Asian Journal of Andrology (2010) 12: 315–321

www.nature.com/aja

Original Article

Vasectomy by epithelial curettage without suture or cautery: a pilot study in humans

John K. Amory[1], John W. Jessen[2], Charles Muller[3], Richard E. Berger[3]

[1]*Department of Medicine, Center for Research in Reproduction and Contraception, University of Washington School of Medicine, Seattle, WA 98195, USA*
[2]*Private Practice Dentistry, Seattle, WA 98195, USA*
[3]*Department of Urology, University of Washington School of Medicine, Seattle, WA 98195, USA*

Abstract

Curettage of the epithelium of the vas deferens might be a safe and effective method of male sterilization. We conducted a pilot study of vasectomy by epithelial curettage with a novel microcurette called the Vas-X in 12 normal men requesting elective sterilization. Seminal fluid analysis was obtained monthly after the procedure for 6 months. Pain was assessed by questionnaire. Three months after the procedure, all men attained sperm concentrations of less than 0.2 million sperm per mL, and seven were azoospermic. Post-procedural pain was minimal. Nine men ultimately achieved and maintained azoospermia; however, 4 to 6 months after the procedure, sperm concentrations increased in three of the 12 subjects, necessitating repeat vasectomy. Microscopic examination of the vas deferens from these failures revealed re-canalization. Vasectomy by epithelial curettage can result in effective sterilization; however, 1/4 of the subjects were not effectively sterilized by the procedure due to re-canalization of the vas deferens. Epithelial curettage will require further refinement to determine if it is a viable form of vasectomy.

Asian Journal of Andrology (2010) 12: 315–321. doi: 10.1038/aja.2009.94; published online 15 February 2010.

Keywords: male contraception, male sterilization, re-canalization, spermatogenesis, vas deferens, vasectomy failure

1 Introduction

Roughly 10% of couples in the United States choose vasectomy as their contraceptive method [1]. Vasectomy is a safe, simple, outpatient surgery performed under local anesthesia in which the vas deferens is located and ligated and/or cauterized through a small scrotal incision. There are approximately 500 000 vasectomies performed in the USA yearly, and worldwide over 50 million men have undergone the procedure [2]. Vasectomies are highly effective, with a failure rate of less than 1% [3–6]. In the last 15 years, the 'no scalpel technique' perfected in the Sichuan Province in China [7], which entails a single puncture in the midline of the scrotal raphe with a pointed hemostat, has become the most frequently used approach. This technique is highly efficacious, particularly when coupled with either cautery or ligation with fascial interposition, but there is no clear-cut advantage of one method over the other [7–9].

A novel microcurette, called the Vas-X, has been developed by two of us (John W. Jessen and Richard E.

Correspondence to: Prof. John K. Amory, Department of Medicine, Center for Research in Reproduction and Contraception, University of Washington School of Medicine, Box 356429, 1959 NE Pacific Street, Seattle, WA 98195, USA.
Fax: +1-206-616-5365 E-mail: jamory@u.washington.edu
Received: 4 November 2009 Revised: 25 November 2009
Accepted: 25 December 2009 Published online: 15 February 2010

Berger) for use in vasectomy. The Vas-X is designed to strip the epithelium of the vas deferens leading to vasal occlusion and sterilization. In addition, the Vas-X might prove easier to use in less-developed areas of the world because the Vas-X has a very simple design, is re-usable (with sterilization) and does not require an electrical supply for use. Pre-clinical work with this device on resected specimens of vas suggested that epithelial curettage might be an effective means of vas occlusion and sterilization. Therefore, we conducted a pilot study in normal men requesting permanent sterilization. After Vas-X vasectomy, subjects were followed with monthly sperm counts for 6 months to examine the efficacy of this approach to male sterilization.

2 Methods

2.1 Subjects

Twelve normal men, age 30–55 years, requesting elective vasectomy were recruited for the study by flyers and newspaper ads. Inclusion criteria were: testicular volumes >15 cm^3 bilaterally, detectable sperm in a baseline semen specimen, the ability to read and sign informed consent documents and complete all follow-up procedures. Exclusion criteria included a history of coronary artery disease, stroke, heart failure, thromboembolic disorder, cirrhosis, prostate or testicular cancer, prior vasectomy or other scrotal surgery, prior male-factor infertility, or current abuse of drugs or alcohol. Subjects were compensated for the time and energy they invested to participate in the study. This study was approved by the Institutional Review Board at the University of Washington. The trial was registered in advance at http://clinicaltrials.gov/ as study # NCT00663533.

2.2 Study procedures

After providing written informed consent, men underwent a screening examination and blood work, as well as two baseline seminal fluid analyses. If blood results were normal and the semen samples revealed motile sperm, subjects were allowed to proceed to Vas-X vasectomy. Vasectomy with the Vas-X (Figure 1A) was performed by first isolating the vas deferens using the standard no-scalpel vasectomy technique. The vas was then hemi-transected at two points approximately 1 cm apart. Next, the Vas-X microcurette was inserted with one hand into the abdominal end of the vas lumen until it tightly engaged the vas lumen (Figure 1B). Next, the forefinger and thumb of the other hand were used to grasp the vas deferens around the Vas-X, which was quickly extracted, removing the vas epithelium (Figure 1C). The Vas-X was then cleaned to remove the epithelial tissue and the stripping procedure was repeated on the testicular end of the vas deferens through the lower hemi-transection site. Lastly, the middle segment of the vas between the two hemi-transection sites was stripped of its mucosa with the Vas-X and opened longitudinally from either end with small iris scissors to provide a 'spacer' between the abdominal and testicular ends of the vas and to encourage scar formation. The wound was inspected for bleeding and the vas was returned to the scrotum. The entire procedure was repeated

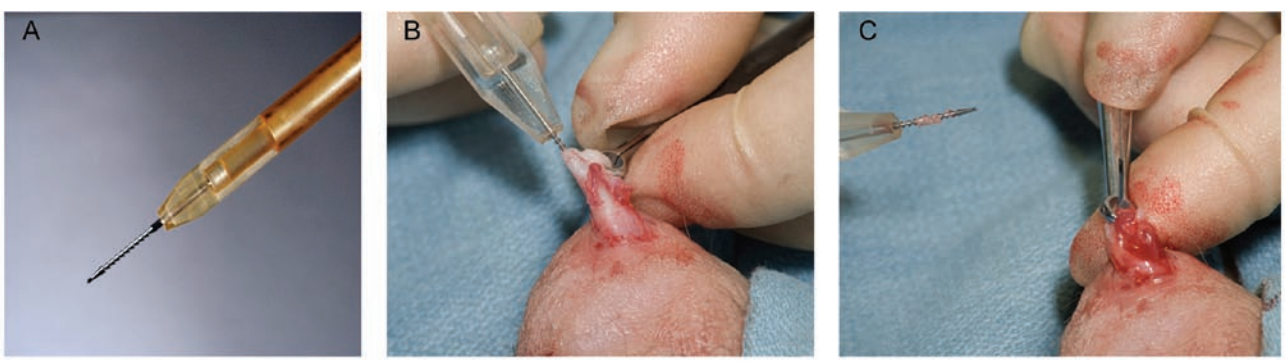

Figure 1. Vasectomy by epithelial curettage using the Vas-X. The vas is uncovered bilaterally using the no-scalpel approach. The Vas-X microcurette (A) is introduced into the hemisected vas, engaging the epithelium (B), which is then stripped out and adheres to the microcurette (C).

on the other vas through the same incision. After the Vas-X vasectomy, men provided monthly seminal fluid samples for 6 months. If the vasectomy failed, subjects proceeded to a routine cautery vasectomy and underwent removal of the segments of vas treated with epithelial curettage.

2.3 Measurements

Semen samples were initially analyzed by computer-aided sperm analysis (Hamilton-Thorne, Boston, MA, USA). Sperm concentrations below 15 million mL^{-1} were manually counted using a hemocytometer according to WHO methods [10]. Azoospermia was defined as the absence of sperm after microscopic examination of the spun semen sample (3 000 × *g*, 15 min) and review of at least 400 fields. Tissue staining of resected vas deferens was performed by the Pathology Laboratory at the University of Washington. Segments of vas deferens treated with the Vas-X were fixed, embedded, sectioned and stained for light microscopy using hematoxylin and eosin, or for immunohistochemistry using the anti-epithelium cytokeratin antibody mixture AE1/AE3 in adjacent 5 μm sections. Post-procedural pain and satisfaction were assessed by study-specific questionnaires. As there were no validated instruments for the assessment post-vasectomy pain and satisfaction, we modeled our acceptability questions on those found in previously published studies of the acceptability of other forms of experimental male contraception [11, 12]. For assessment of pain, three five-option Likert-type questions were created asking the subject to select no pain, mild pain, moderate pain, extreme pain or excruciating pain during the procedure, in the few days after the procedure or 1 month after the procedure. For assessment of acceptability, subjects were asked to select strongly disagree, disagree, undecided, agree or strongly agree in response to the following questions: (1) 'Overall, I was satisfied with the method of contraception'; (2) 'I would recommend this method of contraception to others'. Lastly, subjects were asked to select: a lot better, a little better, about the same, a little worse or a lot worse in response to the question: 'How did this method compare with your expectations?'

2.4 Statistical analysis

Mean sperm concentrations 3 months after the vasectomy (the primary end point) and at other time points were compared with the baseline by paired *t*-tests with a Bonferroni correction for multiple comparisons. Subjects' responses to the pain and acceptability questionnaires were summarized in a descriptive fashion. The association between azoospermia or non-azoospermia and baseline sperm concentration, age and weight was analyzed by univariate and multivariate logistic regression using robust standard errors. STATA version 8.0 (College Park, TX, USA) was used for all calculations. For all comparisons, a two-sided alpha of < 0.05 was considered significant.

3 Results

3.1 Subjects

Thirteen men were screened for inclusion. One man failed screening due to previously undiagnosed liver disease. Therefore, 12 men with a mean age of 38 ± 5 years were enrolled and underwent epithelial curettage vasectomy using the Vas-X. Eleven of the 12 men undergoing vasectomy were Caucasian; one was Filipino. All of the men were in steady long-term relationships, and 11 of the men had fathered children. Eight of the men were relying on condoms for birth control, three were using female hormonal methods and one was relying on the rhythm method and withdrawal.

There were no serious adverse events associated with the procedure. There were no operative complications or wound infections requiring treatment. Adverse events experienced by study subjects in the study period included two subjects with hay fever, and one each with vertigo, headache, food poisoning, insomnia and fatigue. All adverse events were temporary, and in no instance were any of these adverse events considered to be related to study participation. Eleven of twelve subjects completed all study procedures. One subject, #11, failed to make his planned repeat vasectomy twice and was lost to further follow-up.

3.2 Sperm concentrations

Mean sperm concentrations were markedly reduced compared with baseline concentrations ($P < 0.01$) at all time points (Table 1). By 3 months after the vasectomy, all subjects had sperm concentrations of less than 0.2 million sperms per mL of ejaculate and seven of 12 were azoospermic. By 6 months after Vas-X vasectomy, six of 12 men were azoospermic and three additional men had sperm concentrations of less than 0.001 million sperm per mL. These three men demonstrated only rare non-motile sperm on microscopic examination of the centrifuged semen sample. Continued follow-up

Table 1. Sperm concentrations (million mL^{-1}) and rapidly progressive motility in subjects at baseline and monthly after vasectomy by epithelial curettage using the Vas-X.

Subject No.	Sperm concentrations (million mL^{-1})							Progressive motility (%)[a]	
	Baseline	1 m	2 m	3 m	4 m	5 m	6 m	1 m	6 m
1	116	0.2	0.009	0.003	0.001	0*	0*	0	0
2	30	0.1	0.007	0	0	0	0	0	0
3	52	0.007	0.003	0	0	0	0	0	0
4	27	0.075	0.001	0*	0	0.003	0	0	0
5	24	0.1	0*	0*	0	0	0	0	0
6	82	0.008	0.001	0.001	0*	0*	0*	0	0
7	181	7	0.005	0*	4.3	2.7	15	40	35
8	38	0.138	0*	0	0	1.8	5.6	0	30
9	143	4.2	0.35	0.03	0.001	0*	0*	28	0
10	120	0.01	0.001	0	0	0	0	0	0
11	69	48.3	NS	0.153	0.061	NS	0.85	11	N/A
12	94	2.5	0.004	0.025	0*	0	0	0	0

Post-operative rebound of sperm concentration after initial suppression was observed in three subjects (#7, #8 and #11) after three months. m: month after Vas-X vasectomy. [a]Percentage of the Rapidly progressive motility at baseline. NS = no sample, 0* = concentration of less than 0.001 million mL^{-1}, but with rare non-motile sperm observed with microscopic examination of the centrifuged sample. N/A = not available (mailed sample).

of these nine subjects for 12 months has not revealed any additional failure to date.

In contrast, three subjects (#7, #8 and #11) experienced obvious failure of sterilization. Sperm concentrations in these three men appeared to nadir 3 to 4 months after the procedure. Indeed, two of the three failures were azoospermic at month 3. However, 4 to 6 months after the vasectomy, sperm concentrations increased dramatically, even reaching the lower limit of the normal range in one individual. Modeling of factors associated with azoospermia by logistic regression did not reveal a statistically significant association between the attainment of azoospermia at 6 months and age, height or baseline sperm concentration. Moreover, there were no differences in operative technique in the men who failed compared with men with successful surgeries.

3.3 Vas histology

Per protocol, subjects whose vasectomy failed were offered a cautery vasectomy after 6 months. Two of these subjects (#7 and #8) opted to undergo a repeat vasectomy. During this procedure, the treated segment of vas was easily identified operatively. This segment exhibited marked thickening compared with the untreated vas proximally and distally. During the cautery vasectomy, the treated segments of vas were resected and submitted for histological processing. Intact ductus deferens was observed in sections furthest from the treated segment (Figure 2A). These sections strongly reacted with the anti-cytokeratin AE1/AE3 antibody (Figure 2B). In subject #7, the lumen of the left vas appears to be completely scarred shut by the treatment as there is no obvious luminal patency observed by either routine (H&E) or epithelial cytokeratin staining (Figures 2C and D). The in-growth of issue appears to be mainly muscle tissue, with only a few scattered fibroblasts. In contrast, the tissue from the resected segment of the right vas revealed several small patent channels forming within the treated areas; however, no sperms were identified within these channels. In subject #8, the left vas showed a single narrow tube lined with cytokeratin-positive epithelium near the center of the scar (Figures 2E and F). In the right vas of this subject, numerous channels lined by cytokeratin-positive epithelium coursed through the lamina propria adjacent to a scarred central portion (Figures 2G and H). In some, an expanded lumen revealed apparent sperm nuclei.

3.4 Pain and acceptability

The results from the pain and acceptability questionnaires are summarized in Table 2. No subject

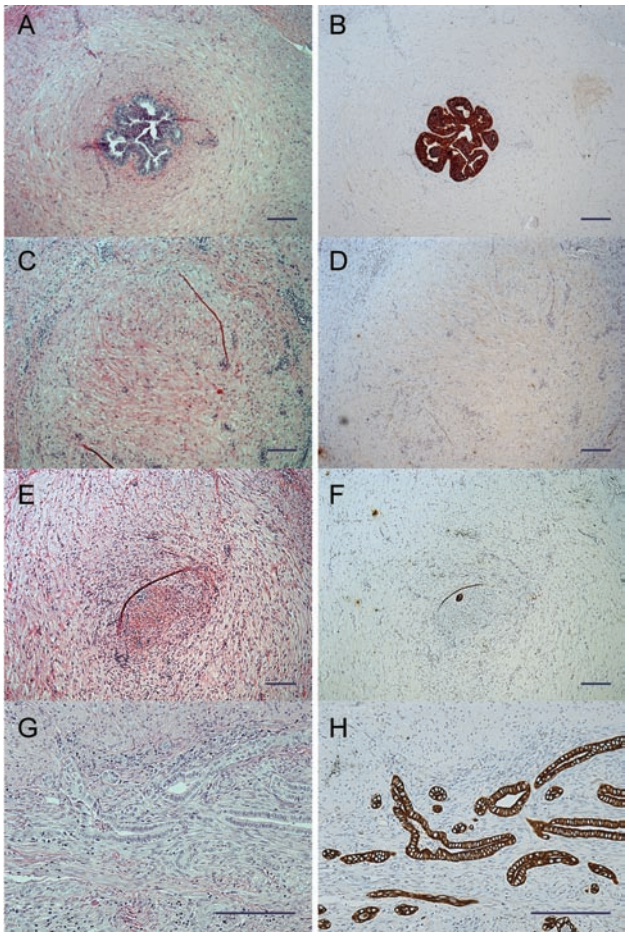

Figure 2. Histological appearance of resected vas deferens from subjects #7 and #8 6 months after failed Vas-X vasectomy. Hematoxylin and eosin stain (A, C, E, G); adjacent section stained with the anti-epithelial cytokeratin stain AE1/AE3 (B, D, F, H). (A), (B): Intact portion of the right ductus deferens of subject #7. (C), (D): Scar tissue with no indication of the epithelium from the left vas of subject #7. (E), (F): Left vas of subject #8 showing the scarred central area with a single epithelium-lined narrow channel. (G), (H): Right vas of subject #8 showing numerous epithelium-lined channels in the lamina propria, some with apparent spermatozoa in the lumen. Scale bars = 100 μm.

experienced extreme or excruciating pain during or after the procedure. Notably, more subjects reported moderate pain in the few days after the procedure compared with during the procedure. However, by 1 month, 11 of 12 men reported having no pain. As a result, satisfaction with this procedure was high, with 10 of 12 men strongly agreeing with the statement 'I was satisfied with this method' and the remaining two men agreeing with the statement. In addition, most of the men would recommend the procedure to others and the procedure was 'worse than expected' for only two of the 12 subjects.

Table 2. Pain and acceptability associated with vasectomy by epithelial curettage using the Vas-X (n = 12).

Grade	I	II	III	IV	V
Pain					
During the procedure	3	6	3	0	0
In the few days afterwards	0	6	6	0	0
One month afterwards	11	1	0	0	0
Acceptability					
I was satisfied with this method	10	2	0	0	0
I would recommend it to others	9	3	0	0	0
How did this method compare with your expectations?	5	2	3	2	0

Pain grade: I, no pain; II, mild pain; III, moderate pain; IV, extreme pain; V, excruciating pain. Acceptability: I, strongly agree; II, agree; III, undecided; IV, disagree; V, strongly disagree. Comparison to expectations: I, a lot better; II, a little better; III, about the same; IV, a little worse; V, a lot worse.

4 Discussion

In this study, we have demonstrated that vasectomy by epithelial curettage with the Vas-X can effectively sterilize men at 1 year of follow-up. However, three of the 12 men in this pilot trial, despite attaining very low sperm concentrations 3 months after the vasectomy, were not effectively sterilized. These men experienced a 'late' failure of their vasectomy (as defined by Labrecque *et al.* [13]), with the re-appearance of sperm in their ejaculates between 4–6 months after the initial epithelial curettage procedure. Because two of these men were azoospermic and the third was near-azoospermic before experiencing failure, it appears that the procedure was initially successful in occluding the vas, but the vas was able to re-canalize several months after the procedure. This re-canalization could be directly visualized in the two individuals who returned for a repeat vasectomy. Microscopic analysis of the segment of the vas that underwent epithelial curettage with the Vas-X revealed what appeared to be re-growth of new vas-like channels through the treatment area. This finding implies that in these individuals the injury to the epithelium mediated by the Vas-X was not sufficient to prevent epithelial re-growth, possibly due to insufficient compression of the vas against the blades of the microcurette before it was extracted. As a result, the technique of

epithelial curettage will require further refinement to determine whether it is a viable alternative to cautery for vasectomy. Improvements such as curettage of a longer segment of the vas and/or instillation of a caustic or toxic agent, such as silver nitrate, into the lumen of the treated segments of vas to prevent re-canalization could be considered for future study.

In addition, we chose to leave the abdominal and treated ends of the vas connected by an 'unroofed' middle segment, which also underwent epithelial curettage with the Vas-X. In theory, this was intended to prevent the abdominal and testicular end of the vas from re-anastomosing while the tissue was forming a luminal scar. A similar method has been extensively tested using electrocautery [14]. However, it is possible that in the setting of epithelial curettage, this approach instead allowed for epithelial stem cells to re-populate the area and form the new lumens visualized in the tissue specimens from the subjects undergoing repeat vasectomy for failure. Moreover, in contrast to the reported histology of the vas in men undergoing cautery vasectomy, which reveals a fibroblastic scar [15], the histology after treatment with the microcurette is predominantly muscular. Whether this accounts for the apparently increased risk of re-canalization is unknown. Future studies of epithelial curettage may need to consider removing the middle segment to prevent the types of failure observed in this study.

If the technique of epithelial curettage for vasectomy can be optimized, it might offer several advantages over current vasectomy techniques that rely on suture or cautery. First, it can be performed with the no-scalpel approach, which is widely practiced and acceptable to patients; however, unlike the no-scalpel technique, it does not require that the vasal blood supply be stripped from the vas deferens, thereby potentially decreasing the potential of vascular injury and bleeding complications. Second, there is no unpleasant smell of burning flesh associated with cautery, and because there is less tissue damage than with cautery, it is possible that men undergoing vasectomy by epithelial curettage might experience less pain. Indeed, men in this study experienced minimal post-operative pain from their procedure, with 11 of 12 men reporting no pain at 1 month. Lastly, if vasectomy via epithelial curettage can be perfected, it may prove easier to use in less-developed areas of the world as the technique is easy to learn and requires less operative skill than other techniques. Moreover, the Vas-X has a very simple design, is re-usable (with sterilization) and does not require an electrical supply for use.

Notably, three of the nine subjects in whom the procedure was successful continued to have rare, non-motile sperm in their ejaculates. The presence of these rare, non-motile sperm has been observed in up to 40% of men undergoing vasectomy [16]. Long-term follow-up has shown that the vast majority of such men eventually become azoospermic [17]. Therefore, the presence of rare, non-motile sperm is thought to be consistent with a successful vasectomy. However, given the novel nature of this procedure, these subjects will continue to be followed up to insure that they do not experience very late failures.

In conclusion, this is the first report of the use of epithelial curettage as a method of vasectomy. We have demonstrated that this approach to male sterilization is effective in a majority of men; however, a subset of men, after initially achieving extremely low sperm counts, failed and experienced the re-appearance of sperm in their ejaculates. Analysis of tissue from these failures demonstrates vasal re-canalization, implying that future studies of this technique will require more extensive curettage, or other measures to prevent late failures. If improvements to the technique are successful, epithelial curettage might offer a simple alternative to cautery or ligation vasectomy for the provision of male sterilization.

Acknowledgment

We thank Ms Marilyn Busher, Ms Kathy Winter, Ms Iris Nielsen, Ms Kathryn Torres Duncan, Ms Constance Pete and Mr Robert Bale for assistance with the clinical aspects of this study, and William Bremner MD, PhD and David W. Amory MD, PhD for their critical review of the manuscript.

This work was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, a division of the National Institute of Health through cooperative agreements U54 HD42454 as part of the Cooperative Contraceptive Research Centers Program and by the Paul G. Allen Family Foundation.

References

1 Piccinino LJ, Mosher WD. Trends in contraceptive use in the United States: 1982–1995. Fam Plan Persp 1998; 30: 4–10.
2 Haws JM, Morgan GT, Pollack AE, Koonin LM, Magnani

RJ, *et al.* Clinical aspects of vasectomies performed in the United States in 1995. Urology 1998; 52: 685–91.
3 Philip T, Guillebaud J, Budd D. Complications of vasectomy: review of 16,000 patients. Br J Urol 1984; 56: 745–8.
4 Fu H, Darroch JE, Haas T, Ranjit N. Contraceptive failure rates: new estimates from the 1995 National Survey of Family Growth. Fam Plan Perspect 1999; 31: 56–63.
5 Jamieson DJ, Costello C, Trussell J, Hillis SD, Marchbanks PA, *et al.* US Collaborative Review of Sterilization Working Group. The risk of pregnancy after vasectomy. Obstet Gynecol 2004; 103: 848–50.
6 Deneux-Tharaux D, Kahn E, Nazerali H, Sokal DC. Pregnancy rates after vasectomy: a survey of US Urologists. Contraception 2004; 69: 401–6.
7 Li SQ, Goldstein M, Zhu J, Huber DH. The no-scalpel vasectomy. J Urol 1991; 145: 341–4.
8 Barone MA, Irsula B, Chen-Mok M, Sokal DC; the investigator study group. Effectiveness of vasectomy using cautery. BMC Urol 2004; 4: 10.
9 Sokal D, Irsula B, Chen-Mok M, Labrecque M, Barone M. A comparison of vas occlusion techniques: cautery is more effective than ligation and excision with fascial interposition. BMC Urol 2004; 4: 12.
10 World Health Organization. Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction, 4th edn. Cambridge: Cambridge University Press; 1999.
11 Zhang L, Shah IH, Liu Y, Vogelsong KM, Zhang L. The acceptability of an injectable once-a-month male contraceptive in China. Contraception 2006; 73: 548–53.
12 Meriggiola MC, Cerpolini S, Bremner WJ, *et al*. Acceptability of an injectable male contraceptive regimen of norethisterone enanthate and testosterone undecanoate for men. Hum Reprod 2006; 21: 2033–40.
13 Labrecque M, Hays M, Chen-Mok M, Barone MA, Sokal D. Frequency and patterns of early recanalization after vasectomy. BMC Urol 2006; 6: 25.
14 Marmar J, Kessler S, Hartanto VH. A minimally invasive vasectomy with the no suture, inline method for vas occlusion. Int J Fertil Women's Med 2001; 46: 257–64.
15 Andonian S, Jarvi K, Zini A, Hermo L. Ultrastructural features of the vas deferens from patients undergoing vasectomy and vasectomy reversal. J Androl 2002; 23: 691–701.
16 Dhar NB, Bhatt A, Jones JS. Determining success of vasectomy. BJU Int 2006; 97: 773–6.
17 Chawla A, Bowles B, Zini A. Vasectomy follow-up: clinical significance of rare, nonmotile sperm in postoperative semen analysis. Urology 2004; 64: 1212–5.