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LEAD POISONING IN CHILDREN

WITH NOTES ON THERAPY *

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ETIOLOGY

The manifestations of lead poisoning in children have been described by several writers, and excellent discussions of the etiology and symptomatology are available.[1] Failure to recognize the disease can be attributed to lack of acquaintance with the symptoms, which are in most cases quite characteristic; therefore a brief résumé of the more important points will be of value.

The disease is usually secondary to a perverted appetite. In this condition, which is known as pica (footnote 1, fourth reference), infants and children may ingest sand, coal, cloth, hair and paint, the last chewed from toys, cribs and woodwork. The derangement of appetite may be only habit, or it may result from gastro-intestinal disturbances, intestinal parasites, mental deficiency or neurosis. In any event, pica, in our experience, is the most frequent forerunner of lead poisoning, as it is of relatively common occurrence and may result in the repeated ingestion of small amounts of lead. Weeks may elapse before symptoms arise, and the perversion of appetite is passed over lightly or not mentioned by the parents who have become accustomed to the strange habits of the child.

SYMPTOMS

The essential clinical picture in lead poisoning is an anemia associated with gastro-intestinal disturbances, such as loss of appetite, constipation, abdominal pain and vomiting. The anemia may become quite marked. It is characterized by reduction in the erythrocyte count with the appearance of basophilic stippling in the cells. Anemia may be the only sign in mild cases. Lead colic, as such, is seldom recognized in children.

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Loss of appetite and constipation are early and very marked symptoms. Vomiting, often of a projectile type, appears in more pronounced cases. The characteristic lead line, a punctate precipitation of black granules in the gum margin above the incisor teeth, is best seen with a hand lens, and if present is good evidence of lead poisoning. It is a deposit of lead sulphide in the gum margin and does not occur in clean mouths. It is only occasionally present in the disease in children.[2]

In severe cases, neuritis [3] and encephalitis occur. Indefinite pains in the joints and muscles, with weakness of the legs, and reflex anomalies may be early signs of lead polyneuritis.[4] Encephalitis [5] appears, especially in lead poisoning of long duration. It is probable that the frequent occurrence of lead encephalitis in children is due to the fact that the lead is ingested in small doses—a method said to be most conducive to severe poisoning. The signs are variable, and may change rapidly, simulating tuberculous meningitis from which it is often only with difficulty distinguished. Vomiting, headache, stupor and convulsions are prominent features. The prognosis of this severe form of the disease has been considered almost uniformly fatal. Convulsions, frequently repeated, or of several hours duration, are the usual terminal manifestation. The spinal fluid [6] is clear, under increased pressure, and may show a positive test for globulin, a slight increase of lymphocytic cells, or both.

Lead amblyopia,[7] though said to be rare, has been reported with lead encephalitis in children. It arises from neuritis of the optic nerve, and atrophy of the retinal cells. Retinal hemorrhages and papilledema may occur.

TREATMENT

Heretofore, treatment has not been entirely satisfactory. Magnesium sulphate and potassium iodide have been used with some degree of success, as have also the de-ionization baths of Oxley.[8] In lead

2. Littlejohn, E. S.: Three Cases of Lead Poisoning in Children M. J. Australia **2**:63 (July 15) 1922.

3. Fisher: Lead Poisoning with Special Reference to the Spinal Cord and Peripheral Nerve Lesions, Am. J. M. Sc. **51**:54, 1892.

4. Friedberg, E.: Chronic Lead Poisoning in Children, Arch. f. Kinderh. **71**:25 (Feb.) 1922; abstr. J. A. M. A. **78**:1172 (April 15) 1922.

5. Strong, R. A.: Meningitis Caused by Lead Poisoning in a Child of Nineteen Months, Arch. Pediat. **37**:352 (Sept.) 1920. Thomas, H. M., and Blackfan, K. D.: Recurrent Meningitis Due to Lead in a Child of Five Years, Am. J. Dis. Child. **8**:377 (Nov.) 1914. Suzuki, T., and Kaneko, J.: Serous Encephalitis in Infants from Lead Poisoning, J. Oriental Med. **2**:55, 1924; abstr. J. A. M. A. **82**: 1819 (May 31) 1924.

6. Weller, C. V., and Christinson, A. D.: Cerebrospinal Fluid in Lead Poisoning, Arch. Neurol & Psychiat. **14**:327 (Sept.) 1925.

7. Gibson, J. L.: Ocular Neuritis Due to Lead Poisoning, M. J. Australia **2**:201 (Sept.) 1917. De Schweinitz, G. L.: Toxic Amblyopias, Alvarenga Prize Essay, College of Physicians of Philadelphia, October, 1894.

8. Oxley: Electrolytic Treatment of Lead Poisoning, Lancet **2**:848, 1914. Gibson, J. L.: Importance of De-ionization in Treatment of Plumbism in Queensland Children, M. J. Australia **1**:272 (April 5) 1919.

encephalopathies, however, little effect has been obtained from either method. The de-ionization method has been adopted in Australia, where the occurrence of lead poisoning in children was of such importance as to require government action in restricting the use of lead paint.

It is the purpose of this paper to call attention to the unrecognized frequency of the condition, and to detail experiences in treatment. The treatment used in the cases to be presented is that recommended by Aub.[9] The mechanism of absorption, transportation, storage, and excretion of the metal is of the utmost importance, but will be considered only as necessitated in explanation of the treatment.[10]

The mechanism of transportation is similar to that of calcium, and circumstances favoring calcium deposition favor lead storage, and conditions effecting calcium removal likewise affect lead. Symptoms of lead poisoning occur when the metal is circulating in the blood stream, or when bound especially in the liver and brain. It is stored in the bones in an inert form, where it may remain indefinitely without causing symptoms. However, under certain conditions, large amounts of the metal are released into the circulation and then acute symptoms recur. This has been known to happen years after removal from exposure to lead.

In the absence of severe symptoms, especially those of encephalitis, deleading, or the withdrawing of lead from the bones and the hastening of its excretion, may be attempted. This is accomplished by making the lead salts more soluble through the production of an acidosis, together with the maintenance of a diet low in calcium. Alkalosis will also produce lead excretion, but to a less extent than acidosis. Aub has found ammonium chloride acidosis to produce the greatest increase in lead excretion.

As deleading is accomplished by bringing the stored lead into solution in patients severely ill with encephalitis, the procedure becomes dangerous through the possibility of aggravating the condition by adding to the circulating poison. Instead, in those severely ill, the deleading process is reversed, to produce storage of the dissolved metal in the bones. Although a diet rich in calcium, together with careful avoidance of acidosis, may be sufficient to cause amelioration of symptoms, it is advisable to administer calcium salts in large doses. In the severely ill patients with persistent vomiting or convulsions, the oral administration of calcium is either impossible or is so slow in its effect that intravenous therapy is required. For this purpose, from 50 to 100 cc. of 2 per cent

9. Aub, J. C.; Fairhall, L. T.: Minot, A. S., and Reznikoff, P.: Lead Poisoning, Medicine 4:1-250 (Feb.-May) 1925.

10. For a complete discussion, the reader is referred to the recent monograph of Aub and his co-workers.

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solution of calcium chloride are given at daily intervals until the convulsions and other dangerous manifestations have ceased.

A rapid subsidence of the symptoms is due to the removal of lead from the circulation. However, improvement does not indicate that the patient is out of danger, as the metal is stored in the bones and under certain circumstances may be released to enter the circulation again and cause acute symptoms. Particularly is this prone to happen during acute infections. Therefore, as soon as the condition of the child permits, deleading should be instituted. In the low calcium diet necessary during periods of deleading, milk, eggs, green vegetables, and many fruits must be omitted entirely. Thus, in very young children deleading is often not feasable because of the inability to provide a diet lacking in these substances. A diet adequate for older children and satisfactory as far as low calcium content is concerned, may contain meat, liver, potato, rice, tomatoes, corn, bananas and milk-free bread. When for any reason, as in very young infants, such a diet cannot be used, the high calcium diet of milk and vegetables should be continued, so as to maintain storage of the lead in the bones, and the patient should be watched carefully for development of acidosis and resulting acute symptoms of lead poisoning. Even in the deleading process recurrence of symptoms should be watched for. The symptoms of recurrence are vomiting, constipation, or increase in the number of stippled cells in the blood. When these occur, treatment should be stopped or reversed.

Since September, 1923, there have been admitted to the Infants and Children's Hospitals seventeen patients showing symptoms attributable to lead poisoning; five were mild cases, twelve were suffering from encephalopathies. This relatively high incidence indicates that lead poisoning is not uncommon. The twelve cases of lead encephalitis represent 14 per cent of all cases of all types of encephalitis seen in the corresponding period. The histories of three cases of lead encephalitis will be reported in detail.

CASE HISTORIES

CASE 1.—P. K., a white girl, aged 2 years, over a period of one year gradually developed an illness characterized by weakness, anemia, vomiting and constipation. On admission to hospital in December, 1923, she was vomiting after each meal, and was markedly constipated. After several days in the hospital, it was noted that she was eating the paint from the crib. Further history obtained at this time revealed that the habit had been present for months.

Physical examination showed a weak, undernourished, mentally subnormal child. A marked tremor and a lead line were noted in the early part of the hospital stay. The blood picture was a secondary anemia, with marked basophilic stippling of the erythrocytes. There was constant glycosuria, but the blood sugar level and glucose tolerance curve were normal.

Course.—Due to the poor physical condition of the child, deleading was considered inadvisable and the treatment to induce storage was instituted. On a high

calcium diet. improvement was slow, but steady. She gained weight, became stronger and less anemic. After five months she was discharged.

Two months later she was readmitted in convulsions. For five days prior to this admission she had been listless and without appetite. The day before admission she was quite drowsy and had a "fruity" odor to the breath. Convulsions had appeared six hours before admission and continued without cessation until respiration ceased two hours after admission to the hospital. Death was due to respiratory paralysis; the cardiac action continued under artificial respiration for three hours. Urinalysis showed a trace of albumin and positive tests for sugar, acetone and diacetic acid.

The spinal fluid was under increased pressure, slightly cloudy, contained 70 cells per cubic millimeter and gave a positive reaction for globulin. Lead analysis made in Dr. Aub's laboratory showed relatively large amounts in the liver, brain and bones, with less of the metal in the other viscera.

Comment.—This case illustrates the typical onset with pica, followed by anemia, vomiting and constipation; the amelioration of milder symptoms by diet alone; and the potential danger that continues to exist after acute symptoms have subsided. It is thought that in this case an increasing acetone body acidosis contributed to the release of lead from the bones, and the sudden appearance of an encephalitis with fatal termination. The mother had been warned against the child's habit of eating paint, and reported that to her knowledge there had been no nibbling of furniture or woodwork since the previous admission.

The attention is called to the spinal fluid findings, which are typical, and to the incidence of glycosuria. Glycosuria is not reported as part of the picture of lead poisoning but has been present in several of our cases. One cannot say whether this represents diabetes due to damage of the pancreas by the metal or a renal glycosuria. The normal blood sugar and normal glucose tolerance curve suggest the latter, although lead was demonstrated in the pancreas.

CASE 2.—J. S., a white boy, aged 23 months, was admitted to the Infants' Hospital Aug. 30, 1924, because of loss of weight, vomiting and constipation. For nine months he had gnawed at the crib and furniture. Physical examination showed a pale, undernourished child lying in a stupor. Two convulsions occurred on the day of admission. The temperature was elevated to 104 F. Blood examination showed a secondary anemia with marked stippling. The urine contained a trace of sugar. A lead line was present.

Course.—As nothing was retained by mouth, parenteral fluids were given repeatedly throughout the first few days. Convulsions were frequent and the condition of the child was grave. Intensive calcium therapy was instituted, with a view to inducing storage of the metal. The persistent vomiting prevented oral medication, so that calcium chloride was given intravenously. There was rapid improvement after daily intravenous injection of 1 Gm. of calcium chloride in 2 per cent solution. As the convulsions ceased and the stupor lessened, marked irritability appeared. Lumbar punctures with removal of considerable quantities of spinal fluid had a quieting effect at this stage.

There were no convulsions after the first few days of treatment. Later evidences of improvement were cessation of vomiting and diminution of irritability. In the hospital stay of one month, the child had received 10 intravenous injec-

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tions of calcium chloride, totaling 15 Gm., and had retained 70 Gm. of the calcium lactate offered by mouth.[11]

When improvement had progressed sufficiently to make further examination possible, it was found the child made no attempt to talk, although he had previously been talking quite well; that objects could not be grasped with the hands, that he could not stand; that hearing was impaired and that he was blind. Examination of the fundi showed what was interpreted as optic atrophy.

Subsequent Course.—After two months at home on a high calcium diet the child was readmitted for a period of deleading. He had improved considerably. The appetite was good, he was gaining weight, the anemia had improved and the weakness of the arms and legs was less marked. He was still quite irritable. Vision seemed to have begun to return and fundus examination showed that the disks were less pale. After two months of a deleading treatment, the child was again discharged. A paresis of the left arm and left leg persisted, for which he continued to receive muscle training.

The patient returned (April, 1926) for another period of observation, now a very active, playful child, well developed and nourished, mentally alert, hearing and understanding well, but only beginning to talk. His appetite was good, the bowels were regular, and there was no vomiting. He still tried to nibble the furniture. The sight and hearing were apparently normal. Examination of the eyegrounds was quite difficult, due to lack of cooperation, but fleeting glimpses of the disks and foveal areas showed nothing abnormal. Weakness of the left arm and left leg continued. The child was quite excitable, with crying spells and occasional attacks of twitching of the left arm.

Comment.—This represents a child with a very severe case of lead encephalitis, complicated by peripheral neuritis, deafness and blindness, in whom the treatment was successful. Improvement has continued steadily, and after nineteen months only slight changes have persisted. There has been only one period of deleading and it is not assumed that the child is free from the metal or that all danger of recurrence of symptoms is past, but by careful observation and cooperation of the parents he has made much improvement; further progress is anticipated. Another period of deleading will be instituted.

CASE 3.—R. H., a white boy, aged 20 months, was admitted to the Infants' Hospital, March 25, 1926, with an illness of three months' duration characterized by constipation, loss of strength, pallor and irritability. For one year he had been biting the window sills and the bars of his crib.

He was an undernourished, pale, restless and very irritable child with occasional muscular twitchings. The respirations were irregular, with periods of apnea. The temperature was elevated to 101 F. The blood showed an anemia with many stippled erythrocytes. Spinal fluid contained only 10 cells per cubic millimeter, but gave a positive test for globulin; a film formed on standing.

11. Calcium lactate was given by mouth instead of calcium chloride, because calcium chloride has been shown by Gamble (Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: Studies of Tetany, Am. J. Dis. Child. 25:455 [June] 1923; Gamble, J. L., and Ross, S. G.: Ibid., p. 471.) and others to be an acid-producing salt, the chloride ion being absorbed from the intestine in excess of the calcium. If calcium is given intravenously, this objection does not apply. Thus, paradoxically, we might give calcium lactate by mouth to produce storage of lead, by the heightened calcium absorption and calcium chloride to produce deleading by the acid action, more of the acid chloride ion being absorbed than of the calcium.

There was an acetone body acidosis as evidenced by acetone in the urine and in the expired air. Lead was demonstrated in the urine. An intradermal tuberculin test was positive.

Course.—On the day following admission, two convulsions occurred followed by unconsciousness, cyanosis and irregularity of pulse and respiration. Forty cubic centimeters of 2 per cent calcium chloride was administered intravenously, followed by 200 cc. of 10 per cent glucose intravenously, to combat the acetone body acidosis. Calcium lactate was offered by mouth. The next day, although the general condition seemed improved, a strabismus developed. Fifty cubic centimeters of 2 per cent calcium chloride was administered intravenously, and 15 grains of calcium lactate every six hours was continued. Convulsions did not recur, and after a few days vomiting ceased, and solid food was retained. The strabismus disappeared but the irritability persisted. The patient was discharged home April 27 on a high calcium diet, to return when his condition had improved sufficiently to warrant deleading. The parents were requested to try to prevent further ingestion of the metal, and to watch closely for recurrence of acute symptoms.

Comment.—This represents another acutely ill patient with early encephalitis, who showed prompt improvement under glucose and calcium therapy.[12] Attention is called to the many points in the history and physical examination which made the condition difficult to distinguish from tuberculous meningitis, particularly in a child who at this age could be assumed to have some tuberculous focus as evidenced by a positive intradermal test.

Although the child is much improved, he is not out of danger, the lead is stored in the bones and care must be exercised in his management until such time as he can be successfully deleaded.

SUMMARY

Lead poisoning is of relatively frequent occurrence in children. In our cases it has usually been associated with pica or with perverted appetite, which causes the ingestion of lead paint with resulting symptoms of anemia, abdominal pain, constipation and vomiting. In the more severe cases, encephalitis ensues, which is often confused with tuberculous meningitis or other forms of encephalitis. Unless proper therapeutic measures are promptly instituted, lead encephalitis is highly fatal.

The administration of calcium salts—calcium lactate by mouth and calcium chloride intravenously, has been demonstrated to produce prompt alleviation of symptoms. Our experience has confirmed these observations. However, the patient is subject to recurrences of acute symptoms of lead poisoning unless excretion of the lead is effected by a deleading process, best accomplished by production of an acidosis, together with a diet low in calcium.

12. As acetone acidosis definitely aggravates the condition, the intravenous administration of glucose would of itself produce some reduction in severity of the symptoms. It was felt to be of definite value in this case.