INDUSTRIAL CANCER

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SYNOPSIS

Many important industries present a potential cancer hazard to their employees. The conditions under which it is not only legal but completely ethical to permit men to be so exposed are discussed in this paper. No hard and fast rules can be laid down to cover every case but certain important precepts must always be followed.

Introduction

One of the penalties that we pay for the benefits of our sophisticated society is an increased liability to certain diseases, of which cancer is one. An enormous toll is taken by tobacco smoking, and by atmospheric pollution, and some food preservatives and even drugs used medicinally are suspect. Besides this, workers in many industries are exposed to a potential cancer hazard and it has been estimated that 80% of cancers result from a re-action to artificial stimuli and are therefore theoretically preventable.

However, should anyone have it in mind to opt out of this disease-ridden environment and retreat to a primitive paradise and live there with nature, the prospect is still without comfort. Some of the most carcinogenic of all substances occur quite naturally: an example is provided by cycasin which arises from a seed and is a nitrosamine-like substance. Nitrosamines are so potent that a single exposure can cause cancer. The increased incidence of primary liver cancer in Africa is thought to be due to the proliferation in humid conditions of Aflotoxin, which is derived from a mould. Moreover, 3 : 4 benzpyrene, a very potent lung carcinogen, is produced when organic material is burned so one would have to pick a warm climate requiring no fires and have a special partiality for uncooked food to avoid natural risks giving rise to cancer.

Industries Which May Give Rise to Cancer

We are concerned here with those cancers which arise occupationally. The industries concerned are many and varied and as examples we may quote the asbestos, dyestuffs, rubber, engineering, cotton, and other industries using certain type of oils, industries using radioactive materials, certain metal industries, the furniture industry, and the boot and shoe industry.

Asbestos

The asbestos industry can give rise to a double hazard—of cancer of the lung, and of cancer of the lining of the lung and abdominal organs—the mesothelioma tumour. Until recent years it was considered that only the asbestos industry itself was at risk, but it is now universally recognised that the user industries are also involved as the degree of exposure necessary for the development of mesothelioma need not be severe or prolonged. *The Asbestos Regulations* of 1969, which came into force on 14 May, 1970, were designed mainly to meet this hazard. The route of entry of asbestos into the body is by inhalation of the fibres.

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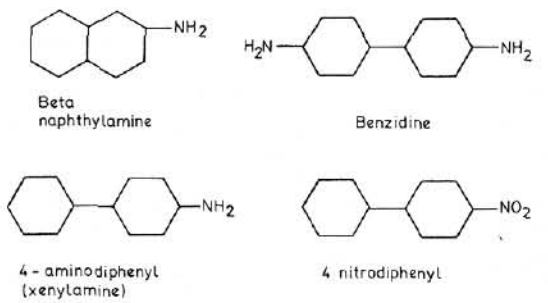


Fig. 1.—*Some potent carcinogens whose use is prohibited in industry*

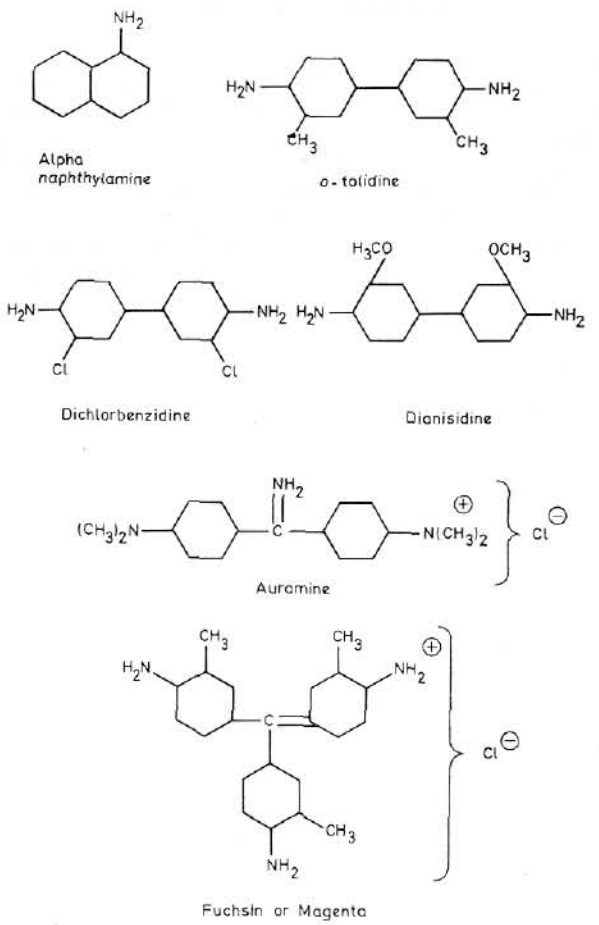


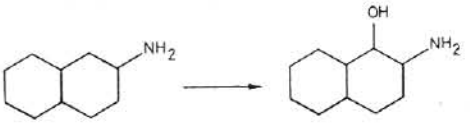
Fig. 2.—*Some carcinogens which may be used in industry subject to strict control*

Dyestuffs

Contact with certain dyestuff's intermediates—by inhalation or by absorption through the skin—can cause tumours of the urinary tract, usually of the bladder. The chemical group mainly responsible is the polycyclic aromatic amines and certain of their substituted compounds (in spite of the old name "aniline cancer", aniline itself is not carcinogenic). The most potent carcinogens are betanaphthylamine, benzidine, 4-aminobiphenyl (xenylamine) and 4-nitrobiphenyl (see Fig. 1) and their salts. The *Carcinogenic Substances Regulations*, 1967, prohibit their use in industry and it is interesting to note that the dyestuffs industry set an excellent example by anticipating this by ten years in its *Code of Practice* (Scott and Williams[4]).

Besides the *prohibited* substances, the *Carcinogenic Substances Regulations* describe *controlled* substances, which can be used in dyestuffs manufacture subject to various laid down precautions. These are regarded as being carcinogenic, although to a considerably lesser degree than the prohibited substances. They are alphanaphthylamine, orthotolidine, dianisidine, dichlorbenzidine and their salts, and auramine and magenta (see Fig. 2). If alphanaphthylamine contains more than 1% betanaphthylamine as an impurity it becomes a prohibited substance.

There are many theories as to what is the exact carcinogenic agent and it is certain that there is no one substance common to all. One theory, for which there is much evidence, is that the carcinogenicity of a substance depends on its conversion in the body to an orthohydroxy amine. Thus betanaphtylamine is metabolised from:

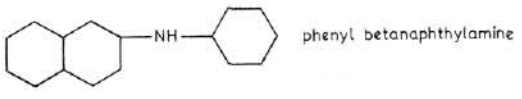


which is the active carcinogen whereas the much less dangerous alphanaphthylamine cannot be converted into this substance.

As evidence for this theory, feeding betanaphthylamine to dogs causes cancer of the bladder and dogs do convert betanaphthylamine to the orthohydroxy amine. Feeding betanaphthylamine to cats does not cause cancer, and cats do not convert it to the orthohydroxy amine, but feeding the orthohydroxy amine itself to cats does cause bladder cancer.

Rubber

Bladder carcinogens were used in the rubber industry at one time before their danger was known. Benzidine was once used as a hardening agent and a naphthylamine aldehyde condensate, containing free betanaphthylamine, was used in processing rubber. These substances have not been used for many years now, but new cases still occur in men who were at one time exposed to them. The apparent anomaly of the present day use of phenyl betanaphthylamine as a rubber anti-oxidant is explained by the fact that in spite of its formula, it is considered to be non-carcinogenic:

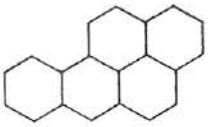


There is a suspicion that there might be an increased incidence of brain tumours in rubber workers. It is not known what the responsible substance is.

Engineering, cotton, and other industries using certain types of oil

Exposure of the skin to a considerable amount of mineral oil, over a long period of time can produce many different pathological conditions of the skin including warts and cancer. The warts may remain benign, or may become malignant if untreated. They are multiple, and usually recurrent. Since removal from exposure does not prevent recurrence, change of occupation will not help the worker who has already developed warts.

The responsible oil is mineral oil. The carcinogenic substance is thought to be in the aromatic fraction, particularly in the polycyclic group with 4 to 6 condensed benzene rings and it is usually 3 : 4 benzpyrene:



Vegetable oils are considered to be safe but are often unsuitable for industry and so solvent-refined mineral oils are used whose carcinogen has been dissolved out with SO_2, furfural, or phenol thus leaving an oil that is mainly aliphatic. Sometimes soluble oils, diluted with water, are used. The problem is complicated by the fact that some additives, such as sulphur, sulphur compounds and certain phenols, may enhance the carcinogenic effect.

Cancer of the scrotum is a form of skin cancer which used to be common in mule spinners in the cotton industry. Because the use of shale oil (which is particularly carcinogenic) has been discontinued and because the cotton industry is, in general, contracting, the hazard is now mainly in the engineering industry where the operative's trousers may be repeatedly soaked by sprays of oil and where he may have to make adjustments while the machine is still in motion.

Since the lesion is on the skin and responds extremely well to early treatment, examination of the man at risk at regular intervals is of prime importance. But it is generally accepted that only those who get large amounts of oil on them repeatedly are at risk and it should be left to the medical officer, after seeing the men at work and after discussion with operatives and supervisors, to decide whom to examine. This will usually be found to be far fewer than expected. The examinations should be carried out at least twice a year. The men must, of course, be protected by the many available safety devices such as treatment of the oil, protection of the machine from splashing and spraying, the use of impermeable aprons, pocketless trousers, good washing and bathing facilities, barrier creams, *etc.* The case of Stokes, Guest, Keen and Nettlefold Ltd. was concerned mainly with the question of medical examination and the Judge's summing-up explains in detail what the Law considers to be the responsibilities of the employer and of the medical officer to the worker.[19]

Industries using radio-active materials

The industries using radio-active materials have a skin cancer and lung cancer hazard due to ionising radiations. Many of the early X-ray workers died from this. The precautions to be taken are stringent and are governed by the *Ionising Radiations* (*Sealed Sources*) and other Regulations.

Chromium

There is a serious lung cancer hazard to workers producing chromates from chromite ore ($FeO.Cr_2O_3$, with often a little magnesium and aluminium oxide too) and possibly also to those who handle certain chrome pigments such as zinc chromate, barium chromate, and lead chromate. Monochromates are thought to present a bigger risk than dichromates. The more soluble compounds are the most carcinogenic, zinc chromate, for example, being more dangerous than barium chromate—which is hardly soluble. The precise chemical substance responsible has not yet been identified—it may be an intermediate in the preparation of

chromate, such as a chromate-chromite mixture. The Industrial Advisory Council is at present considering whether lung cancer in workers employed in the manufacture of chromates should be made a prescribed disease.

Iron ore

In the haematite miners in Cumberland there is an increased incidence of lung cancer. Whether it is due to the high radioactivity of the air in the mines or to the action of iron oxide is not yet quite clear.

Nickel

In refining nickel from ores containing it there is a risk of cancer of the lung and nasal passages.

Cadmium

Exposure to cadmium salts is thought to increase the risk of cancer of the prostate.

Furniture

In the beechwood industry there is an increased incidence of cancer of the lung and of the nasal passages due to inhalation of the dust. The precise agent has not been conclusively isolated and could be the wood, varnish, polish or preservative.

Boot and shoe

Inhalation of dust in the press and preparation rooms of the boot and shoe industry may cause cancer of the nasal sinuses. Again the causative agent has not been isolated.

Other suspect industries

This list is by no means complete and the number of suspect industries continues to increase. But although the eradication of the hazard is vitally important one must keep the picture in its right perspective—only a tiny proportion of all tumours can be regarded as occupational in origin and the use of tobacco alone causes more cancer than all the industrial tumours put together. Even cancer of the bladder, the hazard of the dyestuffs industry, statistically occurs occupationally in only 3% of cases (out of 3000 deaths per annum only 100 are proved to be occupational), although for various reasons the figures of 100 may be inaccurate and an appreciably higher figure might be nearer the true one.

Occupational cancers are usually contracted through inhalation or through contact with, or absorption through, the skin and, less commonly, by ingestion. Their prevention will naturally depend on how carefully the worker is screened from these influences. Carcinogens are completely free from class consciousness, and will attack exposed management or laboratory personnel with the same avidity that they show towards the shop floor.

Concept of Acceptable Risk

Absolute prevention is, in view of the many human factors involved, (including the worker's own degree of co-operation), in some cases unattainable, and the aim must be to reduce the risk to the lowest possible level. This concept of an acceptable risk involves moral as well as practical considerations. It adopts the apparently callous principle of accepting a certain percentage of casualties as inevitable. It is, however, a principle which is used by all of us every day without a second thought. Almost everyone who smokes cigarettes must be aware of the fact that by doing so he is increasing appreciably his chances of developing lung cancer, yet countless millions assess the odds and still accept the risk. When one buys a bicycle for a young child one cannot help thinking that every day children are knocked off their bicycles and injured or even killed; but one assesses the odds, and quite rightly, buys the bike. In other spheres of industry risk is accepted—the chances of a serious or fatal occupational injury are obviously higher in a driver than in a clerk.

Thus the concept of the acceptable risk in industry is neither as revolutionary nor as callous as might first appear. The question is whether it is justifiable to apply it to workmen exposed to a potential risk of cancer. We must be careful here not to make an artificial distinction between cancer and other occupational diseases. The word cancer has emotive overtones to many laymen who tend to put it in a class apart but some noncancerous occupational diseases, such as lead and beryllium intoxication, and asbestosis—to name only a few—can produce severe and distressing symptoms and may prove fatal in the end. One must avoid having two standards of vigilance in industry, one for cancer and one for the others—there must be the same rigorous standard for all.

I believe that it *is* justifiable to apply the concept of acceptable risk to a cancer hazard, providing the following important precepts are rigidly followed:

(1). A carcinogenic substance should never be used where a safe substitute is possible.

(2). When this is *not* possible, a less dangerous material or method should be used, with suitable safety measures.

(3). When this too is not possible, the dangerous substance should only be used when every precaution is taken to reduce the risk to the very minimum.

(4). This minimum must be so low that the chances that an instructed workman using all the preventive measures will contract the disease are to all intents and purposes nil.

(5). The search for a safe substitute must always continue.

The methods used to deal with these hazards are partly governed by the peculiar characteristics of occupational tumours. The most striking is the length of time which elapses between the first exposure to the carcinogen and the first development of the tumour—the so-called latent period. This is, on average, 40 years for mule spinners, 38 years for the mesothelioma tumour due to exposure to asbestos, 18 years for bladder tumours and between 3 to 75 years for cancer of the skin. Moreover, once the process of tumour formation has started, even though it may be many years before the occurrence of any symptoms, removal from exposure may not arrest its development. This causes many problems, as the disease may first manifest itself when the patient has been working for years in a totally different job with a different firm and has perhaps forgotten about his earlier occupation. It may also occur many years after a man has retired and perhaps is living in a totally different part of the country. Since there is no tumour absolutely specific to industry—that is to say, all tumours can arise spontaneously in people who have never been occupationally exposed—its occupational origin may be completely missed. Although this would probably not prejudice either diagnosis or treatment, it would vitiate the statistical figures which can be so valuable in detecting a new hazard and in assessing the dangers of a known hazard and the success of methods used to overcome it.

Need to Keep Statistics

The importance of accurate statistical information in detecting occupational hazards cannot be over emphasised and as an example we may mention the case of the furniture industry hazard. An Ear, Nose, and Throat consultant in Oxford noticed a few years ago that he was seeing a disproportionate number of cases of the uncommon cancer of the nasal passages. The data were referred to a Medical Statistical Unit, who discovered that the features which all

the patients shared in common were that they had, at some time, lived in or near to High Wycombe, worked in the furniture industry there, and the particular wood on which they had all worked was beech. Subsequent cases have confirmed the relationship between this type of cancer and this particular industry as it was carried on decades ago, and it is now a prescribed disease—that is, a sufferer from the disease who worked in this particular branch of the furniture trade is entitled to industrial injury benefit in the same way as is a person who has suffered an industrial injury.

By the use of similar methods it has recently been found that there is an increased incidence of nasal cancer in the Northamptonshire boot and shoe industry. In the period 1953 to '67 out of 46 patients in the area, 21 had worked in the industry, and almost all of them had been employed in two particular processes—in the press and preparation rooms. Work is now being done which may point to a relationship between nasal cancer and the footwear *repairing* industry. The flour industry is being similarly investigated.

Thus a keen clinical awareness, much hard labour and perseverance, and reliable statistics and statisticians are required in the identification of new hazards and in the assessment of the effectiveness of the precautions used against known ones. It is evident that many more as yet unappreciated hazards will be found and the aim must be to identify them as soon as possible and then to eliminate them by effective safety procedures. Legislation will, of course, in the end make this compulsory; but the interest in and the feeling of responsibility for men's health must be present so that Codes of Practice in the particular industry should anticipate and precede legislation and not *vice-versa*. Management must be particularly careful to keep accurate records of a man's occupational history as it may be of inestimable value many years later.

I mentioned earlier that a pre-condition for using a dangerous substance in industry was the rigid observance of certain important principles. I will, very briefly, give some examples of how these principles are applied in various industries.

Substitution

Vegetable oils, or solvent-refined oils (with the carcinogenic fraction removed) are used where possible, instead of mineral oils.

Glass fibre, and many other non-carcinogenic materials, are used instead of asbestos.

Xylene and toluene are used as substitutes for benzene as solvents—exposure to benzene is considered to be responsible for some cases of leukaemia and it should never be used as a solvent. New *Benzene Solvents (Limitations of Use) Regulations* are being formulated prohibiting the use of solvents containing more than 1% benzene, save in exceptional circumstances.

Where it is not possible to find a completely safe substitute, one uses a less dangerous one, for example, crysotile or amosite instead of crocidolite asbestos.

A variation of this is to alter the mode of manufacture of a chemical so that the harmful intermediate is not formed, for example in the dyestuffs industry tobias acid, a betanaphthylamine sulphonic acid used in the synthesis of many dyes, is now made by the sulphonation of betanaphthol followed by amidation, instead of from the highly carcinogenic betanaphthylamine.

Other precautions

To describe all other possible precautions in detail would entail a lecture in itself, so I will very briefly give the headings.

INSTRUCTION OF THE WORKER. Men should always be told of the hazard and of the methods used to protect them and of the contribution which they themselves must make to ensure their absolute safety. The talk should be in language which they can understand and there should be no equivocation. The Works Medical Officer should be the one to tell them; if there is no medical officer it should be a senior member of the staff.

MONITORING OF THE WORKING ENVIRONMENT. The environment should be monitored, for example measurements of asbestos fibre concentration in the air must be made.

SEGREGATION. The hazardous process should be segregated so that only those working on the dangerous material are exposed to it.

ENCLOSURE AND MECHANISATION, so that there is minimal opportunity of contact by skin or by inhalation.

EFFICIENT LOCAL EXHAUST VENTILATION AND GENERAL VENTILATION.

GOOD WORKING CONDITIONS with facilities for men to have a wash, shower, or bath, for change of clothing, and for eating in uncontaminated areas.

PROTECTIVE CLOTHING.

WETTING AND OTHER METHODS OF DUST SUPPRESSION.

MONITORING OF THE MAN, for example, regular examinations of urine in dyestuffs workers; regular skin and scrotum examinations of those exposed to oil in certain circumstances; serial chest X-rays in asbestos workers.

INSTRUCTION CARDS to men who leave the industry or the company so that they will remain under observation.

It will be noticed that the last two headings are not preventive measures but ones which assist in the early diagnosis of disease and they are important because, as I mentioned earlier, one cannot be certain that risk is entirely eliminated because of the human element involved.

Problem of a Suspect Substance

It is not always known for certain whether a substance is, or is not, carcinogenic and a company using it for the first time might be at a loss to know how to deal with the situation. The question should be referred to the suppliers—whose answer should be requested in writing—and to the company medical officer; but one may not get a clear-cut "yes" or "no". The substance may be suspect because its chemical formula is related to that of a known carcinogen and animal experiments might be indicated to assist in forming an opinion; but the problem is then bedevilled by the question of how far the results of animal experiments can be regarded as applicable to man. Ethical considerations rule out experiments on man himself and even if they did not, the long latent period would make such experiments impracticable. Animals having a much shorter life span than man are used but it is well known that different species (and sometimes even different strains of the same species) may react quite differently to the same carcinogens, for example, arsenic is carcinogenic only to man; betanaphthylamine is carcinogenic to the dog and not to the cat. Moreover, the degree of exposure in animal experiments is sometimes totally unrelated to man's industrial exposure. If feeding vast amounts of a substance to rats and mice produces in some of them tumours of the liver or acoustic duct, does that mean that it might cause cancer of the bladder in man? If implanting pellets of a substance into the bladder of a dog results in tumour formation, is it a reasonable deduction that a responsible man, working in a clean, safety-conscious factory with at most minimal contamination of skin or inhalation of dust, is really at risk?

The company, advised by its medical officer, has to make a decision. A lot may depend on the climate of public opinion, and at the moment we are all living in the shadow of the thalidomide tragedy. Are we, perhaps, becoming *too* suspicious because of this? The cyclamate decision certainly indicates an international mood of great caution because there is as yet no evidence that men, eating normal amounts of cyclamate, are at risk. In industry, too, caution must be paramount. Each case must be treated on its own merits and each company competently advised, must answer these questions in accordance with the Law and their own consciences.

In cases where a company has no medical officer there are many recognised consultancy services to whom the matter could be referred. They are often associated with a university and offer highly skilled technical advice—for example, The Department of Occupational Health of Manchester University, The North of England Occupational Health Service, University of Newcastle-upon-Tyne; Dundee and District Occupational Health Service, University of Dundee. The T.U.C. Centenary Institute of Occupational Health, the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, and some private organisations will also give an expert opinion.

Conclusion

I have tried to indicate in the foregoing the main types of cancer hazard in industry, the ethics involved in exposing men to them, and the methods used to reduce the risk to these men to the barest minimum. With the sensible and conscientious application by management, supervision, and workers, of the principles mentioned this minimum can be achieved. Just how small the risk might be is illustrated by the ambition of the dyestuffs industry to reach such a degree of safety that in years to come their workers will have less chance of dying from cancer of the bladder than the unexposed man in the street because the worker will not only be comprehensively protected but he will also have the advantage of early detection (long before any symptoms appear) by the routine urine checks which are legally required. Early diagnosis and treatment improve the prognosis considerably.

With all these sophisticated safety mechanisms in use we can now repeat the earlier question " Is the concept of the acceptable risk justifiable?" and the answer is more readily in the affirmative. Conversely, in their absence the answer must be " no ". No company is justified in exposing men to cancer risks which additional safety measures would lessen and the medical officer should not shrink from the responsibility of advising management that a particular process would involve a risk which it would be immoral to take.

References

Dyestuffs and cancer

1 *The Carcinogenic Substances Regulations*, 1967. (*S.I.*879). (London: H.M.S.O.).

2 *The Carcinogenic Substances (Prohibition of Importation) Order*, 1967. (*S.I.*1675). (London: H.M.S.O.).

3 Scott, T. S. " *Carcinogenic and Chronic Hazards of Aromatic Amines*", 1962. (Amsterdam: Elsevier Publications).

4 Scott, T. S. and Williams, M. H. C. *Br. med. Jl*, 1957, **14,** 150.

Asbestos

5 *The Asbestos Regulations*, 1969. (*S.I.*690). (London: H.M.S.O.).

6 " *Recommendations for Handling Asbestos* ", 1969. (London: Engineering Equipment Users Association).

Oil

7 *The Mule Spinning (Health) Special Regulations*, 1953. (*S.I.* 1545). (London: H.M.S.O.).

8 Bourne, L. B. " *Skin Diseases from Oil—Causes and Prevention*", 1967. (London: British Safety Council).

9 Kipling, M. D. *Trans. Soc. occup. Med.* 1969, **19,** 36.

Furniture

10 Acheson, E. D., Hadfield, E., and Macbeth, R. G. *Lancet*, 1967, **311,** 1.

Boot and shoe

11 Acheson, E. D., Cowdell, R. H., and Jolles, B. *Br. med. J.*, **1,** 385.

Epidemiology

12 Doll, R. " *Prevention of Cancer—Pointers from Epidemiology*," 1967. (London: Rock Carling Fellowship, Nuffield Provincial Hospital Trust).

Radiation

13 *Radioactive Substances Act* 1960. (London: H.M.S.O.).

14 *The Ionising Radiations (Sealed Sources) Regulations*, 1961. (London: H.M.S.O.).

15 *The Ionising Radiations (Unsealed Radioactive Substances) Regulations*, 1969. (London: H.M.S.O.).

General

16 Hunter, D. " *Diseases of Occupation*," 1969. (London: English Universities Press).

17 Clayson, D. B. " *Chemical Carcinogenisis*," 1962. (London: Churchill & Co.).

18 Schilling, R. S. F. " *Modern Trends in Occupational Health*", 1960. (London: Butterworths).

19 *Solicitor's Journal*, 1968, **112,** 821.

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