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STUDIES IN THE INCIDENCE OF CANCER IN A FACTORY HANDLING INORGANIC COMPOUNDS OF ARSENIC

I. MORTALITY EXPERIENCE IN THE FACTORY

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II. CLINICAL AND ENVIRONMENTAL INVESTIGATIONS

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Introduction

The association of arsenic with carcinogenesis has long been suspected in this country. For example, J. Ayrton Paris (1825), a Cornish physician, alleged, during the period of his practice in Penzance (1813–1817), that arsenical fumes from the smelting works occasionally caused scrotal cancer, but later investigation disclosed no definite evidence in favour of his claims. In 1879, Haerting and Hesse, discussing the "Schneeberg lung," implicated the inhalation of arsenical dust as the major cause of the condition, and many later continental investigators in this area have inclined to this view.

The first recorded case in this country of cancer resulting from arsenical medication was that of a clerk, aged 34, who was seen in 1872. He had been under arsenical treatment for psoriasis. He developed a wart which later became a hard-edged sore on the scrotum. This patient was seen by Jonathan Hutchinson (1887), who believed that cancer occurred relatively frequently in those taking arsenic for long periods.

Pye-Smith (1913) collected the records of 31 cases of cancer, mostly amongst patients receiving prolonged arsenical medication for psoriasis. Two cases involving the skin occurred in sheep-dip workers. Legge (1903) gave the first hint in Britain that arsenical dust might possibly damage the lung

when he described a condition of irritation of the upper air passage coincident with keratosis of the skin and pigmentation. The affected persons were sheep-dip workers processing white arsenic and sulphur. Henry (1934), on examination of eight men employed in sheep-dip manufacture, found three with warty growths accompanied by keratoses and pigmentation of the skin, and put forward the view that one or two cases of cancer of the lung in sheep-dip workers may have been caused by arsenic.

During the period 1924–1930, six cases of skin cancer (three fatal) associated with contact with arsenical dust came to the notice of the British Factory Department. In two of these cases exposure was to copper aceto-arsenite, and in the other to arsenical sheep-dip powder. No case of skin cancer has been reported since 1930. Post-mortem examination in one of the fatal cases (copper aceto-arsenite) disclosed a second primary squamous-celled carcinoma below the left knee with secondary deposits in the liver and left kidney. The first primary occurred some years previously in the left axilla. The period of exposure to arsenical dust was nineteen years.

The first fatal case of lung cancer associated with arsenical dust came to the notice of the British Factory Department in 1939, and, since then, two cases (fatal) were reported in 1940 and one case

(fatal) in 1943. In the 1939 case the skin of the trunk and limbs was pigmented, with numerous small, flat, warty growths. There was perforation of the nasal septum. At the apex of the right lung there was a hard mass of cancer, and the glands in its neighbourhood showed evidence of metastases. The period of exposure to sheep-dip powder was thirty-seven years. In one of the 1940 cases post-mortem examination established the cause of death as septic bronchitis caused by a primary oat-celled carcinoma of the lungs. In the 1943 case, the period of exposure to sheep-dip dust was 43 years, and post-mortem examination revealed a columnar-celled adenocarcinoma of the upper lobe of the right lung.

Thus arsenic has long been suspect as a potential carcinogen, and in 1945 the British Factory Department referred the specific question of the occupational relationship of arsenic and cancer of the lung to the Industrial Health Research Board of the Medical Research Council, and a special Committee*

*Members of Committee: Professor M. J. Stewart (Chairman), Dr. A. N. Currie, Dr. S. A. Henry, Professor A. Bradford Hill, Dr. Donald Hunter, Sir Ernest Kennaway, with first Dr. R. S. F. Schilling and later Dr. Joan Faulkner (Secretary).

was set up under the Chairmanship of Professor M. J. Stewart. The Committee initiated a statistical inquiry by Professor A. Bradford Hill and field investigations by Dr. Kenneth Perry, and also arranged for a review of the world literature on arsenic in relation to cancer to be compiled (Neubauer, 1947).

The publication of the two following pioneer papers with their guarded but suggestive conclusions should lead, it is hoped, to an extension of research in industrial centres in other parts of the world where there may be a larger population at risk.

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Introduction

In investigating statistically the mortality experience of the factory under inquiry certain serious difficulties had to be faced. Excluding clerical workers the factory was relatively small, employing in all not very many more than a hundred operatives; further, only a proportion of these would have been in contact with the chemical process and exposed to the specific risk. A long period of years was therefore essential to produce sufficient data to give reliable results. Data for any such period were, however, entirely lacking in the factory records. The information required was as follows: (a) a list of the male employees, divided according to their occupations, for each year from 1943 (the time of inquiry) back to 1900 or thereabouts; (b) the approximate dates of birth of these men so that the age constitution of the population at risk could be computed at different points of time between 1900 and 1943; (c) information regarding all deaths occurring in that period of time. Given these data the recorded numbers of

deaths from different causes could then have been compared with the deaths which would have been expected to occur in a population of the stated size and age constitution if it had been experiencing during the passage of years the national, or local, rates of mortality. Comparison of observation with expectation would have revealed whether or not this group of workers, or some section of it, had experienced any abnormal rates of mortality.

This procedure could, however, not be followed since no details of the employees on the books over so long a period of time were available. A list of the deaths of employees was available and was believed to be comprehensive though lacking the cause of death in some cases. The necessary population figures, to relate to these deaths, were absent.

A different method of approach had, therefore, to be devised, and the only possible one was by means of proportional mortality rates, that is, to see whether the proportion of deaths in these factory workers which was debited to cancer differed



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