

a peculiar sweetish odor, which is somewhat volatile at ordinary temperatures. 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 decomposes in the presence of sunlight with the formation of crystalline tri-ethyl lead oxide, which in the presence of a halogen forms the tri-ethyl lead salt. Crude tetra-ethyl lead and old containers of tetra-ethyl lead are likely to show the presence of this oxide or the halogen salts. The salts are water soluble. They have a peculiar odor not wholly unlike that of tetra-ethyl lead, and when inhaled in even very low concentration they cause violent sneezing and a marked irritation of the mucous membranes. Tetra-ethyl lead is not immediately corrosive when applied to living tissue.

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Tetra-ethyl Lead Poisoning°

A Clinical Analysis of a Series of Non-fatal Cases

by

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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. gr. about 1.62), oily liquid with

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producing illness and death of animals when inhaled as a vapor, when absorbed

It has been shown experimentally that tetra-ethyl lead is capable of

Mode of Entrance

of high fat content, such as adipose tissue, central nervous system, and liver.

predisposes its early localization in relatively high concentration in tissues

to differ from that of the usual lead compounds, in that its solubility in fat

important, perhaps, its distribution in the tissues may be confidently expected

and lungs than is possible in the case of the more common lead compounds. More

properties of the compound which permit of a more rapid absorption through the skin

symptoms and signs produced are due, in all likelihood, to the physical and chemical

order of magnitude as that of other well known compounds of lead. (1) The peculiar

the essential toxic agent in the compound. In fact, its toxicity is of the same

tissues, but after exposure for some time necrosis results. It allowed to remain on 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 absorption into the body, and the clinical features which develop in the course of the poisoning. The peculiarities of the poisoning are striking, so much so that the condition often bears little resemblance to any of the clinical types of lead poisoning except the in-

and inhalation of vapor over a considerable period of time. (The inhalation of the dust of the tri-ethyl lead decomposition products of tetra-ethyl lead has also been seen to produce illness, which, under the conditions of observation, could not be differentiated from that due to tetra-ethyl lead alone.) However, an acute, even fatal poisoning may result from exposure either to a high concentration of vapor for a comparatively short time (several working days), or to a large quantity allowed to remain on a large skin surface.

Symptoms

Under conditions which allow of the absorption of tetra-ethyl lead in any manner, in sufficient quantity, an illness develops in which some or all of the following subjective symptoms appear:

Insomnia. This is one of the earliest and most troublesome symptoms. It may be so severe as to prevent any sleep for days at a time, or it may cause only frequent

through the skin, and when administered orally or 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 kill in from twenty four to seventy two hours, ordinarily from intravenous administration does not produce immediate or even quick death, unless injected in such quantities and at such a rate as to mechanically block large pulmonary vessels. (Tetra-ethyl lead is insoluble with blood and does not cause coagulation. It may well be that poisonous properties depend upon some degree of decomposition of the tetra-ethyl lead molecule.)

In man poisoning is produced as a result of the inhalation of the vapor of tetra-ethyl lead, and also as a result of skin absorption. It may be produced accidentally or carelessly by ingestion, but in the industrial handling of tetra-ethyl lead such a source of poisoning is not encountered to any important degree. Usually, illness in man has been the result of the combination of skin absorption

mind is too active to allow sleep, and that when in a
or dream-like state in which all kinds of grotesque
The attempt to sleep is more fatiguing than to remain awake.
Nausea, Anorexia and Vomiting. These symptoms
morning. A sickening taste, not described as metallic,
development of these symptoms. Such an individual has
positive aversion, though as the day goes on he finds food
and with relish in the evening. However, an attack is
precipitated at any time by the odor of tetrathylammonium
jectional odors.

Vertigo and Headache. Neither of these are primary
something approaching them, in the form of a dull ache
complained of. Occasionally, however, the vertigo is

Muscular Weakness. Some degree of weakness is
a very persistent complaint. It does not appear to be
well established, and appears to be due in most cases to

Itching of the skin is an occasional complaint.

Objective Signs.

The above symptoms are unvaryingly accompanied by

Pallor. This is so uniform as to be a constant
destruction, but rather to a generally inadequate
pronounced fall in blood pressure.

Subnormal Blood pressure. The blood pressure
They represent among the most reliable diagnostic

as low as eighty millimeters of mercury in a patient with a previously normal pressure. The diastolic pressure is relatively lower in almost every case, the pulse pressure being from fifty to seventy millimeters of mercury.

Subnormal Temperature. The temperature is extremely low in the early morning hours, often being as low as ninety six degrees, rarely being above ninety seven in affected persons. It ascends during the day but it usually subnormal throughout the entire twenty four hours.

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

Tremor. A well defined and coarse tremor is seen in most cases. With this the reflexes are exaggerated, and the muscles, themselves, are commonly

is the most striking sign. In such a case there is a continuous tremor, exaggerated when an attempt is made to control it, and increased greatly by sudden, unexpected noises or events. The sudden twitching of an arm or leg may arouse the subject from sleep or cause him to drop an object held in the hand.

Peripheral neuritis, with paralysis or anaesthesia, has not been seen in any of these cases.

There is an increased respiratory rate, and a decreased pulse rate.

Gastric and intestinal cramps are not an important item in the clinical picture. In the few cases in which they have appeared they have not been severe. They have never been the cause of initial complaint. Neither constipation nor diarrhoea is seen often.

Blood Findings. There is no characteristic blood finding. Haemoglobin determinations, carried out regularly on all patients have failed to yield any information. In one or two cases there has been a very slight diminution, but in no case has it been significant. (Determinations made with Dare instrument.) There is little

or nothing in the microscopic examination of the blood to indicate destruction of the erythrocytes. Polychromatophilia and stippling are found in a high percentage of cases of slow absorption over a period of months, but in cases in which there is evidence of rapid absorption stippling is almost uniformly absent. Even in the cases which show polychromatophilia and stippling, (and these are never pronounced blood pictures, such as are frequently seen in ordinary types of lead poisoning), there is no appreciable diminution of erythrocytes.

Lead Line. The appearance of a lead line on the gums is not a constant, nor even a frequent finding. A lead line has been seen in several cases, and in two cases the line has been quite pronounced and characteristic. Yet this is not an early or important item in the diagnosis.

Urinary findings are meager except for the presence of lead. There is a

constant hyperacidity of the urine in all severe cases, the urine retaining strongly acid to Methyl Red during the entire twenty four hours. Albumin does not appear in the urine of even severely poisoned individuals.

Lead Excretion. Lead is excreted in larger quantities than is seen in most cases of lead poisoning. Excretion occurs by way of both kidneys and alimentary tract. Usually the excretion in the faeces exceed that in the urine for a corresponding period of time. However, in one case, the urinary excretion uniformly exceeded that of the faeces. The quantity excreted in a twenty-four specimen of urine has varied from nil up to 5.4 mg of lead.

Clinical Types

In mild cases of poisoning, where the exposure has been slight and brief, insomnia and anorexia, with a slight drop in blood pressure and temperature are frequently the only findings. In such a case the examination of the blood has failed to yield the slightest information. Instead of sleeplessness the victim may complain of being disturbed in his sleep by frightful dreams. In the course of a few days

exposure over a considerable period of time (months) in the blood picture, in addition to the above symptoms in a few such cases also. Here careful examination of a single stippled erythrocyte, without the diminution of erythrocytes. The leucocyte count in such a case is increased one or two thousand above the previous normal. Abnormalities in the blood picture tend to disappear with exposure and the instigation of therapeutic measures.

In more severe cases the symptoms are more pronounced and anorexia are especially pronounced. With the weakness on exertion, and the subnormal blood pressure are prominent symptoms. The persistence of this condition is the chronic fatigue of low grade infectious disease. However, all the symptoms disappear, and no residual symptoms remain.

In acute cases, a central nervous system disorder is an essential characteristic of the condition. The patient is in a constant state of excitement, which may progress to him maniacal. (No case of the writer's has presented such cases have been seen by him. Observations made on the sake of completeness.) The mania resembles an alcoholism in that the victim talks constantly and is in constant motion, the point of attacking him. His struggling to escape, if restrained or quieted in some fashion, he is likely to become violent, even to leaping out of an upper window.

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consideration of the symptoms and signs together with one hand, such poisoning may not safely be excluded. The signs considered characteristic of ordinary lead poisoning of the items which go to make up the clinical aspect of it alone. The conditions which offer the greatest differential diagnosis are tuberculosis, syphilis, chronic sub-acute sinusitis, and other chronic infections with the finding of significant quantities of lead in the urine. The certain differential point in certain cases. However, the diagnosis are likely to be seen in those cases in which there is no exposure to tetra-ethyl lead.

Treatment.

The treatment which has been employed in the past is based upon several considerations, in the absence of any excretion of lead by the poisoned individual in the form of urine at least. It seems obvious, therefore, that this organ is converted into inorganic compounds of lead. From this it follows in the symptomatology of tetra-ethyl lead poisoning that the signs, arise either from a unique distribution of lead in the body or from a difference in the actual quantities present in the body. In these conclusions, the treatment of tetra-ethyl lead poisoning is the same as the treatment of lead poisoning of other types.

as follows:

- (1) Heavy metals combine with and injure living tissue.
- (2) The combination of heavy metal and tissue requires the presence of sufficient concentrations of salts in the blood as to restore the tissue to normal physical state, and provide a form for excretion.

(3) The symptoms of acid intoxication and edema in lead poisoning, especially of the acute type, may be combated by the following means.

The actual treatment consisted of the administration of Sodium Bicarbonate or Sodium Citrate, Magnesium Oxide, and Potassium Bicarbonate sufficient to make and maintain neutrality of the urine. A mixture of such salts are required for this purpose. Magnesium Sulphate was added to the above list, given in small doses day in order to maintain a free diuresis. The bowels were kept open by secretion of lead by means of saline cathartics. Sodium Citrate showed any evidence of the development of acute edema. Potassium and citrus fruit juices were administered.

No Narcotics were used to produce sleep.

that the use of opium compounds and chloral hydrate to relieve insomnia is an exceedingly dangerous practice.)

Therapeutic Results.

It was found that after a thorough alkalinization the severity, usually disappearing in a few days. The

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blood pressure also tended to persist. However, the
of symptoms, and no relapse into previously severe
possible, of course, that this resulted largely from
ethyl lead, and from the rest and diversion occasioned
and recreation. (None of these patients were put to bed
they were dangerously ill, and all of them maintained
of bed.)— On the other hand it is probably not without
delayed effects of either ordinary lead poisoning or
poisoning has appeared in any of these cases. Experimental
study of these patients is to be made the subject of a paper
but on clinical evidence alone the writer feels justified in
method of treatment as the most satisfactory one which he holds the
opinion of the writer that the beneficial effects of potassium
sulphate in arsenic and lead poisoning⁽⁴⁾ and Potassium
explainable on the basis of the principles above stated. A
effect may be obtained from the use of light metal salts of
concentration than these.) The efficacy of these salts in
maniacal types of tetra-ethyl lead poisoning has not been proved
however, that in an acute case of inorganic lead poisoning
symptoms. Such a course of treatment, vigorously continued, results in the
disappearance of cerebral manifestations within a period of a few days.

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