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Vasectomy and Risk of Cancers of Prostate and Testis

VASECTOMY HAS become a popular method of contraception—as many as 50 million couples in the world are estimated to rely on it for fertility control. In addition to being highly effective, the procedure appears to be safe [1]. A suggestion that vasectomy might increase the risk of atherosclerosis, based on a study of a small number of monkeys [2], was not borne out by subsequent research involving monkeys or humans [1]. Concern has recently arisen, however, following publication of a small number of epidemiological studies pointing to an increase in the risk of cancers of the prostate and testis following vasectomy. In October 1991, the WHO held a consultation in Geneva to evaluate research needs in this area. This meeting (which was organised by the WHO Special Programme of Research, Development and Research Training in Human Reproduction) brought together 23 scientists from 10 countries, as well as observers from collaborating organisations. Key background papers prepared for the meeting can be found in this issue of the *European Journal of Cancer*.

As reviewed by Boyle and Zaridze (pp.1048–1055), cancers of the prostate and testis have received less attention from epidemiologists than some other tumours and their aetiology is not well understood. Both cancers are common in many countries and their incidence is increasing. Thus any link with a procedure as common as vasectomy could be of considerable public health importance.

The suggested link with prostate cancer was highlighted by the publication of two studies in the *American Journal of Epidemiology* in December 1990 [3, 4]. Rosenberg and her colleagues [3] reported that an association between vasectomy and prostate cancer had emerged unexpectedly from their system of "case–control surveillance"—a procedure that involves routine screening of potential associations between prior exposures and diagnoses in hospital patients. In their analysis of 220 men with prostate cancer, the relative risk for vasectomy was estimated to be 5.3 (95% C.I. 2.7–10) using as controls hospital in-patients without cancer and 3.5 (95% C.I. 2.1–6.0) using cancer controls. The second study was based on self-administered questionnaires completed by patients entering Roswell Park Memorial Institute in Buffalo, New York [4]. In a case–control analysis involving 614 men with prostate cancer, the relative risk for vasectomy was estimated to be 1.7 (95% C.I. 1.1–2.6). In contrast to the previous study, there was a significant trend in risk with the number of years since vasectomy. The response rate for completing questionnaires was 71% for the cases and 67% for the controls.

Since the procedure of "case–control surveillance" involves the screening of thousands of potential associations between prior exposures and diseases, it is inevitable that many statistically significant associations will emerge by chance. Rosenberg *et al.* [3] emphasised that their findings could do no more than raise the hypothesis. As Guess points out (pp. 1055–1060), the relative risk estimates obtained in this type of study are also likely to be biased upwards. This is because selecting for unusually strong associations also selects for high values of measurement error.

Guess reviews the other epidemiological studies that provide information about the risk of prostate cancer in men who have undergone vasectomy. Another hospital-based case–control study using self-administered questionnaires, at the M.D. Anderson Cancer Center in Texas, suggested a modest increase in risk [5]. The relative risk was estimated to be 1.6 (95% C.I. 1.1–2.3), although the authors noted that their data were subject to the same types of biases as in the other hospital-based studies. A case–control study involving population controls in Los Angeles found a relative risk of 1.4 (95% C.I. 0.9–2.3), with a statistically significant association between the number of years since vasectomy and risk of prostate cancer [6]. Only 55% of the cases eligible for this study were interviewed (19% had died). Another population-based case-control study in Los Angeles was negative (relative risk estimate: 0.5) [7].

The strongest evidence against an association between vasectomy and risk of prostate cancer comes from a follow-up study of men enrolled in the Northern California Kaiser Permanente Medical Care Program [8, 9]. Men who had multiphasic health checkups between 1977 and 1982 were asked whether they had undergone vasectomy and, if so, the year of the operation. The subsequent incidence of prostate cancer was compared in men who reported a history of vasectomy and in matched controls. In the most recent report from this study[9], the relative risk of prostate cancer associated with vasectomy was 1.0 (95% CI 0.7–1.6). The relative risk was approximately 1 regardless of the length of time since vasectomy or the age at which the operation was performed. Another cohort study, known as the Health Status of American Men study, has been reported as showing a slight deficit of prostate cancer in vasectomised men after 8 years of follow-up [10].

All of these studies have been conducted in the United States. Although incidence rates of prostate cancer have been rising in American men, the increases have been just as striking in men aged 60–69 years (in whom vasectomy is uncommon) as in those aged 50–59 years [10]. Howards (pp.1060–1062) considers some possible biological mechanisms for a relationship between vasectomy and prostate cancer, and concludes that all are improbable. Several epidemiological studies which are now in progress will provide further information about this issue, but at present it seems unlikely that there is any real increase in the risk of prostate cancer in men who have undergone vasectomy.

The evidence concerning testicular cancer, which is reviewed by Lynge *et al.* (pp.1064–1066), is even less convincing. Analysis of cases of testicular cancer in Ireland [11] and at a Scottish hospital [12] suggested that vasectomy might accelerate the appearance of a testicular tumour, but the first study included only 3 cases in vasectomised men (all of whom developed symptoms within 8 weeks of vasectomy) and neither study

provided information about possible confounding factors. A population-based case–control study in western Washington state found a relative risk of 1.5 (95% C.I. 1.0–2.2) [13]. The association was confined entirely to Catholic men, and the authors suggested that there might have been underreporting of vasectomy by Catholic controls. Another American case–control study was negative [14]. Jørgensen *et al.* (pp.1062–1064) suggest a mechanism by which vasectomy might possibly accelerate the growth of a testicular tumour, but there is no direct evidence to support this.

After reviewing all of the available biological and epidemiological evidence, the WHO group concluded that any causal relationship between vasectomy and the risk of cancer of the prostate or testis is unlikely. Because even a slight increase in risk would be of concern, the group made recommendations for further research. Nevertheless, it concluded that no changes in family planning policies concerning vasectomy are warranted at present.

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1. Peterson HB, Huber DH, Belker AM. Vasectomy: an appraisal for the obstetrician-gynecologist. *Obstet Gynecol* 1990, 2, 568–572.
2. Alexander NJ, Wilson BJ, Patterson BD. Vasectomy: immunological effects on rhesus monkeys and men. *Fert Steril* 1974, 25, 149–156.
3. Rosenberg L, Palmer JR, Zauber AG, Warshauer ME, Stolley PD, Shapiro S. Vasectomy and the risk of prostate cancer. *Am J Epidemiol* 1990, **132**, 1051–1055.
4. Mettlin C, Natarajan N, Huben R. Vasectomy and prostate cancer risk. *Am J Epidemiol* 1990, **132**, 1056–1061.
5. Spitz MR, Fueger JJ, Babaian RJ, Newell GR. Re: "Vasectomy and the risk of prostate cancer" (letter). *Am J Epidemiol* 1991, **134**, 108–109.
6. Honda GD, Bernstein L, Ross RK, Greenland S, Gerkins V, Henderson BE. Vasectomy, cigarette smoking, and age at first sexual intercourse as risk factors for prostate cancer in middle-aged men. *Br J Cancer* 1988, 57, 326–331.
7. Ross RK, Paganini-Hill A, Henderson BE. The etiology of prostate cancer: what does the epidemiology suggest? *Prostate* 1983, **4**, 333–344.
8. Sidney S. Vasectomy and the risk of prostatic cancer and benign prostatic hypertrophy. *J Urol* 1987, **138**, 795–797.
9. Sidney S, Quesenberry CP, Sadler MC, Guess HA, Lydick EG, Cattolica EV. Vasectomy and the risk of prostate cancer in a cohort of multiphasic health checkup examinees: second report. *Cancer Causes and Control* 1991, 2, 113–116.
10. Perlman JA, Spirtas R, Kelaghan J, Madans J, Cox C, Kleinman J. Re: "Vasectomy and the risk of prostate cancer" (letter). *Am J Epidemiol* 1991, **134**, 107–108.
11. Thornhill JA, Butler M, Fitzpatrick JM. Could vasectomy accelerate testicular cancer? The importance of pre-vasectomy examination. *Br J Urol* 1987, **59**, 367.
12. Cale ARJ, Farouk M, Prescott RJ, Wallace IWJ. Does vasectomy accelerate testicular tumour? Importance of testicular examinations before and after vasectomy. *Br Med J* 1990, **300**, 370.
13. Strader CH, Weiss NS, Daling JR. Vasectomy and the incidence of testicular cancer. *Am J Epidemiol* 1988, **128**, 56–63.
14. Moss AR, Osmond D, Bacchetti P, Torti FM, Gurgin V. Hormonal risk factors in testicular cancer. A case–control study. *Am J Epidemiol* 1986, **124**, 39–52.

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The Therapeutic Challenge of Gliomas

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IN THEORY, a slow growing tumour which does not metastasise should not present a major therapeutic problem. In reality, malignant glioma answers this description and despite multidisciplinary attack remains an elusive problem. Is it over simplistic to say that it is a problem because it resides in a box? Has the fact that it occurs inside the skull got anything to do with the fact that it does not metastasise (or only very rarely)? Is there such a thing as the blood–brain barrier and is this really an acceptable excuse for the failure of chemotherapy and radiosensitisers? Whatever the answers to these questions, all would agree that a new drug which is active in this condition provides a welcome relief. One such drug is reported in the *European Journal of Cancer*, temozolomide. This short comment will review the state-of-the-art treatment of gliomas providing the back cloth against which temozolomide must be tested to assess its real value for the future.

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Inevitably, the major accent on research in the last few years has been refinement of local techniques of detection and destruction of the glioma. These have included physical treatments, immunotherapy and local instillation of cytotoxins and biological response modifiers via the carotid artery route. There is little doubt that stereotactic resection of tumours in the brain has proved a major technical advance [1]. The procedure is of particular benefit in reaching deep seated circumscript lesions but predictably unimpressive in treatment of infiltrating tumours or gliomas in essential areas of the brain. Using the same sort of stereotactic localisation, heat has been used either as a single therapeutic agent [2], or combined with interstitial brachytherapy [3]. Heat alone does produce short lived responses in localised tumours of the order of 20%. When ^{125}I seeds are implanted in addition to microwave heating, more toxicity is reported in the form of reversible seizures, increased neurological deficit and infection. 15 of 31 patients were "improved" in Sneed *et al's.* series, although the definition of improvement is not given. This is a problem area which relates to all reports of