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Results of microsurgical vasoepididymostomy: role of epididymis in sperm maturation

Sherman J.Silber

St Luke's Hospital West, 224 S. Woods Mill Rd, Suite 730, St Louis, MO 63017, USA

One-hundred-and-ninety patients with obstructive azoospermia caused by bilateral epididymal blockage have been followed for ≥4 years after undergoing 'specific tubule' vasoepididymostomy. When anastomosis was required in the corpus epididymidis, the 'patency' rate was 78% and the overall pregnancy rate was 56%. The pregnancy rate for 'patent' cases was 72%, indicating that a high fertility rate can be obtained with spermatozoa that have not passed through the full length of corpus epididymidis. By contrast, with vasoepididymostomy to the caput epididymidis there was a 73% 'patency' rate, but the overall pregnancy rate was only 31%. The pregnancy rate for 'patent' cases was 43%. Spermatozoa from the corpus epididymidis have a higher rate of fertility than spermatozoa from the caput epididymidis, but spermatozoa from proximal areas of the corpus have no less fertility than spermatozoa from the distal corpus epididymidis. The most remarkable observation is that in almost half the cases, spermatozoa which have never journeyed beyond the caput epididymidis seem to be capable of causing pregnancy.

Key words: epididymis/male infertility/spermatozoa/vasoepididymostomy

Introduction

Because of advances in microsurgical techniques, it is now possible to bypass most cases of epididymal obstruction with a high incidence of technical success (Silber, 1978, 1984, 1986). The fertilizing capacity of spermatozoa which have not traversed all sections of the epididymis can ideally be studied with this human clinical model. In every animal that has been studied, spermatozoa from the caput epididymidis are only capable of weak circular motion at most and are not able to fertilize (Orgebin-Crist, 1969). Spermatozoa from the corpus epididymidis can occasionally fertilize but the pregnancy rate is low.

But few of these previous animal studies allowed the spermatozoa time to mature and thereby possibly develop the capacity for fertilization. Spermatozoa were simply aspirated from specific regions of the epididymis and then promptly inseminated. In most studies where the epididymis was ligated to determine if time alone could allow spermatozoa to mature, the obstructed environment was so pathological that no firm conclusions could be reached (Gaddum and Glover, 1965; Paufler and Foote, 1968; Glover, 1969).

In 1969, Orgebin-Crist pointed out that we still did not know with certainty from any of these animal studies whether the factors governing the maturation process of spermatozoa are intrinsic to the spermatozoa themselves and just require time, or whether spermatozoa must pass through most of the epididymis in order to mature. It was entirely possible that aging alone might mature the spermatozoa and that spermatozoa might not need to pass through all of the epididymis in order to develop the capacity to fertilize. Yet because of the animal studies alluded to, and poor results in humans using non-microsurgical techiques, it has always been assumed that epididymal blockage carries a poor prognosis (Hanley, 1955; Hotchkiss, 1970; Schoysman and Drouart, 1972; Amelar and Dubin, 1975).

As long ago as 1931, however, Young's experiments in guinea pigs with ligation at various levels of the epididymis indicated to the contrary: 'that the time consumed by spermatozoa in passing through the epididymis is necessary for a completion of their development, that the changes undergone during this period represent a continuation of changes which start while the spermatozoa are still attached to the germinal epithelium, and are not conditioned by some specific epididymal secretion (Young, 1931).' In fact he observed the same 'inversion' of regions of sperm motility and non-motility in the obstructed epididymis that our group has noted in clinical obstructive azoospermia. The more distal regions have the poorest motility and the more proximal regions have the best motility. Young concluded that in an obstructed epididymis the more distal sperm are senescent, while the more proximal sperm have had time to mature, despite having not traversed the epididymis.

Clinical experience with specific tubule vasoepididymostomy in our group, supports Young's original thesis.

Materials and methods

Patient group

One-hundred-and-ninety patients with bilateral epididymal obstruction who underwent 'specific tubule' vasoepididymostomy have had four or more years of follow-up. One-hundred-and-thiry-nine patients underwent bilateral vasoepididymostomy to the corpus epididymidis and 51 to the caput of the epididymis. In cases where one side was corpus and the other side caput the patient was categorized as corpus. The cause of epididymal blockage was either congenital obstruction, smallpox, chlamydial or gonorrhoeal epididymitis, or secondary blockage caused by pressure build-up after vasectomy (discovered at the time of

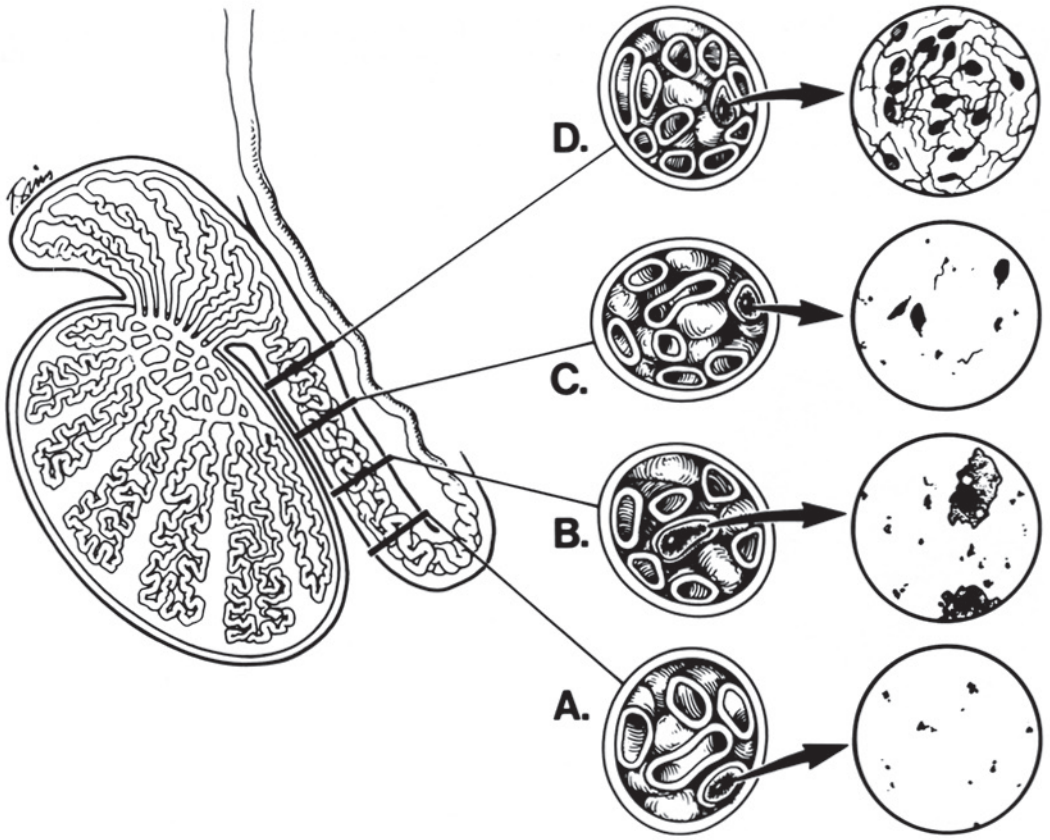

Fig. 1. Serial sectioning of epididymis until the site of most proximal obstruction is bypassed.

vasectomy reversal). The diagnosis of obstructive azoospermia in non-vasectomy reversal cases was made by testicular biopsy demonstrating quantitatively normal spermatogenesis, a palpable vas deferens on physical examination, normal semen volume and azoospermia (Silber and Rodriguez-Rigau, 1981). No cases of obstructive oligospermia are included in this series.

The location of the site of epididymal obstruction was determined at the time of surgery by proximal serial sectioning of the epididymis until normal spermatozoa were found in the fluid coming from the epididymal tubule (Figure 1). Histological sections obtained in the process of transecting proximally up the epididymis confirmed the area of transition from no spermatozoa in the epididymal lumen to an epididymal lumen dilated and packed with spermatozoa.

Factors related to pregnancy and 'patency'

Classical post-operative semen parameters (including numerical count, morphology, percentage motility, quality of motility, velocity of motility and direction of motility) were ascertained at intervals of 3 months, if possible, to yearly. Many patients had as many as 10–15 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 spermatozoa 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 spermatozoa (whether motile or non-motile) in the epididymal fluid. Post-operative counts of spermatozoa and directional motility were related to pregnancy rate, mean time until pregnancy and the level of the caput or corpus epididymidis (proximal, mid or distal) at which the anastomosis was performed.

Surgical technique

All vasoepididymostomies were performed with the 'specific tubule' technique 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 (Silber, 1978, 1984, 1986) (Figure 2). 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, which gave the appearance of many tubules leaking spermatozoa. The vas was 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 spermatozoa from the epididymis in the past has been difficult to obtain.

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

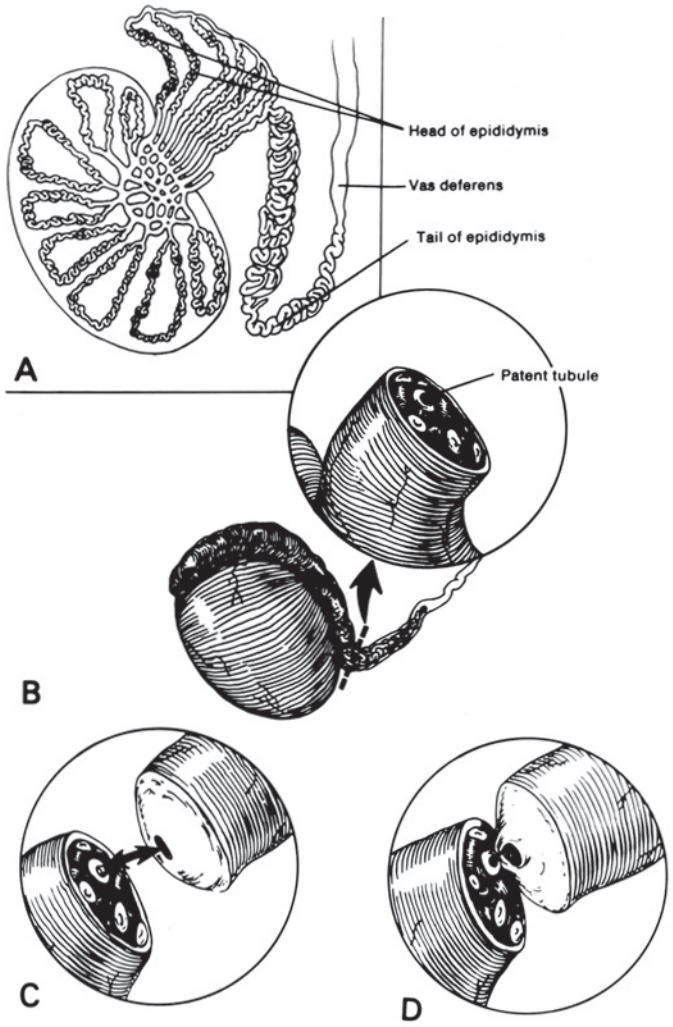

Fig. 2. 'Specific tubule' anastomosis of vas lumen to the epididymis proximal to site of obstruction.

A 10-0 monofilament nylon suture is first placed from outside to inside the tubule which is leaking the fluid containing spermatozoa. 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 end-to-end mucosal anastomosis, and then the outer muscularis of the vas is separately sutured to the outer epididymal tunic with 9-0 nylon interrupted sutures.

Post-operatively 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 4 weeks. Because most patients come from out of town, semen analyses are monitored through local laboratories at varying intervals.

Results

Corpus epididymidis

Of the 139 patients with 4 years follow up undergoing vasoepididymostomy to the corpus epididymidis, 109 had spermatozoa in the ejaculate post-operatively (78%) (Table I).

Table I. Corpus epididymidis lack of relation of post-operative spermatozoa count to pregnancy rate

Spermatozoa count/ml	Pregnant	Not pregnant
Azoospermic	0 (0%)	30
$0-1 \times 10^6$	2 (67%)	1
$1-5 \times 10^6$	5 (63%)	3
$5-10 \times 10^6$	11 (65%)	6
$10-20 \times 10^6$	6 (50%)	6
$10-40 \times 10^6$	17 (81%)	4
40×10^6	32 (74%)	11
Unknown	5	0
Total	78 (56%)	61

Summary: Patency rate, 78%; overall pregnancy rate, 56%; pregnancy rate in 'patent' cases, 72%.

Table II. Corpus epididymidis: relation of % directional spermatozoa motility to pregnancy rate in 'patent' cases

% Directional motility	Pregnant	Not pregnant
0–19	13 (48%)	14
20–39	18 (75%)	6
40–60	19 (76%)	6
>60	22 (81%)	5

Table III. Corpus epididymidis: lack of relation of age of wife to pregnancy rate in 'patent' cases

Age of wife (years)	Pregnant	Not pregnant
<25	14 (78%)	4
25–29	30 (68%)	14
30–35	30 (75%)	10
>35	4 (67%)	2

Seventy eight achieved a successful intra-uterine pregnancy with their wife (56%). Thus, of those 109 patients who had technically 'patent' results, 72% were able to achieve a normal pregnancy. There was no correlation between the post-operative numerical spermatozoa count and the pregnancy rate, except to say that no azoospermic patient impregnated his wife. But in the event of a 'patent' result, the numerical count was not significantly predictive of the chances for the wife to become pregnant within 4 years.

There was, however, a relationship between the occurrence of pregnancy and the post-operative motility of spermatozoa (see Table II). When <20% of the spermatozoa exhibited forward motility, the pregnancy rate in 'patent' cases was only 48%. However, when >20% of the spermatozoa exhibited forward motility, 78% impregnated their wives. Increasing percentages of progressive motility >20% had no greater effect in increasing the likelihood of pregnancy.

Unlike the caput epididymidis cases, the wife's age had no effect on the pregnancy rate (see Table III). More surprisingly the level (proximal, mid or distal) of the anastomosis at the corpus epididymidis had no effect on the pregnancy rate (Table IV) and it also had no effect on the percentage of directional motility.

The numerical spermatozoa count was not related to the level

Table IV. Corpus epididymidis: lack of relation of level of corpus epididymal anastomosis to pregnancy rate in 'patent' cases

	Pregnant	Not pregnant
Proximal corpus	7 (88%)	1
Mid corpus	17 (74%)	6
Distal corpus	54 (71%)	22

Table V. Corpus epididymidis: percent pregnant at varying intervals post-operatively in relation to sperm count in 'patent' cases

Sperm count ($\times 10^6$/ml)	Months				
	6	12	18	24	24
1– 5	56%	22%	22%		
5–10	63%	25%		13%	
10–20	17%	49%		17%	17%
20–40	44%	28%	11%	11%	6%
40	34%	28%	6%	9%	22%
100%	41%	29%	8%	10%	12%

Table VI. Corpus epididymidis: lack of relation of sperm count to mean time until pregnancy in 'patent' cases

Sperm count ($\times 10^6$/ml)	Mean time until pregnancy (months)
1– 5	6.7
5–10	6.0
10–20	10.5
20–40	4.3
40	6.4

Table VII. Head of epididymis: relation of pregnancy to sperm motility in 37 cases with patency

% sperm motility	Pregnancy rate (%)	Pregnant	Not pregnant
0–20	15	2 (13%)	11 (52%)
>20	58	14 (87%)	10 (48%)
Totals	43	16 (100%)	21 (100%)

Table VIII. Head of epididymis: relation of age of wife to pregnancy rate in cases with patency

Age of wife (years)	Pregnancy rate(%)	Pregnant	Not pregnant
25–30	67	12 (75%)	6 (29%)
>30	21	4 (25%)	15 (71%)
Totals	43	16 (100%)	21 (100%)

of the corpus epididymidis at which the anastomosis was performed, nor was technical success of the surgery ('patency') related to the level of the blockage. This is in contrast to caput epididymidis cases where more proximal anastomoses had a poorer technical success rate.

The mean time until pregnancy was not affected by the numerical post-operative spermatozoa count in 'patent' cases (Tables V and VI). For spermatozoa concentrations of $<5 \times 10^6$/ml, the mean time until pregnancy was 6.7 months, and with spermatozoa concentrations $>40 \times 10^6$/ml, the mean time until

Table IX. Head of epididymidis: lack of relation of level of successful vasoepididymostomy to previous failure

	Pregnant	Not pregnant
Repeat after previous failure	6 (38%)	10
Virgin case	10 (29%)	25

Table X. Head of epididymis: relation of post-operative 'patency' to area of anastomosis at head of epididymis

	Proximal caput	Mid caput or mixed	Distal caput
'Patent'	9 (53%)	10 (71%)	17 (89%)
Non-patent (azoospermia)	8 (47%)	4 (29%)	2 (11%)

pregnancy was 6.4 months. Of those patients who did eventually impregnate their wives, 70% did so in the first year and 88% by the second year post-operatively. This appears similar to the curve of a normal population (Vessey *et al.*, 1976).

Caput epididymidis

With the smaller number of 51 cases involving the caput epididymidis the 'patency' rate was 73%, the pregnancy rate overall was only 31% and thus, the pregnancy rate with technically 'patent' cases was 43% (16 out of 37). Thus, spermatozoa from anywhere along the corpus epididymidis were more likely to be fertile than spermatozoa from the caput epididymidis. Furthermore overall higher spermatozoa counts and motility were obtained with anastomosis at the corpus epididymidis than the caput epididymidis, reflecting the greater technical difficulty with caput epididymidis anastomosis. The remarkable finding, however, was that among those with patent results to the caput epididymidis, where spermatozoa were not able to transit through the corpus or tail at all, almost half succeeded in initiating a pregnancy.

Half of the pregnancies occurred after 2 years had passed since the surgery. The other half occurred within the first 6 months, indicating a bimodal distribution of two groups of patients. One group seemed to recover their fertility slowly after a long period of time and the other regained their fertility shortly after surgery. As with corpus epididymidis there was no correlation between the post-operative numerical sperm count and the pregnancy rate, except to say that no azoospermic patient impregnated his wife. But in the event of a 'patent' result, the numerical count was not significantly predictive of the chances for the wife to become pregnant within 4 years. In fact, 31% of the patients whose wives became pregnant had a concentration of $<5 \times 10^6$/ml.

There was, however, a close relationship between the occurrence of pregnancy and the post-operative sperm motility (Table VII). When <20% of the sperm exhibited forward motility, the pregnancy rate was only 15%. However, when >20% of the sperm exhibited forward motility, 58% impregnated their wives. Very few patients had >50% progressive motility and the 'cutoff', in terms of motility having a significant effect on pregnancy, was quite clearly at 20%.

Since most of the patients were referred from out of town, it was difficult to obtain reliable studies on the wife's relative

fertility. But it is striking how well the wife's age correlated with the pregnancy rate in contrast to corpus epididymidis cases (Table VIII). When the wife was <30 years old, the pregnancy rate in cases with spermatozoa 'patency' was 67%. When the wife was >30 years of age, the pregnancy rate was only 21%. The apparent difficulty of the operation did not correlate well with the pregnancy rate. In patients who had a previous failure at vasoepididymostomy, who were referred here for a second attempt, the pregnancy rate was 38%, whereas with cases who had not undergone any previous attempt at vasoepididymostomy, the pregnancy rate was 29% (Table IX).

The numerical sperm count was related to how far proximal in the head of the epididymis the blockage was found. In cases of distal caput blockage, the numerical sperm count post-operatively was higher than in cases of proximal caput blockage. Furthermore, azoospermia following an attempt at vasoepididymostomy was much more likely to occur in cases of proximal caput obstruction (Table X). This is consistent with the view that more proximal anastomoses, necessitated by more proximal obstructions, created technical difficulties that led to a poorer patency rate.

Discussion

The fact that when a technically successful anastomosis to anywhere along the corpus epididymidis is achieved, almost 72% of the wives became pregnant, with a mean time to conception of 6 months, clarifies the issue that spermatozoa do not necessarily have to traverse the entire corpus or cauda epididymidis in the human to achieve fertilizing capacity. The issue of why such good pregnancy rates were achieved needs to be addressed. Firstly, it is clear that with caput epididymidis anastomosis, the pregnancy rates are considerably lower than with corpus epididymidis anastomosis. Thus, there is still some benefit for sperm to have traversed at least the caput into the corpus epididymidis. 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. Considering spermatozoa from 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. In this study a specific tubule anastomosis was performed, rather than creation of a fistula which could lead to lower 'patency' rates and even poorer motility of spermatozoa in the cases that were 'patent' (Schoysman and Drouart, 1972; Amelar and Dubin, 1975). The anastomosis in this series was performed at the most distal site that was just proximal to the site of obstruction, thus allowing the longest possible epididymal length. Newer microsurgical techniques have thus clearly improved the quality of spermatozoa in the ejaculate post-operatively.

It is fascinating that the numerical spermatozoa count had no impact on pregnancy rate, in contrast with motility of spermatozoa. This is in agreement with many clinical studies which demonstrate low spermatozoa counts in a high percentage of normal fertile males (Zukerman *et al.*, 1977; Sherins, 1986; Sokol and Sparkes, 1987; S.J.Silber, in preparation).

If the patient's oligozoospermia is simply a reflection of his low testicular sperm production, fertility may not be poor. But if the oligozoopsermia is caused by residual epididymal pathology, or partial obstruction, poor motility would result and then fertility may be compromised.

Orgebin-Crist (1969) questioned whether factors governing the maturation process of spermatozoa are intrinsic to the spermatozoa, or whether they reside in the epididymis. Epididymal ligation experiments have not always been clear in answering this question because they cause dilatation and epithelial disruption which negatively affect the motility of spermatozoa so retained (Young, 1931; Gaddum and Glover, 1965; Orgebin-Crist, 1967; Paufler and Foote, 1968; Gaddum, 1969; Glover, 1969). Yet Young was able to draw a tentative conclusion in 1931 that sperm maturation may be completely independent of epididymal transport. Others have made similar speculations regarding the corpus and cauda epididymidis (Bedford, 1966; Schoysman and Bedford, 1986).

A vasoepididymostomy model such as the one used here, in which spermatozoa cannot traverse the full length of epididymis, would allow maturation to occur with time only in the vas deferens and help clarify this issue. The fact that spermatozoa, which could not have travelled through any portion of the corpus or cauda epididymidis, were capable of fertilization indicates that a full journey through the epididymis is certainly not required for maturation of spermatozoa sufficient to allow pregnancy. 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 spermatozoa to attain fertilizing capacity.

It should be emphasized that none of these patients underwent any special treatments such as IVF or GIFT and these pregnancies all occurred simply with natural intercourse. In the next few years it may be discovered whether, with in-vitro techniques, >43% of these patients with spermatozoa from the caput epididymidis will or will not be able to accomplish fertilization.

Recent clinical cases have demonstrated that it is even possible, in some circumstances, for spermatozoa which have never traversed any length of epididymis to fertilize the human egg. In two cases reported of vasa efferentia to vas deferens anastomosis, the post-operative ejaculate contained normally motile sperm and the patients' wives became pregnant (Silber, 1988a). In addition, pregnancy from the aspiration of proximal caput epididymal spermatozoa combined with IVF and ZIFT (zygote intra-Fallopian transfer) in cases of irreparable obstruction gives further evidence that transit through the epididymis is not a mandatory requirement for fertilization (Silber *et al.*, 1987; Silber, 1988b). Finally, newer studies of epididymal sperm transport in the human indicate that the human epididymis is not a storage area and indeed spermatozoa pass through the entire human epididymis very quickly, in a mere 2 days; not 11 days as was previously thought (Johnson and Varner, 1988). Thus it is possible that, in the human, the epididymis may not be as essential to spermatozoa development and fertility as it appears to be in most animals.

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