The safety of vasectomy: recent concerns*

T.M.M. Farley,¹ O. Meirik,² S. Mehta,² & G.M.H. Waites³

Vasectomy has been accepted for family planning by approximately 42 million couples worldwide, the majority of whom live in developing countries. It is a highly reliable and safe contraceptive method, which has been extensively studied. Recently, however, renewed concerns have been raised about a possible effect between vasectomy and cancer of the prostate many years after the procedure has been performed. These concerns are based on research conducted in the USA, where there is a high and rising incidence of prostate cancer. This review discusses the evidence for this association and its potential impact in developing countries. The factors influencing the development and growth of prostate cancer are poorly understood and complicate any research into risk factors for the disease. Overall incidences of prostate cancer in some developed countries, such as the USA, are fifty times higher than in some developing countries, such as China. The majority of epidemiological studies on the relationship between vasectomy and prostate cancer have been based in the USA, but the findings are inconsistent and the reported associations weak. On the basis of currently available data, no changes in family planning policies with regard to vasectomy are warranted, but the concerns raised by these studies require that research into any possible association be undertaken in developing countries where vasectomy is widely practised.

Introduction

**Vasectomy: surgical and other methods**

Occlusion of the vas deferens (sperm ducts) by surgical means is an important family planning method and is popularly referred to as “vasectomy” or male sterilization. In recent years simpler and less invasive methods for vasectomy have been introduced (1); for example, the “no scalpel” method, in which the vas deferens is exposed through a small puncture hole, is acquiring widespread acceptability, is quicker to perform, and has a lower complication rate (2). Percutaneous injection into the vas deferens of sclerosing or polymerizing agents, such as polyurethane or silicone, to form plugs is also practised, and has been widely used in China, where it was originally developed. Surgical vasectomy is regarded as a permanent method of family planning, though successful reversal (vasovasostomy) has been performed (1). It is claimed that silicone plug vas occlusion is more easily reversible, though this has yet to be independently established. The surgical vasectomy procedure is safe and only rarely are complications reported (3).

**Worldwide patterns of vasectomy**

Vasectomy is a highly effective method of contraception and, together with use of condoms, is one of the few contraceptive options available to men. It is estimated that a total of 41.5 million couples rely on vasectomy as their method of family planning (Table 1) (4). Use of vasectomy varies considerably between and within regions and countries. Its popularity lags behind female sterilization (estimated world total, 140 million couples) intrauterine devices (100 million), oral contraceptives (65 million) or condoms (45 million). The method is used by a greater proportion of married couples in developed countries, although the total and annual numbers of vasectomies are greater in developing countries. As yet, vasectomy is only rarely performed in Africa.

**Long-term safety of vasectomy**

**General morbidity and survival**

The relationship between vasectomy and long-term morbidity and mortality has been extensively examined (5). A cohort study in the USA involving over 10 000 vasectomized men and a similar number of controls revealed that both groups had similar rates of 98 diseases, including various cancers, autoimmune diseases, and heart disease. The vasectomized men had a lower death rate than the non-vasectomized men, including half the death rate from cancer (6). A more recent study in the USA of the long-term safety of vasectomy also observed that there was no increase in overall cancer mortality; however, there was a significant increase in the risk of lung cancer...
Table 1: Prevalence of vasectomy, by region, in the late 1980s

<table>
<thead>
<tr>
<th>Region and area</th>
<th>% of married couples using vasectomy</th>
<th>Total relying on vasectomy (x10⁶ couples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All developing countries</td>
<td>5</td>
<td>32.3</td>
</tr>
<tr>
<td>Asia and Pacific region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>8</td>
<td>18.1</td>
</tr>
<tr>
<td>India</td>
<td>7</td>
<td>13.0</td>
</tr>
<tr>
<td>Other Asian and Pacific territories</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Hong Kong</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Korea</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Nepal</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Near East and North Africa</td>
<td>&lt;0.5</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>&lt;0.5</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Latin America</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Brazil</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Guatemala</td>
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<tr>
<td>All developed countries</td>
<td>5</td>
<td>9.2</td>
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<tr>
<td>Australia and New Zealand</td>
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<td>10</td>
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<tr>
<td>New Zealand</td>
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</tr>
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<td>12</td>
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<tr>
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<tr>
<td>North America</td>
<td>13</td>
<td>5.2</td>
</tr>
<tr>
<td>Other developed countries</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>World total</td>
<td>5</td>
<td>41.5</td>
</tr>
</tbody>
</table>

* Adapted from ref. 4.

among men who had undergone vasectomy more than 20 years previously (7). A historical cohort study conducted in Sichuan Province, China, showed a lower overall mortality among vasectomized men, though cause of death could not be ascertained (8). These observations are consistent with the results from other investigations that have shown no increase in morbidity, as reflected in hospital admission rates, among vasectomized men (9–12).

**Cardiovascular diseases**

Concerns about the safety of vasectomy with respect to cardiovascular diseases were first raised in the 1970s following studies on rhesus monkeys that suggested an increased risk of atherosclerosis (13), possibly attributable to an elevated level of anti-sperm antibodies. Although a WHO meeting convened in 1981 (14) to review the sequela of vasectomy concluded that there was no clinical or epidemiological evidence of an increase in cardiovascular, endocrine, or autoimmune diseases following the procedure, the concerns raised by the animal studies prompted research on this question among men in both developed and developing countries (6, 8, 12, 15–17). The results obtained did not substantiate the concerns, and showed that there were no adverse long-term effects on the cardiovascular system; the consistency of the results from countries with very different patterns of cardiovascular disease risk factors and incidence provided additional evidence that the original animal observations were not relevant to vasectomized men. Also, subsequent research on monkeys could not reproduce the earlier results (18).

**Testicular cancer**

Around 1990, epidemiological studies carried out in the USA (19) and Scotland (20) suggested that there was an increased risk of testicular cancer following vasectomy. Methodological concerns about the studies were raised during a WHO meeting convened in 1991 (21) to review these and other related results to prostate cancer; consideration of possible biological mechanisms found no plausible explanation for such an association. The majority of testicular tumours are germ cell in origin and the risk factors for testicular cancer appear to be already present at birth. The concerns that vasectomy might cause new, or accelerate the development of existing, testicular tumours have not been substantiated by later research (12).

**Prostate cancer**

Prostate cancer is a disease whose incidence rises steeply with age, and is much commoner among older men. Vasectomy, since it is a permanent contraceptive method, is usually performed on men aged 30–50 years, and became more widely used for family planning in the 1960s and 1970s. Thus it is only recently that the first groups of vasectomized men have reached an age at which there is an appreciable risk of prostate cancer; studies of any relationship between the two are, therefore, only now feasible. Before examining the possible association between vasectomy and prostate cancer, the worldwide and temporal patterns of prostate cancer incidence will be briefly reviewed.

**Incidence.** It is important to distinguish between incidental, clinical, and latent prostate cancer. The latent cancer consists of localized, usually well-differentiated lesions, most often in the peripheral part of the prostate gland. These lesions do not manifest
themselves clinically and are diagnosed at autopsy. Incidental cancers are subclinical lesions with varying potential for malignancy and are usually detected following prostate surgery, which is most frequently performed for the treatment of benign prostatic hyperplasia (BPH), a common condition among elderly men. The prevalence of latent prostate lesions increases with age, reaching almost 50% among men aged >80 years (22), and appears to occur with a similar frequency in different areas of the world (23, 24). Clinical prostate cancer, however, occurs only in a small proportion of men and at widely disparate frequencies in different populations. In developed countries clinical prostate cancer is one of the commonest cancers among men, while in developing countries it has a much lower incidence. Globally, there is a fiftyfold variation in the overall incidence of the disease. For example, in parts of the USA the (age-standardized) annual incidence is 91.2 per 100,000 men, while it is as low as 1.8 per 100,000 in Shanghai. The incidence among men in Bombay is 8.2 per 100,000 (25). Age-specific rates of prostate cancer obtained from cancer registries in various countries are shown in Fig. 1. In the USA the rates among black men are higher than those among white men (data for Detroit are used for purposes of illustration), with no apparent explanation for this difference. In other developed countries, represented in Fig. 1 by Denmark and New Zealand, in both of which vasectomy is a widely used method of family planning, the incidences are lower than in the USA. In contrast, in Bombay and Shanghai, the only developing country populations for which adequate data are available, substantially lower incidences are observed, and the disease is not common. However, the incidence in Bombay and Shanghai rises with age at a similar rate to that in countries with a higher overall incidence of prostate cancer, though this is not apparent from the plots in Fig. 1 because of the scale.

Many studies on the incidence of prostate cancer have not distinguished between the incidental and clinical types. The recent increases in the incidence of prostate cancer in many developed countries may in part be due to an increase in incidental prostate cancer following surgery for BPH. Improved surgical techniques have been introduced, resulting in earlier and more widespread interventions for BPH. Also, new diagnostic techniques, such as the use of prostate-specific antigen levels, ultrasound examinations, and systematic screening for prostate cancer, have led to detection of more prostate cancers, particularly in countries where the incidence is high. In the USA, for example, the age-adjusted incidence of reported prostate cancer increased by 30.3% from 1973 to 1985, while over the same period the age-adjusted mortality increased by only 8.0% (23).

**Risk factors.** Investigation of risk factors for prostate cancer, particularly environmental and behavioural factors, including vasectomy, is difficult because little is known about the underlying pathophysiological causes of the disease (26, 27). The prostate gland depends on androgens for its development and maintenance of its function and morphology (28). Some observations implicate dietary factors in the etiology of clinical cancer. For example, increased rates of clinical prostate cancer among relatives of Japanese migrants to Hawaii (29) and the positive correlation with other tumours that have also shown an association with diet in international comparisons (30), suggest that diet, possibly its fat content, may play an important role in causing clinical prostate cancer (24, 31); however there is no consensus on this issue. Similarly, it has been suggested that variations in circulating hormone levels, in particular testosterone and its metabolites, in different ethnic groups account for differences in prostate cancer incidence (32), but no clear differences have been found in the hormonal levels of prostate cancer cases and controls within the same ethnic group (33).

Presumably clinical prostate cancer develops from lesions similar to the latent cancers that are highly prevalent among older men. The occurrence of similar prevalences of latent prostate cancer, but wide variations in the incidences of the clinical cancer among men from markedly different groups, suggests that the risk factors for latent and clinical prostate cancer, although poorly understood, may be different.

**Vasectomy and prostate cancer**

In 1990 two epidemiological studies in the USA suggested an increase in the risk of prostate cancer fol-

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**Fig. 1. Age-specific incidence of prostate cancer in the 1980s in selected developed and developing countries (from ref. 25).**

![Graph showing age-specific incidence of prostate cancer](https://placeholders.your-image-url.com)

**Detroit, USA** (black)

**Detroit, USA** (white)

**New Zealand** (non-Maori)

**Denmark**

**India**

**China**

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**Table 1. Age-adjusted incidence of prostate cancer in the USA, 1973-1985**

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Incidence per 100,000</th>
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<tbody>
<tr>
<td>50-54</td>
<td>27.0</td>
</tr>
<tr>
<td>55-59</td>
<td>58.0</td>
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<tr>
<td>60-64</td>
<td>108.0</td>
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<tr>
<td>65-69</td>
<td>135.0</td>
</tr>
<tr>
<td>70-74</td>
<td>160.0</td>
</tr>
<tr>
<td>75-79</td>
<td>180.0</td>
</tr>
</tbody>
</table>
following vasectomy. The first of these studies was based on results of hospital-based, case–control surveillance (34) and the conclusions were considered by the authors to be hypothesis-generating, rather than definitive. The other, also a hospital-based case–control study (35), found a non-significant, moderate increased risk of prostate cancer ≥13 years after vasectomy had been performed. Prior to 1990, one cohort study (36) and two case–control studies (37, 38) reported no association between vasectomy and prostate cancer, while a further case–control study (39) reported elevated risks ≥20 years after the procedure. The two 1990 studies resulted in a WHO meeting in 1991 to review available biological and epidemiological evidence on the safety of vasectomy with regard to prostate cancer. At the meeting it was concluded that there was no known biological mechanism to account for any association, and that any causal relationship between vasectomy and cancer of the prostate was unlikely (21). Epidemiological studies under way at that time were expected to provide further information on such relationships.

Two additional studies on the risk of prostate cancer following vasectomy, conducted in the USA, have recently been published (40, 41). These studies used a prospective design in which groups of men were followed over time; one was a historical and the other a concurrent cohort study. Both studies have been carefully analysed and their prospective nature avoids many of the problems of bias in previous case–control approaches. The results indicate that there is an increased risk of prostate cancer (about 1.6 times) following vasectomy, and a trend of increasing risk with time since the procedure, up to a relative risk of about 1.9 among men vasectomized at least 20 years previously. The two studies were conducted among men who were above average socioeconomic status and educational level — one group consisted of health professionals and the other of husbands of registered nurses. However, the results of these new studies are not supported by a re-analysis (42) of Sidney’s cohort study (36), with more cases and person-years of observation, which confirmed the earlier findings of the lack of association between vasectomy and subsequent prostate cancer.

These latest studies, together with other available information, were reviewed at a recent meeting convened by the National Institutes of Health in Bethesda, MD, on 1–2 March 1993, at which WHO was represented. The meeting endorsed the conclusions of the 1991 WHO meeting (21) that no known biological mechanism existed to explain any possible association between vasectomy and prostate cancer and that any causal relationship between the two was unlikely. The meeting also reviewed interim, unpublished results from other ongoing studies of vasectomy and prostate cancer and noted that there was no consistency in the findings and that the reported associations are weak. It was therefore recommended that there was insufficient basis to change clinical and public health practices regarding vasectomy and the procedure should continue to be offered as part of family planning programmes (43). In countries where the incidence of prostate cancer is low (for example, China or India; see Fig. 1) any association of the magnitude observed in the USA, even if substantiated, would be of little significance to individual or public health.

**Implications for family planning programmes**

Recent findings have raised questions about the long-term safety of vasectomy and are of potential public health significance in countries where both prostate cancer and vasectomy are common. In countries where the disease is rare, the potential public health impact of any association is much smaller. However, in countries where vasectomy is a widely used method of contraception, the impact of the recent reports from the USA on family planning programmes and on acceptance of vasectomy could be large. As we have discussed above, the risk factors for prostate cancer are so poorly understood and the incidences so varied between countries that it is not justified to extrapolate the results from the USA to other countries, particularly those with low incidences of prostate cancer. Consequently, there are no grounds, based on the currently available epidemiological data, for changing the recommendation that vasectomy should be offered as part of national family planning programmes. Health care providers should continue to perform the procedure.

Couples seeking family planning should be informed of the benefits and risks of different contraceptive methods, and also of the risks and consequences of not using any family planning method at all. Furthermore, it is important that couples receive information that is relevant to the health situation in their own setting. It is therefore essential that studies on prostate cancer and vasectomy are carried out particularly in developing countries where vasectomy is widely used and the availability of other effective and affordable contraceptive methods is limited. Moreover, individuals who have volunteered for vasectomy have a right to be reassured about the long-term safety of their chosen contraceptive method. Such studies, supported by WHO, are under way—their feasibility has been assessed, and pilot studies will be conducted in 1993 in four developing countries. The main epidemiological study, using
case–control methodology, is expected to start in 1994. In the meantime, WHO will continue to monitor and disseminate any new information that emerges.

Conclusions

Vasectomy is one of the most widely studied surgical procedures and there is extensive evidence about its short- and long-term safety. Earlier concerns about possible adverse effects on the cardiovascular system, or an increase in autoimmune disease, have not been substantiated by careful research conducted in a wide range of countries. The recently reported results from the USA of a possible increased risk of prostate cancer many years after vasectomy has been performed have yet to be confirmed and there is no known biological mechanism or hypothesis to account for such an association. The relevance of these results to men in the USA who have undergone vasectomy has been carefully scrutinized and current recommendations are that vasectomies should continue to be performed and no change in clinical practice is warranted. There is no justification to extrapolate the U.S. results to other countries, particularly those where prostate cancer is not a common disease. Since these results may have an effect on family planning programmes and also raise concerns among men who have been vasectomized, it is essential that the long-term safety of the method be established in countries where vasectomy is a widely used method of contraception. Also, there are no grounds for suggesting any change in family planning policies with regard to vasectomy, and the method should continue to be provided as part of national family planning programmes. It is a simple, safe and highly effective contraceptive method.

Résumé

Sécurité de la vasectomie: nouvelles inquiétudes

Environ 42 millions de couples, dont les trois quarts vivent dans des pays en développement, ont recours à la vasectomie comme moyen de planification familiale. C'est une méthode de contraception fiable et sûre, dont la sécurité à court et à long terme a été largement étudiée. On a commencé à s'inquiéter des éventuels effets indésirables de la vasectomie dans les années 70, des observations sur le singe rhésus ayant évoqué une association avec un risque accru d'athérosclérose. Toutefois, des recherches chez l'homme, réalisées dans les pays développés et dans les pays en développement, n'ont mis en évidence aucune élévation du risque de maladie cardio-vasculaire chez les hommes ayant subi une vasectomie. D'autre part, d'après des études publiées entre 1988 et 1990, il pourrait y avoir un risque accru du cancer du testicule et de la prostate des années après la vasectomie ait été effectuée. Au vu de ces résultats, l'OMS a organisé, en 1991, une réunion chargée d'examiner les preuves épidémiologiques et biologiques d'une telle association. Il a été conclu qu'il n'existait aucun mécanisme biologique connu susceptible d'expliquer une association entre la vasectomie et le cancer du testicule ou de la prostate, et que les travaux actuellement en cours pourraient apporter un complément d'information. En ce qui concerne l'association avec le cancer du testicule, elle n'a été confirmée par aucune étude publiée depuis la réunion.

Deux études, publiées en février 1993, ont de nouveau soulevé le problème d'une éventuelle association entre la vasectomie et la survenue d'un cancer de la prostate des années après l'intervention. Ces deux études étaient prospectives, faisaient appel à des cohortes, et montraient un risque accru d'environ 1,6 fois pour l'ensemble des hommes vasectomisés, et atteignant 1,9 fois chez les hommes ayant subi une vasectomie plus de vingt ans auparavant. Ces observations s'appuient sur des recherches effectuées aux États-Unis d'Amérique, où l'incidence du cancer de la prostate est élevée et en augmentation. Leurs résultats s'écarter de ceux des précédentes études cas-témoins et de cohorte réalisées aux États-Unis d'Amérique et en Europe qui, à une exception près, n'ont montré aucune association systématique entre la vasectomie et le risque de cancer de la prostate. Les facteurs qui influent sur l'apparition et le développement du cancer de la prostate sont mal connus et compliquent les recherches portant sur les facteurs de risque, y compris les risques environnementaux et comportementaux, dont la vasectomie. L'incidence globale du cancer de la prostate, dans certains pays développés comme les États-Unis, est cinquante fois supérieure à celle que l'on observe dans certains pays en développement, par exemple la Chine. Dans ces derniers pays, où l'incidence de ce cancer est faible, l'impact de ces associations sur la santé individuelle et publique est faible; de plus, il reste à savoir si les facteurs de risque observés aux États-Unis sont également présents dans ces pays.

Compte tenu des données épidémiologiques disponibles, il n'y a pas lieu de changer la recommandation selon laquelle la vasectomie doit être
proposée dans le cadre des programmes nationaux de planification familiale. Les agents de soins de santé devront continuer à pratiquer ces interventions. Les couples consultant pour la planification familiale devront être informés des avantages et des risques des différentes méthodes contraceptives, et également des risques et des conséquences de l’abstention de toute méthode de planification familiale. De plus, il importe que les couples reçoivent une information adaptée à la situation sanitaire de leur propre environnement. Il est par conséquent nécessaire d’entreprendre des études sur le rapport entre vasectomie et cancer de la prostate, en particulier dans les pays en développement où la vasectomie est largement utilisée et où le nombre de méthodes contraceptives efficaces et abordables est limité. De plus, les sujets qui se sont portés volontaires pour une vasectomie sont en droit d’être informés quant à la sécurité à long terme de cette méthode contraceptive. De telles études, soutenues par l’OMS, sont en cours; leur faisabilité a été évaluée, et des études pilotes seront effectuées en 1993 dans quatre pays en développement. La principale étude épidémiologique, une étude cas-témoins, devrait démarrer en 1994. Dans l’intervalle, l’OMS continuera à surveiller et diffuser toutes nouvelles informations paraissant sur ce sujet.

References

28. National Cancer Institute Prostate Cancer Work-
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