Lead: devastating impact even at low levels

The relation between intelligence and blood lead levels greater than 10 µg/dL is well defined: IQ declines by 2 to 5 points with every increase of 10 to 30 µg/dL. The effect of lower lead concentrations is less certain. Investigators followed 172 children from age 6 months to 5 years, measuring IQ at ages 3 and 5 years and blood lead concentration at ages 6, 12, 18, 24, 36, and 48 months.

After accounting for 9 possible confounders, including maternal IQ and home environment, each increase of 10 µg/dL in lifetime average blood lead level was significantly associated with a 4.6-point decrease from the expected IQ scores in healthy children (P=0.004) in linear analysis. When the analysis was restricted to the 101 children whose maximum blood lead level never reached 10 µg/dL, the association between higher lead concentration and lower IQ was even stronger. In a nonlinear model, IQ declined by 7.4 points with increases in the lifetime average blood lead concentrations of up to 10 µg/dL. Beyond these lower concentrations, there were further, more gradual declines (an additional 2.5-point decrease for concentrations of 10 µg/dL to 30 µg/dL). These results were unchanged whether lead exposure was categorized as peak, concurrent with testing, or average in infancy.

Comment

As an editorialist notes, the CDC has repeatedly lowered its definition of elevated blood lead levels—it now stands at 10 µg/dL. It is gratifying that the median concentration in U.S. children has fallen almost 4-fold, from 15 µg/dL to 2 µg/dL since gasoline was unleaded. However, almost 300,000 children have lead levels above 10 µg/dL, and many more have levels above 2 µg/dL. What is the primary care physician to do? It is critical that infants receive enough iron, which reduces the gastrointestinal absorption of lead, and it remains important to measure blood lead levels in high-risk children, such as those living in houses built before 1960.

Howard Bauchner, MD
Published in Journal Watch Pediatrics and Adolescent Medicine May 9, 2003

Shigella: a new use for azithromycin?

There are numerous reports of multiresistant shigella in the developing world, and U.S. practitioners in states with large immigrant populations regularly face the problem of treating patients infected with these isolates. Because shigella is highly transmissible from a small inoculum, proper treatment is a public health priority. Options for treatment include many therapies that are effective yet not widely accepted. Investigators in Paraguay compared two such therapies for clinical efficacy and bacteriologic eradication.

Children with clinical dysentery were enrolled in the study and randomized to receive 5 days of oral azithromycin or cefixime. In children with laboratory-confirmed shigella, all isolates were sensitive to both drugs. Clinical improvement was seen at day 3 in 28% of 30 patients in the azithromycin group (93%) and in 25% of 32 patients in the cefixime group (78%). Bacteriologic eradication occurred on day 3 in 93% and 39% of children, respectively.

Comment

In this study, 5-day courses of azithromycin or cefixime for antibiotic-resistant shigella produced excellent results. Azithromycin provides an effective and familiar option for treatment; it had greater efficacy than did cefixime and had a narrower spectrum. It should be used only in cases of diarrhea known to be caused by shigella in which sensitivities demonstrate resistance to the more commonly used therapies, such as amoxicillin and TMP/SMX.

Peggy Sue Weintrub, MD
Published in Journal Watch Pediatrics and Adolescent Medicine May 9, 2003

Daily inhaled steroids benefit patients with mild asthma

The benefit of inhaled glucocorticosteroids for chronic severe asthma is well known. To examine the effect of once-daily inhaled budesonide in patients with less severe disease, researchers conducted a multicenter, placebo-controlled, randomized, double-blind trial in 7214 adults and children with mild persistent asthma (defined as reversible wheezing at least once weekly, but not daily, for less than 3 months).

The risk for a first severe asthma-related event was 44% lower in the budesonide group than in the placebo group. After 3 years, 117 of 3597 budesonide recipients had a severe attack, compared with 198 of 3568 placebo recipients (P=0.0001). Budesonide also was associated with more symptom-free days. A quarter of the placebo group and 15% of the budesonide group required systemic glucocorticoid treatment during the study. FEV1 (before and after bronchodilator treatment) was significantly greater in the budesonide group at 1 year and at 3 years, although the benefit declined with time. Reduced growth (mean difference, −0.43 cm/year) was observed in budesonide recipients aged 5 to 15 years. Differences in growth were greater after 1 year of treatment than after 3 years. One asthma death occurred in the placebo group.

Comment

Treatment with budesonide had a strikingly beneficial effect in this large group of patients with mild persistent asthma. The number of subjects and the flexibility in the use of nonprotocol asthma medications are impressive and increase the credibility of the findings. The negative effects on growth are worrisome, but were previously known and appear to diminish over time.

F. Bruder Stapleton, MD
Published in Journal Watch Pediatrics and Adolescent Medicine April 28, 2003

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Strategies to prevent medication errors in hospital patients

Each year in the U.S., more than 44,000 adult deaths are caused, at least in part, by medical errors. A similar situation exists in pediatric healthcare, and infants and children in intensive care units are especially vulnerable to lasting harm. Most medication errors involve dosage. Children present unique dosing challenges: Dosage depends on weight and age and must be calculated individually, and stock

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solutions often come in adult strengths. Building on recent studies showing that medication errors are often preventable, these investigators analyzed data from two academic medical centers to categorize the major types of medication errors in children and to identify the most effective prevention strategies.

A total of 10,778 medication orders were written for 1020 patients during the study period; 616 orders (5.7%) contained errors, which affected 320 study patients (31%); 118 patients (12%) experienced two or more errors. Most errors occurred at the order stage (77.8%), followed by the administration (12.8%) and transcription (5.8%) stages. The most common errors were in dosage (28.4%) and drug route (17.7%).

Ten prevention strategies were assessed. Three had the greatest potential to reduce error rates: (1) The presence of clinical pharmacists on the unit to monitor ordering might have prevented 58.3% of errors; (2) computerized order entry by physicians might have prevented 65.9% of errors; and (3) improved communication between physician, nurse, and pharmacist might have prevented 47.4% of errors.

Comment ▶ This study is limited by the possible underreporting of drug administration errors and the use of data from only two hospitals. Nevertheless, the results demonstrate the need for system changes if we hope to prevent medication errors.

Harlan P. Gephart, MD
Published in Journal Watch Pediatrics and Adolescent Medicine May 9, 2003

Early drinking: where does it lead?
▶ Underage drinking continues to be a problem in the U.S., and the long-term consequences are largely unknown. In this longitudinal study, investigators first surveyed 6338 seventh graders from 30 California and Oregon schools in 1985, and then reinterviewed 4265 (67%) of these students in twelfth grade and 3369 (53%) at age 23.

Initially, 23% of adolescents were classified as nondrinkers (never had a drink), 46% as experimenters (drank <3 times in the past year and not in the past month), and 31% as drinkers (drank 3 times in the past year or drank in the past month). Compared with nondrinkers, self-reported experimenters or drinkers were significantly more likely to report substance use, academic or employment problems, and other problems (e.g., smoking, criminal behavior) both in grade 12 and at age 23. In a multivariate analysis, grade 7 drinking status was significantly associated with the number of problems in grade 12 and at age 23.

Comment ▶ Although the authors relied on self-reported drinking and did not attempt to identify which early experimenters and drinkers developed later problems, these data suggest that early drinking is associated with future risky behavior. Although it is possible to identify adolescents who drink, successful intervention is much more complicated.

Howard Bauchner, MD
Published in Journal Watch May 16, 2003

Can intensive glycemic control limit atherosclerosis progression in type 1 diabetes?
▶ In the landmark Diabetes Control and Complications Trial (DCCT), patients with type 1 diabetes who were randomized to receive intensive glycemic control had a lower incidence of microvascular complications, but not of adverse cardiovascular events, compared with those who were randomized to receive conventional glycemic control. However, all patients were younger than 40 upon enrollment, and mean follow-up was only 6.5 years.

DCCT participants were invited to undergo carotid ultrasonography at 1 and 6 years after the trial to determine the subsequent progression of carotid intima-media thickness, an index of atherosclerosis. From year 1 to year 6, combined intima-media thickness (a sum of measurements from the common and internal carotid arteries) regressed by an average of 0.155 mm among 618 intensively treated patients and progressed by an average of 0.007 mm among 611 conventionally treated patients (a significant difference between groups). The between-groups difference in glycemic control during the DCCT (mean HbA1c, 7.2% vs. 9.0%, respectively) gradually disappeared by the sixth post-DCCT year (7.9% vs. 8.0%).

Comment ▶ In clinical trials, it has been easier to show the effect of glycemic control on microvascular disease than on macrovascular disease. The present results suggest that intensive glycemic control might limit progression of macrovascular disease in type 1 diabetes but that this effect might take years to see. We need even longer follow-up to assess whether changes in carotid intima-media thickness are associated with reductions in adverse clinical events.

Allan S. Brett, MD
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