VIRUS HEPATITIS IN PREGNANCY

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Viruses in May- 2009

Series of situations with potential problems for mother and baby

- acute infection during pregnancy
- persistent infection during pregnancy
- contact or other exposure during pregnancy
- travel/occupational risks during pregnancy

The inherent biology of the hepatitis viruses determines what happens, and the options for treatment and prophylaxis

Policy issues arising form the biological determinants

screening of pregnant women

action during pregnancy

follow up after pregnancy

wider public health use

Hepatitis A and E are both entero-virus like:

- Transmission is faecal/oral
- The liver is infected via the bloodstream
- Liver damage is due to CPE of the virus +/- CMI
- Neutralising Ab formation is advanced at clinical onset
- Chronic carriage does not ensue
- Severity increases with age
- Breast milk contains virus

But the epidemiology is different

- A still endemic in tropics (but…)
- E occurs in outbreaks in limited regions (India/Africa)
  (but swine reservoir elsewhere…)

HAV susceptibility of women of childbearing age is low
Wherever the infection is endemic because of (usually) asymptomatic childhood infection.

In industrialised countries the risk of exposure is low and many adults have been vaccinated for travel or using A+B vaccine

But

HEV, in outbreaks at least, targets young adults of whom only about 20% are immune.

Vaccine is a long way off.

Impact of pregnancy on the infection:

Both A and E more severe in pregnancy, especially in the third trimester

BUT

HEV notoriously likely to cause acute hepatic failure

Impact of infection on the pregnancy:

Both commonly result in premature delivery with poor outcomes for the baby.

Outcome of acute hepatitis in an Indian hospital series

	HEV	other
Maternal death	54/132	6/88
Death in utero	19 + 8	1+4
stillborn	57	25
Neonatal death	18	12
Live baby	30	46

Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection.
Patra S. Kumar A. Trivedi SS. Puri M. Sarin SK. Annals of Internal Medicine. 147:28-33, 2007

Why is HEV so severe in pregnancy?

Physiological immunosupression

Hormonal influences

Virus genotype

Protein/vitamin deficit (dietary customs)

Prophylaxis of maternal infection:

Recognise major risk factors for maternal infection:

Hep A: travel from industrialised countries

Hep E: resident in outbreak affected area

Hepatitis A

avoidance – of travel/of virus in water/food

vaccination/immunoglobulin – risk assessment

Hepatitis E

avoidance of virus in water/food

? Avoid pig farms etc

Contacts of cases: low risk if adults in first world

Current issues:

Is HEV so rare in Australia that we needn't test for it?

How should we test patients who are jaundiced in pregnancy?

Is superinfection of HAV or HEV in pregnant patients with chronic HBV or HCV or HIV a "sleeping" global problem?

Is HEV yet another unfunded orphan vaccine?

The inherent biology of the hepatitis viruses determines what happens.

Hepatitis B

- Transmission parenteral/sexual
- Viraemia prolonged
- Liver damage due to immune response
- Neutralising antibody late to develop
- Chronicity common outcome
- Virus present in breast milk/saliva

Infection in early life is the key factor determining the global disease load of HBV.

Acute hepatitis B in pregnancy is often severe and carries a high risk of transmission to the infant. This was first described in Sydney almost 40 years ago.

Neonatal hepatitis and Australia antigen. Gillespie A. Dorman D. Walker-Smith JA. Yu JS. Lancet. 2(7682):1081, 1970

It's pathogenesis is as obscure as ever, but the high viral load facilitates transmission and the presence of HBe may be immune modulating in the baby.

Chronic hepatitis B in pregnancy is the major factor determining disease burden in the community.

No association with adverse outcomes for fetus.

No evidence that maternal liver disease is affected.

Only HBV DNA positive mothers transmit – and risk is related to viral load.

Reactivation has not been reported in pregnancy, but virus load increases near term.

Infants most likely to be infected perinatally rather than *in utero.*

Many infected infants become long term carriers with risk of cirrhosis and HCC in later life, others clear. Young Infants have ongoing risk of exposure in household.

Post-exposure prophylaxis with vaccine alone about 90% effective, even better with HBIG.

This justifies universal infant HBV vaccination and, in rich countries, maternal screening and HBIG for babies of HBV DNA (?HBsAg) positive mothers.

Long term issues of vaccine mutants and waning immunity in adult life. Follow up issues….

The inherent biology of the hepatitis viruses determines what happens.

Hepatitis C

Transmission parenteral
Liver damage ?due to immune response
Neutralising antibody ?does not develop
Chronicity common

Chronic hepatitis C in pregnancy

? No effect on pregnancy though some evidence it may affect fertility.

Viral load rises near term.

Transmission to 5-10% babies born to viraemic mothers.

Non-viraemic mothers do not transmit.

Data limited because in many countries most HCVRNA pos mothers are co-infected with HIV.

No consensus on screening in pregancy.

Refining level of risk can be achieved

By qPCR to assess viral load

By testing PBMCs for virus

Infected infants are seldom jaundiced, but "quality of life" may be impaired.

Seroconversion follows "adult" pattern with clearance in approx 50% by 18 months of age.

No consensus about management of persistent infection in children.

Australian ante-natal surveys give different results in different areas.

Central Sydney in 2000

HBsAg 3%
Anti-HCV 4%

Dominant risk factor for HBsAg was birth abroad, and for HCV injecting drugs – but also Tx and birth abroad.

J.Zou et al Procs ISVHLD 2004 pp455-6

What action is/should/could betaken as a result of a positive maternal screening result?

Managing this pregnancy/this baby

Maternal assessment post delivery

Family assessment

Community assessment

Managing this pregnancy/this baby

HBV cut and dried – but difficulties in practice stem from poor pre-test counseling and unclear public health education. Follow up of babies " not recommended" so efficacy is unknown.

HCV may or may not be complicated by current drug use. Follow up of baby difficult and management uncertain. Risk of exposure in drug using households continues.

Maternal assessment post delivery:

Ad hoc at best, yet has great potential to start treatment early. This potential needs to be explicit in pre-test counseling.

Family assessment

HBV :
nuclear family and entry of carriers into surveillance/treatment system

Older generations for assessment of current liver disease status and f/up

Community assessment

There are many cautionary tales (eg pertussis) about complacency after successful introduction of vaccines.

Surveillance based on lab notifications or "opportunistic" serum collections are basically flawed for this purpose, but the cost of rigorous surveillance is prohibitive.

Possible alternative is a health of children survey for many diseases – microarray technology may cut cost of lab work.

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