VIRAL HEPATITIS (Dr Malik's lecture)

done by: Insaf Iyad
reviewed by dr Malik

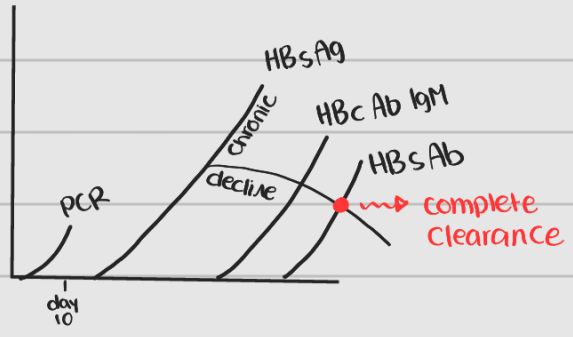
* features for all hepatitis viruses:
  - all cause acute infection, but only B, C, D may become chronic
  - it starts acute then → complete recovery
    → fulminent hepatitis & death
    → becomes chronic → mostly children
  - acute < 6 months < chronic (continous viral replication)
  - presence of symptoms depends on: age, immunity, sex
  - chronicity depends on age (↓ age → ↑ chance chronic)
  - Symptoms:
    ① children: asymptomatic or mild acute (anicteric hepatitis / without jaundice)
    ② adults: severe acute (fever, anorexia, jaundice, rt upper $\frac{1}{4}$ pain, malaise, fatigue, nausea, sometimes hepatomegaly)
  - all hepatitis viruses have the same appearance histologically so we use immunohistochemical stain to differentiate
  - jaundice: appears in severe acute hepatitis / ↑ bilirubin in blood / darker urine (tea color) & lighter stool (clay color)
  - deritis ratio:
    ① liver enzymes change in hepatitis (↑↑↑ ALT, ↑ AST) → $\frac{ALT}{AST} > 1$ indicate viral hepatitis (cytoplasmic damage)
    ② while $\frac{ALT}{AST} < 1$ indicates alcoholic hepatitis (mitochondrial damage)
  - definitive diagnosis of viral hepatitis type → lab investigations (prolonged prothrombin time PT)
  - appearance of symptoms depends on immune response → healthy adults have higher immune response than children & immunocompromized patients → ↑ severe symptoms / ↑ complete recovery / ↓ chance chronic

1 hepatitis A

* genome: ssRNA / naked virus (more resistant) / small genome → higher chance of mutations (but mutations usually lead to nonfunctional virus / family: PicoRNA
* incubation: 10-50 days (highest viral load → most infectous period even though its asymptomatic
* transmission: fecooral (withstands acidity) → contaminated water, dates, seafood, fruits / present briefly in blood (hard to transmit through it) / homosexual practices
* epidemiology: low hygiene developing countries (hyperepidemic)/ most common cause of acute hepatitis in most regions
* can lead to fulminent hepatitis (rapid deteruation function) → acute loss of function → hepatic encephalopathy, seizures (waste can cross BBB because there is no detoxification) / happens when hepatitis in on top of cirrhosis or steatosis
* vaccine: very effective because it has 1 serotype / twinrix vaccine (with B), given 3 times (inactivated, killed virus)
* 1 serotype → previous infection or vaccine give longlife immunity
* paradox epidemiology of hep A: ↓ hygenic countries have ↓ severe acute cases (because most of population got infected in their childhood) while ↑ hygenic countries have ↑ severe acute cases
* support & managment: water & nutrient suppliment (glucose)
* prevention: wash hands / boil food

[2] hepatitis B

* general features:
  - the only DNA hepatitis virus / enveloped / very small genome / has over laping reading frames / partially ds (- → complete, + → incomplete) /
  - reverse transcriptase (RNA dependent DNA polymerase) → no proofreading → ↑ mutations → ↑ antiviral resistance
* transmission: blood borne / IV drug abusers / needle stick injury / sexually / vertically / mother to child (usually chronic)
  ↳ perinatal
* incubation: few months
* higher chance of becoming chronic: <1 year
* areas with ↑ vertical transmission → ↑ endemic (virus stays in body longer)
* lab diagnosis & serologic markers: (which appears first?)
  ① viral DNA (PCR) → earliest
  ② HBsAg → earliest Ag & latest to resolve in acute case
  ③ HBc Ab IgM → earliest Ab
  ④ HBe Ag → like c but with upstream transcription (indicates transmissibility, monitor treatment responce, replaced with viral load measurment) → if present in mother we need to protect the baby (vaccination)
  ⑤ patients with chronic hepatitis have IgG instead of IgM



	HBsAg	Anti-HBs	Anti-HBc	DNA
Susceptible	—	—	—	—
Vaccinated	—	+	—	—
Past Infection	—	+	+	—
Acute Infection	+	—	IgM +	+
Chronic Infection	+	—	IgG +	+

* window period: the period 6-8 months of infection where no marker is detected (Sometimes anti B IgM appears)
* if surface antigen appeared for more than 6 months → Chronic
* epidemicity measure: depends on presence of hep B surface Ag
* chronic hep B can be managed to decrease viral load but it can't be cured (it remains latent)
* prevention: Screening of blood units/don't recap the needle but through it in a sharp container.
* analytical sensitivity test: depends on viral load (they try to lower the detection limit to detect the lowest viral load possible)
* B is the only virus that we don't need reverse transcriptase test to diagnose it.
* nucleic acid amplification testing: detects sAg & anti C Ag

3 hepatitis C

* genome: enveloped / +SS RNA
* transmission: blood borne / most common: injection drug use / sexually / vertical / kneedle stick injury / sharp objects / dialysis in renal failure / using same blade in wet cupping injury / invasive dental procedures / tattoing / piercing / blood transfusion
* hep C vs B: C has lower viral load, less infective, much higher chronicity
* the more severe acute the lesser the chance of becoming chronic (cases that become chronic usually have asymptomatic acute phase)
* managment of acute phase ⟶ supportive.
  managment of chronic phase ⟶ prevent hepatocellular carcinoma leading factors.
*** newest treatment: direct acting antibodies (ex: simprevir) (distract the virus cycle / ↓ side effects (neuro, psycho, ...) / highly effective)
* diagnosis: anti C antibody testing
* prevention: screening blood before transfusion / sharp object hygiene / control sexual practices
* no vaccine because of swift evolution ⟶ evade neutralizing antibodies & immune response.

[4] hepatitis D

* genome: Smallest / -ss RNA
* only comes with B
  ① coinfection → ex: from the same kneedle (most common)
  ② superinfection → D on top of chronic B
* D depends on B for replication, it needs B surface Ag inside hepatocytes to exit cell & infect other hepatocytes
* difference between having B alone or with D:
  D makes progression faster & Symptoms more severe
* Same prevention, vaccine, transmission as B
* if a patient had chronic B then suddenly developed severe symptoms it can be because of D

[5] hepatitis E

* genome: naked / +ssRNA / 7 genotypes
* transmission: fecooral (contaminated water, raw meat & pork)
* diagnosis: Serology (Search for IgM)
* managment: Supportive
* no chronic
* prevention: clean water, cook food, no vaccine
* fulminent hepatitis E is more common than A especially in pregnant women & malnutrition patients