THE LESIONS OF LEAD ENCEPHALITIS IN CHILDREN

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REVIEW

We are told that the clinical effects of lead poisoning on the brain were known to the ancients long before search for microscopical lesions was possible (1). The French writers, Grisolle and Tanquerel des Planches, are said to have given the first good clinical descriptions of lead encephalitis, written nearly a hundred years

ago (2, 3), and now it is familiar to all that young children with depraved appetite, or pica, may swallow plaster or chew paint from furniture, window sills, dolls and toys, and so develop symptoms of lead poisoning over a period of weeks or even months. Children, like lead workers, may develop abdominal pain, constipation and vomiting. Anaemia and basophilic stippling of red blood cells frequently develop, and sometimes a lead line appears on the gums. The urine contains not more than a good trace of protein usually, and in some instances glycosuria has been found (4). As the disease progresses the child becomes irritable and cantankerous, and finally stuporous. Visual disturbances, oedema of optic discs, elevation of blood pressure, and slow pulse may be observed. Projectile vomiting commonly occurs and convulsions generally appear for one or more days before death.

When convulsions set in, it is usually found that the pressure of the spinal fluid is increased; and the fluid contains increased quantities of protein, a few cells, and is sometimes xanthochromic (43). Lead may be demonstrated in the blood in abnormal quantity, and it was shown by Park (5) and by Vogt (6) that a curious disturbance in bone formation develops. The x-ray shows a dense shadow along the line of ossification where lead is deposited in the growing spicules of bone. The latter are found under the microscope to be more numerous than usual, and ossification is retarded. There are, too, characteristic intranuclear inclusion bodies in the kidney and liver (7).

As long ago as 1839 it was possible for Tanquerel des Planches to collect records of examinations of the brain in seventy-one instances of lead poisoning, although characteristic changes were not found to be common to all cases (8).[1] For a century the remarkably varied clinical manifestations of lead encephalitis have been recognized, and they are now perfectly familiar (2, 9). Nevertheless, examination of recent reviews on the subject and of modern textbooks of neurology and pathology shows that as yet no precise pathological lesions in the brain, responsible for the signs and symptoms, have been established as characteristic of lead poisoning (2, 10); and in a very recent monograph concerned with the clinical, anatomical and spectrographic study of the nervous system in acute metallic poisoning, Esser states that information is lacking concerning the changes caused by lead in the central nervous system of man (11).

The wide clinical interest aroused in recent years by the occurrence of acute lead encephalitis in children (12, 13, 14, 15, 16, 17, 18, 19), has been accompanied by few corresponding anatomical studies. The opportunity has lately been afforded to make systematic microscopical examination of the brain in a large series of cases which show an astonishing variety and number of lesions. Similar changes have not been described in any other disease of the central nervous system, and since they appear to be characteristic of lead poisoning, it seems

[1] No lesions were seen in some cases. Yellow discoloration was found in some, and in still others the brain was enlarged or atrophied.

worthwhile once more to review some of the literature devoted to the subject and to describe the characteristic lesions at some length.

In 1888 Westphal reviewed the cases which had been reported (3), and stated that Kussmaul and Maier in 1872 were the first to make histological examination of the brain in lead encephalitis. They examined one case and found wide homogeneous areas around blood vessels in the gray matter, interpreted as increased perivascular connective tissue (20). Von Monakow reported a case in 1879 which showed gross atrophy of the brain, and widening of the adventitial space about blood vessels, together with multiplication of nuclei, collections of cells, fat droplets and pigment. He also described hyperplasia of neuroglia, many minute haemorrhages in the white matter, and numerous abnormal ganglion cells (21). In Seifert's case, reported in 1884, the brain was atrophied and the basilar artery was sclerotic. There was abundant fluid in the subarachnoid spaces and two small gross haemorrhages were found in the brain (22). Likewise Oppenheim, describing one case in 1885, found gross cerebral haemorrhages in a patient with hemiplegia (23). Westphal could find only a small haemorrhage in the left uncinate gyrus of one case and in another several areas of softening together with sclerosis of blood vessels. He assumed that lead caused fine histological changes which could not be detected by the methods then available, though he himself made no microscopical examinations (3).

Following Westphal in 1900 Courtney reported another case with gross cerebral haemorrhages occurring in an adult (24), and in 1912 Cadwalader found a large cerebral haemorrhage in his case, without mention of the cerebral arteries. He described thickening of meninges, increased neuroglia in the cortex and chromatolysis of the Betz cells (25).

Three cases were studied microscopically and reported in 1921 by Hassin (26). Slight changes in nerve cells were found, such as fat accumulation and chromatolysis, and proliferation of endothelial cells, adventitial cells, and of new blood capillaries. Glial cells in excess along blood vessels in the cerebral cortex and cerebellum were found, and thickening of the meninges. There was some infiltration of the meninges with lymphoid cells, and granules of green pigment were found in the brain.

The whole subject of lead poisoning was reviewed at length in 1925 by Aub, Fairhall, Minot and Reznikoff who pointed out the discrepancy between the well-known clinical manifestations and the meagre anatomical findings which had so far been described in the literature (2). Changes in the spinal fluid, the presence of cells, high pressure and increased quantities of protein, were reported in several papers between 1905 and 1924; and on this basis, without examination of the brain, Suzuki and Kaneko speak of serous meningitis in children, caused by lead poisoning acquired from white powders used by Japanese mothers as a cosmetic for the skin (17). From consideration of the changes in the spinal fluid and the histological lesions reported by Hassin it was suggested in the review of Aub, Fairhall, Minot and Reznikoff, that "in so-called lead encephalopathy the meninges are primarily involved, or in other words that the disease is really a meningo-

pathy". They concluded that further information concerning the action of lead on the tissues was not possible from postmortem studies, since its action was apparently too subtle to yield to this type of investigation.

Between the years 1928 and 1934, however, several papers appeared describing new lesions which were found by independent observers. Freifeld reported two cases, lead workers, one in 1928 and one in 1933, showing focal destruction of nerve cells replaced by neuroglia in the cerebral cortex, basal ganglia and pons. She found extraordinary destruction of Purkinje cells in the cerebellum, associated in some areas with new growth of glia. Lesions in the dentate nuclei and thrombi in small vessels were described, in some instances leading to necrosis of tissue. Small perivascular calcium deposits and granules of brown pigment in phagocytic cells were found, and there were perivascular haemorrhages in all parts of the brain. She expressed the opinion that all of the lesions were dependent on vascular damage (27, 28).

In 1929 Tuthill also described focal scars of neuroglia (glial rosettes) in the cortex, basal ganglia, and cerebellum of an infant, and she too saw extensive destruction of Purkinje cells in the cerebellum and gliosis of the molecular layer (29). Scattered minute haemorrhages were found and Tuthill described for the first time lesions which were called concretions. These were scattered in many parts of the brain and cerebellum, and in the walls of blood vessels. They varied in size from small globules to large masses 100 micra in diameter, stained with basic dyes and contained iron. They were thought to be "albuminoid break-down products." It is significant that the patient, a child of 2½ years, after an initial attack of encephalitis, was free from symptoms for about two months before manifestations reappeared and death occurred.

Staemler reported a case in 1929 which he says was essentially like the first case of Freifeld (30), and in 1933 McKhann and Vogt, from consideration of the clinical signs and symptoms, suggested that they might depend on increased intracranial pressure due to intense cerebral oedema (9).

Four more cases, occurring in lead workers, were described in 1933 by Winkelman and Eckel who found lesions in the capillaries, numerous focal lesions in the gray matter of the cerebral cortex, and mentioned the presence of granular perivascular material as evidence of cerebral oedema (31).

The next year, in 1934, Rhea reported a single case in which he saw multiplication of cells in the walls of capillaries and free fluid microscopically in the meninges (32). The conspicuous appearance of the blood vessel in the brain, interpreted by some authors in the past as newly formed growing vessels (26) appeared to Rhea to depend merely on dilatation, and there were a few disseminated microscopical haemorrhages.

THE CLINICAL CHARACTERISTICS IN TWENTY-TWO CASES

Twenty-two cases are described here, all occurring in children. The evidence of lead poisoning is clear in each instance and is shown

in Table I. Most of the cases occurred in colored infants between 13 months and 3½ years of age. One was in a boy of seven, however, and one in a girl of 6 years. Five were white children.

In most cases lead was ingested by nibbling painted articles, usually furniture. Paint may be swallowed in this manner for many months (5 to 18 months in this series) before the onset of neurological disturbances. In one case lead fumes were inhaled from old automobile battery casings burned in the cook-stove. For a period of 3 years after the original convulsions the blood lead remained elevated, and the x-ray showed lead lines in the bones. The child finally died in convulsions and the brain showed both old and fresh lesions, although no evidence could be obtained of exposure to lead fumes or ingestion of lead in the interval. In a second case the first convulsion occurred a month before death, and in a third the child lived for about 6 weeks after the onset of peripheral neuritis. The neurological signs and symptoms were of short duration in the remainder of the cases.

It is curious that 19 of the 22 cases occurred during the five months including June and October, and the tendency of lead encephalitis to appear during the summer and early fall has been mentioned before by Suzuki and Kaneko (17), and by Fukushima and Matsumoto (18), although no explanation was evident.

Complete records of the temperature from the onset of convulsions are not available, but in 21 of the 22 cases fever was present during the stay in the hospital. The temperature was usually irregular and in most cases several degrees of fever were present at times. It would seem from the microscopical sections that the lesions in the brain are sufficient to account for elevation of temperature. There is the possibility, however, discussed in another section of this paper, that fever or the elevated atmospheric temperature of summer and fall may supply the factors which initiate the vascular changes in the brain which in turn are followed by exudate of serous fluid into the tissue.

A marked leucocytosis was observed in most of the cases. The count was 30,000 or above in four of the cases, above 20,000 in eight others, between 10 and 19,000 in seven cases, and normal in two cases. In one case no white count was made, and in a case in the first group there were 58,500 white cells per cu.mm. The degree of leucocytosis

requires care. If the section remains in light green too long, the blood serum, the exudate and all of the tissue, will be stained dark green. Differentiation requires only a few seconds. The section should be dipped quickly in and out of the light green. Proper differentiation is reached when the tissue which does not contain the exudate turns pale green and the areas filled with serous fluid look very dark green *to the naked eye.*

6. Wash in water and examine under the microscope. If necessary, differentiate further.

7. Dehydrate quickly in graded alcohols and xylol.

8. Mount in balsam.

APPENDIX II. CASE REPORTS

Case 1. Autopsy No. 5940. A colored boy, 3 years old. History of pica, malaise for a month, and repeated convulsions for one day. Lead line on gums. Stippled red blood cells. Haemoglobin 60 per cent. *Spinal fluid:* Pandy +, cells 15 per cu.mm. *Temperature:* 99.8° to 101.2°F. *Leukocytes:* 19,000. *Died* in July. Lead line in microscopic sections of ribs. Nuclear inclusion bodies in liver and kidneys.

Case 2.. Autopsy No. 7532. A white girl, 2 years old, who ate the paint from window-sills and toys. She was easily frightened and startled and had screaming spells for two months. Vomiting present at times for one month. Coma, nystagmus, and convulsions for a day. *Blood:* Haemoglobin 45 per cent. Stippled and nucleated red blood cells. *Spinal fluid:* Pandy 3+. Cells, 12 per cu.mm. *Temperature:* 100° to 105°F. *Leukocytes:* 58,500. *Died* in June. Slight lobular pneumonia. Lead line in microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidney.

Case 3. Autopsy No. 10465. A colored boy, 3 years old, who ate house paint. History of vomiting, strabismus, and convulsions off and on for a week. Lead line on gums. *Blood:* Red blood cells 3,950,000. Stippled red cells. *Spinal fluid:* Pandy +. Cells, 5 per cu.mm. Pressure increased (1+). *Temperature:* 38° to 39.6°C. *Leukocytes:* 15,400. *Died* in July. Lead line in microscopical sections of ribs. Intranuclear inclusion in liver and kidneys.

Case 4. Autopsy No. 10637. A white boy 22 months old, who chewed painted furniture for six months. Later constipation, projectile vomiting, and drowsiness appeared for three weeks. He had convulsions and strabismus for three days. *Blood:* Haemoglobin 50 per cent. Stippled red blood cells. *Temperature:* 37° to 38.8°C. *Leukocytes:* 16,400. *Spinal fluid:* Pandy +. Cells 9 per cu.mm. Pressure increased (4+). *Died* in October. Purulent bronchitis, microscopical lead line in ribs, and nuclear inclusions in liver and kidneys.

Case 5. Autopsy No. 10850. A white boy, 13 months old, who gnawed painted furniture for four months. Had a cold and convulsions with fever (104°) for two days a month before death. The first convulsion appeared after the third of a series of daily injections of "cold" vaccine. Later there was spastic paralysis

on the left, and the head and right arm were in constant motion. He was mentally retarded. Several missing teeth and ulcerated gums. *Blood:* Haemoglobin 54 per cent. Stippled red blood cells. *Spinal fluid:* Negative. *Temperature:* 38° to 42°C. *Leukocytes:* 12,300. *Died* in April. Purulent bronchitis and lobular pneumonia. Microscopical lesions of lead poisoning in ribs, and intranuclear inclusions in liver and kidneys.

Case 6. Autopsy No. 11766. A colored boy, 2 years old, who liked to chew paper, plaster, and clothes. For two weeks he was noisy, fretful and disobedient. Enuresis appeared and a tendency to bite and scratch. Occasionally he vomited, and had nystagmus and convulsions for one day. *Spinal fluid:* Pandy 3+. Cells 66 per cu.mm. Pressure increased (1+). *Temperature:* 98 to 105°F. *Died* in December. Lead line in x-ray and in microscopical sections of ribs. Nuclear inclusions in liver and kidneys.

Case 7. Autopsy No. 12168. A colored girl, 3½ years old. Over a year before death there were several periods of vomiting, abdominal pain, constipation, and crying spells. Later she was seen with house paint on her hands and face and a week afterwards vomited persistently for 3 days. This was followed by ascending paralysis, difficulty in speech and swallowing, and dysphagia. Paralysis of extremities and muscles of lower trunk and diaphragm was complete. Weakness of pharyngeal muscles. Occasional convulsive movements of facial muscles. Complete anesthesia to touch and pain over extremities and trunk. Finally, fever, coma and convulsions of facial muscles for several hours before death. *Spinal fluid:* Negative. *Blood:* Haemoglobin 60 per cent. Stippled red blood cells. *Leukocytes:* 19,500 to 22,000. *Temperature:* 37.6° to 38.4°C. *Died* in September, about six weeks after the onset of symptoms. Lead line in x-ray and microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys. Demyelinization of peripheral nerves.

Case 8. Autopsy No. 13334. A colored boy, 3½ years old. History of vomiting for two days. Coma, brachycardia and convulsions for one day. *Blood:* Haemoglobin 45 per cent. Stippled red cells. *Temperature:* 37.4° to 39°C. Leukocytes: 28,000. Blood lead: 0.1 to 0.2 mgm. per cent. Lead line on gums. *Spinal fluid:* Pandy 3+. Cells, 16 per cu.mm. Pressure increased (1+). *Died* in October. Lead line in x-ray and microscopical sections of ribs. Nuclear inclusions in liver and kidneys.

Case 9. Autopsy No. 13698. A colored boy, 2 years old, who ate plaster, ashes, and paint from window-sills. Had abdominal pain and was constipated. History of vomiting for a month. Comatose for four days and had convulsions for one day. Lead line on gums. *Blood:* Haemoglobin 50 per cent. *Blood lead:* 0.5 to 1.0 mgm. per cent. *Temperature:* 37.4° to 38.4°C. *Leukocytes:* 12,880. *Spinal fluid:* Pandy 2+. Cells 30 per cu.mm. *Died* in June. Lead line in bones (x-ray and microscopical). Intranuclear inclusion bodies in liver and kidneys.

Case 10. Autopsy No. 13726. A colored girl, 2 years old, troubled with vomiting for two months. Convulsions chiefly on left side and nystagmus for two days. *Blood:* Haemoglobin 58 per cent. Stippled and nucleated red cells.

Blood lead: 0.1 mgm. per cent. *Spinal fluid:* Pandy 4+. Cells 45 per cu.mm. Pressure increased (2+). *Temperature:* 38.6° to 41°C. *Leukocytes:* 26,350. *Died* in July. Lead line in x-ray and microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys.

Case 11. Autopsy No. 13795. A colored girl, 2 years old, who ate the paint from her dolls for 2 months. Abdominal pain, constipation and vomiting present for two weeks, and convulsions for a day. *Temperature:* 38° to 40.6°C. *Leukocytes:* 25,500. *Haemoglobin:* 78 per cent. *Blood lead:* 0.5 mgm. per cent. Lead line in x-ray and microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys. *Spinal fluid:* Pandy 3+. Cells, 6 per cu.mm. Pressure increased (2+). *Died* in August.

Case 12. Autopsy No. 13830. A colored girl, 3 years old, who sucked painted toys. History of abdominal pain and vomiting for one month, and long period of crying. Stuporous, with spontaneous motion of head and hands, and right-sided convulsions for one day. Gasping respirations. *Temperature:* 35.4° to 40.2°C. *Leukocytes:* 39,000. *Blood:* Haemoglobin 48 per cent. Stippled and nucleated red blood cells. *Blood lead:* 0.5 to 1.0 mgm. per cent. Lead line in x-ray and in microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys. *Spinal fluid:* Pandy 4+. Cells, 11 per cu.mm. Pressure increased (2+). *Died* in September.

Case 13. Autopsy No. 14057. A colored boy, 7 years old. Chewed crayon and chalk. Was drowsy for five weeks and had pain in abdomen and back of head. Vomited at times for four weeks. Two days before death he fell twice on the street and was unconscious for a few minutes. He later became comatose and had convulsions. *Temperature:* 37.4° to 39.5°C. *Leukocytes:* 38,800. *Blood:* Red cells 3,720,000. Normoblasts and stippled red cells in blood smears. *Blood lead:* 0.5 mgm. per cent. Lead line on gums. Lead line in x-ray and in microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys. Widespread bilateral lobular pneumonia (pneumococcus type II). *Spinal fluid:* Pandy 4+. Cells 25 per cu.mm. Pressure 600 mm. of water. *Died* in January.

Case 14. Autopsy No. 14287. A colored girl 3 years old. History of pica. Vomiting, headache, and drowiness for five weeks. Coma, nystagmus and convulsions for one day. Tachycardia, extrasystoles and elevated blood pressure. *Temperature:* 36 to 40.6°C. *Leukocytes:* 25,700. *Blood:* Haemoglobin 62 per cent. Stippled red blood cells. *Blood lead:* 0.5 mgm. per cent. Lead line in x-ray and microscopical section of ribs. Intranuclear inclusion bodies in liver and kidneys. *Spinal fluid:* Pandy 2+. Cells 25 per cu.mm. Pressure increased. *Died* in June.

Case 15. Autopsy No. 14307. A colored boy, 18 months old, who ate flakes of dry paint from the walls. Had anorexia and was fretful for six weeks. Vomited for a week. Cried almost constantly and held hands to head and abdomen for four days. Convulsions for one day. *Spinal fluid:* Pandy 2+. Cells, 15 per cu.mm. *Blood:* Haemoglobin 50 per cent. *Blood lead:* 0.5 to 1.0 mgm. per cent.

Temperature: 37.4 to 39°C. *Leukocytes:* 8,200. *Died* in July. Lead line in bones (x-ray and microscopical). Intranuclear inclusion bodies in liver and kidneys.

Case 16. Autopsy No. 14336. A colored boy, 19 months old, who ate plaster and was constipated for 2 or 3 months. He was fretful and restless, and lost appetite and weight. For a week he was drowsy and vomited. Had convulsions for one day. Lead line on gums. *Blood:* Haemoglobin 35 per cent. *Blood lead:* 0.2 mgm. per cent. *Spinal fluid:* Pandy 2+. Cells 9 per cu.mm. Pressure increased (1+). *Leukocytes:* 10,000 *Temperature:* 37° to 38.4°C. *Died* in July. Lead line in x-ray and in microscopical sections of ribs. Nuclear inclusion bodies in liver and kidneys. Slight lobular pneumonia in right middle lobe.

Case 17. Autopsy No. 14352. A colored boy, 18 months old, who chewed paint from an icebox and sucked an indelible lead pencil. He was constipated and irritable for two weeks, and vomited at times for a week. Had screaming attacks and convulsions for three to four days. *Spinal fluid:* Pandy 2+. Cells 0. Pressure increased (630 mm. of water). *Blood:* 87 per cent. *Leukocytes:* 8,600. *Temperature:* 37.2° to 40.6°C. *Died* in August. Lead line in x-ray and microscopical sections of ribs. Nuclear inclusion bodies in liver and kidneys.

Case 18. Autopsy No. 14354. A colored girl, 6 years old, poisoned by inhaling fumes from battery casings burned for fuel. She had lead encephalitis with convulsions first in July, three years before death. She recovered, though retarded mentally thereafter. A month before death symptoms reappeared and there were anorexia, cough and fever. One week before death she had a single convulsion, and vomited almost daily afterwards. There were frequent violent convulsions for sixteen hours before death. Lead line on gums. *Spinal fluid:* Pandy 3+. Cells 11 per cu.mm. *Blood:* Haemoglobin 75 per cent. Blood lead elevated for three years (0.2 to 0.5 mgm. per cent). *Temperature:* 38.6° to 40°C. *Leukocytes:* 29,000. *Died* in August. Slight lobular pneumonia. Lead line in x-ray of bones three years ago, at intervals afterwards, and on final admission. Lead line in microscopical sections of ribs. Intranuclear inclusion bodies in liver and a few in kidneys.

Case 19. Autopsy No. 14370. A colored girl, 2½ years old, with a history of pica. Vomiting for a week and convulsions for one day. Lead line on gums. *Spinal fluid:* Pandy 2+. Cells 11 per cu.mm. Pressure increased. *Blood:* Stippled and nucleated red blood cells. Haemoglobin 65 per cent. *Blood lead:* 0.2 to 0.5 mgm. per cent. *Leukocytes:* 24,500. *Temperature:* 39° to 41°C. *Died* in August. Lead line in bones on fluoroscopic examination and in microscopical sections. Intranuclear inclusion bodies in liver and kidneys.

Case 20. Autopsy No. 14849. A white girl, 3 years old, who gnawed painted furniture for 18 months. History of vomiting for three months. She was irritable, nervous, cranky and lethargic for a month. Drowsiness and coma appeared during the last two days of life, and finally convulsions. *Spinal fluid:* Pandy 2+. Cells 11 per cu.mm. *Blood:* Haemoglobin 76 per cent. Stippled red cells. *Blood lead:* 0.55 mgm. per 100 gms. *Temperature:* 37° to 40.4°C.

Leukocytes: 31,500. *Died* in June. Lead line in x-ray and in microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys.

Case 21. Autopsy No. 14954. A white boy 2 years old chewed the paint from woodwork and toys for three months. Attacks of vomiting appeared five weeks before the present illness and again for about one day before death. For about twenty hours he was drowsy and had episodes of spasticity and flaccidity, slow respirations, choked discs, stiff neck, ankle clonus and hyperactive reflexes. Finally, deep coma and death. *Spinal fluid:* Pandy 3+. Cells 10 per cu.mm. *Blood:* Haemoglobin 63 per cent. Stippled red cells. *Blood lead:* 0.41 mgm. per cent. *Temperature:* 36.2° to 37.4°C. *Leukocytes:* 21,320. *Died* in September. Lead line in x-ray and microscopical sections of ribs. Intranuclear inclusion bodies in liver and kidneys.

Case 22. Autopsy No. 14974. A colored girl, 2½ years old, with history of pica from 9 to 12 months of age. Had projectile vomiting several times the day before death. Became limp and comatose after vomiting, and a little later convulsions appeared, first on the left and then on the right side. Repeated clonic convulsions at half-hour intervals for thirteen hours until death. *Spinal fluid:* Pandy 2+. Cells 5–10 per cu.mm. *Blood pressure:* 105/70. *Pulse:* Irregular. *Respirations:* Irregular and shallow. *Blood:* Haemoglobin 45 per cent. Red blood cells 2,700,000. Stippled red cells. *Temperature:* 38.2° to 39.2°C. *Leukocytes:* 20,940. *Died* in October. Lead line in bones (x-ray and microscopical). Nuclear inclusions in liver and kidneys. Purulent tonsillitis. Few minute tubercles in one lung and confluent tubercles in a bronchial lymph node. Large crusted pustular lesions on extremities like those of impetigo (present for two weeks).

REFERENCES

(1) Alderson: *Lancet*, 1852, **2**, 73 and 95.
(2) Aub, *et al*: *Medicine*, 1925, **4**, 1.
(3) Westphal: *Arch. f. Psych.*, 1888, **19**, 620.
(4) McKhann: *Amer. Jour. Dis. Child.*, 1926, **32**, 386.
(5) Park, Jackson and Kadji: *Ibid.*, 1931, **41**, 485.
(6) Vogt: *Amer. Jour. Roentgenol.*, 1930, **24**, 550.
(7) Blackman: *Bull. J. H. H.*, 1936, **58**, 384.
(8) Dana: Lead Diseases: Translation from the French of Tanquerel des Planches, 1848.
(9) McKhann and Vogt: *Jour. A. M. A.*, 1933, **101**, 1131.
(10) Baker: *Arch. of Path.*, 1935, **19**, 213.
(11) Esser: *Dtsch. Ztschr. f. d. Gesammte Gerichtliche Med.*, 1936, **26**, 430.
(12) Kato: *Amer. Jour. Dis. Child.*, 1932, **44**, 569.
(13) McKhann: *Arch. Neurol. and Psych.*, 1932, **27**, 294.
(14) Vogt: *Jour. A. M. A.*, 1932, **98**, 125.
(15) Wilcox and Caffey: *Ibid.*, 1926, **86**, 1514.
(16) Thomas and Blackfan: *Amer. Jour. Dis. Child.*, 1914, **8**, 377.

(17) Suzuki and Kaneko: *Jour. of Oriental Med.*, 1924, **2**, 55.
(18) Fukushima and Matsumoto: *Oriental Jour. Dis. of Child.*, 1928, **3**, 27.
(19) McKhann: *Trans. Amer. Neurol. Assoc.*, 1931, 183.
(20) Kussmaul and Maier: *Dtsch. Arch. f. klin. Med.*, 1872, **9**, 283.
(21) Von Monakow: *Arch. f. Psych. u. Nervenheilk.*, 1879-80, **10**, 495.
(22) Seifert: *Berliner Klin. Wchnschr.*, 1884, **21**, 555.
(23) Oppenheim: *Arch. f. Psych. u. Nervenheilk.*, 1885, **16**, 476.
(24) Courtney: *Boston Med. and Surg. Jour.*, 1900, **142**, 136.
(25) Cadwalader: *Jour. of Nervous and Mental Dis.*, 1912, **39**, 153.
(26) Hassin: *Arch. Neurol. and Psych.*, 1921, **6**, 268.
(27) Freifeld: *Virch. Arch.*, 1928, **268**, 456.
(28) Freifeld: *Ibid.*, 1933, **287**, 549.
(29) Tuthill: *Bull. Buffalo Gen. Hosp.*, 1929, **7**, 15.
(30) Staemmler: *Klin. Wchnschr.*, 1929, **81**, 1210.
(31) Winkelman and Eckel: *N. Y. State Jour. Med.*, 1933, **33**, 427.
(32) Rhea: *Internat. Clinics*, 1934, **1**, 203.
(33) Goodwin: *Bull. J. H. H.*, 1934, **55**, 347.
(34) Traube: Gesammelte Beiträge, 1870, **2**, 551.
(35) Grinker: Neurology, 1933, 895.
(36) Brain: Disorders of the Nervous System, 1933, 584.
(37) Weil: Text-Book of Neuropathology, 1933, 314.
(38) Bodian: *Anat. Record*, 1936, **65**, 89.
(39) Okkels: *C. r. Soc. de biol.*, 1930, **102**, 1089.
(40) Keibel and Mall: Human Embryology, 1912, **2**, 74.
(41) Ferraro and Hernandez: *The Psychiatric Quart.*, 1932, **6**, 121.
(42) Weller and Christensen: *Arch. Neurol. and Psych.*, 1925, **14**, 327.
(43) Ginandes: *J. of Mount Sinai Hosp.*, 1935, **2**, 74.
(44) Blackfan and Hamilton: *Boston Med. and Surg. Jour.*, 1925, **193**, 617.