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Biological monitoring of workers exposed to benzene in the coke oven industry

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ABSTRACT Workers in the coke oven industry are potentially exposed to low concentrations of benzene. There is a need to establish a well validated biological monitoring procedure for low level benzene exposure. The use of breath and blood benzene and urinary phenol has been explored in conjunction with personal monitoring data. At exposures of about 1 ppm benzene, urinary phenol is of no value as an indicator of uptake/exposure. Benzene in blood was measured by head space gas chromatography but the concentrations were only just above the detection limit. The determination of breath benzene collected before the next shift is non-specific in the case of smokers. The most useful monitor at low concentrations appears to be breath benzene measured at the end-of-shift.

There is a causal association between regular and prolonged exposure to high concentrations of benzene and the onset of haematotoxic (> 30 ppm) and leukaemogenic (> 100 ppm) effects. The evidence for this association has been adequately reviewed.[1-4]

Much controversy still continues on what level of exposure to benzene constitutes an acceptable risk. Without reliable and quantified exposure data it is impossible to describe the dose response curve relating exposure to effect. Studies are needed to establish quantitative methods for monitoring exposed populations and to assist in advising on regulatory decisions. Biological monitoring, which may be used to assess the uptake of benzene, can be used in conjunction with personal monitoring to determine more accurately the exposure data. The methods adopted for biological monitoring, however, require validation, particularly at low exposure levels.

The current UK occupational exposure limit for benzene is 10 ppm (30 mg/m^3).[5] The proposed European Community Benzene Directive calls for an action level of 1 ppm benzene and a limit value of 5 ppm time weighted average. Any future studies on personal or biological monitoring must consider the need for developing methods that are reliable and precise at these low exposure concentrations.

Historically, urinary phenol has been used as an index of benzene exposure but this form of biological monitoring is unlikely to be of value if benzene exposure is less than 10 ppm.[6] Despite the fact that endogenous phenol obscures any phenol derived from absorbed benzene when the exposure is less than 10 ppm, urinary phenol is still used for monitoring workers, probably because there is no well validated alternative. The measurement of benzene in breath and blood has been proposed as a potential biological monitoring method.[7 8]

In addition to estimating the uptake of benzene in workers attempts have been made to evaluate the biological response. These tests have included cytogenetic studies[9] and haematological tests.[10] Reuvers has suggested that examination of the neutrophil to lymphocyte ratio may be of use in monitoring early effects of exposure.[11]

Workers employed in the production of coke and the recovery of chemical byproducts are potentially at risk from exposure to benzene. In this study we report the results of an evaluation of biological monitoring methods and haematological tests for monitoring workers in the coke oven industry.

Study details and methods

COKING OVENS

A study was carried out in May and June 1986 at two coking ovens, plants A and B. Plant A, commissioned in 1954, produces crude benzole as a byproduct of the coking process with an approximate composition of: benzene 74·6%, toluene 11·0%, xylenes 3·5%, and a mixture of hydrocarbons. Plant B, commissioned in June 1981, produces a crude benzole consisting of approximately: benzene 76%, toluene 7%, xylenes 2·5%, naphthalene 5·5%, and a mixture of hydrocar-

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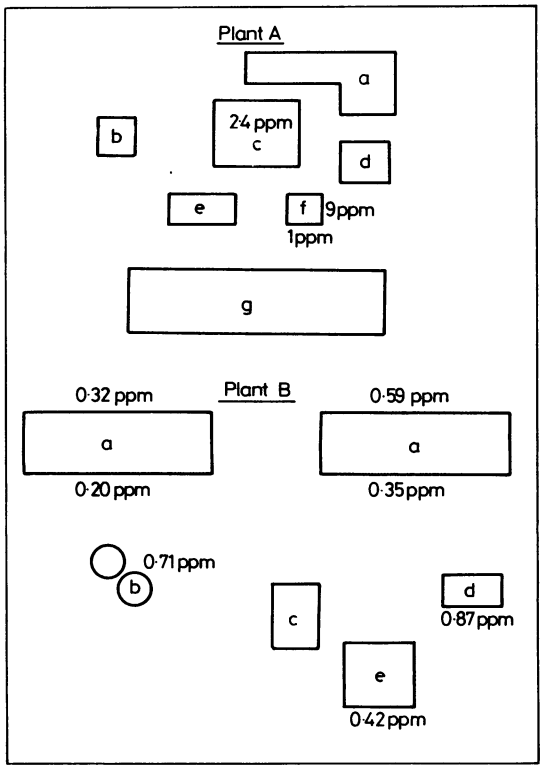

Fig 1 *Schematic diagram of coking ovens and byproducts recovery with typical benzene concentrations. Plant A: (a) storage tanks, (b) loading point, (c) heat exchange, (d) rack coolers, (e) pump house, (f) wells, (g) battery. Plant B: (a) battery, (b) benzole scrubbers, (c) control room, (d) storage tanks, (e) benzole plant.*

bons. A schematic diagram of both plants is presented in fig 1 with some typical atmospheric benzene concentrations.

VOLUNTEERS

The workforce were invited to volunteer after a detailed explanation of the purpose of the study and after full consultation with the trade unions and management. A group of 12 men from workshops located five miles from the nearest plant volunteered to act as unexposed controls. Fourteen men from plant A and 35 men from plant B volunteered to take part.

Each man completed a health and occupational questionnaire that included information on diet, smoking history, and medication. Four benzole tanker drivers agreed to take part in the survey on the days they were visiting the plant. A summary of the volunteer groups is given in table 1. The coke oven process is a 24 hour operation based on three eight

Table 1 *Details of volunteer groups*

	Controls	*Plant A*	*Plant B*	*Drivers*
Total No	12	14	35	4
Average age	35	36	35	56
Non-smokers	7	11	18	3
Smokers	5	3	17	1
Regular medication	1	1	1	1

hour shifts. The benzene exposed men were engaged as battery or benzole attendants. The volunteers were monitored for five consecutive shifts but in some cases it was only possible to monitor some men for three consecutive shifts.

PERSONAL MONITORING SAMPLES

All sampling procedures were carried out at the appropriate medical centre where the background atmospheric benzene concentrations were less than 0·08 ppm.

At the beginning of a shift each man was supplied with a personal monitor. This consisted of a portable pump connected to a charcoal tube located in the breathing zone. The monitors were removed at the end-of-shift and the charcoal tubes were analysed immediately.

BLOOD SAMPLES

Before the monitoring exercise began a blood sample was taken from each man before he started work after at least two days rest. During the study a blood sample (5 ml) was collected from each man at the end-of-shift and transferred to an EDTA bottle. A blood film was prepared immediately and a blood sample (1 ml) returned to the laboratory within 24 hours for routine haematology screening. Duplicate samples (2 ml) were dispensed into head space vials, sealed, and stored at −20 °C for benzene analysis.

BREATH SAMPLES

Breath (alveolar air) benzene was measured directly using a respiratory mass spectrometer. Samples were collected at the beginning of each shift, at midshift, and at end-of-shift.

URINE SAMPLES

A urine sample was collected at the beginning and end of each shift for phenol analysis. The samples were collected in polycarbonate bottles and stored at −20 °C.

Analytical methods

ENVIRONMENTAL BENZENE

The front and back of the charcoal tubes were analysed separately to establish that no breakthrough

had occurred. Benzene was desorbed with carbon disulphide (1 ml) and quantified using a Pye Unicam GCD gas chromatograph fitted with a 5 ft × 4 mm Apeizon L column and a flame ionisation detector.

BLOOD BENZENE

Blood benzene concentrations were determined by head space analysis on a Perkin Elmer Sigma 4 gas chromatograph fitted with a semiautomatic HS6 unit. A 10% Carbowax 1500 on Chromosorb W column was used with a flame ionisation detector. No peak with the retention time of toluene was found in any of the exposed blood samples so this compound was used as an internal standard. The calibration was linear over the range of 0–2·25 μmol/l and the detection limit was 0·05 μmol/l.

BREATH BENZENE

Breath benzene measurements were made directly using a respiratory mass spectrometer (PETRA, VG, gas analysis). The breath inlet system was designed to sample alveolar air, based on the Haldane-Priestley tube.[12] The instrument was calibrated by injecting into the calibration loop prediluted volumes of benzene vapour. The selected ion m/z 78 for benzene was used for monitoring with a detection limit of 0·5 nmol/l.

URINARY PHENOL

Urine samples (1 ml) were treated with 70% perchloric acid (400 μl) and placed in a water bath at 100°C for one hour. Phenol and the internal standard (o-chlorophenol) was extracted with isopropyl ether (2 ml). The ether layer was injected (30 μl) on to a Nucleosil C18 column for high performance liquid chromatography. A Waters 6000A pump and autoinjector (WISP) were used with a Gilson 116 UV detector (280 nm). Phenol and o-chlorophenol were eluted using a solvent mixture of acetonitrile, water, and methanol (2:4:1) at a flow rate of 1 ml/min. The calibration curve was linear over the range 0–1000 μmol/l and the within-batch coefficient of variation was 6·2%.

CREATININE ASSAY

Creatinine in urine was measured by the Jaffé reaction using a Cobas Bio autoanalyser.

HAEMATOLOGY

A Coulter Counter S5 was used to provide a "Coulter profile" that included total red and white cell counts, haemoglobin, mean cell volume, and packed cell volume measurements. The blood films were stained using the May Grunwald-Giesma technique and differential counts were obtained by optical microscopy.

Results

Initially, the data from the two coking ovens were examined separately but there was no significant difference between the two groups and since the conditions and procedures in both plants were similar the data have been combined. Further analysis of the data is based on a control group and an exposed population. The latter is subdivided into battery men (lowest exposure), benzole men (intermediate), and tanker drivers (highest).

BENZENE EXPOSURE

The benzole men are employed in byproduct recovery and are exposed to higher levels of benzene than the battery workers. This is shown in the mean time weighted average exposure levels for benzole men (1·32 ppm benzene) compared with battery men (0·31 ppm). Benzene exposure, however, can occur both through inhalation and by skin absorption.[13]

The highest recorded time weighted average was 4·3 ppm for a benzole worker. The tanker drivers were exposed to air concentrations ranging from 11·5 ppm to 38·2 ppm but these values were for a period of about 50 minutes and were not adjusted to give the time weighted average over an eight hour shift.

BREATH BENZENE

In 80% of the workforce the preshift breath benzene concentrations were below the detection limit (0·5 nmol/l). Where this was not the case, the men were either smokers, benzole attendants, or tanker drivers. No benzene was detected in the breath of the non-smoking controls. The preshift concentration in smokers was generally less than 2 nmol/l; however, one worker had a concentration of 4·5 nmol/l. Figure 2

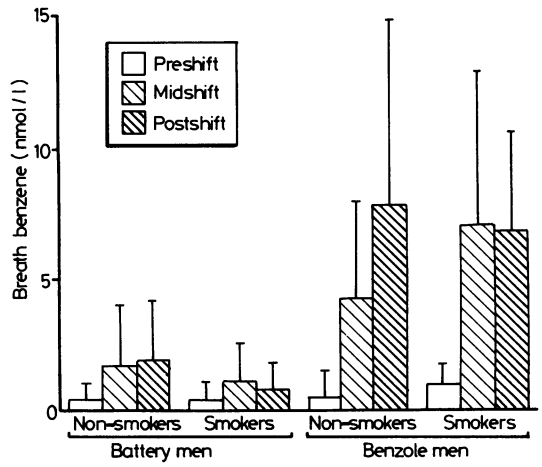

Fig 2 *Comparison of breath benzene concentrations in battery and benzole men.*

shows the general trend of breath benzene concentrations throughout the shift for battery and benzole operators. Breath results show convincingly the difference in exposure between benzole men and battery men. There is no significant difference between preshift values of battery men and benzole men or between smokers and non-smokers. Midshift and postshift concentrations, however, show a definite increase for benzole workers and although battery men also have a slight increase over the shift period, it is possible to differentiate between the two groups. Examination of the preshift breath concentrations for the benzole attendants over five consecutive shifts showed no evidence of accumulation.

BLOOD BENZENE

Table 2 shows the mean blood benzene concentrations for each group of workers and the number of workers with no detectable benzene. Control workers had blood benzene concentrations below the detection limit of 0·05 μmol/l with the exception of one worker. This man, who had a value of 0·06 μmol/l, was a smoker. In the exposed group all but one of the pre-exposure blood concentrations were below the detection limit; an unusually high value of 0·41 μmol/l was found in one smoker. Most battery men (81%) had blood concentrations below the detection limit in samples taken at end-of-shift. The mean concentration was 0·08 μmol/l for those samples which had detectable benzene. The blood benzene concentration in benzole workers ranged from $<0·05$ to 0·76 μmol/l and the mean concentration for those with detectable benzene was higher than that found in the battery men. The tanker drivers had the highest levels, ranging from 0·22 to 1·8 μmol/l.

BLOOD/BREATH BENZENE RATIO

In previous studies in this laboratory with other solvents—for example, toluene and 1,1,1-trichloroethane—we have shown that a relation exists between blood and breath solvent concentrations (typically $R^2 > 0·9$) (unpublished observations). Using data from samples (n = 58) with benzene concentrations above the detection limits, the correlation coefficient in this study, $R^2 = 0·58$, was poorer than expected. This may be due in part to the difficulty in measuring very low levels of benzene in blood by head space gas chromatography.

Table 2 *Concentration of blood benzene in different groups*

	No	*No below detection limit**	*Blood benzene (μmol/l)*
Controls	12	11	—
Pre-exposure blood	44	43	—
Battery men (end-of-shift)	145	117	0·08
Benzol men (end-of-shift)	31	7	0·19
Tanker drivers	4	0	0·82

*0·05 = μmol/l.

URINARY PHENOL

The urinary phenol concentrations ranged from 1 to 25 μmol phenol/mmol creatinine in unexposed workers. These results confirm previously published findings.[14] There was no significant change in the preshift and postshift urinary phenol concentrations in the control group. In the exposed workers 5% of preshift results and 6% of postshift values were above 25 μmol phenol/mmol creatinine. Although there was an upward trend in the postshift urinary phenol concentrations in some of the exposed workers, the range was wide (fig 3). The group mean values for preshift and postshift results did not differ significantly (table 3). It was not possible to link the urinary phenol content to diet. It was not uncommon to find a fall in urinary phenol concentrations over the shift period.

RELATION BETWEEN EXPOSURE AND BIOLOGICAL PARAMETERS

Using only samples that had values above the detection limit the relation between the log of the exposure and the log of benzene in blood and breath and phenol in urine has been examined (table 4). There was a weak correlation between benzene exposure and blood or

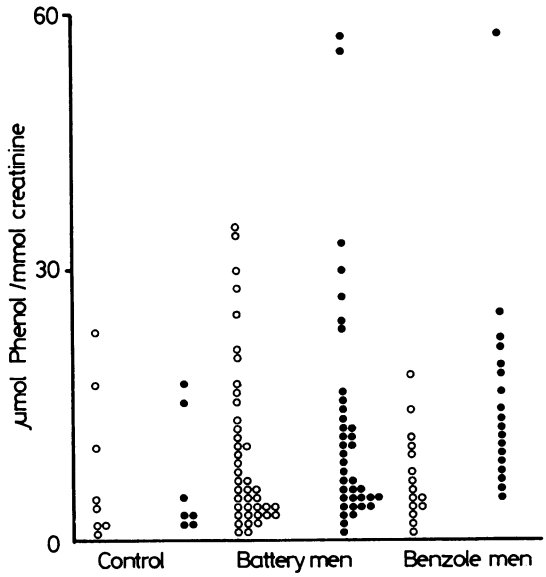

Fig 3 *Urinary phenol concentrations in three groups of workers. ◦ = preshift; • = postshift; ◦ 1–5 samples; ◦◦ 6–10; ◦◦◦ 11–15; ◦◦◦◦ 16–20; ◦◦◦◦◦ 21–25.*

Table 3 *Mean urinary phenol concentration and range*

	μmol phenol/mmol creatinine	
	Preshift	*Postshift*
Controls	6·91 (1·5–25·5)	5·36 (2·0–19·3)
Battery men	9·44 (1·3–35·4)	10·60 (1·5–60·8)
Benzol men	6·10 (1·3–22·0)	13·41 (3·9–59·0)

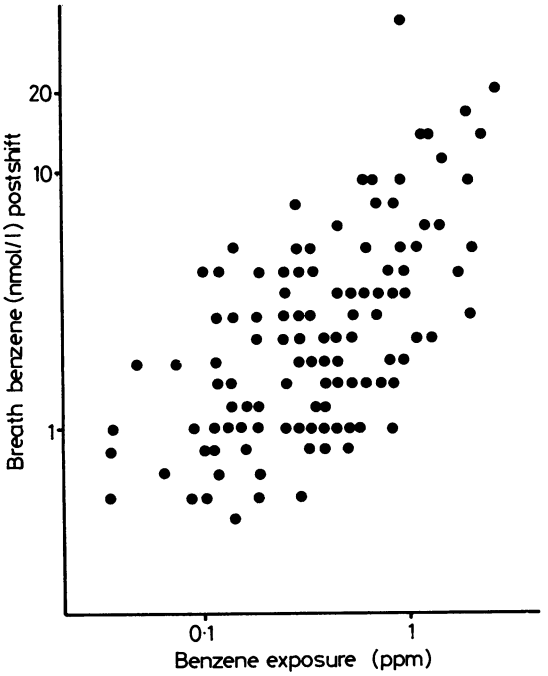

Fig 4 *Postshift breath benzene concentrations and personal benzene exposure (No = 128; R^2 = 0·64).*

Table 4 *Relation between exposure and biological parameters*

	No of samples	*Correlation coefficient R^2*
Blood benzene	56	0·51
Breath benzene	128	
Midshift		0·51
Postshift		0·64
Urine	161	
Postshift		0·25
Post-pre		0·27

breath benzene (fig 4). Breath benzene measured at end-of shift appears to relate more closely than blood benzene to the personal monitor results. Urinary phenol measured at end-of-shift or after the preshift concentration had been subtracted from the end-of-shift value did not show any relation to benzene exposure.

HAEMATOLOGY

All the blood samples examined showed no haematological abnormalities. We found one reversed neutrophil to lymphocyte ratio in a benzole worker but the importance of this finding is not clear.

Discussion

Some authorities recommend the determination of urinary phenol as a biological monitoring method for monitoring workers exposed to benzene.[14] Since interindividual variation in endogenous urinary phenol is large, it has been proposed that the test should be applied only to a group of workers. There are strong arguments against this approach as the advantages of biological monitoring are lost and important practical and ethical considerations are introduced. From the results in two coking ovens, where personal exposure to benzene was typically 1 ppm, we noted that there was no relation between individual exposure and urinary phenol concentration. In this study 95% of the results were within the "normal" range of 1–25 μmol phenol/mmol creatinine. Urinary phenol measurements may have some value if exposure to benzene is in excess of 10 ppm[15] but we can find no reason for using this form of biological monitoring with low level benzene exposure.

Little attention has been paid to the routine determination of benzene in blood. Head space gas chromatography has been used to measure a number of solvents in blood with good sensitivity and specificity. This method, however, is less reliable at very low exposure levels of benzene. The determination of low concentrations of benzene in blood is limited by the presence of interfering substances.

As benzene is present in cigarette smoke and may be detected in the breath of smokers,[16] preshift monitoring of workers exposed to benzene will be non-specific for smokers. We observed that in the majority of smokers examined the preshift breath benzene concentration was less than 2 nmol/l. The American Committee of Governmental Industrial Hygienists (ACGIH) also recommend the use of breath benzene as a monitoring method where the breath sample is taken before work on the day after exposure. The ACGIH action limit is 4·6 nmol/l and in all cases the preshift breath concentrations in this study were below this figure. At this relatively low level the contribution from benzene in cigarettes becomes a confounding factor when monitoring smokers. In midshift and postshift samples there was a clear distinction between the battery men and the benzole men where the concentrations were about 2 and 9 nmol/l respectively. This fourfold increase was noted in the exposure levels (battery men 0·31 and benzole men 1·32 ppm).

We observed no abnormalities in haematological

tests which is in agreement with previous findings.[10] The work of Reuvers[11] prompted us to look at neutrophil to lymphocyte ratios. In one blood sample from a benzole worker we noted a reversal; however, there was no evidence of excessive benzene exposure from any of the environmental or biological measurements. The maximum benzene exposure for this worker, over a five day period, was 2·2 ppm and on this occasion the blood and breath concentrations were 0·28 μmol/l and 9·4 nmol/l respectively. The importance of this finding is not clear since viral lymphocytosis and bacterial neutrophil leucocytosis will render the changes non-specific.

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