A growing body of clinical and experimental evidence suggests that increased lead absorption may impair subsequent behavior and learning ability in school — even in the absence of clinically recognizable symptoms of poisoning.

This book discusses the toxicologic, pharmacologic, nutritional, behavioral, familial, social and environmental factors influencing lead absorption and describes approaches to the coordinated management of each of these factors.

Brief case presentations are used extensively to illustrate the various factors which play a role in the clinical and environmental management of this condition.

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21. Some Practical Problems and Solutions in Lead Poisoning Prevention Programs: An Overview of the Conference

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Introduction

An enormous amount of information in some very good papers has been presented at this meeting. I will try to highlight those points that have the most practical impact on actual practice.

Case Finding versus Case Treatment

Dr. Lin-Fu pointed out that effective case finding is not enough; only a small percentage of children identified as at high risk of lead poisoning actually end up being treated appropriately (Chapter 1). There are at least two reasons for this. The first is an understandable reluctance on the part of the child's provider to treat an asymptomatic patient or to refer him to the university medical center for treatment. This is a problem particularly when rural cases are found and when treatment facilities are distant. The second reason is that there is often poor coordination between those responsible for case finding and those responsible for

treatment. One typical sequence might be an asymptomatic child found on screening to have a blood lead of 40 μg/100 cc. That child may be referred to a practitioner with little more information than the blood lead value, and the practitioner may differ from the health department in the aggressiveness with which he deals with that child. Responsibility for follow-up after referral tends to get blurred, and ultimate disposition may depend more on the curiosity of the parents about the abnormal test than on the adequacy of the treatment. This type of situation is avoided if good, effective communication takes place between referring agencies and practitioners. The goals of both are really the same, prevention of lead poisoning, but agreement on tactics and responsibilities is necessary. Once lines of communication are open, they need to be kept open, so that if questions arise, such as those regarding the latest guidelines and the identification of a good secondary referral center or resource person, they can be answered. The important point is that the referral process is one of the most vulnerable in terms of loss to follow-up and that good communication can ameliorate this problem.

Toxicity and Dose Response

Dr. Hammond (Chapter 2) showed the curvilinear relationship between external dose of lead and blood lead level, and pointed out that the curve gets less steep as it ascends. This offers some reassurance in cases of high exposure. However, the steep early part of the curve implies good absorption at low doses and consequently ubiquitous, if low, blood lead levels.

Dr. Goyer (Chapter 3) mentioned the wide variety of tests that are abnormal in lead intoxication. This is a reflection of the various toxicities of the metal and of the toxicologist's interest in measuring them. However, the availability of these tests does not mean they have a place in routine screening, treatment and follow-up. In fact, their inconstant relation to one another probably means they should be avoided. Effective screening and treatment can be done with free erythrocyte protoporphyrin (FEP), zinc protoporphyrin (ZPP), blood lead and urine lead; other tests should be left to the researcher. Dr. Goyer's other point was the susceptibility of the male gamete to lead. Remember that reproduction is a cycle, starting arbitrarily with the ability of adults to conceive at will, through gestation of normal term offspring, successful lactation, lack of childhood morbidity and mortality and ultimately successful reproduction by the offspring. Lead interferes with virtually all of these steps. It produces oligospermia and teratospermia (Lancranjan et al., 1975) and spontaneous abortion (Nogaki, 1958) in adults, crosses the placenta and intoxicates the fetus (Angle and McIntire, 1964) and, of course, produces childhood morbidity and mortality. The late effects of lead

intoxication on subsequent fertility have not yet been studied. However, some of the children followed in lead poisoning programs are now in their reproductive years and research on their reproductive capacity has yet to be done. I think it biologically plausible that some effects may be seen, but as yet we have no data.

"Critical Effects" and Clinical Disease

Dr. Chisolm (Chapter 18) spoke of critical effects and this concept needs clarification. First, a critical effect is not necessarily a clinical endpoint. It is an effect sought by the toxicologist in his search for points on the dose/response curve. The most obvious of such points is the LD-50, the dose at which half the experimental animals die. For lead, a number of responses have been shown, e.g., death, anemia, protoporphyrinemia, coproporphyrinuria and inhibition of the enzyme amino levulenate dehydratase (ALA-D). The "critical" effect is the one whose dose/response curve begins closest to the origin, i.e., occurs at the lowest dose. For lead, the current critical effect is inhibition of heme synthesis in erythroid cells in the bone marrow, as reflected by elevation of erythrocyte protoporphyrin. Regulators use critical effects as a basis for measures such as allowable levels and thus a great deal of attention is paid to whether a given phenomenon is or is not a critical effect. A critical effect need not be a symptom, sign or clinically definable illness. It simply needs to be a dose-related outcome showing that biologically significant exposure has taken place. The confusion arises when physicians are asked to treat patients whose sole manifestation of exposure is the critical effect, i.e., an elevation of FEP or ZPP accompanied by a high blood lead. In such cases, we are not just treating a laboratory abnormality, we are preventing the occurrence of encephalopathy and its sequellae in a child at high risk and are alerted to the fact that the child's environment contains too much lead and needs to be modified. This point needs emphasis, for it will help maintain good communication between case finders and providers.

Critical effects are thus signals of untoward exposure, but why is a central nervous system (CNS) critical effect emphasized? There is strong clinical suspicion that lead is active on the CNS at doses that do not produce encephalopathy. In order to evaluate such toxicity, however, we are currently forced to use time consuming, expensive methods such as intelligence testing or teacher/parent evaluations of behavior. Studies using such endpoints are always controversial and demand extraordinary investigator commitment, funds, time and method development. A biochemical marker of CNS injury would ease enormously the problems of interpretation and feasibility of study. In addition, if such a marker were a critical effect, i.e., if it responded in a dose-related fashion at a lower level than heme synthesis, then it could become the new focus of regulation.

Thus Dr. Chisolm's work (see p. 211) with homovanillic acid and vanillyl mandelic acid excretion in mild lead intoxication is both exciting and promising.

Dr. Chisolm made another point that deserves emphasis. Of all current tests available, FEP or ZPP is most useful for case finding or screening and blood lead most useful for confirmation and follow-up. This simple scheme is the most interpretable and is practical and productive even in middle class private practice (Dine, 1979).

Pregnancy Outcome and the IQ/Behavior Issue

Although not addressed specifically in a formal paper, the issue of lead and pregnancy came up often enough to deserve attention. The following recommendations seem reasonable, although they may not represent the consensus of the faculty. First, prenatal care should include an occupational history from both parents and also from any adults who come into the house. "Fouling the nest," Dr. Chisolm's term for occupational chemicals brought home on work clothes or other fomites (Chisolm, 1978), is a well described source of chemical intoxication of children. Second, habitual spontaneous abortion, or even a first spontaneous abortion, should call for an occupational history, and perhaps a ZPP, FEP or blood lead if exposure cannot be ruled out. Again, both parents should be questioned. The third issue is really more a question than a recommendation. When is the appropriate time to educate parents about environmental and occupational hazards to their children? At some point, parents should be told about the necessity of occupational hygiene, about paint hazards and about other environmental problems in the same way that they are informed about prevention of poisoning. Children are more susceptible to chemical intoxication than adults, so the absence of illness in the parent is not proof that excess exposure to the child is not taking place through work clothes, tools, paint or straightforward exposure while in utero or lactating. I suggest prenatal visits as the appropriate time to talk about this.

There was also considerable discussion about the significance of the relatively small changes in intelligence quotient (IQ) related to lead burden, reported by Needlemen et al. (1979). Specifically, the discussion centered on whether more frankly retarded children would be found because of this kind of exposure. There are three salient points here. First, the severe mental retardation following lead encephalopathy is very likely due to a mixture of the toxic effect of lead and the nonspecific aftermath of any CNS disaster, and no one proposes that we simply extrapolate arithmetically down the level/response curve to arrive at the effects of low levels. Point two, however, is that any agent that shifts a population IQ mean downward by an arbitrary amount will perforce increase the number in the population found below any specific cutoff point, if the simplistic assumption is

made that the distribution remains similarly shaped. Thus, if the distribution shifts three points, a greater number of children will now be below 70, or 60, or whatever criterion. The third point is that this is a population-based epidemiologic phenomenon, not a patient-based clinical one. Dr. Graef (Chapter 16) noted this when he spoke of the inadvisability of the "three day admission for full developmental work up" of the individual child. This will not be productive in terms of identifying lead-attributable toxicity in the individual, nor will it aid in the identification of a paint, fouling of the nest, or an industrial hazard. Whatever the effect of low doses of lead on CNS function, they are more a regulatory, public health and epidemiologic concern than they are clear-cut causes of obvious clinical dysfunction.

Follow Up: Prospective Study and Clinical Problems

One seemingly attractive proposition to aid understanding of the low dose problem would be to initiate a very large, long term prospective study, with high follow-up rates and measurement of CNS function in various ways. In addition to the usual considerations of cost, time and commitment, however, there is the additional difficulty of the altered management such a group of children would receive. Since lead levels would be known, environmental intervention would have to begin at blood leads 30 μg/100 cc or so. Although the behavior of this group would be of interest, there are still many children in the 30 to 60 μg/100 cc range to whom such data would be relatively inapplicable, especially if negative. There is, I believe, a way out of this dilemma, a validated CNS effect marker. Thus I return again to the importance of the work of Dr. Chisolm and others. Another way would be to take children whose performance had been assessed and to look at lead in shed teeth. This is being done with some of the children who participated in the Perinatal Collaborative Project.

Dr. Chisolm presented an atypical case of a child with an initially low blood lead who turned out to be at risk. This case would not have been evaluated or treated properly if rigid application of Center for Disease Control (CDC) guidelines (CDC, 1978) had been used. Although rigid application of any set of guidelines is not recommended, the CDC guidelines for case finding and follow-up will work almost all the time. They do, of course, need a supplemental dose of clinical judgement and curiosity. This case also brings out a phenomenon known to any practicing epidemiologist. There is an inverse relationship between the "interestingness" of a given patient and the likelihood that he will return for routine follow-up. Considerable ingenuity is necessary to find the "interesting" patients, while those for whom everything is going routinely return unfailingly.

Thus, extra follow-up efforts are to be encouraged, for they sometimes produce surprisingly interesting results.

Dust

The issue of finger contamination with lead dust was brought out by Dr. Charney (Chapter 8). There are two parts to this problem. One is that house dust lead does relate to body burden, and the other is that house dust lead is easily recoverable from finger stick samples. This is another reason to screen with FEP or ZPP, because they are unaffected by much contamination.

Nutrition

Dr. Mahaffey's paper (Chapter 7) on the relationship of diet to susceptibility to lead is the best clinical review of a complicated subject that I have seen. It is unusually clear and should be useful to anyone concerned with this important area.

Program Management

Dr. Siker (Chapter 11) brought out the multiple interfaces that exist in any lead program, and emphasized the necessity of program coordination. This very important point was brought up before and needs emphasis again. A prime time for follow-up loss occurs when a family gets passed from one part of a program to another. Effective coordination and communication between the program parts can prevent this. Dr. Siker also mentioned that in many programs, any physician can obtain a blood lead on a child believed to be at risk. Often, however, the public health nurse is the first to identify such a child. If a list of physicians who are willing to order blood leads or protoporphyrins on such children is made available to the nurses, then the value of the blood test can become part of the child's subsequent medical evaluation. Again, this requires coordination, but it has worked well in North Carolina and deserves a trial.

The Laboratory

The laboratory is crucial in any successful program, and Dr. Mitchell showed some of the pitfalls that even experienced laboratories find (Chapter 12). The point here is that quality control, even when it is up to CDC standards, is no assurance of infallibility. There are obvious sources of variability that are beyond the control of the laboratory, i.e. sample gathering and storage, that introduce bias rather than sampling variation, and thus cannot be dealt with by the lab. A partial solution to this problem, again involving program coordination, is to track samples from collection through arrival in the lab. If a record is kept, the "funny" value attributable to 4 hr of sun exposure in a bus station can at least be suspected. The laboratory should have some person to whom to report suspicious values rather than sending them blithely on to the provider or local health department.

Even when everything works well, recall that any screening program, including lead programs, generates about 50% false positive results on the initial round (Rogan and Gladen, 1978). This has to do with test characteristics as determined by the cutoff value for abnormality and the actual prevalence of the sought after condition. Families should be told that a single positive result does not imply disease in the child and that confirmation will be necessary. This will prevent subsequent confusion and anxiety on the part of families and physicians.

Hazard Abatement: Paint and Other Sources

Hazard abatement is another basic necessity of any program. Good training programs are available and those who have attended them have found them very useful. No child should be returned to a leaded environment, and abatement procedures are the only realistic way that this problem can be avoided. The presentation of the unusual hazard abatement problems in the North Carolina battery factory episode points out that innovation is sometimes necessary. The problem there was that the lead dust brought home by the mostly female workers had contaminated the rugs and cars and house dust and could not be gotten rid of by usual means. That episode is one of three reported outbreaks of undue lead absorption in the children of workers where the source was soiled work clothes (Baker et al., 1977; Morbidity and Mortality Weekly Reports, 1977; Dolcourt et al., 1978). It is the only one in which the workers were women, and again points out the necessity of a good occupational history from both parents. Dr. Chisolm pointed out the wide variety of occupations that involve potential exposure to lead. One that he mentioned, ship breaking, also involves exposure to asbestos.

In general, the occupational exposures of parents should be explored and attention paid to other chemicals besides lead. Another type of history that is going to become necessary is an ''energy'' history. Burning battery cases for hot starter fuel is having a resurgence in North Carolina and perhaps other places as well.

Treatment and the Continuing Paint Problem

Dr. Graef's description of his treatment program (Chapter 16) underlines the fact that treatment is not all that difficult and that consultation and advice are available on a state and sometimes a regional level. The lack of a specialist in lead intoxication is not a reason for ignoring or not seeking out a lead hazard.

Multiple sources of lead for children, i.e., pencils, batteries, work clothes, dustfall, have been mentioned in these papers. Dr. Houk reminded us that the main source of lead is still lead-based paint (Chapter 19). Lead paint poisoning is still a problem, although fewer cases are reported each year. The resultant lack of publicity should not deter further efforts to prevent the disease entirely, since it is one of the few where such efforts undoubtedly pay off.

Summary and a Case Presentation

In summary, there are four parts to lead screening programs: case finding, abatement, laboratory work and treatment. However excellent the individual parts are, they will not work unless coordinated effectively. Children are more susceptible to lead than adults. This is also true of other environmental agents. Thus, occupational exposure histories and education of parents should take place and should not be limited to lead. Finally, research should continue into areas such as the subclinical effects of low lead levels and factors determining susceptibility. However, there is enough knowledge now to prevent the majority of lead-related illness if such knowledge is applied effectively.

Finally, here is a brief case presentation (Osterud et al., 1973). A 27-yr-old male ''hippie'' presented himself to the emergency room with weakness, leg cramps, tarry stools and abdominal pain. He was given an appointment for gastrointestinal x-rays and sent out. He returned 2 days later, having lost a kilogram of weight, and was sent out again because his x-rays had not yet been done. He returned the next day for continued abdominal pain and vomiting. The medical technologist noted basophilic stippling on the blood smear. The patient was found to be lead intoxicated and was successfully chelated. His plumbism

was due to plum wine, homemade in a chipping enamel bathtub. He had drunk 50 gallons of wine (containing about 3.3 mg of lead) over his 5-mo stay at the Green Parrot Goat Farm, a commune of twelve humans, four dogs, four turkeys, two geese, twenty-nine chickens, eleven goats and one parrot. No one else had an elevated blood lead or comparable exposure. The mixed benefits of technologic advance were recognized, and the next year's wine was made in the stainless steel milk cooler.

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