ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN SQUAMOUS CARCINOMA OF THE SKIN, WITH A NOTE ON THE DIAGNOSIS AND PREVENTION OF OCCUPATIONAL SKIN CANCER.

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Part I

Summary and comment on the present knowledge of skin cancer, particularly epidermoid cancer of the skin.

Definitions

Squamous Epithelioma of the Skin (otherwise epidermoid cancer of the skin, squamous cell cancer of the skin)

Malignant growths derived from the stratified squamous epithelium of the skin.

Rodent Ulcer of the Skin (otherwise basal cell cancer of the skin, epithelioma basicellulare)

A variety of cancer which is believed to take origin from the lowest layer of the surface epithelium and which spreads almost exclusively by direct extension.

Surface Cancer

Cancer which originates from any part of the body surface, including squamous and basal cell cancers as above, in addition to cancers arising from mucous membrane or muco-cutaneous junctions, and orificial cancers (e.g. cancer of the lip and cancer of the vulva).

History

Environmental factors, in relation to skin cancer, were first described in connection with occupation and the first description of occupational cancer is found in 'The Chirurgical Works' by Percival Pott (1775). Pott (1713-1788) was born on December 26, 1713 in Threadneedle Street, and was apprenticed at St. Bartholomew's Hospital to Edward Nouse, surgeon. In 1775 he published the description of occupational cancer of the scrotum, due to soot. "There is a disease peculiar to a certain set of people which has not, to my knowledge, been publickly noticed. I mean chimney sweeper's cancer. It is a disease which always makes its first attack on and its appearance in the inferior part of the scrotum; where it produces a superficial painful, ragged, ill-looking sore, with hard and rising edges. The trade call it 'soot wart'."

Cancer of the scrotum was noted by Pott in "climbing boys" aged 13-15.

The next landmark was one hundred years later in 1875 when von Volkmann described industrial skin cancer due to contact with coal tar. The following year (1876) Bell, in Scotland, described paraffin cancer due to shale oil. Mule spinners cancer was described in 1887.

Meanwhile, various attempts were made to produce cancer in experimental animals. No success was achieved until 1915 when the Japanese workers Yamagiwa & Ichikawa, using coal tar, produced cancer of the ears in rabbits. The production of cancer in experimental animals opened up the modern era in cancer research with reference to chemical carcinogenesis, and enabled many compounds to be tested for carcinogenic activity. Until 1930, when Kennaway and Heiger produced cancer by means of 1,2,5,6-dibenzanthracene, no pure chemical substance was a known carcinogen. Following this discovery, many pure chemical carcinogens were isolated. It follows that in occupations in

which the worker is exposed to any of these known chemical carcinogens, that an increased incidence of cancer is to be expected.

In Great Britain, the first official recognition of cancer as an industrial disease is contained in an addition to the third schedule of the Workmen's Compensation Act of 1906. In 1907, an addition to the third schedule of the Act was made that "scrotal epithelioma occurring in chimney sweepers and epitheliomatous cancer or ulceration of the skin occurring in the handling or use of pitch, tar or tarry compounds" were to rank as industrial diseases. In 1914, bitumen, mineral oil and paraffin (or any compound or product or residue of these substances) was added. At present, diseases are 'prescribed' under the National Insurance (Industrial Injuries) Act of 1946, if the disease is thought to be occupational in origin. Skin cancer due to "arsenic, tar, pitch, bitumen, mineral oil or paraffin, or any compound, product or residue of any of these substances, chrome ulcer or its sequelae, scrotal epithelioma, or exposure to x-rays, radium or other radioactive sus$ance" are 'prescribed' within the meaning of the Act. "Ulceration of the skin produced by dust or liquids" is also included in the list of prescribed diseases, and this may cover many other causes of cancer.

While not all the known possible causes of skin cancer are covered by the Act, much progress has been made in the official recognition of occupational influences in cancer production.

Introduction

"The many occupational differences revealed by analyses such as the Registrar General's, afford hints of possible carcinogenic factors which are worth farther statistical and experimental investigation. It is important to emphasize here the great length of the latent period often intervening between the application of the carcinogenic stimulus and the eventual appearance of the tumour. This makes it useless to look for the causes of human tumours in the occupations and habits of affected persons during the parts of their lives immediately preceeding the appearance of the tumours. The tumour of today is often the consequence of stimuli applied 10, 20 or 40 years ago. Our medical histories and therefore our statistical data, of tumour patients are often totally deficient in this respect; detailed inquiry into the occupations and habits of the whole of the patients previous life, remote as well as recent, is rarely undertaken. Here is a great almost virgin field of research, exploration of which ..... must be undertaken if we are to sift out of our complex environment the carcinogenic factors which are yet unrecognized."

The above quotation from 'The Pathology of Tumours' (Willis 1953) outlines the problem on which further work has been attempted and which will be described in Part II. In order to carry out an investigation into possible aetiological factors, the known aetiological factors and other factors which are relevant, will be reviewed briefly and are discussed under the following headings:-

I. Environmental Factors, e.g. physical and chemical factors.

II. Personal Factors, e.g. previous disease, congenital abnormalities, family history.

In a discussion on some principles of aetiology, Halliday (1949) points out that aetiology is always multiple and that part of the cause lies in the individual. He quotes as an example the case of persons drinking water which is contaminated by typhoid organisms. The first person may become seriously ill with typhoid fever, the second person has a mild febrile illness which lasts for a few days, and the third person is not affected in any way. The cause of the first persons illness cannot therefore be the typhoid organisms alone - or the other two persons would have suffered. The difference of reaction in each case was due to an associated factor in the individual. The first person had never had typhoid fever and had never been inoculated prophylactically against the disease; the second had been inoculated against typhoid fever a few years previous; the third had recently recovered from typhoid fever.

With regard to the aetiology of skin cancer, it is important to recognize that it is not only the question "What kind of individual is this" that is important. "What kind of person was this" is equally, if not more, relevant. What environmental factors have influenced him, what changes have occurred in the individual and how have these changes been induced, are questions to which answers should be attempted. The review which follows in Part I will try to present synoptically the available knowledge in answer to the questions. It should be stated here that what follows applies to SKIN cancer, and in particular squamous epithelioma, and not to cancer in general.

III. The Mechanism of Cancer Production

Under this heading is discussed how carcinogens act on the skin in producing cancers, and some of the theories of carcinogenesis.

1. Environmental Factors

Chemical Factors

1. Carcinogenic Hydrocarbons

   a) Soot

   b) Pitch and tar

   c) Mineral oil

2. Arsenic

3. Other chemical factors

1. Carcinogenic Hydrocarbons

a) Soot

This was the cause of the first described occupational cancer, and caused chimney sweeper's cancer of the scrotum. Henry (1950) analysed the occupations of persons who were certified as having died from cutaneous cancer. In total skin cancers, chimney sweepers had the highest incidence of 791.7 per million. In the cases of cancer of the scrotum, chimney sweepers again top the list with an incidence more than twice as great as the next highest - namely, chimney sweepers 543.75 per million against 234.91 per million in textile spinners and piecers.

The exact chemical composition of soot is not known, but Goulden & Tipler (1949) showed that coal smoke or soot contains 0.03% of benzpyrene, which is a known pure chemical carcinogen. (This fact has been suggested as an explanation for the higher incidence of lung cancer in town dwellers.)

Carcinogenic hydrocarbons have been shown to exhibit fluorescence in the region of the mitochondria, and it may be that they are stored in or nearby the mitochondria and exert their action on the cell by way of mitochondrial damage (see under the mechanism of cancer production).

b) Coal Tar and Pitch including Products and Residues.

These are considered together, and are well recognized as the causal agent in cancers among gasworks workers, road tar sprayers, optical lens grinders (who use pitch to embed the glass while grinding) and in many other occupations.

The first pure chemical carcinogen, 1,2,5,6-dibenzanthracene was isolated during researches on the high-boiling carcinogenic fraction of coal tar. Berenblum (1945) proved that tar might contain as much as 1.5%

of 3-4 benzpyrene (a known chemically pure carcinogen).

c) Shale or Mineral Oil

Cancer of the skin due to mineral oil was first described by Joseph Bell in 1876 (Bell 1876) in Scottish shale oil workers, although in the previous year von Volkmann (1875) had described occupational skin tumours in paraffin and tar workers at Halle.

In an analysis of the cases of cutaneous cancer which were statutorily notified to H.M. Chief Inspector of Factories between the years 1920-1949, Henry (1950) found "shale or mineral oil" to be the causative agent in 35.7% of the total number of cases. The occupation of 91.5% of this group was in the manufacture of textiles, 3.72% in chemical and 3.38% in engineering industries.

The composition of the mineral oil varies according to the source of the oil and to the method of refining. It has been shown* that catalytically cracked oil shows a higher carcinogenic potency in animals. This is probably due to the greater number of aromatic (ring) compounds which are produced by this method of refining.

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* See references Smith, W.E., et al., (1951)
Fischer, H.G.M., et al., (1951)
Holt, J.P., et al., (1951)
Blanding, F.H., et al., (1951)

Catalytic cracking of oil was a process developed during the last war and has been used in the United States since 1943 and in the United Kingdom since 1950. The effect of catalytic cracking is to produce high octane petrol from a heavier oil. In doing this, the number of aromatic (ring) compounds are increased and the carcinogenic potency of the residue, after cracking, is greatly increased. This residual oil is used mainly as bunkering for ships and for oil fired boilers.

2. Arsenic

Currie (1947) has reviewed the role of arsenic in carcinogenesis. His conclusion is that it is difficult to assess the function of arsenic in the production of malignant change. Chronic arsenicism may precede malignant changes in the skin in the form of hyperpigmentation, melanosis and hyperkeratoses. Three cases of skin cancer have been noted in the past eighteen years in workers handling arsenical insecticides, and cases have been noted amongst persons engaged in the manufacture of sheep dip. It is also suggested by Currie that arsenic may contribute to the cancers amongst farmers, gardeners and nurserymen who handle arsenical preparations in the form of weedkillers, insecticides and fertilizers.

Ingestion of arsenic leads to hyperpigmentation (melanosis) and the formation of keratoses. These keratoses are regarded as the precursors of arsenic cancer following ingestion of arsenic, although cancer may occur without previous keratoses. Arsenic has been given medicinally for conditions such as psoriasis, asthma, anaemia and other conditions. Arsenic cancers tend to be located on the extremities.

3. Other chemical factors

The 'asbestos corn' in the skin is well known. Wyers (1956) states that in 16 years experience in the asbestos industry, he has never seen malignant change in an asbestos corn. However, he quotes one case in which he has heard of malignant change in an asbestos corn.

The above list contains the "officially accepted" chemical causes of skin cancers in man, that is those for which industrial injury and disablement benefit is payable to the workman. Other possible carcinogens are very numerous. Over seven hundred substances are included in the 'Survey of Compounds which have been Tested for Carcinogenic Activity' (Hartwell, J.L.,

(1951)). This is a review of all compounds which have been tested for carcinogenic activity and gives the result of the tests in synoptic form.

Physical Factors

1. Excess heat
2. Excess local cold
3. X-rays and ionizing radiations
4. Sunlight and ultra-violet light.

PHYSICAL FACTORS

1. Excess Heat.

Henry (1950) directs attention to a number of cases of cutaneous cancer which occur in workers in occupations where the workers are in contact with a source of radiant heat, such as puddlers, glass blowers and finishers, forgemen, metal moulders in foundries and others. In these occupations, the incidence of cutaneous cancer is high. Puddlers have third highest incidence of skin cancers with an incidence of 574.24 per million.

2. Excess Local Cold

In experimental animals, cancers have followed the application of carbon dioxide snow. This was attributed by Boyland (1952) to local cold. Skin cancers on the tips of the ears have followed frostbite and Arctic exposure.

3. X-rays and Ionizing Radiations

This is a well-recognized cause of skin cancer in x-ray and radium workers and in persons who have had radiotherapy. Cancers may occur in any occupations in which the worker is in contact with X-rays or radiations - e.g. radiologists, luminizers, dentists. X-ray burns are often followed by cancer at the site of the burn. The therapeutic uses of X-rays and radium have produced many skin cancers.

4. Sunlight and Ultra-violet Light.

This is often quoted as a cause of skin cancer amongst sailors, farmers and other workers who spend considerable time outdoors. Ramazzini noted the keratotic skin of fishermen, and Unna in 1894 was the first to call this condition precancerous and to trace the condition to the long exposure to sunlight. In order to assess the importance of sunlight as a cause of skin cancer, it is necessary to classify skin cancers into squamous

epitheliomata and basal cell cancers (rodent ulcers). Broders (1919) in a survey of 268 cases of basal cell cancers, found that 56% of the total of the male cases occurred in farmers; among the females, 43.3% were in farm workers. This high incidence in farmers and farm workers has been quoted in support of the sunlight aetiology theory (Mackee & Cipollaro (1937)). Broders concludes that "excessive exposure to sunlight as a cause of the neoplasm has not been borne out by the facts in our series of cases. It was noted that the hand (which is exposed to sunlight at least as much as any part of the body above the clavicles*) did not show lesions". It should here be pointed out that the hand is not, in fact as much exposed to sunlight as the head and neck - the hands are often shaded by the body, held in pockets, or covered by gloves.

In an analysis of cases of squamous cell epitheliomata, Broders (1921) found that 53.9% of all male cases was in farmers. The conclusion that the high incidence of total skin cancer in farmers is due to sunlight, while tempting, does not seem to take enough notice of other factors. The high incidence in farmers may be due to handling animals, (Henry(1950) shows an association between skin cancer and handling horses) or may be due to the handling of fertilizers containing arsenic (Currie 1947) or to other factors which are not known. The conclusion that the high incidence of squamous cell skin cancer in farmers is due entirely to sunlight is not justified by the known facts, although sunlight probably plays an important part.

Prosser White (1934) confirms that outdoor occupations have an excess of cancer of the skin when compared with indoor workers, and the probable cause of this difference is exposure to sunlight.

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* 96.28% of all basal cell cancers in Broders series were shown to be above the clavicles.

In the cancer morbidity surveys of ten United States cities, southern cities, where exposure to sunlight is more intense, had higher skin cancer rates (Haenszel,et al, 1956)

In a discussion of the incidence of surface cancers, that is, cancers of skin and lip, Peller (1948) showed that in the American Armed Forces there was a higher incidence of surface cancers in those who were southern born (below 40° lat.)

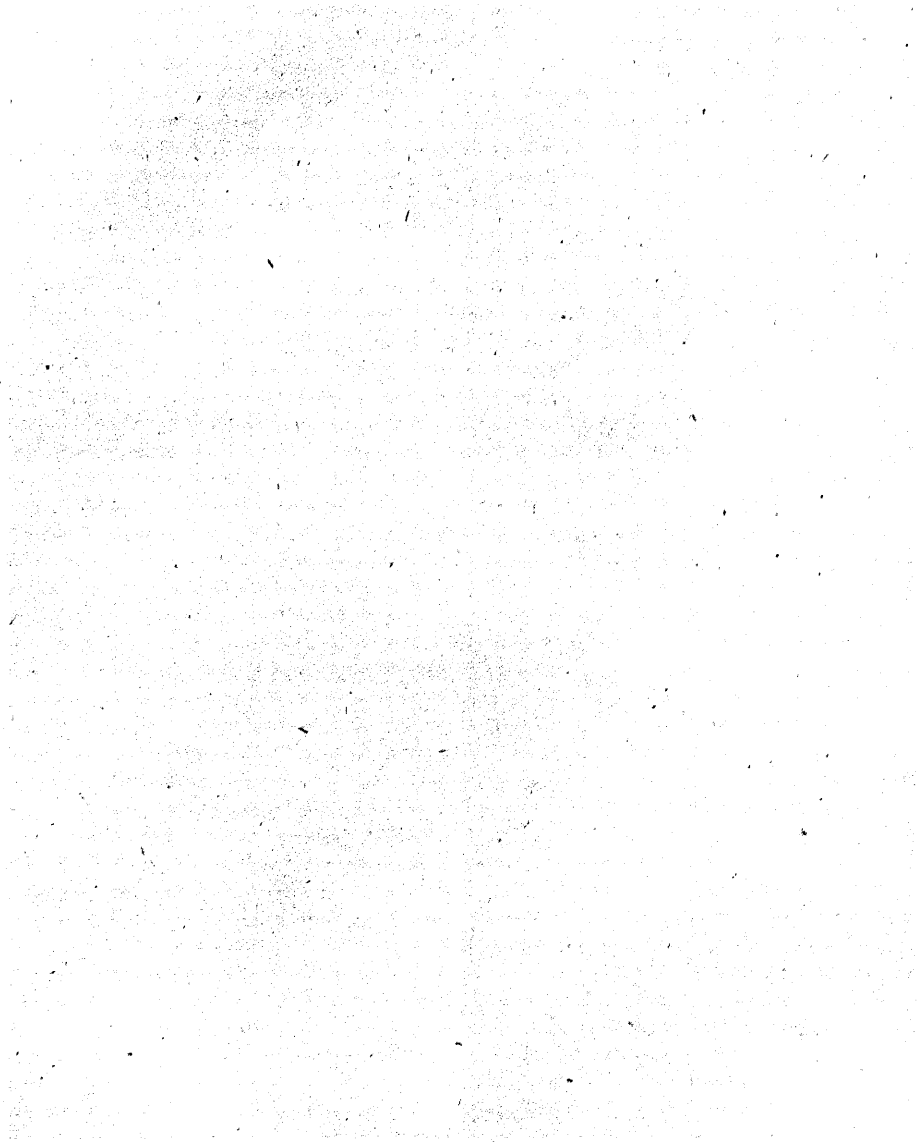
Age	Southern born	Northern born	All
16-34	53%	23%	39%
35-64	47%	29%	36%
All	50%	27%	37%

These men were mixed up in the Forces in a random way as far as their birthplace was concerned.

Peller concludes that "exposure to dermotropic agents in childhood is more effective in changing the distribution of cancer in a population than is exposure in later life". It is interesting to note in this regard that Potts noted cancer of the scrotum in 'climbing boys' aged 13-15. Blum (1940) in an extensive review of sunlight and its relation to cancer of the skin makes the following conclusion "Converging evidence from a number of sources indicates sunlight as an important aetiologic factor in cutaneous cancer of human beings. However, the evidence is tenuous in most instances. The clinical evidence alone is suggestive, but that from animal experiments is necessary to lend solidity to the concept. Caution is necessary, however, in carrying over the evidence from these experiments to the case of man ..... Much more exact data, both clinical and experimental, are required to place the concept on a thoroughly sound footing."

Experimental skin cancers in animals have been produced by exposure to ultra-violet light and it has been suggested by Hueper (1942) that this

ultraviolet light is partly the cause of solar carcinogenesis.



AETIOLOGY

II Personal Factors

1. Family history
2. Selection processes
3. Personal habits
4. Social class
5. History or presence of previous lesion or disease at site of cancer
6. Racial differences, including skin pigmentation
7. Localization of lesions
8. Sex incidence
9. Occupation
10. Environmental factors, except occupation

1. Family History

Broders (1919) in an investigation of 268 cases of basal cell carcinoma (rodent ulcer) found a family history of malignancy in 10.82% of the total. In males, there was a family history of malignancy in 10.3% of cases and in females in 11.85%. Sulzberger (1948) demonstrated familial and racial susceptibility of various animals to chemical carcinogens. Molesworth, quoted by Blum (1940) described a family of eight brothers, six of whom developed cancer of the face. They were all outdoor workers.

2. Selection processes

There are processes of selection in industry by which more susceptible, or less susceptible persons are employed in jobs which carry a risk of skin cancer.

Preplacement and periodical (and statutory) medical examinations of young persons and persons in dangerous trades, may serve to weed out persons with a high potential susceptibility.

Fisher (1953) working in the gas industry is of the opinion that there is a connection between the incidence of tar erythema ('the smarts') and subsequent carcinoma of the skin. Those persons who suffer readily from tar erythema are said to be more prone to subsequent cancer, and persons who suffer readily from tar erythema often remove themselves from such work (or are removed for medical reasons). If Fisher's hypothesis is correct, the resultant population in which cases of skin cancer develop is therefore one which is selected to have a lowered susceptibility to the disease.

3. Personal habits are of great aetiological importance. I have observed at the shale oil refinery at Pumpherston in Scotland the forearms and hands of two workers over the age of 60. Both of these men had extensive skin changes, which have been described under the name of 'shagreen skin'. They

had been employed on oil presses (wax being pressed out of the oil) in their youth for about 10-15 years, in company with many other men. The forearms and hands of all the workers on this process were extensively contaminated by the oil. Many of the workers at this job had to give up due to dermatitis, and a number of others had developed skin cancer. The two elderly workers who still remained at work in the refinery attributed their freedom from trouble and their continued work in the refinery to the fact that they had taken all the precautions available to them. These precautions consisted of a barrier cream (lanolin based) and thorough washing at the end of each work spell. These men were most emphatic that personal cleanliness was of the first importance and quoted to me examples amongst their workmates of men who had not taken full precautions or were notoriously dirty, and who subsequently had to stop work for one of the reasons outlined above. The observations of these men was confirmed to me by the refinery manager who had himself grown up with the industry and was over ten years older than the men in question. These two men were known to him as good workers who took care of themselves and who took an interest in their personal cleanliness.

Scott (1923), who spent his whole life until he died in 1956, in the Scottish shale oil industry, is of the opinion that while acute reactions to paraffin are not affected by attention to cleanliness, that chronic changes such as erythematous dermatitis (syn. 'shagreen skin') are lessened in incidence and severity. Sugiura et al (1956) quote some work as yet unpublished (by W.E. Smith & L. Orris) which shows that the development of tumours in mice, painted with a carcinogenic oil, can be greatly slowed by washing with soap and water after each application. Further delay or complete obviation can be attained by treating the skin with certain barrier

creams prior to each application of the oil, provided that washing is done within 3 hours after the oil is applied.

Ryle & Russell (1947) were able to show a statistical association between the Standardized Mortality Ratio (S.M.R.) from skin cancer and the relative cleanliness or dirtiness of certain occupations. While there is a social class fall in S.M.R. from Class I to Class V, their conclusion after examining the figures for wives, is that there is also an occupational factor in the causation of skin cancer and that the occupational factor is the more important of the two. This occupational factor may, however, be influenced by personal cleanliness, or the lack of cleanliness.

4. Social class

It has been shown by Ryle & Russell (1947), using figures published by the Registrar General, that there is a correlation between mortality from skin cancer and social status for males and females in the age group 20-65. The correlation is more marked in the case of wives - and "would seemingly rule out the possible influence of a purely occupational causation". In the case of the males, where the correlation was not so marked, occupational and environmental factors were thought to be involved. In order to try to disentangle these two factors, the workers were classified into those having clean and dirty jobs. Reference is made to this above under section 3 'Personal habits'.

It has also been shown by Stocks (1938) that cancer (all sites) shows a social gradient from Classes I and II up to Class V. The following table is reproduced from Stock's paper, and is based on figures from the Registrar Generals Decennial Supplement for the years 1922-1932.

Cancer (all sites). S.M.R. at ages 35-65.

Social Class	I & II	III	IV	V
Males	91	99	102	114
Married women	97	102	95	105

5. History or Presence of Previous Lesion or Disease at Site of Cancer.

In many cases of cutaneous cancer which have been reported, there is a history of previous disease or injury, or there may be present some disease or injury scar at the site of the lesion. Broders (1921) found in the case of squamous cell epithelioma that 51.17% were preceded by a "mole, wart, pimple, scab, ulcer, leukoplakia, crack, wen, blister or lump". A history of injury was present in 23.82% of these cases. In basal cell cancers Broders (1919) found that 37.1% were preceded by one of the lesions as listed above and by a history of injury in 9.3% of cases.

Taylor et al. (1941) found a "precancerous lesion" in 45% of their cases of epidermoid cancer of the extremities. With regard to predisposing factors, Smithers (1946) is of the opinion that "all primary skin tumours probably arise in tissue damaged by some kind of irritation". Amongst the irritants are the chemical and physical agents mentioned above and the pre-cancerous lesions which will be mentioned below, of which some may be related to occupation. The following list of previous lesions or disease associated with the skin cancer is taken from many sources, but owes much to the reviews of Willis (1950), Mackee & Cipollaro (1937), and to the monograph by Combes (1954).

(a) Cancer associated with scars. Henry (1950)and Mackee & Cipollaro (1937) call attention to the frequency with which burn scars are followed by skin cancer and quote the 2,000 cases reported by Neve (1923) of cancer due

to the carrying of portable fire baskets in Kashmir. There is some doubt whether these cancers should be included under the heading 'radiant heat' or 'scar'. Schreck (1941) in a review of cutaneous cancer showed that 18% of tumours of the scalp, trunk, legs and arms developed in scars resulting from injury, burns, lacerations, operations and ulceration, and that 2.8% of all the tumours occurred in scars. In contrast 0.7% (3 cases) of 443 tumours of other sites occurred in scars. In Broders (1921) series of epitheliomata, there was a history of burning in 24% of the cases. The origin of certain burns and scars may be occupational.

(b) Cancer associated with chronic ulcers and fistulae

Examples of this are:-

i) Cancer of varicose ulcers

ii) Cancer of other chronic ulcers, variously caused

iii) Cancer of osteomyelitis sinuses

iv) Cancer of other chronic sinuses, variously caused

It is probable that few of the above will be occupationally caused without the pre-existing disease being clearly shown to be occupational in origin.

(c) Cancer associated with skin abnormalities

1. Congenital skin abnormalities

i) Naevi

ii) Defects at muco-cutaneous junctions

iii) Defects at lines of skin fusion.

11. Other skin abnormalities

i) Cancer of sebaceous cysts

ii) Cancer of cutaneous horns

iii) Cancer of keratoses - a) senile keratoses

b) seborrhoeic keratoses

c) arsenical keratoses

iv) Cancer following cutaneous atrophy - of the type with glistening patches and keratoses ('shagreen skin'). The occupation of the person may suggest contact with a known carcinogen in such cases.

v) Cancer associated with papillomatosis.

(d) Cancer associated with skin diseases

i) Lupus vulgaris

ii) Lupus erythematosis

iii) Psoriasis

iv) Leukoplakia (luetic or non luetic in origin)

v) Syphilis

vi) Xeroderma pigmentosum. Sunlight exposure in persons suffering from this disease accelerates the existing tendency in the disease towards the production of epitheliomata. Most sufferers from this disease die at an early age due to the formation of skin cancer.

vii) Any chronic inflamatory dermatosis

viii) Neurofibromatosis (von Recklinghausen's disease)

ix) Leucoderma)
x) Melanoderma) or any combination of these three conditions
xi) Scleroderma)

It should be mentioned that many of the above skin diseases are or were treated by arsenic. It is not possible to separate in many cases the causative roles of the disease and the arsenic in the subsequent production of a skin cancer.

(e) Skin cancer at muco cutaneous areas associated with special disease of these areas.

i) Erythroplasia. This condition attacks orificial mucous membranes and is always followed by cancer.

ii) Leukoplakia vulvae and kraurosis may lead to cancer which involves the adjacent skin.

(f) Cancer associated with the excretion of carcinogenic substances by sebaceous glands, or in sweat.

This remains a theoretical possibility, in view of the difficulty of proof.

6. Racial differences, including skin pigmentation.

It is probable that the question of racial differences in the incidence of skin cancer is due in part to differences in the pigmentation of the skin. Combes (1954) is of the opinion that pigmentation seems to afford "some degree of protection against the carcinogenic effects of solar radiation, epitheliomata being eight times as common in blonds as brunets; and statistics show in those races with more highly pigmented skin a lower incidence of cutaneous cancer. Negroes rarely are afflicted with cutaneous cancer, and natives of the tropics enjoy similar benefits. The highest incidence is in the Scandinavians and Dutch; the Zulus having the lowest."

It is well known in experimental animals that certain strains develop cancers of a particular location with ease and that other strains are very resistant to the development of cancer. In man, Peller (1948) in U.S. showed that the ratio of deaths from cancer of the skin is

White men : Coloured men - 5.1 : 1

White women: Coloured women - 2.7 : 1

Hamilton & Hardy (1949) quote statistics of the Metropolitan Life Insurance

Company which show that the standardized death rate from skin cancer in white males is about three and a half times that for coloured males.

Dorn (1954) in describing the results of a two year survey by the National Institute of Cancer (of U.S.) showed that negroes had a low incidence of skin cancer and a high incidence of genital cancer compares with the white population. The racial difference in the incidence of skin cancer was greatest for the exposed areas; in fact, the risk of skin cancer in these parts is fifteen times as great in whites as in the coloured population.

Ward and Gunther (1954), working in Australia concluded that racial differences existed in the incidence of skin cancer and that persons of British descent (i.e. most Australians) were more susceptible to skin cancer than persons of Scandinavian or N. German ancestry. They quote the average age of skin cancer patients

a) Born in Australia - 61

b) Born elsewhere - 71

In the latter category, the average length of stay in Australia was 44 years. The effects of a higher incidence of sunlight at an earlier age are not, however, taken into account by Ward & Gunther and the remarks above in the section on sunlight, where it has been shown that stimulation by sunlight at an early age is more effective in producing skin cancers, may be sufficient to explain the difference in incidence in the two groups without bringing racial factors into the discussion.

7. Location of lesions

Certain sites in the body show a tendency to develop cancer, although the cancer producing stimulus may be applied generally - e.g. the scrotum is particularly affected in chimney sweepers whose whole skin may be covered with soot, and in mule spinners whose thighs and lower abdomen

may be equally sprayed by the spindle oil. In animals, Sulzberger (1948) has shown that although a mouse's whole back may be evenly tarred, that only certain spots will develop cancers.

The higher incidence of scrotal neoplasms is generally explained in terms of the scrotal rugae. This leads to less efficient cleansing and more prolonged contact of the carcinogen with the skin. In the case of the mouse's backs, no explanation has been offered for this observation.

Pullinger (1945) was able to localize tumours by wounding.

Kennaway (1925) in a discussion of the Anatomic Distribution of Occupational Cancers, shows that soot cancers tend to be localized in the scrotum, that pitch cancers tend to occur mainly in the head and neck and especially on the cheek, lip and eyelid. For a farther discussion of the distribution of occupational cancer, the reader is referred to Part III of this work, under 'Diagnosis of Occupational Skin Cancer', Section vii, site of the cancer.

8. Sex incidence

In his review of squamous cell epithelioma of the skin, Broders (1921) showed that the incidence ratio of male : female was 4 : 1, and in the case of basal cell cancer (Broders 1919) was 1.6 : 1. Mackee & Cipollaro (1937) found that "only about 30% of all cutaneous cancers occur in the female".

In a review of epidermoid cancer of the extremities, Taylor et al. (1941) found a ratio of 1.96 male : 1 female. The Comparative Mortality Index for skin cancer is falling at very nearly the same rate in males as in females (vide Annual Report of the Ministry of Health 1952) 1933 - 1.10; 1938 - 1.00, 1952 - 0.60 - all malignant neoplasms show a rise in males 1952 - 1.20, and a slight fall in females 1952 - 0.90.

Somerford (1930) in a study of 57 cases of squamous cell cancers found more male than female cases in the proportion 3 : 2.

9. Occupation

From the time of Bernandini Ramazzini's work De Morbis Artificum which was published in 1700, the effect of occupation on health has been increasingly studied and reference has already been made to the first description of occupational cutaneous cancer by Percival Pott in 1775. It may appear obvious, but is perhaps worth stating that the effect of occupation is to bring the person into constant contact with a particular type of environment. This environment may be peculiar to one sort of work or may be shared with other occupations. The interaction between the individual and the environment will depend on the nature of the individual and the character of the environment, and in certain circumstances may contribute to the production of cutaneous cancer. The occurrence of skin cancer in an individual may in certain circumstances suggest that there are environmental noxa which bear a causal relationship to the cancer production. In this way, it may be possible to proceed from the individual - or from a number of individuals - to the environment and to identify possible carcinogenic factors. Many environmental occupational factors which can cause disease have been identified in this way, but it is possible that more may be discovered by trying to assess in detail the environment of individuals who are found to be suffering from primary skin cancers of the epidermoid type.

Alternatively, more occupations may be found in which there is a high incidence of skin cancer arising out of already known cancer producing substances.

The method of study adopted by Henry (1947 and 1950) in his authoritative work on the subject of cutaneous cancers, has been to work

backwards from death certificates and from cases of skin cancer which were notified to H.M. Chief Inspector of Factories, to occupation, i.e. all persons whose death has been due to skin cancer or are notified are then classified with respect to occupation. The conclusions from this work have shown a high incidence of cancer in particular occupations and low incidences in others, with many intermediate grades. However, there is one major disadvantage in the death certificate method of checking occupations - the patient is dead and cannot give details. This may, in some cases lead to occupational categories being allotted wrongly - particularly in the 'end occupation' types of work, such as watchman. Henry himself is careful to point out this limitation, and attention is here drawn to it in order to point out that steps have been taken in this survey to try to eliminate such errors by listing, for each person their exact work and the duration for which they did any particular job. This full occupational history is taken so that the significance of each part of the individuals occupation at different times in his life is taken into account in arriving at a final 'loading' of occupation with relation to skin cancer.

It has been demonstrated by Henry (1946, 1947, 1950) and by Cruikshank & Gourevitch (1952) that occupation is a major factor affecting an individual's likelihood to develop skin cancer.

Dorn (1954) in a two year survey of all cancers in a population of nearly 15 million, living in urban areas in U.S.A., found a total of 46,390 new cancers. The incidence of skin cancer was 46% greater in males than in females when the exposed areas were considered separately, but for the covered parts of the skin it was the same in both sexes. This would suggest that the higher male incidence may be due to environmental factors, probably occupational, rather than to some sex difference.

Somerford (1930) in a statistical note on 57 cases of squamous cell cancers, 14 of which arose out of pre-existing skin disease (11 of these were lupus vulgaris, 3 lupus erythematosus and all 14 had been treated by x-rays), concluded, in view of the site incidence (40 were on the face and on the neck, 3 on the limbs, 1 on the body and 6 on the scrotum) against occupation as a cause, "since the face is the part of the body least likely to be brought into contact with irritating substances used in any occupation".

As there is no means of identifying the 14 cases of pre-existing skin disease, which were all treated by x-rays (a known carcinogen) it is not possible to separate cases by areas. However, out of 57 cases, this 14 could reasonably be deducted, thus leaving 43 cases in which occupation may be a factor. It is also probable that the cases of scrotal cancer were not due to x-ray treatment of lupus vulgaris or lupus erythematosus.

The scrotum is a main site of occupational cancer, and in my opinion these six cases are likely to have had an occupational aetiology (see under diagnosis of occupational skin cancer). Occupations were classed according to present occupation only, but five of these men had previously worked in a mill. (? the scrotal cancer cases), and 13 had handled tar or mineral oil.

The conclusions by Somerford with regard to occupation being an unlikely cause of at least some of the cancers, seems therefore to be against some of the facts in his incomplete and to my mind inconclusive investigation. "Of the four patients who had the tumour on the arm, three were tar workers and the other a mulespinner". This, to me, seems clearly to suggest occupation as a cause - both by site of the cancer and by the nature of the substance in contact with the skin.

10. Environmental Factors, except occupation.

While occupational factors in adult life influence largely the type of environment, there is a period prior to adult life in which the home circumstances figure largely in determining the type of environment - the home and housing environment. Henry (1950) in his monograph on 'Cutaneous Cancer in Relation to Occupation' has this to say about hobbies - "Lastly, no searcher after the truth should omit enquiries as to hobbies in addition to occupation, as in the case of a director of a railway, who died of a carcinoma of the hand which, I was informed, he himself considered was due to manipulation of tarred ropes on his luxurious yacht."

Such factors in childhood as general hygiene, diet, the average cleanliness (or dirtiness) at which the skin was maintained, and the sort of housing conditions can easily lead to conditions which appear or persist in adult life. These factors may tend to influence skin cancers - particularly such things as the total exposure to sunlight (both duration and intensity), the frequency of washing (which is often determined to some extent by the available facilities) and the type of skin cleanser used.

III The Mechanism of Cancer Production

1. The Development of Skin Cancer.
2. Cocarcinogenesis
3. Time Lag.

Appendix. List of factors which can cause abnormal growth and development.

1. The Development of Skin Cancer.

It is of importance with regard to the mechanism of cancer production to ascertain how the carcinogenic stimuli act and to trace the biological changes which result thus leading to the final neoplastic transformation. Willis (1953) says of the mode of origin of skin cancer in terms of cellular pathology - "It is not denied that an established tumour grows in bulk by cell proliferation in excess of that of the normal epidermis. What is to be insisted on, however, is that a skin cancer in its early formative stage arises more by a general transformation of pre-existing epidermis than by cellular multiplication, and that only after the formative field has all suffered neoplastic change does the tumour grow solely by multiplication. The two processes, neoplastic transformation and proliferation, overlap, the former predominates during the early genesis of the tumour, the latter often being initially negligible but gradually taking an increasing, and finally exclusive, part in the growth of the tumour".

Haddow (1947) in a review of the mode of action of carcinogens, shows that most carcinogens are or can be growth inhibitors under certain circumstances, and quotes some of his earlier work, in which he showed that the development of cancers might follow a long period of growth repression "... it therefore seems that when the growth of a potentially variable organism is continuously inhibited by a process which allows a sufficient proportion of the affected cells to survive, a relatively small number may undergo an irreversible change in their metabolic properties in virtue of which they are then able to achieve active multiplication in an environment which makes this difficult, or even impossible, for their parent cell."

This general principle was then applied to carcinogenic stimuli "... there seems little doubt of a substantial correlation between

carcinogenicity and growth-inhibitory power, and it therefore seemed a real possibility, as in the case of x-rays and radium, that the mode of action of chemical carcinogens might well be indirect, and that they could operate by retardation of the growth of normal cells, the latter eventually reacting to give a new race of cells with an increased rate of fission. While the correlation on which this view is based seems sufficiently strong to justify it, undoubted exceptions occur which, if they are not enough to invalidate the hypothesis as a whole, indicate that we should regard it as a general approximation. Additional confidence in this view was, however, given by the discovery first of all that various derivatives of 4-aminostilbene possess such inhibitory properties par excellence, and only later that these compounds are, in fact, endowed with carcinogenic properties of an exceptionally interesting kind - an association which would seem to be more than one of chance alone."

The importance of the above is that a hint is given of the <u>origin</u> of cancer cells - i.e. as an adaptation process of normal cells to conditions of impaired growth.

In a recent article, Smithers (1956), supports the view that interference with normal growth may lead to cancer. "The causes of cancer appear as any of those many conditions which lead to the physiological isolation of cells from their fellows in any complicated organism. These multiple causes are seen to be in two main groups: those raising cell activity above that of its control and those lowering the controls. The first group contains most of the irritant, inciting, carcinogenic factors, all those injuries which demand repeated attempts at regeneration, recurrent local hormone stimulation, and any of the intracellular changes which may increase cellular growth potential. The second contains the poorly understood process of ageing,

those nervous and metabolic gradients which largely determine and maintain our growth and form, perhaps some of the cancer-promoting agents which may affect these local control mechanisms, and the general hormone system of diffusable control of homologous tissues and of tissues related in some common function throughout the body."

Sulzberger (1945) points out that many chemical carcinogens which act on the skin are also producers of allergic eczematous hypersensitivity. This resemblance may be due to the growth inhibition properties as pointed out by Haddow, or may be due to other factors. There does however appear to be, in the opinion of Sulzberger, many resemblances between the basic processes of carcinogenesis and the production of allergy.

Schrödinger (1944) in a short book devoted to quantum theory in relation to biology and genetics, suggested that mutations may be due to quantum jumps in the gene molecule. The high stability of the mutation in subsequent transmission or of the cancer cell in producing only cancer cells suggests that when the change has been established that there is no longer any need for the continued presence of the agent which produced the change. As in the case of mutations, so in the case of cancer cells it may be a change in energy level which produces the change from normal to cancer cell. The following figure (after Schrödinger) shows the concept in graphic form.

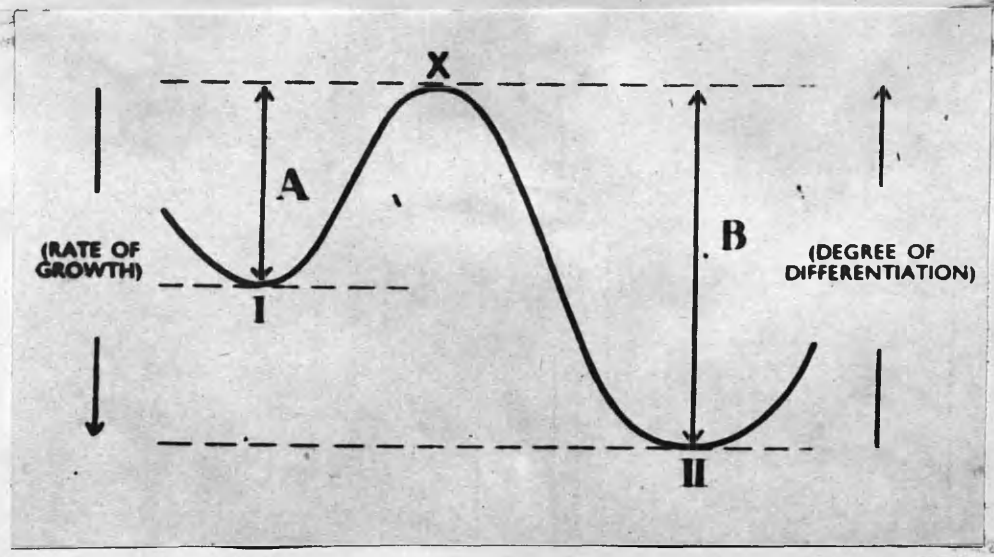


Fig. 1
Probable energy-barrier (X) in the transition from the normal to the malignant state. A = Minimum energy required to effect the change I (normal) II (malignant).

Haddow (1947) in a review of the mode of action of chemical carcinogens says of this theory "An interpretation along these lines (change in energy level) has almost certainly a close connection with other features in the mode of action of carcinogens: for instance, recent work on the metabolism of 3,4-benzpyrene hints that it is not the hydrocarbon itself, or even one of its metabolites, which is the proximate carcinogenic agent, but rather the energy released during the transformation from one metabolite to another. Here, too, may possibly lie the true significance of the allegedly characteristic electronic properties of the carcinogenic molecule. Finally, it may provide a link between the carcinogenic action of x-rays, gamma rays, ultra-violet radiation and chemical compounds, in that all these agents may be sources or carriers of energy in such a form as can readily interfere with the normal growth of the cell."

Peacock (1954) in a discussion of carcinogenesis, concludes that "for an effect to be produced, some work must be done, and whatever the

mechanism involved, there must be some transfer of energy between the carcinogenic molecule and the cell that is in the course of being converted from a normal to a malignant cell. The chemical and physical carcinogens show this in common, and although they initiate the process they certainly cannot be carried along from one cancer cell to the next in series."

The maintenance of the characteristics of the cancer cell is probably due to mutation - and most carcinogenic agents are known to be mutagenic agents, as tested on simpler organisms.

In terms of cell physiology, Warburg (1956) believes that cancer cells arise from normal cells by irreversible damage to respiration. This damage to cell respiration may be produced by a variety of agents: oxygen deprivation, cell respiratory poisons and damage to the mitochondria (which are believed to control cell respiration), by x-rays or carcinogenic hydrocarbons. Once the damage to normal cell respiration has been done, Warburg believes that it is only a matter of time until cell respiration turns from aerobic respiration to glycolysis. "In the struggle for existence by injured cells, some die for lack of energy, while others replace the lost energy of respiration by glycolysis. Owing to the morphological inferiority of the energy of glycolysis, the highly differentiated cells are transformed into undifferentiated cells of uncontrolled growth."

It is possible that the above theory, which has a strong foundation in cell physiology may knit together some of the unexplained ends of how different carcinogens act, and Haddow's theory of interference with normal growth may in fact be interference with normal respiration.

2. Cocarcinogenesis

The acceptance of the experimental findings and the theory of cocarcinogens leads to implications of the greatest moment with regard to

prevention of "Industrially" caused skin neoplasms. It has been shown that one application of a carcinogen (or initiator) is sufficient to produce a skin cancer, provided that a non-carcinogenic stimulus, the cocarcinogen (or promoter) is afterwards applied for a sufficient period. The subsequent tumour incidence is also dependant on the concentration of the carcinogen. The following quotations from original work by Berenblum & Schreck (1947 & 1949) outline the concepts and experimental findings regarding cocarcinogenesis. "The initial change is evidently a specific process (since it is induced by carcinogens but not by croton oil or other irritants); it is also an irreversible process (since its effect can be quantitatively demonstrated after as long an interval as 20 weeks); and it is a very rapid process - possibly even an instantaneous reaction (since a single application of a carcinogen is sufficient to initiate the process in a large proportion of the treated animals). In contract to this, the process involved in the subsequent appearance of the visible wart has a very different mechanism: it is not an instantaneous process (since repeated treatment with the croton oil, or any alternative agent, is required to bring it about); it is not specific (since croton oil, and to a lesser degree, other irritants and wound healing, can produce the effect) and it is not irreversible, at least not in its early developmental stages."

"The latent period is dependent on the efficacy of the promoting action. The initiating process is a sudden and irreversible change in a small minority of cells in the treated area - i.e. the production of 'latent tumour cells'. The concentration of the single application of the carcinogen was the determining factor in the number of tumours induced. Using 9,10-dimethyl 1,2-benzanthracene in liquid paraffin, and expressing concentration ratios 1 : 3 : 9 : 27, tumour yields (in mice) were 1 : 6.6 : 12.4 : 26.5.

The average latent periods of these groups were 14.4, 12.1, 10.6 and 11.8 weeks. Not only was there an increase in tumour bearing animals with increase in concentration of the initiator, but the number of tumours in each tumour bearing animal increased from an average of 1.1 in the lowest concentration to 319 in the highest."

In order to assess the potency of any carcinogen, two factors must be considered - the initiating action and the promoting action. The minimal dose response is a measure of the initiating action and the average latent period is a measure of the promoting action. Any one substance may act both as an initiator and as a promoter - and its action can be separated in the above way into the two components.

Pullinger (1945) was able to increase tumour incidence three times by chronic irritation - i.e. a promoting action.

The importance of the conclusion that a single application of a carcinogen is all that is required to produce a subsequent cancer, provided that a non specific stimulus is subsequently applied need hardly be stressed. Industrial cancer prevention programmes have been designed mainly along the lines of prevention of prolonged contact, or have been designed to minimize contact with the substance thought to be carcinogenic - i.e. they have been directed against the promoting (cocarcinogenic) action of the carcinogen. However, this is bound to fail in its objective of preventing all cancers as long as any single contact with a carcinogen is allowed - non specific stimuli only being required subsequently in order to produce tumours. The absolute avoidance of contact with any substance which is known to be carcinogenic may seem in practice a Utopian concept - but short of absolute avoidance of contact, it seems likely that industrially caused cancers will continue to arise. All efforts should therefore be made to avoid absolutely

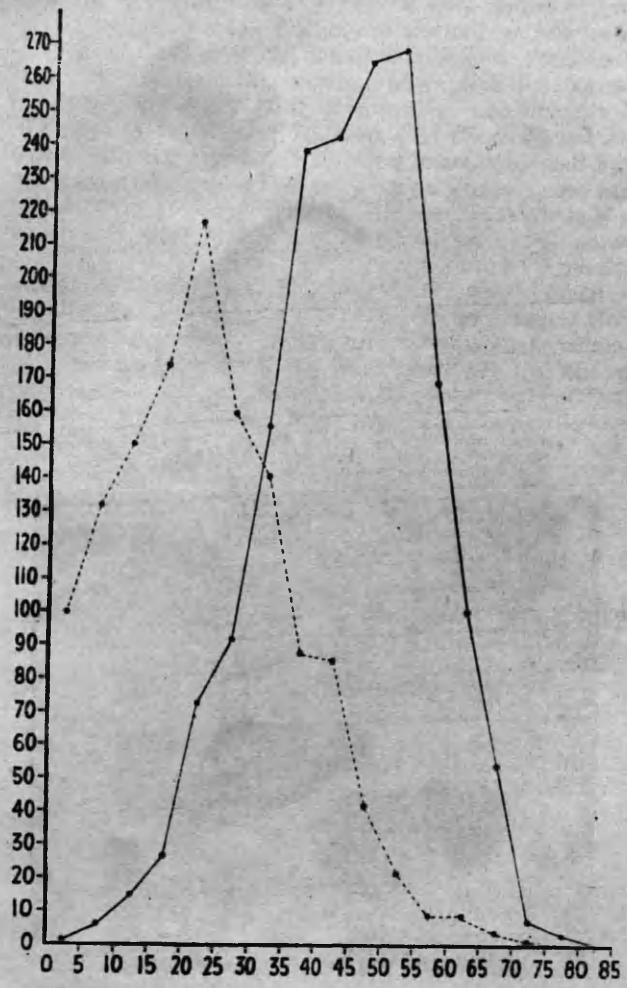
contact with offending substances, and not as in the past, towards minimizing contact.

A farther difficulty in this connection is the sorting out of stimuli into initiators - exposure to which must be avoided absolutely, and promoters - exposure to which should be avoided, but may be minimized. The precancerous lesions which are listed above will probably fall mainly in the class of promoters - but it would be unwise to suggest that in all cases there was no initiating action. Skin cleanliness, washing habits and social class, which are listed above as factors in the field of the person relating to aetiology of skin cancer are probably measures of promoting rather than initiating action.

The field of cancer prevention in industry is therefore seen to be much wider than attention directed to the carcinogenic substance, unless contact with this substance is avoided absolutely. Failing absolute avoidance, no source of possible irritation must be overlooked. Efforts must therefore be directed to the cutting down of non-specific irritation.

The graph below which is reproduced from Henry's review of cutaneous cancer in industry (Henry 1947) shows that pitch, tar and tarry products have a better promoting action than shale and mineral oils, in view of the shorter time lag between exposure and tumour production.

GRAPH 2. TIME ELAPSING FROM ONSET OF EMPLOYMENT TO MANIFESTATION OF A CUTANEOUS PAPILLOMA OR EPITHELIOMA IN 1,335 PERSONS IN CONTACT WITH PITCH, TAR, OR TAR-PRODUCTS COMPARED WITH 1,719 IN CONTACT WITH SHALE OIL, OR MINERAL OIL



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Henry estimates the average latent period for shale and mineral oil to be 50 - 60 years, and for pitch and tar to be 25 years.

There is one reference to a carcinoma which appeared just inside the left vestibule of the nose (it is not stated whether on skin or mucous membrane, or at the junction) following a single application of a refrigerated ammonia-oil mixture. This case has been most carefully documented and reported and the appearance of the epithelioma (confirmed by biopsy) was within six months of application of an ammonia-oil mixture. The opinion of the authors (Shimkin M.B., et al (1954)) is that there was a causal connection between the two events. Another case where there is a possible immediate connection between recent injury* and the appearance of an epithelioma is cited by Kotin & Kohler (1953). A petroleum worker cut the dorsum of his hand and sustained a severe blow on the slowly healing wound. One month later an epithelioma appeared at the site of injury. In both of the above cases, the authors ascribe the role of 'promoter' (cocarcinogen) to the recent event - i.e. to the splash with refrigerated ammonia-oil mixture and to the trauma.

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* See Part II, Cases M23, M24 and F4, for farther examples of recent injury, followed by epitheliomata. The time interval in these cases between the onset of the trauma and the appearance of the tumour was <u>in each case</u> between 3 and 6 weeks after injury. This correlates well with the time in Kotin & Kohler's case.

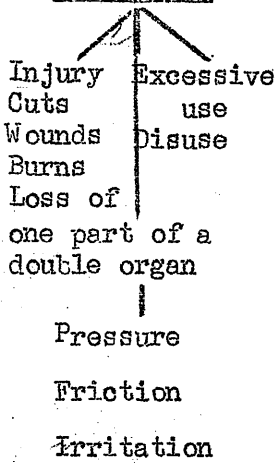
3. Time Lag

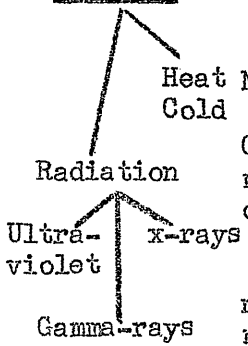
That there is a certain irreducible minimum time from the application of the carcinogen until the time of the appearance of tumours, no matter how strong the solution, how susceptible the animal and so on, has been shown by Sulzberger (1948). Using a single carcinogen without any other kind of stimulation, carcinogenic or non-carcinogenic, it is possible that the time lag is a measure of the promoting action of that substance - the initiating action taking place in a very short time following the first application. It is well known that different substances produce different time-lags.

Appendix

The following scheme, after Bergel (1954) shows the possible primary causative agents and factors of abnormal growth and development. In carcinogenesis a few of these factors are initiators - and many more are likely to be promoters. The importance of this list lies in the fact (which is referred to in detail above) that there is a substantial correlation between carcinogenicity and growth inhibitory power. Many of the agents which are in the list below are growth inhibitors. Some others are growth promoters, deficiency of which leads to failure of growth. This list should be compared with the next list of carcinogens.

Possible Primary Causative Agents and Factors of Abnormal Growth and Development





Chemical

Miscellaneous substances
Cytotoxic and mutagenic compounds (for example, nitrogen mustards and others)
Carcinogenic compounds
Antibiotics

Biochemical

Hormone or enzyme-imbalance (thyroxine, sex-hormones, corticoids)
Vitamin deficiencies (A and B vitamins or co-enzyme deficiencies)
Starvation
Lack or excess of oxygen

Physio-logical

Pregnancy
Exercise

Genetical

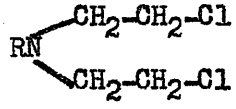
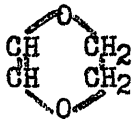
Genes carrying abnormal characters.
Loss of genes causing abnormal cellular anabolism or catabolism or abnormal re-duplication

Viral-Parasitical

Rubella, etc.
Worms, etc.

Boyland (1952) in a review of the mechanism of carcinogenesis prepared a list of known and proved carcinogenic agents, which is reproduced below. This list is especially valuable as it introduces order and system into the chemical carcinogens by grouping them. This list should be compared with that above.

Carcinogenic Agents:-

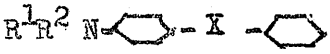
1. Physical		Cellophane[x]
		Local Cold (CO_2 snow)
		X-Rays & Ionizing radiations
2. Inorganic		Nickel
		Na_2 H As O_3
		Be Cl_2
		Zn Cl_2
3. Aliphatic	(a)	Nitrogen Mustards
		
	(b)	Diepoxides
		(Butadiene diepoxide) 
	(c)	Ethylene imines
	(d)	Dimesyl Glycols
	(e)	Urethane
4. Aromatic	(a)	Hydrocarbons
	(b)	Heterocyclics
	(c)	Amines

[x] Many plastic films such as cellophane, polyethylene and others produce malignant tumours when implanted under the skin of rats. If small holes are punched in the films, no tumours result. The significance of these observations is unknown.

Carcinogenic aromatic amines

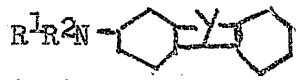
I 

β Naphthylamine

II 

Active where R^1 or $R^2 = CH_3$

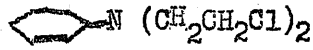
and X is -N=N- as in aminoazobenzene
X is -CH=CH- as in aminostilbene
or X is a single bond as in amino diphenyl

III 

Active when Y is absent as in aminodiphenyl

Active where Y is $-CH_2-$ as in aminofluorene
" " " " -O- " " aminodibenzfurane
" " " " -S- " " aminodibenzthiophene
" " " " -SO- " " aminodibenzthiophene oxide

IV Aromatic Bis (B - Halogenoethyl) amines

e.g. 

For a full list of all compounds which have been tested for carcinogenic activity, the reader should consult the valuable synopsis prepared by Hartwell, J.L. (1951).

PART II.

PRESENT INVESTIGATION

Selection of cases

Case Histories

PART II

The case histories and tables constructed therefrom of patients (fulfilling the necessary criteria) who have squamous cancer of the skin.

PART II

Selection of Cases

It has been shown by Henry (1950), Scott (1923), and by Combes (1954) that cases of skin cancer in which there is a known occupational factor in the aetiology, have fallen almost exclusively into the class of a squamous cell epithelioma and not rodent ulcer (basal cell cancer).

For this reason, the present investigation has been confined to squamous cell cancers.

With the kind permission and co-operation of Dr.A.G.C.Taylor, Dr.T.K.Morgan and members of their staff, in the Radiotherapy Department of the Royal South Hants Hospital, I have been informed of all cases of squamous epithelioma of the skin which come to their notice, and are subject to the following conditions:-

1. The diagnosis of squamous epithelioma is based upon the microscopic appearances of the lesion, either following biopsy or in a surgically excised lesion. A clinical diagnosis is not accepted.
2. The tumour is a primary one of the skin; it is not a secondary deposit from elsewhere.
3. The patient lives within a radius of approximately 30 miles from Southampton and on the mainland. (This excludes the Isle of Wight. The amount of time which would have to be spent in travelling in order to see cases outside of the above area excluded such cases).
4. Cancers of areas which are not cutaneous but muco-cutaneous such as the lip and vulva are excluded - i.e. all orificial cancers are excluded.
5. All cases of skin cancer known to have been produced by radiotherapy are excluded.

The distribution of such cancers will be dependant on the area which has been irradiated, and this area in turn will depend on the location of the disease for which the radiotherapy is being given. No element of uncertainty exists in the aetiology of such cases and the localization of the cancer is fortuitous and will probably not be related to environmental factors.

Case Histories

The findings are presented in each case under the following headings:-

General

Housing

Occupation (with table)

Family history

History of lesion

Microscopic appearances

Condition of skin

Discussion

Male. Date of Birth 30.5.83. Age at lesion 65 M10.

General

This patient has been a sufferer from eczema since 1940 - and his lesion appeared in 1947. He is a rather tense type, who probably worries a lot about his skin but tries hard to conceal his worry.

Housing

The patient has always lived in reasonable houses with no overcrowding. Sanitation was indoors, hot water was easily provided and a bath was provided. He has lived for equal periods in town, suburb and country - as a child in Winchester.

Occupation

All his life he has worked for W.H. Smith in the station news and bookstalls. He started as a delivery boy and soon became a counter server in the stall. He rose gradually, serving in larger establishments until he became manager of the bookstalls in Southampton Central Station. His work was exposed to cold but not to rain except in the very early years as a deliverer of papers. The work was reasonably clean - he had to handle bundles of newspapers, etc. and coinage - but apart from this, and the general dust of a railway station, he was not exposed to any particular hazard.

Family History

There is no family history of cancer or of skin trouble. His mother suffered from asthma, and this may account in part for the chronic eczema from which the patient suffers.

History of lesion

A small spot appeared in the left cheek, high up, under the eye, not in the eyelid, in 1947. It had been present for about two months and

was noted to have a warty top. At this time, he was attending the Skin Department of a local hospital on account of eczema and he showed this condition to the doctor.

Since the age of 21, the patient has worn spectacles. For many years, these were pince-nez type and these spectacles, he thinks, sat on the cheek at the point of the lesion. His present spectacles, which he has had for ten years approximately prior to the appearance of the lesion, do not sit down on this part of the cheek.

Microscopic appearances (following excision)

The appearances are those of a squamous cancer which is highly differentiated and does not show much infiltration.

Condition of skin

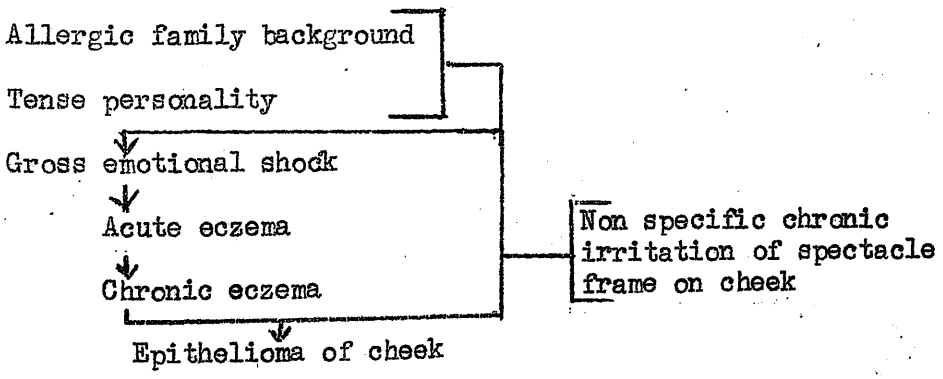
Up until 1940, the patient had a perfectly normal skin. At this time, Southampton Central Station was badly bombed and nothing was left of the three bookstalls of which the patient was then manager. One week later, the first sign of the chronic eczema from which the patient has suffered since had appeared. At this time, he developed lesions in the perianal region and in the groin and on the abdomen under a truss which he wore to control a hernia. The condition at this time became so bad that he had to give up work and enter hospital for inpatient treatment. The very sudden loss of these bookstalls must have represented a serious threat to the patient's livelihood - and the emotional significance of this need hardly be stressed. The very rapid onset of eczema which followed would seem to be connected with the emotional strain referred to above. The hospital record at this time is, unfortunately, not available - but the diagnosis in 1944 is "seborrhoeic eczema".

Discussion

This case would suggest that the patient's cancer was secondary to the chronic eczema from which he suffered. At no time in the treatment of the eczema was tar used, nor indeed any known carcinogen. Treatment was for the most part with bland lotions and emollients.

As a localizing factor, the wearing of spectacles probably had some bearing. Case No. F8 also showed a cancer at the point of contact of spectacle frames - i.e. localization at a source of chronic (non specific) irritation.

A schematic sequence of events with regard to the aetiology of this case would be as follows:-



OCCUPATION

M10

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin.
Paper delivery boy Newspaper and book-seller. News stand Supervisor Manager of several news stands	53 yrs.	Worked for W.H. Smith & Sons	Paper

Male. Date of Birth 18.9.86. Age at lesion 61 M11

General

The patient is the son of a sea captain and in his early years lived in seaport towns. When he was four and until he left school, he spent all of his holidays at sea with his father's boat, which carried dry cargo around the coast of England and occasionally went to the Mediterranean. His time on the ships was spent mainly on deck. At the age of 20, the patient went to U.S.A. and spent twelve years there, mainly in California and Nevada. (Aged 20-32). The climate of these two States tends to be very hot.

On his return to the U.K. (aged 32) he has lived in a country village in the New Forest.

Housing

Up till the age of 15, the patient lived in various houses in seaport towns. There was no overcrowding in any of the houses. Sanitation was in all cases outdoors, there was no bath in any of the houses; hot water was not easily provided, but water was piped to each house. On board ship, where the patient spent his holidays, the washing facilities were poor.

It will therefore be seen that up to this age, the environmental conditions were against ease of maintaining personal cleanliness. However, the patient's father taught him that "cleanliness was next to Godliness" and enforced this. The patients personal cleanliness when seen seemed to show that this lesson had been learned. Fastidious personal cleanliness did seem to be a habit with the patient, as borne out by his present appearance.

Occupation

This patient has been a woodworker all his life. In his early years as an apprentice shipwright and as a coffin maker he had contact with

pitch, though the contact was not prolonged. He estimates that 50% of his working life has been spent outdoors.

His hobby is gardening and he occasionally does some woodwork as a hobby.

Family History

There is no family history of cancer or of skin disease.

History of Lesion

In the spring of 1940 (when the patient was aged 54), a pimple or boil was noted at the site of the lesion. This 'boil' was occasionally cut while shaving and bled on these occasions. The condition did not alter much in size, but in 1947 (patient aged 61), the lesion commenced weeping. On 3.11.47, his hospital records describe an ulcer, with raised edges on the left side of the neck 3.9 x 2.4 cms.

Microscopic appearances

"The structure is chiefly that of a rodent ulcer, but there are areas of cellular irregularity suggesting more malignancy - i.e. low grade carcinoma."

Condition of Skin

This was seen in 1955 (aged 69). His skin is, for the most part, perfectly normal for his age. The exposed areas are suntanned; elasticity is good, and thickness is normal. His unexposed skin is fair and is neither oily nor dry. On the forearms, a few telangiectases were seen. He has less hair on his skin than average. Around the tips of the ears slight degenerative changes were noted - some thinning and glazing with small atrophic white patches. There is no history of other skin disease.

M11

Discussion

The patient seems to have lead a normal sort of life as a wood-worker. The main points of interest with regard to his cancer are:-

i) Although his early environment was relatively poor with regard to cleanliness, he seems to have maintained himself in a good state of cleanliness.

ii) There was a definite exposure to pitch at a young age (14-16) and for some 5 years, mainly to vapours, while coffin making.

iii) He has worked in very sunny areas (California & Nevada) when aged 20-32

iv) He has worked an estimated 50% of his life outdoors.

v) Exposure to known carcinogens has been minimal apart from pitch and sunlight. Wood was the only material handled for prolonged periods.

OCCUPATION

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Apprentice Shipwright	2	Sawing wood and general woodwork. Occasional caulking of ships (1/12 per yr on this).	Pitch was used (hot) for caulking Wood, nails, etc.
Woodworker	5	Making furniture, coffins, etc.	Wood Animal glue Pitch - this was used to line the joints of the coffins though the patient did not do much of this work himself. He did however smell the fumes from the hot pitch for a good part of his working day.
Woodworker	1	Making furniture, boxes, and doing house carpentry.	Wood, etc.
Woodworker and Designer	7	Doing occasional work with tools, mainly employed on 'laying out'.	Wood, etc.
Teaching woodwork	4	-	Wood, etc.
Propeller maker	4	Making wooden propellers for seaplanes.	
Woodworking	36	Carpentry, house joinery and furniture-making.	Wood, etc. Occasionally putty and glue

M12

Male. Date of Birth 30.3.97. Age at lesion 49.

General

The patient when seen in 1955 (aged 58) had suffered from four lesions, one definitely malignant, three clinically malignant, which are given below in synoptic form:-

1. Carcinoma of lip. 22.9.44. first attended hospital. Six months history of ulcer of lower lip. Hard flat tumour of lower lip at junction of left and middle thirds. Treated by radiotherapy. No biopsy.

2. Epithelioma of right hand. 6.11.47 first noted in hospital record. Lesion first noted one year previously. Nodule over the middle metacarpal. Few small pectoral glands in axilla. Biopsy of hand lesion "This must be considered an early squamous carcinoma. The cells are too irregular for a benign tumour, though for the most part the basement membrane is intact and no infiltration is seen." A subsequent dissection of the axilla (Aug. 1949) was carried out. No secondary deposits were noted.

3. Rodent Ulcer left helix. 7.7.52. first noted in hospital record. This lesion was noted at a routine follow-up visit. No biopsy.

4. Epithelioma left hand. 4.1.54 first noted in hospital record. This lesion was between 1st and 2nd metacarpals and was noted at a routine follow-up visit. No biopsy.

It is on account of the second of these lesions that the patient is included in this series.

Housing

The patient has lived all his life in the neighbourhood of Southampton with the exception of a period of less then one year during the first world

war, when he served in the Army.

He has never lived in a house with indoor sanitation, or with a bath, and until the last four years has had no method of heating water easily.

As a child, he lived in a house of five rooms (living and bedrooms) with nine people, three adults and six children. After the age of fifteen, there was plenty of room in the houses in which he lived. When he was aged 41, he was bombed out of one of his houses, and moved back from a Southampton suburb to a large village nearby in which he had spent the first twenty five years of his life.

Occupation

The patient started work at the age of fourteen. He held a number of jobs over a period of 7½ years, and in these jobs he was in contact with a variety of materials (see table). Following on this, he became a road-sweeper, working for Southampton Corporation. He did roadsweeping for eighteen years, a job which involves much dirt, is outside in all weathers, and has altered in character over the years. In his early years in this job, roads were much more dusty than now and horses were more common. Later, roads were more often of tar or asphalt, and horses became uncommon. During the last war he held a job for three years of filling, maintaining and placing out paraffin danger lights and lamps for shelters. This work was partly in and partly out of doors. For the last eleven years he has been employed in laying tarmac and laying paving stones. Tar spraying has been an occasional job. He estimates that 40% of his job is in contact with tar, mainly in the form of a pebble-tar mixture for road making, and that 60% of the time is spent laying paving stones. Cement and sand are the principal materials used in this work.

The patient keeps quite a large garden as a hobby. He does not use insecticides or chemical manures.

M12

Family History

The patient's father died at the age of 82 from a cancer of forearm, which "crept up the arm and ate into a blood vessel". The patient's father was a "chemical miller" and crushed bones, etc. There is no family history of any disease and no other relative has died of cancer. The patient has one brother and four sisters all alive and well. He has two children aged 29 and 22 in good health.

History of Lesion

The condition began as a slight scab, which was occasionally knocked off. There was no bleeding - a dry and scaly patch was left behind. After an interval of about six months, a swelling appeared and this swelling pricked "as if something was inside". The swelling appeared on exactly the area on which the scab began. He sought advice about the swelling at about one year after the first scab had appeared. On examination of his hand on 6.11.47, a tender nodule was noted over the middle metacarpal, in its distal portion, behind the head and slightly towards the radial side. Other skin changes were noted (see below).

Microscopis appearance (Surgical excision)

"This must be considered an early squamous carcinoma. The cells are too irregular for a benign tumour though for the most part the basement membrane is intact and no infiltration is seen."

Condition of Skin

The patient noted that the skin of the hands and forearms was dry, shiny, thinner and wrinkly (inelastic) about two or three years prior to the first appearance of the lesion. This came on gradually and in the winter his skin tended to crack. The condition got worse and when seen he had the

classical precancerous dermatosis of 'shagreen skin' on the forearms and hands. His unexposed skin is normal for his age. The hands show flat keratoses, the largest of which is 2mms. in diameter, telangiectases, many cracks, occasional areas of peeling not associated with keratoses and the whole skin on the backs of the hands is dry and scaly, thin and shiny, especially over the knuckles. The skin on the forearm is beginning to show the same changes, but in an early not an advanced stage. The skin of the face and back of neck also shows similar but mild changes, the tips of the ears being most affected.

Discussion

The patient's father died of a cancer of the skin. A striking feature of the case is the number of cancers from which the patient has suffered. In summary, the lesions have appeared as follows -

1. Carcinoma of lip aged 47 (Clinical diagnosis).
2. Changes of 'shagreen skin' noted by the patient on backs of the hands. It is probable that the condition was present for longer, as it was not until cracking was present, due to the inelasticity of the skin, that the patient took note.
3. Epithelioma of back of right hand aged 50 (Microscopical diagnosis).
4. Rodent ulcer tip of left helix aged 52 (Clinical diagnosis).
5. Epithelioma left hand aged 57 (Clinical diagnosis).

It appears possible that further malignant lesions may arise on the backs of the hands and forearms, especially the hands, as the skin on these areas is typically precancerous in appearance.

Occupation is, in my opinion, a likely causal factor in these skin changes. The patient's work has been almost always out of doors and fully

exposed to the weather. The skin changes on the hands and tips of the ears seem to indicate weather (and particularly sunlight) as a causal factor. The rather dirty nature of his occupation as a road sweeper in contact with tar may also have contributed. In the six years after ceasing to be a road sweeper, he worked in contact with paraffin for three years and in contact with tar, cement and sand for the last three.

Although in this case the aetiology of the cancer is probably a result of the patient's occupation, he would not be notified to H.M. Chief Inspector of Factories as his work falls outside of the scope of factory legislation.

The family history of skin cancer is possibly accounted for by the patient's father's occupation. The site of this cancer (arm) would suggest an environmental origin, but a familial tendency to skin cancer cannot be ruled out.

OCCUPATION

M12

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin.
Errand boy	½	-	Groceries of all kinds
Grocers boy	½	-	
Bakers roundsboy	¾	-	Bread
Pipefitter's Mate	½	Helping pipefitter. Red lead was used for jointing and mineral oil to clean pipe.	Red lead, mineral oil.
Storeman	4/12	In a Grocers wholesalers	Groceries.
Baking and delivering bread	1½		Flour and bread. (Was baking bread only).
Army Private	1	Infantry	Oil for rifle.
Plant Operator	8/12	Nitric acid was made in a pot and used for guncotton.	Nitric acid. He was burned on the right forearm by this
Cordite exploding and burning	10/12		Cordite
Post Office Linesman	1¼	Putting in poles and putting up lines	Telegraph poles and lines (? creosote on poles).
Road Sweeper	18	Sweeping street refuse, etc. into piles Was a dusty job in summer, a dirty muddy job in winter.	Street dirt
Lampman	3	Filling and maintaining and delivering paraffin oil burning danger lights.	Paraffin
Roadman	3	60% laying paving stones 40% Tarmac laying with pebble-tar mixture. Occasional tar spraying.	Cement, sand. Tar

Male. Date of Birth 14.11.07. Age at lesion 39. M15

General

This patient was brought up on farms under what were rather poor housing conditions until the age of fifteen. He has held a variety of unskilled jobs all his life. He is an epileptic, having suffered from this disease since infancy. In childhood, he had one fit every two weeks, but in the last fifteen years he has had only two fits. He takes phenobarbitone gr. $\frac{1}{4}$ b.d. and has done so for many years.

Housing

Until the patient was fifteen, his housing conditions were poor. There was a slight degree of overcrowding, and washing facilities were bad: water was not piped to the house, there was no bath and no means of heating water easily. Sanitation was outdoors. Conditions improved slightly thereafter. He has not lived in crowded conditions since, but there has never been a bath or easy means of providing hot water in the houses in which he has lived.

Occupation

The patient has held a series of unskilled jobs all his life. The three main jobs he has held being cowman, stevedore and paint sprayer. Full details are given in the table.

Family History

There is no family history of skin disease or of cancer, and the patient does not know of any relative who suffers from epilepsy.

History of Lesion

The lesion began as a 'wart' at the outer corner of the left eye. There is no history of injury, and the skin in this area was perfectly normal

M15

prior to the development of the lesion. From the first sign of the wart until the biopsy was three weeks.

Microscopic appearances showed 'marked growth of squamous epithelioma'.

Condition of Skin

The patient has a good thickness skin, medium oily, elastic, and medium dark in colour. There are no degenerative changes and his exposed and unexposed skin are normal.

Discussion

No reason can be suggested for the appearance of a cancer in this patient's skin. Henry (1950) has noted an association between people handling animals and cancer, and this case may fall in that category.

OCCUPATION

M.15

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all Materials in contact with the skin.
Paper round	1		
Milking cows, cleaning and some general farm work	4	Mainly as a cowman	
Stevedore	15		Skins, wool, copper.
Cowman	2	Had skin trouble for 1/12	
Builders labourer	¾		
Cowman and farm hand	6	Mainly as a cowman	
Laundry maintenance worker	1	Mainly builders labourer and handyman	
Paint spraying	5		Cellulose and aluminium paint. White spirit.

Male. Date of Birth 13.11.19. Age at lesion 28. M16

General

The patient, one of a family of seven, has lived all his life, apart from war service, in a village on the edge of the New Forest. He joined the Royal Artillery at the beginning of the war and was demobilized 6 years later, having served most of his time afloat as a gunner in merchant ships and for over half a year as a gunner-hand on a fleet oiler. On return to civilian life he again lived in the same village.

Housing

This has been rather poor, and at most times between birth and the age of 20 there was an average of 8 persons living in a house with 3 bedrooms and 1 living room. Sanitation was outdoors, there was no bath in the house, although water was piped to the house and hot water was said to be provided easily.

Occupation

The patient's first job as a labourer in a tar distillery brought him into contact with pitch, tar and bitumen. As a young lad he used to be covered in pitch and tar at the end of his day's work. Tar erythema has been experienced many times (at least x 25) during the first 2 years in this job.

As a plasterer his skin was in contact with lime, cement and sand and proprietary quickset plasters, but his skin did not at any time show any reaction, apart from a tendency to dryness, to these substances.

In the Army, rifle oil and grease were the only materials handled apart from the one and a half years during which he served on a tanker. The work on this tanker brought him into contact with fuel oil. This contact was mainly arms and legs but was, on occasions, all over when hoses burst or

M16

other such trouble happened. He was sailing mainly in semi tropical areas and shorts only were worn. The oil was, therefore, able easily to contaminate his skin.

On his return to civilian life, he again handled pitch and tar and in addition naphthalene.

Family History

The patient's father, who worked in the same tar distillery, took his son(the patient) into his gang. Although the patient's father did not suffer, as far as is known, from malignant disease, he did suffer from tar warts and had skin changes on his forearms (presumably due to tar). Between the ages of 55-60 the patient's father "had 14 tar warts cut off his neck and some off his arms".

No other member of the family, including uncles and aunts are known to have had cancer. The patient's eldest brother had an operation for a 'brain tumour' following a head injury received during the war. It seems from the history of trauma (and pension) that this condition was probably traumatic in origin.

History of lesion

Up until December 1944 (aged 25) the patient noted no abnormality in his skin anywhere or in particular over the right shin. At this time, the patient was working on the oil tanker and had a small wound on the front of the shin, halfway up the leg. A fuel oil line burst and flooded around, thus contaminating the wound. Within three weeks, the patient noted a lump or pimple at this site. This lump went away and nothing further was noted until 1948 (January). At this time a lump was again noted, and following on the swelling some pain was experienced. The top of the swelling was warty

M16

and used to discharge. It is the patient's opinion that his trouble dates from the oil contamination of the wound and he is quite emphatic about this and about the fact that the swelling which was the epithelioma arose at the site and in the scar of this wound. Prior to surgical excision the lesion was described as "an epithelioma on the anterior part of the leg, halfway between the knee and the ankle, measuring 5 x 4 cms". No glands were noted.

Microscopic appearances

"The specimen is a definite epithelioma, probably slow in growth, as it is highly differentiated. The tumour penetrates through the sub-epithelial fibrous layer almost to the fat."

Condition of skin

Apart from the scar at the site of the excision of his epithelioma the patient's skin is a normal, elastic, slightly oily fair skin, poor in hair and slightly pigmented in the exposed areas. He shows no sign of shagreen skin or tar melanosis and his pores are not enlarged or blocked.

Discussion

This cancer appears to have a definite environmental aetiology. My view is that the carcinogen was pitch which was handled aged 14 - 17 and that the injury in 1944 (aged 24) which was contaminated by mineral oil was the cocarcinogen. Whether the trauma or the mineral oil was the precipitating factor remains a matter for speculation. The age of the patient is much in favour of an occupational cause of the cancer and the clear history of pitch handling, together with the history of injury and oil contamination, makes occupational factors almost certain.

The mineral oil (bunker fuel) was more likely to be a promoter (cocarcinogen) than an initiator (carcinogen) from what I know of the

constitution of such oil. Until recently, when the process of catalytic cracking of oil was introduced, bunker fuels contained almost no aromatic (cyclic) hydrocarbons. Straight-chain (paraffinic) hydrocarbons show practically no carcinogenic activity.

The practice of washing tar off the skin with naphthalene should also be mentioned as a possible source of non-specific irritation.

Although this case seems clearly occupational in origin, it was not notified to H.M. Chief Inspector of Factories by any of the doctors who saw the case as an industrially caused cancer.

OCCUPATION

M16

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin.
Labourer	3	Loading solid and semi-solid bitumen into trucks either by shovelling or in drums. Loading and breaking pitch, occasionally handling tar. He joined the gang in which his father worked.	Bitumen, pitch and tar
Plasterer's labourer	3	Using plaster and plastering.	Cement, lime, sand and quickset plaster (for ceilings)
Army	5½)1½)4	Infantry Maritime Royal Artillery Gunner 1¾ yrs. Gunner-hand on a tanker 1½ yrs. General Home Duties 2/3 yrs.	Rifle oil (lubricating oil) Grease Fuel oil
Labourer	1	Breaking and loading pitch into trucks. Handling tar. Digging and bagging naphthalene (out of pans)	Pitch and tar Naphthalene

Male. Date of Birth 9.1.74. Age at lesion 76. M19

General

This patient has spent most of his life at sea. His father was a sailmaker and the sea is obviously in his blood.

Housing

As a boy he lived in accommodation which was reasonably good by the standards of the day. Four children and four adults shared a house with six bed and living rooms. Sanitation was outdoor; there was no means of providing easily hot water; there was no bath in the house, but water was piped to the house. From the ages of fifteen and until he was fifty five, he spent his time at sea with very occasional short stays ashore. After coming ashore permanently, he has lived in the country in reasonably good housing.

Occupation

The patient started work at the age of 12 and spent 30 years at sea. Next, he spent 18 years strawberry and poultry farming, and this was followed by 6½ years as a rigger-boatman. Since 1944, he has been retired.

He was in contact with Stockholm (wood) tar which he handledevery other day for about 10 years and also on occasions with coal tar, pitch, yacht varnish, linseed oil (boiled) and coal.

Family History

The patient is the second boy in a family of six boys and four girls. Two of the patients sisters are dead: one died when aged 3 of diphtheria and convulsions; the other died aged 72 from unknown cause. Two brothers have died - one of consumption when aged over 40, the other following an internal operation aged 63. The patient thinks that cancer was the cause of death of this brother. There is no other history of cancer or any history of skin

disease in the family.

Apart from one child who died aged 3 of meningitis, the patient has 3 sons and 2 daughters alive and well.

History of lesion

In January 1949 (the patient was aged 75) the patient noted a painless swelling behind the left ear. This lump was movable under the skin but did not seem to grow until November, when it began to get larger. The lump was thought at first to be a sebaceous cyst which had become infected, but as it did not improve with poultices, he was sent to hospital.

Microscopic appearances

The lesion on biopsy was reported as "a malignant tumour, lying in the subcutaneous tissues, formed by columns of cells with a tendency to form imperfect glands. It is probably a type of squamous carcinoma".

Condition of skin

The exposed skin of the patient shows degenerative changes. In the forearms and especially in the hands, the skin is typical "sailor skin" - thin, atrophic, inelastic, with white patches and areas of light brown pigmentation. There are a few telangiectases and occasional keratoses. The striking features are the brown-white background of the skin and the glazed appearance of the back of the hands. His hands cut and abraid very easily and some scabs were present, arising from injury, when the patient was seen. He says that "his hands bleed very easily" - this is due to the very poor quality of the skin.

On the face, the skin was pink and slightly peeling. The tips of the ears show marked degenerative changes and on the neck the skin is thin and has many comedones at the back.

M19

The unexposed skin is extremely pale and inelastic and of below average thickness.

He says that his skin is sensitive and tender, and he has noticed the thinness of his skin when working. In the summer, he dare not expose his skin to strong sunlight as he peels and goes red. He has never produced a good tan. His colouration is that of the typical red-head with very pale skin and blue eyes.

In the tropics (and he spent about 1½ years altogether in tropical climates) he always avoided the sun as much as he could, otherwise he peeled.

Once, he had a cargo of pitch, and the dust from this "peeled his skin as much as the sun would".

Discussion

This cancer appeared on the exposed skin of the neck in an old sailor aged 76. Typical precancerous changes were present on the hands and forearms and degenerative changes were present on the neck. The patient's colouring was such that he stood up badly to sunlight. It would therefore seem possible that environment was one factor in the aetiology of this cancer. Another possible factor is the constitutional one of poor resistance to sunlight due to lack of pigment formation. However, it would be reasonable to assume, if the above is correct, that the constitutional factor would not have an adverse effect on his susceptibility in the absence of sunlight - and his work brought him into the weather at most times and seasons.

OCCUPATION

M19

Age at which patient started work: 12

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Telephone Exchange Operator	3		
Cabin boy - cook	½		
Ordinary seaman, able-seaman and up to 1st Mate	23	Yachting around the world, coasting, trawling. 1½ years in tropics. Had to paint and maintain the ships, rigging, etc.	Used to tar the bottom of coasting ships with coal-tar Stockholm tar was used for rigging, etc. Hands used to be covered in this. Tallow was often used as a skin cleanser for tar, in addition to being handled. Coal and china clay were handled as cargoes. Pitch - one cargo of this was handled and the dust of this "peeled his skin as much as the sun would".
Navigator R.N.R.	4½		
Poultry & Strawberry farming	18		
Rigger-boatman	6½	In a yacht yard. Painting, pumping and general work.	
Retired	7		

Male. Date of Birth 10.3.86. Age at lesion 64. M23

General

This patient has worked for the last 25 years out of doors in all weather as a Customs waterguard. He comes of a family of six of which he is the eldest. His father worked in the straw hat making industry (which is an industry located around Luton and Bedford) and the patient did some work at this trade from a young age, as much of the work was home work.

Housing

During the patient's childhood and up until the time he joined the Navy (at the age of 14¾) he lived near Luton, Bedfordshire, in a house with four rooms (living room and bedrooms). There were eight people in this house for most of that period - two adults and six children. Sanitation was outdoor, water was piped to the house, there was no bath in the house, nor was there any means of providing hot water easily.

During his service in the Royal Navy the patient spent part of his service in submarines.

From the age of 45 he has lived in a house in Lymington, Hants, with no overcrowding, indoor sanitation, a good supply of hot water and a bath.

Occupation

The early contact with dyes is difficult to assess. The dyes were in solution and were sprayed in a mist onto the straw hats.

The latter part of his life was spent mainly outdoors in all weathers. Apart from gardening, he has no regular hobby.

Family History

He comes of a family in which there is no history of cancer, skin trouble or other disease and who survive to ripe ages.

M23

History of lesion

The patient is of the opinion, which he stated quite definitely and emphatically, that his condition began as a result of an injury. In 1950, six weeks before he was seen at hospital, he was out picking cob nuts. While doing this he received a prick on the cheek which, in the patient's opinion was on the exact spot at which the swelling later appeared. I suggested to the patient that the prick may have been near the spot - but he was unshakeable in his belief that the lesion which followed was a result of the prick and was identical in location. The spot came up later "like a mosquito bite" but continued to enlarge. He then consulted his own doctor, who sent him to hospital.

Microscopic appearances

The report on a biopsy specimen is "This is a squamous carcinoma".

Condition of skin

In the exposed areas, his skin is thin, shiny and inelastic. Pigmentation is normal. There are occasional spidery telangiectases. The skin of the face is smooth, thin and relatively hairless. Unexposed skin is rather dry, of normal thickness and poor elasticity.

The principal changes noted are thinness of the skin in exposed areas and a generalised loss of elasticity.

There is no history of skin disease.

Discussion

The possible environmental causative agents in this case may be listed as follows:-

i) The dye used to colour straw hats. This exposure was short (six months only) but was at a young age (aged 15).

M23

ii) Outdoor work - as a seaman in the Navy and later as a Coastwatcher, for over 25 years.

iii) The very definite history of injury, following which the cancer appeared.

In the light of the theory of cocarcinogenesis, it would appear possible that exposure to sunlight in the long continued outdoor work was the carcinogenic stimulus and that the injury was the localizing and precipitating (cocarcinogenic) factor.

OCCUPATION

Age at which patient started work: 13.

M23

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Grocer's errand boy	4/12		
Baker's Assistant and errand boy	5/12		
Straw hat factory worker	6/12	Millinery plat (straw from China) and handling dyes - blowing dye on to straw hats out of a bottle which was held in the hand.	? Vegetable dyes) Blue and ? Aniline dyes) red and ? Arsenic dyes) green dyes
Service in Royal Navy as a boy, a seaman, a torpedoman (electrician) and submarine cox'n	20		Occasional contact with mineral oil
Coastguard service)	2	As a coastwatcher. He spends his time outdoors, patrolling a stretch of the coast.	
H.M.Customs)	27		

Male. Date of Birth 5.4.08. Age at lesion 41. M24

General

This case shows the onset of a cancer four weeks following a prick on the nose by a needle while sewing asbestos. The patient is a tough ex-regular soldier who came of a rather poor home and spent five years in India with the Army.

Housing

Until the patient joined the Army at the age of 19, he lived in rather poor, though not overcrowded housing conditions. Water was not piped to the house, there was no bath nor easy means of providing hot water and sanitation was outdoors. Apart from his twelve years of Army service, his housing conditions have since been satisfactory. In the Army, he was living under reasonable conditions, except for some periods on active service during the war. He spent five years in India from 1928-33, that is when he was aged 20-25.

Occupation

After three years as a gardener and one year as an underfootman and butler, the patient spent six years in the Army, mainly as a tank driver. On coming out of the Army, he worked intermittently as a driver and labourer for 3½ years (out of 6, the remainder being unemployed), before joining the Army again as a driver. On leaving the Service, he became a lagger in the docks. In this work he came in contact with asbestos and other lagging materials such as magnesia blocks.

Family history

There is no family history of cancer or of skin trouble.

History of lesion

The patient was sewing asbestos cloth round a pipe and accidentally pricked his nose with a needle while doing this. In less than two months he had a wart-like growth at the exact spot where he had injured his nose. The patient is certain that there is a causal connection between the injury and the 'wart'.

Microscopic appearances are those of "a squamous carcinoma".

Condition of skin

Apart from some slight evidence of degenerative change on the forearms and backs of hands - a few thin patches and occasional keratoses - the skin is normal. Thickness and elasticity are average. The unexposed skin shows no sign of degeneration or of other change.

Discussion

This patient has had a series of mainly outdoor jobs and has spent a period of five years in India between the ages of 20 and 25.

He gives a very clear cut history of trauma, followed in four weeks by the appearance of a 'wart'. The patient is in no doubt whatever regarding the causal connection between the needle prick and the subsequent epithelioma which appeared at the exact site of the needle prick.

It may or may not be of importance that the patient was sewing asbestos cloth at the time. Asbestos implantation, subcutaneously by the needle prick is a possibility which cannot be ruled out. Wyers (1956) in a discussion on asbestos "corns" quotes one case known to a colleague of his(A.I.G.McLoughlin) of neoplastic change in an asbestos corn, but in 16 years of work in the asbestos industry, Wyers has never seen a case of neoplastic change in the skin. The carcinogenic effect of asbestos in the lungs is well known, but the

M24

evidence of its carcinogenicity to the skin while slight, cannot be ignored.

OCCUPATION

M24

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Gardener and odd job man	3	Gardening and looking after chickens and goats.	
Houseboy (Under-Footman and butler)	1		
Army	6	Tank driving mainly. India 5 years	
Driving	2	From 1933-38. The rest of this time he was unemployed.	
Labouring	1½		
Army	6	4 years as a driver, 2 years as a supervisor of P.O.W.	
Lagger	5	On ships.	Asbestos. Magnesia blocks.
Electrician's Mate	6		

Male. Date of Birth 12.8.02. Age at lesion 45. M29

Housing

The patient has lived all his life in Southampton. Up till the age of 15, the patient lived in a house with five rooms (excluding kitchen and bathroom) with two adults and seven children. Sanitation was outdoors and there was no bath. Water was piped to the house and there was an easy means of providing hot water. After the age of 15, housing was good, without crowding and with all modern amenities.

Occupation

Apart from labouring jobs for nearly three years after leaving school, the patient has been an apprentice joiner and a joiner. Details are given in the table.

Family history

There is no family history of skin disease. Both the patients parents died of cancer; his father of bladder cancer and his mother of ? stomach (internal) cancer. He has four brothers and six sisters, all alive and well.

History of lesion

The patient's wife first noted a small lump in the left upper eyelid. From the time of its appearance until a year and a half later, when it was excised, the lesion grew very slightly, reaching a final size of 6 mms. in diameter. There was superficial ulceration noted prior to excision. Microscopic appearance was that of a horny papilloma, with one area showing an epithelioma, Grade I.

Condition of skin

The patient's skin is normal fair skin, in keeping with his age.

M29

A few freckles and small degenerated placques were noted on the exposed skin of the extensor surfaces of the forearms.

Discussion

No cause can be suggested for this lesion apart from the possible association with a previous acute allergeric dermatitis ("teak poisoning").

OCCUPATION

M29

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin.
Odd jobs	9/12	Pirelli Cable Works	Copper cables.
Labourer	2	In a shipyard	
Apprentice joiner	5	In shop and outside. 2 years of this time in shipping	Wood of all kinds
Joiner	23		

Male. Date of Birth 19.11.07. Age at lesion 44. M30

General

In this case three main factors appear to be concerned in the aetiology -

i) The presence of a naevus (wart).

ii) Heavy mineral oil exposure while at work.

iii) Chronic eczema since age 16, said to have been caused by handling oily pipes. The disease and the treatment have to be taken into account.

Housing

The patient has always lived in a suburb of Southampton. There has been ample room at home and at no time has there been overcrowding. Sanitation was indoors and there has always been a bath with easy means of heating water.

Occupation

As a machinist, he has a chronic heavy contamination of his exposed skin by cutting oils. Paraffin makes his eczema break out and he avoids contact with this. At no time has he used barrier creams. He blames his occupation for the start of his eczema (from which he still suffers).

He is, and has for many years been a keen gardener.

Family History

No relative has suffered from cancer. One of his sisters suffers from skin trouble and attends hospital occasionally on this account.

History of lesion

Since childhood, the patient had a lesion in the right nasolabial fold at the site which subsequently became malignant. He was known as

"bladder-lip" to some of his contemporaries at school. The condition was quite static until he cut it while shaving 14 years prior to the diagnosis of cancer was made. After he had cut it, it became wart-like and remained that way until two months prior to excision. At this time the 'wart' started to grow rapidly for no known reason.

Microscopic appearances were those of an epithelioma.

Condition of Skin

Until the age of 16, the patient's skin was completely normal apart from the naevus. At this time, he developed an eczema which has remained with him in varying degrees of severity ever since. He attributes the origin of this condition to his work (see above). The eczema has at times been severe and very extensive and he has had spells in hospital under treatment for the condition. At present the hands and popliteal areas only are affected. He has had no treatment of his skin by tar. On examination, his skin is of normal thickness and elasticity, is medium dry and very white. In sunlight he goes red and not brown. There is very little difference between the exposed and unexposed skin.

Discussion

It is difficult to sort out the various factors into order of importance, but there seems to be no doubt about the connection between the naevus and the subsequent epithelioma in view of the identical site and the fact that the epithelioma seemed to arise from the naevus.

The connection of the chronic eczema (which was due to oil, in the patient's opinion) and the exposure to oil per se in the aetiology of the lesion is more difficult to sort out.

It has been shown in part I that both chronic eczema and oil contact

M30

are known aetiological factors. Whether in this case chronic eczema and oil should be regarded as precipitating factors in a pre-existing naevus can only be a matter for speculation. It is possible that the association of these three factors is more than co-incidental and that the subsequent cancer bears a relationship to one or all of them.

OCCUPATION

M30

Age at which patient started work: 15.

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Apprentice Machinist and Machinist.	30	As a boy he filled and drained tubes with linseed oil. As a machinist, he has been in constant contact with cutting oils. These oils tend to spray out, due to rotation of machine parts or pipe which is being machined.	Cutting oil - an oil-water emulsion, often with additives of a detergent nature Paraffin and paint - these substances, if handled, make his eczema worse.

Male. Date of Birth 27.12.85. Age at lesion 67. M33

General

This patient gives a history of chronic ulceration of the leg, arising from an accident when he was aged 30. Malignant changes supervened in what was a chronic varicose ulcer and the leg was amputated.

Housing

All his life the patient has resided in Southampton in the same house. When he was young, four adults and seven children lived in the three-bedroom and two living-room accommodation of this house. There has never been more than ten persons and never less than four in the house. Sanitation is outdoors, there is no bath in the house, and there is no means of providing hot water easily.

Occupation

For most of his life the patient has been a woodwork machinist, making mouldings, stairs etc. This work involves little movement and he had to stand by the machine while operating it. No seating was provided. (The Factories Act of 1948 makes provision of seats obligatory if the work can be done while sitting).

Family history

Cancer of "the bowels" was the cause of death of the patient's mother. No other relative had cancer. The patient's mother had a chronic eczema of the hands and arms, but no other relative had any skin trouble.

History of lesion

When the patient was bathing (aged 30) an eyelet from his boot stuck in his leg. The wound bled a little and after a few days became inflamed. The inflammation settled and in a month an ulcer appeared. This ulcer got

worse but then healed by pressure bandaging of the leg. The ulcer was situated on the inner aspect of the leg at the junction of the middle and lower limbs.

The ulcer would heal and break down - always following a knock or blow; never for no reason. Subsequently the ulcer refused to heal, and at this time, two years after the first appearance of the lesion, he had a haemorrhage from the ulcer and was off work for six months. The ulcer then healed.

Over the next 28 years the ulcer kept breaking down and healing, but on each occasion the ulcer tended to get larger. Finally, the ulcer would not heal and at this time a biopsy was taken.

Microscopic appearances

"The edge of a varicose ulcer, in places becoming frankly malignant."

Condition of Skin

Owing to amputation, the condition of skin in the area of the ulcer was not available for inspection. Elsewhere the skin is of average thickness, fair, slightly dry and of good elasticity for age (though it is relatively inelastic). Exposed skin has slight pigmentation - otherwise exposed and unexposed areas are similar.

His case record confirms that the ulcer was a varicose one and he had the usual associated skin changes around the margin of the ulcer.

Discussion

This is a case of malignant change in a chronic varicose ulcer. The patient's mother had a chronic eczema. His principal occupation, in which he was required to stand still without moving much, may have contributed to the aetiology of varicose veins, varicose dermatitis and varicose ulceration.

M33

The malignant change in the ulcer was not probably affected by his occupation, unless trauma may have played a part.

OCCUPATION

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Errand Boy	1		
Cycle Repairer	6		Oil (lubricating), rubber solution.
Woodwork Machinist	38	Making stairs, mouldings, on a wood-work machine	Wood

Male. Date of Birth 23.11.97. Age at lesion 51. M39

General

This cancer occurred in a small, fragile nervous man, who looked as if he had been poorly nourished as a child. His record of illness over the years is of sickness absence considerably above the average.

Three main factors appear to be relevant to the discussion of aetiology in this case:-

i) Eczema of the face (and elsewhere) aged 9.

ii) Lupus vulgaris at the site of the cancer, present for 5 years.

iii) The occupational contact of 48 years with soot, coal ash and clinker in the firebox of railway locomotives.

Housing

Until the age of 30, the patient lived in Brighton in a house of 5 rooms (excluding kitchen and bathroom). At the peak, there were four adults and four children living in this house. Water was piped to the house, hot water was easily provided, there was no bath, and sanitation was outdoor. From Brighton, the patient moved to Eastleigh and occupied, with his wife and son a house of 5 rooms, with all modern amenities. He still lives in this house.

Occupation

From the table it will be seen that the patient has spent practically the whole of his working life as a boilermaker, working on one particular job.

Family history

The patient's mother died at the age of 70 of cancer of the bowel. He has a sister aged 48 who suffers from colitis. There is no history of skin trouble in the family.

M39

History of Lesion

In 1944, nine years prior to the biopsy diagnosis of squamous epithelioma, the patient noted a scaly patch on the left side of the forehead. This patch was about 1 cm. in diameter and remained like this for two years. At the end of this time, the patch grew larger and by the third year of its presence the patient sought the advice of a dermatologist, owing to breakdown of the centre of the area and to weeping. The lesion was diagnosed as lupus vulgaris and calciferol treatment was given, but the condition did not improve. An 'ulcerating tumour' was noted in July 1953 which was biopsied.

Microscopic appearances.

"Fragments of loose connective tissue, infiltrated by interweaving strands of basi-squamous cell carcinoma".

Condition of skin

The patient first had skin trouble in childhood aged 9 to 10, when for 1 year he suffered from eczema. This eczema affected the face and elsewhere. There was some weeping at the height of the disease. Since the age of ten, he has had no return of this or any other skin disease until in 1944 he began the lupus vulgaris which finally became cancerous, and which has been described above.

On examination, the patient's skin was rather inelastic and thin for his age, but normal otherwise, apart from the scar at the site of his skin cancer.

Exposed skin shows slight pigmentation, but the unexposed skin is lily-white. He shows no changes suggestive of occupational degeneration.

Discussion

The important facts in this case seem to be -

M39

i) The previous history of skin disease - eczema for a year aged 9 - 10, and lupus vulgaris for nine years.

ii) The patient's occupation, which brought him into contact with the firebox soot of railway engines and with lubricating oils.

It seems likely that both the lupus vulgaris and the irritation from soot (on a normally exposed area) may be put forward as causal agents. He was also in contact with mineral oil as lubricating oils. That the lupus itself, a form of chronic skin disease, may lead to cancer is undeniable, as also is the fact that coal soot and mineral oil are known carcinogens on the skin. Which of these factors is more important (if one is) is difficult to decide. The important point is that the cause of this cancer probably lies in one of these factors or in a combination of them.

OCCUPATION

Age at which patient started work: 14

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Toy assembler	½		
Apprentice boiler-maker	5)	48 years in total, working for the railways as a boilermaker, maintaining and repairing locomotives. Mainly inside fireboxes.	Clinker soot and ash are found inside the fireboxes. "Verdigris" (green scale on the copper from which the firebox is made) Lubricating oil - much of this used in the course of his job.
Boilermaker	43)		

Male. Date of Birth 31.1.04. Age at lesion 49. M41

General

This patient has lived in and around Southampton all his life - and for most of his working life he has been associated with the bitumen and tar trade as a representative. As a child he was at boarding school from age 7 to 17.

Housing

At all times, this patient has lived under good housing conditions without overcrowding and in houses with adequate hot water, baths and indoor sanitation.

Occupation

Apart from an initial two years and a half, after starting work at the age of 16½ in an office clerical job, the patient has worked as a representative (salesman) in the bitumen and tar trade. His work involves much travelling and he spends quite a lot of time in the open, often visiting sites where tar or bitumen is being used - e.g. on roads. If complaints are made regarding the quality of the product, he goes to the site where the product is being used in order to make sure that it is being laid and used correctly. In this way, he suffers some exposure, particularly to the fumes. During the last three years of the war, he was in charge of bitumen "armour plating" of ships and had charge of a gang of men in Southampton Docks. This work involved melting bitumen and pouring it in moulds around the exposed parts of ships - e.g. the bridge. The patient occasionally helped with the actual melting and pouring during this time and was again exposed. He is also exposed slightly while inspecting asphalt and tar plants.

His main hobby is repairing and maintaining his car.

Family History

The patient's mother died aged 81 of cancer of the stomach and a sister died aged 56 of breast cancer. There is no history of skin trouble in the family.

History of lesion

In March 1952, the patient noted a small swelling or "sore" which appeared on the right hand, on the dorsum, over the junction of 1st and 2nd metacarpals. This sore grew from a pimple and got larger, and occasionally broke down in the middle. He had no injury to this site.

Microscopic appearance

"The lesion is a well differentiated low grade squamous carcinoma".

Condition of skin

His exposed skin on the hands and to a lesser extent on the forearms shows marked degenerative changes, with areas of depigmentation and loss of elasticity. No telangiectases or keratoses were noted. The appearances are those of shagreen ('sailor') skin.

His complexion is fresh and ruddy. The tips of the ears do not show any signs of degenerative change. In the scalp, he has a slight degree of seborrhoea. The skin is dry and very fair and burns easily in the sun. His unexposed skin is normal.

Discussion

The likeliest cause of this man's cancer would appear to be exposure to tar. Bitumen is not a likely cause as I know of no case in the literature or from personal experience in the oil industry, of skin cancer in workers exposed only to bitumen. This agrees with Henry's experience (Henry 1950).

M41

The shagreen skin appearance on the hands would support an environmental cause, as also would the fact that the cancer appeared on the hands (see Part III, Diagnosis of Occupational Skin Cancer).

Mineral oil, in the form of lubricating oil, as used in cars would also have to be considered in view of the patient's hobby of working on his car.

One other possible environmental factor is x-ray - he had five barium meals in connection with a peptic ulcer. However, the exposure levels here would be low.

An interesting feature of the case is the absence of degenerative changes on the tips of the ears: this suggests that sunlight is not important in this case and that the environmental carcinogen was handled, in view of the obvious degenerative changes on the skin of the hands.

In conclusion tar is therefore the most likely cause of this cancer, with some exposure to mineral oil as a possible contributory factor.

OCCUPATION

M41

Age at which patient started work: 16½

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Office work	2½		
Sales Representative and supervisor	30	Bitumen and tar trade	Did not handle tar, but in inspecting roadmaking and asphalt plant, had contact with the fumes. During the war, he was working with bitumen and tar used for armouring ships. On this job, he actually helped at times with the pouring.

Male. Date of Birth 1.9.90. Age at lesion 64. M43

General & Housing

This patient was born into a rich family - in his own words "his father was a very wealthy man" and has lived in comfort all his life. He has lived in houses with more than enough room for the occupants, and surrounded by all modern conveniences. Up until the age of five he lived in London and from five onwards has lived in the country, though he has worked in London. At the age of 60 he retired and has lived since in the country near Southampton. The patient has suffered from chronic bronchitis and dilatation of the heart which began when he was a young man.

Occupation

The patient has worked in a bank from the age of 16 for 39 years. His work was firstly as a clerk and secondly as a manager in the securities department. The work was mainly brain-work and involved some writing.

Family history

There is no family history of cancer or of skin trouble. One brother died aged 44 of Friedreich's ataxia.

History of lesion

In October 1953, the patient's wife noticed some increase in redness near the inner corner of the eye. The lesion was painless and became larger. It grew in size until it was 1" long, and lying beneath the inner extremity of the lower lid. The swelling was freely movable on the deep structures. The surface was smooth and not ulcerated.

Microscopic appearances

"The excised specimen is an anaplastic squamous cell cancer."

Condition of skin

The patient has a dry, hairless, rather thin and very white skin. The forearms show slight pigmentation. Elasticity is average for age. He suffers easily from sunburn and has to be very careful in strong sunlight. His skin produces some pigment but he can get burned and peeling in spite of this.

Discussion

No environmental factors can be suggested in this case which may have contributed to the aetiology of this cancer. The physical environment of this patient appears to have been extremely favourable throughout his life and no other factor such as familial disease, previous lesion or injury can be suggested. It is possible that this cancer arose at a muco-cutaneous junction, but would appear to be rather low down in the lid for this.

Male. Date of Birth 25.7.05. Age at lesion 49. M44

General

This case illustrates the point made by Henry (1950) about hobbies (see Part I, Personal Factors, 10) being important. In this instance, the patient is a keen sailor and spends most of his spare time either sailing or working on his motor boat.

Housing

As a child, and up to the age of 20, the patient lived in a house with an average occupancy of two persons per available room. There was no bath in the house, water was piped in, but no means was available of providing hot water easily. Sanitation was outdoors and the house was in a town. After the age of 20, and apart from war years, he lived in uncrowded houses with good modern standards of plumbing.

Occupation

He has, apart from an initial half year of work as an apprentice painter and decorator, worked all the time for a firm of wine and spirit merchants. Apart from intake of alcohol, there appears to be little occupational hazard in the job - and the patient is a very occasional drinker only.

The patient's hobby is his motor-boat. This week-end cruiser is looked after and maintained by the patient. In doing this, he has come into contact with paint, paraffin, lubricating oil, and tar. The paraffin and lubricating oil are used in the engine. He has used pitch and tar quite a lot and has suffered once from tar erythema in the course of tarring the bottom. The tar erythema from which he suffered was in April, 1954, and the lesion first appeared in September, 1954.

Family history

One brother died aged 63 of a cancer of the stomach. There is no skin trouble in the family nor are there any illnesses which run in the family. Seven siblings are alive and well.

History of lesion

In September 1954, the patient noted a swelling in the right cheek which was "like a blind boil". The skin in this situation was previously normal, and he has had no scar or previous injury. The swelling grew in size and was noticed to have a warty top. The swelling was excised within a month of its appearance.

Microscopic appearances

"Well differentiated squamous carcinoma. Malignancy probably of a low grade."

Condition of skin

His unexposed skin is fair, of average elasticity and thickness, and neither oily nor dry. The exposed skin of face, neck and forearms and hands shows well marked pigmentation. Degenerative changes, slight in degree of the 'sailor skin' variety are present on the forearms and hands. He has never suffered from any skin disease except for tar erythema as mentioned above.

In cleaning his forearms and hands after working on his engine, he has used petrol and paraffin to clean his skin.

Discussion

Occupation in regard to his spare time hobby of boating seems to provide the clue to the aetiology of this cancer. Three possibilities emerge with regard to boating:-

M44.

i) Tar. In view of the amount handled to tar the bottom every spring and the definite history of tar erythema five months prior to the appearance of the lesion, tar appears to be a distinct aetiological possibility.

ii) Sunlight. As a sailor, he would be exposed to the weather - and his forearms show the degenerative changes of shagreen (sailor) skin. His degree of pigmentation on what is a very fair skin would also support the amount of exposure in his case being considerable.

iii) Mineral Oil. He describes himself as a dirty worker - oil and grease gets all over him when he does a job - and he removes this contamination with petrol or paraffin.

It is possible that all of the above have played some part in the aetiology of his cancer. The association in time of his tar erythema merits special mention.

His normal work in the wine and spirits trade seems free from skin hazard.

OCCUPATION

Age at which patient started work: 14

M.L.

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin
Apprentice painter and decorator	½		
Cellarman	2	In wine and spirits business.	
Storeman	3		
Delivery	4½		
Window dressing and delivery	15		
Hobby, sailing			Tar, paraffin, lubricating oil and paint.

Female. Date of Birth 9.10.81. Age at lesion 66. F2

General & Housing

This patient has lived in comfortable circumstances all her life. She has never lived in overcrowded conditions and has always had adequate sanitary and washing facilities.

Occupation

She has spent ten years as a florist's assistant and one and a half years as a shop assistant. For the rest of her life she has been a housewife. Her work as a florist was in constructing wreaths, etc. most of the time. The shop assistant work was in a drapery store.

Family history

There is no family history of cancer or skin disease.

History of lesion

In December 1946, the patient noted a "blackhead" near the inner corner of the left eye. This lesion grew and became cauliflower-like and in March 1947 was excised. Prior to December 1946 the skin at the site of the lesion was completely normal.

Microscopic appearances

"The lesion is a squamous epithelioma".

Condition of skin

The appearances of the patient's skin are normal for her age. She gives a history of allergy to sunflowers, in the form of a rash of the forearms and hands about six months prior to the appearance of the lesion on her face. This rash lasted for a few days only.

Discussion

There is nothing in the patient's history or in the environment

F2

which can be suggested as having any bearing on the apperance of the lesion. The scar seemed clear of the muco-cutaneous junction.

Female. Date of Birth 5.9.95. Age at lesion 51. F3

General

In this case, there is nothing in the environment as far as can be ascertained which has any bearing on the development of the cancer.

Housing

The patient has lived all her life in the Southampton area. She has always lived in reasonable housing, with no overcrowding. Until she moved house at the age of 46, she had outdoor sanitation, no means of providing easily hot water, and no bath in the house.

Occupation

See table.

Family history

The patient's father died of cancer of the pancreas and intestines, and the patient's mother died of cancer of the pancreas. There is no family history of skin trouble.

History of lesion

The patient first noted a little lump in the left side of the neck in March 1947. This lump hurt slightly when she washed. There was no previous lesion, scar or ulcer at the site. The lump was growing in size. On 28.4.47, the lump was excised and was then about the size of a pea.

Microscopic appearances

"The specimen shows an epithelioma Grade I, i.e. probably relatively benign. The tumour is highly differentiated (keratinized), shows little infiltration, and there is marked round cell reaction."

Condition of skin

The patient's skin is normal in all respects for her age. The

F3

colour is medium-dark, the thickness is above average, and the skin is medium in oiliness. Her skin tans readily in the exposed areas, and never burns. She considers that her skin is hard and insensitive.

Discussion

No environmental factor, nor any other factor can be put forward as a possible cause of this patient's cancer.

OCCUPATION

F3

Age at which patient started work: 14½

Work or Job Title	Duration	Description of process, hazards, etc.	Name and description of all materials in contact with the skin.
At home	2½	Housework	
Housemaid	2½	General housework.	
Laundry worker	1	Putting sheets through a calendering machine	
Housework	1½		
Housework since married	35½	No other jobs.	

Female. Date of Birth 22.10.84. Age at lesion 63. F4

General

This patient lived in England until she was aged 12. From this age and until she was aged 43 she lived in Tasmania, and has since lived in England. She has lived fairly comfortably all her life.

Housing

This has always been perfectly satisfactory with regard to quality of accommodation. She has never lived in overcrowded conditions and has always lived in houses with bath and good hot water systems. In Tasmania, sanitation was outdoors.

Occupation

The patient has always done housework. She started immediately she left school as her mother died at this time and she continued to look after her father until his death. Since this time she has looked after some other relatives (aunts) until their death a few years ago. She now takes in university students during term.

Family history

The patient's paternal grandmother died of cancer (intra abdominal). An aunt of the patient (her mother's sister) suffered all her life from eczema.

History of lesion

In early spring, before Easter 1948, the patient was cleaning the chimney of her living room fire. At this time she struck her right hand on a bracket at the back of the fire. Her hands at this time were contaminated by soot and soot got into the abrasion. She then washed her hands and continued at work without applying a dressing.

F4

A hard lump began in about three weeks. This lump grew fairly rapidly until it was about the size of a sixpence. At this time the lump was removed, i.e. six weeks from the date of injury, three weeks from the time the lump was first noted.

Microscopic appearances

"Epithelioma, Grade 2. Well marked infiltration of deeper tissues".

Condition of skin

The skin on the backs of the hands has many freckles and is thin. Telangiectases are present but no keratoses. There are a few patches of extreme thinness. The unexposed skin is inelastic and dry, and within normal limits for her age.

Discussion

There is, in this case, a very clear story of minor injury, with soot contamination of the wound, being followed in three weeks by a swelling. This swelling, six weeks after the injury, proved to be an epithelioma. The condition of the skin in the area affected was perfectly normal prior to this injury.

It would, therefore, seem more than likely that there is a causal relationship between the injury as described above and the subsequent appearance of the tumour.

Female. Date of Birth 23.6.18. Age at lesion 28. F6.

General and Housing

My first impression of this patient was of a harassed, overworked, chronically tired and undernourished woman, looking much older than her years, who had absolutely no interest in herself. Her hair was unbrushed, her clothes were hanging off her and required washing and mending, and her skin around her feet and ankles showed days old mud splashes. On entering her house, the stale odour was overpowering. Flies buzzed around in swarms and the top of tables, chairs and floor were covered in varying degrees of thickness by dirt, fat and general assorted debris and filth. Conditions in the house were perhaps due in some measure to the lack of amenities - cooking was performed on an old fashioned range; water was drawn in buckets just outside the door; there was no means of providing hot water other than by heating a small quantity on the top of the old fashioned range; all water which was used had to be carried out of the house as there is no drainage from within.

Externally, the house is a picturesque thatched cottage with a pear tree growing up the wall. Internally, it is a damp overcrowded slum, with a total absence of amenities which are taken for granted by most people in this century.

The patient has suffered from asthma since the age of fourteen. Her father died when she was about three years old and her mother moved around from one lodging to another for some 8 years thereafter, finally marrying again. The occupation of the mother during this period is a matter for speculation. Since the age of 14 the patient's asthma has become steadily worse, until in the last 1½ years she has suffered from some secondary circulatory failure. She has taken ephedrine and adrenalin since about eighteen years of age. Adrenalin has been self administered and the

resultant scars on the arms are profuse in the areas used. A cold is now enough to precipitate gross dyspnoea and her ankles swell badly if she does not take diuretics.

Throughout the patient's life there has never been a means of providing hot water easily in her various dwellings, and during her married life has not had water piped to the house. Sanitation has always been outdoors.

Occupation

After leaving school, the patient worked for three months as a packer of chocolates. Following this, she worked for 5½ years in a laundry on various jobs - sorting, packing, ironing and calendering. On leaving the laundry she became a housewife.

Family history

One aunt died of cancer of the uterus. Apart from this, there is no family history of cancer, skin trouble or allergic disease.

History of lesion

Prior to May 1949, the patient had noted nothing abnormal in the skin on her sternum. It should here be pointed out that her skin condition generally was not normal, though it appears to be accepted by her as such (see below under 'Condition of skin'). During May 1949, the patient noted a "whitehead" which she broke. This lesion discharged and then grew larger. There was no pain accompanying the lesion. The lesion grew to about the size of a pea and had a grey-black crust on top "as if I never washed it". She had no lumps anywhere else, though she suffered occasionally from previous "whiteheads".

F6

Microscopic appearance

A biopsy of the lesion is reported "a squamous papilloma, showing early malignant change".

Condition of skin

The general appearance of the patient and of the skin suggest a chronic lack of washing. Over the shoulders and scapular regions the skin shows engrained dirt. There are many septic spots or scars resulting from these spots. The pores are large and are blocked by oily secretion or by blackheads. The skin is oily, of average elasticity and thickness and is neither fair nor dark, but in between in colour.

The skin of the posterior aspects of both arms shows marked changes due to constant adrenalin injections. (The patient's syringe was lying about the kitchen when I went in and was used without sterilizing). These changes are due to local areas of necrosis following injections. (In view of the fact that these injections were self-administered, it would be hard to find a more awkward site - but as the doctor gave her an injection there she had always used that site!)

Under her chin, on the left side, she has a neuro-dermatitis. This condition is very irritable and wakes her at night. The skin is glazed and of poor quality and shows evidence of being scratched.

The general condition of the skin is, like the general condition of the patient, poor.

Her skin never burns on exposure to sunlight - her ability to form pigment is good.

Discussion

It is hard to say which feature in this case began the obvious

F6

lack of care which the patient displays for herself. Probably a combination of poor housing, children, a rather poor childhood and eventual illness, lead to the present condition in which the patient no longer tries, either with regard to herself or with regard to her environment, to maintain cleanliness. The picture of this woman represents to my mind a survival of past conditions into the middle of the twentieth century. A social document of some length could be written as a commentary.

Whether this background has any relation to the development of her cancer is a matter which cannot be settled with satisfaction, but the features of this case which are unusual are:-

i) The age of the patient. She was 28 when the biopsy was taken. Such youthfulness suggests that the cause of the cancer is different from the usual.

ii) The very bad environmental conditions, coupled with lack of washing, leading to skin changes.

iii) The associated general debility and asthma.

iv) The possibility of some of the drugs which were taken for asthma entering into the aetiology.

v) The advanced physiological age of the patient, 45, when compared with her chronological age of 37.

Female. Date of Birth 18.1.91. Age at lesion 61. F7

General

This lady has lived all her life in or near Eastleigh, a 'railway town', in which is situated a large railway repair depot.

Housing

Until the patient was fifteen, she lived in rather crowded conditions in a house in the country. There was water from a pump, outdoor sanitation, no bath in the house nor any means of heating water easily. Between the ages of 15 and 25, she was in service and lived under better housing conditions. She has had her own house (a council house) for the last 30 years and has enjoyed up to date plumbing. There has been no overcrowding.

Occupation

The patient has done domestic type work all her life. As a girl and young woman, she was in service, after which she spent two years as a hospital cleaner. Following this, she married and has done housework ever since. She is a keen gardener.

Family history

The patient's mother died of cancer of the uterus at the age of 79. Two of the patient's sisters aged 66 and 52 have had a breast removed on account of cancer. There is no history of skin trouble or allergic illness in the family.

History of lesion

The patient had a 'mole' in the left groin for many years. Ten years ago, a black lump appeared, about as big as a walnut. This lump grew slowly and finally ulcerated, six months prior to excision. The patient thinks that she had a cyst removed from the groin 25 years ago, but a careful

search of hospital records has failed to show any trace of this. The presence of a previous mole is undoubted - but the question of the cyst operation cannot be resolved by the patient, or by any existing hospital record.

Microscopic appearances

"A well differentiated keratinising squamous carcinoma showing comparatively shallow penetration."

Condition of skin

The patient's skin is normal for her age. It is slightly oily, well pigmented and shows a few senile keratoses on the neck. The forearms are freckled. Soap powders irritate her skin and she therefore does not use these.

Discussion

This cancer appears to have arisen in a pigmented naevus. Whether she had an operation for a cyst at the same site 25 years ago is a question on which a decision has not been possible in spite of careful search of hospital records. The patient's memory on the site of the cyst is vague. Against the forementioned operation is the fact that when she had the cancer excised the surgeon at this time made no note of previous operation in the history, neither did he notice a previous scar. The opinion of this surgeon is that he would probably have noticed a previous scar at the site if it had been present. It is not therefore possible to know accurately if there was previous trauma (in this case, operative incision) at the site of the cancer, which may have caused malignant change in the naevus. It is, however, clear that the cancer developed in association with the naevus.

Female. Date of Birth 14.4.89. Age at lesion 62. F8

General

This patient, who comes from an upper middle class family, has lived in an environment which by contemporary standards has always been good. The lesion was situated on her left cheek at the exact point where her spectacle frames rest.

Housing

I cannot do better than to quote from a letter which the patient wrote to me. "I have done my best with your questionnaire but the housing form defeated me. My family moved a good deal, and I cannot possibly remember the exact number of rooms in each house; but perhaps what I have written may give the pointers which you want. I was born in Clifton, Bristol and lived there with my family until 1908, attending day schools; first St.Helen's School (private) and then Clifton High School, (independent). We lived in various Clifton family houses, where there was ample space, dining room, drawing room, study, schoolroom, nursery, etc. There were all modern conveniences according to the time. I was resident at St. Hugh's College, Oxford, from 1908-1911, returning home for the vacations. From 1911 I was resident in various independent boarding schools, returning home for holidays.

In 1917 the family moved to a family house in Devon. In 1917 I became Head Mistress of St.Clare, Penzance, resident, and in 1936 Head Mistress of Danesfield, Walton-on-Thames, also resident. When the War made conditions impossible for keeping on that school I joined the staff at St. Swithun's School, Winchester, at first non-resident, and then resident in one of the boarding houses where all appointments were very modern. In 1949 I retired and lived in a modernised cottage at Cheriton (Hants) where there

was a bathroom with water from a bore pumped by an automatic electric pump, and an Elsan closet. In December last I moved here."

This environment seems always to have been of good standard.

Occupation

From school, the patient went to College for 3 years, after which she became a school mistress for 38 years, until her retiral in 1949.

Family History

No relatives have suffered from cancer and there is no family history of skin disease or allergy.

History of lesion

In the Autumn of 1950, the patient noted a pimple which afterwards became a lump, situated on the left cheek. This lesion became harder and grew in size until about March 1951. From this time on, it did not grow larger, but broke down and discharged slightly. On 4.6.51 the lesion was excised. This lesion was situated on the cheek at the exact point of contact of her spectacle frames on her cheek. In 1949, the patient had a swelling which began similarly and which was situated in exactly the same spot, underneath the right eye. (The small scars in each case show the spots, and they are alike and correspond to the point of contact of the spectacle frame). This earlier lesion under the right eye was excised by a surgeon in Winchester and following an enquiry by me, he was kind enough to reply as follows:- "I am very sorry but I am afraid I cannot be of much help to you in the matter of the lesion on the right side of this patient's face. It appeared to be a simple mole and was not sent for section. I think it is possible that it might have been a basal cell carcinoma, but I cannot believe that it was an epithelioma even in its early stage."

The similarity between these two occurrences which happened within ten months of one another may be more than coincidental, though in view of the apparent simplicity of the lesion under the right eye, there may be no connection.

Microscopic appearances

The excised specimen is reported to be "a squamous epithelioma, poorly keratinizing".

Condition of skin

The patient's skin is normal for her age, rather inelastic, of normal thickness, tending to be dry, and fair in colour. On her face she shows some freckles and a few dilated veins. Two small scars are present at the sites of excision of the lesions on her cheeks. The patient suffers from slight submammary intertrigo in hot weather.

Discussion

In view of the lesions developing on each side at the point of contact of her spectacle frames, it was thought worth while to investigate the types of frames which had been worn. The frames have been as follows:-

i) Gold frames (rolled gold)

ii) Pince-nez - these spectacles, which were still in the patient's possession, but had not been worn for about 25 years, did not touch the cheek.

iii) Imitation tortoiseshell. These frames were worn for about 15 years, together with a rimless pair.

iv) Rimless - the glass of the lens being in contact with the cheek.

v) Flesh coloured plastic. These frames were in use for a period of about ten years, prior to development of the cancer.

F8

The imitation tortoiseshell and the flesh colour plastic spectacle frames are different forms of cellulose - and in common with other plastics may have contained traces of plasticisers. It is not possible to be more specific than this without tracing the frames to their source. This has proved to be impossible, in spite of contacting the optician by whom the spectacles were provided.

Downing (1952) says "Minute repeated injuries may result in the appearance of epitheliomas of the skin. I think the commonest evidence of this occurrence in dermatologists offices is the large number of epitheliomas seen on the bridge of the nose and behind the ears, caused by the constant wearing of eye glasses." (Case M10 may also be due in part to trauma from eye glasses).

It may be that chalk accumulated at the point of contact of the frames with the face. Another case (F13) aoccurred in a schoolmistress who handled chalk.

Of these possibilities, I think that the spectacle frame is the more likely, both as a physical irritant (the lesion was at the exact point of contact of the frame) and possibly as a chemical one.

Female. Date of Birth 31.7.82. Age at lesion 70. F13

General

The findings in this case, from an environmental viewpoint, are that the environment has probably not contributed by any of the known environmental factors towards the production of this skin cancer.

Housing

The patient has lived all her life in the country with the exception of a short period of less than four years, aged 14-18, when she was a pupil teacher and lived in a suburban area. She has never lived in overcrowded houses. Up till the age of 55, and with the exception of her short suburban stay, she has lived in a house with outdoor sanitation, no piped water, no bath and no means of providing easily hot water. Since the age of 55, she has lived under better conditions and sanitation is indoor, water is piped to the house and easily heated, and a bath is available.

Occupation

At the age of 13½, the patient left school and began study as a pupil teacher. In four years she became a fully qualified teacher and was the sole teacher in two different country schools for a period of 37 years. Then, at the age of 57, she married and has been a housewife since. Her occupation has been almost always indoors. Chalk (she only used white chalk) has been the only material handled. She is right handed, and undoubtedly the right hand would tend to become contaminated by the chalk. The situation of the cancer on the upper part of the hand and at a site of possible contact with a stick of chalk, may suggest that this chalk may be a possible factor in the aetiology of the condition.

F13

Family history

Apart from a brother who died aged 67 from cancer of the lung, there is no history of cancer or skin disease in the family. 'Nervous trouble' which the patient suffers from was also experienced by her father.

History of lesion

Prior to Christmas of 1952, the patient noted no difference in the area on which the lesion developed when compared with the surrounding skin. It should be mentioned briefly here (more fully below) that there were skin changes present in the hands in association with rheumatoid arthritis.

There is no history of injury. A painless 'scar' was first noted "like a pimple or a wart". This became larger, and when it reached ¼" in diameter, the patient saw her doctor and the lesion was excised in August, 1953.

Microscopic appearances.

"The lesion is a squamous epithelioma. Penetration is shallow."

Condition of skin

The skin of the hands shows changes which are secondary to rheumatoid arthritis. The rheumatoid arthritis began six years prior to the appearance of the squamous epithelioma. The skin changes are a general thinning of the skin over the hands and fingers, with a shiny glazed appearance of the skin, particularly of the fingers. The circulation in this skin is less good than that in the rest of the skin. The rheumatoid arthritis is of moderate degree - the fingers can all move, but not through a full range. Ulnar deviation of the hand is evident and there is swelling around all the joints.

On the forearms, the skin is freckled and has a few tiny red spots (? Campbell de Morgan spots). The unexposed skin is normal for age, inelastic,

neither oily nor dry, and fair in colour. The exposed skin is slightly pigmented. There is no history of skin disease or burns.

Discussion

This patient has not at any time come in contact with known carcinogens. She has, however, for 37 years as a schoolmistress handled chalk in the course of her duties. White chalk* only was used. Also, she has suffered from rheumatoid arthritis for 6 years prior to the onset of the squamous carcinoma. No treatment has been given for the rheumatoid arthritis as she has never consulted a doctor about it and has accepted it as 'rheumatics'.

It may be that the skin atrophy (and interference with normal growth of skin) which is a part of the rheumatoid arthritis has some aetiological connection with the appearance of this lesion. Any interference with normal growth is known to be a possible factor in carcinogenesis (see Part I).

It has recently been shown by angiography that in rheumatoid arthritis there is a very great closing down (or loss) of blood vessels in the affected areas. It is probable that the associated skin changes are due to impaired nutrition of the skin consequent upon the poor blood supply. The carcinogenic factor may thus possibly be the interference in normal growth due to poor blood supply.

* White chalk is calcium sulphate (plaster of Paris).

Part III

Conclusions, together with a note on the diagnosis and prevention of occupational skin cancer.

Part III - CONCLUSIONS

1. Average age of onset.
2. Percentage of working life spent outdoors.
3. Site of cancer, with regard to exposed or covered areas.
4. Colour of skin, hair (age 21) and eyes.
5. Degenerative changes in the skin.
6. Family history
    a) of cancer in any form in father, mother, brother, sister
    b) of skin disease in any form
    c) of allergy.
7. General health.
8. Skin cleansers.
9. Housing.
10. Social class.
11. Reaction of skin to sunlight.
12. Traumatic Squamous Cancer of the skin.
13. Aetiology of the cases whose histories appear in Part II.
14. Environment and occupation in the aetiology of the cases.
15. The diagnosis of occupational skin cancer.
16. The prevention of occupational skin cancer.

1. The average age of onset:-

in males was 52.53 years

in females was 63.43 years

in males and females was 56.09 years.

The younger age onset in males is noted.

2. Percentage of working life spent outdoors:-

in males was 48.0%

in females was 5.71%

in males and females was 36.2%

	Males	Females
75% or more outside	3	0
50-75% outside	6	0
Less than 50% outside	6	7

60% of males spent over 50% of their working life outside.

3. Site of the Squamous Cancer, with regard to exposed or covered area:-

	Males	Females	Both
Normally exposed area	86.8%	71.5%	82.6%
Normally covered area	6.6%	28.5%	13.5%
Doubtful	6.6%	-	4.5%

There is a greater number of cancers in exposed areas than in covered areas. In the males, the excess of cancers in exposed areas is greater than in females.

4. Colour of skin, hair (aged 21) and eyes:-

a) Skin

Very fair -	4
Fair	12
Medium fair	2

Medium dark 3

Dark 1

Most of the cases have skin which can be classified as fair or very fair.

b) Hair (aged 21)

Auburn	2
Blonde	1
Light brown	6
Medium Brown	6
Dark Brown	6
Black	1

Most of the cases had brown hair at the age of twenty one.

c) Eye Colour

Brown	6
Blue	16

5. Degenerative changes in the skin

These changes were classified as +++, ++, +, or - .

	Males	Females	Both
+++	2	0	2
++	2	0	2
+	2	1	3
-	9	6	15

Degenerative changes are relatively more common and more severe in the male than in the female cases.

6. Family History

a) Family History of cancer in any form, in father, mother, brother or sister.

	Males	Females	Both
Positive	6	3	9
Negative	9	4*	13

(* Of this number, two had a family history of cancer; one in paternal grandmother, one in an aunt.)

b) Family History of skin disease in any form.

	Males	Females	Both
Positive	4	1	5
Negative	11	6	17

c) Family History of allergy.

	Males	Females	Both
Positive	3	1	4
Negative	12	6	18

7. General Health

	Males	Females	Both
Good	10	4	14
Moderate	5	2	7
Poor	0	1	1

8. Skin Cleansers

The following agents are mentioned as the normal skin cleansers by the patients - some patients mention more than one, and the agents are given in order of number of times mentioned:-

Lifebuoy Bar Soap -	7
Lifebuoy Toilet Soap	7
Palmolive Toilet Soap	5
Yellow Bar Soap	4
Toilet soap (unspecified)	4
Fairy Soap	3
Lux Toilet Soap	1
Baby soap	1
Knights Castille Toilet Soap	1

The top two places are occupied by carbolic soaps. The phenol content may possibly be of significance.

Other agents used as occasional cleansers are as follows:-

Paraffin	3
Petrol	1
Naphthalene	1
"Grease solvent"	1
Tallow	1

The use of hydrocarbons as skin cleaners is, without doubt, an unwise thing. Depending on which hydrocarbon is used, the possible actions on the skin are:-

1. A carcinogen
2. A cocarcinogen (irritant)
3. A sensitizing agent
4. A defatting agent

In this connection, there is a lot of work to be done in educating workpeople in the dangers of improper cleansing agents and in the provision

of good cleansing agents and good facilities such as washrooms, hot water and towels.

9. Housing

The general housing conditions of the cases can be classed as follows:-

	Size in relation to number of occupants. Overcrowded			Sanitation		Bath		Hot water provided easily		Water Piped to house	
	++	+	-	In	Out	Yes	No	Yes	No	Yes	No
Males	1	6	8	4	11	4	11	7	8	14	1
Females	0	2	5	3	4	3	4	3	4	5	2
All	1	8	13	7	15	7	15	10	12	19	3

The picture which emerges is of housing conditions which are not particularly good, especially when viewed from the availability of hot water and baths. While it is not suggested that good personal hygiene cannot be maintained in such conditions, the presence of a bath and adequate hot water makes the whole business much easier - and therefore it is more likely that higher standards will be achieved.

Overcrowding in the above table is not defined in terms of floor area per person. A single + is given if, on room occupancy there are two people per available room (i.e. excluding rooms which cannot be used for living or sleeping). The sign ++ is used if the number is over $2\frac{1}{2}$. Under 2 persons per room is shown as negative. From the table, it will be seen that 13 are classed as negative, 8 as + and 1 as ++.

In terms of social class, the housing conditions indicate that the lower end of the scale is probably more heavily represented than the upper end.

10. Social Class

The following table shows the social class of the patients and the social class of their father, when the patients were aged 5 - 10. The latter grouping is to try to show the social class in childhood, as well as the adult social class to which the patient belongs.

All occupations are classified in accordance with the "Classification of Occupation 1950" ((1951), H.M.S.O. London).

Case No.	Patient aged 5-10 Fathers occupation	Soc. class	Patient's occupation as given	Soc. class	Patient's occupation as ascertained ✱	Soc. class	
M10	Coachman	IV	Book, Stationery & News Stand Trade	II	Paper roundsboy to manager of several station bookstalls (over 53 years) R	II	
M11	Master Mariner	II	Woodworker	III	Always a woodworker, though he started as an apprentice shipwright. Used pitch to line coffins. Domestic carpenter for 36 years R	II	
M12	Chemical Miller	IV	Pavier	IV	Various odd jobs, as roundsman, but mainly a road sweeper. (24 years)	V	
M15	Farm Labourer	V	Paint Sprayer	IV	Stevedore 15 yrs., Cowman 12 yrs., Paintsprayer 5 yrs., other $2\frac{3}{4}$ yrs.	IV	
M16	Labourer	V	Labourer	V	Tar distillery labourer 4 yrs., Plasterers labourer 3 yrs., Army $5\frac{1}{2}$ yrs., (R.A.Gunner)	V	
M19	Sailmaker	III	Old age pensioner	-	Telephone Operator 3 yrs., Seaman 1st Mate $27\frac{1}{2}$ yrs., Poultry and strawberry farmer 18 yrs., Boatman $6\frac{1}{2}$ yrs., Retired 7 yrs.	III	
M23	Brickmaker Straw hat maker	IV	Retired	-	R.N.Seaman to submarine coxswain 20 yrs. Coastwatcher & Customs Waterguard 29 years.	III	
M24	Farm carter & Royal Marine	IV	Labourer	V	Gardener 3 yrs., Houseboy 1, Army $8\frac{1}{2}$ yrs., Labourer $1\frac{1}{2}$ yrs., Army 6 yrs., Lagger 5 yrs., Electrician's Mate 6 yrs.	V	
M29	Joiner	III	Joiner	III	Labourer $2\frac{3}{4}$ yrs., Joiner 28 yrs.	III	
M30	Shipwright	III	Machinist	III	Machinist, turning metals 30 yrs.	III	

Case No.	Patient aged 5-10 Fathers Occupation	Soc. Class	Patient's occupation as given	Soc. Class	Patient's occupation as ascertained*	Soc. Class	
M33	Engine Driver	III	Retired woodcutter machinist	-	Cycle repairer 6 yrs., woodworking machinist 38 yrs.	III	
M39	Horse Groom	IV	Boilermaker	III	Boilermaker 48 years	III	
M41	Master Mariner	II	Representative	III	Office work 2½ yrs., Sales representative tar & bitumen trade 30 yrs.	III	
M43	Retired (Retired Merchant)	- I	Retired	-	Worked all his life in banking, in various jobs over 39 years.	II	Father was a wealthy retired merchant.
M44	Coachman	IV	Window dresser and driver	IV	Works for wine and spirit merchants - cellarman 2 yrs., storeman 3 yrs., delivery 4½ yrs., window-dress and delivery 15 yrs. Hobby - boats	IV	
F2	Engineer on boats	III	Housewife Council Clerk		Draper shop Asst. 2½ yrs., Florist Asst. 10 yrs., Housewife 45 yrs.	III	
F3	Seaman	III	Housewife Docker		Laundry worker 1, Housewife and housework 42 yrs.	III	
F4	Secretary of an Agricultural Soc.	III	Domestic duties (Single)		Housework, 23 yrs.	IV	
F6	Coalminer	III	Housewife (Agricultural labourer)		Chocolate packer ¼ yr., laundry worker 5½ yrs., Housewife 15 yrs.	V	
F7	Farm Carter	IV	Housewife Labourer		Domestic work 12 yrs., hospital cleaner 2 yrs., Housewife 30 yrs.	V	Father was "with horses all his life"
F8	Secretary to school & School Governors	III	Retired Schoolmistress (Single)		Schoolmistress 38 yrs.	II	
F13	Carpenter	III	Retired Schoolmistress ex Naval P.O.		Schoolmistress 41 yrs., Housewife 16 yrs.	II	

* For full details, see under Occupation in case histories. R = retired.

i) Social class by father's occupation, patient aged 5-10.

	I	II	III	IV	V
Males	1	2	4	6	2
Females	-	-	6	1	-
Both	1	2	10	7	2

ii) Social class by patient's occupation as given.

	I	II	III	IV	V	Retired
Males	-	1	5	3	2	4

Females. As married females take their social class from their husband, it is not possible to classify social class on occupation as given.

iii) Social class by occupation, as ascertained

	I	II	III	IV	V
Males	-	3	7	2	3
Females	-	2	2	1	2
Both	-	5	9	3	5

iv) Social class by father's occupation (1/3) and patient's occupation as ascertained (2/3).

This is an attempt to summarize the social class of the individual throughout his life. Although the childhood period is shorter in time, its effects in the period of formative growth are greater and the proportion of 1/3 is therefore allotted.

The social class distribution is therefore:-

	I	II	III	IV	V
Males	-	2 2/3	6	3 1/3	2 2/3
Females	1/3	1 1/3	3 1/3	1	1 1/3
Both	1/3	4	9 1/3	4 1/3	4

The trend in males is towards the lower social classes and in the combined male and female total, the number in I and II is $4\frac{1}{3}$, whereas

the number in IV and V is 8 1/3. The males particularly show a strong trend to the lower social classes.

This would tend to confirm the findings of Ryle & Russell (1947) and of Stocks (1938) which are mentioned in Part I.

11. Reaction of the skin to sunlight.

Does the skin form pigment easily?

	Male	Female	Both
Yes	4	4	8
No	11	3	14

Amongst the men, there is a greater number of cases who cannot form pigment easily.

12. Traumatic Squamous Cancer of the skin.

The relationship between trauma and cancer has been discussed in Part I in a very general way. The observed connection between burns, scars and cancer is well known, though much difference of opinion exists as to whether trauma is the carcinogen or the cocarcinogen in such cases. It would appear to me to be able to function in both capacities. The localization of tumours in experimental animals by wounding is well known and has been referred to in Part I. Here the trauma is thought to act as a cocarcinogen. If trauma is presumed to be a causal factor in the production of cancer, the following criteria, which were first stated by Ewing (1935), would require to be demonstrated:-

1. The authenticity and the adequacy of the trauma.
2. The previous integrity of the injured part.
3. The tumour arises at the point of injury.
4. A reasonable time limit must be observed between the injury and the appearance of the tumour.

5. The positive diagnosis of the presence and nature of the tumour is essential.

(These criteria apply to all cases of supposed traumatic cancer and not solely to skin cases.)

In the cases which I have seen, three appear to fulfill Ewing's criteria, Nos. M23, M24 and F4; and one case shows localization of cancer at site of previous injury - M16. For full details of their histories, reference should be made to Part II. Their histories are shown briefly in the table below, set out under five headings to correspond with Ewing's criteria.

Case No.	Nature of trauma	Any previous lesion at site	Did tumour arise at point of injury	Time elapsing from trauma to histological diagnosis	Positive histological diagnosis	Comments
M23	Prick on cheek while picking cob nuts	No	Yes	6/52	Squamous Carcinoma	
M24	Prick by a needle while sewing asbestos cloth	No	Yes	8/52	Squamous Carcinoma	
F4	Struck back of hand on a chimney projection, sustaining a soot contaminated wound.	No	Yes	6/52	Epithelioma, Grade 2.	History of swelling 3/52 after injury
M16	Contused wound of shin due to an oil pipe. Fuel oil contaminated the wound.	No	Yes	4 yrs	Epithelioma	Patient worked in a tar distillery. This may be a case of localization of tumour at site of previous scar.

It is necessary to accept the patients statements for the first four of the five criteria, but as far as possible these statements have been cross checked for time and other details with the hospital record. An attempt was also made to shake the patients in their stories, bearing in mind traumatic determinism - that is that after the lesion has appeared, the patient will come up with a story of injury. In each of these three cases, the patient was quite sure that the injury was causally connected with the lesion. It is impossible to be absolutely certain in a strictly scientific sense when reliance has to be placed on a story told some time after events have taken place, but, in spite of checking and because of trying to shake the patients in their stories and of being unable to do this, I believe that these cases are causally related to the trauma described. It is necessary to be somewhat sceptical about such stories in cancer cases, and I have therefore given my own views as fully as would seem necessary in order to show that while I share the scepticism and have seen many cases of undoubted traumatic determinism, that in my view these three cases are cases of traumatic cancer.

The time interval in these cases is of interest - six weeks in two and eight weeks in one until histological diagnosis was made. The lesion was noted in three weeks in one case and had been present in each of the other cases for about two weeks before removal and section. The close correlation of the three times and the short time interval from trauma to cancer seems to me to be of importance.

One more case shows trauma in the form of low grade chronic irritation by spectacle frames as the possible cause - i.e. F8. In this case the patient sustained a cancer of one cheek, and a lesion on the other cheek (which was not examined histologically) within ten months of each other.

Both of these lesions were at the exact point of contact of the spectacle frame with the cheek.

Case No. M10 also shows a cancer of the cheek at the site of contact of spectacle frames, although in this case there is also a chronic eczema.

13. Aetiology of the cases investigated and written up in Part II.

A synoptic presentation of the aetiological factors in the cases which were investigated appears below. It will be seen from this that in six of the cases the aetiology is unknown. This does not mean that in the remainder of the cases (16 = 72.8%) that the aetiology is known with certainty. However, in all cases which are not labelled as unknown, possible aetiological factors can be suggested, and in some it is my opinion that aetiology is not in any way obscure. By way of classification with regard to the aetiology being known, a system of ++'s was awarded as follows:-

++++ Practically certain

+++ Very probable

++ Probable

+ Possible

- Unknown.

Rating in + or -	No. and age at lesion	Aetiology.
++	M10 Aged 65	This patient has a family history of allergic illness. Following on a gross psychological shock, the patient developed generalized eczema which became chronic. Seven years later he developed a cancer of the face at a point where his spectacle frames sat on his cheek. (See F8)
++	M11 Aged 54	This man, a carpenter for most of his life, had a definite exposure to pitch for 2 years (aged 14-16) while coffin-making. He worked in a very sunny area (California and Nevada) aged 30-32, and spent 50% of his working life out of doors.
++++	M12 Aged 50	Four surface cancers have been diagnosed in this man: three clinically and one by biopsy. His occupation for most of his life was a street sweeper in contact with road dust and outside in all weathers. His exposed skin shows classical precancerous degenerative changes.
-	M15 Aged 39	Unknown
++++	M16 Aged 29	This cancer appears to have a definite occupational cause. The patient handled pitch in a tar distillery aged 14-17 and had an injury which was contaminated by mineral oil aged 25. He had a swelling at this site 3/52 later which subsided. 4 years after this, his cancer appeared at the site.
++++	M19 Aged 76	This seaman who has spent almost 100% of his working life out of doors and has on occasion used pitch and tar and Stockholm (wood) tar shows typical precancerous changes (shagreen skin) in a very fair skin (associated with red hair). Occupation and lack of skin pigment would seem to be the main factors in this case.
+++	M23 Aged 64	As a Customs Waterguard (coastwatcher) this man was outside in all weathers for 25 years. He received a prick on the cheek while picking cob nuts and six weeks later had an epithelioma at this site.
+++	M24 Aged 41	There is a clear history of trauma (a prick by a needle), followed within less than two months by the appearance of a "wart" (which proved to be an epithelioma) at the site of injury. The needle was sewing asbestos cloth.
-	M29 Aged 45	The aetiology is not known. There may possibly be a connection between the 'teak poisoning' (allergic dermatitis) and the cancer, but the interval of 22 years seems long. No other factor can be suggested.
++	M30 Aged 44	Naevus present since birth. This naevus (wart) was occasionally cut while shaving. Finally grew rapidly. Since aged 16, patient has been heavily exposed to mineral oil - greases and cutting oil - and since that age has suffered from a chronic eczema

Rating in + or -	No. and age at lesion	Aetiology.
++++	M33 Aged 67 (or less	Malignant change in a chronic varicose ulcer. Occupation may have aggravated the condition by preventing healing of the varicose ulcer: his work as a woodworking machinist involved continuous and rather immobile standing.
+++	M39 Aged 51	Eczema of face aged 9. Lasted 1 year. Lupus vulgaris 5 years prior to development of cancer. His work as a boiler-maker brought him into contact with the soot ash and clinker in railway engine (coalfired) fireboxes.
+++	M41 Aged 49	Intermittent contact with pitch, tar and bitumen (asphalt) for 27 years, with closer contact during 3 years at end of war. Hobby is repairing and maintaining his car - and he gets his hands covered with oil. Cleanses hands by washing in paraffin.
-	M43 Aged 63	Unknown.
++	M44 Aged 49	This man who has worked in the wine and spirits trade, spends most of his spare time sailing in his motor boat or working on it. In this connection he has been exposed to tar (sufficiently to suffer from tar erythema) and spends a lot of time outdoors in the sun and weather. His forearms show degenerative changes of 'sailor skin'.
-	F2 Aged 66	Unknown
-	F3 Aged 51	Unknown
+++	F4 Aged 63	While doing housework, at which she had worked all her life, the patient struck her hand on a chimney projection and sustained a soot contaminated wound. Six weeks later, a swelling appeared which was an epithelioma.
-	F6 Aged 28	The youthfulness of the patient at the time of the lesion would suggest an aetiology which could be demonstrated. In this case, the various possible factors cannot satisfactorily be sorted out and the reader is referred to the full case history. Unknown.
+	F7 Aged 61	An ulcer in a pigmented area - ? previous naevus, with malignant change.
++	F8 Aged 62	Probably due to continued irritation from spectacle frames (See M10)
+	F13 Aged 70	Possibly connected with cutaneous atrophy associated with rheumatoid arthritis, or with schoolroom chalk.

The aetiology of these cases may be classed thus:-

Aetiology known?		Males	Females	All
Practically certain	++++	4	0	4
Very probable	+++	4	1	5
Probable	++	4	1	5
Possible	+	0	2	2
Unknown	-	3	3	6
	Total	15	7	22

It will be seen that most of the male cases fall in the top three groups, and that only one fifth of these cases are classified as unknown. This distribution of cases is reversed in the female cases, most of which fall in the last two groups - over half being in the last two groups. It has been shown that on close investigation of proved squamous cancer cases, that in 14 out of 22 cases (63.8%) the aetiology could be classified as probable, very probable or practically certain. The difference in male and female cases in so small a sample cannot be rated accurately, but the trend which shows the largest number of the male cases falling in the probable or better classes and the smallest number of female cases in the same categories should be noted.

Another point for comment is the number of cases in which it is possible to make a reasonable deduction, following investigation, concerning the aetiology. Particularly in the male cases, I would suggest that large scale investigation might yield worth while results.

The large proportion of male cases about which a deduction can be made with regard to aetiology is certainly unusual in a group of cancer cases.

14. Environment and occupation in aetiology of the cases.

Case No.	Have known environmental factors contributed to this squamous cancer?	Reasons and Remarks	Are there possible other factors in this squamous epithelioma?	Reasons and Remarks	Was environmental or other factor a contributor to aetiology (State what factor and reasons)
M10	No	-	Yes	1. Chronic eczema 2. ? Irritation from spectacle frames.	Other factors appear to be important.
M11	Possibly	Handled pitch briefly when young.	No	-	Environmental, possibly.
M12	Yes	Road sweeper and tar worker. Has 'shagreen skin' in exposed areas and has had four surface cancers.	No	-	Environmental.
M15	No	-	No	-	Not known
M16	Yes	Pitch and tar handler in a tar distillery. Also, handled mineral oil. Patient was aged 28 when squamous cancer developed.	No	-	Environmental.
M19	Yes	A sailor with typical precancerous changes in his exposed skin ("sailor skin")	Yes	Poor resistance to sunlight, due to lack of function of pigment in skin (he was red haired)	Environmental Constitutional factor.
M23	Yes	Worked for 25 yrs in all weathers. History of injury preceeding development of the squamous cancer.	No	-	Environmental, probably.
M24	Yes	There is a clear history of trauma by pricking the skin with a needle. The cancer arose within a month of this happening.	Yes	The prick with the needle arose while sewing asbestos cloth. There is a remote possibility of implantation of asbestos.	Environmental

Case No.	Have known environmental factors contributed to this squamous cancer?	Reasons and Remarks	Are there possible other factors in this squamous epithelioma?	Reasons and Remarks	Was environmental or other factors a contributor to aetiology (State what factor and reasons)
M29	Probably not	There may be a connection between the incidence of previous allergic dermatitis due to teak and the subsequent cancer.	No	-	Not known
M30	Possibly	Mineral oil exposure +++ at work.	Yes	Chronic varicose eczema.	Both environmental factors (oil) and constitutional factors (chronic eczema) may contribute in this case.
M33	Yes	Chronic varicose ulcer (following trauma originally).	No	-	Standing still at work may have tended to prolong varicose ulceration.
M39	Possibly	His work as a boilermaker was in the firebox of railway locomotives, which are coal fired and produce soot.	Yes	History of eczema, aged 9, for 1 yr. Lupus vulgaris at site of cancer, present 5 years.	
M41	Yes	He has worked in intermittent slight contact with pitch tar and asphalt for 27 yrs. Also, he has as his hobby car work and gets oil ++ on hands. This he cleans with paraffin.	No	-	Environmental.
M43	No	-	No	-	Not known
M44	Possibly	He has had tar erythema while tarring his boat, and he spends a lot of his spare time out of doors with the boat	No	-	Tar possibly played a part in the aetiology of this cancer. (Hobby of boating).

Case No.	Have known environmental factors contributed to this squamous cancer?	Reasons and Remarks	Are there possible other factors in this squamous epithelioma?	Reasons and Remarks	Was environmental or other factor a contributor to aetiology (State what factor and reasons)
F2	No	-	No	-	-
F3	No	-	No	-	Environment shows nil discoverable.
F4	Yes	Cancer was noted 3/52 following an injury while clearing soot from the chimney.	No	-	Environmental
F6	Yes	Lack of cleanliness is an outstanding feature of this case - both in person, in clothes and in home.	Yes	Continual drug taking for asthma	Environmental probably. Drugs for asthma is another possibility.
F7	No	-	Yes	? previous naevus (pigmented)	-
F8	No	-	Yes	i) irritation from spectacle frames. ii) ? schoolroom chalk.	? chronic irritation from spectacle frames.
F13	No	-	Yes	i)? schoolroom chalk. ii)? any association with rheumatoid arthritis or skin changes associated with this disease.	? other factor.

In the preceeding table, the cases are placed in four classes, with the following result:-

	Male	Female	All
Environment and occupation directly concerned	6	1	7
" " " indirectly "	1	0	1
" " " possibly "	4	1	5
" " " not "	4	5	9*

The majority of cases thus fall in categories where environment and occupation may have contributed to the causation of their cancers. This finding may help to support the argument, advanced on the work of others in Part I, that squamous cancers are more likely to have environmental and occupational factors in their aetiology than basal cancers.

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* Out of this, five have no known or possible suggested aetiology. In the remaining four cases, the aetiology is known but is not connected with environment or occupation.

15. The Diagnosis of Occupational Skin Cancer.

i) Case history

In order to ascribe a skin cancer to causes arising out of occupation, it is necessary to examine in some detail the present and past occupations of the person who is suffering from the cancer. A careful history should include not only the job-title, but some idea of what the work performed actually was in each job. Any substances which came into contact with the skin should also be noted, together with duration of contact.

The general environmental factors such as housing etc., should also be investigated, and hobbies (vide supra) should be enquired into.

From such an occupational and environmental history, it should be possible to arrive at some conclusion about the likelihood or otherwise of skin cancers from known causes. From unknown causes it may give a clue as to aetiology, in that some new cause may be suspected.

ii) Association with other skin diseases or skin changes

This association may favour the occupational origin of the cancer, as in "shagreen" skin or may suggest a non-occupational cause as in xeroderma pigmentosum. Full examination of the patient together with a careful skin examination should sort out such relationships.

iii) Precocious appearance of skin cancer

The likelihood of a cancer being industrial in origin may be heightened if a cancer appears in an individual who is below the normal cancer age, and who has no history of chronic skin disease. Potts in 1775 noted scrotal cancer in "climbing boys" who were aged 13-15. Jenkins (1948) in his monograph "Dermatoses among Gas and Tar Workers" noted the average age of Tar Works' employees suffering from epitheliomata as 49, the youngest

being a pitch worker of 27. A colour plate of a man suffering from an epithelioma due to tar is shown in the Atlas of Skin Diseases by Semon & Moritz (1943). His age is given as 41.

iv) Type of Skin Cancer

Out of a total of 4,632 cases of cutaneous cancer in 3,530 persons which were notified to H.M. Chief Inspector of Factories between the years of 1920 and 1949, 105 were rodent ulcers - i.e. of 4,632 cases 1.8% were rodent ulcers. It will thus be noted that industrially caused cancers of the skin are much more likely to be squamous epitheliomata.

It would also seem likely on theoretical grounds that skin irritants and carcinogens applied externally would tend more to affect the superficial than the deep cells, thus producing epidermoid cancers in greater numbers than basal cancers (rodent ulcers).

Of all cases of fatal skin tumours recorded by the Registrar General between 1911 and 1945 (a total of 27,215) just over 6% were due to sarcoma or melanoma. Of the cases remaining (25,545 = 94% approx.), 77% were cases of squamous epithelioma and 23% were rodent ulcers.

Type of Cancer	Percentages of All skin cancer deaths 1911-1945	All notified skin cancers 1920-1949
Squamous Epithelioma	72	98.2
Rodent Ulcer	22	1.8
Other	6	0

As an extension of the view that industrially notified cancers are mainly squamous epitheliomata, and that environmental factors may be the main causal agent of such cancers, it may be reasonable to draw two conclusions:-

1) That cases of squamous epithelioma in general will tend to have more in the way of environmental aetiology (whether arising from the industrial or other environment) than other forms of skin cancer.

2) That in view of the extremely small percentage (1.8%) of rodent ulcers in the 'notified' series, that the environment is not very important as a causal agent in rodent ulcers in factories.

For these reasons, the environmental investigations made have been confined to cases of squamous cell cancer. It was also felt that histological confirmation was a more reliable basis for work than clinical impressions with regard to the type of cancer (see Part II Selection of Cases).

A survey of cancer incidence in the population of Iowa (Haenszell, W. et al 1956) showed the distribution of all skin cancer cases noted as follows:-

	Percentage				
All types	Basal & Baso squamous cell cancers	Squamous cell cancers	Melanoma	Epithelial cancer	Other types
1,067	46.8	38.4	5.2	7.1	2.5

These cases were noted in a cancer survey which tried to elicit information about all cancer cases in the area as early as possible in the illness, by collecting cases from all sources (hospitals, clinics, family doctors, etc.) within the State.

When these figures of incidence are compared with deaths (the previous table from the Registrar General) it will be seen that the number of squamous cell cancers in the Iowa series is approximately half the number of the skin cancer deaths; and the number of basal cell cancers in the Iowa series is approximately double the number in the skin cancer deaths.

This difference is interesting, and while the two series are not directly comparable as it probably reflects a difference in mortality in these two different types of cancer, it also seems to show up the fallacies which so easily arise by lumping all skin cancer under one heading. It is clear from the evidence of the pathologist, and from the difference in clinical picture, and from the occupational incidence amongst many other reasons, that these two forms of skin cancer are separate and distinct and should be treated separately. The differences between cancers of the cervix and body of the uterus are well recognized - and no discussion is now attempted on 'cancer of the uterus' without breaking these cancers down into the two widely differing groups. A similar breakdown is required in skin cancer and before progress can be made in the occupational classification of skin cancer in large numbers, it will be necessary to obtain the co-operation of the Registrar General in producing analyses which show not only present occupation, but previous occupations, and which show the precise type of cancer. Cases which have been confirmed by microscopic examination of the skin should be separated from cases diagnosed clinically.

The Registrar General in analysing the 1951 census is still using 'Skin Cancer' as a heading in the occupational volume, and in the Cancer Registry, occupations are not being recorded.[=] This seems a pity.

The Iowa survey shows also the difference in distribution by site of squamous and basal cell cancers under the following headings:-

Site	Basal and baso-squamous cell cancers	Squamous cell cancers
Face, head and neck	55.8%	33.5%
Other and unspecified	24.7%	47.1%

= Personal communication.

This confirms the different behaviour of the two forms of cancer by showing their different distribution.

This table should also be compared with the tables under Section vii below, Site of the Cancer.

v) Multiplicity of Surface Cancers

It is unlikely that any individual will develop more than one surface cancer without there being some aetiological factor which should become apparent on investigation. Case No. M12 is a good example of this.

Certain skin diseases may eventually lead to several cancers, and in these cases the underlying disease should be obvious to the examiner.

In other cases, the cause of the multiple cancers will lie in environmental factors - and particularly in occupational exposure. Jenkins (1948) quotes the case of one pitch worker who at the age of 36, with 20 years service, had suffered from 9 previous scrotal lesions (either papillomata or carcinomata) in addition to the epithelioma with which he now presented.

In the absence of obvious non occupational skin disease it would, therefore, be wise to suspect environment and in particular occupation, as an aetiological factor in any case of multiple surface cancers ('surface' cancers include orificial cancers at muco-cutaneous junctions such as lip, nose, etc.)

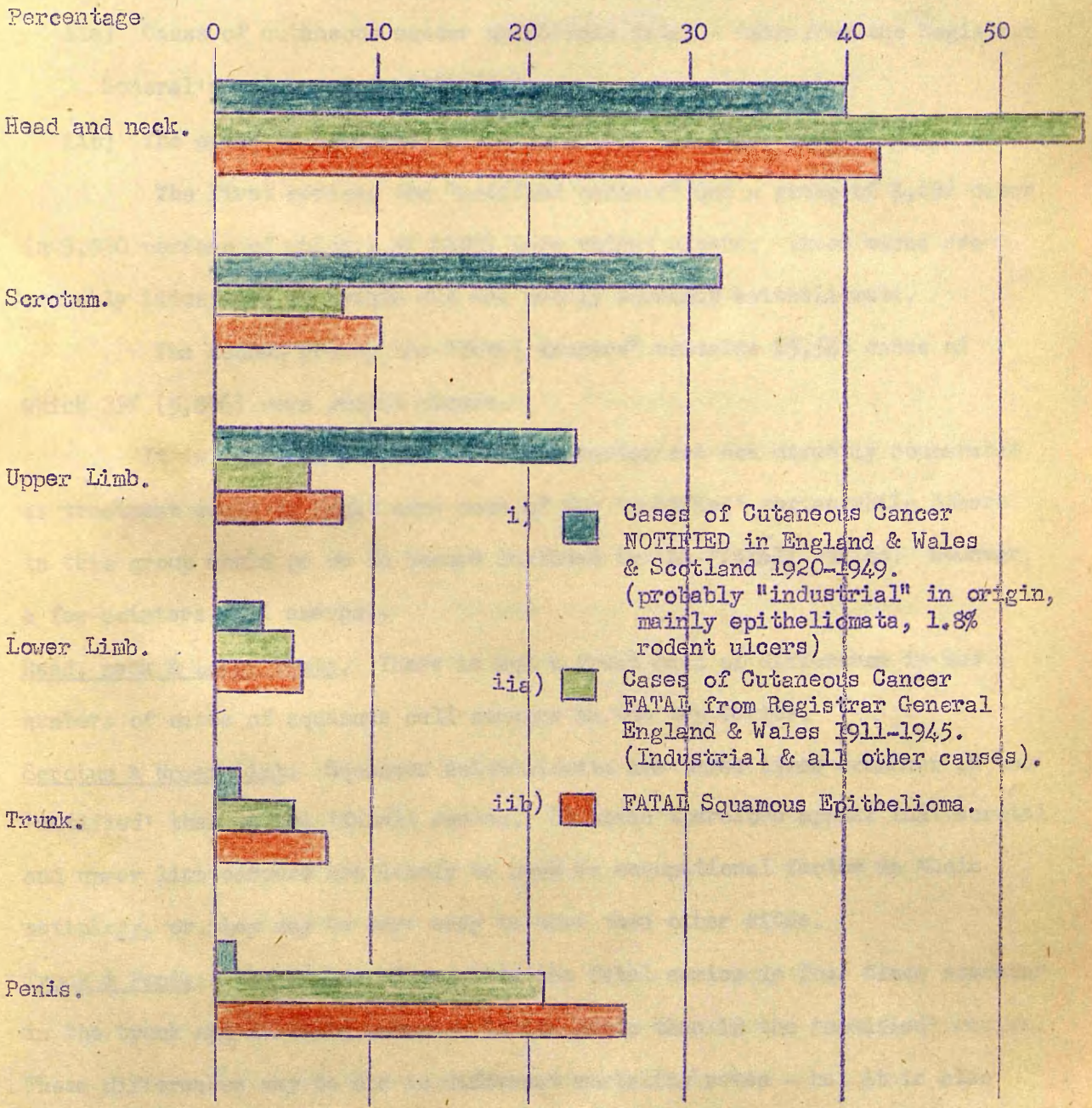
vi) Sex

It is probable that more occupational cancers will occur in males than in females.

vii) Site of the Cancer

The following figure has been constructed from figures which have been collected by Henry (1950).

Cutaneous Cancer: a Comparison by areas affected of cases notified by industry and cases notified at death to the Registrar General.



In 1% of Fatal Cases, the site was not stated.

This figure shows the percentage of cancer by various sites in two series.

i) Cases of cutaneous cancer which were notified in England, Wales and Scotland in the years 1920 - 1949.

iia) Cases of cutaneous cancer which were fatal - taken from the Registrar General's returns from 1911-1945.

iib) The cases of squamous epithelioma from the above series.

The first series, the "notified cancers" was a group of 4,632 cases in 3,530 persons of which 1.8% (103) were rodent ulcers. These cases are probably industrial in origin and are mainly squamous epitheliomata.

The second group, the "fatal cancers" contains 25,545 cases of which 23% (5,896) were rodent ulcers.

It is appreciated that these two series are not directly comparable as treatment would no doubt cure some of the 'notified' series while others in this group would go on to become included in the 'fatal' series. However, a few pointers will emerge:-

Head, neck & Lower Limbs. There is not a great deal of difference in the numbers of cases of squamous cell cancers in the two series.

Scrotum & Upper Limb. Squamous epitheliomata are three times commoner in the 'notified' than in the 'fatal' series. It would therefore appear that scrotal and upper limb cancers are likely to have an occupational factor in their aetiology, or they may be more easy to cure than other sites.

Trunk & Penis. The number of cases in the fatal series is four times commoner in the trunk and 17 times commoner in the penis than in the 'notified' series. These differences may be due to different mortality rates - but it is also possible that occupational factors play a lesser part in the aetiology of

these cancers. If mortality differences exist, why should the limb figures (upper and lower) be so different?

It is interesting to note that scrotal epithelioma is presumed to be industrial in origin by virtue of site alone, as it is 'prescribed' under the National Insurance (Industrial Injuries) Act of 1946; all the other statements of 'prescribed' diseases are in terms of causal agents.

16. The Prevention of Occupational Skin Cancer.

Recognition of the hazard is a primary step in prevention. In view of the relatively long latent period between exposure and the development of skin changes which is common to carcinogens, it is important with regard to new substances and processes to try to predict carcinogenicity in order that precautions shall be adequate. Recognition of a hazard may therefore involve research on a considerable scale or the taking of precautions on suspicion.

The chemical family to which the substance belongs may give a clue in some instances. Undoubtedly the most unfortunate way to recognize any cancer hazard is by the appearance of the disease, as has so often happened in the past.

In the "Outline of Occupational Disease Control through Engineering" (Bulletin No.83, Washington D.C.) the U.S. Department of Labour gives eight methods for the control of industrial health hazards:-

1. Substitution of less toxic material
2. Enclosure of harmful process (with automatic operation)
3. Isolation of the harmful process from the remainder of the plant with special protection for workers necessarily included in the area isolated.

4. Local exhaust ventilation

5. General ventilation

6. The use of wet methods.

7. The use of personal protective devices particularly respiratory protection

8. Decreasing the daily exposure through short work periods.

In principle, the steps which should be taken to deal with a cancer hazard follow the same steps as should be taken to deal with any other toxic hazard. These steps will be commented upon briefly and the special points in dealing with cancer hazards will be noted.

1. Substitution. This is the ideal method of dealing with any toxic hazard because by this method the hazard should cease to exist - i.e. a non-toxic substitute is provided for the toxic material.

2. Enclosure. By this method, the toxic substance is kept enclosed, thus preventing handling. It is not, however, a foolproof method as spills, leaks and other accidents can and do occur. In this way contact with the toxic substance can be made.

3. Protective Clothing. By this means it is hoped that the worker can be protected against the hazard. However, as was pointed out by Sir Thomas Legge, any method over which the worker has no control (i.e. substitution and enclosure) is better than one over which he has control (clothing). It is difficult to remove protective clothing which is heavily contaminated without getting some trace of the offending substance on to the skin.

These methods are mentioned briefly, as they are standard methods of prevention. With regard to skin cancer, certain special considerations apply in addition to the above, or certain general factors require more than

usual stress. These are given in detail below.

i) Education of the worker in the nature of the hazard is important. In this way he can appreciate the need for care in handling in order to prevent skin contact with the offending substance. It is not possible to secure as good co-operation from the worker if he does not understand the need for doing certain things which he may be told to do, or not to do, as the case may be.

It is also important that the worker should be told something of how skin cancers appear in their early stages, so that at the first sign or suggestion of abnormality of any kind he knows to report immediately for medical opinion. In this way, any case which does develop should receive early treatment and thus be cured.

ii) Skin cleansing. If the worker does come into contact with the offending substance, the importance of immediate washing should be pointed out and enforced. It may also be good practice where skin contact is possible but not definite to insist on a shower being taken by each worker on completion of the job or shift. The importance of the provision of good washing facilities is emphasized; no man will wash in an ice cold building in tepid water. Contaminated clothing should be discarded and should not be worn again until it has been laundered. The use of suitable cleansing agents should be checked: it is foolish to allow the skin to be cleansed by any substance which is capable on its own of producing dermatitis or any skin irritation. Too often, solvents are used on the skin and these solvents, although they are not in themselves carcinogens, may hasten the appearance of a cancer by their co-carcinogenic action; or they may produce dermatitis.

iii) Chronic Irritation. There is good evidence to suggest that chronic irritation of one sort or another predisposes to cancer of the skin (see Part I for discussions of this). It is therefore important as part of preventive measures to minimize any factor which may produce skin irritation of any kind.

iv) Selection of Workers.

(a) Age. If workers have to be exposed to a known possibly carcinogenic substance, it would seem advisable to select people whose expectation of life is shorter than the average duration of exposure which is required to produce a cancer. In this way, using older workers, the tragedies of deaths from cancer in young or middle aged workers, or the problems of having to treat cancers should arise with much less frequency.

This method of selection of workers is at present used in the dye industry in relation to the bladder cancer hazard which exists there.

(b) Condition of the skin. A normal skin should be a sine qua non of selection. Any evidence of any skin disease should disqualify. Persons with a history of any chronic or severe skin disease should be rejected. Particular care should also be taken to note the presence of any moles, naevi, etc. at the time of the original examination, in order to provide a base-line for future periodic medical examinations. It should be emphasized that in order to examine any patients skin completely, that it is necessary to have the patient completely naked and in a good light, preferably daylight.

If possible, dark skins should be preferred to fair skins. There is evidence, at any rate in connection with solar skin reactions, that dark skinned races suffer less than fair skinned races. (see Part I).

v) Periodic Medical Examinations. This as a technique of prevention is much less useful than the preplacement examination. At a preplacement medical, the patients can be sorted out into those who are suitable for the job and those who are not. At a subsequent examination, only changes which have occurred in the interval can be noted, and these changes will be relatively few. It should also be noted that in the case of skin cancer, the education of the worker should cause the worker to report at once any change which he notes in the condition of the skin.

With regard to early diagnosis and treatment and maintenance of good morale in jobs of high hazard, there is no doubt that periodic medical examinations are helpful.

vi) Barrier Creams. The use of these substances is based on the "invisible glove" type of propaganda, so dear to the manufacturers of these products. The use of a barrier presupposes contact - and so, as a method of prevention ranks very low. It is doubtful if a complete barrier exists, but there is also no doubt that contact can be reduced by use of appropriate barrier substances. In the prevention of cancer of the skin, their use of necessity indicates that other and better methods of prevention either have not, cannot, or will not be used. As a method of skin cancer prevention, therefore, the use of barrier substances on the skin is a resort of desperation and an unreliable and unsatisfactory method.

vii) Single Contact. It has been shown that a single contact with a carcinogenic substance is sufficient to produce a cancer, provided that a non-specific stimulus is afterwards applied. (See Part I, cocarcinogenesis).

The importance of avoiding contact by appropriate methods is therefore heightened (and the need for avoidance of any form of chronic irritation should be stressed if contact is made with any carcinogenic substance).

The whole of the thinking with regard to cancer prevention in industry should be reorientated towards avoidance of any contact and not as at present in some quarters to minimizing contact, while being prepared to admit some contact. In support of this view, the following extract from an extensive review by Shubik & Sicé (1956) of chemical carcinogens and the testing of substances for carcinogenic action is quoted. "It has not yet been conclusively demonstrated that any preventive measures other than total removal are effective against carcinogenic hazards". Measures designed to cut down the amount and duration of contact should be replaced by measures based on absolute avoidance. The reader is particularly requested to re-read at this point the conclusions in Part I (under cocarcinogenesis) arising out of the concept of a single contact being capable of producing cancer. (See page 36)

It is realised that contact cannot always be avoided absolutely in practice - but there is a great need today to change the type of thinking which presupposes contact as a normally occurring phenomenon. Such contact, in well designed plants, should only occur in emergency - and suitable measures, such as education of the worker, the use of protective clothing and so on should be arranged against the emergency. Prevention of exposure is nowadays, in many cases, a matter of good engineering design of plants in order to enclose dangerous substances and keep these substances away from the worker.

It is still an all too common observation to find a carcinogen which could be enclosed being handled in an open manner, by workers who have little or no idea of the hazard to which they are exposed.

When the hazard has been recognized and a control programme is worked out, the only remaining step is to carry this programme into effect. As it usually involves the spending of money, proper justification for this expenditure should be presented with the control programme. Eckardt (1956) summarizes the position when he says "It is not that industry is reluctant to assume its justified costs in the field of environmental cancer control; it is rather that industry needs to be educated to the nature and extent of the problem and to realistic measures for its control."

Conclusion

The principles on which any attempts to prevent occupational skin cancer are based are neither complex nor new. In order to carry out preventive programmes, the hazard must first be recognized. Sir Thomas Legge laid down in his famous axioms the foundations of a preventive approach to any industrial hazard: these axioms apply as much today as they did over 50 years ago when they were propounded.

A number of additions can be made to ordinary preventive methods in the special instance of skin cancer, and these concern medical examinations with a view to selection of normal skins; education of the worker; skin cleansing; the effect on the skin of non specific chronic irritation and the extreme importance of absolute avoidance of contact in place of minimal contact, together with avoidance of any cause of chronic non specific irritation of the skin.

Lastly, any control programme must be realistic and must be carried out.

Summary

Part I

The history of occupational skin cancer is traced briefly from the first description by Percival Pott in 1775 up till the present time, with mention of the official "prescribing" of the disease. The present state of knowledge regarding the aetiology of squamous cancer as it appears from a survey of the literature, is summarized under various heading with comments.

Chemical Factors — Among chemical factors in the aetiology of squamous skin cancer are the hydrocarbons - polycyclic compounds being the important ones. Well recognized substances are soot, pitch and tar, and mineral oil. Numerous chemically pure hydrocarbons have been described which are carcinogenic to animals. In Great Britain, the Factory Department recognize skin cancer due to soot, pitch and tar, and mineral oil as occupational diseases (since 1907). Arsenic is another chemical cause of skin cancer.

Physical Factors — Physical factors which have produced squamous cancers of the skin are excess heat, excess local cold, x-rays and ionizing radiations, sunlight and ultra-violet light.

Personal Factors — The family history is reviewed. In some animals, familial susceptibility to skin cancer is recognized.

Selection — Selection processes, by which the incidence of skin cancer may be altered in a group - for example by means of preplacement medical examinations, or men only being selected - are examined.

Habits — The importance of personal habits, with particular attention to cleanliness, in preventing skin cancer is shown. The

statistical correlation between the numbers of skin cancers in an occupation and the relative cleanliness of the work is commented on.

Social Class

There is a statistical correlation between mortality from skin cancer and social class.

Previous lesions or diseases

Previous skin lesions, arising from injury and disease, will predispose to squamous skin cancer. Amongst the common predisposing causes are scars (especially burn scars), chronic ulcers and fistulae, congenital skin abnormalities and certain skin diseases. Of the skin diseases lupus vulgaris, lupus erythematosus, psoriasis, leukoplakia, syphilis, xeroderma pigmentosum, various chronic inflammatory dermatoses, neurofibromatosis, leukoderma, melanoderma and scleroderma are all known to be followed in some cases by squamous skin cancer.

Racial differences

Racial differences are noted in the incidence of skin cancer, pigmentation of the skin having some bearing on the protection of the skin against cancer caused by sunlight. There is no doubt that in animals racial difference occur: some strains of mice are skin cancer prone. In man, such differences are more difficult to detect. In Australia, persons of British descent were shown to be more susceptible to skin cancer than persons of Scandinavian or North German ancestry.

Localization of lesions

The lesions of skin cancer tend to localize in particular places, in spite of generalized or widespread carcinogenic stimulation. This has been demonstrated in mice. The tendency for special sites to be affected by skin cancer is well known - for example, the scrotum in industrial skin cancer due to mineral oil.

Sex incidence

Sex incidence shows an excess of squamous skin cancer in males.

Occupation

Occupation is a most important factor in any discussion of squamous skin cancers. The effect of occupation is to bring the person into constant contact with a particular type of environment. The resultant interaction between the person and the environment in the production of skin cancer has been studied in a number of ways: by analysis of notification of skin cancer to H.M. Chief Inspector of Factories; by analyses of hospital series of cases; and in the present study by a detailed investigation into the whole working life of the patient, together with details of other "occupations" such as hobbies. Other environmental factors, varying from housing, general hygiene and the type of environment to which the patient may have been subjected in special circumstances, for example in the Services, are also of importance.

The Mechanism of Cancer Production

The mechanism of cancer production is examined in the literature, with a view to seeking possible clues which could lead to prevention of certain of the skin cancers which are found. The origin of cancer cells appears to be in a growth disorder, probably an inhibition of growth, in previously normal cells. Known carcinogens are examined in the light of these theories.

Cocarcinogenesis

Cocarcinogenesis introduces a most important concept. It has been shown that a single application of a carcinogen is all that is necessary to produce a cancer in experimental animals, provided that it is followed by a cocarcinogenic stimulus. A cocarcinogenic stimulus is one which of itself cannot produce a cancer. However,

if it follows a single application of a carcinogen, it can "activate" the carcinogen and produce a cancer. In this work lies a field which is, as yet, in its full implications, unrealized in most industries. Preventive programmes are at present based on minimizing exposure to cancer producing substances, while admitting that some slight exposure may take place. Absolute avoidance of contact is the only logical method of prevention, and should be the target. It will also be necessary to recognize cocarcinogenic stimuli - particularly any stimuli giving rise to chronic irritation, and to eliminate these as far as possible.

Time Lag

A time lag occurs in every case between the application of a carcinogenic stimulus and the appearance of a lesion. The importance of this knowledge is in seeking far enough backwards in time for a cause, when a patient reports with a cancer.

Summary

Part II

The case histories and tables constructed therefrom of patients (fulfilling the necessary criteria) who have squamous cancer of the skin.

Part II. Present investigation.

It has been shown that cases of skin cancer in which there is a known occupational factor in the aetiology, fall almost exclusively into the class of squamous skin cancers. For this reason the present investigation has been confined to squamous skin cancers, subject to the following conditions.

1. The diagnosis is a histological and not a clinical one.
2. The tumour is primary in the skin.
3. The patient lives within accessible distance of Southampton.
4. The cancer is not an orificial one (i.e. at or near a muco-cutaneous junction).
5. The patient has had no radiotherapy prior to biopsy (or excision of specimen from which the diagnosis was established).

Case Histories

M10. Male. Date of Birth 30.5.83. Age at lesion 65.

This patient has always lived in reasonable housing conditions and has worked all his life for W.H.Smith in railway station bookstalls, working his way up to manager of several bookstalls. There is a family history of allergic illness.

Following on gross psychological shock, the patient developed a generalized eczema, which became chronic. Seven years later he developed a cancer of the face at a point where the spectacle sits on the cheek. At no time was any tar preparation used in the treatment of his eczema.

The history would suggest that the cancer developed secondarily to the chronic eczema and was localized by the chronic irritation from the spectacle frames.

Case F.8. also shows localization of the tumour at the site of contact of spectacle frames.

M11. Male. Date of Birth 18.9.80. Age at lesion 61.

The patient, a son of a sea captain, spent much of his early life at sea. He was taught that "cleanliness was next to Godliness" and has been rather fastidious all his life about personal cleanliness. He has worked all his life as a woodworker. In his early years aged 20-32, he was in U.S., in California and Nevada (hot and sunny) and was employed for some time as a coffin maker, being exposed to fumes of pitch (used for lining the coffins).

Over half of his working life has been spent out of doors. There is no family history of skin disease or cancer.

His cancer appeared first when the patient was aged 61, although he had a boil or pimple for seven years prior to this, at the same site on the left side of his neck. The general condition of his skin was healthy with a few degenerative changes.

The important points in the history with regard to his cancer appear to be:-

1. His fastidious cleanliness
2. The small but definite exposure to pitch
3. The work in hot sunny areas aged 20-32
4. Over half of his working life was spent out-doors
5. Apart from pitch and sunlight, he has been exposed to no other carcinogens.

M12. Male. Date of Birth 30.3.97. Age at lesion 49.

This patient has suffered from four surface cancers. His housing conditions have been rather poor and he has worked as road sweeper or very similar jobs for most of his working life. This work involves exposure to road dirt, tar, and to the weather all the year round. Tar spraying has been an occasional job. The patient's father died of cancer of the forearm.

The four lesions from which the patient suffered were:-

1. Carcinoma of lip aged 47 (clinical diagnosis)
2. Epithelioma, back of right hand aged 50 (microscopic diagnosis)
3. Rodent ulcer tip of left helix aged 52 (clinical diagnosis)
4. Epithelioma, back of left hand (clinical diagnosis)

He has marked changes of shagreen skin on the exposed skin, his unexposed skin being normal for his age.

The patient's occupation would therefore appear to be the major contributory factor to the production of his cancer, and although the diagnosis of three of the malignancies are clinical, it would be reasonable to assume that he did in fact suffer from multiple cancers. The multiplicity, together with the associated skin changes of shagreen skin and the age of the patient, favour strongly an occupational origin.

M15. Male. Date of Birth 14.11.07. Age at lesion 39.

This patient has lived in poor social conditions all his life. He is an epileptic and has worked in various unskilled jobs - cowman, docker, paint sprayer. There is no family history of skin disease, cancer or epilepsy.

The cancer was situated at the outer corner of the left eye, clear of the lid margins on the skin of the face. From the first sign of the

growth until biopsy showed an epithelioma, the time was three weeks. The patient's skin is normal for his age. No reason can be suggested for the appearance of this tumour and its cause remains unknown.

M16. Male. Date of Birth 13.11.19. Age at lesion 28.

This patient developed a cancer on the right shin at the site of an injury which occurred three years previously. The injury was caused by a fuel oil line striking against the leg, and the wound was contaminated by heavy fuel oil.

The patient's father, who worked as a labourer then as a ganger in a tar distillery, suffered from skin changes on his forearms and from tar warts and "had 14 tar warts cut off his neck and some off his arms". No malignancy was known to the patient's father.

From the ages of 14-17, the patient worked in his father's gang in the tar distillery, loading bitumen, breaking pitch, and often going off work with his skin heavily covered and contaminated by pitch and tar. Tar erythema was a common occurrence and the patient estimates that he has had tar erythema on at least 25 occasions.

The general condition of the patient's skin is normal. This case appears to be clearly of occupational origin and to be due to the handling of pitch and tar. The age of the patient (28) is strongly in favour of occupation being the cause in the absence of skin disease. Although this case appears to be occupational in origin, it was not notified to H.M.Chief Inspector of Factories by any of the doctors who saw the case.

M19. Male. Date of Birth 9.1.74. Age at lesion 76.

This patient developed a cancer on the skin of the neck behind the left ear. All his life the patient was a sailor, and on "retiring" he

took up strawberry and poultry farming for 18 years, and followed this by becoming a rigger-boatman for 6½ years. He thus led an outdoor life, some of it in tropical climates.

His colouring when young was typically ginger - a very fair skin, easily burnt by the sun, blue eyes and carroty hair. In the tropics, he lived as much as possible out of the sun, as he always peeled and reddened: never did he form pigment.

His exposed skin showed the classical picture of "sailor skin" with atrophic patches, keratoses, glazing, thinness, inelasticity and occasional telangiectases.

The cause of this cancer would appear to be a combination of sunlight and of very poor resistance to it, due to the patient's colouring. Occupation, being outdoor, brought him into contact with the elements.

M23. Male. Date of Birth 10.3.86. Age at lesion 64.

This patient has, for most of his working life, been outdoors - in the Navy and in H.M. Customs Waterguard. There is no family history of skin disease or cancer. His cancer developed on the face, six weeks after receiving an injury while picking cob nuts. The cancer developed at the exact spot at which the prick occurred - and the patient could not be shaken in this story. He is quite sure of the connection between the prick and the subsequent swelling.

The patient's skin is normal on unexposed areas, but rather dry and inelastic. On the exposed areas, his skin is thin, shiny and inelastic, and on the face, smooth and relatively hairless.

The cancer appears to bear some relation to the recent injury - and it is probable that the injury acted as a localizing and precipitating

factor (cocarcinogen) in a skin that was exposed to the elements for many years and was showing some degenerative changes. His occupation caused him to be so exposed to the elements.

M24. Male. Date of Birth 5.4.08. Age at lesion 41.

This case shows the onset of a cancer four weeks following a prick on the nose by a needle while sewing asbestos. The patient is a tough, ex-regular soldier, who came of a rather poor home and spent five years in India with the Army. His other occupations have been as a gardener, and as a lagger and electrician's mate on ships. There is no family history of cancer or skin disease.

The patient is quite certain of the connection between the prick on the nose and the subsequent warty growth which developed at the exact site of the prick four weeks later. Like the previous case, the injury appears to bear a definite relationship to the appearance of the cancer. Asbestos implantation may have occurred. There is only one known case of skin cancer arising out of an asbestos corn in the literature, and this patient did not have a corn. It is more probable that the prick acted as a cocarcinogenic stimulus.

M29. Date of Birth 12.8.02. Male. Age at lesion 45.

This patient has worked for nearly all his life as a joiner (28 years), apart from 2¾ years as a boy, prior to becoming apprenticed when he did odd labouring type jobs.

At the age of 45, a horny papilloma, which ulcerated centrally, developed on his left upper eyelid.

The patient's parents both died of cancer - his father of bladder cancer and his mother of intra-abdominal cancer (? intestinal).

Apart from an acute allergic dermatitis due to teak, the patient has suffered from no skin trouble.

No cause can be suggested for this lesion, but it may possibly be associated in some way with the acute allergic dermatitis which he suffered from.

M30. Male. Date of Birth 19.11.07. Age at lesion 44.

This patient has always lived in good housing conditions. He has worked as a machinist in contact with cutting oils, by which his skin is contaminated chronically and heavily. Since childhood, he has had a naevus in the right nasolabial fold - earning him the nickname of "bladderlip" as a child. Until the age of 16, the patient's skin was perfectly normal, apart from the naevus. At this time, he developed an eczema, which has remained with him in varying degrees ever since. He attributes the origin of his eczema to exposure at work to paraffin and oils. The eczema has been both extensive and severe at times. At no time was it treated by tar applications.

The condition of his skin when seen by me was good - his eczema was confined to the hands and popliteal areas.

Fourteen years prior to excision of the lesion, he cut his naevus while shaving, and it became wart-like. The condition remained thus until two months prior to excision when the wart started to grow rapidly. No reason is known for this sudden start of rapid growth.

In this case, the aetiology of his cancer is probably connected with the following factors:-

1. The presence of the naevus
2. The heavy mineral oil exposure
3. The cut while shaving
4. The chronic eczema.

If the patient's assumption about the aetiology of his chronic eczema is correct, then factors 2 and 4 above are related to his occupation.

M33. Male. Date of Birth 27.12.85. Age at lesion 67.

This patient had a chronic varicose ulcer of the leg from the age of 30. Malignant change supervened and the leg was amputated. His work was a wood-working machinist. In this job, he stood all the time, with very little movement.

He gives a family history of chronic eczema in his mother, who died of intestinal cancer.

The skin of his leg broke down for the first time following an injury at the age of 30. The skin healed and broke down (always following trauma) until two years later, when the ulcer refused to heal. After a haemorrhage, the ulcer healed and resumed its course of breaking down and healing, but getting longer. Finally, the ulcer went for some time without any sign of healing and a piece of tissue from the edge was reported as "becoming frankly malignant".

Owing to the amputation, the skin of the affected leg was not seen. Elsewhere, the skin was normal for age.

His occupation may have contributed to the varicose veins (by prolonged standing), the subsequent malignant change in the ulcer was probably not affected by occupation unless trauma played a part.

M39. Male. Date of Birth 23.11.97. Age at lesion 57.

The skin cancer in this case occurred on the left side of the forehead. The patient was a small fragile man, who looked as if he had been poorly nourished as a child. He grew up to enjoy rather poor general health.

For 48 years, the patient has worked as a boilermaker on the railways, maintaining and repairing locomotives, and mostly working inside the firebox. In the firebox, he was in contact with soot, coal, coal ash and clinker.

There is no family history of skin trouble - the patient's mother died of cancer of the bowel.

In 1944, nine years prior to the diagnosis of skin cancer, the patient developed a patch of lupus vulgaris at the same site. This patch grew larger and broke down in the centre (in spite of treatment). An "ulcerating tumour" was noted in 1953 and a biopsy showed malignancy.

The patient suffered from eczema (affecting the face amongst other parts) for one year from the age of 9 - 10.

The causes of this cancer appear to be

1. Eczema
2. Lupus vulgaris
3. Occupational heavy contact with soot.

M41. Male. Date of Birth 31.1.04. Age at lesion 49.

This patient had a cancer of exposed skin on the dorsum of the right hand, which appeared after he had been employed in the tar and bitumen trade for 30 years.

Apart from an initial 2½ years as an office cleaner, he has worked mainly as a salesman in the tar and bitumen trade. He spends quite a lot of time outside, often visiting sites where bitumen is being used. During the war, he was engaged in actual bitumen pouring, used for plastic armour on ships. Exposure to pitch and tar also occurred while inspecting plants.

The patient's mother died of cancer of the stomach (aged 81) and a sister died (aged 56) of breast cancer. There was no family history of skin

trouble.

The patient's exposed skin on hands and to a lesser extent on the forearms shows the typical degenerative changes of "shagreen skin". His skin is dry and very fair and burns easily in the sun. He has a slight seborrhoea of the scalp. Unexposed skin is normal.

In view of the site of the cancer, and the associated shagreen skin, the cause of the condition is probably tar.

M43. Male. Date of Birth 1.9.90. Age at lesion 64.

This patient developed a cancer of the lower eyelid near the inner canthus. He gives no family history or history of cancer or skin trouble. His environment, both at home (he came of wealthy parents) and at work (in a bank) appears to have been exceptionally good. The patient's skin is dry, very white, rather thin and hairless. He suffers easily from sunburn and does not ever form enough pigment to offer protection. The situation of the cancer appears to be far enough from the lid margin to eliminate muco-cutaneous origin and to be not far enough down for spectacle frame irritation. No environmental causal factors can be suggested in this case.

M44. Male. Date of Birth 25.7.05. Age at lesion 49.

This patient developed a cancer of the right cheek, which was excised within a month of its appearance. There is no family history of skin trouble; one brother died aged 63 of cancer of the stomach.

The patient has lived in good housing conditions all his life and has worked in the wine and spirits trade as a cellarman, storeman, delivery man and window dresser for a total of 25 years. His hobby has been his motor weekend cruiser - and he spends nearly all of his spare time either sailing or doing maintenance on the boat. He has suffered from tar erythema while using tar on the bottom of his boat, and has come into contact with paraffin

and mineral oil when working on the engine. His skin shows degenerative changes in the exposed areas (of the shagreen skin type) particularly on the forearms. The degree of pigmentation of what is a very fair skin would also suggest prolonged exposure to the elements.

It is therefore probable that his hobby has contributed to the causation of his cancer - a point well made by Henry (1950). Tar and sunlight are probably the most important factors in this cancer.

F2. Female. Date of Birth 9.10.81. Age at lesion 66.

This patient developed a cancer near the inner canthus of the left eye.

Apart from an allergic rash of the forearms and hands which appeared six months before the cancer, she has no history of skin trouble. Her work was mainly as a florist's assistant (10 years) and as a housewife. No cause can be suggested for this lesion.

F3. Female. Date of Birth 22.10.84. Age at lesion 63.

There is, in this case, a very clear story of minor injury, with soot contamination of the wound, being followed in three weeks by a swelling. This swelling, six weeks after the injury, proved to be an epithelioma. The condition of the skin in the affected area was perfectly normal prior to the injury.

The patient's occupation has been housework all her life. She has lived in good housing conditions in England and in Tasmania, where she lived for 21 years.

F6. Female. Date of Birth 23.6.18. Age at lesion 28.

The age of this patient at the time of development of the cancer should be noted. Such youthfulness suggests that the cause of the cancer is

different from the normal.

Other unusual features in the case are the very bad environmental conditions under which she lived. It is hard to say which feature in this case began the obvious lack of care which the patient displays for herself. Probably a combination of poor housing, childbearing, a rather poor childhood and eventual illness had lead to the present conditions in which the patient no longer tries, either with regard to her environment or herself, to maintain cleanliness.

From the age of 14, she suffered from asthma - and this has progressed to chronic dyspnoea on exertion with cardiac failure and oedema.

The skin of her arms, which she uses to give herself adrenalin injections (from an unsterilized syringe) is pitted and scarred. The general condition of the skin suggests a chronic lack of washing - engrained dirt, scars from septic spots, blackheads, etc. The skin is oily and forms pigment easily. A neurodermatitis was present under the chin. The cancer appeared over the upper sternal area, first as a "whitehead", which she broke. This lesion discharged and then grew larger, until it had a grey-black crust on top. Biopsy showed a squamous papilloma showing early malignant change.

The following list of factors are unusual with regard to her case.

1. The age of the patient (28)
2. The bad environmental conditions, coupled with the lack of washing and cleanliness.
3. The associated general debility and asthma.
4. The possibility of some of the drugs which were used for the treatment of her asthma, entering into the aetiology.
5. The advanced physiological age of the patient, 45, when compared with her chronological age of 37.

F7. Female. Date of Birth 18.1.91. Age at lesion 61.

This cancer, which occurred in the left groin, appears to have arisen from a mole which was operated on ten years previously (at the age of 57). The patient also gives a history that she had a cyst at the same site which was removed 25 years prior to this. A careful search of hospital records has not, however, brought confirmation of this, and the notes on the operation ten years ago make no mention of any scar or previous operation. The patient has done housework all her life.

There is a family history of cancer: the patient's mother died of cancer of the uterus and two sisters have each had a breast removed on account of cancer.

The patient's skin is completely normal for her age.

The cancer therefore appears to be causally connected with the pigmented naevus which was removed ten years ago - and which itself may have been preceeded by a "cyst" - and with the operation for its removal.

F8. Female. Date of Birth 14.4.89. Age at lesion 62.

This cancer occurred on the left cheek of a retired schoolmistress a t the exact point on the face at which the spectacle frame rested. Bilateral lesions occurred within 10 months of each other. The earlier lesion on the right cheek was apparently simple (a lesion was excised, thought to be a simple mole, and was discarded without histological examination). Spectacles have been worn continuously for over 30 years.

The patient has had good housing and social amenities all her life. She has no family history of skin disease, allergic illness or cancer. Her health has always been good.

The patient's skin is normal for her age. This case seems clearly to be connected with the wearing of spectacles.

F13. Female. Date of Birth 31.7.82. Age at lesion 70.

This patient developed a cancer on the right hand, on the skin over the V formed by the junction of the 1st and 2nd metacarpal bases. She has worked as a schoolmistress and as a housewife all her life.

The lesion began as a painless "scar" which developed into a pimple or wart, and grew larger. When it was $\frac{1}{4}$" in diameter, it was excised. The skin of her hands was thin and atrophic, showing the changes which are associated with rheumatoid arthritis. The rheumatoid arthritis developed six years prior to the cancer beginning. At no time has she had any treatment for the rheumatoid arthritis. The rest of her skin is normal for her age, except for some increase in freckling.

One brother died of lung cancer - otherwise there is no history of skin trouble or cancer.

The patient has "suffered from her nerves" for many years (since about age 21) and her father was the victim of similar trouble. It has recently been shown by angiography that in rheumatoid arthritis there is a very great closing down (or loss) of blood vessels in the affected areas. The associated skin changes are therefore likely to be due to impaired nutrition. The carcinogenic factor may thus be interference with normal growth (due to impaired blood supply).

Summary

Part III. Conclusions.

1. The average age of onset

in males was 52.2 years

in females was 63.4 years

in males and females was 56.0 years

2. The percentage of working life spent out of doors

in males was 48.0

in females was 5.71

in males and females was 36.2

60% of males spent over 50% of their working life outside.

3. There is a greater number of cancers in normally exposed areas than in covered areas. In males, the excess of cancers in exposed areas is greater than in females.

4. Most of the cases have skin which can be classified as fair or very fair.

5. Most of the cases had brown hair at the age of 21.

6. The eye colour was blue in 16 and brown in 6.

7. Degenerative changes in the skin are more common and more severe in the male than in the female cases. 15 cases had no degenerative changes and 7 cases had changes, varying from slight to marked.

8. A family history of cancer in any form in father, mother, brother or sister was found in 9 cases and was absent in 13.

9. A family history of skin disease in any form was found in 5 cases and was absent in 17.

10. A family history of allergy was found in 4 cases and was absent in 18.

11. General health was assessed as good in 14 cases, moderate in 7 and poor in 1.

12. A list of the common skin cleansers used by the patients was topped by carbolic soaps. The phenol content may possibly be of some significance.

13. The housing conditions under which the patients lived showed that the majority lived under conditions which could be classified in general terms as fair or poor.

14. Patients were classified by social class. The social class of the patient's father was also taken into account and a table of distribution in which the patients' social class counted for 2/3 and the patients' father's social class counted for 1/3 showed:-

	I	II	III	IV	V
Males	0	2 2/3	6	3 1/3	2 2/3
Females	1/3	1 1/3	3 1/3	1	1 1/3
Both	1/3	4	9 1/3	4 1/3	4

There is a trend towards the lower end of the scale, especially in males.

15. The skin reaction to sunlight was assessed by the answer to the question of ease or not of pigment formation and suffering from sunburn. Amongst the men, there is a greater number of cases in which pigment is not easily formed.

16. The relation of trauma to cancer of the skin is discussed. Particular mention is made of Ewing's criteria. Three cases in the present investigation appear to fulfil these criteria and one other case shows localization of the cancer at the site of a previous injury. The time interval in each of the three cases between the trauma and the appearance of the cancer was between 6 to 8 weeks.

17. The various aetiological factors which were elicited during the present investigation were collected together and a table was then prepared showing, in the following way, the certainty or the uncertainty of the aetiology of each:-

Number of cases

4	++++	aetiology practically certain
5	+++	" very probable
5	++	" probable
2	+	" possible
6	-	" unknown

Most of the male cases fall in the top three groups. It was shown that on close investigation of proved squamous cancer cases that in 14 out of 22 cases (63.8%) the aetiology could be classified as probable, very probable or practically certain. In view of this high figure, it is suggested that a much larger scale investigation into the aetiology of squamous skin cancer in males would probably lead to worthwhile results.

18. The diagnosis of occupational skin cancer is discussed. It is necessary, before describing a cancer as occupationally caused, to investigate the patient's occupation or occupations (including hobbies and spare-time interests) as fully as possible. Associated skin diseases or skin changes may favour occupational origin (for example shagreen skin). The precocious appearance of a cancer will tend to occur more often in occupationally caused cancer than in others. The type of skin cancer in known occupational cancers has been, for the most part, squamous epitheliomata. Multiplicity of surface cancers will tend to occur more often in occupational cancers (with the exception of multiple cancers

associated with xeroderma pigmentosum, burns, or other obvious skin diseases). Occupational skin cancers will tend to occur more often in males.

The site of the cancer in occupational cancers will tend to favour the face, scrotum and upper limbs (especially backs of the hands and the forearms).

19. The prevention of occupational skin cancer will follow the ordinary methods for dealing with industrial hazards, (substitution, enclosure, protective clothing and so on), but certain special considerations are seen to emerge.

Recognition of the hazard may be long delayed and efforts should be made in any case of suspicion (arising say from the chemical nature of the substance) to speed up the latent interval by appropriate research.

Education of the worker in the nature of the hazard is important, together with instructions in cleanliness and the early reporting of any suspicious lesions.

Skin cleansing is a most important matter in preventing chronic irritations of the skin - and the facilities required, together with the actual cleansing agents, are important.

There is good evidence to suggest that chronic irritation can aid the production of cancer by acting as a cocarcinogen, and steps should be taken to minimize any factor which may produce skin irritation.

Selection of workers is a good preventive method - by age, to select the older age groups, by unblemished dark skins, free from disease. It is important in this connection to examine the whole skin, - that is the patient should be naked - in a good light.

Periodic medical examinations of those who are exposed to a known hazard is another preventive method.

Barrier creams can be used, but tend to give a false sense of security.

It has been shown that a single contact with a carcinogen is sufficient to produce a cancer, provided that non specific stimulation (usually in the form of some chronic irritation) is afterwards provided.

The approach to prevention of industrial cancers will, in the light of this knowledge, have to be re-orientated towards absolute avoidance of contact and not, as in many cases nowadays, to minimizing contact. Non specific chronic irritation should also be avoided.

Lastly, any programme of control must be realistic and must be carried out.

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