Lead Poisoning in Children

Foreword

As pointed out by Jacobziner in this symposium, lead intoxication in children in the United States is largely a disease of the slum areas of the big cities, where housing is old and deteriorated.

Residents of such areas are often largely Negro, with some Puerto Ricans and a scattering of Caucasian children. Poverty with its problems of serious crowding, high rates of unemployment, large families, broken homes, absent fathers and mothers during working hours—all contribute to lack of supervision of small children and failure to protect them from opportunity for environmental exposure.

The continuing stream of migrants to cities in the North as a consequence of social and economic pressures in the South and in Puerto Rico continues to flood these old neighborhoods. New public housing, safe from the standpoint of risk of lead exposure, cannot be developed fast enough to keep pace with the demand. Since slum clearance and public housing programs are expensive, and slow at best, complete removal of sources of exposure to lead still lies in the far future.

With present population situations, public health programs as described by Jacobziner require large sums of money and large numbers of trained people. Case finding is tedious and in large cities the case loads of social agencies are huge. Necessary laboratory facilities, particularly for quantitative lead determinations, are not widely available. Educational programs geared both to the general public and to the medical profession are onerous in themselves. Cooperation from landlords in the correction of housing violations is not everywhere obtainable.

Nevertheless, every city must make extreme efforts to introduce and sustain preventive programs. Lead intoxication responds well to therapy if detected early, before the onset of encephalopathy. The economic cost to our communities from the brain damage of plumbism is infinitely greater than the expenditures for case finding and prophylaxis. When this is fully realized over the country, the same accomplishments of New York and some other cities will become more general. This is the most immediate approach to the eradication of lead intoxication in children.

Speaking very generally, the permanent solutions to this problem are linked closely with the profound sociologic problems of modern living; they will fade away slowly with the reforms which affect profoundly the many ramifications of our culture.—*Joseph Greengard, M.D., Director, Division of Pediatrics, Cook County Hospital, Chicago, Illinois.*

Lead Poisoning in Childhood:

Signs, Symptoms, Current Therapy, Clinical Expressions

JOSEPH GREENGARD, M.D.*

From the Cook County Children's Hospital and the Hektoen Research Institute, Chicago, Illinois

When detected early, before the onset of encephalopathy, lead intoxication subsides rapidly under therapy. Here for the pediatrician is an outline of the problems inherent in early detection, along with summaries of the therapeutic measures being used at one center for the early case as well as the case with the dread complication of lead encephalopathy.

THE number of deaths from all poisonings in United States children is approximately 1,500 per year. Nonfatal cases are estimated to be 100 to 150 times that number.[1] A major source of poisoning is lead, accounting for many deaths and much residual brain damage. Though largely a phenomenon of large cities, lead intoxication can and does occur in rural areas.

This discussion describes the manifestations of lead poisoning in young children, and more specifically, in toddlers between 18 months and five years of age. The central nervous system in this age group is particularly susceptible to the effects of this poison and the development of encephalopathy.

Lead poisoning is linked closely with poverty and poor housing. The actual incidence in big cities seems to be increasing in spite of the fact that physicians and public health officials have been aware of its presence for many years and have devoted much attention to its management. Progress has been made in treatment, and, undoubtedly, many cases of acute encephalopathy have been avoided by early recognition; there is still, however, no therapy which is truly effective. Early symptoms of this syndrome are so vague and nonspecific that the patient often fails to seek medical aid early, and the physician, when he is finally consulted, sometimes fails to consider lead poisoning as a possibility.

* Director, Division of Pediatrics, Cook County Hospital, Clinical Professor of Pediatrics, University of Illinois, College of Medicine, Senior Attending Pediatrician, Michael Reese Hospital, Chicago, Illinois. Address: 700 South Wood Street, Chicago, Illinois 60612.

Etiology of Lead Poisoning

Pica. The usual portal of entry is by ingestion. This involves a consideration of pica, defined as an abnormal craving for non-nutritious or even harmful substances such as clay, plaster, ashes, charcoal and the like. Perhaps the most enlightening description of this interesting condition is that of Marcia Cooper,[2] based on a study of 784 Baltimore children, 21.9 per cent of whom had pica. A predominance of children with the habit were Negro children, and in most cases the habit was established in the second year of life and disappeared by the fourth or fifth year.

The most common form of pica was the eating of dirt, although plaster, ashes, and paint were also consumed. Cooper stresses that this is not merely random mouthing to satisfy oral curiosity among her study children; it is a persistent and purposeful pursuit of the substance. With respect to plaster, she states that those with a craving for it dug it from the walls with great determination. This description certainly fits those children in my experience with lead intoxication whose source of lead was wall plaster. There is still no good explanation for the insatiable appetite some individuals have for the substances concerned in pica, though the association with anemia and the conjecture that pica may represent iron hunger has been suggested.

Source of Lead. An important contributory factor is poor slum housing with buildings 30 to 50 years old. Here the walls and ceilings are often in serious disrepair with cracked plaster and peel-

FIG. 1. X-ray of the abdomen in a child who has recently ingested large amounts of lead paint-containing plaster. Paint chips are clearly seen in the large bowel.

ing paint. These give ready access to the prying fingers of the child. In addition, repeated coats of high lead-containing paint have soaked into the plaster over the long years. Chrome green, chrome yellow, and white lead paints are common sources; Chisolm[8] estimates that small chips of such dried paint may contain 100 mg. or more of lead.

Kehoe[10] has calculated that 8 to 12 per cent of ingested lead is absorbed. The continued ingestion over many months results in lead intoxication. In the past the role of inhalation was important due to the popular use of old storage battery casings as fuel in heaters; this has been recently well controlled by city ordinances, though sporadic outbreaks still occur such as we experienced in December of 1959.[10]

Summer vs. Winter. Seasonal factors are of great importance in the overt manifestations of lead intoxication. Children with high increments of lead may be symptom-free during the winter and develop serious difficulty with the advent of sunny warm weather. Most patients are seen between May and October.

In other months one encounters scattered cases whose symptoms are brought on by intercurrent infection. Just why this is predominantly a summer disease is not well understood, though there is some animal experimental evidence to incriminate the role of increased heat and humidity[1] and of ultraviolet rays in summer sunlight.[23]

Symptoms and Signs

Lead intoxication usually has an insidious onset with vague complaints. Parents often note a change in their child's disposition. Instead of being active and happy, he becomes listless. Associated with this are gastro-intestinal symptoms—loss of appetite, intermittent vomiting, abdominal pain and frequent constipation. The child may also seem pale.

These symptoms and signs are not striking and, in the age group involved, may not arouse much concern. If the mother consults a physician, he too finds little on physical examination to indicate serious illness. He will frequently not pursue any special laboratory procedures unless he is by past experience alerted to the problem of plumbism. As a result, the complaints are passed off as "flu" or some digestive disorder; not infrequently, an antibiotic is given along with instructions to return if there is no improvement.

With the advent of central nervous system involvement, there may be drowsiness and the child may evidence clumsiness or definite ataxia; the latter is a common sign of lead encephalopathy. Not infrequently the seriousness of the brain involvement is not appreciated until the onset of dramatic symptoms such as severe and repeated convulsive seizures, coma, or even respiratory arrest. These last will, of course, bring the child to the hospital, but all too often with a fatal outcome. With brain involvement there may also be focal neurologic signs, though these are usually not striking. Fever is sometimes also present along with changes in cardiac rate and rhythm.

Approaches to Diagnosis

Clinical Expressions. Greenberg *et al.*[9] have described the value of a history of pica in a case finding program by the New York City Health Department. It is certainly an important clue to the diagnosis, but parents rarely volunteer this history. When in cross examination pica is uncovered, most parents seem surprised that the doctor deems it unusual.

Pallor due to anemia of the iron deficiency type is an almost constant accompaniment of lead in-

toxication in this age group. It should be given equal weight by the examining physician with pica. Its mechanism of production is still to some extent controversial. Recent experimental data seem to support its being due to two factors: (1) interference by lead with the enzymatic incorporation of iron into protoporphyrin; and (2) diminished survival time of red blood corpuscles.

Basophilic stippling of erythrocytes has long been described as a characteristic of lead poisoning. In actual practice, the percentage of children revealing this finding on ordinary blood examination with light microscopy is a relatively low 30 to 40 per cent. Experimental studies utilizing electron microscopy have revealed enlightening data on this aspect.

Bessis and Breton-Gorius [2] showed that basophilic-stippled cells contain mitochondria which are not present in normal mature mammalian erythrocytes. Pirrie [21] and McFadzean and Davis [16] showed that basophilic-stippled cells are removed from the circulation at an accelerated rate by the reticulo-endothelial system; this was demonstrated by finding that erythrocyte counts remained high in the guinea pig poisoned by lead, but previously splenectomized or subjected to reticulo-endothelial blockade by trypan blue.

As noted below, the sulfhydryl enzyme, delta aminolevulinic acid dehydrase, is partially inhibited by lead, and its substrate appears in large amounts in the urine. As a consequence the synthesis of heme from iron and protoporphyrin is interfered with to a significant degree. The presence of increased amounts of coproporphyrin III in the urine of children with lead poisoning is based on this interference with heme synthesis, and, while not specific, is an extremely important diagnostic finding and a guide to therapy as well.

Parents and physicians are obviously impressed by catastrophic symptoms such as repeated convulsions, coma, and respiratory arrest. Early symptoms of intoxication are another matter, however; the recognition of early lead encephalopathy is a challenge of great significance, since it is only in the early stages that good results may be achieved.

A high index of suspicion by the physician is an essential component. This involves an awareness of the etiologic factors noted above. Thus, any child aged one to three years living in a deprived area where deteriorated housing is prevalent, and who presents during the summer months with vague symptoms should be under suspicion for lead poisoning. If the mother volunteers a story of pica or should such a history be elicited on questioning, the possibility is even stronger.

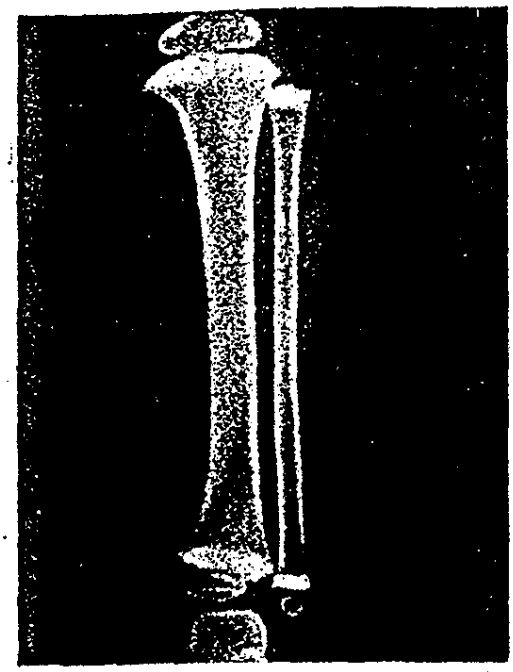

FIG. 2. Dense "lead lines" are seen in these x-rays of the upper and lower tibial and fibular metaphyses of a child with lead intoxication.

A urine specimen should be obtained as soon as possible and analyzed for coproporphyrin III. A strongly positive reaction is a high presumption of lead intoxication; the child must be hospitalized and the diagnosis pursued further.

Radiography. The x-ray is a valuable aid to presumptive diagnosis. The abdomen may show flecks of radiopaque material in the intestinal tract, occasionally in large amounts as seen in Figure 1 when lead-containing plaster has been recently ingested. The bones may reveal a dense line at the metaphysis as seen in Figures 2 and 3, the knee being a particularly good area to demonstrate this. "Lead lines" are frequently also striking at the iliac crests as in Figure 4 and the tips of the scapulae.

In Figure 5 the lumbar spine is demonstrated in a three and one-half-year-old child who had lead intoxication. Lead lines are seen in the vertebral bodies (this film was kindly supplied by Dr. Harvey White of Children's Memorial Hospital, Chicago, and is unique in our experience).

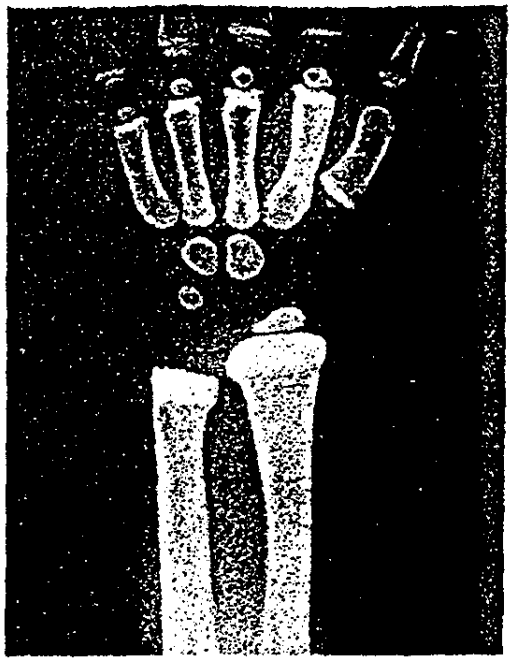

FIG. 3. Wrist and hand of the same child in Figure 2. Note the dense metaphyseal lines in the radius and ulna, in the metacarpals and phalanges, and the concentric rings on the carpal bones.

When encephalopathy is advanced, with marked cerebral edema and increased intracranial pressure, splitting of the sutures, particularly the sagittal and coronal, may also be seen.

Tests for Lead. When clinical and radiologic findings are presumptive, a blood sample should be drawn in a lead-free syringe, placed in a lead-free tube with a hard rubber stopper, and submitted to the appropriate laboratory for lead analysis. This is the one specific diagnostic finding in lead intoxication. Values up to 0.06 mg. (60 mcg.) per 100 ml. of whole blood are considered within the normal range, whereas 0.08 mg. (80 mcg.) and higher are found in true lead intoxication. In the child with lead encephalopathy very high values are obtained; we have seen levels as high as 825 mcg. per 100 ml.

Kehoe[10] states that the rapid rate of lead absorption in young children is responsible for their high rate of encephalopathy. Unfortunately, most hospitals are unable to perform lead analyses and blood and urine specimens must be sent out—a time-consuming process.

Urinary lead determinations are much less reliable. Methods of collection without contamination are difficult; urine lead levels may also be disproportionately low because of impairment of renal function in this disease.

Treatment

Encephalopathy. Within the past six years we have treated 182 cases of lead encephalopathy at the Cook County Hospital in Chicago.[10-12] Our programs of management are based upon clinical studies of these patients.

We first classify the individual case as moderate or severe. Frequently this is difficult, because a child who is conscious and seemingly not too severely involved on admission may unpredictably develop convulsions and lapse into coma eight to 12 hours later.

The definitive clinical diagnosis of encephalopathy is based upon spinal fluid findings, yet the lumbar puncture itself may precipitate grave or even fatal complications, unless carried out with great precaution. This hazard is the sudden release of fluid under increased pressure with resultant herniation of the cerebellar tonsils through the foramen magnum or of the temporal lobes through the tentorium.

When the diagnosis of encephalopathy is suspected, the needle must be introduced with great care, using a three way stop cock connected with a manometer. The fluid is never allowed to spurt

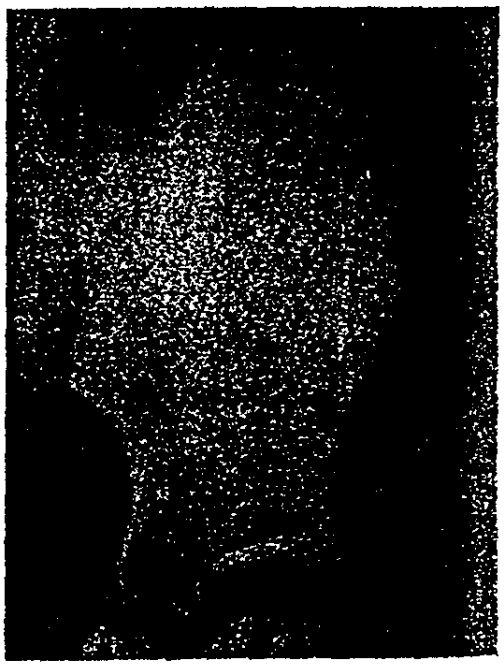

FIG. 4. Lead lines are seen here in the alae of the ilium due to repeated lead intoxication.

out, but is diverted into the manometer so that the pressure may be read directly. If the child is crying hard, a few moments are allowed to pass until the often falsely high pressure reading stabilizes.

About one or two milliliters of fluid are carefully collected; the needle is then withdrawn, the puncture site being compressed with a sterile sponge for a few moments and then sealed so that fluid will not seep externally or into the tissues. Even with the greatest precautions, catastrophes do occasionally occur. In suspected cases the lumbar puncture is a necessity to rule out intracranial infections requiring specific treatment.

Severe encephalopathy, characterized by convulsions, coma and at times respiratory arrest, always challenges the therapeutic ingenuity of the attending physician. Convulsions are unusually protracted, repeated, and very difficult to control. The barbiturates are notoriously ineffective in the patient with lead encephalopathy; in our opinion, they actually carry a definite hazard of precipitating respiratory arrest, since the dosage may be pushed to the point of medullary paralysis in an attempt to control the seizures. It is extremely important to exert every means to control convulsions, however, since the accompanying and ensuing anoxia contributes to resultant brain damage.

Paraldehyde is a safe drug; it is usually given rectally in a dosage of 0.6 cc. per kilogram up to 10 cc. It may be given intramuscularly, or, rarely, even intravenously when more rapid action is desired. If paraldehyde proves ineffective, an inhalation anesthetic, such as ether, may be used. This will often stop a convulsion promptly, but it may recur after a brief period of time.

Chloral hydrate, another useful drug, is administered per rectum in dosage of 0.05 Gm. per kilogram body weight; no more than 1 Gm. per day should be given. Chlorpromazine may be helpful in poteutiating other anticonvulsants. Dilantin has proved to be of little value in controlling the convulsions of lead encephalopathy.

When otherwise intractable, it may be necessary to administer a barbiturate, but only with great caution. This is best done using amobarbital or pentobarbital intravenously. A syringe is filled with a solution containing a dose calculated at 0.1 grain per kilogram of body weight. The needle is introduced into the vein and the barbiturate injected slowly until the convulsion ceases. This will usually occur when about 3/4 to 1 grain of the drug has been injected; at this point, the injection is stopped. We *do not* give barbiturates intramuscularly, orally, or rectally in divided doses for this condition. Morphine, of course, is absolutely contraindicated.

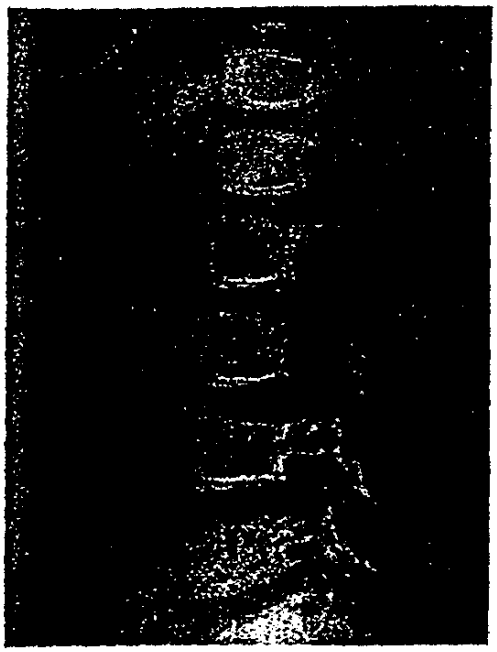

FIG. 5. Lead lines are seen in this x-ray of the vertebral bodies. (Courtesy of Dr. Harvey White, Children's Memorial Hospital, Chicago.)

Since the brain dysfunction seems based principally on severe cerebral edema, symptomatic therapy to overcome this edema is essential. In our hands intravenous urea has been useful.[13] A concentrated solution (30%) may be used if the need is felt to be urgent, but we prefer a 4 per cent solution, because there is less likelihood of thrombosing veins, or of producing sloughs if some of the solution should leak into the surrounding tissues.

Urea is administered by fairly rapid intravenous drip, about 60 drops per minute, through a polyvinyl catheter threaded several inches into the vein. The dosage is 1 Gm. per kilogram of body weight. This amount will produce sustained diuresis up to 12 hours. Because of the likelihood of rebound of the cerebral edema after this period, the doses are repeated regularly every eight hours for two to three days. The serum levels of electrolytes, blood urea nitrogen, and creatinine are checked daily.

Moderate hypothermia by application of the water mattress and air cooling seems also to be useful in reducing brain volume and in decreasing the demand for oxygen by ganglion cells.[14]

We recommend its use in the severe encephalopathy, exercising care not to reduce the body temperature below 96° F. Myocardiopathies have been described in severe lead intoxication,[17] and disturbances in cardiac rhythm are common in our experience. Excessive cooling may bring about circulatory collapse.

In the hope of further reducing cerebral edema and brain volume, we supplement the hypothermia by giving a corticosteroid, methyl prednisolone sodium succinate, parenterally in relatively large doses over three or four days. We have treated 83 patients with severe lead encephalopathy in this manner, but have been unable to demonstrate a statistically significant change in survival rates.[12]

Extensive craniectomy has been recommended for severe encephalopathy with marked brain swelling.[3] We have used this operation in 25 severe, sometimes moribund, children with lead encephalopathy.[21] Though in an occasional selected case the method may be life saving, we have found its routine use unrewarding and have abandoned it for our patients.

Chelating Agents. Chelating agents are of considerable importance in the management of lead intoxication, particularly in the early case. Severe encephalopathy can undoubtedly be prevented by early diagnosis. Unfortunately, this is often not possible for reasons noted above.

Calcium disodium edetate is the agent which has been used over the longest period of time.[4, 22] There are, however, two important shortcomings to its use in encephalopathy: (1) dosages within the range of safety remove only a small fraction of the body burden of lead over a period of several days, and this is not sufficiently rapid with a convulsing or comatose child; (2) in addition, the institution of EDTA therapy not infrequently produces an exacerbation of the symptoms for the first 48 to 72 hours.

Chisolm[6] has stated that experimental studies in animals have shown the lead-EDTA chelate to be significantly dissociable in body fluids. Furthermore, the inhibition of heme synthesis by lead is intensified by the administration of EDTA in the experimentally poisoned animal. Since the inhibition of sulfhydryl enzymes by lead can be reversed by 2,3 dimercaptopropanal (BAL), he investigated the effect of alternate and simultaneous doses of EDTA and BAL in lead poisoned children by measuring the levels of delta aminolevulinic acid (ΔALA) in the blood, urine, and plasma.

This substance, a precursor of heme, is the substrate of ΔALA dehydrase, a sulfhydryl enzyme which is inhibited by lead. Delta aminolevulinic acid was found to be increased four to 25 fold in the child with lead intoxication; and each injection of EDTA was followed by a further 10 to 150 per cent increase in the plasma concentration. This rise was sharply reversed by each dose of BAL when these two drugs were given alternately.

On this basis, Chisolm has recommended a new therapeutic approach to lead encephalopathy, employing EDTA and BAL in combination. In our patients during the summer of 1964, 11 children with acute encephalopathy were treated by his technic, six recovered and five died. The method should be pursued further—it would seem to be a rational approach. BAL alone has been abandoned in most centers as an unsatisfactory chelating agent in lead.

We have also been employing penicillamine on an experimental basis. Our results have been conflicting, but sufficiently interesting to pursue the investigation further.

Complications of Lead Intoxication

Respiratory Arrest. Complications in lead encephalopathy may be severe. Coma with accompanying respiratory arrest is perhaps the most ominous. Attention to details of management are of extreme importance here. A convulsing, unconscious child must be kept under constant nursing and medical supervision. To prevent further injury, a soft mouth gag is employed to protect the tongue from being bitten, and the eyes are protected by lubricant and dressings.

A laryngoscope, suction, endotracheal tubes and mechanical respirator must be kept readily available for an emergency. If apnea occurs, the child will require resuscitation and assisted respiration, and in most instances, via tracheostomy. This complication is of extremely grave import. Though children may be maintained by the Bennett, Byrd or Morch artificial respirator for many days, the ultimate outcome is almost invariably fatal. In our series, however, five of 20 patients have recovered after varying periods with the respirator. Methyl prednisolone succinate had been given to all of these, and is one reason why we are inclined to administer a steroid for severe encephalopathy.

Anemia. The anemia of lead intoxication may be an important factor in the shock seen in the severe lead encephalopathy. Blood transfusions are used in such cases, and are also necessary when surgical procedures under general anesthesia are contemplated in these children whose hemoglobin levels may be as low as 5 to 7 grams per cent.

All of these children require iron therapy which can usually be administered in the form of oral ferrous sulfate. In those instances where the hemoglobin level is quite low, or if for social as well as medical reasons the physician wishes to be certain that sufficient iron is quickly administered, it may be given intramuscularly as an iron dextran preparation while the patient is still hospitalized.

Gastro-intestinal Tract. In all children whose x-ray films show large collections of lead-containing material in the gastro-intestinal tract, repeated saline enemas, dulcolax suppositories, or cathartics should be given as the first phase of therapy. The chelating agent is not employed until after the radiopaque material has been removed completely. All other medications such as calcium disodium edetate is withheld for at least 24 hours because of its effect in aggravating symptoms, and they are never given orally.

Gastro-intestinal bleeding occurs with a fair degree of frequency. It was encountered in six of our 38 children with severe encephalopathy. This may be due to acute peptic ulceration of the duodenum, since such lesions are found at autopsy not infrequently.

When bleeding occurs with a stress ulcer, it is apt to be severe and uncontrollable; surgical intervention may be necessary. The stool should be followed carefully with daily tests for blood in these cases.

We give calcium carbonate and aluminum gel preparations along with anticholinergic drugs prophylactically in all patients with severe lead encephalopathy.

Shock. This occurs frequently in these children and is an ominous complication. In our series of eight children, it resulted fatally in seven. Blood pressure must be taken at regular intervals with these patients, and may have to be kept up by means of plasma expanders and vasopressor drugs. Steroids are of value here, also, as potentiating agents. Low molecular dextran solution intravenously seems to be of value in overcoming sludging of blood in the peripheral circulation. Serum electrolytes must be followed carefully in these cases, particularly when diuretics are employed, in order to correct any specific losses quickly.

Nephritis. The kidney is a target organ of lead intoxication and EDTA is also a nephrotoxic substance. We have seen instances of acute urinary suppression, an extremely grave complication and usually fatal. Chisolm [7] has pointed out the frequency of aminoaciduria, often severe, in children with lead intoxication, and has concluded that its association with hypophosphatemia and glycosuria is significant of a renal tubular dysfunction as seen in the Fanconi syndrome. This triad has occurred most frequently in those children with severe intoxication, but was reversible, although long term follow up would be necessary to determine whether or not permanent impairment had occurred.

In this connection, Henderson [13] reported follow up studies on children in Queensland, Australia who had acquired lead intoxication from powdered white lead paint many years previously. Many of these had died of chronic nephritis. In 187 who could be located, he found hypertension and proteinuria in 17. We have no personal data on this subject.

Prevention

The prime consideration in therapy of lead intoxication is removal of the child from the source of lead. While this is axiomatic, it is extremely difficult to accomplish this practically. In a city like Chicago, with thousands of dilapidated old dwellings in the poorer neighborhoods and several hundred patients suffering from appreciable lead intoxication each year, the task of removing such children from further contact with lead containing paint and plaster is enormous. In spite of good cooperation by the Health Department, a dozen or more repeaters are seen each year at Cook County Hospital. Sometimes this second attack is fatal. The best one can do is to try to correct the environmental factor in each individual case.

To re-emphasize, we must stress once more that the only truly satisfactory approach to the management of lead intoxication remains its prevention. This is a difficult problem; it involves a cooperative effort by practicing physicians, public health agencies, welfare clinics, housing authorities, building commissioners, avenues of communication, school teachers, and the general electorate who supply the funds through governmental agencies to deal with the problem of slums.

Bibliography

1. Baetzer, A. M. *et al.*: Arch. Environ. Health 1: 463, 1960.
2. Bessis, M. and Breton-Gorius, J.: Etude au microscope electronique des granulations ferrugineuses des erythrocytes normaux et pathologique—Anemies hemolytique, hemoglobinopathies, saturnisme. Rev. d'Hemat. 12: 45, 1957. Quoted by Chisolm, J. J.: Disturbances in the biosynthesis of heme in lead intoxication. J. Pediat. 64: 174, Feb. 1964.
3. Bucy, P. C. and Buchanan, D. N.: Simulation of intracranial tumor by lead encephalopathy in

children, with remarks concerning surgical treatment of the latter. J. A. M. A. 105: 244, 1935.
4. Byers, R. K.: Lead poisoning, review of the literature and report on 45 cases. Pediatrics 23: 585, 1959.
5. Chisolm, J. J.: Childhood lead intoxication: a preventable summer disease. Pediatrics Digest 6: 29, July 1964.
6. Chisolm, J., Jr.: The use of edathamil calcium disodium (EDTA) and 2,3. dimercaptopropanol (BAL) in combination for the treatment of acute lead encephalopathy. J. Ped. 63: 843, 1963.
7. Chisolm, J., Jr.: Aminoaciduria as a manifestation of renal tubular injury in lead intoxication and a comparison with patterns of aminoaciduria seen in other diseases. J. Ped. 62: 1, 1962.
8. Cooper, M.: Pica. Springfield, Ill., Charles C Thomas, 1957.
9. Greenberg, M., Jacobziner, H., McLaughlin, M. C., Fuerst, H. T. and Pellitteri, O.: Pediatrics 22: 756, 1958.
10. Greengard, J. *et al.*: Lead encephalopathy in children, intravenous use of urea in its management. New Eng. J. Med. 264: 1027, May 18, 1961.
11. Greengard, J., Voris, D. C. and Hayden, R.: The surgical therapy of acute lead encephalopathy. J. A. M. A. 180: 660, 1962.
12. Greengard, J., Adams, B. and Berman, E.: Acute lead encephalopathy in young children, evaluation of therapy with corticosteroid and moderate hypothermia. J. Ped. 66: 707, 1965.
13. Henderson, D. A.: A followup of cases of plumbism in children. Australasian Annals of Medicine 3: 219, 1954.
14. Ingraham, F. D. and Matsen, D. D.: Neurosurgery of Infancy and Childhood. Springfield, Ill., Charles C Thomas, Publisher, 1954.
15. Kehoe, R. A.: The metabolism of lead in man in health and disease. Archives of Environmental Health and Disease 2: 418, 1961.
16. Kehoe, R. A.: The metabolism of lead in health and disease. J. Roy. Inst. Publ. Health & Hygiene 24: 177, 1961.
17. Kline, T. S.: Myocardial changes in lead poisoning. A.M.A. J. Dis. Child. 99: 48, 1960.
18. McFadzean, A. J. S. and Davis, L. S.: On the nature and significance of stippling in lead poisoning with reference to the effect of splenectomy. Quart. J. Med. 18: 57, 1949.
19. McLaurin, R. L. and Nichols, J. B., Jr.: Extensive cranial decompression in treatment of severe lead encephalopathy. Pediatrics 20: 653, 1957.
20. Nelson, W. E.: Textbook of Pediatrics. Philadelphia, Pa., W. B. Saunders & Co., 1964, p. 1561.
21. Pirrie, R.: The effect of splenectomy and reticuloendothelial blockade upon the anemia of lead poisoning in guinea pigs. J. Path. Bact. 64: 211, 1952.
22. Statement on diagnosis and treatment of lead poisoning in childhood. Pediatrics 27: 676, 1961.
23. Rapaport, M. and Rubin, M.: Amer. J. Dis. Child. 61: 245, 1941.
24. Rosomoff, H. L. and [illegible] T. A.: A study of brain volume and [illegible] pinal fluid pressure during hypothermi[illegible] . J. Physiol. 183: 19, 1955.

READER'S CHECK LIST

Experimental Animals

Comparative Hematology. WARREN ANDREW, M.D., Ph.D., Indiana University School of Medicine. New York, Grune and Stratton, 1965. 188 pp. 116 figures plus 14 full-color plates. $22.75.

A summary of the major findings with respect to leukocytes, erythrocytes and analogous cells in a great array of multicellular creatures including common laboratory animals.

The Pharmacological Basis of Therapeutics, Ed. 3. Edited by L. S. GOODMAN and A. GELNIER. New York, Macmillan, 1965. 1,784 pp. $22.50.

Jam-packed with information in its nearly two-thousand double-columned pages, this masterwork correlates pharmacologic observations and principles with clinical and therapeutic phenomena. Along with discussions of the various drugs, anesthetics, hormones, vitamins and poisons, there is an excellent exposition of the characteristics and principles of use of the antibiotics, sulfonamides and related agents.

Vision Screening of the Preschool Child; Report of a Study. R. A. SAVITZ, R. B. REED and I. VALADIAN. For sale by Supt. of Documents, U. S. Govt. Printing Office, Washington, D. C. 20402. 70 pp. 45 cents.

A report of a survey of 94 young slum children in Boston by assorted tests. Six probable cases of amblyopia (corrected vision of less than 20/40) were discovered. "These children are culturally deprived, and it is interesting to speculate about the possible role of sensory deprivation in the etiology of amblyopia."

The Foetus and the New-Born: Recent Research. Brit. Med. Bull. Vol. 22, No. 1, Jan. 1966. $5.00.

Nineteen stimulating papers by 27 leading British investigators survey a diversity of phenomena in biochemistry, physiology, metabolism and resuscitation.

General

Recent Advances in Paediatrics, 3rd Ed. DOUGLAS GAIRDNER, Editor. Boston, Little, Brown and Co., 1965. 360 pp. $13.50.

A collection of 15 comprehensive and well organized reviews by well known authorities in England. Scot

(Continued on page 291)