

## **Chapter 8 Citations**

### **1. Age at first measles-mumps-rubella vaccination in children with autism and school-matched control subjects: a population-based study in metropolitan atlanta.**

#### **Abstract**

##### ***“OBJECTIVE:***

To compare ages at first measles-mumps-rubella (MMR) vaccination between children with autism and children who did not have autism in the total population and in selected subgroups, including children with regression in development.

##### ***METHODS:***

A case-control study was conducted in metropolitan Atlanta. Case children (N = 624) were identified from multiple sources and matched to control children (N = 1824) on age, gender, and school. Vaccination data were abstracted from immunization forms required for school entry. Records of children who were born in Georgia were linked to Georgia birth certificates for information on maternal and birth factors. Conditional logistic regression was used to estimate odds ratios (ORs).

##### ***RESULTS:***

The overall distribution of ages at MMR vaccination among children with autism was similar to that of matched control children; most case (70.5%) and control children (67.5%) were vaccinated between 12 and 17 months of age. Similar proportions of case and control children had been vaccinated before 18 or before 24 months. No significant associations for either of these age cutoffs were found for specific case subgroups, including those with evidence of developmental regression. More case (93.4%) than control children (90.6%) were vaccinated before 36 months (OR: 1.49; 95% confidence interval: 1.04-2.14 in the total sample; OR: 1.23; 95% confidence interval: 0.64-2.36 in the birth certificate sample). This association was strongest in the 3- to 5-year age group.

## **CONCLUSIONS:**

Similar proportions of case and control children were vaccinated by the recommended age or shortly after (ie, before 18 months) and before the age by which atypical development is usually recognized in children with autism (ie, 24 months). Vaccination before 36 months was more common among case children than control children, especially among children 3 to 5 years of age, likely reflecting immunization requirements for enrollment in early intervention programs.”

### **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/14754936>

### **References**

Destefano, F., T. K. Bhasin, W. W. Thompson, M. Yeargin-Allsopp, and C. Boyle. "Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta." *Pediatrics* 113.2 (2004): 259-66.

## **2. Assessing the association of early life antibiotic prescription with asthma exacerbations, impaired antiviral immunity, and genetic variants in 17q21: a population-based birth cohort study**

### **Abstract**

#### **“Background**

The relationship between early-life antibiotic use and the development of wheeze and asthma has been reported in several studies but might arise as a consequence of bias rather than causal relationship. We investigated the association between antibiotic prescription and subsequent development of atopy, wheeze, and asthma exacerbations, and the relation of early life antibiotic prescription with anti-infective immunity and genetic variants on asthma susceptibility locus 17q21.

#### **Methods**

Children in a population-based birth cohort were followed from birth to age 11 years. Information on antibiotic prescription, wheeze, and asthma exacerbations was extracted from medical records, and the effect of antibiotic prescription assessed with longitudinal analyses. We assessed immune responses of peripheral blood mononuclear cells, taken at age 11 years, to viruses (rhinovirus and respiratory syncytial virus; RSV) and bacteria (*Haemophilus influenzae* and *Streptococcus pneumoniae*) in children who either received at least one or no antibiotic prescriptions in infancy. Finally, we assessed the association of 17q21 polymorphisms with antibiotic prescription.

## **Findings**

Of 984 families who gave consent, we extracted data for 916 children. We noted significantly higher risk of physician-confirmed wheezing after antibiotic prescription (hazard ratio [HR] 1.71, 95% CI 1.32–2.23;  $p < 0.0001$ ) and severe wheeze or asthma exacerbation after antibiotic prescription (HR 2.26, 95% CI 1.03–4.94;  $p = 0.041$ ). In children who wheezed, the hazards of exacerbations (2.09, 1.51–2.90;  $p < 0.0001$ ) and admissions to hospital (2.64, 1.49–4.70;  $p = 0.0009$ ) were significantly increased in the 2 years after the first antibiotic prescription. Children who received antibiotics in infancy had significantly lower induction of cytokines, which are important in host defence against virus infections to both RSV and rhinovirus; there were no differences in antibacterial responses. Variants in 17q21 were associated with an increased risk of early life antibiotic prescription.

## **Interpretation**

The association between antibiotics and asthma might arise through a complex confounding by indication. Hidden factors that may increase the likelihood of both early life antibiotic prescription and later asthma are an increased susceptibility to viral infections consequent upon impaired antiviral immunity and genetic variants on 17q21.”

## **Links**

[http://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(14\)70096-7/abstract](http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(14)70096-7/abstract)

## **References**

Semic-Jusufagic, Aida, Danielle Belgrave, Andrew Pickles, Aurica G. Telcian, Eteri Bakhsoliani, Annemarie Sykes, Angela Simpson, Sebastian L. Johnston, and Adnan Custovic. "Assessing the Association of Early Life Antibiotic Prescription with Asthma Exacerbations, Impaired Antiviral Immunity, and Genetic Variants in 17q21: A Population-based Birth Cohort Study." *The Lancet Respiratory Medicine* 2.8 (2014): 621-30

## **3. Complementary and alternative medicine for prevention and treatment of the common cold.**

### **Abstract**

“To review the evidence supporting complementary and alternative medicine approaches to treatment and prevention of the common cold in adults.

### ***QUALITY OF EVIDENCE:***

MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched from January 1966 to September 2009 combining the key words common cold or influenza with echinacea, garlic, ginseng, probiotics, vitamin C, and zinc. Clinical trials and prospective studies were included.

### ***MAIN MESSAGE:***

For prevention, vitamin C demonstrated benefit in a large meta-analysis, with possibly increased benefit in patients subjected to cold stress. There is inconsistent evidence for Asian ginseng (*Panax ginseng*) and North American ginseng (*Panax quinquefolius*). Allicin was highly effective in 1 small trial. For treatment, *Echinacea purpurea* is the most consistently useful variety; it was effective in 5 of 6 trials. Zinc lozenges were effective in 5 of 9 trials, likely owing to dose and formulation issues. Overall, the evidence suggests no benefit from probiotics for prevention or treatment of the common cold.

### ***CONCLUSION:***

Vitamin C can be recommended to Canadian patients for prevention of the common cold. There is moderate evidence supporting the use of *Echinacea purpurea* and zinc lozenges for treatment. Ginseng and allicin warrant further research.”

### **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/21322286>

### **References**

Mousa, H. A.-L. "Prevention and Treatment of Influenza, Influenza-Like Illness, and Common Cold by Herbal, Complementary, and Natural Therapies." *Journal of Evidence-Based Complementary & Alternative Medicine* (2016)

#### **4. Pneumococcal vaccination reduced the risk of acute otitis media: Cohort study**

##### **Abstract**

“Seven-valent pneumococcal conjugate vaccine (PCV7) was introduced to Japan in 2009, and after that invasive pneumococcal disease has gradually decreased. There are few data, however, on the effectiveness of PCV7 against acute otitis media (AOM) in Japan.

##### ***METHODS:***

From 10 daycare centers in Sapporo, Japan, 614 parents participated in the survey. Each parent reported whether their child subject had received one or more doses of PCV7, and, if so, the exact dates of receiving PCV7 were verified by reviewing their maternal and child health handbooks marked by a pediatrician. AOM was diagnosed by otorhinolaryngologist or pediatrician. Cox's proportional hazard model was used for calculating the hazard ratio (HR) of AOM incidence reduced by PCV7 inoculation.

##### ***RESULTS:***

Inoculation of PCV7 significantly reduced the risk of AOM (crude HR, 0.63; 95% CI: 0.50-0.79). Adjusting for potentially confounding variables reduced the risk further (adjusted HR, 0.32; 95% CI: 0.23-0.44). On stratification by subject age on 30 April 2012, PCV7 was significantly associated with a reduced risk of AOM in both infants < 3 years old, and in children  $\geq$  3 years.

##### ***CONCLUSION:***

PCV7 is effectiveness in reducing the risk of AOM both in infants < 3 years old, and in young children  $\geq$  3 years in Japan.”

##### **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/25615843>

##### **References**

Hasegawa, Junko, Mitsuru Mori, Satoko Showa, Aiko Matsushima, Hirofumi Ohnishi, Takeshi Tsugawa, Yuko Yoto, and Hiroyuki Tsutsumi. "Pneumococcal Vaccination Reduced the Risk of Acute Otitis Media: Cohort Study." *Pediatrics International Pediatr Int* 57.4 (2015): 582-85.

#### **5. Structural maturation of neural pathways in children and adolescents: in vivo study.**

##### **Abstract**

“Structural maturation of fiber tracts in the human brain, including an increase in the diameter and myelination of axons, may play a role in cognitive development during childhood and adolescence. A computational analysis of structural magnetic resonance images obtained in 111

children and adolescents revealed age-related increases in white matter density in fiber tracts constituting putative corticospinal and frontotemporal pathways. The maturation of the corticospinal tract was bilateral, whereas that of the frontotemporal pathway was found predominantly in the left (speech-dominant) hemisphere. These findings provide evidence for a gradual maturation, during late childhood and adolescence, of fiber pathways presumably supporting motor and speech functions.”

### **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/10082463>

### **References**

Paus, T. S. A. A. "Structural Maturation of Neural Pathways in Children and Adolescents: In Vivo Study." *Science* 283.5409 (1999): 1908-911.

## **6. The Risk of Melanoma in Airline Pilots and Cabin Crew: A Metaanalysis**

### **Abstract**

“Airline pilots and cabin crew are occupationally exposed to higher levels of cosmic and UV radiation than the general population, but their risk of developing melanoma is not yet established.

#### ***OBJECTIVE:***

To assess the risk of melanoma in pilots and airline crew.

#### ***DATA SOURCES:***

PubMed (1966 to October 30, 2013), Web of Science (1898 to January 27, 2014), and Scopus (1823 to January 27, 2014).

#### ***STUDY SELECTION:***

All studies were included that reported a standardized incidence ratio (SIR), standardized mortality ratio (SMR), or data on expected and observed cases of melanoma or death caused by melanoma that could be used to calculate an SIR or SMR in any flight-based occupation.

#### ***DATA EXTRACTION AND SYNTHESIS:***

Primary random-effect meta-analyses were used to summarize SIR and SMR for melanoma in any flight-based occupation. Heterogeneity was assessed using the  $\chi^2$  test and I<sup>2</sup> statistic. To assess the potential bias of small studies, we used funnel plots, the Begg rank correlation test, and the Egger weighted linear regression test.

#### ***MAIN OUTCOMES AND MEASURES:***

Summary SIR and SMR of melanoma in pilots and cabin crew.

## ***RESULTS:***

Of the 3527 citations retrieved, 19 studies were included, with more than 266 431 participants. The overall summary SIR of participants in any flight-based occupation was 2.21 (95% CI, 1.76-2.77;  $P < .001$ ; 14 records). The summary SIR for pilots was 2.22 (95% CI, 1.67-2.93;  $P = .001$ ; 12 records). The summary SIR for cabin crew was 2.09 (95% CI, 1.67-2.62;  $P = .45$ ; 2 records). The overall summary SMR of participants in any flight-based occupation was 1.42 (95% CI, 0.89-2.26;  $P = .002$ ; 6 records). The summary SMR for pilots was 1.83 (95% CI, 1.27-2.63,  $P = .33$ ; 4 records). The summary SMR for cabin crew was 0.90 (95% CI, 0.80-1.01;  $P = .97$ ; 2 records).

## ***CONCLUSIONS AND RELEVANCE:***

Pilots and cabin crew have approximately twice the incidence of melanoma compared with the general population. Further research on mechanisms and optimal occupational protection is needed.”

## **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/25188246>

## **References**

Sanlorenzo, Martina, Mackenzie R. Wehner, Eleni Linos, John Kornak, Wolfgang Kainz, Christian Posch, Igor Vujic, Katia Johnston, Deborah Gho, Gabriela Monico, James T. Mcgrath, Simona Osella-Abate, Pietro Quaglino, James E. Cleaver, and Susana Ortiz-Urda. "The Risk of Melanoma in Airline Pilots and Cabin Crew." *JAMA Dermatol JAMA Dermatology* 151.1 (2015): 51.

## **7. Zinc gluconate and the common cold: a controlled clinical study.**

### **Abstract**

“A report in 1984 on the success of zinc gluconate against common cold symptoms could not be confirmed in three subsequent studies, which are now known to have used formulations that inactivated zinc. A non-chelating formulation including glycine, which releases 93% of contained zinc into saliva, was tested in a randomized, placebo-controlled, double-blind trial in 73 young adults. Efficacy was recorded in symptom diaries using a symptom severity rating. Patients' symptoms first appeared 1.34 days prior to entry to the study in both groups. Disappearance of symptoms occurred after an additional 4.9 days for zinc-treated patients versus 6.1 days for placebo-treated patients. A difference was noted in the efficacy of treatment if it was started 1 day after symptom onset: cold duration was an additional 4.3 days in zinc-treated patients compared with 9.2 days for placebo-treated patients. Cough, nasal drainage and congestion were the symptoms most affected, and only mild side-effects were noted.”

### **Links**

<http://www.ncbi.nlm.nih.gov/pubmed/1397668>

**References**

Godfrey JC<sup>1</sup>, Conant Sloane B, Smith DS, Turco JH, Mercer N, Godfrey NJ." Zinc gluconate and the common cold: a controlled clinical study." J Int Med Res. 1992 Jun;20(3):234-46.