

SHELL DEVELOPMENT COMPANY

MAY 2 1950

TO

K. R. EDL

SHELL DEVELOPMENT COMPANY
MAY 11 28, 1950
EMERYVILLE, CALIF.

FROM

C. H. HINE, M.D., CONSULTING TOXICOLOGIST

SUBJECT CERTAIN PROBLEMS OF ENVIRONMENTAL CANCER IN THE PETROLEUM INDUSTRY

As you are undoubtedly aware there has arisen in many sources an increased concern about the incidence of cancer in the productive working age group. Since it is my understanding that certain Departments of the Company will have occasion in the future to have an increased contact with high boiling and non-volatile petroleum mixtures, I have prepared the following memorandum for your information. I can see no cause for immediate concern, however, it is rightly the province of your group to have access to information about the problem of occupational cancer.

Any chemical agent which on proper exposure, directly or indirectly, causes cancerous growth in one, several, or all types of human tissues represents an environmental carcinogen. There is considerable evidence substantiating the increase in cancer due to environmental causes. While such factors as improvement in diagnosis and treatment doubtlessly increase the number of cases recognized, there is little doubt that there is a quantitative widening of the spectrum of environmental carcinogens. For example there has been a marked increase in the number of lung cancers recorded during the past 40 years from many parts of the world. The extrinsic origin of this phenomenon is suggested by the fact that the increase has been more pronounced in males than in females. At present there is a lack of proof that a single extrinsic agent is wholly responsible for this development. It is well established that several agents with highly different physical and chemical properties may cause pulmonary malignancies of occupational origin.

In only relatively few instances can the origin of environmental cancer be traced to contact with well defined chemical agents possessing established carcinogenic qualities. Among such compounds are arsenic, benzol, and aromatic amines, in addition to radio-active elements.

A large group of environmental tumors are caused by exposure to ill defined mixtures of organic chemicals, the carcinogenic components of which are incompletely known. The members of this group include tar, pitch, asphalt, soot, crude mineral oils, paraffin oil, shale oil, anthracene oil, lubricating and fuel oil, creosote and bitumens. The highly diverse chemical and physical properties of these compounds make it improbable that they exert their specific pathogenic action on a common mechanism. Certain theories have been proposed concerning the possible mechanisms in producing cancer. The first of these theories is based on the known action of the aromatic amines and carcinogens contained in tar, and predicates a direct action on cellular substrate. This action may be catalytic by interfering with normal cellular enzymatic activity or by combining with proteins

PLAINTIFF'S EXHIBIT 101

003343

PLAINTIFF EXHIBIT

500428 SHEL

PLAINTIFF'S EXHIBIT

resulting in the formations of allergens. A second theory relates that carcinogens do not possess direct carcinogenic properties, but that they act through changing some normal chemical constituent of the cell or tissue fluid so that it becomes endowed with carcinogenic properties. A third theory concerns agents which may cause quantitative or qualitative changes in some intricate endocrine gland or the liver, which responds with a generation within the body of abnormal endogenous carcinogenic products. Cancers of this type may be produced by hepatotoxic agents such as azo dyes or chlorinated hydrocarbons.

Human contacts with soot, carbon black, pitch, asphalt, crude petroleum, shale oil, paraffin oil, lubricating and fuel oil, anthracene oil and other distillations and fractionation products of coal and petroleum apparently cause the majority of environmental cancers in man.

The specific carcinogenic agent or agents in these products is not known. However, it is probable that 3,4-benzpyrene account for at least a portion of this activity.

Despite the observation that tar products, petroleum, and oil shale products account for the majority of environmental cancer in man, Gafafer, on analyzing the incidence rate of cancer among the employees of an oil refinery, did not find any significant difference from that of the general population. Huesper, an authority in Occupational Cancer Problems states that he feels that the validity of this report is highly questionable, due to difficulty in obtaining factual data. The A.P.I. is in the process of undertaking a survey among certain members of the Institute who have kept adequate medical records; their report should be forthcoming in about a year. Information of a highly confidential type has reached me that Esso has conducted such a survey and has obtained information which is causing considerable concern. The role which the inhalation of tar dust and fumes plays in the production of cancer in man is still unsettled. Animal experimental evidence shows that soot containing gasoline motor exhaust products cause cancer of the lungs after inhalation, or sarcoma of the subcutaneous tissue after injection in mice and rats. However, the lung cancer rate among males in Pittsburgh was found to be lower than that of any other large city surveyed with the exception of Denver.

Huesper has pointed out that the great majority of cancers which can be traced to occupational origin in modern times have resulted from carcinogens which entered industrial processing during the last 50 years. In the following table are presented all the known or commonly suspected chemical agents causing cancer that are present in the oil industry. As a general rule occupational cancers arise at the site where the particular carcinogen has the most prolonged and intense contact with the tissue. Consequently, we would expect the majority of cancers in the petroleum industry to occur on the skin, mucous membrane and surface organs.

003344

CHH/mw

cc: N. W. Jacobsen
R. R. Ward

C. H. Hine
C. H. HINE, M.D., Consulting Toxicologist

TABLE 1

CERTAIN RECOGNIZED AND SUSPECTED CARCINOGENIC AGENTS ENCOUNTERED IN THE OIL INDUSTRY
SHOWING THE ORGANS OR SYSTEMS CHIEFLY AFFECTED

Substance	Organ or System
Aniline and derivatives	Bladder, ureter, kidney
Anthracene, crude	Skin
Aromatic organic chemicals	Liver
Asphalt	Skin Eye
Benzidine and derivatives	Bladder, ureter, kidney
Benzol	Blood forming organs
Benzol derivatives	Blood forming organs
Chlorinated aliphatic hydrocarbons (?)	Liver
Creosote	Skin Lip Eye
Mineral oil, crude	Skin Lip Respiratory system Eye
Naphthylamine, beta	Bladder, ureter, kidney
Oil shale	Skin
Paraffin oil, crude	Skin
Pitch	Skin Lip Bladder Eye
Soot	Skin Bladder
Spindle oil	Skin
Tar	Lip Skin Respiratory system Bladder Blood forming organs Eye

003345

A number of agents encountered in the petroleum industry elicit pre-cancerous reactions which are characteristic to a certain extent of causative agents and which represent various transitional stages between the original normal tissue and the final cancer. In Table 2 are enumerated certain of the more common of these agents together with the portion of the body affected and a description of the lesion.

003348

Precancerous Lesions	Etiologic Agent
atrophy: Skin grossly thinned and glistening in patches, associated with keratotic areas.	Pitch, tar, asphalt, radioactive substances, radiation (including ultraviolet rays).
xema: Dry seborrheic patches on skin	Arsenic, asphalt, pitch, soot, tar.
leucoderma: Flat, discrete, scaly area on skin with raised pearly borders. Usually on parts of skin exposed to carcinogen, but may occur in unexposed parts, particularly about sweat glands, with arsenic.	Anthracene, arsenic, asphalt, creosote, crude mineral oil, paraffin, pitch, sodium nitrate, soot, tar, radioactive substances, radiation (including ultraviolet rays).
hyperkeratosis: Rough, fissured keratotic plaques with small, hard, wart-like horns, usually on hands and soles. May become nodular and ulcerate.	
varicose: Form of hyperkeratosis.	
debridement: Breakdown of keratotic lesions.	
leukoderma: Absent pigmentation alone.	
leuko-melanoderma: Patchy increased and absent pigmentation of skin. Most common in areas of highest pigmentation, and may involve oral mucosa.	Anthracene, arsenic, asphalt, creosote, crude mineral oil, paraffin, pitch, tar, radioactive substances, radiation (including ultraviolet rays).
melanoderma: Increased pigmentation alone.	
leukoderma: Dry, scaly, parchment-like skin, with enlarged pores, associated with leukomelanoderma.	Crude mineral oil, paraffin oil, radioactive substances, radiation.
hemorrhage: Varying size with telangiectasis. Located mainly in trigone and about ureteral orifices.	Aniline, benzidine, beta-naphthylamine and derivatives.
polyps: Polypous or villous, pedunculated or sessile, often multiple about trigone and ureteral orifices.	
polyps: Pedunculated, develop mainly on lids, occasionally on eyeball.	Arsenic, asphalt, creosote, crude mineral oil, pitch, tar, radiation (including ultraviolet rays).

003347

Precancerous Lesions	Etiologic Agent
<p>ONES AND BONE MARROW:</p> <p>Blood dyscrasias: Hyperplastic, hypoplastic, aplastic, or hemolytic anemia. Thrombocytopenic purpura with spleen not markedly enlarged. Transitory leukopenia, monocytosis.</p>	<p>Benzol and derivatives, radioactive substances, radiation.</p>
<p>LUNGS:</p> <p>Pneumoconioses: Bituminosis, asbestosis, "lipoid" pneumonia, chronic chemical pneumonia, arsenical dermatosis, chromate ulcer of hands, perforated nasal septum (chromate, arsenic).</p>	<p>Asbestos, arsenic, tar, soot, oil, mist, chrome salts, chrome pigments, nickel carbonyl.</p>

Many of these pre-cancerous manifestations regress spontaneously from exposure the causative agent ceases, however, some of them are followed by or transformed into malignant growths. It is advised, therefore, to examine certain workers periodically for such reactions when they are known to be exposed to these carcinogenic agents, and when such warning signals appear the worker should be removed from his environment.

003348