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Absorption and Excretion of Mercury in Man

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Absorption and Excretion of Mercury in Man

V. Toxicity of Phenylmercurials

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Introduction

In a previous report [1] it has been pointed out that all organic mercurials probably do not have the same degree of toxicity and in particular that at least some of the phenylmercurials do not appear to possess a high degree of toxicity.

The purpose of the present study is to examine in detail published data on the toxicity of phenylmercurials for man and lower animals and to record some new data on human exposure. The latter has been made possible by an opportunity to study three groups of persons whose occupational exposure has been to a single phenylmercurial; in two groups to phenylmercury benzoate (PMB) and in the third to phenylmercuric acetate (PMA). Earlier studies have included observations on human exposures in which phenylmercurials have been involved along with several other organic and inorganic compounds of mercury; in other words, mixed exposures.[1-4]

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Review of Literature on Phenylmercurials

An intensive search of the literature of the past 30 years has been made for all references to phenylmercurials. If any significant published work has been overlooked it is not due to lack of diligence in conducting this

search. Studies dealing with humans and other animals have been included.

Phenylmercuric Acetate (PMA).—Human: Eastman and Scott in studying the use of PMA as a contraceptive observed 14 women who used PMA jelly two to five times a week for six months and 100 women who used this preparation one to five times a week for more than a year. Each application was of 6 ml of 0.05% PMA jelly, containing 1.788 mg of mercury. The former group was found to have an average urinary mercury of 83μg per 24 hours, compared with an average of 22μg before use of the jelly. In no case was there evidence of vaginal irritation or other toxic effect.[6] Danger to the spouse is illustrated in a case reported by Cohen in 1958.[7] A husband with known hypersensitivity to a popular mercurial antiseptic developed dermatitis of the penis after his wife used a contraceptive jelly containing 0.02% PMA.

The vesicant action of PMA and of several other organomercurials was reported by Goldblatt in 1945.[8] The author describes a case due to PMA in which the blister fluid contained 12μg Hg/gm. He noted that even under carefully controlled conditions the workers showed mercury in the urine although none showed symptoms of poisoning. No figures are given on degree of exposure or on urinary mercury levels.

PMA was one of several mercurials involved in a report by Cotter in 1947.[9] In this study, as in others of mixed exposures, it is not possible to evaluate the role of any individual compound. Chemicals other than mercurials may also have been involved.

In a review of organomercurials used as seed disinfectants, Swensson included PMA along with several other mercury compounds.[10] Among the materials studied he found $HgCl_2$ to have the highest toxicity, followed by PMA, methyl and ethyl mercury chloride, and methyl and ethyl mercury dicyandiamides, in that order.

A case of skin burn due to PMA was reported by Sunderman et al in 1956.[11] The delayed nature of the skin reaction led the authors to conclude that hypersensitivity rather than primary irritation was the mechanism. Additional cases of dermatitis have been described by Morris,[12] PMA being one of three organomercurials implicated.

An extensive study of human exposure in which PMA was one of several organomercurials involved was reported by Dinman et al in 1958.[16] The mixed nature of the exposure makes it impossible to evaluate the role of PMA.

Animal: Efforts to arrive at an LD_{50} dose for PMA were made by Eastman and Scott.[6] They found that for intravenous administration the LD_{50} for rats and mice was 20 mg/kg and for rabbits 5 mg/kg. Rats given up to 4 mg/kg of PMA intraperitoneally for ten days showed no toxicity, and rabbits given up to 0.2 mg/kg IV five days a week for ten weeks had no abnormal findings.

Vaginal and oral absorption of PMA in rats was studied by Laug and Kunze.[13] In their report they comment on the storage of mercury in the kidney and its significance when repetitive exposure occurs. Additional studies on the absorption, excretion, and storage of PMA (and mercuric acetate) in rats were subsequently reported by the same observers.[14,15] In the latter report it is stated that PMA in the diet at levels of 0.5 ppm for one or two years will produce renal lesions in female rats and that 10-20 times as much Hg acetate was required to produce the same lesions. No explanation is offered for the interesting difference between the response of female and male rats.

Japanese observers have reported that pregnant albino rats treated with PMA vaginally and subcutaneously produced an increased percentage of abnormal embryos.[17] Most of the embryonal abnormalities were found in the central nervous system, while degenerative lesions were found in the liver and kidneys of the treated animals.

Autoradiographic and tracer techniques, using radioactive Hg^{203} have been used in a number of studies of PMA by research groups in Sweden.[18-23] Kita in Japan has

conducted similar studies.[24] These investigations have produced a large amount of interesting data on absorption, excretion, and distribution of PMA in several animal species for subcutaneous, oral, and intravenous administration. The significance of these studies when related to human exposures is, of course, difficult to evaluate.

Detailed studies by Gage and Swan showed that PMA was much less toxic than certain methyl mercury compounds and no more toxic than inorganic mercury salts.[25] Methyl mercury salts were found to cause central nervous system lesions, but the same damage was not produced by PMA.

Other Phenyl Mercurials

The literature dealing with phenylmercurials other than PMA is rather scanty. This is particularly true of unmixed exposures involving humans.

Phenylmercuric Propionate (PMP).—An experimental study by Gemmill and Bowman in 1950 showed that PMP strongly inhibited the action of the enzyme invertase.[26] Phenylmercuric butyrate was found to have a similar effect.

Linfield et al studied the effects of a 70% cationic fabric softener which contained 0.85% of PMP.[27] They found no evidence of skin irritation or sensitization among 1,500 hospitalized patients who came in contact with treated fabrics over a period of six months. The concentration of PMP in the fabrics ranged from 30 to 63 ppm.

Absorption of mercury from undergarments treated with PMP in a form similar to that used by Linfield was studied by Goldwater and Jacobs.[28] All of five human subjects tested showed absorption of mercury if the undergarments contained more than 40 ppm of mercury, but there was no measurable absorption when the concentration was below 10 ppm. No skin irritation or sensitization or other toxic manifestations were observed.

Several reports of human exposures in which PMP has been present as one of a number of mercurials have been published.[1-4] Since it was not possible to evaluate the role of PMP in these studies, they are merely mentioned without comment.

Phenylmercuric Nitrate (PMN).—Weed and Ecker in 1931 reported a case of a man who ingested 250 ml of a 1:1,250 solution of PMN (200 mg of PMN) with no sign of toxic response.[5]

The use of PMN in the treatment of fungus infections of the skin was studied by Levine in 1933.[29] He reported that a lotion of 1:1,000 PMN was too irritating but that a 1:1,500 PMN ointment with 10% glycerin was satisfactory. Mercurial burns were reported in seven of about 200 patients.

Birkhaug[30] fed PMN 1:2,000 in drinking water to mice for ten weeks without any fatalities. He found that the minimum lethal dose (MLD) for rabbits by intramuscular or intraperitoneal injection of PMN was 0.01 gm/kg and by mouth about three times that quantity. He, himself, took 0.16 gm of PMN by mouth and experienced loose stools and slight abdominal pain for about 30 hours after the ingestion.

While the principal medicinal use of PMN has been as an antiseptic and germicide for external application, there is on the market a proprietary throat lozenge containing this compound. The label states that each lozenge contains 0.3 mg of PMN. A German study of a similar remedy containing 0.3% phenylmercuric borate purported to show negligible toxicity.[31]

Biskind found that application of 1:1,250 solutions of PMN to the human vagina did not cause irritation but a 1:750 solution in 10% alcohol produced a chemical burn.[31A]

The Council on Pharmacy of the American Medical Association published a review of studies on PMN and phenylmercuric chloride in 1934.[32] Among the conclusions were: "It is apparent from these studies that phenylmercuric nitrate is a mercurial of relatively low toxicity for man and animals," but the report went on to say that claims to this effect "must be advanced with caution."

A more recent review by Lundgren and Swensson[33] led the authors to conclude that

the acute oral and parenteral toxicity in animals is about the same for alkyl, phenyl, and inorganic compounds of mercury. A similar conclusion had been reached by these observers in an earlier study.[34]

Enzyme studies with PMN have shown depression of cytochrome oxidase, succinoxidase, catalase, and several dehydrogenases.[35] The reactivity of PMN and of *p*-chloromercuribenzoate with sulfhydryl groups has also been shown.[35,36]

Miscellaneous Phenylmercurials.—A few references to other phenylmercurials can be found in the literature. The irritant action of phenylmercuric oleate (PMO) was studied by McCord et al in 1941.[37] Five of nine human subjects reacted to 2% PMO but none to a 1% application. In rabbits, all concentrations above 0.1% caused skin reactions.

A study by Goldberg et al [38] showed that an aqueous solution containing 0.1% phenylmercuric dinaphthylmethane disulfonate can penetrate the skin and connective tissue into the underlying muscle.

Phenylmercuric pyrocatecholate was one of several organomercurials studied by Hagen.[39] By using rats and mice, he found that this compound gave off practically no vapors but might offer a dust hazard.

Possible hazards due to the use of phenylmercurials in paint have been studied.[40] Mice were kept for six months in cages painted with 0.1% phenylmercuric dinaphthylmethane disulfonate, 0.65% phenylmercuric hydroxyquinolinate, 0.24% and 1.2% phenylmercuric *p-tert*-octylphenate. All exposed animals showed normal growth curves, negative autopsy findings, and "negligible" amounts of mercury in kidneys and liver.

Human exposure to phenylmercuric pyrocatechin was reported on by Massmann in Germany in 1957.[41] He observed 26 workers who were exposed to atmospheric concentrations between 0.24 and 3.20 mg Hg/cu m and whose urinary mercury levels were as high as 6 mg/liter. Finding no signs or symptoms of poisoning after exposure up to five and six years, he concluded that this compound is relatively nontoxic.

Our Observations

As mentioned above, it has been possible to study three groups of human subjects whose occupational exposure has involved a single phenylmercury compound. In two of the groups the chemical was phenylmercuric benzoate (PMB) and in the third phenylmercuric acetate (PMA). No references dealing with PMB were found in the literature. Data gathered by other observers dealing with workers exposed to phenylmercury oleate (PMO) have also been available to us for review.

For purposes of discussion, the groups studied will be designated X, Y, Z, and Q. Mention of the processes which resulted in mercury exposure might permit identification of one or more of the industries concerned so that no detailed description can be given. The plants using PMB will be designated plants X and Y, and the one using PMA will be called plant Z. Plant Q is the one using PMO.

In plants X, Y, and Z, observations included numerous air analyses for both mercury vapor and mercury-containing dust. Urine samples were analyzed for mercury in all cases. Albumin, sugar, and specific gravity were included in the urinalyses. Blood levels of mercury were measured in all persons in plant Y and some in plant X. In a few instances, samples were lost in transit. Mercury in blood and urine was determined by the method of Jacobs.[42]

For plant X, results of physical examinations done by a local physician were available for review as were complete blood cell counts. Workers in plant Y were examined for signs of mercurialism by one of us (L.J.G.), but those in plant Z were not examined.

Plant X.—The findings in plant X are summarized in Tables 1 and 2.

Comment on Plant X: It is obvious that the completeness of the studies in plant X leaves much to be desired. The histories

TABLE 1.—*Plant X Air Analyses, May, 1962*

Sample	Location	Method	Hg, Mg/Cu M
1	Storage room manuf. bldg.	I_2-KI Unijet	None
2	Mixing tank manuf. bldg.	I_2-KI Unijet	40.00
3	Lab I, draw-down hood	I_2-KI Unijet	None
4	Analytical lab	Hg vapor meter	0.00
5	Lab II	Hg vapor meter	
	(*a*) In sink		0.04
	(*b*) In trash barrel		0.03
	(*c*) Elsewhere		0.00
6	Grinding room	Hg vapor meter	0.04 (max)
7	Storage warehouse	Hg vapor meter	
	(*a*) Near floor		0.08
	(*b*) Over open paper boxes		0.04
	(*c*) General air		0.02

Samples 1, 2, and 3 represent total Hg. Source of Hg was phenylmercuric benzoate (PMB).

TABLE 2.—*Studies in Plant X, April, 1962*

Case No.	Mercury: Urine	Mercury: Blood	Hgb, Gm %	Hct, %	WBC	Eosin, %
1	95		13.2	43.5	6,800	5
	788	9.0				
2	653		14.4	44.0	6,200	8
3	50		12.4	41.0	6,350	0
	53	3.0				
4	4		14.0	46.0	8,450	8
	<1	0.6				
5	600		14.7	45.5	11,100	2
6	368		13.0	44.5	11,450	2
7	0		13.2	42.0	8,450	4
	4	5.7				
8	26		13.0	44.5	5,850	1
9	186		14.0	46.0	9,000	2
10	3		14.0	46.0	5,750	1
11	8	4.9				
12	135		13.8	44.0	7,150	2
13	60					
14	<1	<1.0				
15	103					
16	412		13.4	43.0	8,600	0
	103	6.0				
17	72		13.6	42.0	6,200	0
	180	3.0				
18	105		15.8	49.0	10,200	13
19	57		13.4	44.0	9,300	4
20	108		12.6	41.0	8,350	6
21	220		14.4	45.5	8,050	3
22	215		14.5	47.0	9,400	2
23	44		13.8	44.0	8,350	2

Hg in urine in μg/liter. Hg in blood in μg/100 ml. Where two values are given for mercury in urine, the second was a reexamination after three weeks.

and physical examinations were done by a local physician who reported no signs or symptoms of mercury poisoning among the personnel. Routine urinalyses and blood cell counts were done at a local hospital. None of the urines showed albumin or other abnormalities. Eosinophil counts between 4% and 13% in seven of 23 persons is a striking finding for which no ready explanation was apparent. If and when the opportunity arises, this feature will be investigated further.

Only one location showed a significantly high level of mercury in the air. This was due to mixing of dry PMB powder. The two operators in the area were protected by impervious clothing and a helmet with forced air supply.

About the only inference that can be drawn from these incomplete observations is that a group of workers were exposed to sufficient PMB to result in urinary excretion of mercury up to nearly 800μg/liter and that they showed no detectable abnormality suggestive of mercury intoxication. The reported eosinophilia remains to be explained. The location of the plant made parasitic infestation highly improbable, and there was no evidence of allergic reactions.

Plant Y.—The results of air studies in plant Y are presented in Tables 3 and 4. Table 3 gives the direct readings for mercury vapor as measured with a Beckman mercury vapor meter and Table 4 total mercury collected in iodine-iodide solution and analyzed by a modified Barnes method. Figures for blood and urine are shown in Table 5.

Comment on Plant Y: It can be seen in Tables 3 and 4 that the mercury levels in the air were highest in location C. The fact that the readings on the mercury vapor meter and the amounts found in the I_2-KI samples were in the same general range strongly suggests that most or all of the mercury present in the air was in the form of mercury vapor rather than as PMB.

There is no consistent pattern for mercury in urine and blood. The highest values would have been expected for those working in location C, but apparently the nature and intensity of exposure was not such as to be

TABLE 3.—*Plant Y Mercury Vapor Meter Readings, February, 1963*

Location (3-11 PM Shift)	Hg, Mg/Cu M
A. Finishing area	
1. Work table	0.040-0.060
2. Above stacked product	0.080-0.120
3. On floor	0.120-0.180
4. Handling product	0.320
5. Packing	0.080-0.100
6. Top of unboxed product	0.080-0.100
7. Packing	0.060-0.080
8. Handling product	>0.250 (momentarily)
9. Examination table	0.040-0.070
10. Handling product	>0.100
B. Machine 227	
1. On desk	0.001-0.018
2. Entire area	0.001-0.010
C. Sheeting room	
1. Rear area near rolls	0.350-0.400
2. On examining bench	0.350-0.400
3. At examination bench	0.250-0.350
4. At collection end	0.350-0.500
D. Laboratory	0.020-0.030
E. Coating machine	
1. Rewind floor	0.028-0.052
2. Over coating liquid	0.040
3. Rewind	0.030-0.040
4. Wind	0.058
5. Station 1, inside	0.180
6. Side of station 1	0.034-0.420
7. Station 2	0.060
F. Storage	
1. Around packages	0.020-0.060
2. Toward floor	0.040-0.090
G. Baling	
1. In room	0.000-0.010
2. In trucks	0.020->0.100
(Worker bends over truck; sometimes enters truck)	
H. Cutting	
1. Not cutting	0.020
2. Cutting	0.040

Source of Hg was phenylmercuric benzoate (PMB).

TABLE 4.—*Plant Y Total Mercury, February, 1963*

Location	Hg, Mg/Cu M
A. Finishing area	
1. No activity	0.040
2. Inspection	0.080
3. Inspection	0.090
B. General atmosphere	0.000
C. Sheeting room	
1. On examining bench	0.350
2. Near rolls	0.330
3. Final process	0.240
E. Coating	
1. Starting	0.085
2. Middle	0.080
3. Near heater	0.000
F. Storage	0.060
G. Baling	0.080

Source of Hg was PMB.

reflected in that type of picture. It is interesting that only three of 21 exposed persons showed any mercury in their blood and nine had no detectable mercury in the urine. Only two workers had urinary mercury values greater than 100μg/liter, the highest value being 240μg/liter.

Medically, the group showed nothing remarkable at the time of these examinations. Mild hypertension was found in an obese woman of 47 and in a 51-year-old man with a history of previous kidney trouble. One man showed a slight tremor of the hands and another had a mild localized gingivitis. None showed albuminuria and none complained of any abnormal symptoms.

One significant feature was elicited in the histories and was confirmed by records in the plant medical office. This was a history of dermatitis in 12 of the employees. Several had had more than one episode; but there were no cases of dermatitis during the six months prior to this survey, that is, between August, 1962, and February, 1963.

The process involving PMB was introduced in April, 1961. Cases of dermatitis of the hands began to appear within a few weeks and created a troublesome problem for the next year or so. In July or August, 1962, a more stable, purer form of PMB replaced the earlier product and greater emphasis was given to the wearing of gloves. It is not possible to evaluate the relative importance of these two factors in putting an end to the dermatitis problem. Since all exposed employees do not wear their gloves at all times, it is not improbable that the improved PMB was at least partly responsible for the favorable change in the situation.

In considering the dermatitis problem in plant Y it must be pointed out that an organic resin and several other chemicals were present in the product along with the PMB. No adequate tests were conducted to establish the possible role of the other materials. Patch tests with the finished product at a time when it contained the unstable PMB had been conducted on humans and animals by a commercial testing laboratory.[43] These tests resulted in a high percentage of reac-

TABLE 5.—*Plant Y Mercury in Blood and Urine, February, 1963*

No.	Sex, Age	Operation and Location		Duration, Mo	Blood	Urine
1	F, 51	Inspect & packing	A	22	0	Lost
2	F, 45	Inspect & packing	A	22	0	240.0
3	M, 24	Sheeting	B	4	0	0
4	M, 23	Sheeting	B	22	0	165.0
5	F, 51	Inspect & pack sheeting	C	22	0	0
6	F, 24	Inspect & pack	C	9	4.2	40.5
7	F, 29	Inspect & pack	C	18	0	5.0
8	F, 47	Inspect & pack sheeting	C	22	2.2	37.0
9	F, 53	Inspect & pack sheeting	C	22	0	0
10	F, 45	Inspect & pack sheeting	C	22	0	10.0
11	M, 39	Laboratory	D	27	6.6	15.0
12	M, 41	Laboratory	D	27	0	0
13	M, 20	Coating	E	15	0	0
14	M, 26	Coating	E	22	0	7.0
15	M, 23	Coating	E	13	0	40.0
16	M, 51	Coating	E	22	0	75.0
17	M, 43	Baler	G	22	0	0
18	M, 30	Slitting	H	22	0	0
19	M, 22	Slitting	H	22	0	45.0
20	M, 54	Cutting	H	22	0	7.0
21	M, 21	Cutting	H	22	0	0
		Controls				
C 1	M, 38			0	2.2	0
C 2	F, 27			0	0.9	Lost
C 3	F, 21			0	0	4.0
C 4	M, 52			0	0	0
C 5	M, 36			0	4.5	7.0
C 6	M, 51			0	0	0
C 7	M, 27			0	0	0
C 8	M, 58			0	—	0
C 9	M, 36			0	0	19.0
C10	M, 22			*	0	0
C11	M, 24			†	0	90.0

* Last Dec 20, 1962.

† Last Dec 30, 1962.

0 indicates none detected. Blood values are micrograms per 100 ml. Urine values are micrograms per liter. Samples taken toward end of work shift. Thirteen of 18 operators were employed for the entire time since this process was introduced. All samples negative for albumin. Letters correspond to locations as in Tables 3 and 4.

tions but tell nothing as to the component responsible. The fact that phenylmercury compounds have so frequently been associated with skin reactions [7,8,11,12,31A,37] naturally caused the finger of suspicion to point to PMB. Further tests, using the individual components, are being planned.

Plant Z.—The findings in plant Z are given in Table 6.

Comment on Plant Z: Since the workers in this plant did not remain constantly in any one location, no attempt has been made to correlate specific exposures with evidence of absorption. Samples from nine of the 17 locations tested showed no detectable mercury. The other areas were found to have between 0.05 and 0.10 mg Hg/cu m. The variability of exposure may account in part for the irregular pattern of blood and urine mercury levels.

TABLE 6.—*Plant Z Mercury in Blood and Urine, February, 1963*

No.	Duration, Months	Mercury	
		Blood	Urine
1	30.0	29.0 (0)	0 (0)
2	24.0	17.0 (1)	49 (158)
3	12.0	<1.0	0
4	30.0	0.0	15
5	30.0	0.0	0
6	18.0	5.0	0
7	0.5	0.0	150
8	4.0	7.0 (0)	0 (0)
9	12.0	0.0 (1)	0 (21)
10	4.0	0.0	23
11	30.0	0.0	0
12	30.0	7.0	0
13	30.0	0.0	4
14	30.0	55.0 (1)	138 (0)
15	12.0	0.0	0
16	6.0	0.0	0
17	30.0	0.0	12
18	30.0	0.0	0
19	24.0	0.0	0
20	Intermittent	0.0 (9)	12 (217)
21	Intermittent	45.0 (2)	0 (0)
22	Intermittent	38.0 (3)	0 (0)
23	Intermittent	38.0 (7)	95 (108)

Total mercury in air in 17 locations, 0-0.1 mg/m³. Blood values are micrograms per 100 ml. Urine values are micrograms per liter. Figures in parentheses are for repeat analyses two months after the original tests. Source of Hg was phenylmercuric acetate (PMA).

In one respect, the data appear to have some degree of consistency, namely, that there was a low level of both exposure and absorption.

Plant Q.—The data for plant Q were collected by other observers and made available to us for review. They are mentioned here only because no previous reference to human absorption of phenylmercuric oleate (PMO) was found in the literature.

Urinary mercury levels were determined on 24 persons, the range being from about 100μg to about 700μg per liter. None of the exposed workers was reported as showing any evidence of toxic effects. Tests for at-

mospheric levels of mercury showed a wide range of concentrations.

General Comment

One of the responsibilities of the industrial toxicologist is to evaluate and interpret data derived from animal experimentation as well as that obtained through observations of human exposures. Both are important and both have limitations. Ordinarily it is not possible to obtain from human experience the same degree of completeness and control as is possible when animals are studied in the experimental laboratory. On the other hand, animal data are of only academic interest unless they have some meaning in relation to human occupational exposures. The ultimate test subject is man.

In reviewing published reports on phenylmercurials one is at once impressed by the apparent lack of unanimity as to the relative toxicity of the several compounds. On one hand there is the work of Fitzhugh and his group [15] in which renal lesions are said to have occurred in female rats which had received 0.5 ppm of PMA in their diet. On the other hand there is the report of Massmann [41] on 26 humans who had been exposed up to six years to atmospheric concentrations of phenylmercuric pyrocatechin between 0.24 and 3.20 mg/cu m with no clinical evidence of injury. Human experience with PMA does not appear to confirm the high toxicity for rats reported by Fitzhugh. Donald Hunter in his textbook *Diseases of Occupation* states that he had not heard of any cases of human poisoning due to phenylmercurials.[44]

The apparent discrepancies may not be so puzzling if one recognizes the many variables involved. These include (*a*) differences in species of the test animals, including humans; (*b*) differences in routes of administration or absorption; (*c*) differences in dosage; and (*d*) differences in the type of phenylmercurial tested. It is reasonable to assume that this group of compounds is similar to other chemicals in that different responses may be expected depending upon how the variables are manipulated.

One general conclusion cannot be disputed, namely, that present knowledge on the toxicity of phenylmercurials is very meager. This being so, there is a place for any new data, even though incomplete, pending the time when more comprehensive studies can be made.

The findings in the present series of studies justify only the most limited conclusions. About all that can be said is that under the conditions existing at the plants which were studied no evidence was found that PMA, PMB, and PMO have a high degree of toxicity for man. The fact that measurements of atmospheric mercury in plant Y, where PMB was involved, showed that most or all of the mercury in the air was in the form of mercury vapor suggests that the toxicity of PMB is actually that of the mercury vapor that is liberated. This hypothesis is supported by the studies of Berlin [22] which show that when PMA is given intravenously to mice, the phenylmercuric radical breaks down to inorganic mercury.

Summary

A review of the literature on phenylmercurials reveals a great lack of unanimity as to the relative toxicity of various compounds in this group.

Dermatitis due to phenylmercurials has been described frequently but no case of occupational systemic poisoning in a human has been reported.

Studies involving phenylmercuric acetate, phenylmercuric benzoate, and phenylmercuric oleate do not point to a high degree of toxicity of these compounds for humans.

Additional observations on human exposures are needed before definite conclusions can be drawn.

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Addendum

Shortly after the date when this paper was submitted for publication, Hirschman, Fein-

gold, and Boylen reported a case of acrodynia in a 5-year-old child who was found to be excreting abnormal amounts of mercury in his urine and who presumably had been exposed to phenylmercuric propionate in a house paint (Hirschman, S. Z.; Feingold, M.; and Boylen, G.: Mercury in House Paint as a Cause of Acrodynia: Effect of Therapy With n-Acetyl-d,l-Penicillamine, *New Eng J Med* 269:889 [Oct 24] 1963).

The authors state that "Both ingestion of the paint and inhalation of its vapor could have resulted in mercury toxicity." The fact that a 3-year-old brother and both parents, who slept in the same room as the patient, showed no mercury in the urine and no signs of mercury intoxication suggests that a route of absorption other than inhalation of vapor was involved. In the report it is stated that "the patient had helped his mother paint part of the kitchen and bedroom four months before the onset of symptoms. There was no definite history of ingestion of paint although this remains a possibility." No mention is made as to whether or not remnants of the paint were accessible to the child.

REFERENCES

1. Goldwater, L. J.; Jacobs, M. B.; and Ladd, A. C.: Absorption and Excretion of Mercury in Man: IV. Tolerance to Mercury, Arch Environ Health 7:568, 1963.
2. Goldwater, L. J.; Jacobs, M. B.; and Ladd, A. C.: Absorption and Excretion of Mercury in Man: I. Relationship of Mercury in Blood and Urine, Arch Environ Health 5:537, 1962.
3. Ladd, A. C.; Goldwater, L. J.; and Jacobs, M. B.: Absorption and Excretion of Mercury in Man: II. Urinary Mercury in Relation to Duration of Exposure, Arch Environ Health 6:480, 1963.
4. Jacobs, M. B.; Ladd, A. C.; and Goldwater, L. J.: Absorption and Excretion of Mercury in Man: III. Blood Mercury in Relation to Duration of Exposure, Arch Environ Health 6:634, 1963.
5. Weed, L. A., and Ecker, E. E.: The Utility of Phenyl-Mercury-Nitrate as a Disinfectant, J Infect Dis 49:440, 1931.
6. Eastman, N. J., and Scott, A. B.: Phenylmercuric Acetate as a Contraceptive, Hum Fertil 9:33, 1944.
7. Cohen, M. M.: An Avocational Dermatitis, Maryland Med J 7:236, 1958.
8. Goldblatt, M. W.: Vesication and Some Vesicants, Brit J Industr Med 2:183, 1945.
9. Cotter, L. H.: Hazard of Phenylmercuric Salts, Occup Med 4:305, 1947.
10. Swensson, A.: Investigations on the Toxicity of Some Organic Mercury Compounds Which are Used as Seed Disinfectants, Acta Med Scand 143: 365, 1952.
11. Sunderman, F. W.; Hawthorne, M. F.; and Baker, G. L.: Delayed Sensitivity of the Skin to Phenylmercuric Acetate, AMA Arch Industr Health 13:574, 1956.
12. Morris, G. E.: Dermatoses From Phenylmercuric Salts, AMA Arch Environ Health 1:53, 1960.
13. Laug, E. P., and Kunze, F. M.: The Absorption of Phenylmercuric Acetate From the Vaginal Tract of the Rat, J Pharmacol Exp Ther 95:460, 1949.
14. Prickett, C. A.; Laug, E. P.; and Kunze, F. M.: Distribution of Mercury in Rats Following Oral and Intravenous Administration of Mercuric Acetate and Phenylmercuric Acetate, Proc Soc Exp Biol Med 73:585, 1950.
15. Fitzhugh, O. G.; Nelson, A. A.; Laug, E. P.; and Kunze, F. M.: Chronic Oral Toxicities of Mercuri-Phenyl and Mercuric Salts, Arch Industr Hyg Occup Med 2:433, 1950.
16. Dinman, B. D.; Evans, E. E.; and Linch, A. L.: Organic Mercury: Environmental Exposure, Excretion, and Prevention of Intoxication in Its Manufacture, AMA Arch Industr Health 18:248, 1958.
17. Murakami, U.; Kameyama, Y.; and Kato, T.: Effects of a Vaginally Applied Contraceptive with Phenylmercuric Acetate Upon Developing Embryos and Their Mother Animals, Annual Report of the Research Institute of Environmental Medicine, Nagoya University, Japan, 1955, p 88.
18. Friberg, L.; Odeblad, E.; and Forssman, S.: Distribution of Two Mercury Compounds in Rabbits After a Single Subcutaneous Injection, AMA Arch Industr Health 16:163, 1957.
19. Bergstrand, A.; Friberg, L.; and Odeblad, E.: Localization of Mercury in the Kidneys After Subcutaneous Administration, AMA Arch Industr Health 17:253, 1958.
20. Swensson, A.; Lundgren, K. D.; and Lindstrom, O.: Distribution and Excretion of Mercury Compounds After Single Injection, AMA Arch Industr Health 20:432, 1959.
21. Swensson, A.; Lundgren, K. D.; and Lindstrom, O.: Retention of Various Mercury Compounds After Subcutaneous Administration, AMA Arch Industr Health 20:467, 1959.
22. Berlin, M., and Ullberg, S.: Accumulation and Retention of Mercury in the Mouse: II. An Autoradiographic Comparison of Phenylmercuric Acetate With Inorganic Mercury, Arch Environ Health 6: 602, 1963.
23. Berlin, M.: Renal Uptake, Excretion, and Retention of Mercury: II. A Study in the Rabbit

During Infusion of Methyl- and Phenylmercuric Compounds, Arch Environ Health 6:626, 1963.

24. Kita, T., et al.: Absorption of Drugs: II. Distribution of Hg^{203} Labelled Organic Compounds in Some Organs, Yakugaku Kenkyu 32:662, 1960.

25. Gage, J. C., and Swan, W.: Toxicity of Alkyl and Aryl Mercury Salts, Biochem Pharmacol 8:77, 1961.

26. Gemmill, C. L., and Bowman, E. M.: Effects of Mercurial Compounds on Invertase, J Pharmacol Exp Ther 100:244, 1950.

27. Linfield, W. M.; Sherrill, J. C.; Casely, R. E.; Noel, D. R.; and Davis, G. A.: Studies in the Development of Antibacterial Surfactants: I Institutional Use of Antibacterial Fabric Softeners, J Amer Oil Chem Soc 37:248, 1960.

28. Goldwater, L. J., and Jacobs, M. B.: Unpublished data, 1961.

29. Levine, B.: Use of Phenylmercuric Nitrate in Tinea and Yeast Infections of the Skin, JAMA 101: 2109, 1933.

30. Birkhaug, K. E.: Phenyl-Mercuric-Nitrate, J Infect Dis 53:250, 1933.

31. Kneucker, R.: Erfahrungen mit Merfenhalspastillen, Munchen Med Wschr 99:1181, 1957.

31A. Biskind, L. H.: Phenyl Mercury Nitrate: Its Clinical Uses in Gynecology, Surg Gynec Obstet 57: 261, 1933.

32. AMA Council Report: Phenylmercuric Nitrate and Phenylmercuric Chloride, JAMA 102: 1224, 1934.

33. Lundgren, K. D., and Swensson, A.: A Survey of Results of Investigations on Some Organic Mercury Compounds Used as Fungicides, Amer Industr Hyg Ass J 21:308, 1960.

34. Lundgren, K. D., and Swensson, A.: Phenylmercuric Compounds as Problem of Industrial Hygiene, Nord Hyg T p 207, 1950.

35. Cook, E. S., and Perisutti, G.: The Action of Phenylmercuric Nitrate, J Biol Chem 167:827, 1947.

36. Hellerman, L.; Chinard, F. P.; and Deitz, V. R.: Protein Sulfhydryl Groups and the Reversible Inactivation of the Enzyme Urease, J Biol Chem 147:443, 1943.

37. McCord, C. P.; Meek, S. F.; and Neal, T. A.: Phenyl Mercuric Oleate, Skin Irritant Properties, J Industr Hyg Toxic 23:466, 1941.

38. Goldberg, A. A.; Shapero, M.; and Wilder, E.: Penetration of Phenylmercuric Dinaphthyl Methane Disulfonate Into Skin and Muscle Tissue, J Pharm Pharmacol 2:89, 1950.

39. Hagen, U.: Toxikologie organischer Quecksilberverbindungen, Arch Exp Path Pharmakol 224: 193, 1955.

40. Goldberg, A. A., and Shapero, M.: Toxicological Hazards of Mercurial Paints, J Pharm Pharmacol 9:469, 1957.

41. Massmann, W.: Beobachtungen beim Umgang mit Phenylquecksilberbrenzkatechin, Zbl Arbeitsmed 7:9, 1957.

42. Jacobs, M. B.; Goldwater, L. J.; and Gilbert, H.: Ultramicrodetermination of Mercury in Blood, Amer Industr Hyg Ass J 22:276, 1961.

43. Confidential report.

44. Hunter, D.: Diseases of Occupations, London: English Universities Press, 1955, p 280.

Acute mercury poisonings have declined along with the decline of California's mining industry, but cases still do occur where mercury is being recovered by ore reduction. Actual exposures to mercury have increased over the past ten years, especially with the growth of research and technological facilities. Today, there is hardly a home or public building without some small quantity of mercury to be found in switches, thermostats, etc. Even children's games and toys have recently unwisely appeared, utilizing this metal. Thus, the population at risk has increased a hundredfold and the need for caution in preventing the access of poisonous mercury vapor into room air has reached the level of the public in general, as well as those industries specifically working directly with the metal.—Technical Information Service, California State Department of Public Health, Mercury Poisoning, *Occup Health,* 1963.