Hepatitis A Virus (HAV)

Virology & Transmission

Feature	Description
Virus type	RNA virus, **non-enveloped**
Transmission route	**Fecal–oral** (contaminated food/water)
Incubation period	Average **21 days** (range **14–50 days**)
Chronic infection?	**Never** becomes chronic
Vaccine available?	Yes – highly effective

Clinical Features

Feature	Notes
Jaundice	Common in adults, rare in children
Dark urine	Due to **conjugated bilirubin**
Pale stools	From reduced bile in intestines
Nausea & vomiting	Part of viral prodrome
Fever & malaise	Common early symptoms
Fatigue	May persist for weeks

Serology – Diagnosis & Timeline

Marker	Meaning	Timing	Interpretation
IgM anti-HAV	Detects **acute infection**	Peaks in weeks 2–3, disappears by 6 months	Acute Hepatitis A
Total anti-HAV (IgG + IgM)	Shows **past infection or vaccine immunity**	Lifelong	Immune (past infection or vaccinated)
ALT	Rises with liver injury	Peaks with symptoms	Supports liver inflammation
Fecal HAV	Virus in stool (infectious period)	Appears before symptoms	High infectivity

Serological Course Summary

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Time 0 – Exposure
Fecal HAV appears early (weeks 1–2)
ALT rises with symptoms
IgM anti-HAV appears → indicates acute infection
IgM disappears by month 6
Total anti-HAV (mostly IgG) remains lifelong

Test Interpretation Table

IgM anti-HAV	Total anti-HAV	Interpretation
Positive	Positive	**Acute Hepatitis A**
Negative	Positive	Past infection or **vaccinated**
Negative	Negative	Susceptible → **consider vaccine**

Epidemiology & Endemicity Patterns

Endemicity	Infection Age	Pattern of Spread
High	Early childhood	Person-to-person, few outbreaks
Moderate	Late childhood/young adults	Waterborne outbreaks + person-to-person
Low	Young adults	Food/waterborne outbreaks, sporadic
Very Low	Adults (travelers)	Occasional outbreaks

Complications (Rare but Important)

Complication	Notes
Fulminant hepatitis	Severe liver failure, rare

Cholestatic hepatitis	Prolonged jaundice
Relapsing hepatitis	Recurrence of symptoms

💊 **Treatment & Prevention**

Type	Notes
Treatment	No antivirals – **supportive care only**
Prevention	- Safe food & water 🤢

- Good hygiene 🧼
- HAV **vaccine** for high-risk groups 💉 |

| **Post-exposure prophylaxis** | **Vaccine or immunoglobulin** within 2 weeks |

📍 **Special Notes**

- During **incubation**, patients **shed virus** — check household members 🧼
- Vaccine = **2 doses**, lifelong protection 🛡️

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🧬 **Hepatitis B Virus (HBV) — Complete Breakdown**

🔬 **Basic Virology**

Feature	Description
Virus type	**DNA virus**, enveloped 🧬
Family	Hepadnaviridae
Genome	4 genes (S, C, X, P)
Main antigens	HBsAg, HBcAg (core), HBeAg (e antigen)

📦 **Modes of Transmission**

Route	Examples
Perinatal 👶	From infected mother to baby (main route in endemic areas)
Parenteral 💉	IV drug use, blood transfusion, dialysis
Sexual ❤️	Unprotected sex, especially men who have sex with men
Household 🧼	Contact with infected bodily fluids

🧠 **Note**: HBV is found in **blood**, **semen**, **saliva**, and **vaginal secretions** — NOT in feces or urine significantly.

📊 **HBV Concentration in Body Fluids (from slide)**

Body Fluid	Virus Load Level
Blood	High 🔴
Semen / vaginal fluid	High
Saliva / breast milk	Moderate
Sweat / tears	Low
Urine / feces	Very low / not important ❌

⏳ **Incubation Period**

- **Average**: 60–90 days
- **Range**: 45–180 days

😷 **Clinical Features**

Feature	% Affected
Jaundice	<5 yrs: <10%

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>5 yrs: 30–50% |

| **Fever, nausea, vomiting**| Common in prodrome | | **ALT elevation** | Typical in acute phase | | **Chronicity risk** | Age-dependent (see below 👇) |

📉 **Outcome by Age at Infection**

🧠 From your second chart: The younger the age → the **higher the chance of chronic infection** 😐 The older the age → the **higher the chance of symptoms** 😷

Age at Infection	Chronicity Risk (%)	Symptoms Likely?

Birth	90%	❌ Rare symptoms
1–6 months	70%	Rare
7–12 months	40–60%	Low-moderate
1–4 years	~20–40%	Some symptoms
Adults	5–10%	✅ Often symptomatic

🧪 **Serologic Markers of HBV**

Marker	What it Detects	What It Means 💡
HBsAg	Surface antigen	**Infection is present** (acute or chronic)
anti-HBs	Antibody to surface antigen	**Immunity** (vaccine or past infection) 🛡️
HBcAg	Core antigen (not measured in serum)	N/A
anti-HBc (IgM)	IgM antibody to core	**Acute infection**
anti-HBc (IgG)	IgG to core	**Past or chronic infection**
HBeAg	"e" antigen = active replication	**High infectivity**
anti-HBe	Antibody to "e" antigen	**Lower infectivity**
HBV DNA	Viral load	**Level of active virus** — used for treatment monitoring

🔄 **Serologic Course – Acute HBV with Recovery (from slide)**

📈 **Weeks After Exposure**: 0 → 4 → 8 → 12 → 24 → 52

Time Frame	What Happens 🧪
Early weeks	**HBV DNA** appears first → **HBsAg** appears soon after
~Week 4–8	**HBeAg** positive = high infectivity
~Week 8–12	**ALT rises**, symptoms appear 😷
~Week 12–24	**IgM anti-HBc** positive → **diagnostic for acute HBV**
~Week 24–32	**HBsAg clears** → **anti-HBs** appears = recovery 🛡️
After 6 months	**anti-HBc IgG** and **anti-HBs** remain lifelong if recovered

🧠 **Window Period**: HBsAg disappears, but anti-HBs hasn't appeared yet → ✔ Only **IgM anti-HBc is positive** during this phase.

🔁 **Progression to Chronic HBV Infection**

- HBsAg persists **beyond 6 months** = chronic infection
- **IgM anti-HBc** becomes **negative**, only **IgG** remains
- **anti-HBs never appears** in chronic patients

📈 **Phases of Chronic HBV (from chart)**

Phase	HBeAg	HBV DNA	ALT	Notes
Immune tolerant	+	High	Normal	Common in perinatal infection
Immune clearance	+	Fluctuating	High	Best time to treat 💊
Inactive carrier	– (anti-HBe +)	Low	Normal	Low inflammation
Reactivation	–/+	High	High	Especially after immunosuppression ⚠️

👶 **Phases of Perinatal-Acquired Chronic HBV**

⚠️ **Why is this different?**

- Babies infected at birth often **don't show symptoms** 😐
- They develop **chronic infection silently**, going through **phases** that may last years.
- Immune system doesn't attack the virus at first → "immune tolerant"

Phase	Key Features 🧠	HBeAg	HBV DNA	ALT	Notes
1. Immune Tolerant👶	Common in infants & children infected perinatally. No liver damage yet.	✅	Very High	Normal	No inflammation despite high virus. Lasts years.
2. Immune Active / Immune Clearance🔥	Body starts attacking infected liver cells →	✅	High	↑↑	ALT rises. This is the **best time to**

	inflammation begins.				**treat**. Can cause liver fibrosis.
3. Inactive Carrier 😌	Immune system controls the virus. Liver damage stops.	❌ (anti-HBe+)	Low or undetectable	Normal	Low risk of progression. May last for life or revert later.
4. Reactivation Phase ⚠️	Virus escapes immune control → replication resumes, inflammation returns.	✅ / ❌	↑↑	↑↑	May occur spontaneously or after immunosuppression (e.g., chemo). Treat if active.

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🧬 Hepatitis C Virus (HCV)

🔬 Virology Overview

Feature	Description
Virus type	Single-stranded **RNA virus** 🧬
Envelope?	✅ Yes (enveloped)
Family	Flaviviridae
Genotypes	6 major genotypes (affect treatment)
Replication site	Inside hepatocytes (liver cells)

🚑 Transmission Routes

Route	Examples
Percutaneous 🩸	IV drug use, transfusions (before 1990s), dialysis
Sexual ❤️‍🔥	Less common than HBV — high in HIV co-infection cases
Perinatal 👶	From infected mother (low risk, ~5%)
Other	Tattoos, needle-stick injuries, organ transplants

🧠 No vaccine exists because of **HCV's genetic variability**.

⏳ Incubation Period

- **Average**: 6–7 weeks
- **Range**: 2–26 weeks

😷 Clinical Features

Feature	Notes
Jaundice 💛	In only ~30% of patients with acute infection
Fatigue 😴	Most common chronic symptom
Nausea, myalgia, low-grade fever 🤒	Non-specific
Cirrhosis & liver cancer	Develop in some chronic cases over 20–30 years ⚠️

📊 Natural History of HCV Infection

Outcome	% of Patients
Spontaneous clearance	15–30%
Chronic infection	**70–85%** 😢
→ Of those, develop cirrhosis	~20–30%
→ Of cirrhotics, HCC risk	~1–4%/year

🧪 HCV Serologic Timeline (from your slide)

Time Since Exposure	Marker	What Happens 🕒
Week 1–3	**HCV RNA** appears	First detectable marker (viremia)
Week 4–8	**Anti-HCV antibodies** appear	Positive whether infection is current or past
Week 6+	**ALT** may rise	Indicates liver damage

🧠 Key Point:
Anti-HCV stays positive even if the patient has cleared the virus. That's why we need **HCV RNA** to confirm **active infection**.

🧪 HCV Markers Explained

Test	Detects	Interpretation 🔍
Anti-HCV (EIA)	Antibodies to virus	🧪 **Screening test**: positive in current or past infection
HCV RNA PCR	Viral RNA	✅ If positive = **active infection**
Quantitative RNA	Viral load	Helps monitor treatment response
Genotype test	Type of virus strain	Affects drug choice & duration

❓ Anti-HCV Positive → What next?

HCV RNA	Interpretation
+	**Active infection** → start treatment
–	Cleared infection or false positive

💊 HCV Treatment

Treatment	Details
Direct-Acting Antivirals (DAAs) 💊	Oral meds, taken for 8–12 weeks
Cure rate	>95% 🎉
Common drugs	Sofosbuvir, Ledipasvir, Glecaprevir, etc.
Side effects	Minimal ✅
Reinfection risk?	Yes, especially in IV drug users ⚠️

🛡️ Prevention (No Vaccine)

Method	Notes
Blood screening 🩸	All donors tested
Safe injections 💉	Avoid needle sharing
Use protection ❤️	Reduce sexual risk
Treat and cure existing patients	Stops transmission 🔁

📊 Hepatitis B vs Hepatitis C — Key Differences

Feature	HBV	HCV
Virus type	DNA	RNA
Vaccine?	✅ Yes	❌ No
Chronicity rate	5–10% (adults)	**70–85%**
Cure available?	❌ Control only	✅ **DAAs cure it**
HCC risk	High if chronic	High if cirrhosis develops
Serology	Complex (many antigens)	Simpler (Anti-HCV + RNA only)

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🧬 Hepatitis D Virus (HDV) — Complete Breakdown

🔬 Virology Overview

Feature	Description
Virus type	**RNA virus**, enveloped 🧬
Family	Unclassified (delta agent)
Genome	Circular, single-stranded RNA
Unique feature	**Requires HBV** to replicate (needs HBsAg) 🧬🔗

🧠 You **cannot** get Hepatitis D without being infected with **Hepatitis B**.

🚦 Modes of Transmission

Mode	Examples
Percutaneous 💉	IV drug use, contaminated needles
Permucosal 😳	Sexual contact, body fluid exposure
Perinatal (rare) 👶	Possible but not common

❗ Two Infection Patterns

Type	Description 📖	Outcome 🧠

Coinfection	Patient gets HBV and HDV at the same time	Often **self-limited**, but more severe
Superinfection	Patient already has chronic HBV, then gets HDV	Often leads to **chronic HDV**, cirrhosis, liver failure ⚠️

⚠️ **Which is More Dangerous?**
🔥 **Superinfection** is worse — higher risk of:

- Decompensated liver disease
- Progression to cirrhosis
- Liver failure
- Chronic HDV infection

⏳ **Serologic Timeline (from your slides)**
🧪 **Coinfection (HBV + HDV together):**

Marker	Timing 🕒	Interpretation
HBsAg	Positive	HBV infection
Total anti-HDV	Appears later	HDV exposure
IgM anti-HDV	Positive	Indicates acute HDV infection
HDV RNA	Appears early	Active viral replication
ALT	↑ during symptoms	Liver inflammation

✓ May be self-limiting; patient often **clears both viruses**.

🧪 **Superinfection (HDV on top of chronic HBV):**

Marker	Interpretation
HBsAg	Already positive (chronic HBV)
anti-HBc IgM	❌ Negative — confirms **not new HBV infection**
IgM anti-HDV	✅ Positive — new **HDV infection**
HDV RNA	✅ Positive — shows **active HDV replication**
ALT	High — inflammation flare

✓ Often becomes **chronic HDV infection** ✓ Can cause **rapid liver failure** even without cirrhosis 😱

🔍 **How to Differentiate Co-infection vs Superinfection?**

Feature	Coinfection	Superinfection
HBsAg	Positive	Positive (chronic)
anti-HBc IgM	✅ Positive (new HBV)	❌ Negative (old HBV)
IgM anti-HDV	Positive	Positive
HDV RNA	Positive	Positive
Outcome	Usually self-limited	Often progresses to chronic HDV

🎯 This confirms the **#1 way to distinguish** superinfection from coinfection:
If **anti-HBc IgM is negative**, it's **superinfection**. If **anti-HBc IgM is positive**, it's **coinfection**.
📌 **Also:**

- **Superinfection → higher ALT, faster liver failure, cirrhosis risk**
- **Coinfection → acute hepatitis, usually clears as HBV clears**

🧪 **HDV Markers Summary**

Marker	What it Means
HBsAg	Required for HDV entry and replication
IgM anti-HDV	Acute or recent HDV infection
Total anti-HDV	Current or past HDV infection
HDV RNA	Confirms active replication

💊 **Treatment of HDV**

Treatment Option	Notes
Pegylated Interferon α 💉	Best available treatment (48–72 weeks)
Nucleos(t)ide analogs ❌	Not effective for HDV alone (only for HBV control)
New drugs (e.g., Bulevirtide)	Promising for chronic HDV (not widely available yet)

🛡️ **Prevention of HDV**

Prevention Type	How to Do It ✅
HBV vaccination 💉	**Prevents HDV too!** → no HBsAg = no HDV
Post-exposure	Same as HBV: vaccine + HBIG if exposed
Avoid	Needle sharing, unprotected sex, blood contact

🧠 No specific HDV vaccine — **HBV vaccine protects against both**!

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🦠 **Hepatitis E Virus (HEV)**

🔬 **Virology Overview**

Feature	Description
Virus type	**Single-stranded RNA, non-enveloped** 🧬
Family	Hepeviridae
Genotypes	4 main genotypes — 1 & 2 infect humans

📦 **Transmission**

Route	Details
Feco-oral 🚽	Contaminated drinking water (main route)
Zoonotic (rare)	Undercooked pork, wild game (genotype 3 & 4)
Vertical 👶	From mother to fetus (especially dangerous!)

⏳ **Incubation Period**

- **Average**: 40 days
- **Range**: 15–60 days

😷 **Clinical Features**

Feature	Notes
Jaundice, fever, fatigue	Common in adults 😷
Self-limiting	Usually resolves without treatment ✅
ALT rises	Indicates liver inflammation
IgM anti-HEV	Detects acute infection
IgG anti-HEV	Indicates past exposure
HEV RNA in stool 💩	Detects active viral shedding

⚠️ **Complications**

Risk Group	Complication
Pregnant women (3rd trimester)	High risk of **fulminant hepatitis** and **death (15–25%)** 🚑
Immunosuppressed	May develop **chronic HEV** (especially genotype 3)
Elderly	More severe disease possible

🧪 **Serology – Timeline of HEV Infection**

Marker	Appears When? 🕒	What It Means 💡
IgM anti-HEV	Early in infection	Acute HEV → usually disappears in 3–6 months
IgG anti-HEV	After IgM	Past infection or later-stage illness 🛡️
HEV RNA	In stool and blood early	Indicates active replication 🧪
ALT	Rises with symptoms	Liver inflammation indicator

📊 **HEV Timeline Summary (Based on Your Slide Image)**

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0 → 6 weeks:

⬆️ HEV RNA in stool (first)

⬆️ IgM anti-HEV appears with symptoms (ALT ↑)

➡️ IgG anti-HEV rises and remains

⬇️ IgM fades over time

🛡️ **Prevention & Control**

Measure	Description
Safe drinking water 🚰	Boil water or use clean bottled water
Avoid raw food 🍤	Especially raw shellfish or unpeeled vegetables

Traveler precautions ✈️	No ice, peel fruits, avoid tap water
Vaccine?	Exists in China (not yet worldwide)

💊 **Treatment**

Type	Notes
Acute HEV	Supportive care only (hydration, rest) ✅
Chronic HEV	In immunosuppressed: may need Ribavirin 💊

🧠 **Compare with Hep A:**

Feature	HEV	HAV
Transmission	Feco-oral	Feco-oral
Envelope	❌ Non-enveloped	❌ Non-enveloped
Chronic infection	❌ Except in immunocompromised	❌ Never chronic
Pregnancy risk	⚠️ Very high risk (15–25% death)	Not severe
Vaccine	✅ Only in China 🇨🇳	✅ Worldwide