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Cancer of the Urinary Bladder – Epidemiology and Aetiology

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Summary. A brief review of the geographical variations in bladder carcinoma incidence is given and the known aetiological factors, e. g. industrial exposition and pharmaceutic drugs, are surveyed.

Key words: Urinary bladder cancer - Epidemiology - Industrial cancer.

Cancer of the bladder is a world-wide disease but its incidence varies considerably in different countries. The data available from W. H. O. (14) show that the highest mortality rates are found in England and Wales but figures are not available for all countries. In Egypt, for example, where the disease is associated with bilharzia the incidence is very high. It is estimated that 12% of all cases of cancer occuring in Cairo are in the bladder.

In England, bladder cancer is the sixth commonest malignant disease in men and it is three times commoner in men than in women. Susceptibility to the disease increases with age which suggests that the "oncogenic force" increases as we grow older or, the effect of the mechanism that controls cell growth diminishes. Between 1962 and 1970 there has been a 50% increase in the number of people contracting the disease compared with 17% increase in cancer of the bronchus (Registrar General's Statistical Review 1973). Part of this increase may of course be due to the fact that we are an ageing population and the number of people at increased risk is steadily going up. However, a similar increase in incidence has also been noted in the United States.

In England the disease is commoner in towns than in rural areas and this has been noted in several other countries including Sweden and suggests that exposure to atmospheric pollution associated with urbanisation may be a contributory factor.

Of particular interest is a small group of patients in whom there has been occupational exposure to carcinogenic substances. These account for a very small proportion of all cases and in the majority of patients no occupational hazard can be identified. This occupational risk was observed first by Rehn (12) in four aniline dye workers in Germany. Since then it has been shown that the carcinogenic substances used in dyeing were 2-naphthylamine and to a lesser extent benzidine and 4-amino-diphenyl. In persons exposed to these substances death from bladder cancer appeared to be 30-40 times commoner than in unexposed persons (3). These chemicals are also used for hardening rubber and it was found in one area in England where they make rubber tyres that there was a high incidence of bladder cancer due to a substance related to 2-naphthylamine (2). There is also some evidence that workers in the electric cable industry exposed to rubber have developed the disease (5).

The identification of these substances is of considerable importance in preventive medicine. In some countries their use in industry has been prohibited by law. Workers who have already been exposed are also kept under careful surveillance. This involves regular cytological examination of urine. As a result of these preventive measures there are now very few cases of cancer produced by industrial exposure but as new industrial processes are constantly being developed a watch has to be kept for possible hazards.

Cigarette smoking has been associated with bladder cancer in many surveys. This, of course, is a dominant factor in bronchial carcinoma and it seems to play a similar although less pronounced part in the genesis of tumours of the urinary bladder. Studies in the U.S.A. (13, 15) and Demark (10) suggest that the risk for smokers is two to three fold. This has also been shown in the U.K. in one study by Deeley and Cohen (6). In a recent survey, however, carried out on British doctors over a period of 20 years by Doll and Peto (7), they were unable to demonstrate a significant association between smoking and deaths from

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bladder cancer. The numbers, however, were relatively small and although no positive relationship could be found it cannot be excluded. It would appear that when bladder cancer is thought to be related to smoking the latent period is considerably longer than in bronchus cancer so that death from bronchial disease may occur before a bladder tumour developed.

Two recent reports have also suggested that extensive coffee drinking may predispose to bladder cancer (4, 8). It has been postulated that the caffeine in coffee may be concerned but there is no direct evidence to support this. Experimental rats exposed to caffeine developed bladder tumours but the dosage was equivalent in the human to drinking about 85 cups of coffee per day!

The substances in the urine that derive from dyes which are thought to cause cancer are known chemically as aromatic amines. It was therefore a reasonable supposition that there might exist in the urine other substances of this nature occurring naturally which might be responsible for bladder tumours of unknown origin. The only substances of this type which have been demonstrated were derivatives of the amino-acid tryptophane (11). The interest in tryptophane metabolism was stimulated when it was suggested that some of its metabolites were carcinogenic and might be responsible for a proportion of cases in which no industrial hazard can be implicated. It was shown in a small series of 41 cases studied by Price that 20 who developed bladder cancer had an abnormal tryptophane metabolism but this work has not been confirmed.

Drugs may have some effect in causing tumours in the bladder. Phenacetin has been reported as having an association with urothelial tumours particularly in the renal pelvis and occasionally in the bladder (1). We have also seen several cases of bladder carcinoma develop in patients who had received treatment with the cytotoxic drug cyclophosphamide.

Further studies on the causation of bladder cancer must be based on patients suffering from the disease. Many classes of compounds seem capable of producing tumours of the urothelium. It would seem likely that the carcinogenic agent is present in the urine. The situation of the tumour at the ureteric orifice points to the fact that it is probably a urinary "irritant" rather than blood borne.

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