

ROLE OF EPIDIDYMIS IN SPERM MATURATION

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ABSTRACT—One hundred ninety patients with obstructive azoospermia caused by bilateral epididymal blockage have been followed up for four years or longer after undergoing "specific tubule" vasoepididymostomy. When anastomosis was required in the corpus epididymis, the "patency" rate was 78 percent, and the overall pregnancy rate was 56 percent. The pregnancy rate for "patent" cases was 72 percent, indicating that a high fertility rate can be obtained with sperm that have not transited the full length of corpus epididymis. By contrast, with vasoepididymostomy to the caput epididymis there was a 73 percent "patency" rate, but the overall pregnancy rate was only 31 percent. The pregnancy rate for "patent" cases was 43 percent. Sperm from the corpus epididymis have a higher rate of fertility than sperm from the caput epididymis, but sperm from proximal areas of the corpus have no less fertility than sperm from the distal corpus epididymis. The most remarkable observation is that in almost half the cases sperm that have never journeyed beyond the caput epididymis seem to be capable of causing pregnancy.

Because of advances in microsurgical techniques, it is now possible to bypass most cases of epididymal obstruction with a high incidence of technical success.¹⁻³ Whether or not sperm which have not traversed all of the epididymis are capable of fertilization in the human can be ideally studied with this clinical model. In every animal that has been studied, sperm from the caput epididymis are only capable of weak circular motion at most and are not able to fertilize.⁴ Sperm from the corpus epididymis can occasionally fertilize, but the pregnancy rate is low.

But few of these previous animal studies allowed the sperm time to mature and thereby possibly develop fertilizing capacity. Sperm were simply aspirated from specific regions of the epididymis and then promptly inseminated. In studies where the epididymis was ligated to determine if time alone could allow sperm maturation, the obstructed environment was so pathologic that no conclusions could be reached.

In 1969 Orgebin-Crist⁴ pointed out that we did not know from any of these extensive studies whether the factors governing the maturation process of sperm are intrinsic to the sperm themselves and just require time or sperm must

transit the whole length of the epididymis. It was entirely possible that aging alone might mature the sperm, and that sperm might not need to pass through all of the epididymis to develop the capacity to fertilize. But because of these animal studies, and poor results in humans using non-microsurgical techniques, it has always been assumed that epididymal blockage carries a poor prognosis.⁵⁻⁸

Material and Methods

Patient group

One hundred ninety consecutive patients with bilateral epididymal obstruction who underwent "specific tubule" vasoepididymostomy have had four or more years of follow-up. One hundred thirty-nine patients underwent bilateral vasoepididymostomy to the corpus epididymis, and 51 to the caput of the epididymis. The cause of epididymal blockage was either congenital obstruction, smallpox, chlamydial or gonorrheal epididymitis, or secondary blockage caused by pressure buildup after vasectomy (discovered at the time of vasectomy reversal). The diagnosis of obstructive azoospermia in nonvasectomy reversal cases was made by testicle biopsy demonstrating quantitatively normal

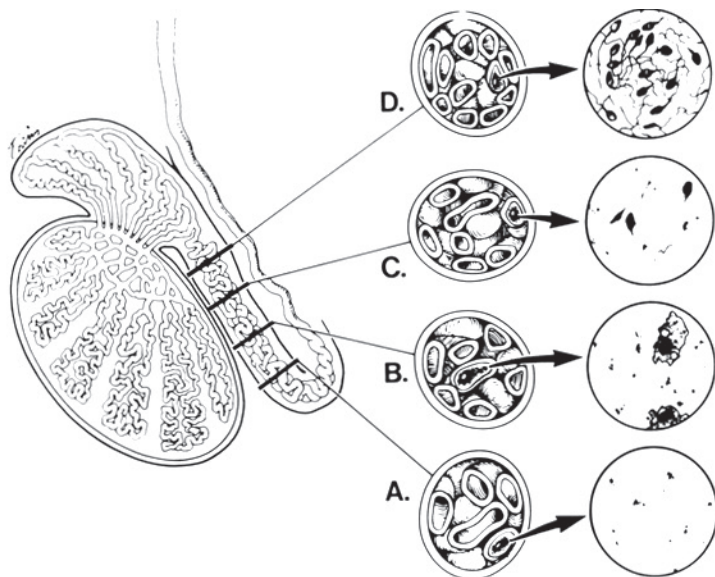


FIGURE 1. Serial sectioning of epididymis until site of proximal-most obstruction is bypassed.

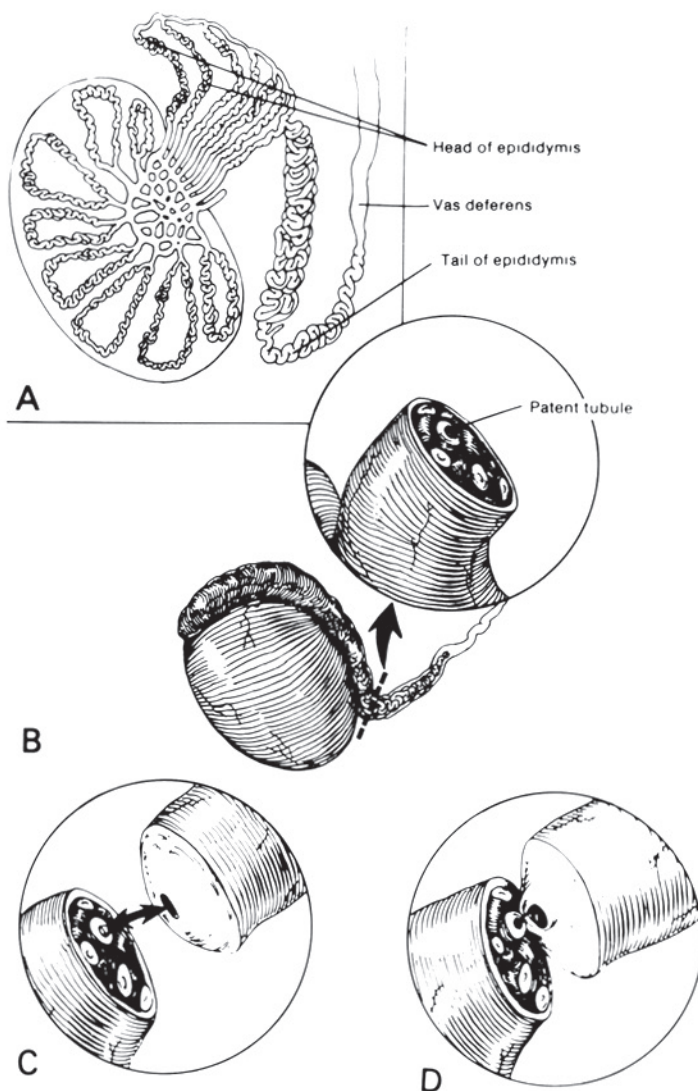


FIGURE 2. "Specific tubule" anastomosis of vas lumen to epididymis proximal to site of obstruction.

spermatogenesis, a palpable vas deferens on physical examination, normal semen volume, and azoospermia.⁹ No cases of obstructive oligospermia are included in this series.

The localization of the site of the epididymal obstruction was determined at the time of surgery by proximal serial sectioning of the epididymis until normal sperm were found in the fluid coming from the epididymal tubule. Histologic sections obtained in the process of transecting proximally up the epididymis confirmed the area of transition from no sperm in the epididymal lumen to an epididymal lumen dilated and packed with sperm.

Factors related to pregnancy and "patency"

Classic postoperative semen parameters (including numerical count, morphology, percent motility, quality of motility, velocity of motility, and direction of motility) were ascertained at intervals of three months to yearly. Many patients had as many as 10 to 15 semen analyses performed, and the mean of the semen analyses obtained after a leveling off of the rise after surgery was used in tabulation. The area of the epididymis, the degree of dilatation of the epididymal tubule, volume of fluid efflux, and the quality of sperm in the fluid proximal to the obstruction were recorded. The epididymis was serially sectioned proximally until there was a good volume of fluid efflux and a copious number of long-tailed sperm (whether motile or non-motile) in the epididymal fluid. Postoperative sperm count and directional motility were related to pregnancy rate, mean time till pregnancy, and the level of the caput or corpus epididymis (proximal, mid, or distal) at which the anastomosis was performed.

Surgical technique

All vasoepididymostomies were performed with the "specific tubule" technique we have described, which involves an end-to-end anastomosis of the inner lumen of the vas to the epididymal tubule, mucosa-to-mucosa in a leakproof fashion.¹⁻³ Virtually all of the earlier literature on vasoepididymostomy involved a longitudinal cut through the epididymal tunic and into the epididymal tubule which resulted in a random cutting of the epididymal tubule in many of its convolutions. This gave the appearance of many tubules leaking sperm. Then the vas would be sutured to that outer epididymal tunic hoping that a fistula would form. Because of the high rate of technical failure with that methodology, reliable data on the fertility of

TABLE I. *Lack of relation of postoperative sperm count to pregnancy rate*

Sperm Count (Per cc)	Pregnant (%)	Not Pregnant
Azoospermic	0 (0)	30
0 to 1×10^6	2 (67)	1
1 to 5×10^6	5 (63)	3
5 to 10×10^6	11 (65)	6
10 to 20×10^6	6 (50)	6
20 to 40×10^6	17 (81)	4
40×10^6	32 (74)	11
Unknown	5	0
TOTALS	78 (56)	61

sperm from the epididymis have been difficult to obtain.

With the "specific tubule" technique used in this series, the epididymis was transected proximally until the point was reached where many sperm were found (Figs. 1 and 2). Fluid at every level was examined under a phase contrast microscope in the operating room for the presence and quality of sperm. The anastomosis of the vas to the epididymis was performed at the transition point from no sperm to the point where there was an abundant amount of sperm in the fluid coming from the epididymal tubule.

A 10-0 monofilament nylon suture is first placed from outside to inside the tubule which is leaking the sperm fluid. The first stitch is then completed with an inside-to-outside stitch in the vas mucosa. Usually four to five 10-0 nylon interrupted sutures complete the leakproof mucosal anastomosis, and then the outer muscularis of the vas is separately sutured to the outer epididymal tunic with 9-0 nylon interrupted sutures.

Postoperatively, the patient is allowed to go home a day later, but is restricted from most activity (other than at home) for the first week, and is allowed no heavy exertion or exercise for four weeks. Because most patients come from out of town, semen analyses were monitored through local laboratories at varying intervals.

Results

Corpus epididymis

Of the 139 patients with four years' follow-up undergoing vasoepididymostomy to the corpus epididymis, 109 (78%) had sperm in the ejaculate postoperatively (Table I). Seventy eight (56%) achieved a successful intrauterine preg-

TABLE II. *Relation of percent directional sperm motility and level of corpus epididymis to pregnancy rate*

Relationship	Pregnant (%)	Not Pregnant
Directional motility (%)		
0-19	13 (48)	14
20-39	18 (75)	6
40-60	19 (76)	6
60	22 (81)	5
Level of corpus epididymis		
Proximal corpus	7 (88)	1
Mid corpus	17 (74)	6
Distal corpus	54 (71)	22

nancy with their wives. Thus, of those 109 patients who had technically "patent" results, 72 percent were able to achieve a normal pregnancy. There was no correlation between the postoperative numerical sperm count and the pregnancy rate, except to say that no azoospermic patient impregnated his wife. But as long as there was a "patent" result, the numerical count was not significantly predictive of the chances for the wife getting pregnant within four years.

There was, however, a relationship between the occurrence of pregnancy and the postoperative sperm motility in "patent" cases (Table II). When less than 20 percent of the sperm exhibited forward motility, the pregnancy rate in "patent" cases was only 48 percent. However, when over 20 percent of the sperm exhibited forward motility, 78 percent impregnated their wives. Increasing percentage of progressive motility beyond 20 percent had no greater effect in increasing the likelihood of pregnancy. More surprisingly the level (proximal, mid, or distal) of the anastomosis at the corpus epididymis had no effect on the pregnancy rate, and it also had no effect on the percentage of directional motility (Table II).

The numerical sperm count was not related to the level of the corpus epididymis at which the anastomosis was performed, nor was technical success of the surgery ("patency") related to the level of the blockage. This is quite in contrast to caput epididymis cases where more proximal anastomoses had a poorer technical success rate.

The mean time till pregnancy was not affected by the numerical postoperative sperm count in "patent" cases. For sperm counts less than 5 million sperm/cc, the mean time till pregnancy was 6.7 months, and with counts

greater than 40 million sperm/cc, the mean time till pregnancy was 6.4 months.

Caput epididymis

With the small number of 51 cases involving the caput epididymis, the "patency" rate was 73 percent; the pregnancy rate overall was only 31 percent; and thus the pregnancy rate with technically "patent" cases was 43 percent (16 of 37). Thus, sperm from anywhere along the corpus epididymis were more likely to be fertile than sperm from the caput epididymis. Furthermore, overall higher sperm counts and motility were obtained with anastomosis at the corpus epididymis than the caput epididymis reflecting the greater technical difficulty with caput epididymis anastomosis. The remarkable finding, however, was that among those with patent results to the caput epididymis (where sperm were not able to transit through the corpus or tail at all) almost half were able to get their wives pregnant.

Comment

The fact that when a technically successful anastomosis to anywhere along the corpus epididymis is achieved, almost 72 percent of the wives get pregnant with a mean time to conception of six months, clarifies the issue that *sperm do not necessarily have to traverse the entire corpus or cauda epididymis in the human to achieve fertilizing capacity*. The issue of why such good pregnancy rates were achieved needs to be addressed. First, it is clear that with caput epididymis anastomosis, the pregnancy rates are considerably lower than with corpus epididymis anastomosis. Thus, there is still some benefit for sperm to have traversed at least the caput into the corpus epididymis. But the remarkable finding is that there is no further improvement either in motility or pregnancy rate for anastomoses that are more distal in the corpus. Anywhere along the corpus, the chances for pregnancy are equivalent.

The lower pregnancy rates in previous clinical series most probably relate to a number of factors. First, it is apparent that anastomosis to the caput epididymis carries a lower success rate, and many previous "macro" approaches to vasoepididymostomy were automatically performed in all patients to the caput.^{5,6} Second, most previous clinical series have not only been "macro" approaches rather than microsurgical, but they made no attempt to obtain a specific tubule anastomosis. Rather a fistula was

created, which may have led to lower "patency" rates, and poorer sperm motility in the cases that were "patent."^{7,8} It is fascinating that the numerical sperm count had no impact on pregnancy rate, but sperm motility did. This goes along with many clinical studies which demonstrate low sperm counts in a high percentage of normal fertile males.

In 1969 Orgebin-Crist⁴ asked the key question of whether the factors governing the maturation process of sperm are intrinsic to the sperm or do they reside in the epididymis. Many experiments were performed to ligate various regions of the epididymis to see if aging alone matures the sperm, or if sperm need to pass through specific regions of the epididymis to mature. These epididymal ligation experiments all caused dilatation and epithelial disruption which could hurt the maturation of caput sperm so retained. These experiments could not allow for the deleterious effects of the ligation experiment on the activity of the duct epithelium.^{4,10-15}

Thus in 1969 Orgebin-Crist still posed the question of whether or not sperm that have not progressed completely through the epididymis are capable of fertilization.⁴ Orgebin-Crist suggested the possibility that sperm could mature in the vas deferens without the need of traversing the full length of the epididymis. A vasoepididymostomy model, in which sperm had never traversed the full length of epididymis, might possibly allow sperm to mature on their own in the vas deferens. Later Bedford¹⁴ speculated that although the potential of the vas deferens for sperm maturation is unknown, it is possible that the corpus and cauda regions of the epididymis are not required for maturation of human spermatozoa.

The fact that sperm which could not have travelled through the entire length of corpus or cauda epididymis were capable of fertilization, indicates that a full journey through the epididymis is not required for maturation of sperm sufficient to allow pregnancy. Furthermore, the fact that pregnancy occurred in almost half of the patent cases to the caput indicates that transit beyond the head of the epididymis is not an absolute requirement for sperm to attain fertilizing capacity. However, it is apparent that these sperm do have limited fertilizing capacity since the pregnancy rate for caput sperm is still lower than that following vasovasostomy or vasoepididymostomy to the corpus epididymis.^{2,3,16}

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