MALE INFERTILITY

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and

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¶*This study includes the Analytical Data of 1268 Infertile couple investigated over a period of 4 years and 6 months. A male factor compromising fertility was diagnosed in 687 couples. The Different aspects of male Infertility— aetiological factors, diagnostic aids and therapeutic modalities—are discussed.*

Beginning in August 1975, over a period of 4 years and 6 months, 1268 couple were investigated and treated for problems of infertility. Following the routine clinical evaluation of both partners by the author, the preliminary investigations—Seminal study, mid-cycle post-coital test, premenstrual endometrial biopsy and hysterosalpingography—were completed in a particular order.

In addition to the clinical examination of the male, seminal study and post-coital test were also conducted in all cases. Six hundred and eighty seven men were adjudged to have some form of reproductive dysfunction contributing to the barren union giving a rather high incidence of male infertility viz. 54.18 per cent.

Disorders in the male reproductive function are usually associated with inadequate number or quality (or both) of spermatozoa in the ejaculate, disturbance of the function of sex accessory glands, inability to produce ejaculate, or inability to deliver the ejaculate into the female reproductive tract. Poor seminal quality associated with vascular abnormalities (varicocele), or endocrine disturbances, and disorders of the excretory accessory ducts such as block are the more clinically important types of reproductive failures of the male. Aetiology of male infertility

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as diagnosed in our series is given in Table I. Azoospermia was the commonest disorder encountered in just more than one half of the infertile men. Oligospermia without varicocele was the next common entity diagnosed in about 25 per cent of the defective men. Varicocele as the cause for oligospermia and infertility was diagnosed in 96 men (13.97%). Other factors such as necrospermia, sexual dysfunctions, anatomical defects and aspermia were only minor contributory factors.

TABLE I
Male Infertility & Aetiological Factors

From August 1975 to December, 1979
Total Infertile couple investigated: 1268
Male factors diagnosed in: 687 (54.18%)

Male factor	No. of patients	Percentage
Azoospermia	394	57.35
Oligospermia	173	25.18
Oligospermia with varicocele	96	13.97
Necrospermia	14	2.04
Sexual problems	5	0.73
Aspermia	3	0.44
Anatomical defects	2	0.29

Azoospermia

This was the commonest finding at the seminal study encountered in 394 of the 687 infertile men investigated (57.35%). Considering the total number of infertile couple evaluated (1268), the incidence of azoospermia is 31.07%.

To establish the cause for azoospermia, bilateral testicular biopsy was performed in 210 subjects. The testicular morphology was normal, denoting ductal obstruction, in 74 men (35.20%). The other subjects were suffering from varying grades of testicular failure, the only reversible type in this group was spermatogenic arrest encountered in 32 (15.20%). The other 50 per cent of azoospermic subjects were having irreversible type of tubular pathology such as tubular fibrosis in 33 (16.00%), Germinal cell aplasia in 23 (11.00%), Klinefelters' syndrome in 20 (9.50%) and multiple lesions in 28 (13.10%). From this study we have observed that only 50 per cent of azoospermic men have scope for any form of treatment, and the rest must be given proper guidance to accept A.I.D. or adoption. (Table II).

Size of the testes in azoospermic men offers a guide to decide the need for testicular biopsy. (Table III). Among the 123 men with normal sized testes about 80 per cent had reversible pathology, whereas 87 men with small sized testes had a predominantly irreversible type of lesion in about 90 per cent of subjects. Hence it is held that in the former group testicular biopsy is a must to differentiate obstructive azoospermia from testicular

TABLE II
Testes Biopsy in Azoospermia (210 men)

Normal Spermatogenesis		Testicular Failure									
		Spermatogenic arrest		Tubular fibrosis		Germ cell aplasia		Klinefelter		Multiple lesion	
No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
74	35.20	32	15.20	33	16.00	23	11.00	20	9.5	28	13.1
106 (50.40%) (Reversible changes)				104 (49.60%) (Irreversible tubular changes)							

TABLE III
Size of Testes and Morphology in Azoospermia

Size of testes	Normal Spermato-genesis		Testicular Failure									
			Spermato-genic arrest		Tubular fibrosis		Germcell aplasia		Kline-felter		Multiple lesion	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	Reversible change						Irreversible pathology					
Normal testes (123)	70	56.90	28	22.80	8	6.50	9	7.30	—	—	8	6.50
	98		(79.70)				25	(20.30)				
Small testes (87)	4	4.60	4	4.60	25	28.7	14	16.10	20	20.0	20	23.0
	8		(9.20)				79	(90.80)				

failures, and the latter group can be saved from the botheration of undergoing the biopsy procedure since they are predictably irreversible.

Results of treatment of azoospermia were quite disappointing, and nothing much could be done even in those men with a reversible type of testicular morphology. Five subjects with left sided varicocele, in whom the testicular biopsy was suggestive of spermatogenic arrest, were subjected to varicocelectomy with no improvement in seminal quality. Epididymo-vasal anastamosis was tried in 11 subjects with proved ductal block, and none of them showed any improvement. Among the two men (Post-vasectomy) who had sperms in the ejaculate following vasal anastamosis one could impregnate his wife.

In view of the fact that 50 per cent of azoospermic men have irreversible testicular failure, and the other 50 per cent with reversible testicular changes do not respond favourably with any form of treatment modalities, therapeutic insemination with donor semen (A.I.D.) has gained considerable importance. In fact, among the 240 couples registered for AID, 206 husbands were azoospermic. Predictably, the results for AID were quite satisfactory, with about 76 per cent conception rate in those undergoing treatment for atlest 6 consecutive cycles.

Varicocele

Varicocele is a well established cause of male infertility, and probably the one which gives impressive results with surgical correction. The seminal picture of subfertile men with varicocele is that of oligo-spermia of varying degrees, but of more importance is the marked impairment of sperm motility and also a definite increase of immature and tapering sperm forms in the ejaculum (Stress pattern). Testicular biopsy shows germinal cell hypoplasia and premature sloughing of immature sperm forms within the lumina of the seminiferous tubules. These cells are similar to those seen in the ejaculum and include the tapering forms and the spermatids.

The major problem in varicocele seems to be retrograde blood flow from the renal vein into the scrotal circulation secondary to incompetent values in the internal spermatic venous system. The problem

can be corrected by interrupting the course of the internal spermatic vein to prevent retrograde flow rather than by removing the dilated scrotal veins. This venous abnormality is usally left-sided, and hence the corrective surgery is needed in majority of cases only on the left side. In our series we have preferred the Ivanissevich procedure modified by Amelar and Dubin where the internal spermatic veins are ligated and partially excised at the internal inguinal ring.

While 67 subfertile men were operated only 57 could be followed after the surgery. Among them 43 (75.43%) had marked improvement in semen quality, and 23 (40.36%) succeeded in impregnating their wives. The pregnancies occurred at a mean of 8.6 months, with 12 conceptions (52.20%) occurring within 6 months, and 20 conceptions (87.00%) within 1 year of surgery. Results of varicocelectomy were more rewarding in those men with an initial sperm count of more than 10 million than those with less than 10 million (Table IV).

Idiopathic Oligospermia

This includes a wide group of subfertile men, and this diagnostic category embraces various, still-unidentified, pathologic states. These subjects do not have any demonstrable endocrinopathies, and most male partners of infertile couples fall within this diagnostic group. The common denominator is oligospermia associated with infertility. The gonadotropin levels are within normal limits, and testicular biopsy shows nonspecific damage to the seminiferous epithelium (adult seminiferous tubule failure). Some of these patients could have partial defects in steroidogenic enzyme activities which have been shown to respond to gonadotropin therapy, eventhough, in general, no adequate form of therapy is available. Recently it has been shown that, in some of these patients, ow normal levels of testosterone can be demonstrated which respond to stimulation with gonadotropins.

In the absence of precise and specific diagnosis, therapy of oligospermic subfertile male is difficult, tedious, and frequently unrewarding. Of the various forms of treatment available Gonadotropin therapy, whether direct (H.C.G. administration) or indirect via clomiphene citrate holds definite promise for a select group of subfertile men. Our experience with Human Chorionic Gonadotropin and Clomiphene Citrate (Fertyl) in subfertile oligospermic men (idiopathic) is as follows:

Human Chorionic Gonadotropin (H.C.G.)

Our regime of 3000 units of HCG twice

TABLE IV
Effect of Varicocelectomy on Oligospermia

Initial sperm count	Total patients		No. improved semen quality		No. Achieved conception	
	No.	%	No.	%	No.	%
Below 10^6	32	56.14	24	75.00	11	34.40
10^6 to 19^6	9	15.78	8	88.88	5	55.60
20^6 and above	16	28.08	11	66.75	7	43.75
Total:	57	100.00	43	75.43	23	40.36

a week for 10 weeks, was tried in 36 infertile men of whom 26 oligospermic patients ould be regularly followed. These patients were between 23 to 42 years and had a period of infertility ranging from 1 to 26 years (mean—4.3 years). Following treatment, 9 patients (34.61%) showed definite improvement and 7 (26.92%) could achieve pregnancy (Table V). Therapeutic response was more marked in those men with an initial sperm count of more than 10 million than in those with less than 10 million. The pregnancies occurred within 1 year of treatment; the earliest was after 2 months of therapy.

TABLE V

Human Chorionic Gonadotropin in Oligospermia

No. of oligospermic men treated	No. showing improvement		No. conception	%
	No.	%		
26	9	34.61	7	26.92

Clomiphene Citrate (Fertyl) (Table VI)

ence appears to show sufficient effectiveness in some oligospermic men, without producing undesirable side effects. Even-though its therapeutic application is in the most preliminary stage, it is a drug with a potential for becoming a part of the therapeutic armamentarium.

In this preliminary study we have selected 49 infertile men for treatment with clomiphene citrate (Fertyl). In this empirical study gonodotropin assays and testicular biopsies were not employed for selection of patients. Among the 49 men registered only 33 had regular treatment and follow-up, and of them 2 were azoospermic by the initial seminal study. Thus, there were 31 oligospermic subfertile men who had regular treatment with Fertyl. Age of these patients ranged from 23 to 45 years, with a mean of 32.10 years, and the duration of infertility ranged from 1 to 13 years (mean—4.85).

Fertyl was administered in a dose of 25 mgms (½ tab.3 daily for 25 days, with five days' rest, for 6 to 9 months or till pregnancy resulted in the wife. Semen study was repeated every 2 months. Obvious improvement in the seminal quality was observed in 23 (74.19%) of the 31 oligospermic men; 8 could (25.80%) impregnate their wives within 1 to 7 months of therapy. All the 3 parameters, namely, sperm count, viability and moti-

TABLE VI

Results of Clomiphene (Fertyl) Treatment in 31 Oligospermic Men

Particulars	Mean Sperm count (million)	Mean sperm motility (%)	Motility grading		
			II %	II+ %	III %
Before treatment	10.43	36.50	20.00	6.60	nil
After treatment	20.16	49.40	50.00	16.60	3.40

Improvement in semen quality in 23 (74.19%) Conception in 8 (25.80%).

Oligospermic subfertile men without any other diagnosable endocrine, anatomical, or sexual disorders are benefited by the administration of clomiphene citrate (Fertyl), as a method for improving spermatogenesis by the endogenous release of gonadotropins. Current experi-

lity grading had improved in those men who had achieved pregnancy following Fertyl therapy (Table VII).

TABLE VII

Concretion Following Clomiphene (Fertyl) Treatment in 8 Couples Changes in Seminogram

Case No.	Base line seminal picture			Following Fertyl therapy			Treatment-Conception Interval
	Count	Motility	Grade	Count	Motility	Grade	
I	34^6	40%	I	40^6	90%	II	One month
II	15^6	50%	II	22^6	35%	II	Two months
III	10^6	50%	I	12^6	80%	I	Four months
IV	15^6	20%	II	40^6	10%	III	Two months
V	15^6	30%	II	98^6	100%	II	Four months
VI	20^6	40%	II	28^6	100%	II+	Three months
VII	8^6	30%	II	—	not known	—	Two months
VIII	8^6	50%	II	9^6	50%	II	Seven months

This preliminary study on treatment of 'idiopathic oligospermia' definitely goes to prove that some patients respond by improving the seminal quality and resulting conception. The results appear comparable, whether treated by exogenous administration of gonadotropin or endogenous release of gonadotropin by Clomiphene citrate. If more careful patient selection is followed, better results could be anticipated. By determination of gonadotropin levels, serum testosterone concentration and the testicular morphology in oligespermic subjects the responsive group can be selected. Patients with 'Pregerminal hypofertility', identified by oligospermia of varying degree, normal serum FSH, LH and testosterone levels and testicular biopsy showing spermatogenic hypoplasia, can be predicted to respond favourably than these with 'primary germinal hypofertility'.

Conclusion

A brief summary of the therapy of the infertile male is presented. The significance of 'couple-directed' approach to infertility problem, and the importance of proper evaluation of the male partners by a team familiar with the disorders of the reproductive system in both sexes are highlighted. Careful and detailed evaluation of the 'infertile' males certainly brings to prominence those with a reversible disorder who could be hopefully treated.