Chronic Hepatitis B

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Chronic Hepatitis B

- Mauritius – Low Prevalence
- Vaccination programme well implemented
- **BUT**
- Many Chronic HBV around
  - At risk of Hepatic Decompensation
  - At risk of cirrhosis
  - At risk of Hepatocellular Carcinoma
- Worryingly An increased incidence of Acute HBV

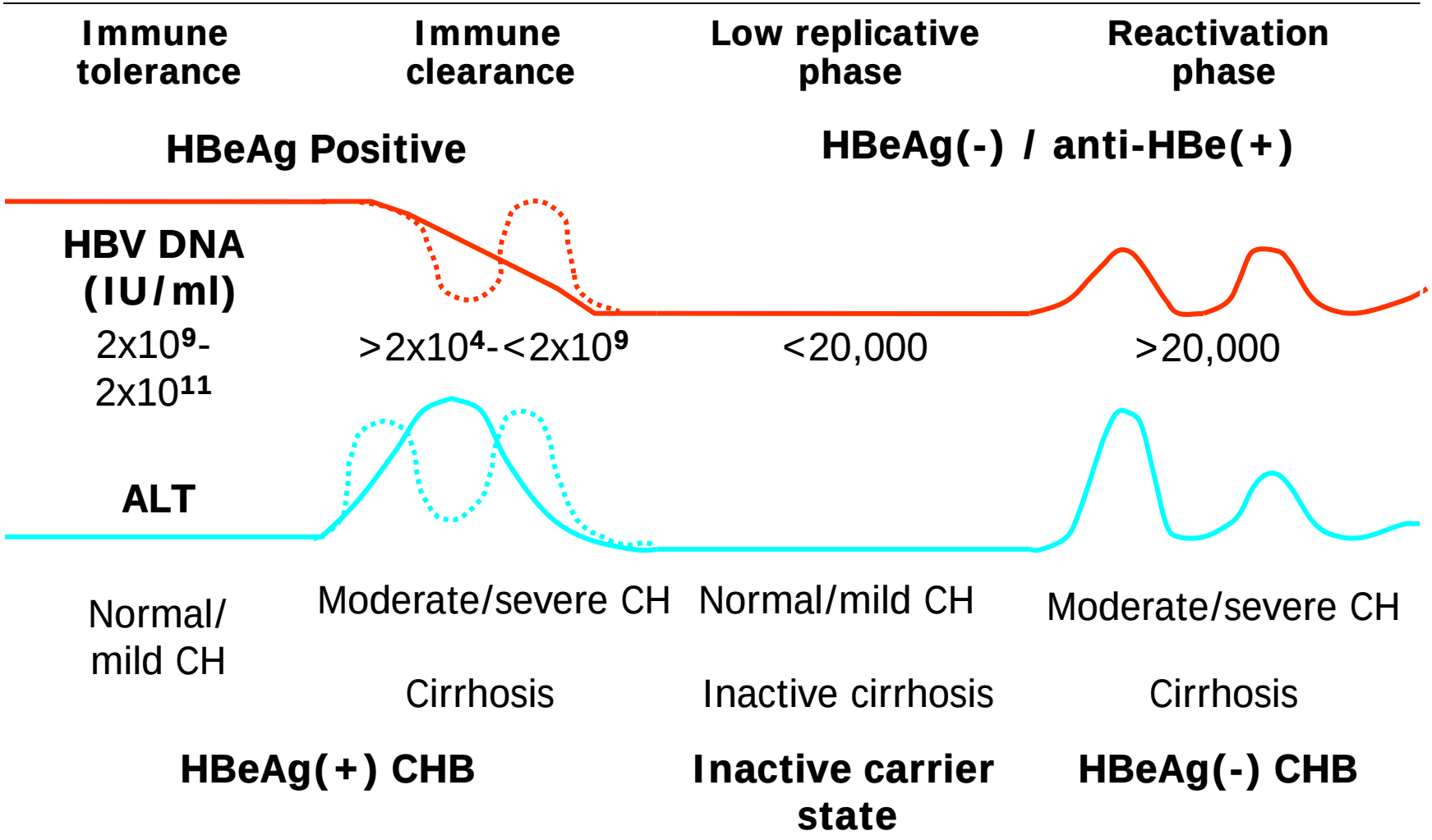
Case Presentations

- A Philippino – ? The law needs to be changed
- A Teacher – We should listen to our patient
- 3 Brothers – Perinatal or early childhood infection
  - 3 different presentations
  - 3 different treatments
- A Businessman – Money can improve healthcare & outcome
- Patient operated in a hospital – Nosocomial Infection
- Hepatitis B and pregnancy – An underestimated issue
- Hepatitis B and chemotherapy – Another important issue

‘Chronic HBV infection is a dynamic state of interactions among HBV, the hepatocytes and the immune system’

Long term Follow-up required

Natural history of Hepatitis B (CHB) infection



Adapted from Fattovich G. Sem Liver Dis. 2003;23:47-58

Philippino

- 25 yrs old male – Blood tests done for working visa
- HBs Ag Pos
- Hepatitis B is 100 times more infective than HIV
- Hepatitis B is 10 times more infective than HCV
- HBs Ag Pos LFTs entirely normal
- Doctor please treat

Philippino

- 25 yrs old male – Blood tests done for working visa
- HBs Ag Pos LFTs entirely normal
- High prevalence of HBV in Philippines (Asia-Pacific Region)
- Likely acquired perinatally or in childhood
- Long Immune tolerant phase
- Rx: No treatment required but
- Follow-up important as Liver injuries may occur if the host's immune responses change

Teacher

- May 1996 – Age 35 AST 238 ALT 204
- HBs Ag Pos HBe Ag Pos
- Measurement of HBV DNA not possible in 1996
- Immune Clearance phase of CHB
  - Active Inflammation of Liver
  - Cirrhosis develops

Teacher

- Patients in the immune clearance phase develop Cirrhosis develop at an annual incidence of 2.4% per year
- TREATMENT REQUIRED

Treatment proposed in 1996

- Standard Interferon – s.c three times per week
- Aim is to seroconvert i.e
  - Get rid of the HBeAg
  - Develop HBeAntibodies
- Problems are:
  - Expensive
  - Lots of Side-Effects
  - Success Rate is only 20 to 30%

Teacher

- Interferon is a protein (cytokines) that your body is constantly making.
- INF-alpha and INF-Beta
- When you have a viral infection such as a flu the body makes more interferon
- Immunomodulator
- Interferon treatment helps the body fight the Hepatitis B virus by getting rid of the HBe Ag

Teacher

- Tired all the time
  - Looking after the husband
  - Raising the kids
  - The work at the college was very demanding
- Immune System needs a boost

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- Tired all the time
  - Looking after the husband
  - Raising the kids
  - The work at the college was very demanding
- Immune System needs a boost
  - Took a sabbatical year from work
  - Sleep well, Healthy Food & Exercise

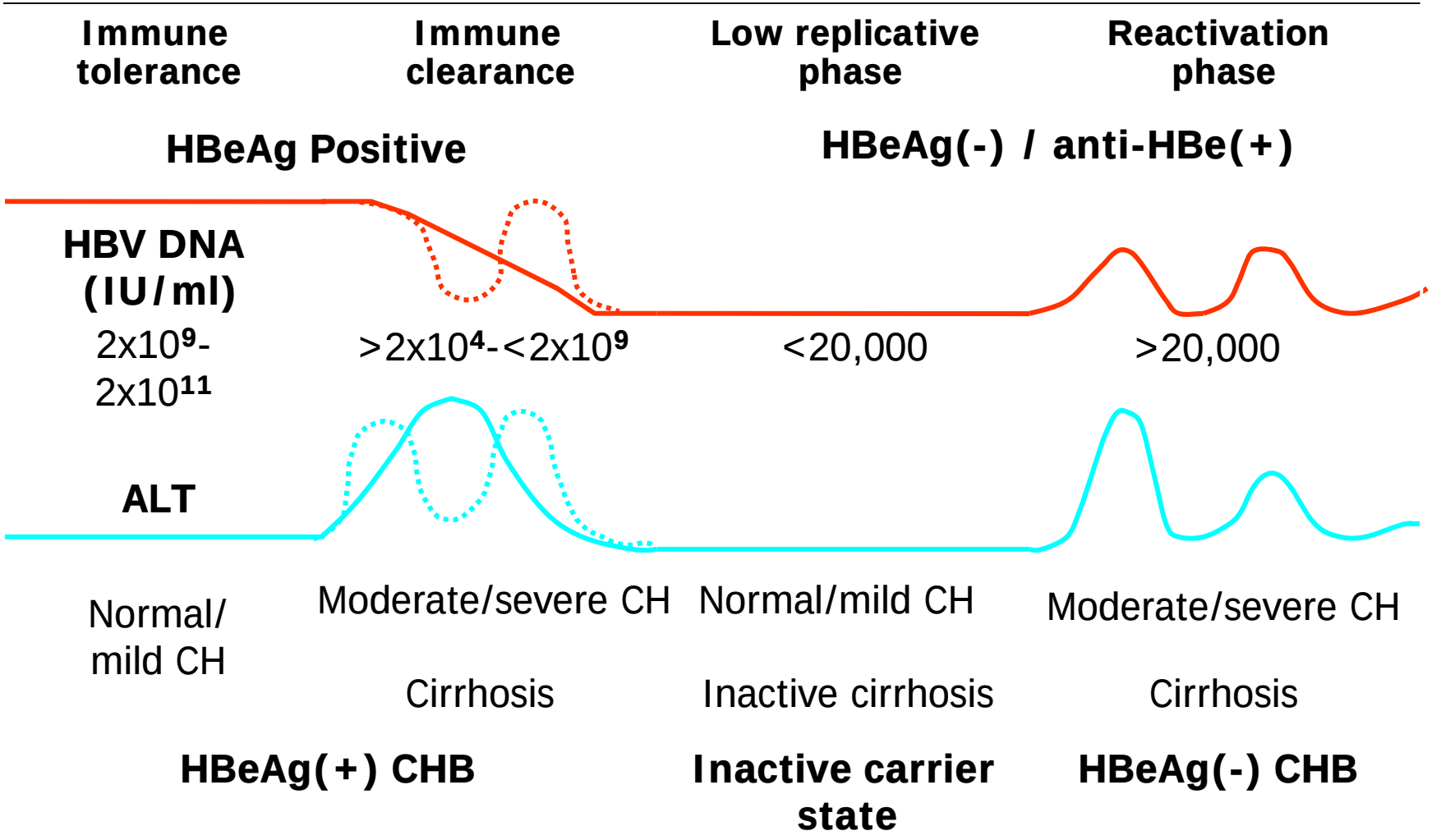
Teacher

- Disappeared for a year and a half
  - Self Monitoring of LFTs

Teacher

- Disappeared for a year and a half
  - Self Monitoring of LFTs
- 1998 – LFTs Normal
- Has seroconverted
- HBe Ag NEG HBe Ab POS

Natural history of Hepatitis B (CHB) infection



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3 Brothers

- Vertical Transmission from mother to baby in the perinatal period
- Horizontal Transmission carries a 20 to 30% risk of chronicity
- Hepatitis B is also parenterally transmitted
  - Sexually
  - Contaminated Body Fluids
  - Sharing of needles
  - Body peircing
  - Tatoos

Patient (Brother No. 1)

- HBs Ag Pos HBe Ag Pos
- July 2008 – AST 61 ALT 72
- Aug 2008 – HBV DNA 266,518 iu/ml
- Immune Clearance phase of CHB
  - Active Inflammation of Liver
  - Cirrhosis develops
- Treatment required

Treatment

- Treatment of Finite Duration
- Long-term Treatment

Treatment of Finite Duration

- Pegylated Interferon – alpha 2a x 48 weeks
- Aim is to seroconvert i.e
  - Get rid of the HBeAg
  - Develop HBeAntibodies
- Problems are:
  - Expensive
  - Lots of Side-Effects
  - Success Rate is only 30%

Patient (Brother No. 1)

- Rx Pegylated Interferon
- Had a rough time
  - Tiredness
  - Loss of appetite
  - Wt Loss
  - Irritable/Not sleeping
- April 2009 HBV DNA 606,964 iu/ml

Patient (Brother No. 1)

- Rx Long term treatment
  - Nucleoside Analogues
    - Lamivudine
    - Telbivudine
  - Nucleotide Analogues
    - Adefovir
    - Entecavir
    - Tenofovir
- Inhibit viral polymerase – Used in HIV

Patient (Brother No. 1)

- Rx Lamuvidine 150 mg daily
  - April 2009 – HBV DNA 606,964 iu/ml
  - Nov 2009 – HBV DNA 1,873 iu/ml
- Beware of Resistance Close, Follow-up required
  - Lamivudine resistant strains develop at 20% per year
  - By year 5, 80% will be resistant to Lamuvidine

Patient (Brother No. 1)

- May 2010 – HBV DNA 41,840,000 iu/ml
- What to do?

Patient (Brother No. 1)

- May 2010 – HBV DNA 41,840,000 iu/ml
- What to do?
  - Add Tenofovir 300 mg daily
  - OR Adefovir or Entecavir
- July 2010 – HBV DNA 25,582 iu/ml
- Sept 2010 – HBV DNA 2,383 iu/ml
- Feb 2011 – HBV DNA 195 iu/ml
- July 2011 – HBV DNA 89 iu/ml

Liver Injuries & Cirrhosis

- In the immune clearance phase immune mediated liver injuries may be episodic or persistent
- Patients in the immune clearance phase develop Cirrhosis develop at an annual incidence of 2.4% per year
- With HBe Ag seroconversion, the disease enter an inactive phase. Transaminases Normal. Cirrhosis do not develop
- Relapse may occur with development of precore or basal core promptor mutations
- HBe Ag Negative Chronic Hepatitis. Cirrhosis develop 2.9% per year

Brother No. 2

- Oct 2003 – Age 41 AST 339 ALT 795
- HBs Ag Pos HBe Ag Neg HBe Ab Pos
- HBV DNA 115 meq/ml (<0.7)
- HBe Ag Negative Chronic Hepatitis. Without treatment Cirrhosis develop at rate of 2.9% per year

Brother No. 2

- Oct 2003 – Rx Lamivudine
- April 2006 – HBV DNA Negative
- LFTs consistently normal since
- Interferon gives sustained HBV DNA suppression in only 20%

Brother No. 3

- GP in Australia
- Presented with decompensated liver cirrhosis
- Started on Lamividine
- Had a Liver Transplant
- Now on Lamivudine & Adefovir to prevent recurrence

Hepatitis B

- Carcinogenic
- HCC without cirrhosis
- But if cirrhosis present Risk of HCC is higher

Screening for HCC

- In those with cirrhosis Annual Incidence is 2 – 6%
- Ultrasound 6 monthly
- Sensitivity is low (20 – 50%) But Specificity 92 – 96%
- MRI with angiography is better. High sensitivity for lesions 1 – 2 cms

Screening for HCC

- Focal Lesion with contrast enhancement
- AFP > 400 ng/ml
- Imaging is 98% sensitive and 100% specific
- Liver Biopsy best avoided - 2 to 5 % risk of tumour seeding in the needle tract

Cirrhosis & HCC

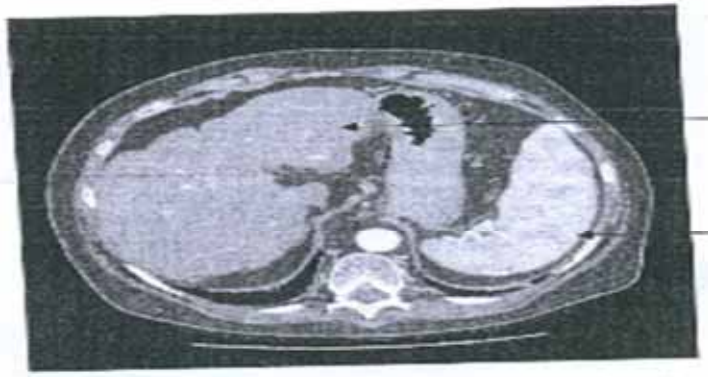

Fig. 14.1 CT scan showing the cirrhotic liver. Note the shrunken liver with irregular outline and enlarged spleen, due to portal hypertension.

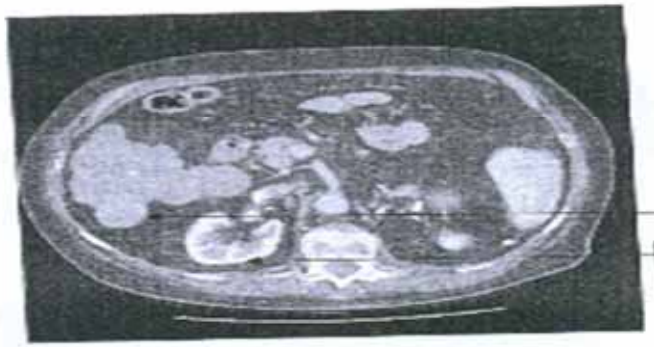

Fig. 14.2 A CT scan showing a round lesion at the tip of the right lobe of the liver, with intense contrast enhancement seen during the arterial phase.

Alpha Fetoprotein

- May be normal if HCC is < 2 cm in diameter
- AFP may be significantly elevated (> 400 ng/ml) in chronic viral hepatitis or acute hepatic necrosis

40 yrs old man

- Sept 2010 – Jaundice Hepatitic Picture
  - Had major surgery
  - Blood transfusion
  - HBs Ag positive
  - HBc Ig M antibodies positive
- Acute Hepatitis B
- ? Related to blood transfusion

40 yrs old man

- Blood donors traced
- HBs Ag NEG
- Nosocomial Infection ?
- Reported to Public Health

32 yrs old female

- Pregnant
- HBs Ag pos
- What to do?

Hepatitis B and Pregnancy

- Perinatal transmission results in a high frequency of Chronic Infection
- It occurs at and near the time of birth – Exposure to cervical secretions and maternal blood
- Rx Vaccination is effective
- Adding Hepatitis B Immunoglobulin reduces the risk further
- Prevent only 80 to 95% of cases
- Not 100% - Transplacental (intra-uterine) transmission

32 yrs old female

- HBe Ag Positive
- HBV DNA > 170,000,000 iu/ml
- Risk of transplacental transmission HIGH

32 yrs old female

- Risk of transplacental transmission HIGH
- Risk is significantly reduced by Mother taking Lamuvidine in the last trimester
- Newborn must be given HBs Immunoglobulins + Vaccination at birth

Teacher

- May 1996 – Age 35 Immune Clearance phase of CHB
  - HBe Ag Pos AST 238 ALT 204
- 1998 – Seroconverted HBe Antibodies Pos
- Inactive Carrier
- 2010 – Breast Cancer
  - Surgery
- Chemotherapy

HBV reactivation

- In HBV patients who require immunosuppressive therapy, reactivation is frequent
  - 14 to 50%
- High mortality: 3.7 to 60%
- During or after immunosuppressive therapy:
  - Allogenic bone marrow transplantation
  - Haematological chemotherapy
  - Solid organ cancer chemotherapy
  - High doses of corticosteroids, or azathioprine

1. Hoofnagle J, et al. Ann Intern Med. 1982;96:447-49. 2. Scullard GH, et al. Gastroenterol. 1981;81:987-91. 3. Steinberg JL, et al. J Med Virol. 2000;60:249-55. 4. Pariente EA, et al. Dig Dis Sci. 1988;33:1185-91. 5. Oksuzoglu B, et al. Jpn J Clin Oncol. 2002;32:543-45. 6. Hammond A, et al. Dtsch Med Wochenschr. 1999;124:687-90

Teacher

- 2010 – Breast Cancer
  - Rx Surgery
- Then Chemotherapy
- Rx Lamuvidine

Rheumatoid Arthritis

- 2000 – Severe Rheumatoid Arthritis
  - Rx NSAIDs + Steroids
- Abn LFTs
- LFTs normalise when drugs stopped
- What to do?

Rheumatoid Arthritis

- 2000 – Severe Rheumatoid Arthritis
  - Rx NSAIDs + Steroids
- Abn LFTs
- HBs Ag POSITIVE HBe Ag NEG
- Rx Lamuvidine
- On NSAIDs + Intermittent steroids. LFTs Normal

‘Chronic HBV infection is a dynamic state of interactions among HBV, the hepatocytes and the immune system’

Long term Follow-up required

Important Advances

- Better treatment for Chronic Hepatitis B
- Better results for pregnant mothers
- Acute flares during or after chemotherapy can be prevented
- Complications can be prevented
- Be careful – Acute Hepatitis B are seen not infrequently

Thank You