FERTILITY AND STERILITY
Vol. 31, No. 3, March 1979

Printed in U.S.A.

EPIDIDYMAL EXTRAVASATION FOLLOWING VASECTOMY AS A CAUSE FOR FAILURE OF VASECTOMY REVERSAL

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Twenty-eight men undergoing vasectomy reversal who were found to have no sperm in the proximal vas fluid on one or both sides underwent microscopic epididymal exploration. In 33 of 39 cases so explored, normal sperm were found in the epididymal fluid of the corpus, despite absence of sperm in the vas fluid. Epididymal histology distal to this site revealed extensive interstitial sperm granulomas resulting from rupture of the epididymal duct. Testicular biopsy revealed normal spermatogenesis. Secondary epididymal obstructions were noted when there was copious fluid in the vas deferens proximal to the vasectomy site as well as when there was scanty fluid. It is concluded that persistent azoospermia after an accurate microscopic vasovasostomy results from the secondary epididymal obstruction induced by rupture of the epididymal duct related to the pressure increase after vasectomy. Fertil Steril 31:309, 1979

It has been previously demonstrated that failure to recover a normal semen analysis after vasectomy reversal is very frequently due to obstruction of the anastomosis.[1, 2] However, another major cause of failure to recover fertility despite an accurate vasovasostomy was found to be the pressure-mediated effects of the vasectomy itself.[3, 4] The recovery of a normal semen analysis was correlated with the presence of an abundance of normal sperm in the vas fluid on the testicular side of the vasectomy site at the time of vasovasostomy. This fluid was less likely to harbor normal sperm the longer the duration of time that had passed since the vasectomy. Furthermore, the presence of a sperm granuloma at the vasectomy site, venting the high pressure that would otherwise build up, virtually ensured the presence of good quality sperm in the vas fluid. A sperm granuloma at the vasectomy site was associated with less dilatation of the proximal vas deferens. The question as to how these pressure-induced changes proximal to the vasectomy site made the recovery of fertility less likely after an accurate reanastomosis, however, was unanswered by these studies. By exploring the epididymis in cases in which there were no sperm in the vas fluid at the time of vasectomy reversal or when a demonstrably accurate vasovasostomy still resulted in azoospermia, we wished to determine whether microanatomical changes in the epididymis induced by the pressure increase subsequent to vasectomy might be the major factor responsible for failure of an otherwise accurate vasovasostomy.

Received August 10, 1978; accepted November 15, 1978.
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METHODS

Twenty-eight men underwent microscopic epididymal exploration and serial transections with biopsy. All of these patients were noted to have no sperm in the vas fluid on the testicular side of the vasectomy site at the time of intended vasovasostomy. Thirteen of the patients had persistent azoospermia after a previous vasovasostomy, and no sperm were noted in the vas fluid at the time of that vasovasostomy. Fifteen of the patients had not had a previous vasovasostomy. Ages ranged from 27 to 55 years.

All patients underwent several semen analyses preoperatively to determine that they were azoospermic. The operative permit for vasovasostomy included complete scrotal and/or inguinal exploration with epididymal dissection and multiple sectioning if indicated. Each of the 28 patients underwent a bilateral scrotal exploration in which the vas deferens was first freed and isolated above and below either the vasectomy site or the former vasovasostomy site. Under ×10 to ×25 magnification with an operating microscope, the vas deferens was first transected proximally, that is, on the testicular side of the vasovasostomy or vasectomy site. Fluid from this testicular side of the vas deferens was then sampled with a micropipette and examined for volume and characteristics observable under the dissecting microscope. This fluid was then placed on a slide and examined as a wet mount under a laboratory microscope for the presence or absence of sperm; if sperm were present, the quality of motility was recorded. The slide was then fixed and stained and examined under oil immersion for sperm morphology and other constituents in the vas fluid. In cases where a previous vasovasostomy had been performed, a vasogram in the abdominal direction determined whether or not the former anastomosis was properly patent (Fig. 1).

All of these patients who did not have sperm present in the vas fluid then underwent epididymal exploration in anticipation of a possible microscopic vasoepididymal tubule anastomosis.[5] Beginning as far distally as possible, the epididymis was serially transected 0.5 cm at a time and observed under the operating microscope under ×25 magnification. With each transection the one specific tubule leaking epididymal fluid was observed and fluid was sampled from it. This fluid was then examined in a fashion similar to the vas fluid. Serial sectioning was continued proximally up the epididymis to the level where spermatozoa were noted, or until the head of the epididymis was reached. The lowest level at which spermatozoa were noted was then selected for the site of vasoepididymal anastomosis end-to-end. All distal segments of epididymis thus serially removed were submitted for histologic examination.

In 11 of these 28 patients the need for epididymal exploration was bilateral; in 17 the exploration was only unilateral. Thus, a total of 39 epididymides were examined. In 13 of these 39 cases a testicular biopsy was also performed with an atraumatic "no-touch" technique, and the specimen was fixed with Zenker's solution. Of these 28 patients, 4 had a sperm granuloma at the vasectomy site on one side. In all four of these cases the vas fluid harbored abundant, morphologically normal sperm on this side, but on the other side there were no sperm in the vas fluid. Similarly, 13 other patients (making a total of 17) had normal sperm in the vas fluid on one side and therefore underwent only unilateral epididymal exploration. Of the 28 patients, 11 underwent bilateral epididymal exploration because there were no sperm in the vas fluid on either side.

RESULTS

Vas Deferens Fluid. This study represents a selected group of cases in which no sperm were found in the vas fluid. Of 39 vasa so examined, 20 had a very scanty volume of fluid which was translucent. In 19 of the 39 vasa examined, the fluid was copious in amount and was under considerable pressure. Sixteen of those nineteen men had thick, creamy fluid, and three had a more normal-appearing, translucent fluid. Creamy fluid harbored an abundance of macrophages and/or "amorphous debris." Previous electron microscopic studies of thin sections of such "debris" have shown that it often represents products of sperm head breakdown.[6] When the vas fluid contained no sperm, but was *crystal clear*, patients reliably recovered normal semen analysis after vasovasostomy. Therefore such patients did *not* undergo epididymal dissection, and are not included in this study.

Epididymal Fluid. In 33 of 39 cases, despite absence of sperm in the vas fluid, an abundance of sperm was noted in the epididymal fluid at some point between the junction of the tail of the epididymis with the corpus epididymidis and the area of the proximal corpus epididymidis. In 30 of those cases sperm were present near the distal corpus epididymidis. Of the 33 samples of epididymal fluid which harbored sperm, 9 had actively motile sperm and 24 had morphologically normal but nonmotile sperm. In 6 of the 39 cases no sperm were noted in the epididymal fluid. In two of those cases the transection was discontinued in the region of the distal corpus (these were among the earlier cases in the series). In two of the six cases the transection did not extend proximal to the corpus epididymidis. In only two of the six cases with no sperm in the epididymal fluid did the exploration extend well into the head of the epididymis.

In all of these cases epididymal fluid was present. In 15, the epididymal fluid appeared creamy

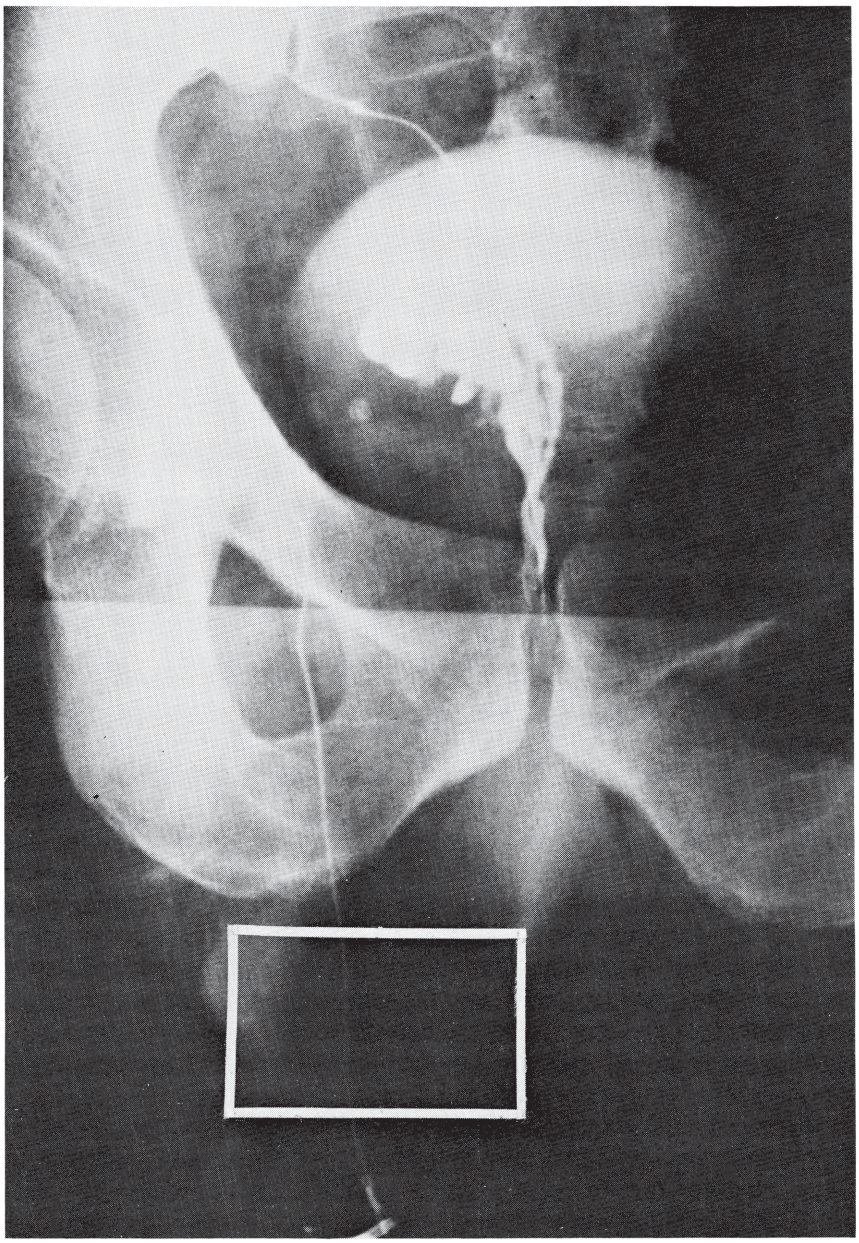

FIG. 1. A vasogram demonstrates completely normal patency *(inset)* after microsurgical vasovasostomy despite persistent azoospermia.

under the operating microscope, and 6 of the 15 samples contained no sperm. In 8 cases the epididymal fluid was clear and in 11 cases it was translucent. In five cases we did not have accurate records of the appearance of that fluid under the operating microscope.

Of the 19 cases in which there was a large volume of fluid which harbored no sperm in the vas deferens, the epididymal fluid contained sperm in 18 cases and did not contain sperm in only 1 case. Of the 20 cases in which the vas fluid was scanty, the epididymal fluid in 15 harbored sperm and in 5 it did not. When the epididymal fluid did not harbor sperm the fluid in the epididymis was creamy. Clear or translucent epididymal fluid always harbored sperm. In all cases the epididymal tubule clearly was dilated.

Testicular Biopsy. Nonquantitative examination of the testicular biopsy in 13 cases demonstrated normal mature sperm in the seminiferous tubules in all cases. Spermatogenesis appeared to be progressing adequately through all stages. There was a suggestion of an accumulation of immature cells and sloughing but this was not as

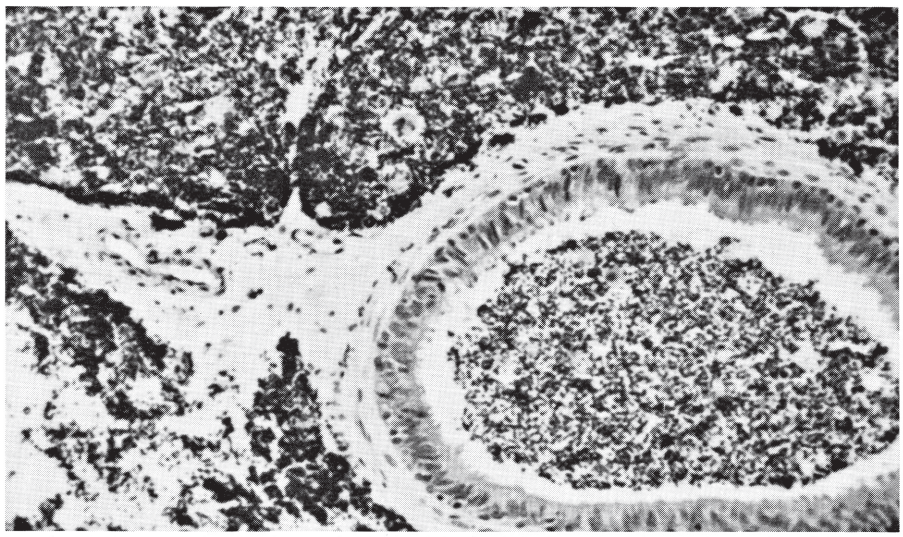

FIG. 2. Epididymal histology reveals extensive interstitial sperm granuloma surrounding an epididymal tubule congested with senescent sperm.

dramatic as the appearance of normal sperm in the seminiferous tubules in all cases in which no sperm were found in the vas fluid.

Epididymal Histology. Examination of the epididymis distal to the level at which normal sperm were found in the epididymal fluid revealed dilated epididymal ducts, sperm extravasation into the interstitium, and intertubular sperm granuloma formation with macrophages containing sperm heads and plasma cells (Figs. 2, 3, and 4). Within the epididymal tubules themselves at the section near the site of transition, many sperm were noted within the tubule (Fig. 5). Distal to the area of transition, sperm were not detected in the epididymal tubules (Fig. 6). When no sperm were found in the epididymal fluid (six cases), the epididymal histology did not show interstitial sperm granuloma formation nor did it show sperm within the epididymal tubule.

DISCUSSION

In our previous studies we noted that the increase in intravasal pressure transmitted toward the epididymis and testis after vasectomy appeared to be the major factor affecting recovery of a normal semen analysis after an anatomically successful vasovasostomy. The capacity for epididy-

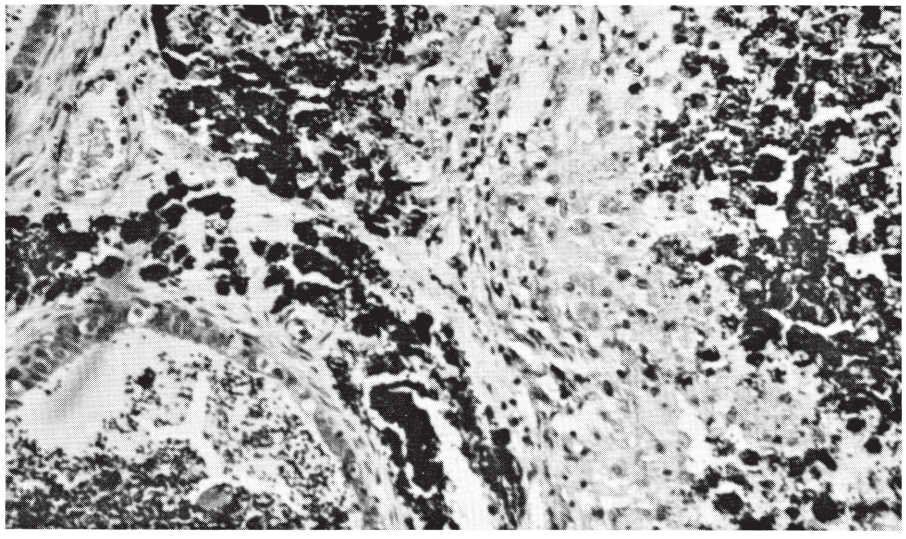

FIG. 3. Diffuse extravasation of sperm into interstitium of epididymis with widespread formation of sperm granuloma.

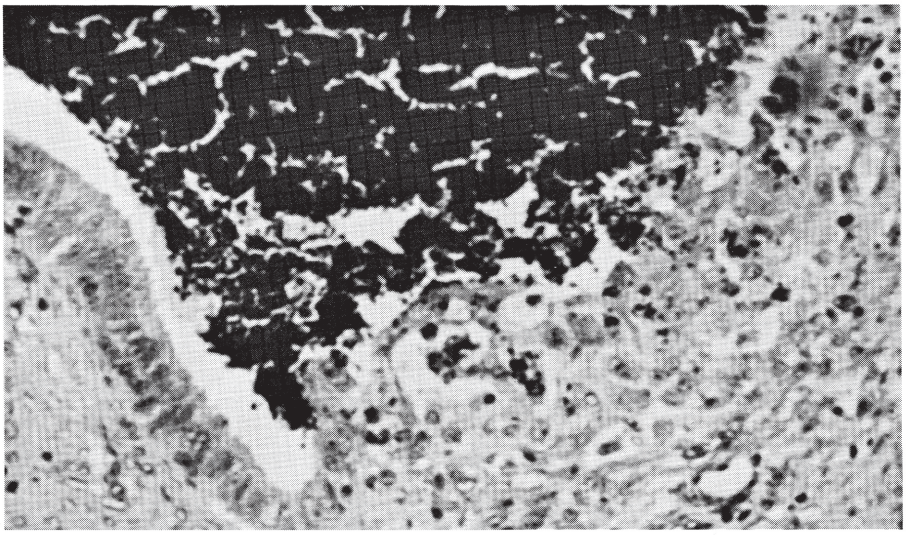

FIG. 4. Site of epididymal sperm extravasation.

mal fluid reabsorption is probably a major source of protection after vasectomy.[7] The formation of a sperm granuloma at the vasectomy site is another important source of protection for some patients, representing leakage at the vasectomy site which minimizes dilatation of the proximal vasal system.[3] There remain several unanswered questions. Is the absence of sperm in the vas fluid on the testicular side of the vasectomy a result of pressure-mediated damage within the testis, the rete testis, or the epididymis? Why should some patients with very high intravasal pressure for more than 20 years have good quality sperm in the vas fluid whereas others with the same degree of pressure have no sperm in the vas fluid?

The role of autoimmunity is also confusing. Alexander and Schmidt[8] have shown that the incidence of antisperm antibody levels appeared only slightly higher in men who had sperm granulomas than in those who did not have sperm granulomas at the vasectomy site. The appearance of a sperm granuloma at the vasectomy site did not predict that an individual would be much more likely to develop antisperm antibodies. Yet, from our clinical data the presence of a sperm granuloma, which would seem to ensure greater likelihood of immune stimulation, confers remarkable protection from the pressure-induced changes of vasectomy.

In studies with vasectomized rhesus monkeys, Alexander[9] demonstrated massive dilatation of

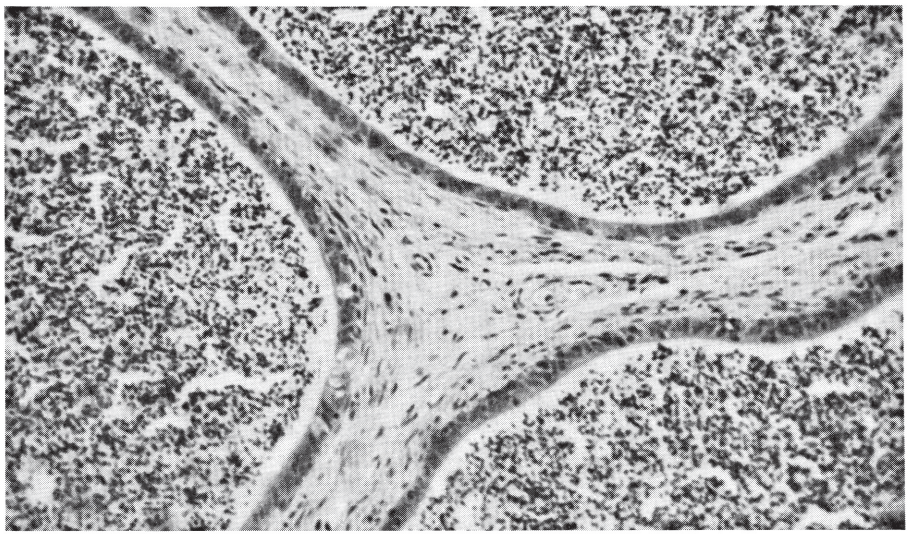

FIG. 5. Section through epididymal tubule proximal to the site of sperm extravasation. The cut ends of its many convolutions are seen to be massively congested with sperm.

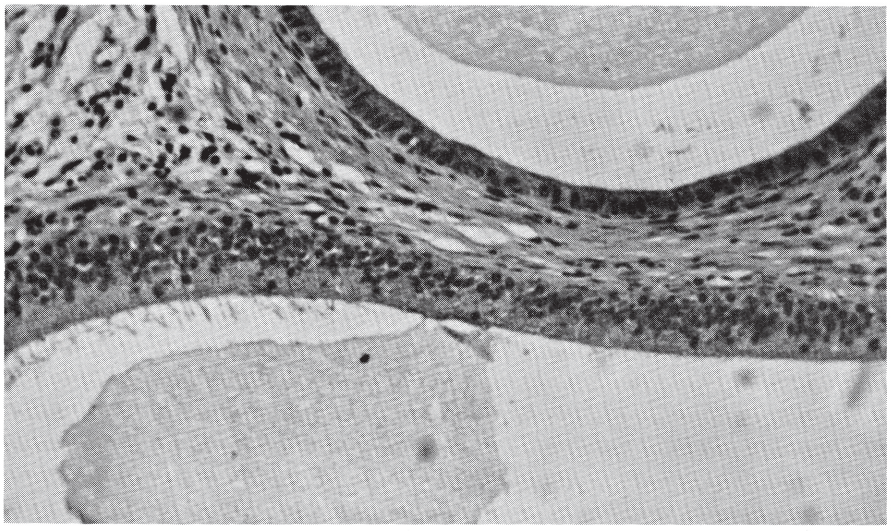

FIG. 6. Section through epididymal tubule distal to site of sperm extravasation. The epididymis here is devoid of sperm.

the ductuli efferentes with macrophage invasion suggesting sperm reabsorption at that site. Bedford[10] performed extensive long-term studies on the effect of vasectomy in a variety of animals, including rabbits, hamsters, rats, and rhesus monkeys. He noted increasing distention of the epididymis with the duration of time after vasectomy in all of the animals studied. Testicular tissue was histologically normal in all cases, but the cauda epididymidis showed massive dilatation with dense accumulations of sperm.[10] There was no infiltration of any type of leukocyte unless rupture of the epididymal duct had occurred. By 8 months the corpus epididymidis began to show dilatation with a series of lesions and ruptures as well as scars in the interstitium of the epididymis. No macrophages were found in the epididymal tubule until this leakage occurred and interstitial sperm granuloma developed. Interestingly, Bedford noted very little epididymal damage in the rhesus monkey. de Kretser[11] also noted that sperm production by the testes appears to continue with little specific damage to the seminiferous tubules. However, in most animals, ligation of the vas was followed by distention of the epididymal ducts with rupture and granuloma formation. Pardanani et al.[12] noted the appearance of epididymal lesions following vasectomy in human but were not able to determine the nature of the lesions or to explore the epidiymis surgically for fear of interfering with ductal continuity.

The problem in determining the site of pressure-induced damage following vasectomy in humans has been one of microsurgical technique. Transecting the epididymis would destroy ductal continuity and conceivably ruin any chance for successful recovery of sperm output. Conventional techniques for vasoepididymostomy that were available made such an exploration unjustified. Once an accurate technique for anastomosing the inner lumen of the vas deferens directly to the epididymal tubule was available, we felt it reasonable to explore patients who had no sperm in the vas fluid at the time of vasovasostomy, or who were azoospermic after accurate vasovasostomy.[5]

It is clear from this series of epididymal explorations that secondary ductal obstruction in the epididymal region (caused by rupture of the dilated epididymal tubule with consequent interstitial sperm granuloma formation) is the major cause of persistent azoospermia in patients who have had an accurate vasovasostomy. In a smaller group, ruptures may occur at the level of the vasa efferentia or the rete testis. In most cases, however, the level of secondary obstruction is near the junction of the distal corpus and tail of the epididymis (where the epididymal tubule first becomes remarkably thinned out). The volume of fluid in the vas does not give any indication of this secondary obstruction; only the absence of sperm in this fluid indicated secondary obstruction.

It would appear that the reason patients with sperm granuloma at the vasectomy site almost always have good quality sperm in the vas fluid is that the decompression allowed by the sperm granuloma in this region lessens the pressure in

the epididymis and thus also lessens the likelihood of a subsequent epididymal sperm granuloma resulting from rupture of the epididymal duct.

The approximately equivalent incidence of sperm antibodies in patients with and without sperm granulomas at the vasectomy site is most probably explained by the observation that if a sperm granuloma does not appear at the vasectomy site, it is more likely to appear in the epididymis; in either event sperm antibody formation is just as likely to be induced. However, in neither case does it appear that antibody formation is the major cause of the persistent infertility in these patients. Sperm antibodies may be an excellent marker of sperm extravasation in the epididymis or at the vasectomy site, but the cause of poor semen appears to be more micromechanical than autoimmune.

One could speculate that perhaps those patients who have sperm in their vas fluid at the time of vasovasostomy and who remain severely oligospermic with poor sperm motility after an accurate vasovasostomy might have partial rather than total epididymal obstruction from the same cause, that is, tubular rupture and extravasation. We have reported that most patients with oligospermia after inaccurate vasovasostomies have partial obstruction at the vasovasostomy site to account for their poor sperm count. Reoperating upon them with accurate microscopic technique resulted in normal sperm count in the majority.[1] Therefore, it is possible that the same type of partial obstruction, but in the epididymis, could be the cause of poor sperm counts in patients who have a demonstrably accurate vasovasostomy. Our data *suggest* that, although sperm autoimmunity may play an important role in indicating ductal disruption, the major cause for failure of vasovasostomy, whether due to inadequate microsurgical technique or secondary epididymal disruption, ultimately is micromechanical. Therefore, with the development of more accurate techniques for vasoepididymal anastomosis, many otherwise hopeless cases may be salvaged.

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