Persistent Effects of Maternal Smoking during Pregnancy on Lung Function and Asthma in Adolescents

Hollams E *et al.*

American Journal of Respiratory and Critical Care Medicine (Nov 2013)

The extent to which maternal smoking in pregnancy (MSP) has persisting effects on respiratory health remains uncertain and the mechanisms involved are not fully understood. Alterations in immune function have has been proposed as a mechanism contributing to respiratory disease. They determined whether MSP increases risk of respiratory disorders in adolescence and, if so, whether this occurs via decreased lung function, altered immune function, and/or enhanced atopy. Methods: Data on spirometry, bronchial responsiveness, respiratory symptoms, total and allergen-specific IgE and IgG4, immune function and inflammatory markers were obtained from 1129 participants in the 14 year follow-up of the Western Australian Pregnancy (Raine) Cohort and related to MSP using regression analyses.

MSP was reported for 21.0% (237/1129) of participants, with 92 (8.1%) reporting current smoking. MSP was associated with some altered immune measures at age 14. MSP was strongly related to reduced lung function in current non-smokers (FEF25-75, p=0.016, FEV1/FVC, p=0.009) and increased risk for: current asthma [OR 1.84(95% CI 1.16-2.92), p=0.01]; current wheeze [1.77(1.14-2.75), p=0.011]; and exercise-induced wheeze [2.29 (1.37-3.85), p=0.002], but not for BHR or atopy. Adjustment for immune measures and/or lung function in multivariate models did not greatly alter these associations and the increased risks for asthma and wheeze were not modified by sex, atopy or maternal history of asthma or atopy. They cocluded that maternal smoking in pregnancy increases risk of asthma and wheezing in adolescence; mechanisms go beyond reducing lung function and exclude altering immune function or enhancing atopy.

Higher Vitamin D Levels in Pregnancy Could Help Babies Become Stronger

Children are likely to have stronger muscles if their mothers had a higher level of vitamin D in their body during pregnancy, according to a study published in the January 2014 edition of the Journal of Clinical Endocrinology and Metabolism.

Low vitamin D status has been linked to reduced muscle strength in adults and children, but little is known about how variation in a mothers status during pregnancy affects her child.

Low vitamin D concentrations are common among young women in the UK, and although women are recommended to take an additional 10mcg/day of vitamin D in pregnancy, supplementation is often not taken up.

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In the study, vitamin D levels were measured in 678 mothers in the later stages of pregnancy. When the children were aged 4 years, grip strength and muscle mass were measured.

Results showed that the higher the levels of vitamin D in the mother, the higher the grip strength of the child, with an additional, but less pronounced association between mothers vitamin D and childs muscle mass.

These associations between maternal vitamin D and offspring muscle strength may well have consequences for later health; muscle strength peaks in young adulthood before declining in older age and low grip strength in adulthood has been associated with poor health outcomes including diabetes, falls and fractures, said Nicholas Harvey, Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom.

It is likely that the greater muscle strength observed at age 4 years in children born to mothers with higher vitamin D levels will track into adulthood, and so potentially help to reduce the burden of illness associated with loss of muscle mass in old age, he said.

The 678 women who took part in the study are part of the Southampton Womens Survey -- one of the largest and best characterised such studies globally.

Umbilical Cord Serum Interleukin-6, C-Reactive Protein, and Myeloperoxidase Concentrations at Birth and Association with Neonatal Morbidities and Long-Term Neurodevelopmental Outcomes

Sorokin Y *et al.*

American Journal of Perinatology (Dec 2013)

Umbilical cord serum samples were collected at birth from 400 newborns delivered within a multicenter randomized controlled trial of repeated versus single course of antenatal corticosteroids (ACs), in women at increased risk for PTB. Newborns were followed through discharge and were evaluated between 36 and 42 months corrected age with neurological examination and Bayley Scales of Infant Development. Umbilical cord serum concentrations of IL-6, CRP, and MPO were determined using enzyme-linked immunoassays. Multivariate logistic regression analyses explored the relationship between umbilical cord serum IL-6, CRP, and MPO levels, adverse newborn outcomes, and PTB The aim of the study is to determine if umbilical cord serum concentrations of interleukin-6 (IL-6), C-reactive protein (CRP), and myeloperoxidase (MPO), in pregnancies at risk for preterm birth (PTB), are associated with neonatal morbidities and/or altered neurodevelopmental outcomes in the children. Study Design<Univariate analysis revealed that umbilical cord IL-6 above the 75th percentile was associated with increased respiratory distress syndrome (RDS) and chronic lung disease (CLD), but not with necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), or neonatal sepsis; however, this association was not significant after adjusting for GA at delivery and treatment group. No significant associations between CRP or MPO and RDS, CLD, NEC, sepsis, or IVH were evident. Regression analysis revealed that CRP above the 75th percentile was associated with a decreased risk of CLD (odds ratio, 0.10; 95% confidence interval, 0.02-0.41). No associations between umbilical cord IL-6, CRP, or MPO and MDI 32 weeks of gestational age (GA). Results<70 or PDI<70 were evident. Umbilical cord serum concentrations of IL-6, CRP, and MPO, above the 75th percentile, were associated with more frequent PTB<Elevated umbilical cord

serum concentration of CRP is associated with reduced risk for CLD even after adjusting for GA at delivery. Occurrence of levels 32 weeks of GA. Conclusion>75th percentile of IL-6, CRP, and MPO in umbilical cord serum was associated with PTB<32 weeks of GA. Elevated umbilical cord serum concentrations of IL-6, CRP, and MPO at birth were not associated with poor neurodevelopmental outcomes.

Lower risk of atopic dermatitis among infants born extremely preterm compared with higher gestational age

Barbarot S *et al.*

British Journal of Dermatology 169 (6), 1257-64 (Dec 2013)

Their objective was to determine whether the risk of AD is influenced by preterm birth.

They investigated the relationship between gestational age (GA) and AD using data from two independent population-based cohorts, including a total of 2329 preterm infants, of whom 479 were born extremely preterm.

There was a lower percentage of children with AD in the extremely preterm group compared with those born at a greater GA (Epipage cohort, 2-year outcome: 13.3% for 24-28 weeks, 17.6% for 29-32 weeks, 21.8% for 33-34 weeks, P = 0.02; LIFT cohort, 5-year outcome: 11% for 24-28 weeks, 21.5% for 29-32 weeks, 19.6% for 33-34 weeks, P = 0.11). After adjusting for confounding variables, a lower GA (< 29 weeks) was significantly associated with decreased risk of AD in the Epipage cohort [adjusted odds ratio (aOR) 0.57, 95% confidence interval (CI) 0.37-0.87; P = 0.009] and the LIFT cohort (aOR 0.41, 95% CI 0.18-0.90; P = 0.03).

They concluded that very low GA (< 29 weeks) was associated with a lower risk of AD compared with higher GA (29-34 weeks) and full-term birth.

Correcting Mutations by RNA Repair

Reenan R.

NEJM 2014;370:172-174

Therepatic approaches to mendeles disorders use tactics from gene replacement to small molecules designed to correct functional defects, from drugs that force the synthesis of full long the proteins that would otherwise be truncated to oligonucleotides that alter RNA splicing. The repair machine in a process called adenosine to inosine RNA editing Enzyme called ADARs (adenosine diamines acting on RNA) chemically modify adenosine to inosine in RNA transcript. When cellular machine see the inosine as a guanosine residue, the final effect is the conversion of adenosine to guanosine (A^{a}D). So they incorporate A^{a}G changes. Therefore, more than half the amino acids of the genetic code can be altered and repaired.

Mistargeting of Peroxisomal EHHADH and Inherited Renal Fanconis Syndrome

Klootwijk ED *et al.*

NEJM 2014;370:129-138

In renal Fanconis syndrome, dysfunction in proximal tubular cells leads to renal losses of water, electrolytes, glucose and low-molecular-weight nutrients.

In 5 families with autosomal dominant inheritances this kind Fancons syndrome heterozygose missence mectation of enzyme EHHADH created a new mutochondrial targeting motif in the N-terminal portion of it which is involved in peroxisamal oxidation of faty acids causing some changes in proximal tubul mutochondria which causes abnormality in the tube function.

Increased incidence of neonatal respiratory distress in infants with mucopolysaccharidosis type II (MPS II, Hunter syndrome

Dodsworth C, Burton B

Molecular Genetics and Metabolism 111 (2), 203-4 (Feb 2014)

Records were reviewed on all patients with mucopolysaccharidosis type II (Hunter syndrome) seen at a single institution from 1999 to 2013 to identify those with a history of neonatal intensive care. Eleven of 34 patients were in a neonatal intensive care unit and all had respiratory distress with 8 diagnoses of respiratory distress syndrome and 3 of transient tachypnea of the newborn. None of the infants were premature; four were delivered by cesarean section. These findings suggest that respiratory distress is more commonly observed in neonates with MPS II than in the general population. This may reflect airway disease already present in this disorder at the time of birth.

Neurobiology of attention deficit hyperactivity disorder

Wankerl B *et al.*

Fortschritte der Neurologie-Psychiatrie 82 (1), 9-29 (Jan 2014)

The origin of ADHD is multifactorial and both the aetiology and pathophysiology of ADHD are as yet incompletely understood. The monoamine deficit hypothesis of ADHD postulates a dysbalance in the interaction of the neurotransmitters dopamine, noradrenaline and serotonin. Pathophysiological mechanisms involved in ADHD include alterations in fronto-striatal circuits. The currently proposed animal models of ADHD are heterogeneous with regard to their pathophysiological alterations and their ability to mimic behavioural symptoms and to predict response to medication. Some evidence points to a genetic basis for ADHD which is likely to involve many genes of small individual effects. In summary, specific neurobiological substrates of ADHD are unknown and multiple genetic and environmental factors appear to act together to create a spectrum of neurobiological liability.