COAL TAR AND CUTANEOUS CARCINOGENESIS IN INDUSTRY

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FOREWORD

THE PROPERTY of carcinogenic potency is widely distributed among chemical compounds. Well over 300 have been found capable of inducing malignancy in laboratory animals, and about 35 capable of inducing benign tumors. While these figures may appear high, cognizance must be taken of the fact that the investigations upon which they are based were done on mice, rats, dogs, rabbits and other laboratory animals under various environmental and inherent variables. By no means can it be categorically stated that this or that substance, because of its chemical structure, is carcinogenic. On the other hand neither is one justified in divesting any chemical of carcinogenic potency since many which are under certain conditions safe, under other more favorable conditions and in the presence of unknowns, enzymotic, catalytic or infectious in nature, may be carcinogenic. The term, therefore, cannot be interpreted as an "invariable property" of certain chemicals or of substances of related chemical structure.

An effort has been made in this text to present the carcinogenic nature of certain fractions of coal tar in a practical way, especially as it applies to the workman in industry. Naturally some reference must be made to efforts to induce cutaneous malignancy in animals, but the reader must avoid the pitfall of blandly applying the results of animal experimentation to man. Certain animals are more resistant to certain chemicals, others more susceptible. Likewise, contributing factors encountered in industry are lacking in animal experimentation.

The growing chemical industry and world wide investigation of the cause and nature of cancer prompted the preparation of this short text as a source of information for the dermatologist and industrial physician.

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INTRODUCTION

In a discussion of the nature of cancer, Loeb divided principal factors which must, of necessity, be considered potential causes as (1) constitutional factors; and (2) stimulating factors. The latter he interpreted as originating "either within the organism itself or in the outer environment." These stimulating factors act on the healthy tissue cells and make them cancerous. This metamorphosis of normal cells into malignant cells can be induced in all tissues which contain the potentiality of proliferation.

The assumption of atavistic tendencies has been observed as a result of a variety of extrinsic causes, among which are (1) certain viruses; (2) hormones, especially those of the steroid type; (3) certain metazoic parasites; and (4) the so-called carcinogenic hydrocarbons, including tar.

II

THE GENERAL NATURE OF CARCINOGENESIS

EPITHELIOMA, carcinoma, or for that matter, any malignant neoplasm differs from a benign new growth not only in the more rapid proliferation of its cellular elements but in the development of structural abnormalities, immature elements predominating. These two factors are *permanent* characteristics of cancer cells and not *temporary* or *transitory* as in non-malignant growths, which reach a certain size and may then remain stationary or even regress. One might conceive of malignant neoplasms as defects in cellular coordination due to the presence or absence of some trace substance which upsets tissue equilibrium and is responsible for stimulation of the active vegetative cellular units. Regardless of cause, the change is permanent and irreversible.

It is now known that this basic difference between malignant and non-malignant tissue is probably determined by differences in biochemical structure and metabolism. Many factors, both intrinsic and extrinsic, hereditary, and acquired, as already mentioned, working interdependently or individually, are capable of initiating these revolutionary diversions. The exact methods are unknown.

Statistically the great majority of malignant cutaneous tumors develop in the latter decades of life; but this incidence is not absolute, since the maximum incidence at any age is influenced by other factors, especially environmental noxae. Chief among these are radiant energy of many types, epidermal irritation of a mechanical nature and the presence in the skin of specific carcinogenic hydrocarbon fractions, from an endogenous or exogenous source, or a combination of any of these. This responsibility of a variety of noxae in carcinogenesis is not unique, since such is true in many other biologic phenomena. It is, however, a feature which contributes to our difficulty in interpretation of the biologic properties of carcinogenic chemicals and in an estimation of their ultimate significance.

Predisposing states or constitutional factors which must be recognized as influencing the tendency to development of cutaneous cancer from protracted exposure to carcinogenic fractions of tar include:

AGE

a. The sum of stimuli affecting tissues and organs increases with age.
b. Tissues undergo involutional changes with increasing age which impede their return to normal.
c. The skin becomes drier with advancing age, and undergoes many degenerative changes which make it more susceptible to environmental trauma to which it is exposed.
d. In the case of many precancerous dermatoses a "lag period" of 10-30 years intervenes before development of malignancy.

SEX

The reason for prevalence of cutaneous malignancy in men is readily apparent, entirely aside from the fact that the average woman will seek immediate medical attention for any defect or the slightest irritation of her skin. Roffo found the incidence of epithelioma in men to be 70.9% as compared to women 29.1%.

COMPLEXION AND RACE. Blonds and those with fair skins are more susceptible, especially to chemicals and radiant energy. The negro skin is resistant. Basal cell epithelioma is rare in this race.

PREEXISTENT DERMATOSES. Such dermatoses as seborrhea, ichthyosis, pyogenic infections, acne, cutaneous injuries and poor hygiene, act as predisposing factors.

III

THE TARS

THE CANCER producing potentiality of tar depends upon its source and chemical constituents. It might be advisable to explain briefly just what is meant by "tar." When speaking of it, many think of the thick, viscous, black, asphalt-like material used to pave roads. This is not necessarily tar; tar varies in color from black to light brown; and in consistency, from a fragile, brittle solid to a watery liquid. There are many features of tar chemistry which are still subject to controversy among organic chemists; and many components of both coal and petroleum tars which have not yet been fractionated or identified.

In a broad sense, any residue remaining after the destructive distillation of organic matter is a tar.

There are four groups of substances, all basically of vegetable origin, designated as "tars," and used in medicine. These are coal tar; the wood tars (the tar oils—juniper tar, pine tar, beech tar, and birch or Russian tar); bituminous shale tar (the source of ichthyol) and lastly, petroleum tar (from crude oil).

CRUDE COAL TAR

Although all tars are to some degree carcinogenic, either directly or indirectly (through their ability to initiate precancerous lesions), only coal tar is thought to actually contain active carcinogenic chemicals. These vary in type and quantity depending on the geologic and geographic source of the tar, its method of extraction and distillation.

Coal tar is a by-product in the manufacture of illuminating gas, and is of great commercial value. As the coal decomposes at temperatures ranging from 450 to 1200° C., ammonia, steam, coal gas and crude tar are evolved, leaving an amorphous mass of coke in the retorts.

When first introduced into medicine it represented the black deposit recovered at temperatures of 450-700° C. from the horizontal retorts in the illuminating gas plants. The small quantities required for medical purposes were washed with water to remove the ammonia, then heated to 70° C. to remove the water content. It was called "retort tar" or "gas house tar" and consisted roughly of the following fractions determined by the method of fractional distillation.

Tar acids	24-45%
Naphthalene fraction	0- 3%
Anthracene fraction	5-10%
Pitch and carbon	35-60%

The evolution of the illuminating gas industry in the last quarter century has resulted in the substitution of as much as 60% petroleum and steam for much of the coal, thus furnishing an illuminating gas containing a mixture of carbon monoxide and hydrogen (from the split H_2O). This process requires the use of high temperatures (900-1200° C.) rapidly achieved in vertical retorts, so that the tar residue now contains not only distillation products from coal, but petroleum distillates as well.

Low temperature, horizontal retort tar is a relatively thin, brown liquid (orange or red), fairly rich in complex phenolic compounds with paraffin side-chains; unsaturated compounds, a minimum of naphthalene and anthracene compounds, no solid aromatic fractions and little free carbon. It has an odor of hydrogen sulfide and phenol (due to phenol, molecular sulfur and mercaptans), never naphthalene, as high temperature tar. On rare occasions, especially when brown coals or lignites are the parent materials (as in the British Isles), the tar may be solid at room temperature owing to the presence of solid paraffins.

The specific gravity of low temperature tar is lower than that of high temperature tar (0.95-1.06 at 25° C.), due to the presence in high temperature tars of more aromatic hydrocarbons, such as naphthalene and anthracene. Low temperature tars have a tendency to impart a red color to any water that comes in contact with them, particularly if that water is alkaline.

High temperature distillation results in a tar low in phenols and neutral oils but rich in solid aromatic hydrocarbons and much free carbon and pitch. It is usually much thicker in consistency, less mobile and jet black in color. The greater content of naphthalene, anthracene and carbon makes this type of distillate more valuable commercially than medically. The same may be said for tar obtained from high temperature coke ovens, as shown in the following assay:

Tar acids	14-25%
Naphthalene fraction	4-10%
Anthracene fraction	9-12%
Pitch and carbon	40-67%

Coke is the residue of pitch which has been subjected to intense heat (1200+° C.) in the absence of oxygen, resulting in distillation of all traces of oils and volatile matter. This residue is almost pure carbon.

COAL TAR DISTILLATION

Ordinarily the companies dealing in tar and tar products purchase their tar from every source possible, illuminating gas plants, coke ovens, etc. By a process of controlled redistillation, chemicals and oils of various types are obtained at different temperature levels (see Table I).