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Key terms: alipahtic hydrocarbon; alveolar air; aromatic hydrocarbon; blood; concentration; exercise; exposure; human experiment; rest; toxicology; white spirit

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Exposure to white spirit
I. Concentration in alveolar air and blood during rest and exercise

by IRMA ÅSTRAND, M.D., ÅSA KILBOM, M.D., and PER ÖVRUM, M.Sc.[1]

ÅSTRAND, I., KILBOM, Å. and ÖVRUM, P. Exposure to white spirit: I. Concentration in alveolar air and blood during rest and exercise. *Scand. j. work environ. & health* 1 (1975) 15—30. Fifteen healthy male subjects were exposed to 1,250 and 2,500 mg/m^3 of white spirit in inspiratory air during rest and excercise on a bicycle ergometer. The white spirit contained approximately 83 % aliphatic and 17 % aromatic components. The duration of each exposure period was 30 minutes. The pulmonary ventilation, the cardiac output, and the concentration of white spirit (subdivided into aromatic and aliphatic components) in alveolar air, arterial blood, and venous blood were determined during and after exposure. The concentration of aliphatic and aromatic components in alveolar air tended to level off towards the close of each period. The resting level of the aromatic components increased approximately 2.0 times, and that of aliphatic components about 2.5 times, during exercise with increased intensities. The concentration of aliphatic components in arterial and venous blood increased at the start of each exposure period but tended to level off towards the close of the period. The resting value increased fourfold in work at the highest intensity. However, the concentration of aromatic components rose sharply during each period. The arterial blood concentration was about 15 times higher at the end of exposure during the heaviest exercise intensity than at rest. Pulmonary ventilation appeared to be more important to uptake in arterial blood than to circulation. The results are believed to be due to the differing solubilities of aliphatic and aromatic components in blood. Measurement of the concentration of white spirit in venous or arterial capillary blood is suggested as a biological check on exposure.

Key words: toxicology, human experiment, aromatic hydrocarbons, aliphatic hydrocarbons, white spirit.

White spirit, mineral spirit, or ligroin is a very common solvent. It is employed as a cleaning agent in the home and in the care of cars and bicycles. It is widely used as a scourer in the manufacturing industry. It is also used in the painting trade, in which dangers of exposure to white spirit have been debated. Some people even feel that the effect of exposure is sufficient to warrant a ban on the substance.

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White spirit has only rarely been studied with respect to its effect on man and animals (5). The effect of sniffing similar solvents has been described in Sweden (6).

White spirit is mainly a mixture of aliphatic and aromatic hydrocarbons. The number of components and their mutual proportions vary, one possible reason why no threshold limit value has been set for white spirit.

The white spirit most commonly sold in Sweden consists of 83 % aliphatic and 17 % aromatic components. It was the white spirit used throughout the examinations described in this article.

SUBJECTS

Fifteen men 20 to 34 years of age served as subjects. They were all students or employees of the Department of Occupational Medicine.

The subjects were given careful clinical examinations, in which particular attention was devoted to the function of respiratory and circulatory organs. Lung function was tested with a Bernstein spirometer and using the helium dilution technique. Exercise tests were performed on a bicycle ergometer (Monark, Varberg, Sweden) at a number of submaximal and one maximal exercise intensity in which electrocardiograms (ECGs) were recorded and oxygen uptakes measured. The same method was used as in previous studies of toluene (1), methylchloroform (3), and styrene (2).

All subjects were healthy at the time of the examination, and none had ever suffered from any disease which might have had a detrimental effect on respiratory or circulatory organs. Values for hemoglobin concentration, hematocrit, and erythrocyte sedimentation rate were within normal limits for all subjects. The lung function tests were also normal (table 1).

Table 2 indicates mean values for measurements made in conjunction with exercise on a bicycle ergometer without exposure. Values from submaximal and maximal exercise were normal and not significantly different from the values of previous studies (1, 2, 3). The differences in subject response to different solvents may therefore not be ascribed to physiological differences in subjects. Three subjects developed occasional ectopic beats in their ECGs in conjunction with exercise. Otherwise, there were no ECG changes of any importance.

EXPERIMENTAL DESIGN

At present no threshold limit value has been set for white spirit in air. It was therefore difficult to select the levels of exposure. In initial trials subjective discomfort in the form of nausea, vertigo, and a feeling of being severely affected appeared at an exposure to 5,000 mg/m^3. Symptoms even appeared at 2,500 mg/m^3, although to a lesser degree. We decided to expose subjects to levels from 1,000 to 2,500 mg/m^3 in air so as to avoid severe subjective discomfort, since these concentrations still permit an accurate analysis of the content in alveolar air and blood.

Table 1. Anthropometric and respiratory data from resting measurements of 15 male subjects 20 to 34 years of age. Mean values ± their standard errors are given.

Body height cm	Body weight kg	Vital capacity l	Residual volume l	Forced expiratory volume %	Maximum voluntary ventilation l/min
179 ± 1	74.5 ± 1.6	5.9 ± 0.2	1.6 ± 0.1	82 ± 2	184 ± 9

Table 2. Results from submaximal and maximal exercise on a bicycle ergometer without exposure to white spirit. Mean values ± their standard errors are given. ($\dot{V}_E$ = pulmonary ventilation per unit of time; $\dot{V}O_2$ = oxygen uptake per unit of time)

Work load W	No. of subjects	Heart rate beats/min	$\dot{V}_E$ BTPS l/min	$\dot{V}O_2$ STPD l/min	Blood lactate mmol/l
50	15	94 ± 2	27.4 ± 0.8	1.02 ± 0.01	1.9 ± 0.2
100	15	114 ± 3	40.2 ± 1.0	1.56 ± 0.02	2.3 ± 0.2
150	15	138 ± 4	58.4 ± 1.5	2.24 ± 0.03	4.3 ± 0.4
Maximal exercise	15	185 ± 3	156.7 ± 6.4	3.78 ± 0.11	16.6 ± 0.5

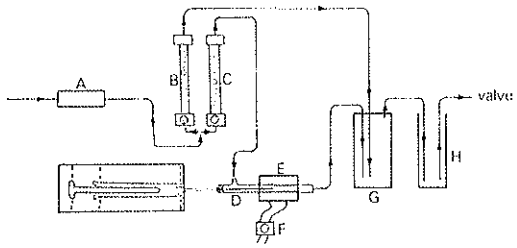


Fig. 1. The vapor was produced as follows: Compressed air was passed through a charcoal filter (A) to two rotameters (B and C) connected in parallel, both supplied with valves for the regulation of air flow. Air from one rotameter (C) passed through a glass tube (D) which was partially located in a tube heater whose output could be regulated with a rotary transformer (F). With an infusion device (Unita 1, Braun Melsungen Apparatebau, Laboratorieinstrument Skafte & Claesson AB, Göteborg, Sweden), adjustable for different piston speeds for 5 or 50 ml syringes, solvent could be injected into the warm zone of the glass tube where it was vaporized in the air passing through the tube. The air passing the rotameters (B and C) was mixed in a closed vessel (G) and passed via a tube to the bottom of a cylinder (H) from which inspiratory air was drawn into the breathing valve with the aid of a metal tube. Air containing white spirit was supplied to the cylinder (H) at a rate of about 60 l/min. This volume was never less than a subject's pulmonary ventilation. The device was located in a fume cupboard, and surplus vapor was exhausted.

The air mixture was prepared in a manner similar to the method used in previous studies (fig. 1).

The concentration of white spirit in inspiratory air was continuously monitored with a gas indicator (Hydrocarbon analyser, Model 116, Scott Research Lab. Inc., Plumsteadville, Pa., U.S.A.). The production of a certain white spirit concentration (with 83 % aliphatic and 17 % aromatic components) was accurate enough to provide contents which varied from 1,200 to 1,300 mg/m^3 at an intended content of 1,250 mg/m^3 and from 2,450 to 2,550 mg/m^3 at an intended content of 2,500 mg/m^3. All air concentrations are henceforth stated in mg/m^3 at 25°C unless otherwise specified.

The trials were generally conducted in the same manner as in previous studies. They started with the introduction of catheters into a brachial artery and a medial cubital vein. Exposure then took place at rest and during submaximal exercise on a bicycle ergometer. Each exposure period comprised 30 minutes, and each subject was exposed for four periods at each session.

Five subjects were exposed to both approximately 1,250 and 2,500 mg/m^3 of white spirit in inspiratory air at rest (30 + 30 min) and during exercise (30 + 30 min) at an intensity of 50 W (300 kpm/min). Fifty watts corresponds to about the intensity found in light physical vocational work (4).

Four subjects were exposed to approximately 1,250 mg/m^3 of white spirit in inspiratory air during rest (30 min) and during exercise (30 + 30 + 30 min) at intensities of approximately 50 W (300 kpm/min), 100 W (600 kpm/min), and 150 W (900 kpm/min).

Two subjects were exposed to approximately 2,500 mg/m^3 of white spirit in ordinary air and to approximately 2,500 mg/m^3 in an air mixture consisting of 21 % oxygen, 4 % carbon dioxide, and 75 % nitrogen during rest (30 + 30 min) and during exercise (30 + 30 min) at an intensity of 50 W (300 kpm/min).

Two subjects were exposed to 1,250 mg/m^3 of white spirit in inspiratory air during rest (30 min) and during exercise (30 + 30 + 30 min) at an intensity of 100 W (600 kpm/min).

Two subjects were exposed to approximately 1,000, 1,250, 1,500, and 2,000 mg/m^3 of white spirit in inspiratory air at rest (30 + 30 + 30 + 30 min).

The sequence of the different exposure periods in each type of trial was always the same and is shown in the figures in the section reporting results. Fig. 2 shows the layout of each exposure period.

Alveolar air samples were collected in a glass syringe from a breathing valve during exposure and in glass tubes after exposure. Arterial and venous blood samples were taken from the catheters and collected in 15 ml glass bottles. Previous studies present the details of the technique used (1, 2, 3). The mean value of the last two determinations in each exposure period was used for the concentration in alveolar air and for the

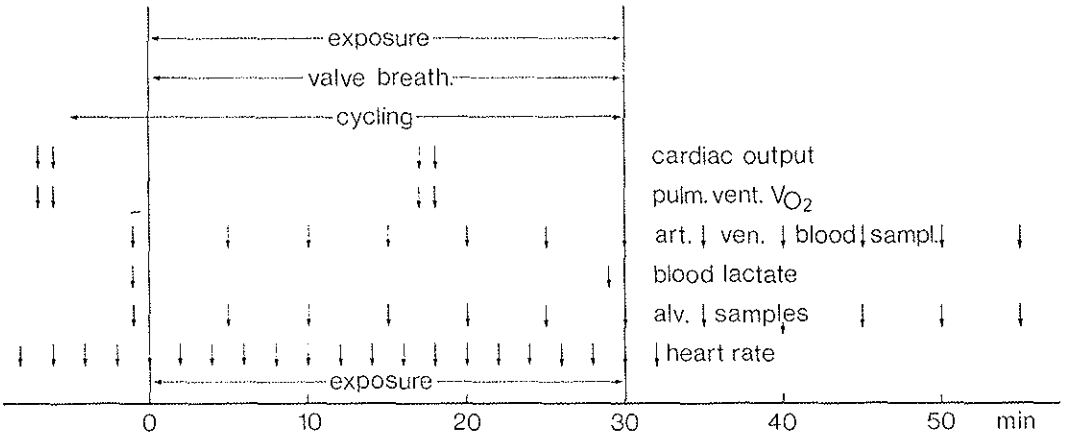


Fig. 2. Times at which cycling was started and at which different measurements and samplings were taken before, during, and after a 30-minute exposure period.

aliphatic components in blood. However, for the aromatic concentration in blood the final value was stated when it was also the highest value, as was almost always the case. Otherwise, the mean value of the last two values was stated.

Heart rate was determined using ECG recordings. The mean value of the three final determinations in each exposure period was used. Blood samples for lactic acid assay were taken at the end of each exercise period.

The oxygen uptake and the volume of expiratory and alveolar air were determined with the Douglas bag method after about 20 minutes of each exposure period.

Cardiac output was determined for six subjects. A double determination was made during rest prior to exposure and after about 20 minutes during each exposure period, both during rest and exercise. The mean value was used.

The volume of expiratory air was continuously measured in bags (specially made of polyester-laminated aluminium foil) for four subjects throughout their entire exposure, i.e., for 2 hours, and the air's white spirit content was assayed. The volume of inspiratory air was estimated as being the same as the volume of expiratory air (no more than 1 % error), and the organism's uptake of white spirit, divided into the two components, was calculated as the difference between the total amounts in inspiratory and expiratory air. The measurements were taken from two subjects exposed to 1,250 and 2,500 mg/m^3 of white spirit during rest and during exercise at an intensity of 50 W (300 kpm/min) and using two subjects exposed at rest to 1,000, 1,250, 1,500 and 2,000 mg/m^3.

After four completed periods of exposure the concentration of white spirit in the form of aliphatic and aromatic components in alveolar air and blood was followed until their levels were under the limit of detection, i.e., generally after 1 more hour. The exact times for samplings are shown in the figures.

ANALYSIS METHODS

Respiratory volumes, blood lactate, and heart rate were determined according to the methods described in a previous study on toluene (1). The oxygen and carbon dioxide contents of expiratory air were determined using an oxygen analyzer (Beckman model E2) and a carbon dioxide analyzer (Beckman LB2), respectively, and oxygen uptake was calculated. A series of air samples was assayed with the aforementioned automatic analyzers and the manual Haldane technique. The mean deviation amounted to 0.00 % with a standard deviation of 0.06 % and to −0.08 % with a standard deviation of 0.04 %, respectively. Ten assays were made

with the automatic analyzers on one and the same air sample with an oxygen content in the 16 to 21 % measurement range. The mean value for the oxygen content expressed in percentage was 17.62 with a standard deviation of 0.02 %. The corresponding value for the carbon dioxide content was 3.59 % with a standard deviation of ± 0.03 %.

Respiratory rate was recorded with the aid of a heat receptor located in the breathing valve, and tidal air was calculated. Dead space in subjects, including the valve, was estimated at 150 cm^3, and alveolar ventilation was calculated. No correction was made for any larger dead space during exercise, since differences are small at the measured ventilations.

Cardiac output was determined by using the dye dilution technique in the same manner as in a methylchloroform study (3). In our view the blood loss (approximately 100 ml) in conjunction with these measurements, including the loss arising in blood sampling, had no effect on results. For the errors of the methods which are not specifically indicated Kilbom (9) can be consulted.

The white spirit content in blood was determined with a head space method (3) and a gas chromatograph (Model F 30, FID, Perkin-Elmer Ltd., Beaconsfield, Buckinghamshire, England) fitted with a stainless steel column (1 m long, 2.2 mm inner diameter) packed with 0.75 % $\beta\beta$-oxidiproprionitrile on chromosorb G (80—100 mesh). The carrier gas flow (N_2) was 30 ml/min, and the column temperature 45°C. The error of the method for a single determination was calculated from double determinations on blood with contents from 1 to 4 mg/kg of blood and was ±0.15 mg/kg or 8.3 % of the mean value (1.85 mg/kg).

The contents in air were determined with a gas chromatograph (Model F 11, FID, Perkin-Elmer Ltd., Beaconsfield, Buckinghamshire, England) supplied with a stainless steel column (0.7 m long, 2.2 mm inner diameter) packed with 0.75 % $\beta\beta$-oxidiproprionitrile on chromosorb G (80—100 mesh). The column temperature was 25°C.

The stationary phase used was well suited to the task of separating aromatic components from other hydrocarbons (aliphates, olefins). Aromatic hydrocarbons have a relatively long retention time in this stationary phase. All n-aliphates up to and including undecane (boiling point 196°C) emerge before xylene in the chromatogram. Therefore it is possible to distinguish aromatic compounds from most of the other components in white spirit with boiling points between 150 to 200°C (fig. 3).

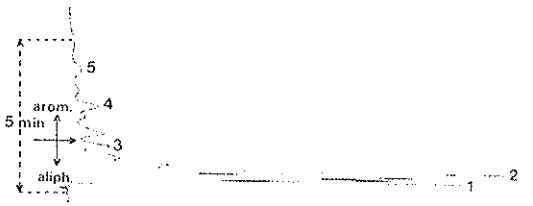


Fig. 3. Chromatogram for white spirit (Perkin-Elmer F 11, FID, column length 0.7 m, inner diameter 2.2 mm, 0.75 % $\beta\beta$-oxidipropionitrile on chromosorb G, 80—100 mesh, T = 30°C, 0.75 ml injected by a standard gas at 976 mg/m^3). The arrow following peak 3 represents the borderline between aromatic and nonaromatic components. (Peak 1 = n-nonane, peak 2 = n-decane, peak 3 = n-undecane, peak 4 = pseudocumene and peak 5 = 1, 2, 3 trimethylbenzene)

In an effort to facilitate assays and calculations we allowed n-decane (b.p. 174°C) to represent nonaromatics and pseudocumene (1, 2, 4 trimethylbenzene, b.p. 169°C) to represent aromatics. Both lay within the boiling point interval for the white spirit in question (150—200°C). In the prevailing analytical conditions these components were also relatively well separated from other components, in both blood and expiratory air.

The white spirit used in the experiments contained 17 % aromatic components, including 1, 2, 4 trimethylbenzene (pseudocumene), n-propylbenzene, mesitylene, and 1, 2, 3 trimethylbenzene. Gas chromatographic analysis of white spirit from different oil companies (Esso Varnolene, Texaco White Spirit, Shell kristallolja, Nynäs nafta, BP Renolin, Gulf White Spirit) produced chromatograms which were relatively similar with peaks at the same retention times. However, the ratio between maximun peaks varied somewhat, but the difference between brands was relatively slight.

RESULTS

Pulmonary ventilation and blood circulation

During exercise three subjects displayed occasional atrial premature beats in their ECGs of the same type as during rest. One subject developed atrial premature beats exclusively in conjunction with exposure. One subject displayed gradual flattening and, ultimately, inversion of the T wave during exposure, indicating possible action on the myocardium. This subject displayed no other changes. He had no subjective symptoms, and the ECG picture had normalized at the time of a check made a few days later in conjunction with exercise.

Values for alveolar ventilation, oxygen uptake, and heart rate at rest were of a normal magnitude (table 3). Values during exercise at 100 W (600 kpm/min) and 150 W (900 kpm/min) were not comparable to the corresponding data in table 2. The rise in magnitude found — a mean increase in heart rate for four people of 6 and 10 beats/min, respectively, and a mean increase in oxygen uptake of 0.15 and 0.20 l/min, respectively — often takes place in conjunction with exercise lasting for 30 minutes and was therefore probably not ascribable to exposure (7).

No differences were noted in heart rate, alveolar ventilation, or oxygen uptake either at rest or during exercise at an intensity of 50 W during exposure to 1,250 mg/m^3 and 2,500 mg/m^3 (table 3).

At a work intensity of 50 W the subjects utilized an average of 27 % of their maximal aerobic work power (max $\dot{V}O_2$), at 100 W approximately 46 %, and at 150 W 65 %. Lactate concentration in blood indicated that work loads of 50 and 100 W may be regarded as relatively light exercise and 150 W as moderately heavy exercise (table 3).

Cardiac output was normal at rest and increased in an ordinary manner as work increased, both in exposure to 1,250 mg/m^3 and to 2,500 mg/m^3. These values were of the same magnitude as in previous studies (2, 3).

In two subjects the alveolar ventilation

Table 3. Data from 15 male subjects during rest and exercise with exposure to 0 mg/m^3, about 1,250 mg/m^3 (1,038 parts aliphatic and 212 parts aromatic), and about 2,500 mg/m^3 (2,075 parts aliphatic and 425 parts aromatic) of white spirit. When the number of subjects was < 3, extreme values are given; otherwise the mean value ± its standard error are given. (V_A = alveolar ventilation per unit of time, dead space estimated at 150 cm^3 for all subjects; VO_2 = oxygen uptake per unit of time)

Work load and level of exposure	No. of subjects	$\dot{V}_A$ BTPS l/min	Alveolar conc. aliphatic mg/m^3	Alveolar conc. aromatic mg/m^3	Arterial blood conc. aliphatic mg/kg	Arterial blood conc. aromatic mg/kg	Venous blood conc. aliphatic mg/kg	Venous blood conc. aromatic mg/kg	Heart rate at 25—30/min	VO_2 STPD l/min	Blood lactate conc. mmol/l	No. of subjects	Cardiac output l/min
0 mg/m^3													
rest	6	7.7 ± 0.4	—	—	—	—	—	—	66 ± 5	0.33 ± 0.01	—	6	5.6 ± 0.4
1,250 mg/m^3													
rest	11	8.6 ± 0.3	256 ± 14	27.8 ± 2.5	1.7 ± 0.1	0.2 ± 0.0	1.3 ± 0.2	0.2 ± 0.0	63 ± 3	0.30 ± 0.01	1.4 ± 0.2	2	4.6— 7.6
50 W	9	23.0 ± 1.1	513 ± 54	40.1 ± 7.5	3.5 ± 0.3	0.9 ± 0.1	2.4 ± 0.4	0.6 ± 0.1	93 ± 6	1.03 ± 0.03	1.4 ± 0.1	3	10.0 ± 0.2
100 W	6	40.1 ± 1.9	562 ± 18	43.5 ± 7.6	5.1 ± 0.5	1.7 ± 0.1	3.7 ± 0.7	1.2 ± 0.3	124 ± 5	1.74 ± 0.06	1.9 ± 0.3	2	13.1—14.7
150 W	4	58.6 ± 4.2	622 ± 40	59.1 ± 11.0	6.9 ± 0.3	2.9 ± 0.3	5.4 ± 0.5	2.6 ± 0.3	158 ± 8	2.39 ± 0.09	3.3 ± 0.5	2	18.4—20.9
2,500 mg/m^3													
rest	7	7.2 ± 0.3	563 ± 44	56.4 ± 5.2	3.4 ± 0.3	0.6 ± 0.1	2.2 ± 0.2	0.4 ± 0.1	65 ± 3	0.31 ± 0.01	—	5	5.2 ± 0.4
rest + CO_2	2 a	18.8 ± 20.7	730— 859	78.2—76.5	5.6— 8.3	0.8—1.5	2.1—3.4	0.3—0.7	62—59	0.34—0.29	—	2	6.3— 5.1
50 W	7	23.2 ± 0.9	981 ± 61	74.0 ± 4.9	8.2 ± 0.5	1.9 ± 0.2	6.7 ± 0.3	1.3 ± 0.1	94 ± 6	1.04 ± 0.03	1.3 ± 0.2	4	10.0 ± 0.5
50 W + CO_2	2 a	45.7 ± 52.1	1403—1121	93.5—74.8	8.1—11.0	2.0—4.0	6.6—5.9	1.9—1.7	93—88	1.26—1.10	1.5—2.4	2	11.1—10.8

a The first value stated is always derived from the same subject.

increased from approximately 7 to 20 l/min at rest and from 23 to 49 l/min during cycling at an intensity of 50 W when pulmonary ventilation was increased through the addition of 4 % carbon dioxide (table 3). This increase was not attended by any increase in heart rate, although there was a slight increase in oxygen uptake and cardiac output at a work intensity of 50 W. Thus as blood circulation remained almost unchanged pulmonary ventilation increased sharply.

Alveolar air and arterial blood concentrations during exposure

The concentrations of the two white spirit components in air and blood differed considerably and are therefore reported separately.

Aliphatic components. After a 30-minute exposure at rest to approximately 1,040 mg/m^3 of the aliphatic component in white spirit, the concentration in alveolar air amounted to 255 mg/m^3, i.e., approximately 25 % of the concentration in the inspiratory air (table 3). The corresponding arterial blood concentration was approximately 1.7 mg/kg. When alveolar ventilation about tripled during 50 W exercise, the alveolar concentration increased to about 515 mg/m^3, i.e., about 50 % of the concentration in inspiratory air, whereas the arterial concentration rose to 3.5 mg/kg (fig. 4 a).

In exposure at rest to approximately 2,075 mg/m^3 of the aliphatic component, the concentrations in both alveolar air and arterial blood about doubled those of the lower level of exposure. Alveolar air and arterial blood concentrations in exercise at 50 W approximately doubled those of the resting level, just as in exposure to the lower exposure level (table 3, fig. 4 a).

When exercise intensity was increased successively with an attendant increase in alveolar ventilation to nearly 60 l/min at 150 W, the alveolar concentration rose stepwise to about 60 % of the concentration in inspiratory air (table 3, fig. 5 a). The corresponding arterial concentration was about twice as great as at 50 W.

When alveolar ventilation at rest was increased by adding 4 % carbon dioxide to inspiratory air, the alveolar concentration rose from about 20 % (two subjects) to about 40 % of the level in inspiratory air (table 3, fig. 6 a). During work at an intensity of 50 W and after the addition of 4 % carbon dioxide the alveolar concentration rose from about 50 to 60 % of the level in inspiratory air. The increase in concentration corresponded to the increase obtained through increased alveolar ventilation during exercise while breathing white spirit vapors in ordinary air. Generally speaking, the arterial concentrations paralleled the changes in the composition of alveolar air.

During these different types of experiments, there was a tendency, at least in some subjects, for the increase in alveolar and arterial concentration to slow down towards the end of each period (figs. 4 a, 5 a). This leveling-off became more apparent during protracted exposure (90 min) at a constant exercise intensity of 100 W (fig. 7 a).

Aromatic components. In exposure at rest to approximately 210 mg/m^3 of the aromatic component of white spirit in the inspiratory air, the concentration in alveolar air after 30 minutes amounted to about 30 mg/m^3, i.e., approximately 15 % of the concentration in inspiratory air (table 3). The corresponding arterial blood concentration was approximately 0.2 mg/kg. When alveolar ventilation during 50 W work was tripled, the alveolar concentration increased to about 20 % of the concentration in inspiratory air. This increase for the aromatic components was far less than for the aliphatic components. However, the arterial blood concentration increased far more [from 0.2 to 0.9 mg/kg as compared to 1.7 to 3.5 mg/kg (fig. 4 b)].

In exposure at rest to a content twice as great, i.e., 425 mg/m^3 of the aromatic component in inspiratory air, the alveolar air concentration was about twice as high as in exposure to the lower concentration (table 3). The arterial blood concentration was approximately three times higher. The alveolar air concentration in work at 50 W, as compared to rest, increased from about 27 to 35 % of the

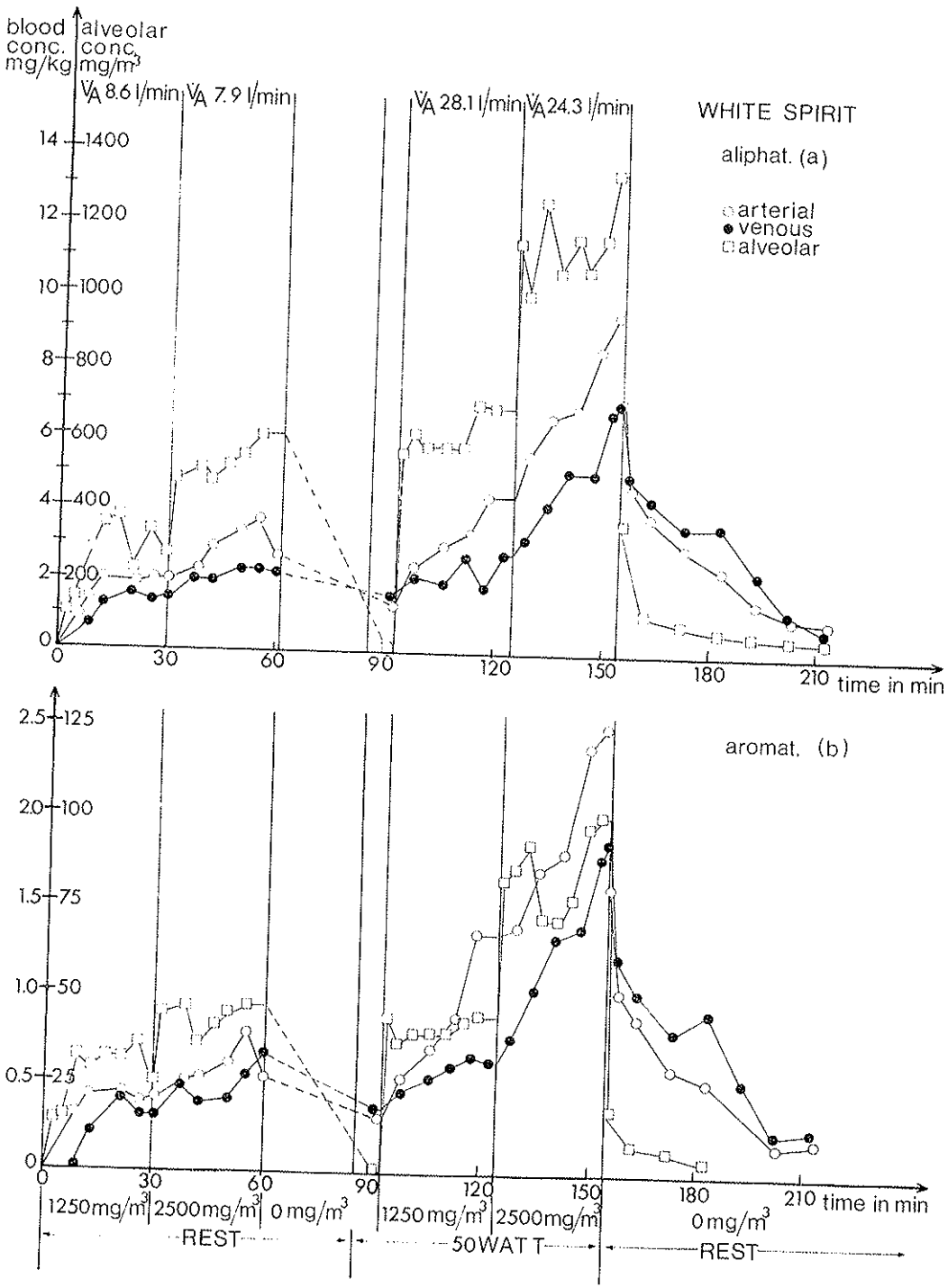


Fig. 4. The concentration of aliphatic (a) and aromatic (b) components of white spirit in alveolar air, arterial blood, and venous blood in one subject during and after exposure to approximately 1,250 and 2,500 mg/m³ of white spirit in inspiratory air. Exposure was provided at rest and during exercise at an intensity of 50 W (300 kpm/min). ($\dot{V}_A$ = alveolar ventilation in l/min)

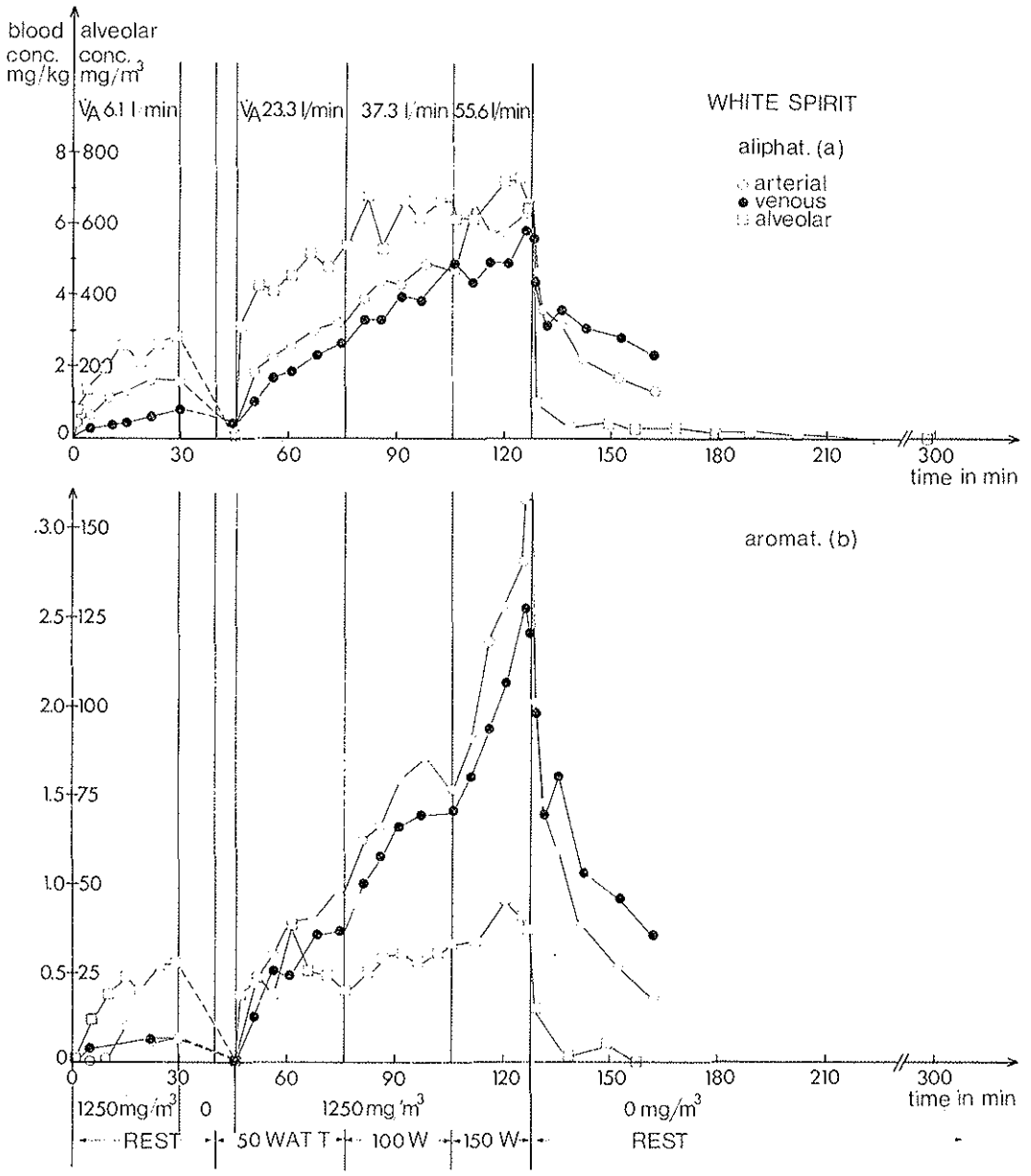
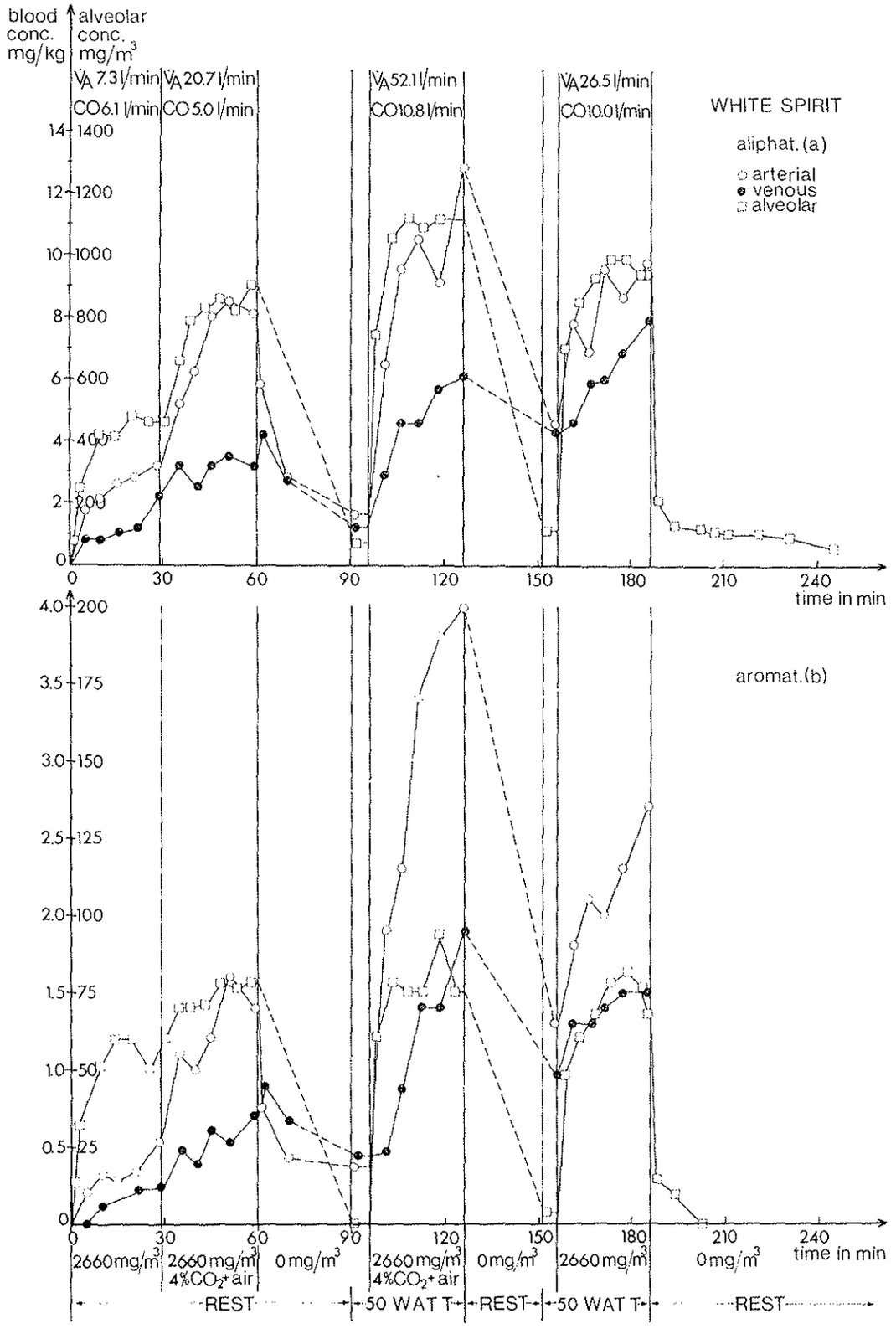


Fig. 5. The concentration of aliphatic (a) and aromatic (b) components of white spirit in alveolar air, arterial blood, and venous blood in one subject during and after exposure to approximately 1,250 mg/m³ of white spirit. Exposure was provided at rest and during exercise at intensities of 50 W, 100 W, and 150 W (300, 600 and 900 kpm/min). ($\dot{V}_A$ = alveolar ventilation in l/min)

inspiratory air concentration, whereas the concentration in arterial blood about tripled (table 3).

With increasing pulmonary ventilation the alveolar concentration increased only slightly, whereas arterial concentration rose steeply; this evolution is a sharp contrast to the corresponding one for the aliphatic components (table 3, fig. 5 b).

With carbon dioxide added the alveolar concentration increased only slightly at rest, whereas the arterial concentration


blood conc. mg/kg
alveolar conc. mg/m³
V̇A 7.3 l/min
CO 6.1 l/min
V̇A 20.7 l/min
CO 5.0 l/min
V̇A 52.1 l/min
CO 10.8 l/min
V̇A 26.5 l/min
CO 10.0 l/min
WHITE SPIRIT
aliphat. (a)
arterial
venous
alveolar
14 1400
12 1200
10 1000
8 800
6 600
4 400
2 200
0
0 30 60 90 120 150 180 210 240
time in min
4.0 200
3.5 175
3.0 150
2.5 125
2.0 100
1.5 75
1.0 50
0.5 25
0
aromat. (b)
0 30 60 90 120 150 180 210 240
time in min
2660 mg/m³
2660 mg/m³ 4%CO₂+air
0 mg/m³
2660 mg/m³ 4%CO₂+air
0 mg/m³
2660 mg/m³
0 mg/m³
REST
50 WAT T
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REST

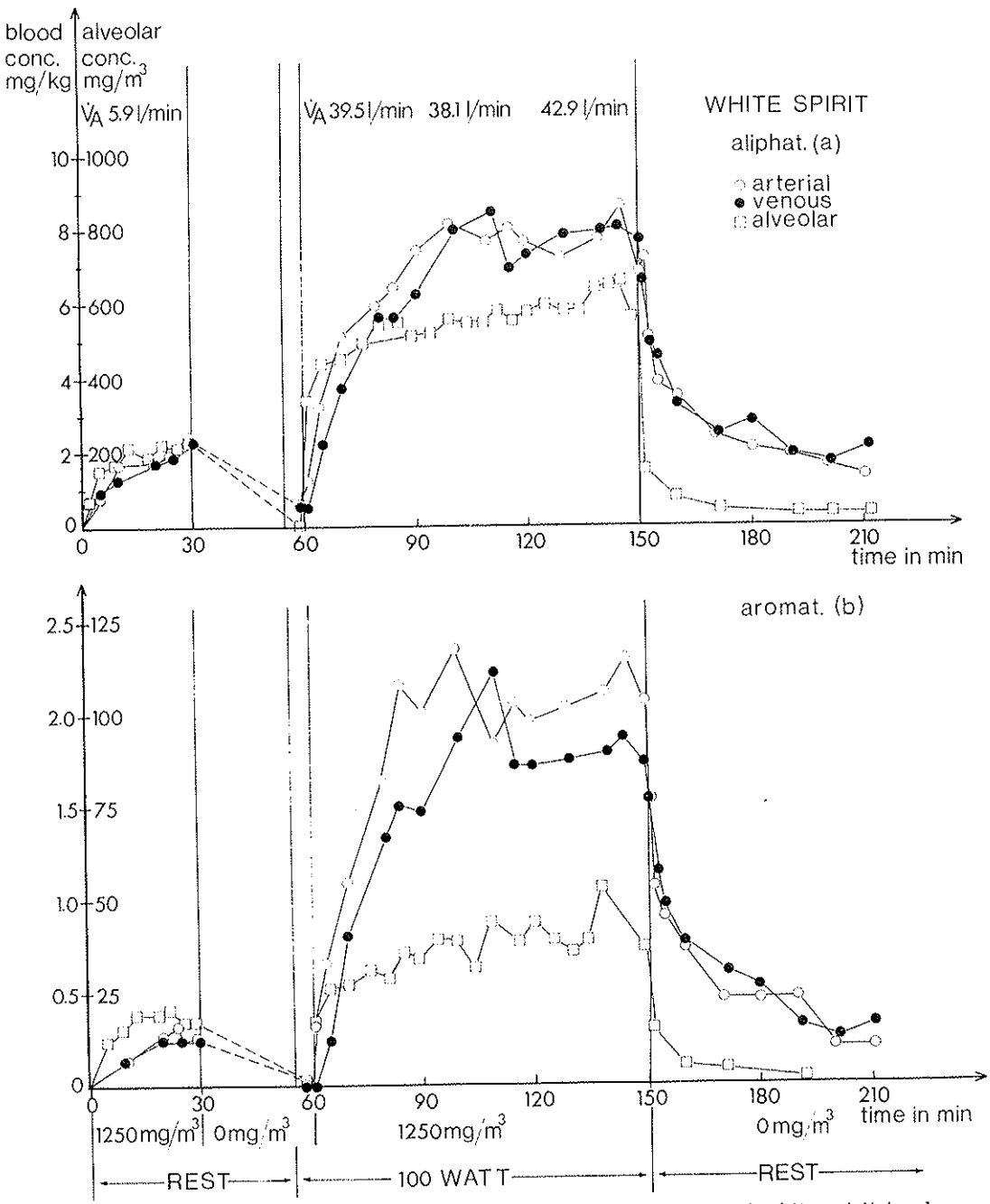

Fig. 7. The concentration of aliphatic (a) and aromatic (b) components of white spirit in alveolar air, arterial blood, and venous blood in one subject during and after exposure to approximately 1,250 mg/m³ of white spirit. Exposure was provided at rest and during exercise at an intensity of 100 W (600 kpm/min). ($\dot{V}_A$ = alveolar ventilation in l/min)

← *Fig. 6.* The concentration of aliphatic (a) and aromatic (b) components of white spirit in alveolar air, arterial blood, and venous blood in one subject during and after exposure to approximately 2,660 mg/m³ of white spirit. Exposure was provided at rest and during exercise at an intensity of 50 W (300 kpm/min) with white spirit added to the air and to an air mixture consisting of 4 % carbon dioxide and air. ($\dot{V}_A$ = alveolar ventilation in l/min; CO = cardiac output in l/min)

rose sharply (see fig. 6 b). The alveolar concentration was also only slightly elevated when the same air mixture was inspired during 50 W exercise, whereas the arterial concentration increased considerably. No direct comparison can be made of values during exercise with and without the addition of carbon dioxide, since the latter experiments were made when values were initially elevated. The increase in arterial blood concentration must have been mainly caused by an increase in ventilation because cardiac output was only slightly affected by carbon dioxide inspiration, both at rest and during exercise (table 3).

Alveolar concentration in these three types of experiments leveled off after about 10 minutes of exposure and then remained unchanged in each 30-minute period. However, the arterial blood concentration rose continuously throughout each period. The arterial blood concentration also rose in the transition from rest to exercise and during increasing exercise intensities. The arterial content displayed a kind of leveling-off only after protracted exposure during 90 minutes (fig. 7 b).

Figs. 8 and 9 elucidate the relationship between the arterial and alveolar concentrations of aliphatic and aromatic components following a period of exposure for all subjects. A linear relationship between the two variables was found for the aliphatic components (fig. 8). However, the spread was relatively great. The corresponding spread in one and the same subject was far less (8). In a corresponding relationship for the aromatic components, the spread was wider. All arterial blood concentrations measured at rest were lower than the values measured at the same exposure during exercise (fig. 9).

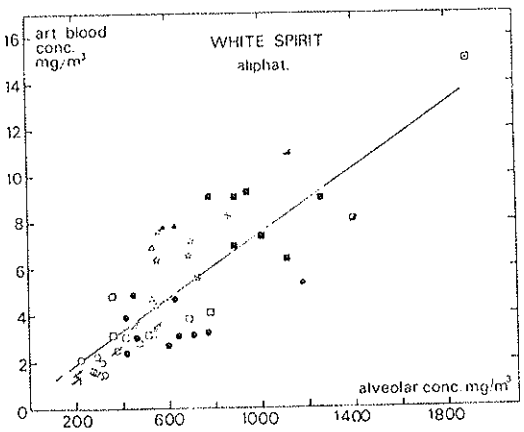

Fig. 8. Relationship between the concentration of aliphatic components in arterial blood and alveolar air after 30 minutes of exposure at rest and during exercise. Each symbol stands for a single exposure period, i.e., a single subject may be represented by more than one symbol. Symbols: ○ rest, 1,250 mg/m³; □ 50 W, 1,250 mg/m³; ● rest, 2,500 mg/m³; ■ 50 W, 2,500 mg/m³; △ 100 W, 1,250 mg/m³; ☆ 150 W, 1,250 mg/m³; ▲ 100 W, 1,250 mg/m³ (60 and 90 min); ⊗ rest, 2,500 mg/m³ + CO_2; ◪ 50 W, 2,500 mg/m³ + CO_2; ∅ rest, 1,000 and 1,500 and 2.000 mg/m³; ⊙ rest, 5,000 mg/m³ (pretrial); ⊡ 50 W, 5,000 mg/m³ (pretrial). (Regression line y = 0.508 + 0.007 x)

Venous blood concentration and arteriovenous difference during exposure

The venous blood concentration of aliphatic components paralleled the arterial concentration with a tendency towards a lesser increase at the end of each period (figs. 5, 6 and 7), while the concentration of aromatic components in venous blood rose during each period, analogous to the arterial concentration (figs. 4, 5 and 6). The arteriovenous difference for both the aliphatic and aromatic components, expressed in mg/kg of blood, increased only slightly as the arterial concentration increased. However, the release from arterial blood per unit of time, expressed in mg/min, increased as cardiac output increased in conjunction with exercise. It should be noted that the venous concentration obtained in these experiments stemmed from peripheral and not central venous blood. In view of a different distribution of the blood circulation at rest as compared to during exercise, the peripheral venous blood concentrations do not provide the same information during these two conditions. Since venous concentrations paralleled arterial concentrations, the aliphatic venous concentration was obviously better correlated to alvealor concentration than was the case for the aromatic concentration (figs. 8 and 9).

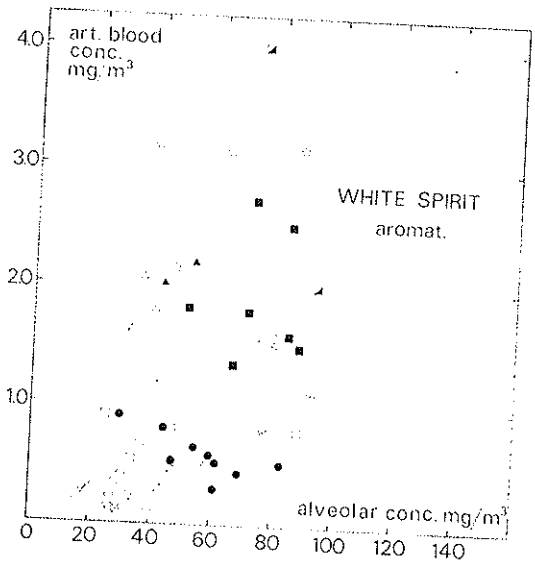

Fig. 9. Relationship between the concentration of aromatic components in arterial blood and alveolar air after 30 minutes of exposure at rest and during exercise. Symbols: ○ rest, 1,250 mg/m³; □ 50 W, 1,250 mg/m³; ● rest, 2,500 mg/m³; ■ 50 W, 2,500 mg/m³; △ 100 W, 1,250 mg/m³; ☆ 150 W, 1,250 mg/m³; ▲ 100 W, 1,250 mg/m³ (60 and 90 min); ⊗ rest, 2,500 mg/m³ + CO_2; ◪ 50 W, 2,500 mg/m³ + CO_2; ∅ rest, 1,000 and 1,500 and 2,000 mg/m³; ⊙ rest, 5,000 mg/m³ (pretrial); ⊡ 50 W, 5,000 mg/m³ (pretrial).

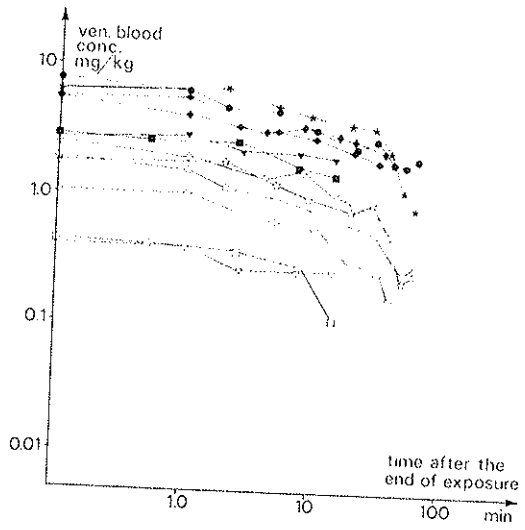

Fig. 10. Concentration of aliphatic and aromatic components of white spirit in venous blood at the end of and at different times after different types of exposure to white spirit. Each type of symbol represents one individual. (Filled symbols = aliphatic components; open symbols = aromatic components)

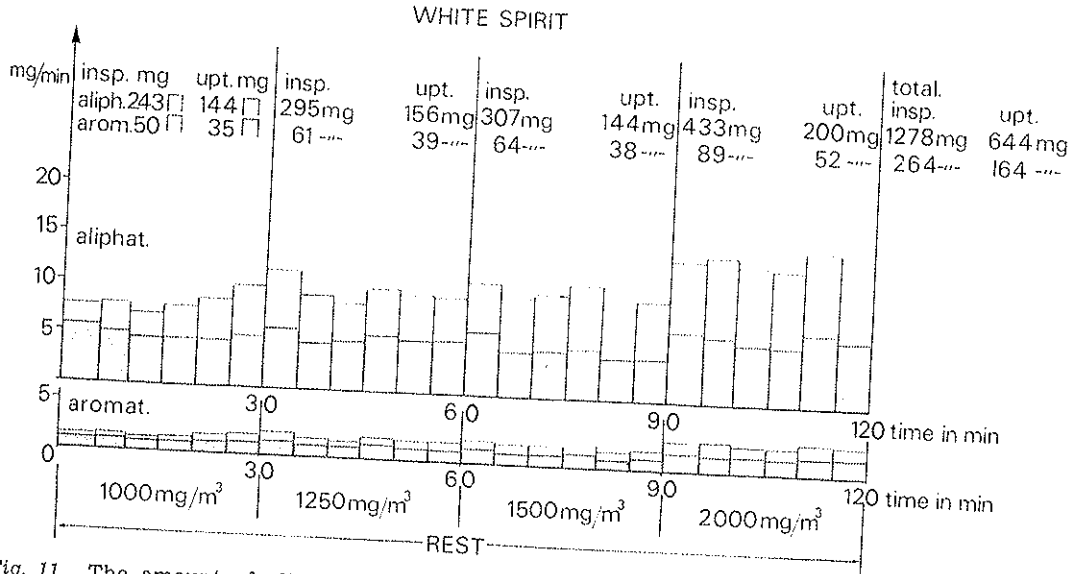

Fig. 11. The amount of aliphatic and aromatic components supplied in inspiratory air ($\dot{V}_I$ x concentration) and taken up by the organism (V_I x concentration − V_E x concentration) in exposure to approximately 1,000, 1,250, 1,500, and 2,000 mg/m³ of white spirit at rest by one subject. The total amount supplied and taken up during each 30-minute period and the total amounts are stated at the top of the figure.

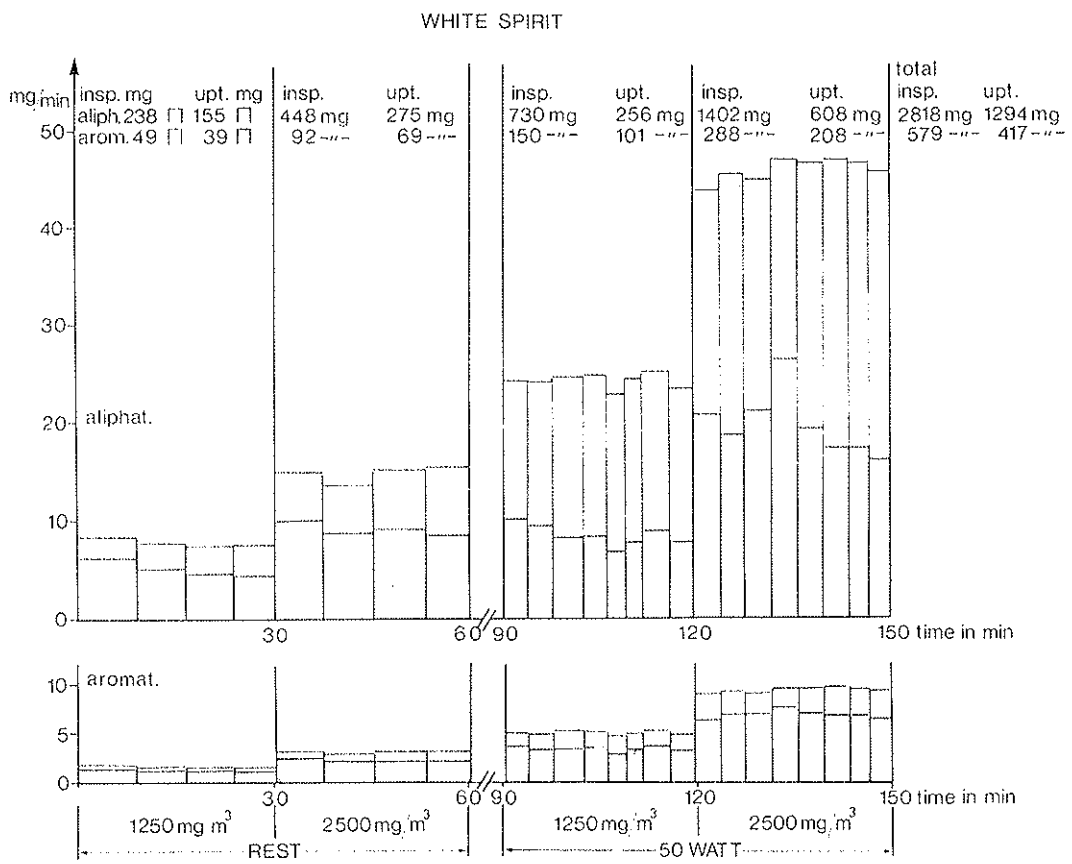

Fig. 12. The amount of aliphatic and aromatic components supplied in inspiratory air ($\dot{V}_I$ x concentration) and taken up by the organism ($\dot{V}_I$ x concentration - $\dot{V}_E$ x concentration) in exposure to approximately 1,250 and 2,500 mg/m³ at rest and during 50 W exercise (300 kpm/min) by one subject. The total amount supplied and taken up during each 30-minute period and the total amounts are stated at the top of the figure.

Concentration in alveolar air and in arterial and venous blood after the end of exposure

Figs. 4, 5, 6, and 7 show that the aliphatic concentration in alveolar air dropped to about 50 mg/m³ of air or less 20 minutes after exposure. The corresponding aromatic component declined to about 0.2 mg/m³ of air. Assay values were then relatively unreliable. Since tests in industry cannot generally be taken within 20 minutes of the end of exposure, it is obviously impossible to estimate the degree of prior exposure by determining the alveolar air concentration after exposure, at least when brief exposures are involved. Measurable amounts remained much longer in the blood. The rate of decline in venous concentration is shown in fig. 10. It was not linear in a log-log system.

Uptake in the organism

The total uptake of aliphatic and aromatic components in the organism was obtained in experiments with continuous measurement of the amounts in inspiratory and expiratory air. The uptakes amounted to 59, 53, 47, and 46 % of the total amount of aliphatic components supplied during four resting exposure periods, as illustrated in fig. 11. The corresponding uptakes for the aromatic components were 70, 64, 59, and 58 %. The uptake was accordingly greater at the start than at the end of the

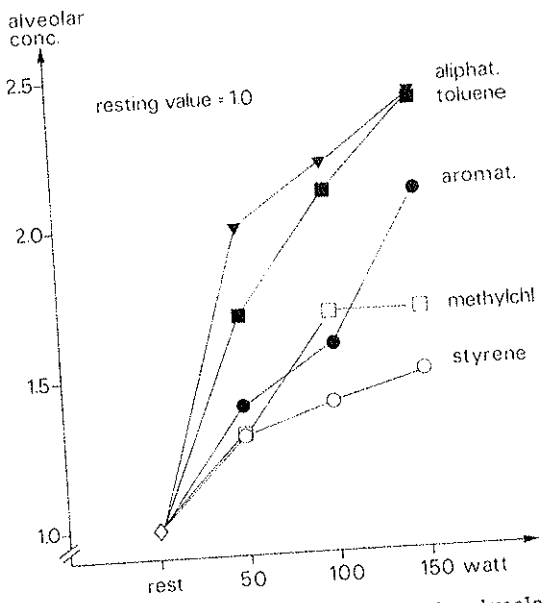

Fig. 13. Concentration of solvents in alveolar air at rest and during exercise at different intensities with constant exposure to toluene, methylchloroform, styrene, and aliphatic and aromatic components of white spirit. The resting value for the different substances was 1.0. The number of subjects was fewer at 150 W than at the other loads.

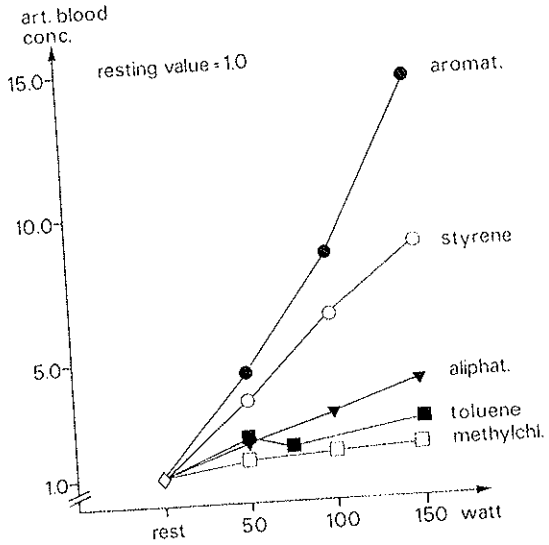

Fig. 14. Concentration of solvents in arterial blood at rest and during exercise at different intensities with constant exposure to toluene, methylchloroform, styrene, and aliphatic and aromatic components of white spirit. The resting value for the different substances was 1.0. The number of subjects was less at 150 W than at the other loads.

2 hours of exposure. Uptake averaged 50 % for the aliphatic components and 62 % for the aromatic components.

In exposure during two resting periods an uptake of about 63 % was obtained for the aliphatic components, and one of about 78 % for the aromatic components (fig. 12). During 50 W exercise the uptake amounted to about 39 % for the aliphatic components and to 69 % for the aromatic components. Thus, the uptake declined in percentage during exercise, especially for the aliphatic components, whereas the aromatic components declined only slightly. However, the total uptake, measured in milligrams per period of exposure, was slightly greater during exercise than at rest for both the aliphatic and aromatic components.

DISCUSSION

In the report of a styrene study (2) the solubility of different solvents in blood was discussed with respect to their concentrations in alveolar air and arterial blood under different conditions. The following was noted in closing: (a) initial alveolar concentration is far lower in relation to the level of exposure when subjects are exposed to a relatively soluble solvent, such as styrene, than is the case when they are exposed to a less soluble solvent, such as toluene or methylchloroform; (b) alveolar concentration increases to a lesser degree during enhanced pulmonary ventilation in exposure to an easily soluble solvent than in exposure to a relatively insoluble solvent; and (c) arterial concentration during each exposure period increases to a far greater degree, both during rest and during exercise, in exposure to an easily soluble solvent than to a relatively insoluble solvent. These findings are valid when membrane permeabilities are identical and when any metabolism takes place slowly.

Corresponding arguments can be advanced for the aliphatic and aromatic components in white spirit. The aliphatic components reacted as if they were not too

a The first value stated is always

soluble in blood, whereas aromatic components appeared to be relatively soluble substances (figs. 13 and 14).

Total uptake in the organism should be greater for a substance which is readily soluble in blood and other organs, and uptake should increase in step with the amounts supplied in conjunction with exercise. At rest the uptake of the aliphatic components did prove to be lower than the uptake of the aromatic components. During exercise the uptake percentage declined for the aliphatic component, whereas uptake of the aromatic component remained practically unchanged. This difference suggests that the aromatic components accumulated in the body more readily than the aliphatic components did. If toxicity is assumed, the substance with greater solubility in blood probably presents a greater risk than the substance less soluble in blood. Fat-solubility, however, is probably decisive in neurotoxicity. Respiration and blood circulation were unaffected by exposure to white spirit, as was analogously the case in exposure to toluene, methylchloroform, and styrene. Respiration was more important to uptake than blood circulation.

Since the exposed organism ultimately accumulates at least the aromatic components in white spirit and the degree of impression may be expected to be greater the greater the uptake, measuring only the content in inspiratory air can obviously not to be relied upon. Measurements of this type should be supplemented with biological measurements, especially in cases of relatively heavy exposure. Alveolar air samples, which are relatively easy to take, unfortunately fail to provide sufficiently accurate information on the uptake of aromatic components in blood, and these components are presumably of the greatest interest. Information on blood uptake can only be obtained by means of assays of venous or arterial capillary blood (2).

ACKNOWLEDGMENT

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