

## Absence of Antisperm Antibodies in Anejaculatory Men

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**Antisperm antibodies were assessed in the serum samples of 73 men unable to ejaculate naturally and on the sperm cells of 13 of these men. None of the serum samples were found to be positive by sperm agglutination or sperm immobilization methods and antibodies were detected by an immunobead assay on the sperm cells of one of the 13 men examined.**

**Key words:** Agglutinating antibodies, immobilizing antibodies, immunobead assay.

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A relatively uninvestigated area of reproductive physiology is the changes of sperm quality in the anejaculatory man. Specimens obtained by electroejaculation or vibrator stimulation from these men may vary greatly in total sperm numbers but sperm motility and forward progression are usually low (Brindley, 1984; Ohl et al, 1989). The often unusually high concentration and total numbers of sperm cells found in ejaculates induced by electrical or vibrator stimulation suggests that there is a retention of sperm cells in the genital system. This physiologic obstruction to normal passage of the sperm cells may result in increased pressure in the genital tract, initiating an autoimmune response to sperm as seen in cases of congenital absence of the vas deferens

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(Girgis et al, 1982) and vasectomy (Ansbacher, 1973). Autoantibodies against sperm have been associated with decreased motility characteristics in infertile men (Mathur et al, 1986; Menge and Beitner, 1989), and if present in anejaculatory men, this could explain the low motility seen in their specimens.

The purpose of this investigation was to determine the occurrence of antisperm antibodies in the serum samples and on the sperm cells of men undergoing electroejaculation for the treatment of anejaculatory infertility.

### Materials and Methods

A total of 73 men seeking treatment for anejaculatory infertility at the University of Michigan Electroejaculation Program entered the study. All men were unable to ejaculate without medical assistance. The majority of the men had spinal cord injuries (SCI—57 patients). Of the remaining men, 12 had been rendered anejaculatory by retroperitoneal lymphadenectomy (RPLND) performed because of testis cancer, and the other patients had a variety of diagnoses (one each with diabetic neuropathy, multiple sclerosis, myelodysplasia, and psychogenic anejaculation).

All men capable of achieving orgasm (mostly RPLND patients) were checked for retrograde ejaculation and found to have none. All were placed on sympathomimetic medications to bring about emission, all failed to respond to this treatment.

Prior to electroejaculation, serum samples for antibody determination were obtained from all of the 73 men. Electroejaculation was carried out as previously described (Ohl et al, 1989). Antegrade ejaculates were collected directly into a sterile specimen container and any semen emitted into the bladder was collected via urethral catheterization following the electrical stimulation. Semen samples obtained by these techniques from 13 of the patients were submitted for direct antibody determination. These were the last 13 patients to enter the study, and they consisted of 12 men with SCIs and one with a RPLND.

Sperm antibodies were measured in the serum by a modified tray agglutination technique (TAT) and sperm immobilization test (SIT) (Menge et al, 1982). After heating at 56°C for 30 minutes, serum samples were analyzed twice by TAT and SIT with sperm from different donors. Serum samples were assayed at starting dilutions of 1:16 for the TAT and 1:4 for the SIT. Known positive and negative control sera were run in each assay. If, in either method, there appeared to be a positive response at the lowest dilution, the assay was repeated using lower dilutions.

The direct immunobead binding test (IBT) was performed on sperm cells from the antegrade and retrograde fractions of the ejaculates. The sperm cells were enhanced for motility and washed free of seminal components by centrifugation over an 80% Percoll-medium mixture at 400 × g for 15 minutes (Bronson et al, 1982). The medium consisted of Ham's F-10 containing 0.5% bovine serum albumin and 20 mmol/L HEPES buffer. The sperm pellet was removed with a pipet, resuspended, washed once in the medium, and diluted to 5 × 10<sup>6</sup> sperm/mL before adding the immunobeads (IB). The sperm samples examined were screened with an IB mixture to detect IgA, IgG, and IgM bound antibodies and, if positive, they were assayed against the individual Ig classes in the IBT.

### Results

None of the 73 serum samples proved positive by the TAT or SIT assays, and only one sperm sample of the 13 examined was found to be positive by IBT. This sample showed that 60% of the motile sperm were bound by anti-IgA IB and none by anti-IgG IB. This individual was a SCI patient with no history of genital tract infections.

### Discussion

Our results give no suggestion that the anejaculatory condition, even for periods of up to 27 years (our patient with congenital myelodysplasia), predisposes men to autoimmunity against sperm cells. This conclusion is drawn from a population

of patients who might be considered at risk for development of antibodies because of their basic disease processes. The patient with antibody-bound sperm did exhibit an unusually low motility that ranged from 1% to 5% over the course of three electroejaculations. Sperm antibodies have been found in response to infection/inflammation of the genitourinary tract (Fjallbrant and Nilsson, 1977), which are common in SCI patients, and have been described as a possible cause of subfertility in men with testis tumors (Nagler, 1986).

Our findings are similar to the study of 16 anejaculatory men with spinal cord injuries done by Dahlberg and Hovatta (1989) in which none of the specimens obtained showed sperm-agglutinating antibodies in the serum, and none of the seven antegrade sperm specimens were found to be positive by the mixed-antiglobulin reaction assay.

The results of our study and those of Dahlberg and Hovatta (1989) are in sharp contrast to the report on eight anejaculatory men by Hirsch and co-workers (1989). These authors found antibodies on the sperm of all the men with an enzyme-linked immunosorbent assay and with an IBT in the serum of four of the eight men with spinal cord injury that had undergone electroejaculation. The reasons for the discrepancy among the studies is not known. While different assays were used, it is unlikely that this could account for such a great disparity. It is possible that their patient population of spinal cord injured men experienced more complications from their paraplegic state, such as recurrent epididymitis, and the probable ensuing testicular damage initiated an autoimmune response. The incidence of positive IBTs with sperm of men from infertile couples was reported to be approximately 10%, whereas no positive IBTs were found in the fertile group (Adeghe et al, 1986).

Semen samples from infertile men have shown a negative association between the presence of antisperm antibodies in the ejaculate or serum and the motion characteristics of the sperm cells (Mathur, 1986). Elevated serum titers of sperm antibodies, especially the immobilizing type, were associated with significant inhibitory effects on the forward progression and total progressive motility of ejaculated sperm of men from infertile couples (Menge and Beitner, 1989).

Following vasectomy, and in cases of congenital absence of the ductus deferens, obstruction of sperm outflow creates sufficient pressure to cause extravasation of sperm from the genital ducts. This

in turn initiates an autoimmune response in the majority of patients. The evidence suggests that this response is initiated in the epididymis and rete testis. Antisperm antibodies were found in the epididymal fluids obtained from men undergoing vasovasostomy, and afterwards in the semen, whereas before the repair, antisperm antibodies were rarely detected in the seminal plasma (Linnet et al, 1982). Similar findings were reported in a study of men with congenital aplasia of the vas, with antisperm antibodies being found in the epididymal secretions of two of three men, and in the serum of all three men (Kay et al, 1988). Epididymal samples from these men possessed low sperm concentration and decreased sperm motility and forward progression.

Compared to patients with bilaterally or unilaterally occluded ductus deferens, such as occurs after vasectomy or in cases of congenital aplasia, in which there is an anatomic obstruction, neurogenic anejaculation creates a physiologic impairment of sperm transport. This impairment of flow must not be great enough to cause high pressure, extravasation, and subsequent antibody development. There may be an intermittent discharge of fluid from the genital ducts which serves to decrease excess pressure. Experimental evidence of this phenomenon exists in rabbits subjected to long periods of sexual rest (Prins and Zaneveld, 1980).

In conclusion, we believe that in men with anejaculation, the often observed low motility and poor forward progression of sperm cells in induced ejaculates are unlikely to be the result of antisperm antibodies.

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