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Safety and effectiveness of vasectomy

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Objective: To recommend further research on vasectomy based on a systematic review of the effectiveness and safety of vasectomy.

Design: A systematic MEDLINE review of the literature on the safety and effectiveness of vasectomy between 1964 and 1998.

Main Outcome Measure(s): Early failure rates are <1%; however, effectiveness and complications vary with experience of surgeons and surgical technique. Early complications, including hematoma, infection, sperm granulomas, epididymitis-orchitis, and congestive epididymitis, occur in 1%–6% of men undergoing vasectomy. Incidence of epididymal pain is poorly documented. Animal and human data indicate that vasectomy does not increase atherosclerosis and that increases in circulating immune complexes after vasectomy are transient in men with vasectomies. The weight of the evidence regarding prostate and testicular cancer suggests that men with vasectomy are not at increased risk of these cancers.

Conclusion(s): Publications to date continue to support the conclusion that vasectomy is a highly effective form of contraception. Future studies should include evaluations of the long-term effectiveness of vasectomy, evaluating criteria for postvasectomy discontinuation of alternative contraception for use in settings where semen analysis is not practical, and characterizing complications including chronic epididymal pain syndrome. (Fertil Steril® 2000;73:923–36. ©2000 by American Society for Reproductive Medicine.)

Key Words: Vasectomy, sterilization, male contraceptives, pregnancy, prostate cancer, cardiovascular disease, testicular cancer, epididymal pain syndrome

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Vasectomy is a simple and highly effective contraceptive method with a low morbidity rate and an extremely low mortality rate (1, 2). Worldwide, approximately 42–60 million men or 5% of married couples of reproductive age rely on vasectomy as a contraceptive method (3, 4). A large international variation in the prevalence of vasectomy exists among reproductive age married couples. Vasectomy is prevalent in New Zealand (23%), the United States (11%), the Netherlands (11%), South Korea (11%), Australia (10%), China (8%), and India (7%) (2). Because of the important role that vasectomy plays as a method of contraception worldwide, it is timely to review the current literature on safety and effectiveness and to recommend further research on this method of contraception.

MATERIALS AND METHODS

We reviewed the available medical literature on efficacy and safety of vasectomy with automatic searches in MEDLINE between the years 1964 and 1998. Search key words included vasectomy, sterilization, male contraception, and vasovasostomy. Primary sources were retrieved and reviewed.

RESULTS

Prevalence and Incidence of Vasectomy in the United States

Approximately 4.21 million women of reproductive age (10.9% of women aged 15–44) in the United States rely on vasectomy for family planning (5). Among women 35–44, almost 20% rely on this method. The percentage of women relying on vasectomy as their contraceptive method has remained stable since 1982, increasing only slightly from 10.9% to 11.7% between 1982 and 1988 but returned to the 1982 level in 1995 (Table 1). The proportion of women 30–34 years of age relying on vasectomy decreased from 14% in 1988 to 10% in 1995.

Most women reporting vasectomy as their contraceptive method are nonHispanic whites—14% of this group, compared with only 4% and

TABLE 1

Percentage of vasectomy users 15–44 years of age in the United States by age, marital status, education, income, and intention to have more children.

Characteristic	Percentage of vasectomy users with indicated characteristic*		
	1982	1988	1995
Overall	10.9	11.7	10.9
Age group (y)			
15–19	0	0	0
20–24	4	2	1
25–29	6	6	5
30–34	15	14	10
35–39	18	20	19
40–44	23	22	20
Marital status			
Never married	2	2	1
Currently married	16	17	17
Formerly married	3	4	4
Education			
≤11 y	8	7	6
12 y	14	15	13
≥13 y	11	13	12
Income†			
<149%	6	4	3
150–299%	10	12	11
≥300%	14	14	15
Intends to have more children			
Yes	0	0	0
No	19	19	18

Note: See ref. 5.

* Women aged 20–44 only.

† Percentage of federal poverty level.

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TABLE 2

Trends in the percentage of nonHispanic white and nonHispanic blacks using vasectomy among contraceptive users 15–44 years of age, according to age in the United States.

Race or ethnicity	Percentage of female contraceptive users relying on vasectomy*						
		Age group (y)					
	All	15–19	20–24	25–29	30–34	35–39	40–44
NonHispanic white							
1982	13	0	4	7	18	21	25
1988	14	0	2	8	17	24	26
1995	14	0	1	6	13	23	24
NonHispanic black							
1982	2	0	1	1	2	4	3
1988	1	0	0	0	2	1	2
1995	2	0	0	1	2	2	4

* See ref. 5.

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2% of Hispanic and nonHispanic black women, respectively, who rely on vasectomy as their primary method. Trends since 1982 reflect no change in this distribution (Table 2). However, the decline in the reliance on vasectomy since 1988 among 30–34 year olds is accounted for primarily by the decline of this method among the nonHispanic white women.

The National Survey of Men reported that 12% of married men aged 20–39 had a vasectomy (6, 7), with the largest proportion being in the 35- to 39-year-old group (21.6%). Vasectomies were far more common in white (13.5%) than in black men (1.6%) and among men with a high school education (13.7%) or more than a high school education (10.9%). Only 4.8% of men with less than a high school education reported having had a vasectomy. Married men in the Midwest and western United States had higher rates of vasectomy (15.7% and 15.1%, respectively) than men in the northeast (7.9%) or in the southern (7.1%) United States. The husband's age, race, education, and religion had strong effects on the likelihood of male sterilization, whereas the wife's characteristics played a lesser role. Having an unintended last pregnancy using a male method was a strong predictor of having had a vasectomy.

Vasectomy is first incident in men in their 20s, peaks in the 30s and 40s, and drops rapidly in the 50s (7–9). The procedure has been in use since the 1940s, resulting in a vasectomy prevalence nearing 25% when weighted for men who were between the ages of 40 and 59 years in 1987 (8, 9). A strong birth-cohort effect exists in these data so that the prevalence of vasectomy in 1987 is lower for men >60 years of age.

Data from a retrospective survey of urology, general surgery, and family physician practices conducted in 1991 estimated that there are approximately 500,000 vasectomies performed annually in the United States, or 10.3 procedures per 1,000 men aged 25–49 years (6–9). The rate is highest in the Midwest (14.5 per 1,000), and lowest in the Northeast (8.8 per 1,000). Urologists perform most vasectomies (71.7%), with family practitioners (15.4%) and general surgeons (12.9%) performing the remaining procedures.

Surgical Techniques and Contraindications

In the United States, vasectomy is typically performed as an outpatient procedure under local anesthesia (6–9). Conventional incisional vasectomy and no-scalpel vasectomy are the two most common surgical techniques for approaching the vas (10, 11). The incisional method of vasectomy uses a scalpel to make one or two incisions each 1- to 2-cm long in the scrotum. The no-scalpel vasectomy, which has been widely used in developing countries (12) and is becoming common in the United States, uses a sharp pointed forceps-like instrument to puncture the scrotum. A clamp holds the

vasa in place just under the skin, so that the forceps can puncture the skin, grasp a vasa, and pull it out to be cut and occluded. Both approaches into the scrotum require injection of local anesthesia.

Surgical methods also vary by method of vas occlusion and length of vas removed (10, 13). Several surgical techniques for occluding the vas have been developed with the goals of avoiding recanalization of the vas, enhancing potential for reversal or avoiding side effects associated with increased pressure on the testicular end of the ligated vas. Vas occlusion differs by the method of ligation (nonabsorbable suture, cautery, clips, or some combination) and by whether the testicular side of the vas is left unsealed (open-ended vasectomy, which is rarely used) or sealed (closed-ended vasectomy, which is more commonly used) (10, 13). Any of these methods may be used with interposition of the fascia between the cut ends. A method of vasectomy used in China is a percutaneous technique involving chemical occlusion with a combination of cyanoacrylate and phenol (10).

Contraindications and Counseling

There are no permanent contraindications to vasectomy, but vasectomy should be delayed in the presence of local infection, acute systemic infection, signs or symptoms of sexually transmitted disease, filariasis, elephantiasis, intrascrotal mass, or hypersensitivity to the anesthetic agents to be used (14). Conditions that may increase the risks or difficulties of performing the operation include previous scrotal trauma, large varicocele or hydrocele, previous surgery for cryptorchidism, inguinal hernia, and certain coagulation disorders. When possible, the condition should be improved or controlled before surgery. When any of these conditions are present, the patient should be informed about the possible increased risk.

Vasectomy should only be performed after proper counseling about the effectiveness and safety of the procedure and after patients have given informed consent. Generally, participation of both partners in the counseling session is desirable but should not be a condition for provision of the method. Counseling should include [1] other possible contraceptive methods, [2] emphasis on the intended irreversibility of the procedure, [3] the small possibility of method failure, [4] the possibility of regret, and [5] what happens at the operation. Ideally, the decision should be made with sufficient time for proper consideration of the options. Hesitation about vasectomy or expressed marital instability should signal the potential for postvasectomy regret and indicate the need for further counseling about vasectomy and vasovasectomy.

Effectiveness

Vasectomy is considered one of the most reliable family-planning methods currently available. Pregnancy rates associated with vasectomy are reported in the range of 0 to 2%, with most reporting $<1\%$. However, although vasectomy is widely considered highly effective, the specific failure rates associated with different techniques have not been well quantified in clinical trials.

Studies have consisted primarily of retrospective reviews of case series from a single practice using a single method of vas occlusion. Comparative studies often consist of retrospective reviews of vasectomies using one method of occlusion by one practitioner, followed by another series using a different method by the same practitioner. No long-term study, similar to that available for female sterilization (e.g., the Collaborative Review of Sterilization [CREST] Study) (15), has been conducted. Unlike the data available for tubal sterilization, no study documents the major differences between pregnancy outcomes of different methods of vasectomy. The longest prospective study reported in the literature followed men for <2 years. Many reports do not provide detailed information on the length of the follow-up period, the extent of loss to follow-up, or methods of analysis. Compliance with follow-up visits in most practices is low, rendering retrospective reports of failures problematic (16).

The end points or definition of vasectomy failure also vary among studies. There are different definitions of early, late, overt, or technical failures. Late failures, or the occurrence of a pregnancy, appear to be unambiguous, but follow-up of the cohort for long periods of time is usually not complete, and the denominators of reported late pregnancy rates are often omitted. Concepts of time-to-azoospermia, or number or spacing of ejaculations-to-azoospermia, or time-to-motility are intermixed, and the data are unavailable to judge their interrelationship.

Although definitions vary among investigators, early failure of the procedure is considered to have occurred when significant numbers of spermatozoa or any motile spermatozoa persist continuously later than 4 months after vasectomy. Ideally, two semen analyses separated by variable lengths of time beginning at 10–12 weeks after vasectomy and 4–6 weeks apart, or after 20–25 ejaculations are recommended to determine the absence of sperm, to allow time for clearance of stored sperm, and to detect early failures or recanalizations (17–19). However, this ideal regimen is not always followed (13). The International Planned Parenthood Federation (IPPF) recommends that another method of contraception should be used until the semen is sperm free, or where analysis is not possible, until the man has ejaculated at least 20 times postvasectomy (14).

Shortly after the procedure, before sperm are sufficiently cleared from the reproductive tract, early user failure can result from unprotected coitus. In fact, most early failures are considered user failures, although this is not well documented because distinctions between user failure and technical early failures or early recanalizations are not systematically reported. In preliminary data from a survey of 288 urologists responding to a questionnaire, 33 of 74 reported

pregnancies (44.6%) in the previous 5 years were due to unprotected coitus or broken condoms (20).

For some, technical failures are synonymous with all early failures, whereas for others, technical failures are nonsignificant numbers of immotile spermatozoa present 1 year or later after vasectomy (21, 22). Some make the distinction between overt failures that have between 5 and 20×10^6 motile sperm or in excess of 20×10^6. Depending on the definition, the rate of early failure has varied from 0.3% (26) to 0.6% (19). On the basis of case series data, one or another method of vas occlusion may appear to be superior to others in pregnancy outcomes, but the differences based on these data are small. Furthermore, the most effective method of occlusion in combination with different vas delivery techniques (no-scalpel vs. standard incisional methods) has not been evaluated in a clinical trial.

Late failure occurs when motile spermatozoa reappear in the ejaculate after proof of success of vasectomy, signifying that recanalization has occurred (19, 23). Recanalizations can occur soon after a vasectomy and result in early failures or several years after vasectomy. Failures occurring years after the procedure are usually detected only after a pregnancy has occurred. However, issues surrounding paternity may lead to underreporting of pregnancies after vasectomy. In some marriages, women might not inform their husbands if a pregnancy occurred, because they might fear being accused of infidelity. They might simply have an abortion without informing their husband. Conversely, a pregnancy in a man's nonspousal partner may be attributed to another man.

The available information suggests that the life span and fertilizing potential of sperm remaining in the male reproductive tract postvasectomy is considerably shorter than the time necessary to clear all sperm from the reproductive tract. Immediately after vasectomy, fertilizing capacity is lost, and decline in sperm motility occurs (24–26). Two studies provide data that the loss of fertilizing capacity is lost between 3 and 8 days postvasectomy using the zona-free hamster oocyte penetration test (25, 26). However, the time before sperm are no longer observed in the semen (azoospermia) varies widely, and overall, studies find that approximately 95% of men will be azoospermic by 4 months postvasectomy or after approximately 23 ejaculations.

Several studies have sought to determine the significance of "lurking sperm" (19, 24–28). Primarily on the basis of few pregnancies observed in spouses of men with immotile sperm who have resumed unprotected intercourse, it is widely accepted that immotile sperm have no fertilizing capacity. One study that investigated failures only among men with persistent sperm (27) found that 33% of men had immotile sperm at 12 weeks postvasectomy, and 7.7% had reappearing immobile sperm after azoospermia was determined at 12 weeks. Sperm were present in 9.7% of prereversal ejaculates, suggesting the possibility of late vasectomy failures (28).

The experience of the practitioner and the number of vasectomies annually performed is considered a large factor in the effectiveness of the method. Although most surgical approaches used by competent, experienced surgeons are considered highly successful, there are many situations in which surgeons do not perform vasectomies or may perform only a few within any given year.

A recent pilot study conducted in Mexico using simple ligation and excision suggests that the median time to azoospermia is 10 weeks, with 93% of men being azoospermic by week 20 (29). The failure rate was quite high in this study and the inexperience of the surgeons and the lack of fascial interposition used in the procedure were both cited as possible explanations for the high failure rate. However, it was impossible to separate which were due to inexperience of the practitioner and which were due to the lack of fascial interposition.

The literature is not consistent about follow-up protocols and varies according to the assumptions made about the requirement for azoospermia. There is a need for reliable postvasectomy follow-up protocols that ensure the success of the method while reducing user failures by requiring a minimum amount of time before users can dispense with the use of additional contraceptive methods. This is particularly crucial for developing world settings, where the option of a follow-up semen analysis is not available. When azoospermia is used as the criterion for a successful vasectomy rather than infertility parameters, which can be achieved in a shorter period of time, men must be followed for longer periods of time. The documented low rate of compliance with the long-term regimens suggests that, in practice, these regimens serve few identifiable purposes.

On the other hand, assuming that immotile sperm lack fertilizing capacity, Philp et al. (30) suggests that men with persistent spermatozoa should be offered a special clearance if, after at least 7 months, two consecutive counts show immotile sperm in concentrations of $<10{,}000$/mL. Edwards (31) recommends that clearance could be given within 4–6 weeks, because by that time all motile sperm would be cleared.

Others recommend that semen be examined at 3 weeks postvasectomy to demonstrate reduced numbers of sperm, all of which are immotile. This ensures that the vasectomy is a technical success and that the biologic limit of sperm viability has been exceeded. However, others cite the rare occurrence of "stored sperm pregnancies" and late recanalizations as justification for highly conservative follow-up regimens, including yearly semen analysis (19). Fear of litigation if a pregnancy occurs without documentation of azoospermia is also cited as a rationale for these regimens.

In summary, although vasectomy is reported to be highly

effective and the differences in effectiveness appear small, no long-term carefully conducted study on the long-term effectiveness of the method is available, nor are clinical trial data available on different methods of vas occlusion.

Vasectomy Reversal

Approximately 1–3 per 1,000 vasectomized men will request a reversal (8, 32). The success of a reversal, as measured by pregnancy rates, ranges from 30%–60% (33). Sharlip (34) reports that the maximum pregnancy probability for vasectomy reversal is 67%. Factors that explain the failure to achieve pregnancy in the remaining couples that are known and documented in the literature include partner infertility, epididymal dysfunction, and antisperm antibodies, although these explanations may not capture the complexity of these failures. In addition, although comparative trials are lacking, most surgeons agree that the success of a reversal depends on the microsurgical technique used (35, 36). Other factors that may influence success rates include the skill of the surgeon, the occlusion technique originally used, the presence of sperm granulomas, and the time interval between vasectomy and reversal.

Available data suggest that success of the procedure declines with time since vasectomy (35, 36). In a study of 1,469 men who underwent microsurgical vasectomy reversal procedures, rates of patency (return of sperm to the semen) and pregnancy vary with time. For intervals of <3 years patency and pregnancy were 97% and 76%, respectively, 3–8 years, 88% and 53%, 9–14 years 79% and 44%, and 15 years 71% and 30% (36).

Men with intervals of >10 years since vasectomy tend to require an epididymostomy for vas reversal, a technically challenging technique. All vas reversal procedures have $\geq$10% chance of scarring off immediately, eliminating the chance for a reversal success. Among men who require an epididymostomy for vas reversal, because it is more technically challenging and is not typically performed by the average practitioner, scarring is more likely. However, when this technique is used by an experienced practitioner, the pregnancy rate is likely to be improved. So rather than a linear decline with time, a technique-specific rate is likely to more adequately reflect the effectiveness of vasectomy reversal.

Peterson et al. (37) suggest that there may be a trade-off between efficacy of an occlusion method and potential for reversibility. For example, open-ended vasectomies may be associated with a lower rate of congestive epididymitis and have a higher potential for reversal but may be associated with higher pregnancy rates. Removing a large portion of the vas may be associated with a low pregnancy rate, but reanastamosis in this situation may be more difficult, with a low potential for reversibility. Cautery and coagulation methods tend to effectively seal off the ends of the vasa, but these require a more technically difficult vasoepididymostomy.

Antisperm antibody in relation to the success of vasovasostomy have been examined (38, 39). Titers of >160 have been associated with a pregnancy induction rate of zero (38). Although this finding suggests that men with high prereversal levels would have a low probability of success, such testing cannot be used to select candidates because some men with high sperm antibody titers still achieve pregnancies.

Intraoperative and Early Postoperative Complications

Intraoperative and early postoperative complications include bleeding or hematoma, infection, acute epididymitis, and need for hospitalization. The incidence of intraoperative and early postoperative complications of vasectomy varies with the surgical technique and the number of vasectomies performed annually by the practitioner (40, 41). A national survey of a probability sample of urologists, family physicians, and general surgeons (32% response rate) reported that the incidence of hematoma was 4.6% for physicians performing 1–10 vasectomies annually, 2.4% for those performing 11–50 annually, and 1.6% for those performing >50 annually (6). The corresponding incidences of hospitalization were 0.8%, 0.3%, and 0.2%.

The incidence of infection was 3.5%, with no mention of variation by number of vasectomies performed. Higher infection rates have been reported in some series (42–44). Although most infections are minor, there is one published case report of lethal gangrene due to group A beta hemolytic streptococcus with onset 2 days after an outpatient vasectomy in a previously healthy young man (45).

Several studies have shown that complication rates after incisional vasectomy are higher than following no-scalpel vasectomy. In a study involving 1,203 vasectomies performed by 28 physicians in Thailand, the complication rate was 3.1% (16 of 523) with incisional vasectomy and 0.4% (3 of 680) with no-scalpel vasectomy ($P<.02$) (41).

In a patient-questionnaire study of 256 men undergoing vasectomy at two Copenhagen hospitals (88% response rate) (46), the patient-reported incidence of complications at one hospital where the no-scalpel technique was used exclusively was compared with that at the other hospital, where incisional vasectomy was used exclusively. The self-reported rates of bleeding were similar with no-scalpel and incisional vasectomy (17% and 14%, $P=.57$), whereas the rates of infection were lower with no-scalpel vasectomy (4% and 18%, $P=.002$), as were pain at rest (11% and 22%, $P=.05$), use of analgesics (29% and 53%, $P<.001$), and physician contacts (8% and 22%, $P = .009$).

Sperm granulomas represent inflammatory reactions to extravasated spermatozoa and have been identified in 15%–40% of vasectomy reversal procedures (47). Although most sperm granulomas are small and asymptomatic, painful sperm granulomas may occur in 2%–3% of vasectomies,

typically in the second or third postoperative week (15, 40). Another complication of vasectomy closely related to sperm granulomas is vasitis nodosa, which is characterized by a localized proliferation of ductal structures after injury to the vas deferens (47). In most cases it is initially diagnosed as an incidental histologic finding at vasovasostomy.

Open-ended vasectomy, or leaving the testicular end of the vas open, is performed to avoid the increased intraluminal pressure that leads to postvasectomy pain syndrome and to increase the chances of successful reversal. Some have shown that leaving the vas open eliminates potential for damage from increased pressure and is less likely than closed-ended vasectomy to be associated with congestive epididymitis, and in some cases, sperm granulomas (48–50). Others report that the method appears to result in increased rates of spontaneous recanalization (51, 52). However, the method of occlusion of the closed end and the use of fascial separation of the two ends seem to modify the rate of spontaneous recanalization (49).

Long-Term Complications: Chronic Pain and Epididymitis

Congestive epididymitis presents as pain and testicular tenderness on the affected side. Generally, the occurrence of epididymitis is uncommon and is reported in 0.4%–6.1% of vasectomies (53, 54). Congestive epididymitis can occur sooner or later after vasectomy and linger. Typically, it lasts weeks to months, and it is extremely rare for it to last >1 year. It is usually treated with analgesics and antibiotics.

Congestive epididymitis has been attributed to pressure within the epididymis from sperm production in the presence of an occluded outlet. (The term "epididymitis" might be a misnomer, because the condition is thought to result from mechanical pressure rather than from an inflammatory process.) In one large series, the frequency of congestive epididymitis with closed-ended vasectomy was reported to be higher than with open-ended vasectomy (6% vs. 2%; relative risk = 3.0 (95% confidence interval [CI] = 1.2–7.5) (50). Even among closed-end vasectomy the incidence varies by method of occlusion. An incidence of 5.6% was reported with ligation of both testicular and prostatic ends of the vas in 288 procedures, 3.8% with bipolar cautery of both ends in 1,000 patients, and 2.8% with monopolar cautery of both ends in 1,600 patients (data on statistical significance not presented) (55).

Among the reported long-term complications of vasectomy is a syndrome of chronic noninfectious epididymal pain and induration beginning months to years after vasectomy (56). This syndrome has been attributed to long-standing obstruction with dilatation of the epididymal ducts, extravasation of sperm and sperm granulomas with an inflammatory reaction. The syndrome appears to be quite rare, and the attribution to vasectomy is based on case reports.

Although there are no comparative studies of this specific syndrome in men with and without vasectomies, there are comparative data from the Health Status of American Men study (HSAM) (57) on the incidence of epididymitis-orchitis in men with and without vasectomies. The late-onset chronic epididymal pain syndrome reported by Selikowitz and Schned (56) seems to fall within the diagnostic category of epididymitis-orchitis in the HSAM study. In this study, 10,590 men with vasectomies were paired with neighborhood controls without vasectomies (8, 57). The incidence rates of epididymitis-orchitis in the first 12 months after vasectomy were 87.7 per 10,000 person-years in the men with vasectomies and 9.7 per 10,000 person-years in controls. The incidence rates after the first 12 months were 24.7 and 13.6 per 10,000 person-years. The cumulative incidences were 0.9% and 0.1% in the first 12 months and 1.8% and 1.0% in the period from 12 months postvasectomy to the end of follow-up (median, 7.9 years postvasectomy).

Although the difference in incidence rates between men with and without vasectomies was highest in the first 12 months after vasectomy (approximately 8 cases per 1,000 person-years, relative risk of 9.0), the difference in incidence rates remained elevated beyond 12 months postvasectomy (approximately 1 case per 1,000 person-years, relative risk of 1.8). Based on these data, further study is needed to characterize this risk. However, because of the low incidence of all forms of epididymitis-orchitis, any study of a specific chronic form of epididymitis-orchitis would be difficult to conduct.

Epididymitis nodosa is an epididymal lesion that is analogous to vasitis nodosa and is thought to be the result of long-standing obstruction to the vas. This lesion has been found in some patients undergoing epididymidectomy for late-onset chronic pain and epididymal induration after vasectomy (58). Radiological and histopathological features of this and other epididymal lesions associated with chronic postvasectomy pain have been described (58–60).

Mortality

Two large studies of mortality among men undergoing vasectomy have found lower rates of mortality among men with vasectomies than among their matched controls (8, 63). In both studies, the lower mortality was likely related to the self-selection for vasectomy and the most appropriate interpretation was that of no evidence for an overall increase in mortality associated with vasectomy. Giovannucci et al. (63) found that the relative risk of all-cause mortality was 0.85 (95% CI = 0.76–0.96) and the relative risk of all-cause mortality among men who had a vasectomy 20 years earlier was 1.11 (95% CI = 0.92–1.33). The relative risk of mortality from cancer was 1.01 (95% CI = 0.82–1.25).

However, the relative risk of mortality from cancer among men who had a vasectomy at least 20 years earlier was 1.44 (95% CI = 1.07–1.92), despite nearly identical reported smoking prevalence and number of cigarettes

smoked in the two groups. This increased risk in mortality was largely attributable to an unexpected and unexplainable increase in lung cancer deaths. This increase in deaths from lung cancer, like the decrease in deaths from colon or rectal and renal cancer, were likely chance findings. There were fewer cancer deaths than expected in men who had their vasectomy within the past 20 years (observed = 104; expected = 123).

Antisperm Antibodies and Immune Complexes

Antisperm antibodies are found in approximately 50%–70% of men after vasectomy (64–66) and in every mammalian species studied (67). Percentages of men with antibodies detected after vasectomy vary between 52% and 68% at 6 months, and 52%–60% after 1 year, and antibodies have been found to persist in the circulation for several years.

The daily production of millions of sperm after vasectomy is believed to stimulate antisperm antibodies. Not all men develop detectable levels of antisperm antibodies (68), although men who have high preoperative sperm counts are likely to have sustained or early high levels of antisperm antibodies (69).

It may be that nonresponders have a genetically programmed low immunological response to sperm antigens (70). The precise antigens involved in the immune response are still poorly defined. Approximately 20% of men with vasectomies develop antibodies to internal nuclear sperm antigens called protamines (71). Many other andrologic pathologies have some autoimmune antisperm reaction (66). With the exception of men diagnosed as infertile because of antisperm antibodies without any other andrological pathology, men with vasectomies have the highest level of antibody (66–72). The major impact of antisperm antibodies tends to be on the reduced rate of pregnancy after vasectomy reversal.

Increases in circulating immune complexes (CICs) occur after vasectomy also, but these progressively disappear after the third month postsurgery (73). Initially, there was concern that increased CICs observed in animals (74, 75) and humans (76) may account for the increased risk of atherosclerosis in vasectomized cynomolgus macaques (77). A series of basic studies in laboratory animals were undertaken to understand whether CICs might cause local disease in the testis or epididymis or in other, more remote organs. This decade-long series of investigations was followed by extensive human studies aimed at clarifying the potential role of vasectomy and CICs and cardiovascular disease. In rabbits, but not in long-term vasectomized monkeys, immune complex deposits in the kidneys and mild glomerulonephritis were found, suggesting the circulation of immune complexes may have systemic effects on sites distant from the testes (74, 75).

A marked increase in atherosclerosis in two species of monkeys was reported in a 1980 study of vasectomized cynomolgus monkeys maintained on a high-cholesterol diet for 10 months (77). However, in 1988, the same investigators published data that did not support their initial findings and were consistent with epidemiologic studies showing no effect of vasectomy on cardiovascular disease risk in monkeys (78).

Clinical evaluations (79) and several large cohort and case-control studies provided no support for the presence of an effect of CICs on immunologic disease, including testicular or kidney changes in humans (8, 57, 63, 80, 81). Furthermore, several clinical and epidemiologic studies failed to demonstrate any association between vasectomy and atherosclerosis in humans, as manifested by cardiovascular disease (82–88).

A study conducted to examine whether the presence of antisperm antibodies after vasectomy is influenced by coronary heart disease (CHD) risk factors reported that CHD risk factors were unrelated to antibody levels and did not confound the vasectomy status/antibody relationships (88). These studies in humans provide compelling evidence against any relationship between vasectomy and cardiovascular disease, together with the lack of ability to replicate the original results in monkeys (78). This is one controversy about vasectomy that has been completely resolved.

No changes in blood coagulation factor assays and measurement of thrombin monomer and circulating platelet aggregate ratios have been reported postvasectomy, resting concerns that vasectomy might potentiate thrombotic disease (89). Other studies have pursued the question of whether vasectomy changes testicular hormone production and endocrine function (90, 91). These studies demonstrated that mean levels of FSH, LH, testosterone, and estradiol are within the normal ranges postvasectomy.

Prostate Cancer

Five original cohort studies (8, 92–97) and 10 case-control studies (98–108) investigating the relationship between vasectomy and prostate cancer have been published since 1983 (Table 3). On the basis of these studies and other reports (109, 110), it seems unlikely that vasectomy and prostate cancer are causally linked. Inconsistent results, lack of strong data on plausible mechanisms, small elevations in risk, and the possibility of detection bias argue against such a relationship.

Through 1993, data from five case-control studies (98–104) and three cohort studies (92, 93, 95, 96) were published. Among the case-control studies, all of which reported elevations in risk, and elevations with increasing years since vasectomy, the possibility of detection, surveillance, and misclassification bias could not be ruled out (111). Because low-grade prostate cancer can easily be detected with screening, factors associated with detection can seem to be risk factors. Most vasectomies are performed by urologists in the

TABLE 3

Studies of vasectomy and prostate cancer.

Reference	Study type	Study size	Cases with vasectomy	Estimate of relative risk and 95% CI
Case-control studies				
Ross et al. (98)	Population	110 matched case-control pairs	NR	0.5 (0.2–1.4)
Honda et al. (99)	Update of Ross et al.	216 matched case-control pairs	58	1.4 (0.9–2.3), overall 2.2 (1.0–4.8), 20–29 y postvasectomy 4.4 (0.9–21), 30+ y postvasectomy
Newell et al. (100)	Hospital-based	343 cases 360 controls	NR	1.6 (1.1–2.3)
Spitz et al. (103)	Update of Newell et al.		NR	2.2 (1.1–4.3), ≥27 y postvasectomy
Mettlin et al. (101)	Hospital-based	614 cases 2,588 controls	27	1.7 (1.1–2.6) 2.2 (1.0–4.6) (13–18 y postvasectomy)
Rosenberg et al. (102)	Hospital-based	220 cases, 571 noncancer controls 960 cancer controls	22	5.3 (2.7–10.0) (noncancer controls) 3.5 (2.1–6.0) (cancer controls)
Rosenberg et al. (112)	Hospital-based	355 cases 2,048 controls	18	1.2 (0.6–2.7) 1.4 (0.5–4.2) (15+ y postvasectomy)
Hayes et al. (104)	Population	Blacks 471 cases 589 controls Whites 494 cases 703 controls	7 blacks 49 whites	Blacks 1.6 (0.5–4.8) White 1.1 (0.6–1.8) 1.5 (0.8–2.7), 20+ y postvasectomy 2.0 (1.0–4.0), <35 y of age
Hsing et al. (105)	Hospital and population	136 cases 158 hospital cancer controls 158 hospital noncancer controls 322 neighborhood controls	14	2.0 (0.7–6.1) (hospital cancer controls) 3.3 (1.0–11.3) (hospital noncancer controls) 6.7 (2.1–21.6) (neighborhood controls)
John et al. (106)	Population-based	1,642 cases 1,636 controls 324 Japanese-Americans	172	All 1.1 (0.8–1.4) Blacks 1.0 (0.6–1.8) Whites 0.9 (0.7–1.3) Japanese 1.8 (1.0–3.4) Chinese 1.0 (0.4–2.2)
Zhu et al. (107)	HMO case-control	175 cases 258 controls	61	0.9 (0.6–1.3) 0.8 (0.5–1.4), 20+ y postvasectomy
Platz et al. (108)	Hospital-based			1.6 (0.6–4.3) with family history of prostate cancer 1.5 (0.8–2.7) 1.6 (0.8–3.1), 20+ y postvasectomy 1.2 (0.4–1.4), <20 y postvasectomy 2.1 (1.0–4.3), 40+ y of age
Cohort studies				
Sidney et al. (92, 93)	Retrospective 6.8-y follow-up	5,119 vasectomized men each matched to 3 nonvasectomized men	68	1.0 (0.7–1.6)
Giovanucci et al. (96)	Prospective 166,870 person-years	10,055 vasectomized men 37,800 nonvasectomized men U.S. health professionals	59	1.7 (1.2–2.2) 1.8 (1.2–2.6), 22+ y postvasectomy 1.6 (1.2–2.1), non-A1* cases 1.8 (1.2–2.7), non-A1, 22+ y postvasectomy
Giovanucci et al. (95) (1993)	Retrospective	Husbands of women in Nurses Health study	54	1.6 (1.0–2.4) 1.9 (1.1–3.1), 20+ y postvasectomy 2.1 (1.0–4.4), stage C or D
Hiatt et al. (94)	(update) 8–15 y of follow-up	43,432 men from Kaiser Permanente Medical Care Program	NR	0.8 (0.5–1.3)
Möller et al. (97)	Registry Cohort 6.5 mean y of follow-up	73,917 vasectomized men	12	1.0 (0.8–1.1)

* A1 refers to cancer stage.

Schwingl. Safety/effectivensss of vasectomy. Fertil Steril 2000.

United States; thus, men with vasectomies may be more likely to know and have access to urologists, making their chances of being screened and their cancer detected higher than their nonvasectomized counterparts.

A case-control study (102) based on data from a surveillance system screened these data regularly to detect previously unrecognized associations between several exposures and diseases. The relative risk emerging from this study was highly elevated (OR = 5.3; 95% CI = 2.7–10.0) but was subsequently refuted by a second case-control study published by the same investigators in 1994 based on additional data collected in the same surveillance system (112). Findings that emerge from screening for strong associations tend to seem more highly statistically significant and stronger than they actually are, and together, these two studies illustrate how relative risks detected in screening can have an upward bias (113).

Data from the cohort studies published during this time were inconsistent. A retrospective cohort study conducted in the United Kingdom found no increased risk of prostate cancer in men with vasectomies (114). However, the follow-up was short; men with vasectomies were followed for an average of 6.6 years, with no vasectomies occurring >14 years in the past. An HMO cohort study (92–94) reported that the risk of prostate cancer in men with vasectomy was 1.0 (95% CI = 0.7–1.6), regardless of length of the interval (<10 years, 10–20 years, or >20 years) between vasectomy and multiphasic health checkup, or the age at vasectomy (<40 years vs. >40).

Two cohort studies, published by Giovannucci et al. (95, 96), reported moderate positive associations between vasectomy and prostate cancer, and relative risks increased over time since vasectomy. These two cohort studies provided the strongest evidence to date in support of a causal explanation. In these studies >40% of the vasectomies among cases had been performed 20 or more years before cancer diagnosis. In both of these studies the risk increased with increasing time since vasectomy. In the retrospective cohort study (95), men who were ≥40 years of age when they had their vasectomy had the highest risk 20 years after vasectomy. The increased risk persisted when the analysis was restricted to men who had at least one digital rectal examination (DRE) in the time interval preceding cancer detection, indicating that detection bias was unlikely to appreciably influence the results (96).

Although attempts were made to ascertain the presence of detection bias in the cohort studies, it was conceivable that patterns of long-term increasing risk could also be due to increased opportunity for detection such as that which was observed in the Honolulu Heart Program (115). In that study, overall long-term cancer mortality was lower in participants than nonparticipants, yet long-term prostate cancer mortality was higher in participants. The most likely explanation seems to be detection bias.

The combined evidence prompted the National Institutes of Health (NIH) to convene an expert panel in 1993 to provide recommendations to clinicians and public health authorities. However, after review of all existing data, the NIH panel concluded that, overall, the associations in the literature to date were weak and that detection bias could not be ruled out (116). The panel recommended that providers should continue to offer vasectomy and perform the procedure; that vasectomy reversal is not warranted to prevent prostate cancer; and that screening for prostate cancer should not be any different for men who have had a vasectomy than for those who have not.

Since 1993, one cohort study in Denmark (97) and five case-control studies, three of which were conducted in the United States (104, 106, 107), one in China (105), and one in India (108), have been published. No increased risk of prostate cancer was found in a Danish (97) computerized record linkage study, although the results were considered inconclusive, because the period of risk was substantially <15 years. In a case-control study of black and white men, no overall elevation in risk was found among white men, but a statistically nonsignificant elevated excess risk was reported in black men (104). Among men 20 or more years since vasectomy, a nonsignificant excess risk of 1.5 was reported; a significant risk was observed in men vasectomized before the age of 35.

Two recent case-control studies constitute the strongest evidence among the case-control studies against an association (117). Among 1,642 population-based incident cases from a multiethnic population (106), no consistent association of prostate cancer risk with vasectomy, age at vasectomy, or time since vasectomy was observed. Analyses limited to cases with high-grade tumors did not show stronger results. In data from the Group Health Cooperative HMO (107), no overall increased risk of prostate cancer in men with vasectomies and no increased risk by age at or time since vasectomy were found. The risk of prostate cancer was increased, however, among men with a positive family history of prostate cancer.

Case-control studies from developing countries reported small increased risks of prostate cancer in men with vasectomies (105, 108). In the Chinese study (105), however, only 10% of the cases were beyond 10 years since vasectomy; cases had high rates of prostatitis and benign prostatic hypertrophy compared with the controls, suggesting that cases may have been under greater urologic surveillance. In addition, wide confidence intervals existed around the elevated estimates.

In the Indian study (108), an increased risk in the same range as studies in the United States were reported; however, men >20 years beyond vasectomy had virtually the same risk as men closer in time to the procedure. Men >40 years of age at vasectomy had a twofold increased risk. Half of the cases had been vasectomized after the age of 40, and 82% of

TABLE 4

Studies of vasectomy and testicular cancer.

Registry or cohort studies	No. of men with vasectomy	No. of cases with vasectomy	Estimate of relative risk and 95% CI
Goldacre et al. (120)	1,764	1	2.1 (0.1–11.6)
Thornhill et al. (121)	23,148 man-years	3	3.8 (0.8–11.0)
Cale et al. (122)	3,079	8	4.2 (1.8–8.2)
Nienhuis et al. (114)	13,246	4	0.5 (0.1–1.4)
Giovannucci et al. (63)	13,124	0	—
Möller et al. (97)	73,917	70	1.0 (0.8–1.3)
Case-control studies	**No. of cases**	**No. of cases with vasectomy**	**Estimate of relative risk and 95% CI**
Moss et al. (124)	173	15	0.6 (0.3–1.2)
Swerdlow et al. (125)	259	22	1.1 (0.6–2.0)
Strader et al. (123)	333	46	1.5 (1.0–2.2)
UK Testicular Cancer Study Group (119)	794	81	1.1 (0.8–1.5)
Rosenberg et al. (112)	132	7	0.8 (0.4–1.9)

Schwingl. Safety/effectivensss of vasectomy. Fertil Steril 2000.

the cases were at least 20 years from the procedure. Bias resulting from unequal access to vasectomy and to detection of prostate cancer that exists in the United States is not likely to be as strong in India, because a wide cross section of the population has been vasectomized and men are not routinely screened for prostate cancer.

A meta-analysis of the results of studies to date indicated a slightly elevated risk of prostate cancer among men with vasectomies overall (OR = 1.23; 95% CI = 1.01–1.49) but showed that this effect varied widely depending on the study design, study base, potential for detection bias, and potentially inadequate control selection. In particular, risk estimates from hospital-based case-control studies were significantly increased compared with estimates of population-based case-control studies. Given that men with vasectomies have lower mortality than men without vasectomies (63), the prevalence of vasectomy may be lower in hospital controls than in men in the general population, leading to an overestimate of the association between vasectomy and prostate cancer in the hospital-based studies.

In addition, studies that were judged to be affected by detection bias had a summary OR = 1.91 (95% CI = 1.4–2.6), compared with those less likely to be affected (OR = 1.11; 95% CI = 0.96–1.29). Similarly, those studies likely to be affected by inadequate control selection had an OR = 2.24 (95% CI = 1.42–3.54), whereas those judged unlikely to have this problem had an OR closer to unity (OR = 1.11; 95% CI = 0.94–1.31). This finding suggests that the heterogeneity of study results is likely to be explained by bias, such that the studies with bias operating will have higher risk estimates than those in which the bias has been adequately controlled.

Future studies of this topic will be difficult in the United States, because a recently published study suggests that there have been changes in practice toward men with vasectomies by urologists (118), even in light of the NIH recommendations to make no changes. More than 90% of urologists responding to a survey stated that the prostate cancer and vasectomy studies had little or no effect on their practice of vasectomy. However, 27% reported screening men with vasectomies earlier for prostate cancer, and 20% said they would be reluctant to recommend a vasectomy to a man with a strong family history of prostate cancer. Also, epidemiologists undertaking studies of complications of vasectomy should be aware that vasectomy is occasionally performed for noncontraceptive purposes in older, higher-risk patients.

In summary, although several epidemiologic studies in which an elevated incidence of prostate cancer was found in association with vasectomy exist, there are also a number of large, well-designed studies in which an elevation in risk was not found. Overall, the weight of the evidence suggests that there is no association between vasectomy and prostate cancer.

Testicular Cancer

Until the recent publication of a registry study by Möller et al. (97) and a case-control study by the United Kingdom Testicular Cancer Study Group (119), the studies on this association have included only small numbers of cases (Table 4). Among the four studies reporting an elevation in risk (120–123), all were based either on small numbers or were subject to confounding or misclassification bias. Two others showed no increased risk (124, 125). The first studies in Scotland and Ireland suggesting an elevated incidence of testicular cancer in men with vasectomies were based on one

and three cases in these men, respectively (120, 121). The largest number of cases with vasectomies was reported in a population-based case-control study in the state of Washington (123). In this study, the small observed elevation in risk was confined to Catholic men in the study and was considered to be due to probable underreporting of vasectomy in the Catholic controls. A second small study in Scotland reported an elevated incidence of testicular cancer in a cohort of men with vasectomies, but the investigators did not control for confounding factors (122).

No association of vasectomy with testicular cancer was reported in a recent, small case-control study (113), which included only seven cases of testicular cancer in men with vasectomies. Although the theoretical concern has been raised that vasectomy could potentially accelerate growth of an existing testicular tumor or act as a late-stage promoter, there has been no reported evidence that vasectomy is associated with an increased risk of testicular cancer after many years. Based on two exposed cases 10 or more years after vasectomy, the reported relative risk was 0.7 (95% CI = 0.2–3.2) in this study.

The record linkage study by Möller et al. (97) and the case control study by the United Kingdom Group (119), the largest studies to date, report no elevated risk among men with vasectomy. These studies offer the most convincing evidence that vasectomy is not likely to induce or accelerate testicular tumors. In summary, testicular cancer rates are not increased among men with vasectomy.

Long-Term Psychological Effects

In a long-term follow-up of all men undergoing vasectomy in one Swedish county (n = 108) 95% reported satisfaction five years later (126). Presterilization predictors of poststerilization regret in both the person undergoing the procedure and in the spouse of the person undergoing the procedure have been studied (127). An important finding was that for both wives of men undergoing vasectomy and husbands of women undergoing tubal ligation, the regret of only the spouse who did not undergo the procedure was affected by their perception of the other spouse's regret. A Chinese study found that men who had a vasectomy were more likely to have depressive symptoms on the Centers for Epidemiologic Studies Depression scale (CES-D) than controls (128). Applicability of the latter finding to conditions in the United States is questionable because of differences in patient selection factors.

Other Potential Long-Term Effects

Long-term alterations in testicular morphology and endocrine function have been reported in studies of men with vasectomies (129, 130). Fisch et al. (130) reported that certain men after vasectomy have abnormalities in seminiferous tubule and Leydig cell functions of the testes. These abnormalities are unrelated to the interval after vasectomy and are not identifiable with routine static hormonal measurements. These men are also less likely to have antisperm antibodies. In two small studies of lipoproteins in men who had undergone vasectomy, one study (n = 62) found no changes in cholesterol level or lipoprotein levels (131), whereas another found a reduction in high-density lipoprotein cholesterol (132). Bone mineral density in the lumbar spine and femoral neck is not affected by vasectomy (133).

Advantages and Disadvantages

A primary disadvantage of this method is that like other nonbarrier methods, it provides no protection from sexually transmitted diseases. The acceptability of vasectomy by large populations is somewhat limited. However, differential access to and knowledge about vasectomy may explain the dramatic differences in vasectomy by race, ethnicity, and income. Data on the acceptability of vasectomy in the United States among groups of men having the lowest vasectomy rates are sparse. Some researchers have attempted to explain differences in vasectomy rates by cultural differences. However, an evaluation of a US training program, sponsored by the Association of Voluntary Surgical Contraception (AVSC), strongly suggests that vasectomy would be quite acceptable to a wider range of men if there was more information about the method where these men and their families receive health services (134).

Family physicians in 17 states were trained in no-scalpel vasectomy at 43 sites, including community health centers, state or county public health departments, Planned Parenthood clinics, hospital-based clinics, Indian health centers, and a military hospital. An evaluation of the program found that successful expansion or initiation of vasectomy services requires sufficient number of providers committed to serving men and providing a quality service; outreach to clients to inform them about the availability of vasectomies; marketing strategies; and the commitment of funds to subsidize vasectomies for men who cannot afford them.

The increases in caseloads in clinics that offered free vasectomies or priced services lower than urologist fees demonstrated that demand exists among men who previously had no source other than private physicians for a vasectomy and lacked insurance coverage for the procedure. Research on the initiation of vasectomy services in developing countries highlights similar findings and adds that sustained promotional campaigns are most successful (135–137).

A strong argument in favor of vasectomy is that it can relieve the female burden of contraception. In promotional campaigns in developing countries, interviews with 218 couples in six countries found that men cited concern for women's health as the principal reason for having a vasectomy. The report concludes that encouraging men to have a vasectomy for their partner's sake and stressing that it is a man's turn to take responsibility for family planning may be effective in promotional strategies (138).

Compared with either no contraceptive method or 14

other methods currently used, vasectomy is one of the most cost-effective. In a 5-year analysis, considering the costs of acquiring and using the method, the cost of side effects, and the cost of unintended pregnancy, vasectomy ranked second of all methods and had an annualized cost of $760 in a managed payment model and $355 in a public payer model, second only to the Copper-T IUD in cost-effectiveness. Although the initial cost is high, the method becomes extremely cost-effective over time for those who desire no more children (139).

Suggested Research

Long-term effectiveness studies with high follow-up rates are needed to document long-term failure rates of vasectomy for different methods of vas occlusion, use of fascial interposition, or importance of the length of the vas removed. In addition, these studies should characterize the incidence of long-term complications such as chronic epididymal pain syndrome. Cross-sectional studies documenting the presence of sperm in men with vasectomies up to 10 years postvasectomy would also be desirable to document the long-term efficacy of the method.

Randomized studies of methods of occlusion are needed to determine pregnancies and infertility end points in relation to these methods. Data on the efficacy of various occlusion methods in combination with the no-scalpel method of vasal delivery are lacking (31). Such studies would be especially useful for developing countries in which the choice of whether to use clips or cautery rather than ligation and excision has more serious cost implications.

In addition, there is a need for shorter-term studies to help define the extent of follow-up needed to provide sufficient evidence of infertility. Such studies are needed to develop evidence-based guidelines on recommended numbers and timing of postvasectomy visits and the use of alternative contraception in settings where semen analysis is not practical.

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