A REVIEW ON SPERM_AGGLUTINATING ANTIBODIES IN SERUM AND SEMEN OF INFERTILE MALE

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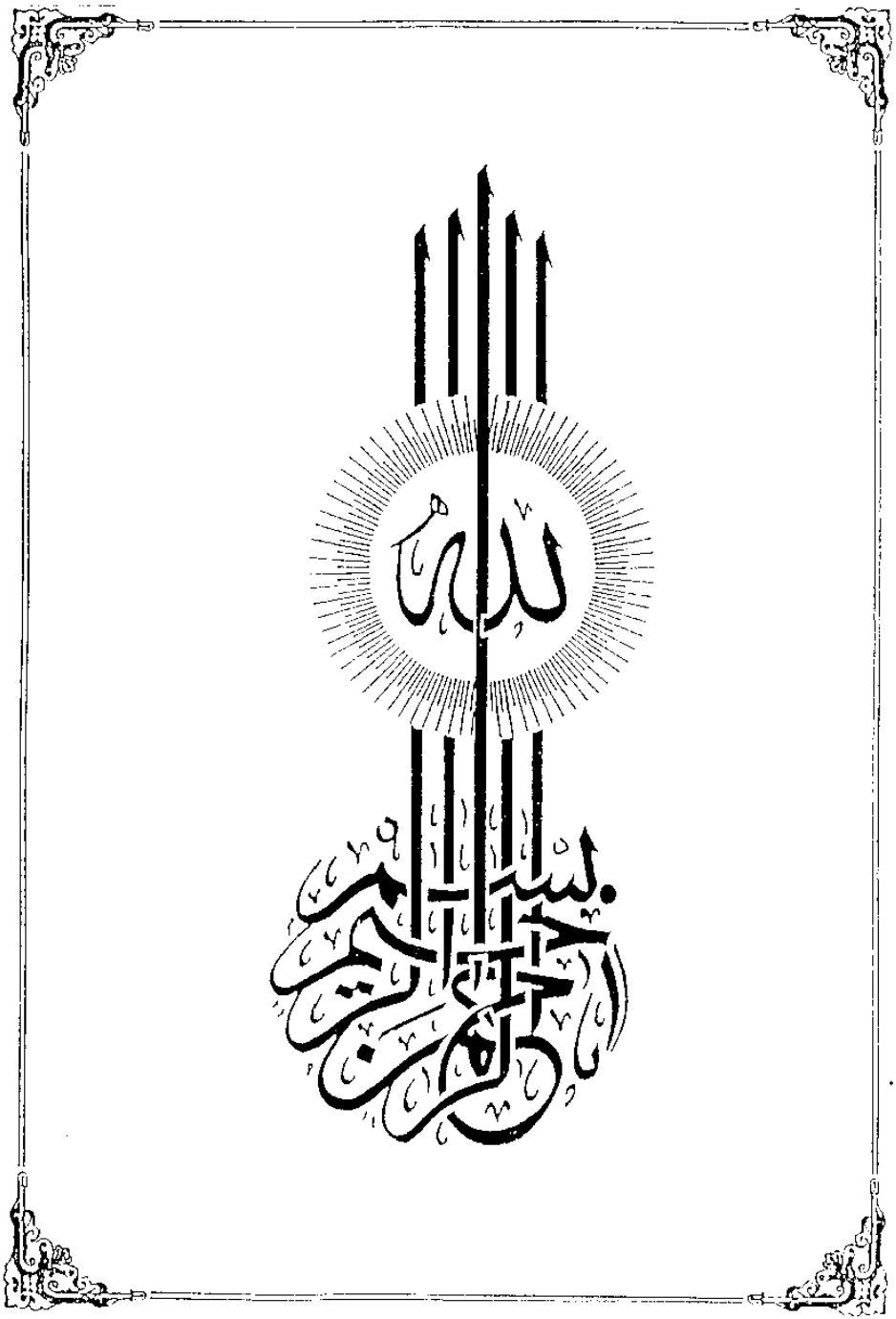
بسم الله الرحمن الرحيم

قال تعالى

لله ملك السموات والأرض . يخلق ما يشاء ، يهب لمن يشاء
إناثا ويهب لمن يشاء الذكور ، أو يزوجهم ذكرانا وإناثا ، ويجعل
من يشاء عقيما ، إنه عليم قدير .

صدق الله العظيم



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INTRODUCTION
AND
AIM OF WORK

INTRODUCTION

Male infertility is multifactorial. The semen is a complex composed of cells and secretions elaborated from the male reproductive tract for fertilization of the ovum. The cells i.e spermatozoa are of paramount importance. The journey through the male and female reproductive tract is not always joyful, but may be difficult and sometimes completely impossible. The successful completion of the journey requires many millions of spermatozoa showing vigorous progressive movement. This movement might be impeded by so many factors among which the immunologic ones might be important (Beer and Neaves, 1978).

Since semen appears late in life and since tolerance to self antigens develops early in life, then semen may be potentially autoantigenic. Under certain conditions an individual may evoke an immune response to the elements of his own semen (Hekman and Rumke, 1976). In fact the ability of spermatozoa to produce an immunologic response has been known since the turn of this century (Landsteiner, 1899).

According to Schoenfled et al. (1976), 10-15% of marriages are infertile. In 20% of these, the infertility state is unexplainable i.e no apparent organic causes can be found. 15-20% of these unexplained infertility

were found to be caused by immunological factors (Glass and Vaidya , 1970).

Both cell-mediated and humoral immune responses against spermatozoa in both serum and seminal fluid were reported to occur (Fiberg, 1982). The humoral immunity proved to display different types of antibodies which include sperm-agglutinating, sperm immoblizing and sperm-cytotoxcity antibodies. The latter two types are complement dependant.

The first observations of circulating sperm-agglutinating antibodies in man were made by Wilson (1954) and Rumke (1954).

The majority of these antibodies belong to immunoglobulin G "IgG" and to a lesser extent immunoglobulin A and M (IgA & IgM) (Friberg, 1974 a).

The couple with immunological infertility has a long history of infertility probably produced by repeated encourgment based on apparently normal findings on routine investigations. A good but variable sperm count with marked autoagglutination of the ejaculate coupled with poor postcoital test should arouse the suspicion of antisperm antibodies in otherwise unexplained infertility (Fjallbrant and Obrant, 1968).

AIM OF THE REVIEW

The review will be confined to sperm-agglutinating antibodies in serum and semen of males with unexplained infertility. However, a quick touch on the female side will be included in a way to look on the other side of the coin to have the real magnitude of the problem which is in many instances a bipolar problem.

The review will encompass, in short, the antigenicity autoimmunity of spermatozoa, the incidence of sperm-agglutinating antibodies, and the significance as well as the trials to treat the condition.

Chapter I

Historical Perspective

HISTORICAL PERSPECTIVE

Infertility, as existing on the basis of exposure to semen, was suggested as early as 1871 by Darwin who put forward a direct relationship between sexual promiscuity in women and infertility. However, the demonstration of antigenicity of spermatozoa was made by Landsteiner (1899) and Metchnikoff (1900) who observed that injection of sperms or testicular extracts into experimental animals resulted in antibody formation. Immediately, reports appeared which could be used to support the rationale of inducing sterility by immune methods. However, the cumulative evidences were so motivating to extend these attempt to human beings. Mayer (1922) postulated that sex intemperance in women could lead to premature rupture of ovarian follicles and, thus affect fertility. He speculated that during sexual abstinence, fertility could return and cited evidence that during World War 1, abstinence facilitated postwar pregnancies in previously infertile couples. Rosefeld (1926) took note of isolated, vague reports from birth control clinics which showed that women who had been injected with semen could avert pregnancy for about 20 months . Hovever, he injected three female patients vith human sperms, but was unable to demonstrate a definite positive result in their sera. Mud and Mud (1929) employed electrophoretic

methods to demonstrate that human sperms injected into the rabbit induced antibodies which were found to be species as well as organ specific.

Agglutination of human spermatozoa was demonstrated by certain strains of bacillus coli (Rosenthal, 1931). This was thought to reduce fertility chances. However, other bacilli failed to show agglutination of sperms. Baskin (1932) could immunize 20 females by injecting them with sperm. The immunization lasted about one year and he could determine the degree of immunization by determining the antisperm antibodies in the blood.

Species specificity of spermatozoa was shown to be dominant rather than absolute. Cross-reactions were found between sperm of different species (Henle et al., 1938). The human spermatozoa were found to react to some extent, with bull spermatozoa. Rabbit anti-bull anti sera exhibited marked reactions with human sperms. In an attempt to characterize the antigenic nature of mamalian sperms, these workres studied bull sperms and found a heat-labile, head-specific and tail-specific antigens and heat-stable antigen common to both head and tail. This last antigen was found to be species specific. Using heterologous antisera, these workers revealed three different cross-reacting antigens in bull sperms. Of

these, two were located in the head and the third was located in the tail. Lewis (1941) demonstrated that anti-testis sera reacted with brain tissue and vice versa. Both organs were shown to have similar antigenic properties. Both revealed cross reaction with corpus luteum. Otherwise, both organs showed complete organ specificity.

Adjuvants started to gain recognition for their ability to potentiate antibody response. Freund et al. (1953) established that autologous or homologous testicular extracts incorporated into adjuvant induced selective destruction of the spermatogenic tissue in guinea pigs.

The gelatin agglutination test (GAT) of Kibrick et al. (1952) was originally designed for studies of rabbit antisera to spermatozoa. It was first introduced for use in humans by Rümke (1954). It has been widely used and has been followed by a vast number of techniques and their modifications. All these tests are intended to detect titres and types of antisperm antibodies.

However, it was only during the 1950s when people started to touch on male infertility caused by immune response to spermatozoa. This was made possible by the work of Wilson (1954) who demonstrated that agglutination of normal human sperms was produced by the

seminal plasma and blood sera of two patients whose spermatozoa exhibited autoagglutination. Rumke (1954) demonstrated sperm-agglutinating antibodies in two azoospermic cases. Since then, the subject of detection and search for incidence of sperm antibodies attracted the attention of many investigators.

As for the antigencity of semen, a close antigenic relationship between spermatozoa and seminal plasma was described (Weil et al., 1956). Seminal plasma was claimed to possess a highly antigenic material (Weil, 1961). Sperm specific antigens were demonstrated to exist in the spermatozoa obtained from the mature testis and epididymis of guinea pigs (Isojima and Stepus, 1959).

In their search for the causes of antisperm antibody formation, Rumke and Hellinga (1959) found occlusion of vas deferens to be a prominent cause resulting in spermatostasis and then extravasation of spermatozoa with their resultant presentation to the immune system. Then it became easier for phade and Padakone (1964) to explain the appearance of circulating antisperm antibodies in high titres following vasoligation.

The blood-genital tract barrier was described by Johnson (1970) as an efficient mechanism that prevents

the escape of antigens from the reproductive tract into the host environment and on the other hand prevents the entery of antibodies and immune cells into the genital tract.

Rumke (1973) found that the presence of circulating sperm-agglutinating antibodies in titres below 1:32 to be compatible with fertility. Since then this value was taken as the upper limit of the normal above which treatment is ought to be considered. Then Friberg (1974a) reported that when a serum titre above 1:32 is found, antibody activity can be experienced in the ejaculate.

The fact that antibody formation against spermatozoa in man is an autoimmune phenomenon justified Halim and associates (1974) to use corticosteroids as immunosuppressive agent prior to artificial insemination. They used low-dose regimen. Later on this low-dose regimen was employed with variable success rates.

However, Shulman (1976) was the first to report on high-dose regimens which on sebsequent works proved to be more successful.

The pioneer studies on testosterone as a treatment for immunological infertility was performed by Schoysman