

Tetraethyl Lead Poisoning

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A Clinical Analysis of Forty Non-fatal Cases

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Lead in various forms has been recognized as one of the important occupational poisons for a long time. The zealous study and the insistent presentation of the characteristics of the condition have outlined a clinical picture which is a matter of general medical instruction and knowledge, in spite of the controversial nature of certain diagnostic details. The manufacture and handling of tetra-ethyl lead, resultant upon its recent development for important industrial purposes, has brought about the appearance of a type of lead poisoning, which because of its unique character, is made the subject of the present paper.

Tetra-ethyl lead is a clear, heavy (sp. g. about 1.62) oily liquid with a peculiar sweetish odor, which is somewhat volatile at ordinary temperature. It is insoluble in either hot or cold water, ^{but soluble in} alcohol and acetone, and miscible in all proportions with fats and oils. It is not, ^{immediately} corrosive, but when applied to living tissue for some time it brings about necrosis. If allowed to be in contact with the skin for half an hour or more little or no sensation is produced but desquamation occurs after a day or two leaving white and glistening patches. However, if removed from the skin (best done with kerosene) within a short time after its application no harmful effect on the skin is produced.

It would be assumed that such a compound of lead is a general protoplasmic poison and in fact chemists in general have regarded it as such. Observation and experimentation have confirmed the truth of this assumption, and have shown the extent of toxicity, the avenues of admission into the body, and the clinical features which develop in the course of the poisoning. The peculiar-

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ities of the poisoning are very striking, so much so that the condition bears little resemblance to any of the clinical types of lead poisoning except the infrequent lead encephalitis. Nevertheless, it can not be doubted that the lead is the essential toxic agent in the compound. The peculiar symptoms and signs produced are due, in all likelihood, to the physical and chemical properties of the compound which permit of a more rapid absorption through the skin and lungs than possible in the case of the more common lead compounds. More important, its distribution in the tissues may be confidently expected to differ from that of the usual lead compounds in that its solubility in fats predisposes its localization in relatively high concentration in tissues of high fat content, such as adipose tissue, central nervous system and liver.

Modes of Entrance. It has been shown experimentally ~~animals~~ ^{of animals} that tetra-ethyl lead is capable of producing illness and death when inhaled as a vapor, when ^{absorbed through} ~~applied to~~ the skin, when administered orally ^{or} ~~when~~ ^{injected} intravenously. (1) Under any one of these conditions death may be brought about in the course of three to six hours, though minimal lethal doses do not kill under twenty-four hours ordinarily. The intravenous injection does not produce immediate death, unless injected in such quantities and at such a rate as to produce mechanical blocking of the blood vessels.

(1) Unpublished experiments from the Research Laboratory of the Ethyl Gasoline Corporation, Dayton, Ohio.

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the reason that no coagulation is produced in the blood by the presence of tetra-ethyl lead, which is immiscible with blood.) Men, too, have been seen to become ill as a result of inhalation of vapor of tetra-ethyl lead, and also as a result of absorbing the fluid through the skin. ^{Usually} ~~were frequently~~, however, illness in men has been produced by the combination of these conditions over a considerable period of time. *State condition of exposure.*

Symptoms and Signs. Under conditions which permit of inhalation of concentrated vapor of tetra-ethyl lead, or skin contact with undiluted tetra-ethyl lead, or both, for sufficient periods of time an illness develops in which some or all of the following subjective symptoms appear; insomnia, nausea, vertigo, anorexia, headache and muscular weakness. A sickening taste which is not described as metallic, is frequent. Itching or burning of the skin occasionally is complained of. These are unvaryingly accompanied by the objective signs of pallor, low blood pressure, ^{increased respiratory rate} subnormal temperature and loss of weight. There is usually a slowing of the pulse. A well defined and rather coarse tremor is an almost constant finding, and the reflexes are frequently exaggerated. The muscles themselves are hyperirritable, responding easily to mechanical stimulation. Gastric cramps, although occasionally present, are not severe, and are almost never a matter of complaint on the part of the patient. Neither constipation nor diarrhoea is experienced. A lead line has been seen by the writer in but two cases and here a severe pyorrhoea lent some doubt as to the nature of the blue discoloration.

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Examination of the blood shows no constant significant findings. A slight anemia sometimes develops but the changes characteristic of ordinary lead poisoning are usually ~~conspicuous by their~~ ^{absent} ~~absence~~ ^{five} in only ~~five~~ out of forty cases has stippling of the erythrocytes appeared, and in these only ~~one~~ ^{two} showed enough change to be found except by the most patient searching. Urinary findings are meager. There is an hyperacidity of the urine in all severe cases, the urine remaining acid to Methyl Red during the entire twenty-four hours.

Analysis of Symptoms and Signs. The insomnia is one of the earliest and most persistent symptom. It is so severe as to be a complete inability to sleep for days at a time, and as it becomes less pronounced it frequently occurs every second night. It is not ordinarily followed by any intense fatigue even in persons who are doing heavy manual labor during the day. Any sleep which is obtained by the affected person is likely to be fitful and disturbed, with twitching of the body, frequent movements, and crying out. The complaint is frequently made by the patient that his mind is too active to allow sleep, and that when asleep or awake he is in a dream or dreamlike state in which all kinds of grotesque and unusual situations arise. The nausea, vomiting, lack of appetite and vertigo are all especially pronounced in the early part of the day and usually wear off during the course of the day. An individual in this situation often goes without breakfast, the very thought or sight of which nauseates him, but eats heartily and with relish in the evening. However, an attack of nausea and vomiting may be

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immediately precipitated by the odor of the tetra-ethyl lead. The vertigo is not pronounced except in very severe cases, and is usually an indefinite feeling of dullness, half dizziness and half headache.

The blood pressure changes are seen early and are the most reliable early findings. The systolic pressure may go as low as eighty millimeters of mercury, but is usually between ninety and one hundred in persons whose pressure was previously normal. The diastolic pressure is relatively lower in almost every case, the pulse pressure being fifty to sixty millimeters.

The temperature is extremely low in the early morning hours, often being as low as ninety-six, rarely being above ninety-seven in an affected person. It ascends during the day but ordinarily is subnormal through the entire twenty-four hours.

Loss of weight is a constant finding varying from slight to great decreases such as fifteen pounds in two or three weeks.

The severity of the tremor is quite variable, but some degree of it is almost constant. In some cases it is the most striking symptom, and the one most complained of. In the more severe cases, sudden twitchings of an arm or leg, usually the former, occur to such an extent as to arouse the subject from sleep or cause him to drop an object held in the hand.

These symptoms and signs together with the somewhat exaggerated reflexes, present a picture of a degree of central nervous system involvement which is not seen in any but the most acute cases of *inorganic* lead poisoning. Indeed they suggest a degree of selective localization in nervous tissue, which might be anticipated from a consideration of

Clinical types. In mild cases, where exposure has been slight, insomnia and anorexia, with a slight drop in blood pressure in which the most pronounced drop is in the diastolic pressure, are frequently the only findings. Indeed the insomnia is sometimes replaced by a disturbed sleep in which frightful dreams are conspicuously frequent. In the course of a few days the condition disappears almost entirely, though frequently leaving the blood pressure lowered for from one to three weeks. In more severe cases the symptoms are more numerous and pronounced, ~~and the duration of the second is as prolonged as to extend over a period of many weeks or even months.~~ Loss of weight, insomnia and anorexia are especially pronounced. However, when the insomnia disappears improvement comes surely and with the return of the appetite the subjective symptoms usually disappear almost completely. Weakness on exertion, lassitude and the subnormal blood pressure, occasionally persist for long periods of time, and by their persistence suggest the fatigue of chronic infectious diseases. In very severe cases the nervous system involvement is seen at once to be the essential characteristic of the condition. The patient is irritable, "nervous", and is in a constant state of excitement which may progress to such an extent as to render him maniacal. (*) The mania resembles an alcoholic delirium very strikingly. In it the victim talks constantly and is usually in constant fear of animals and persons who are on the point of attacking him. His struggling to escape or to defend himself is

(*) The writer has not had occasion to study or treat any such cases. They are described from the statements of other physicians and are included for the sake of completeness. ✓

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continuous, and unless restrained or quieted in some other fashion he is likely to jump out of the window or injure himself in some other fashion. The outcome of such a case ^{has been} almost uniformly fatal, death occurring apparently from exhaustion.

Diagnosis. The diagnosis of tetra-ethyl lead poisoning is to be made from a careful consideration of the symptoms and signs together with a history of exposure. However, none of the items which go to make up the clinical aspect of this condition is characteristic of it alone. A careful differential diagnosis must be made from tuberculosis, syphilis, chronic myocarditis and other chronic infections with systemic intoxication.

Treatment. The treatment which has been employed in the cases herein discussed has been based on several considerations. It seems likely that tetra-ethyl lead is converted in the tissues to inorganic lead compounds capable of reacting with proteins in the way that heavy metal salts are generally known to do. (There is some experimental evidence that this is the case.)

From this it would appear that the variations in the symptomatology of tetra-ethyl lead poisoning as opposed to ordinary lead poisoning, ~~differing as they do from ordinary lead poisoning,~~ arise either from a unique distribution of lead in the ~~tissues~~ or from a great difference in the ^{actual} quantity present in the ~~body~~. Assuming the correctness of these conclusions the treatment of tetra-ethyl lead poisoning need not differ from the treatment of lead poisoning of other types.

Accordingly a type of treatment was employed

which has demonstrated its efficacy in several types of heavy metal poisoning. The experimental basis of this method and the clinical evidences ~~which point~~ of its value appear elsewhere. (3) The principles underlying it are as follows:

- (1) Heavy metals combine with and produce coagulation of living tissue.
- (2) This combination of heavy metal and tissue can be both prevented and broken by the presence of sufficient concentrations of salts of the light metals, in such a way as to restore the tissue to normal physical state and free the heavy metal in soluble form for excretion.
- (3) The symptoms of acid intoxication ^{and} edema, with consequent retarded excretion, associated with heavy metal poisoning, especially of the acute type, may be combatted effectively by the same means.

In general the treatment consisted of administering mixtures of sodium bicarbonate, sodium citrate, calcium carbonate and magnesium oxide in quantities sufficient to make and maintain neutrality of the urine. In the more severe cases magnesium sulphate was added to the above list, given in small doses throughout the day in order to maintain free diuresis. Large quantities of water and citrus fruit juices were administered.

No narcotics were used in producing sleep. (It can not be emphasized too much that the use of opium compounds and chloral hydrate in this and similar types of insomnia is an extremely dangerous procedure)

It was found that after a thorough alkalization the insomnia decreased in severity, usually disappearing in a few days. The appetite returned almost immediately and with it loss of weight came to an end.

In several cases general weakness, nervous irritability, as evidenced by tremors and somewhat exaggerated reflexes, together with disturbed sleep, persisted for considerable

However, there was no increase in the severity of the symptoms and no relapse into previously severe symptoms in a single case. It is possible of course, that this resulted largely from cessation of exposure to tetra-ethyl lead, and from the rest and diversion occasioned by light out of door exercise and recreation. (Rest in bed was impossible for most of these cases, ^{for the reason that they could not remain quiet in bed} ~~therefore~~ they were permitted to amuse themselves and to keep occupied in light out of door recreation.) ^{hardly} it is ~~not~~ without significance On the other hand, that none of the delayed effects of either ordinary lead poisoning or of this particular type of lead poisoning ^{has} ~~appeared~~ ~~occurred~~ in any of these cases. Experimental evidence obtained in the study of these patients is to be made the subject of a later publication, inasmuch as ^{the experiments are not} ~~this evidence is not~~ complete at this time. But on clinical evidence alone the writer feels justified in presenting the above method of treatment as the most satisfactory method which can now be offered. Its efficacy in the acute maniacal types of tetra-ethyl lead poisoning has not been determined. It is ~~rather~~ suggestive, however, that in an acute case of inorganic lead poisoning, with pronounced cerebral symptoms, such a treatment vigorously carried out resulted in an almost immediate and complete recovery.