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Meeting convened by Task Force for Epidemiological Research on Reproductive Health and Task force of methods for the regulation of male fertility of the World Health Organization, Geneva, Switzerland. The meeting was convened to evaluate research needs and priorities regarding the relationship of vasectomy to cancers of the testis and prostate.

Risk Factors for Prostate and Testicular Cancer

P. Boyle and D.G. Zaridze

INTRODUCTION

CANCER OF THE prostate and testis both represent important forms of cancer in man although from a different perspective. It has been estimated that in 1980 there were nearly one quarter of a million new cases of prostate cancer diagnosed internationally [1] and within the European Community this represents the second commonest form of cancer in men with an estimated 85 000 new cases each year [2]. The incidence rate increases at a much faster rate with age than for any other epithelial cancer and, given the aging of the population (see Brody [3] for example) seems destined if for no other reason to become much more common in absolute terms. Testicular cancer is not so numerically important but with a clear peak in early life it represents the commonest form of cancer in men aged between 20 and 40 in many westernised countries. Thankfully, there have been major treatment advances in testicular cancer which have led in most countries to notable reductions in the mortality rates: the single exception to this observation appears to be those countries of central and eastern Europe [4].

The purpose of this working paper is to provide a background review of the epidemiology of cancer of the prostate and testicular cancer focussing on general risk factors, with reference to the role of vasectomy specifically excluded and covered elsewhere [5].

PROSTATE CANCER

Despite being one of the commonest forms of cancer, relatively little is known about the aetiology of cancer of the prostate. In 1980 it was estimated that prostatic cancer was the fifth most frequent cancer in men, with an estimated 235 800 cases occurring annually worldwide [1]. The incidence continues to increase [6] and incidence and mortality rates of cancer of the prostate demonstrate wide international variation with, for example, a 120-fold difference present between area of highest and lowest incidence, according to the most recently available statistics [7]. Increases continue to take place in the incidence of prostate cancer in Scotland and Connecticut [8] as well as the Scandinavian countries [9].

Figures 1–3 present the time trends in mortality rates from prostate cancer in Canada, Japan and Sweden: these three countries are chosen as they cover the range of prostate cancer variation. The mortality rate is increasing in all three countries and has been since 1955. In 1988 prostate cancer comprised 2.5% of all cancer deaths in Japan with the corresponding figure for Canada being 10.6% and for Sweden, 17.7%. This emphasises the importance of prostate cancer as a public health problem. When the age-specific mortality rates for these same countries are examined by birth cohort, it is suggestive that rates are beginning to stabilise in the younger cohorts in Canada (Fig. 4) and Japan (Fig. 5) and less noticeably in Sweden (Fig. 6).

Migrant studies have demonstrated that migrants from low-to high-incidence areas acquire a higher risk for prostatic cancer [10–12], with an increase in risk already apparent in the first generation of migrants from Japan and China. Haenszel [10] has shown that migrants from Ireland, Norway, Canada and Sweden have higher prostatic cancer rates than other United States whites, while migrants from Austria, Poland, U.S.S.R. and Italy show lower rates.

The cancer experience of special population groups, whose lifestyle habits distinguish them from the general population and

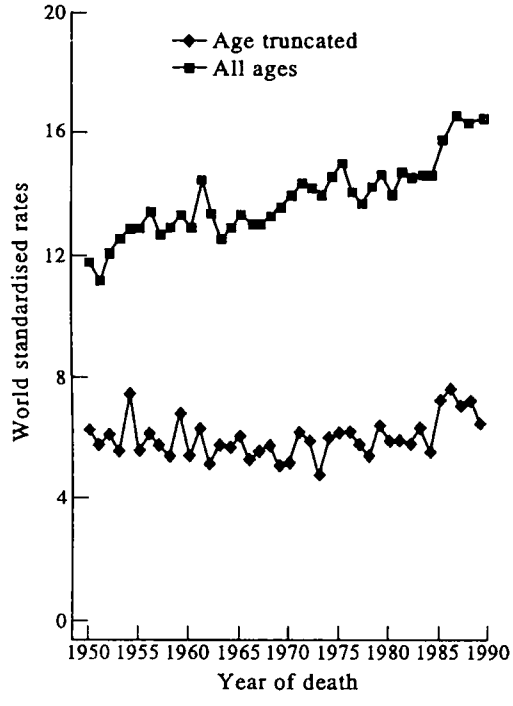

Fig. 1. All ages and truncated (aged 35–64), age-standardised mortality rates per 100 000 person-years for prostate cancer in Canada, 1950–1989.

Correspondence to P. Boyle.
P. Boyle is at the Division of Epidemiology and Biostatistics, European Institute of Oncology, via Ripamonti 332/10, 20141 Milan, Italy, and D.G. Zaridze is at the Institute of Carcinogenesis, Russian Cancer Research Centre, Moscow, Russia.
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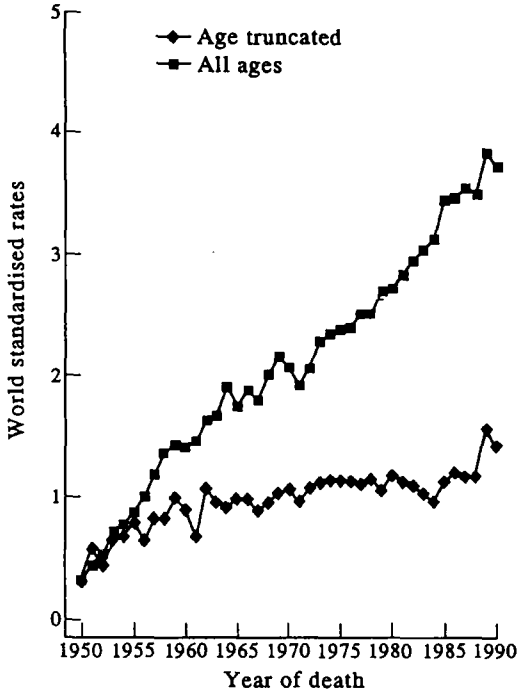

Fig. 2. All ages and truncated (aged 35–64), age-standardised mortality rates per 100 000 person-years for prostate cancer in Japan, 1950–1990.

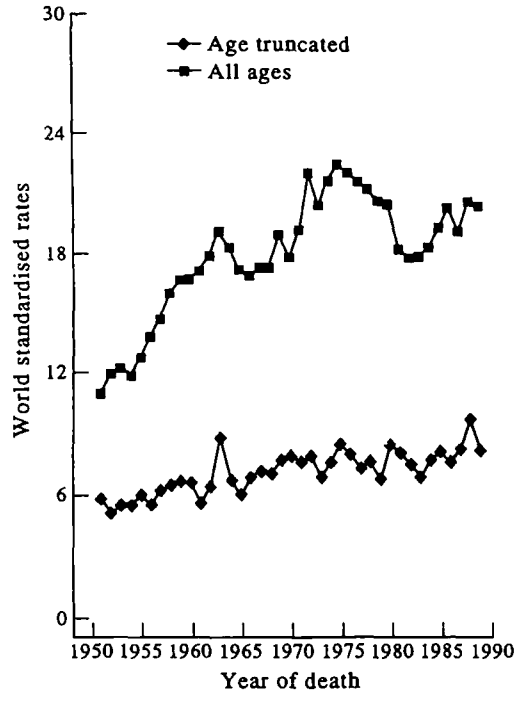

Fig. 3. All ages and truncated (aged 35–64), age-standardised mortality rates per 100 000 person-years for prostate cancer in Sweden, 1951–1989.

also from the nearby population, is of great interest in relation to cancer sites in which certain lifestyle factors are claimed to be of aetiological importance. The most studied of such groups are Seventh Day Adventists and Mormons, whose cancer and cardiovascular disease experience and lifestyle pattern have been the subject of rigorous studies.

In general, currently available evidence on cancer among Seventh Day Adventists and Mormons is consistent with the hypothesis that one or more components of the typical Adventists' and Mormons' lifestyle account for a large proportion of their reduced risk of cancer. However, the rates for prostatic cancer in Seventh Day Adventists do not differ from those in control populations [13], while the incidence of prostatic cancer is higher among Mormons than among non-Mormons [14].

The descriptive epidemiology of prostate cancer can be summarised as providing compelling evidence that prostate cancer may be preventable. Different populations around the world experience different levels of prostate cancer and these levels change systematically with time. When migration takes place, migrant groups quickly acquire the prostate cancer pattern of their new home. Furthermore, groups of individuals whose lifestyle differentiates themselves from other members of the same community experience different prostate cancer levels. While the data on blacks in Africa and the U.S.A. provide some evidence of a genetic component to prostate cancer risk, it is clear that lifestyle determines to a large extent the risk of prostate cancer.

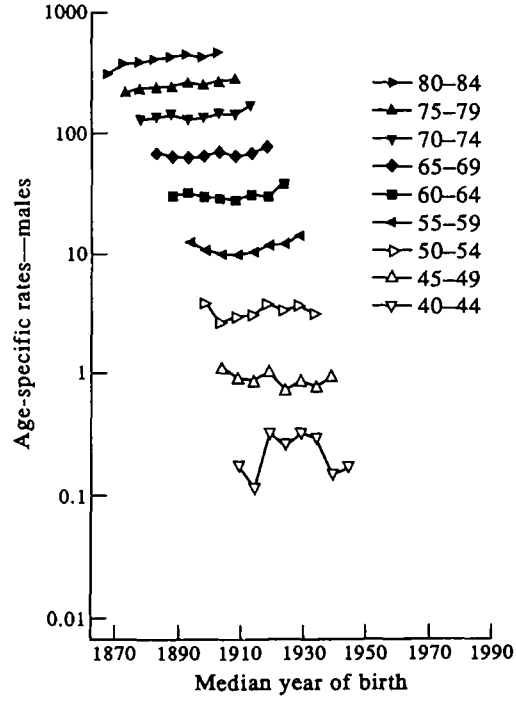

Fig. 4. Age-specific rates per 100 000 presented by age and median year of birth (cohort) for prostate cancer in Canada, 1950–1989.

SUSPECTED AETIOLOGICAL FACTORS

Hormones

It is not within the scope of this document to give a detailed review of endocrinological factors in the aetiology of cancer of the prostate: only a brief mention will be made with some important references quoted and it can be easily summarised. In research directed to the search for endocrine or biochemical factors that could be implicated in prostate carcinogenesis, determination of steroid and peptide hormone concentrations in plasma of patients with the disease has failed to consistently identify any endocrine disturbance, or any difference from the normal asymptomatic male which could lead to a greater understanding of prostate cancer aetiology [15, 16].

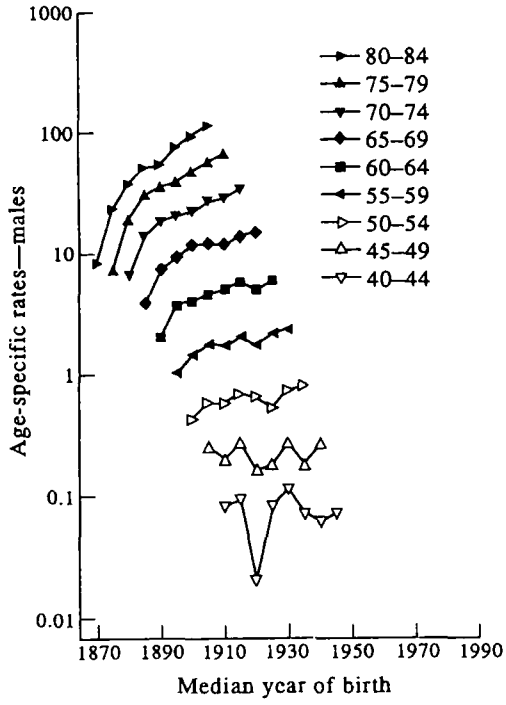

Fig. 5. Age-specific rates per 100 000 presented by age and median year of birth (cohort) for prostate cancer in Japan, 1950–1989.

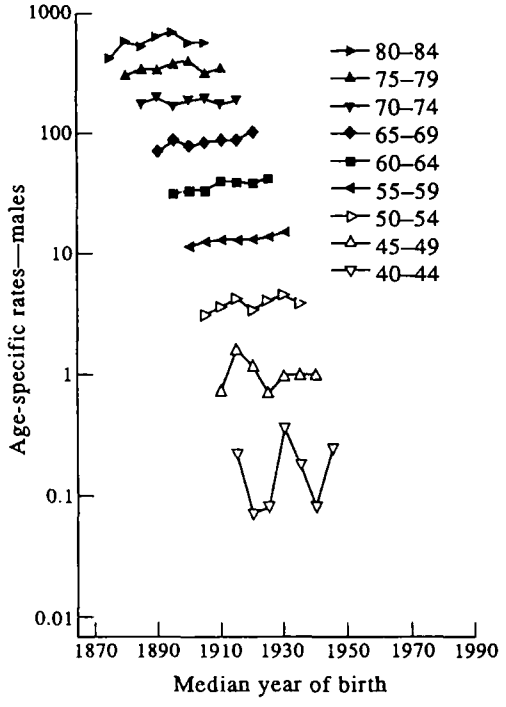

Fig. 6. Age-specific rates per 100 000 presented by age and median year of birth (cohort) for prostate cancer in Sweden, 1955–1989.

Sex hormones have been implicated in the aetiology of cancer of the prostate, primarily on the basis that the growth and development of this organ requires the presence of sex hormones. The hormonal hypothesis in the aetiology of prostatic cancer is supported by the discovery of steroid hormone receptors in prostatic carcinoma [17], by the success of oestrogen treatment of prostatic cancer patients [18] and, finally, by the fact that it was possible to induce prostatic carcinoma in experimental animals by prolonged administration of male sex hormones [19]. In addition, it has been shown that the levels of testosterone and dihydrotestosterone are higher in neoplastic prostatic tissue than in the normal prostatic gland, as is the uptake of testosterone and its conversion to its metabolite dihydrotestosterone (DHT). The level of testosterone in neoplastic tissue has been found to be higher than in the hyperplastic prostate, while conversely, the levels of dihydrotestosterone were higher in the hyperplastic prostatic gland [20–22]. This is not, however, straightforward to interpret since DHT may well be increased due to the effects of the benign prostatic hyperplasia itself.

Furthermore, the hormonal hypothesis in the development of prostatic cancer has received only equivocal support from epidemiological studies and clinical observations.

Sexual activity and marital status

Sexual activity, which is merely an indicator or indirect measure of hormonal status, has been related to the occurrence of prostatic cancer [23, 24]. Prostatic cancer patients seem to have a greater sexual drive than controls, but are less sexually active. According to Rotkin [23], prostatic cancer patients experience both puberty and first intercourse at a later age than controls.

Prostatic cancer mortality rates are associated with marital status, increasing in the following order: single, married, widowed, divorced [25, 26]. It has also been suggested that among married men the risk of prostatic cancer is higher in those with children than among those without children [27].

The results of case–control studies in general show the same pattern. Steele *et al.* [28] found that among prostatic cancer patients there was a significantly lower proportion of single men than in the control group. In other studies, prostatic cancer patients had significantly more children than controls [29–31].

However, these associations with marital status are more difficult to interpret today than previously with regard to their interpretation, *vis-a-vis* sexual drive and sexual activity due to changes in society's attitudes.

Diet

The hypothesis relating prostatic cancer to a high-fat diet, through possible influence on hormone metabolism, has arisen from observations of the international distribution of prostatic cancer [29, 32]. Several correlation studies report a positive correlation between prostatic cancer frequency and a high-fat intake [32–36] and also with the frequency of other diet-related cancers such as colorectal and breast cancer [32, 34, 37]. In addition, there is limited evidence to suggest that diet influences the hormonal profile of men [38].

Hypotheses relating prostatic cancer risk to a high-fat diet, through a possible influence on hormone metabolism, have arisen through observation of the international distribution of prostate cancer occurrence and *per capita* fat intake [8]. Recent interest has focused on three aspects of diet: animal fat intake, beta-carotene intake and milk consumption.

Schuman [39] reported a case–control study of 223 cases in Minnesota, U.S.A. and found an increased risk [odds ratio (OR) = 2.45] associated with infrequent consumption of carrots and an increased risk (OR = 1.68) for frequent consumption of ice-cream. Graham *et al.* in a study based on 260 cases, found an increased risk (OR = 3.0) for high animal fat consumption. The same study found an increased risk (OR = 1.8) associated with frequent consumption of foods rich in vitamin A among men aged over 70.

Snowdon *et al.* [41] examined 247 prostate cancers which occurred in a prospective study of Seventh Day Adventists. They found no effect of intake of fruits and vegetables. However, they found a significantly increased risk (OR = 2.4) associated with frequent milk consumption and a significant risk (OR = 3.6) associated with a heavy intake of milk, cheese, eggs and meat. Heshmat [43], reporting a case–control study of 181 cases, found that intake of vitamin A from plant and animal sources was higher in cases than in controls. They also found that cases consumed significantly greater amounts of fats than controls.

Hirayama [43] reported findings from a cohort study conducted in Japan which yielded 183 prostate cancer cases. He reported a reduced risk of death associated with frequent consumption of green and yellow vegetables in men aged less than 75 years. However, he found the reverse situation, i.e. a positive association, in men aged over 75. These results are difficult to reconcile. No data regarding fats were reported.

Talamini *et al.* [44] reported a case–control study from Northern Italy based on 166 cases. They reported a non-significant increased risk (OR = 1.2) for men who consumed green vegetables five or more times per week. Prostate cancer risk was increased by frequent weekly consumption (five or more times) of milk and dairy products (OR = 2.5) and meat (OR = 1.7). Ross [45] reported a case–control study of prostate cancer with 142 cases interviewed. In those with a high fat diet, an increased risk (OR = 2.0) was found to be associated with low beta-carotene intake. Significant risks were found for high fat intake among black subjects with a trend in risk apparent among whites.

Ohno *et al.* [46] found no association with dietary fat intake in their case–control study but among men aged over 70, they found an increased risk (OR = 2.9) associated with low beta-carotene intake. By contrast, Kolonel *et al.* [47], based on a larger case–control study (452 cases) found an increased risk (OR = 1.6) associated with higher levels of dietary beta-carotene intake among men aged over 70. They also found an increased risk (OR = 1.7) associated with high usual consumption of saturated fat among men aged over 70.

Mettlin *et al.* [48] reported findings from a case–control study of 371 cases in Buffalo, New York. A decreased risk for high beta-carotene intake was found for both younger (less than 69 years) men (OR = 0.3 in highest quintile) but not among older (70+ years) men (OR = 1.0 in highest quintile). This study also found a trend toward increased risk for intake of fat from meats and a significantly increased risk associated with preference for whole milk (OR = 1.9). Mills *et al.* [49] reported follow-up on a Seventh Day Adventist cohort which yielded 180 cases of prostate cancer. Increasing consumption of fruits was associated with a significantly decreased risk and a suggestive positive association with animal product consumption did not persist after adjustment.

These findings are difficult to summarise concisely. Increased fat intake could increase the risk of prostate cancer and while milk consumption is apparently associated with increased risk it has not been shown to be independent of intake of fat. The association with vegetable intake is very confusing: some studies are positive, some negative and a smaller number are null. It is clear, however, that there are dietary determinants of prostate cancer risk but their precise nature requires to be identified in a variety of populations in a variety of study designs.

The suggestion from some studies (see Mayne [50] for review) that increased beta-carotene/vitamin A/vegetable intake could increase the risk of prostate cancer deserves to be taken seriously particularly in view of the possible protective role, and use as a chemoprevention agent, against many common forms of cancer. It has been shown that vitamin A can enhance carcinogenesis in animal models [51]. With specific regard to the prostate, it has been shown that vitamin A may influence the synthesis of testosterone and that vitamin A has metabolic interactions with zinc (which may itself be a prostate cancer risk factor). Further, vitamin A can enhance proliferation of prostatic epithelial cells [52] and hence progress on occult tumours. However, support for a possible protective effect of vitamin A is supported by laboratory findings which have shown that vitamin A and synthetic retinoids inhibit and reverse carcinogen-induced hyperplastic and anaplastic lesions in mouse prostate organ cultures [53].

In studies which have examined the effect of dietary intake of trace elements on the frequency of cancer, a direct correlation has been established between estimated zinc and cadmium intake and mortality from prostatic cancer, as well as cancer of the large bowel, breast, uterus and skin. This finding is suggested not to represent the direct effect of increased zinc and cadmium intake but rather to be an indirect effect of zinc and cadmium on cancer risk by their antagonism with selenium, which was found to be inversely correlated with mortality from the above cancer [54]. There is evidence that levels of zinc in neoplastic prostatic tissue are significantly lower than in normal prostatic glands, whereas in glands with benign prostatic hyperplasia, levels of zinc are significantly elevated [55–57]. The suggestion of the possible role of cadmium in prostatic carcinogenesis is based on the ability of cadmium to modify the capacity of the prostate to take up zinc [58].

The currently available epidemiological evidence by no means provides definitive evidence that prostate cancer risk is increased by increased intake of vitamin A or beta-carotene-rich foods or supplements. It merely highlights an area of possible concern in epidemiology, particularly when making dietary recommendations to bring about cancer prevention.

Body mass index

In the American Cancer Society cohort, overweight males were shown to have a 30% increased prostate cancer mortality compared to men within 10% of their 'ideal' weight [59]. Among Seventh Day Adventists, the risk of fatal prostate cancer was 2.5-fold higher among overweight men [41]. Two case–control studies were inconclusive [29, 40]. More recently, Talamini *et al.* [44] found a substantial dose–response gradient in a case–control study in northern Italy. With the risk set to 1.0 in the lowest tertile of body mass index (kg/m^2) the risk rose to 2.3 (95% confidence interval (2.1,4.8) in the second tertile and to 4.4 (1.9,9.9) in the highest: the trend was highly significant ($P < 0001$).

Given these findings and the association between energy intake and increased weight, it is important to have information on dietary intake of vitamin A and beta-carotene adjusted for total energy intake. As Willett [60] has pointed out, people who have high energy intakes generally eat more of everything: thus they will apparently have an increased carotene/vitamin A intake due to what could be an artefact. It is essential to look at the micronutrients associated with prostate cancer risk after adjustment for estimated energy intake: this does not appear to have been done to date.

Occupation

In experimental conditions several cadmium compounds have been reported to be carcinogenic [61], although administration of cadmium components failed to produce any changes in the prostate gland of experimental animals [62, 63]. The results of cohort studies suggest an increased risk of prostatic cancer among those who were exposed to cadmium oxide [64, 65]. A case–control study in which exposure to dietary sources of cadmium was related to prostatic cancer risk produced negative results [66].

In cohort studies of rubber workers, an excess of prostatic cancer death was observed [67–69]. In one of these studies excess of prostatic cancer deaths were claimed to be the result of exposure to cadmium [67]. However, this hypothesis was subsequently rejected [70]. An attempt to find a specific work experience with specific exposure in the rubber industry has not yet been successful.

While several studies have demonstrated an increased risk of prostate cancer among farmers and agriculture workers [71] a recent study from New Zealand did not provide support for this association [72]. A feature of studies of occupation and prostate cancer has been that findings in one are not replicated in the others and a new set of occupations are found to be associated with higher risk (see discussion in [72]).

Genetic factors

Prostate cancer was found to be significantly more frequent in the male relatives of index patients than in controls [27, 73]. Furthermore, the high levels reported in blacks worldwide—Africa, the Caribbean and North America—suggest a possible independent genetic component to the risk of this disease.

Sexually transmitted infection

There is evidence from experimental studies that certain tumour-associated viruses isolated from a human prostate carcinoma (Herpes virus 2, Simian virus 40 and cytomegalovirus) and able to induce oncogenic transformation of hamster embryo cells [74–76]. A number of studies have demonstrated the presence of virus-like particles in tissue removed from patients with prostatic cancer [77] or have shown increased antibody titres in such patients [78].

In several case–control studies, a higher proportion of cases than controls reported a previous history of venereal disease [24, 28, 73]. (This may also reflect the tendency, discussed above, of prostatic cancer cases to have a greater sexual drive.) Some studies have observed an increase in breast and cervical cancer among wives of men with prostatic cancer [79] but others failed to confirm the previous findings [80].

Benign prostatic hyperplasia

The relationship between benign prostatic hyperplasia and prostatic cancer remains controversial [8]. The two most frequently quoted studies on the relationship between benign prostatic hyperplasia and prostatic cancer have produced contrasting results [30, 31]. In the second study, both prospective and retrospective approaches were used. The results obtained from the prospective study demonstrate a relative risk of prostatic cancer 3.7 times greater among benign prostatic hyperplasia patients, and indicate that prostatectomy produces a considerable reduction in subsequent cancer risk. The retrospective study of patients with prostate cancer and controls admitted with benign prostatic hyperplasia has shown a relative risk of 5.1 for the prostatic cancer group. These findings are at variance with the results of a prospective study of patients who had subtotal prostatectomy and controls, in which the relative risk of prostatic cancer in the benign prostatic hyperplasia group was estimated to be 0.9 [30]. Furthermore, it is generally accepted that carcinoma arises in the outer part of the prostate, while benign prostatic hyperplasia is more often found in the inner part of the gland [81, 82].

DISCUSSION

The association of the hormonal profile of men with diet and, most probably, diet-associated differences in the hormonal milieu of populations at different risk of prostatic cancer, suggest that diet determines the risk of prostatic cancer through its influence on sex hormone metabolism. As has been shown above, prostatic cancer is a disease of old age, and its incidence increases rapidly with age, suggesting that the hormonal status of elderly men and the changes which occur with advancing age should be of importance in the aetiology of prostatic cancer.

Carcinogenesis is recognised as a multistage process which results from a complex interaction of multiple factors. There are two clearly defined stages in the natural history of prostatic cancer. The end point of the first stage of carcinogenesis in the prostate is the development of a latent cancer (small, focal, clinically unrecognisable tumour), while the second stage evolves into an invasive clinically overt tumour. While little is known about the factors involved in the first stage of prostatic carcinogenesis, the second stage, which is associated with tumour growth, promotion and progression, is most probably related aetiologically to environmental factors prevalent in the high-risk populations, frequently defined as "lifestyle" factors.

Some epidemiological observations, however, are compatible with the hypothesis that there is a genetic component in the aetiology of prostatic cancer. First of all, cancer of the prostate was found more frequently in the male relatives of index patients than in controls [83, 84]. Secondly, the incidence of prostatic cancer has been reported to be high not only among North American blacks, who consume a western diet, but also in blacks living in Africa [85], whose diet is mainly vegetarian. Thirdly, according to the most recent incidence statistics [7, 86], prostatic cancer incidence among Japanese and Chinese in most areas of the U.S.A. is still less than half that of white Americans, while their rates for colorectal cancer (cancer with high-fat diet-related aetiology) are of the same order as those of white and black Americans. The above suggests either than Chinese and Japanese may be less susceptible to prostatic cancer than blacks and/or Caucasians, or that there are some unknown exogenous factors to which the latter but not the former ethnic groups are exposed.

Where are we now with the epidemiology of prostatic cancer? The disease is increasing in incidence in many parts of the world at differing disease risks and we do not understand which risk factor(s) are driving these spatial and temporal differences. The findings from aetiological studies are inconsistent in regards to the likely important variables: these are probably dietary and hormonal in origin but it is not clear which one is the true risk factor. There is some agreement that neither cigarette smoking nor alcohol drinking are important risk factors for prostate cancer. From the available evidence, it is probable that a diet high in fat and milk increases the risk of prostate cancer. It is difficult to ignore the various suggestions that beta-carotene/vitamin A-rich diets could be associated with an increased risk of prostate cancer. This is particularly true at a time when these micronutrients are being proposed for cancer prevention strategies. Finally, it is difficult to escape the feeling that prostatic

cancer has not attracted the interest from epidemiologists that its numerical importance deserves: the increases in numbers of cases programmed into the aging population clearly identify prostate cancer as a priority for further research and prevention.

TESTICULAR CANCER

The age–incidence curve of testicular cancer has two peaks, one in the twenties and one later in life [7, 87], possibly reflecting the relative frequency of different histological types, since teratomas have an earlier peak incidence than the more frequent seminomas, or reflecting the role of different risk factors applying to different birth cohorts. Testicular cancer has been increasing in frequency throughout this century [88]. Further, there is evidence that the incidence, specifically of teratomas, is now increasing predominantly in young men in many regions, including Scotland [89], New Zealand [90] and the Nordic countries [9] including Denmark [91]. The incidence rate has tripled in Victoria, Australia between 1950 and 1985 with increasing cohort-based trends in both seminoma and non seminoma, and a trend towards an earlier age at onset incidence for non-seminomas has been detected [92]. The highest incidence rates are observed in western populations and the lowest ones in oriental populations and blacks [7]. Efficacious chemotherapy, particularly the introduction of *cis*-platinum, has substantially reduced mortality from this disease over the last two decades although the time trends have varied between countries as a result of differences in the availability and utilisation of treatments [4]. This has also greatly altered the relationship between incidence and mortality rates: mortality can no longer be viewed as a surrogate for the incidence of testicular cancer.

Cryptorchidism is the only established risk factor for testicular cancer [93–98] with relative risks of order of 2–4 consistently found and a population attributable risk of approximately 10% in North America not restricted to the retrieved testis [95]. However, even although cryptorchidism is increasing in frequency in England and Wales, the proportion of cases of testicular cancer with mal-descent remains constant at around 10% [99]. The elevated risk is apparently not related to age at orchidopexy [100]. It is not known whether the temperature of the testis has some risk *per se* as would be expected with variation in time of descent. Other potential factors, such as *in utero* exposure to oestrogens [101], higher social class [87], occupational exposure to farming or chemical substances, marital status or mumps or diabetes have been studied but there is no clear evidence as to their role. There may be an increased risk of testicular cancer associated with premature birth [102] although this requires confirmation. Small excess risks have been reported among men with inguinal hernia and a reported history of testicular injury; the same study reported no association with a number of other factors including cigarette smoking and coffee consumption [98].

Correlation studies suggest an association with high dietary fat intake [34] which has never been properly investigated and assessed in an epidemiological study. A more recent study from Denmark, where the highest rates of testicular cancer are found, reported no association with height, weight and body mass index and risk of testicular cancer [103]. Incidence rates of testicular cancer have increased in Denmark steadily since 1943 [91]. It appears that men born just before or during the Second World War (1939–1945) are at a lower risk of testicular cancer compared to that expected against a background of a continually increasing trend [104].

These and other findings suggest that testicular cancer is initiated early in life and may, in fact, resemble in epidemiological terms a congenital malformation which does not appear until later in life. This is being investigated in a number of large epidemiological studies nearing completion around the world whose results could greatly clarify the role of certain aetiological factors in the causation of this disease.

CONCLUSIONS

For different reasons, prostate cancer and testicular cancer are important diseases for men. The incidence of both diseases appears to be increasing for reasons which are not at all understood. Both these forms of cancer should be priority areas for future epidemiological research and intervention.

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Is Vasectomy a Risk Factor for Prostate Cancer?

Harry A. Guess

Recently, several case–control studies have suggested that vasectomy may predispose to prostate cancer. Other studies have found no increase in risk. All of these studies have a number of limitations. Taken together, these studies do not provide convincing evidence that vasectomy increases the risk of prostate cancer. However, in view of the high prevalence of prostate cancer and the growing worldwide importance of vasectomy as a form of contraception, further epidemiological research is warranted. After briefly commenting on the experimental studies we will examine the epidemiological studies in more detail. This will be done by first summarising the designs and main findings of the most relevant published studies and then discussing methodological issues relating to the studies taken as a whole. Finally, we will present conclusions and offer recommendations for future research.
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EXPERIMENTAL STUDIES

ANIMAL STUDIES of vasectomy have shown considerable variability between species, making it difficult to extrapolate these findings to humans [1]. While an excess of spontaneous liver tumours following vasectomy has been clearly demonstrated in one strain of mice [2], it would be premature to draw any conclusions about human prostate cancer risk from this. Various types of anti-sperm antibodies have been demonstrated serologically in a high proportion of men following vasectomy [3]. Morphological changes in the human testis following vasectomy have been well documented [4], however, the authors argued convincingly that the fibrotic changes appeared to result from the mechanical obstruction produced by vasectomy rather than

Correspondence to H.A. Guess, Dept of Epidemiology, Mc Gau-Greenberg Hall, CB 7400 The University of North Carolina, Chapel Hill, North Carolina 27599–7400, U.S.A.
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