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Pregnancy after vasovasostomy for vasectomy reversal: a study of factors affecting long-term return of fertility in 282 patients followed for 10 years

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The aim of this study was to determine the eventual fertility of those patients following vasectomy reversal who have no pressure-induced secondary epididymal blockage. These patients underwent simple vasovasostomy because at the time of the reversal surgery there were sperm present in large numbers in the vas fluid. It was possible to obtain long-term follow-up on 326 early patients who underwent vasectomy reversal 8–10 years ago. Two hundred and eighty-two of those patients had sperm in the vas fluid. These patients were studied for pregnancy rate and post-operative semen parameters in relation to presence or absence of sperm in the vas fluid at the time of vasectomy reversal, duration of time since vasectomy, pre-operative serum antisperm antibody titers, the influence of varicocoele and quantitative evaluation of testicular biopsy. All of the 44 patients with no sperm in the vas fluid remained azoospermic following vasovasostomy. Of the 282 patients with sperm in the vas fluid, 228 (81%) eventually impregnated their wives. Twenty-four patients with sperm in the vas fluid (9%) were azoospermic and did not impregnate their wives. Of the 258 patients who had sperm patency, the pregnancy rate was 88%. The number of mature spermatids per tubule in the testis correlated closely with the post-operative sperm count in patent cases. Quantitative evaluation of the testicular biopsy revealed normal spermatogenesis, even in patients with azoospermia or severe oligospermia post-operatively. Technical failures were due to blockage either at the vasovasostomy site, or epididymal blockage unrecognized at the time of vasovasostomy. Sperm count had a minimal impact on the likelihood of pregnancy so long as there was patency, and there was no discrepancy between sperm count and actual testicular sperm production as determined by testicular biopsy. Pregancy was not related to the presence or absence of a varicocoele, pre-operative serum sperm antibody levels, or testicular biopsy findings.

Key words: vasovasostomy/vasectomy reversal/fertility

Introduction

Vasectomy is the most popular method of birth control in the world today (Liskin *et al.*, 1983). More than half a million vasectomies are performed in the United States each year. Because of the fear of child death in the developing world, changing views about family life in the Western world and the increasing prevalence of divorce and remarriage, there are now a large number of men requesting reversal of vasectomy. For many years the pregnancy rate after surgical re-anastomosis of the vas had been very low and a variety of explanations had been offered for the relatively poor success in reversing vasectomy (O'Connor, 1948; Dorsey, 1953; Phadke and Phadke, 1967; Derrick *et al.*, 1973; Middleton and Henderson, 1978). With the advent of microsurgical techniques, pregnancy rates improved considerably, suggesting that purely micro-mechanical factors were associated with the low success rates, but long-term follow-up on large numbers of patients was not available and the matter remains somewhat controversial (Silber, 1977a, 1978b,c). Theories for the consistently poor results with vasectomy reversal have included development of sperm antibodies, damage to the deferential nerve and testicular damage (Ansbacher, 1971; Linnet and Hgort, 1977; Pabst *et al.*, 1979; Sullivan and Howe, 1977; Middleton and Urry, 1980; Brickel *et al.*, 1982; Fowler and Marino, 1983; Jarrow *et al.*, 1985). Yet some investigators questioned any correlation between sperm antibodies in the serum and subsequent fertility after vasovasostomy (Thomas *et al.*, 1981) and the effect, if any, of vasectomy on the testis in humans and animals has also been very controversial (Silber, 1978c). Segregating the various studies by species has not cleared up the confusion. If any testicular damage occurs, the mechanisms generally agreed upon would be either autoimmune, or pressure related (Paufler and Foote, 1969; Alexander, 1973; Bedford, 1976; Bigazzi *et al.*, 1976; Silber, 1978c).

The pressure increase subsequent to vasectomy has been well established, as well as the effect of this pressure on epididymal dilatation, perforation and sperm inspissation in the epididymis, causing secondary epididymal obstruction (Silber, 1978a, 1979, 1984). It was found that the incidence of this confounding secondary epididymal blockage increased with the duration of time following vasectomy and never occurred if there was a sperm granuloma at the vasectomy site (Silber, 1977a,b, 1978c). Despite the dismal finding of no sperm in the vas fluid in patients with secondary epididymal blockage, the testicular biopsy always appeared normal (Silber, 1979; Silber and Rodriguez-Rigau, 1981). This apparent effect of pressure increase after vasectomy led to the suggestion that the testicular end of the vas not be sealed at the time of vasectomy, so as to lessen the pressure build-up and possibly increase the ease of reversibility (notwithstanding the potentially damaging immunological consequences) (Alexander and Schmidt, 1977; Silber, 1977b; Shapiro and Silber, 1979). The present study was set up to determine what the fertility rate would be for this favorable group of patients who had no epididymal damage as evidenced by sperm being present in the vas fluid.

A large group of patients who had undergone microsurgical vasovasostomy with no evidence of pressure-induced secondary epididymal blockage has been carefully studied for 9–10 years. An attempt was made to relate in these patients the presence or absence of varicocoele, post-operative semen analyses, pre-operative serum sperm antibody titers and quantitative evaluation of testicular biopsy to the chance for pregnancy. This study reviews the results in patients who were thought to have no epididymal blockage. Patients with no sperm in the vas fluid, all of whom exhibited secondary epididymal obstruction, will be the subject of a subsequent paper.

Materials and methods

Three hundred and twenty-six men, who had previously been vasectomized, underwent vasectomy reversal and received extensive long-term follow-up. In 44 men no sperm was found in the vas fluid. All such patients have been found to be azoospermic after vasovasostomy, and require a vasoepididymostomy instead. In the remaining 282 cases, there was sperm in the vas fluid and a vasovasostomy was performed. The vasovasostomy involved a meticulous, two-layer microsurgical technique performed by the same surgeon, with accurate mucosa-to-mucosa approximation (Silber, 1977a). Almost all the patients had proven prior fertility as evidenced by previous fatherhood. All patients were followed up for 9–10 years.

Standard semen analyses were obtained at intervals of every month to twice a year. Forty-two of the patients (14.8%) had a varicocoele on the left side demonstrable on physical examination. None of the patients with varicocoele underwent varicocoelectomy. A random group of 98 patients had blood drawn 1 day prior to surgery for serum levels of sperm agglutinating antibody (Kibrick method) and immobilizing sperm antibody (Isojima method). A flaw in the study is that semen levels of antibodies were not determined, only serum levels.

In a random group of 22 of the patients, quantitative testicular biopsy was performed at the time of vasovasostomy (Steinberger and Tijoe, 1968; Zuckerman *et al.*, 1978; Silber and Rodriguez-Rigau, 1981). Seventeen of the patients undergoing testicular biopsy at the time of vasovasostomy had sperm patency post-operatively and five did not. The specimen was fixed in Zenker's solution and cut into 4-μm sections. A total of at least 20 circular-shaped seminiferous tubules was analyzed in each patient. The number of mature spermatids (Sc + Sd) and pachytene spermatocytes was counted in all of the tubules and divided by the number of tubules, to obtain the count of mature spermatids and pachytene spermatocytes per tubule. The clinical sperm count (average of all counts available) after 1 year of follow-up was then compared in each patient to the predicted sperm count, based on the graph previously developed (Figure 1), relating the number of mature spermatids per tubule to sperm density (Silber and Rodriguez-Rigau, 1981).

Results

The overall, long-term pregnancy rate and sperm patency rate is summarized in Table I. The overall pregnancy rate in this selected group of cases with sperm in the vas fluid was 81%.

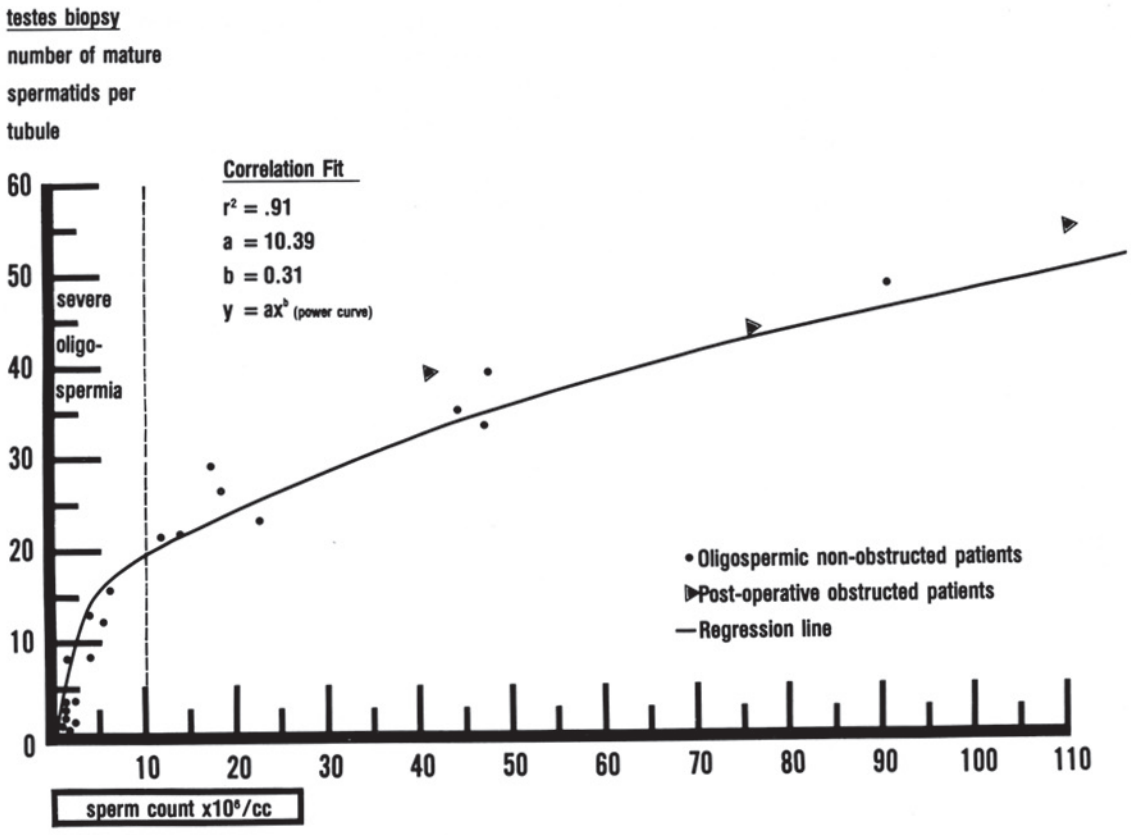

Fig. 1. Quantitative testicular biopsy and sperm count.

None of the azoospermic patients succeeded in impregnating their wives. If azoospermic patients are excluded, 88.4% of patients with sperm patency post-operatively eventually impregnated their wives. This compares to Vessey's expected pregnancy rate of 96% for previously fertile couples discontinuing contraception (Vessey *et al.*, 1978).

The frequency distribution of semen parameters post-operatively in men who did and did not impregnate their wives is summarized in Tables II and III. There was remarkably little difference in pregnancy rate among men with low or high sperm counts. Similar findings were seen with sperm motility of >20%. However, the pregnancy rate was somewhat lower with motility of <20%. Above those lower limits, the pregnancy rate was not seriously affected by low semen parameters. These post-operative semen parameters in patent cases were not very different from previously reported pre-vasectomy semen parameters (Zuckerman *et al.*, 1977).

Table I. Overall long-term pregnancy rates in patients undergoing vasovasostomy 10 years follow-up (sperm seen in vas fluid)

	Combined 1975 and 1976–1977 series	Original 1975 series
Total patients	282 (100%)	42 (100%)
Total pregnant	228 (81%)	32 (76%)
Azoospermic	24 (9%)	5 (12%)

Table II. Pregnancy rate according to distribution of motile sperm count in men with sperm patency following vasovasostomy (10-year follow-up)

Total motile sperm count (per ejaculate)	Total patients	Pregnant	Not pregnant
0–10 000 000	32 (12%)	25 (78%)	7
10–20 000 000	31 (12%)	27 (87%)	4
20–40 000 000	32 (12%)	30 (93%)	2
40–80 000 000	79 (31%)	68 (86%)	11
80 000 000	84 (33%)	78 (92%)	6
Totals	258 (100%)	228 (88%)	30

Table III. Pregnancy rate according to percentage sperm motility in men with sperm patency following vasovasostomy (10-year follow-up)

Motility	Total patients	Pregnant	Not pregnant
0–20	24	18 (75%)	6
20–40	70	66 (94%)	4
40–60	82	71 (86%)	11
60–80	62	55 (88%)	7
80	20	18 (90%)	2
Totals	258 (100%)	228 (88%)	30 (100%)

Table IV. Lack of effect of varicocoele (not operated on) on pregnancy rate following vasovasostomy

	No. of patients	Patients with varicocoele	Patients without varicocoele
Pregnant	228 (80.9%)	33 (78.5%)	195 (81.2%)
Not pregnant	54 (19.1%)	9 (21.4%)	45 (18.8%)
Totals	282 (100%)	42 (14.8%)	240 (85.2%)

As summarized in Table IV, a left-sided varicocoele was clinically apparent in 42 of the 282 patients (14.8%). Varicocoeles were not operated on, and yet the pregnancy rate was not significantly different in patients with varicocoele as opposed to patients without varicocoele. Table V summarizes the relationship of post-operative serum antisperm antibody titers to the pregnancy rate after vasovasostomy. Similarly to varicocoele, the presence of high immobilizing titers or agglutinating titers had no influence on the pregnancy rate.

The results of quantitative analyses of testicular biopsies are summarized in Tables VI and VII. In the 16 patients biopsied who had sperm present in the vas fluid, post-operative sperm count was fairly well predicted by the number of mature spermatids (Sc + Sd) per seminiferous tubule in the testicular biopsy. The close correlation (exponential curve) of mature spermatids per tubule to sperm count has been well demonstrated in a previous study and is corroborated by these data (Silber and Rodriguez-Rigau, 1981). Of these 16 patients, two did not impregnate their wives. The semen parameters in these two were no different from patients who did achieve impregnation. The ratio of pachytene spermatocytes to mature spermatids showed a close one-to-one correlation in all patients and was not significantly different in the two patients who failed to impregnate their wives.

Table VII summarizes the quantitative data on testicular biopsies in patients who had persistent blockage post-operatively. Five of these six patients were azoospermic post-operatively and one of them was severely oligozoospermic (1 800 000/cm^3) despite an accurate vasovasostomy. None of these wives became pregnant. The mature spermatid count per tubule and, thus, the 'expected' sperm count were within the normal range of all six. The ratio of pachytene spermatocytes to mature spermatids was no different from patients who achieved impregnation.

Discussion

The high pregnancy rate in this group of patients requires some explanation. There have been many speculations about the failure to achieve fertility after reversal of vasectomy, including autoimmune changes and damage to the testis. This study suggests that the pregnancy rate in patients who have patency accurately re-established without epididymal damage is eventually not significantly less than a normal population of couples. Vessey *et al.* (1978) demonstrated that among couples with proven prior fertility, 96.5% conceive within 4 years of discontinuing contraception. In these couples with patent results after vaso-vasostomy who had no evidence of epididymal pressure damage, 88% conceived with long-term follow-up. Of course, these men had demonstrated prior fertility. Those patients with no sperm in the vas fluid were excluded because they had secondary epididymal blockage and required a completely different surgical approach than vasovasostomy.

Failure to achieve patency could be caused either by a partial or complete stricture at the vasovasostomy site, or by secondary pressure-induced blockage in the epididymis. The presence of these epididymal blockages has been confirmed in four different species of animals (Bedford, 1976) as well as in humans (Silber,

Table V. Relationship of serum sperm antibody titers to pregnancy rate after vasovasostomy

	Total studied	Immobilizing titer (Isojima)		Agglutinating titer (Kibrick)	
		2	10	0	20
Husband not azoospermic					
Wife pregnant	75	29 (39%)	18 (24%)	42 (56%)	30 (40%)
Wife not pregnant	11	4 (46%)	2 (16%)	6 (54%)	6 (54%)
Husband azoospermic	12	5 (42%)	3 (25%)	7 (58%)	5 (42%)
Entire group studied	98	38 (39%)	23 (24%)	56 (57%)	41 (42%)

Table VI. Quantitative study of testicular biopsy in patients who had sperm patency

Patient	Years since vasectomy	No. of mature spermatids per seminiferous tubule		Ratio of pachytene spermatocytes to mature spermatids	Expected sperm count (per cm^3)	Actual sperm count (per cm^3)
		Right	Left			
G.B.	9	–	24.0	1.19	19 000 000	20 000 000
R.D.	4	–	17.2	1.17	7 000 000	6 600 000
W.B.	10	43.3	–	0.89	78 000 000	82 000 000
C.B.	16	30.3	–	0.91	33 000 000	37 200 000
M.B.	2	–	27.7	0.96	26 000 000	35 800 000
R.C.	5	–	18.0	1.33	8 000 000	5 800 000
S.C.	9	31.8	27.8	1.06	31 000 000	30 000 000
M.C.	1	28.6	–	1.04	30 000 000	24 850 000
A.B.	1	22.6	–	1.15	17 000 000	24 500 000
P.C.	5	14.0	–	1.64	4 000 000	3 000 000
A.C.	6	30.1	27.9	1.16	32 000 000	30 000 000
R.C.	5	29.9	27.8	1.11	30 000 000	38 000 000
R.B.	22	40.4	–	1.18	63 000 000	70 000 000
M.C.	5	–	36.1	1.01	50 000 000	63 000 000
M.C.	4	–	30.9	1.28	37 000 000	40 800 000
A.F.	6	33.2	–	1.11	41 000 000	36 000 000

Table VII. Quantitative study of testicular biopsy in patients who had little or no sperm patency

Patient	Years since vasectomy	No. of mature spermatids per tubule		Ratio of pachytene spermatocytes to mature spermatids	Expected sperm count (per cm^3)	Actual sperm count (per cm^3)
		Right	Left			
J.C.	10	31.9	30.2	1.00	34 000 000	0
N.D.	20	35.7	36.8	1.05	52 000 000	0
J.D.V.	8	–	29.1	1.24	32 000 000	0
C.C.	16	27.7	26.7	1.27	26 000 000	0
P.D.V.	5	30.3	–	1.19	33 000 000	0
R.C.	17	–	28.0	1.21	28 000 000	1 800 000

1979, 1984). The effect of a poorly performed or strictured vas anastomosis has also been well documented (Silber, 1977a).

Quantitative study of testicular biopsies revealed no differences between those patients who impregnate their wives and those who did not. In non-obstructed patients there was no significant difference between the expected sperm count (based on the number of mature spermatids per tubule) and the actual clinical sperm count post-operatively. In those patients who had persistent post-operative azoospermia, testicular biopsy showed no quantitative abnormalities in the testicle, indicating blockage either at the epididymal or at the vasovasostomy site.

Varicocoele is considered a common cause of male infertility, yet no deleterious effect could be found in the presence of a varicocoele on pregnancy rates of patients undergoing vasovasostomy.

It has been previously shown that the success rate of vasovasostomy decreases with the duration of time since the vasectomy (Silber, 1977a). The decrease in success with longer duration of time since vasectomy is directly related to the absence of sperm in the vas fluid at the time of vasovasostomy, and this is caused by the interruption of epididymal patency by pressure-induced sperm extravasation and inspissation (Silber, 1979). The incidence of this pressure-mediated interruption of epididymal patency is reduced dramatically by the presence of a sperm granuloma at the vasectomy site, which serves as a release valve to prevent the pressure increase that would otherwise occur

proximal to the vasectomy site (Silber, 1977b, 1978c; Shapiro and Silber, 1979). When there is no sperm in the vas fluid, vasoepididymostomy proximal to the site of epididymal blockage is required (Silber, 1978a, 1984). None of the patients in this study was thought to require vasoepididymostomy, and so they were a very favorable group.

It thus appears that the fertility rate and pregnancy rate may be higher than previously expected in patients with no epididymal blockage who undergo technically 'successful' vasovasostomy.

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