

# BRITISH MEDICAL JOURNAL

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## Pointers

**Primary Amoebic Meningoencephalitis:** This usually fatal disease, caused by free-living saprophytic amoebae, probably occurs in Britain, for two examples were found during the review of specimens in a London pathology museum, one dated 1909 reputedly from Essex, the second dated 1937 from Belfast (p. 449).

**Intermittent Corticotrophin in Asthma:** Improvement in respiratory function lasted longer than the enhancement of adrenocortical activity, as judged by plasma cortisol levels (p. 455).

**Alcoholism and Blood Group:** A controlled investigation of ABO blood group and secretor status in 1,000 alcoholics shows an unexplained increase in group A non-secretors (p. 457).

**Response to Gastric Stimulants:** Impairment of response to gastric stimulants such as penta-gastrin can occur after repeated testing (p. 459).

**Haemolytic Anaemia in Pregnancy:** Prednisolone was effective in controlling haemolysis in 5 of 6 pregnant Nigerians with severe haemolytic anaemia (p. 461).

**Fatal Appendicitis in Children:** Analysis of the 204 deaths in England and Wales during the five-year period 1963-7 (p. 466).

**Chronic Bronchitis:** Comparative trial of trimethoprim-sulphamethoxazole and ampicillin suggests that the trimethoprim mixture is useful and safe (p. 470).

**Hb H Disease in Pregnancy:** Management (p. 473).

**Epilepsy in Childhood:** Current Practice article on drug treatment (p. 475).

**Road Accidents:** Trapped casualties (p. 478).

**First-aid:** Proposals for "a 'crash-course' on a national scale" (p. 485).

**Specialty of Family Medicine:** Training programme at Tel Aviv University (p. 487).

**Personal View:** Dr. Anthony Ryle (p. 490).

**Nurses:** Letters (pp. 491-2). Pay claim (p. 506).

**Junior Doctors' Representation:** Letters (pp. 497-8).

**Leptospirosis:** Three recent deaths (p. 505).

**Specialist Registration:** Minister's intentions (p. 506). Letters on G.M.C.'s proposals (p. 499). Constitution of G.M.C. (*Supplement*, p. 43).

**Medicines Commission:** Membership (p. 504).

**B.M.A. Committees:** Overseas Affairs, Public Health, Armed Forces, and Charities (*Supplement*, pp. 41-43).

## Cancer from Mineral Oil

Skin cancer due to mineral oil was first noted during the latter part of the nineteenth century among mule spinners in the cotton industry. The first patient that S. A. Henry<sup>1</sup> could trace died in 1875. Between 1920 and 1943 no fewer than 1,441 cases of skin cancer attributable to industrial exposure to mineral oil were notified. Of these the scrotum was affected in 885 instances. Nearly all of those affected were cotton workers, and only 50 worked in the engineering industry. Scrotal cancers were more frequently fatal than cancers arising on the hands and forearms. A few women cotton workers developed cancer of the vulval skin.

First made a notifiable industrial disease under Section 66 of the Factory Act in 1920, statutory recognition had been given to cancer of the skin due to exposure to mineral oil for compensation purposes in 1914. Legislation designed to protect workers from the carcinogenic effects of mineral oil was not introduced until 1953.<sup>2</sup> By this time the industry itself had introduced protective measures. Among the measures enforced are the compulsory use of a highly refined, so-called "white oil" for lubricating spindles and regular six-monthly medical examination of all workers.

The first warning signs that cancer from mineral oil could be a problem in the engineering industry went largely unheeded. They came in the form of a paper by C. N. D. Cruickshank and J. R. Squire in 1950.<sup>3</sup> These workers collected records of 12 cases of scrotal cancer in men exposed to mineral oil in the engineering industry in the Birmingham region. Then came a report that an unusual proportion of cases of cancer of the hand and forearm in the Birmingham area during the 10 years 1941-50 were in "metal workers" and probably due to exposure to mineral oil.<sup>4</sup> Two cases of scrotal cancer specifically in "tool-setters" were later described by J. G. Fife.<sup>5</sup> At present in the Birmingham area among a population of some 5 million the Regional Cancer Registry collects approximately 1,500 cases of skin cancer and 14 cases of epithelioma of the scrotum each year. Tool-setting figures prominently as an occupation, especially among the patients with scrotal cancer.

Most nuts and bolts in this country are made in machines into which the metal is fed as a continuous coil, or bar, and shaped into the finished product by a series of noisy cutting operations. These are facilitated by the cooling and lubricant action of streams of so-called "cutting oils." The machines are fully automatic, but every so often need the attention of the tool-setter to fit new cutting edges or make other adjustments. Today in the larger and more up-to-date plants the job of the tool-setter need not be a particularly oily one most of the time. Overalls, aprons, hot and cold water, soap, and plenty of rags to remove oil from the surfaces of machinery are available. In some small factories conditions are less favourable and medical supervision is virtually absent.

Against this background came the case of *Stokes v. Guest Keen and Nettlefold* in 1968,<sup>6</sup> in which a widow was awarded £10,000 because her

husband, a tool-setter, died from cancer of the scrotum attributed to exposure to mineral oil. The case arose in one of the bigger and cleaner factories and might never have been recognized as a case of industrial cancer or come to court if it had arisen in a smaller concern. As a result, notices warning of the dangers of exposure to mineral oil have been renewed or displayed more prominently in engineering shops, and by the distribution of pamphlets the attention of workers has been drawn to the hazards—particularly the danger of delay in seeking medical advice. Recently, too, the Department of Employment and Productivity and the Factory Inspectorate have jointly produced a new and more informative warning pamphlet.<sup>7</sup>

Despite these efforts a visit to some engineering factories would probably still show men not wearing aprons, men wearing oil-soaked overalls and putting oily rags in their trouser pockets, and men with oil on their faces and hands who make little use of the washing facilities provided. It is an unwritten basic human right that a man cannot be forced to keep himself clean, and some men in this country seem to regard cleanliness as an infringement of manhood, though the position has perhaps improved since Henry Butlin, in these columns in 1892,<sup>8</sup> contrasted English chimney sweepers with some of their Continental counterparts, particularly in Switzerland and Germany.

Is the answer to make the oil safe to use? Mineral oils consist of three types of compound—paraffins, naphthenic compounds, and aromatic compounds. It is thought that most of the carcinogenicity of cutting oils is attributable to compounds in the aromatic fraction, particularly the polycyclic aromatics containing 4 to 6 condensed benzene rings.<sup>9, 10</sup> But some straight chain aliphatic compounds such as dodecane<sup>11</sup> have been shown to enhance the carcinogenic activity of polycyclic aromatic compounds for mouse skin. Some commonly used additives such as sulphur itself and certain other sulphur-containing compounds may also do so,<sup>12</sup> and so may certain phenols.<sup>13</sup>

For some engineering purposes it might be possible to use the highly refined "white oils" recommended for use in the textile industry, but they are relatively expensive, would be scarce if the demand increased, and suffer from the disadvantage that they do not have quite the same physical properties as oils used at present. They also have poor solvency for some of the additives used in special metal-working oils.

Doubtless now that attention has been drawn to the need for less hazardous oils they will be developed, though they will be more expensive. But it would be a mistake at present to rely on them as the immediate or only solution to the problem.

General practitioners have an important role in the diagnosis of the condition. Clearly the significance of a wart or ulcer on the scrotum or vulva needs careful assessment. Another aspect of the problem is that not all skin cancers of industrial origin are being notified,<sup>14</sup> and there is no means of finding out what the short-fall is. An important reason for failure to notify is lack of awareness that skin cancer of industrial origin often arises long after exposure to the causative agent has ceased, and frequently after a person has retired from work altogether. These problems would be partly solved if employers were required by law to introduce six-monthly medical examinations by experienced factory doctors of workers heavily exposed to mineral oils. How many workers should be covered by such a recommendation is difficult to say, but medical resources are too few for all workers exposed to mineral oils to be included.<sup>15</sup> At least a beginning could be made with those occupations in which there is an established risk, such as tool-setting and jute manufacture.<sup>16, 17</sup>

## A New Synthetic Antimycotic

Since the discovery of nystatin nearly twenty years ago the treatment of fungus infections has been mainly with antibiotics. Nystatin can cope with most forms of candidiasis, while griseofulvin, rediscovered as an antimycotic some years later, can deal with the dermatophytoses and amphotericin B with systemic mycoses, histoplasmosis, coccidioidomycosis, and deep-seated forms of candidiasis. Some of these treatments, particularly the last-named owing to its toxic effects, leave something to be desired, and the advent of a totally new drug with some promise in this direction is consequently welcome.

Such a drug is described by M. Plempel and his colleagues,<sup>1</sup> of the Bayer laboratories in Elberfeld. Known at present only as BAYb 5097, it is bis-phenyl(2-chlorophenyl)-1-imidazolyl-methane, and is one of 600 similar derivatives recently synthesized and presumably examined for any useful form of activity. It has no action on bacteria, but inhibits the growth of a large variety of fungi, including plant as well as human pathogens, in concentrations usually about 1 µg./ml. The species of which multiple strains have been tested with consistent results include the principal dermatophytes, *Candida*, *Aspergillus*, and *Penicillium* species, *Histoplasma capsulatum*, *Coccidioides immitis*, *Cryptococcus neoformans*, and *Sporotrichum schenckii*.

The L.D.<sub>50</sub> for animals is about 1,000 mg./kg. body weight, and doses of 150 and 60 mg./kg. daily have been given to animal and man respectively with no evident ill effects. Presumably because of its low solubility in water very little is absorbed after parenteral injection, but by a mechanism which is not altogether clear its absorption from the alimentary tract is good, a single dose of 40 mg./kg. in man pro-

<sup>1</sup> Henry, S. A., *Cancer of the Scrotum in Relation to Occupation*. London, Oxford University Press, 1946.

<sup>2</sup> Ministry of Labour and National Service, *The Mule Spinning (Health) Special Regulations 1953* (S.I. 1545). London, H.M.S.O. 1953.

<sup>3</sup> Cruickshank, C. N. D., and Squire, J. R., *British Journal of Industrial Medicine*, 1950, 7, 1.

<sup>4</sup> Cruickshank, C. N. D., and Gourevitch, A., *British Journal of Industrial Medicine*, 1952, 9, 74.

<sup>5</sup> Fife, J. G., *British Journal of Industrial Medicine*, 1962, 19, 123.

<sup>6</sup> Stokes v. Guest Keen and Nettlefold (Bolts and Nuts) Ltd., *Solicitors Journal*, 1968, 112, 821.

<sup>7</sup> Department of Employment and Productivity, *Cancer of the Skin Caused by Oil*, pamphlet No. SHW 295A. London, H.M.S.O. 1969.

<sup>8</sup> Butlin, H. T., *British Medical Journal*, 1892, 1, 1341; 2, 1; and 2, 66.

<sup>9</sup> Bingham, E., Horton, A. W., and Tye, R., *Archives of Environmental Health*, 1965, 10, 449.

<sup>10</sup> Dietz, W. A., King, W. H., Priestley, W., and Rehner, J., *Industrial and Engineering Chemistry*, 1952, 44, 1818.

<sup>11</sup> Horton, A. W., Denman, D. T., and Trosset, R. P., *Cancer Research*, 1957, 17, 758.

<sup>12</sup> Horton, A. W., Bingham, E. L., Burton, M. J. G., and Tye, R., *Cancer Research*, 1965, 25, 1759.

<sup>13</sup> Boutwell, R. K., and Bosch, D. K., *Cancer Research*, 1959, 19, 413.

<sup>14</sup> Sutton, M., *British Medical Journal*, 1969, 1, 116.

<sup>15</sup> Lloyd, W. J., *British Medical Journal*, 1968, 4, 830.

<sup>16</sup> Kinnear, J., Rogers, J., Finn, O. A., and Mair, A., *British Journal of Industrial Medicine*, 1955, 12, 36.

<sup>17</sup> Roe, F. J. C., Carter, R. L., and Taylor, W., *British Journal of Cancer*, 1967, 21, 694.

<sup>1</sup> Plempel, M., Bartmann, K., Buchel, K. H., Regel, E., *Deutsche Medizinische Wochenschrift*, 1969, 94, 1356.

<sup>2</sup> Oberster-Lehn, H., Baggesen, I., and Plempel, M., *Deutsche Medizinische Wochenschrift*, 1969, 94, 1365.