LEAD ENCEPHALOPATHY IN A COOPERAGE

BY

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Advances made in the industrial field have led not only to a reduction in the total number of cases of plumbism, but also to a relative decrease in the severe forms of the disease, including encephalopathy. Of 6,638 cases of plumbism occurring during the years 1900 to 1909, 262 were cases of encephalopathy, an incidence of 3.9%, (Legge, 1934), whereas of 634 cases notified to the Factory Department during the years 1939 to 1948, only five showed symptoms of encephalopathy, less than 0.8%. It is generally agreed that severe exposure by inhalation of dust, fume, or vapour is necessary to produce encephalopathy. Today, in large industrial concerns, inspection and control are so thorough that such exposure seldom arises. The cooperage described in this paper had escaped inspection, and two coopers contracted lead poisoning, one of whom developed encephalopathy, before the presence of a severe lead hazard was brought to light.

Of all the manifestations of inorganic lead poisoning in the adult, encephalopathy is the most serious and the least common. The last cases to be recorded in Britain would appear to be those of Chalmers (1940) and Nussey and Drybrough-Smith (1940). Encephalopathy in children differs somewhat from that seen in adults, the whole clinical and pathological picture suggesting a more intense reaction: it will not be discussed.

Grisolle (1836) distinguished three main forms of encephalopathy: convulsive, comatose, and delirious, of which the convulsive was the most serious and the most common. As Tanquerel (1839) pointed out, these forms occur more often in combination than singly. The onset of encephalopathy may be sudden. When apparently well, the patient may fall in an epileptiform attack or pass rapidly into coma or mania. More often there is warning, either in the form of other manifestations of lead poisoning or in the occurrence of various symptoms which frequently precede the onset of frank encephalopathy, namely intense headache; restlessness; depression; insomnia and disturbed dreams; hallucinations; pallor; faintness; vertigo; disturbances of vision; and transient paralysis and aphasia, paresthesie, and tremors of the hands and face (Aub, Fairhall, Minot, and Reznikoff, 1925; Hamilton, 1925).

The disturbance of cerebral function caused by lead varies in degree, from the restlessness, irritability, impairment of memory and lack of concentration encountered in all forms of lead poisoning, to the confusion, delirium, mania, and coma of advanced encephalopathy. The delirium does not appear to differ essentially from severe delirium produced by other causes, but the concurrence of convulsions may present a characteristic picture. These may take the form of major epilepsy with loss of consciousness, but Tanquerel (1839) considered that partial preservation of consciousness was more common.

Papilledema, retinal haemorrhages, and subsequent optic atrophy are well recognized complications of lead encephalopathy. Primary optic atrophy due to lead is also said to occur. In the potteries, Prendergast (1910) found total blindness in 7.7%, and partial blindness in 10.2% of women with plumbism. Although the onset may be of dramatic suddenness, it is usually gradual, and eventual recovery is the rule. Transient attacks of loss of vision, affecting the whole or part of the visual field, have also been described, and are usually attributed to spasm of the retinal or cerebral arteries. Paralysis of the extrinsic eye muscles is not uncommon; abnormalities in pupillary reactions and accommodation are rare. At one time or another lesions of all the cranial nerves have been attributed to lead. Arterial hypertension not infrequently accompanies encephalopathy, and there may be some degree of pyrexia. Some impairment of mentality, either temporary or lasting, was found by Alice Hamilton (1925) in 19 out of 59 cases of encephalopathy reviewed by her. One of her cases suffered from recurrent epilepsy after apparent recovery and similar cases have been described by other writers. As might be expected,
an anxiety state and hysteria may follow encephalopathy in some cases.

The relationship between lead on the one hand and arteriosclerosis, nephritis and hypertension on the other, is now a matter of dispute, but in the past lead was accepted as a causal factor in these conditions, and cases of cerebral arteriosclerosis and of uremia have been included in accounts of saturnine encephalopathy. The mortality rate in different recorded series varies from 25% to 75% (Aub and others, 1925). Hamilton (1925) and Cantarow and Trumper (1944) have reviewed the literature of this subject.

Many conflicting reports of the pathological changes in encephalopathy have been published. Aub and his co-workers (1925) concluded that the condition was primarily meningitis with secondary involvement of the brain, “a meningo-encephalopathy”. The more recent work of Freifeld, Tuthill, Staemler, Winkelman, and Eckel and Rhea (quoted by Blackman, 1937) support the older view that lesions in the nervous system are secondary to changes in the vessels. Blackman (1937), who made detailed pathological studies of 22 children who had died of encephalopathy, concluded that “the lesions in the brain are for the most part dependent on vascular damage and the collection of exudate”.

The most frequent finding in the cerebrospinal fluid is a raised pressure. An increase in protein and in the number of lymphocytes may also occur, but these changes are seen more often in children than in adults, in whom they do not appear to be a constant or marked feature. Mosny and Malloizel (1907), quoted by Aub and others (1925), found that the cell count averaged 100 lymphocytes per c.mm. in encephalopathy, but their findings have not been borne out by subsequent observation.

Cantarow and Trumper (1944) observed concentrations of lead ranging from 0-001 to 0-040 mg. per 100 ml. of cerebrospinal fluid in patients with no history or evidence of abnormal exposure to lead, and concentrations as high as 0-35 mg. per 100 ml. in subjects with lead poisoning with no nervous manifestations. They quote Duensing as reporting values of 0-22 mg. and 0-493 mg. per 100 ml. in two cases of lead poisoning with neurological manifestations.

Since 1923, when 149 cases of encephalopathy due to tetra-ethyl lead occurred in the United States of America, attention has been focused on this form of lead poisoning, and series of cases have been reported by Kehoe (1925), Macle (1935), Cassells and Dodds (1946), Singh (1949), and others. The fat soluble nature of tetra-ethyl lead predisposes its early localization in tissues of high fat content, in particular the nervous system (Kehoe, 1925). Its action on nervous tissue is probably therefore direct and not, as appears to be the case in inorganic lead poisoning, indirect through changes in the vessels. The cerebral symptoms of tetra-ethyl lead poisoning differ in many respects from those of inorganic lead encephalopathy. Convulsions are rare, papilloedema, optic atrophy, loss of vision, temporary paralyses, paresthesiae and aphasia do not apparently occur, and no permanent cerebral sequelae were noted in over 80 cases (American Public Health Association, 1943). The pressure of the cerebrospinal fluid may be raised during delirium, but shows no evidence of a meningeal reaction (Macle, 1935). The marked drop in blood pressure and slowing of the pulse so frequently seen in tetra-ethyl lead poisoning are not features of inorganic lead encephalopathy. For these reasons it would be unwise to draw any conclusions about inorganic lead encephalopathy from the findings in tetra-ethyl lead poisoning.

Case Report

The patient, a man of 39 years, was first seen as an out-patient on March 30, 1949. His main complaints were of headache, vomiting, and general weakness, but sugar and acetone were found in his urine and on questioning he admitted to loss of weight and polyuria. A provisional diagnosis of diabetes mellitus was made.

On admission to hospital the next day there was no acetone and only a trace of sugar in his urine, and it was clear that diabetes was not the cause of his symptoms. He was somewhat confused and his headache was extremely severe. He volunteered no information and tolerated questioning and examination with reluctance. No suspicion of a lead hazard was aroused at this time, and much of the following history was obtained at a later date when the patient was more coherent. He had been a cooper for over 20 years but for eight months had been working for a firm chiefly concerned with the repair of barrels used for white lead. One of his mates had been off work with colic and constipation. He was a very heavy beer and spirits drinker, although he had been taking less during the last week or two. His father, also an alcoholic, had died of cirrhosis of the liver. Except for a chronic winter cough he had previously been healthy.

For six months he had been troubled by headache, general weakness and morning anorexia, and had lost about a stone in weight during that period. The headache had been at first slight and infrequent, but recently it had been practically continuous and of such severity that the patient could not remain still during the day and had slept little at night. It was mainly frontal, was aggravated by stooping, occurred at no particular time of the day, and for six weeks had been associated with vomiting. Although he had first noticed a general weakness and ease of fatigue, latterly this had been most marked in his right arm, the grip being particularly
affected so that he had found it difficult to use his hammer at work. At the onset of his symptoms he had suffered from obstinate constipation lasting two weeks and associated with lower abdominal colic. There had been no further constipation, but occasional bouts of diarrhea.

For six weeks he had suffered from periodic diplopia and blurring of vision, slight deafness and occasional tinnitus in both ears. He had also experienced attacks of dizziness when walking, which caused him to stagger, though he had not fallen; there was no actual sense of rotation and he did not deviate in any particular direction. On one occasion there had been transient weakness of both hands, lasting only a few minutes, and once whilst at work he had become suddenly but temporarily blind. It was not clear whether this was a total or partial visual field defect. He could only remember that for a minute or two he had been unable to see his mate, who had dismissed the matter with some cryptic remark about his drinking habits. He had a slight cough, and a few days before admission he had coughed up about two ounces of bright red blood. He gave a history of polyuria for some months and of recent thirst, and he had noticed an unpleasant taste in his mouth which might be described as metallic. About ten days before admission his doctor had given him a cough mixture; his symptoms had been very severe during the following week. (This prescription was dated March 19, 1949, and contained 2% gr. potassium iodide in each dose. It is thought that he took very little of this medicine, and the exacerbation of symptoms at that time may have been coincidental.)

Examination on Admission.—The patient was of average muscular development, with little subcutaneous fat. His eyes were watery and suffused, his skin and mucous membranes pale, and there was slight but definite beaking of the finger nails. The pulse, temperature, and respirations were normal. The breath was offensive and the mouth foul, with furred tongue and gingivitis. The blood pressure was 125/85 mm. Hg, and no abnormality was detected in the heart, lungs, abdomen, or external genitalia. Rectal examination was normal.

The findings in the nervous system were: fine tremor of the lower lip and outstretched hands; speech normal, but cerebration slow and memory poor; no evidence of meningism; pupils normal in appearance and reactions; bilateral slight papilledema, more marked on the right; retinal vessels normal with no hemorrhages or exudates; slight weakness of the right external rectus muscle, but no diplopia during examination and no nystagmus; slight middle ear deafness on the left side; other cranial nerves intact; slight generalized muscular weakness; loss of power most marked in the right arm, the grip of the right hand being particularly affected; no wasting or fibrillation; no spasticity; tendon reflexes brisk and equal; superficial reflexes normal; all forms of sensation normal and Romberg's sign absent; no intention tremor or dysdiadochokinesia, but movements of the arms and legs shaky and the gait unsteady.

At this stage the suggested diagnosis was bronchial carcinoma with secondary deposits in the brain. Radiographs of the skull and chest were, however, normal. Lumbar puncture gave a clear fluid under very high pressure, some 10 ml. of which was cautiously withdrawn. Examination of the fluid revealed protein 60 mg. % with a slight increase in globulin; gold curve 0112210000; sugar 70 mg. %; chlorides 650 mg. %; no increase in cells: Wassermann reaction negative in all dilutions. The blood Wassermann reaction was also negative, the non-protein nitrogen 35 mg. %, and the urine contained no albumin, casts, or red cells. An electrocardiogram was normal.

Progress.—The patient was given magnesium sulphate by mouth, and, when his condition permitted, hypertonic retention enemata. Severe headache and frequent vomiting persisted, although temporarily abolished by lumbar puncture. He became incontinent of urine and faces. Papilledema increased, and a small retinal hemorrhage appeared in the right eye. He was much troubled by diplopia. During the day he was more confused, and was difficult to control. At night he passed into a noisy, agitation delirium, shouting, swearing, and dancing about on his bed. When not thus engaged he maintained a ceaseless rambling chatter. He was disorientated as to time and place, and clearly the victim of frightening hallucinations. Repeated injections of soluble phenobarbitone were necessary to control the delirium.

Although there was amnesia for the nights on which he had been delirious, he was able, some days later, to give an account of the hallucinations from which he had suffered at other times. They were mostly visual and had first occurred some days before admission, when he was much troubled by a man in woman's clothing, who came into the bedroom at night, though the door was locked, and attempted to get into the bed. When the patient tried to come to grips with him he disappeared. More recently, while in hospital, the hallucinations had been of a terrifying nature; enormous black men thrusting at him with their spears or men with machine-guns trained on him. Sometimes there was micropsia, in which all the doctors had tiny hands. To a lesser extent he suffered from auditory hallucinations, people calling him by name and passing offensive remarks about him.

On several occasions his urine contained a trace of sugar, but as the blood sugar remained normal this glycosuria was presumably due to a low renal threshold associated with the raised intracranial pressure.

By the fifth day a slight improvement in his condition was apparent. Although noisy and confused at night, he was more easily restrained, and by day he appeared rational. Headache remained severe. During the course of a further examination at this time a blue line was observed near the gum margin, most marked where infection was severe, and myoedema was elicited in the muscles of the shoulder girdle and upper arms. For the first time lead poisoning was suspected. The possibility of a lead hazard was admitted by the patient and confirmed by a visit to the cooperage where he had worked.
Examination of the blood revealed marked punctate basophilia with increased polychromasia; hemoglobin 9.7 g. (65% Haldane); red blood cells 3,500,000; colour index 0.9; reticulocytes 4.5%; white blood cells 9,500, with a normal differential count. A red cell fragility test showed marked increased resistance to hypotonic salines. The Van den Bergh test was negative and the icteric index 2 units; the thymol turbidity 2 units and the alkaline phosphatase 5 units. So far as these tests were concerned there was no evidence of liver damage. Urea concentration and clearance tests gave results within normal limits.

Lumbar puncture was repeated on the sixth day, about 20 ml. of cerebrospinal fluid being withdrawn. The pressure was still extremely high, and a rise of cell count to 10 per c.mm. was noted. Analysis of blood and cerebrospinal fluid revealed a high lead content: blood 0.33 mg. per 100 g.*, cerebrospinal fluid 0.06 mg. per 100 g. The patient was then given calcium lavulinate intravenously (20 ml. of a 10% solution), followed by a high calcium and phosphorus diet, supplemented by calcium lactate orally (5 gr. t.d.s.). No extra iron or vitamins were administered. Sedatives at night and magnesium sulphate by mouth and rectum were continued. Complete relief of headache following lumbar puncture lasted some eight hours on this occasion. Urine collected on the seventh day contained 0.9 mg. of lead per litre*, and the total urinary excretion of lead during the 24 hours was 0.9 mg.

From this time the patient's condition improved more rapidly. Headache occurred less frequently and was easily relieved by mild analgesics. His behaviour was occasionally strange at night, but in general he slept well and assured us with obvious relief that there were "no more devils". Incontinence ceased. His appetite improved and he lost no more weight, although it was several weeks before he began to gain. Muscular power increased. The retinal haemorrhages was absorbed and the papilledema regressed. Clinical improvement was accompanied by a fall in the pressure of the cerebrospinal fluid. On the tenth day this was 150 mm. on the thirteenth day 95 mm. and on the fifteenth day 80 mm. of cerebrospinal fluid. The blood pressure remained normal.

This satisfactory progress was interrupted on the nineteenth day by a noticeable recurrence of symptoms. The patient felt "off colour", and complained that for a short time he had been unable to control the movements of his hands. Later severe headache and insomnia returned. On the twenty-second day the pressure of the cerebrospinal fluid was considerably increased, although the protein had fallen to 50 mg.% and the cells to 2 per c.mm. By the twenty-fourth day he was confused, irrational and emotionally unstable, weeping at the slightest provocation. There were no further hallucinations, but he suffered from various delusions, accusing the nursing staff of keeping him awake at night, and of leaving clues around the ward for him to solve, so that he might work out his own salvation. This setback was short-lived. By the twenty-seventh day he was mentally normal and there was no headache; the cerebrospinal fluid pressure was 250 mm. The blood pyruvic acid was 0.8 mg.% on the twentieth day and 0.95 mg. % on the twenty-sixth day. With the method employed for estimation both these figures are within normal limits.

On the thirtieth day there was still slight papilledema in the right eye, and some weakness of the right arm. There was no tremor, ataxia, or incoordination. By the thirty-seventh day the only abnormalities on physical examination were a lead line, myoidema of the arms, and clubbing of the fingers. The cerebrospinal fluid was normal. The patient felt well. He was then given a normal diet without supplementary milk or calcium. For a few days there was a return of headache, and after ten days a rise in the cerebrospinal fluid pressure to 200 mm. was noted. For the next two weeks a low calcium diet was given. There was no return of headache. More drastic methods of de-leading were not attempted.

The blood picture had meanwhile shown a steady improvement. The number of stippled cells per million red cells fell from 16,000 on the fourteenth day to 4,500 on the twenty-second day. Dr. Charles St. Hill reported on Giensa stained marrow films obtained on the twenty-sixth day:

"There is considerable increase in red cell production. The immature cells appear normal up to the late (polychromatric) normoblast stage. At this stage about 4% of normoblasts show punctate basophilia. The mature red cells from the marrow contain 23,000 stippled cells per million red blood cells." These findings are in agreement with the recent work of McFadzean and Davis (1949). We were, however, unable to obtain a positive reaction for iron in the stippled cells, using films fixed in methyl alcohol. A red cell fragility test on the thirty-seventh day was normal.

Examination of blood on the sixty-second day showed hemoglobin 11.8 g. (80% Haldane); red cells 4,500,000; reticulocytes 2%; stippled cells 700 per million red blood cells.

The progressive decrease in the concentration of lead in the blood and cerebrospinal fluid and in the amount excreted daily in the urine can be seen in Table 1 and Fig. 1. This fall was maintained during relapse, and was not apparently affected by reduction of the calcium intake.

After nine weeks in hospital the patient was discharged. He had no complaints. The lead line was less distinct; myoidema and finger clubbing were still present. The cerebrospinal fluid was normal; the pressure 120 mm. Shortly afterwards he obtained light work with another firm of cooperers where there was no exposure to lead.

Six months after his first admission to hospital the patient's only complaint was an occasional feeling of faintness, chiefly when he was worried; otherwise he claimed to be in perfect health. For the previous two months he had been taking a normal diet without extra milk and had limited himself to two pints of beer a day. His wife, however, complained that he was now extremely irritable and hypersensitive and made
constant accusations against her of infidelity for which there was apparently no justification. She confirmed that he was now sober in his habits.

Physical examination revealed no abnormality. The lead line had completely disappeared from his gums, and, surprisingly, the finger nails were no longer beaked. Blood pressure was 140/85 mm. Hg; cerebrospinal fluid normal; blood count: hemoglobin 14.8 g. % (100% Haldane); red blood cells, 5,100,000; no stippled cells seen; non-protein nitrogen 35 mg. %; no abnormality detected in the urine. The daily urinary excretion of lead had diminished, but the concentration of lead in the blood had risen slightly since the last estimation (Table 1).

When next examined, after nine months' observation, no material change was apparent in the patient's physical condition. He was referred for a psychiatric opinion to Dr. Ivan Leveson, who reported as follows:

"He complains that he finds mental effort difficult, is indecisive and unable to understand things as well as previously. Prior to his illness he was very active and sociable, whereas now he has no inclination to mix with his friends, and lacks interest. He finds himself frequently thinking about his hallucinatory experiences, and the fact that he 'saw' men in his wife's bedroom, during the acute phase of his illness, has led him to doubt her fidelity. During examination he is pleasant, frank, cooperative and coherent, and there is no evidence of any acute emotional disorder."


### Table 1

**Summary of Analytical Data**

<table>
<thead>
<tr>
<th>Days after Admission</th>
<th>C.S.F. (mg. Pb in 100 g)</th>
<th>Blood (mg. Pb in 100 g)</th>
<th>Daily Output (ml.)</th>
<th>S.G.</th>
<th>Urine Mg. Pb/litre</th>
<th>Mg. Pb/litre converted to S.G. of 1024</th>
<th>Daily Urinary Excretion Pb (mg.)</th>
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Collection of Specimens.—All specimens for analysis were collected in lead-free containers. On the seventh, eighth, and ninth nights the patient was confused and the possibility that urine collected during this period was contaminated cannot be excluded. Thereafter he was scrupulously careful. For lumbar puncture and venepuncture new autoclaved needles and syringes were used, but these were not treated to remove traces of lead. As a check, therefore, samples of blood on the twenty-second and one hundred and ninety-sixth days, and of cerebrospinal fluid on the twenty-second day, were taken with syringes and needles previously treated with nitric acid. The results of analysis of these specimens were in general conformity with those obtained by the less scrupulous technique. This finding, the absence of sudden unexplained variations and the low figures eventually obtained, lead one to suppose that no material contamination occurred.

To obviate the variations in urinary lead concentration which take place throughout any 24-hour period, analysis was carried out on the whole 24-hour specimen. The mg. per litre figure thus obtained was also converted to a standard specific gravity of 1024, as recommended by Levine and Fahy (1945). The total daily urinary excretion of lead was calculated, as this appears to afford the most satisfactory data for following the progress of a case of poisoning.

Air samples were collected by means of a hand-operated pump, and absorption in acetic acid.

Method of Analysis.—Analysis of all specimens was carried out by a dithizone method based on that described by Snyder (1947). The figures for lead concentration in cerebrospinal fluid and blood are accurate to within 0.005 mg. per 100 g., and in urine to within 0.005 mg. per litre. For this reason results recorded as “nil” in the cerebrospinal fluid should, to be exact, be stated as “less than 0.005 mg. of lead per 100 g.”
LEAD ENCEPHALOPATHY IN A COOPERAGE

Conditions in the Cooperage

Since a severe lead hazard is now uncommon in industry in this country, a more detailed description of the cooperage is important.

It was in 1940, when the shortage of timber made this profitable, that the firm first undertook the repair of barrels which had contained white lead. They failed to give notification that the work was in progress, and therefore evaded inspection.

The building, a ramshackle barnlike structure, was of the most primitive nature. Apart from large open doors, and windows high up in the walls, there was no system of ventilation. The floor, which was rough and pitted, was dry-swept. There were no washing facilities and no canteen, and although they did not eat on the premises the men smoked when they liked and drank tea periodically. Each man wore an apron over his ordinary clothes. The dust of white lead was evident everywhere, particularly on the men’s hands, hair, and clothing.

Most of the barrels had contained dry white lead. Before cooping these the men had instructions to don masks, damp the barrel, empty out any white lead in the bottom, and replace the lid. Depending on the cooper himself, most or all of these precautions were disregarded; when the work was carelessly performed clouds of dust rose up from the barrels and from the floor around them. Even more dangerous were barrels which had contained white lead ground in linseed oil; this had set hard and to soften it a small wood fire was lighted in the bottom of the barrel, which after a few minutes could be scraped clean. Perhaps the most serious hazard was a small brazier, on which an apprentice was heating a kettle for the coopers’ cup of tea; for fuel he was using parts of a barrel thick with ground white lead. This was probably responsible for the high lead content of the surrounding air when no work was in progress.

Analyses of atmosphere samples gave the following figures:

1. General air sample some 5 yds. from brazier (no active work in progress):
   20 mg. lead per 10 cu.m.
2. Air at face level, when working on white lead barrel with prescribed precautions:
   50 mg. lead per 10 cu.m.
3. Same barrels, but working with extreme carelessness:
   660 mg. lead per 10 cu.m.
4. Air at face level, when working on ground white lead barrel, after heating in the usual manner:
   830 mg. lead per 10 cu.m.
5. Fumes issuing from brazier:
   1,300 mg. lead per 10 cu.m.

Lane (1936) has suggested that the maximum permitted contamination of the atmosphere with lead be fixed at 2 mg. per 10 cu.m., and this figure, or slightly less, is generally accepted in Great Britain and in the United States of America.

Three coopers and two apprentices were employed. The coopers performed identical work with apparently similar risks; the apprentices were given lighter and less hazardous tasks. The apprentices had not been long at the job; they were well, they had no lead line and their blood was normal. All three coopers showed a blue line on the gum margins. Two, who had been working for ten years on lead barrels, had no symptoms of intoxication, and although they looked pale, their hemoglobin was over 90% (Haldane); one had a stippled count of 4,000, the other of 400 per million red blood cells. The third cooper had been working on the barrels for three years. He had suffered from periodic constipation and colic; he looked pale and his blood count showed hemoglobin 9-7 g. (65% Haldane); reticulocytes 3-5%; stippled cells 4,000 per million red blood cells.

We were informed that our patient had been an extremely careless worker. He took none of the prescribed precautions, and in particular was in the habit of rolling his own cigarettes when his hands were covered with white lead.

Discussion

Predisposing Factors.—Of four coopers, exposed to apparently similar risks, two developed lead poisoning and two remained in good health. Personal idiosyncrasy may be postulated to explain this fact, but it is difficult to prove. Alcoholics are particularly susceptible to lead poisoning, and the effect on the brain of alcohol or a vitamin B deficiency might well render it more vulnerable to the toxic action of lead. The man with encephalopathy was an alcoholic, but his mate, an even heavier drinker than he, was perfectly well after ten years’ exposure, and the other cooper who showed evidence of intoxication was a teetotaller. Kehoe (1947) stresses the generally unrecognized variability of lead exposure from person to person and from time to time in the same occupation. Atmospheric samples taken during work in the cooperage showed that extreme carelessness increased the lead concentration tenfold; this finding alone might account for apparent differences in susceptibility among the coopers.

Diagnosis.—The possibility of lead poisoning in this case was at first overlooked, through failure to obtain a good history and to insist on a detailed examination of a confused and uncooperative patient.
But even when it is realized that a patient has been exposed to lead, the diagnosis of encephalopathy presents considerable difficulty. The condition is so uncommon that cerebral symptoms in lead workers are much more likely to be due to causes other than lead. High concentrations of lead in the blood and in the urine are proof only of absorption, not of intoxication, but normal or low levels are of value in excluding the diagnosis, since severe absorption is necessary to produce encephalopathy. In the present state of our knowledge the diagnostic significance of lead in the cerebrospinal fluid is doubtful. There appears to be no definite relationship between the concentration in the cerebrospinal fluid and symptoms of encephalopathy, a point illustrated in this case by the absence of lead during relapse.

The clinical picture of encephalopathy is not distinctive. In its various forms it is closely simulated by hypertensive encephalopathy, uremia, idiopathic epilepsy, neurosphilitis, pellagra without cutaneous manifestations, Wernicke's encephalopathy, delirium tremens and other causes of severe delirium, cerebral tumour, encephalitis, meningitis, and intoxications with various drugs.

Although in our case there was eventually ample proof of absorption of lead, and also of intoxication as evidenced by the blood changes, the possibility that the cerebral condition was due to other causes had to be seriously entertained.

Headache, vomiting, and papilledema, and the progressive nature of his symptoms suggested a "space-occupying" lesion, and the history of cough, hemoptysis, and loss of weight, with beaking of the finger nails, pointed to a primary lesion in the lungs. The close resemblance to cerebral tumour has been noted in many accounts of encephalopathy.

Wernicke's encephalopathy was also considered. Rapid improvement without the exhibition of any of the vitamin B group, and the normal blood pyruvic acid just before and after relapse, rendered this diagnosis unlikely.

Delirium tremens was the only other condition which presented a real problem in diagnosis. The history of cerebral symptoms over some months, the absence of tachycardia, pyrexia, leucocytosis or severe constitutional symptoms, and the presence of definite papilledema were the main differentiating features.

**Clinical Features.**—The case described here was, in the main, characteristic of the delirious type of lead encephalopathy, but certain features merit further discussion.

**Arterial Hypertension.**—According to Traube (1878) and Vaquez (1904) hypertension is an invariable accompaniment of lead encephalopathy, and Cantarow and Trumper (1944) concluded that many, if not indeed the majority, of the phenomena of lead encephalopathy are due to hypertension, particularly the convulsive manifestations and the subjective and objective ocular abnormalities.

A sufficient number of cases of lead encephalopathy with normal blood pressures have now been recorded to disprove the contentions of Traube and Vaquez, and the case reports of Hamilton (1925), Evans (1932), Chalmers (1940), and Nussey and Drybrough-Smith (1940) show clearly that all the major manifestations of encephalopathy, including coma, delirium, convulsions, and transient visual disturbances and aphasia, may occur in the absence of hypertension. Evans noted constriction of the retinal arteries in the periods between convulsions, when the blood pressure was 120/70 mm. Hg and attacks of severe headache were followed by temporary homonymous hemianopia. Our patient experienced transient blindness once, and a temporary weakness of both hands on two occasions, but at no time was the blood pressure found to be raised.

It seems likely that arterial spasm is the underlying cause of the transient paresis, aphasia and amaurosis which occur in hypertensive and lead encephalopathy, as is the case in the similar phenomena associated with migraine. It is interesting that they have not been observed in poisoning with tetra-ethyl lead, which appears to act directly on the nervous tissue rather than on the vessels. Fishberg (1939) has suggested that, in the instances of lead encephalopathy without hypertension, "it would seem plausible, though not proved, that the vasoconstriction is largely confined to the cerebral vessels without sufficient splanchnic and other vasoconstriction to produce hypertension."

**Cerebrospinal Fluid.**—From his study of cases in children, McKhann (1932) concluded that the signs of lead encephalopathy were pathognomonic, not of lead poisoning, but only of increased intracranial pressure. While it is improbable that raised intracranial pressure can account for all the manifestations of encephalopathy, particularly the transient phenomena just discussed, the constant relationship between cerebral symptoms and increased cerebrospinal fluid pressure was a noticeable feature of our case; a fall in pressure accompanied the initial clinical improvement, and a rise occurred during relapses.

Fig. 1 shows an approximate parallel between the concentration of lead in the blood and cerebrospinal fluid, although the infrequency of the estimations probably gives an artificial stability to the
LEAD ENCEPHALOPATHY IN A COOPERAGE

It is interesting that Straube (1948) has recently demonstrated a similar relationship between the content of lead in the blood and cerebrospinal fluid in lambs given increasing doses of lead acetate.

Haemoptysis.—The cause of haemoptysis in this case was not revealed, but may have been associated with chronic bronchitis. There appears to be no conclusive evidence that increasing specific lesions in the respiratory organs. The finger clubbing was also unexplained.

Relapse.—This does not appear to be common during recovery from encephalopathy due to inorganic lead, although it is not infrequently seen in tetra-ethyl lead poisoning (Machle, 1935). Alice Hamilton (1925) records a case similar to ours, though more severe.

Treatment.—The symptomatic treatment of lead encephalopathy includes lumbar puncture and injections of hypertonic salines to lower intracranial pressure, sedatives (in particular the barbiturates) for the control of convulsions and mental excitement, and measures to combat dehydration and starvation. In children, Bucy and Buchanan (1935) and other workers have recommended decompression for the relief of raised intracranial pressure and to reduce the likelihood of complications. The curative treatment of lead poisoning is the subject of much controversy. Whilst no workers question the beneficial effect of calcium in lead colic, due at least in part to a local action on the intestinal muscle, several authorities express doubt as to its value in other forms of lead poisoning. In the case of encephalopathy described in this paper, a high calcium and phosphorus diet, with additional calcium intravenously and by mouth, was started on the sixth day in hospital. By this time the patient had been free from exposure for over a week, and the bowel frequently purged with magnesium sulphate. The rapid decrease in urinary lead excretion, evident from the seventh to the nineth days, may have been taking place for some days previously. Following the administration of calcium there was undoubtedly marked clinical improvement, but this improvement ran parallel with the fall in cerebrospinal fluid pressure, and may have been due, at any rate in part, to repeated lumbar puncture. A normal calcium intake during the sixth week, and subsequently a low calcium diet, were not accompanied by any rise in the lead content of the blood, cerebrospinal fluid, or urine. There was, it is true, a return of headache and a rise in the pressure of the cerebrospinal fluid during the sixth week, but these did not recur when a low calcium diet was given, and a much more serious relapse had taken place when the patient was receiving large amounts of calcium. No definite conclusions can therefore be drawn regarding the effect, if any, of the administration of calcium in this case. While under treatment in hospital my patient’s progress, as judged by the concentration of lead in the blood and urine, was essentially similar to that described by Kehoe, Thamann, and Cholak (1933) in patients to whom no calcium was given. Later, although the concentration of lead in the urine continued to fall, that in the blood remained disturbingly high; it was actually greater on the one hundred and ninety-sixth day than on the twenty-seventh (Table I). This was considered a contraindication to any measures designed to mobilize “stored” lead.

The one therapeutic measure which appeared to be of undoubted value was the repeated withdrawal of cerebrospinal fluid by lumbar puncture.

The number of recorded cases of inorganic lead encephalopathy in adults, treated by various modern methods, is too small for statistical analysis of results to be of much value.

Summary

A cooperage is described in which a severe lead hazard caused two cases of lead poisoning; one patient developed encephalopathy.

The syndrome of lead encephalopathy in adults is reviewed. The difficulties in diagnosis, the possible causes of apparent susceptibility to lead, the absence of hypertension in this and other cases, and the treatment of encephalopathy are discussed. Some of the essential differences between this form of encephalopathy and that due to tetra-ethyl lead are outlined.

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