[CANCER RESEARCH 46, 4178–4183, August 1986]

Determination of Polycyclic Aromatic Hydrocarbons in the Urine, Benzo(*a*)pyrene Diol Epoxide-DNA Adducts in Lymphocyte DNA, and Antibodies to the Adducts in Sera from Coke Oven Workers Exposed to Measured Amounts of Polycyclic Aromatic Hydrocarbons in the Work Atmosphere

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ABSTRACT

Workers in coke oven plants have a higher incidence of lung cancer than the general population. They are esposed to a variety of chemicals, in particular the polycyclic aromatic hydrocarbons (PAH), including benzo(*a*)pyrene. To evaluate the genotoxic effects of PAH exposure, air samples and urine samples were analyzed for PAH by capillary gas chromatography and high-performance liquid chromatography, respectively. Since benzo(*a*)pyrene is activated to 7β,8α-dihydroxy-(9α,10α)-epoxy-7.8.9. 10-tetrahydrobenzo(*a*)pyrene (BPDE) and binds to DNA, we hate used ultrasensitive enzymatic radioimmunoassay and synchronous fluorescence spectrophotometry to measure BPDE-DS.4 adducts in lymphocyte DNA. The results show that workers were esposed to high concentrations of atmospheric PAH. However. the mean PAH esposure levels are reduced 60% when the workers wore masks during work. When compared to exposure levels. the urinary excretion of PAH was relatively low. Approximately one-third of the workers had detectable putative BPDE-DNA adducts in lymphocytes by ultrasensitive enzymatic radioimmunoassay. and 10% of the samples had emission peaks at 379 nm by synchronous fluorescence spectrophotometry. The four most positive samples were the same in both of the assays. Antibodies to an epitope(s) on BPDE-DNA were found in the sera of approximately one-third of the workers. Detection of DNA adducts and antibodies to these adducts are internal indicators of exposure to benzo(*a*)pyrene.

INTRODUCTION

Emissions from coke ovens pose a significant risk of cancer to the exposed coke workers. This is based on epidemiological surveys (1. 2) as well as experimental animal studies (3) and chemical analyses of coke oven emissions (4). Epidemiological studies indicate an excess relative risk for lung cancer as high as 16-fold for topside coke oven workers with 15 yr of exposure or more (2). Chemical analyses of coke oven emissions have revealed the presence of over 100 different PAH[2] some of which are known to be potent carcinogens in experimental animals (4).

PAH have long been of concern as a potential human health hazard. There is considerable evidence that PAH are enzymatically converted to reactive metabolites that bind covalently to cellular macromolecules (for review. see Ref. 5). The covalent binding of reactive metabolites to DNA is considered to be an important step in tumor initiation by these carcinogens (6). In fact. the carcinogenic potency of a number of PAH correlates with their ability to form specific covalent adducts with DNA (6–8). However, the persistence of BPDE-DNA adducts *per se* is apparently not sufficient for tumor induction (9). BP, a prototype of the carcinogenic PAH and the most thoroughly studied one. is metabolized to the chemically reactive isomers BPDE I and II, resulting in the formation of covalent BPDE-adducts with DNA (5).

Sensitive methods are required to detect carcinogen-DNA adducts in exposed individuals. Immunoassays. *i.e.*, ELISA and USERIA (10–16). synchronous fluorescence spectrophotometry (17–19), ^{32}P-postlabeling assay (20). and HPLC ^{32}P assay (21) are methods currently being developed to detect the presence of carcinogen adducts in DNA. Recent reports have indicated the presence of BPDE-DNA adducts in human lung tissue of patients with cancer of the lung and in human WBC from occupationally exposed groups (15, 18. 19, 21). The purpose of this study was to quantify the carcinogenic exposure and bioavailability of PAH by analysis of airborne PAH, urinary PAH levels. and the amounts of BP derivatives bound to DNA in peripheral blood lymphocytes of coke oven workers exposed to high levels of PAH in the uork environment. In addition, we examined the sera from these workers for antibodies to an epitope(s) on BPDE-DN.4.

MATERIALS AND METHODS

Chemicals. The solvents used were either "all glass distilled" in the laboratory or HPLC grade from Rathburn. Ltd.. Walkerbyrn, Scotland. PAH standards were obtained from Fluka. Buchs. Switzerland [benz(*a*)anthracene. fluorene. and pyrene]; Koch-Light. Ltd.. Suffolk. United Kingdom [benzo(*a*)fluorene. benzo(*a*)pyrene, benzo(*e*)pyrene, and fluorene]: BDH. Ltd., Poole. United Kingdom (chrysene and fluoranthene); ICN Pharmaceuticals. Inc.. Plainview, NY (2,2'-binaphthyl): TCI. Tokyo, Japan (3,6-dimethylphenanthrene).

Amberlite XAD-2 was obtained from Fluka. Buchs. Switzerland. and cleaned by Soxhlet extraction with methanol. acetone. and cyclohexane prior to use. Proteinase (Pronase) was purchased from Calbiochem Corp. (La Jolla, CA) phenol (nucleic acid grade) from Bethesda Research Laboratories. Inc. (Gaithesburg, MD); chloroform and isoamyl alcohol from J. T. Baker Chemical Co. (Phillisburg, NJ); alkaline phosphatase-conjugated goat anti-rabbit IgG (Fab_2) from Cappel Laboratories. West Chester. PA; [^{3}H]PNPP, Econofluor, from New England Nuclear. Boston. CIA: and PNPP from Sigma Chemical Co., St. Louis. MO.

Subjects. Topside coke oven workers (22 smokers, 8 exsmokers and 8 nonsmokers) were investigated. The age. sex. number of cigarettes smoked per day. and medication were scored for all subjects. Urinary PAH analyses were performed on 15 smokers and 9 nonsmokers and DNA analyses on all 38 subjects. The urine and blood samples were

Received 10/4/85; revised 4/11/86; accepted 4/30/86.

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[2] The abbreviations used are: PAH, polycyclic aromatic hydrocarbons: BP. benzo(*a*)pyrene; BPDE. 7β,8α-dihydroxy-(9α,10α)-epoxy-7.8.9.10-tetrahydrobenzo(*a*)pyrene; ELISA. enzyme-linked immunosorbent assay; PNPP, paranitrophenyl phosphate: POM. polycyclic organic matter: SFS. synchronous fluorescence spectrophotometry: USERIA. ultrasensitive enzyme radioimmunoassay: HPLC. high-performance liquid chromatography.

collected at the end of the work shift. The urine samples were immediately frozen. and blood samples were transported to the laboratory at 4°C. The serum for antibody studies was frozen at −70°C. Eighty % of these workers wore a full-face respiratory protection system with airfilte mask. Exposure levels of PAH were determined by personal air sampling both inside and outside the respirator worn by topside workers. Four samples from different persons were collected using a sampling system consisting of a membrane filter (Versapor 800; Gelman. Inc.) and a back-up section of Amberlite XAD-2 resins. The sample volumes outside and inside the respirator were 0.449–0.480 m^3 and 0.905–0.943 m^3, respectively.

Analysis of Airborne PAH. The particulate PAH collected on the filter and the gaseous PAH adsorbed on the XAD-2 resins were extracted in a Soxhlet apparatus for 24 h with methylene chloride containing 2,2'-binaphthyl and 3.6-dimethylphenanthrene as internal standards. The extracts were carefully concentrated to a smaller volume under a gentle stream of highly purified N_2. The PAH were transferred to freshly distilled cyclohexane and cleaned by liquid/liquid extraction with dimethyl formamide/water as described by Bjerseth (23). The PAH were analyzed by a Hewlett-Packard gas chromatograph. Model 5730A. equipped with a SE-54 fused silica column and a flame ionization detector.

Analysis of Urine Samples. Creatinine levels in each of the urine samples were determined spectrophotometrically using the Jaffe reaction. Urine samples with a creatinine concentration below 5 mol/liter were excluded from statistical analysis. Furthermore. urine samples with a volume of less than *50* ml were not analyzed. The analytical method for the determination of urinary PAH levels consisted of the following steps: (*a*) extraction of PAH and their metabolites from urine using commercial preparative cartridges containing C_{18}-modified silica: *b*) reduction of metabolites to parent PAH by hydriodic acid: and *(c)* analysis of the PAH by HPLC with fluorescence detection. A detailed description of the procedure has been given elsewhere (24). In the present study anthracene was not included in the analysis. In earlier studies (25), anthracene constituted between 2 and 7% of the sum of the 10 major PAH in urine samples from exposed workers.

DNA Isolation. Twenty-five ml of peripheral blood were collected. and the lymphocytes were separated by the Lymphoprep method and immediately frozen. DNA was prepared from lymphocytes as previously described by treatment with proteinase K. extracted with chloroform:isoamyl alcohol (24:1) followed by two sequences of proteinase treatment, phenol extractions. and ethanol precipitation overnight at −20°C (19). The 260 nm/280 nm absorbance ratio of DN.4 after purification was over 1.7.

Synchronous Fluorescence Spectrophotometry for Detection of BPDE-DNA Adducts. The DNA samples were acid hydrolyzed in 0.1 M HCl at 90°C for 3 h as described before (19). The samples were assayed at room temperature using Perkin-Elmer Fluorescence Spectrophotometer 650-40 with Perkin-Elmer Model 3600 data station by scanning excitation and emission synchronously with a constant wavelength difference of 34 nm. The hydrolysis products of BPDE-DNA [benzo(*a*)pyrene-tetrols and -triol] give a specific emission peak at 379 nm (19). *SFS* assays for BPDE-DNA were performed only once on 1-ml volumes containing 100 μg of sample DNA per ml.

Ultrasensitive Enzyme Radioimmunoassay for Detection of BPDE-DNA Adducts. The rabbit antiserum used reacts with BPDE-DNA (14) and to a lesser extent chrysene-modified DNA (18). BPDE-modified calf thymus DNA was used as the standard reference DNA and alkaline phosphatase-conjugated goat anti-rabbit IgG (Fab_2) as the secondary antibody, a mixture of [^{3}H]PNPP and PNPP as the substrate. and Econofluor 2 as the scintillate.

The USERIA was performed as described before (26). Briefly. polyvinyl microtiter plates were precoated with 0.2 ng of BPDE-DNA. washed, and treated with 2% horse serum for 1 h. Test samples were double-stranded or sonicated double-stranded DNA. An equal volume of a 1:3 $\times 10^5$ dilution of rabbit anti-BPDE-DNA antiserum was added to each sample and to tubes containing serially diluted double-stranded BPDE-DNA prepared in 10- or 25-μg/ml solutions of double-stranded calf thymus DNA for the standard curve. Each antigen-antibody solution was added to microtiter wells containing single-stranded BPDE-DNA as the solid phase competitor and to a well containing single-stranded coid thymus DNA ior specificity control. After 90-min incubation at 37°C the plates were washed. and alkaline phosphatase-conjugated goat anti-rabbit IgG (Fab_2) (1:500) was added and incubated 1 h at 37°C. The plate was washed. 100 μl of 10 to 20 pmol of tritiated PNPP and *80* to 90 pmol of PNPP per well in 10 mM MgCl were added, and the plate was incubated for 4 h at 37°C. Finally, 20 μl from each well were then diluted in 2 ml of buffer and mixed with 4 ml of Econofluor 2, and the hydrolyzed [^{3}H]PNP was separated in the organic phase to measure radioactivity.

ELISA for Detection of Antibody to BPDE-DNA Adducts. Human sera were tested for the presence of antibodies as described before (18). Briefly. 20 ng of BPDE-modified DNA (test antigen) or unmodified DNA (control antigen) were attached by drying to the wells of polyvinylchloride microtiter plates (Costar. Cambridge. MA). Human serum samples were tested using triplicate tests and 4 log, serial dilutions. The binding of immunoglobin was detected using goat anti-human immunoglobin reagents and the avidin-biotin horseradish-peroxidase system (ABC L'ectastain kit: Vector Laboratories. Burlingame. CA).

The enzyme reaction was developed by the addition of 100 μl of the substrate solution [0.05 M citrate buffer (pH 4.0):*o*-phenylenediamine dihydrochloride (1.0 mg/ml):30% H_2O_2 (*0.5* μl/ml)] to each of the wells. The enzyme reaction was stopped after 20 min by the addition of 50 μl of *2.5* M H_2SO_4 per well. The plates were read. and the absorbance at 490 nm was recorded.

The mean ± SD of triplicate ELISA absorbance readings was determined and used to establish the significance of antibody reactions. Antibody reactions were considered positive when the mean absorbance values of the triplicate test wells were significantly greater than control test absorbance values. The ELISA absorbance significance levels were established as the mean absorbance. obtained using a particular serum dilution on unmodified DNA. plus 2 SDs. Antibody data are reported as titer end points which represent the highest serum dilution which produced a significant level of specific antibody binding.

RESULTS

Typical capillary gas chromatograms of filter (*a*) and XAD-2 (b) extract are shown in Fig. 1. A typical distribution of particulate and gaseous PAH is shown in Table 1. Other POM identified included dibenzofuran. dibenzothiophene. carbazole. benzo(*def*)dibenzothiophene, benzothionaphthene. and benzophenanthridine. The total amounts of particulate and gaseous PAH in the air samples collected outside and inside the respirators are shown in Table 2.

The concentration of total PAH in the atmosphere outside the respiratory device varied from 212–315 μg/m^3 (Table 2). Inside the mask the PAH concentration vaned from 51–162 μg/m^3. The corresponding concentrations of BP were 7–9 μg/m^3 and 1–4 μg/m^3, respectively. The respirators were able to remove 49–76% of the PAH and 49–87% of BP.

Urinary excretions of PAH in exposed smokers and nonsmokers are shown in Fig. 2. The results are given in μg/mmol of creatinine in order to correct for varying dilution of the urine samples. The urinary excretion of PAH was relatively low. as compared to results recently obtained for aluminum plant workers *(25)*. The mean value for PAH in nonsmokers was 0.57 μg/mmol of creatinine and 0.87 μg/mmol of creatinine for smokers. A reasonable explanation for this low urinary PAH level is that the majority of coke oven workers (80%) wore full-face masks. Fig. 3 shows levels of various PAH in workers' urine. There were no significant qualitative or quantitative differences in PAH excretion between nonsmokers and smokers.

Lymphocyte DNA from the workers was analyzed for BPDE-DNA adducts. By SFS. 4 of 38 DNA samples isolated from peripheral lymphocytes demonstrated a peak at 379 nm of emission with the wavelength difference (AX) of 34 nm indicat-

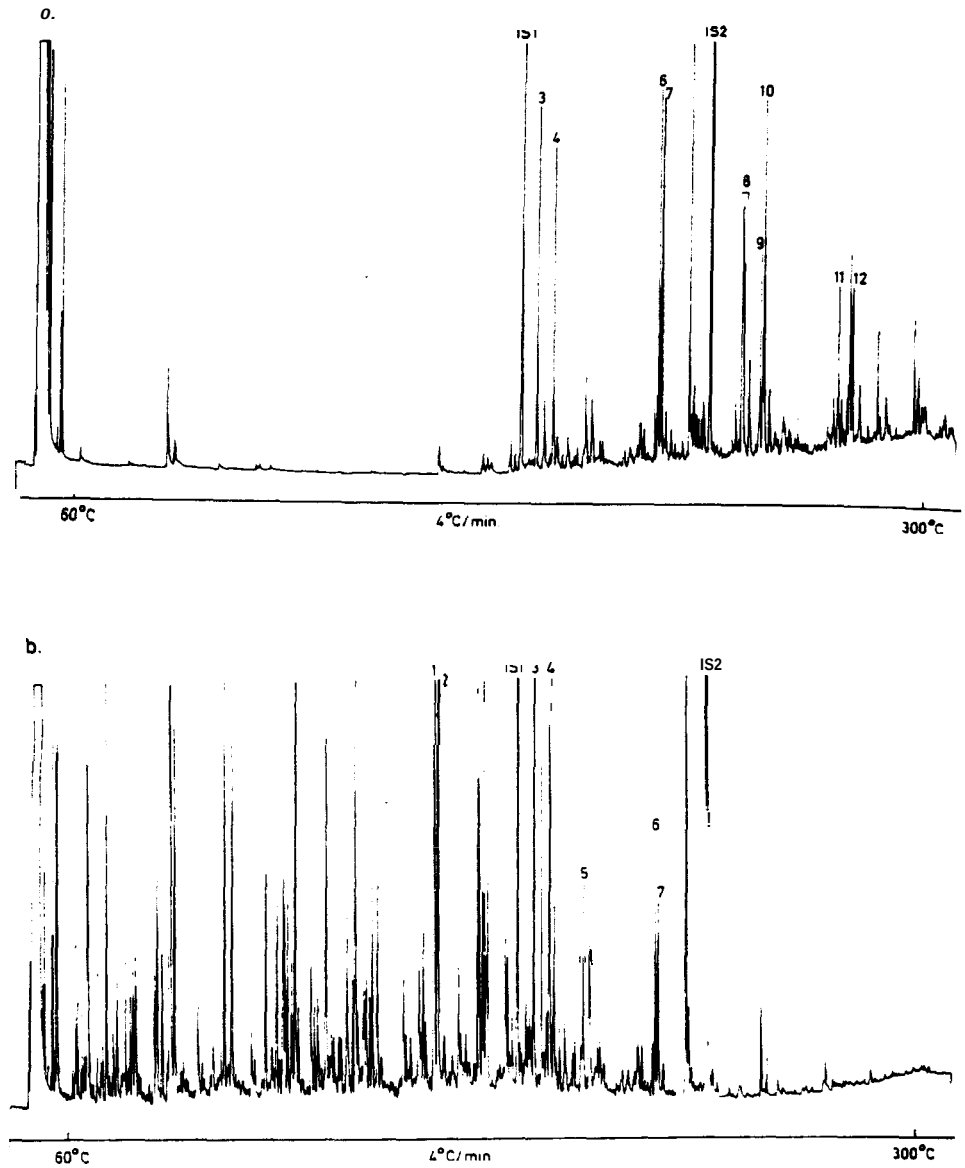


Fig. 1. Typical gas chromatograms of filter extract (*a*) and XAD-2 extract (*b*). Main components are: *1*, phenanthrene; 2. anthracene: 3, fluoranthene: *4*, pyrene; *5*, benzo(*a*)fluorene; *6*, benz(*a*)anthracene; 7, chrysene/triphenylene; *8*, benzo(*b*+*j*+*k*)fluoranthene; 9, benzo(*e*)pyrene; *IO*. benzo(*a*)pyrene; *11*, indeno(1,2,3-*c*+*d*)-pyrene: *12*. benzo(*g*+*h*+*i*) perylene; *IS1*, 3,6-dimethylphenanthrene:*IS2*, 2,2′-binaphthyl.

ing putative BPDE-DNA adducts in lymphocytes (Table 3). The amount of adducts detected ranged from 2.2 fmol/μg of DNA to **0.38** fmol/μg of DNA. Three of the **4** positive samples were smokers. By USERIA. **13** of the **38** samples tested (34%) had detectable levels of BPDE-DNA antigenicity (Table 3). The level of adducts ranged from **> 13.7** to 0.1 fmol of BPDE per μg of DNA. The mean level of BPDE adducts for these cases was **1.7** fmol of BPDE per μg of DNA. The 4 positive samples in the SFS assay were also found to have a high percentage of inhibition and the highest values in the USERIA. Fifty % of the nonsmokers and 37% of the exsmokers were positive, and no significant difference in the level of BPDE-adducts could be demonstrated as measured by USERIA (except for one female worker having >13.7 fmol of BPDE per μg of DNA): **0.41 ± *0.25*** fmol/μg of DNA for nonsmokers and **0.49 ± 0.10** fmol/μg of DNA for exsmokers. The mean level of the BPDE-DNA adduct for the smokers was 0.93 ± 0.75 fmol/μg of DNA ***(P C* 0.05** compared with the nonsmokers). Twenty of the 38 individuals were retested for BPDE-DNA adduct level after a 3-wk vacation. As shown in Table 3, by **USERIA.** the level of BPDE-DNA adducts for all but one of the individuals either remained the same or decreased after the 3-wk vacation period. By **SFS,** all 20 samples were negative.

Antibodies to BPDE-modified DNA were studied in sera from the same workers. As shown in Table 4, at the first bleeding 12 of 38 (32%) serum samples were positive, *i.e.*, containing antibodies to an epitope(s) on BPDE-DNA. Nine mo later 13 of 38 (34%) of the sera tested from the same workers were positive. During a period of 9 mo **no** change in specific antibody titers to BPDE-DNA could be detected for 21 individuals. **8** lost titers. and 9 gained titers. There was observed ***no*** statistically significant correlation between antibody titers and years of employment at the coke oven plant.

DISCUSSION

It has long been recognized that products from incomplete combustion and destructive distillation products of coal **are** carcinogenic to humans. Over the past 200 yr it has **been** demonstrated that a variety of industrial populations, exposed either to emissions from these processes or to handling of the products. are at an increased risk for developing cancer of the lung, skin. and urinary organs. Workers on coke ovens **are** exposed to a rather complex mixture of dusts, vapors, **and** gases. Analysis of the topside coke-oven samples from the **work** atmosphere showed that the exposure to PAH is high. **The**

mean concentration is 266 $\mu g/m^3$ for total PAH (90 $\mu g/m^3$ for particulate PAH. 176 $\mu g/m^3$ for gaseous PAH) and 8 $\mu g/m^3$ for BP. These findings are in good agreement with previous studies (4). Furthermore, our results show that the mean PAH exposure lev ' were reduced 60% when the workers wore full face masks du _ work. For instance the masks reduced the average exposure for BP from 8 $\mu g/m^3$ to 3 $\mu g/m^3$. The fact that 80% of the workers in this study wore masks can explain the relatively low mean value of PAH excreted in urine.

Formation of specific adducts in target cell DNA is assumed to be an important initial event in the carcinogenic process. and some studies have shown that the carcinogenic potency of various PAH correlates with their ability to form specific adducts (6–8), while others have not found this association (9). A quantitation of these adducts may give us an indication of the biologically effective dose. In recent years quantitation of carcinogen-DNA adducts has become possible by using specific polyclonal and monoclonal antibodies as well as biophysical methods which recognize specific alterations within the DNA molecule at the fmol level. The level of BPDE-DNA adducts measured is a result of BP exposure, metabolic activation and deactivation of BP. and DNA repair capacity. Our results show that 34% of the topside coke oven workers had detectable putative BPDE-DNA adducts in lymphocytes by USERIA. and 10% of the samples had emission peaks at 379 nm. In a recent study 66% of the coke oven workers had detectable putative

Table 1 *A typical distribution of particulate* and gaseous *PAH* outside rhe *respiratory device*

	PAH ($\mu g/m^3$)	
	Paniculate	Gaseous
Acenaphthylene		28.3
Acenaphthene		3.8
Fluorene		14.0
2-Methylfluorene		2.5
1-Methylfluorene		1.8
Phenanthrene	3.0	46.0
Anthracene	1.3	15.0
3-Methylphenanthrene	0.4	3.2
2-Methylphenanthrenr	0.7	4.3
2-Methylanthracene	0.1	2.6
4,5-Methylenephenanthrene	0.8	4'
4- and or 9-methylphenanthrene	0.1	2.8
1-Methylphenanthrene	0.4	3.0
Fluoranthene	8.0	13.6
Benz(*e*)acenaphthylene	1.5	2.1
Pyrene	7.1	9.7
Ethylmethylenephenanthrene	1.3	2.0
Benzo(*a*)fluorene	2.3	1.4
Benzo(*b*)fluorene	2.3	2.0
4-Methylpyrene		
2-Methylpyrene and/or methyl-fluoranthene	1.1	0.5
1-Methylpyrene	0.7	0.6
Benzo(*g+h+i*)fluoranthene	1.0	0.6
Benzo(*c*)phenanthrene	0.9	0.5
Cyclopenteno(*c+d*)pyrene	1.5	0.4
Benz(*a*)anthracene	5.8	1.7
Chrysene and triphenylene	7.0	1.6
Benzo(*b*)fluoranthene Benzo(*j*)fluoranthene Benzo(*k*)fluoranthene	4.3	
Benzo(*e*)pyrene	4.7	
Benzo(*a*)pyrene	7.3	
Perylene	1.8	
Indeno(1,2,3-*c+d*)pyrene	4.5	
Dibenz(*a,c* and/or *a,h*)anthracenes	1.2	
Benzo(*g+h+i*)perylene	4.4	
Anthanthrene	2.4	
Coronene	3.2	
Sum identified PAH	81	168

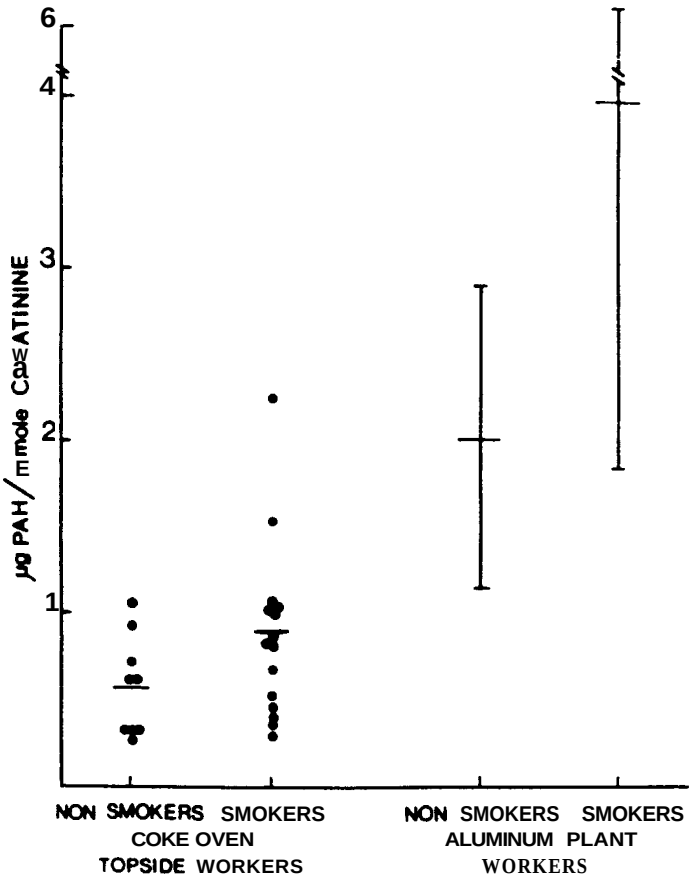


Fig. 2. PAH levels of urine samples from exposed workers (9 nonsmokers and 15 smokers) compared to results obtained for aluminum plant workers (25).

Table 2 Concenrration of PAH and *POM* ($\mu g/m^3$) outside and inside the respirator

	Sample A		Sample B		Sample C		Sample D	
	Paniculate	Gaseous	Particulate	Gaseous	Particulate	Gaseous	Particulate	Gaseous
Outside respirator								
PAH	82	130	81	168	100	189	97	218
POM	ND[a]	11	2	15	2	16	2	20
PAH + POM	82	141	83	183	102	205	99	238
Total P9H	212		249		289		315	
Total PAH + POM	223		266		307		337	
Inside respirator								
PAH	15	36	35	73	31	87	56	106
PO51	0.4	4	1	7	1	8	1	11
"AH + POM	15	40	36	80	32	95	57	117
›tal PAH	51		108		118		162	
..otal PAH + POM	55		116		127		174	

[a] ND, not determined.

Table 3 *Detection of BPDE-DNA adducts in lymphocyte DNA from coke oven workers using both competitive USERIA and SFS*

Sample	Age (yr)	Sex	Employment yr	Smoking cigarettes/day	Air-filtering masks	USERIA (fmol/μg DNA)		SFS (fmol/μg DNA)	
						Working	Vacationing	Working	Vacationing
1	41	F	3	Never	+	>13.7	0.15	2.2	ND[b]
2	40	M	18	7	+	2.0	0.14	0.4	ND
3	38	M	13	3	−	1.8	NT	0.5	NT
4	60	M	20	Exsmoker	+	0.4	0.12	ND	ND
5	28	M	2	7	+	1.0	0.15	0.6	ND
6	21	M	1	Never	+	0.7	NT	ND	NT
7	53	M	8	Exsmoker	−	0.5	0.1	ND	ND
8	41	M	20	14	−	0.4	0.1	ND	ND
9	34	M	3	Exsmoker	+	0.6	NT	ND	NT
10	22	M	1	4	+	0.2	0.14	ND	NT
11	28	M	8	Never	+	0.1	0.1	ND	ND
12	25	M	6	21	+	0.1	0.15	ND	ND
13	23	M	2	Never	−	0.4	NT	ND	NT

[a] Samples taken 3 wk after leaving workplace during vacation period.
[b] ND. not detected level of sensitivity: 0.2 fmol/μg DNA. SFS: 0.1 fmol/μg DNA. USERIA: NT. not tested.

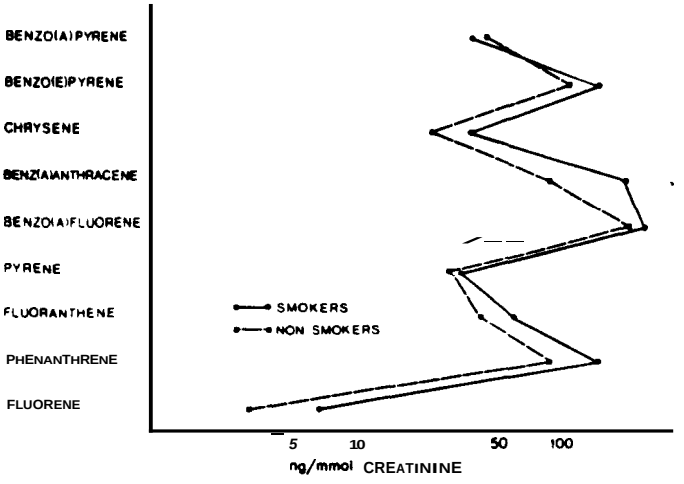


Fig. 3. Mean values for concentrations of individual PAH in workers' urine.

BPDE-DNA adducts by USERIA and 76% by SFS **(18).** In another study. 28% of the roofers and 35% of the foundry workers were positive by USERIA (15). A third study found that 2% of the aluminum workers had detectable BPDE-DNA adducts. while 9 nonsmokers working in the laboratory.were all negative **(19).** It is interesting that the 4 most positive were the same in both of the assays. Furthermore. our study demonstrates that the level of BPDE-DNA adduct remained the same or decreased for 90% of the workers retested by USERIA after 3 wk of vacation. By SFS. all 20 samples were negative after the vacation period.

Approximately one-third of these individuals also have developed antibodies against an epitope(s) on BPDE-DNA adducts. In a recent study by Harris and coworkers 28% of the workers had antibodies against this particular adduct (18). However. the exact structural component these antibodies react with should be determined. They may cross-react with adducts formed by related compounds having chemical structures or configurations closely related to a BPDE-DNA adduct. *e.g.*, chrysene-modified DNA (Ref. 18; Footnote 3). Furthermore. our results demonstrate that during a period of 9 mo. 9 workers gained titers and 8 workers lost titers. The persistence of the antibody titer needs to be investigated in serial samples from workers in such industries taken over a period of time. When compared to our previous study of coke oven workers in another plant the antibody titers in the study reported here were lower, *i.e.*, 25–625. Whether antibodies to carcinogen-DNA adducts may be useful indicators in epidemiological studies is currently being evaluated.

Table 4 *Presence of antibodies to BPDE-DNA adducts in sera from coke oven workers*

No.	Antibody titer[a]	
	September 1983	May 1984
Never smokers		
1	625	625
2		
19		
26	125	
28		
30		25
31		
34		
Exsmokers		
4	125	
5	125	
8		
10	25	25
13		
16		
18	25	
22	125	125
Smokers		
3		
6		25
7		
8		125
9	125	125
11		
12		125
14		
17		125
20	125	
21		
23		125
24	625	
25		
27	25	
29	125	
32		25
33		
35		125
36		
37		125
38		

[a] Antibody to BPDE-DNA was not detected in the sera when a number is not listed.

This is one of the first studies to compare two basically different methods to detect adducts in humans. It should be emphasized that USERIA and the SFS assay are measuring different end points: *i.e.*, USERIA utilizes an antibody to detect carcinogen-DNA adducts where the epitope recognized by the antibody is sterically intact. whereas the SFS assay measures a physical property of the adduct and acid hydrolysis-increased

'C. C. Harris. unpublished results.

detectability of a carcinogen. In addition. it is possible that the USERIA may recognize DNA-adducts of non-BPDE chemicals having the same epitope(s), and the SFS assay may measure moieties from non-BPDE chemicals that have adducted DNA. Even though the exposure to PAH in this coke oven plant is high, adducts were not detected in all of the samples. This probably reflects variation in exposure, balance between metabolic activation and deactivation, DNA repair capacity, and the sensitivity of the applied assays. The bioavailability of the PAH compounds adsorbed to airborne particles is also an important factor. PAH associated with various adsorbing particles may not be taken up by the organism to the same extent because of particle size distribution or adsorbing capacity of the particles. For instance. workers in primary aluminum production plants are also exposed to considerable amounts of PAH in the workplace atmosphere. but epidemiological studies show no or only a very small increase in lung cancer incidence in this industn (27, 28). This is in accordance with the finding that no significant increase In frequencies of sister chromatid exchange is obsened and that only 2% of the workers have detectable BPDE-DNA adducts (19. 25). Such studies among particular populations where epidemiological studies have shown an increased risk of cancer should provide useful information and may help in cancer prevention.

ACKNOWLEDGMENTS

We wish to thank Dr. Erikstad for help with the sampling. C. Bjørnstad and G. Tveten for skillful technical assistance. and Dr. Poirier who kindly supplied rabbit antibody to BPDE-DNA. Financial support from the Royal Norwegian Council for Scientific and Industrial Research is gratefully acknowledged.

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