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AMERICAN PETROLEUM INSTITUTE
MEDICAL ADVISORY COMMITTEE

Minutes of Meeting
May 7-8, 1945
Hotel Statler
St. Louis, Missouri

MEMBERS PRESENT:

McIver Woody - Chairman
D. V. Stroop - Secretary

J. M. Adams	D. M. English	M. N. Newquist
W. O. Armstrong	T. M. Frank	I. E. Percy
V. C. Baird	A. E. Hoag	B. B. Reeve
F. F. Boys	R. A. Jewett	O. S. Somerville

MEMBERS ABSENT:

Wm. Russell Lewis	J. F. Peattie
W. A. Morrison	H. S. Thomson

ASSOCIATES PRESENT:

E. W. Adams	Standard Oil Co, (Indiana),	Chicago, Ill.
L. C. Beard, Jr.	Socony-Vacuum Oil Co., Inc.	New York, N. Y.
R. S. Bonsib	Standard Oil Co. (N.J.)	New York, N. Y.
R. C. Cole	Phillips Petroleum Co.	Bartlesville, Okla.
Wm. Grant, Jr.	Humble Oil & Refining Co.	Houston, Texas
H. R. Kemmerer	Shell Oil Company	Wood River, Ill.
A. J. Koewing, Jr.	Socony-Vacuum Oil Co., (Lubrite Div.)	East St. Louis, Ill.
E. P. Lankelma	Standard Oil Co. (Ohio)	Cleveland, Ohio
H. R. Warrick	The Texas Company	New York, N. Y.
F. M. Watkins	Sinclair Refining Co.	East Chicago, Ind.

GUESTS:

Wm. W. Brooks, M.D.	Phillips Petroleum Co.	Phillips, Texas
R. H. Gould	" " "	Bartlesville, Okla.
F. F. Heyroth, M.D.	Kettering Laboratory	University of Cincinnati

I

Choice of Chairman for 1945.

Following a review of the origin and purpose of the Medical Advisory Committee, McIver Woody was chosen to serve as chairman for 1945.

JAM 016809

II

API 06766

Medical Problems in Hydrocarbons

By invitation Doctor Heyroth reviewed data and sources of data on the toxi- [illegible] which recently have become important because of the rapid

Action: The committee tendered Doctor Heyroth a vote of appreciation and thanks for his presentation and requested him to send a copy of his review to the secretary so that copies could be distributed to members and associates.

III

List of Current Medical Problems

A canvass of members resulted in the listing of a number of substances and mixtures which may be injurious to persons through contact, absorption, or inhalation. In addition a number of subjects involving matters of policy and administrative practices were suggested for committee consideration.

The committee discussed several bases for classifying problems for inclusion in its program of work, as follows:

1. By groups of substances or mixtures, such as types of hydrocarbons, inhibitors, additives, catalysts, or acids.

2. By the manner in which substances may injure persons, such as skin contact, absorption, or inhalation.

3. By the method of solution to be used on problems, such as cooperative compilation of clinical data, literary research, or laboratory research.

Action: The committee did not agree upon a comprehensive classification of the full list of problems but it was in agreement on four studies which should be initiated in 1945, as follows:

1. The study of medical policies and practices and formulation of tentative procedures for guidance of medical men in industry.

2. A study of chlorinated compounds, particularly chlorinated cutting oils used in petroleum products, and of their effects.

3. A study of possible carcinogenic properties of hydrocarbons and petroleum products.

4. Preliminary reviews and studies as to the toxic effects and properties of hydrocarbons, products and substances other than those included in items 2 and 3.

The chairman was authorized to appoint four subcommittees to undertake these studies.

Notes by Secretary: (1) An outline of the field of interest of members, as developed at the meeting, is appended to these minutes.

(2) The chairman announced the memberships of subcommittees, as follows:

a. Subcommittee on Medical Policies and Practices

R. A. Jewett, Chairman
J. M. Adams
T. M. Frank
W. A. Morrison
J. F. Peattie
I. E. Percy
H. S. Thomson
McIver Woody, Ex Officio
D. V. Stroop, " "

b. Subcommittee on Chlorinated Compounds

F. F. Boys, Chairman
A. E. Hoag
M. N. Newquist
B. B. Reeve
McIver Woody, Ex Officio
D. V. Stroop " "

c. Subcommittee on Carcinogenicity

M. N. Newquist, Chairman
J. M. Adams
A. E. Hoag
Wm. Russell Lewis
I. E. Percy
McIver Woody, Ex Officio
D. V. Stroop, " "

d. Subcommittee on Permissible Concentrations

V. C. Baird, Chairman
W. O. Armstrong
D. M. English
T. M. Frank
O. S. Somerville
McIver Woody, Ex Officio
D. V. Stroop, " "

IV

Contribution and Dissemination of Information

Contributions of literature reviews were contributed to the Committee by the following:

1. Library of the Technical and Research Division, The Texas Company

"The Carcinogenicity of Bituminous Compounds," April 30, 1945

2. Chemical Division, Socony-Vacuum Oil Co., Inc.

"Carcinogenic Hydrocarbons," April 27, 1945

API HISTORY OF THE SUBCOMMITTEE ON CARCINOGENICITY

1945-1950

API

HISTORY

OF THE

SUBCOMMITTEE

ON

CARCINOGENICITY

1945-1950

4009-6-3

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6-13-45.

Technical Memo No. 45-214
Chemical Division
Socony-Vacuum Oil Co., Inc.
Research and Development
Laboratories
Paulsboro, New Jersey
April 27, 1945

ATTENTION

Mr. P. V. Keyser, Jr.
Dr. A. A. O'Kelly
Dr. W. P. Hawthorne

Carcinogenic Hydrocarbons,
Literature Survey

A brief literature survey of the cancer-producing hydrocarbons has been made as requested by Dr. L. C. Beard in his letter (W. M. Holaday/ P. V. Keyser, Jr.) of April 12, 1945.

Carcinogenic activity has been noted in various types of compounds including hydrocarbons, amino, azo and nitro compounds, hormones, and inorganic compounds. This report will be confined to the hydrocarbons and hydrocarbon fractions identified as carcinogenic.

Most of the carcinogenic hydrocarbons were originally identified in the pyrolysis products of coal, wood, petroleum and shale. In some cases these hydrocarbons exist, as such, in the original materials. The active hydrocarbons are almost without exception polynuclear aromatic hydrocarbons and are conveniently classified under the parent hydrocarbons from which they might be derived. Thus, the three main types are classified as benzopyrenes, cholanthrenes, and benzanthracenes.

Identified Carcinogenic Hydrocarbons

(7),(22),(45),(24),
(12),(10),(5),(28),
(29),(38),(47)

I. Benzopyrenes

1,2-benzopyrene
3,4-benzopyrene
1,2,3,4, dibenzopyrene

II. Cholanthrenes

cholanthrene
20-methyl cholanthrene
16,20-dimethyl cholanthrene
20-ethyl cholanthrene
15,16-benzdehydrocholanthrene

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A contribution of information to Members of API Medical Advisory Committee.
6-13-45.

THE CARCINOGENICITY
OF
BITUMINOUS COMPOUNDS

***

Literature Review

April 30, 1945

N O T E

In view of the immense amount of published information on various phases of the cancer problem it should be emphasized that this literature review gives only a rapid survey of developments in the field of cancer research as applied directly to the petroleum, coal tar, oil shale and allied industries. While it is far from being complete, yet it is believed that most of the important work in this particular field has been covered, either in the report itself or in one of the bibliographical references given in the appendix and referred to at the bottom of page 1.

M. P. Doss

THE CARCINOGENICITY OF BITUMINOUS COMPOUNDS

It has long been recognized that the incidence of skin cancer is greater among workers in certain industries and occupations than among the population as a whole. Attention was first directed in 1787 to the very high death rate resulting from scrotal cancer of chimney sweeps; it is eight times more common in these workers than in the general public in England, and in the United States the ratio of cancer cases in chimney sweeps is double that of the general population[78]. In practically all cases it is the scrotum that is attacked; this is also the site in mule spinners cancer discussed later. Workers in other industries coming into direct contact with tars, pitches, shale oils, etc. likewise show a high incidence of skin cancer, for example, laborers in plants making briquettes, tar roofing, wood preservatives, artificial gas, insulating compounds, shale products, etc.

However, in spite of the recognition of the fact that bituminous compounds were apparently the cause of skin cancer, it was not until relatively recently that skin cancer was produced in laboratory animals by direct application of tar. This was accomplished by the Japanese investigators Yamigawa and Ichikawa[122] in 1915. Since then a great deal of very careful work has been done in synthesizing and testing various organic compounds, particularly polycyclic hydrocarbons and derivatives. For lengthy reviews of this work, see References 8-12, 14, 17, 20, 22, 23, 26-29, 32-34, 74, and 87; particularly the review by J. L. Hartwell of the National Cancer Institute covering 696 chemical substances, of which 169 are reported to be carcinogenic[41]. L. F. Fieser summarizes our knowledge in this field as follows[34]:

> "As judged by all available data for the production of skin and subcutaneous tumors in rats and mice, methylcholanthrene probably is the most potent of the known chemical carcinogens. Systematic studies of synthetic model compounds have shown that the methyl group is of no importance to the functioning of the compound; that much, if not all of the efficacy of cholanthrene is retained in the analogous hydrocarbon 5,10-dimethyl-1,2-benzanthracene; and that the most significant structural feature of cholanthrene or methylcholanthrene is the 1,2-benzanthracene ring system with a

carbon substituent at the meso position 10. 10-Methyl-1, 2-benzanthracene evokes sarcomas in mice nearly as rapidly as methylcholanthrene, and, though it is distinctly less effective in the production of skin cancer, the substance constitutes the nearest approach in a simple model compound to a simulation of the biological properties of the hydrocarbon of more complicated structure.

"All twelve possible monomethyl derivatives of the inactive 1, 2-benzanthracene have been synthesized and tested for carcinogenic activity, and of these the 10-isomer is the most potent. The meso-substituted 9-methyl compound stands next in order of potency, followed closely by the 5-methyl derivative, which produced sarcomas in mice with a latent period about twice as long as that observed with 10-methyl-1,2-benzanthracene. Methylcholanthrene and benzpyrene can be regarded as 1, 2-benzanthracenes substituted at the meso positions 10 and 9, respectively, and in model compounds the combination of the two types of substitution is particularly favorable. 9,10-Dimethyl-1,2-benzanthracene produced skin tumors in mice with remarkable rapidity and in this test surpasses methylcholanthrene in speed of action, though it is less effective when administered by subcutaneous injection. The thiophene isologue of the hydrocarbon has comparable properties."

Numerous attempts have been made to isolate the definite carcinogenic compounds in coal tar by means of distillation, solvent extraction, etc.[73], but while very potent fractions have been obtained, the individual compounds have been difficult to separate. Kennaway and Hieger [16] proved the carcinogenicity of 1,2,5,6-dibenzanthracene, the first pure carcinogenic hydrocarbon known. Cook, Hieger and Hewitt [24] in 1933 isolated 1,2-benzpyrene, 4,5-benzpyrene and 1,2-benzanthracene and estimated that the original coal tar pitch contained not less than 0.003% of the potent 1,2-benzpyrene.

Several investigators [22, 24, 25] have attempted to correlate carcinogenesis with <u>fluorescence</u>. For example, the cancer-producing material formed by the action of $AlCl_3$ on tetrahydronaphthalene shows a blue-violet fluorescence, showing three bands, 4000, 4180 and 4400 A.U., which are similar to the fluorescence spectrum of 1,2-benzanthracene [44]. Kennaway and Hieger [62] suggest the possibility of the use of the fluorescence spectrum for the preliminary examination of materials suspected of being carcinogenic.

An important fact brought out by several investigators is that the temperature to which a tar, shale oil or petroleum oil has been subjected determines its carcinogenic activity. In general, it would seem that temperatures up to 500°C. are without effect [52] but above that temperature carcinogens are formed, the maximum yield lying between 800 and 900°C. [53, 59]. Tar and pitch from gas works are far more active than that from coke ovens [58], accounting for 70% of all cases of tar cancer in the United States while the coke oven product causes only 5% [113].

While petroleum residues resulting from moderate heat treatment are inactive [120], yet by passing an inactive California petroleum through a tube at 880°C. Kennaway and Leitch obtained a very active carcinogen [59, 60]. Even an inactive medicinal paraffin oil heated to 380°C. under 50 atms. pressure acquired some carcinogenic activity [101].

Kennaway [56] likewise obtained an active material by passing isoprene through a tube filled with H_2 and heated to 820°C. Watson [115] achieved similar results with turpentine at 850°C.

Acetylene yields an active product on being passed through a red hot tube [59] but it must be pointed out that treatment with $AlCl_3$ at room temperature also produces an active compound [61].

On the other hand, synthetic lubricating oils produced by $AlCl_3$ polymerization at temperatures up to 150°C. were entirely inactive [121]. It is suggested that the condensation products of acetylene are of a more complicated nature and probably more unsaturated than those obtained from ethylene.

The carcinogenic activity of tars depends apparently not only on the temperatures of their formation but also on the chemical compound used as the base stock [100]. For example, a tar made from pinene at 850°C. was far more active than one from turpentine made similarly, the relative potencies being 100:19. Pinene tars made at 500, 600, 750, 850 and 950°C. had relative potencies

of 0, 12, 24, 100 and 64. Oxidation of a synthetic tar at 100°C. reduced its potency from 100 to 63, and at 150-160°C. its potency fell to 0. Oxidation with an acetone solution of $KMnO_4$ reduced the potency to 24; with pyridine as a solvent, almost to 0. The active constituents of synthetic tars form crystalline picrates, the remaining filtrate being almost inactive, and the picrate extremely potent.

Shale oil is carcinogenic, probably as a result of the high temperatures to which oil shale is subjected [104]. However, temperatures below 400°C. give a relatively inactive product, 500°C. and above being required [101].

In England where high-temperature tar is used in briquette manufacture, there are many cases of skin cancer among the workmen, which is not the case in France where the low temperature product is used.

The greatest amount of investigation of any type of occupational cancer has been carried out on mule spinners cancer in the cotton mills of Lancashire, England. Southam and Wilson [88] in 1922 first called attention the excessive occurrence of cancer in mule spinners. Women workers are not affected and about 70% of all cancer among mule spinners is of the scrotum [84], apparently due to the fact that a mule spinner at work walks to and fro in front of his machine, leaning over the moving frame from time to time to join up broken ends of the yarn. The base of the frame is on a level with the groin and the spindles on the frame as they rapidly revolve throw off oil from their bearings onto the clothes. In the hot mills the men perspire freely and so wash off the natural grease of the skin, thus allowing the oil closer contact [15]. Irritation by the trousers and overalls also helps the process. It is interesting to note that no trouble of this sort was noticed in England until mineral oil replaced animal and vegetable oils as a lubricant [16]. Henry [43] estimates that 0.25% of all cotton mule spinners in England suffer from scrotal cancer. On the other hand in the United States during 1926, for example, there were only 33 deaths from cancer of the

scrotum, of which only three of the victims were textile workers and three were mule spinners; four of the six were born in England and the other two in Canada [45], which tends to show that mule spinner cancer is rarely contracted in the United States. In a woolen mill in the United States employing about 200 mule spinners no cases of scrotal cancer were found [84]. Since the method of operating this equipment is the same in both countries this striking contrast is attributed by Hamilton [40] to the fact that Scottish shale oil is used in the Lancashire mills. However, the literature is not entirely clear as to the origin and type of the oil used in Lancashire in mule spinning [53].

Leitch [70] brings out a fact of possible significance, to the effect that cancer is not known in woolen spinning mills, even though the same machines are used as in the cotton factories, but points out that the room temperatures in the cotton mills are much higher, possibly resulting in more relaxation of the tissues of the scrotum and permitting entry of oil into the sebaceous follicles. Breckbank [16], however, states that in the woolen industry piecing of broken ends of yarn is done with both hands with a forward level bending movement of the body and thus there is not the same friction of the clothes on the scrotum as in the cotton mills. He admits, however, that the same oil is used in both types of mills.

As a result of the preliminary investigation of Southam and Wilson mentioned above, the Manchester Cancer Commission, consisting of more than fifty members, was organized in 1925 under the direction of Dr. C. C. Twort to investigate the mineral oils used in Manchester cotton mills. Lubricating oils from the various fields throughout the world were found to have widely varying degrees of activity. A sample of Venezuela oil was very potent while Russian and Pennsylvanian samples were on an average less than one-tenth as active. Purified medicinal oil had no carcinogenic properties and several saponifiable oils, such as sperm, olive, rape, cottonseed and neatsfoot oil, failed to produce

tumors when applied to mice, even under the most severe experimental conditions. In general terms, the more saturated were the constituent hydrocarbons of the lubricating oil, the less capable were they of inducing cancer in experimental animals, the physical characteristics being the same [101].

This preliminary report was criticised severely in an editorial in the "Petroleum Times" of London [4], in that while various oil companies (Anglo-American, Anglo-Persian and Shell-Mex) had contributed £1,000 for two years for the support of this investigation, yet the Manchester Cancer Commission had not availed itself of the services and advice of experts from the oil industry relative to the characteristics and methods of treatment of petroleum oils. The Institute of Petroleum Technologists, while making no definite criticisms at this time of the work of the commission, formed a committee of its own to follow closely the work in progress [63]. In 1934 Dr. A. E. Dunstan, Dr. F. H. Garner and Mr. James Kewley of the Institute of Petroleum Technologists are shown as members of the Manchester Commission [21].

In 1933, Twort and Lyth [104] of the Manchester Cancer Committee reported that by means of solvents, extracts were obtained of high refractivity and correspondingly high carcinogenicity. Their recommendations for the selection of an oil of low carcinogenicity were as follows:

When selecting from several mineral oils with similar gravity, specify that with the lowest refractive index; when selecting from those with similar refractive index, specify that with the highest gravity; when selecting from those with similar refractivity, specify that with the highest viscosity; and when selecting from origin alone, choose in the following order: Russian, Pennsylvanian, Texas, Mid-continent, Mexican, Californian, Persian, Rumania, Borneo, Venezuelan, shale.

However, it should be emphasized at this point that these authors state definitely that "adequate refining of any of the oils handled, of no matter what origin, results in a product ..... possessing only a very low

carcinogenicity" [104]. Also, that a single extraction of an unrefined distillate with SO_2 may profoundly lower the activity of a previously very dangerous oil, while a second extraction may render it almost inert. They state that "it is probably commercially feasible to treat oils of any origin, or oils of any degree of carcinogenic activity, so that they may be less dangerous than even the very best of the straight oils used today". They evidently assume that untreated textile oils are used in the Lancashire mills.

Lyth of the Commission further stated [71] that when the refractivity* of an oil was less than 0.5500 it was found to be non-toxic, while when the value was greater than 0.5600, the oil was highly toxic. Pennsylvanian oils and certain mildly treated oils were an exception. The iodine value of an oil seems to afford an indication of its toxicity, providing the oil has not been treated and again the higher the value, the more potent the oil. The toxicity increases in the same order as iodine value, except for Pennsylvanian oils which again occupy too high a position. The permanganate values are not regarded as of any value in connection with estimating the toxicity of oils.

Lyth adds that extraction with alcohols, acetone, etc., clay and acid treatment, leads to a reduction in the potency, especially in the case of the more potent oils but a corresponding reduction in the refractivity does not always occur. Where a marked reduction in the refractivity does occur, there is, without exception, a marked decrease in carcinogenicity; with a marked increase in refractivity, a corresponding increase in potency. Where the refractivity is not much altered, the potency may or may not be affected and further tests are necessary.

In spite of the apparent definite findings and recommendations of the Manchester Cancer Commission, the Cancer Research Committee of the Institute of Petroleum Technologists [51] was not convinced that "the so-called incidence of

* (Refractivity = $\frac{\text{Refractive Index} - 1}{\text{DENSITY}}$)

cancer is in any shape or form connected with the use of spindle oils". No elaboration of this statement was given, but was possibly based on refined oils only being used as textile lubricants.

An editorial in the "Petroleum Times" of London in 1937 once again attacked the conclusions of the Manchester Committee, pointing out that only one oil from each of a number of countries was examined [5].

In 1937 the Federation of Master Cotton Spinners Association sent out a letter to its members recommending that when purchasing spindle oils a guarantee should be obtained that the oil conforms to the specifications of the Manchester Cancer Commission, and that tests had shown that many of the oils in use at that time conformed to the specification.

While throughout the reported work of the Manchester Cancer Commission it is stated repeatedly that acid or solvent treatment of a potent oil greatly reduces or eliminates its activity [97, 102, 104, 71], yet in 1939 Twort and Lyth [107] investigated acid and clay treated distillates from a Borneo oil and found them to be active, the maximum potency being at a viscosity of 200-250 cp at 25°C. Molecular distillation gave a greater concentration of the carcinogenic material than was obtained by ordinary distillation at from 3 - 10 mm. In confirmation of previous findings the middle fractions of this Borneo oil were mostly responsible for pathological changes in the organs.

A carcinogenic shale oil was separated by molecular distillation into fractions which were subjected to chromatographic adsorption. Two apparently pure hydrocarbons have been isolated and are being investigated [2,109].

A recent report (1941) by C. C. Twort of the Manchester Cancer Commission [109] states that animal tests are variable, lengthy and costly and that a more reliable estimate of the carcinogenicity of oils can be obtained from the refractive index and viscosity. (Yet the data on which selection of these two properties was based were obtained by means of this variable skin test.)

Woodhouse of the Birmingham Cancer Research Laboratory also states that mouse tests to determine carcinogenicity are difficult to correlate with human tendencies to cancer unless these animal tests are strongly positive or negative [121]. For example, two oils were tested (a) from a spinning mill where no cases of mule spinners cancer had been recorded, and (b) from a mill where six cancers had recently been reported. Mouse tests indicated slight carcinogenic properties in the case of the two oils but a greater action on mice of (a) than (b).

Dr. E. M. Brockbank, chairman of the Manchester Cancer Commission, has briefly summarized the investigations of the Commission in a recent publication [16]. He lists the hygienic precautions to be exercised in mule spinning and urges the adoption of the oil specification given previously by Twort. He also makes this interesting generalization: "As a general rule an oil that is strongly dermatitic will not be strongly carcinogenic and vice versa". This is also mentioned by Kennaway [61] who states that cyclohexene (which is non-carcinogenic) is extremely irritating to the skin and should produce cancer if chronic irritation were an essential factor in carcinogenesis.

As mentioned previously, shale oils are very carcinogenic and in the Scottish shale industry the case incidence of skin cancer is about 0.1% per annum among the oil workers but 0.5% among the paraffin workers [53] (this is based on a 28 year record). This activity of paraffin is restricted by Schwarz and Tulipan [84] to the crude product, the refined wax being inactive, which view is supported by Wood [119] who states that the active components are present only in the crude paraffin oils.

With regard to the refining of petroleum oils, Wood [120] made an investigation of refineries in Pennsylvania and found no scrotal cancer, which was confirmed by Heller [42]. However, Heller found evidence of carcinogenic compounds in Mid-Continent oils as refined in plants in Ohio and Indiana. Here oil boils are fairly common and in some cases lead to skin cancer. In one case

a paraffin pressman in the Middle West was treated for "wax boils" for three years when a cancerous growth developed on the right forearm and was removed, but eight years later a second similar growth in the same place had to be removed. Heller also found records of cases of skin cancer in another refinery, using crude from the Lima field; eight cases had occurred in this refinery and one was fatal. All of these cancers were preceded by warts. The length of exposure before malignancy appeared varied from four to thirty four years. The part most often affected was the scrotum and all but one man worked in the paraffin department. These cases were caused by unrefined oils and Hamilton [40] states that so far there is no proof of the occurrence of skin cancer in the U.S. from the use of refined lubricating and spindle oils which have been acid-treated.

Heller [42] believes that the relative freedom from occupational cancer in the U.S. is due to the mechanization of industrial processes, preventing direct contact with the pitch and tar; the extensive employment of negroes, who are apparently less subject to skin irritants than whites; the use of refined lubricants from crudes which are poor in carcinogenic properties, and the use of tar from coke-ovens instead of from gas works.

Phillips [77] reports the particulars of a study carried out by the U.S. Public Health Service as to the incidence of occupational cancer in Texas. The records of 1190 individuals having microscopically verified skin cancers were analyzed, covering the period 1920 to 1940. The occupation of the largest group of these patients was outdoor work (farming and ranching); the work of housewives comes next in order, followed by various activities requiring moderate outdoor life. The professions were next, followed by laborers and carpenters. The railroad and petroleum industries furnished few cutaneous cancers.

Gafafer and Sitgreaves in a U.S. Public Health report issued in 1940 [37] analyze 70 cases of cancer recorded for the male members of the sick benefit plan of an oil refining company during the period 1933-38; there were 46 deaths. The death rate was 0.78 per 1000 and a frequency of 1.2 per 1000 (all U.S. death rate

0.96 per 1000). Almost 70% of the deaths were related to the digestive system and the rate for this site was higher than in the total population. Deaths from cancer of the genito-urinary system was 6.5% of the total, compared to 15.0% in the case of the total population.

In 1934 Campbell [20, 21] made laboratory tests on mice with dust obtained from tarred roads. This dust caused warts and cancer of the skin and in six months 24 out of 59 mice showed typical tar warts, half of which developed malignancy. This finding was confirmed by Kling, Samsonow and Heros, [64, 65] who also separated a substance containing the benzopyrene nucleus from the tar. However, Hogouneg [47] is doubtful of the danger from road tar since it usually takes years of direct contact of coal tar to the skin to produce skin cancer. (Teutschlaender [91] calls attention to the fact that almost all industrial cancers require an exposure of about ten years before growth appears, although a few cases may arise much later.) Valade [111] likewise is of the opinion that while primary lung tumors can be induced in mice painted with tar or exposed to inhalation of dust from tar roads, yet these results cannot be transferred to humans. Animals other than mice should be employed in experiments and an inquiry should be carried out on workers exposed daily to such dusts.

While the manufacture of briquettes in England is attended by a high cancer rate, [58] since high-temperature tar is used, yet in the few plants in the U.S. making briquettes cancer is entirely absent, partly due to the lack of contact with the binder since the process here is entirely mechanized and partly due to the use of petroleum asphalt as a binder, [42]. This finding was confirmed by Wood [120] in his investigation of briquette manufacture in Pennsylvania.

The addition of glycerides [89] reduces the carcinogenic potency of mineral oils but not to as great an extent as lanolin. Speakman and Chamberlain [89] state that while alcohols have not been used for this purpose there can be little doubt that such polar compounds will reduce the risk of cancer formation by promoting emulsification, since an oil which is easily and completely removed from the skin

must carry less risk than one which is difficult to emulsify. These investigators also believe that polar compounds in a mixture with mineral oil may, however, function in yet another way. It is known that the carcinogenic agents of mineral oil when associated with unsaturated compounds are free to concentrate at any surface to which the oil is applied, the non-polar paraffin molecules offering little or no resistance. However, when oil-soluble polar compounds, such as oleyl alcohol or wool-fat ether, are mixed with mineral oil they concentrate at the surface, excluding the less polar carcinogenic hydrocarbons.

Sequeira [86] stresses the necessity of absolute cleanliness of body and clothing, the application of castor oil [85] to exposed surfaces and medical inspection every three months. Brockbank [15] suggests a mixture of lanolin and olive oil be applied to the skin.

Duckham advocates the use of an oil-solvent cleanser similar to the ether soap used in hospitals in order to remove all of the lubricant from the pores [3].

In view of the suggested use of lanolin the following should be of particular interest: Dr. E. V. Cowdry, of the Washington University School of Medicine, St. Louis, has just announced (N.Y. Herald Tribune April 29, 1945) that cells can be sensitized to become cancer cells by treating them with a substance which does not cause cancer and which will even prevent powerful cancer-producing chemicals from exhibiting that property.

For example, when the powerful carcinogen methylcholanthrene is mixed with lanolin it is without action when applied to the skin of mice, although alone it always results in cancer. However, when these mice were then treated with methylcholanthrene in benzene they developed cancers more quickly and tumors of greater virility than mice which had not received the cancer-preventing treatment.

MPD-VL
DWS

REFERENCES

1. Anon., Cancer from Spindle Oil. Oil and Color Trades J., July 2, 1937, 38.
A letter sent out by the General Committee of the Federation of Master Cotton Spinners' Association recommends that when purchasing spindle oil members should obtain a guarantee that the oil conforms to a specification of the Manchester Cancer Committee which recently issued a formula claimed to minimize the so-called cancer-producing elements of mineral oil. Tests showed that many of the oils in use at present conform to this specification and are obtained at regular prices.

2. Anon., Cancer and Mineral Oils. Oil and Color Trades J., 102, 695 (1942)
The report of the Manchester Committee on Cancer, issued for the year ended October, 1941, states that in efforts to isolate and characterize individual carcinogenic hydrocarbons from shale oil, recently appreciable quantities of crystalline material have been obtained, but it is too early to discuss results in detail. As far as can be judged, all fractions obtained from Venezuelan Oil by chromatographic adsorption are active. Proprietary colloids have varying effects, depending on the conditions of the experiment. A colloid containing a chlor-compound was found less efficacious than an olive oil-lanoline mixture as protection against the carcinogenic action of shale oil, while the reverse appeared to be the case when the carcinogenic agent used was benzpyrene.

3. Anon., The Problem of Cancer. Petroleum Times, 23, 59, 300 (1930)
(a) The following appeared in a recent issue of the British Medical Journal in connection with the use of mineral lubricating oils in the Lancashire cotton mills: "The Manchester Cancer Committee, while studying the part played in the production of malignant growths by the lubricating oils used in cotton mills, has obtained information about the carcinogenetic power of various oils and the concentration within them of a cancer-producing principle. In the course of this research, two pure compounds of known chemical composition have been proved capable of producing tumors, and a study has been made of the factors which change a non-carcinogenic into an active carcinogenic substance. Already some of the methods for destroying the cancer-producing power of certain oils have proved to be effective, at least in part, and one method led to the preparation of a purified oil which, when subjected to vigorous test, has failed altogether to produce cancerous growths. Representatives of the cotton industry, after comparing this oil with the crude untreated oil have said that its lubricating power is unimpaired, and the Manchester Committee is therefore able to hold out the hope that before long it may be possible to put on the market an oil which fulfills the needs of industry without being a source of danger to the workers."

Assuming that the use of spindle oils be such a source of danger, it almost necessarily follows that other lubricating oils which come into closer physical contact with the worker must be sources of higher potential danger than any of the light lubricating oils used in the looms of the Lancashire cotton industry. It might be proved upon investigation that little difficulties would present themselves in the production of a spindle oil which is non-carcinogenic, and lest the present attack widens itself to include the whole range of mineral lubricating oils, it would be advisable to make an investigation of the most embracing character.

examns., gas-works tar and pitch were responsible for 70.2% of the cases while coke-oven tar and pitch were held responsible for only 5.4%. Coke-oven tar is much the less injurious especially when cognizance is taken of the fact that coke-oven tar is used much more extensively. The presence of olefins in gas-works tar seems to be of particular importance and may be a cause of oil cancer. Occupational cancer does not occur in the briquet mfg. industry. Mineral oils vary in carcinogenic activity according to their olefin or unsatd. hydrocarbon content. There is no method for the detn. of the amt. of olefins in the various crude oils; if such a method existed, it would be possible to measure the cancer-producing power of mineral oils. Cancer is not attributable to the occupagion of mule spinner in the U.S., possibly because of the carefully refined lubricating oils used on the machines, thus ensuring relative freedom from olefins or unsatd. hydrocarbons.

43. Henry, S. A. Study of Fatal Cases of Cancer of the Scrotum. J. Am. Med. Assn., 109, 1667 (1937)

44. Hieger, I., Spectra of Cancer-producing Tars and Oils and of Related Substances. Biochem. J., 24, 505-11 (1930)

45. Hoffman, F. L. Mule Spinners Cancer. Monthly Labor Rev. of U.S., 27, 457-475 (1928)

46. Hoffman, W. J. Industrial Cancer. Prevent. Med., 6, 7-34 (1936)
One of the seven types of industrial cancer discussed is cancer of skin in workers exposed to coal, tar, pitch, soot, shale, petroleum and arsenic. They may cause an epitheliomatous form of cancer.

47. Hogouneng, L. The Cancerigenic Hydrocarbons from Tar and the Tarring of Roads. Ann. Hyg. Publ. Sociale, 27, 1-7 (1939)
The cancerigenic hydrocarbons found in coal tar produce skin cancer in exposed workers usually only after direct contact with the skin for long periods of time. It is believed that man is much more resistant to the action of these materials than lab. animals.

48. Hueper, W. C. Cancer in Relation to Occupation and Environment. Bull. Am. Soc. Control Cancer, 25, No. 6 (June, 1943)
Owing to industrial development, the general population and factory workers in particular, are exposed to many new environmental factors, many of which are disease producing. Occupational cancers are caused by numerous chemical and physical agents. Among them are the heavy metals, nitrites, aromatic amino compounds, benzol, asbestos, mineral oil, soot, radio-active substances, ultraviolet radiation and X-rays. The author cites statistics taken mainly from the records of industrial concerns, but points out their shortcomings.

Cancer of the urinary tract due to coal-tar is the most recent addition to the list of occupational cancers. It is most frequent in the aniline dye and related industries.

49. Home Office, Rept. of Departmental Comm. to Consider Evidence as to Occurrence of Epitheliomatous Ulceration Among Mule-Spinners. (London, 1926)
Contains a bibliography on cancer among petroleum refiners.