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Isopropanol exposure: environmental and biological monitoring in a printing works

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ABSTRACT Occupational exposure to isopropanol was studied in 12 workers by testing environmental air, alveolar air, venous blood, and urine during their work shift. Isopropanol, which ranged in environmental air between 7 and 645 mg/m3, was detected in alveolar air, where it ranged between 4 and 437 mg/m3, but not in blood or in urine. Alveolar isopropanol concentration (Ca) was significantly correlated with environmental isopropanol concentration (Ci) at any time of exposure. The value of the arithmetical Ca/Ci ratio was 0·418 (SD 0·101). Acetone, which is a metabolite of isopropanol, was found in alveolar air, blood, and urine in concentrations that were higher during exposure than before. Alveolar and blood acetone concentrations were highly correlated with alveolar isopropanol concentrations at any time during exposure. Acetone ranged between 0·76 and 15·6 mg/l in blood, between 4 and 92 μg/l in alveolar air, and between 0·85 and 53·7 mg/l in urine. Alveolar (Ca) and blood (Cb) acetone concentrations were highly correlated (r = 0·67), with a Cb/Ca ratio of 101. Alveolar isopropanol uptake ranged between 0·03 and 6·8 mg/min and was highly correlated with environmental isopropanol concentration (r = 0·92). During exposure, acetone eliminated by the lungs ranged between 20 and 273 mg in seven hours and in urine between 0·3 and 9·6 mg in seven hours. Acetonuria was higher the next morning than at the end of exposure.

Isopropanol is a solvent widely used in industry and in the home and it was used for tepid sponging in feverish children[1] before it was known to be responsible for the potentiation of hepatic and renal toxicity caused by haloalkanes.[2–4] It is also suspected of being a carcinogenic agent after the discovery of an abnormal incidence of paranasal and sinus cancers in employees manufacturing isopropyl alcohol.[5] The uptake and metabolism of isopropanol after ingestion has been studied in man[6] and animals,[7–11] but the uptake of isopropanol from the lung and its metabolism in man have not yet been clearly elucidated. The present study was carried out on a group of workers exposed to isopropanol with the aim of examining the uptake of isopropanol from the lung under industrial conditions.

Materials and methods

We studied the occupational exposure to isopropanol in 12 workers employed in a printing works by testing environmental air, alveolar air, venous blood, and urine. For each worker we took nine samples of environmental air, nine samples of alveolar air, five samples of venous blood, and three samples of urine.

Air samples

Air samples, which were all instantaneous,[12 13] were collected before the start of the work shift, after the first half hour, and then hourly during the seven hours of the whole afternoon work shift. Each alveolar air sample was collected simultaneously with one environmental air sample. Alveolar Ventilation ($\dot{V}A$) was measured on two or more occasions during the work shift.[12]

Blood samples—Blood samples were collected before exposure, after the first hour, and then every two hours until the end of work. Each blood sample was collected simultaneously with one alveolar air sample. The blood samples, which were put in glass vials, were analysed by a head space technique.

Urine samples—Urine samples were collected before exposure, after the end of work, and the next morning. A head space technique was used to analyse the specimens.

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The samples were collected on four different days, examining three workers a day.

The concentration of isopropanol and its metabolite acetone were measured in all the air, blood, and urine samples using gas chromatography. For the analyses a Perkin-Elmer mod F 17 gas chromatograph with FID was used: column 2 m × 3 mm outside diameter (steel column), packed with Carbowax 1500 0·2% on Carbopack C 80–100 mesh; temperature: injector and detector 200°C, oven 90°C; carrier gas: nitrogen; flow rate: 20 ml/min. Before analysis all air samples were kept at a temperature of 60°C and blood and urine samples at 37°C.

Results

Isopropanol was detected in environmental and alveolar air samples collected during the whole work shift, but in no other air samples nor in any blood or urine samples. The concentration of isopropanol ranged between 8 and 647 μg/l in environmental air and between 3 and 439 μg/l in alveolar air during the work shift. Table 1 shows the individual values of isopropanol concentration in environmental and alveolar air.

At each sampling time studied during the work shift, a good correlation was found between the environmental and alveolar isopropanol concentration (fig 1). Considering all the data collected at the various intervals, the correlation between the alveolar and environmental concentrations of isopropanol was highly significant (fig 2). The slope of the regression line shown in fig 2 suggests that the mean alveolar concentration of isopropanol corresponds to 53·9% of the environmental concentration.

Figure 3 shows the individual and mean values of the arithmetical ratios between the alveolar (Ca) and environmental (Ci) concentrations of isopropanol (Ca/Ci). According to this, over 50% of the individual values of Ca/Ci ratios fall between 0·3 and 0·5.

The mean value of the arithmetical Ca/Ci ratio, equal to 0·418, is lower than that given by the slope of the regression line in fig 2 (0·539).

Acetone was detected in all the samples of alveolar air, blood, and urine collected. Before the work shift the mean acetone concentration was 3·7 μg/l (SD 3·8) in alveolar air, 1·4 mg/l (SD 0·5) in blood, and 3·9 mg/l (SD 7·6) in urine (table 2). Acetone was detected in environmental air samples during the work shift only in the case of the first three workers listed in the tables, who were exposed to the highest concentrations of isopropanol (table 1). The mean acetone concentration was 13 μg/l (SD 9), 18 μg/1 (SD 18), and 15 μg/l (SD 12) in the atmosphere of the work place of the first, second, and third workers respectively. By comparison with these environmental acetone concentrations, the first three workers showed a mean alveolar acetone concentration (table 3) of 38 μg/l (SD 18), 50 μg/l (SD 29), and 41 μg/l (SD 16). These figures show that, as regards the first three workers, acetone concentration was higher in alveolar than in environmental air. During the work shift, acetone ranged between 3 and 93 μg/1 in alveolar air, 0·76 and 15·6

Table 1 *Isopropanol concentrations (μg/l) in environmental (Ci) and alveolar (Ca) air and alveolar ventilation (V̇A)*

Case No	*V̇A l/min*		*Times of the work shift (hours)*									
			0·5	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*M*	*SD*
1	11·3	Ci	591	581	419	396	620	460	526	352	493	100
		Ca	247	294	247	184	272	259	280	267	256	33
2	11·9	Ci	479	550	369	459	620	539	526	278	478	109
		Ca	408	274	271	141	290	259	333	181	270	83
3	9·5	Ci	544	647	419	531	343	544	266	467	470	123
		Ca	439	364	285	282	266	220	138	184	272	96
4	12·9	Ci	167	114	123	69	63	59	67	128	99	40
		Ca	44	55	45	32	18	25	29	46	37	13
5	12·8	Ci	212	140	187	136	51	64	129	253	146	69
		Ca	101	58	70	58	15	28	35	64	53	27
6	15·6	Ci	268	155	189	129	79	80	81	90	134	68
		Ca	105	82	70	57	30	25	29	29	53	30
7	13·6	Ci	182	256	364	152	81	99	234	287	207	97
		Ca	56	105	112	62	12	36	35	95	64	36
8	13·3	Ci	170	220	301	167	80	113	260	266	197	78
		Ca	37	77	80	57	13	20	84	88	57	30
9	16·9	Ci	177	208	487	182	56	65	242	226	205	133
		Ca	51	75	160	45	25	24	27	143	69	54
10	14·6	Ci	26	14	18	35	21	32	—	—	24	8
		Ca	6	6	5	20	12	14	—	—	10	6
11	13·1	Ci	10	10	15	8	20	28	—	—	15	8
		Ca	5	5	3	5	6	17	—	—	7	5
12	11·9	Ci	25	8	16	36	40	27	—	—	25	12
		Ca	6	5	6	8	18	11	—	—	9	5

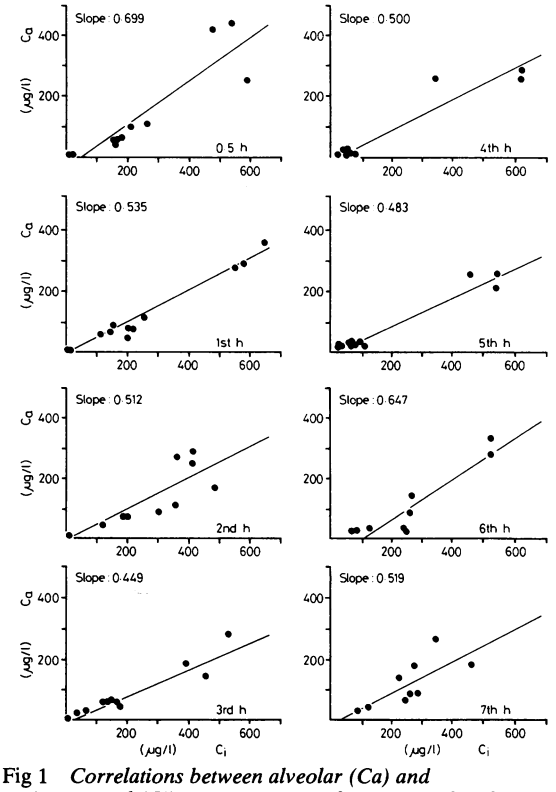

Fig 1 *Correlations between alveolar (Ca) and environmental (Ci) concentrations of isopropanol at the various times studied:*

½ h: Ca = 0·699 Ci − 41; r = 0·90; n = 12; p < 0·001
1st h: Ca = 0·535 Ci − 13; r = 0·99; n = 12; p < 0·001
2nd h: Ca = 0·512 Ci − 9; r = 0·83; n = 12; p < 0·001
3rd h: Ca = 0·449 Ci − 7; r = 0·95; n = 12; p < 0·001
4th h: Ca = 0·500 Ci − 5; r = 0·96; n = 12; p < 0·001
5th h: Ca = 0·483 Ci − 7; r = 0·98; n = 12; p < 0·001
6th h: Ca = 0·647 Ci − 58; r = 0·93; n = 9; p < 0·001
7th h: Ca = 0·519 Ci − 13; r = 0·75; n = 9; p < 0·05.

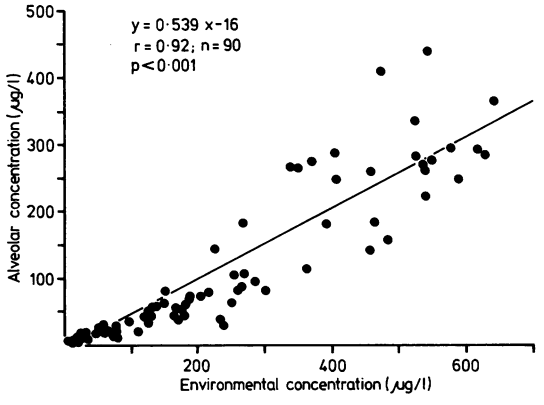

Fig 2 *Correlation between alveolar (Ca) and environmental (Ci) concentrations of isopropanol; all individual data.*

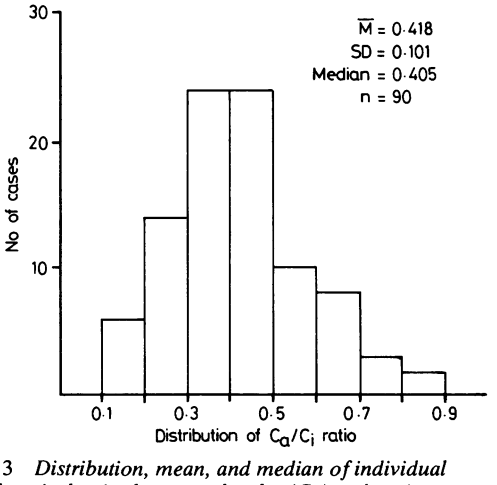

Fig 3 *Distribution, mean, and median of individual arithmetical ratios between alveolar (Ca) and environmental (Ci) concentrations of isopropanol (Ca/Ci).*

Table 2 *Results of biological monitoring before, during, and after exposure*

Subject No	*Before exposure*				*During exposure*				*After exposure*	
	Alveolar acetone conc (μg/l)	*Blood acetone conc (μg/l)*	*Urine acetone conc (μg/l)*	*(μg/m')*	*Alveolar isopropanol uptake (mg/7 h)*	*Blood acetone conc (μg/l)*	*Urine acetone conc (μg/l)*	*(μg/m')*	*(next morning) Urine acetone conc (μg/l)*	*(μg/m')*
1	4	1340	500	—	1680	8200	5400	6·0	38200	39·9
2	8	2470	1470	—	1805	7192	18200	19·5	41600	49·9
3	5	630	27700	—	1410	7635	14300	22·8	53700	54·6
4	2	1490	1750	1·6	232	3435	3650	4·0	4040	2·0
5	1	1830	3190	1·7	373	3400	4590	3·0	3400	1·1
6	1	1590	1790	2·3	434	2735	4160	4·7	4150	4·6
7	3	810	500	0·3	492	4302	1800	0·9	850	0·8
8	14	770	1130	0·8	443	5012	1080	0·5	2280	1·9
9	2	1170	5420	8·6	688	3000	1950	1·4	2230	1·8
10	1	1920	800	1·4	70	2715	2180	1·1	1840	1·4
11	3	1280	1410	1·6	23	1170	920	0·7	3630	2·3
12	1	1780	1130	0·3	48	1725	1600	0·8	1540	1·0
M	3·7	1423	3899	2·1	641	4210	4986	5·4	13122	13·3
SD	3·8	539	7619	2·5	635	2330	5515	7·6	19264	21·1

Table 3 *Acetone concentrations (μg/l) in alveolar air (Ca) and in blood (Cb)*

Subject No		*Time of work shift (hours)*								*Mean*	*SD*
		0·5	*1*	*2*	*3*	*4*	*5*	*6*	*7*		
1	Ca	11	27	39	40	58	66	27	35	38	18
	Cb	—	3600	—	5370	—	8210	—	15620	8200	5298
2	Ca	18	23	36	31	71	93	88	44	50	29
	Cb	—	3990	—	6060	—	8240	—	10480	7192	2795
3	Ca	16	36	36	61	38	58	30	56	41	16
	Cb	—	5740	—	11420	—	9060	—	4320	7635	3211
4	Ca	8	10	5	14	24	21	19	18	15	7
	Cb	—	2140	—	3680	—	4850	—	3070	3435	1136
5	Ca	8	14	15	20	23	19	15	15	16	4
	Cb	—	2660	—	4250	—	2850	—	3840	3400	767
6	Ca	14	11	20	19	23	11	19	13	16	4
	Cb	—	2420	—	3510	—	1240	—	3770	2735	1155
7	Ca	10	7	17	24	8	15	6	14	13	6
	Cb	—	2340	—	4190	—	3330	—	7350	4302	2168
8	Ca	10	4	10	24	14	12	68	22	20	20
	Cb	—	1690	—	3930	—	4150	—	10280	5012	3683
9	Ca	14	8	61	48	18	8	65	60	35	25
	Cb	—	2420	—	3240	—	2990	—	3350	3000	415
10	Ca	3	6	3	4	6	4	—	—	4	1
	Cb	—	2400	—	3030	—	—	—	—	2715	—
11	Ca	6	3	4	4	9	5	—	—	5	2
	Cb	—	1580	—	760	—	—	—	—	1170	—
12	Ca	4	4	3	5	9	22	—	—	8	7
	Cb	—	1760	—	1690	—	—	—	—	1725	—

mg/l in blood (table 3), and between 0·9 and 18·2 mg/l in urine (table 2). The concentration of acetone in urine collected from the end of work to the next morning ranged between 0·85 and 53·7 mg/l (table 2).

A significant correlation between the alveolar (x) and blood (y) concentrations of acetone was found at the first, third, and fifth hours of the work shift, but not at the seventh or before the start of work (table 4); correlation between all the data collected before and during the work shift is shown in fig 4.

Acetone concentration both in alveolar air and in blood was better correlated with the isopropanol concentration in alveolar air (Ca) than with the isopropanol concentration in environmental air (Ci) or with the isopropanol difference between Ci and Ca. Figure 5 shows that in the correlation with alveolar isopropanol concentration, the alveolar concentration of acetone rises according to the duration of exposure. The correlation between alveolar acetone concentration and alveolar isopropanol concentration existed at all hours of the work shift studied except the sixth hour (r = 0·49).

Figure 6 shows that blood acetone concentrations are related to alveolar isopropanol concentrations and rise according to the duration of exposure.

The elimination of acetone by the lungs during the work shift was calculated by multiplying alveolar acetone concentration by $\dot{V}A$ and time ($Ca \times \dot{V}A \times t$). At the various hours of the work shift the acetone eliminated by the lungs, expressed as a percentage of the isopropanol absorbed, rose greatly especially until the third or fourth hour of exposure (fig 7).

Table 4 *Correlation between alveolar (x, μg/l) and blood (y, mg/l) concentrations of acetone*

Time of exposure	*No of cases*	*Intercept*	*Slope*	*r*	*Significance*
Before exposure	12	+1·5	−0·39	−0·28	NS
1st h	12	+1·3	+109	+0·96	$p < 0·001$
3rd h	12	+1·3	+119	+0·80	$p < 0·01$
5th h	9	+2·2	+82	+0·89	$p < 0·01$
7th h	9	+6·5	+11	+0·05	NS

According to the observation that the alveolar and blood concentrations of acetone were better correlated with isopropanol in alveolar air than with isopropanol in environmental air or its Ci-Ca differ-

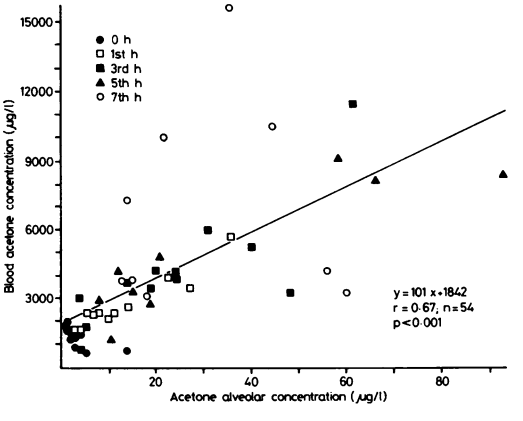

Fig 4 *Correlation between blood and alveolar concentrations of acetone; all individual data before and after exposure to isopropanol.*

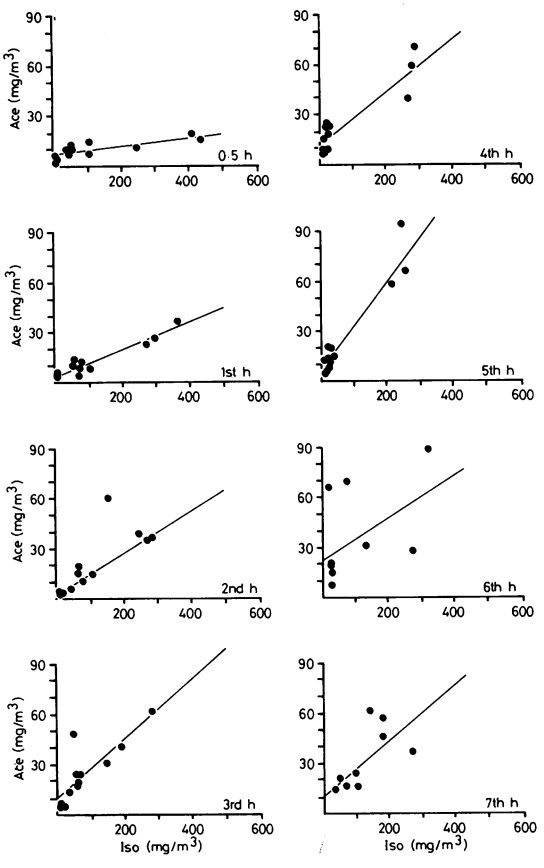

Fig 5 *Correlations between alveolar acetone concentrations (Ace) and alveolar isopropanol concentrations (Iso) at various times of exposure:*
½ h: Ace = 0·023 Iso + 7; r = 0·77; n = 12; $p < 0·01$,
1st h: Ace = 0·081 Iso + 3; r = 0·95; n = 12; $p < 0·001$,
2nd h: Ace = 0·124 Iso + 3; r = 0·78; n = 12; $p < 0·01$,
3rd h: Ace = 0·179 Iso + 10; r = 0·83; n = 12; $p < 0·001$,
4th h: Ace = 0·161 Iso + 12; r = 0·91; n = 12; $p < 0·001$,
5th h: Ace = 0·267 Iso + 7; r = 0·95; n = 12; $p < 0·001$,
6th h: Ace = 0·119 Iso + 24; r = 0·49; n = 9; p = NS
7th h: Ace = 0·162 Iso + 11; r = 0·68; n = 9; $p < 0·05$.

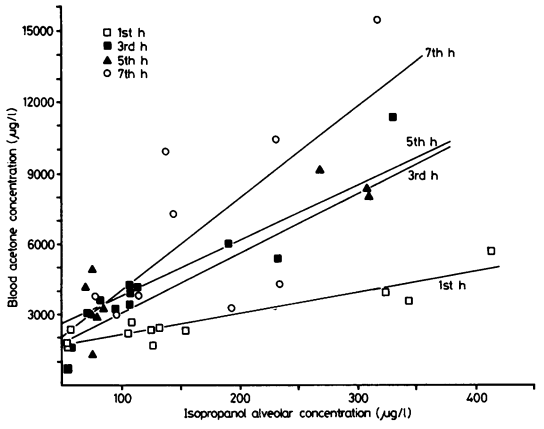

Fig 6 *Correlations between blood acetone concentrations and alveolar isopropanol concentration at various times of exposure*
1st h: Ace = 8·9 Iso + 1691; r = 0·92; n = 12; $p < 0·001$
3rd h: Ace = 30·4 Iso + 1853; r = 0·94; n = 12; $p < 0·001$
5th h: Ace = 23·4 Iso + 2658; r = 0·92; n = 9; $p < 0·001$
7th h: Ace = 38·7 Iso + 2185; r = 0·69; n = 9; $p < 0·05$.

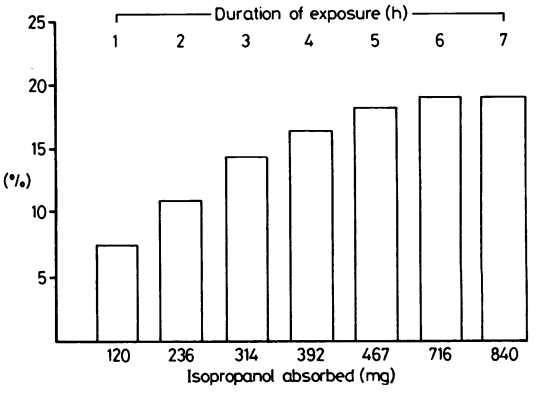

Fig 7 *Acetone eliminated by lungs during exposure to isopropanol expressed as mean percentage of absorbed isopropanol.*

ence, we considered alveolar isopropanol concentration as the best index for calculating the amount of isopropanol absorbed by the lungs. Seeing that the mean arithmetical Ca/Ci ratio of isopropanol was 0·418 (fig 3) we calculated the isopropanol absorption as follows:

$$\text{alveolar isopropanol uptake} = \text{Ca } (\mu g/l) \times \frac{R}{Ca/Ci} \times VA \text{ with } R = 1 - Ca/Ci = 0·582.$$

The individual values of isopropanol uptake per minute are shown in fig 8, which shows that a significant correlation (r = 0·92) existed between alveolar uptake and the environmental concentration of isopropanol. The total amount of isopropanol absorbed during the whole period of the work shift was calculated for the individual workers by multiplying the mean absorption per minute by the time of exposure (table 2).

The blood acetone concentrations determined during the work shift calculated as the mean of the four determinations made (table 2) were significantly correlated with the total amount of

Table 5 *Correlation between alveolar isopropanol uptake (mg/7 h) and blood acetone and urine acetone concentrations and between urine and blood acetone concentrations (mg/l) in nine subjects*

	Intercept	*Slope*	*r*	*p*
Alveolar isopropanol uptake (x)/blood acetone conc (y = μg/l)	2350	3·1	0·91	<0·001
Alveolar isopropanol uptake (x)/end-exposure urine acetone conc (y = mg/l)	−235	7·6	0·78	<0·05
Alveolar isopropanol uptake (x)/end-exposure urine acetone conc (y = μg/m′)	−1·5	0·01	0·75	<0·05
Alveolar isopropanol uptake (x)/next-morning urine acetone conc (y = mg/l)	−9904	31·7	0·92	<0·001
Alveolar isopropanol uptake (x)/next-morning urine acetone conc (y = μg/m′)	−12·5	0·035	0·94	<0·001
Blood acetone conc (x)/end-exposure urine acetone conc (y = mg/l)	− 3·1	1·85	0·66	<0·1
Blood acetone conc (x)/end-exposure urine acetone conc (y = μg/m′)	− 6·3	2·7	0·69	<0·05
Blood acetone conc (x)/next morning urine acetone conc (y = mg/l)	−28·3	9·02	0·91	<0·001
Blood acetone conc (x)/next morning urine acetone conc (y = μg/m′)	−31·7	9·8	0·90	<0·001

Table 6 *Total elimination of acetone by the lungs during exposure and by the kidneys during and after exposure*

Subject No	*Acetone eliminated By lungs (mg/7 h)*	*In urine (mg/17 h)*
1	180	25·8
2	273	38·1
3	173	42·3
4	84	2·9
5	90	1·9
6	110	4·8
7	75	0·9
8	125	1·3
9	274	1·7
10	22	1·3
11	20	1·7
12	31	0·9
Mean	121	10·3
SD	88	15·6

isopropanol absorbed during the whole work shift (table 5). Urine acetone concentrations determined both at the end of the work shift and the next morning (table 2) were also significantly correlated with the total isopropanol absorbed (table 5) and with the mean blood acetone concentration found during the whole work shift (table 5). The alveolar elimination of acetone during the whole work shift turned out to be many times higher than the total amount of acetone eliminated in urine both at the end of exposure and the next morning (table 6).

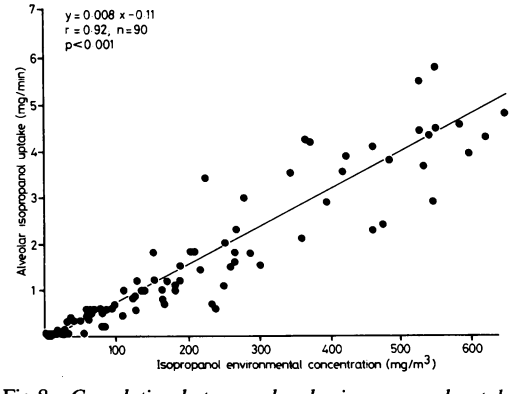

Fig 8 *Correlation between alveolar isopropanol uptake (Ca × R/(Ca/Ci) × VA, with Ca = alveolar isopropanol concentration (μg/l), R = 1—Ca/Ci = 0·582, Ca/Ci = 0·418) and environmental isopropanol concentration.*

Discussion

ISOPROPANOL IN ENVIRONMENTAL AND ALVEOLAR AIR

Our data on the alveolar concentration of isopropanol show that a highly significant correlation existed with environmental isopropanol concentration at all the times of exposure (fig 1). The ratio between alveolar and environmental concentration (Ca/Ci) was not affected by the duration of exposure (fig 1), environmental concentration (figs 2 and 3), or alveolar ventilation. The observation that the mean and median value of the arithmetical isopropanol Ca/Ci ratio are 0·418 and 0·405 respectively and that more than 50% of the individual Ca/Ci ratio values fall between 0·3 and 0·5 (fig 3) suggests that the variability of the Ca/Ci ratio might reasonably fall in the region of these two values. This hypothesis is suggested by the fact that we used instantaneous samples and that alveolar air cannot instantaneously reflect momentary variations in environmental air but needs a lapse of time for the wash in or wash out of the alveoli if there is any variation in the atmosphere. On the basis of the finding that, despite our instantaneous sampling technique, a correlation existed between alveolar and environmental concentration, it seems conceivable that the above mentioned values might express the actual value of the isopropanol Ca/Ci ratio. In our experience[13] in the alveolar air of workers each inhaled solvent reaches a concentration that, with environmental concentration, shows a ratio (Ca/Ci) characteristic of the solvent under consideration. Folland *et al*,[14] who studied 13 workers occupationally exposed to isopropanol, reported environmental and alveolar data according to which the isopropanol Ca/Ci ratio turns out to be between 0·247 and 0·400. The assessment of the Ca/Ci ratio is of basic importance because from it we can arrive at alveolar retention (Retention (R) = 1−Ca/Ci) and then estimate alveolar uptake (R × VA × Ci).

ISOPROPANOL IN BLOOD

Blood isopropanol concentrations have been measured in cases of acute poisoning in man. Adelson[15] found no correlation between the severity of poisoning and the blood level of isopropanol, which ranged in all his cases between 1·3 and 2·0 g/l. King *et al*[16] found a blood isopropanol concentration of 4·4 g/l in a man who swallowed about a litre of "rubbing alcohol" in 10 minutes, 45 minutes before his admission to the hospital. Laham *et al*[9] and Laham *et al*[10] detected isopropanol in the blood of rats exposed to environmental concentrations of isopropanol ranging from 500 ppm (1225 mg/m3) to 8000 ppm (18 600 mg/m3). The blood isopropanol concentrations were 30 and 503 mg/l after four hours of exposure to 1225 and 18 600 mg/m3 respectively. The simultaneous determination of acetone in rats' blood showed a ratio between acetone and isopropanol in blood that was three in the lowest exposure (500–1000 ppm) and unity in the highest exposure (8000 ppm).

Our data show that the first three workers listed in the tables were exposed to a mean environmental concentration of isopropanol corresponding to 470–493 mg/m3 (table 1), which is about half the threshold limit value (980 mg/m3 by ACGIH, 1981). In none of these three workers, nor in any others, were we able to detect isopropanol in the blood or urine. The mean blood acetone concentration (table 2) in these first three workers was 7192-8200 μg/l with ranges in individual tests from 3600 to 15 620 μg/l. Extrapolating from data on rats[9 10] we would have expected a blood isopropanol concentration of 1·2–5·2 mg/l—that is, one-third of the blood acetone values (3600–15 620 μg/l). Our detectable limit for isopropanol in blood was 1 mg/l and so we can conclude that under the conditions of exposure we studied, the ratio of acetone to isopropanol in blood should be higher than three. Our inability to detect isopropanol in blood is possibly because the apparent volume of isopropanol distribution in the human body is so large that the resultant blood concentration is lower than our technical limit of detection.

ACETONE CONCENTRATIONS

The chief metabolite of isopropanol is acetone, which may be detected in the urine after one hour and in expired air within 15 minutes.[6] High concentrations of acetone in the blood of people poisoned with isopropanol were reported by Glasser *et al*[17]; Folland *et al*[14] reported an alveolar acetone concentration of 46 and 18 μg/l in workers exposed to an environmental isopropanol concentration of 1000 and 343 μg/l respectively. Our data on acetone determination in workers before the start of isopropanol exposure showed a concentration of 3·7 μg/l (SD 3·8) in alveolar air, 1·4 mg/l (SD 0·5) in blood, and 3·9 mg/l (SD 7·6) in urine. Wigaeus *et al*[18] reported that physiological concentrations of acetone in alveolar air were 1·7 μg/l (SD 0·5), in blood 1·3 mg/kg (SD 0·6), and in urine 1·4 mg/kg (SD 1·1); the endogenous levels of blood acetone we found were similar. On the other hand, the concentrations of acetone in the urine and in the breath before exposure differ. We now know that the third worker (table 2) had worked an overtime shift that finished about 10 hours before our examination. This explains his high urine acetone concentration (27·7 mg/l) before exposure (table 2).

It is well known that the alveolar concentration of acetone is related to blood acetone concentrations and that the blood/air partition coefficient of acetone plays a decisive part in establishing its concentration in blood and alveolar air. The blood/air partition coefficient, known also as the solubility coefficient in blood, was found in experiments in vitro to range between 218 and 275.[18–21] In healthy men with an endogenous blood acetone concentration of 1·3 mg/kg and an endogenous alveolar acetone concentration of 1·7 μg/l the blood/air partition coefficient is 765.[18] On the other hand, in volunteers with different levels of exposure the acetone solubility coefficient ranged from 30 to 100 during exposure.[20] In the same experiments the solubility coefficient ranged between 400 and 340 after the end of exposure during the four hours of the elimination phase studied. Previously we had found in a group of workers exposed to acetone in factories a solubility coefficient of 114.[19] In the present investigation we found, on the basis of the slopes of the regression lines, a blood/air partition coefficient of acetone equal to 109, 119, and 82 at the first, third, and fifth hours of exposure respectively (table 4). Considering all the data together (fig 4), the solubility coefficient turned out to be equal to 101, which is similar to that of 114 which we found previously in workers exposed to acetone. Statistical analysis showed that a good correlation between the alveolar concentration of acetone and isopropanol existed at all the times except at the sixth hour of the work shift, when the correlation coefficient turned out to be 0·49 (fig 5). A correlation coefficient between 0·68 (seventh hour) and 0·95 (fifth hour) was found at all the other hours. Figure 5 clearly shows that the alveolar concentration of acetone, during exposure, rises not only as a function of alveolar isopropanol concentration but also as a function of the duration of exposure. According to the slopes of the regression lines reported in fig 5 it is clear that the alveolar acetone concentration as a percentage of alveolar isopropanol concentration rises from 2·3% at the

first half-hour to 26·7% at the fifth hour of exposure. As regards the correlations in fig 5, it is worth emphasising that the slopes were very similar—0·179, 0·161, and 0·162 at the third, fourth, and seventh hours respectively. Despite the result at the fifth hour (slopes = 0·267), these figures seem to suggest that the alveolar acetone concentration, as a function of alveolar isopropanol concentration, does not vary after the third hour of the work shift. This suggests that a steady state between the uptake of alveolar isopropanol and its metabolism to acetone should be reached within three hours of exposure.

At all the sampling times studied, a significant correlation (fig 6) was again found between blood acetone concentration and alveolar isopropanol concentrations. The correlation coefficients were 0·92, 0·94, 0·92, and 0·69 respectively at the first, third, fifth, and seventh hours of the work shift. The slopes at the third, fifth, and seventh hours were similar, 30·4, 23·4, and 38·7 respectively, compared with the one at the first hour of the work shift, which was 8·9. These results support the view that a steady state condition exists after the third hour of exposure.

ISOPROPANOL UPTAKE

Since alveolar concentration is an expression of time integrated exposure, we preferred to calculate the alveolar isopropanol uptake by using the individual values of alveolar isopropanol concentration (μg/l) determined at the various hours of exposure rather than the environmental isopropanol concentrations. This is in accordance with the observation that the acetone concentration determined, both in the alveolar air and in the blood of workers exposed to isopropanol, was better correlated with isopropanol in alveolar air than with isopropanol concentration in environmental air. The individual data on alveolar isopropanol uptake (mg/min) calculated as mentioned above—that is, starting from the alveolar concentration of isopropanol (μg/l)—were significantly correlated with environmental isopropanol concentrations (fig 8). On the basis of the slope of the regression line in fig 8, it appears that the amount of isopropanol contained in eight litres of environmental air was absorbed, on average, every minute by the lungs. In other words, it may be said that the mean alveolar clearance of isopropanol was equal to eight litres of environmental air per minute. The alveolar uptake of isopropanol calculated for the seven hours of the work shift ranged between 232 and 1805 mg (in the first nine workers listed in table 2). The blood acetone concentrations in these nine workers determined as the mean of the four determinations carried out during the work shift were significantly correlated with the amount of isopropanol absorbed during the seven hours (r = 0·90, table 5). From this correlation, it may be estimated that 1 g of isopropanol absorbed in seven hours gives a mean blood acetone concentration of about 5·5 g/l.

ACETONE ELIMINATION

An examination of the urinary acetone concentrations at the end of exposure and the next morning shows that both the concentration and the excretion rate of acetone were higher the next morning than at the end of exposure (table 2). Some acetone concentrations the morning after exposure were better correlated with the seven-hour alveolar isopropanol uptake (table 5: r = 0·92–0·94) than were the concentrations at the end of the work shift (r = 0·78–0·75). From fig 7 it may be seen that the mean lung acetone elimination as a percentage of the alveolar isopropanol absorbed rises quickly within the first three hours and slowly thereafter. On the other hand, table 7 shows that in each individual worker the acetone eliminated by the lungs, expressed as a percentage of the alveolar isopropanol absorbed, varied according to the level of exposure. It was the lowest (10·7–15·1%) in the first three workers, who were exposed to the highest isopropanol concentrations (table 1: 470–493 mg/m3), and proportionately higher (15·2–39·8%) in the other workers, who were exposed to the lowest isopropanol concentrations (table 1: 99–207 mg/m3). In table 7 the clearance of acetone from the lung and renal clearance are reported. The clearance of acetone from the lung, except in the last worker listed, showed a narrow range (41–97 ml/min). The renal clearance of acetone, on the other hand, showed a value ranging between 0·1 and 3 ml/min, 30 or more times lower than that of clearance from the lung. An examination of the data in table 7 suggests that

Table 7 *Elimination of acetone by the lungs and kidneys*

Subject No	*Alveolar* acetone elimination*	*Pulmonary† clearance of acetone (ml/min)*	*Renal‡ clearance of acetone (ml/min)*
1	10·7%	52	0·7
2	15·1%	90	2·7
3	12·3%	54	3·0
4	36·2%	59	1·2
5	24·1%	63	1·5
6	25·3%	97	1·8
7	15·2%	41	0·2
8	28·2%	59	0·1
9	39·8%	217	0·5

*Acetone eliminated by lungs as percentage of isopropanol absorbed during work shift.
†Acetone eliminated by lungs during work shift divided by blood acetone concentration as mean of four determinations carried out during work shift.
‡Acetone eliminated in urine during work shift divided by blood acetone concentration as mean of four determinations carried out during work shift.

elimination of acetone in alveolar air in terms of percentage values (10·7–39·8%) depends inversely on the level of isopropanol exposure, while in terms of pulmonary clearance it seems to be independent of the level of isopropanol exposure (pulmonary clearance between 41 and 97 ml/min in eight out of the nine workers tested). Our findings, which show that kidney excretion of acetone is low, agree with the results reported in men exposed to acetone[18] and with other studies[22] indicating that the renal excretion of acetone occurs by simple diffusion.

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