pared to daily energy intake in a controlled setting,[1] and we observed a similar threefold difference among children in their everyday environment.[2] Dr Goldman points out that averaging individual measurements reduces the variability of the mean. It was for this reason that we used a statistical test to compare the observed coefficient of variation for the day's energy intake to the expected coefficient of variation for the day. Specifically, we compared the observed coefficient of variation to that which would be expected if there were no covariance between eating occasions. This procedure indicated that some, but not all, of the reduction in variability was due to the statistical phenomenon described by Dr Goldman. Birch et al did not test the observed coefficient of variation for the day's intake against a null hypothesis, but they did observe that energy intakes at consecutive meals were inversely correlated, ie, that children consuming higher than their own average intake at one eating occasion were likely to consume less energy than their own average at the next eating occasion.

Dr Goldman is also concerned that the statistical significance of our results is attributable to the inclusion of spurious zero intakes. The expected value of the coefficient of variation of the day's caloric intake under the null hypothesis of independence was 29.0% when computed using only occasions at which non-zero energy intake was reported, which indeed is not significantly different ($t = 1.8$, $df = 180$, $P = .76$) from the observed value of 30.3% (see Table 1[2,p545]). However, we believe that excluding all zero intake occasions from analysis distorts reality substantially. Surely some eating occasions at which zero energy intake was reported are real.

In this context we considered two compromise solutions. In the first, all snacks were combined and the coefficient of variation for the day was based on four eating occasions: breakfast, lunch, dinner, and snacks for the 181 children. The expected value under independence was 32.3%, which is significantly higher than the observed value of 30.3%, which remained unchanged ($t = -3.3$, $df = 180$, $P = .001$). In the second, children reported to consume no energy at lunches in year 1 ($n = 1$) or year 3 ($n = 59$) were excluded. This approach excluded children who ate lunch at school but whose parents reported no intake, as well as children who truly did not eat lunch on the days of the recalls. There is no way to distinguish these two groups. In this analysis, the expected value of the coefficient of variation for the day under independence computed using six eating occasions (breakfast, lunch, dinner, and three separate snacks) for the 121 remaining children was 32.6%, which is significantly greater than the observed value of 29.4% ($t = -4.0$, $df = 120$, $P < .001$). The expected value under independence computed with snacks combined was 31.9%, also significantly greater than the observed value ($t = -3.5$, $df = 120$, $P = .001$). In each case there was less observed variability in daily caloric intake than would be expected under the assumption of independence.

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REFERENCES

1. Birch LL, Johnson SL, Andresen G, et al. Variability of young children's energy intake. *New Engl J Med*. 1991;324:232–235.
2. Shea S, Stein AD, Basch CE, Contento IR, Zybert P. Self-regulation of energy intake in young children in their everyday environment. *Pediatrics*. 1992;90:542–546.

Preventing Lead Poisoning in Kids: A Win-Win Opportunity

To the Editor.—

For many, it is hard to believe that small amounts of lead pose a risk to children. In the February issue of *Pediatrics*, Dr Edgar Schoen cautioned physicians that the recent national focus on lead is overstated.[1] Although Dr Schoen is correct that early lead studies were inadequately designed, he ignores later research which is well-designed and clearly implicates lead. In doing so, he seriously underestimates the hidden cost to our society of this pervasive toxin.

Several recent studies have indicated that low blood levels of lead (10 to 25 µg/dL) can cause a persistent, dose-related decrease in a child's IQ (three to six points) or motor development. These projects followed children from birth and were designed to weed out the effect of lead from confounding variables. They either rigorously controlled for interfering factors (eg, income, maternal IQ) or neutralized their influence by studying homogeneous populations.

The three most important of these reports are (1) a study of 245 Cincinnati 6-year-olds that found a dose-related decrease in motor development with lead levels 7 to 20 µg/dL[2]; (2) a study of 494 Australian 7-year-olds that revealed a 5-point decrease in IQ coincident with an increase in their lead levels, as toddlers, from 10 to 30 µg/dL[3]; and (3) a study of 148 Massachusetts 11-year-olds who lost 6 IQ points with each 10 mcg/dL increase in blood lead level experienced at 2 years of age.[4] A dose-response curve was demonstrated even at levels below 10 µg/dL. These observations have been confirmed in non-human primates.[5] Finally, the impact of these findings is strengthened when one considers that, because of the "noise" from interobserver and test-retest variability, the bias in developmental assessments is to underestimate small but significant effects.

It is this research that persuaded the CDC to lower it's action level from 25 to 10 µg/dL, thereby increasing the number of children considered at risk to hundreds of thousands. Dr Schoen wryly refers to this as "less lead becoming more disease." Some say that a potential 3- to 6-point drop in IQ is too little to warrant screening. . .but, that's a parent's prerogative to decide. Our job is to help them to make an informed decision. The fact is that standard practice usually limits toxic exposures to less than one-tenth the dose which causes ill effects. Certainly, if a bilirubin of 20 mg/dL caused a 5-point decrease in IQ it wouldn't be tolerated for a minute!

In his conclusion, Dr Schoen raises a critical question. . .Is the funding of lead abatement programs appropriate while other urgent health needs are underfunded? Yes. . .it is! Obviously, we have to use our resources wisely. We need to lobby for a less costly way to screen. However, we must not just toss needy groups into the ring to fight over funding. Our challenge is to be ingenious and fortunately, in the case of lead, we have a classic win-win opportunity.

It's obviously a win for the hundreds of thousands of children who will do better in school and have greater job opportunities. But, it's also a win for society because of lowered medical and education costs, increased taxes from higher lifetime earnings, and abatement jobs created for unemployed workers. In 1991, the government analyzed the cost of abatement vs the savings from lowered medical and education expenditures and higher lifetime wages.[6] It estimated that a lead program would save the nation about $28 billion! And that may be a low estimate. It doesn't consider other benefits such as higher tax revenues from increased earnings or decreased legal, welfare, and penal expenses.

Critics worry that the government is underestimating the cost of abatement, but technologies (eg, flexible encapsulants) are being developed that will lower costs substantially. Also, existing programs like California's $100 million weatherizing project are being redesigned to make homes more energy efficient and lead-safe. . .simultaneously.

One lesson is clear, prevention is cheaper than treatment! Our challenge today is to design creative and forward thinking solutions to keep lead and other hazards from whittling away at our most valuable resource. . .our children.

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REFERENCES

1. Schoen E. Childhood lead poisoning: definitions and priorities. *Pediatrics*. 1993;91:504–505
2. Dietrich K, Berger OG, Succop PA. Lead exposure and the motor developmental status of urban six-year-old children in the Cincinnatti prospective study. *Pediatrics*. 1993;91:301–307
3. Baghurst P, et al. Environmental exposure to lead and children's intelligence at the age of seven years. *N Engl J Med*. 1992;327:1279
4. Bellinger DC, Stiles KM, Needleman HL. Low-level lead exposure, intelligence, and academic achievement: a long term follow-up study. *Pediatrics*. 1992;90:855–861
5. Rice D. Behavioral impairment produced by developmental lead exposure: evidence from primate research. In: Needleman H, ed. *Human Lead Exposure*. Boca Raton, FL: CRC Press 1992:137–152
6. Binder S, Falk H. Strategic plan for the elimination of childhood lead poisoning. Washington, DC: US Dept. of Health and Human Services; February 1991; Appendix II:20

Helicobacter pylori in Children With Acquired Immunodeficiency Syndrome

To the Editor.—

It has been demonstrated that the presence of *Helicobacter pylori*-associated gastritis is rare in adults with acquired immunodeficiency syndrome (AIDS).[1] To investigate the prevalence of *H pylori* infection in pediatric AIDS patients, we examined 19 children, aged 1 to 14 years (mean age 5 years 11 months), of mainly central African ethnic origin. They were compared to an asymptomatic control population of comparable age (n = 52; mean age = 5 years, 10 months) and ethnic origin. Positivity for *H pylori* was assessed by means of a second generation enzyme-linked immunosorbent assay test for the detection of IgG antibodies to *H pylori* (MALAKIT® HELICOBACTER PYLORI, Biolab, Limal, Belgium). Blood samples were taken during routine blood sampling before the monthly administration of γ-globulins in the patients with AIDS and during preoperative blood analysis in the control population.

None of the AIDS-infected patients had a positive serology for *H pylori* compared to 10/52 patients (19.2%) in the control population. This difference is statistically significant ($P < .05$).

Whether these findings reflect a false negative result, due to a failure in the production of antibodies against *H pylori* in these immunodeficient children or a significantly lower prevalence of *H pylori* infection in pediatric patients with AIDS when compared to healthy children remains to be evaluated. However, despite the well-established humoral immune defect in HIV infected patients, the presence of antibodies against other frequently encountered pathogens can be detected in these children.

We, therefore, postulate that the absence of antibodies against *H pylori* in our population of children with AIDS actually reflects a significantly lower prevalence of *H pylori* infection. The reason for this is not clear, but it is possible that an almost constant treatment with antibiotics in patients with AIDS may act as a preventive factor against *H pylori* infection in these patients.

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REFERENCE

1. Edwards PD, Carrick J, Turner J, Lee A, Mitchell H, Cooper DA. *Helicobacter pylori*-associated gastritis is rare in AIDS: antibiotic effect or a consequence of immunodeficiency? *Am J Gastroenterol*. 1991;86:1761–1764

Which Is the Most Appropriate Dosage of Liposomal Amphotericin-B (AmBisome) for the Treatment of Fungal Infections in Infants of Very Low Birth Weight?

To the Editor.—

Lackner et al[1] report on the excellent efficacy and lack of toxicity of 1 to 5 mg/kg per day of liposomal Amphotericin-B (AmBisome) administered to two infants of very low birth weight with disseminated fungal infection.

We agree with the authors when they say that success in the treatment of two cases does not allow extrapolation of the same therapeutic schedule to an infants with identical multisystemic immaturity.

We would like to report two cases from our own clinical experience with distinct characteristics. They were both infants of very low birth weight, with disseminated fungal infection, in whom clinical improvement was evident after the administration of AmBisome but in lower doses than those reported by Lackner et al.[1] In one of the cases, a transitory and reversible hepatic dysfunction occurred during AmBisome treatment.

The first case refers to a premature newborn (gestational age of 31 weeks and birth weight of 960 g), who showed at the 21st day of life a clinical picture of septicemia due to *Candida albicans*, isolated from blood, urine, and central venous catheter tip.

The second case refers to a premature newborn (gestational age of 31 weeks and birth weight of 975 g), who presented at the 14th day of life a mixed infection caused by *Staphylococcus epidermidis* (isolated from blood and umbilical catheter tip) and *Candida parapsilosis* (positive cultures from urine and endotracheal tube).

The diagnosis of disseminated fungal infection was justified, because the two newborns showed persistent bradycardia, bradypnea, grey-like coloration of the skin and thrombocytopenia, despite broad-spectrum antibiotic therapy for several days for suspected bacterial sepsis. The two newborns were exposed to several risk factors associated with fungal infections: central venous catheter, parenteral nutrition (the second patient received intravenous fat emulsions), endotracheal tube, and previous broad-spectrum antibiotic therapy. In both cases, the treatment consisted of removal of central catheters and the administration of AmBisome at an initial dose of 1 mg/kg per day intravenously as a continuous infusion for 2 hours. After a week, we increased the dose of AmBisome to 1.25 mg/kg per day for another week.

Five days after initiation of treatment there was a marked clinical improvement, normalization of platelet counts in the peripheral blood, and negative blood culture in case 1. Urine culture became sterile between days 4 and 9 of therapy. No electrolyte disturbance or impairment of renal function were detected. However, during AmBisome treatment, the second patient showed significant increases in serum γ-glutamyltranspeptidase (from 6 to 125 U/L), alkaline phosphatase (from 235 to 1696 U/L), and slight increases in serum-conjugated bilirubin, alanine aminotransferase, and aspartate aminotransferase. These effects were reversible, because all values returned to within normal range 1 month after discontinuation of the drug.

These two cases reinforce the idea that liposomal Amphotericin B is effective in the treatment of very low birth weight infants with disseminated fungal infections. Several studies already have demonstrated that liposomal Amphotericin B is far less toxic than the conventional drug. In the cases presented here, several factors could contribute to neonatal cholestasis. Nevertheless, the blood chemistry disturbance followed a reasonable temporal sequence from drug administration in doses up to 1.25 mg/kg per day.

The problem consists of finding the minimal effective dose, associated with less adverse events. The prompt initiation of antifungal therapy, whether the fungal infection is confirmed or just clinically suspected, is one of the most important measures to reduce the morbidity and mortality of this disease.[2]

Until controlled studies are performed to establish the most appropriate dosage of liposomal amphotericin for the treatment of very low birth weight infants with disseminated fungal infections, we have no alternative but to find it empirically.