Vaccine Refusals Increase Despite School Immunization Requirements

Vaccine Refusal, Mandatory Immunization, and the Risks of Vaccine-Preventable Diseases.


Complacency regarding susceptibility and severity of vaccine-preventable diseases and concerns about vaccine safety have led to increased rates of non-medical exemptions from school immunization requirements.

**Background:** Despite school requirements, deviations from recommended immunization schedules, including vaccine refusals, continue to increase. This trend poses significant risks, both to the individual and the community.

**Design:** Review of historic and current literature.

**Discussion:** By the early 1980s, the U.S. legally imposed school immunization requirements, with variations by state. Medical exemptions are currently allowed in all states, religious exemptions in most, and personal (philosophical) exemptions permitted in 21 states. In recent years, the rate of non-medical exemptions has dramatically increased, particularly in states that allow exemptions due to personal beliefs. Because there is marked geographic clustering of non-medical exemptions, the accumulation of susceptible children in a given area increases the risk of disease outbreaks in that region. Geographic clustering may occur due to characteristics of the local population, opinions of health care providers/community leaders, and local media coverage. Heterogeneity of school policies and attitudes of the school officials responsible for vaccine compliance may also influence exemption rates. As a result, complexity of procedures allowing non-medical exemptions is inversely proportional to the exemption rate. Studies have demonstrated that measles risk is 22 to 35 times higher in an unvaccinated child. During recent measles outbreaks, cases have almost universally occurred in unvaccinated individuals—either those with non-medical exemptions or those too young for vaccination. A case-control study reveals that parents of exempt children are much more likely than those of vaccinated children (51% to 60% vs 15% to 18%) to believe that their children have low susceptibility to vaccine-preventable diseases, the severity of the diseases is low, and that safety and efficacy of vaccines is low. The most frequent reason for vaccine refusal (in 69%) is concern regarding harmful effects of the vaccine. Primary care providers, including those of unvaccinated children, are cited by parents as the most frequent source of vaccine information, and several studies have highlighted the significant influence of clinicians on parental decisions regarding vaccines. Providers caring for a high proportion of exempt children are less likely to show confidence in vaccine safety and are less likely to perceive vaccines as providing benefit to individuals and the community. The American Academy of Pediatrics encourages clinicians with high confidence in vaccines to continue relationships with families that refuse immunization, and to engage in ongoing respectful dialogue to address parental concerns.

**Reviewer's Comments:** Ironically, it is precisely because vaccines are so effective at reducing the incidence, morbidity, and mortality of infectious diseases that public perception of the threat of these diseases has changed so drastically. Provisions for personal exemptions to school immunization "requirements" suggest that there is essentially no requirement after all. Without effectively enforced school policies, our ability to control disease outbreaks through the use of vaccines greatly depends on heightened efforts to educate our patients.

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Mandatory Vaccine for Hepatitis A Results in Significant Drop in Hepatitis A Infection

The Effect of Universal Toddlers-Only Hepatitis A Virus Vaccination Program on Seropositivity Rate in Unvaccinated Toddlers: Evidence for Reduced Virus Circulation in the Community.


In this study, the mandatory vaccination for hepatitis A in toddlers only resulted in a significant drop of community-acquired hepatitis A infection.

**Objective:** To determine if a mandatory hepatitis A vaccine program in toddlers only can have a significant reduction in community-acquired hepatitis A infection.

**Methods:** Serological testing for hepatitis A was performed in children aged 11 to 15 years in a township in Southern Israel, where there is a high occurrence of hepatitis A infections. There was a 98.8% presence of hepatitis A immunoglobulin (IgG) concentrations. There was no mandatory hepatitis A vaccine program during this surveillance time. In 2000, there was a toddler-only vaccine program for hepatitis A instituted in this community. The vaccines were free as part of the national health program. In this study, blood samples were studied for presence of hepatitis A IgG prior to and after the mandatory vaccination in children at age 16 to 20 months. The hepatitis A vaccine was given at 18 and 24 months of age.

**Results:** There were 629 serum samples taken from 1991 to 2007 in the unvaccinated children aged 16 to 20 months. The vaccine program started in 2000. Prior to the vaccine program, the seropositive rate was 19% to 20% positive titers to hepatitis A; after the initiation program, the rates dropped to 2.5% to 3.0% in the children in this small community.

**Conclusions:** The mandatory vaccination for hepatitis A in toddlers resulted in a significant drop of community-acquired hepatitis A infection.

**Reviewer's Comments:** The prevalence of 20% infection rate in this toddler group prior to mandatory vaccine and the drop to 2% a few years after vaccine shows the reduction of spread from toddlers within this community. Children at these younger ages are the vectors for spread of hepatitis A, and with mandatory vaccination it showed a marked reduction of disease burden in younger children. By encouraging patients here in the United States to be immunized with the hepatitis A vaccine, it will help reduce the spread of disease in this age group and may have an effect on a larger proportion of the population.

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Fears of Negative Effect of Minimum Interval Schedule for DTaP Unfounded

Effects of a Minimum Interval Immunization Schedule for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccination During a Pertussis Outbreak.

Bronson-Lowe D, Anderson SM:
Arch Pediatr Adolesc Med; 163 (May): 417-421

Contrary to concerns, the use of a minimum interval schedule for DTaP actually had a positive effect on receiving other vaccines, not a negative one.

Background: Although the pertussis vaccine resulted in significantly lower rates of disease from its introduction in the 1950s through the 1980s, since that time, the number of cases each year has been increasing. Infants are scheduled to receive a vaccination for pertussis at 2, 4, and 6 months of age, with a minimum of 8 weeks between doses. However, in outbreak conditions, some have proposed a quicker schedule, with the first dose given at 6 weeks of age, and subsequent doses 4 to 8 weeks later. This could affect the chance of receiving other vaccines at scheduled intervals.

Objective: To determine how a minimum interval schedule for the diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine would affect the administration of the inactivated polio (IPV) and pneumococcal conjugate vaccines (PCV).

Design/Methods: This was a retrospective cohort study of infants in Arizona. All vaccines administered in that state are reported to the Arizona State Immunization Information System. Two separate cohorts were created in February 2008 over a period that contained an outbreak of pertussis. In one of these cohorts, the minimum intervention schedule was used; in the other, the normal schedule of vaccines was performed. Demographic data were abstracted in order to control for other factors related to vaccination administration.

Results: Data were available for 45,129 children, 19,228 of which were in the minimum interval schedule group and 25,901 of which were in the normal schedule group. Children in the minimum interval group were more likely to receive all the vaccines. By 1 year of age, they were 34% more likely to have received 3 doses of DTaP (relative risk, 1.3), 27% more likely to have received 3 doses of IPV (RR, 1.3), and 37% more likely to have received 3 doses of PCV (RR, 1.4). They were also significantly more likely to have received all 3 doses of DTaP at a younger age (24 weeks vs 30 weeks).

Conclusions: Contrary to concerns, the use of a minimum interval schedule for DTaP actually had a positive effect on receiving other vaccines, not a negative one. Infants on a minimum interval schedule for DTaP were significantly more likely to receive all 3 doses of the vaccine in a shorter period of time. They were also more likely to receive their other vaccines on time as well. Fears that a minimum interval for pertussis vaccination in an outbreak setting might have negative consequences on other immunizations seem unfounded.

Reviewer's Comments: It is counterintuitive that taking the DTaP off the standard schedule and adding in extra visits for shots actually increased the uptake of all vaccines. At the very least, this is good evidence that the minimum interval schedule should be used in outbreaks without concern.

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Shorter Antibiotic Course for Septic Arthritis May Be Reasonable

Prospective, Randomized Trial of 10 Days Versus 30 Days of Antimicrobial Treatment, Including a Short-Term Course of Parenteral Therapy, for Childhood Septic Arthritis.


High-dose oral antibiotic treatment following 2 to 4 days of intravenous treatment is probably a viable option for treatment of septic arthritis.

Background: The standard therapy for pediatric septic arthritis is a combination of parenteral and oral antibiotics for several weeks +/- surgical lavage. However, few large-scale studies support a lengthy course of antibiotics.

Objective: To determine if antibiotic treatment duration of septic arthritis can be shortened.

Design: Randomized multicenter unblinded noninferiority trial.

Participants/Methods: Patients aged 3 months to 15 years with suspected septic arthritis were recruited at 7 referral Finnish hospitals from 1983 to 2005 and randomized to receive antibiotics intravenously for 2 to 4 days, followed by oral treatment at the same dose for a total of 10 or 30 days. Patients were also randomized to receive clindamycin 40 mg/kg/day or a first-generation cephalosporin 150 mg/kg/day. Between 1983 and 1997, children aged <4 years also received ampicillin/amoxicillin 200 mg/kg/day (for Haemophilus influenzae type b) until causative agent was identified. Needle aspiration of the joint was performed once to obtain fluid for bacterial culture. No other surgical procedures were performed unless clinical response was unsatisfactory. X-rays, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were obtained at periodic intervals.

Results: 130 patients with culture-positive septic arthritis completed the study. Mean age was 6.5 years, and lower extremities, most commonly the hip, were affected in 85%. Staphylococcus aureus was the causative agent in 58%, H influenzae b in 18%, Streptococcus pyogenes in 12%, and S pneumoniae in 8%. In total, 48% were randomized to receive 10 days of antibiotics; 52% were randomized to 30 days. However, the treating physician had the option of continuing antibiotics beyond the specified treatment course if response was considered suboptimal or CRP was >20 mg/L and antibiotics other than clindamycin or a cephalosporin could be used. Five patients in the 10-day group received antibiotics for >10 days, and 3 patients in the 30-day group received antibiotics >30 days. Sixty-one (47%) patients received an antibiotic other than clindamycin or cephalosporin. There was no difference between the 2 groups in CRP, ESR, or WBC counts during treatment or at 2 weeks, 3 months, and 1 year follow-up. At 3 months and 1 year, there was no difference in clinical outcome. One patient in the 30-day group had recurrent infection. No other patients had relapse, recurrence, residual dysfunction, or growth disturbance.

Conclusions: Use of high-dose antibiotics for 10 days is not inferior to 30 days in the treatment of pediatric septic arthritis.

Reviewer’s Comments: This study needs to be interpreted carefully. Although it was a prospective study, there were several deviations from protocol. For instance, almost half of the patients were treated with antibiotics not specified in the protocol, and the authors do not provide data about whether those patients also received high doses. It is difficult to draw definitive conclusions from this paper.

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Bleach Baths Decrease Severity of Impetiginized AD

Treatment of Staphylococcus aureus Colonization in Atopic Dermatitis Decreases Disease Severity.

Huang JT, Abrams M, et al:

Pediatrics; 123 (May): e808-e814

Bleach baths, when used adjunctively, improve impetiginized eczema and are well-tolerated over at least 3 months.

Objective: To determine the prevalence of Staphylococcus aureus colonization in patients with impetiginized atopic dermatitis (AD) and to determine whether treatment with bleach baths and intranasal mupirocin improves eczema severity.

Participants/Methods: Patients with moderate-to-severe eczema and signs of impetigo (weeping, crusting, and/or papules) presenting to a pediatric dermatology clinic were randomly assigned to 1 of 2 groups. Both groups were treated with 14 days of oral cephalexin. The treatment group was then instructed to add 4 ounces of 6% bleach to a 40-gallon bath for a 5- to 10-minute bath twice weekly without submerging the head and also to apply mupirocin ointment intranasally twice daily for 5 consecutive days each month over a 3-month period. The placebo group was instructed to bathe without bleach at least twice weekly and to apply petrolatum intranasally in the same fashion as the mupirocin was applied in the treatment group. Both groups were instructed to pat dry and apply emollients liberally after bathing. The primary outcome was the Eczema Area and Severity Index (EASI) score.

Results: 31 participants were analyzed on an intent-to-treat basis. While no one withdrew due to adverse events, 3 parents withdrew consent due to inconvenience of study appointments and marked improvement in the children's condition. S aureus grew from 87.1% of the lesional skin cultures and from 80.6% of the nares cultures. Of these positive cultures, 7.4% of the skin cultures and 4.0% of the nares cultures grew MRSA. At the study's onset, the mean EASI score was 19.7. The treatment group's decrease in mean EASI scores at 1 month and 3 months was 10.4 and 15.3, respectively, compared to 2.5 and 3.2 for the placebo group, demonstrating a statistically significant improvement in the treatment group. However, when focused on the head and neck, the EASI scores did not differ between the treatment and placebo groups. There was no significant difference in compliance between groups.

Conclusions: For patients with impetiginized moderate-to-severe eczema who were initially treated with oral cephalexin, bleach baths and intranasal mupirocin substantially improved their eczema after both 1 month and 3 months of therapy.

Reviewer's Comments: While this study had a small sample size, its results demonstrate an inexpensive, well-tolerated, and effective therapy for impetiginized moderate-to-severe eczema. Considering its questionable benefit for eliminating S aureus colonization, this reviewer wonders if the intranasal mupirocin played any role in the treatment group's improved eczema scores.

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Use of Ferrous Fumarate Sprinkles Does Not Improve Tx Adherence Over Drops

Iron Supplementation of Low-Income Infants: A Randomized Clinical Trial of Adherence With Ferrous Fumarate Sprinkles Versus Ferrous Sulfate Drops.


Although parents report less difficulty incorporating ferrous fumarate sprinkles into their child's daily routine, they are not more adherent with its daily use compared to ferrous sulfate drops.

Background: Iron deficiency is common in young toddlers and infants. Its prevalence ranges from 15% to 35% and it has been linked to neurocognitive impairment. Adherence to daily supplementation with multivitamin or iron drops has been plagued by poor adherence.

Objective: To compare the adherence with daily iron supplementation of ferrous fumarate sprinkles compared to ferrous sulfate drops.

Design/Participants: This was a randomized clinical trial in which healthy infants age 5 to 7 months were enrolled at their 6 month well-child check.

Methods: Enrollment sites were an urban academic hospital-based ambulatory clinic and a community health center. Children with pre-existing conditions associated with iron deficiency or anemia or with use of iron supplementation in the prior month were excluded. Infants were randomized to receive one packet of sprinkles added to prepared food or 1 mL of Tri-Vi-Sol with Iron drops given orally on an empty stomach once daily. Treatment assignment was not blinded. Outcomes measured included adherence, side effects, and experience with administration. Adherence was categorized for each encounter as high (5 to 7 days), some (1 to 4 days), or none (0 days). The study was powered to detect a 70% versus 40% adherence between groups (sprinkles vs drops).

Results: 150 infants were enrolled in the study. Those who enrolled did not differ demographically from those who declined enrollment. The study population was 52% African American and 29% Latino, and most were breastfed (80%). Most caregivers spoke English, graduated high school (81%), and received WIC (91%). There were no differences between intervention groups. Adherence was poor in both the sprinkle and drops groups. High adherence ranged from 32% to 63% in the drops group and 31% to 46% in the sprinkles group. However, the drops group was more likely to have at least 4 assessments with high adherence (22.0% vs 9.5%). The drops group reported greater fussiness compared to the sprinkles group (24.0% vs 1.9%). However, this side effect was not related to adherence. Of note, caregivers in the sprinkles group were more likely to report concerns about using a new product (12% vs 0%) and safety of the product for infants (14.0% vs 1.3%).

Conclusions: Use of ferrous fumarate sprinkles did not lead to improved adherence compared with daily ferrous sulfate drops.

Reviewer's Comments: Poor adherence to iron deficiency treatment continues to be a thorn in the primary care pediatrician's side. The ferrous fumarate sprinkles seemed like an ingenuous solution to the problem of adherence. While it didn't work, the larger lesson here is that we should neither underestimate nor dismiss the public's concern about the use of new medications because their perceptions may thwart our efforts to improve adherence with new medication formulations. We must work to ensure that new medicines are safe and we need to effectively convey this information to parents.
Iron Deficiency Nearly Twice as Common in Children With Febrile Seizures

The Association Between Iron Deficiency and Febrile Seizures in Childhood.
Hartfield DS, Tan J, et al: 
Clin Pediatr (Phila); 48 (May): 420-426

Iron deficiency is nearly twice as common in children with febrile seizures, either simple or complex, when compared to age-matched controls with fever. In children presenting with a febrile seizure, screening for iron deficiency should be considered.

**Objective:** To determine the relationship between febrile seizures and an abnormal iron status in young children with febrile seizures compared to controls.

**Design/Participants:** This was a retrospective case-controlled study of children aged 6 to 36 months who presented to an emergency department in Alberta, Canada, over a 5-year period (2001 to 2006) with a febrile seizure, simple or complex, and had a complete blood count (CBC) done during the evaluation. Controls were patients with a febrile illness alone who also had a CBC done. Patients were excluded if they had a CNS infection, an underlying blood disorder, or a past history of an afebrile seizure.

**Methods:** To make a diagnosis of iron deficiency, the authors utilized a combination of an increased red cell distribution width (RDW) and a decreased mean cell volume (MCV). An MCV <70 and an RDW >15.6% were considered abnormal. A hemoglobin <11 mg/dL was the study's definition of anemia.

**Results:** 361 cases of febrile seizures and 390 controls were included in the study. Mean age was about 18 months. The authors found that in patients with febrile seizures, 9% of all cases had iron deficiency and 6% had iron deficiency anemia. For control patients, 5% had iron deficiency and 4% had iron deficiency anemia. This amounted to an increased odds ratio of 1.83 (95% CI, 0.98 to 3.45) of having a febrile seizure associated with iron deficiency compared to controls. No difference was found in those with simple and those with complex febrile seizures.

**Conclusions:** The authors concluded that iron deficiency is nearly twice as common in children with febrile seizures, either simple or complex, when compared to age-matched controls with fever. In children presenting with a febrile seizure, the results suggest that patients should be screened for iron deficiency.

**Reviewer's Comments:** Younger children are more susceptible to febrile seizures. One theoretic basis for this increased susceptibility may be the lack of maturational changes in inhibitory and excitatory neurotransmitters. Because iron is a cofactor in a number of enzymatic reactions involving neurotransmitter production and DNA replication, there exists the potential for disruption of normal cell and organ function, particularly in the central nervous system in the setting of low iron stores. Disruption of normal neurotransmitter activity from iron deficiency could predispose these children to febrile seizures. An interesting follow-up study would be to determine if treating the iron deficiency resulted in a lowering of the likelihood of seizure recurrence.

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**ADHD Medication Use May Improve Academic Achievement During Elementary School**

*Positive Association Between Attention-Deficit/ Hyperactivity Disorder Medication Use and Academic Achievement During Elementary School.*

Medication use in children with ADHD appears to be associated with increased academic performance.

**Background:** Attention-deficit hyperactivity disorder (ADHD) is a common condition in children that is associated with increased levels of inattention, activity, and impulsivity. More than half of affected children are treated with prescription medication that has been proven effective in large trials. Unfortunately, fewer children are treated than would be optimal. Children with ADHD can have poorer school performance than normal children. In the past, research has not shown that academic performance has increased with medication treatment, although some of these studies had methodological issues.

**Objective:** To examine whether medication use for ADHD contributes to improved academic performance in elementary school.

**Design/Methods:** This was a retrospective cohort study using data from the Early Childhood Longitudinal study - Kindergarten Class of 1998 to 1999. Data were collected in 5 waves: twice in kindergarten and then once in first, third, and fifth grades. Mathematics and reading achievement was measured by achievement tests paralleling the National Assessment of Educational Progress. The diagnosis of ADHD was reported by parents in the last 4 waves of the study. In the last wave, parents were asked if their child was currently on medication for ADHD. If they were, further information was collected on the length of treatment.

**Results:** Data were available on 594 children with ADHD. Children who were on medication for their ADHD had an average mathematics achievement score that was 2.9 points higher than the average score of children who were not receiving medication. Those children with ADHD who were treated for at least 2 waves of the study had an average reading achievement score that was 5.4 points higher than those not treated with medication. Children who had an individualized education program had a less significant association with a higher reading score than those without an individualized education plan. These increased scores in math and reading are equivalent to score gains of 0.2 and 0.3 school years, respectively.

**Conclusions:** Medication use in children with ADHD appears to be associated with increased academic performance. Children with ADHD who were treated with medication had significantly increased achievement scores in mathematics and reading, especially if treated for longer periods of time. The use of an individualized education plan lessened the impact of medication on reading score improvements. The gains achieved by medication still did not fully compensate for the effect of having ADHD on lowering achievement scores in general.

**Reviewer's Comments:** There are two big points to take home here. First, this is another reason why we should make sure kids with ADHD receive the recommended medication. Second, this is a stark reminder that, although medication helps children with ADHD normalize their academic performance, they are still at a disadvantage.

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ADHD More Likely in Pediatric Patients Hospitalized for Trauma

Screening for Attention-Deficit/Hyperactivity Disorder in a Select Sample of Injured and Uninjured Pediatric Patients.

Maxson RT, Lawson KA, et al:
J Pediatr Surg; 44 (April): 743-748

Patients with certain injury mechanisms, including bicycle accidents and falls, are more likely to have positive screens for ADHD. Identification and treatment of these patients might lessen the burden of injury recidivism.

**Objective:** To compare rates of attention-deficit/hyperactivity disorder (ADHD) in injured and uninjured hospitalized pediatric patients.

**Participants/Methods:** Patients aged 6 to 12 years who were admitted for trauma to Children's Medical Center in Dallas from 2004 to 2006 constituted the database. Parents were questioned regarding the mechanism of injury and patients were included in the study if they were injured in an auto-pedestrian collision, auto-bicycle collision, other bicycle collision, or a fall. Control patients were those admitted for appendicitis. To screen for ADHD, one parent of each patient completed the Vanderbilt Attention-Deficit/Hyperactivity Disorder Parent Rating Scale, a screening tool which requires 18 answers regarding behavior in the past 6 months. A positive screen on this scale was felt to be indicative of ADHD traits. Other demographic information, including previous diagnosis of ADHD, was also collected.

**Results:** 133 patients with trauma and 157 patients with appendicitis were included in the study. Mean age for each group was around 9 years. The authors found that injured patients were 3.25 times more likely to have a positive ADHD screen than those hospitalized with appendicitis (OR, 3.25; 95% CI, 1.57 to 6.72). This encompassed all types of injury mechanisms studied. Only 34% of those in the ADHD group were receiving treatment at the time of injury. There was not a mention in the study of the total percentage that had been diagnosed prior to hospitalization with ADHD, but in 24% of those with a positive screen for ADHD, parents reported having no knowledge of the disease. Those with positive screens were more likely to be male, to have non-excellent school performance as reported by parents, and to have been previously seen in an ED for an injury-related diagnosis.

**Conclusions:** The authors concluded that patients with certain injury mechanisms, including bicycle accidents and falls, may warrant screening and possible referral for ADHD. They hypothesize that identification and treatment of these patients might lessen the burden of injury recidivism. Thus, ADHD screening might be an effective injury prevention initiative for a trauma service.

**Reviewer's Comments:** It's not hard to imagine the potential spin-off studies from this paper, such as a comparison of injury rates among those with ADHD who are on or off medication or even the screening of adult trauma patients for ADHD, as it is estimated that 30% to 70% of children with ADHD will continue to have symptoms as adults.

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BUS May Be Comparable to Radiography in Identifying Fractures in Children

The Utility of Bedside Ultrasonography in Identifying Fractures and Guiding Fracture Reduction in Children.
Patel DD, Blumberg SM, Crain EF:
Pediatr Emerg Care; 25 (April): 221-225

Bedside ultrasonography shows promise in the diagnosis of fractures in children, and with more research, might be an adequate replacement for radiographs.

Background: In general, physicians have relied on x-rays or fluoroscopy in order to diagnose fractures in children. These tests are slow, may require sedation, and involve significant radiation exposure. However, the use of bedside ultrasound may remove some of these limitations and still allow for an accurate diagnosis. However, little research has been performed in children to see if this technique might hold promise in the emergency department (ED) setting.

Objective: To determine if bedside ultrasonography (BUS) is useful in identifying long bone fractures in children, and if those fractures might need reduction.

Design: Prospective cohort study.

Methods: Eligible participants were children between the ages of 2 and 17 years presenting to an urban pediatric ED with a suspected fracture of the radius, ulna, tibia, or fibula. Three pediatric ED physicians with no prior formal experience with ultrasonography were trained in its use during a 2-hour session. Before children were examined with radiographs, one of these physicians performed a bedside ultrasound. If they diagnosed a fracture, they further estimated the angulation and displacement of the fracture. After ultrasound, all patients underwent radiographs as a gold standard. Blinded orthopedic physicians later determined the agreement between ultrasound and radiograph for the identification of fractures, the need for reduction, and the quality of performed reduction.

Results: 33 patients were enrolled and the mean age was 9.1 years. Studies were performed on 66 bones, of which 56 (85%) were in the upper extremities. About 60% of the examined bones had a fracture and one third required reduction. The overall agreement between bedside ultrasound and radiographs was 95% in identifying fractures, 92% in identifying the need for reduction, and 92% in identifying the quality of the reduction. The sensitivity and specificity of bedside ultrasound was 0.97 and 0.85 for fracture identification, 0.93 and 1.00 in identifying the need for reduction, and 1.00 and 0.80 in judging the adequacy of reduction.

Conclusions: BUS certainly shows promise in the diagnosis of fractures in children, and with more research, might be an adequate replacement for radiographs. BUS was almost as sensitive as radiographs in identifying fractures in children. It was less precise, but still impressive, in the identification of the need for reduction. Further research and training may lead to BUS replacing radiographs in children.

Reviewer's Comments: Although BUS may not be ready to replace radiography entirely for the diagnosis and management of fractures in children, it appears to show real promise and may replace radiography in the future.

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**Pump Tx vs Injections Does Not Influence Metabolic Parameters in Young Diabetics**

*A Randomized Prospective Study of Insulin Pump vs. Insulin Injection Therapy in Very Young Children With Type 1 Diabetes: 12-Month Glycemic, BMI, and Neurocognitive Outcomes.*


For children aged <5 years, the initiation of pump therapy versus continuing intensive injection therapy did not differ in significantly influencing metabolic parameters, such as hemoglobin A1c or BMI, or neurocognitive or parental stress outcomes after 1 year of therapy.

**Objective:** To compare the use of an insulin pump versus intensive injection therapy in children aged <5 years with diabetes mellitus.

**Participants/Methods:** Children aged <5 years at the James Whitcomb Riley Hospital in Indianapolis were enrolled from 1999 to 2003. Families were selected based on a history of good compliance and the use of at least twice daily injections at home. Patients were randomized to begin either pump or intensive injections for 6 months. After 6 months, the injection group switched to the pump. The pump group, in a study design change done because of parental apprehensions, was given the option of switching or continuing on the pump at 6 months. At the start of the study and at 3, 6, 9, and 12 months, hemoglobin (Hgb) A1c and body mass index (BMI) were measured. At the start and at 6 and 12 months, neurocognitive assessment (using the Stanford-Binet Intelligence Scale), parenting assessment (using the Parenting Stress Index), and child behavior assessment (using the Child Behavior Checklist) were done.

**Results:** 35 patients, with an average age of slightly more than 3.5 years, completed the study. The authors found that for both groups (pump and intensive injections), there was a significant decline in Hgb A1c to 8.9 in the pump group and 8.5 in the injection group, but there were no significant differences between the groups. Both groups had some improvement in the Child Behavior Checklist. In all other areas studied, BMI, neurocognitive testing, and parenting stress, there were no significant changes between the 2 groups.

**Conclusions:** The authors concluded that in a research setting, for children aged <5 years, the initiation of pump therapy versus continuing intensive injection therapy did not differ in significantly influencing metabolic parameters, such as Hgb A1c or BMI, or neurocognitive or parental stress outcomes after 1 year of therapy.

**Reviewer's Comments:** Children with the onset of diabetes aged <5 years have an increased risk of cognitive deficits compared to those children diagnosed later. The use of insulin therapy in this age group has special inherent problems, including the unpredictable pattern of meals, variations in periods of activity, increased sensitivity to insulin, and an increased vulnerability to severe hypoglycaemia, as toddlers cannot accurately relay symptoms of low blood sugar. In this study for this age group, the theoretic advantages of insulin pump therapy as a closer mimic of physiologic insulin release did not translate into significant measurable benefits in metabolic or neurocognitive outcomes after 1 year compared to injections alone. It remains to be seen whether longer periods on the pump might demonstrate such an advantage.

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Should Phototherapy Be Used Universally for Jaundice in Newborns?

Numbers Needed to Treat With Phototherapy According to American Academy of Pediatrics Guidelines.

Newman TB, Kuzniewicz MW, et al:

*Pediatrics;* 123 (May): 1352-1359

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**Background:** Although recommendations of the American Academy of Pediatrics (AAP) for treatment of hyperbilirubinemia are specific, they correctly state that they are based on "uncertain estimates and extrapolations." The studies that have been used to estimate the number needed to treat (NNT) with phototherapy had different cutoff values for beginning and ending treatment than that recommended by the AAP. The true NNT is unknown.

**Objective:** To determine the true efficacy of phototherapy for jaundice in infants and to calculate the NNT to prevent 1 exchange transfusion.

**Methods:** A cohort of children was gathered from medical records in the Northern California Kaiser Permanente Medical Care Program, which covers >3 million members. Eligible infants were those born alive between 1995 and 2004, at >=2 kg, and at >=35 weeks' gestation. All data were drawn from electronic databases of the health care system. AAP guidelines were used to determine who should receive phototherapy and for how long. Infants in this analysis were those who had a total serum bilirubin level within 3 mg/dL of the threshold for age and risk group. Infants were excluded if their bilirubin was already declining or if the direct bilirubin was >2 mg/dL. Phototherapy was identified by procedure code.

**Results:** Of 281,898 infants in the birth cohort, 22,547 were eligible for analysis. Of these, about 31% had a procedure code for phototherapy. Based on review, the procedure code for phototherapy was both sensitive and specific for actually having undergone phototherapy. Phototherapy began within 8 hours of a qualifying total serum bilirubin level in about 75% of cases, for a total of 5251 infants. Of these, only 1.6% ever exceeded the level where exchange transfusion would be recommended. For infants with a negative direct antiglobulin test, phototherapy was very effective, with an adjusted odds ratio of 0.16. For infants with a total serum bilirubin above the treatment threshold, the NNT to prevent 1 exchange transfusion was 222 for boys and 339 for girls. There was significant variation in the effectiveness across subgroups, with high effectiveness in infants aged <1 day and low effectiveness in infants aged >3 days.

**Conclusions:** Although phototherapy appears to be effective, its actual effectiveness is highly variable across different groups. (1) Phototherapy does prevent exchange transfusions according to AAP guidelines. (2) The actual effectiveness varies across groups; however, with some high NNTs. (3) Further research should investigate the cost-effectiveness of phototherapy in infants.

**Reviewer's Comments:** Although it appears effective, it may be that tailored phototherapy for certain subgroups may be more cost-effective. This is an area that begs for a cost-effectiveness analysis.

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**Clinical Features Do Not Predict Time to Presentation for Pediatric Stroke**

*Pediatric Stroke: Do Clinical Factors Predict Delays in Presentation?*

Hartman AL, Lunney KM, Serena J:

*J Pediatr;* 154 (May): 727-732

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**Age, initial clinical symptoms, and clinical outcome are not associated with time to presentation for children with acute ischemic stroke.**

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**Background:** Children who have strokes often have nonspecific symptoms (such as altered mental status), which may lead to delay in presentation and diagnosis.

**Objective:** To identify clinical factors associated with delay in diagnosis in children with acute ischemic stroke.

**Design:** Retrospective chart review.

**Methods:** Charts were reviewed for all children aged 1 month to 15 years admitted for first-time stroke in San Diego County between 1995 and 2000. Acute ischemic stroke was defined as sudden onset of neurologic deficit, localized to the brain, lasting >24 hours, accompanied by findings on MRI or CT consistent with clinical findings. Data were collected about sociodemographics, medical history, family history, clinical signs and symptoms, risk factors, laboratory and imaging results, and treatment. Delay in presentation for evaluation was determined by time of onset of clinical symptoms in patient history and categorized as <6 hours, 6 to 24 hours, and >24 hours. The Glasgow Outcome Scale (GOS), a 5-point scale (1 = death, 2 = persistent vegetative state, 3 = severe disability, 4 = moderate disability, 5 = good recovery), was used to measure clinical outcome.

**Results:** 125 cases met study criteria; 51 of these had acute ischemic stroke, and time data about onset of clinical symptoms and presentation to a medical facility were available for 37. Nine children (24%) presented within 6 hours, and an additional 15 (41%) presented within the first 24 hours. Time to presentation was not statistically associated with gender, age, or initial symptoms (including hemiparesis, seizures, altered mental status, fever, ataxia, speech/language abnormalities, and headache). However, the 3 children with headache presented within 6 to 12 hours. Congenital heart disease was associated with presentation after 24 hours, and sickle cell disease was associated with presentation within 24 hours. There was no association between GOS and time to presentation. However, children presenting with altered mental status were more likely to die, and no patients presenting with hemiparesis died.

**Conclusions:** Age, initial clinical symptoms, and clinical outcome are not associated with time to presentation for children with acute ischemic stroke. Patients with sickle cell disease are more likely to present earlier, and those with congenital heart disease are more likely to present later.

**Reviewer’s Comments:** This is a very small study, and the authors acknowledge that the study may not be adequately powered to make any conclusions. Sickle cell patients generally receive education about stroke recognition, and this likely contributes to early recognition. Early recognition of hemiparesis, which is easier for parents to detect than altered mental status, may result in better outcomes. While it seems intuitive that early recognition could result in improved outcomes, this study does not help to answer that question.

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Definitions of, Referral Patterns for Palliative Care Vary Greatly Among Pediatricians

Pediatricians’ Perceptions of and Preferred Timing for Pediatric Palliative Care.

Pediatricians’ definitions and referral patterns for palliative care, when polled, revealed great variability.

Background: Both the Institute of Medicine and the American Academy of Pediatrics (AAP) have stated a need for greater availability of and referrals to pediatric palliative care services in children facing life-threatening illnesses. Despite this, referral rates remain low, and people speculate that this may be due to misperceptions of palliative care.

Objective: To investigate how pediatricians define palliative care and their referral patterns in 13 life-limiting diseases.

Design: Survey study.

Participants: Practicing pediatricians in California and Florida.

Methods: Investigators designed a survey to assess their 3 outcomes of interest: definition of, time of referral, and for which diseases practitioners would refer; 400 pediatricians were selected from the AAP database of practicing pediatricians and were sent the survey.

Results: 40% of participants submitted the survey. Of these, 75% were in private and/or outpatient practice, while 25% were inpatient and/or at an academic setting. Fifty percent defined palliative care as hospice care, while 30% defined it differently but without consensus on an alternative definition. Twenty percent stated they did not know its definition. Fifty percent had made a hospice referral before, while one third did not know if services existed in their community. Time to referral varied by disease but, overall, an early referral was rare. For most diseases, almost 50% of pediatricians noted they would wait to refer to palliative care until curative therapy was no longer the goal. Cancer was the most likely disease to get a referral followed by cystic fibrosis and then metabolic/storage disorders.

Conclusions: There is a lack of consensus on the definition of palliative care among practicing pediatricians. Participants typically wait to refer until curative therapy is no longer an option.

Reviewer’s Comments: As a pediatric palliative care physician, I was not surprised by the disparate definitions, as the equating of palliative care and hospice has been a barrier for early referrals in my experience. I was also not surprised to find that most clinicians would wait to refer until there is no curative option. These results validate our struggle to increase our early referrals as we feel an early referral increases collaboration, understanding, and therefore success with families, patients, and clinicians. One critique of this article is that the investigators created their own survey but gave no evidence that it was validated. As the much-needed research in palliative care begins, we need to make sure that it has a high level of quality with a strong foundation, and such a foundation starts with validated metrics.

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**Adenoidectomy Does Not Increase Risk of Asthma, Atopy**

*Effect of Adenoidectomy on Respiratory Function: A Randomised Prospective Study.*

Mattila PS, Hammaren-Malmi S, et al:

*Arch Dis Child; 94 (May): 366-370*

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**Adenoidectomy, in conjunction with tympanostomy tubes, does not increase the risk for asthma.**

**Background:** For children, recurrent respiratory infections and asthma often go hand in hand. Infection can often result in an exacerbation, and there is some evidence that repeated respiratory infections, especially early in life, can predispose one to asthma. Children with repeated respiratory infection also are prone to recurrent otitis media.

**Objective:** To investigate effects of adenoidectomy on lung function.

**Design:** Randomized controlled trial.

**Participants:** Children aged 1 to 4 years with recurrent or persistent otitis media who were referred to a university hospital otorhinolaryngology department.

**Methods:** All patients received bilateral tympanostomy tubes and were randomized to undergo adenoidectomy or not at the time of tympanostomy tube placement. Patients were then followed for 3 years. Families kept diaries of all episodes of otitis media. Lung function and atopy were measured 3 years after adenoidectomy. Exercise-induced bronchoconstriction was measured by respiratory resistance before and after exercise. Bronchial inflammation was measured by exhaled nitrous oxide, and skin prick testing for multiple allergens was used to test for atopy.

**Results:** Of 217 children who were randomized, 166 completed 3 years of follow-up. No differences were seen between groups in episodes of otitis media, respiratory resistance before and after exercise, bronchial inflammation, or skin prick testing. Logistic regression analysis showed that, while adenoidectomy was not associated with abnormalities in respiratory resistance or bronchial inflammation, a history of recurrent otitis media during the first year of follow-up was associated with abnormalities in both respiratory resistance and bronchial inflammation.

**Conclusions:** Adenoidectomy does not increase development of asthma or atopy. In addition, there was no impact of adenoidectomy on the subsequent occurrence of recurrent otitis media.

**Reviewer's Comments:** Recall that the authors found before that children with recurrent otitis media undergoing adenoidectomy have an increased risk of asthma. It seems apparent from this study that it is not the adenoidectomy but, more likely, recurrent respiratory infections and/or recurrent episodes of otitis media that increase asthma risks. It should be noted, however, that approximately 25% of patients who were randomized initially dropped out of the study. The authors report that the primary reason for dropout was the unwillingness to continue with follow-up visits, as children were reported to have no medical problems requiring a medical visit. Since more children in the adenoidectomy group dropped out, this could well have created study bias that may have masked some negative effects of adenoidectomy.

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Order of Vaccine Administration Impacts Pain Experience

Order of Vaccine Injection and Infant Pain Response.

Ipp M, Parkin PC, et al:

Arch Pediatr Adolesc Med; 163 (May): 469-472

Administering the DPTaP-Hib vaccination prior to the pneumococcal conjugate vaccine (PCV) causes less pain compared to administering the PCV first.

**Background:** Parents who refuse immunizations for their children frequently cite pain as a reason. It is known that some vaccines are more painful than others. What is not known is if the order of administration affects the cumulative pain experience.

**Objective:** To determine if the pain response after administration of the diptheria, polio, and tetanus toxoids and acellular pertussis and *Haemophilus influenzae* type B vaccine (DPTaP-Hib) and the pneumococcal conjugate vaccine (PCV) differed based on order of administration.

**Design:** Randomized double-blinded study.

**Participants:** Infants aged 2 to 6 months were assessed who did not have a known acute febrile illness, chronic health problem, or allergy to either immunization. Use of systemic analgesic was not an exclusionary factor.

**Methods:** 120 participants were randomly chosen to receive either the DPTaP-Hib or PCV first followed by the other vaccine. Administrators, caregivers, and patients were all blinded, and needles appeared identical. Participants were videotaped, and 2 investigators reviewed their reactions just before and just after administration. Their pain reaction was scored using the Modified Behavioral Pain Scale. Parents also evaluated their children's pain using the visual analog scale. Investigators also noted presence or absence of crying.

**Results:** Pain after the first injection was significantly lower when the DPTaP-Hib was administered first. Similarly, the overall pain score after administration of both vaccines was significantly lower when the DPTaP-Hib was administered first. Finally, in all participants, pain increased after the second immunization was administered, regardless of which vaccine was given first.

**Conclusions:** Administration of the DPTaP-Hib vaccine first resulted in less pain after the first injection and less pain overall following administration of both vaccines as compared to administering the PCV first.

**Reviewer's Comments:** Our understanding of pain and the perception of pain is rapidly growing. Researchers have learned that earlier painful stimuli appear to have a negative impact on future reactions to painful stimuli. Therefore, it is important to determine the least painful way to deliver preventative medicine both to increase the likelihood that parents will agree to immunizations and to minimize the negative impact on later painful experiences and perceptions. This was an excellently designed study, with a simple question and clean results, that adds to this growing body of knowledge.

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A number of factors, both maternal and perinatal, seem to be associated with autism spectrum disorder and warrant further investigation.

Background: Autism is a complicated condition with a host of potential associations, both genetic and environmental. The existence of twin and sibling concordance suggests a familial disposition, but incomplete concordance also means that there are likely outside factors as well. Although a number of factors have been associated with autism, no one factor has been shown to have a positive association consistently. These differences may be due, in part, to differences in study methodology.

Objective: To examine risk factors for autism spectrum disorders using rigorous methodologies and broad ascertainment.

Participants/Methods: The study population was 8-year-old children born in 1994 and living at 1 of the 3 most populous counties in the state of Utah; these 3 counties house about two thirds of the total population of the state. As part of the Autism and Developmental Disabilities Monitoring Network, multiple source screening occurred at all public schools and all major health sites in the area. Trained abstractors went to each site and reviewed records to look for autism spectrum disorder triggers that could lead to further investigation. Records were requested on 4549 children; 532 had an autism spectrum disorder trigger and 196 met criteria for diagnosis. These children were matched to 100 controls each on gender and birth year. Multivariate logistic regression was performed to determine associations with prenatal, perinatal, and neonatal factors.

Results: A number of factors were found to be significantly associated with a greater risk of autism spectrum disorder. These included having a mother aged >35 years (odds ratio [OR], 1.7) and being a first-born child (OR, 1.8). Children who presented in a breech position were also at higher risk (OR, 2.1) as were those born by cesarean section (OR, 1.7); after controlling for breech position as a cause of cesarean section, the association with cesarean section disappeared. Neonatal factors were not found to be associated with an increased risk of developing autism spectrum disorder.

Conclusions: A number of factors, both maternal and perinatal, seem to be associated with autism spectrum disorder and warrant further investigation. (1) Prenatal factors such as advanced maternal age and first in birth order seem to be associated with a higher risk of autism spectrum disorder. (2) Perinatal risk factors such as breech presentation also have a higher risk of autism. (3) Neonatal risk factors were not found to be associated with a higher risk.

Reviewer's Comments: With so much time spent perseverating on the vaccine issue, it is nice to see a study looking for factors with scientific evidence behind them. More work is needed to determine causes of autism and what might be done to treat it.

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Do Children Outgrow Egg Allergies, Regardless of Whether They Avoid Eggs?

Dietary Advice, Dietary Adherence and the Acquisition of Tolerance in Egg-Allergic Children: A 5-Yr Follow-Up.

Allen CW, Kemp AS, Campbell DE:
Pediatr Allergy Immunol; 20 (May): 213-218

Adherence to dietary egg avoidance is not associated with resolution of IgE-mediated egg allergy in children.

Background: IgE-mediated egg allergy is among the 3 most common childhood food allergies, with an estimated prevalence of 1% to 2% among 2-year-old infants. Current treatment recommendations include egg allergen avoidance. However, there is little evidence to support these recommendations, and it is unknown how strictly parents adhere to them.

Objective: To determine the type of advice given to parents for treatment of their children's egg allergy, how closely parents adhere to this advice, and whether adherence is related to allergy resolution.

Participants/Methods: Parents of children diagnosed with IgE-mediated egg allergy and seen in a tertiary pediatric allergy clinic received mailed questionnaires. Parents were asked what type of recommendations they received regarding management of their child's allergy and how adherent they had been to these recommendations. Information was also available for those children (about half) who had undergone an oral challenge to determine whether they had outgrown their allergy.

Results: 167 of 199 parents completed the questionnaire. Of these, 84 children had undergone an in-hospital oral egg challenge (27 positive, 57 negative). Average age of children was 6.6 years, and it had been about 5.5 years since their first reaction. Many children in the study group had coexistent food allergies (83%), concurrent asthma (56%), and atopic dermatitis (69%). Although most parents received advice--some of which was conflicting--from multiple sources (allergy specialist, dietician, pediatrician, general practitioner), the source was not associated with adherence. Moreover, advice on the degree of egg avoidance was unrelated to the severity of the child's initial reaction. Oftentimes, parents did not follow these recommendations: 32% did not avoid egg all the time, 80% did not avoid cooked egg, and 65% did not avoid traces of egg. There was no association between severity of the initial reaction to egg and parents' adherence to recommendations. Importantly, neither the severity of the initial reaction to egg nor parents' adherence to egg avoidance recommendations was associated with whether or not children outgrew their egg allergy.

Conclusions: Parents of children with egg allergy often did not adhere to recommendations to avoid giving their children eggs. However, children outgrew egg allergy even in the face of this non-adherence.

Reviewer's Comments: This article reminds us that we need to be clear with parents about the limits of our understanding about the efficacy of our treatments for food allergies. Food allergies in a child create increased burden and a high level of stress for parents. It is not easy for parents to consistently eliminate some allergens from a child's diet, and failure to follow strict adherence can cause guilt for parents who believe their lapses to be responsible for persistence of their child's allergy.

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Steps for Reducing Admissions for Dehydration in Exclusively Breastfed Infants

A Nationwide Study on Hospital Admissions Due to Dehydration in Exclusively Breastfed Infants in the Netherlands: Its Incidence, Clinical Characteristics, Treatment and Outcome.

Pelleboer RAA, Bontemps STH, et al:
Acta Paediatr; 98 (May): 807-811

In this study from the Netherlands, the incidence of exclusively breastfed infants hospitalized with dehydration was low, with recommendations for home breast pumps, early weighing, and appropriate lactation support advised.

Objective: To determine the incidence of hospitalization of exclusively breastfed infants in the Netherlands for dehydration or undernutrition as well as evaluations and treatment.

Participants/Methods: All pediatric admissions in the Netherlands from 2003-2005 were assessed through the Dutch Paediatric Surveillance Unit, which is a database involving all practicing Dutch pediatricians. In the time period studied, all admissions for infants aged <3 months due to dehydration or failure to thrive were monitored. Severe dehydration was defined as weight loss >10% compared to birth weight. Clinical features studied included signs and symptoms, lactation-related interventions, in-hospital hydration treatments (eg, nasogastric tube, IV drip), and continuation of breastfeeding at discharge.

Results: 158 cases of exclusively breastfed infants were included in the study. Most (106 of 158 [67%]) were aged <11 days. Median weight loss was 9.3%. Median age was 5 days at admission. Of infants, 34% had >10% weight loss; 4% had a serum sodium >=150 mmol/L, but only 12% of all cases had serum sodium measurements obtained. The most common clinical presentations were lethargy, jaundice, or clinical dehydration (11% to 25%). In 3%, seizures with hypoglycemia or shock were the presenting problems. Insufficient volume intake was noted in 61%. In only 31% was a breast pump available at home compared with in-hospital availability of breast pumps at 82% and lactation consultants at 73%. About two thirds were offered formula as treatment, with 30% receiving fluids by nasogastric drip. Only 22% received IV fluids. All patients fully recovered, with admissions lasting in most cases up to 3 days. About one third continued to be exclusively breastfed at discharge. The incidence of hospitalization for dehydration for exclusively breastfed newborns in the Netherlands was 58 per 100,000 per year and, for severe dehydration, 20 per 100,000 per year.

Conclusions: Hospitalization for severe dehydration for young exclusively breastfed infants in the Netherlands is low. The authors recommend extended use of breast pumps at home and more extensive screening of serum sodium and glucose as part of the evaluation process.

Reviewer's Comments: It is striking how much less interventional the evaluations and treatments are in the Netherlands compared with the U.S. Electrolyte measurements are relatively uncommon, as is IV hydration. It would be hard to imagine an infant being admitted to a U.S. hospital without phlebotomists having a field day. The authors do argue for a more aggressive approach in their country. However, the statement that "all fully recovered" is a powerful finding. As for the U.S., the American Academy of Pediatrics' recommendation of reweighing between 72 and 96 hours after birth remains an extremely important process to minimize the likelihood of an infant becoming severely dehydrated.

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Are 2 LAIV Doses Necessary in Previously Unvaccinated Children?

Efficacy and Safety of 1 and 2 Doses of Live Attenuated Influenza Vaccine in Vaccine-Naive Children.


One dose of live attenuated influenza vaccine provides clinically significant protection against influenza in young children previously unvaccinated against influenza; 2 doses provides additional protection.

Objective: (1) To assess the efficacy, immunogenicity, and safety of 1- and 2-dose regimens of live attenuated influenza vaccine (LAIV) in children aged 6 to 36 months and (2) to investigate whether vaccine excipients such as egg protein or hydrolyzed gelatin contribute to the vaccine's adverse effects.

Participants/Methods: Children aged 6 to <36 months were enrolled during the 2001-2002 influenza seasons in South Africa, Brazil, and Argentina. Subjects were randomized to 1 of 4 treatment arms: (1) LAIV and LAIV in year 1 then LAIV in year 2; (2) LAIV and placebo in year 1 and LAIV in year 2; (3) excipient placebo and excipient placebo in year 1 and saline placebo in year 2; and (4) saline placebo and saline placebo in year 1 and saline placebo in year 2. Nasal swabs were obtained to test for influenza within 4 days of onset of flu-like symptoms. Vaccine efficacy was defined in terms of incidence rates.

Results: 3200 children were enrolled. During year 1, the vaccine's efficacy against strains antigenically similar to those in the vaccine was 73.5% for the LAIV-LAIV group and 57.7% for the LAIV-placebo group. In year 2, the efficacy rate for the LAIV-LAIV-LAIV group was 73.6% and for the LAIV-placebo-LAIV group was 65.2%. The difference between these 2 groups' efficacy rates was not significantly significant. The efficacy rate in year 2 for the LAIV-LAIV-placebo group was 57% higher than the placebo-placebo-placebo group. Adverse effects were similar among all 4 treatment arms (26.7% to 29.1%). The most frequently reported adverse events were fever, upper respiratory infection, rhinitis, and coughing. Serious adverse events were reported in 5.0% of LAIV-LAIV recipients, 3.8% of LAIV-placebo recipients, 3.4% of excipient placebo recipients, and 4.1% of saline-placebo recipients. Those serious events were most frequently bronchiolitis and pneumonia.

Conclusions: The LAIV in children aged 6 to <36 month was fairly effective in year 1 after 1 dose (57.7%) but even more effective after 2 doses (73.5%). In those who received LAIV in year 2, there was no difference in efficacy between those who received 2 LAIVs in the previous year versus those who received just 1 the previous year. Adverse effects were similar among placebo and treatment groups, and there was no difference between the excipient placebo and the saline placebo.

Reviewer's Comments: The efficacy for LAIV in children aged 6 to <36 months demonstrated in this study is encouraging, but there are a few caveats. First, this study was supported financially by LAIV's manufacturer, MedImmune. Second, LAIV is currently indicated only in children aged >24 months or older, not down to 6 months, as this study included.

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Rib, Sternal, Scapular Fractures--Consider Child Abuse!

Bullock DP, Koval KJ, et al:
J Pediatr Orthop; 29 (April/May): 231-237

In a study of a large pediatric inpatient database, fractures most likely to be related to a diagnosis of child abuse involved the rib, sternum, or scapula.

**Objective:** To identify characteristics of physical abuse cases that raise suspicion for child abuse, particularly from an orthopedic perspective.

**Participants/Methods:** The authors used the 1997, 2000, and 2003 Kids' Inpatient Databases, which approximate a nationally representative sample. All discharges in patients aged <18 years in which a physical injury was denoted were eligible for study. Specific cases were then identified by ICD-9 codes for child abuse or accidental injury. Risk factors were identified by patient demographics, location and setting, timing of admission, and nature of sustained injuries.

**Results:** Of >6.2 million discharges in the databases, 10.66% had a type of physical injury identified. Of these, 1.74% (11,554) involved child abuse. The strongest demographic predictor of child abuse was age <1 year (with an adjusted relative risk [RR] of 11.46). Other risk factors included age 1 year to <2 years (RR, 3.04) and Medicaid as a primary payer (RR, 1.99). Risk was increased for winter and weekday presentations. Fractures that had the highest adjusted RRs for coded child abuse were rib or sternum (RR, 5.34) and scapula (RR, 3.22). The only fracture in which the adjusted RR for coded child abuse was lower was pelvic fracture (RR, 0.29). Of cases of child abuse, 28% had a fracture requiring orthopedic management.

**Conclusions:** In the setting of physical injury, young age is a strong predictor of the increased likelihood of child abuse. Orthopedic management in the setting of child abuse occurs in more than one fourth of cases.

**Reviewer's Comments:** Clearly, fractures of all kinds, particularly when inconsistent with the mechanism of injury or the child's developmental abilities, should raise the suspicion of child abuse. While most pediatricians are familiar with the tibia/fibula, radius/ulna, or femur fractures as presentations involving child abuse, this study demonstrates that rib or sternal fractures have the highest likelihood of being caused by abuse.

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Higher-Dose Intranasal Steroid Spray More Effective for Allergic Rhinitis

**Efficacy and Safety of Once-Daily Fluticasone Furoate Nasal Spray in Children With Seasonal Allergic Rhinitis Treated for 2 Wk.**


Fluticasone furoate nasal spray is an effective and safe drug at 110 g in a daily nasal spray for children aged 2 to 11 years with seasonal allergies.

**Objective:** To determine the safety and efficacy of intranasal fluticasone furoate (FF) in children with seasonal allergic rhinitis.

**Design:** 2-week, randomized, double-blind placebo-controlled study.

**Participants:** Children aged 2 to 11 years with allergic rhinitis.

**Methods:** The study was conducted in 57 centers in the United States. Children who were selected had confirmed allergies to seasonal allergens via skin prick testing or blood IgE tests. Children were excluded if they had conditions such as serious medical issues, adverse effects with previous glucocorticoid usage, or had tuberculosis or psychological disorders. During this period, children were not able to take any anti-allergy or anti-rhinitis medication, unless they were aged <6 years, and this was on an as-needed basis. There were 3 groups: group 1 received 55 g of FF spray daily, group 2 received 110 g of FF spray daily, and group 3 (controls) received saline spray. There were 4 clinic visits during the 2-week study to evaluate allergy symptoms. Parents kept records of daily symptoms scores.

**Results:** There were 554 patients in total who were enrolled in the study. There were 448 children aged 6 to 11 years and 105 aged 2 to 6 years. There was equal distribution of children among the 3 groups. The 110-g FF dose group showed the greatest improvement of symptoms. The 55-g FF dose group showed some improvement, but it was not significant. The safety profile showed the drug was well tolerated, and adverse events were similar among all 3 groups. Headache was the number 1 complaint among all 3 groups. Plasma samples taken from patients at the end of the 2-week trial showed that, after 1.5 hours post dosage, there was no significant detectable amount of FF in the blood. Of those patients with quantifiable amounts of FF in the blood, the amount was <30 pg/mL, which is <3 times the lower limit of quantification.

**Conclusions:** FF intranasal spray was effective in treating seasonal allergic rhinitis at the 110-g daily dosage rate in children aged 2 to 11 years.

**Reviewer's Comments:** This study shows that the 110-g dosage of FF was both effective and safe. The 55-g dose of FF, while safe, was not effective as a sole treatment for seasonal allergic rhinitis. The safety profile showed that, in 14% of patients, there were some detectable levels of FF in the blood. The only concern is whether, over the long-term period (ie, beyond 2 weeks of treatment), there is a cumulative effect, since most patients will use a medication for >2 weeks during seasonal allergy season.

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Need for Resuscitation at Birth Predicts Risk for Cognitive Developmental Deficit

Resuscitation at Birth and Cognition at 8 Years of Age: A Cohort Study.
Odd DE, Lewis G, et al:
Lancet; 373 (May 9): 1615-1622

Mild perinatal physiologic compromise, suggested by the need for resuscitation at birth, may cause sufficient neuronal or synaptic damage to affect cognition in later childhood.

Background: It is widely believed that clinically important brain damage following a perinatal hypoxic event occurs only if there are signs of encephalopathy in the neonatal period. Mild degrees of perinatal hypoxia are much more common, but the long-term effect on cognitive function is not clear.

Objective: To investigate the effect of a perinatal hypoxic event on childhood intelligence quotient (IQ) scores.

Participants/Methods: Subjects were selected from the Avon Longitudinal Study of Parents and Children. All were products of full-term pregnancies and lived at least to age 8 years. From 11,482 infants identified, 3 groups were delineated: (1) those who were resuscitated, had no signs of encephalopathy, and required no further neonatal care, (2) those who were resuscitated and required additional care for signs of encephalopathy, and (3) those who were healthy, required no resuscitation, and had no signs of encephalopathy. Information about resuscitation efforts, including positive pressure ventilation and/or chest compressions, was obtained from maternity unit medical records. Diagnosis of encephalopathy was based on seizure activity, tone abnormality, hyperreflexia, and high-pitched cry. Cognitive function was assessed at approximately age 8 years using a modified Weschler intelligence scale for children (WISC-III). Impaired IQ was defined by a score of <80.

Results: Need for resuscitation in otherwise asymptomatic infants was associated with a low full-scale IQ score. The absolute risk for a low IQ score was 6.5% for reference group infants, 9.8% for asymptomatic resuscitated infants, and 23.1% for resuscitated infants with encephalopathy.

Conclusions: Mild perinatal physiologic compromise, suggested by the need for resuscitation at birth, may cause sufficient neuronal or synaptic damage to affect cognition in later childhood. Substantial perinatal compromise, presenting with encephalopathy, incurs an even greater risk of impaired cognition.

Reviewer's Comments: This study supports the theory of a "continuum of reproductive casualty," which proposes that severe perinatal cerebral insults may cause death or immediately apparent neurologic deficit, but that milder events may lead to more subtle defects that manifest only as the child ages. While the intention of Apgar scoring is to provide assessment only to determine need for resuscitation, parents often ascribe greater significance as a predictive device. On the contrary, Apgar scores have not been shown to predict neonatal mortality or subsequent cerebral palsy. This study, however, suggests that need for resuscitation (likely reflected by low Apgar score) may serve as an indicator of developmental risk after all.

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