

CHEMICAL AGENTS AND RELATED OCCUPATIONS

VOLUME 100 F
A REVIEW OF HUMAN CARCINOGENS

This publication represents the views and expert
opinions of an IARC Working Group on the
Evaluation of Carcinogenic Risks to Humans,
which met in Lyon, 20-27 October 2009

LYON, FRANCE - 2012

IARC MONOGRAPHS
ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS

SHALE OILS

Shale oils were considered by previous IARC Working Groups in 1984 and 1987 ([IARC, 1985, 1987](#)). Since that time, new data have become available, which have been incorporated into this *Monograph*, and taken into consideration in the present evaluation.

1. Exposure Data

1.1 Identification of the agent

Chem. Abstr. Serv. Reg. No.: 68308-34-9

Chem. Abstr. Serv. Name: Shale oils

Crude shale oil is the product of thermal processing of raw oil shale. Oil shale is sedimentary rock containing mainly mineral components and organic matter called kerogen, which has a low solubility in organic solvents. Oil shale has a low boiling-point and it produces liquid organic products (oils) on thermal decomposition. Crude shale oils differ principally from crude petroleum in that they contain higher concentrations of organic nitrogen compounds and arsenic. Materials encountered in oil-shale processing include raw oil shale, crude shale oil, spent shale, oil-shale ash, synthetic crude oil (or 'syncrude') and refined products. Operations include retorting, upgrading and refining ([IARC, 1985](#)).

Crude shale oils are viscous, waxy liquids made up of hydrocarbons (alkanes, alkenes and aromatic compounds) and polar components (organic nitrogen, oxygen and sulfur compounds). Crude shale oils are very complex

mixtures, and only few of the compounds have been identified.

To recover the oil from the shale, its organic portion (kerogen) must be decomposed thermally. This thermal decomposition, known as retorting, converts the solid organic material of the shale into liquid and gaseous fractions and a solid carbonaceous residue. The liquid fraction, the so-called shale oil, consists of condensable hydrocarbons (C_{5+}) and small quantities of decomposition water. The gaseous product is a mixture of carbon monoxide, carbon dioxide, hydrogen, nitrogen, hydrogen sulfide, methane, and other hydrocarbons (C_{4-}). The carbonaceous residue, a coke-like material, is obtained in a mixture with the inorganic minerals of the original oil shale ([Weiss, 2005](#)).

1.2 Uses

Oil shales occur in many parts of the world. The areas where they are found range in size from small occurrences of little or no economic value to thousands of square miles. Oil shales also differ in geologic age, from Cambrian (570–500 million years ago) to Tertiary (65–2 million years ago). Total world resources of extractable oil shale are conservatively estimated at 2.6 trillion barrels ([AAPG, 2009](#)).

Early applications of shale oils included use as a source of paraffin waxes and burning oils for lamps, as well as for medicinal purposes. Later on, shale oils were used to prepare gasoline, diesel oils and lubricants from its light, intermediate and heavy distillates, respectively. The fuel oils, representing the major part of liquid products from the internal combustion (gas-generator type) retorts, have been used in the manufacture of gas-turbine fuel oil, automobile gasoline, and additives for high-sulfur petroleum fuel oils. (Aarna, 1978; Öpik & Kaganovich, 1981). In the People's Republic of China, shale oil has been used to generate electric power and as a refinery feedstock (Dickson, 1981). Products included gasoline, kerosene, diesel fuel and coke (Qian, 1982; IARC, 1985).

Oil-shale industries are operating in Europe (Estonia), South America (Brazil) and Asia (China). The largest operations are in Estonia, where approximately 12 million tonnes of oil shale is mined annually (underground and open-pit mining). About 85% of this material is burned as fuel in electric power-plants in north-eastern Estonia; the remainder is retorted for shale oil and used to manufacture fuels and petrochemicals. In Brazil, oil shale is mined in open pits and is retorted for shale oil, liquefied petroleum gas, sulfur and fuel gas (AAPG, 2006).

1.3 Human exposure

According to the US National Occupational Exposure Survey (1981–83), approximately 350 workers (including approximately 150 women) were potentially exposed to shale oil (NIOSH, 1990).

Very few studies were identified that assessed occupational exposures to shale oil. Most studies of this industry assessed exposures to other contaminants: free crystalline silica in the form of quartz; asbestos (Kangur, 2007), diesel exhaust (Scheepers *et al.*, 2002; Muzyka *et al.*, 2003, 2004; Knudsen *et al.*, 2005), trace elements (arsenic,

cadmium, lead, mercury, nickel), hydrogen sulphide, uranium and radon, carbon monoxide, phenol, polynuclear aromatic compounds, such as benzo(a)pyrene and 1-nitropyrene (Kuljukka *et al.*, 1996, 1998; Anderson *et al.*, 1997; Boffetta *et al.*, 1997; Kivistö *et al.*, 1997; Scheepers *et al.*, 2002, 2003), aromatic compounds, such as benzene and toluene (Anderson *et al.*, 1997; Kivistö *et al.*, 1997; Marcon *et al.*, 1999; Scheepers *et al.*, 2002; Sørensen *et al.*, 2004), sulfur dioxide, and dust in shale mines, retorts, tips and brick-works (Louw *et al.*, 1986).

2. Cancer in Humans

Most of the literature addressing the carcinogenicity of shale oils dates back to the early part of the 20th century, with compelling evidence from case series of skin cancer, particularly of the scrotum, in the United Kingdom. These case series are substantial in scale, including 65 cases of scrotal cancer that occurred in the period 1900–21 in the Scottish shale-oil industry (Scott, 1922a, b). Exposure of cotton-textile workers (mule spinners) exposed under non-hygienic conditions to lubricating oil that included shale oil during varying time periods, was strongly associated with cancer of the scrotum (Southam, 1928; Brockbank, 1941). Even in the absence of methodologically rigorous epidemiologic studies, this association has become accepted as causal.

As the oil-shale industry has risen and fallen over time in various parts of the world, a modest epidemiological literature has been developed. The size and prospects for the industry have fluctuated dramatically over time in relation to the price of oil, resulting in a haphazard approach to epidemiology that addresses the health of workers in the industry. Furthermore, varying technologies for releasing the oil from the shale have different implications for exposures of

the workforce. A morbidity survey of several hundred workers in the USA employed at an oil-shale demonstration facility suggested an increased risk for abnormal sputum cytology and no excess of skin cancer ([Rom et al., 1985](#)).

The most extensive epidemiological study of cancer among oil-shale workers addressed causes of death among 6359 Scottish workers employed in the period 1950–62 and followed for vital status through 1982 ([Miller et al., 1986](#)). The focus was on the subset of 3161 men who worked in mining, retorting, or refining, with maximum potential exposure to shale oil. A total of 1868 of these men died, 802 before the start of mortality follow-up and 1066 during the follow-up, i.e. between January 1968 to December 1982. Mortality of the workers from lung, stomach, colon, rectum, bladder, and kidney cancers was similar to or lower than that of an external population. Only skin cancer, with six observed deaths, was in excess, with an estimated relative risk of 4.9 (95%CI: 2.2–10.9). This elevation in skin-cancer mortality is consistent with the case series noted previously. A more detailed evaluation of the exposure conditions for 212 lung-cancer cases compared with 221 men with other diseases, mostly cardiovascular problems, revealed no associations with occupational exposures. In contrast to the skin-cancer mortality excess, a survey of 1664 living workers from the same cohort revealed no increase in self-reported skin tumours ([Seaton et al., 1986](#)). No lung-cancer excess was reported among workers in the shale-oil industry employed at a facility in central Sweden between 1942 and 1966. Comparison of 51 lung-cancer deaths with 206 referent deaths did not indicate any association of shale-oil exposure with lung cancer ([Seldén, 1987](#)).

Overall, based on the case series, with some corroborating epidemiological studies, there is evidence that exposure to shale oil is causally associated with skin cancer, particularly of the

scrotum. Data pertaining to other cancer sites, including lung, remain inadequate to draw a conclusion on any association due to the limited research done thus far, the limited quality of the exposure data, and the poor precision of the estimates in the completed studies.

3. Cancer in Experimental Animals

A large number and a wide variety of animal studies have been conducted to analyse shale-derived oil and its precursors, or the by-products of shale-oil processing. The resulting picture is quite complex, as experimental results are affected by several factors, including: (1) the nature of the material under study (raw shale, spent shale, crude, hydro-treated or refined shale oil, retort process-water, or oil-shale ash); (2) the mineral composition of the original shale and the type of retort process; and (3) the fractionation procedure used to separate and/or characterize the active constituents of the complex mixture.

[Table 3.1](#) includes some of the studies considered as the most representative of the carcinogenicity of shale oils as well as studies published since the previous evaluation ([IARC, 1985](#)).

3.1 Raw and spent oil-shale

3.1.1 Skin application

Solvent extracts from both raw and spent oil-shale containing benzo[*a*]pyrene were applied to mouse skin and induced skin papillomas and carcinomas ([Berenblum & Schoental, 1944](#); [Hueper, 1953](#); [Rowland et al., 1980](#); [IARC, 1985](#)).

3.1.2 Intratracheal administration

Crude shale oil and its aromatic fractions were enclosed in bee's wax pellets – which allow slow release of the content – and implanted in the lungs of rats. The substances induced a

Table 3.1 Carcinogenicity studies of shale-oils in experimental animals

Species, strain (sex) Duration Reference	Dosing regimen, Shale oil Animals/group at start	Incidence and/or multiplicity of tumours (%)	Significance	Comments
Raw and spent oil shale				
Mouse, Swiss, (F) Lifetime Rowland et al. (1980)^a	Dermal application of raw shale oil and TOSCO II retort 2.5 mg in 1/60 ml, twice/wk Raw shale oil contains 0.66 µg/ml B[a]P Spent shale oil contains 1.4 µg/ml B[a]P 50 or 100 animals/group	Control: 0/100; sham control: 0/50 Spent shale: 3/50 (6%) papillomas, *3/50 (6%) carcinomas; Raw shale oil: 0/50 Number of survivors not indicated	*[<i>P</i> = 0.0356 vs control]	Raw oil shale from Colony Oil shale development, Parachute Creek, Colorado
Rats, Wistar (F) 24 mo Dagle et al. (1990)	Intra-tracheal administration of 0.2 ml of beeswax pellet containing 0, 0.6, 6, 60 mg crude shale oil, three of its chemically derived fractions, or crude petroleum. Equal volumes of beeswax and tricapyrylin were used in the vehicle-control pellets. 30 animals/group	Rats with lung epidermoid carcinomas at three doses Control, 0; Crude, 1, 3, 9; Neutral, 0, 1, 6; Basic, 2, 2, 8; PNA, 1, 9, 10 Number of survivors not indicated	<i>P</i> < 0.05	Crude shale oil from Anvil Points Mine, Colorado. Chemically derived fractions were: neutral, PNA, and basic. Number of effective rats not noted.
Rat, Fisher 344, sex (NR) 24 mo Holland et al. (1983)^a	Inhalation of raw oil shale and spent oil shale, 0 or 90 mg/m ³ respirable fraction 5 h/d, 4 d/wk for 24 mo. Positive control, 10 mg/m ³ quartz 62 animals/group	Lung adenomas, SCC, or adenocarcinomas Control: 1/17 adenoma; sham control: 0/15; positive control: 4/57 (7%) adenomas, 13/57 (23%) carcinomas Raw: 1/50 (2%) adenoma; 11/50 (22%) carcinomas; spent: 3/57 (5%) adenomas, 10/57 (17%) carcinomas	[NS]	Shale from Anvil Points, Colorado No information on survival or latency period was provided.
Hamster, Syrian golden, sex (NR) 16 mo Holland et al. (1983)^a	Inhalation of raw oil shale and spent oil shale 0 or 50 mg/m ³ , 4 hr/d, 4 d/wk	No lung tumours in any of the groups. Number of survivors not indicated	–	Results are preliminary
Crude shale-oils from low-temperature retorting				
Mouse, strain A, C57BL, hairless, sex (NR) 20 mo Hueper (1953)^a	Dermal application of two Green River crude shale oils, once/wk for one yr Unspecified amount in xylene (6 mo) then in ethyl ether (6 mo) 42 untreated strain A mice 1) NTU crude-shale oil 100 strain A, 25 C57BL 2) Fisher-assay crude-shale oil 50 strain A, 30 hairless	Skin tumours Untreated A, 0/42 1) A, 1/38 (3%) papilloma; C57BL, 4/19 (21%) squamous-cell carcinomas 2) A, 2/45 (4%) squamous-cell carcinomas; hairless, 1/10 (10%) squamous cell carcinoma	–	1) Nevada-Texas-Utah (NTU) retort processed at 538–816 °C 2) Fischer-assay retort processed at 371–538 °C No controls for C57BL and hairless mice

Table 3.1 (continued)

Species, strain (sex) Duration Reference	Dosing regimen, Shale oil Animals/group at start	Incidence and/or multiplicity of tumours (%)	Significance	Comments
Mouse, C3H/He (F, M) 700 d Wilson & Holland (1988)	Dermal application of 2.5–5 mg shale derived crude oils in 50 µl of 60% acetone and 40% cyclohexane (v/v), 3 × /wk for 700 d. In addition to solvent-exposed controls there were untreated controls and B[a]P positive controls. 20 animals/sex/group	% M, F with skin papillomas and/or carcinomas at 2.5, or 5 mg 1) 95/85, 95/95 2) 70/75, 90/85 3) 60/35, 60/75 No tumours in the solvent- or untreated-control groups	$P < 0.05$, Significant differences between male and female occurred only in time to tumour (not shown)	Oak Ridge oil-shale repository: 1) PCSO, Anvil Points, Colorado 2) OCSO, Piceance Creek Basin, Colorado 3) PCSO-UP, hydrated PCSO
Mouse, A/Jax (M) 23–25 wk Smith & Witschi (1983)^a	Intratracheal administration of paraho crude shale-oil 0, 500, 1250, 2500 mg/kg in corn oil, 3 × /wk for 8 wk 30 animals/group	Lung tumours 0, 7/16 (44%)*, 6/12 (50%)*, 3/5 (60%)*	* $P < 0.05$, all three exposed compared with control	
Shale-oil distillates, blends and other commercial products				
Mouse, C3H/HeN (F, M) 105 wk Clark et al. (1988)	Dermal application of seven shale-oil derived distillates, 25 mg, 3 × /wk for 21 wk Mineral oil (USP) was used on controls. Benzo[a]pyrene was used as a positive control. 25 animals/sex/group	Tumours at injection site Oil, % surviving mice with carcinoma/fibrosarcoma Control 0/2; benzo[a]pyrene 96/4; Crude oil, 50/4*; Hydro-treated oil, 0/0; Naptha, 12/4*; JP-4, 24/21*; Jet-A, 4/8*; Diesel, 1/1; Residum, 6/0*	* $P < 0.05$ carcinoma and/or fibrosarcoma	Hydrotreated Syncrude was prepared from crude shale oil retorted from shale oil in a procedure designed to simulate commercial production
Mouse, CC57Bl (M, F) Lifetime Bogovski et al. (1990)	Dermal application of crude shale oil or industrial residue produced from a blend of shale oils In benzene, 0 or 18 mg, twice/wk for 6 mo (50 times); one group received benzene and another was untreated 29 M and 40 F/group	Skin carcinomas: 0/61 (benzene control); 2/60 (3%) (crude shale oil); 3/56 (5%) (industrial residue)	NS	

^a Summarized in [IARC \(1985\)](#)

B[a]P, benzo[a]pyrene; d, day or days; F, female; h, hour or hours; M, male; mo, month or months; NR, not reported; NS, not significant; SCC, squamous-cell carcinoma; vs, versus; wk, week or weeks; yr, year or years

dose-dependent increase in lung cancer (epidermoid carcinomas) ([Dagle et al., 1990](#)).

3.1.3 Inhalation

An aerosol generated from a Write Dust Feed packed with a raw-shale sample from Anvil Points, Colorado, and one spent-shale sample from a direct-heated retort induced lung adenomas and carcinomas in rats during 24 months of exposure, but not in hamsters during 16 months of exposure ([Holland et al., 1983](#)).

3.2 Crude shale oils from low-temperature retorting

3.2.1 Skin application

Crude shale oils from a variety of locations around the world and processed by heat transfer or retort combustion at temperatures below 1000 °C consistently induced squamous cell papillomas and carcinomas when repeatedly applied to the skin of mice ([Hueper, 1953](#); [IARC, 1985](#)). Shale-derived crude oils and a hydro-treated product induced papillomas and carcinomas in mouse skin during nearly two years of treatment ([Wilson & Holland, 1988](#)).

The inner surface of rabbit ears painted with the heavy fraction of the generator (semi-coking) oil obtained from the Estonian oil-shale in gas generators at Kohtla-Järve induced squamous cell carcinomas in 8% of the rabbits. In one surviving rabbit, metastases of the carcinomas were found in the regional lymph nodes, the liver, and the lungs ([Vahter, 1959](#); [IARC, 1985](#)).

3.2.2 Intratracheal administration

Intratracheal administration of a crude shale oil at three dose levels significantly increased the incidence of lung tumours in mice across all dose groups ([Smith & Witschi, 1983](#); [IARC, 1985](#)).

3.3 Crude shale oils from high-temperature retorting

3.3.1 Skin application

Crude shale oils processed in chamber ovens above 900 °C induced squamous cell papillomas and carcinomas when applied to the skin of mice ([Larionov, 1947](#); [Bogovski, 1958, 1961](#); [Turu, 1961](#); [Bogovski & Vinkmann, 1979](#); [IARC, 1985](#)). Chamber-oven oil applied to the inner surface of rabbit ears resulted in multiple squamous-cell papillomas and keratoacanthomas and cornifying and non-cornifying squamous-cell carcinomas in 22% of the rabbits. In one rabbit, metastases in the lung and liver were found ([Vahter, 1959](#); [IARC, 1985](#)).

3.4 Shale-oil fractions

Assessment of fractionations of shale oil were undertaken to determine the extent to which exposure to fractions containing known carcinogens such as benzo[a]pyrene correlates with carcinogenic activity.

3.4.1 Skin application

Chromatographic fractions of shale oil prepared by adsorption on aluminium oxide and elution with various solvents induced benign and malignant skin tumours in mice ([Berenblum & Schoental, 1943](#); [IARC, 1985](#)). Chromatographic fractions of high-temperature (800–1000 °C, chamber-oven) shale oil were collected on silica-gel column and further fractionated into five fractions on aluminium oxide eluted with various solvents. Some of the fractions induced carcinomas and sarcomas with metastases in mice, and papillomas but not carcinomas in rabbits ([Bogovski, 1961, 1962](#); [IARC, 1985](#)).

3.4.2 Subcutaneous and/or intramuscular administration

Intramuscular injection of various thermo-distillation products and multiple chromatography fractions of crude shale oil into the thigh of mice induced sarcomas at the site of injection ([Hueper & Cahnmann, 1958](#); [IARC, 1985](#)). Chromatographic fractions of chamber-oven tar injected intramuscularly into the thigh of mice induced sarcomas at the injection site and lung tumours in some of the mice, which were also reported in historical controls ([Bogovski, 1961, 1962](#); [IARC, 1985](#)).

3.5 Shale-oil distillates, blends and other commercial products

3.5.1 Skin application

Application to the skin of mice of individual distillates and blends of distillates from shale oil – including products such as ‘green’ oil, ‘blue’ oil, unfinished gas oil, machine lubricating oil, fuel oil, wood-impregnating oil, tar, bitumen, coke, and lacquer – induced papillomas, spindle-cell sarcoma, and squamous-cell carcinomas ([Twort & Ing, 1928](#); [Hueper, 1953](#); [IARC, 1985](#)). Heavy fractions of shale oils appeared to be more carcinogenic than light fractions. The latter induced only benign tumours while heavy fractions induced benign and malignant tumours with a shorter latency period ([IARC, 1985](#)).

Crude oil, naphtha, and jet fuels derived from shale induced squamous-cell carcinomas and fibrosarcomas when applied to the skin of mice, whereas hydro-treated and diesel-distilled shale oil did not produce tumours ([Clark *et al.*, 1988](#)). Crude shale oil and industrial residue derived from a blend of shale oils induced two and three skin carcinomas (in 60 and 56 animals), respectively. No tumours were observed in controls ([Bogovski *et al.*, 1990](#)).

Tolichthol, a product obtained from the acid residue of rectification of shale-oil aromatic fractions – containing up to 22% (w/w) sulfur compounds – did not induce tumours during 24 months after application to the skin ([Vinkmann & Mirme, 1975](#)).

3.5.2 Intratracheal administration

Shale-oil coke (a raw-shale distillation residue) did not produce tumours in Syrian golden hamsters after intra-tracheal instillation ([Rowland *et al.*, 1980](#)).

3.6 Synthesis

Inhalation of either raw oil shale or spent oil shale produced lung tumours in rats. Application of an extract of spent oil shale produced skin tumours in mice. Skin application of crude oils from both low- and high-temperature retorting induced skin tumours in mice and rabbits; the oils obtained from high-temperature retorting had higher carcinogenic activity. A low-temperature crude oil produced lung tumours in mice after intra-tracheal instillation. Various fractions of shale oils were carcinogenic when applied to the skin of mice and rabbits. Shale-oil distillates, residues, blends and commercial products of the oil-shale industry were tested in mice by dermal application, and produced skin tumours. Distillation fractions from less highly refined shale oils were more carcinogenic than the more highly refined products.

4. Other Relevant Data

4.1 Humans

Shale oil-plant workers in Estonia were examined for chromosomal damage and aneuploidy in peripheral blood cells by means of tandem-labelling fluorescence in situ hybridization. One

group of 12 workers was engaged in benzene production from shale oils and another group, of five workers, engaged in coke operations. The control group of eight was from a nearby village. No significant difference in the extent of DNA breakage was detected in nucleated cells in blood smears of exposed *vs* control subjects. In contrast, modest but significantly increased frequencies of breakage affecting both chromosomes 1 and 9 were observed in the cultured lymphocytes of the benzene-exposed workers compared with the unexposed controls (Marcon *et al.*, 1999). [The Working Group noted that workers were likely to be also exposed to other carcinogens such as benzene and coke-oven emissions.]

Peripheral blood lymphocytes from 49 smoking and non-smoking coke-oven workers from a shale-oil plant in Estonia and 10 controls from a nearby village were examined for the presence of aromatic DNA adducts by use of the [³²P]-postlabelling techniques. Mean DNA-adduct levels in the exposed group did not differ from those in the controls; however, smokers had significantly higher levels of DNA adducts compared with non-smokers (Kuljucka *et al.*, 1998).

4.2 Experimental systems

Low-temperature shale-derived crude oils and oil-shale retort waters showed mutagenic activity in bacteria, fungi, and mammalian cells in culture. These two agents also induced chromosomal effects in mammalian cells *in vitro* and *in vivo* (IARC, 1985, 1987). Data on the genotoxic activities of raw and spent shale and oil-shale ash, and oil-shale retort-process waters were inconclusive at the time.

Dichloromethane extracts of oil-shale ash were evaluated in a mutagenicity assay with an arabinose-resistant *Salmonella typhimurium* strain. These extracts were highly mutagenic in the absence of an exogenous metabolic activation system. Similar results were obtained with

oil-shale ash extracts prepared with ethyl acetate/methanol as the extraction solvent (Whong *et al.*, 1983).

Shale oil and acid-base-neutral solvent fractions were evaluated with the morphological cell-transformation assay in Syrian hamster embryo cells in the presence of an exogenous source of metabolic activation. The unfractionated crude oil, the basic fraction, and the PAH fraction produced a positive response in the assay (Frazier & Andrews, 1983).

Genotoxicity assays were conducted on industrial Kiviter shale oil and its two fractions, the low-temperature fraction (230–350 °C) and the rectification residue obtained in the laboratory, as well as the industrial rectification residue. Human lymphocytes exposed to the shale oil and each of the rectification samples had significantly increased frequencies of sister chromatid exchange compared with the controls, irrespective of the presence or absence of exogenous metabolic activation. Shale oil and the industrial rectification samples also significantly increased the frequency of chromosomal abnormalities compared with the controls, with and without metabolic activation (Bogovski *et al.*, 1990).

4.3 Synthesis

Shale oils are genotoxic in experimental systems. There are only few data to determine an underlying mechanism for the carcinogenicity of shale oils.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of shale oils. Shale oils cause cancer of the skin (observed in the scrotum).

There is *sufficient evidence* in experimental animals for the carcinogenicity of shale oils.

Shale oils are genotoxic in experimental systems. There is weak evidence to determine a mechanism of action underlying the carcinogenic effects of shale oils, based on two studies with lymphocytes in exposed workers.

Shale oils are *carcinogenic to humans (Group 1)*.

References

- AAPG (2006). *Energy Minerals Division: Will Oil Shale Be a Major Player?* AAPG Explorer, May 2006 [http://www.aapg.org/explorer/divisions/2006/05emd.cfm]
- AAPG (2009). *Energy Minerals Division: Technical Area: Oil Shale*. American Association of Petroleum Geologists [http://emd.aapg.org/technical_areas/oil_shale.cfm]
- Aarna A (1978). *Chemical Engineering in the Estonian SSR*. Tallinn: Perioodika, pp.29–34
- Anderson D, Hughes JA, Veidebaum T *et al.* (1997). Examination of ras (P21) proteins in plasma from workers exposed to benzene emissions from petrochemical plants and healthy controls. *Mutat Res*, 381: 149–155. doi:10.1016/S0027-5107(97)00162-0 PMID:9434871
- Berenblum I & Schoental R (1943). Carcinogenic constituents of shale oil. *Br J Exp Pathol*, 24: 232–239.
- Berenblum I & Schoental R (1944). The difference in carcinogenicity between shale oil and shale. *British Journal of Experimental Pathology*, 25: 95–96.
- Boffetta P, Jourenkova N, Gustavsson P (1997). Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. *Cancer Causes Control*, 8: 444–472. doi:10.1023/A:1018465507029 PMID:9498904
- Bogovski P, Veidebaum T, Tamme J, Poldvere E (1990). *Carcinogenicity and Mutagenicity of the shale-oil produced in the Estonian Kiveri retort*. In *Complex Mixtures and Cancer Risk*. Vainio H, Sorsa M, McMichael AJ, editors. Lyon: International Agency for Research on Cancer
- Bogovski PA (1958). [On the blastomogenic action of oil-shale generator tar.] (Russ.). In: *Problems of Industrial Hygiene in the Shale-Oil Industry in the Estonian SSR*. Bogovski PA editor. Tallinn: Valgus, Vol. 3, pp. 172–185.
- Bogovski PA (1961) [Carcinogenic Action of Estonian Oil Shale Processing Products] (Russ.), Tallinn: Academy of Science Estonian SSR, pp. 108–115, 138–148, 154–161, 189, 192–204.
- Bogovski PA (1962). On the carcinogenic effect of some 3,4-benzopyrene-free and 3,4-benzopyrene-containing fractions of Estonian shale-oil. *Acta - Unio Internationalis Contra Cancrum*, 18: 37–39.
- Bogovski PA & Vinkmann F (1979). Carcinogenicity of oil shale tars, some of their components, and commercial products. *Environ Health Perspect*, 30: 165–169. doi:10.1289/ehp.7930165 PMID:446447
- Brockbank EM (1941). Mule-spinner's Cancer. *BMJ*, 1: 622–624. doi:10.1136/bmj.1.4190.622 PMID:20783633
- Clark CR, Walter MK, Ferguson PW, Katchen M (1988). Comparative dermal carcinogenesis of shale and petroleum-derived distillates. *Toxicol Ind Health*, 4: 11–22. PMID:3388444
- Dagle GE, Smith LG, McDonald KE *et al.* (1990). Pulmonary carcinogenesis in rats given implants of shale oil in beeswax pellets. *J Toxicol Environ Health*, 29: 399–407. doi:10.1080/15287399009531400 PMID:2325153
- Dickson PF (1981). *Oil shale*. In: *Kirk RE & Othmer DF, eds, Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed. Vol.16, New York: John Wiley & Sons, pp. 333–357.
- Frazier ME & Andrews TK Jr (1983). Transformation of Syrian hamster embryo cells by synfuel mixtures. *J Toxicol Environ Health*, 11: 591–606. doi:10.1080/15287398309530370 PMID:6312062
- Holland LM, Gonzales M, Wilson JS, Tillery MI (1983). *Pulmonary effects of shale dusts in experimental animals*. In: *Health Issues Related to Metal and Nonmetallic Mining*. Wagner WL, Rom WN, Merchant JA, editors. London: Butterworth, pp. 485–496.
- Hueper WC (1953). Experimental studies on cancerigenesis of synthetic liquid fuels and petroleum substitutes. *AMA Arch Ind Hyg Occup Med*, 8: 307–327. PMID:13091431
- Hueper WC & Cahnmann HJ (1958). Carcinogenic bioassay of benzo (a) pyrene-free fractions of American shale oils. *AMA Arch Pathol*, 65: 608–614. PMID:13532114
- 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
- Kangur M (2007). Occupational exposure to asbestos during renovation of oil-shale fuelled power plants in Estonia. *Int J Occup Saf Ergon*, 13: 341–346. PMID:17888242
- Kivistö H, Pekari K, Peltonen K *et al.* (1997). Biological monitoring of exposure to benzene in the production of benzene and in a cokery. *Sci Total Environ*, 199: 49–63. doi:10.1016/S0048-9697(97)05481-8 PMID:9200847
- Knudsen LE, Gaskell M, Martin EA *et al.* (2005). Genotoxic damage in mine workers exposed to diesel exhaust, and the effects of glutathione transferase genotypes. *Mutat Res*, 583: 120–132. PMID:15876548

- Kuljukka T, Savela K, Vaaranrinta R *et al.* (1998). Low response in white blood cell DNA adducts among workers in a highly polluted cokery environment. *J Occup Environ Med*, 40: 529–537. doi:10.1097/00043764-199806000-00005 PMID:9636933
- Kuljukka T, Vaaranrinta R, Veidebaum T *et al.* (1996). Exposure to PAH compounds among cokery workers in the oil shale industry. *Environ Health Perspect*, 104: Suppl 3539–541. doi:10.2307/3432819 PMID:8781379
- Larionov LT (1947). *On the carcinogenic properties of Estonian shale tars*. In: *Materials on the Toxicology of Oil Shale Products. Proceedings of the Industrial Hygiene and Occupational Diseases Research Institute*. Lazarev NV editor. Leningrad, Vol. 11, Part I, pp. 111–118.
- Louw SJ, Cowie HA, Seaton A (1986). Epidemiologic studies of Scottish oil shale workers: II. Lung function in shale workers' pneumoconiosis. *Am J Ind Med*, 9: 423–432. doi:10.1002/ajim.4700090504 PMID:3717167
- Marcon F, Zijno A, Crebelli R *et al.* (1999). Chromosome damage and aneuploidy detected by interphase multi-colour FISH in benzene-exposed shale oil workers. *Mutat Res*, 445: 155–166. PMID:10575426
- Miller BG, Cowie HA, Middleton WG, Seaton A (1986). Epidemiologic studies of Scottish oil shale workers: III. Causes of death. *Am J Ind Med*, 9: 433–446. doi:10.1002/ajim.4700090505 PMID:3717168
- Muzyka V, Bogovski S, Scheepers P *et al.* (2003). Effects of occupational exposure to diesel exhaust on porphyrin metabolism in lymphocytes of workers employed at black coal and oil-shale mines. *Am J Ind Med*, 44: 70–74. doi:10.1002/ajim.10239 PMID:12822138
- Muzyka V, Scheepers PTJ, Bogovski S *et al.* (2004). Porphyrin metabolism in lymphocytes of miners exposed to diesel exhaust at oil shale mine. *Sci Total Environ*, 322: 41–50. doi:10.1016/S0048-9697(03)00404-2 PMID:15081736
- NIOSH (1990). *National Occupational Exposure Survey (1981–83)*. Cincinnati, OH: US Department of Health and Human Services, Public Health Service, National Institute for Occupational Safety and Health. <http://www.cdc.gov/noes/noes4/x3554sco.html>
- Õpik I, Kaganovich I (1981). *Oil shale of the Baltic basin: Power engineering and thermal processing*. In: *Proceedings of the 6th IIASA resources Conference, World Oil-Shale Resources and Their Potential Development*. Golden CO editor. Laxenburg, Austria: International Institute For Applied Systems Analysis
- Qian JL (1982). *Oil shale industry of China*. In: *Synfuels' 2nd World-Wide Symposium*. New York: McGraw-Hill, pp.1–12.
- Rom WN, Krueger G, Zone J *et al.* (1985). Morbidity survey of U.S. oil shale workers employed during 1948–1969. *Arch Environ Health*, 40: 58–62. PMID:3994419
- Rowland J, Shubik P, Wallcave L, Sellakumar A (1980). Carcinogenic bioassay of oil shale: long-term percutaneous application in mice and intratracheal instillation in hamsters. *Toxicol Appl Pharmacol*, 55: 522–534. doi:10.1016/0041-008X(80)90054-X PMID:7434364
- Scheepers PTJ, Coggon D, Knudsen LE *et al.* (2002). BIOMarkers for occupational diesel exhaust exposure monitoring (BIOMODEM)—a study in underground mining. *Toxicol Lett*, 134: 305–317. doi:10.1016/S0378-4274(02)00195-9 PMID:12191893
- Scheepers PTJ, Micka V, Muzyka V *et al.* (2003). Exposure to dust and particle-associated 1-nitropyrene of drivers of diesel-powered equipment in underground mining. *Ann Occup Hyg*, 47: 379–388. doi:10.1093/annhyg/meg036 PMID:12855488
- Scott A (1922a). The occupation dermatoses of the paraffin workers of the Scottish shale oil industry. *British Medical Journal*, 2: 381–385.
- Scott A (1922b). On the occupation cancer of the paraffin and oil workers of the Scottish shale oil industry. *BMJ*, 2: 1108–1109. doi:10.1136/bmj.2.4896.1108-a
- Seaton A, Louw SJ, Cowie HA (1986). Epidemiologic studies of Scottish oil shale workers: I. Prevalence of skin disease and pneumoconiosis. *Am J Ind Med*, 9: 409–421. doi:10.1002/ajim.4700090503 PMID:2940860
- Seldén A (1987). Shale oil workers: absence of lung cancer hazard replicated. *Am J Ind Med*, 11: 485–487. doi:10.1002/ajim.4700110411 PMID:3578301
- Smith LH, Witschi HP (1983). *The Mouse Lung Tumor Assay: A Final Report (Oak Ridge natl Lab. 5961)*. Oak Ridge, TN.
- Sørensen M, Poole J, Autrup H *et al.* (2004). Benzene exposure assessed by metabolite excretion in Estonian oil shale mineworkers: influence of glutathione s-transferase polymorphisms. *Cancer Epidemiol Biomarkers Prev*, 13: 1729–1735. PMID:15533900
- Southam AH (1928). Occupational cancer of mule-spinners. *BMJ*, 2: 437–438. doi:10.1136/bmj.2.3531.437 PMID:20774126
- Turu H (1961). On the blastomogenicity of tar obtained by processing of granular oil shale in a solid heat carrier installation. *Eesti NSV Tead. Akad. Toim.*, 10: 13–18.
- Twort CC & Ing HR (1928). Studies on carcinogenic agents (Ger.). *Z Krebsforsch*, 27: 308–351. doi:10.1007/BF02314235
- Vahter H (1959). [Experimental Data on the Morphogenesis of Tumours Induced by Shale Oils] (Russ.), Tartu State Publishing House 'Scientific Literature', No. 79, pp. 99–105.
- Vinkmann FY, Mirme HY (1975). *Studies on the eventual cancerogenic activities of some commercial products of the Estonian oil-shale industry (Epo-glue and Tolichthon)*. In: *Experimental and Clinical Oncology*. Loogna G editor. Tallinn: Estonian SSR, Valgus, Vol. 2, pp. 76–80.
- Weiss HJ (2005). *Oil Shale*. In: *Ullmann's Encyclopedia of Industrial Chemistry*, 7th Ed. [online], Weinheim, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

- Wilson JS & Holland LM (1988). Periodic response difference in mouse epidermis chronically exposed to crude-oils or BaP: males vs. females. *Toxicology*, 50: 83–94. doi:10.1016/0300-483X(88)90123-0 PMID:3388432
- Whong WZ, Stewart JD, Adamo DC, Ong T (1983). Mutagenic detection of complex environmental mixtures using the Salmonella/arabinose-resistant assay system. *Mutat Res*, 120: 13–19. doi:10.1016/0165-7992(83)90068-4 PMID:6339913

