Preeclampsia, Pregnancy Induced Hypertension & Gestational Diabetes

CONFLICTS IN PREGNANCY

Case

- 31 year old woman 6 weeks pregnant
- No symptoms
- Random blood glucose in clinic is 180
- Abnormal glucose tolerance test
- Incidence in pregnancy is up to 3-10%
- What is it?

Diagnosis: Gestational Diabetes

- In pregnancy maternal pancreas islet cells hypertrophy
- Conflict between how much glucose goes to the fetus vs. to the mother's body.
- Placental hormone "resistin" induces insulin resistance in mother – shunting glucose to the placenta.

Complications of gestational diabetes ?

- Macrosomia
- Shoulder dystocia
- Increased rate of C section and bleeding complications

Big Baby

22 year old female 6 months pregnant

- Presents to the ER with headaches
- Blood Pressure is 160/110
- Protein is noted in her urine
- She has low platelets
- You are worried – you had a similar patient who had seizures and died!

Pre-eclampsia

- Illness of pregnancy
- PIH, Pre-eclampsia, Eclampsia
- very high blood pressure, seizures and death
- More common in first pregnancy
- More common in twin births

Fairly common disease

- 2-8 % pregnancies
- 10% pregnancies may have PIH
- Common, mysterious, & can kill you? Why?

Here is a clue

- Get rid of the placenta – ecclampsia goes away
- Placenta is combination of maternal and paternal genes.
- Invades the uterus
- There is a balance that determines the degree of invasion and control the mother gives up

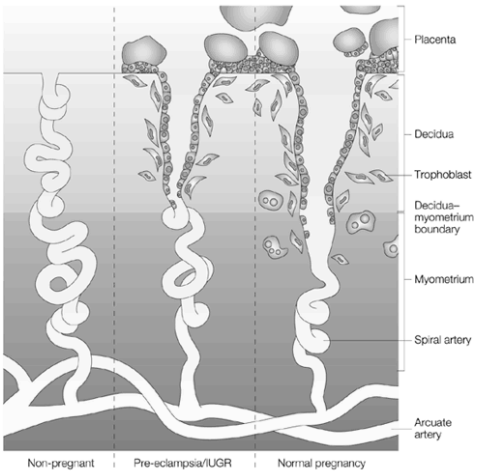
Risk Factors

- Multiple gestation – twins, triplets
- Hydatid Mole
- These give you a large placenta

The placenta

- "A ruthless parasitic organ existing soley for the maintenance and protection of the fetus, perhaps too often to the disregard of the maternal organism"
- Page, E.W. 1939

Spiral Arteries



Out of balance!

- Shouldn't all parties agree on keeping both mother and baby happy and healthy?

Paternal genes

- Paternal genes are shared in the fetus but not with the mother. Interests lie mostly with the fetus.
- Paternal derived genes might attempt to extract more resources from mother than mother would like to give up

Maternal genes

- Promote control over resource delivery to placenta
- Can withhold resources from one reproductive effort that can be diverted to other needs

Implantation

- Inflammation
- Implantation and trophoblast invasion does not occur without a fight.
- Maternal NK (Natural Killer) cells cause inflammation around the early placenta – can resist invasion and can induce abortion

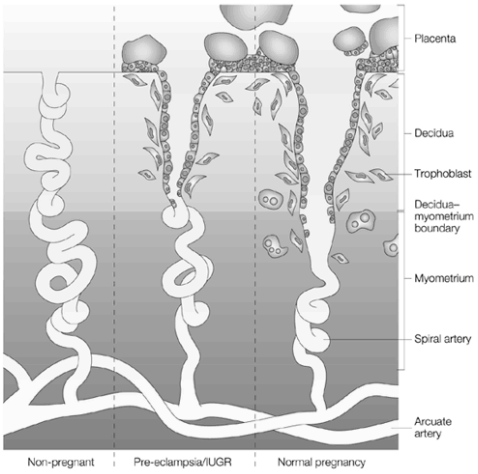
Cryptic mate choice

- Investment in pregnancy balanced against future health and investment in other offspring
- 50% spontaneous abortion rate (early miscarriage)

Paternal genes

- Would be expected to resist efforts to prevent implantation and trophoblast invasion
- Might be expected to increase resource delivery to the fetus at expense of mother.

Trophoblast invasion



Pregnancy induced hypertension

- The placenta is a low pressure venous system
- Raising maternal arterial pressure increased flow.
- 600cc blood per hour
- Increased flow means increased glucose and nutrients to the fetus
- Paternally derived trait

Pre-eclampsia

- Uterine spiral arteries resistance to invasion of uterus by trophoblasts
- Trophoblasts induce cytokines and free fatty acid production -> increase vascular resistance in the mother
- This raises her blood pressure
- Can lead to increased nutrient delivery to fetus

Eclampsia

- Process gets out of hand – cyokines damage mother's arteries and organs with diffuse inflammation
- Causes hemolysis, thrombosis, seizures, death

Sounds Far Fetched?

- OK lets make some predictions
- If a father has several kids with a mother – paternal genes might not benefit from injuring the mother to benefit a fetus.
- Conversely, a mother might "trust" sperm from partner she has previous children with and be more likely to allow implantation
- Do multiple pregnancies decrease the risk?

Multiparity & Preeclampsia

- Nulliparous women have higher risk
- Previous pregnancy decreases risk

- How does this occur?

Male reproductive proteins

- Antigens to certain proteins might be neutralized by female antibodies
- Increases the chance of successful pregnancy

- You might also predict change in sexual partners would increase the risk…

MHC and preeclampsia

- Major histocompatibility antigens seem to be important in pregnancy, spontaneous abortion, and preeclampsia
- Maternal KIR (AA) with fetal HLA-C

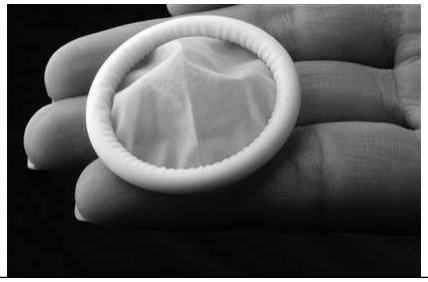
- Trowsdale J, MoffettA. NK receptor interactions with MHC class I molecules in pregnancy. SeminImmunol (2008), doi:10.1016/j.smim.2008.06.002

Danger of a One Night Stand!

- Change in sexual partners has effects:
- Increases risk of preeclampsia
- Duration of cohabitation decreases risk

Condoms increase risk!

- Exposure to male sperm decreases risk
- Barrier methods increase risk
- Male reproductive proteins seem to decrease the likelihood of reproductive conflict over time



Confounder: STDS?

- Sperm donor IVF increased the risk
- Washed semen – tests for and removes STDs
- Autologous sperm donor less likely to cause preeclampsia than stranger sperm donors
- Suggests that MRPs affect tolerance of sperm and possibly implantation of embryo from a recognized male
- Occurs even when the MRPs are not present

Male or Female Effect?

- Increased successful implantation from long-duration partners
- Is the female altering sperm composition
- Or is the sperm changing?
- Female tolerance of more fertilized eggs?
- Maybe both?

EsplinMS, FausettMB, FraserA, KerberR, MineauG, CarrilloJ, etal. Paternal and maternal components of the predisposition to preeclampsia. NEnglJMed 2001;344:867–72.

Dangerous Male

- Preeclampsia specialists
- Certain males have higher risk of inducing preeclampsia
- Are these males more likely to have multiple partners?

Egg donation

- In implanted oocyte IVF - fetus does not share any genes with mother – rate of preeclampsia is 30%!
- Lack of expressed maternal counter adaptations to paternal attempts to increase blood pressure.

SalhaO, SharmaV, DadaT, NugentD, RutherfordAJ, TomlinsonAJ, etal. The influence of donated gametes on the incidence of hypertensive disorders of pregnancy. Hum Reprod 1999;14:2268–73.

Summary

- Paternal genes increase resource extraction
- Maternal genes resist these effects
- Tug of war – usually these balance out
- PIH, Ecclampsia, Gestational Diabetes occur when sides are out-of-balance.