THE POTENTIAL CONTRIBUTION OF MOBAND TO THE EPIDEMIOLOGY OF CEREBRAL PALSY

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THE TWO TRADITIONAL RISK FACTORS FOR CP

- PREMATURE BIRTH
  - 50 fold higher risk in infants < 28 wks.
  - In high-income countries, birth < 37 weeks accounts for some 40% of CP cases.
- BIRTH ASPHYXIA

  Long thought my many to be the basic cause of CP, with very expensive implications for obstetric malpractice lawsuits. But:
  - Some degree of birth asphyxia is very common, and most infants recover completely
  - Prenatally compromised infants often respond poorly to the stress of labor
  - No reduction in CP prevalence with major increases in c-section rates

SOME RECENTLY HYPOTHESIZED RISK FACTORS FOR CP

- COAGULATION
  - Perhaps as much as 5-10% of CP is from perinatal stroke. It is plausible, but not proven, that some may have polymorphisms of the coagulation system
- THYROID HORMONES
  - Low thyroxine after birth a risk factor (not certain if causal) in preterm; possibly also at term. A syndrome which is a form of CP (neurologic cretinism) linked to iodine deficiency in endemic goiter areas.
- INFECTION/INFLAMMATION
  - Increasing evidence for a role of antepartum infection, especially in preterm birth (Fetal Inflammatory Response Syndrome - FIRS)

CP GENETICS

- Genes only a modest factor in CP
- Recurrence risk in siblings is about 1-2%, a 5 to 10-fold elevation in risk, similar to many polygenic birth defects.
- Most consistent molecular genetic finding:
  - Apoliprotein E - A modest association with CP (odds ratios of 2-4) in some (but not all) studies with presence of epsilon 2 or 4 allele, in contrast to having the epsilon 3 allele.

MOBAND

A COMBINATION OF THE TWO LARGEST PREGANCY COHORTS IN EXISTENCE CREATED TO STUDY CP

1. Mothers and Babies in Norway (MoBa)

2. The Danish National Birth Cohort (DNBC)

Key reference: Tollanes et al: BMJ Open 2016 Sep 2;6(9):e012777

MOBAND CHARACTERISTICS

- Some 210,000 children, among whom 438 cases of CP were ascertained in the two national CP registries.
- Norway: 112,509 pregnancies, recruited at weeks 13-17, 1999-2009.
- Denmark: 100,417 pregnancies, recruited at weeks 6-10, 1996-2003.
- CP prevalence is just over 2/1,000 live births

MOBAND DATA

- DNBC
  - Brief questionnaire at 6-10 weeks
  - Telephone interviews at 16,31 weeks
  - Nutritional questionnaire at 25 weeks
- MoBa
  - Questionnaire at 13-17 weeks
  - Nutritional questionnaire at 22 weeks
  - Questionnaire at 30 weeks

MOBAND SPECIMENS

- DNCB
  - Blood at 6-10 weeks
  - Blood in mid-pregnancy
  - Cord blood
- MoBa
  - Blood and urine at 13-17 weeks
  - Cord blood

WHAT CAN MOBAND TEACH US ABOUT CP?

- MOBAND is by far the largest cohort study initiated in pregnancy and linked to CP cases.
- Recent studies of CP etiology are from administrative data and contain no information obtained in pregnancy in real time from mothers except for medical records.
- No studies of CP in relation to either maternal interviews during pregnancy or biological specimens in pregnancy.
- To use MOBAND data, approval is needed from MOBAND steering committee and from each of the two cohorts.
- I serve on the scientific advisory committee to MOBAND

IMPLICATIONS FOR CP PREVENTION RESEARCH

- I think CP will be prevented, like heart disease, a little bit at a time.
- In heart disease, several clinical syndromes were aggregated – angina, heart attack, sudden death – and risk factors were examined for the aggregated clinical picture
- Similarly, I suspect that to find important, intervenable risk factors, it will be more productive to focus on risk factors clusters (e.g. prematurity, term birth with labor problems) rather than on clinical sub-types (e.g. diplegia, hemiplegia).

MOBAND ILLUSTRATION #1

- Tanja Gram Petersen* et al: Maternal thyroid disorder in pregnancy and risk of cerebral palsy in the child: A population-based cohort study (in submission)
- Examines CP in relation to thyroid disorders
  - Self-reported thyroid disorders at 13-17 weeks of pregnancy. Question did not distinguish hypo from hyperthyroidism
  - Thyroid medication use at 13-17 weeks in MOBA and at 31 weeks in DNBC
- Some weak relationships found.
- Next step – INVESTIGATE THE SERUM SAMPLES!
- * Graduate student in epidemiology, University of Copenhagen

MOBAND ILLUSTRATION #2

- Diana Haggerty* proposes to investigate a nutritional-inflammatory interaction
- She hypothesizes that an interaction between unbalanced maternal intake of two polyunsaturated fatty acids and perinatal exposure to an inflammatory event increases the risk of CP in offspring.
- Both variables will be obtained from the maternal interviews about health and diet conducted during pregnancy in DNBC and MoBa.
- Next step – INVESTIGATE THE SERUM SAMPLES!

* Has poster in this conference

FURTHER IMPLICATIONS

- It will be key to move quickly from suggestions emerging from examination of questionnaire data to examination of biological specimens
- Especially important to focus on term births, where less is understood than in preterm births, because CP in preterm births has been the subject of considerable research in prospective cohorts, and we have identified some risk factors.
- If one topic ought to be explored in depth to identify risk factors in clinical, interview and biological data with high potential for intervention, I would recommend infection and inflammation.

THANKS FOR LISTENING

I’M HAPPY TO TAKE QUESTIONS