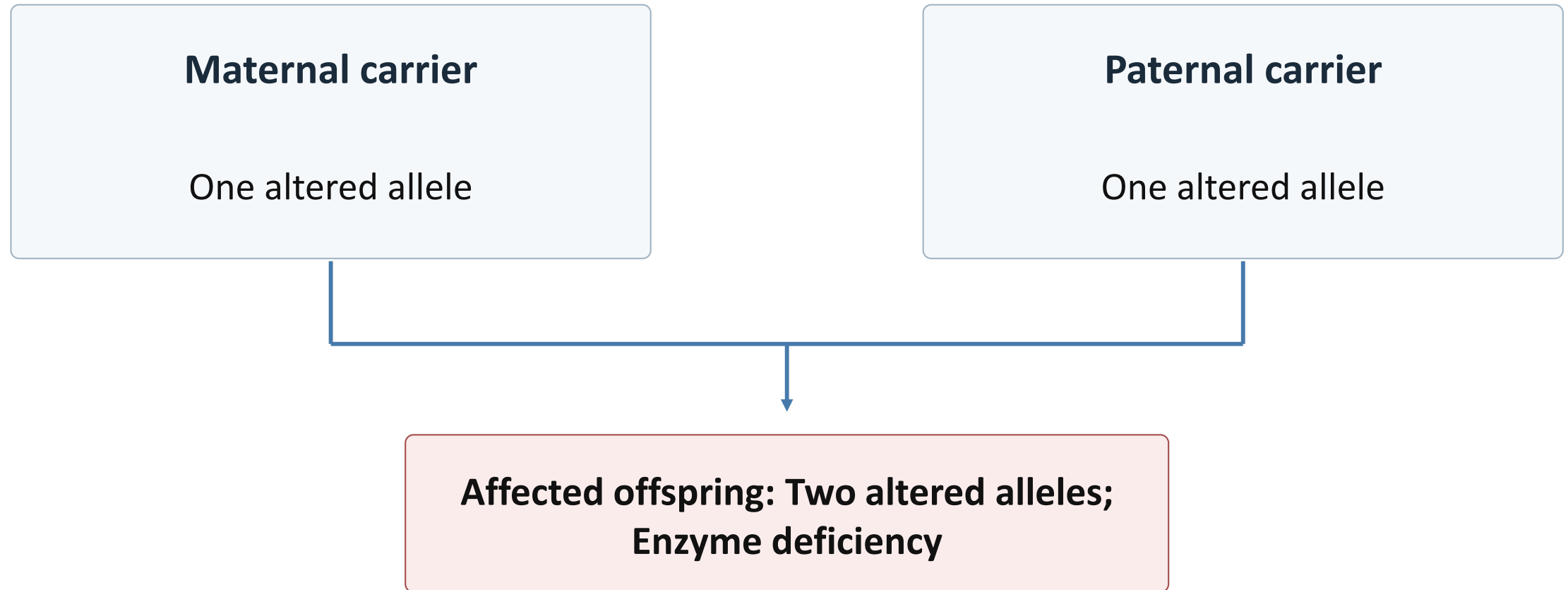


This schematic emphasizes a possible course, not an inevitable progression.

AFLP and disordered fatty acid metabolism

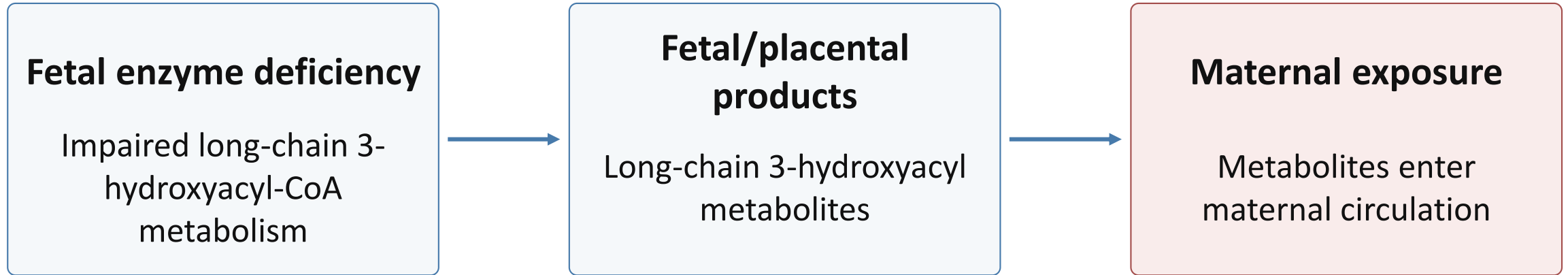
- The source links some cases to inherited deficiency of mitochondrial long-chain fatty-acid oxidation.
- The implicated enzyme is long-chain 3-hydroxyacyl-CoA dehydrogenase.
- The fetal–placental unit is central to the proposed maternal injury pathway.
- This mechanism is described for a subset, not all AFLP cases.

Inheritance creates a fetal enzymatic deficit



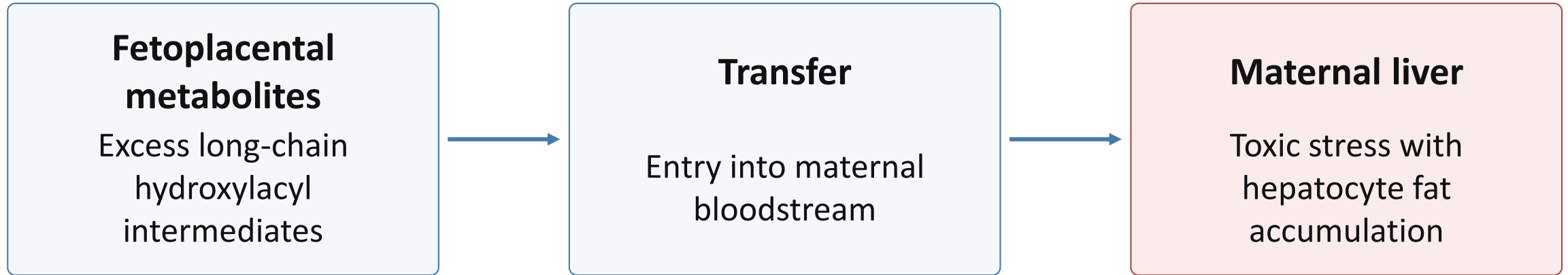
Familial mechanism in a subset of cases; The parental carrier states are independent inputs.

The fetal–placental metabolic link



The fetus and placenta may remain clinically well while maternal hepatic dysfunction develops.

Maternal hepatotoxicity: Proposed pathway



This as an unusual example of fetal metabolism producing maternal disease.

Genetic mechanism: Interpret the limits

Supported causal model

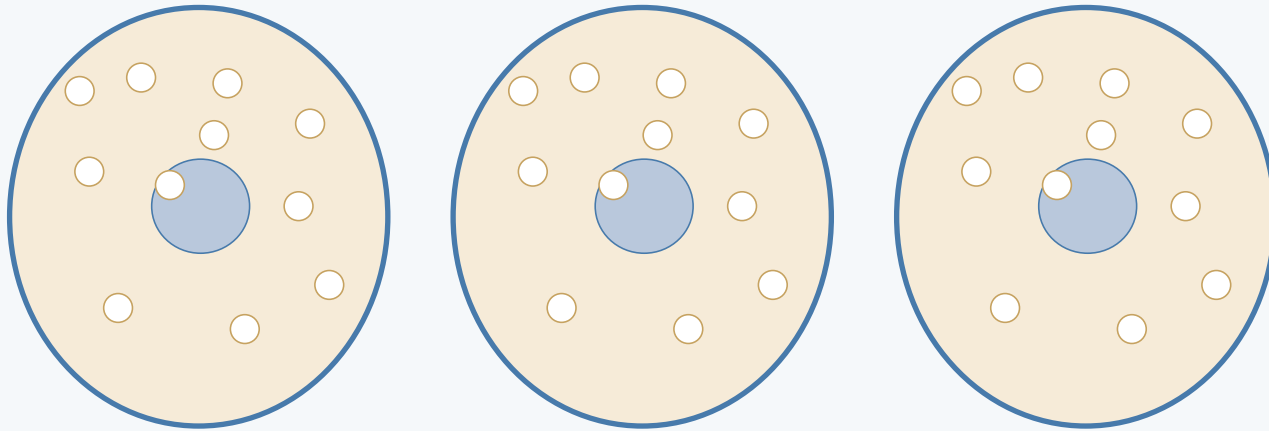
- Both parents carry a relevant mutant allele.
- An affected fetus lacks enzyme function.
- Metabolites of fetoplacental origin injure the mother.

Important limitations

- The textbook says this occurs in a subset.
- Do not infer carrier status in every patient.
- The model does not explain all pregnancy-related steatosis.

Microvesicular steatosis: The histologic hallmark

Conceptual hepatocyte schematic — not H&E microscopy



Diagnostic morphology

Numerous small
cytoplasmic lipid droplets
distributed diffusely
among hepatocytes.

Severe AFLP: Additional histologic abnormalities

- Diffuse microvesicular hepatocellular steatosis is the characteristic finding.
- More severe cases may show lobular disarray and hepatocyte dropout.
- Collapse of the reticulin framework can accompany loss of hepatocytes.
- Portal tract inflammation may be present.

AFLP morphology overlaps with other injuries

Characteristic AFLP features

- Diffuse microvesicular steatosis.
- Hepatocyte dropout and reticulin collapse in severe cases.
- Cholestasis may coexist.

Why viral hepatitis may be confused

- Severe AFLP can show lobular disarray.
- Portal inflammation and hepatocyte loss are not unique to AFLP.
- Tissue findings require clinical and gestational context.

Cholestasis can accompany acute fatty liver

- The Robbins morphology description notes possible accompanying cholestasis.
- Bile retention is not exclusive to intrahepatic cholestasis of pregnancy.
- The dominant AFLP lesion remains diffuse microvesicular steatosis.
- Coexisting cholestasis must be interpreted within the full lesion pattern.

Case: An evolving AFLP phenotype

A patient in the third trimester develops nausea, jaundice and bleeding.

Observed findings

- Symptoms arise late in pregnancy.
- A liver injury syndrome progresses over days.
- Microvesicular steatosis is the characteristic histologic lesion.

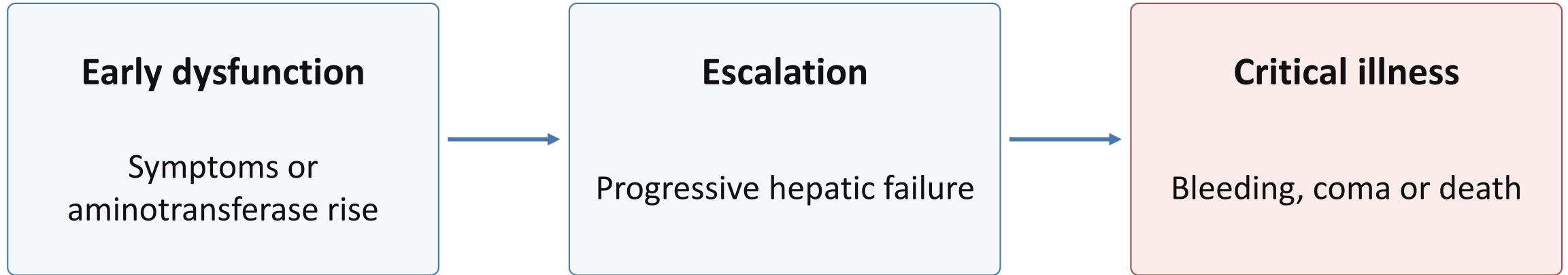
Diagnostic task

What disease mechanism links a fetal–placental metabolic process to maternal hepatopathy?

AFLP: Maternal clinical manifestations

- Nausea and vomiting may accompany evolving hepatic dysfunction.
- Jaundice reflects impaired bilirubin handling.
- Bleeding is a serious manifestation consistent with hepatic failure.
- At the extreme, encephalopathic coma and death can occur.

AFLP may deteriorate rapidly



Not every patient follows this trajectory; Rapid evolution is the warning emphasized by Robbins.

AFLP can overlap clinically with preeclampsia

20%–40%

Presenting symptoms may be those of coexistent preeclampsia.

Shared clinical setting

Late-pregnancy systemic illness with biochemical hepatic injury.

Different lesions

AFLP: Microvesicular steatosis; Preeclampsia: Periportal microvascular hemorrhagic injury.

AFLP: Intervention follows the pregnancy link

- The source identifies termination of pregnancy as the primary treatment.
- This recommendation follows the fetal–placental contribution to maternal toxic exposure.
- AFLP requires recognition as a potentially fast-progressing systemic emergency.
- The textbook excerpt does not specify delivery timing protocols or drug regimens.

Intrahepatic cholestasis of pregnancy

Core symptom

New-onset pruritus in the second or third trimester.

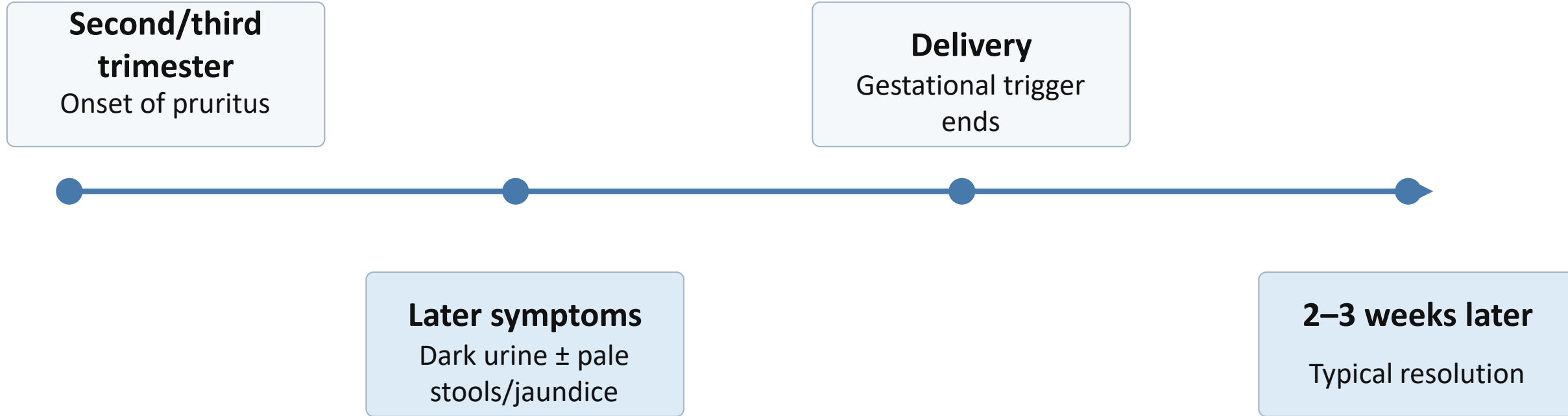
Biochemical pattern

Marked bile-salt elevation;
Bilirubin may rise mildly.

Natural history

Usually resolves within 2–3 weeks after delivery.

ICP: Symptom sequence and resolution



The temporal relationship is diagnostically informative.

Pruritus is the clinical hallmark of ICP

- Pruritus commonly begins during the second or third trimester.
- The itching is due to retention of bile salts.
- The itching may be intensely distressing despite relatively limited jaundice.
- Severity of maternal pruritus and magnitude of bilirubin elevation are distinct features.

Additional cholestatic symptoms

- Dark urine follows pruritus in approximately 10%–25% of cases in the source.
- Light-colored stools may occur occasionally.
- Jaundice may occur but is not required for the typical pruritic presentation.
- These findings reflect altered biliary excretion rather than vascular necrosis.

ICP biochemistry: Bile salts versus bilirubin

Bile salts

- Serum bile salts are markedly increased.
- Retention is linked to pruritus.
- The bile salt abnormality is central to the syndrome.

Bilirubin / alkaline phosphatase

- Bilirubin elevation is mostly conjugated.
- Bilirubin rarely exceeding 5 mg/dL.
- Alkaline phosphatase may be slightly increased.

ICP pathogenesis: Interacting susceptibilities

Gestational hormones

Altered endocrine milieu of pregnancy.

Environmental influences

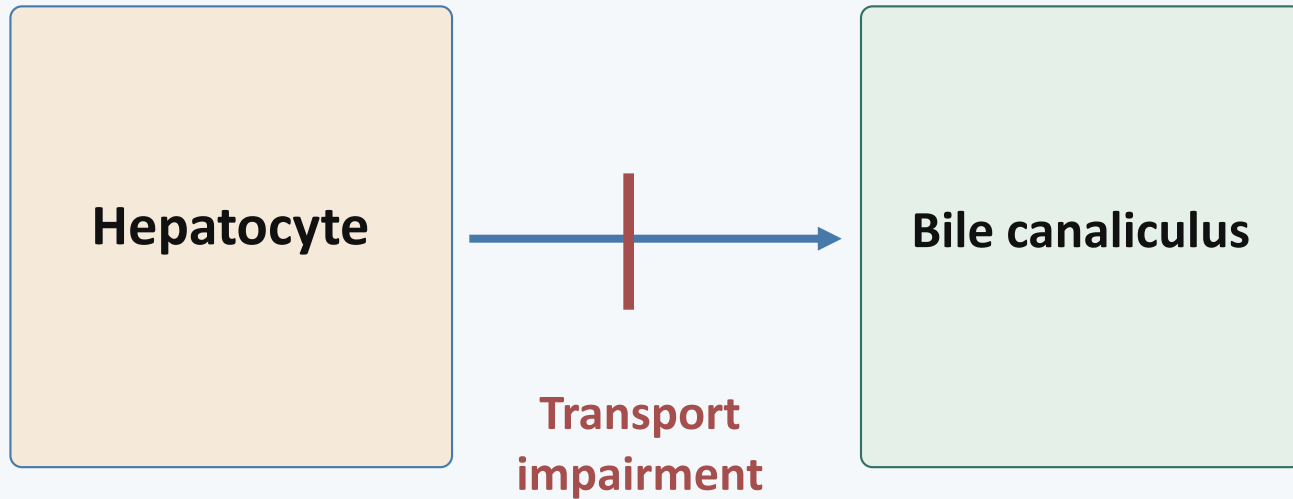
Non-genetic susceptibility.

Transporter defects

Impaired proteins involved in bile export.

Together these factors may engender canalicular cholestasis; No single universal cause is specified.

Canalicular bile retention: Conceptual model



Conceptual transport model — not tissue image

Consequence

Bile constituents accumulate when canalicular export is impaired.

ICP: Pregnancy-related and transport-related factors

- Altered hormonal state is a proposed contributor to gestational cholestasis.
- Environmental factors also contribute in the model presented by Robbins.
- Defects involving transporter proteins are implicated in susceptibility.
- Their interaction produces canalicular cholestasis rather than diffuse steatosis.

ICP outcome: Maternal burden and fetal concern

Maternal symptom burden

Bile-salt-associated pruritus may be exceptionally distressing.

Fetal concern

The source describes a modest risk of fetal loss.

Resolution

The maternal cholestatic syndrome commonly abates postpartum.

ICP resolves after delivery—but may recur

- Resolution typically within two to three weeks following delivery.
- A subsequent pregnancy may precipitate recurrence.
- The pregnancy dependency supports a hormonal and transporter interaction.
- Resolution of maternal symptoms does not negate the described fetal risk.

Three pregnancy-associated hepatic syndromes

Dimension	Preeclampsia / HELLP	Acute fatty liver	Intrahepatic cholestasis
Typical context	Hypertensive pregnancy syndrome	Usually third trimester	Second or third trimester
Dominant process	Periportal vascular injury	Microvesicular steatosis	Canalicular cholestasis
Major danger	Hematoma, rupture, coagulopathy	Rapid hepatic failure	Fetal loss; Maternal pruritus
Notable association	HELLP / eclampsia	May coexist with preeclampsia	May recur in later pregnancies

Biochemical and morphologic discrimination

Feature	Preeclampsia / HELLP	AFLP	ICP
Hepatic enzymes	Mild to marked rise	Rise may be modest or severe	Source emphasizes bile salts
Hepatic morphology	Periportal fibrin / necrosis	Diffuse microvesicular fat	Canalicular cholestasis
Other defining clue	Hypertension / hemolysis / platelets	Failure, bleeding, GI symptoms	Pruritus; Bilirubin usually modest
Severe outcome	Coagulopathy or rupture	Coma and death	Fetal loss risk

Different mechanisms can converge on jaundice

Infectious cause

Viral hepatitis and hepatocyte injury.

Metabolic or vascular cause

Acute fatty liver or preeclamptic hepatic injury.

Cholestatic cause

Canalicular retention of bile constituents.

These are alternative etiologic categories—not sequential steps in one pathway.

Diagnostic exercise: Pruritus predominates

A pregnant patient develops intense itching in the third trimester.

Observed findings

- Bile salts are markedly elevated.
- Bilirubin is only mildly increased.
- The syndrome later resolves postpartum.

Diagnostic task

Which pregnancy-related liver syndrome best fits this pattern?

Diagnostic exercise: Hematologic clues predominate

A pregnant patient develops hypertension and liver enzyme elevation.

Observed findings

- Hemolysis and thrombocytopenia are present.
- Hepatic injury may initially be subclinical.
- Severe disease can cause periportal hemorrhagic injury.

Diagnostic task

Which named syndrome organizes these findings?

Diagnostic exercise: Microvesicular change

A third-trimester patient develops progressive vomiting, jaundice and bleeding.

Observed findings

- The deterioration is rapid.
- Hepatocytes contain diffuse microvesicular fat.
- A fetoplacental mitochondrial oxidation mechanism is possible.

Diagnostic task

What diagnosis and specific pathogenesis are suggested?

Integrated case answers

Presentation	Favored interpretation	Discriminating source feature
Pruritus + bile salts	Intrahepatic cholestasis	Canalicular retention; Postpartum resolution
Hemolysis + low platelets	HELLP / preeclampsia	Periportal fibrin and hemorrhagic injury
Late severe disease + microvesicular fat	Acute fatty liver	Fetoplacental metabolism in a subset

Mechanism-driven synthesis

Vascular injury

Fibrin and hemorrhage → periportal necrosis.

Metabolic toxicity

Fetoplacental metabolites → microvesicular steatosis.

Transport dysfunction

Bile retention → pruritus.

Independent mechanisms; Infection is an additional major category when jaundice presents.

Final clinicopathologic priorities

- Pregnancy-associated hepatic dysfunction has infectious, vascular, metabolic and cholestatic causes.
- Preeclampsia/HELLP: Periportal fibrin, hemorrhage and possible necrosis or rupture.
- AFLP: Diffuse microvesicular steatosis and potentially rapid hepatic failure.
- ICP: Pruritus, bile-salt elevation, postpartum resolution and fetal risk.
- Critical clinical decisions require obstetric and hepatology assessment beyond this pathology overview.

Primary source and scope

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).

Chapter 18: Liver and Gallbladder, printed pages 786–787.

Sections: Hepatic Disease Associated With Pregnancy; Preeclampsia and Eclampsia; Acute Fatty Liver of Pregnancy; Intrahepatic Cholestasis of Pregnancy.

The lecture reflects the supplied textbook excerpt rather than an updated clinical practice guideline.