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Key terms: alveolar air; arterial blood; blood/air partition; butyl alcohol; coeddicient; distribution; exposure; man; uptake; water air partition coefficient

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Exposure to butyl alcohol

Uptake and distribution in man

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ÅSTRAND, I., ÖVRUM, P., LINDQVIST, T. and HULTENGREN, M. Exposure to butyl alcohol: Uptake and distribution in man. *Scand. j. work environ. & health* 3 (1976) 165—175. Twelve subjects were exposed to 300 or 600 mg/m³ of butyl alcohol in inspired air during rest and during exercise on a bicycle ergometer. Exposure lasted 2 h. The results were puzzling in view of the high blood/air partition coefficient for butyl alcohol. The arterial blood concentration was low. The concentration in the last part of the expired air, i.e., the "alveolar" concentration, was low. The quotient of "alveolar" concentration $\times$ 100/inspired concentration was low in relation to the low percentage uptake. However the high solubility of butyl alcohol in water may explain the results. Butyl alcohol was probably partially taken up in the water of the dead space mucous membranes during inspiration. It was then partially released from the membranes. Therefore the concentration of butyl alcohol in the last part of expiration was probably not the same as the concentration in the alveolar air.

Key words: butyl alcohol, exposure, man, arterial blood, alveolar air, uptake, blood/air partition coefficient, water air partition coefficient.

Butyl alcohol is the name of four alcohols with the same formula, C_4H_9OH . Normal butyl alcohol is the most common form and is the alcohol referred to in this article. It is used as a solvent for paint and varnish in automotive and general painting and as a solvent in plastic manufacturing. In the textile industry it is used in the plastic coating of various materials. Butyl alcohol is also employed as a solvent for glue in the plastics and rubber industry. About 4,000

tons are consumed each year in Sweden, and a large number of people are exposed to butyl alcohol in their everyday work.

The American threshold limit value (TLV) for butyl alcohol in air is 100 ppm or 300 mg/m³ of air at 25°C and a barometric pressure of 760 mm Hg. One hundred parts per million was selected because irritation of the airways and the eyes is avoided when this value is respected (8, 10). The French TLV is also 100 ppm (9). In 1973, 0.1 mg/m³ (6, 7) was suggested as the Russian value. Such a low value was proposed because it was felt that certain reflexes might be affected by levels around 1—2 mg/m³. The official Swedish value is 50 ppm (5).

Few studies have been made of the effect of butyl alcohol on the central ner-

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vous system or long-term effects on health (8). Nor has the uptake and distribution of butyl alcohol in the body of man been studied to any great extent.

Butyl alcohol has been made the subject of the present study because of its widespread use in industry and because it is an alcohol. As such its properties differ from those of the solvents previously studied (1). Alcohols with a small number of carbon atoms are highly soluble in water, in contrast to the other substances previously investigated. The solubility of butyl alcohol in water is 7.9 g/100 g of water, i.e., 8 %.

SUBJECTS

The subjects consisted of a group of 12 men, 21 to 34 years of age. Their state of health was carefully examined, particular attention being devoted to the function of respiratory and circulatory organs. The method employed has been described elsewhere (2, 3).

All the subjects were healthy. None had ever had any illness that could affect the results in the exposure trials. All the values from the spirometric examination

were normal (table 1). This was also the case for values obtained in conjunction with exercise at four different work intensities. All the subjects had a normal physical work capacity (table 2). No significant ECG changes were recorded.

None of the subjects had been exposed to solvents in their everyday work. Subjects were asked not to consume any form of alcohol for 24 h prior to exposure.

EXPERIMENTAL DESIGN

The experiments were performed generally in the same manner as in the previous studies of solvents (1). Thus catheters were introduced into a brachial artery and a medial cubital vein. The subjects were exposed to butyl alcohol through a breathing valve and a mouthpiece. Each exposure period lasted 30 min, and each subject was exposed for four periods, i.e., for a total of 2 h.

Subjects were exposed to butyl alcohol in inspiratory air in a concentration of 100 or 200 ppm, i.e., 300 or 600 mg/m³ of air, during rest and during exercise on a bicycle ergometer. The Swedish TLV for butyl alcohol in air is, as mentioned earlier,

Table 1. Means and standard errors of the means of the height, weight, and respiratory data, taken at rest, of the 12 male subjects 21 to 34 years of age. (FEV % = forced expiratory volume for 1 s as the percentage of vital capacity; MVVf = max voluntary ventilation at free rate)

Body height (cm)	Body weight (kg)	Vital capacity (l)	Residual volume (l)	FEV (%)	MVVf (l/min)
182 ± 2	76.2 ± 2.4	6.2 ± 0.2	1.7 ± 0.1	86 ± 1	215 ± 12

Table 2. Means and standard errors of the means of the 12 subjects' results from an exercise test on a bicycle ergometer without exposure to butyl alcohol. ($\dot{V}_E$ = pulmonary ventilation; $\dot{V}O_2$ = oxygen uptake per unit of time)

Exercise intensity (W)	Heart rate (beats/min)	$\dot{V}_E$ BTPS (l/min)	$\dot{V}O_2$ BTPS (l/min)	Blood lactic acid (mmol/l)
50	97 ± 2	26.2 ± 1.0	0.99 ± 0.03	2.3 ± 0.1
100	117 ± 2	38.3 ± 1.1	1.55 ± 0.02	2.7 ± 0.3
150	142 ± 4	54.5 ± 2.0	2.16 ± 0.03	4.5 ± 0.5
Maximum	186 ± 3	134.4 ± 4.3	3.66 ± 0.13	15.4 ± 0.6

Fig. 1. Twelve subjects were exposed during four consecutive 30-min periods at rest and during exercise according to two alternatives, series I and II. A 20-min pause with no exposure was inserted when there was a shift from rest to exercise. During the final 5 min of that pause the subject was cycling at a work load of 50 W. (Low = about 300 mg/m³ and high = about 600 mg/m³ of butyl alcohol in the inspiratory air)

50 ppm or 150 mg/m³ of air at 25°C and a barometric pressure of 760 mm Hg. All concentrations given henceforth will be converted to milligrams per cubic meter at 25°C and at the prevailing barometric pressure unless otherwise noted. The air mixtures were prepared in a manner similar to the one employed in the previous studies (3).

The concentration of butyl alcohol in inspiratory air was continuously followed with a gas indicator and a strip chart recorder (Hydrocarbon analyzer, model 116, Scott Research Lab. Inc. Plumsteadville, Pa., U.S.A.). The concentration was constant in each experiment. During the course of the investigation, the concentration varied from 295 to 350 and from 590 to 610 mg/m³.

Subjects were exposed according to the following two alternatives (fig. 1): series I: Six subjects were exposed to butyl alcohol in inspiratory air at a concentration of approximately 600 mg/m³ at rest (30 min) and during physical exercise (30 + 30 + 30 min) at an intensity of about 50 W (300 kpm/min); series II: Six other subjects were exposed to butyl alcohol in inspiratory air at a concentration of approximately 300 mg/m³ at rest (30 min) and during physical exercise (30 + 30 + 30 min) at intensities of about 50, 100, and 150 W (300, 600 and 900 kpm/min).

Fig. 2 illustrates the experimental design with respect to measurements and samplings during and after an exposure period.

The volume of expiratory air was continuously measured throughout the entire exposure, i.e., for 2 h, with the Douglas bag technique. The butyl alcohol content in each bag was analyzed. The volume of inspiratory air was assumed to be the same as the volume of expiratory air (<1 % error), and the amount of butyl alcohol taken up in the body was calculated as the difference between the total quantities in inspiratory and expiratory air. The mean value for pulmonary ventilation/min ($\dot{V}_E$) was calculated for every 30-min period and for each subject. The mean value for the six subjects in each series was then calculated. The figures describing the results show how the collection of the volume of expiratory air was fractionated.

The oxygen content of expiratory air was analyzed and oxygen uptake was calculated for the latter half of each exposure period during rest and for the last 5—10 min of each period of exercise. The mean value of two determinations for each period and subject was used. Determinations of oxygen uptake and of lactic acid concentration in blood were performed so that an assessment of exercise intensity in

relation to individual work capacity (max $\dot{V}O_2$) could be made.

Alveolar air samples for butyl alcohol assay were extracted from the breathing valve with a glass syringe during exposure and with a glass tube after the conclusion of exposure (3). Samples of arterial and venous blood (about 0.5 g) were taken straight from the catheters into 15-ml glass bottles for butyl alcohol assay. Details of this sampling procedure have been presented in previous studies (2, 3). A mean value is given for the concentration of butyl alcohol in alveolar air and in the arterial and venous blood of each subject and each 30-min period on the basis of the final three measurements.

The concentrations in alveolar air and in arterial and venous blood were followed for about 1 h after the conclusion of exposure. The times at which the samples were taken are shown in fig. 2.

ECGs were recorded continuously throughout the entire exposure. Heart rates were determined every other minute from the ECG records, and the mean value of the three final determinations in each exposure period was used.

ANALYTICAL METHODS

The volume of expiratory air, blood lactic acid concentration, and the heart rate were determined according to methods

described elsewhere (2). The oxygen and carbon dioxide content of expiratory air was determined with automatic analyzers (model OM 11 and LB2, respectively, LKB-Beckman Instr. AB, Vällingby, Sweden), and oxygen uptake was calculated. The errors of the methods are described elsewhere (4).

The concentration of butyl alcohol in inspiratory and expiratory air was determined with a gas chromatograph (model F 30, FID, Perkin-Elmer Ltd., Beaconsfield, Buckinghamshire, England) fitted with a stainless steel column (2 m long, 2.2-mm inner diameter) packed with 1 % OS-124 on Chromosorb G, 60—80 mesh. The flow rate of the carrier gas (nitrogen) was 30 ml/min, and the column temperature 100°C. One-milliliter samples were injected.

The concentration of butyl alcohol in alveolar air was assayed with a gas chromatograph (model F 11, FID, Perkin-Elmer Ltd., Beaconsfield, Buckinghamshire, England) fitted with a stainless steel column (1 m long, 2.2-mm inner diameter) packed with 8 % carbowax 1540 on Chromosorb W, 80—100 mesh. The flow rate of the carrier gas (nitrogen) was 30 ml/min, and the column temperature 35°C. One-milliliter samples were injected.

On the basis of the chromatogram, the butyl alcohol content was determined with the aid of standard air samples with known concentrations of butyl alcohol.

Fig. 2. Times for different measurements and samplings prior to, during, and after a 30-min period of exposure.

Table 3. Means and standard errors of the means of results obtained during rest and exercise on a bicycle ergometer with exposure to butyl alcohol in the inspiratory air. Series I: exposure to about 600 mg/m³ at rest (30 min) and during exercise at an intensity of 50 W (30 + 30 + 30 min). Series II: exposure to about 300 mg/m³ at rest (30 min) and during exercise at intensities of 50, 100, and 150 W (cf. fig. 1). Each period (1—4) lasted 30 min, and each series lasted 2 h and included six subjects. ($\dot{V}_E$ = pulmonary ventilation; $\dot{V}O_2$ = oxygen uptake per unit of time)

Exposure	Heart rate (beats/min)	$\dot{V}O_2$ STPD (l/min)	Blood lactic acid (mmol/l)	$\dot{V}_E$ BTPS (l/min)	Butyl alcohol concentration		
					Alveolar air (mg/m ³)	Arterial blood (mg/kg)	Venous blood (mg/kg)
Series I							
1	68 ± 3	0.32 ± 0.01	2.0 ± 0.2	10.5 ± 0.4	157 ± 15	0.5 ± 0.0	0.2 ± 0.0
2	97 ± 5	0.94 ± 0.02	2.2 ± 0.3	24.6 ± 0.4	183 ± 18	1.1 ± 0.1	0.4 ± 0.1
3	98 ± 6	0.96 ± 0.02	1.6 ± 0.1	24.7 ± 0.5	178 ± 15	1.1 ± 0.1	0.4 ± 0.1
4	101 ± 9	0.94 ± 0.04	1.6 ± 0.2	24.7 ± 0.9	172 ± 19	1.1 ± 0.1	0.4 ± 0.1
Series II							
1	63 ± 3	0.31 ± 0.02	1.7 ± 0.2	11.2 ± 0.5	67 ± 7	0.3 ± 0.1	0.2 ± 0.0
2	92 ± 4	0.98 ± 0.03	1.7 ± 0.2	25.2 ± 0.9	87 ± 4	0.6 ± 0.1	0.3 ± 0.1
3	120 ± 6	1.65 ± 0.06	2.0 ± 0.5	37.5 ± 0.9	80 ± 6	0.9 ± 0.2	0.5 ± 0.0
4	145 ± 7	2.34 ± 0.10	4.1 ± 0.3	52.6 ± 1.8	94 ± 8	1.3 ± 0.1	0.9 ± 0.1

The butyl alcohol level in blood was determined with a "head-space" method. The analysis was performed with a gas chromatograph (model F 11, FID, Perkin-Elmer Ltd., Beaconsfield, Buckinghamshire, England) fitted with a stainless steel column (2 m long, 2.2-mm inner diameter) packed with 1 % fraconitil II on Chromosorb G, 80—100 mesh. The flow rate of the carrier gas (nitrogen) was 30 ml/min, and the column temperature 70°C. The level of butyl alcohol in the "head-space" was calculated on the basis of individual blood samples with known concentrations of butyl alcohol. The samples were prepared as follows: 1 μ l of an aqueous solution of butyl alcohol containing 0.5 μ g of butyl alcohol/ μ l of water was injected into a 15-ml glass bottle containing a known quantity of blood, usually 0.5 g, and 100 μ l of ACD² solution. On the basis of the content in the "head-space" of the standard, the butyl alcohol content of individual samples was calculated. The error of the method for a single determination was calculated from 10 double determinations made on blood with a butyl alcohol content of 0.81 mg/kg and found to be ± 0.086 mg/kg, i.e., 10.4 %. The lowest detectable level of butyl alcohol in blood was 0.08 mg/kg.

² ACD refers to acidum citricum, dextrose.

RESULTS

Pulmonary ventilation and blood circulation

Pulmonary ventilation, oxygen uptake, blood lactic acid concentration, and heart rate displayed ordinary magnitudes during exposure at rest. No significant differences were recorded at rest between the measurement values during exposure to the two different concentrations (table 3).

During exercise on the bicycle ergometer pulmonary ventilation, oxygen uptake, and heart rate were of the same magnitude at the respective intensities during exposure in comparison to non-exposure (tables 2 and 3), nor were any differences recorded between measurement values in exposure to the two different concentrations during cycling at an intensity of about 50 W (300 kpm/min).

At the intensities of 50, 100, and 150 W the subjects utilized about 25, 45, and 65 %, respectively, of their physical work capacities. These values, plus the attendant lactic acid concentrations in blood, suggest that 50 W can be regarded as light physical exercise, 100 W as moderate, and 150 W as heavy physical exercise for the subjects taking part in the study. None of the subjects were troubled by the exposure, either at rest or during exercise.

No significant ECG changes were recorded at rest or during exercise. Thus no subject displayed an increased incidence of ectopic beats during exposure in comparison with nonexposure.

Uptake in the organism

The amount of butyl alcohol taken up in the organism was measured as the difference between the amounts in inspiratory and expiratory air (table 4). One example from each series of exposure is shown in figs. 3 and 4.

At rest about 80 mg were taken up during a 30-min exposure to 600 mg/m³, whereas the absorbed amount was halved when the exposure concentration was halved. The amount taken up constituted about 47 % of the amount supplied.

In exercise at an intensity of about 50 W during three consecutive 30-min periods and exposure to 600 mg/m³, the absorbed quantities amounted to 160, 155, and 145 mg, respectively, and corresponded to 39, 38, and 36 % of the amount supplied.

At exercise intensities of about 50, 100, and 150 W during three consecutive 30-min periods and exposure to 300 mg/m³, the absorbed quantities amounted to about 80, 130, and 195 mg, respectively, and

corresponded to 37, 40, and 41 % of the amount supplied.

Thus the percentage uptake declined in the transition from rest to work. On the other hand there was no change in uptake during continued exercise irrespective of whether the intensity was maintained or increased. The total uptake during the 2-h exposure amounted to about 535 mg in series I (high exposure — light exercise) and to about 450 mg in series II (low exposure — rising exercise intensity).

Alveolar air and arterial blood concentration of butyl alcohol during exposure

After 30 min of exposure at rest to 600 mg/m³ of butyl alcohol in inspiratory air, the concentration in alveolar air amounted to about 155 mg/m³ and corresponded to about 25 % of the concentration in inspiratory air (table 3). The concentration in alveolar air rose only slightly, i.e., to about 30 % of the concentration in inspiratory air, during exercise for three consecutive periods at an intensity of 50 W. During this work load the pulmonary ventilation was increased about 2.5 times in comparison to that recorded during resting conditions (fig. 5).

During exposure at rest to 300 mg/m³ the concentration in alveolar air amounted to about 65 mg/m³ after 30 min and corresponded to about 22 % of the concentra-

Table 4. Mean and standard errors of the means of the amount of butyl alcohol in milligrams in the inspiratory air and of the amount taken up per each 30-min period and after 2 h of exposure to approximately 600 and 300 mg/m³ during rest and exercise. Series I: exposure to about 600 mg/m³ at rest (30 min) and during exercise with an intensity of 50 W (30 + 30 + 30 min) (n = 6). Series II: exposure to about 300 mg/m³ at rest (30 min) and during exercise with intensities of 50, 100, and 150 W (30 + 30 + 30 min) (n = 6).

Series	Exposure period	Amount given (mg)	Amount taken up (mg)	Uptake (% of given amount)
I	1	171 ± 9	78 ± 3	46 ± 2
	2	406 ± 15	159 ± 15	39 ± 3
	3	406 ± 17	154 ± 15	38 ± 4
	4	404 ± 17	145 ± 15	36 ± 3
	1—4	1,380 ± 55	536 ± 51	39 ± 3
II	1	90 ± 4	43 ± 5	48 ± 4
	2	220 ± 8	81 ± 14	37 ± 6
	3	326 ± 8	130 ± 21	40 ± 7
	4	460 ± 15	193 ± 27	41 ± 5
	1—4	1,093 ± 22	449 ± 66	41 ± 6

Fig. 3. The amount of butyl alcohol supplied and taken up in one subject during exposure to approximately 600 mg/m³ of butyl alcohol in the inspiratory air. Exposure was provided at rest and during exercise at an intensity of about 50 W (300 kpm/min). The total amount taken up in 2 h amounted to 419 mg, i.e., about 34 % of the supplied amount of 1,243 mg. During the first 15 min after the end of exposure about 50 mg of butyl alcohol was expired.

Fig. 4. The amount of butyl alcohol supplied and taken up in one subject during exposure to approximately 330 mg/m³ in the inspiratory air. Exposure was provided at rest and during exercise at intensities of about 50, 100, and 150 W (300, 600 and 900 kpm/min). The total amount taken up in 2 h amounted to 493 mg, i.e., about 43 % of the supplied amount of 1,154 mg. During the first 15 min after the end of exposure about 18 mg of butyl alcohol was expired.

Fig. 5. The concentration of butyl alcohol in the alveolar air and in the arterial and venous blood of one subject during and after exposure to approximately 600 mg/m³ of butyl alcohol in the inspiratory air. Exposure was provided at rest and during exercise at an intensity of about 50 W (300 kpm/min). $\dot{V}_E$ = pulmonary ventilation in liter per minute. (The same experiment as in fig. 3)

tion in inspiratory air. In exercise of rising intensity amounting to 50, 100, and 150 W, the alveolar concentration rose to 87, 80, and 84 mg/m³, respectively, and corresponded to about 30 % of the concentration in inspiratory air (table 3, fig. 6).

The arterial blood concentration of butyl alcohol after 30 min at rest in series I (high exposure) was about 0.5 mg/kg (table 3). The concentration rose to 1.1 mg/kg during exercise at 50 W. This concentration remained unchanged throughout the three periods of exercise. The arterial concentration in series II (low exposure) amounted to 0.3 mg/kg after 30 min at rest, i.e., about half of the concentration obtained with twice the level of exposure. The concentration amounted to 0.6, 0.9 and 1.3 mg/kg, respectively, during exercise at the three rising intensities.

In principle the venous blood concentration paralleled the arterial blood concentration. Earlier investigations (1) pre-

sent comments on peripheral venous concentration, arteriovenous difference, and the calculation of uptake in reference to the cardiac output and the arteriovenous difference in blood.

DISCUSSION

A surprising feature of a comparison between the present results and the results obtained in previous experiments was the relationship between alveolar air concentration, arterial blood concentration, and the butyl alcohol uptake (1). The substances previously studied were toluene, methylchloroform, styrene, white spirit, methylene chloride, and trichloroethylene.

The exposure level of 300 mg/m³ of air was selected as the lowest level and not 150 mg/m³, which corresponds to the TLV, because no butyl alcohol could be found in the blood with the assay technique described, even after 30 min of exposure at levels around the TLV. Thus the concentration in arterial blood was low. After 30 min of exposure at rest to 300 and to 600 mg/m³ of butyl alcohol, the arterial blood concentration was still low, i.e., 0.3 and 0.5 mg/kg, respectively. However, the alveolar concentrations were simultaneously low, corresponding to about 25 % of the concentration in inspiratory air.

The values are extraordinary in view of the blood/air partition coefficients for the substances compared (1). (The term "partition coefficient" refers to the ratio of concentrations of a substance in two immiscible phases at equilibrium and at 37°C). According to the unpublished results of Lindqvist the coefficient for butyl alcohol happens to be about 1,200 but those for the other substances are considerably less, i.e., they range from about 1 to 32 (1). In view of its coefficient, the concentration of butyl alcohol in arterial blood should be higher than that of the other substances. Even if the coefficients, determined in vitro, cannot be used for direct calculations of absolute blood concentrations, they still provide some idea of the relative levels of compared substances (1).

The fact that the butyl alcohol uptake never amounted to more than about 50 %

of the quantity supplied was also remarkable, particularly as the blood/air partition coefficient for butyl alcohol, as already mentioned, is very high. The highest percentage uptake recorded hitherto is a figure of about 70 % for styrene and for the aromatic components of white spirit (1). No partition coefficient has been determined for the aromatic components but the coefficient for styrene is 32 (1). Thus butyl alcohol uptake should have been analogously greater.

Finally the ratio between the alveolar concentration and the concentration in inspiratory air was small in relation to the uptake percentage (1). For all the other substances this relationship, i.e., percentage uptake — air concentrations, could be plotted on a straight line with a small standard deviation, whereas the relationship for butyl alcohol clearly fell outside

that line (fig. 7). Thus the cited alveolar concentration of butyl alcohol as a percentage of the concentration in inspiratory air was not related to uptake in the same manner as those of the other substances.

These divergent results may have been due to the fact that butyl alcohol is readily soluble in water, whereas the other substances studied were insoluble or only slightly soluble in water. As previously mentioned, the blood/air partition coefficient for butyl alcohol is about 1,200, but the water/air coefficient is also about 1,200 (Lindqvist, to be published). Two simple experiments were performed in order to ascertain the consequences of solubility in water.

A bag was filled with 10 l of air containing butyl alcohol at a concentration of 600 mg/m³. For about 30 s the air was pressed through a glass tube, packed with

Fig. 6. The concentration of butyl alcohol in the alveolar air and in the arterial and venous blood of one subject during and after exposure to approximately 330 mg/m³ of butyl alcohol in the inspiratory air. The exposure was provided at rest and during exercise at intensities of about 50, 100, and 150 W (300, 600 and 900 kpm/min). $\dot{V}_E$ = pulmonary ventilation in liters per minute. (The same experiment as in fig. 4)

Fig. 7. The amount taken up as the percentage of the supplied amount of butyl alcohol in relation to the alveolar concentration as the percentage of the concentration in inspiratory air. The determinations were made after 30 min of exposure both at rest and during exercise. The regression line was calculated on the basis of measurements made during exposure to methylene chloride, trichloroethylene, aliphatic and aromatic components of white spirit and styrene (1); $y = -0.72x + 74.9$; $SD = \pm 5$; $r = -0.93$.

water-saturated filter paper, into an empty bag. The concentration of butyl alcohol in this second bag was measured at 210 mg/m³. Thus the remainder must have been absorbed in the tube. Pure air from another 10-l bag was then pressed at the same rate through the tube with butyl alcohol into an initially empty bag. The butyl alcohol concentration in the latter sack was thereafter found to be 54 mg/m³. The experiment shows that butyl alcohol is rapidly dissolved in water but is also released from water to air.

A similar experiment was performed with one subject. Following a maximal expiration, the subject performed a maximal inspiration of gas containing a concentration of 600 mg/m³ of butyl alcohol. The subject then expired the same volume of gas into four different bags. In bag 1, the volume of which was calculated as being equivalent to the volume of the subject's anatomical dead space, the butyl alcohol concentration was measured at 129 mg/m³. The concentrations in bags 2, 3, and 4, which should have contained alveolar air, amounted to 87, 51, and 36

mg/m³, respectively. The oxygen content of bag 1 was 20.5 %, i.e., very close to the concentration in inspiratory air, and this value indicates that a very small amount of alveolar air was present. This experiment also showed that butyl alcohol had been dissolved in water, i.e., in the mucous membranes of the dead space. If this were not the case, then the butyl alcohol concentration in bag 1 would have been the same as in the inspiratory air.

In view of the high blood/air partition coefficient, almost all of the butyl alcohol should have been extracted from the air carried to the alveoli, but the air had probably lost a relatively large amount of its butyl alcohol before reaching the alveoli. Most of the butyl alcohol absorbed in the water in the mucous membranes during inspiration is probably retained there. Diffusion from water to blood in the mucous membranes probably takes place very slowly. The layer of cells which separates the water from the blood happens to be relatively thick, and the water/blood partition coefficient is relatively small, i.e., about 1.0. In the expiratory phase butyl alcohol is released from the mucous membranes of the dead space into the air flowing from the alveoli, since the alveolar air probably contains a very low concentration.

The preceding remarks may explain why the arterial blood concentration was relatively low, why the final portion of the expired air had a higher concentration than was expected, and why the uptake was modest, despite a very high blood/air partition coefficient for butyl alcohol.

Thus butyl alcohol is not only taken up in the alveoli, but also in other parts of the respiratory tract. The corresponding phenomenon probably failed to occur with the other substances examined (1), because they were not absorbed in the water of the mucous membranes but were taken up by the blood passing the alveoli.

It should be noted that the concentration in the "alveolar" air, samples of which were taken according to accepted practice, and in the arterial blood were "false" in the sense that they failed to reflect the amounts taken up. Therefore the ratio between percentage uptake and "alveolar" air/inspiratory air can only be used for

gases which are taken up in the alveoli, i.e., the relationship does not apply for water-soluble substances.

The carriage of a substance to different organs in the body is provided by the blood. As previously mentioned, the concentration of butyl alcohol in blood was low since part of the uptake apparently took place before the gas reached the alveoli. Even if part of the uptake in dead space ultimately diffused into the arterial blood, the concentration there still remained very low. The low blood concentrations must mean that the risk of a large uptake in other organs, such as the central nervous system, is smaller for butyl alcohol than for the other substances studied to date. In any event, this is the case for exposure lasting 2 h as in the present study.

One subject in series II (low exposure — rising work intensity) differed from the others by displaying an uncommonly small uptake. His total uptake amounted to 190 mg and represented about 19 % of the quantity supplied. All the other subjects had values ranging from 30 to 53 %. The subject was in extremely good physical condition. He had the lowest pulmonary ventilation and oxygen uptake at 100 and 150 W and probably even the smallest cardiac output at these intensities. On the other hand, he displayed about the same respiratory rate as the other subjects, probably because this rate is governed by the pedaling rate. However, these circumstances do not explain his low uptake. It may have been because this subject's pulmonary ventilation was more even with less variation in flow rate, and therefore the uptake in and release from the

mucous membranes was larger than for other subjects, i.e., the net uptake was relatively slight.

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