LEAD INDUSTRIES ASSOCIATION

60 EAST 42ND STREET

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To the Members of the Lead Industries Association:

A REVIEW OF CERTAIN HEALTH PROBLEMS ASSOCIATED WITH LEAD

Dr. William E. George, Chief Medical Officer of the Consolidated Zinc Proprietary, Ltd., Sydney, Australia, delivered at the annual meeting of our Association last April an address on "Problems in Plumbism" so interesting to his hearers that many requests for copies have been received.

Dr. George having spoken from handwritten notes, no distribution of his address was possible until it had been developed into manuscript, and the facts that the author left our shores soon after the meeting and has been traveling almost continuously in the intervening months have delayed the reproduction until now.

Under the revised title set forth at the head of this bulletin, a copy of Dr. George's address is herewith. In it, seemingly important aspects of the overall problem of plumbism which have hitherto had relatively little attention in this country are set before us. Of two American industrial physicians to whom the manuscript was submitted, one has commented that the problem of the effect of lead on the kidney is one which should be brought vigorously into the open, and the second has made the observation that, the author having been "on the road" while preparing the manuscript, the extent to which, with few exceptions, he has been able to both raise and answer a series of questions is truly remarkable.

The account of the 1956 episode on the fourth page is the first publication of a case in which the results of Versene administration have been used to support a claim that lead poisoning was the cause of chronic kidney damage.

A limited supply of additional copies of Dr. George's paper is available for distribution to our members on request.

Manfred Bowditch
Director of Health and Safety

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A REVIEW OF CERTAIN HEALTH PROBLEMS ASSOCIATED WITH LEAD*

Dr. William E. George
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Among problems in plumbism which are of special medical interest at the present time are the following:-

1. The use of Versene in relation to industrial lead exposure when it is administered:

   (a) Curatively

   (b) Diagnostically - i.e. the production of a high urinary lead excretion in workers with an industrial lead exposure who

   i. have never shown clinical evidence of plumbism, or

   ii. have suffered from episodes of acute lead poisoning many years previously, or

   iii. are suffering from chronic degenerative disease which could possibly be considered to be caused, aggravated, or accelerated in onset by exposure to minimal quantities of lead insufficient to produce clinical manifestations of lead poisoning.

   (c) Prophylactically

   i. to prevent the onset of disabling plumbism in lead workers with raised urinary lead excretion but with no signs of clinical plumbism,

   ii. to prevent the possible later development of chronic degenerative disease in lead workers, both with and without raised urinary lead excretion, but with no signs of clinical plumbism,

   iii. to all lead workers, to diminish bone and soft tissue storage of lead.

2. The value of oral administration of Versene as compared with its administration by intrevenous infusion.

*A presentation at the 29th Annual Meeting, Lead Industries Association, Chicago, Ill., April 24-25, 1957, with revisions by the author.

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3. Possible short-range and long-range harmful effects of Versene administration.

4. The amount of urinary lead excretion produced by Versene in persons with no industrial lead exposure.

5. The relationship of cardiovascular-renal disease to

(a) Antecedent attacks of acute lead poisoning.

(b) Exposure during a working life to quantities of lead insufficient to produce clinical symptoms of lead poisoning but known to be higher than those to which the general community is exposed. This may be revealed by:

i. high urinary lead concentrations,

ii. high urinary lead excretions following Versene administration,

iii. high bone lead concentration discovered during life or at autopsy.

(In this regard, the work of Dr. D. A. Henderson, in Australia, appears to have established that excessive lead exposure in childhood is frequently followed by the development of a progressive renal lesion which ultimately leads to early death from renal failure.)

References

D. A. Henderson: "A Follow-up of Cases of Plumbism in Children" Australasian Annals of Medicine (1954) III, 3, 219

D. A. Henderson: "Chronic Nephritis in Queensland" Australasian Annals of Medicine (1955) IV, 3, 163

D. A. Henderson: "The Renal Content of Bone in Chronic Bright's Disease" Australasian Annals of Medicine (1957) (To appear shortly)

(In a fourth paper, Henderson will describe the renal pathology resulting from excessive lead absorption during childhood.)

(c) The intermittent release from storage in the tissues of increased amounts of lead as a result of infection, starvation, diet variation, etc.

6. The use of the measurement of bone lead concentration to ascertain the relationship of some cases of chronic cardiovascular-renal disease to excessive lead absorption, either in childhood or in industry.

7. The importance of sweat as a vehicle for the excretion of absorbed lead and the effects generally of temperature on lead absorption and excretion.

References

D. O. Shiels: "The Elimination of Lead in Sweat" Australasian Annals of Medicine (1954) III, 3, 225

D. O. Shiels: "Industrial Lead Poisoning in Relation to Climate" Australasian Annals of Medicine (1955) August

8. The effects of diet on lead absorption and excretion, including the possibility of the existence of metabolic chelating agents.

It is impossible to refer to all the above aspects in the time available, but reference will be made to some of them, especially to those to which most attention has been paid by Australian investigators.

As far as industrial lead poisoning is concerned, many years ago, in what were apparently very bad working conditions, acute lead poisoning frequently occurred at Broken Hill, where oxidised carbonate ore was then being mined and smelted, and at Port Pirie, where lead smelting and refining were conducted. Commissions of Enquiry were held in 1920 at Broken Hill and in 1925 at Port Pirie, and in the reports of both, the incidence of lead poisoning was commented upon.

Following these enquiries, working conditions in both industries were greatly improved, compensation was provided for incapacity as a result of lead poisoning, and medical boards were established to examine and certify.

There has been very little evidence of clinical lead poisoning in either place for many years. At Broken Hill, since 1940, only five cases of lead poisoning have been certified. Four of these cases quickly recovered with treatment and returned to work - three of them had been working in a limited retreatment process of an old dump consisting of highly oxidised material. At Port Pirie, only one case of plumbism has been certified in the last six years. In both places, notification by medical practitioners of suspected cases of lead poisoning is required under the Act. Recent interviews with general practitioners in both localities confirm that they are seeing no evidence of absorption of harmful quantities of lead.

Several hundred cases of lead poisoning occurred in the early nineteen-thirties in lead mines situated in the north of Queensland. At that time, carbonate ore was being mined and smelted. Medical supervision of workers was instituted, working conditions were improved and the incidence of lead poisoning speedily decreased. Today, with the mining of sulphide ore, cases of lead poisoning occur only among men employed in the smelter section of the operations. Two or three such clinical cases occur per year, though quite a number of men show laboratory evidence of excessive lead absorption. Men so affected are given work away from a lead hazard.

Secondary industry contributes a few cases of lead poisoning per year in all states - e.g. among bridge painters employed removing old lead paint from bridges, and among men engaged in the handling of scrap batteries. Such men are medically examined regularly and it is unusual for clinical lead poisoning to develop. Men showing raised urinary lead excretion are given work away from this hazard.

In 1956, the "Versenate test" for lead poisoning was raised at Broken Hill in a claim for compensation for lead poisoning. A miner there became disabled as a result of chronic nephritis. He was twice examined by the statutory medical board and a certificate that his disablement was due to lead poisoning was refused. He had worked at Broken Hill, in sulphide ore only, since 1924. He had never suffered from symptoms of acute or subacute lead poisoning and his urinary lead excretion was 0.02 mgm per litre. He was sent to Sydney, where he was given an infusion of a Versenate. This resulted in the urinary excretion of 0.6 mgm of lead per litre. In his report following his examination of the man, his physician stated that this result indicated:

(a) that the worker had an abnormal quantity of lead stored in his body,

(b) that he had been exposed to excessive quantities of lead at his work, and

(c) that the result of Versene administration confirmed his opinion that the chronic nephritis from which the worker was suffering was due to lead poisoning. He quoted the opinions of many industrial physicians that lead could cause renal damage.

It is thought that this is the first occasion on which the results of lead excretion in the urine following Versene administration have been used to support a claim that chronic nephritis was due to lead poisoning. We feel that, probably, if Versene is given to any worker exposed to an industrial lead hazard, a high urinary lead excretion will follow, compared with that produced in persons with no industrial exposure. In the present state of our knowledge, we do not know that we could satisfy a court that an abnormally high amount of lead, set in the bones as calcium lead phosphate or lying in the soft tissues, does not shorten the life of a worker or prejudicially affect his health. We feel that we have insufficient information of the quantities of lead which could be produced, by the administration of Versene, in the urine of industrial lead workers with no symptoms of illness and with no signs of disease. If this is greater in amount than that which can be produced in nonexposed workers in similar age groups, is it of any clinical significance?

Some interesting work on the excretion of lead in the sweat has been reported by Shiels. Shiels has pointed out that, at Mount Isa in the tropical north of Australia where lead mining and smelting are carried out, all persons excreting 0.30 mgms or more of lead per litre of urine have some evidence of clinical lead poisoning, whereas in Melbourne, in the temperate south of Australia, only 62 per cent of workers excreting 0.30 mgms per litre or more show clinical evidence of lead poisoning. He shows that, at Mount Isa, the daily excretion of fluid is of the order of one litre of urine and 2.5 litres of sweat per day, whereas in Melbourne, the

daily excretion of fluid is about 0.5 litres of sweat and 1.5 litres of urine. Thus, with 0.30 mgms of lead per litre of urine and a like concentration in the sweat in each place, the total daily lead excretion in fluids at Mount Isa would be more than one mgm per day, whereas in Melbourne, the daily lead excretion in fluids would amount to about 0.60 mgms only. At Mount Isa the blood, organs and tissues of the body would be in contact with more than one mgm of lead per day. At Melbourne, with the urine showing the same lead concentration, the tissues would be in contact with only 0.6 mgm of lead. There would thus be a greater chance of finding cases of lead poisoning among persons excreting 0.30 mgs per litre of urine at Mount Isa than among those excreting 0.30 mgs in Melbourne.

On the other hand, assuming a constant amount of lead absorption daily, there would be a greater excretion of lead in the hotter months than in the colder months, so that there would be presumably less tissue lead storage. There would be less chance of lead poisoning developing in the summer than in the winter, provided conditions of exposure were the same. Shiels concludes that increased elimination of lead in the sweat may have an important bearing on variations in the evidence of lead absorption as shown by the amount of urinary lead.

Referring to <u>nonindustrial lead poisoning</u>, some very interesting work has been reported recently from Queensland. This state has always been very "lead conscious" because of a former lead hazard to children. For more than 50 years, clinicians in Queensland have been convinced that one of the sequelae of lead poisoning in childhood there has been the development of chronic renal disease at a comparatively early age. In 1929, Nye concluded that children in Queensland were exposed to a lead hazard whilst playing, during the wet season, on the lead painted wooden verandahs so common there. They licked rain drops off the verandah railings. He showed that there was an abnormally high incidence of lead poisoning among Queensland children, e.g., from 1917 to 1926, 428 children were treated for lead poisoning in the Brisbane Children's Hospital, whilst during the same period, only four children were treated for lead poisoning in Sydney, three in Melbourne and one in Adelaide.

Along with this high incidence of lead poisoning in children, study of the death rate from chronic nephritis showed that the death rate from this disease in Queensland in the 10-40 age group was more than three times as great as that in other states.

As a result of this and of many other reports, legislation was introduced in Queensland about 1930 which forbade the use of lead-containing paint on the interior of houses at heights which children could reach. Within the last year, in Queensland, the legislation has been further amended and now the sale or manufacture of lead carbonate as a paint substance has been completely forbidden. No building may be painted, either interiorly or exteriorly, with a lead paint of any description, except that, on certain decorative boards high up in the buildings, such as fascia boards, a lead paint of up to 5 per cent may be used. Red lead may still be used on structural steel.

It is now claimed that, in recent years, an improvement in the statistics of death from chronic nephritis in younger age groups is evident.

Dr. D. A. Henderson, as a result of work at the Queensland Institute of Medical Research, has recently reported some extremely interesting conclusions on the

relationship between acute lead poisoning in childhood and the development of chronic renal disease. It would appear that he has convincing evidence that this connection does, in fact, exist. His work has appeared in the "Australasian Annals of Medicine" at intervals since 1954. References to these papers have been given above.

In his first paper, Henderson describes how he studied the after histories of children who had been treated for lead poisoning in the Hospital for Sick Children, Brisbane, between 1915 and 1935. There were 431 children in the group, with ages ranging from 2 to 12 years and comprising 169 males and 232 females. The follow-up was made by enquiries in the Department of the Registrar General, at electoral offices, and by examination of marriage records, death registers, etc. Some information was obtained of 352 of the 401 children. Of these 352 children, death certificates were seen for 101 females and 64 males. These included five war deaths. XII of these deaths occurred between the ages of 1 and 40 years. The mortality rate for the whole series of children was 40,604 per 100,000, whereas the average mortality rate from all causes in the general population of Queensland for persons aged 1 to 40 years is 263 per 100,000.

Of the 165 deaths, no fewer than 54 were certified as being due to chronic nephritis; an additional 14 deaths were certified as being due to other possible renal causes, e.g. cerebral hemorrhage, giving a total mortality rate, from renal causes, in this group of 26,932 per 100,000. The average mortality rate from all renal causes in the general population of Queensland in the 15-40 age group is 36 per 100,000.

The duration of life before death from renal causes, after admission to hospital with the diagnosis of lead poisoning, varied from 6 years to 34 years.

Even after the subtraction of all renal and vascular deaths, an excess of mortality from other causes was noted. Many of the other causes of death certified could represent the sequelae to lead poisoning, e.g. such certified causes of death as "dementia," "encephalitis," "convulsions," "acute nephritis of pregnancy," etc. There was also a high death rate in the group from infective causes which could possibly be related to chronic ill-health associated with decreased resistance.

Of the 187 members of the series still alive, information about 101 was obtained. Of these, 17 have hypertension and albuminuria, 3 have hypertention, 5 are mentally defective, 3 have psychoses and 2 are blind as a result of optic atrophy.

In his second paper, "Chronic Nephritis in Queensland," published in 1955, Henderson concludes that, since 1890, Queensland has had a higher mortality from chronic nephritis than the remainder of Australia. This higher mortality was observed to affect first the younger age groups and then older age groups in succession, until the oldest age group to be affected, 50-59 years, was involved about 1930. This higher mortality has now begun to decline, first in the younger age groups and, if the present trend continues as appears likely, the mortality in the 50-59 years age group should drop to that of the other states of Australia about 1990.

When the increased mortality was at its maximum, chronic nephritis was one of the commonly certified causes of death for persons under the age of 40 years. Approximately 160 persons between the ages of 10 and 60 years died each year in Queensland in excess of the number who would have died had the death rate from this disease been the same as that in other states.

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Henderson points out that this excess mortality is best explained by the action of some nephrotoxic agent on the children of Queensland which would have commenced acting about 1870 and gradually diminished after about 1920. This agent initiated changes in the kidney which lead to death from chronic nephritis in from 10 to 40 years.

In this second paper, Henderson leaves it at that, but in his third paper, entitled "The Lead Content of Bone in Chronic Bright's Disease," he concludes that this nephrotoxic agent was excessive lead absorption in childhood. In this paper, he reports the results of the analysis of the lead content of bone from the calvarium and from portion of a rib from 669 autopsies in Brisbane (possible lead exposure in childhood) and 197 in Sydney (no childhood exposure). He found that the bone lead content of persons without chronic Bright's disease and who resided in Queensland is of the same order as those who had lived outside that state. He also shows that the lead content of bone from subjects aged 20 to 49 years, born and dying in Queensland from chronic Bright's disease, is significantly higher than that of subjects not suffering from this disease. In 36 males and 31 females, aged 20 to 49 years, born and dying in Queensland from chronic nephritis, the mean bone lead content was 7.31 mgs per 100 gms of moist bone in males and 7.97 in females, whilst for persons in the same age group and not suffering from chronic Bright's disease, the mean was 3.91 mgms per 100 grams in males and 3.34 mgms in females (calvarium bone).

Henderson found that, as a result of autopsies on patients dying outside Queensland, most cases of chronic renal disease among them could be allotted by clinicopathological examination to one of three defined and generally accepted etiological groups:

(a) chronic glomerulonephritis,

(b) chronic pyelonephritis, and

(c) those associated with hypertension as the primary condition.

When, however, an attempt was made to allocate to one of the above groups the 59 cases of death from chronic nephritis in Queensland in the 20 to 49 age group, it was found that only 12 of these could be so classified - five to chronic glomerulonephritis, three to pyelonephritis, four to hypertension. Forty-seven were regarded as being of undetermined cause. These cases could only be labeled "hypertension with renal failure." They had no history of acute nephritis, of long-standing urinary infection, or of oedema, prior to that associated with terminal cardiac failure. Their urinary findings gave no indication of the etiology of this renal condition and the general histological picture was one of marked disappearance of renal tissue without indication of cause.

The bone lead content of the 12 subjects with chronic Bright's disease of known cause was found to be of the same order as that of persons not suffering from this disease.

For the 25 females and 22 males in the group for which no etiological diagnosis was made, the mean lead values in the calvarium were 8.45 mgms per 100 gms in males and 8.66 in females.

Henderson then proceeds to discuss the possible origin of this high bone lead and enumerates three possible causes:

(a) As all had chronic renal disease, retention of normally absorbed lead by failing kidneys may have been responsible.

(b) There may have been some disturbance of metabolism whereby a large proportion of normal lead intake was absorbed.

(c) There may have been excessive absorption of lead due to excessive exposure.

Each of these possibilities is discussed. He finally concludes that there had been in these cases excessive absorption due to excessive exposure.

In those with a high bone lead, in only one male was there a history of industrial lead poisoning. Four males had a history of lead poisoning in childhood and a sibling of another had suffered from childhood lead poisoning. There has been no industrial exposure to lead of females in Queensland, and no other lead hazard to adult females is known to exist. Six of the females with chronic Bright's disease and a high bone lead content had histories of lead poisoning in childhood.

Summarizing his conclusions, Henderson points out that it is known that there was in Queensland for many years a serious and widespread lead hazard to children and that it has been shown that, where a lead hazard exists, investigations of siblings and associates of children with plumbism will reveal many additional instances of grossly excessive lead absorption, with few, if any, acute clinical manifestations. The above facts make it most probable that the excessive lead in the bones of nearly all these young individuals with chronic Bright's disease was acquired during their childhood. He goes on to say that his investigations provide a link between the chronic nephritis in Queensland and excessive lead absorption in childhood.

He further suggests that the estimation of the lead content of bones in cases of chronic Bright's disease may well have a wider application. He points out that plumbism, both industrial and nonindustrial, clinical and subclinical, occurs in most civilized communities and that, despite some doubt, particularly in America, there is a great deal of evidence that lead absorption can produce chronic renal disease. He suggests that cases of chronic Bright's disease occurring outside Queensland may also be due to plumbism and that the routine determination of bone lead at autopsy, in cases of chronic renal disease without obvious cause, may elucidate their etiology. This is supported by the fact that, in the group born outside Queensland, thereby avoiding the special hazard in childhood, a number of cases of chronic Bright's disease had high bone lead. It so happens that all these were males in the older age groups, suggesting an industrial exposure.

Henderson emphasizes that the bone lead content is of etiological significance only when considered in conjunction with clinical and histological data.

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Henderson finally concludes that some cases of chronic Bright's disease in Queensland in the 20-49 age group can be ascribed by clinicopathological studies to known causes, but the larger proportion, 63 per cent in the present series, cannot be so allotted. The bone lead content of those cases of known etiology is the same as that of persons dying without chronic Bright's disease, whereas the bone lead content of the group of unknown etiology is significantly higher. This high bone lead content is due, with few exceptions, to excessive absorption during childhood. Bone lead content can be used, in cases of chronic Bright's disease, as a valid indication of excessive lead absorption, and its estimation may provide a clue to the etiology of some of them.

In a fourth paper, Henderson intends to discuss the pathology of the kidney associated with the presence of high bone lead content.