

From the Institute of Pharmacology (Head: Professor Ib Holm-Jensen, M.D.),  
University of Aarhus, Aarhus, Denmark.

## Absorption of Mercury Vapour from the Respiratory Tract in Man

By

F. Nielsen Kudsk

(Received June 2, 1965)

It is well-known that inhalation of air contaminated with mercury vapour may lead to poisoning from the absorption of toxic amounts of mercury from the respiratory tract.

Extensive studies within the field of industrial hygiene, first performed by NEAL *et al.* (1937 & 1941), have revealed a valid correlation between the mercury concentration in the atmosphere and the incidence of chronic mercury poisoning. On the basis of these studies, industrial hygienists in the U.S.A. have fixed a toxic threshold limit value for mercury vapour and inorganic mercury compounds in the atmosphere at  $100 \mu\text{g}/\text{m}^3$  under conditions involving constant daily exposure within normal working hours. This threshold value is still maintained by the American Conference of Governmental Industrial Hygienists (ACGIH 1964). British investigators have advised a threshold limit value of  $75 \mu\text{g}/\text{m}^3$  (BUCKELL *et al.* 1946; BROOKS & HOLMES 1958). In Soviet Russia, the toxic threshold limit value for metallic mercury has been set at  $10 \mu\text{g}/\text{m}^3$  and for mercuric chloride at  $100 \mu\text{g}/\text{m}^3$  (ELKINS 1961).

Some diversity of opinion thus exists as to the maximum allowable concentration of mercury and its inorganic compounds in the atmosphere: until our knowledge of the toxicity to man of low concentrations of mercury in the air has been extended, the fixation of a toxic threshold value must therefore to some extent be left to individual judgement. Among the difficulties encountered in fixing unequivocally the lowest level of toxic concentrations in the air is the fact that the mildest symptoms of mercury poisoning, which are of a psychopathological character, may also occur in persons who have not been exposed to

## MERCURY ABSORPTION FI

mercury. Thus, TURRIAN *et al.* (1956) found a correlation between the average mercury concentration in the incidence of certain psychopathological symptoms of poisoning present in 15 out of 58 subjects with mercury concentrations of  $10-600 \mu\text{g}/\text{m}^3$ . This was also abnormally high among subjects with mercury concentrations below  $100 \mu\text{g}/\text{m}^3$ , but did not present the fully developed picture of chronic poisoning.

In animal experiments (rats), FRIBERG (1960) observed that inorganic mercury was absorbed in considerable quantities in the brain more firmly than in any other organ of the body. This was performed by BERLIN & ULLBERG (1964) who used  $^{203}\text{HgCl}_2$  resulted in considerable accumulation in the matter of the *cerebellum*, and in the *callosa*. BERLIN & JOHANSSON (1964) demonstrated that rats that had inhaled air contaminated with mercury for 4 hours contained 10 times as much mercury in the brain as given a similar intravenous dose of  $^{203}\text{Hg}$ . The rate of absorption was not stated. Thus, absorption of mercury from the respiratory tract is more than absorption by other route to the brain. This may perhaps also offer a correlation between the demonstrated between the concentration of mercury in the air and the incidence of psychopathological symptoms including tremor.

### Absorption of inhaled mercury.

Detailed knowledge of the extent to which mercury is absorbed in the respiratory tract will clearly be of great importance to fix more precisely the maximum daily intake of mercury under constant exposure to mercury vapour.

It seems that the extent of absorption of mercury in the respiratory tract in animals and man has not been determined. On the basis of a comparison of the mercury excreted in the urine and the concentration in the blood (1909) reported that the uptake of mercury was about 10% when the concentration was less than  $100 \mu\text{g}/\text{m}^3$ . (1948) contested GÖTHLIN's method of determining the uptake, that his determinations of the mercury in the blood possibly had an appreciable negative error. The method is incomplete. In a small number of experiments

001411



ad: Professor Ib Holm-Jensen, M.D.),  
Aarhus, Denmark.

## Mercury Vapour from the Respiratory Tract in Man

n Kudsk

ne 2, 1965)

of air contaminated with mercury  
the absorption of toxic amounts of

of industrial hygiene, first performed  
revealed a valid correlation between the  
sphere and the incidence of chronic  
these studies, industrial hygienists in  
old limit value for mercury vapour  
in the atmosphere at  $100 \mu\text{g}/\text{m}^3$  under  
exposure within normal working  
conditions maintained by the American Conference  
on Governmental Hygiene (ACGIH 1964). British investigators  
found a limit value of  $75 \mu\text{g}/\text{m}^3$  (BUCKELL *et al.* 1946;  
in Russia, the toxic threshold limit value  
is  $10 \mu\text{g}/\text{m}^3$  and for mercuric chloride

exists as to the maximum allowable  
concentrations of organic compounds in the atmosphere;  
exposure to man of low concentrations of  
mercury, the fixation of a toxic threshold  
must not be left to individual judgement.  
In fixing unequivocally the lowest  
permissible concentration in the air is the fact that the mildest  
symptoms which are of a psychopathological  
nature occur in persons who have not been exposed to

mercury. Thus, TURRIAN *et al.* (1956) demonstrated a causal relationship  
between the average mercury concentration in the atmosphere and the  
incidence of certain psychopathological and neurological symptoms of  
poisoning present in 15 out of 58 workers who had been exposed to  
mercury concentrations of  $10\text{--}600 \mu\text{g}/\text{m}^3$ . The frequency of symptoms  
was also abnormally high among workers who had been exposed to  
concentrations below  $100 \mu\text{g}/\text{m}^3$ , but none of the affected workers exhib-  
ited the fully developed picture of chronic mercury poisoning.

In animal experiments (rats), FRIBERG (1959) and ROTHSTEIN & HAYES  
(1960) observed that inorganic mercury administered parenterally accumu-  
lated in considerable quantities in the brain and was bound there more  
firmly than in any other organ of the body. In experiments on mice  
performed by BERLIN & ULLBERG (1963), a single intravenous dose of  
 $^{203}\text{HgCl}_2$  resulted in considerable accumulation, especially in the grey  
matter of the *cerebellum*, and in the *tuber cinereum* and *corpus subforn-  
icatus*. BERLIN & JOHANSSON (1964) demonstrated that the brains of mice  
that had inhaled air contaminated with mercury vapour ( $10 \text{ mg Hg}/\text{m}^3$   
for 4 hours) contained 10 times as much mercury as the brains of mice  
given a similar intravenous dose of  $\text{Hg}(\text{NO}_3)_2$ . The rate of injection was  
not stated. Thus, absorption of mercury from the respiratory tract seems  
more than absorption by other routes to lead to its accumulation in the  
brain. This may perhaps also offer an explanation of the correlation  
demonstrated between the concentration of mercury in the atmosphere  
and the incidence of psychopathological and neurological manifestations,  
including tremor.

### Absorption of inhaled mercury.

Detailed knowledge of the extent to which mercury is absorbed from  
the respiratory tract will clearly be of great importance in an attempt to  
fix more precisely the maximum daily dose that can be tolerated during  
constant exposure to mercury vapour in the inspired air.

It seems that the extent of absorption of mercury vapour from the  
respiratory tract in animals and man has not previously been clearly  
determined. On the basis of a comparison of the amounts of mercury  
excreted in the urine and the concentrations in the inspired air, GÖTHLIN  
(1909) reported that the uptake of mercury by man was almost complete  
when the concentration was less than  $250 \mu\text{g}/\text{m}^3$ . However, HOLM-JENSEN  
(1948) contested GÖTHLIN's method of analysis and expressed the view  
that his determinations of the mercury concentrations of the inspired air  
possibly had an appreciable negative error and that absorption was in fact  
incomplete. In a small number of experiments performed on three volun-

001412



teers, GERSTNER (1931) found an absorption of 34–77% on inhalation of air containing from 10 to 100  $\mu\text{g}/\text{m}^3$ . In dogs breathing air containing from 3 to 26 mg mercury per  $\text{m}^3$ , FRASER *et al.* (1934) found a fairly constant absorption from the respiratory tract, averaging 25%. BATTIGELLI (1960) expressed the opinion that this also applies to human beings. By means of the mercury-vapour detector described by WOODSON (1939), SHEPHERD *et al.* (1941) performed a few experiments in which they found that the air expired by persons who breathed air with a mercury content of 60  $\mu\text{g}/\text{m}^3$  did not contain mercury. On the other hand, when the mercury concentration of the atmosphere was increased to 200  $\mu\text{g}/\text{m}^3$ , the expired air contained about 10  $\mu\text{g}/\text{m}^3$ . In rats exposed to an atmosphere containing 1 mg mercury per  $\text{m}^3$ , GAGE (1961) found an absorption from the lungs of about 50%. HAYES & ROTHSTEIN (1962) exposed rats to an atmosphere with a mercury content of 1.4 mg/ $\text{m}^3$  for from 30 minutes to 5 hours.  $^{203}\text{Hg}$  was added as a tracer. By calculating the amounts of inhaled mercury from the minute volume of breathing (fixed in relation to the weight of the animals) and determinations of the total amounts of mercury found in the animals, the authors concluded that the absorption from the respiratory tract was complete.

### Material and Methods

#### Personal investigations.

In order to throw light on the extent to which mercury vapour is absorbed from the respiratory tract in man, I have studied in four volunteers (including myself) the ratio of the average mercury concentration in the expired air to that of the inspired air. This ratio was determined at different constant concentrations of mercury in the inspired air and for roughly constant minute volumes. The influence, if any, of the respiratory rate on the absorption was also studied. An attempt was made to gain some impression of the variations in mercury concentration in the expired air during the individual expirations.

The mercury concentrations in the inspired air were determined both by ultraviolet photometry in a slightly modified form of the mercury-vapour detector designed by RUSSELL (cited by BROOKS & HOLMES 1958) and manufactured by "Hanovia", and by the chemical method previously described (NIELSEN KUDSK 1964) as a control. Only the latter method was used for determining the average concentration of mercury in the expired air.

In a series of previous experiments in which direct determinations of the mercury concentration in expired air were performed by means of the mercury-vapour detector, I had observed that the results were affected by the amount of water vapour of the expired air; further studies showed that under such conditions the results read on the detector were too low. This observation probable explains why SHEPHERD *et al.* (1941) found only 5% or none at all of the inhaled mercury in the expired air, as they used a detector of a similar construction. After some experimentation, I succeeded in reducing the water-vapour content of the expired air by condensation to such an extent that the negative recording of the residual water vapour by the detector became negligible and constant, without any concurrent loss of mercury in the condenser system.

The continuous direct recording of the mercury concentration in the expired air by

means of the mercury-vapour detector and rendered possible by this method was used in the determination of the expired amounts of mercury for the curves obtained show only to a limited extent of the expired air, partly because of the relatively large dead space of the condenser recorded by the detector at flow rates below 1 l/min. Likewise, it is only possible to determine the expired air with a limited accuracy on the basis of a clear from such a graph of the mercury concentration during abnormally slow and maximal expiration. Under these circumstances the last portion of the expir

#### Experimental set-up.

The experiments were performed in a room of 100 m<sup>3</sup> volume. The mercury vapour was conveyed into the room at a constant rate, which was adjusted to the concentration desired during the experiments. I had ascertained that the volume of air cleared of mercury every minute fairly close to the room (in m<sup>3</sup>/min.), i. e. chemical conversion did not occur. The rate at which mercury vapour was maintained a steady-state concentration is thus determined by the ventilation rate, provided the ventilation period. The air in the room was agitated by the distribution of the mercury vapour. In order to obtain within a reasonable time, the mercury vapour rate. When the desired concentration was obtained, the rate. When the constancy of the mercury concentration was maintained, the mercury-vapour detector for a suitable period, the room was  $23 \pm 1^\circ\text{C}$ .

The experimental set-up employed for the determination of the mercury concentration in the expired air is shown in semi-diagrammatic form in Figure 1. The expired air is drawn through two condensers connected in series. The air then emerges in a constant-temperature water bath, where it is re-circulated by means of a pump through the condenser placed outside the water bath. Before the collection of condensed water. From the condenser, the air is conducted into the mercury-vapour detector, where it is recorded by the recorder. A stopcock is inserted into the system for temporary closure that is not at once passed on by the air pump. The air is supplied with a valve for the supply of dry mercury-free air transported by the pump for a short period, which is operated from an a.c. stabiliser, sensibly described (NIELSEN KUDSK 1964) at a pressure of the atmosphere and at a constant rate of 7 l/min by a flow-meter manufactured by Fischer & Porter.

As already mentioned, the "Hanovia" mer



absorption of 34–77% on inhalation of . In dogs breathing air containing ER *et al.* (1934) found a fairly respiratory tract, averaging 25%. BATTI- at this also applies to human beings. ctor described by WOODSON (1939), w experiments in which they found reathed air with a mercury content . On the other hand, when the mer- e was increased to 200  $\mu\text{g}/\text{m}^3$ , the . In rats exposed to an atmosphere GE (1961) found an absorption from OTHSTEIN (1962) exposed rats to an of 1.4  $\text{mg}/\text{m}^3$  for from 30 minutes cer. By calculating the amounts of lume of breathing (fixed in relation terminations of the total amounts of thors concluded that the absorption etc.

## Methods

which mercury vapour is absorbed from the ur volunteers (including myself) the ratio of red air to that of the inspired air. This ratio ations of mercury in the inspired air and for any, of the respiratory rate on the ab- de to gain some impression of the variations uring the individual expirations. ed air were determined both by ultraviolet the mercury-vapour detector designed by nd manufactured by "Hanovia", and by the EN KUDSK 1964) as a control. Only the latter concentration of mercury in the expired air. hich direct determinations of the mercury by means of the mercury-vapour detector, l the amount of water vapour of the expired nditions the results read on the detector were why SHEPHERD *et al.* (1941) found only 5% pired air, as they used a detector of a similar l succeeded in reducing the water-vapour such an extent that the negative recording of became negligible and constant, without any ystem. mercury concentration in the expired air by

means of the mercury-vapour detector and a connected potentiometer recorder that was rendered possible by this method was used in all the experiments, with simultaneous collec- tion of the expired amounts of mercury for subsequent chemical determination. However, the curves obtained show only to a limited extent the fluctuations in the mercury concentra- tion of the expired air, partly because an appreciable mixture of the expired air occurs in the relatively large dead space of the condenser system, and partly because the results recorded by the detector at flow rates below about 2 litres per minute are a little too low. Likewise, it is only possible to determine the average concentration of mercury in the expired air with a limited accuracy on the basis of these curves. Nevertheless, it appears clear from such a graph of the mercury concentration in the expired air directly recorded during abnormally slow and maximal expirations (preceded by deep inspirations) that in these circumstances the last portion of the expired air is virtually free from mercury vapour.

## Experimental set-up.

The experiments were performed in a room with a net volume of 40  $\text{m}^3$ . From an ad- joining room, mercury vapour was conveyed through a plastic tube into the experimental room at a constant rate, which was adjusted on the basis of the ventilation of the room and the concentration desired during the experiment concerned. In some so far unpublished experiments, I had ascertained that the volume of air in the experimental room which is cleared of mercury every minute fairly closely corresponds to the ventilation rate of the room (in  $\text{m}^3/\text{min.}$ ), i. e. chemical conversion or appreciable adsorption of mercury does not occur. The rate at which mercury vapour is to be conveyed into the room in order to maintain a steady-state concentration is thus equal to the product of that concentration and the ventilation rate, provided the ventilation is constant during the experimental period. The air in the room was agitated by two electric fans in order to ensure an even distribution of the mercury vapour. In order to obtain the desired steady-state concentra- tion within a reasonable time, the mercury vapour was at first led into the room at a high rate. When the desired concentration was obtained, the supply was adjusted to the calcu- lated rate. When the constancy of the mercury concentration had been checked by the mercury-vapour detector for a suitable period, the tests were begun. The temperature of the room was 23  $^{\circ}\text{C}$ .

The experimental set-up employed for the determination of the mercury concentration in the expired air is shown in semi-diagrammatic form in fig. 1. The expired air is conducted through two condensers connected in series. The second condenser (a Friedrichs type) is emerged in a constant-temperature water bath adjusted to 11  $^{\circ}\text{C}$ . The water from the bath is re-circulated by means of a pump through the Friedrichs condenser and a double-surface condenser placed outside the water bath. Both condensers are provided with a reservoir for the collection of condensed water. From the condenser system the expired air is con- ducted into the mercury-vapour detector, which by means of a connected potentiometer recorder records the mercury concentration. After the detector, a breathing bag of astatic rubber is inserted into the system for temporary collection of the part of the expired air that is not at once passed on by the air pump. In the same place, the system is provided with a valve for the supply of dry mercury-free air. This valve is actuated when the volume of air transported by the pump for a short period exceeds that of the expired air. The pump, which is operated from an a.c. stabiliser, sends the air through a mercury absorber previ- ously described (NIELSEN KUDSK 1964) at a pressure of about 100 mm mercury above that of the atmosphere and at a constant rate of 7 litres per minute. The flow rate is measured by a flow-meter manufactured by Fischer & Porter.

As already mentioned, the "Hanovia" mercury-vapour detector was used in a slightly



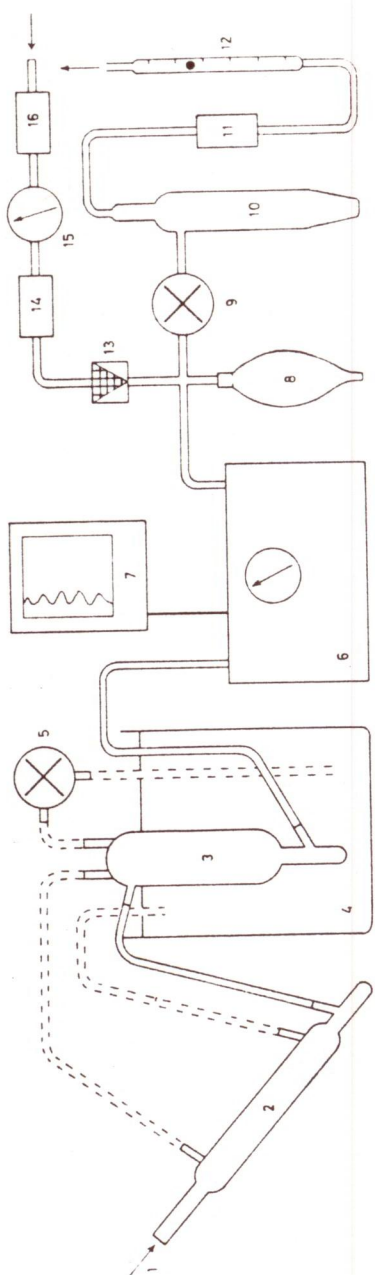


Fig. 1. Diagram showing the experimental set-up for the determination of mercury in expired air. 1, inlet for expired air; 2, double-surface condenser (Quickfit, Type C 5/23); 3, Friedrichs condenser (JP "Pyrex", Type 1810); 4, constant-temperature water bath at 11 °C; 5, water pump; 6, mercury-vapour detector ("Hanovia", Type E3472); 7, potentiometer recorder ("Varian", Type G-11A); 8, breathing bag, 2.5 litres (astatic rubber); 9, air pump ("Reciprotor", Type 406 G); 10, mercury absorber; 11, air vessel; 12, flow-meter; 13, respiratory valve; 14, air-drying filter (silica gel); 15, "wet" gas meter; 16, mercury-absorbing iodised charcoal filter.

## MERCURY ABSORPTION I

modified form. The modifications made to the circuit for the zero adjustment, (2) power supply to the built-in air pump, and (4) careful tightening of the absorber by the use of a screwdriver. By these modifications and re-calibration by the use of mercury vapour, it was possible to obtain a sensitivity of  $\pm 1.5 \mu\text{g}/\text{m}^3$  when the most sensitive mercury pump used was completely tight, and the possible demonstrable loss of mercury; nor did any

### Experimental procedure.

Immediately before each experiment, the sensitivity of the circuit was determined by means of the detector apparatus described, with the absorber cut out. The air-flow rate was set at 7 litres per minute.

Then the entire apparatus was "washed" with mercury-free air. The volunteer under test now expired the air contained in the expired air wash period of 5 minutes. Mercury-free air, which was used in the experiments, was measured by means of the detector apparatus. After the experiment, the apparatus was again washed with mercury-free air before the experiment. In all the experiments the subject inhaled through the nose and expired it through the mouth and the apparatus. During expiration, the volunteer

The mercury concentration in the expired air was determined during the experimental period by means of the detector (fig. 1). On the basis of the fluctuation graph, the number of expirations during the experimental period, already mentioned, the curves obtained did not differ from the average concentration of mercury in the expired air calculated on the basis of the amount of mercury absorbed and the volume of expired air measured at the end of the experimental period.

The mercury concentration in the air expired at frequent intervals, both before and after the experiment, was determined (NIELSEN KUDSK 1964): this was in agreement with those obtained by the detector apparatus during the experiments with mercury (dithizone determinations).

## Re

The results of the experiments with expired air were determined with a sensitivity of  $\pm 10\%$ . The average tidal volumes (ATPS) were  $\pm 10\%$ . The error of the calculated values in the table as percentages of the inspired air were  $\pm 15\%$  at the lowest concentrations in the expired air and  $\pm 15\%$  at higher concentrations.

001415



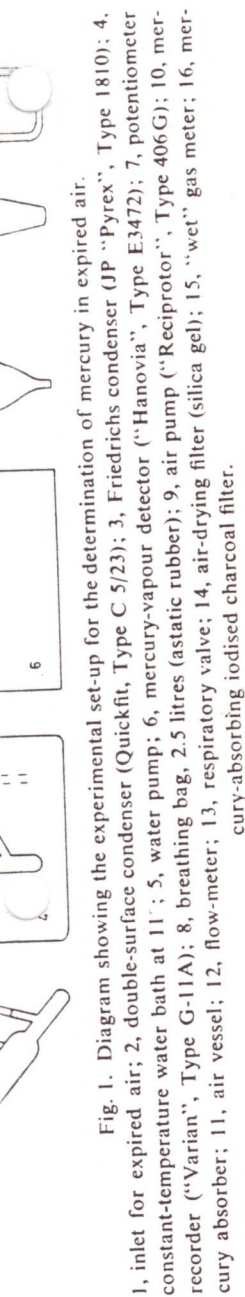


Fig. 1. Diagram showing the experimental set-up for the determination of mercury in expired air.

1, inlet for expired air; 2, double-surface condenser (Quickfit, Type C 5/23); 3, Friedrichs condenser (JP "Pyrex", Type 1810); 4, constant-temperature water bath at 11°; 5, water pump; 6, mercury-vapour detector ("Hanovia", Type E3472); 7, potentiometer recorder ("Varian", Type G-11A); 8, breathing bag, 2.5 litres (astatic rubber); 9, air pump ("Reciprotor", Type 406 G); 10, mercury absorber; 11, air vessel; 12, flow-meter; 13, respiratory valve; 14, air-drying filter (silica gel); 15, "wet" gas meter; 16, mercury-absorbing iodised charcoal filter.

modified form. The modifications made consisted in (1) a slight change in the electric circuit for the zero adjustment, (2) power supply through an a.c. stabiliser, (3) removal of the built-in air pump, and (4) careful tightening of all the air-duct systems of the instrument. By these modifications and re-calibration by means of air containing known concentrations of mercury vapour, it was possible to obtain a sensitivity of 3 µg and a measuring accuracy of  $\pm 1.5$  µg/m<sup>3</sup> when the most sensitive measuring range was used. The "Reciprotor" air pump used was completely tight, and the passage of air through it did not give rise to any demonstrable loss of mercury; nor did any such loss occur in the breathing bag.

### Experimental procedure.

Immediately before each experiment, the mercury concentration in the air of the room was determined by means of the detector while the air was being passed through the apparatus described, with the absorber cut out. By adjusting the a.c. supply voltage to the pump the air-flow rate was set at 7 litres per minute.

Then the entire apparatus was "washed" with mercury-free air. The absorber was then inserted, and the volunteer under test now expired air through the apparatus. The amount of mercury contained in the expired air was collected in the fluid of the absorber for a period of 5 minutes. Mercury-free air, which was supplied to the system only in a few experiments, was measured by means of the gas meter shown in fig. 1. At the end of the experiment, the apparatus was again washed with mercury-free air, after which the absorber was again cut out, and the mercury concentration in the room air was determined just as before the experiment. In all the experiments, the volunteers inspired the air through the nose and expired it through the mouth and a short length of plastic tubing connected with the apparatus. During expiration, the volunteers closed their nostrils with their fingers.

The mercury concentration in the expired air was also recorded graphically throughout the experimental period by means of the potentiometer recorder connected with the detector (fig. 1). On the basis of the fluctuations in the mercury concentration shown by the graph, the number of expirations during the experimental period could be counted. As already mentioned, the curves obtained did not permit an accurate determination of the average concentration of mercury in the expired air, and this concentration was therefore calculated on the basis of the amount of mercury collected during the experimental period and the volume of expired air measured at the ambient temperature ( $23 \pm 1^\circ\text{C}$ ).

The mercury concentration in the air of the experimental room was determined at frequent intervals, both before and after the experiments, by the chemical method previously described (NIELSEN KUDSK 1964): the results of these determinations were in close agreement with those obtained by the detector. The condensed water collected from the condenser system during the experiments did not contain demonstrable amounts of mercury (dithizone determinations).

### Results

The results of the experiments are shown in table 1. The volumes of expired air were determined with a margin of error of less than  $\pm 5\%$ . The average tidal volumes (ATPS) involve errors that do not exceed  $\pm 10\%$ . The error of the calculated amounts of expired mercury, given in the table as percentages of the inspired amounts, is less than  $\pm 20\%$  at the lowest concentrations in the expired air (about 10 µg/m<sup>3</sup>) and less than  $\pm 15\%$  at higher concentrations.

001416



Table 1.

Results of the experiments showing the percentages of mercury absorbed during inhalation of air containing mercury at various concentrations in relation to the average tidal volumes (ATPS). The table also shows the expired amounts of mercury, as percentages of the amounts inspired. These figures are taken as expressions of the percentage that a notional dead space for mercury absorption represents of the average tidal volume.

Volunteer sex, weight	Hg conc., inspired air, in $\mu\text{g}/\text{m}^3$	Hg conc., expired air, in $\mu\text{g}/\text{m}^3$	Expired Hg, as percentages of inspired Hg	Absorbed Hg, as percentages of inspired Hg	No. of expirations in 5 min.	Average tidal volume, in litres (ATPS)
F.N.K., M, 92 kg	49.3	10.1	20.4	79.6	24	1.45
	54.7	10.4	19.0	81.0	23	1.52
	47.5	10.7	22.5	77.5	22	1.59
	99.0	18.0	18.1	81.9	24	1.45
	109	15.0	13.8	86.2	19	1.84
	102	15.8	15.5	84.5	25	1.40
	193	28.8	15.0	85.0	20	1.75
	205	39.0	18.9	81.1	28	1.25
	210	37.6	17.8	82.2	26	1.35
	345	50.2	14.5	85.5	23	1.52
	330	60.9	18.4	81.6	25	1.40
	340	58.8	17.2	82.8	22	1.59
	52.0	8.6	16.5	83.5	25	1.40
	52.0	9.7	18.5	81.5	31	1.13
	50.2	11.5	22.9	77.1	25	1.40
B.P., M, 63 kg	98.0	14.3	14.5	85.5	24	1.46
	98.0	17.6	17.8	82.2	31	1.13
	104	18.0	17.3	82.7	20	1.75
	201	24.4	12.2	87.8	22	1.59
	193	30.1	15.6	84.4	26	1.35
	207	33.3	16.0	84.0	31	1.13
	370	49.3	13.3	86.7	21	1.67
	345	53.8	15.6	84.4	22	1.59
	340	52.4	15.5	84.5	25	1.40
	55.6	14.3	25.7	74.3	60	0.58
	52.0	16.8	32.2	67.8	58	0.60
	50.2	16.4	32.6	67.4	61	0.57

## MERCURY ABSORPTION

Volunteer sex, weight	Hg conc., inspired air, in $\mu\text{g}/\text{m}^3$	Hg conc., expired air, in $\mu\text{g}/\text{m}^3$	Expired perce inspi
G.L.M., F, 54 kg	96.0	22.2	2
	106	21.8	20
	102	25.8	2
	204	48.7	2
	201	49.5	20
	193	47.2	20
	377	106.9	20
	350	83.2	20
	348	83.5	20
O.C., M, 73 kg	52.0	14.0	20
	53.8	15.2	20
	50.2	14.0	20
	98.0	26.8	20
	97.0	23.4	20
	108	26.8	20
	198	42.2	20
	198	49.6	20
	196	48.7	20
	371	79.5	20
	350	80.9	20
	340	89.4	20

A study of the results obtained shows that the absorption of mercury occurred in the individual volumes with small variations. The ratio of the expired to the inspired mercury seems to be largely independent of the concentration in the inspired air, although absorption is higher at a wider margin of error of the determination. The results in the respiratory tract thus seem to be independent of the absorption of mercury. Incidentally, the results show that air with a varying content of mercury is absorbed in through the nostrils of a volunteer. During this passage, the loss of mer

001417



mercury absorbed during inhalation  
relation to the average tidal volumes  
amounts of mercury, as percentages of the  
expirations of the percentage that a notional  
amounts of the average tidal volume.

Absorbed Hg, as percentages of inspired Hg	No. of expirations in 5 min.	Average tidal volume, in litres (ATPS)
79.6	24	1.45
81.0	23	1.52
77.5	22	1.59
81.9	24	1.45
86.2	19	1.84
84.5	25	1.40
85.0	20	1.75
81.1	28	1.25
82.2	26	1.35
85.5	23	1.52
81.6	25	1.40
82.8	22	1.59
83.5	25	1.40
81.5	31	1.13
77.1	25	1.40
85.5	24	1.46
82.2	31	1.13
82.7	20	1.75
87.8	22	1.59
84.4	26	1.35
84.0	31	1.13
86.7	21	1.67
84.4	22	1.59
84.5	25	1.40
74.3	60	0.58
67.8	58	0.60
67.4	61	0.57

Volunteer sex, weight	Hg conc., inspired air, in $\mu\text{g}/\text{m}^3$	Hg conc., expired air, in $\mu\text{g}/\text{m}^3$	Expired Hg, as percentages of inspired Hg	Absorbed Hg, as percentages of inspired Hg	No. of expirations in 5 min.	Average tidal volume, in litres (ATPS)
G.L.M., F, 54 kg	96.0	22.2	23.1	76.9	58	0.60
	106	21.8	20.5	79.5	66	0.53
	102	25.8	25.3	74.7	65	0.54
	204	48.7	23.8	76.2	63	0.56
	201	49.5	24.6	75.4	61	0.57
	193	47.2	24.5	75.5	62	0.57
	377	106.9	28.2	71.8	62	0.57
	350	83.2	23.7	76.3	54	0.65
	348	83.5	23.9	76.1	59	0.59
O.C., M, 73 kg	52.0	14.0	26.9	73.1	58	0.60
	53.8	15.2	28.2	71.8	61	0.57
	50.2	14.0	28.3	71.7	52	0.67
	98.0	26.8	27.2	72.8	57	0.61
	97.0	23.4	24.0	76.0	56	0.62
	108	26.8	24.8	75.2	53	0.66
	198	42.2	21.3	78.7	53	0.66
	198	49.6	25.0	75.0	54	0.65
	196	48.7	24.7	75.3	54	0.65
	371	79.5	21.5	78.5	54	0.64
	350	80.9	23.1	76.9	52	0.67
	340	89.4	26.2	73.8	50	0.70

A study of the results obtained shows that the extent to which absorption occurred in the individual volunteers was subject to only relatively small variations. The ratio of the absorbed to the inspired amounts of mercury seems to be largely independent of the mercury concentration in the inspired air, although absorption was a little less at the lowest concentration in the inspired air ( $50 \mu\text{g}/\text{m}^3$ ), even if allowance is made for the wider margin of error of the determinations there. Adsorptive processes in the respiratory tract thus seem to be of only minor importance in the absorption of mercury. Incidentally, I performed a few experiments in which air with a varying content of mercury vapour was allowed to pass in through the nostrils of a volunteer and out through the oral cavity. During this passage, the loss of mercury was about 2% at a concentration

001418



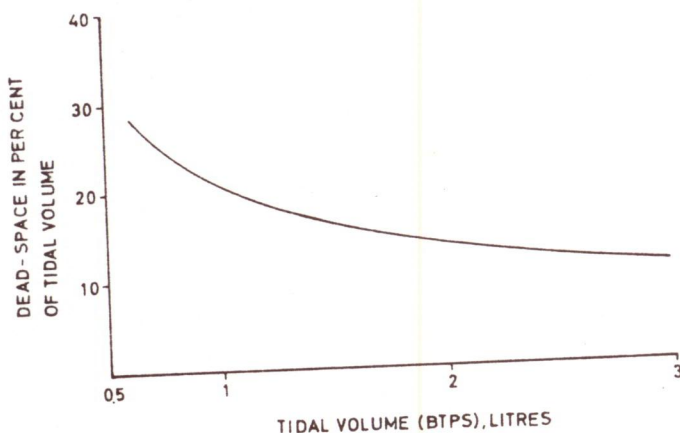


Fig. 2. Graph showing the relationship between the physiological dead space, as a percentage of the tidal volume, and the tidal volume. Based on results of ASMUSSEN & NIELSEN (1956).

of  $350 \mu\text{g}/\text{m}^3$  and less at lower concentrations, as determined by means of the mercury-vapour detector connected with the apparatus described above.

The percentage that the amount of expired mercury constitutes of the amount inspired may be regarded as an expression of the percentage that a notional dead space for mercury absorption represents of the average tidal volume (ATPS) listed in the table. ASMUSSEN & NIELSEN (1956) studied the physiological dead space as a function of the tidal volume (BTPS) in four young men. On the basis of their results, I have constructed the curve shown in fig. 2, indicating the relationship between the physiological dead space, as a percentage of the tidal volume, and the tidal volume. The average tidal volumes (ATPS) listed in table 1 are based on measurements at  $23^\circ$  of the volumes of expired air, saturated with water vapour at that temperature. The corresponding tidal volumes (BTPS) measured and saturated with water vapour at body temperature will thus be about 8.5% larger.

A comparison of the figures in table 1 and the curve in fig. 2 shows that the notional dead space for mercury fairly closely corresponds to the physiological dead space. However, at the lowest concentrations in the inspired air the dead space for mercury was a little higher in several of the experiments.

The results of the experiments thus suggest that the uptake of metallic mercury from the inspired air chiefly occurs from the alveoli of the lungs and that this alveolar absorption is almost complete and independent of variations in the mercury concentration in the inspired air within the

## MERCURY ABSORPTION

range from 100 to  $350 \mu\text{g}/\text{m}^3$ . The concentration of  $50 \mu\text{g}/\text{m}^3$  suggests or probably almost insignificant, in from the respiratory tract in man. with mercury will thus presumably mercury that at a close approxin mercury concentration in the inspi

## Dis

Absorption is most commonly d by which a substance from the site blood. In the experiments reported the uptake of mercury from the HAYES & ROTHSTEIN (1962) found vapour (with added  $^{203}\text{Hg}$ ), tempo in the lungs for a few hours, after wl similar to that observed after int chloride. However, these authors d of the brain; according to the com SON (1964) mentioned above, howe the animal has inhaled mercury v: 10 times as large as that taken up corresponding dose of mercuric ni that metallic mercury vapour was mercuric ions in human whole blo The oxidation mainly occurred in followed by an equilibration of the HUGHES (1957) called attention to t in lipoids, compared with its solubil view that metallic mercury – as di bound to SH-groups – readily and taining cell membranes (the alveo metallic form in the organism and and carried to sensitive tissues, such is oxidised and linked up with the S of this hypothesis, HUGHES referred & b), who both in autopsied patie found that inhalation of mercury va considerable amounts of mercury in

The processes by which mercury through the alveolar and capillary w





VOLUME (BTPS), LITRES

between the physiological dead space, as a percentage of the tidal volume. Based on results of ASMUSSEN & NIELSEN (1956).

concentrations, as determined by means of the apparatus described

of expired mercury constitutes of the average tidal volume. An expression of the percentage that absorption represents of the average tidal volume. ASMUSSEN & NIELSEN (1956) studied the function of the tidal volume (BTPS) in their results, I have constructed the curve between the physiological dead volume, and the tidal volume. The data in table 1 are based on measurements of expired air saturated with water vapour at that tidal volumes (BTPS) measured and body temperature will thus be about

table 1 and the curve in fig. 2 shows that the uptake of mercury fairly closely corresponds to the percentage of the tidal volume at the lowest concentrations in the inspired air was a little higher in several of the

as suggest that the uptake of metallic mercury occurs from the alveoli of the lungs and is almost complete and independent of the concentration in the inspired air within the

range from 100 to 350  $\mu\text{g m}^{-3}$ . The slightly lower uptake at a mercury concentration of 50  $\mu\text{g m}^{-3}$  suggests that adsorptive processes are of less, or probably almost insignificant, importance in the absorption of mercury from the respiratory tract in man. A person breathing air contaminated with mercury will thus presumably take up per minute an amount of mercury that at a close approximation is equal to the product of the mercury concentration in the inspired air and his alveolar ventilation.

### Discussion

Absorption is most commonly defined as the sum of all the processes by which a substance from the site of absorption enters the circulating blood. In the experiments reported here, this definition was applied to the uptake of mercury from the inspired air. In experiments on rats, HAYES & ROTHSTEIN (1962) found that, after inspiration of mercury vapour (with added  $^{203}\text{Hg}$ ), temporary retention of the mercury occurs in the lungs for a few hours, after which it shows a distribution in the body similar to that observed after intravenous administration of mercuric chloride. However, these authors did not determine the mercury content of the brain; according to the comparative studies by BERLIN & JOHANSSON (1964) mentioned above, however, the mouse brain takes up, after the animal has inhaled mercury vapour, an amount of mercury about 10 times as large as that taken up after intravenous administration of a corresponding dose of mercuric nitrate. CLARKSON *et al.* (1961) found that metallic mercury vapour was rapidly taken up and oxidised to mercuric ions in human whole blood at physiological oxygen tensions. The oxidation mainly occurred in the erythrocytes and was rapidly followed by an equilibration of the mercury between plasma and cells. HUGHES (1957) called attention to the high solubility of metallic mercury in lipoids, compared with its solubility in water and air. He expressed the view that metallic mercury – as distinct from mercuric ions, which are bound to SH-groups – readily and rapidly diffuses through lipid-containing cell membranes (the alveolar walls), temporarily exists in its metallic form in the organism and is then dissolved in the blood lipoids and carried to sensitive tissues, such as that of the brain; here the mercury is oxidised and linked up with the SH-groups of the proteins. In support of this hypothesis, HUGHES referred to investigations by BRIGATTI (1949a & b), who both in autopsied patients and in animal experiments had found that inhalation of mercury vapour resulted in the accumulation of considerable amounts of mercury in the brain.

The processes by which mercury vapour from the alveolar air passes through the alveolar and capillary walls and the interstitial tissue into the

001426



blood and is transported in this medium are thus not fully clarified. It may be assumed that a considerable part of the mercury vapour passes through these structures by diffusion, without being converted, and that the remainder is oxidised and temporarily deposited in these structures. Similarly, it may be thought that mercury may be transported in the blood both in the form of unconverted metal dissolved in the lipoids and in an oxidised form ( $\text{Hg}^{++}$ ) bound to the SH-groups of the haemoglobin and plasma albumin.

The volunteers used in the experiments reported here had been previously exposed to mercury in the inspired air only occasionally or not at all. One of the males (O.C.) had previously undergone unilateral thoracoplasty. All the volunteers were moderate smokers, and no restrictions as to smoking or food intake were imposed during the period of the experiments.

It should be of interest to study the absorption in persons who have been exposed to mercury vapour in the inspired air for prolonged periods. It also seems reasonable to study the factors that may be assumed to influence the absorption. Thus, I found, entirely by accident, that ingestion of alcohol to an appreciable extent reduced the absorption of mercury. This phenomenon, which was studied by a slightly modified technique, will be described in a paper to be submitted for publication.

### Summary

Studies on the absorption of mercury vapour from the respiratory tract in four volunteers who breathed air with mercury concentrations ranging from 50 to 350  $\mu\text{g}/\text{m}^3$  are reported. Determinations of the ratio of the expired to the inspired amounts of mercury gave an expression of the fraction that a notional dead space for mercury absorption represented of the average tidal volume measured during the experimental period. A comparison with the results reported by other authors on the size of the physiological dead space in relation to the tidal volume showed that the notional dead space for mercury absorption was of the same magnitude as the physiological dead space and, within the range investigated, largely independent of the mercury concentration in the inspired air. It was also demonstrated that the last part of the air expired during maximal expiration contained only negligible amounts of mercury. It is therefore reasonable to assume that almost complete absorption of mercury vapour occurs from the alveolar parts of the lungs in normal individuals.

### REFERENCES

- American Congress of Governmental Industrial Hygienists: 1964. *Arch. Environm. Hlth.* 1964, 9, 545-548.
- Asmussen, E. & M. Nielsen: Physiological dead space and during muscular exercise. *Acta physiologica Scandinavica* 1964, 2, 1-12.
- Battigelli, M. C.: Mercury toxicity from industrial sources—literature—part I. *J. Occup. Med.* 1960, 2, 1-12.
- Berlin, M. & S. Ullberg: Accumulation and autoradiographic study after a single intravenous injection of mercury. *Environm. Hlth.* 1963, 6, 589-601.
- Berlin, M. & L. G. Johansson: Mercury in man and after intravenous injection of mercury. *Environm. Hlth.* 1964, 7, 1-12.
- Brigatti, L.: Il contenuto in mercurio degli alimenti e l'assorbimento mercuriale. *Med. Lavoro* 1961, 46, 1-12.
- Brigatti, L.: Distribuzione del mercurio negli organi e nei tessuti con vapori di mercurio. *Med. Lavoro* 1961, 46, 13-24.
- Brooks, R. O. R. & A. Holmes: *The control of mercury in the environment*. MED/R 2350, Atomic Energy Research Establishment, Harwell, 1958.
- Buckell, M., D. Hunter, R. Milton & K. M. Macdonald: Mercury in man and after intravenous injection of mercury. *Industr. Med.* 1946, 3, 55-63.
- Clarkson, T. W., J. Gatzky & C. Dalton: Studies on the distribution of mercury in blood. *Univ. of Rochester AEC Report No. 1961-10*.
- Elkins, H. B.: Maximum acceptable concentration of mercury in the atmosphere. United States. *Arch. Environm. Hlth.* 1961, 18, 1-12.
- Fraser, A. M., K. J. Melville & R. L. Stehle: The proportion of mercury absorbed and excreted in man. *Macol. & Exper. Therap.* 1934, 51, 147.
- Friberg, L.: Studies on the accumulation, metabolism and excretion of mercury ( $\text{Hg}^{203}$ ) after prolonged subcutaneous administration. *Toxicol.* 1956, 12, 411-427.
- Gage, J. C.: The distribution and excretion of mercury in man. *Med.* 1961, 18, 287-294.
- Gerstner, F.: *Die quantitative Bestimmung kleiner Mengen von Quecksilber auf verschiedene Probleme*. Diss. d. Technischen Hochschule in Baden, 1931.
- Göthlin, G. F.: Kvicksilfverhaltig luft och förorening i medicinsk läroanstalt. *Hygienisk Tidsskrift* 1931, 1, 1-12.
- Hayes, A. D. & A. Rothstein: The metabolism of mercury by isotope techniques. *J. Pharmacol. & Exper. Therap.* 1948, 84, 1-12.
- Holm-Jensen, I.: *Biologisk bestemmelse af kvicksilber*. Thesis, Universitetsforlaget, Aarhus 1948.
- Hughes, W. L.: A physicochemical rationale for the toxicity of mercury compounds. *Ann. N.Y. Acad. Sci.* 1957, 6, 1-12.
- Neal, P. A., R. R. Jones, J. J. Bloomfield, J. J. Edwards & R. H. Flinn: Chronic mercurialism in hatters' fur-cutters. *Public Health Bulletin* No. 234, 1937.
- Neal, P. A., R. H. Flinn, T. I. Edwards, W. L. Hughes & J. J. Bloomfield: Mercurialism and its control in the hatter's industry. *Public Health Bulletin* No. 263, 1941.



m are thus not fully clarified. It  
art of the mercury vapour passes  
ut being converted, and that  
rily deposited in these structures.  
rcury may be transported in the  
metal dissolved in the lipoids and  
e SH-groups of the haemoglobin

ents reported here had been pre-  
red air only occasionally or not at  
asly undergone unilateral thoraco-  
e smokers, and no restrictions as  
d during the period of the experi-

absorption in persons who have  
inspired air for prolonged periods.  
factors that may be assumed to  
d, entirely by accident, that inges-  
at reduced the absorption of mer-  
udied by a slightly modified tech-  
be submitted for publication.

vapour from the respiratory tract  
th mercury concentrations ranging  
Determinations of the ratio of the  
mercury gave an expression of the  
or mercury absorption represented  
during the experimental period. A  
y other authors on the size of the  
the tidal volume showed that the  
rption was of the same magnitude  
within the range investigated, largely  
tion in the inspired air. It was also  
air expired during maximal expira-  
s of mercury. It is therefore reason-  
e absorption of mercury vapour  
ings in normal individuals.

## REFERENCES

- American Congress of Governmental Industrial Hygienists: Threshold limit values for 1964. *Arch. Environm. Hlth.* 1964, 9, 545-554.
- Asmussen, E. & M. Nielsen: Physiological dead space and alveolar gas pressures at rest and during muscular exercise. *Acta physiol. scand.* 1956, 38, 1-21.
- Battigelli, M. C.: Mercury toxicity from industrial exposure - A critical review of the literature-part I. *J. Occup. Med.* 1960, 2, 337-344.
- Berlin, M. & S. Ullberg: Accumulation and retention of mercury in the mouse, I. An autoradiographic study after a single intravenous injection of mercuric chloride. *Arch. Environm. Hlth.* 1963, 6, 589-601.
- Berlin, M. & L. G. Johansson: Mercury in mouse brain after inhalation of mercury vapour and after intravenous injection of mercury salt. *Nature* 1964, 204, 85-86.
- Brigatti, L.: Il contenuto in mercurio degli organi di soggetti senza e con precedente assorbimento mercuriale. *Med. Lavoro* 1949a, 40, 233-239.
- Brigatti, L.: Distribuzione del mercurio negli organi di conigli intossicati in modo subacuto con vapori di mercurio. *Med. Lavoro* 1949b, 40, 240-250.
- Brooks, R. O. R. & A. Holmes: *The control of mercury metal in the laboratory*. AERE MED/R 2350, Atomic Energy Research Establishment, Harwell, Berkshire, England 1958.
- Buckell, M., D. Hunter, R. Milton & K. M. A. Perry: Chronic mercury poisoning. *Brit. J. industr. Med.* 1946, 3, 55-63.
- Clarkson, T. W., J. Gatz & C. Dalton: Studies on the equilibration of mercury vapor with blood. *Univ. of Rochester AEC Report No. 582*, 1961.
- Elkins, H. B.: Maximum acceptable concentrations. A comparison in Russia and the United States. *Arch. Environm. Hlth.* 1961, 2, 45-49.
- Fraser, A. M., K. J. Melville & R. L. Stehle: Mercury laden air: the toxic concentration, the proportion of mercury absorbed and the urinary excretion of mercury. *J. Pharmacol. & Exper. Therap.* 1934, 51, 147.
- Friberg, L.: Studies on the accumulation, metabolism and excretion of inorganic mercury ( $\text{Hg}^{203}$ ) after prolonged subcutaneous administration to rats. *Acta pharmacol. et toxicol.* 1956, 12, 411-427.
- Gage, J. C.: The distribution and excretion of inhaled mercury vapour. *Brit. J. industr. Med.* 1961, 18, 287-294.
- Gerstner, F.: *Die quantitative Bestimmung kleinster Quecksilbermengen und ihre Anwendung auf verschiedene Probleme*. Diss. d. Technischen Hochschule "Fredericiana" zu Karlsruhe in Baden, 1931.
- Göthlin, G. F.: Kvicksilfverhaltig luft och fall af kronisk kvicksilfverförgiftning vid en medicinsk läroanstalt. *Hygienisk Tidskrift* 1909, p. 138-183.
- Hayes, A. D. & A. Rothstein: The metabolism of inhaled mercury vapor in the rat studied by isotope techniques. *J. Pharmacol. & Exper. Therapeut.* 1962, 138, 1-10.
- Holm-Jensen, I.: *Biologisk bestemmelse af kviksølv i luft ved hjælp af daphnia magna*. Thesis, Universitetsforlaget, Aarhus 1948.
- Hughes, W. L.: A physicochemical rationale for the biological activity of mercury and its compounds. *Ann. N.Y. Acad. Sci.* 1957, 65, 454-460.
- Neal, P. A., R. R. Jones, J. J. Bloomfield, J. M. Dallavalle & T. I. Edwards: A study of chronic mercurialism in hatters' fur-cutting industry. *U.S. Public Health Service, Public Health Bulletin No. 234*, 1937.
- Neal, P. A., R. H. Flinn, T. I. Edwards, W. H. Reinhart, J. W. Hough, J. M. Dallavalle et al.: Mercurialism and its control in the felt-hat industry. *U.S. Public Health Service, Public Health Bulletin No. 263*, 1941.

001422



- Nielsen Kudsk, F.: Chemical determination of mercury in air. *Scand. J. clin. Lab. Invest.* 1964, 16, Suppl. 77.
- Rothstein, A. & A. D. Hayes: The metabolism of mercury in the rat studied by isotope techniques. *J. Pharmacol. & Exper. Therap.* 1960, 130, 166-176.
- Russell, M. C. B.: Unpublished work. Quoted by Brooks, R.O.R. & A. Holmes, 1958, loc. cit.
- Shepherd, M., S. Schuhmann, R. H. Flinn, J. W. Hough & P. A. Neal: Hazard of mercury vapor in scientific laboratories. *J. Research National Bureau of Standards* 1941, 26, 357-375.
- Turrian, H., E. Grandjean & V. Turrian: Industriehygienische und medizinische Untersuchungen in Quecksilberbetrieben. *Schweiz. med. Wschr.* 1956, 86, 1091-1096.
- Woodson, T. T.: A new mercury vapor detector. *Rev. Sci. Instruments* 1939, 10, 308-311.

*Acta pharmacol. et toxicol.* 1965, 23

From the Institute of Pharmacology (I)  
University of Aarhus

## The Influence of Ethyl A Mercury Vapour fr

F. Niels

(Received J

In a previous paper I have reported of metallic mercury from the re inhaled air containing mercury vap 50 to 350  $\mu\text{g}/\text{m}^3$  (NIELSEN KUDSK 19

In a determination of the ratio of mercury, I found that a notional dead space was of the same order of magnitude within the range studied, largely in relation to the inspired air. The notional dead space was found to be dependent on the size of the physiological dead space. However, at a concentration of 50  $\mu\text{g}/\text{m}^3$ , the notional dead space indicates that mercury absorption is of little importance for mercury absorption. It was also demonstrated that the last expiration was virtually free from mercury.

On the basis of these results it is concluded that the most complete absorption of mercury occurs in the lungs in normal individuals. A person breathing with mercury vapour will thus preserve a certain amount of mercury that at a close approximation is equal to the mercury concentration in the inspired air. Processes that may be thought of as influencing the mercury vapour and its transport in relation to the fixation of a maximum amount of mercury in the atmospheric air were

001423