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Key terms: alveolar concentration; arterial concentration; distribution; exposure; man; partition coefficient; rest; solubility; trichloroethylene; uptake; work

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Exposure to trichloroethylene

I. Uptake and distribution in man

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ÅSTRAND, I. and ÖVRUM, P. Exposure to trichloroethylene: I. Uptake and distribution in man. *Scand. j. work environ. & health* 4 (1976) 199—211. Fifteen healthy male subjects were exposed to about 540 and 1,080 mg/m³ of trichloroethylene (TRI) in the air during rest and exercise on a bicycle ergometer. Each subject was exposed during four 30-min periods. The arterial blood concentration increased linearly with the concentration in the alveolar air. The uptake of TRI was about 55 % of the supplied amount at rest. At a work load of 150 W during the fourth period the percentage uptake decreased to about 25 %. For one fairly thin subject the uptake was near zero at the end of exposure. This development was probably due to the relatively low solubility of TRI in blood and tissues. The uptake of TRI may be estimated from pulmonary ventilation and the concentration in alveolar and inspiratory air.

Key words: exposure, trichloroethylene, alveolar concentration, arterial concentration, rest, work, uptake, solubility, partition coefficient.

Trichloroethylene (Cl₂C:CH Cl) is one of the most common and widely used solvents. It is often referred to as TRI, and this designation will be used in the present article.

Approximately 15,000 metric tons of TRI are consumed in Sweden each year, and a large number of people are exposed to it in their work. It is mainly used as a degreasing agent in the metal-working and engineering industry. It is also employed as a solvent in glues and as a cleaning agent.

The absorption, metabolism, distribution, and elimination of TRI in man and animals have been the subject of many investigations, as has the effect of TRI on the nervous system, the heart and the cir-

culatory organs. Summaries and conclusions from such studies are to be found in two recently published reports from the National Institute for Occupational Safety and Health (11, 13).

The two reports show that about 60 % of inspired TRI is taken up in the body of man and that about 75 % of the amount taken up is metabolized (5, 12). The values cited were obtained when subjects were exposed to up to about 200 ppm (1,080 mg/m³) for 5 h in the laboratory. The reports also show that a number of cases of sudden, inexplicable death have occurred in conjunction with exposure to TRI (9). These deaths may have been due to cardiac arrhythmias triggered by exposure to TRI under certain conditions and in combination with physical exertion.

Even though there are a large number of studies on TRI, none appear to have been performed in which the arterial blood concentration was measured or in which uptake was measured exactly both at rest and during work. Measurements

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Table 1. Body height, body weight and respiratory data taken at rest from 15 male subjects 22 to 29 years of age; mean values and standard errors of the means are given. (FEV₉₀ = forced expiratory volume for 1 s as the percentage of vital capacity; MVVf = maximal voluntary ventilation at free rate)

Body height (cm)	Body weight (kg)	Vital capacity (l)	Residual volume (l)	FEV (%)	MVVf (l/min)
181 ± 2	72.6 ± 2.4	6.0 ± 0.2	1.8 ± 0.1	81 ± 2	204 ± 9

Table 2. Results of 15 subjects from the exercise test on a bicycle ergometer without exposure to trichloroethylene; mean values and standard errors of the means are given. ($\dot{V}_E$ = 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	95 ± 4	25.3 ± 0.6	0.99 ± 0.03	2.6 ± 0.2
100	120 ± 5	38.7 ± 0.9	1.53 ± 0.02	2.9 ± 0.2
150	152 ± 5	57.7 ± 2.1	2.27 ± 0.04	6.1 ± 0.6
max. work	189 ± 2	140.1 ± 6.2	3.52 ± 0.14	17.0 ± 0.5

of this kind are described in the present report. The study features the same general design as previously published reports on solvents (1, 7).

SUBJECTS

A group of fifteen men, 22 to 29 years of age, were used as subjects. Six of them were gainfully employed and the others were students. No subject had previously been exposed to solvents except on isolated occasions.

MEDICAL EXAMINATION

The health of the subjects was carefully examined, special attention being devoted to the function of respiratory and circulatory organs. The same method was employed as in earlier studies on solvents (2, 3). The subjects were asked not to consume alcohol in any form for 24 h prior to exposure.

All the subjects were found to be healthy at the time of the examination, and no one had previously suffered from any illness that might affect the results

of the exposure trials to be performed. All the results from the spirometric examination were normal (table 1). All the values measured during submaximal and maximal work on the bicycle ergometer were normal, and the subjects displayed ordinary physical work capacities (table 2). These capacities were of the same magnitude as those of subjects in the earlier exposure studies. No significant ECG changes were recorded.

STUDY DESIGN

The experiments were conducted along the same general lines as the previous studies (4). The first step was to introduce catheters into a brachial artery and a medial cubital vein. The subject was then exposed to TRI. Each period of exposure lasted 30 min, and each subject was exposed for four periods, i.e., for a total of 2 h.

Subjects were exposed to TRI in the inspiratory air through a breathing valve fitted with a mouthpiece both at rest and during work on a bicycle ergometer. The concentration was about 100 or 200 ppm, i.e., about 540 or 1,080 mg/m³ of TRI in the air.

The Swedish TLV for TRI in air is 30 ppm or about 160 mg/m³ at a temperature of 25°C and a barometric pressure of 760 mm Hg. Henceforth, all air concentrations have been converted to milligrams per cubic meter at 25°C and a pressure of 760 mm Hg unless otherwise indicated. The air mixtures were prepared in the same manner as in the previous studies (4). The concentration of TRI in inspiratory air was continuously followed with a gas indicator (Hydrocarbon analyzer, model 116, Scott Research Lab. Inc., Plumsteadville, Pa., U.S.A.). At the intended concentration of 540 mg/m³ the actual concentration varied from 521 to 553 mg/m³; and at the intended concentration of 1,080 mg/m³, from 1,067 to 1,093 mg/m³ of air.

Subjects were exposed according to the following three alternatives (fig. 1): series I: five subjects were exposed to about 540 and 1,080 mg/m³ of TRI in inspiratory air during rest (30 + 30 min) and during exercise (30 + 30 min) at an intensity of about 50 W (300 kpm/min); series II: five subjects were exposed to about 540 mg/m³ of TRI in inspiratory air during rest (30 min) and during exercise (30 + 30 + 30 min) at an intensity of about 50 W (300 kpm/min); series III: five subjects were exposed to about 1,080 mg/m³ of TRI in inspiratory air during rest (30 min) and during exercise (30 + 30 + 30 min) at intensities of about 50, 100 and 150 W (300,

600 and 900 kpm/min).

Fig. 2 shows the times at which the measurements were made and samples taken.

The volume of expiratory air was continuously measured in bags, made of polyester-laminated aluminium foil, throughout the entire exposure, i.e., for 2 h. The TRI concentration was analyzed in both inspiratory and expiratory air. The volume of inspiratory air was assumed to be the same as the volume of expiratory air (< 1 % error), and the uptake of TRI in the organism was calculated as the difference between the total amounts in inspiratory and expiratory air. The mean value for pulmonary ventilation per minute was calculated on the basis of all measurements (bags) during each 30-min period for each subject. The figures describing the results show how the collection was fractionated into 20 to 30 different bags in the three types of exposure experiments.

The oxygen content of expiratory air was analyzed, and oxygen uptake was calculated for the latter half of each exposure period at rest and for the final 5–10 min of exercise. The mean value for two determinations in each period was used. These measurements, like the determination of lactic acid concentration in blood, were performed so that an assessment of exercise severity could be made for each subject.

Fig. 1. Fifteen subjects were exposed to trichloroethylene (TRI) for four consecutive 30-min periods at rest and during exercise according to three alternatives, series I, II and III. A 20-min pause with no exposure was inserted when there was a shift from rest to exercise. During the final 5 min of the 20-min pause the subject was cycling at a work load of 50 W. (Low = about 540 mg/m³ and high = about 1,080 mg/m³ of TRI in inspiratory air)

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

Alveolar air samples for TRI assay were extracted from the breathing valve with a glass syringe during exposure and with a glass tube after the conclusion of exposure. Arterial and venous blood samples (approximately 0.5 g) for TRI assay were taken straight from the catheters into 25-ml glass bottles. Preceding studies on solvents provide the details of these techniques (2, 3). A mean value for the concentration of TRI in alveolar air, arterial blood, and venous blood was calculated for each subject and each 30-min period on the basis of the last three measurements.

After conclusion of the four periods of exposure, the concentration of TRI in alveolar air and blood was followed for an additional 2 h. The exact times for sampling are shown in fig. 2 and in the figures describing the results. The final value in each 30-min period for each subject was used in the calculation of the mean values for the relative concentrations 30, 60, 90, and 120 min after the conclusion of exposure.

The ECG was recorded continuously during exposure, and heart rate was determined every other minute from these records. The mean value for the final three determinations during each exposure period was used.

ANALYTICAL METHODS

The volume of expiratory air, the blood lactic acid concentration, and the heart

rate were determined according to methods described in the toluene study (2). The oxygen and carbon dioxide content of expiratory air was determined with an oxygen and a carbon dioxide analyzer (model OM 11 and LB 2, respectively, LKB-Beckman Instr. AB, Vällingby, Sweden), and oxygen uptake was calculated. An analysis was performed on a series of air samples with the previously mentioned automatic analyzers and manually according to the Haldane technique. The mean deviation was -0.444 ± 0.056 (SD) and -0.021 ± 0.046 (SD), respectively. Accordingly, in the analysis of air samples from the experiments, the oxygen concentration was corrected for a systematic deviation of -0.44 . When the analyzers were used on the assays of one and the same air sample, the mean value for the oxygen concentration expressed as the percentage was 17.95 and $SD \pm 0.007$. The corresponding value for the carbon dioxide concentration was 3.09 and $SD \pm 0.005$.

The TRI concentration 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 2.5 % SE 30 on Chromosorb G, 80-100 mesh. The carrier gas flow was 30 ml/min, and the column temperature 75°C . A 1-ml sample was injected.

The TRI concentration in alveolar air was determined 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 0.9 % $\beta\beta$ -oxidipropionitril on Chromosorb G, 80—100 mesh. The carrier gas flow was 30 ml/min, and the column temperature 35°C. A 1-ml sample was injected.

On the basis of the chromatograms the TRI concentration in air was calculated with the aid of standard air samples with known TRI concentrations.

The TRI concentration in blood was determined with a "headspace" method (3). 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 2 % $\beta\beta$ -oxidipropionitril on Chromosorb G, 60—80 mesh. The carrier gas flow was 30 ml/min, and the column temperature 40°C. The concentration of TRI in the "head-space" was calculated on the basis of individual blood samples and standard air samples with known TRI concentrations. The error of the method for a single determination was calculated from 10 double assays of

blood, for which the concentrations ranged from 3.31 to 3.34 mg of TRI/kg of blood and amounted to ± 7.3 % of the mean value.

RESULTS

Pulmonary ventilation and blood circulation

Pulmonary ventilation, oxygen uptake, and heart rate were of ordinary magnitudes during exposure at rest (table 3). During exercise on the bicycle ergometer, no significant differences were obtained for pulmonary ventilation, oxygen uptake, and heart rate during exposure in comparison with the nonexposure values (tables 2 and 3).

During exposure to about 540 mg/m³ of TRI, when compared to that of about 1,080 mg/m³ (table 3), no significant differences were found for pulmonary ventilation, oxygen uptake, and heart rate either at rest or during exercise at an intensity of 50 W (300 kpm/min).

At a work intensity of 50 W (300 kpm/min) the subjects utilized an average of 28 % of their maximal aerobic work

Table 3. Results during rest and exercise with exposure to trichloroethylene in the inspiratory air. Each series lasted 2 h and included 5 subjects; each period (1—4) lasted 30 min (see fig. 1); mean values and standard errors of the means are given. ($\dot{V}_E$ = pulmonary ventilation; $\dot{V}O_2$ = oxygen uptake per unit of time)

Exposure period		Heart rate (beats/min)	$\dot{V}O_2$ STPD (l/min)	Blood lactic acid (mmol/l)	$\dot{V}E$ BTPS (l/min)	TRI concentration			
						Alveolar air (mg/m ³)	Arterial blood (mg/kg)	Venous blood (mg/kg)	
Series I									
1	540 mg/m ³ rest	67±3	0.30±0.01	2.1±0.5	9.6±0.4	124±9	1.1±0.1	0.6±0.1	
2	1,080 mg/m ³ rest	67±4	0.30±0.01	2.0±0.4	10.2±0.5	280±18	2.6±0.0	1.4±0.3	
3	540 mg/m ³ 50 W	98±5	0.94±0.04	2.4±0.4	25.5±0.4	245±12	2.7±0.2	1.7±0.4	
4	1,080 mg/m ³ 50 W	102±6	0.95±0.03	1.5±0.3	26.0±0.4	459±44	6.0±0.2	3.3±0.8	
Series II									
1	540 mg/m ³ rest	64±7	0.31±0.01	1.9±0.2	10.9±0.8	127±11	1.3±0.1	0.5±0.1	
2	540 mg/m ³ 50 W	97±5	1.00±0.03	2.2±0.4	25.2±0.6	218±7	2.8±0.1	1.8±0.3	
3	540 mg/m ³ 50 W	99±6	1.00±0.04	1.5±0.2	25.9±1.0	234±12	3.1±0.3	2.2±0.4	
4	540 mg/m ³ 50 W	100±7	1.01±0.03	2.0±0.2	26.0±1.0	244±16	3.3±0.3	2.2±0.4	
Series III									
1	1,080 mg/m ³ rest	68±6	0.36±0.02	2.1±0.3	10.6±0.2	212±7	2.1±0.2	1.2±0.1	
2	1,080 mg/m ³ 50 W	90±5	1.02±0.02	1.7±0.1	24.2±0.7	407±30	5.2±0.5	2.9±0.7	
3	1,080 mg/m ³ 100 W	121±6	1.65±0.03	2.1±0.4	37.6±1.4	542±33	7.5±0.7	4.8±1.1	
4	1,080 mg/m ³ 150 W	146±5	2.34±0.05	3.1±0.6	54.3±3.1	651±53	9.0±1.0	7.4±1.1	

Table 4. Amount of trichloroethylene in milligrams in the inspiratory air and amount taken up per each 30-min period and after 2 h of exposure to approximately 540 and 1,080 mg/m³ of TRI in inspiratory air during rest and exercise; mean values and standard errors of the means are given. Each series lasted 2 h and included 5 subjects; each period (1—4) lasted 30 min.

Exposure period	Given amount (mg)	Taken up amount (mg)	Uptake in % of given amount
Series I			
1 540 mg/m ³ rest	149 ± 6	79 ± 4	53 ± 2
2 1,080 mg/m ³ rest	313 ± 15	156 ± 9	50 ± 2
3 540 mg/m ³ 50 W	395 ± 6	160 ± 5	40 ± 2
4 1,080 mg/m ³ 50 W	803 ± 12	308 ± 16	38 ± 2
1—4	1,681 ± 26	702 ± 31	45 ± 2
Series II			
1 540 mg/m ³ rest	155 ± 13	81 ± 7	52 ± 2
2 540 mg/m ³ 50 W	390 ± 10	179 ± 2	46 ± 1
3 540 mg/m ³ 50 W	401 ± 16	157 ± 2	39 ± 2
4 540 mg/m ³ 50 W	402 ± 15	147 ± 9	37 ± 2
1—4	1,348 ± 41	565 ± 8	44 ± 1
Series III			
1 1,080 mg/m ³ rest	322 ± 3	186 ± 7	58 ± 2
2 1,080 mg/m ³ 50 W	749 ± 21	378 ± 18	51 ± 3
3 1,080 mg/m ³ 100 W	1,164 ± 42	418 ± 39	36 ± 3
4 1,080 mg/m ³ 150 W	1,672 ± 92	419 ± 84	25 ± 5
1—4	3,907 ± 151	1,402 ± 307	42 ± 3

Fig. 3. The amount of trichloroethylene (TRI) supplied and taken up in one subject during exposure to approximately 540 and 1,080 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at an intensity of 50 W (300 kpm/min). The total amount taken up in 2 h amounted to 688 mg, i.e., about 42 % of the 1,646 mg supplied. Approximately 57 % was taken up during the first period and about 30 % during the final period.

Fig. 4. The amount of trichloroethylene (TRI) supplied and taken up in one subject during exposure to approximately 540 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at an intensity of 50 W (300 kpm/min). The total amount taken up in 2 h amounted to 542 mg, i.e., about 41 % of the 1,315 mg supplied. Approximately 56 % was taken up during the first period and about 30 % during the final period.

power (max $\dot{V}O_2$). At 100 W (600 kpm/min) and 150 W (900 kpm/min) they utilized about 47 and 66 %, respectively. These percentage figures, like the lactic acid concentrations in blood during exercise at the corresponding intensities, suggest that 50 W can be regarded as relatively light work for these subjects, 100 W as moderately heavy work, and 150 W as heavy work. All the subjects completed the different 30-min periods with no unpleasant effects from exposure.

No significant ECG changes were recorded at rest or during exercise. Thus the incidence of ectopic beats did not increase during exposure, when compared to that during nonexposure.

Samples were taken for checks on changes in carboxyhemoglobin concentrations in view of the fact that other chlorinated hydrocarbons are known to induce an increase (4, 6). The blood after exposure did not contain any more carboxyhemoglobin than before exposure.

Uptake in the organism

The amount of TRI taken up in the organism was calculated on the basis of mea-

surements of the TRI concentration and the volume of inspiratory and expiratory air during exposure (table 4). One example from each series of experiments is shown in figs. 3, 4 and 5. Uptake at rest amounted to about 80 mg in 30 min during low exposure (series I and II) and to about 170 mg during high exposure (series III); it constituted about 55 % of the amount supplied.

The percentage uptake dropped to about 40 % during work at an intensity of 50 W (fig. 3). The uptake declined successively with exposure to a low level during work at an intensity of 50 W for 1.5 h (fig. 4). It amounted to about 180 mg during period 2, dropping to 160 mg and 150 mg in periods 3 and 4, respectively, and constituted 45, 40 and 35 %, respectively, of the amount supplied (table 4).

Uptake rose from about 185 mg at rest to 380 mg during period 2 and to about 420 mg during periods 3 and 4 with exposure to 1,080 mg/m³ during rest and during increasing work intensity (fig. 5). In relative terms, there was a drop in the percentage uptake from about 60 % at rest to 25 % during work of the amount supplied (table 4).

Fig. 5. The amount of trichloroethylene (TRI) supplied and taken up in one subject during exposure to approximately 1,080 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at intensities of 50, 100 and 150 W (300, 600 and 900 kpm/min). The total amount taken up in 2 h amounted to 879 mg, i.e., about 23 % of the 3,789 mg supplied. Approximately 57 % was taken up during the first period and about 6 % during the final period.

Fig. 6. The concentration of trichloroethylene (TRI) in the alveolar air and the arterial and the venous blood of one subject during and after exposure to approximately 540 and 1,080 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at an intensity of 50 W (300 kpm/min). This is the same experiment as in fig. 3. (V_E = pulmonary ventilation in l/min)

The variation in the percentage uptake between different subjects was relatively slight during the first periods. However, in all three series it was greater in the fourth period than in the other periods. Uptake variation was the greatest during period 4 in series III, i.e., after 1.5 h of exposure to a high concentration during increasing work intensity. In fig. 5 the results are given from one subject who displayed a very slight uptake at the end of the fourth period.

Alveolar air and arterial blood concentration of trichloroethylene during exposure

The concentration in alveolar air amounted to about 125 mg/m³ and corresponded to about 23 % of the concentration in inspiratory air after 30 min of exposure at rest to about 540 mg/m³ of TRI in inspiratory air (table 3, series I and II). The corresponding arterial blood concentration was about 1.2 mg/kg. During work at an intensity of 50 W pulmonary ventilation was about 2.5 times greater than at rest, and the alveolar

concentration was almost twice as great as at rest. The arterial blood concentration more than doubled under the corresponding conditions (table 3, fig. 6).

During rest in exposure to about 1,080 mg/m³ of TRI in inspiratory air (series I and III), the alveolar air concentration and the arterial blood concentration were about doubled in comparison to the values during exposure to half that concentration (table 3). During work with an intensity of 50 W, alveolar air and arterial blood concentrations increased in about the same way as in exposure to 540 mg/m³ (fig. 6).

During work with intensities of 50, 100 and 150 W (series III) pulmonary ventilation increased from about 11 l/min at rest to about 24, 38 and 54 l/min, respectively. The alveolar concentration rose from about 210 to 405, 540 and 650 mg/m³, respectively, corresponding to 20, 40, 50 and 60 %, respectively, of the concentration in inspiratory air (table 3). The corresponding arterial blood concentrations rose from about 2.1 to 5.2, 7.5 and 9.0 mg/kg of blood, respectively (table 3). In fig. 7 the results are given from one subject with a relatively poor uptake.

During all exposure periods the increase

Fig. 7. The concentration of trichloroethylene (TRI) in the alveolar air and in the arterial and the venous blood of one subject during and after exposure to approximately 1,080 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at intensities of 50, 100 and 150 W (300, 600 and 900 kpm/min). This is the same experiment as in fig. 5. ($\dot{V}_E$ = pulmonary ventilation in l/min)

Fig. 8. The concentration of trichloroethylene (TRI) in the alveolar air and in the arterial and the venous blood of one subject during and after exposure to approximately 540 mg/m³ of TRI in inspiratory air. Exposure was provided both at rest and during exercise at an intensity of 50 W (300 kpm/min). This is the same experiment as in fig. 4. ($\dot{V}_E$ = pulmonary ventilation in l/min)

in alveolar air and arterial blood concentrations tended to decline towards the end when compared to that in the beginning of the periods. This leveling off in concen-

tration was the most apparent during the third and fourth periods of constant exposure to 540 mg/m³ (series II, fig. 8).

In fig. 9 the relationship is shown between arterial blood and alveolar air concentrations at the end of each exposure period for all subjects. The relationship was linear, and the arterial blood concentration was closely correlated to the alveolar air concentration.

Fig. 9. The relationship between the concentration of trichloroethylene in arterial blood and alveolar air at the end of each exposure period both at rest and during exercise. Each symbol stands for one exposure period, i.e., one subject is represented by four symbols. Symbols: Δ rest 540 mg/m³; $\blacktriangle$ rest 1,080 mg/m³; $\circ$ 50 W 540 mg/m³; $\bullet$ 50 W 1,080 mg/m³; $\square$ 100 W 1,080 mg/m³; $\blacksquare$ 150 W 1,080 mg/m³; $\star$ 50 W 540 mg/m³ 60 min; $\star$ 50 W 540 mg/m³ 90 min. (Regression line $y = -0.489 + 0.014 x$)

Venous blood concentration and arteriovenous trichloroethylene difference during exposure

The concentration in peripheral venous blood at the end of the resting exposures amounted to about half of the corresponding arterial concentration (table 3). During work with an intensity of 50 W the concentrations rose to about 60 % of the arterial concentrations and during the intensities of 100 and 150 W to 65 and 80 %, respectively. The absolute arteriovenous difference (mg/kg of blood) increased during work with the intensities of 50 and 100 W. However, at the highest intensity of 150 W, there was a pronounced decline (table 3, fig. 7).

Cardiac output may be estimated to be about 5 l/min at rest and to rise to 10, 13.5 and 18 l/min during the work intensities of 50, 100 and 150 W, respectively (1, 3). On the basis of these values and the respective arteriovenous differences, the release from blood to other organs, i.e., total uptake, could be calculated for each 30-min period. These calculations gave results of uptake at rest that were in relatively close agreement with the exact measurements made via the respiration. During work, however, the estimated value was always higher than the measured value. Thus the estimated value for resting uptake amounted to 73–148 % of the measured value, whereas the corresponding estimated value during work amounted to 115–263 % of the measured value. The lack of agreement between measured and

estimated values was probably caused by the fact that peripheral venous blood did not contain the same amount of TRI as central venous blood. This problem was pointed out in previous studies. The redistribution of cardiac output at the transition from rest to work may also have played a role.

Excretion of trichloroethylene after exposure

Figs. 6, 7 and 8 show that the concentration of TRI in alveolar air and arterial and venous blood dropped very rapidly after the conclusion of exposure. However, 30 min after exposure, the rate of excretion was much slower than at the start (table 5). All the subjects had TRI in their alveolar

Table 5. The concentration of trichloroethylene in the alveolar air and blood of 15 male subjects after exposure; there were five subjects in each series; mean values and the standard errors of the means are given. (Series I: exposure to 540 and 1,080 mg/m³ at rest and during 50 W; series II: exposure to 540 mg/m³ at rest and during 50 W; series III: exposure to 1,080 mg/m³ at rest and during 50, 100 and 150 W)

Series	TRI concentration		
	Alveolar air (mg/m ³)	Arterial blood (mg/kg)	Venous blood (mg/kg)
I			
end of exposure	459 ± 44	6.0 ± 0.2	3.3 ± 0.8
after 30 min	70 ± 5	1.2 ± 0.2	1.3 ± 0.2
» 60 »	40 ± 4	0.6 ± 0.1	0.7 ± 0.1
» 90 »	35 ± 9	0.4 ± 0.0	0.6 ± 0.0
» 120 »	31 ± 8	0.3 ± 0.0	0.5 ± 0.0
» about 300 min	8 ± 1		
» » 420 »	5 ± 0.5		
» » 19 h	2 ± 0.3		
II			
end of exposure	244 ± 16	3.3 ± 0.3	2.2 ± 0.4
after 30 min	51 ± 3	0.8 ± 0.0	0.9 ± 0.1
» 60 »	28 ± 2	0.4 ± 0.0	0.5 ± 0.1
» 90 »	21 ± 1	0.3 ± 0.0	0.5 ± 0.1
» 120 »	16 ± 1	0.2 ± 0.0	0.4 ± 0.0
» about 300 min	9 ± 2		
» » 420 »	4 ± 0.5		
» » 19 h	2 ± 0.2		
III			
end of exposure	651 ± 53	9.0 ± 1.0	7.4 ± 1.1
after 30 min	105 ± 18	1.7 ± 0.2	2.4 ± 0.4
» 60 »	69 ± 8	1.0 ± 0.1	1.4 ± 0.2
» 90 »	55 ± 2	0.8 ± 0.0	1.1 ± 0.1
» 120 »	45 ± 1	0.7 ± 0.0	0.9 ± 0.1
» about 300 min	14 ± 2		
» » 420 »	8 ± 1.3		
» » 19 h	4 ± 0.5		

air about 19 h later. Table 5 shows that the intersubject spread in concentrations was great on every measurement occasion. It should be noted that the values in table 5 are grouped according to the degree of exposure. In each group all subjects were exposed in exactly the same manner. No assessment of the degree of exposure, made on the basis of alveolar air samples (one or more), can be reliable because of the normally wide spread in intersubject findings. This was also pointed out in the previous studies (1). Stewart et al., however, concluded from their experiments that breath analysis is a superior method for monitoring workplace exposure (13, 14, 15, 16).

Vesterberg et al. discusses other forms of TRI excretion in part II of this article (17).

DISCUSSION

The amount of TRI taken up by the body was about 55 % of the amount supplied at rest irrespective of the degree of exposure. During the final period with a high exposure and the highest work intensity (150 W) uptake dropped to about 25 %. The resting uptake was in close agreement with the uptakes of 58 and 64 % found in the literature (5, 12). However, the percentage uptake declined as work intensity increased. In other words at higher work loads the rate of diffusion to the blood from the alveoli was slower than the rate of supply to the alveoli.

The relatively slow rate of diffusion can be explained in several ways, the most significant of which is the relative insolubility of TRI in blood. The partition coefficient for blood/air is approximately 9 (1, 8). (The term "partition coefficient" refers to the ratio of concentrations of a substance in two immiscible phases at equilibrium and 37° C.) The corresponding coefficient for styrene is for example 32. The relatively poor solubility of TRI in blood is also reflected by the fact that the alveolar concentration during the course of exposure increased as the arterial blood concentration increased.

However, the results reported in figs. 5 and 7 suggest that the solubility in tissues also affects uptake. The rate of diffusion

from arterial blood to the tissues dropped sharply during the last period. This drop is particularly apparent in the results shown for the subject in the figures. As uptake dropped from 12 % to 1 % during that period, the concentration rose in venous blood. At the close of the period the TRI concentration in venous blood approached the concentration in arterial blood; this phenomenon suggests imminent saturation of the tissues. The alveolar content was relatively high throughout the period.

As saturation approaches, the venous concentration rises and ultimately becomes as high as the arterial concentration. The uptake in the lungs drops simultaneously with an attendant increase in the alveolar concentration and results in turn in a higher arterial blood concentration, etc.

The values illustrated in figs. 5 and 7 were obtained from a subject with a relatively light body weight and a relatively high physical work capacity per kilogram of body weight (max $\dot{V}O_2/\text{min} = 51 \text{ ml/kg}$). Therefore his body fat made up only a relatively small proportion of his body weight, and this probably contributed to early saturation in his case.

All three factors, i.e., relatively poor solubility in blood, relatively poor solubility in the tissues, and a small amount of total body fat in all subjects, probably contributed to the percentage drop in uptake during the course of exposure.

The ratio between arterial blood concentration and alveolar air concentration increased from 10 to 15 during the course of exposure. In other words the partition coefficient obtained under the existing circumstances was relatively stable, i.e., neither high nor low (1), and corresponds to a substance with neither poor nor high solubility in blood and tissues. TRI was the fourth in solubility among the seven substances examined hitherto (1).

The uptake of TRI can be estimated with relatively high accuracy by measurement of the concentration in alveolar air and inspiratory air and measurement or approximation of pulmonary ventilation (1, 10). The arterial concentration can be estimated from the concentration in alveolar air. Both these biological measurement methods should serve as excellent supplements to conventional measurements of the content in ambient air.

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