

Cond abstract of a Talk at Ocular Snake Society Feb. 1927

The Behavior of Lead in The Animal Organism.

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A. It is well known that lead is only slightly toxic for animals and man when absorbed slowly. Many times the single lethal dose may be found in the tissues of apparently normal animals. Furthermore, experimental animals and men may go through all the activities of an apparently normal life without showing any evidence of interference with any normal function, at any time in spite of having taken into their bodies large quantities of lead.

The explanation of this apparent lack of toxicity in the case of rabbits is shown by experimental studies on the distribution of lead in the tissues, and the excretion of lead from the body.

Data compiled from the analyses of the tissues of many rabbits which have accumulated lead without developing lead poisoning at any time, show a characteristic distribution of lead in the tissues. Selective absorption is shown by the liver, the kidneys, the central nervous system, and the bones. The skeleton does not absorb all the lead. In fact the concentration of lead found in the bones is rarely higher than that found in the other tissues mentioned above. But, because of the enormous mass of the skeleton as compared with that of the liver, kidney, and central nervous system, most of the lead is found in the skeleton. Thus this large bulk of comparatively inert tissue, physiologically,

is able to take up large quantities of lead, and in so doing maintains a low concentration throughout the entire body.

A study of excretion in relation to the total lead content and the distribution of lead in the tissues, shows that there is a continuous excretion, the magnitude of which is proportional to the total lead content of the animal. Furthermore, in spite of a great diminution of the total lead in the body, as a result of prolonged and continuous excretion, the distribution of lead in the tissues remains proportionally constant, except in the case of the nervous system. (In this tissue the relative concentration steadily increases as lead is lost from the body.) This can occur only as a result of a continual shifting of lead in the tissues. As the excretory organs (liver, intestine and kidney) give up lead, they absorb lead from the blood, which being depleted as to its lead content, takes up more lead from the tissues through which it passes. The cycle continues thus until most of the lead is lost from the body.

Thus because of its manner of distribution and its continuous excretion lead is only slightly toxic, ordinarily, and even large amounts may fail to induce poisoning.

B. Lead poisoning, however, occurs in experimental animals under proper conditions. It may occur when the actual quantity of lead in the animal body is quite small.

Acute symptoms and death from lead poisoning occur as the result of the administration of a single sufficiently large dose, or following the frequent repetition of doses, one of which is not apparently injurious. Also, illness and death from lead

poisoning may occur at a time in which no lead is being administered or absorbed. When this latter occurs there is always some contributory factor. Anaesthesia, starvation, difficult parturition, intercurrent acute infection, or experimental administration of acids, alkalies, and many neutral salts, may precipitate an attack of illness and perhaps death as a result of lead poisoning.

No matter how the poisoning is induced certain common facts are seen. The rate of excretion of lead is high, the blood content is high, and there is a striking variation in the distribution of lead in the tissues from that found in the loaded but symptomless animal.

These facts lead to the following conclusions. Poisoning is produced when the lead concentration in the blood is high. High concentration in the blood may be produced in any one of three ways. Lead may be absorbed into the blood from the outside at a more rapid rate than it can be distributed into the tissues. Or, in spite of the rate of absorption sufficiently slow to allow distribution, the total quantity taken in may be such as eventually to bring about a high concentration in all the tissues, including the blood. Obviously in both of these cases excretion does not keep pace with absorption, and if excretion be impaired for any reason, poisoning will be hastened. Finally, lead may be poured out of the tissues into the blood, so to speak, as a result of ~~the~~ changes in the tissues themselves.

The data indicate that the tissues most easily subject to change in this direction are the liver and kidneys. The skeleton takes part in the process but apparently at a slower rate. The central nervous system, on the other hand, shows a decided ten-

The variety of the conditions which may precipitate acute poisoning in the rabbit during a period of complete freedom from absorption compels a search for some mechanism common to all whereby lead may be brought out of the tissues into the blood. Such a search brings us to the recognition of the similarity of behavior of lead in the tissues as compared with that of the lead-protein compounds under laboratory conditions. In the presence of certain proteins lead is bound, so to speak, and is only very slightly soluble. In the presence of ^{sufficient concentration of} acids, alkalies and neutral salts, however, the heavy metal protein precipitates are seen to resolve and to free the heavy metal from its relatively insoluble and little diffusible state.

It is difficult to conceive of any other combination of the heavy metal in the tissues which may be affected by so many variables. On this basis the influence of parturition, acute infection, fatigue and other types of illness with their attendant increased production and decreased elimination of acids, together with administered acids, alkalies and many neutral salts may all be readily understood. Thus becoming freely diffusible and mobile in the body lead may be expected to enter the blood stream in high concentration and to be carried into tissues such as the central nervous system which are highly susceptible to injury, as well as to be excreted at a greatly increased rate.

Further evidence of the probable correctness of this interpretation is offered by the relative efficacy of the salts in producing the above effects. Those salts which are most effective in resolving heavy metal-protein precipitates are seen to be most effective in bringing about changes in distribution of lead in the tissues, and in promoting excretion. Thus the ammonium salts (includ-

ing the carbonate) and certain salts of potassium as the iodide and sulphocyanate are strikingly effective in both.

C. A consideration of clinical facts as well as indirect evidence gained by studies on excretion of lead in man indicate the great likelihood that the distribution and excretion of lead in man are influenced by the same set of factors as have been observed in the case of rabbits. Direct proof is difficult if not impossible to obtain because of the necessity of obtaining human tissues for analysis under conditions which do not allow of the influence of acute illness and disease on the ante-mortem distribution of lead.

Concluding on the basis of the indirect evidence that the facts as regards lead distribution in man are as observed in the rabbit, the principles on which the treatment of lead poisoning should be based are capable of simple statement.

(1). Persons, without symptoms, but known to contain large quantities of lead must be regarded as potential cases of lead poisoning. The normal distribution of lead in their tissues should not be disturbed, except as they are kept under the closest observation, and slow elimination of lead should be maintained over a long period of time, during which further absorption is prevented. Intercurrent infections are especially to be feared, and in the event of their occurrence every effort should be made to prevent the development of the starvation or intoxication acid accumulation which so frequently results.

The use of especially efficacious methods of lead elimination is fraught with grave danger to the subject except under the most careful observation, and, in general, it is advisable to use materials which produce their effect slowly.

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(2). The patient with lead poisoning is already suffering as a result of abnormal distribution of lead. In his case every effort must be made to restore the normal relations of lead distribution. He should not be treated for greater elimination of lead. Careful observation will usually serve to indicate why his symptoms are present. Several possibilities present themselves, but the most important and more frequently effective means of producing a subsidence of symptoms is to neutralize the acid intoxication which is usually present by proper quantities of alkaline salts.

After the disappearance of the symptoms of active poisoning the case of this man is in no wise different from that of the group discussed previously.