VACCINES – CONTROLLED COMPARISON STUDIES – Vaccinated v Unvaccinated

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Pilot comparative study on the health of vaccinated and unvaccinated 6- to 12-year-old U.S. children

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Abstract

Vaccinations have prevented millions of infectious illnesses, hospitalizations and deaths among U.S. children, yet the long-term health outcomes of the vaccination schedule remain uncertain. Studies have been recommended by the U.S. Institute of Medicine to address this question. This study aimed 1) to compare vaccinated and unvaccinated children on a broad range of health outcomes, and 2) to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors. A cross-sectional study of mothers of children educated at home was carried out in collaboration with homeschool organizations in four U.S. states: Florida, Louisiana, Mississippi and Oregon. Mothers were asked to complete an anonymous online questionnaire on their 6- to 12-year-old biological children with respect to pregnancy-related factors, birth history, vaccinations, physician-diagnosed illnesses, medications used, and health services. NDD, a derived diagnostic measure, was defined as having one or more of the following three closely-related diagnoses: a learning disability, Attention Deficient Hyperactivity Disorder, and Autism Spectrum Disorder. A convenience sample of 666 children was obtained, of which 261 (39%) were unvaccinated. The vaccinated were less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but more likely to have been diagnosed with pneumonia, otitis media, allergies and NDD. After adjustment, vaccination, male gender, and preterm birth remained significantly associated with NDD. However, in a final adjusted model with interaction, vaccination but not preterm birth remained associated with NDD, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% CI: 2.8, 15.5). In conclusion, vaccinated homeschool children were found to have a higher rate of allergies and NDD than unvaccinated homeschool children. While vaccination remained significantly associated with NDD after controlling for other factors, preterm birth coupled with vaccination was associated with an apparent synergistic increase in the odds of NDD. Further research involving larger, independent samples and stronger research designs is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health.

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Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports.

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ABSTRACT

Background: Vaccinations have prevented millions of infectious illnesses, hospitalizations and deaths among US children. Yet the long-term health outcomes of the routine vaccination program remain unknown. Studies have been recommended by the Institute of Medicine to address this question. **Specific Aims**: To compare vaccinated and unvaccinated children on a broad range of health outcomes, and to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remains significant after adjustment for other measured factors. **Design**: A cross-sectional survey of mothers of children educated at home. **Methods**: Homeschool organizations in four states (Florida, Louisiana, Mississippi, and Oregon) were asked to forward an email to their members, requesting mothers to complete an anonymous online questionnaire on the vaccination status and health outcomes of their biological children ages 6 to 12. **Results**: A total of 415 mothers provided data on 666 children, of which 261 (39%) were unvaccinated. Vaccinated children were significantly less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but significantly more likely to have been diagnosed with pneumonia, otitis media, allergies and NDDs (defined as Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and/or a learning disability). After adjustment, the factors that remained significantly associated with NDD were vaccination (OR

3.1, 95% CI: 1.4, 6.8), male gender (OR 2.3, 95% CI: 1.2, 4.3), and preterm birth (OR 5.0, 95% CI: 2.3, 11.6). In a final adjusted model, vaccination but not preterm birth remained associated with NDD, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% CI: 2.8, 15.5). **Conclusions**: In this study based on mothers' reports, the vaccinated had a higher rate of allergies and NDD than the unvaccinated. Vaccination, but not preterm birth, remained significantly associated with NDD after controlling for other factors. However, preterm birth combined with vaccination was associated with an apparent synergistic increase in the odds of NDD. Further research involving larger, independent samples is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health.

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Lack of effectiveness of the 23-valent polysaccharide pneumococcal vaccine in reducing all-cause pneumonias among healthy young military recruits: a randomized, double-blind, placebo-controlled trial.

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Abstract

BACKGROUND: Streptococcus pneumoniae infections have periodically caused significant morbidity and outbreaks among military personnel, especially trainees. This study evaluated the effectiveness of the 23-valent polysaccharide pneumococcal vaccine (PPV23) in reducing pneumonia in healthy military trainees.
METHODS: From 2000-2003, 152723 military trainees from 5 US training camps were enrolled in a double-blind, placebo-controlled trial of PPV23. Participants were closely monitored during basic training for radiographically confirmed pneumonia etiology and loss-of-training days. Participants were also followed using electronic medical encounter data until 1 June 2007 for three additional outcomes: any-cause pneumonia, any acute respiratory disease, and meningitis.
RESULTS: Comparison of demographic data by study arm suggested the randomization procedures were sound. During basic training, 371 study participants developed radiographically confirmed pneumonia. None had evidence of S. pneumoniae infection, but other etiologies included adenovirus (38%), Chlamydophila pneumoniae (9%), and Mycoplasma pneumoniae (8%). During the follow-up period, many study participants, in both the vaccine and placebo groups, had clinical encounters for the medical outcomes of interest. However, Cox's proportional hazard modeling revealed no evidence of a protective vaccine effect during recruit training (radiographically confirmed pneumonia) or up to 6.7 years after enrollment (any-cause pneumonia, any acute respiratory disease, or meningitis).
CONCLUSIONS: Data from this large, double-blind, placebo controlled trial do not support routine use of PPV23 among healthy new military trainees.

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Haemophilus influenzae oral vaccination for preventing acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease.

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Abstract

BACKGROUND: Chronic bronchitis and chronic obstructive pulmonary disease (COPD) are serious conditions in which patients are predisposed to viral and bacterial infections resulting in potentially fatal acute exacerbations. COPD is defined as a lung disease characterised by obstruction to lung airflow that interferes with normal breathing. Antibiotic therapy has not been particularly useful in eradicating bacteria such as non-typeable Haemophilus influenzae (NTHi) because they are naturally occurring flora of the upper respiratory tract in many people. However, they can cause opportunistic infection. An oral NTHi vaccine has been developed to protect against recurrent infective acute exacerbations in chronic bronchitis.
OBJECTIVES: To assess the effectiveness of an oral, whole-cell, non-typeable H. influenzae (NTHi) vaccine in protecting against recurrent episodes of acute exacerbations of chronic bronchitis and COPD in adults. To assess the effectiveness of NTHi vaccine in reducing NTHi colonising the respiratory tract during recurrent episodes of acute exacerbations of COPD.
SEARCH METHODS: We searched the following databases: CENTRAL (2014, Issue 6), MEDLINE (1946 to July week 3, 2014), EMBASE (1974 to July 2014), CINAHL (1981 to July 2014), LILACS (1982 to July 2014) and Web of Science (1955 to July 2014). We also searched trials registries and contacted authors of trials requesting unpublished data.
SELECTION CRITERIA: We included randomised controlled trials comparing the effects of an oral monobacterial NTHi vaccine in adults with recurrent acute exacerbations of chronic bronchitis or COPD when there was overt matching of the vaccine and placebo groups on clinical grounds. The selection criteria considered populations aged less than 65 years and those older than 65 years.
DATA COLLECTION AND ANALYSIS: Two authors independently assessed trial quality and extracted data

from original records and publications for incidence and severity of bronchitis episodes and carriage rate of NTHi measured in the upper respiratory tract, as well as data relevant to other primary and secondary outcomes.

MAIN RESULTS: We identified six placebo-controlled randomised controlled trials with a total of 557 participants. They investigated the efficacy of enteric-coated, killed preparations of H. influenzae in populations prone to recurrent acute exacerbations of chronic bronchitis or COPD. The vaccine preparation and immunisation regime in all trials consisted of at least three courses of formalin-killed H. influenzae in enteric-coated tablets taken at intervals (for example, days 0, 28 and 56). Each course generally consisted of two tablets taken after breakfast over three consecutive days. In all cases the placebo groups took enteric-coated tablets containing glucose. Risk of bias was moderate across the studies, namely due to the lack of information provided about methods and inadequate presentation of results. Meta-analysis of the oral NTHi vaccine showed a small, non-statistically significant reduction in the incidence of acute exacerbations of chronic bronchitis or COPD by 2.048% (risk ratio (RR) 0.97, 95% confidence interval (CI) 0.84 to 1.12, P value = 0.68). There was no significant difference in mortality rate between the vaccine and placebo groups (odds ratio (OR) 1.62, 95% CI 0.63 to 4.12, P value = 0.31).We were unable to meta-analyse the carriage levels of NTHi in participants as each trial reported this result using different units and tools of measurement. Four trials showed no significant difference in carriage levels, while two trials showed a significant decrease in carriage levels in the vaccinated group compared with placebo. Four trials assessed severity of exacerbations measured by requirement for antibiotics. Three of these trials were comparable and when meta-analysed showed a statistically significant 80% increase in antibiotic courses per person in the placebo group (RR 1.81, 95% CI 1.35 to 2.44, P value < 0.0001). There was no significant difference between the groups with regards to hospital admission rates (OR 0.96, 95% CI 0.13 to 7.04, P value = 0.97). Adverse events were reported in all six trials with a point estimate suggestive that they occurred more frequently in the vaccine group, however, this result was not statistically significant (RR 1.43, 95% CI 0.70 to 2.92, P value = 0.87). Quality of life was not meta-analysed but was reported in two trials, with results at six months showing an improvement in quality of life in the vaccinated group (scoring at least two points better than placebo).

AUTHORS' CONCLUSIONS: Analyses demonstrate that NTHi oral vaccination of patients with recurrent exacerbations of chronic bronchitis or COPD does not yield a significant reduction in the number and severity of exacerbations. Evidence is mixed and the individual trials that show a significant benefit of the vaccine are too small to advocate widespread oral vaccination of people with COPD.

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High-dose vitamin A with vaccination after 6 months of age: a randomized trial.

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Abstract

BACKGROUND: The World Health Organization recommends vitamin A supplementation (VAS) at routine vaccination contacts after 6 months of age based on the assumption that it reduces mortality by 24%. The policy has never been evaluated in randomized controlled trials for its effect on overall mortality. We conducted a randomized double-blind trial to evaluate the effect of VAS with vaccines.

METHODS: We randomized children aged 6 to 23 months 1:1 to VAS (100000 IU if aged 6-11 months, 200000 IU if aged 12-23 months) or placebo at vaccination contacts in Guinea-Bissau. Mortality rates were compared in Cox proportional-hazards models overall, and by gender and vaccine.

RESULTS: Between August 2007 and November 2010, 7587 children were enrolled. Within 6 months of follow-up 80 non-accident deaths occurred (VAS: 38; placebo: 42). The mortality rate ratio (MRR) comparing VAS versus placebo recipients was 0.91 (95% confidence interval 0.59-1.41) and differed significantly between boys (MRR 1.92 [0.98-3.75]) and girls (MRR 0.45 [0.24-0.87]) (P = .003 for interaction between VAS and gender). At enrollment, 42% (3161/7587) received live measles vaccine, 29% (2154/7587) received inactivated diphtheria-tetanus-pertussis-containing vaccines, and 21% (1610/7587) received both live and inactivated vaccines. The effect of VAS did not differ by vaccine group.

CONCLUSIONS: This is the first randomized controlled trial to assess the effect of the policy on overall mortality. VAS reduced the mortality rate in girls but not in boys. VAS had no overall effect, but the effect differed significantly by gender. More trials to ensure an optimal evidence-based vitamin A policy are warranted.

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Zinc supplementation for preventing mortality, morbidity, and growth failure in

children aged 6 months to 12 years of age.

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Abstract

BACKGROUND: Zinc deficiency is prevalent in low- and middle-income countries, and contributes to significant diarrhoea-, pneumonia-, and malaria-related morbidity and mortality among young children. Zinc deficiency also impairs growth.

OBJECTIVES: To assess the effects of zinc supplementation for preventing mortality and morbidity, and for promoting growth, in children aged six months to 12 years of age.

SEARCH METHODS: Between December 2012 and January 2013, we searched CENTRAL, MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase, African Index Medicus, Conference Proceedings Citation Index, Dissertation Abstracts, Global Health, IndMED, LILACS, WHOLIS, metaRegister of Controlled Trials, and WHO ICTRP.

SELECTION CRITERIA: Randomised controlled trials of preventive zinc supplementation in children aged six months to 12 years compared with no intervention, a placebo, or a waiting list control. We excluded hospitalised children and children with chronic diseases or conditions. We excluded food fortification or intake, sprinkles, and therapeutic interventions.

DATA COLLECTION AND ANALYSIS: Two authors screened studies, extracted data, and assessed risk of bias. We contacted trial authors for missing information.

MAIN RESULTS: We included 80 randomised controlled trials with 205,401 eligible participants. We did not consider that the evidence for the key analyses of morbidity and mortality outcomes were affected by risk of bias. The risk ratio (RR) for all-cause mortality was compatible with a reduction and a small increased risk of death with zinc supplementation (RR 0.95, 95% confidence interval (CI) 0.86 to 1.05, 14 studies, high-quality evidence), and also for cause-specific mortality due to diarrhoea (RR 0.95, 95% CI 0.69 to 1.31, four studies, moderate-quality evidence), lower respiratory tract infection (LRTI) (RR 0.86, 95% CI 0.64 to 1.15, three studies, moderate-quality evidence), or malaria (RR 0.90, 95% CI 0.77 to 1.06, two studies, moderate-quality evidence). Supplementation reduced diarrhoea morbidity, including the incidence of all-cause diarrhoea (RR 0.87, 95% CI 0.85 to 0.89, 26 studies, moderate-quality evidence), but the results for LRTI and malaria were imprecise: LRTI (RR 1, 95% CI 0.94 to 1.07, 12 studies, moderate-quality evidence); malaria (RR 1.05, 95% 0.95 to 1.15, four studies, moderate-quality evidence).There was moderate-quality evidence of a very small improvement in height with supplementation (standardised mean difference (SMD) -0.09, 95% CI -0.13 to -0.06; 50 studies), but the size of this effect might not be clinically important. There was a medium to large positive effect on zinc status. Supplementation was associated with an increase in the number of participants with at least one vomiting episode (RR 1.29, 95% CI 1.14 to 1.46, five studies, high-quality evidence). We found no clear evidence of benefit or harm of supplementation with regard to haemoglobin or iron status. Supplementation had a negative effect on copper status.

AUTHORS' CONCLUSIONS: In our opinion, the benefits of preventive zinc supplementation outweigh the harms in areas where the risk of zinc deficiency is relatively high. Further research should determine optimal intervention characteristics such as supplement dose.

Dan Med J. 2012 Jan;59(1):B4378. PMID: 22239846

Combining vitamin A and vaccines: convenience or conflict?

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Abstract The present thesis is based on 11 papers from 1995-2010. The studies have mainly taken place at the Bandim Health Project in Guinea-Bissau, West Africa, but a reanalysis of a randomised trial from Ghana is also included. My research has explored the consequences of combining high-dose vitamin A supplementation and childhood vaccines. Vitamin A deficiency is associated with increased mortality. To protect against the consequences of vitamin A deficiency the World Health Organization recommends that high-dose vitamin A supplements be given together with routine vaccines to children between 6 months and 5 years of age in more than 100 low-income countries. The recommendation is based on logistical considerations. The consequences of combining vitamin A and vaccines were not investigated in randomised trials prior to the implementation of this policy - it was assumed that the interventions were independent. My first project aimed to study the effect on the immune response to measles of providing vitamin A together with measles vaccine. We found that the two interventions were not independent. Vitamin A enhanced the antibody response to measles vaccine given at 9 months of age significantly, especially in boys. The effects were sustained over time; the children who had received vitamin A with their measles vaccine were more protected against measles at 6-8 years of age. Though vitamin A supplementation had a beneficial effect on the immune response to measles vaccine, it intrigued me that the effect of vitamin A supplementation on overall mortality was not always beneficial. While vitamin A was beneficial when given after 6 months of age, and two studies had shown a beneficial effect when given at birth, all studies testing the effect between 1-5 months of age had found no effect. These time windows are dominated by three different childhood vaccines: BCG vaccine given at birth, diphtheria-tetanus-pertussis (DTP) vaccine given between 1-5 months of age, and measles vaccine given at 9 months of age. These vaccines have been shown to have strong effects on mortality from infectious diseases in general, so-called

non-specific effects. The live BCG and measles vaccine protects against more mortality than can be ascribed to the prevention of tuberculosis and measles, respectively. The inactivated DTP vaccine worryingly has been associated with increased mortality from other infectious diseases. Both positive and negative effects are strongest for girls. I proposed the hypothesis that vitamin A amplifies not only the specific vaccine effects, as we saw for measles vaccine, but also the non-specific effects of vaccines on mortality from other infectious diseases. According to my hypothesis, vitamin A would enhance the non-specific beneficial effects on mortality of BCG and measles vaccine, but also the negative effects of DTP vaccine. Hence, the hypothesis offered an explanation for the mortality-age pattern after vitamin A supplementation. Since it was formulated, I have aimed to test this hypothesis. Since it is associated with ethical problems to randomise children above 6 months of age to vitamin A supplementation, and to randomise children in general to recommended vaccines, we have had to be pragmatic when designing the trials. Hence, our studies have taken many different forms. We conducted an observational study during a vitamin A campaign in which missing vaccines were also provided, and a randomised trial testing the effect of two different doses of vitamin A during another campaign; we tested the effect of providing vitamin A with BCG at birth in two randomised trials, and we reanalysed data from one of the original randomised trials of vitamin A supplementation from the perspective of vaccination status. In all studies the main outcome was mortality. The results document that vitamin A supplements do more than protect against vitamin A deficiency. They support the hypothesis that vitamin A supplements interact with vaccines with important consequences for mortality. First, a smaller dose of vitamin A was more beneficial than a larger dose for girls. Second, the effect of vitamin A given with DTP vaccine was significantly different from the effect of vitamin A given with measles vaccine, and children, who received vitamin A with DTP vaccine, had higher mortality than children, who had received vitamin A alone, or who did not receive anything. Third, vitamin A given with BCG at birth interacted negatively with subsequent DTP vaccines in girls. Fourth, the effect of vitamin A to older children in Ghana depended on vaccination status, being beneficial in boys, but harmful in girls who received DTP vaccine during follow-up. The results also show that boys and girls respond differently to vitamin A and vaccines.

BMC Public Health. 2011 Apr 13;11 Suppl 3:S20. PMID: 21501438 **Free PMC Article**

Impact of vitamin A supplementation on infant and childhood mortality.

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Abstract

INTRODUCTION: Vitamin A is important for the integrity and regeneration of respiratory and gastrointestinal epithelia and is involved in regulating human immune function. It has been shown previously that vitamin A has a preventive effect on all-cause and disease specific mortality in children under five. The purpose of this paper was to get a point estimate of efficacy of vitamin A supplementation in reducing cause specific mortality by using Child Health Epidemiology Reference Group (CHERG) guidelines.

METHODS: A literature search was done on PubMed, Cochrane Library and WHO regional data bases using various free and Mesh terms for vitamin A and mortality. Data were abstracted into standardized forms and quality of studies was assessed according to standardized guidelines. Pooled estimates were generated for preventive effect of vitamin A supplementation on all-cause and disease specific mortality of diarrhea, measles, pneumonia, meningitis and sepsis. We did a subgroup analysis for vitamin A supplementation in neonates, infants 1-6 months and children aged 6-59 months. In this paper we have focused on estimation of efficacy of vitamin A supplementation in children 6-59 months of age. Results for neonatal vitamin A supplementation have been presented, however no recommendations are made as more evidence on it would be available soon.

RESULTS: There were 21 studies evaluating preventive effect of vitamin A supplementation in community settings which reported all-cause mortality. Twelve of these also reported cause specific mortality for diarrhea and pneumonia and six reported measles specific mortality. Combined results from six studies showed that neonatal vitamin A supplementation reduced all-cause mortality by 12 % [Relative risk (RR) 0.88; 95 % confidence interval (CI) 0.79-0.98]. There was no effect of vitamin A supplementation in reducing all-cause mortality in infants 1-6 months of age [RR 1.05; 95 % CI 0.88-1.26]. Pooled results for preventive vitamin A supplementation showed that it reduced all-cause mortality by 25% [RR 0.75; 95 % CI 0.64-0.88] in children 6-59 months of age. Vitamin A supplementation also reduced diarrhea specific mortality by 30% [RR 0.70; 95 % CI 0.58-0.86] in children 6-59 months. This effect has been recommended for inclusion in the Lives Saved Tool. Vitamin A supplementation had no effect on measles [RR 0.71, 95% CI: 0.43-1.16], meningitis [RR 0.73, 95% CI: 0.22-2.48] and pneumonia [RR 0.94, 95% CI: 0.67-1.30] specific mortality.

CONCLUSION: Preventive vitamin A supplementation reduces all-cause and diarrhea specific mortality in children 6-59 months of age in community settings in developing countries.

BMC Public Health. 2011 Apr 13;11 Suppl 3:S23. PMID: 21501441 **Free PMC Article**

Preventive zinc supplementation in developing countries: impact on mortality and morbidity due to diarrhea, pneumonia and malaria.

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Abstract

BACKGROUND: Zinc deficiency is commonly prevalent in children in developing countries and plays a role in decreased immunity and increased risk of infection. Preventive zinc supplementation in healthy children can reduce mortality due to common causes like diarrhea, pneumonia and malaria. The main objective was to determine all-cause mortality and cause-specific mortality and morbidity in children under five in developing countries for preventive zinc supplementation. **DATA SOURCES/ REVIEW METHODS**: A literature search was carried out on PubMed, the Cochrane Library and the WHO regional databases to identify RCTs on zinc supplementation for greater than 3 months in children less than 5 years of age in developing countries and its effect on mortality was analyzed.
RESULTS: The effect of preventive zinc supplementation on mortality was given in eight trials, while cause specific mortality data was given in five of these eight trials. Zinc supplementation alone was associated with a statistically insignificant 9% (RR = 0.91; 95% CI: 0.82, 1.01) reduction in all cause mortality in the intervention group as compared to controls using a random effect model. The impact on diarrhea-specific mortality of zinc alone was a non-significant 18% reduction (RR = 0.82; 95% CI: 0.64, 1.05) and 15% for pneumonia-specific mortality (RR = 0.85; 95% CI: 0.65, 1.11). The incidence of diarrhea showed a 13% reduction with preventive zinc supplementation (RR = 0.87; 95% CI: 0.81, 0.94) and a 19% reduction in pneumonia morbidity (RR = 0.81; 95% CI: 0.73, 0.90). Keeping in mind the direction of effect of zinc supplementation in reducing diarrhea and pneumonia related morbidity and mortality; we considered all the outcomes for selection of effectiveness estimate for inclusion in the LiST model. After application of the CHERG rules with consideration to quality of evidence and rule # 6, we used the most conservative estimates as a surrogate for mortality. We, therefore, conclude that zinc supplementation in children is associated with a reduction in diarrhea mortality of 13% and pneumonia mortality of 15% for inclusion in the LiST tool. Preventive zinc supplementation had no effect on malaria specific mortality (RR = 0.90; 95% CI: 0.77, 1.06) or incidence of malaria (RR = 0.92; 95 % CI 0.82-1.04).
CONCLUSION: Zinc supplementation results in reductions in diarrhea and pneumonia mortality.

Am J Clin Nutr. 2009 Sep;90(3):629-39. PMID: 19640958 **Free full text**

Does vitamin A supplementation interact with routine vaccinations? An analysis of the Ghana Vitamin A Supplementation Trial.

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Abstract
BACKGROUND: The World Health Organization recommends vitamin A supplementation (VAS) at vaccination contacts after 6 mo of age to reduce mortality. However, it is unknown whether the effect of VAS is independent of vaccinations. One of the original VAS trials from Ghana had collected vaccination information.
OBJECTIVE: We reanalyzed the data to explore the hypothesis that VAS reduces mortality in children who had bacille Calmette-Guérin or measles vaccine as their most recent vaccine but increased mortality when diphtheria-tetanus-pertussis vaccine (DTP) was the most recent vaccine. On the basis of previous studies, we expected the effects to be strongest in girls.
DESIGN: At enrollment, children aged 6-90 mo were randomly assigned to receive VAS or placebo every 4 mo for 2 y. Vaccination status was assessed at enrollment and after 1 and 2 y by reviewing the children's health cards. Lack of a health card was presumed to mean that the child had not been vaccinated.
RESULTS: VAS had a beneficial effect only in children with no record of vaccination at enrollment (n = 5066); the mortality rate ratio (MRR) was 0.64 (95% CI: 0.47, 0.88) compared with 0.95 (95% CI: 0.72, 1.26) in children with one or more vaccinations (n = 6656). Among vaccinated children, the effect of VAS differed between boys (MRR: 0.74; 95% CI: 0.51, 1.08) and girls (MRR: 1.18; 95% CI: 0.84, 1.67) (P = 0.046 for interaction). VAS had a negative effect in measles-vaccinated girls who were missing one or more doses of DTP at enrollment, a group who often received DTP during follow-up (MRR: 2.60; 95% CI: 1.41, 4.80).
CONCLUSIONS: The effect of VAS differed by vaccination status. This is potentially problematic because VAS is provided at vaccination contacts.

Pediatr Allergy Immunol. 2008 Sep;19(6):544-51. PMID: 18266826 Need Review of full-text.

Measles, mumps and rubella infections and atopic disorders in MMR-unvaccinated and MMR-vaccinated children.

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Abstract. Vaccinations have been incriminated in the increase of atopic disorders. Especially the measles-mumps-rubella (MMR) vaccination is often refused by people having a notion that these infectious diseases are beneficial for a healthy development of a child's immune system. This practice endangers herd immunity and is the cause of repeated outbreaks. As the clinical course of infections and also its possible impact on the development of atopy may be different in vaccinated and unvaccinated individuals, we explored in vaccinated and unvaccinated children associations of MMR infection with atopic disorders. Using data from a previously conducted study on the relationship between the diphtheria-tetanus-pertussis-(inactivated) poliomyelitis vaccination in the first year of life and atopic disorders, the study population of 1872 8-12-yr-old was divided as children MMR-unvaccinated and children MMR-vaccinated in the first year of life. Within each group the

association between MMR infections and atopic disorders (both as reported by the parents) was assessed. We found a statistically significant positive association between measles infection and 'any atopic disorder' [adjusted odds ratio, OR (95% confidence interval, CI): 1.77 (1.20-2.61)] in the MMR-vaccinated group, mainly because of the relationship with eczema. For rubella there was a negative association with eczema and food allergy in the unvaccinated group: adjusted OR (95% CI): 0.57 (0.38-0.85) and 0.23 (0.07-0.76), respectively. All other associations were not statistically significant. **We found a positive relationship between measles infection and any atopy in a group of MMR-vaccinated children and a negative association between rubella infection and eczema and food allergy in unvaccinated children.** However, we cannot conclude that these relationships are causal. The negative association with rubella may be an artefact. This study shows no evidence for any protective effects from MMR diseases for the development of atopy and therefore supports conclusions found elsewhere that childhood vaccinations do not cause atopy.

***NB* - no discussion here of atopic disorders in vaccinated v unvaccinated children !**

J Allergy Clin Immunol. 2008 Mar;121(3):626-31

Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma.

McDonald KL[1], Huq SI, Lix LM, Becker AB, Kozyrskyj AL.

[1]Faculty of Medicine, Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada.

Abstract

BACKGROUND: Early childhood immunizations have been viewed as promoters of asthma development by stimulating a T(H)2-type immune response or decreasing microbial pressure, which shifts the balance between T(H)1 and T(H)2 immunity.

OBJECTIVE: Differing time schedules for childhood immunizations may explain the discrepant findings of an association with asthma reported in observational studies. This research was undertaken to determine whether timing of diphtheria, pertussis, tetanus (DPT) immunization has an effect on the development of childhood asthma by age 7 years.

METHODS: This was a retrospective longitudinal study of a cohort of children born in Manitoba in 1995. The complete immunization and health care records of cohort children from birth until age 7 years were available for analysis. The adjusted odds ratio for asthma at age 7 years according to timing of DPT immunization was computed from multivariable logistic regression.

RESULTS: Among 11, 531 children who received at least 4 doses of DPT, the risk of asthma was reduced to (1/2) in children whose first dose of DPT was delayed by more than 2 months. The likelihood of asthma in children with delays in all 3 doses was 0.39 (95% CI, 0.18-0.86).

CONCLUSION: We found a negative association between delay in administration of the first dose of whole-cell DPT immunization in childhood and the development of asthma; the association was greater with delays in all of the first 3 doses. The mechanism for this phenomenon requires further research.

Dr. McDonald and colleagues of the University of Manitoba (2008) published in the J. of Allergy and Clinical Immunology on the effect of delaying DPT vaccination so that the vaccination occurred- but was given later rather than earlier in infancy. A total of 11,531 kids were studied. A delay of two months in the initial DPT shot was associated with a 50% cut in asthma diagnosis.

Pediatr Allergy Immunol. 2008 Feb;19(1):46-52. PMID: 18086216

Reported pertussis infection and risk of atopy in 8- to 12-yr-old vaccinated and non-vaccinated children.

Bernsen RM[1], Nagelkerke NJ, Thijs C, van der Wouden JC.

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Abstract. Pertussis infection has been suspected to be a potential causal factor in the development of atopic disease because of the effect of pertussis immunization on specific IgE antibodies. Although several studies found a positive association between pertussis infection and atopic disorders, this relationship has not yet been studied in a population stratified by vaccination status. To assess the association between pertussis infection and atopic disorders in pertussis-unvaccinated children and in pertussis-vaccinated children. Using data from a previously conducted study on the relationship between the diphtheria-tetanus-pertussis-(inactivated) poliomyelitis vaccination in the first year of life and atopic disorders, the study population of 1872 8-12 yr old was divided into children pertussis-unvaccinated and children pertussis-vaccinated in the first year of life. Within each group, the association between pertussis infection and atopic disorders (both as reported by the parents) was assessed. In the unvaccinated group, there were no significant associations between pertussis infection and atopic disorders. In the vaccinated group, all associations between pertussis infection and atopic disorders were positive, the associations with asthma [odds ratio (OR) = 2.24, 95% confidence interval (CI(95%)): 1.36-3.70], hay fever (OR = 2.35, CI(95%): 1.46-3.77) and food allergy (OR = 2.68, CI(95%): 1.48-4.85) being significant. **There was a positive association between pertussis infection and atopic disorders in the pertussis vaccinated group only**. From the present study, it cannot be concluded whether this association is causal or due to reverse causation.

Petrik and colleagues documented that vaccine ingredients (adjuvants) injected in mice at levels equivalent to those given to humans caused motor deficits, cognitive deficits, and neural loss. This was a controlled experiment documenting harm from vaccine ingredients. It is important to further the finding because sometimes vaccine safety studies that report no effects use "control groups" for comparison who get injected with adjuvants, rather than injected with placebo. Neuromolecular Medicine. 2007; 9(1):83 – 100.

J Allergy Clin Immunol. 2006 Jan;117(1):59-66. PMID: 16387585

Allergic disease and sensitization in Steiner school children.

Flöistrup H[1], Swartz J, Bergström A, Alm JS, Scheynius A, van Hage M, Waser M, Braun-Fahrländer C, Schram-Bijkerk D, Huber M, Zutavern A, von Mutius E, Ublagger E, Riedler J, Michaels KB, Pershagen G; Parsifal Study Group.

[1]*Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. Helen.Floistrup@ki.se*

Abstract

BACKGROUND: The anthroposophic lifestyle has several features of interest in relation to allergy: for example, a restrictive use of antibiotics and certain vaccinations. In a previous Swedish study, Steiner school children (who often have an anthroposophic lifestyle and are unvaccinated) showed a reduced risk of atopy, but specific protective factors could not be identified.
OBJECTIVE: To investigate factors that may contribute to the lower risk of allergy among Steiner school children.
METHODS: Cross-sectional multicenter study including 6630 children age 5 to 13 years (4606 from Steiner schools and 2024 from reference schools) in 5 European countries.
RESULTS: The prevalence of several studied outcomes was lower in Steiner school children than in the reference group. Overall, there were statistically significant reduced risks for rhinoconjunctivitis, atopic eczema, and atopic sensitization (allergen-specific IgE > or =0.35 kU/L), with some heterogeneity between the countries. Focusing on doctor-diagnosed disease, use of antibiotics during first year of life was associated with increased risks of rhinoconjunctivitis (odds ratio [OR], 1.97; 95% CI, 1.26-3.08), asthma (OR, 2.79; 95% CI, 2.03-3.83), and atopic eczema (OR, 1.63; 95% CI, 1.22-2.17). Early use of antipyretics was related to an increased risk of asthma (OR, 1.54; 95% CI, 1.11-2.13) and atopic eczema (OR, 1.32; 95% CI, 1.02-1.71). Children having received measles, mumps, and rubella vaccination showed an increased risk of rhinoconjunctivitis, whereas measles infection was associated with a lower risk of IgE-mediated eczema.
CONCLUSION: Certain features of the anthroposophic lifestyle, such as restrictive use of antibiotics and antipyretics, are associated with a reduced risk of allergic disease in children.

Am J Public Health. 2004 Jun;94(6):985-9. PMID: 15249303 **Free PMC Article**

Vaccination and allergic disease: a birth cohort study.

McKeever TM[1], Lewis SA, Smith C, Hubbard R.

[1]*Clinical Science Building, City Hospital, Nottingham NG5 1PB, England, UK. tricia.mckeever@nottingham.ac.uk*

Abstract

OBJECTIVES: We examined the effect of vaccination for diphtheria; polio; pertussis and tetanus; or measles, mumps, and rubella on the incidence of physician-diagnosed asthma and eczema.
METHODS: We used a previously established birth cohort in the West Midlands General Practice research database.
RESULTS: We found an association between vaccination and the development of allergic disease; however, this association was present only among children with the fewest physician visits and can be explained by this factor.
CONCLUSIONS: Our data suggest that currently recommended routine vaccinations are not a risk factor for asthma or eczema.

Am J Public Health. 2004 Jun;94(6):985-9. PMID: 15249303 **Free PMC Article**

Vaccination and allergic disease: a birth cohort study. ***REVISION - JP.***

McKeever TM[1], Lewis SA, Smith C, Hubbard R.

[1]*Clinical Science Building, City Hospital, Nottingham NG5 1PB, England, UK. tricia.mckeever@nottingham.ac.uk*

Abstract

OBJECTIVES: We examined the effect of vaccination for diphtheria; polio; pertussis and tetanus; or measles, mumps, and rubella on the incidence of physician-diagnosed asthma and eczema.
METHODS: *We used a previously established birth cohort in the West Midlands General Practice research database, allowing examination of vaccination records of 29238 children.*
RESULTS: *We found an association between vaccination and the development of allergic disease – asthma and eczema. The risk of allergic asthma was 5.04% in vaccinated children v 0.36% in unvaccinated children. It was noted that unvaccinated children made fewer visits to doctors.*
CONCLUSIONS: *Vaccination status was associated with an increased incidence of asthma and eczema-JP*

AUTHOR CONCLUSIONS: Our data suggest that currently recommended routine vaccinations are not a risk factor for asthma or eczema, *BECAUSE WE POSTULATE THAT FEWER DOCTOR VISITS WAS THE REAL CAUSE OF THE INCREASED ALLERGY INCIDENCE !!!*

Int J Epidemiol. 2004 Apr;33(2):374-80.

The introduction of diphtheria-tetanus-pertussis vaccine and child mortality in rural Guinea-Bissau: an observational study.

Aaby P[1], Jensen H, Gomes J, Fernandes M, Lisse IM.

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Abstract

BACKGROUND and objective: Previous studies from areas with high mortality in West Africa have not found diphtheria-tetanus-pertussis (DTP) vaccine to be associated with the expected reduction in mortality, a few studies suggesting increased mortality. We therefore examined mortality when DTP was first introduced in rural areas of Guinea-Bissau in 1984-1987. Setting Twenty villages in four regions have been followed with bi-annual examinations since 1979.

SUBJECTS: In all, 1657 children aged 2-8 months. Design Children were weighed when attending the bi-annual examinations and they were vaccinated whenever vaccines were available. DTP was introduced in the beginning of 1984, oral polio vaccine later that year. We examined mortality for children aged 2-8 months who had received DTP and compared them with children who had not been vaccinated because they were absent, vaccines were not available, or they were sick.

MAIN OUTCOME MEASURE: Mortality over the next 6 months from the day of examination for vaccinated and unvaccinated children.

RESULTS: Prior to the introduction of vaccines, children who were absent at a village examination had the same mortality as children who were present. During 1984-1987, children receiving DTP at 2-8 months of age had higher mortality over the next 6 months, the mortality rate ratio (MR) being 1.92 (95% CI: 1.04, 3.52) compared with DTP-unvaccinated children, adjusting for age, sex, season, period, BCG, and region. The MR was 1.81 (95% CI: 0.95, 3.45) for the first dose of DTP and 4.36 (95% CI: 1.28, 14.9) for the second and third dose. BCG was associated with slightly lower mortality (MR = 0.63, 95% CI: 0.30, 1.33), the MR for DTP and BCG being significantly inversed. Following subsequent visits and further vaccinations with DTP and measles vaccine, there was no difference in vaccination coverage and subsequent mortality between the DTP-vaccinated group and the initially DTP-unvaccinated group (MR = 1.06, 95% CI: 0.78, 1.44).

CONCLUSIONS: In low-income countries with high mortality, DTP as the last vaccine received may be associated with slightly increased mortality. Since the pattern was inversed for BCG, the effect is unlikely to be due to higher-risk children having received vaccination. The role of DTP in high mortality areas needs to be clarified.

Autoimmunity. 2002 Jul;35(4):247-53. PMID: 12482192

Clustering of cases of insulin dependent diabetes (IDDM) occurring three years after hemophilus influenza B (HiB) immunization support causal relationship between immunization and IDDM.

Classen JB[1], Classen DC.

[1]Classen Immunotherapies Inc., 6517 Montrose Avenue, Baltimore, MD 21212, USA. classen@vaccines.net

Abstract

OBJECTIVE: The hemophilus vaccine has been linked to the development of autoimmune type 1 diabetes, insulin dependent diabetes (IDDM) in ecological studies.

METHODS: We attempted to determine if the Hemophilus influenza B (HiB) vaccine was associated with an increased risk of IDDM by looking for clusters of cases of IDDM using data from a large clinical trial. All children born in Finland between October 1st, 1985 and August 31st, 1987, approximately 116,000 were randomized to receive 4 doses of the HiB vaccine (PPR-D, Connaught) starting at 3 months of life or one dose starting after 24 months of life. A control-cohort included all 128,500 children born in Finland in the 24 months prior to the HiB vaccine study. Non-obese diabetic prone (NOD) mice were immunized with a hemophilus vaccine to determine if immunization increased the risk of IDDM.

RESULTS: The difference in cumulative incidence between those receiving 4 doses and those receiving 0 doses is 54 cases of IDDM/100,000 (P = 0.026) at 7 years, (relative risk = 1.26). Most of the extra cases of IDDM appeared in statistically significant clusters that occurred in periods starting approximately 38 months after immunization and lasting approximately 6-8 months. Immunization with pediatric vaccines increased the risk of insulin diabetes in NOD mice.

CONCLUSION: Exposure to HiB immunization is associated with an increased risk of IDDM. NOD mice can be used as an animal model of vaccine induced diabetes.

Sood and colleagues, writing in the Journal of Pediatrics, gave HIB vaccines to animals and then exposed them to the HIB virus. This is what is called a controlled experiment. It is the kind that allows cause and effect statements to be made: this kind of control cannot be usually be done with humans…..Know that approximately 90% of the vaccinated group came down with HIB. And – there was a control group of

unvaccinated rats who also were exposed to the same HIB virus. but only 17% of the unvaccinated rats got HIB. Read it

BMJ. 2000 Dec 9;321(7274):1435-8. PMID: 11110734 **Free PMC Article**

Routine vaccinations and child survival: follow up study in Guinea-Bissau, West Africa.

Kristensen I[1], Aaby P, Jensen H.

[1]Bandim Health Project, Apartado 861, Bissau, Guinea-Bissau.

Abstract

OBJECTIVE: To examine the association between routine childhood vaccinations and survival among infants in Guinea-Bissau.

DESIGN: Follow up study.

PARTICIPANTS: 15 351 women and their children born during 1990 and 1996.

SETTING: Rural Guinea-Bissau.

MAIN OUTCOME MEASURES: Infant mortality over six months (between age 0-6 months and 7-13 months for BCG, diphtheria, tetanus, and pertussis, and polio vaccines and between 7-13 months and 14-20 months for measles vaccine).

RESULTS: Mortality was lower in the group vaccinated with any vaccine compared with those not vaccinated, the mortality ratio being 0.74 (95% confidence interval 0.53 to 1.03). After cluster, age, and other vaccines were adjusted for, BCG was associated with significantly lower mortality (0.55 (0.36 to 0.85)). However, **recipients of one dose of diphtheria, tetanus, and pertussis or polio vaccines had higher mortality than children who had received none of these vaccines (1.84 (1.10 to 3.10) for diphtheria, tetanus, and pertussis).** Recipients of measles vaccine had a mortality ratio of 0.48 (0.27 to 0.87). When deaths from measles were excluded from the analysis the mortality ratio was 0.51 (0.28 to 0.95). Estimates were unchanged by controls for background factors.

CONCLUSIONS: Children vaccinated against diphtheria, tetanus, and pertussis or polio had a death rate nearly 2 times that of unvaccinated children. These trends are unlikely to be explained exclusively by selection biases since different vaccines were associated with opposite tendencies. Measles and BCG vaccines may have beneficial effects in addition to protection against measles and tuberculosis.

J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: 10714532

Effects of diphtheria-tetanus-pertussis or tetanus vaccination on allergies and allergy-related respiratory symptoms among children and adolescents in the United States.

Hurwitz EL[1], Morgenstern H.

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Abstract

BACKGROUND: Findings from animal and human studies confirm that diphtheria and tetanus toxoids and pertussis (DTP) and tetanus vaccinations induce allergic responses; associations between childhood vaccinations and subsequent allergies have been reported recently.

OBJECTIVE: The association of DTP or tetanus vaccination with allergies and allergy-related respiratory symptoms among children and adolescents in the United States was assessed.

METHODS: Data were used from the Third National Health and Nutrition Examination Survey on infants aged 2 months through adolescents aged 16 years. DTP or tetanus vaccination, lifetime allergy history, and allergy symptoms in the past 12 months were based on parental or guardian recall. Logistic regression modeling was performed to estimate the effects of DTP or tetanus vaccination on each allergy.

RESULTS: The odds of having a history of asthma was twice as great among vaccinated subjects than among unvaccinated subjects (adjusted odds ratio, 2.00; 95% confidence interval, 0.59 to 6.74). The odds of having had any allergy-related respiratory symptom in the past 12 months was 63% greater among vaccinated subjects than unvaccinated subjects (adjusted odds ratio, 1.63; 95% confidence interval, 1.05 to 2.54). The associations between vaccination and subsequent allergies and symptoms were greatest among children aged 5 through 10 years.

CONCLUSIONS: DTP or tetanus vaccination appears to increase the risk of allergies and related respiratory symptoms in children and adolescents. Although it is unlikely that these results are entirely because of any sources of bias, the small number of unvaccinated subjects and the study design limit our ability to make firm causal inferences about the true magnitude of effect.

Lancet. 1999 May 1;353(9163):1485-8. PMID: 10232315

Atopy in children of families with an anthroposophic lifestyle.

Alm JS[1], Swartz J, Lilja G, Scheynius A, Pershagen G.

[1]Department of Laboratory Medicine, Karolinska Institute and Hospital, Stockholm, Sweden. Johan.Alm@sos.ki.se

Abstract

BACKGROUND: Increased prevalence of atopic disorders in children may be associated with changes in types of childhood infections, vaccination programmes, and intestinal microflora. People who follow an

anthroposophic way of life use antibiotics restrictively, have few vaccinations, and their diet usually contains live lactobacilli, which may affect the intestinal microflora. We aimed to study the prevalence of atopy in children from anthroposophic families and the influence of an anthroposophic lifestyle on atopy prevalence.
METHODS: In a cross-sectional study, 295 children aged 5-13 years at two anthroposophic (Steiner) schools near Stockholm, Sweden, were compared with 380 children of the same age at two neighbouring schools in terms of history of atopic and infectious diseases, use of antibiotics and vaccinations, and social and environmental variables. Skin-prick tests were done for 13 common allergens, and we took blood samples from children and their parents for analysis of allergen-specific serum IgE-antibodies.
FINDINGS: At the Steiner schools, 52% of the children had had antibiotics in the past, compared with 90% in the control schools. 18% and 93% of children, respectively, had had combined immunisation against measles, mumps, and rubella, and 61% of the children at the Steiner schools had had measles. Fermented vegetables, containing live lactobacilli, were consumed by 63% of the children at Steiner schools, compared with 4.5% at the control schools. Skin-prick tests and blood tests showed that the children from Steiner schools had lower prevalence of atopy than controls (odds ratio 0.62 [95% CI 0.43-0.91]). There was an inverse relation between the number of characteristic features of an anthroposophic lifestyle and risk of atopy (p for trend=0.01).
INTERPRETATION: Prevalence of atopy is lower in unvaccinated children from anthroposophic families than in children from other families. Lifestyle factors associated with anthroposophy may lessen the risk of atopy in childhood.

Epidemiology. 1999 May;10(3):337-9. PMID: 10230847

Hepatitis B vaccine and liver problems in U.S. children less than 6 years old, 1993 and 1994.

Fisher MA[1], Eklund SA.

[1]Department of Epidemiology, University of Michigan, Ann Arbor 48109, USA.

Abstract. Data to assess the benefits and risks of hepatitis B vaccine for the general population of U.S. children are sparse. This study addressed the problem of external validity found in previous studies of high risk populations by evaluating the benefit of hepatitis B vaccination for the general population of American children. We calculated the risk of liver problems among hepatitis B vaccinated and non-hepatitis B vaccinated children using logistic regression. Hepatitis B vaccinated children had an unadjusted odds ratio of 2.94 and age-adjusted odds ratio of 2.35 for liver problems compared with non-hepatitis B vaccinated children in the 1993 National Health Interview Survey. Hepatitis B vaccinated children had an unadjusted odds ratio of 2.57 and age-adjusted odds ratio of 1.53 for liver problems compared with non-hepatitis B vaccinated children in the 1994 National Health Interview Survey dataset.

In 1999, Fisher and Ekland reported in the journal Epidemiology: "we calculated the risk of liver problems among hepatitis B vaccinated and non-hepatitis b vaccinated children using logistic regression. Hepatitis B vaccinated children…" were found to have 3 fold increase in liver problems compared to non vaccinated children.

Epidemiology. 1997 Nov;8(6):678-80. PMID: 9345669

Is infant immunization a risk factor for childhood asthma or allergy?

Kemp T[1], Pearce N, Fitzharris P, Crane J, Fergusson D, St George I, Wickens K, Beasley R.

[1]Department of Medicine, Wellington School of Medicine, New Zealand.

Abstract. The Christchurch Health and Development Study comprises 1,265 children born in 1977. The 23 children who received no diphtheria/pertussis/tetanus (DPT) and polio immunizations had no recorded asthma episodes or consultations for asthma or other allergic illness before age 10 years; in the immunized children, 23.1% had asthma episodes, 22.5% asthma consultations, and 30.0% consultations for other allergic illness. Similar differences were observed at ages 5 and 16 years. These findings do not appear to be due to differential use of health services (although this possibility cannot be excluded) or confounding by ethnicity, socioeconomic status, parental atopy, or parental smoking.

Lancet. 1995 Apr 29;345(8957):1071-4. PMID: 7715338

Is measles vaccination a risk factor for inflammatory bowel disease?

Thompson NP[1], Montgomery SM, Pounder RE, Wakefield AJ.

[1]Inflammatory Bowel Disease Study Group, Royal Free Hospital School of Medicine, London, UK.

Abstract Measles virus may persist in intestinal tissue, particularly that affected by Crohn's disease, and early exposure to measles may be a risk factor for the development of Crohn's disease. Crohn's disease and ulcerative colitis occur in the same families and may share a common aetiology. In view of the rising incidence of inflammatory bowel disease (Crohn's disease and ulcerative colitis), we examined the impact of measles vaccination upon these conditions. Prevalences of Crohn's disease, ulcerative colitis, coeliac disease, and peptic ulceration were determined in 3545 people who had received live measles vaccine in 1964 as part of a measles vaccine trial. A longitudinal birth cohort of 11,407 subjects was one unvaccinated comparison cohort, and 2541 partners of those vaccinated was another. Compared with the birth cohort, the relative risk of developing Crohn's disease in the vaccinated group was 3.01 (95% CI 1.45-6.23) and of developing ulcerative colitis was 2.53 (1.15-5.58). There was no significant difference between these two groups in coeliac disease prevalence. Increased prevalence of inflammatory bowel disease, but not coeliac disease or peptic ulceration,

was found in the vaccinated cohort compared with their partners. These findings suggest that measles virus may play a part in the development not only of Crohn's disease but also of ulcerative colitis.

In 1995 as published in Lancet by Thompson et al, 3545 MMR vaccinated persons were compared to some 11,000 non vaccinated MMR persons. Total risk of inflammatory bowel disease was 3 fold higher in those who received vaccination. Lancet. 1995 Apr 29;345(8957):1071-4.

N Engl J Med. 1986 Dec 18;315(25):1584-90. PMID: 3491315

Hemophilus influenzae type B disease in children vaccinated with type B polysaccharide vaccine.

Granoff DM, Shackelford PG, Suarez BK, Nahm MH, Cates KL, Murphy TV, Karasic R, Osterholm MT, Pandey JP, Daum RS.

Abstract.. We studied 55 cases of invasive Hemophilus influenzae type b disease occurring in children at least three weeks after vaccination with type b polysaccharide vaccine. Their mean age at the time of immunization was 27.8 months (range, 18 to 47). Meningitis developed in 39 patients, of whom 3 died and 6 had neurologic sequelae. We investigated certain host factors that may have contributed to the failure of the vaccine. The geometric **mean concentration of antibody to type b polysaccharide in convalescent-phase serum from 31 of the vaccinated patients who had hemophilus disease was significantly lower than that in serum from 25 patients of similar age with the disease who had never been vaccinated (0.59 vs. 3.46 micrograms per milliliter, P less than 0.001)**. However, only 3 of 46 patients in whom the vaccine failed and who were tested for hypogammaglobulinemia had this finding, and none of 33 children tested for IgG2 had low serum concentrations of this immunoglobulin subclass, which is thought to be important in the immune response to polysaccharide antigens. In addition, all but 1 of the 46 patients in whom the vaccine failed and who were tested for IgG antibody to tetanus toxoid protein, a thymic-dependent antigen, had normal values, and 19 of 20 tested for hemolytic complement activity had normal levels. In white children, the presence of the Gm immunoglobulin phenotype (1,2,3, 17; ;5,13,21) was associated with a sevenfold increase in the relative risk of vaccine failure (P less than 0.003). We conclude that vaccine failure may be related in part to genetic factors, and that most vaccinated children in whom Hemophilus influenzae disease develops have deficient antibody responses to the type b polysaccharide despite normal serum concentrations of immunoglobulin and normal antibody responses to tetanus toxoid.

Granoff and colleagues publishing in the New England Journal of Medicine (1986) studied a group of children who got HIB Meningitis even though they were vaccinated. These kids were compared to other kids who did not get the vaccine, but also got HIB meningitis. The idea was to try and figure out why the vaccine failed. Kids who were vaccinated had very low immune responses to the disease compared to kids who had not been vaccinated.

Classen and colleagues published (2002) in the journal Autoimmunity. First, they gave the HIB vaccine to mice and showed that the vaccine itself triggered insulin-dependent diabetes in mice… and then also a comparison: 116,000 HIB vaccinated children had a significantly higher rate of diabetes compared to 128,000 children who did not have the vaccine. Read it

Autoimmunity. 2002 Jul;35(4):247-53. PMID: 12482192

Clustering of cases of insulin dependent diabetes (IDDM) occurring three years after hemophilus influenza B (HiB) immunization support causal relationship between immunization and IDDM.

Classen JB[1], Classen DC.

[1]*Classen Immunotherapies Inc., 6517 Montrose Avenue, Baltimore, MD 21212, USA. classen@vaccines.net*

Abstract

OBJECTIVE: The hemophilus vaccine has been linked to the development of autoimmune type 1 diabetes, insulin dependent diabetes (IDDM) in ecological studies.

METHODS: We attempted to determine if the Hemophilus influenza B (HiB) vaccine was associated with an increased risk of IDDM by looking for clusters of cases of IDDM using data from a large clinical trial. All children born in Finland between October 1st, 1985 and August 31st, 1987, approximately 116,000 were randomized to receive 4 doses of the HiB vaccine (PPR-D, Connaught) starting at 3 months of life or one dose starting after 24 months of life. A control-cohort included all 128,500 children born in Finland in the 24 months prior to the HiB vaccine study. Non-obese diabetic prone (NOD) mice were immunized with a hemophilus vaccine to determine if immunization increased the risk of IDDM.

RESULTS: The difference in cumulative incidence between those receiving 4 doses and those receiving 0 doses is 54 cases of IDDM/100,000 (P = 0.026) at 7 years, (relative risk = 1.26). Most of the extra cases of IDDM appeared in statistically significant clusters that occurred in periods starting approximately 38 months after immunization and lasting approximately 6-8 months. Immunization with pediatric vaccines increased the risk of insulin diabetes in NOD mice.

CONCLUSION: Exposure to HiB immunization is associated with an increased risk of IDDM. NOD mice can be used as an animal model of vaccine induced diabetes.