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.

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.

Hepatitis B

- Definitions
  - Immune tolerant
    - ALT persistently normal
    - HBeAg positive
    - HBV DNA ≥ 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

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.

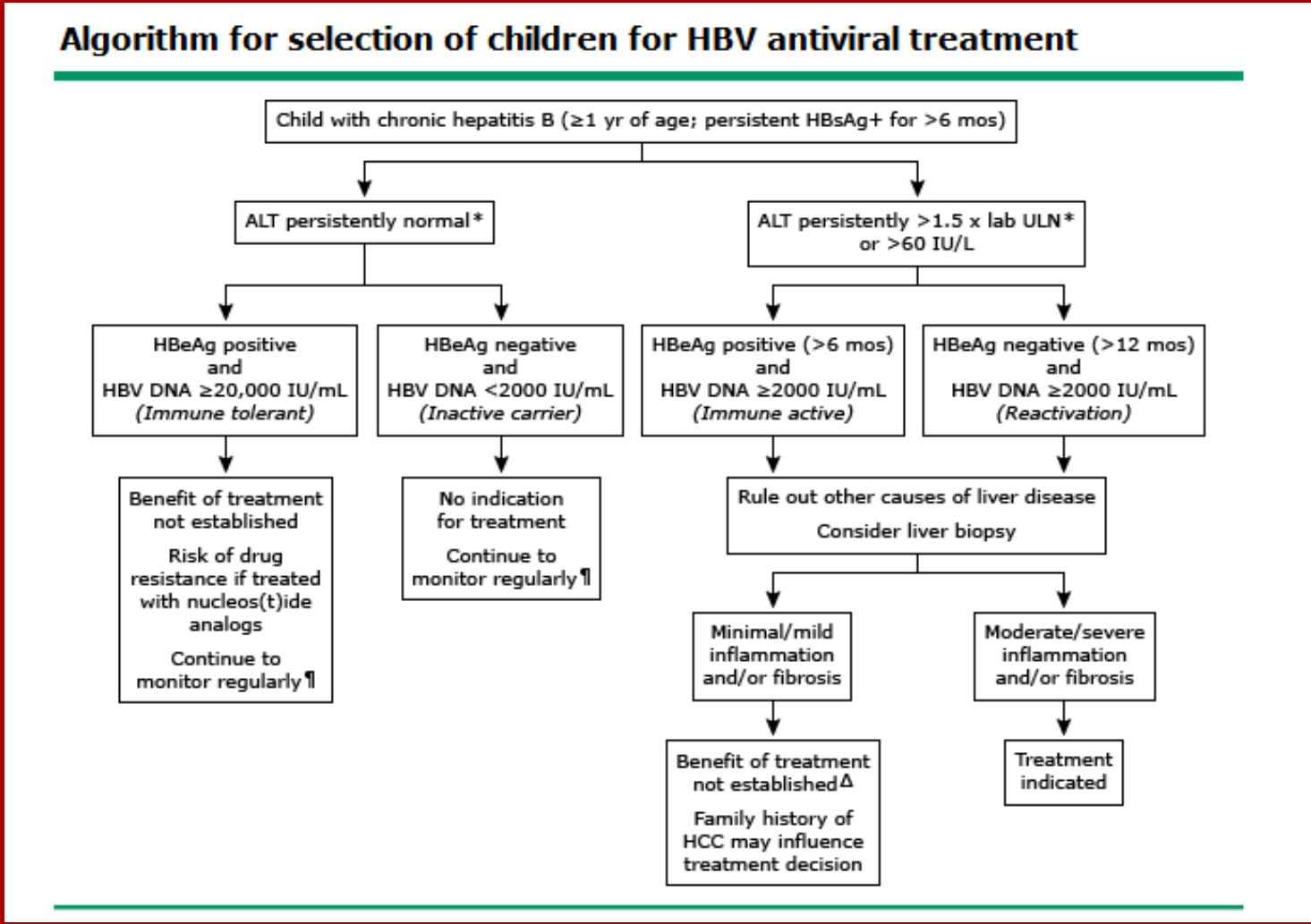
Hepatitis B

- 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.

HEPATITIS B



Jonas MM, Block JM, Haber BA, et al. Treatment of children with chronic hepatitis B virus infection in the United States: Patient selection and therapeutic options. Hepatology 2010. Copyright © 2010 American Association for the Study of Liver Diseases. Reproduced with permission from John Wiley & Sons.

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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.

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.

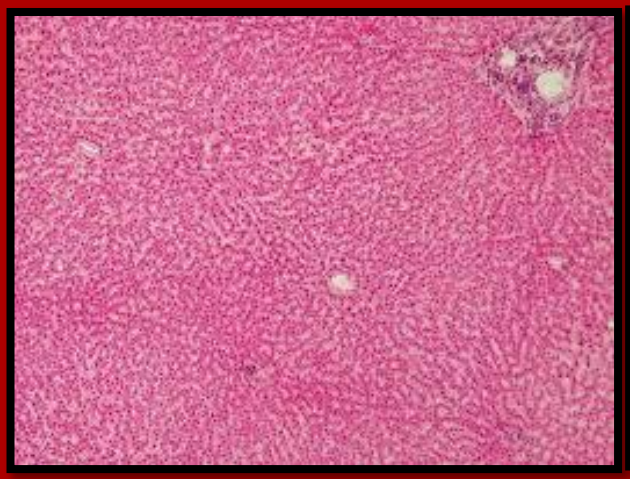
Hepatitis B

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

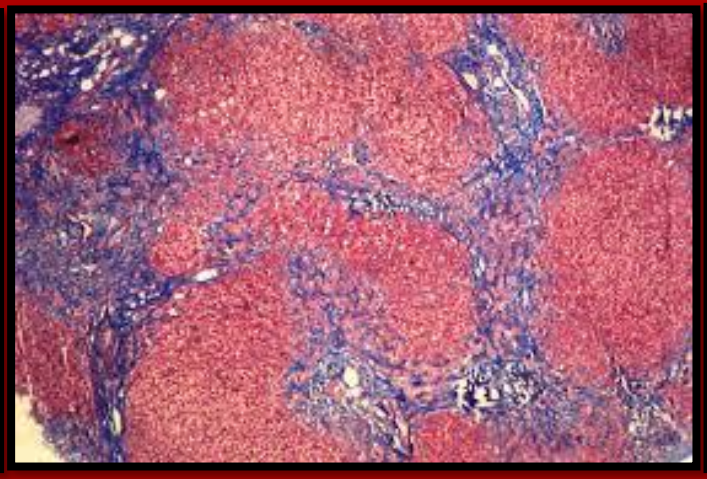
Hepatitis B

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

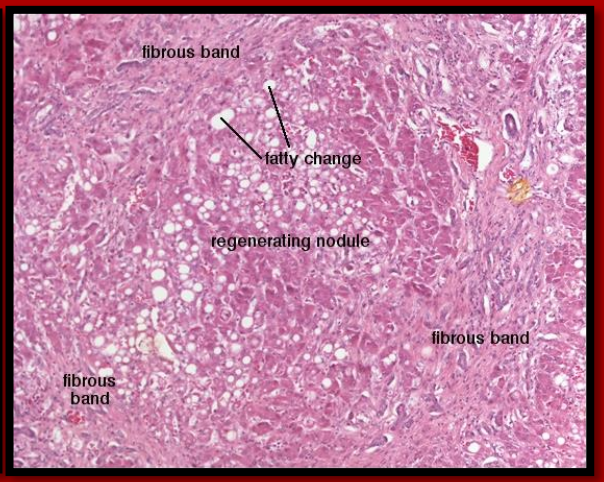
Histology of Fibrosis vs. Cirrhosis



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.

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.

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.

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.

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Case 2

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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 coinfected 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.

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.
  - Adolescents should be advised regarding prevention of sexual transmission.

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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