

Hepatitis A Virus

Transmission • immune-mediated injury • clinical course • diagnosis

Pathology teaching lecture

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Identify the virologic characteristics and fecal–oral transmission of HAV.
- Trace infection, host immunity, hepatocyte injury, and clinical evolution.
- Interpret acute versus previous infection using anti-HAV IgM and IgG.
- Recognize unusual complications and explain why chronic HAV does not occur.
- Apply prevention and clinicopathologic reasoning to short clinical scenarios.

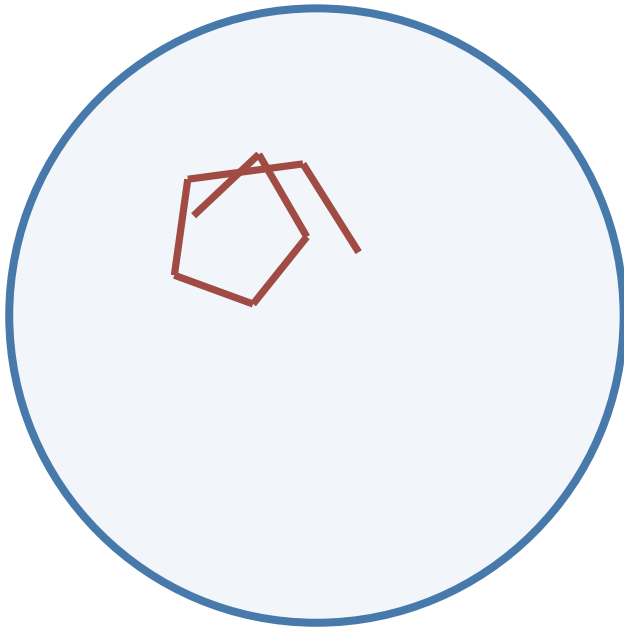
HAV within the spectrum of viral hepatitis

- Hepatotropic viruses A–E share liver tropism but differ in transmission and persistence.
- HAV typically causes an acute, self-limited hepatitic illness.
- Unlike HBV and HCV, HAV does not produce chronic hepatitis or a carrier state.
- Clinical and histologic features alone cannot reliably specify the virus.

Virologic identity of hepatitis A

- Small, nonenveloped, positive-sense single-stranded RNA virus.
- Belongs to the picornavirus family, genus Hepatovirus.
- Icosahedral capsid; A diameter of approximately 27 nm.
- These structural features describe the pathogen—not the mechanism of hepatocyte death.

Virion organization: Conceptual model



Nonenveloped capsid

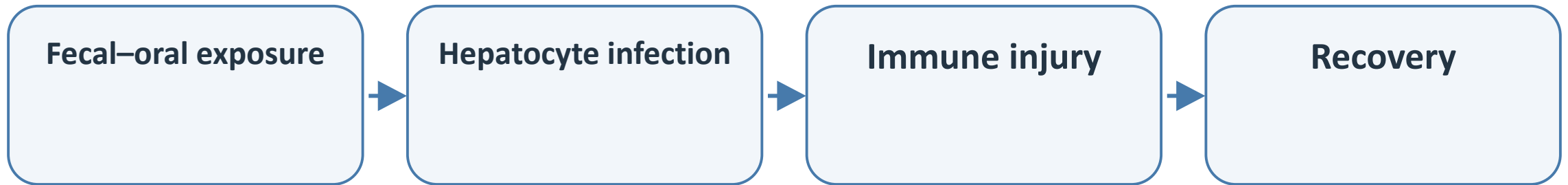
Positive-sense ssRNA genome

Picornaviridae • Hepatovirus

~27 nm (Robbins)

Original conceptual virion schematic, not an electron micrograph

Why HAV belongs in acute hepatitis



- Virus enters the host by an exposure route linked to fecal contamination.
- The immune response causes transient hepatocellular injury.
- Infection reaches hepatocytes and provokes an antiviral immune response.
- Viral clearance is ordinarily followed by recovery and lasting immunity.

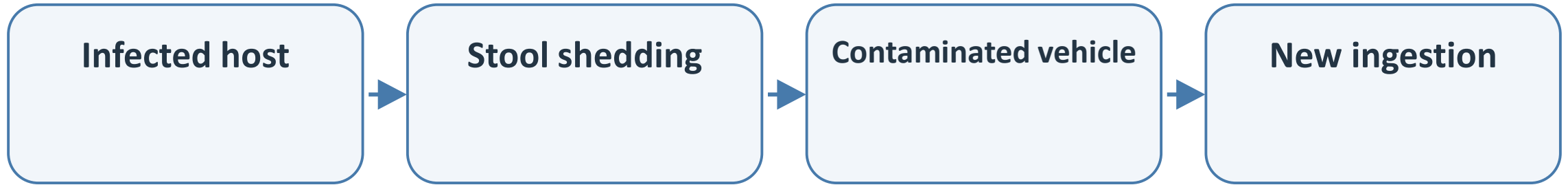
Contrast with other hepatotropic viruses

Feature	HAV	HBV / HCV	HEV
Typical route	Fecal–oral	Primarily parenteral / blood-related	Fecal–oral
Persistent infection	No chronic hepatitis	Chronic disease can occur	Chronicity possible in immunocompromised hosts
Key teaching point	Acute illness with immunity	Important chronic liver diseases	Acute disease; special host risks

The defining natural-history distinction

- HAV infection is self-limited in nearly all patients.
- It does not establish a persistent carrier reservoir.
- Prolonged symptoms or a relapse are not equivalent to chronic viral infection.
- That distinction changes diagnostic counseling and long-term risk assessment.

The fecal–oral route

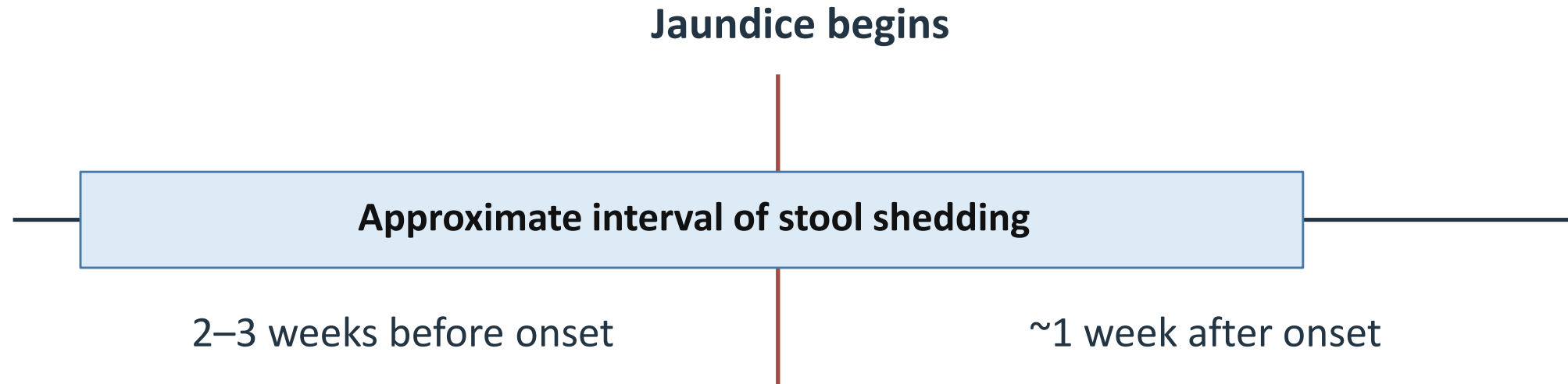


- Virus shed in stool contaminates food, water, hands, or the immediate environment.
- Close contact and contaminated common sources both support transmission.
- Ingestion introduces HAV to a susceptible individual.
- This is the core epidemiologic mechanism.

Why sanitation matters

- HAV is endemic where sanitation and hygiene are inadequate.
- Contaminated water and food are important transmission vehicles.
- Environmental conditions that permit fecal contamination amplify outbreaks.
- Improved sanitation reduces opportunities for exposure.

Timing of fecal shedding



- Transmission can therefore precede recognition of a symptomatic case.
- Absence of visible icterus does not imply absence of infectious exposure.

Timing is from the Robbins HAV section; Not to quantitative scale

Why cases transmit before diagnosis

- Peak infectivity in acute viral hepatitis may overlap late incubation and early symptoms.
- A presymptomatic person may contaminate shared environments.
- Contact tracing based only on the day jaundice appears can miss earlier exposure.
- A transmission history must look backward into the incubation period.

Close personal contact as an exposure

- Close contact with an infected individual is a major epidemiologic setting.
- Repeated opportunities for fecal–oral contamination enable person-to-person spread.
- Clusters may develop before the first recognized patient becomes jaundiced.

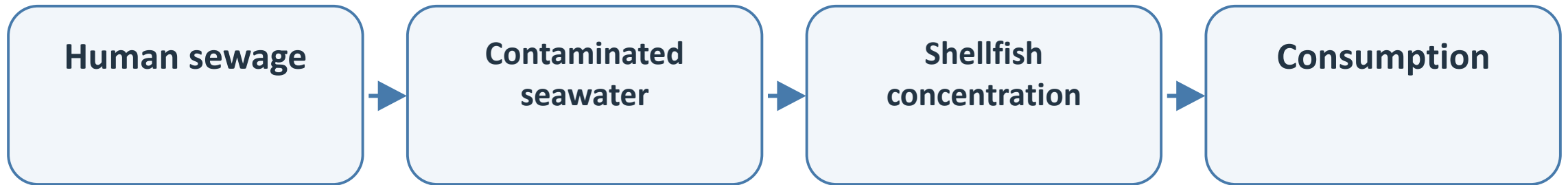
Institutional outbreaks

- Schools and nurseries as potential outbreak settings.
- Shared facilities and close contact support multiple linked exposures.
- An outbreak investigation should consider shared food, water, and contact networks.
- The relevant transmission mode remains fecal–oral.

Water-associated epidemics

- Contaminated water can lead to epidemic transmission.
- Overcrowding and unsanitary conditions increase the risk.
- A shared water source may expose many susceptible hosts simultaneously.
- Epidemic clustering differs from independent sporadic infections.

Shellfish as a foodborne vehicle



- Raw or lightly cooked oysters, mussels, and clams are highlighted.
- Consumption may produce sporadic infections even in high-income countries.
- Shellfish can concentrate viruses from sewage-contaminated seawater.
- The exposure links marine contamination to human fecal waste.

Sexual and blood-borne transmission

- Sexual transmission can occur, particularly with fecal–oral exposure.
- Viremia is transient, making blood-borne transmission rare.
- Donated blood is not routinely screened for HAV.
- These less-common pathways do not displace fecal–oral spread as the dominant route.

Maternal–fetal transmission

- No maternal–fetal transmission for HAV.
- This contrasts with the clinically important perinatal routes of some other hepatitis viruses.
- Do not extrapolate the transmission characteristics of HBV to HAV.

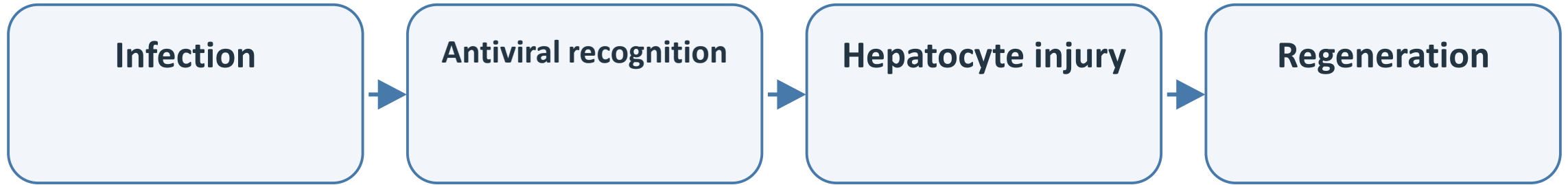
Seroprevalence reflects past exposure

- Anti-HAV seropositivity may indicate previous infection or immunity.
- In high-resource settings, historical exposure typically increases with age.
- Robbins provides age-related US seroprevalence as an epidemiologic example.
- Seropositivity alone does not establish a current symptomatic illness.

Epidemiology is time- and setting-dependent

- HAV as an important cause of clinically evident acute hepatitis.
- The textbook also records an increase in reported US cases in its source context.
- Case counts and exposure patterns can change with outbreaks, immunity, and sanitation.
- Historical figures must not be presented as real-time surveillance data.

HAV pathogenesis in four linked events



- Host exposure is followed by hepatocyte infection.

- Cytotoxic effector mechanisms injure the liver.

- Antiviral lymphocytes recognize infected cells.

- Resolution follows immune control and hepatocyte regeneration.

A receptor identified

- Hepatocyte HAVcr-1, also called TIM-1.
- TIM-1 is a glycoprotein discussed in relation to entry by multiple viruses.
- Receptor biology is distinct from the immune-mediated injury mechanism.
- This is a textbook statement, not an independently updated receptor review.

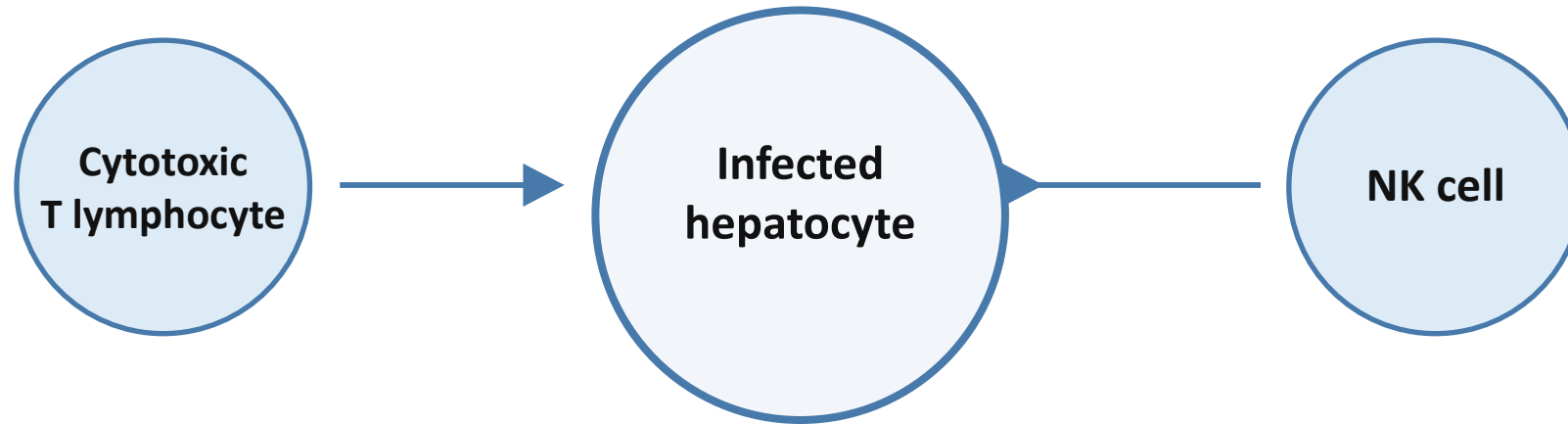
HAV is not directly cytopathic

- Robbins explicitly describes HAV as noncytopathic.
- The predominant mechanism of hepatocellular injury is antiviral immune attack.
- Infected hepatocytes can be killed by cytotoxic T lymphocytes and NK cells.
- Thus, tissue injury reflects host–virus interaction rather than direct lysis by HAV.

Cellular immune effectors

- Cytotoxic T lymphocytes recognize and eliminate infected hepatocytes.
- Natural killer cells also participate in killing infected cells.
- This response reduces infected-cell burden but produces hepatocellular damage.
- Inflammatory recruitment accompanies the injured liver parenchyma.

Immune-mediated hepatocyte injury



Immune recognition and killing

Schematic: Immune effector cells are shown apart from tissue architecture

HAV itself is described as noncytopathic.

Necrosis and apoptosis are different

Necrosis

- Cell swelling
- Membrane disruption
- Cellular-content release

Apoptosis

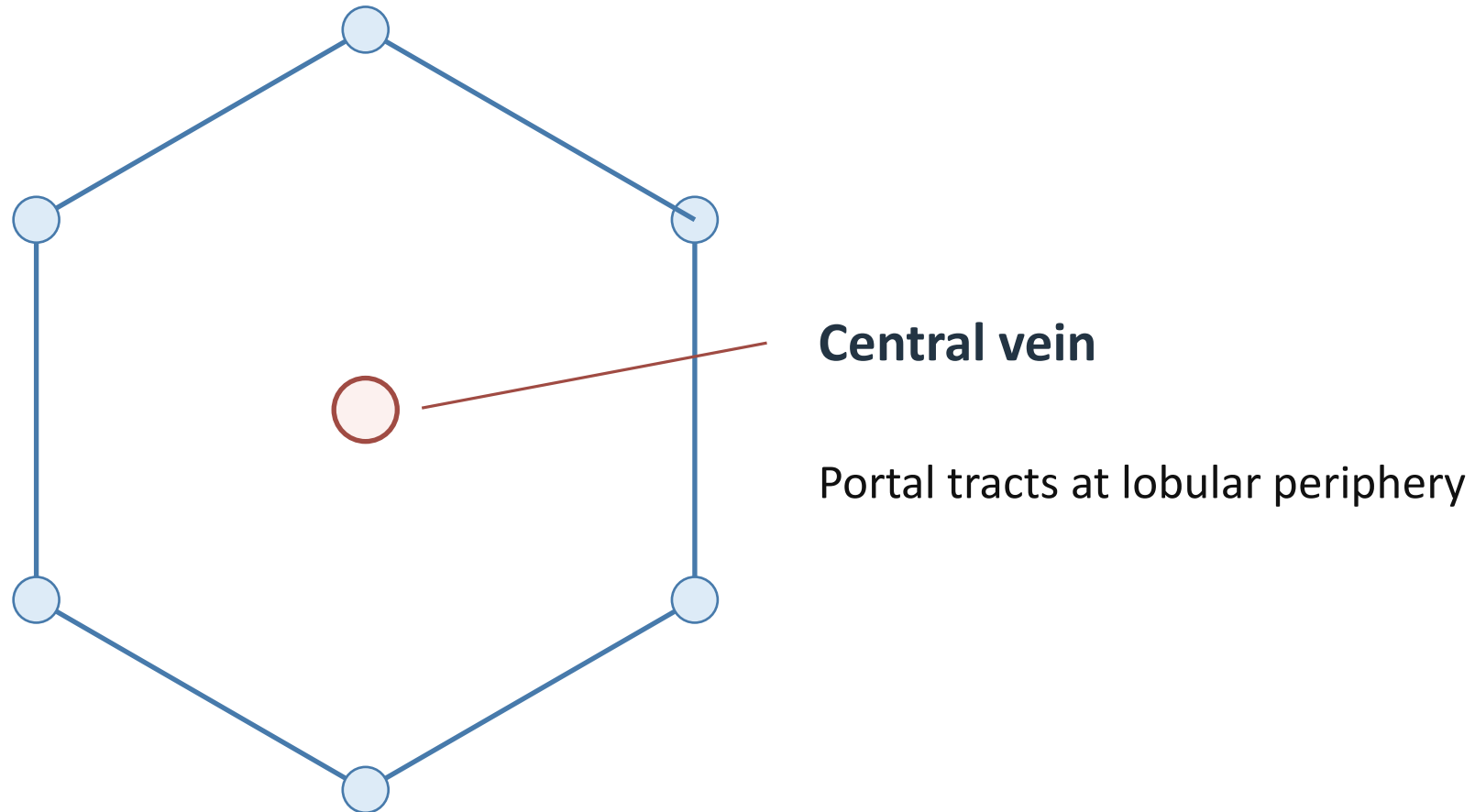
- Cell shrinkage
- Nuclear condensation
- Acidophilic body formation

Interpretive comparison: Terminology differs by clinical context

Acute hepatitis: Portal and lobular inflammation

- Acute viral hepatitis can show inflammation within portal tracts and lobules.
- The infiltrate is predominantly lymphocytic.
- Plasma cells and eosinophils may be present in variable numbers.
- This pattern overlaps with several nonviral inflammatory liver diseases.

The hepatic lobule as an injury map



Schematic classical lobule; Not histologic image or diagnostic micrograph

Apoptotic hepatocytes: Acidophil bodies

- Apoptotic hepatocytes appear shrunken and deeply eosinophilic.
- Chromatin condensation and cell fragmentation accompany apoptosis.
- “acidophil bodies” for apoptosis in hepatitis.
- The eponym “Councilman bodies” is reserved by convention for yellow fever.

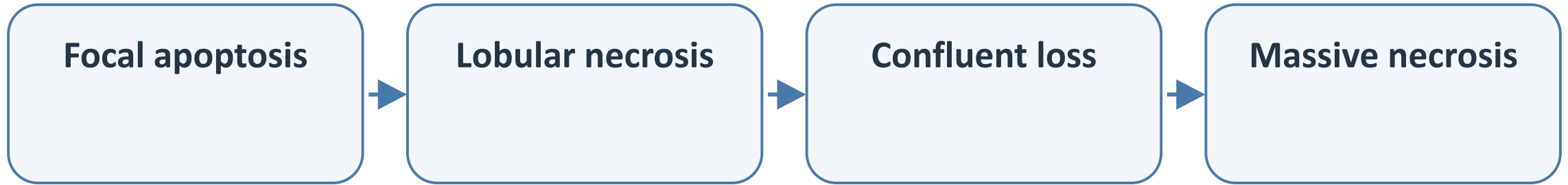
Macrophages clear injured parenchyma

- Macrophages phagocytose debris from necrotic hepatocytes.
- Pigmented macrophages may mark prior sites of hepatocyte death.
- Lobular inflammation and phagocytic clearance are linked processes.
- These changes are not specific for HAV.

Severe acute injury: Confluent necrosis

- Confluent necrosis is loss of contiguous groups of hepatocytes.
- Bridging necrosis can connect vascular structures.
- Panacinar necrosis may obliterate an entire lobule.
- Extensive cell loss can progress to massive hepatic necrosis and liver failure.

Morphologic severity spectrum



- The same acute disease framework can span limited hepatocyte apoptosis to extensive dropout.
- Morphologic severity and clinical liver failure are related but not interchangeable.
- Severe necrosis reduces functioning liver mass.

Why histology cannot type hepatitis A

- Acute hepatitic patterns are shared across hepatotropic viruses.
- Drug reactions, autoimmune hepatitis, and Wilson disease can overlap morphologically.
- Etiologic typing therefore requires appropriate serologic or molecular testing.
- A biopsy may assess injury, but HAV is not diagnosed by a unique H&E signature.

Chronic hepatitis morphology is a contrast, not HAV evolution

Acute HAV

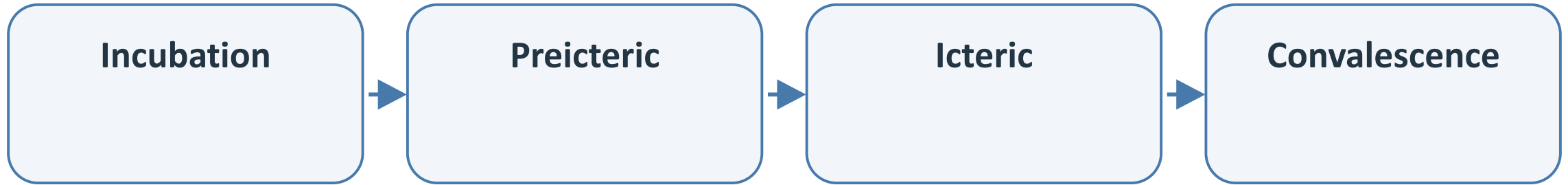
- Time-limited inflammatory injury
- Recovery expected
- No chronic carrier state

Chronic viral hepatitis

- Persistent inflammation
- Fibrosis may accumulate
- HBV/HCV are major causes

Interpretive comparison: Terminology differs by clinical context

The four clinical phases of acute hepatitis



- Incubation precedes obvious illness.

- A symptomatic preicteric interval can follow.

- Icteric symptoms may then become apparent.

- Convalescence follows as the liver injury resolves.

Incubation: 2–6 weeks

- The source gives a 2–6-week incubation period for HAV.
- The patient may appear well while infection develops.
- Exposure inquiry must include the weeks before symptom onset.
- A remembered meal or contact immediately before jaundice may be unrelated.

Subclinical infection is possible

- Acute hepatitis can occur without overt symptoms.
- A clinically silent episode may be recognized later by antiviral antibodies.
- The absence of jaundice is not evidence against prior HAV exposure.
- Symptom-based surveillance can therefore miss infections.

The preicteric presentation

- Fatigue and appetite loss are prominent nonspecific symptoms.
- These complaints alone cannot establish an etiologic diagnosis.
- A relevant exposure history and hepatitis testing guide recognition.
- This phase may precede visible jaundice.

Icteric presentation

- Patients often develop jaundice during symptomatic acute infection.
- Icterus reflects accumulation of bilirubin.
- Recognition of jaundice occurs after part of the stool-shedding interval.
- Clinical severity requires evaluation beyond the presence of yellow discoloration.

Jaundice links function to appearance

- Altered bile handling can cause bilirubin retention.
- Bilirubin accumulation produces yellow skin and scleral discoloration.
- A prolonged cholestatic course is an uncommon HAV complication.
- Icterus alone does not establish acute liver failure.

Usual time to recovery

- Most patients recover within 3 months.
- Nearly all have resolution by 6 months.
- Recovery represents clearance of the acute infection.
- This timeline is consistent with the absence of chronic HAV infection.

Course of illness and immune markers

Incubation

Symptoms begin

Recovery

Long term

IgM anti-HAV

Detected from onset; Persists 3–6 months

IgG anti-HAV

Appears during recovery; Persists for years

IgM suggests recent infection; IgG reflects durable immune memory.

IgM anti-HAV identifies a recent response

- IgM anti-HAV appears at the onset of symptoms.
- Persistence for approximately 3–6 months.
- IgM positivity supports a recent/acute HAV infection in the appropriate setting.
- The test result should be interpreted in the clinical context.

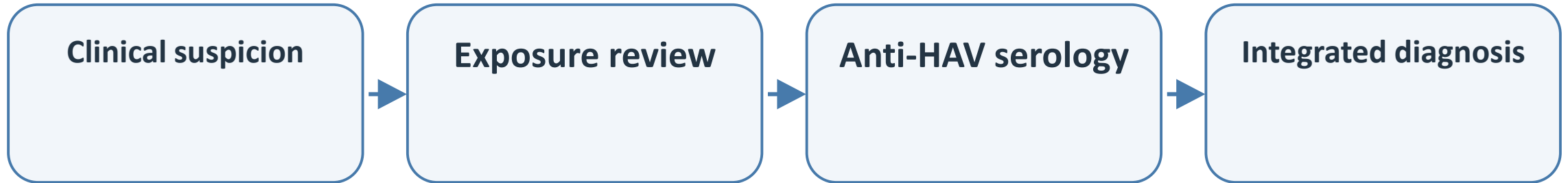
IgG anti-HAV marks durable immunity

- IgG anti-HAV appears during recovery.
- It persists for years and confers long-term immunity.
- IgG positivity without evidence of an acute IgM response favors prior immune exposure.
- Antibodies after vaccination may also signify immunity.

Anti-HAV results: Practical interpretation

IgM anti-HAV	IgG anti-HAV	Interpretive principle
Positive	May be positive	Recent infection likely with compatible clinical context
Negative	Positive	Prior infection / immunity, not proof of acute HAV
Negative	Negative	No anti-HAV serologic evidence of previous exposure
Any discordance	Any discordance	Review timing, exposure, and clinical course

A focused diagnostic reasoning sequence



- Identify acute hepatitic symptoms and relevant epidemiologic exposure.
- Interpret anti-HAV IgG as evidence of prior immune response.

- Use anti-HAV IgM to evaluate suspected recent HAV infection.
- Consider alternative causes when the presentation or test pattern is discordant.

Why laboratory and morphology must agree

- H&E inflammatory patterns overlap across different causes of hepatitis.
- IgM and IgG reflect infection timing and host immune response.
- Clinical course provides an independent consistency check.
- Discordant information should prompt reassessment rather than forced attribution.

Acute liver failure is uncommon but important

- Acute liver failure in 0.1%–0.3% of HAV infections.
- This event is uncommon relative to uncomplicated recovery.
- An otherwise self-limited virus can still cause life-threatening acute hepatic injury.
- The low frequency must not lead to dismissal of rapidly worsening symptoms.

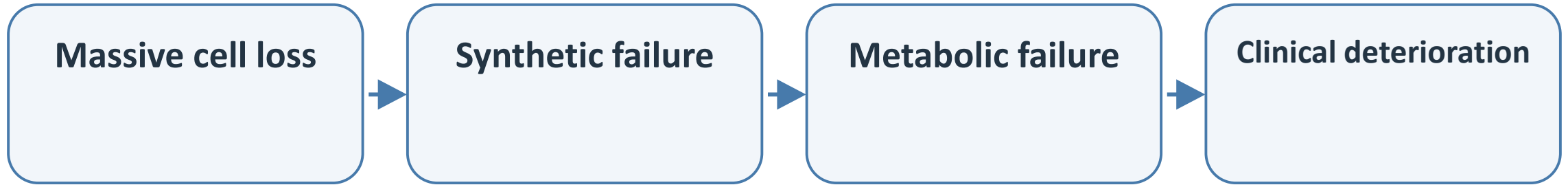
Chronic liver disease increases vulnerability

- The source particularly notes acute liver failure in patients with liver disease of another cause.
- Reduced hepatic reserve may increase consequences of an acute insult.
- HAV does not need to become chronic to worsen preexisting chronic liver disease.
- Clinical interpretation must distinguish baseline disease from the acute superimposed infection.

What constitutes acute liver failure?

- A syndrome of encephalopathy and coagulopathy after acute liver injury.
- definition, onset is within 26 weeks and without preexisting liver disease.
- A patient with preexisting chronic liver disease requires different syndrome classification.
- Neither isolated jaundice nor isolated transaminase elevation is sufficient.

Failure of synthesis and detoxification



- Reduced coagulation-factor synthesis contributes to coagulopathy.
- Massive hepatocyte loss may cause multiorgan complications.

- Failure to detoxify ammonia contributes to encephalopathy.
- Assessment of function matters more than transaminase magnitude alone.

A dangerous laboratory paradox

- In severe liver failure, transaminases can fall as viable hepatocyte mass is lost.
- Worsening jaundice, coagulopathy, or encephalopathy despite falling enzymes is alarming.
- A falling enzyme level cannot be equated automatically with recovery.
- This principle follows the general acute liver failure discussion.

Prolonged cholestasis after HAV

- Some patients have a prolonged cholestatic course.
- Cholestasis denotes impaired bile formation or flow with retained solutes.
- Persistence of jaundice in this setting does not prove chronic HAV infection.
- Serial assessment should distinguish prolonged recovery from liver failure.

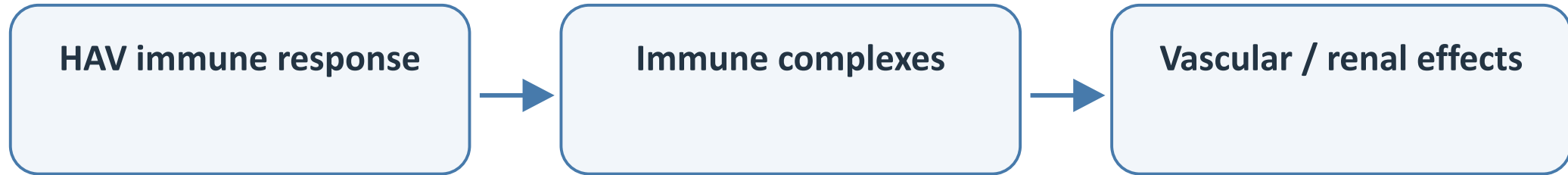
Relapsing disease after initial improvement

- Relapses within 6 months of the original onset.
- Relapse represents renewed clinical activity during an acute disease course.
- It is not equivalent to a stable chronic carrier state.
- A renewed episode should still be assessed for alternative causes.

Extrahepatic manifestations: The overview

- Rash and arthralgia can accompany HAV infection.
- Immune-complex mechanisms are invoked in rare systemic complications.
- The organ systems involved may include skin, kidney, and vessels.
- Extrahepatic manifestations do not establish chronic viral persistence.

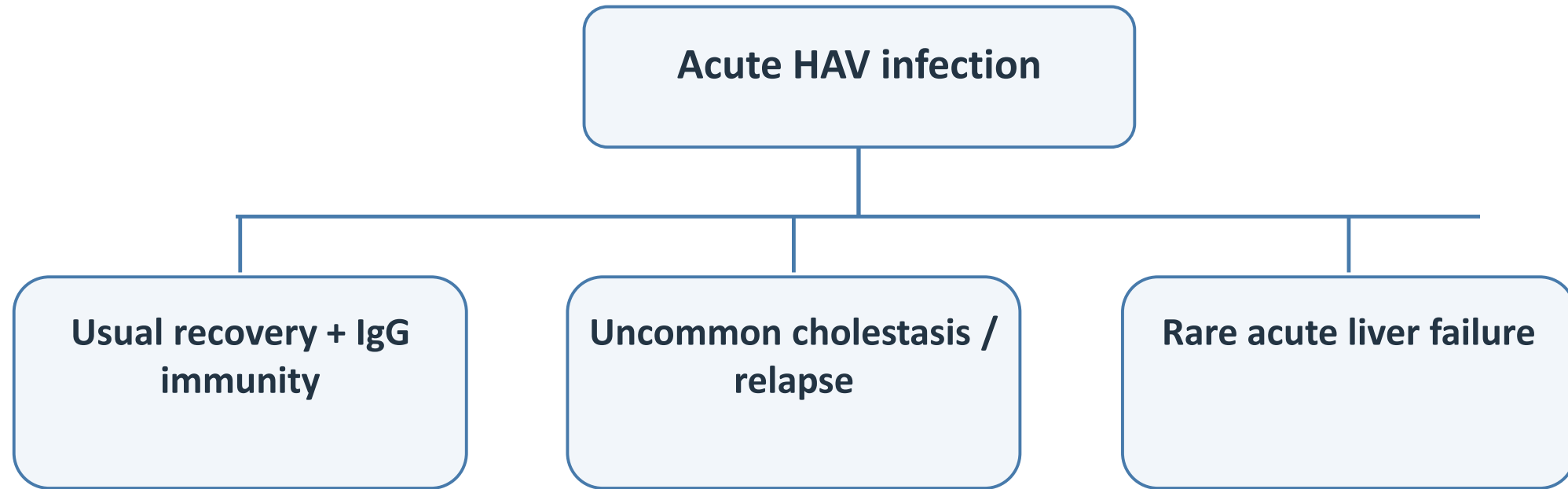
Immune-complex associated manifestations



Schematic causal overview; No disease-specific microscopic specimen depicted

- Leukocytoclastic vasculitis is listed among the possible manifestations.
- Glomerulonephritis can represent renal involvement.
- Cryoglobulinemia is another reported immune-complex phenomenon.
- These are uncommon and require diagnostic evaluation in context.

Typical and atypical outcomes



No chronic HAV hepatitis or persistent carrier state

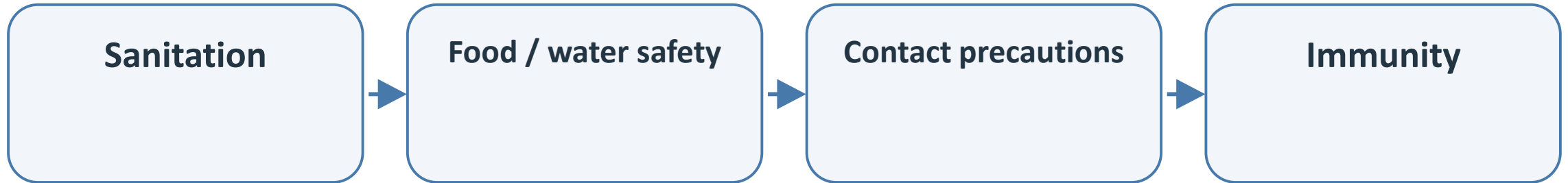
Why HAV does not create a carrier state

- The virus is cleared rather than maintained as a persistent transmissible infection.
- IgG anti-HAV remains after recovery even when acute infection has resolved.
- The host may be antibody-positive without continuing to harbor HAV.
- Never equate seropositivity with infective carriage.

Vaccination interrupts the susceptible-host pathway

- HAV vaccination is effective in preventing infection.
- Vaccine-derived immunity reduces the population of susceptible hosts.
- Vaccination is complementary to sanitation and exposure prevention.
- Specific schedules and postexposure protocols are beyond the supplied Robbins excerpt.

Prevention targets the exposure chain



- Protect food and water from fecal contamination.
- Consider implicated shellfish and environmental sources during investigations.

- Reduce close-contact transmission through hygienic practices.
- Vaccination reduces susceptibility before exposure.

Case 1: Jaundice after a shared meal

Clinical reasoning exercise

- An adult reports fatigue and anorexia, then jaundice several weeks after eating shellfish with a group.
- Which exposure feature raises concern for HAV?
- Which antibody class best supports a recent infection?
- Why might other exposed persons remain asymptomatic at first?

Case 1: Interpret the evidence

- Shellfish may concentrate HAV from contaminated seawater.
- IgM anti-HAV supports recent infection in the appropriate context.
- The 2–6-week incubation explains a delayed symptomatic presentation.
- Subclinical infection and presymptomatic shedding complicate outbreak detection.

Case 2: Recurrent jaundice without chronicity

Clinical reasoning exercise

- A patient improves after acute HAV and experiences recurrent symptoms months later.
- Relapse within 6 months as an uncommon outcome.
- Why should this not automatically be labeled chronic hepatitis A?
- What further evaluation is needed if the course is clinically discordant?

Case 3: Deteriorating liver function

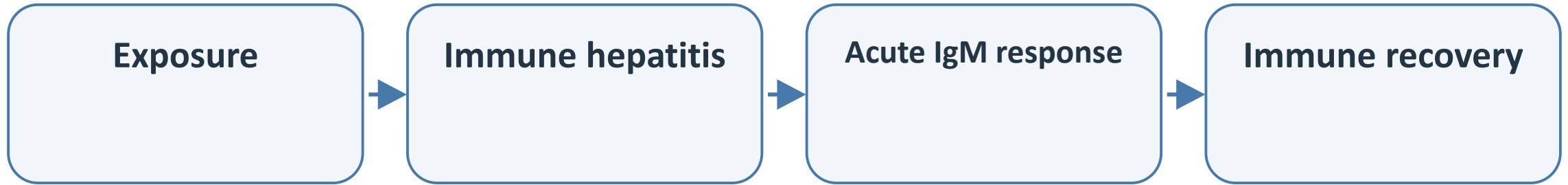
Clinical reasoning exercise

- A patient with acute hepatitis develops confusion and a prolonged coagulation test.
- Which clinical syndrome must be considered urgently?
- Would falling transaminases independently indicate recovery?
- Which underlying-liver-disease history would alter the syndrome classification?

Case 3: Clinicopathologic interpretation

- Encephalopathy and coagulopathy are features of acute liver failure.
- Extensive hepatocyte necrosis can reduce functional liver mass.
- Falling transaminases may coexist with worsening liver failure.
- Preexisting liver disease changes formal classification and clinical reserve.

Integrated concept: HAV infection in one pathway



- Transmission is predominantly fecal–oral, with shedding before jaundice.
- Symptoms and IgM antibody characterize the acute period.
- HAV-infected hepatocytes are injured by cytotoxic immune cells.
- Recovery brings IgG-associated immunity; Chronic hepatitis does not develop.

Five decisions to remember

- Is the exposure compatible with fecal–oral transmission?
- Is the illness acute, and does IgM anti-HAV support it?
- Is the patient improving or showing functional deterioration?
- Could cholestasis, relapse, or immune-complex disease explain atypical findings?
- Has immunity and prevention been addressed?

Textbook references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition. Elsevier.
- Primary textbook section: Hepatitis A Virus; background section: Viral Hepatitis.
- Additional context: Clinicopathologic Syndromes of Viral Hepatitis; Hepatocyte and Parenchymal Responses; Acute Liver Failure.
- All schematics were newly constructed as editable teaching diagrams; no textbook figures are reproduced.