# TOXICOLOGICAL HAZARDS OF MERCURIAL PAINTS

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The toxicological hazards of ingestion of mercury by absorption through the skin from mercurial ointments and through the lungs from mercury laden air are reviewed. Mice living for 6 months in cages painted with antifungal mercurial paints show no significant Hg levels in the kidneys, liver, lung or spleen. From this it is inferred that no toxic hazard to humans working in rooms treated with these mercurial paints should result. Using the literature figure of 100 μg. Hg/c.m. of air as the upper safe limit for continuous exposure of man for 8 hours per day and assuming that 25 per cent of the inhaled mercury is absorbed it has been deduced that the maximum safe continuous peroral intake of mercury is 1·3 μg./kg./day. This figure should assist in deciding the maximum permissible amount of mercury salts in food and drinking water. Guinea pigs have been given 150 times this dose daily for 6 months and found to remain in perfect health. The hazard arising from the possibility of contamination of foodstuffs by flaking of an antifungal mercurial paint is thought to be negligible.

UNTIL recent years hydrargyrism was a hazard confined to industrial workers continually handling mercury and its salts, and to people undergoing inunction therapy with mercurial ointments. During the last two decades, however, mercurial preparations have gained wide use as bactericides and fungicides both in the medical and industrial fields; accordingly the proportion of the population now exposed to toxic hazard has considerably increased. These uses have been previously reviewed[1,2]. More recently there has been a trend to incorporate organo-mercurial compounds in paints and varnishes particularly for use in industrial premises, for example, breweries and bakeries, where walls are prone to troublesome fungal growths because of humid conditions. Apart from the possible hazard to personnel manufacturing and applying these paints—hazards which can be largely controlled by suitable precautions—it is natural to enquire into the general health risk entailed by the widespread use of mercurial additives in paint. Hazard can arise from the continual breathing of the air inside the painted room if the organo-mercurial compound should have any appreciable volatility, and from flaking of the paint with consequent possible contamination of foodstuffs. The work now reported was undertaken to add further information to our knowledge of these hazards.

It is pertinent to the object in mind briefly to review previous work on the toxicological hazards met with in the use of mercury and its derivatives in order to arrive at threshold figures below which risk of toxaemia may be considered negligible. It is remarkable that up to the present time no Official Committee has laid down upper permissible limits for mercury in foodstuffs or drinking water.

Various general reviews[3–10] on metallic poisons have appeared which give reference to mercurialism. Two methods have been used for assessing mercury accumulation in the body after a known exposure: (i) the determination of the amount of mercury in the urine and faeces over a long period until the value falls to zero and (ii) the analysis of the organs for mercury in those cases where autopsy can be performed. Stock[11], from extensive analyses of 67 human cadavers, showed that the kidney and hypophysis are the organs in which circulating mercury preferentially accumulates. Sollemann and Schneiber[12], in post mortem analyses of suicides who had used corrosive sublimate, found the highest concentration of mercury in the kidney (38 μg./g.).

Considerable work has been carried out on absorption of mercury through the skin, as determined by the urinary excretion of mercury, during the inunction therapy of syphilis and psoriasis; the rate of absorption depends to a considerable extent[13] upon the ointment base employed. In this connection it is necessary to know the mercury content of normal urine; a reliable estimate would appear to be 5 to 20 μg./l. Thus, Borinski[14] reported that 38 of 75 normal humans excreted as much as 10 μg. of mercury daily in their urine and faeces despite absence of any known exposure to mercury; while Lane[10] found the average urinary level to be 20 μg./l. in psoriasis patients who had not been previously treated with mercurials. Cole and others[15] examined six men who had been given 18–30 rubs with mercurial ointments and found that after four weeks the median figures for elimination of mercury were about 100 μg./day in the urine and 300 μg./day in the faeces. Inman, Gordon and Trinder[16] record that, in a series of psoriasis patients inuncted twice daily for 6 weeks with 2 per cent ammoniated mercury in soft paraffin over an area averaging 65 per cent of the total body area, the urinary level of mercury was about 130 μg./l. during the first week, rising to 500 μg./l. by the sixth week and then falling slowly to the normal figure in 7 to 9 months. No clinical toxicity was observed; nevertheless Inman and colleagues call attention to the risk of toxicity which the prolonged use of mercury ointments entails and consider a urinary level in excess of 300 μg./l. to be potentially dangerous. Examples[17,18] of the nephrotic syndrome attributable to mercurial ointments have been described and the opinion[19] has been held that syphilitic nephrosis is more likely to be caused by the mercury than by the syphilis. There is much evidence, however, that it is necessary to apply mercurial ointments for longer than 6 months before symptoms appear.

The distribution of mercury in mice, after the subcutaneous injection of mercury and calomel ointments has been determined by Maren, Epstein and Hand[20]. It would appear from their results that mercury levels in the kidney are a fairly reliable index of the extent of chronic absorption in the case of exposure to metallic mercury but with exposure to calomel, liver analyses are also necessary. Maren and colleagues comment upon the fact that there was no significant loss of weight in the experimental mice or, indeed, any other gross sign of toxaemia observable despite the high concentrations of mercury in the liver and kidney. Laug,

Vos, Umberger and Kunze[21] determined the absorption of various mercurial ointments in rabbits after inunction into a clipped area of the back comprising about 8 per cent of the total body area; after 24 hours the animals were killed and the organs analysed. With calomel the concentration of mercury in $\mu$g. Hg/g. of wet tissue was much the highest in the kidney (kidney, 21–26; liver, 0·78–1·02). Covering the inunction site was found to increase absorption fourfold.

Much work has been done on the hazard involved in breathing air containing mercury vapour. Stock and Zimmerman[22] kept animals in cages through which was passed air which had been loaded with mercury vapour at 50°; substantial quantities of mercury were found in the bodies at autopsy. Frazer, Melville and Stahl[23] exposed dogs to air containing 1890 $\mu$g. Hg/c.m. for 8 hours a day for 40 days: there was no ostensible sign of mercurialism but the daily excretion of mercury was about 500 $\mu$g. for dogs weighing 12 kg., showing that on an average 24 per cent of the mercury in the inhaled air had been absorbed. Attention[24] has previously been called to the risk arising from the spilling of metallic mercury in chemical and physical laboratories, particularly in the neighbourhood of steam pipes. The results of exposure of 38 men to various atmospheric concentrations of mercury has been reported by Shepherd, Schumann and Flinn[25] who found no evidence of mercurialism in men constantly exposed to an atmosphere containing 70 $\mu$g. of Hg/c.m.

Bidstrop, Bonnell, Harvey and Locket[26] observed symptoms of chronic mercury toxaemia in 27 of 161 men repairing D.C. meters; 58 men working on the repair of A.C. meters (which do not contain mercury) were unaffected. It was observed[26] that excretion of more than 300 $\mu$g. of Hg/day is accompanied by manifest symptoms of hydrargyrism and the excretion level was related to the concentration of mercury in the atmosphere. A concentration of 100 $\mu$g. Hg/c.m. of air was considered the upper safe limit; this is identical with the figure which had been previously laid down by the American Bureau of Standards[27] for the upper safe limit for continuous exposure for 8 hours per day. By assessing the rate of normal quiet breathing for an adult man at about 8 litres/minute and assuming from the work of Stock and Zimmerman[22] that 25 per cent of the inhaled mercury is absorbed, it is deducible that a man breathing air containing 100 $\mu$g. of Hg/c.m. for 8 hours a day will absorb about 100 $\mu$g. of Hg/day. For a 70 kg. adult this is a mercury intake of 1·3 $\mu$g./kg./day. In the light of present knowledge this must be taken as the upper safe limit for continuous daily absorption and it gives a basis for assessing the possible hazard of working in a room which had been painted with, or of continually consuming food which has been contaminated with a mercurial paint.

## Experimental

Groups of 20 mice were kept in cages 18 in. × 15 in. × 10 in. (46 × 38 × 25 cm.), the four sides and ceiling of which had been heavily coated with the mercurial antifungal paint. The front of the cages (18 in. × 15 in.) had a small wire grid 8 in. × 5 in. for admission of light and air. The

painted surfaces were covered with heavy gauge wire mesh ½ in. away from the paint, in order to prevent the ingestion of paint by contact or gnawing. The room temperature was 21°. The animals were kept in the cages for 6 months, weighed as a group each week and fed and watered *ad libitum*. At the end of this period 4 animals were taken at random from each cage, killed, the organs examined histologically and analysed for mercury content by the dithizone procedure.

The fungicidal organomercurials used were selected from substances now in commercial use and were as follows:

*Paint No.* 1. Emulsion paint containing 0·1 per cent w/w phenylmercuric dinaphthylmethane disulphonate. *Paint No.* 2. Emulsion paint containing 0·65 per cent w/w phenylmercuric 8-hydroxyquinolinate.

TABLE I

MERCURY CONTENT OF ORGANS OF MICE WHICH HAD BEEN KEPT IN CAGES PAINTED WITH MERCURIAL PAINT FOR 6 MONTHS

| | Liver | | Kidney | | Lungs | |
|---|---|---|---|---|---|---|
| Paint No. | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) |
| 1 | 1·87 | 0 | 0·38 | 0 | 0·28 | 0 |
| | 1·56 | 0 | 0·42 | 1 | 0·35 | 0 |
| | 1·32 | 0 | 0·38 | 0 | 0·21 | 0 |
| | 1·63 | 0 | 0·46 | 0 | 0·27 | 0 |
| 2 | 1·47 | 0 | 0·23 | 0 | 0·17 | 0 |
| | 1·87 | 0 | 0·41 | 0 | 0·27 | 0 |
| | 1·54 | 2 | 0·53 | 1 | 0·23 | 0 |
| | 1·16 | 0 | 0·29 | 0 | 0·18 | 0 |
| 3 | 1·85 | 0 | 0·45 | 0 | 0·31 | 0 |
| | 1·58 | 2 | 0·45 | 0 | 0·22 | 0 |
| | 1·74 | 0 | 0·46 | 0 | 0·39 | 0 |
| | 1·45 | 0 | 0·37 | 0 | 0·20 | 0 |
| 4 | 2·02 | 0 | 0·41 | 0 | 0·37 | 0 |
| | 1·67 | 0 | 0·29 | 0 | 0·24 | 0 |
| | 1·75 | 0 | 0·47 | 1 | 0·32 | 0 |
| | 1·90 | 3 | 0·40 | 3 | 0·26 | 0 |

* μg. Hg in total organ.

*Paint No.* 3. Oil paint containing 0·24 per cent phenylmercuric *p-tert.*-octyl phenate. *Paint No.* 4. Oil paint containing 1·2 per cent phenylmercuric *p-tert.*-octyl phenate. The first three of these paints have the mercury content which is recommended for use; the last has four times this content. At the end of the 6 months' period the average weight in each group had increased from 20–23 g. to 30–34 g. The mice appeared normal, there being no visible sign of toxaemia. The only deaths which occurred were from fighting and cannibalism; these were 1 in Group 1; 3 in Group 2; 4 in Group 3 and 1 in Group 4. In the four groups there were 5 healthy litters during the period. In the group of 20 controls kept in ordinary cages the average weight increase was from 20–22 g. to 30–33 g.; there were 3 deaths in this group and 2 litters.

Histological examination of the kidneys, lungs, liver and spleens showed no abnormality; the mercury content of the organs is shown in Table I.

In order to obtain information on the risk involved if old paint should flake and accidentally find its way into foodstuff, small daily doses of

phenylmercuric dinaphthylmethane disulphonate were fed to guinea pigs. This was the only one of the three additives which is water soluble and hence easy to administer over a long period. A group of four guinea pigs was given 50 g. of bran containing the pure organomercurial each morning; after this was eaten the animals were given greenstuff and oats *ad libitum*. The dose of the organomercurial amounted to 0·5 mg./kg./day (Group A). A further group of four guinea pigs was given 0·05 mg./kg./day in the same manner (Group B). The animals were weighed each week and after six months two from each group were killed and their

TABLE II

MERCURY CONTENT OF GUINEA PIG ORGANS AFTER FEEDING WITH MERCURIAL EACH DAY FOR 6 MONTHS

| Daily dose | Guinea pig No. | Liver | | Kidney | | Lung | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|
| | | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) |
| Group A .. .. | 1 | 22·4 | 3 | 4·5 | 58 | 4·0 | 0 | 0·6 | 0 |
| 0·5 mg./kg./day .. | 2 | 35·8 | 4 | 5·4 | 77 | 5·0 | 1 | 0·5 | 0 |
| Group B .. .. | 5 | 23·6 | 0 | 3·9 | 7 | 4·7 | 1 | 0·6 | 0 |
| 0·05 mg./kg./day .. | 6 | 29·2 | 1 | 4·8 | 7 | 5·0 | 0 | 0·8 | 0 |

* Per g. wet tissue.

TABLE III

MERCURY CONTENT OF GUINEA PIG ORGANS AFTER FEEDING WITH MERCURY FREE DIET FOR A FURTHER 6 WEEKS

| Group | Guinea pig No. | Liver | | Kidney | | Lung | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|
| | | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) | Weight (g.) | Hg* (μg.) |
| Group A .. .. | 3 | 26·5 | 0 | 4·4 | 11 | 5·0 | 0 | 0·7 | 0 |
| | 4 | 32·8 | 2 | 5·1 | 9 | 5·2 | 1 | 0·6 | 4 |
| Group B .. . | 7 | 27·1 | 0 | 4·1 | 2 | 4·8 | 1 | 0·8 | 0 |
| | 8 | 28·4 | 0 | 4·6 | 4 | 5·6 | 0 | 0·7 | 1 |

* Per g. wet tissue.

organs examined and analysed. The remainder were kept on normal diet for a further 6 weeks, killed and the organs examined and analysed to gain information on the rate of elimination of mercury.

In both groups the average weight increased regularly from 325–350 g. to 650–700 g., a rate of increase which is normal for guinea pigs of this age over a 6 month period. At the end of this period all the animals were alert, active and behaved normally; their fur had an excellent bloom. In the first group each animal had received an average of 100 mg./kg./6 months; in the second group 10 mg./kg./6 months. The single dose toxicity figures of this compound have previously been reported by Goldberg, Shapero and Wilder[28,29] to be: LDO 50 mg./kg.; LD50 70 mg./kg. and LD100 80 mg./kg. Table II shows the mercury content of the organs at the end of the initial 6 months and Table III the analyses after a further 6 weeks on the mercury free diet during which time elimination of the accumulated mercury was taking place.

It can be seen from Table II that, after oral ingestion of phenylmercuric dinaphthylmethane disulphonate, mercury accumulates principally in the kidney and liver; at the top dose (0·5 mg./kg./day) the amounts being about 360 $\mu$g. in the total kidney and 100 $\mu$g. in the total liver; none appears to be deposited in the lung and spleen. After 6 weeks on mercury-free diet these amounts had been reduced to about 50 $\mu$g. in the total kidney; the liver, lung and spleen being free from significant mercury.

## Conclusions

The results in Table I indicate that there is no measurable or significant volatility of mercurial from any of the paints used and accordingly that there should be no health hazard to personnel working in a room the walls of which have been painted with these preparations. Even with the paint containing four times the recommended amount of mercurial additive (Group 4) the amount of mercury found in the kidneys and liver was negligible excepting in one animal where 3 $\mu$g. was found in each organ. It is probable that this animal had gained access to and gnawed the paint since in no case was mercury found in the lungs.

The possibility of food contamination with flakes of the mercurial paint is a more difficult hazard to assess although a number of relevant comments can be made. The dose of mercurial in Group A guinea pigs corresponds to an oral intake of mercury of 200 $\mu$g./kg./day for 6 months and Group B, 20 $\mu$g./kg./day of mercury for 6 months. These intakes are respectively 150 and 15 times the amount, namely, 1·3 $\mu$g./kg./day (100 $\mu$g./man/day), which is accepted as the safe upper limit for continuous intake of mercury in inspired air. An intake of 100 $\mu$g./man/day by mouth must therefore be considered to be within the safe limit. It is pertinent to consider the probability of this dosage being exceeded by contamination of foodstuffs. The approximate area covered by 1 kg. of paint is 200 sq. ft. (200,000 sq. cm.); with the highest amount of mercurial additive recommended, 0·1 per cent combined mercury in the wet paint, the amount of mercury in the surface of the painted area is about 5 $\mu$g./sq. cm. Accordingly, all of the mercurial in the paint which might flake off 20 sq. cm. of surface could be consumed per day by the same person indefinitely without exceeding the accepted upper safe limit. It must be admitted that the probability of this amount being exceeded or even reached in the most careless establishment is very remote.

## References

1. Goldberg, *Mfg. Chem.*, 1951, **22**, 186.
2. Goldberg, *Chim. et Ind.*, Numero special du XXIII Congrès de Chimie Industrielle de Milan, Sept., 1950.
3. Esse, *Dtsch. Z. ges. gerichtl. Med.*, 1937, **27**, 253.
4. Robinovitch, *Canad. med. Ass. J.*, 1934, **30**, 386.
5. McDonald, *Industr. Med.*, 1941, **10**, 447.
6. *Industr. Hyg. Sect.*, **2**, 66.
7. Pinto and Bowditch, *New Engl. J. Med.*, 1941, **225**, 949.
8. Ferrari, *Med. Klin.*, 1940, **36**, 1005.
9. Stock, *Ber.*, 1942, **75B**, 1530.
10. Lane, *Brit. med. J.*, 1954, **1**, 978.
11. Stock, *Biochem. Z.*, 1943, **316**, 108.

12. Sollemann and Schneiber, *Arch. Internat. Med.*, 1936, **57**, 42.
13. Wild and Roberts, *Brit. med. J.*, 1926, **1**, 1076.
14. Borinski, *Klin. Wschr.*, 1931, **101**, 149.
15. Cole, *Arch. Derm. Syph., N.Y.*, 1933, **27**, 1.
16. Inman, Gordon and Trinder, *Brit. med. J.*, 1956, **2**, 1202.
17. Oertel, *Dtsch. Arch. Klin. Med.*, 1940, **185**, 357.
18. Ludwig, *Helv. Med. Acta*, 1945, **12**, 543.
19. Zollinger, *Schweiz. Z. Allg. Path. Bakt.*, 1955, **18**, 155.
20. Maren, Epstein and Hand, *J. Amer. pharm. Ass., Sci. Ed.*, 1944, **33**, 91.
21. Laug, Vos, Umberger and Kunze, *J. Pharmacol.*, 1947, **89**, 52.
22. Stock and Zimmermann, *Biochem. Z.*, 1929, **216**, 243.
23. Frazer, Melville and Stahl, *J. Industr. Hyg.*, 1934, **16**, 77.
24. Ziener, *Chemia (Buenos Aires)*, 1940, **11**, 208.
25. Shepherd, Schumann and Flinn, *J. Res. Nat. Bur. Standards*, 1941, **26**, 357.
26. Bidstrop, Bonnell, Harvey and Locket, *Lancet*, 1951, **2**, 856.
27. Neal and Goodman, *Occupational Hazards*, 1943, **5**, 10 and 24.
28. Goldberg, Shapero and Wilder, *J. Pharm. Pharmacol.*, 1950, **2**, 20.
29. Goldberg, Shapero and Wilder, *ibid.*, 1950, **2**, 89.