

# OCCUPATIONAL EXPOSURES DURING COAL-TAR DISTILLATION

---

Occupational exposures during coal-tar distillation were considered by a previous Working Group in 2005 ([IARC, 2010](#)). Since that time new data have become available, which have been incorporated in this *Monograph*, and taken into consideration in the present evaluation.

## 1. Exposure Data

### 1.1 Manufacturing process

Coal tar is obtained by cooling the gas that is formed during the destructive distillation of coal to approximately ambient temperature. It is a black, viscous liquid composed primarily of a complex mixture of condensed-ring aromatic hydrocarbons. It may contain phenolic compounds, aromatic nitrogen bases and their alkyl derivatives, and paraffinic and olefinic hydrocarbons. Coal-tar pitch is the residue from the distillation of coal tar ([Betts, 1997](#)).

The largest source of tar and pitch is the pyrolysis or carbonization of coal. Until the end of the Second World War, coal tar was the main source of benzene, toluene, xylenes, phenol, cresols and cresylic acids, pyridine and methylpyridines, naphthalene, anthracene, creosote, tar paints, road tars and pitch binders ([Betts, 1997](#)). However, by the 1990s, over 90% of the world production of these aromatic chemicals was derived from the petrochemical industry, and coal tar became chiefly a source of anti-corrosion coatings, wood preservatives, feed-stocks for the

manufacture of carbon black and binders for electrodes ([Betts, 1997](#)).

Coal-tar distillation products comprise essentially the distillate (primarily a complex mixture of mono- and polycyclic aromatic hydrocarbons) and the residue from the distillation (pitch) ([Betts, 1997](#)).

The part of coke-oven tar that is normally distillable at atmospheric pressure boils at up to ~400 °C and contains principally aromatic hydrocarbons. These include (in order of the distillation fraction): benzene, toluene and the xylene isomers, tri- and tetra-methylbenzenes, indene, hydrindene (indane), and coumarone; polar compounds, including tar acids (phenol and cresols) and tar bases (pyridine, picolines (methylpyridines) and lutidines (dimethylpyridines)); naphthalene, contaminated with small but significant amounts of thionaphthene, indene and other compounds; methylnaphthalene isomers; biphenyl, acenaphthene and fluorene; anthracene and phenanthrene; pyrene and fluoranthene ([Betts, 1997](#)).

Much less is known about the composition of pitch, the residue from coal-tar distillation. Studies of coke-oven pitch indicate that it contains: four-membered aromatic hydrocarbon

**Table 1.1 Concentrations of PAHs in the air and urine of workers in coal-tar distillation**

| Reference<br>Country<br>Year of study                                     | Job/task  | No. of<br>subjects | No. of<br>samples           | No. of<br>smokers | PAH  | Air ( $\mu\text{g}/\text{m}^3$ ) |               | Urinary<br>1-hydroxypyrene<br>( $\mu\text{mol}/\text{mol creatinine}$ ) |                |           |    |
|---|---|--------------------|-----------------------------|-------------------|--|----------------------------------|---------------|---|----------------|-----------|----|
|   |   |                    |                             |                   |  | Mean                             | Range         | Mean  | Range          |           |    |
| <a href="#">van de Ven &amp; Nossent (1984)</a><br>the Netherlands<br>NR  | Coal-tar distillation<br>Operators, cleaners,<br>maintenance  | NR                 | 49                          | NR                | Sum of 11 PAHs   | 31                               | < 1–277       |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               | 26; 8.5   | < 2–280;       | 3.7       | NR |
|   |   |                    |                             |                   |  |                                  |               | 14; 5.1   | < 2–96         | 11.8      | NR |
|   |   |                    |                             |                   |  |                                  |               | 4.7; 1.4  |                | 4.0       | NR |
|   |   |                    |                             | 16; 5.2           |  | 4.6                              | NR            |   |                |           |    |
| <a href="#">Jongeneelen <i>et al.</i> (1986)</a><br>the Netherlands<br>NR | Coal-tar distillation<br>Operator pitch unit<br>Operator batch distillery<br>Operator pump station<br>Cleaner | 1                  | Air; urine<br>8; 2          | 0                 | Sum of 11 PAHs;<br>pyrene<br>1-Hydroxypyrene   |                                  |               |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   |                |           |    |
| <a href="#">Price <i>et al.</i> (2000)</a><br>United Kingdom<br>1998      | Tar distillation<br>Low-temperature<br><br>High-temperature   | 8                  | 8                           | 1                 | Total 19 PAHs<br>HSE 11 <sup>a</sup><br>Benzo[ <i>a</i> ]pyrene<br>Pyrene<br>1-Hydroxypyrene | 12.17                            | 3.99–38.59    |   |                |           |    |
|   |   |                    |                             |                   |  | 0.008                            | < 0.004–0.008 |   |                |           |    |
|   |   |                    |                             |                   |  | ND                               | ND            |   |                |           |    |
|   |   |                    |                             |                   |  | 0.037                            | 0.013–0.068   |   |                |           |    |
|   |   |                    |                             |                   |  | 279.04                           | 51.9–1130.5   |   | 0.36           | 0.21–1.05 |    |
|   |   |                    |                             |                   |  | 0.95                             | 0.15–4.87     |   |                |           |    |
|   |   |                    |                             |                   |  | 0.283                            | 0.019–0.642   |   |                |           |    |
|   |   |                    |                             |                   |  | 1.24                             | 0.14–6.73     |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   | 2.60           | 0.78–5.69 |    |
|   |   |                    |                             |                   |  |                                  |               |   | Median         | 90%       |    |
|   |   |                    |                             |                   |  |                                  |               |   | 63.62          | 455.17    |    |
|   |   |                    |                             |                   |  |                                  |               |   | Sum of 16 PAHs |           |    |
|   |   |                    | 1-Hydroxypyrene             |                   |  |                                  |               |   |                |           |    |
|   |   |                    | Sum of hydroxy-phenanthrene |                   |  |                                  |               |   |                |           |    |
| <a href="#">Preuss <i>et al.</i> (2003)</a><br>Germany<br>1999–2001       | Tar distillation  | 18                 | NR                          | NR                | Sum of 16 PAHs<br>1-Hydroxypyrene<br>Sum of hydroxy-phenanthrene                             |                                  |               |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   |                |           |    |
|   |   |                    |                             |                   |  |                                  |               |   |                |           |    |

<sup>a</sup> Benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*a*]pyrene, benzo[*g*/*hi*]perylene, indeno[1,2,3-*cd*]pyrene, dibenzo[*a,h*]anthracene, anthracene, cyclopenta[*cd*]pyrene  
 ND, not detected; NR, not reported; PAHs, polycyclic aromatic hydrocarbons  
 Conversions used for 1-hydroxypyrene: 1  $\mu\text{mol}/\text{mol creatinine}$  = 1.93  $\mu\text{g}/\text{g creatinine}$  = 0.013  $\mu\text{mol}/\text{L}$  = 2.84  $\mu\text{g}/\text{L}$  = 2.84  $\mu\text{g}/\text{mL}$

ring systems (e.g. chrysene, fluoranthene, pyrene, triphenylene, naphthacene and benzanthracene); five-membered ring systems (picene, benzo[*a*]pyrene and benzo[*e*]pyrene, benzo-fluoranthenes and perylene); six-membered ring systems (dibenzopyrenes, dibenzofluoranthenes and benzoperylene); and seven-ring systems (coronene). Other aromatic chemicals present in pitch include methyl- and polymethyl-derivatives, mono- and polyhydroxy-derivatives, and heterocyclic compounds (Betts, 1997).

For a more detailed description of the coal-tar distillation process, see the previous IARC Monograph (IARC, 2010).

## 1.2 Occupational exposure

Concentrations of PAHs in the ambient air and in urine of workers in coal-tar distillation have been measured in several studies. The results are summarized in Table 1.1. The levels of PAH exposures overall were similar in installations that used the high-temperature process and much lower in the low-temperature distillation facility. A study from Germany (Preuss *et al.*, 2003) showed high air concentrations of total PAHs as well as urinary 1-hydroxypyrene levels.

## 2. Cancer in Humans

A previous Working Group (IARC, 2010) concluded that there was *sufficient evidence* in humans for the carcinogenicity of occupational exposures during coal-tar distillation. Two large surveillance programmes provided evidence of an increased risk for skin cancer among coal-tar distillers. Notifications of skin cancer in England during 1911–38 were analysed in relation to occupation and more than 700 skin cancers attributed to exposure to coal tar among coal-tar distillers had been recorded; crude mortality rates of scrotal cancer were very high among

coal-tar distillers (Henry, 1946). Occupational health surveillance in a German coal-tar distillation plant identified 606 individuals with skin lesions during 1946–96, a third of whom had also malignant skin tumours (squamous-cell and basal-cell carcinoma); 20 cases of scrotal cancer (squamous-cell) were observed (Letzel & Drexler, 1998). No indication of an increased risk for skin cancer was found in more recent cohort-mortality studies, but mortality studies are not sufficiently sensitive to identify potential risks for skin cancer. The findings for other cancer sites were inconsistent. A modest, non-significant increase in mortality was reported for lung cancer in one British and one Dutch study (Maclaren & Hurley, 1987; Swaen & Slangen, 1997), and a significant excess in the incidence of buccal cavity and pharyngeal cancers was reported in a French study (Moulin *et al.*, 1988).

Since the previous evaluation (IARC, 2010) there have been no further relevant studies of cancer risk associated with occupational exposures during coal-tar distillation.

## 3. Cancer in Experimental Animals

Three high-temperature tars – one undiluted and two as benzene extracts – produced skin tumours, including carcinomas, when applied to the skin of mice. Each one of five blast-furnace tars and two extracts of blast-furnace tars produced skin tumours, including carcinomas, after topical application to mice (IARC, 1985). Likewise, each one of five pharmaceutical coal-tar preparations caused skin tumours, including carcinomas, when applied to the skin of mice (IARC, 1985).

Two unspecified coal tars caused skin tumours, including carcinomas, after application to the skin of mice. Lung tumours but not skin tumours were produced in rats after application of coal tar to the skin. In one study, an

unspecified coal tar produced tumours when applied to the ears of rabbits (IARC, 1985).

No data were available to the Working Group on the carcinogenicity of distillation fractions of low-temperature tars or of products derived from these tars (IARC, 1985).

In addition, several individual polynuclear aromatic compounds for which there is *sufficient evidence* of carcinogenicity in experimental animals have been measured at high concentrations in air samples taken from certain areas in coal-tar distillation plants (IARC, 2010).

## 4. Other Relevant Data

### 4.1 Mechanistic considerations relevant to the carcinogenic hazards of exposures during coal-tar distillation

#### 4.1.1 Experimental systems

In previous IARC Monographs (IARC, 1985, 1987, 2010) coal-tar pitch and roofing-tar emissions were found to be mutagenic in *Salmonella typhimurium* (in the presence of an exogenous metabolic activation system) and in two mammalian cell systems (in the presence and absence of an exogenous metabolic activation system). Coal-tar pitch and roofing-tar emissions induced sister chromatid exchange in Chinese hamster ovary cells and enhanced viral transformation in Syrian hamster embryo cells (both in the absence and presence of an exogenous metabolic activation system). Samples of therapeutic coal-tars, extracts of coal-tar shampoos, an industrial coal-tar-pitch and vapours escaping from a coal-tar sample at 37 °C were all mutagenic in *Salmonella typhimurium* in the presence of an exogenous metabolic activation system.

Coal tar applied topically to the skin of male Parkes mice produced a complex pattern of DNA

adducts in skin and lung tissues when analysed by means of <sup>32</sup>P-postlabelling (Schoket *et al.*, 1988), with one adduct spot tentatively identified as benzo[ghi]perylene (Hughes *et al.*, 1993).

Benzo[ghi]perylene was shown to be photo-mutagenic in *Salmonella typhimurium* strains. It induced DNA strand-breaks (comet assay) in V79 Chinese hamster lung fibroblasts with photo-activation (Yan *et al.*, 2004; Platt & Grupe, 2005; Platt *et al.*, 2008a; IARC, 2010). The major metabolic intermediate of benzo[ghi]perylene is the K-region oxide, 3,4-epoxy-3,4-dihydro-benzo[ghi]perylene (Platt *et al.*, 2008b).

Male B6C3F1 mice fed a diet containing coal tar from manufactured gas plant residue produced a complex pattern of aromatic adducts in DNA of the liver, lung, and fore-stomach, which increased with dose and time of treatment; one of the adducts was identified as the *anti*-benzo[a]pyrene-7,8-diol-9,10-oxide-deoxyguanosine-adduct (Culp & Beland, 1994; Culp *et al.*, 2000). In a similarly designed feeding study, a complex pattern of aromatic DNA adducts was produced in the lung, fore-stomach, and spleen tissues of mice; it was demonstrated that the benzo[a]pyrene content alone in the coal tar could not account for the aromatic DNA-adduct levels (Weyand *et al.*, 1991). In the lung of female A/J mice fed a diet containing coal tar from manufactured gas plant residue, three major aromatic DNA adducts were identified as being derived from benzo[b]fluoranthene, benzo[a]pyrene, and 7H-benzo[c]fluorene (Weyand & Wu, 1995; Koganti *et al.*, 2000). The 7H-benzo[c]fluorene-DNA adduct was also observed in mice who received topical application of manufactured gas plant residue (Cizmas *et al.*, 2004); the structure of this adduct is unknown, although a diol epoxide structure has been proposed (Wang *et al.*, 2002).

In the previous IARC Monograph (IARC, 2010) benzo[b]fluoranthene was found to be both genotoxic and carcinogenic in experimental studies. 7H-benzo[c]fluorene gave inconclusive results when tested for mutagenicity in *Salmonella*

*typhimurium* strains TA98 and TA100 in the presence of rat liver S9 (IARC, 1983), but it was found to be carcinogenic to mice (IARC, 2010).

Coal tar applied topically to *lambda-lacZ* transgenic mice (MutaMouse<sup>®</sup>) strongly increased the mutation frequency in epidermal cells. Isolated epidermal cells from C3H/Tif/hr hairless mice that had been given coal tar had higher levels of DNA strand-breaks (as analysed in the comet assay) (Thein *et al.*, 2000). In female B6C3F1 mice fed diets containing coal tar, cell proliferation was increased in the small intestine. *K-ras*, *H-ras*, and *p53* mutations were observed in the coal tar-induced tumours, the most abundant being *K-ras* mutations in fore-stomach and lung tumours (Culp *et al.*, 2000).

Chemical analyses of high-temperature coal tars have identified a series of polycyclic aromatic hydrocarbons that are both genotoxic and carcinogenic in experimental studies. Among these compounds are benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*a*]pyrene, dibenz[*a,h*]anthracene, chrysene, and indeno[1,2,3-*cd*]pyrene (IARC, 1983, 1985, 2010). These polycyclic aromatic hydrocarbons may contribute in part to the genotoxic and tumorigenic activities of coal tars.

Both naphthalene and benzene are constituents of coal tars produced by various processes (IARC, 1985). Both chemicals are genotoxic and induce tumours in experimental animals (IARC, 1982, 2002). Benzene is considered to be carcinogenic to humans (IARC, 2002).

#### 4.1.2 Humans

In previous *Monographs* (IARC, 1985, 2010) short-term assays were reviewed to assess the genotoxic effects of coal-tar exposure in humans. Patients treated with coal-tar ointments produced urine that was mutagenic in *Salmonella typhimurium* strains TA98 and YG1024 in the presence of an Aroclor-1254-induced rat-liver metabolic activation system. In the *S. typhimurium* strain

YG1024, *GSTM1*-null patients had higher levels of mutagens in their urine than *GSTM1*-positive patients.

DNA-adduct measurements that involved coal-tar workers or patients undergoing coal-tar therapy have focused solely on detection of benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adducts. In the skin and white blood cells (monocytes, lymphocytes, and granulocytes) of a group of eczema patients topically treated with coal-tar ointments the presence of aromatic DNA adducts was demonstrated by means of <sup>32</sup>P-postlabelling analysis. One of the adducts co-migrated with the benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adduct (Godschalk *et al.*, 1998). Analysis of the same adduct by use of an HPLC/ fluorescence method in a group of 26 psoriasis patients showed that the percentage of subjects with adducts did not exceed the 95 percentile control-subject value (Pavanello *et al.*, 1999). The white blood cells of 23 psoriasis patients undergoing clinical coal-tar therapy were examined for the presence of benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adducts with an enzyme-linked immunosorbent assay (ELISA). These adducts were detected and the adduct levels decreased with time after treatment, but no relationship could be ascertained between the level of exposure and the number of adducts and no difference in DNA-adduct formation was found between smoking and non-smoking patients (Paleologo *et al.*, 1992). PAH diolepoxide-DNA adducts and *GSTM1* genotype were determined in white blood cells of 57 psoriasis patients and 53 controls by use of ELISA and polymerase chain reaction (PCR), respectively. These DNA adducts were slightly elevated in patients compared with controls. There was no relationship between the presence of the *GSTM1* gene and the number of adducts (Santella *et al.*, 1995). Skin-biopsy samples from 12 psoriasis patients receiving coal-tar ointments contained aromatic DNA adducts, measured by <sup>32</sup>P-postlabelling analysis (Schoket *et al.*, 1990). In another <sup>32</sup>P-postlabelling study no significant

effects were reported of a similar treatment of psoriasis patients on the levels of benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adducts in peripheral blood lymphocytes (Pavanello & Levis, 1994). In a study of 111 Korean painters using coal-tar-based paint, the levels of aromatic DNA adducts measured by <sup>32</sup>P-postlabelling analysis were slightly higher compared with 17 on-site control workers (Lee *et al.*, 2003).

In lymphocytes of 49 coal-tar workers a significant increase of chromosomal aberrations, sister chromatid exchange, and satellite associations was observed, compared with values in non-exposed controls (Yadav & Seth, 1998).

Increased levels of p53 protein were found in skin biopsies of atopic eczema patients treated topically with coal-tar; a correlation was observed between p53 and aromatic DNA-adduct levels measured in the same tissue by <sup>32</sup>P-postlabelling analysis (Godschalk *et al.*, 2001).

## 4.2 Synthesis

In experimental systems, coal tars were mutagenic in bacteria and mammalian cells, and induced sister chromatid exchange and morphological cell transformation in cultured mammalian cells. Coal tar was also mutagenic *in vivo*, in transgenic mice. Mouse-lung tumours induced by coal-tar treatment had mutations in the *K-ras* proto-oncogene.

Epidemiological studies in humans and studies in experimental animals were consistent with respect to coal-tar exposures being carcinogenic to the lung. Coal tars produced lung and skin tumours in mice and rats after exposure by inhalation, lung tumours in rats after dermal treatment, and skin tumours in mice after dermal treatment. Coal tar was a mouse skin-tumour initiator (see Section 3).

Indications on the role of PAH in the mechanism of action of exposure to coal tar are based on the detection of DNA adducts of several PAHs, e.g. benzo[*ghi*]perylene, benzo[*b*]fluoranthene,

7*H*-benzo[*c*]fluorene and benzo[*a*]pyrene in *in vitro* studies, with DNA adducts of benzo[*b*]fluoranthene, benzo[*c*]fluorene and benzo[*a*]pyrene being detected in lung tissues of exposed animals. The benzo[*a*]pyrene DNA adduct was identified as an *anti*-benzo[*a*]pyrene-7,8-diol-9,10-oxide-deoxyguanosine-adduct.

In studies in humans, the urine from patients undergoing coal-tar treatments was mutagenic in bacteria. Peripheral blood lymphocytes of workers occupationally exposed to coal tars had increased chromosomal damage. Measurements of PAH-DNA adducts in human studies are based exclusively on detection of benzo[*a*]pyrene-DNA adducts, in particular *anti*-benzo[*a*]pyrene-7,8-diol-9,10-oxide-deoxyguanosine.

In conclusion, studies in experimental systems and in surrogate tissues of humans provide strong evidence for a genotoxic/mutagenic mechanism underlying the effects of occupational exposures during coal-tar distillation.

## 5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during coal-tar distillation. Occupational exposures during coal-tar distillation cause cancer of the skin (including, but not limited to, cancer of the scrotum).

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal tars.

Studies in experimental systems and in tissues of humans provide strong evidence for a genotoxic mechanism underlying the effects of occupational exposures during coal-tar distillation in humans. The detection of *anti*-benzo[*a*]pyrene-7,8-diol-9,10-epoxide-DNA adducts in the peripheral blood lymphocytes of exposed humans suggests the participation of benzo[*a*]pyrene in the genotoxic mechanism of this exposure in humans.

Occupational exposures during coal-tar distillation are *carcinogenic to humans (Group 1)*.

## References

- Betts WD (1997). *Tar and pitch*. In: *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., New York: John Wiley & Sons [online edition]
- Cizmas L, Zhou GD, Safe SH *et al.* (2004). Comparative in vitro and in vivo genotoxicities of 7H-benzo[c]fluorene, manufactured gas plant residue (MGP), and MGP fractions. *Environ Mol Mutagen*, 43: 159–168. doi:10.1002/em.20011 PMID:15065203
- Culp SJ & Beland FA (1994). Comparison of DNA adduct formation in mice fed coal-tar or benzo[a]pyrene. *Carcinogenesis*, 15: 247–252. doi:10.1093/carcin/15.2.247 PMID:8313515
- Culp SJ, Warbritton AR, Smith BA *et al.* (2000). DNA adduct measurements, cell proliferation and tumor mutation induction in relation to tumor formation in B6C3F1 mice fed coal-tar or benzo[a]pyrene. *Carcinogenesis*, 21: 1433–1440. doi:10.1093/carcin/21.7.1433 PMID:10874023
- Godschalk RW, Ostertag JU, Moonen EJ *et al.* (1998). Aromatic DNA adducts in human white blood cells and skin after dermal application of coal-tar. *Cancer Epidemiology, Biomarkers & Prevention*, 7: 767–773.
- Godschalk RW, Ostertag JU, Zandstee AM *et al.* (2001). Impact of GSTM1 on aromatic-DNA adducts and p53 accumulation in human skin and lymphocytes. *Pharmacogenetics*, 11: 537–543. doi:10.1097/00008571-200108000-00008 PMID:11505223
- Henry SA (1946). *Cancer of the Scrotum in Relation to Occupation*. New York: Oxford University Press.
- Hughes NC, Pfau W, Hewer A *et al.* (1993). Covalent binding of polycyclic aromatic hydrocarbon components of coal-tar to DNA in mouse skin. *Carcinogenesis*, 14: 135–144. doi:10.1093/carcin/14.1.135 PMID:8425262
- IARC (1982). Some industrial chemicals and dyestuffs. *IARC Monogr Eval Carcinog Risk Chem Hum*, 29: 1–398. PMID:6957379
- IARC (1983). Polynuclear aromatic compounds, Part 1, chemical, environmental and experimental data. *IARC Monogr Eval Carcinog Risk Chem Hum*, 32: 1–453. PMID:6586639
- IARC (1985). Polynuclear aromatic compounds, Part 4, bitumens, coal-tars and derived products, shale-oils and soots. *IARC Monogr Eval Carcinog Risk Chem Hum*, 35: 1–247. PMID:2991123
- IARC (1987). Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1 to 42. *IARC Monogr Eval Carcinog Risks Hum Suppl*, 7: 1–440. PMID:3482203
- IARC (2002). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. *IARC Monogr Eval Carcinog Risks Hum*, 82: 1–556. PMID:12687954
- IARC (2010). Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. *IARC Monogr Eval Carcinog Risks Hum*, 92: 1–853. PMID:21141735 PMID:18756632
- Jongeneelen FJ, Bos RP, Anzion RBM *et al.* (1986). Biological monitoring of polycyclic aromatic hydrocarbons. Metabolites in urine. *Scand J Work Environ Health*, 12: 137–143. PMID:3726495
- Koganti A, Singh R, Rozett K *et al.* (2000). 7H-benzo[c]fluorene: a major DNA adduct-forming component of coal-tar. *Carcinogenesis*, 21: 1601–1609. doi:10.1093/carcin/21.8.1601 PMID:10910965
- Lee KH, Ichiba M, Zhang J *et al.* (2003). Multiple biomarkers study in painters in a shipyard in Korea. *Mutat Res*, 540: 89–98. PMID:12972061
- Letzel S & Drexler H (1998). Occupationally related tumors in tar refinery workers. *J Am Acad Dermatol*, 39: 712–720. doi:10.1016/S0190-9622(98)70043-X PMID:9810887
- Maclaren WM & Hurley JF (1987). Mortality of tar distillation workers. *Scand J Work Environ Health*, 13: 404–411. PMID:3433042
- Moulin JJ, Mur JM, Wild P *et al.* (1988). Epidemiologic study of the mortality among the employees of a coal tar distillery *Rev Epidemiol Sante Publique*, 36: 99–107. PMID:3413326
- Paleologo M, van Schooten FJ, Pavanello S *et al.* (1992). Detection of benzo[a]pyrene-diol-epoxide-DNA adducts in white blood cells of psoriatic patients treated with coal-tar. *Mutat Res*, 281: 11–16. doi:10.1016/0165-7992(92)90030-L PMID:1371585
- Pavanello S, Favretto D, Brugnone F *et al.* (1999). HPLC/fluorescence determination of anti-BPDE-DNA adducts in mononuclear white blood cells from PAH-exposed humans. *Carcinogenesis*, 20: 431–435. doi:10.1093/carcin/20.3.431 PMID:10190558
- Pavanello S & Levis AG (1994). Human peripheral blood lymphocytes as a cell model to evaluate the genotoxic effect of coal-tar treatment. *Environ Health Perspect*, 102: Suppl 995–99. PMID:7698093
- Platt KL, Aderhold S, Kulpe K, Fickler M (2008a). Unexpected DNA damage caused by polycyclic aromatic hydrocarbons under standard laboratory conditions. *Mutat Res*, 650: 96–103. PMID:18160334
- Platt KL & Grupe S (2005). Microsomal biotransformation of benzo[ghi]perylene, a mutagenic polycyclic aromatic hydrocarbon without a “classic” bay region. *Chem Res Toxicol*, 18: 700–710. doi:10.1021/tx049698a PMID:15833030
- Platt KL, Grupe S, Fickler M (2008b). The 3,4-oxide is responsible for the DNA binding of benzo[ghi]perylene, a polycyclic aromatic hydrocarbon without a “classic” bay-region. *Chem Biol Interact*, 176: 179–187. doi:10.1016/j.cbi.2008.07.010 PMID:18755170
- Preuss R, Rossbach B, Müller J *et al.* (2003). [Eine deutschlandweite Studie zur inneren und äusseren Exposition gegenüber polycyclischen aromatischen

- Kohlenwasserstoffen (PAK) am Arbeitsplatz.] *Gefahrst Reinhalt L*, 63: 7–14.
- Price I, Scobbie E, Cocker J (2000). *Survey of occupational Exposure to Polycyclic Aromatic hydrocarbons*. No. JS200329. Environmental Measurement Group, Health and Safety Laboratory. London: Health and Safety Executive
- Santella RM, Perera FP, Young TL *et al.* (1995). Polycyclic aromatic hydrocarbon-DNA and protein adducts in coal-tar treated patients and controls and their relationship to glutathione S-transferase genotype. *Mutat Res*, 334: 117–124. PMID:7885362
- Schoket B, Hewer A, Grover PL, Phillips DH (1988). Covalent binding of components of coal-tar, creosote and bitumen to the DNA of the skin and lungs of mice following topical application. *Carcinogenesis*, 9: 1253–1258. doi:10.1093/carcin/9.7.1253 PMID:3383342
- Schoket B, Horkay I, Kósa A *et al.* (1990). Formation of DNA adducts in the skin of psoriasis patients, in human skin in organ culture, and in mouse skin and lung following topical application of coal-tar and juniper tar. *J Invest Dermatol*, 94: 241–246. doi:10.1111/1523-1747.ep12874576 PMID:2299199
- Swaen GMH & Slangen JMM (1997). Mortality in a group of tar distillery workers and roofers. *Int Arch Occup Environ Health*, 70: 133–137. doi:10.1007/s004200050197 PMID:9253642
- Thein N, Møller P, Amtoft H *et al.* (2000). A strong genotoxic effect in mouse skin of a single painting of coal tar in hairless mice and in MutaMouse. *Mutat Res*, 468: 117–124. PMID:10882890
- van de Ven, C, Nossent, C (1984). [Who deals with pitch... *Occupational hygiene study in a coal-tar processing plant.*] 195. Gezondheidsleer, V146 Luchthygiene en – verontreiniging. Health education, air quality and air pollution.
- Wang JQ, Weyand EH, Harvey RG (2002). Synthesis of suspected carcinogenic metabolites of 7H-benzo[c] fluorene, a coal-tar component implicated in causation of lung tumors. *J Org Chem*, 67: 6216–6219. doi:10.1021/jo011149b PMID:12182663
- Weyand EH & Wu Y (1995). Covalent binding of polycyclic aromatic hydrocarbon components of manufactured gas plant residue to mouse lung and forestomach DNA. *Chem Res Toxicol*, 8: 955–962. doi:10.1021/tx00049a009 PMID:8555411
- Weyand EH, Wu Y, Patel S *et al.* (1991). Urinary excretion and DNA binding of coal-tar components in B6C3F1 mice following ingestion. *Chem Res Toxicol*, 4: 466–473. doi:10.1021/tx00022a011 PMID:1912335
- Yadav JS & Seth N (1998). Effect of polycyclic aromatic hydrocarbons on somatic chromosomes of coal-tar workers. *Cytobios*, 93: 165–173. PMID:9779589
- Yan J, Wang L, Fu PP, Yu H (2004). Photomutagenicity of 16 polycyclic aromatic hydrocarbons from the US EPA priority pollutant list. *Mutat Res*, 557: 99–108. PMID:14706522