



CHILDHOOD HEPATITIS B AND C

WHERE ARE WE?

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**LET'S START
WITH SOME
CASES!**

CASE 1

4 yo adopted Chinese male who upon arrival to the United States is screened and found to have Hepatitis B (HBsAg positive). Further lab work shows that he is HBeAg negative, his liver enzymes are normal and his viral load (HBV DNA) is <2000 IU/mL.

WHAT DO YOU DO NEXT?

CASE 2

16 yo white female in foster care with a history of IV drug abuse who is HBsAg positive, HBeAg positive with an ALT of 120 and a viral load of 60,000 IU/mL.

WHAT DO YOU DO NEXT?

CASE 3

4 yo white male whose mother was an IV drug abuser who is now in the custody of his MGM and presents with screening positive for Hepatitis C and elevated ALT (ALT=165). Repeat ALT 2 months later shows persistent elevation (ALT=157).

WHAT DO YOU DO NEXT?

CASE 4

16 yo Ukrainian American male who has been a Hepatitis C patient of yours since age 4 when screening upon arrival to the United States after adoption revealed his disease. For 12 years he has had normal liver enzymes, ultrasounds and alpha-fetoproteins, but continued viral load. He presents for his annual follow-up and states “I want to be treated for my Hepatitis C.”

WHAT DO YOU DO NEXT?

HEPATITIS B

- Double-stranded DNA hepatitis B virus (HBV).
 - Mode of transmission
 - Vertical (perinatal transmission)
 - Parenteral
 - Sexual
 - Incubation period 50-180 days.
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HEPATITIS B

- Perinatal transmission
 - Rates vary from 20 – 90%.
 - Depends on maternal HBsAg titer and HBeAg status.

HEPATITIS B

- At-risk populations of childhood
 - Infants born to HBV-infected women.
 - Infants/children living in community groups with endemic HBV.
 - Immigrants/adopted children from regions of the world with high prevalence of HBV.
 - Household contacts of individuals with chronic HBV.
 - Adolescents engaging in high-risk behaviors.
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HEPATITIS B

- Definitions
 - Immune tolerant
 - ALT persistently normal
 - HBeAg positive
 - HBV DNA $\geq 20,000$ IU/ml
 - Inactive carrier
 - ALT persistently normal
 - HBeAg negative
 - HBV DNA < 2000 IU/ml

HEPATITIS B

- Definitions (cont'd)
 - Immune active
 - ALT persistently >1.5 normal lab value (>60 IU/L)
 - HBeAg positive (> 6 mo)
 - HBV DNA ≥ 2000 IU/ml
 - Reactivation
 - ALT persistently >1.5 x normal (>60 IU/L)
 - HBeAg negative (>12 mo)
 - HBV DNA ≥ 2000 IU/ml
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HEPATITIS B

- Acute HBV infection
 - Variable course
 - Asymptomatic to fulminant hepatitis
 - Universal vaccination has substantially reduced fulminant hepatitis frequency (Taiwan 5.36 to 1.71 per 100,000 over the past 20 years).
 - Serum sickness-like syndrome with fatigue, jaundice, anorexia, nausea, RUQ discomfort.
 - The older the patient, the milder the symptoms.

HEPATITIS B

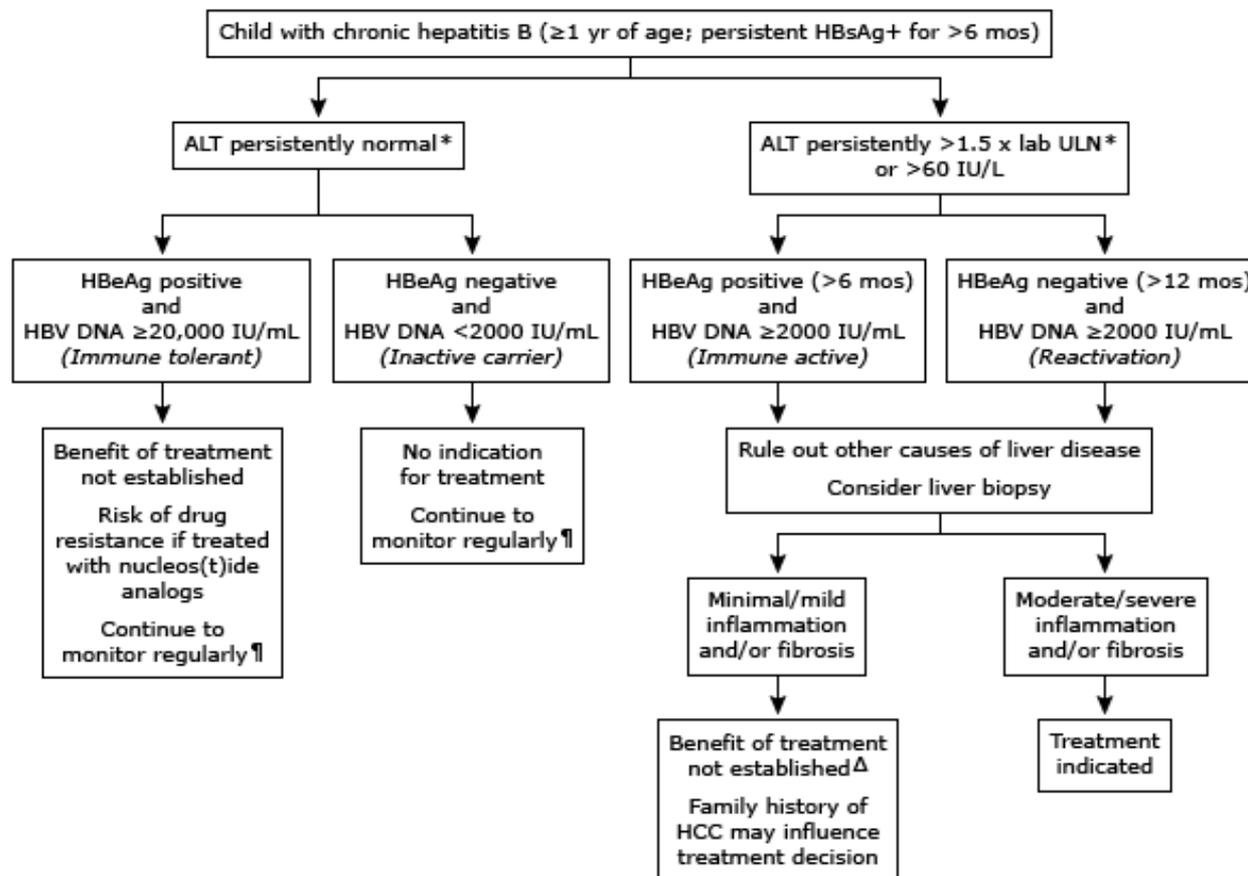
- Development of chronic disease varies based on the age of acquisition.
 - Infants: 90% chance of developing chronic disease.
 - Children 1 – 5 years: 30% chance.
 - Children > 5 years: 6% chance.

HEPATITIS B

- Natural History Variable!
 - If from an endemic country (more likely perinatal acquisition)
 - Usually remain HBeAg positive
 - Have high levels of viral replication
 - But, histologic injury is typically mild
 - Spontaneous seroconversion < 2–5%
 - If from a non-endemic country (less likely perinatal acquisition)
 - Frequently clear HBeAg and HBV DNA in the first 2 decades of life
 - Those who seroconvert spontaneously typically have higher ALT levels early in life.
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HEPATITIS B

Algorithm for selection of children for HBV antiviral treatment



HEPATITIS B

- If we decide to treat, what medications are available and licensed for use in children in the US?
 - Interferon alfa
 - Entecavir
 - Lamivudine
 - Others? (Rare circumstances)

INTERFERON ALFA – 2B

- More favorable response in genotype A and B.
 - Six month course.
 - Six million units per m^2 (max 10 MU) subQ TIW x 24 weeks.
 - Observation 6 to 12 months thereafter.
 - Not associated with resistance.
 - Multiple courses does not increase seroconversion.
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INTERFERON ALFA – 2B

Side effects

- Fever
- Myalgia
- Headache
- Arthralgia
- Anorexia
- Psychiatric complications

ENTECAVIR

- Oral, long term indefinitely unless there is seroconversion.
- Approved ≥ 2 yoa.
- 24% HBeAg seroconversion vs 2% placebo
- Treatment would continue for 1 year following seroconversion.
- Can be used if IFN fails.
- Also not associated with resistance.

LAMIVUDINE

- 3 mg per kg (max 100 mg)
- Drug resistance develops in up to 25%!
- Therefore, IFN or entecavir are recommended over this medication.

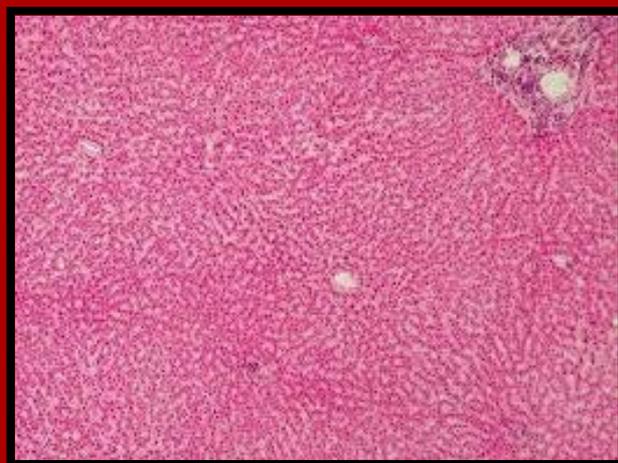
HEPATITIS B

- Annual rate of spontaneous clearance (conversion to HBeAg negative and HBeAb positive)
 - 0 – 3 years of age < 2%
 - > 3 years of age ~ 5%

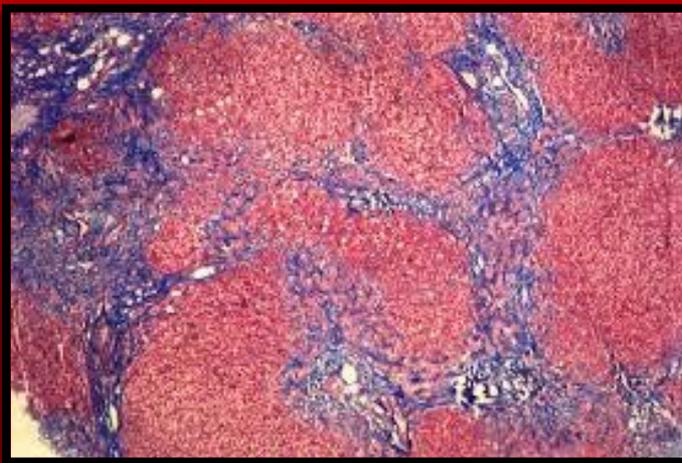
HEPATITIS B

- Cirrhosis
 - Infrequent in childhood.
 - Only 3% in a large (n=292) study of children HBsAg+ and elevated AST.
 - Higher incidence if coinfecting with HDV or HCV.
 - However, moderate or severe fibrosis is common > 50% of children with chronic HBeAg-positivity with elevated ALT.
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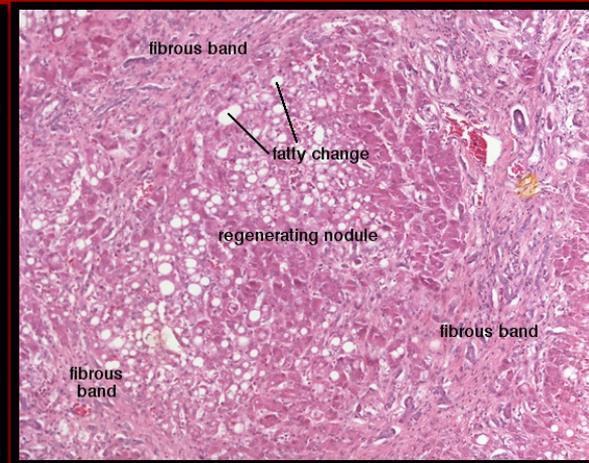
HISTOLOGY OF FIBROSIS VS. CIRRHOSIS



Normal



Fibrosis



Cirrhosis

HEPATITIS B

- What about Hepatocellular Carcinoma Risk?
 - Related to duration of disease.
 - Related to degree of histologic injury.
 - Related to the viral load.
 - So, rare in children overall, BUT ... has been described in children even after viral replication ceases.
 - Taiwan: Children with HCC majority Genotype B
 - Use RUQ US and alpha-fetoprotein annually.
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HEPATITIS B

- Chronic HBV disease
 - Occasionally associated with extrahepatic manifestations
 - Glomerulonephropathy
 - Polyarteritis nodosa

HEPATITIS B

- Treatment overview
 - No treatment is highly successful.
 - Carefully select patients with chronic HBV infection for treatment during childhood.
 - If immune tolerant or inactive phases, do NOT treat.
 - If immune active with moderate/severe histologic findings, interferon alfa or entecavir are first line choices.
 - Use RUQ ultrasound and alpha-fetoprotein level for HCC surveillance annually.
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HEPATITIS B

- Prevention
 - HBV vaccine:
 - Universally recommended for all infants (series of 3 doses over 6 – 9 months).
 - Catch up immunizations for older, unimmunized children.
 - HBV-exposed family members/close contacts.

HEPATITIS B

- Prevention (continued)
 - HBV immune globulin indications for use:
 - Infants born to HBsAg positive mothers
 - Postexposure prophylaxis within 24 hours after exposure (if no vaccination in the past)
 - Household contacts
 - Avoid sharing of shavers, toothbrushes, nail clippers, tweezers

HEPATITIS B

- Prevention (continued)
 - Universal precautions for handling abrasions, bleeding, etc.
 - Adolescents should be advised regarding prevention of sexual transmission.
 - monogamous-vaccinate sex partner
 - multiple partners-use of condoms

HEPATITIS B

- Prevention (continued)
 - Children with chronic hepatitis B should be allowed to participate in all regular activities including school and sports.
 - No special arrangements need to be made other than universal precautions in day care centers, schools, sports and camps.

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4 yo adopted Chinese male who upon arrival to the United States is screened and found to have Hepatitis B (HBsAg positive). Further lab work shows that he is HBeAg negative, his liver enzymes are normal and his viral load (HBV DNA) is <2000 IU/mL.

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CASE 2

16 yo white female in foster care with a history of IV drug abuse who is HBsAg positive, HBeAg positive with an ALT of 120 and a viral load of 60,000 IU/mL.

WHAT DO YOU DO NEXT?

HEPATITIS C

- Single-stranded RNA hepatitis C virus (HCV).
- Mode of transmission
 - Vertical (perinatal transmission)
 - Parenteral
 - Sexual
- Incubation period: 30 – 150 days

HEPATITIS C

- Perinatal transmission
 - Rates are ~ 5%.
 - Rates increase to 15 – 20% if the mother is coinfectd with HIV.

HEPATITIS C

- Clinical features
 - Chronic infections will develop in 60 – 80% of exposed children.
 - Majority of patients are asymptomatic in childhood.

HEPATITIS C

- Clinical features (continued)
 - Acute liver failure from HCV infection in immunocompetent patients has not been reported.
 - End-stage liver disease with cirrhosis in childhood – reported but rare.

HEPATITIS C

- Diagnosis
 - Laboratories: liver panel, HCV IgG Antibody (after 18 mos. of age) and HCV RNA (after 2 mos. of age)
 - Positive anti-HCV antibody (IgG) after > 18 months of age = exposure to HCV.
 - Active infections can only be confirmed by positive HCV RNA.

HEPATITIS C

- Diagnosis (continued)
 - HCV genotype analysis indicated if treatment is being considered.
 - HCV RNA testing in the first 2 months of life is problematic:
 - false positives (due to transient viremia)
 - false negatives (due to low levels not detectable)
 - So.... wait until after 2 months of age to check HCV RNA and repeat test 6 months later.
 - Spontaneous clearance after perinatal acquisition – Variable rates.
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HEPATITIS C

- Because chronic Hepatitis C generally has a slow progression to fibrosis and severe disease is rare in children, follow up without treatment until adulthood may be a valid treatment for most children.
- Children with Hepatitis C who demonstrate persistently elevated serum aminotransferases or those with progressive disease (i.e. fibrosis) should be considered for treatment.

HEPATITIS C

- Treatment
 - Subcutaneous weekly pegylated interferon-alpha injections for 48 weeks (genotypes 1 or 4) or 24 weeks (genotypes 2 or 3) plus oral ribavirin.
 - Response = nondetectable HCV RNA by the end of the treatment period.
 - Pegylated interferon/ribavirin therapy approved for ≥ 3 years of age.
 - Seroconversion – overall 59% (genotypes 2/3 have higher rates of conversion than genotype 1).

HEPATITIS C

SIDE EFFECTS OF MEDICATIONS

- Fever*
- Fatigue*
- Myalgias*
- Arthralgias*
- Headache*
- Nausea
- Growth deficits**
- Bone marrow suppression***
- Psychiatric complications (1/3)

* usually resolves after several weeks

** usually rebounds after therapy completion

*** usually returns to baseline within weeks after cessation of therapy

HEPATITIS C

- Prevention
 - HCV vaccine: none available.
 - HCV immune globulin: none available.
 - Household contacts: avoid sharing of shavers, toothbrushes, nail clippers, tweezers.

HEPATITIS C

- Prevention (continued)
 - Universal precautions for handling abrasions, bleeding, etc.
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HEPATITIS C

- Prevention (continued)
 - Children with chronic hepatitis C should be allowed to participate in all regular activities including school and sports.
 - No special arrangements need to be made other than universal precautions in day care centers, schools, sports and camps.

HEPATITIS C

- Hepatocellular Carcinoma
 - Although rare, remember ultrasound and alpha-fetoprotein should be used for annual screening.

CASE 3

4 yo white male whose mother was an IV drug abuser who is now in the custody of his MGM and presents with screening positive for Hepatitis C and elevated ALT (ALT=165). Repeat ALT 2 months later shows persistent elevation (ALT=157).

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THANK YOU!



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