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Management of the Infertile Couple

by

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I must thank the Post-Graduate Committee of the Kandang Kerbau Hospital for inviting me to participate in the current post-graduate talks though I am not a member of your academic staff and I deem it a great honour.

Secondly, I have been delegated the difficult task of addressing on a subject which is rapidly gaining importance day by day demanding a high degree of scientific and technological knowledge in order to understand the many intricate mechanisms that confront the question of Infertility.

It sounds incredible that in a world where the population is increasing at the alarming rate of 68,000 individuals per day, where the demographers are constantly reminding us that the world population will double itself in 2000 A.D. to six billions, and where the structure of our human society is being threatened out of its existence unless adjusted to a more equitable pattern of economy: that there still should be found students of research engaged on problems of sterility and Infertility.

However, one should not lose sight of the humanitarian aspect of this problem. If the Gynaecologist can bring joy and happiness to these frustrated infertile couples by restoring the normal basic physiological status in order to gratify the parental instincts which God has given to every mankind then, we, the Gynaecologists would have gone a long way to justify the cause of our speciality.

With these preliminary remarks I shall now proceed with the humble apology that it is impossible to do justice to a complex problem like infertility within the short space of time allotted.

The management of the infertile couple can be divided into two distinct headings:—

1. Investigations.
2. Management and treatment.

The former is the most important, for only by a systematic and methodical line of approach may the actual cause of the infertility be discovered before any rational treatment can be prescribed. At the outset, it may be well to draw your attention to the confusion that has existed in the past to the usage of terms such as sterility and infertility when discussing this subject.

The Committee of the R.C.O.G. sitting on the Royal Commission on Population in England in 1947 helped to define their respective status.

Sterility

The original definition given by Meaker in 1934 is the one accepted and reads as follows:—

"The inability to initiate the reproductive process." It is applicable to the male and the female partners as well as to marriages. It includes both groups of cases e.g. one where the germ cells may be wanting e.g. spermatozoa or ova, as well as those where the germ cells are healthy and normal but there is a block in the transportation system whether in the vas, or the tubes. Hence Sterility is absolute except in the latter case where the situation may be reversed by surgery.

Fertility

This is defined as the ability to produce an offspring and takes into account the reproductive capacity of both partners. Unlike sterility, fertility is not absolute and may manifest several degrees, e.g. infertile, subfertile, fertile and hyperfertile couples.

I shall now focus on "Infertility" as the theme of my talk. It is important to differentiate between primary infertility and secondary infertility. This latter implies that there has at

least been one pregnancy before and further by talking of the "infertile couple," as such it emphasizes the importance of both partners, each contributing his or her quota towards the ultimate result.

A few statistical reports will show how simple remedies, advice and guidance and even simple surgical procedures are all that is needed in over-coming some of the problems of the infertile couple.

Green Armytage in a series of 397 patients complaining of infertility found 4% to have intact hymen.

Stallworthy in a similar group of 581 patients found 5% had not even consummated their marriages. Tyler observed the male to be a contributory causative factor in 60% of infertile matings. Meaker attribute 30% of the failures in infertile marriages to the male partner. Moorewhite and Green Armytage in their recent text book (the Management of impaired fertility) writes, the husband is responsible for 30% of the causes of barren marriages.

From these above statistical data, the role of the male in the investigation of infertile couples is established beyond doubt. It may be interesting to consider at this stage to what extent this question of infertility may be a national problem. Here again, the Royal Commission on Population found that 8% of all married couples in any one year will be found to be sterile in the United Kingdom. Similar data for our country has not been worked out as yet.

Infertility Clinic

In order to conduct a systematic, co-ordinated plan of investigations to elicit all possible factors contributing to the infertility, a well organised clinic is essential with the requisite staff and facilities available.

One must remember it is a specialised clinic and not an appendage to a busy gynaecological outpatient department. An intelligent diagnosis is essential or else the treatment will be sketchy, haphazard and amateurish. The potentials of an infertile clinic should consist of:—

1. Facilities for evaluating male fertility factors.
2. Facilities for evaluating female fertility factors.
2. Liaison with the Radiological, serological and pathological departments of the hospital.
4. Co-operation with the urologists for genito-urinary investigations.
5. Close relationship with the Medical Units to assess Endocrine factors relating to Pituitary, Thyroid, Pancreatic and adrenal conditions.
6. Availability of a psychiatrist to assess the psychological component of infertility.
7. Facilities for Biological assays and estimation of Keto-Steroids with Dept. of Biochemistry.
8. Finally the investigation of "Immunological Factors" in conception—introduced by Albert Tyler, e.g. antigen antibody concept of fertilisation.

The ideal situation for such a clinic would be in a gynaecological unit situated within the precincts of a general hospital, to save the patient travelling long distances from one department to another.

A general survey in my own practice shows that 20% of all gynaecological patients seeking advice are for infertility. Half of these cases respond to the standard treatment of dilatation, curettage and insufflation of the tubes with many becoming pregnant within 3 to 6 months of surgery; another 15% react favourably to reassurance, general treatment with tonic and vitamins, and coitus restricted to the ovulatory phase of her menstrual cycle. This leaves behind 7% of the total number of infertile patients who require more elaborate investigations. The bulk of these manifest blocked tubes, anovulation, endocrinpathies (mainly obesity) fibroids and other adnexal conditions in the females and oligospermia, asthenospermia, azoospermia and even necrospermia in the male.

Investigation Of The Male

A systematic review includes:—

1. History relating to general, marital, coitus and dietetic habits; addictions to alcohol, tobacco and other drugs and evidences of venereal and other diseases likely to affect the testis.
2. Psychological examination by a psychiatrist in cases of impotence and lack of libido.
3. Full physical examination with particular reference to the genital tract to detect evidences of undescended or absent testis, hydrocele, varicocele, and other penile deformities.
4. A full semi-nological examination by a seminologist if possible.

5. Complete medical check to rule out endocrine factors.

Investigation Of The Female

This must also be conducted on similar lines, e.g.—

1. Full personal history relating to marital habits, coital frequency, dietetic habits and drug addictions.
2. An equally detailed gynaecological history with particular references to menarche, puberty, menstrual patterns and other evidences of genito-urinary tract inflammations.
3. Psychiatric assessment of emotional factors pertaining to infertility.
4. Complete physical and gynaecological examination to detect congenital anomalies and genital hypoplasia.
5. Investigation to detect endocrine defects.
6. Specific examination to test for evidences of:—
   (a) Ovulation
   (b) Tubal patency.
   (c) Endometrial pattern compatible with nidation of fertilised ova.
   (d) Unhealthy leucorrheal discharges with special reference to vaginal Ph.
7. Usually in selected cases the detection of chromosomal pattern of the individual indicating certain matings to be infertile.

Post Coital Test

The fate of the spermatozoa following coitus until it fertilizes the discharged ova in the fallopian tube is of extreme importance. Any impediment or failure to achieve this will result in infertility. Where the male partner is capable of producing active healthy spermatozoa in sufficient concentration the factors controlling sperm migration have an important bearing. In its passage through the vagina, cervix, uterus and finally the tube, the physiological and biochemical properties peculiar to each will contribute its quota towards an efficient transmission.

The nature of this complex problem is far from complete today and much of our knowledge is based upon animal experiments. The fate of the spermatozoa in the vagina and cervix can be studied by relatively simple methods and should be a normal routine in investigating the infertile couple. It entails examination of the secretions from the posterior vaginal pool and cervical canal following coitus. Marion Sims in 1868 was the first to study the fate of the spermatozoa in the cervical canal.

Normally the **vaginal secretion** is hostile to the spermatozoa with a ph. of 4.5 a degree of acidity not compatible with sperm survival. The seminal fluid on the other hand has a ph. of 7.7-8 and the cervical secretion a ph. between 7-8. This hostile environment in the normal vagina is offset by the buffering capacity of the Semen The cervical secretion on the other hand exerts a more salutary effect on the spermatozoa being slightly alkaline and particularly favourable to sperm penetration. This becomes more marked at time of ovulation when the secretion becomes less viscid, less cellular and more glairy. It develops the properties of spinnbarkeit and fern-crystallisation. In fact, if one exposes the cervix with a bivalve speculum at time of ovulation the cervical mucus may be seen to flow only in a cascade.

Technique Of Post-Coital Test

A few cardinal points must be remembered:-

1. Coitus must take place during the presumptive ovulatory phase and report to the gynaecologist within 12 hours.
2. A period of 4-5 days abstinence must be insisted upon and there should be no prior usage of jellies, douches or other chemicals for at least 48 hours previously.
3. The patient having been placed in the lithotomy position, no lubricant must be used to visualise the cervix.
4. With a syringe mucus should be obtained from the distal portion of the cervical canal and placed on a slide.
5. Using a second syringe material is obtained from the posterior vaginal fornix and placed on a second glass slide.
6. Both these slides are examined under the microscope.

Normal Findings

1. **Vaginal Secretion.**

   With a normal sperm count numerous spermatozoa will be seen but most of them will be non-motile. If only a few are seen it may be construed that rapid migration has occurred out of vagina.

2. **Cervical Secretion.**

   Under normal circumstances, numerous actively mobile spermatozoa will be seen and

20 per H.P.F. (high power field) may be accepted as a good reading. 75% of the sperms should be actively motile up to 12 hours after coitus and 20% even after 24 hours in fecund couples. The longest period of viability of sperms in the cervical canal has been found to be five days (Lane—Roberts).

Some Abnormal Readings

A. **No spermatozoon in vagina and cervical secretion.**

This implies — (a) faulty coital technique
(b) ejaculatio praecox
(c) hypospadias
(d) azoospermia.

B. **Spermatozoon in vaginal secretion and none in cervical secretion.**

This implies non receptivity of cervical mumus to sperm migration and may be due to:—

(a) increased viscosity.

(b) or abormal secretion resulting from inflammation, e.g. cervicitis and endocervicitis or cervical polyp.

C. **Non-motile spermatozoon in cervical secretion.**

This implies cervical hostility and probably results from chemical and physical abnormalities inherent in cervical mucus. Usually an adequate volume of cervical fluid is necessary in the face of a normal sperm count for normal sperm migration or else there will be inadequate buffering to counteract vaginal accidity.

Kurzrok and Miller (1928) described an **"in vitro Test"** to demonstrate cervical penetration by bringing into contact the spermatozoa and cervical mucus on a glass slide and visualize the sperms actually migrating into the mucus. This was thought to be due to a lytic enzyme present in the semen which dissolve the mucus and reduce its viscosity. The significance of this mucolysis is highly conjectural and only a positive result is of value.

Thus the post-coital test can be considered to be the one most important single test which will furnish the maximum information on sperm cervical relationship in an otherwise healthy couple.

Evaluation Of Male Factors In Infertility

It is only in recent years that there has been an upsurge of interest in problems associated with male fertility and that for reasons I have already mentioned in the beginning. Until now man has basked in the glory of his own masculinity taking for granted that his capacity for bearing children was not to be questioned. Sadly enough the truth of this is no longer infallible, and virility and fertility do not go hand in hand. A seminal appraisal is the first requisite and should conform to the following standards: though there is marked variation in the range of abnormalities:—

1. Physical Characteristic—usually a whitish coagulum.
2. Liquefaction—normal semen will liquify within 15 minutes.

   Any delay is abnormal and may indicate a delay or non-release of sperma tozoa from its coagulum base.
3. Volume — This is important from the point of view of buffering mechanism of vaginal acidity. Normal range varies from 2½-5cc. Volume below 1.5 cc is abnormal.
4. Ph. value—semen is slightly alkaline with a ph. of 7.7 and this is remarkably constant even in abnormal specimens.
5. Sperm concentration—The normal range is taken as between 60-100 millions per c.c. The American Society for the study of sterility accepts 20-40 million per c.c. as being within normal concentration. Cases are recorded where pregnancies have occurred with concentrations very much lower. However, the general agreement is the lower the spern count the lower the incidence of pregnancy.
6. **Sperm Characteristic.—**

This includes (a) MOTILITY
(b) Abnormal forms
(c) Agglutination
(d) A Presence of Leucocytes.

The American Society for study of sterility has laid down as minimum standards that 60-70% of the sperms should be vigorously motile within two hours of liquefaction. Normally, motility should be estimated at 2, 4 and 6 hours respectively. About 20%-30% should still be actively motile at end of this period in a normal fertile specimen. The percentage of abnormal forms should not exceed 20%. Higher figures definitely indicate lowered fertility index. Agglutination is an important phenomena but more difficult of evaluation. It comes under the study of immunological factors in infertility and it is still in its early experimental stage. Presence of leucocy-

tes is suggestive of inflammation of the genital tract. Normally leucocytes are absent. The source is usually Seminal Vesicles, Prostate or Posterior Urethra, Infertile specimens may show the following abnormal sperm features:—

1. oligo-spermia
2. necro-spermia
3. Astheno-spermia
4. azoospermia.

I shall only discuss the last condition as the others are well described in standard books on this subject. To diagnose azoosperimia one should examine a centrifuged deposit of the specimen; which may show a few sperms and thus becomes a case of extreme oligo-spermia although from the point of view of fertility both conditions are hopeless.

Azoospermia is either the result of:—

(a) Blockage of the genital tract:—

(i) Epididymal canal
(ii) Vas Deferens
(iii) Ejaculatory ducts.

(b) Absence of spermatogenic tissue.

The former may be diagnosed by radiographic methods while the latter on testicular biopsy.

Evaluation of Female Factors in Infertility

Having ruled out medical, endocrinological, anatomical and psychological causes and before embarking upon specialised forms of investigation, I would like to mention what has been termed **non-specific** infertility factors in female infertility. This includes:—

1. appendicitis in childhood
2. chronic sinusitis
3. chronic pyelitis
4. Atypical infection of teeth
5. Chronic constipation.

Except in the case of appendicitis the adverse effects on fertility are probably the result of toxic effects on the reproductive system. One important toxin which working women may be exposed to and cause infertility, is lead.

A. Ovulation.

Not only is it an evidence of normal ovarian function but also an index of normal gonadotrophic activity of the anterior pituitary of the woman. Without ovulation there can be no pregnancy. The various means of detecting ovulation are only too well known and I shall only enumerate them:—

1. subjective symptoms
2. basal body temperature
3. vaginal smears
4. endometrial biopsy
5. cervical changes
6. biochemical assays
7. Peritoneocopy
8. Culdoscopy

B. Tubal Patency Studies by Insufflation.

First introduced by Rubin in 1920 it has today become the universally adopted method of testing tubal patency. In 1925 Rubin introduced the kymographic method of studying human tubal peristalsis whereby oscillation arising from peristalsis were recorded on a smoked revolving drum. This gave in addition information on tubal function. Negative insufflation should be followed up with hystero-salpingographic studies. This will reveal not only the site of tubal blockage but abnormal states, e.g. tubal kinking, hydrosalpinx, tuberculosis, diverticula, hypoplasia. In diagnosing tubal block on Xrays, one must remember the possibility of a functional block arising from tubal spasms, or

Tubal Block < organic < partial / complete.
Tubal Block < functional < partial / complete.

C. Gynaecography

First introduced by Peterson in 1921 and later popularised by Stein of Chicago. It is of value in diagnosing large polycystic ovaries associated with Stein Leventhal syndrome. I will advise my audience to refer to specialised text books on this subject for further information.

Treatment of the Infertile Couple

Having given a brief account of the various factors involved in the investigation of the infertile couple, I shall devote a few lines on the treatment. This will include both the male and the female partners and I shall only enumerate the main methods of treatment.

The various types of treatment available are:—

I. Medical:—
   (a) Hormones
   (b) Vitamins
   (c) Short Wave diathermy
   (d) anti-biotics.

II. Surgery

III. Irradiation methods (to induce ovulation) < Gonads / Pituitary

IV. Artificial insemination

V. Artificial induction of ovulation

I shall conclude by mentioning a few words on artificial induction of ovulation first described by Gemzeble in 1958 with the use of human F.S.H. In 1960 he described the first case of human pregnancy resulting from the use of Human Gonadotrophin. Since then this work has been repeated in U.S.A. and Great Britain and it looks as though we have at last discovered a powerful weapon with which to induce ovulation. However, these pertinent questions have now to be answered:—

1. Are ova so derived readily fertilizable?

2. What will be the risk of congenital abnomalities? The recommended dosage is from 6 to 10 daily injections of human F.S.H. followed in 24-48 hours later by 3 day treatment with human C.G.H. (B.M.J. 1963:1:136.)

The deterent factor lies in the difficulties of collecting human pituitary glands and expenses involved therein. This may be solved by extracting F.S.H. from human menopausal urine now being attempted. Greenblatt (Fertility and sterility 1961:12:402) has been able to induce ovulation by chemical methods. The results have yet to be assessed. However, the day is not far off when induction of ovulation will no longer remain a difficult uncertain and an impracticable task.