A NOTE ON EXPERIMENTAL LEAD POISONING.

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The incidence of Industrial Lead Poisoning is closely related to those sections of the manufactures which involve the production of dust. In white-lead works, paint-grinding shops, litharge grinding, electrical accumulator works, etc., the dust takes the form of minute particles of the special compound of lead manipulated by the workman. In smelting, desilverising, trimming metals and in file cutting, finely divided metallic lead, or a lead oxide, is present in the workshop air.

In a Special Report on Lead Poisoning in Paint and Colour Manufactures, Dr T. M. Legge points out that at least 80 per cent. of the cases of poisoning collected by him in paint workshops are related to the processes in which the lead compound is handled in the dry state (dusty processes).

It is also commonly recognised that the special danger in emptying Dutch stoves in the white-lead works, and mash-making in paint-grinding works, to take two specific instances, comes from the white-lead dust thrown into the air; and further that, when proper provision is made for the withdrawal of the dust by powerful exhaust fans, the amount of poisoning associated with these two processes is greatly diminished. The substitution of one process for another is also often followed by a distinct diminution in the incidence of the poisoning, and I have been able to show that the decrease in the poisoning in a white-lead factory followed the introduction of a particular change in the method of setting the beds, so that the resulting corroded lead was much harder and therefore freer from dust than in the original process,

and therefore less dust was produced in its removal when the stacks were emptied.

From the undoubted association of lead poisoning with the dusty operations in the manufacture of lead compounds, I thought it of some interest to enquire experimentally into lead poisoning by subjecting animals to the inhalation of lead dust in air. The best animal to use for such experiments was at once suggested by the fact that cats and dogs when allowed to roam at will in a white-lead works rapidly become poisoned, and ultimately die with similar symptoms to those observed in man. "It is impossible to keep a cat, they always die of lead poisoning here," is a common saying in the lead factories. Rats, with which many of the factories swarm, appear to be immune, and are never found dead or dying from lead poisoning. Cats were used for this reason, and because they are easy to deal with, and such animals as guinea-pigs are somewhat too small, and, in common with rabbits, differ more in their alimentary system from man than do cats. A further series of experiments, to be published later, have also been carried on with cats, alcohol being given in addition to the lead, and causing a more rapid appearance of the symptoms of lead poisoning than when lead alone is used.

The lead dust in air may presumably be absorbed through two channels:

(*a*) The gastro-intestinal canal—by the dust in the air becoming deposited upon the pharynx and nasal mucous membrane and then swallowed.

(*b*) By direct inhalation of the particles of dust into the lung.

That dust can gain direct access to the lungs is evidenced by the dark stained sputum in persons exposed to dusty atmospheres, as coal miners, grinders, etc.; and the following experiment shows the difficulty of removing white-lead dust from the air by moist chambers or water.

Four 750 c.c. wash bottles were arranged in series with india-rubber tubes so that air could be drawn through the apparatus by means of a water pump. The whole apparatus was washed out with water, including the rubber junction tubes $\frac{1}{4}$ inch in diameter, and some 2 ft. long. A bottle containing white-lead dust was attached to the distal end and gently shaken in the hand. Within three minutes of the pump being started white-lead dust was observed in the proximal flask. The rate of flow was two litres in 35 secs. The dust had passed through three sets of wet $\frac{1}{4}$ inch rubber tube and through the three moist wash bottles.

There therefore appears to be considerable probability that white-

lead dust can find its way into the lung direct, and as in the white-lead and paint-making industries the workmen are frequently subjected to sudden puffs of white-lead dust an attempt was made to reproduce in an experimental manner the working conditions. It was necessary however to somewhat shorten the period during which the experimental animals were exposed to inhalation of lead dust, so somewhat larger quantities of lead dust were used over shorter periods than would be the actual case in a paint mill or other industrial process. This point will be referred to again.

Apparatus.

For the purpose of the experiments a large cage was constructed 6 ft. by 3 ft. 6 ins. by 3 ft., having the two long sides and the top glazed so that the animals could be watched during the whole of the experiment; the remainder of the cage was lined with sheet zinc. At one end was placed an electric fan making 2000 revolutions per minute. Immediately in front of the fan and in the roof of the cage was a $\frac{3}{4}$ inch hole through which passed the stem of an ordinary glass funnel. This was covered with a piece of sheet lead through which passed a rod terminating inside the cage in a disc so arranged that it could be pulled up (without opening the cover of the funnel) and so prevent the white-lead or other lead compound from falling through the funnel until required. At the end of the cage farthest from the fan a wire cage was placed in which the animal could lie down without discomfort. Through the back wall on a level with the animal's head a 1 inch hole was drilled through the cage for the purpose of taking air samples. A cork, through which passed a glass tube plugged with cotton wool, was pushed into the hole. The tube was then connected with an aspiratory jar and a measured quantity of air drawn through the cotton wool plug, in which the lead present was afterwards estimated. Two large holes plugged with cotton wool were also made in two other situations to allow of ventilation in the cage. A fourth hole was made through the side of the cage near the fan, through which a glass tube could be passed and steam let into the cage at the termination of the experiment. Two doors were also provided for manipulating, cleaning, etc.

Method of Experiment.

The cage was in the first place well cleaned out after the previous experiment by means of steam and then water, followed by mopping

out and drying by a small charcoal stove and hot bricks. It was then well ventilated by running the fan with both doors open. The animal under experiment was then placed in the cage and the doors closed tightly. A weighed quantity of the lead compound well dried and in fine powder was then placed in the funnel and the fan started. Small quantities of the dust were now allowed to drop into the cage by lowering or raising the rod through the funnel; as the dust dropped some was taken up by the motion of the fan and stirred up into the cage air. The dust was allowed to fall gradually, about ten minutes being required to pass in 50 grms. The respirations of the animal were noted during the experiment. At the end of 15 minutes a further quantity of dust was started in the manner described above, and at the end of 30 minutes the fan was stopped. Steam was then turned into the cage for a few minutes, after which the door was quickly opened and the animal removed, taken outside the laboratory and thoroughly brushed with a hard brush to remove all dust adhering to its coat.

Immediately the first quantum of dust had been added to the cage air five litres of air were aspirated off in about 60 seconds through the glass tube plugged with cotton wool.

If the animal showed any disposition to lick itself during the experiment it was immediately stopped, but as a rule the cats curled up and went to sleep either facing, or with their backs to the fan; they made no attempts to get out of the wire cage and appeared entirely indifferent to their surroundings. In only a few instances did they cough or sneeze, white-lead dust in particular being evidently non-irritating, whereas litharge dust on several occasions caused coughing. I have noticed a similar difference between the dust produced in litharge and white-lead grinding in a factory. The litharge dust is much heavier than the white lead and becomes deposited on the cage walls more rapidly. Flue dust on the other hand is very fine and circulates longer in the cage air.

Lead compounds used.

Three varieties of lead compound were used in these experiments: three animals (cats) were experimented with, a fourth cat being used as control and fed with a lead compound, and a fifth kept in the laboratory as a general control.

The compounds of lead used were:—

A. *Flue dust* from the "market plot" in desilverising. This dust

contains from 50 % to 60 % PbO. The dust is produced as follows. In the process of desilverising zinc is added to the molten lead containing the silver and gold, and the zinc, which contains practically all the precious metals, is separated from the lead by the difference of melting point, etc. The "poor lead," or lead from which the zinc has exhausted the precious metals, is run into a pot called the "poor pot" or "market pot," holding some 30 tons of metal. Air and steam under pressure are then forced through the molten mass, oxidising the zinc and at the same time some of the lead. The exhaust from the pot passes into a flue and underground chamber, where the dust is collected. A considerable amount of dust finds its way into the air of the factory during the process of blowing.

B. *Litharge* obtained from the air ducts leading from a litharge grinding plant. This dust may escape and be inhaled by the persons engaged on the grinding machine. The litharge lumps are broken up by hand and shovelled into the hopper of the grinding machine.

C. *White lead* obtained from the air ducts leading from the packing machines used in packing dry white lead into barrels. Persons engaged in white-lead or paint manufacture are liable to inhale this dust. White lead from the air ducts of the packing machines etc. finds its way to the potteries as "off colour lead" and is used in making glazes and fritts.

Experiments[1].

A. *Flue dust.* Cat w. = 3 kgs. subjected to inhalation of "flue dust" on 10 occasions from Nov. 15th to Dec. 18th, 1905. Final weight 2·5 kgs., loss = 0·5 kg.

Colic Dec. 3rd and Dec. 18th. Extensor paralysis of front paws, weakness of back muscles, slight retinal haemorrhage.

B. *Litharge.* Cat w. = 3·77 kgs. subjected to inhalation of litharge dust on 10 occasions, Nov. 22nd to Dec. 18th, 1905. Final weight 3·0 kgs., loss = 0·77 kg.

Slight paralysis of hind limbs, no eye changes. Colic Dec. 6th.

C. *White lead.* Cat w. = 4·1 kgs. subjected to inhalation of white lead on eight occasions, Nov. 28th to Dec. 18th, 1905. Final weight 3·04 kgs., loss = 1·06 kg.

Dec. 1st, Colic, hind leg stiff and extensor paralysis. No eye changes.

[1] Full details of the experiments are given in the Tables.

D. *Flue dust Control.* Cat w. = 2·75 kgs. Fed with flue dust.
Nov. 16th, 1905 to Dec. 18th, 1905, Sundays excepted.
Total quantity taken 7·25 grms.
Slight stiffness hind limbs, no retinal change, Colic Dec. 7th.

The method first tried for estimating the amount of lead present in the cage air was as follows. The cotton wool in the glass tube was dissolved in dilute nitric acid and the contained lead precipitated and weighed as sulphate.

This method was found to give somewhat unequal results, and was discarded, the lead being dissolved out of the cotton wool with nitric acid, filtered, and finally determined by the molybdate method with tannic acid as indicator.

It will be seen that the amount of dust used was gradually increased, 20 grms. and finally two lots of 30 grms. being used during the experiments. It will also be noticed that a considerable variation in the respirations occurred, particularly with the cat which was subjected to the litharge dust. I noticed throughout that the litharge dust was apparently much more irritating to the lung, and produced far more discomfort than the other two varieties of dust used. Both the white-lead cat and flue-dust cat remained for the most part quite quiet during the experiments, the cats going to sleep during the whole of the time; but with the litharge cat the animal very rarely remained still, was constantly sneezing, and was apparently feeling distinctly uncomfortable. It never sat down and went to sleep like the other cats, whilst its respirations were more frequent than the flue-dust or white-lead cats.

It will be noticed on comparing the weights of the cats that the flue-dust cat shows the same amount of diminution in weight as the cat fed on the flue dust. All the cats show progressive diminution in their weight. Control cats kept under similar conditions in the laboratory increased considerably in weight when not fed with lead dust, and it was noticed in the experimental cats that the diminution in weight was rather rapid at first.

The first noticeable change in the experimental cats was an alteration in the appearance of the face due to the wasting of the orbital and buccinator fat giving the animal a pinched appearance curiously like the facial appearance presented by men who have worked for long periods in dangerous positions in lead works.

Colic was the next symptom observed, the cats first showing a disinclination to eat their food, and then showing signs of abdominal discomfort, which at times became more pronounced. Obstinate con-

stipation appeared about the same time, the faeces of the experimental cats contrasting sharply with those of the control cats in the laboratory fed on the same diet without exposure to lead.

Weakness of the muscles was also noticed, especially the muscles of the back and the extensor muscles of the limbs, the latter causing the animal to adopt a curious stiff gait. It walked on the tips of its toes, and in endeavouring to turn round was obliged to arch its back and draw its feet close together to prevent its falling over. When attempting to turn when running down the laboratory after a ball it invariably fell over. The back muscles were distinctly weak, so much so that if the animal was held up by placing one's forefinger and thumb behind its ears it hung straight, and any attempt to twist or claw the holder's hand was impossible, whereas a normal cat held in the same way soon causes itself to be dropped. When jumping off a table on to the floor, the cat fell upon its belly, the extensor muscles being evidently unequal to the strain.

The four cats were further examined with an ophthalmoscope for eye changes, but in only one, the flue-dust cat, was any distinct eye change noticed, and the examinations had to be discontinued as the use of the atropine even in small doses caused acute salivation and running from the nose.

The loss of weight appeared at first progressive, but when the loss had proceeded to a certain point the weight remained fairly constant, the white-lead cat alone showing a tendency to rise in weight at the termination of the experiments. Glibert, who fed rabbits with pills of white lead, found there was no great loss of weight and that the loss apparently had no relation to the onset of symptoms of acute poisoning. My experiments were not carried as far as the death of the animal by acute poisoning, all the animals being killed when distinct signs of poisoning had supervened.

No blood examinations were made, as the examination of persons working in lead factories, although showing a certain degree of secondary anaemia, does not show any specific changes.

A few experiments were made in addition to the inhalation observations, regarding the solubility of the white lead and litharge in gastric juice obtained from a normal man.

The two samples[1] of gastric juice were obtained by means of a stomach tube after a test breakfast of tea and toast taken fasting.

[1] Both samples were tested for digestive efficiency and acidity. No. 2 shewed a slight excess of both total and volatile acidity over normal gastric contents.

To 10 c.c. of each of these samples of gastric juice were added:

A. 0·1 grm. Lead Sulphate
B. 0·1 „ White Lead.
C. 0·1 „ Litharge.

The mixtures were then digested at 37° C. for one hour: the digests centrifuged; and 2 c.c. of the supernatant fluid removed with a pipette and titrated against an ammonium molybdate solution, 1 c.c. of which was equal to 0·0008 grm. PbO. The digests were made in duplicate and two estimations made of each.

The average quantities of PbO present in the digests were:

1.	A.	Lead Sulphate.	0·080 %.
	B.	White Lead.	0·048 %.
	C.	Litharge.	0·040 %.
2.	A.	Lead Sulphate.	0·046 %.
	B.	White Lead.	0·042 %.
	C.	Litharge.	0·034 %.

It would appear therefore that very little difference exists in the solubility of the three compounds in normal gastric juice, but that, if anything, the lead sulphate is the more soluble. The observation tends to throw doubt on the advantage of the sulphuric acid sanitary drink in use in the various lead works.

Certain objections suggest themselves in the foregoing inhalation experiments. Firstly it may be objected that the animals would swallow the lead dust in the air breathed, the dust becoming deposited upon the pharynx and nasal mucous membrane and so swallowed. There is, however, sufficient evidence in both the wash bottle experiment and in the production of industrial diseases in other trades than lead works, that dust finds its way into the lung. Miners' phthisis, grinders' rot, stone masons' phthisis, are cases in point, while in the particular case of the experiments detailed the quantity of lead present in the cage air was so small that the animal if it swallowed the whole of the dust it breathed in would not obtain as much as the control cat which was fed with lead.

The further criticism that the animals obtained lead dust from their coats is not, I think, a serious one, for the greatest care was exercised after each experiment to thoroughly brush and dust the animal's coat before it was returned to the cage.

A further objection that arises is the fact that the animals were subjected to somewhat more severe conditions than those under which industrial lead poisoning takes place. The objection is not so serious as would at first sight appear. A man engaged in tipping barrels of dry white lead into a hopper of a paint-grinding mill, unless the mill hopper be provided with a very efficient exhaust draught, gets a puff of dust into his face at the moment of emptying the white-lead barrel, a process that is continued at intervals during the day. Again, in the lower part of the paint mill at the moment of mash-making dust generally finds its way out at the lower levels. In stripping white-lead beds during the emptying of the earthenware pots into the trays clouds of dust are frequently produced, and when the corrosions are placed in the washing apparatus or wash beck a cloud of dust is always given off if the workman is in a hurry or careless. Although therefore the workman is not working in a confined space and having clouds of lead dust blown into his face for half an hour, as were the experimental animals, yet during the day and week he is subject to constant small doses of lead dust; and, if at any time the dose inhaled is somewhat larger than his metabolic process can easily deal with, some evidences of poisoning supervene. So much is this the case that a break-down of the dust preventing apparatus in a white-lead factory is generally followed in a day or two by symptoms among the men working, while the poisoning is always more associated with the dusty parts of the machinery or processes than the actual handling of the raw material.

Further, the men employed in the dusty processes are frequently covered with lead dust, and it is no uncommon thing to be able to wipe off distinct white-lead dust from a workman's eyelids after he has performed certain manipulations. Even should the amount of lead dust inhaled by the animals much exceed that of industrial processes, poisoning undoubtedly does take place in a dusty lead process, and the fact that the animal becomes poisoned somewhat more rapidly does not militate greatly against the cause of the poisoning. The largest number of cases of poisoning by lead reported from white-lead and paint-grinding works are first attacks occurring during the first nine months of exposure.

The experiments detailed above were performed for an essay submitted to the International Labour Bureau in 1906. Since that date the experiments have been considerably extended, my friend Dr F. W. Goodbody having collaborated with me, and we hope shortly to publish

our results, which are entirely confirmatory of the experiments detailed herein.

My experiments on the inhalation of lead dust show that poisoning by lead may take place through the lung as well as through the gastro-intestinal tract, and that susceptible animals exposed for short periods to air laden with lead dust develop symptoms of lead intoxication in a way analogous to the poisoning which takes place in men engaged in industrial processes, and exposed to the deleterious effects of lead-dust laden air.

Finally, as confirmatory evidence, it is interesting to note that at the end of the first fortnight of the experiments both myself, my friend, and the laboratory assistant all developed colic and constipation simultaneously during the week-end. On examining the cage we found a number of cracks where lead dust had undoubtedly escaped into the laboratory air at a point on a level with our faces; after these were properly closed no further trouble was experienced.

TABLE I.

Lead Dust Inhalation Experiments.

Animal No. 1. Cat. Weight = 3·000 kgs. Market Pot dust (PbO 50 %, ZnO 50 %). Details of the exposures in the special cage.

Date	Weight of animal kgs.	Total quantity of dust used gms.	Duration of exposure mins.	Average respirations per minute	PbO gms. per litre cage air	Notes
Nov. 15. 05	3·000	12	30	24	0·0019	
,, 17. 05	3·300	12	60	34	0·003	
,, 22. 05	2·800	40	60	40	0·003	
,, 28. 05	2·650	40	60	57	0·003	Face pinched. Vomiting.
Dec. 1. 05	2·500	40	20	45	0·004	
,, 3. 05	2·500	60	11	70	0·0014	Colic.
,, 6. 05	2·500	60	20	30	0·0016	Slight extensor paralysis.
,, 8. 05	2·500	60	20	35	0·0020	Back muscles weak.
,, 13. 05	2·750	60	15	30	0·0014	Colic.
,, 18. 05	2·250	60	20	20	0·0017	? Retinal haemorrhage.

TABLE II.

Lead Dust Inhalation Experiments.

Cat No. 3. Litharge dust from packing and grinding machine. (Cyclone dust collector.) Animal exposed to dust as No. 1.

Date	Weight of animal kgs.	Total quantity of litharge dust used gms.	Duration of experiment mins.	Average respirations of animal per min.	PbO gms. per litre in cage air	Notes
Nov. 22. 05	3·770	20	30	91	0·00019	
,, 24. 05	3·770	40	60	103	0·0001	Jerky respiration.
,, 28. 05	3·590	40	60	125	0·0558	Animal sneezing and coughing.
,, 29. 05	3·250	40	20	68	0·0781	Do. do.
Dec. 3. 05	3·300	40	20	87	0·0031	
,, 6. 05	3·300	60	20	81	0·0033	Animal fell over. Slight paralysis of hind limbs.
,, 8. 05	3·000	60	30	79	0·0026	
,, 11. 05	3·000	60	26	58	Lost	
,, 13. 05	3·000	60	20	33	0·0020	
,, 18. 05	3·000	60	20	65	0·0016	Colic. No eye changes.

TABLE III.

Lead Dust Inhalation Experiments.

Cat No. 4. White-lead dust from air duct of packing machine. Animal exposed as No. 1.

Date	Weight of animal kgs.	Total quantity of white-lead dust used gms.	Duration of experiment mins.	Average respirations per min.	PbO gms. per litre in cage air	Notes
Nov. 28. 05	4·00	40	30	43	0·0033	
,, 29. 05	4·300	40	20	44	0·0043	
Dec. 1. 05	4·000	60	20	40	0·00502	Colic.
,, 3. 05	3·500	60	20	26		Asleep during exp.
,, 6. 05	3·500	60	20	33	0·00273	Colic.
,, 8. 05	3·500	60	30	23	0·00273	
,, 11. 05	3·000	60	20	26	0·00262	
,, 13. 05	3·000	60	20	31	0·00273	Hind limb stiff. Colic.
,, 18. 05	3·040	60	20	26	0·00192	No eye changes.

TABLE IV.

Control Experiment, Cat fed with Flue dust.

Dust mixed with food (fish), given in first lot of food in the day.

Date	Weight of animal, kgs.	Quantity of PbO taken in dust, gm.	Notes
Nov. 16. 05	2·750	0·05	
,, 17. 05	2·750	0·05	
,, 18. 05	—	0·05	
,, 20. 05	2·500	0·10	
,, 25. 05	—	0·10	
,, 26. 05	—	—	
,, 27. 05	—	0·10	
,, 28. 05	—	0·10	Vomiting.
,, 29. 05	—	0·10	
,, 30. 05	—	0·10	
Dec. 1. 05	—	0·10	
,, 2. 05	—	0·10	
,, 3. 05	—	—	
,, 4. 05	2·000	0·5	Dose increased, as no symptoms.
,, 5. 05	—	0·5	
,, 6. 05	—	0·5	
,, 7. 05	—	0·5	Colic.
,, 8. 05	2·000	0·5	
,, 9. 05	—	0·5	
,, 10. 05	—	—	
,, 11. 05	—	0·5	
,, 12. 05	—	0·5	
,, 13. 05	—	0·5	
,, 14. 05	—	0·5	
,, 15. 05	—	0·5	
,, 16. 05	—	0·5	
,, 17. 05	—	—	
,, 18. 05	2·000	0·5	Slight stiffness in hind limbs, retinal arteries tortuous?

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