Varicocele and Male Infertility II

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Introduction

F. H. Comhaire

Many diseases were, at the beginning, merely defined by the description of their clinical appearance. Next, the pathogenic mechanisms underlying the diseases were recognized. Since then, the proof of presence of the pathogenic agent or agents has been required to confirm the diagnosis.

However, it sometimes happens that the pathogenic agent can be demonstrated without the disease being clinically evident. Confusion arising from this observation may cause endless, often purely emotional discussions between "believers" and "non-believers". Moreover, if the disease involves potential disturbance of male fertility, the problem is further obscured by the difficulty of defining man's fertility. Indeed, during the short history of andrology, the criteria for judging a man and his ejaculate as potentially fertile or infertile have repeatedly changed. Andrological "landmarks" in general do not hold up for long, and some scientists continue to set themselves the task of proving the "old" definitions invalid.

Certainly, such developments are necessary to make science more exact and to improve medical care. However, while this research is being done, the male partners of barren marriages continue to seek advice and treatment. Common sense and an empirical approach in the handling of these cases may result in obviously encouraging results, which non-believers will ascribe to "witchcraft" and believers will see as confirmation of their opinions.

Varicocele probably is the example of such a disease or condition. The puzzle of varicocele consists of many pieces; the exact place of each piece is not yet clear and many pieces are still missing. The large number of adolescent males who have varicocele makes it difficult to consider this condition a disease. On the other hand, as a result of their varicocele some men present so severe an alteration of their vital capacity to reproduce, that in them this condition must be considered pathological.

As usual, both believers and non-believers probably are right to some extent. However, our knowledge about varicocele will not increase if non-believers waste their efforts in trying to prove the believers wrong, and vice versa.

When Ekke Jecht and I decided to organize this symposium we tried to attract the main authorities in the field of varicocele research. An excellent opportunity for this task was the inclusion of the symposion on varicocele as an integral part of the 2° International Congress of Andrology, held in Tel Aviv which attracted leading andrologists from five continents. Though we know that at the end of the symposium the puzzle will not be complete, we certainly hope some progress will have resulted.

Varicocele and Male Infertility II
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I. Physiopathology

New Concepts in Pathogenesis and Treatment of Varicocele

A. Shafik

Varicocele is an established cause of male infertility. Its controversial etiology initiated several investigations into its anatomical, physiological and pathological aspects. A new concept of varicocele pathogenesis and treatment is described here.

Physioanatomical Considerations

Fasciomuscular Tube of the Spermatic Cord

The fasciomuscular tube consists of three layers which are extensions of the anterior abdominal wall musculature. These layers comprise the external and internal spermatic fasciae, and between them, the m. cremaster with fascia. Microscopic studies showed the tubal fasciae to consist mainly of elastic fibers impregnated with collagen and arranged in a crisscross pattern, lending the fasciae a textile nature (Fig. 1) [19].

The fasciomuscular tube is divided into two compartments, the anterior, or pampiniform and the posterior, or vasal, the two being separated by a "transverse fascial septum" deriving from the internal spermatic fascia (Fig. 2) [4, 19]. The pampiniform compartment, surrounded by a fascial tube from the internal spermatic fascia, encloses the pampiniform plexus and the testicular artery. The vasal compartment, surrounded by a similar fascial tube, ensheathes all of the ductus deferens with its artery, the vasal venous plexus and the m. cremaster internus [5, 9].

The Musculi Cremaster

There are two mm. cremaster, the externus and internus. The m. cremaster externus arises from the mm. obliquus internus abdominis and transversus abdominis, extends along the spermatic cord and testicle, and inserts into the tunica vaginalis. It exists in three patterns: single, double, and most commonly, diffuse (Fig. 3) [5].

The m. cremaster internus, as identified in the human (Fig. 2) [5, 9], originates from the m. transversus abdominis and descends in the spermatic cord, commonly in the vasal compartment and rarely in the pampiniform

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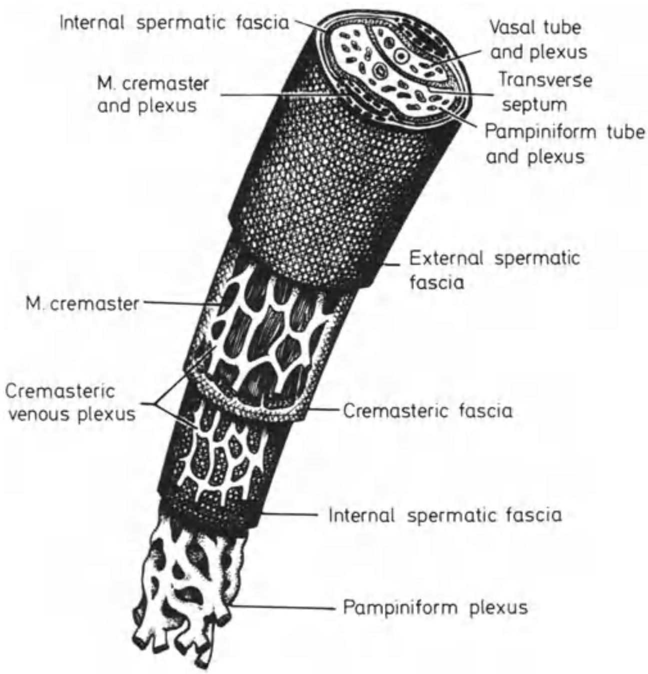

Fig. 1. The fasciomuscular tube and the venous plexuses related to it. The crisscross textile nature of the fasciae is demonstrated. (From Shafik et al. [19])

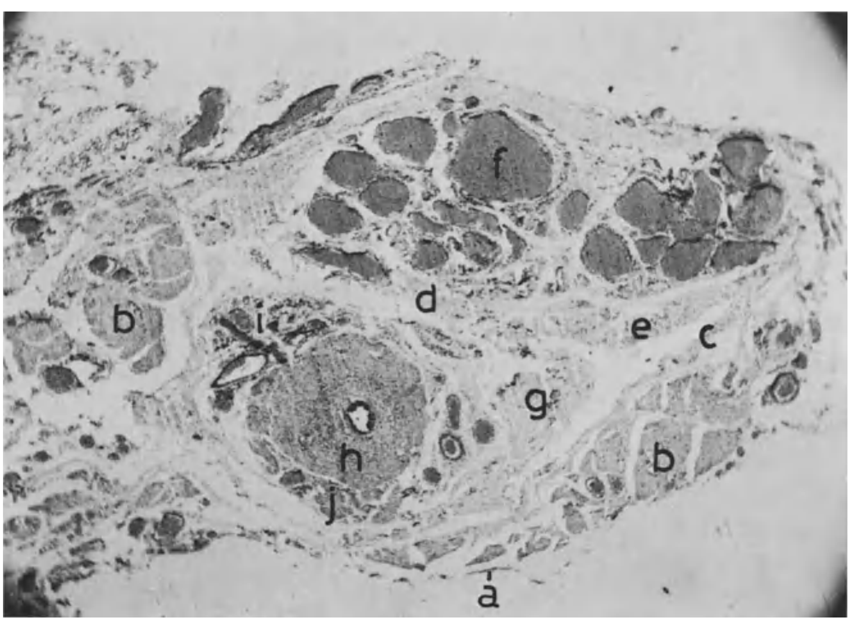

Fig. 2. Transverse section of the spermatic cord showing the cord compartments, the venous plexuses, and the m. cremaster internus. Hematoxylin and eosin, × 28. *a* external spermatic fascia; *b* m. cremaster; *c* internal spermatic fascia; *d* transverse septum; *e* pampiniform tube; *f* pampiniform plexus; *g* vasal tube; *h* ductus deferens; *i* vasal plexus; *j* m. cremaster internus. (From Shafik et al. [19])

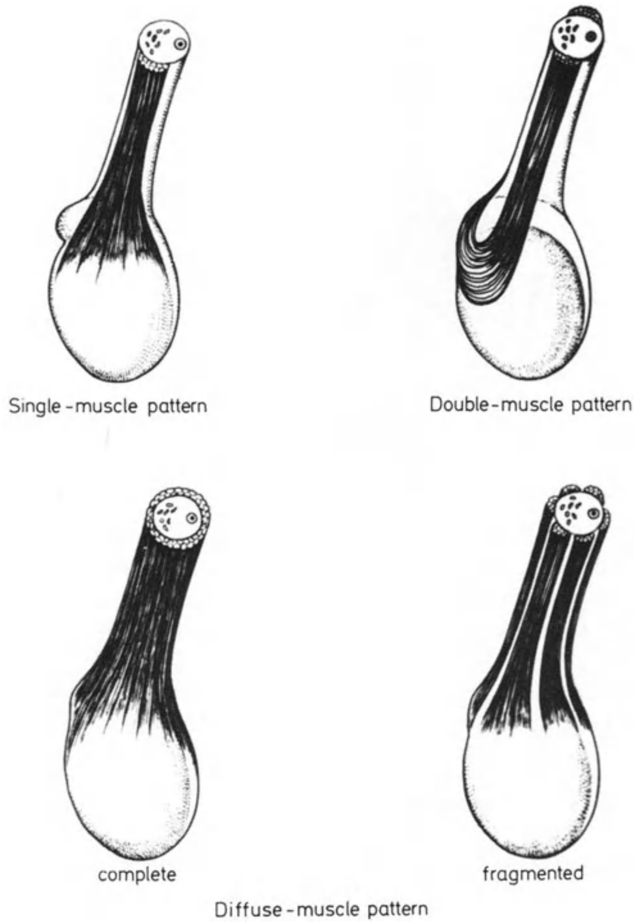

Fig. 3. Diagram of the m. cremaster patterns. (From Shafik [5])

compartment. It inserts into the tunica vaginalis. In spite of their similar origin and common termination, there is no connection between the mm. cremaster externus and internus since they are separated by the internal spermatic fascial tube. The m. cremaster internus seems to help in the draining of the ductus deferens.

The Scrotal Ligament

At the scrotal bottom is the scrotal ligament, a small fibromuscular band which ties the dartos closely to the testicle at its lower pole (Fig. 4) [6, 10]. It consists of muscle bundles with collagen fibers scattered between them, and is more developed and muscular in children than in adults. Elsewhere, the dartos is loosely connected with the underlying fasciomuscular tube by areolar tissue.

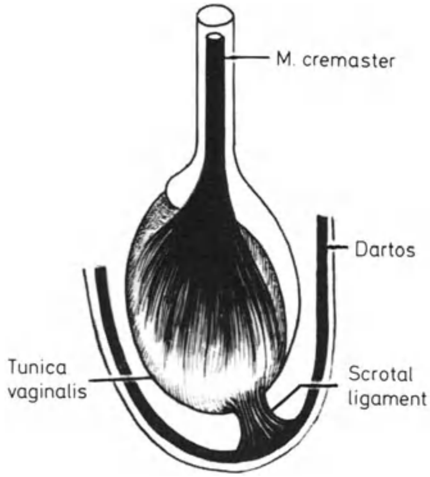

Fig. 4. Diagram of the scrotal ligament. (From Shafik [10])

The ligament plays a significant role in testicular thermoregulation in that it provides the mechanism which keeps the testicular movements in harmony with those of the dartos. Furthermore, it constitutes a connection, along the testicle, between the dartos and the m. cremaster, thus synchronizing the action of both muscles [10]. Absence of the scrotal ligament disturbs the thermoregulatory mechanism of the testicle, and leads to the syndrome of "aligamentous testicle" which may cause male infertility [16].

The Fasciomuscular Pump

A study of the anatomical and histological structure of the fasciomuscular tube has shown that it has more important functions than being a mere fascial covering of the spermatic cord and the testicle [4, 5, 19]. It acts as an "autoelastic stocking" which supports the cord veins. In addition, it constitutes a "pump" by which the blood is pushed up the cord. For this purpose, the spermatic and cremasteric fasciae are provided with a very large number of elastic fibers. The crisscross pattern of fibers provides the fasciomuscular tube with maximal efficiency necessary to its functional performance. The tube possesses a sphincteric action on the cord veins which is greatly potentiated by the contraction of the m. cremaster (Fig. 5). This mechanism participates in pumping the blood from the testicle and the cord.

The pumping effect is augmented by division of the fasciomuscular tube into two compartments by the transverse fascial septum. The spermatic cord is thus composed of two units, each representing a separate pump containing its own venous plexus, the anterior containing the pampiniform plexus and the posterior containing the vasal plexus. Each pump is surrounded by a layer of elastic fascia (internal spermatic fascia) and supported by a muscular cushion (m. cremaster). The two units are wrapped together by an outer common elastic fascia (external spermatic fascia). This arrangement helps to increase the fasciomuscular pump efficiency.

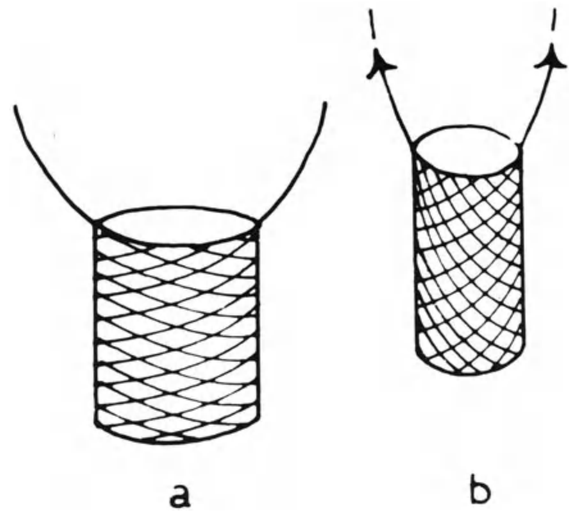

Fig. 5a, b. Diagram of the sphincteric action of the fasciomuscular tube. **a** The tube at rest; **b** the tube during contraction. (From Shafik [11])

The impregnation of the elastic fibers of the fasciomuscular tube with collagen has an important function. Being inelastic, the collagen fibers limit excessive relaxation of the tube. This prevents tubal subluxation which might result from venous stagnation during erect posture.

Venous Plexuses of the Spermatic Cord

A previous study [4] has shown that the cord veins are arranged into two systems; the superficial consists of the cremasteric plexus, and the deep one includes the pampiniform and vasal plexuses. The two systems are separated by the internal spermatic fascia and wrapped together by the external spermatic fascial tube (Fig. 2).

The Pampiniform Plexus. The largest plexus is the pampiniform, which lies in the anterior cord compartment. At the lower part of the cord the veins are of small size with poor muscularization. Valves are found in two to three central veins (Fig. 6). At the midcord and external inguinal ring level, the veins are larger, more muscular, and valveless (Fig. 7). The plexus, at the midinguinal level, consists of two large, well-muscularized and valveless veins surrounded by three to four small ones.

The Vasal Plexus. A small plexus which lies in the posterior cord compartment is the vasal plexus. It is formed of small, poorly muscularized and valveless veins arranged around the ductus deferens (Fig. 8).

The Cremasteric Plexus. The veins of the cremasteric plexus lie between the m. cremaster bundles; a few are found scattered in the cremasteric and external spermatic fasciae (Fig. 8). They are smaller than the pampiniform veins, poorly muscularized and valveless.

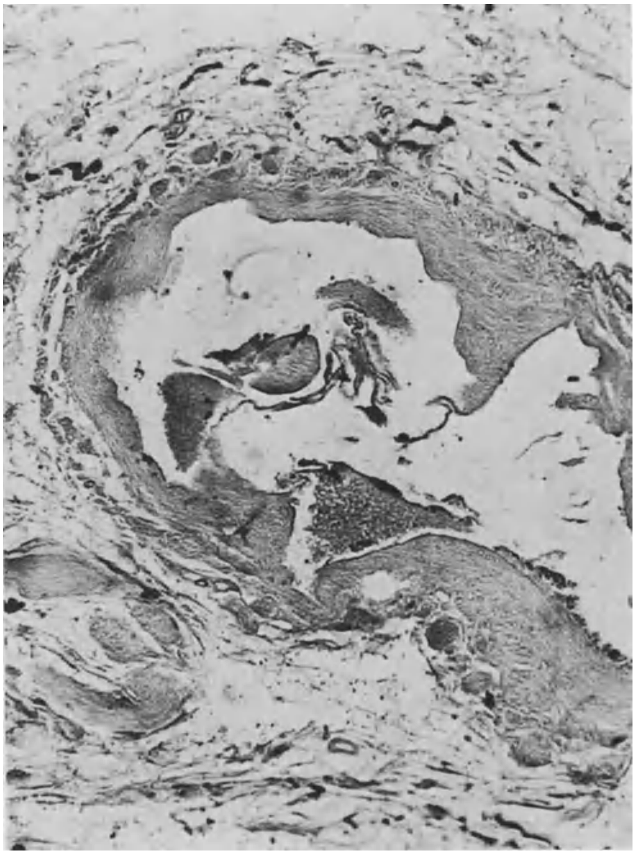

Fig. 6. Photomicrograph showing a valve in a pampiniform vein. Gomori, × 250 (From Shafik [4])

Communicating Veins. The small, poorly muscularized and valveless veins which connect the three cord plexuses are the communicating veins. They traverse the cremasteric and spermatic fasciae and transmit blood in both directions. They are especially abundant between the pampiniform and cremasteric plexuses.

Venous Return from the Testicle

The pampiniform and vasal plexuses collect the venous blood from the testicle and epididymis, while the cremasteric plexus drains the fasciomuscular tube. In the erect position, blood is returned to the heart by the pumping action of the fasciomuscular tube, the m. cremaster being the main component of the pump [5, 19]. Each plexus presents certain anatomical features in adaptation to its function [4]. Adequate muscularization of the pampiniform veins augments the

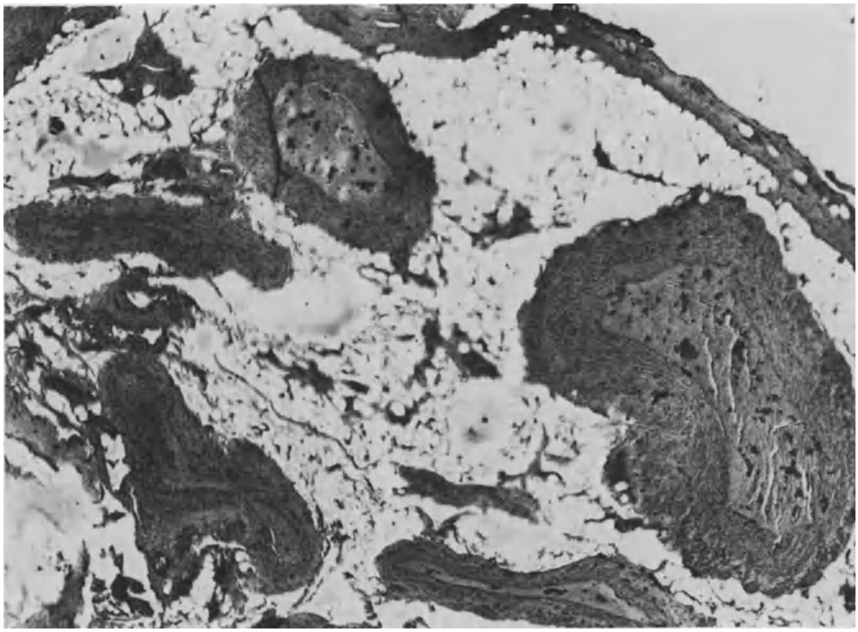

Fig. 7. Photomicrograph of the spermatic cord at the external inguinal ring level, showing that the pampiniform veins are fairly muscular. Hematoxylin and eosin, × 100. (From Shafik [4])

pumping mechanism efficiency of the pampiniform plexus. The pampiniform valves provide a protective mechanism against testicular congestion. Snapping shut when the venous pressure rises during increased intra-abdominal pressure, they prevent the full force of this high venous pressure from being transmitted to the testicle. With increased venous pressure and closure of the pampiniform valves, the blood draining from the testicle escapes via the communicating veins to the other valveless plexuses from where it is ejected upwards through the fasciomuscular tube pumping action. These natural mechanisms are designed to prevent testicular congestion and its injurious effects on spermatogenesis.

The location of the cremasteric plexus between the m. cremaster bundles increases its venous drainage efficiency. This is important, as the plexus may have to cope with extra blood escaping from the pampiniform veins when the pampiniform valves shut upon venous pressure elevation. Further, as the cremasteric veins lie outside the strong internal spermatic fascial tube and are poorly muscularized and valveless, they yield easily in adaptation to the extra blood volume. For this reason, cremasteric plexus dilatation and varicosity occur early in varicocele [4].

The vasal veins are well supported by the ductus deferens and by their location within a narrow fascial compartment. This renders the veins less liable to dilatation and varicosity.

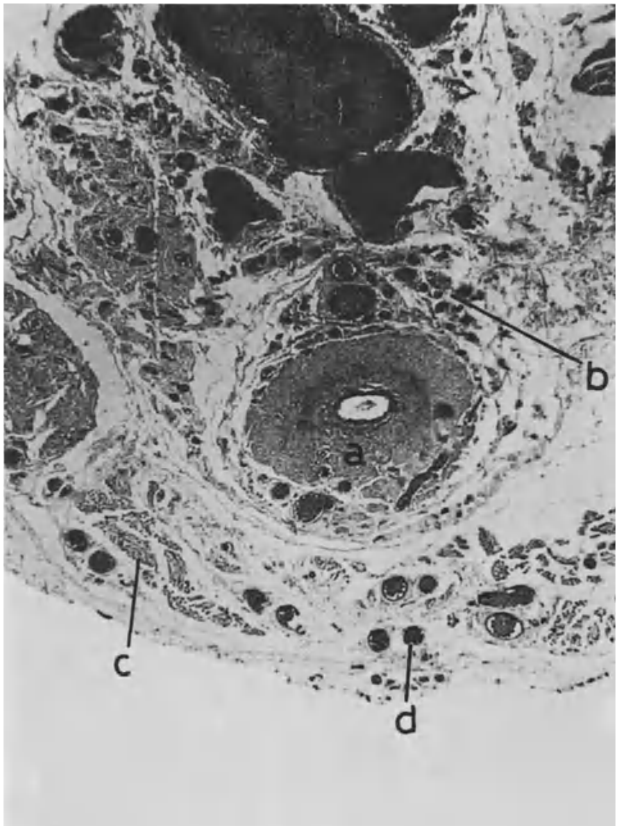

Fig. 8. Photomicrograph of the lower part of the spermatic cord showing the vasal venous plexus in the posterior cord compartment. The cremasteric plexus lies between the cremasteric muscle bundles and fascia: *a* ductus deferens; *b* vasal plexus; *c* m. cremaster; *d* cremasteric plexus. Hematoxylin and eosin, × 100. (From Shafik [4])

Pathogenesis of Varicocele

The Tubovalvular Antireflux Mechanism

The tubovalvular antireflux mechanism is provided by the fasciomuscular tube and the testicular vein valves to protect the testicle from the high venous tension induced by increased intra-abdominal pressure [4–6, 11, 19]. As a prolongation of the abdominal wall muscles, the tube remains in harmony with changes in them. When these muscles contract, increasing intra-abdominal pressure, there is simultaneous contraction of the m. cremaster (being a part of the mm. obliquus internus and transversus), as well as traction on the spermatic fasciae in a longitudinal direction (being extensions from the m. obliquus externus and fascia transversalis). This mechanism effects constriction of the fasciomuscular tube and tightens the elastic stocking around the cord veins and the testicle, thus preventing venous reflux from the abdominal veins to the testicle (Fig. 5). Together with the shutting of the valves of the testicular veins, this mechanism prevents the full force of the high venous pressure from being transmitted to the testicle.

The location of the valves in the testicular system of veins varies. However, whether they are located low down in the pampiniform veins as demonstrated by Shafik [4] or high up in the testicular vein as recorded by Revington [2] and Kohler [1], the valves function to prevent venous reflux to the testicle. Nevertheless, the scarcity and inconsistent position of the valves emphasize the importance of the tubular antireflux mechanism as compared with the valvular one [11].

The Role of the Fasciomuscular Tube in Varicocelogenesis

A study of the fasciomuscular tube in primary varicocele showed that it was flabby and capacious, with degeneration and atrophy of the m. cremaster and the elastic fibers [5, 19]. Due to tubal subluxation, the sphincteric action of the tube is lost, efficiency of the pumping mechanism is reduced, and the cord veins are supported less and cannot withstand increased venous pressure during muscular contraction. In addition, the squeezing effect of the elastic fibers is lost, owing to their atrophy. As a result, the tubovalvular antireflux mechanism is disturbed: the veins become engorged with blood and dilated, which in turn renders the valves incompetent. This throws an additional load onto the already weakened tube and pumping mechanism. The chain of events which lead to a varicocele is thus initiated.

The tube, in addition to its function as a venous pump, suspends the testicle in its normal position in the scrotum. Tubal subluxation leads to a lowered testicular position which results in further blood stagnation and varicosity.

In light of this new concept, a varicocele is considered to result from dysfunction of the fasciomuscular venous pump, attributable to a subluxated tube rather than to a disease of the veins themselves [5, 19]. An operation [3] in which the tube is plicated by multiple purse-string stitches has been successfully practiced for the correction of the atrophic subluxated tube and the cure of a varicocele. In severely atrophic tubes, as in advanced and recurrent varicoceles, a fascia lata graft of the tube produced satisfactory results [7].

The Role of the Fasciomuscular Tube in Testicular Thermoregulation

The fasciomuscular tube, by its sphincteric action on the cord veins, plays an important role in the temperature-regulating mechanism of the testicle [5, 8]. On contraction, the tube – especially its cremasteric component – compresses the cord veins. The resulting diminished blood volume and shrinking of the exposed cord surface area prevent heat loss. Meanwhile, the testicular temperature increases owing to the testicle being drawn near the warmer body surface. Tubal relaxation leads to an increased blood volume within the cord veins, a greater exposed cord surface area, and a lowered testicular position – a mechanism which favors heat loss. The active contractile function of the m. cremaster is so marked in some animals that the testicle can be retracted within the abdomen and extruded into the scrotum voluntarily. This occurs in most rodents, many insectivores, and bats [20].

Venous Tension in Varicocele

A recent study on venous tension patterns in the cord veins [12, 13] has shown that the average normal venous tension with the individual at rest is 58.7 mm Hg on the right side and 59.9 mm Hg on the left side. In varicocele patients, venous tension on the right, nonvaricose side is slightly above normal with an average of 59.6 mm Hg, whereas on the left, varicose side, it is considerably higher, the average being 79.6 mm Hg. During Valsalva's maneuver, the venous tension on the left, varicose side is elevated to an average of 83.8 mm Hg.

These figures demonstrate conclusively the presence of venous hypertension in varicose veins, which is an effect of venous backflow as evident from the marked increase in venous tension after Valsalva's maneuver. These data further show that the high venous tension is not transmitted across the communicating veins from the varicose to the contralateral side, as indicated by the nearly normal tension values in the latter.

Venous reflux and hypertension eventually lead to congestion, dilatation, and varicosities of the cord veins. Cord congestion results in impaired venous drainage of the testicle with a consequent testicular congestion and possibly accumulation of toxic testicular metabolites. The latter could be responsible for inhibiting the spermatogenic function of the testicle.

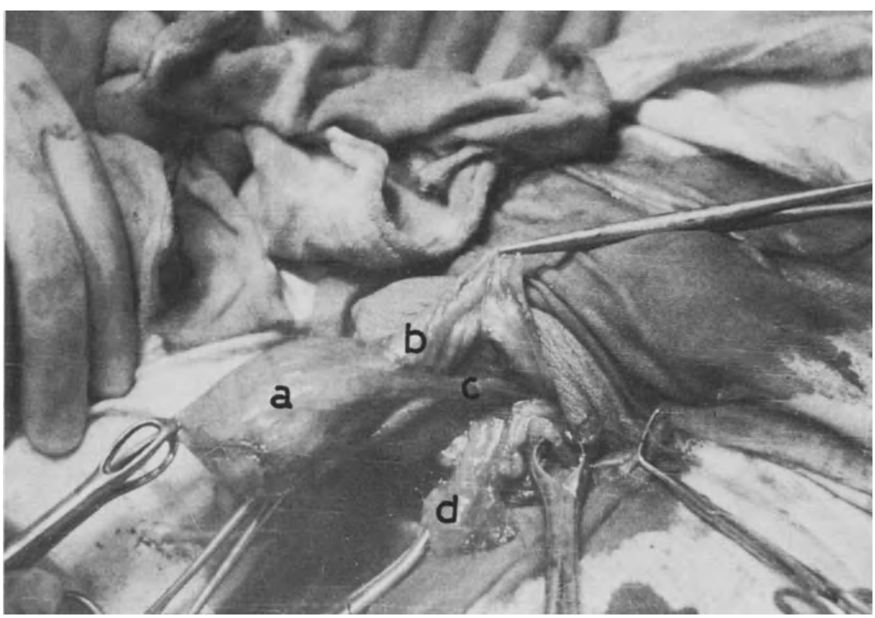

Fig. 9. Operative view showing normal fat pattern in infertile subject: *a* testicle; *b* spermatic cord; *c* fasciomuscular tube, opened; *d* posterior extratunicary pad of fat. (From Shafik and Olfat [17])

Scrotal Fat and Varicocele

The anatomy of the scrotal fat was studied histologically in 28 normal cadavers and in 44 infertile subjects [17, 18]. Two fat patterns were described, normal and infertile. According to its relation to the fasciomuscular tunics of the spermatic cord, fat can be extra-, inter-, and intratunicary.

In the normal fat pattern, a small extratunicary triangular pad of fat is consistently encountered posterior to the cord (Fig. 9). It is continuous over the pubic ramus with the suprapubic fat. Intratunicary fat occurs as small granules between the cord veins.

Of the 44 infertile subjects, 38 showed excess and abnormally distributed fat, a condition I describe as "scrotal lipomatosis", of which two types are recognized: extratunicary and intratunicary [17]. In the former, a thick pad of fat containing multiple small tortuous veins exists posterior to the spermatic cord (Fig. 10). The latter presents in two patterns, diffuse and lobular. The diffuse pattern occurs both in obese subjects and in those of normal build. The fat takes the form of a diffuse sheet which covers, and is adherent to, the cord veins (Fig. 11). The lobular pattern (Fig. 12) occurs exclusively in the obese. The fat lobules are easily separable from the cord veins. Each lobule has a pedicle which can be traced along the inguinal canal to the extrapertioneal fat. The pedicles gather in the inguinal canal to form a "lipomatous cord" which suspends the testicle high in the abdomen.

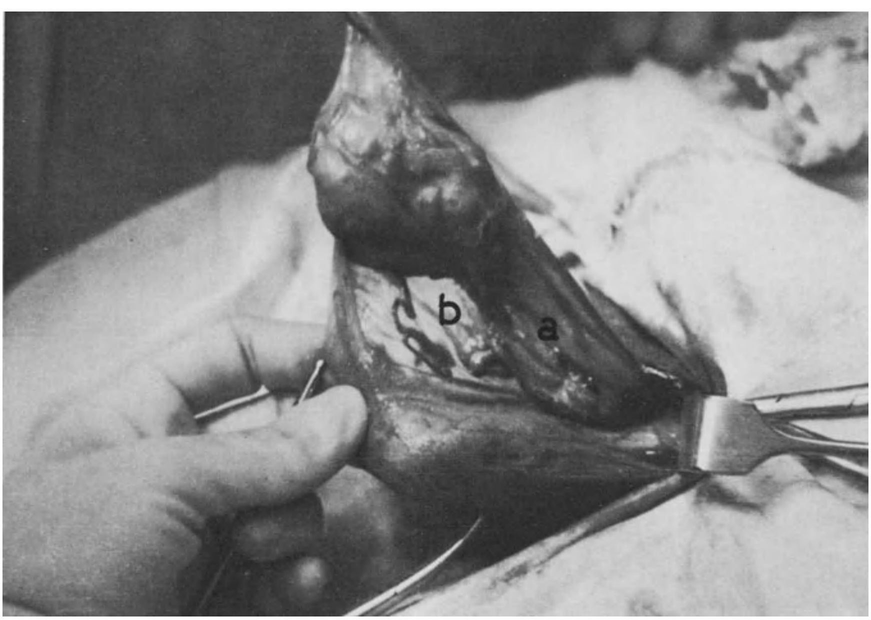

Fig. 10. Operative view of lobular lipomatosis in infertile subject showing the posterior extratunicary pad of fat containing tortuous veins: *a* spermatic cord; *b* extratunicary fat. (From Shafik and Olfat [17])

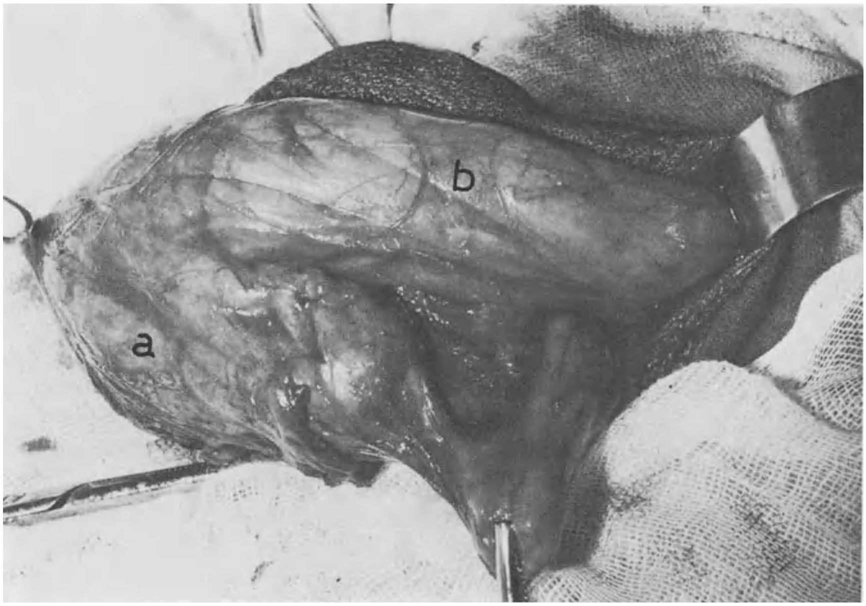

Fig. 11. Operative view showing diffuse lipomatosis of the spermatic cord in infertile subject. The fat extends down to cover the testicle: *a* fat pads covering the testicle; *b* spermatic cord. (From Shafik and Olfat [17])

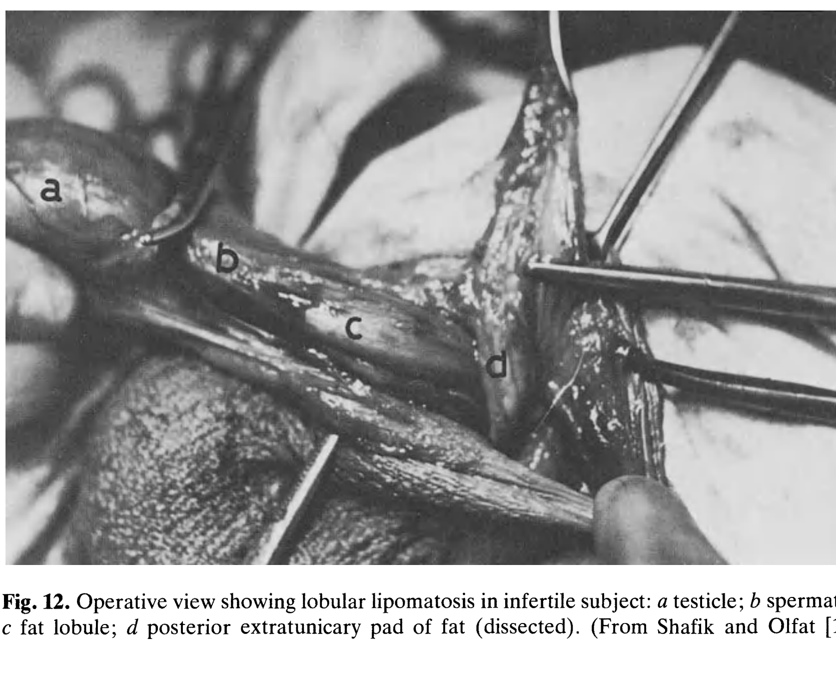

Fig. 12. Operative view showing lobular lipomatosis in infertile subject: *a* testicle; *b* spermatic cord; *c* fat lobule; *d* posterior extratunicary pad of fat (dissected). (From Shafik and Olfat [17])

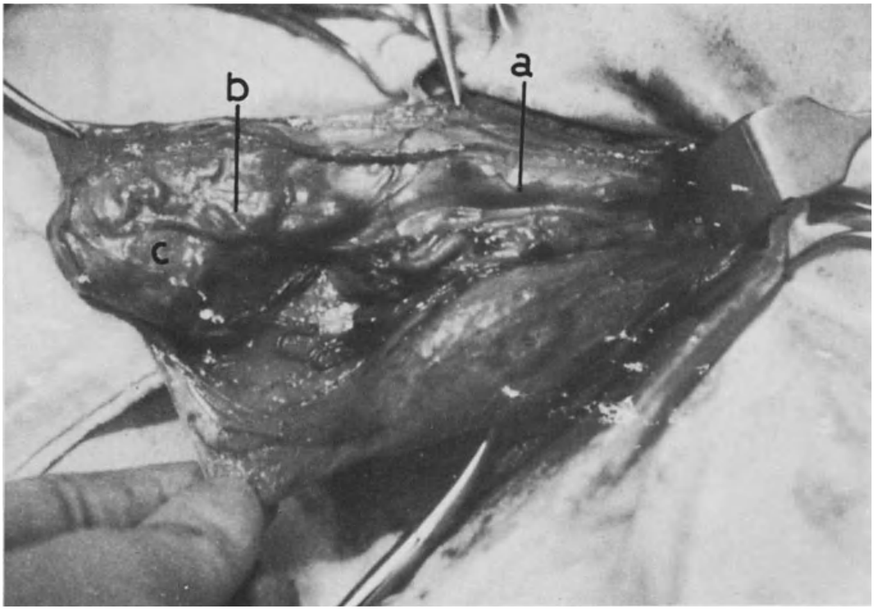

Fig. 13. Operative view showing cremasteric and pampiniform varicosity in infertile subject with lobular lipomatosis. Extratunicary and intratunicary fat were removed: *a* pampiniform varices; *b* cremasteric varices; *c* testicle. (From Shafik and Olfat [17])

Cord Varicosity in Scrotal Lipomatosis

At operation the cremasteric veins were found to be dilated and tortuous in all of the 38 cases of scrotal lipomatosis [17]; pampiniform varicosity was also present in 20 cases (Fig. 13). Cord varices were not palpable clinically, being masked by lipomatosis. However, in seven patients with diffuse lipomatosis there was scrotal redundancy, which could indicate cord varicosity.

Cord varices in scrotal lipomatosis seem to be due to venous stasis, resulting from the intratunicary fat compressing the veins and interfering with the venous pumping mechanism [17]. Scrotal redundancy in diffuse lipomatosis is due to cord varicosity. However, it is not evident in lobular lipomatosis, despite cord varicosity, as the testicle is supported by the "lipomatous cord".

Pathology of Varicocele

A study of the histopathological changes of the cord veins in 28 patients with left-sided varicocele was performed [14]. Twenty-five patients were infertile and three had fathered children.

The cremasteric veins were varicose in all cases. They were best identifiable over the anterior aspect of the tunica vaginalis, being the only veins in this area. The veins were small and tortuous. They lay under the glistening external

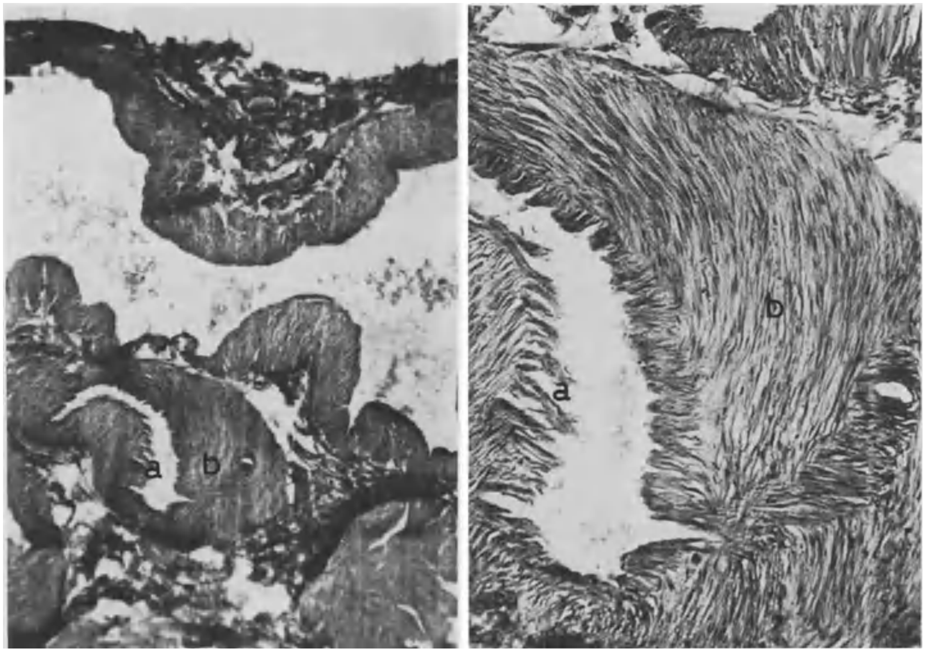

Fig. 14. Photomicrograph of varicose pampiniform veins. The intima shows papillary projections. The media is greatly thickened and its muscle bundles are hypertrophied: *a* intima; *b* media. Hematoxylin and eosin; *left* × 50, *right* × 185. (From Shafik and Olfat [14])

spermatic fascial tube, and varicosity became less manifest as the veins were followed up the cord. The pampiniform plexus, which was revealed after the internal spermatic fascial tube had been opened, occupied the anterior cord compartment. The varicosity was maximal at the back of the testicle, and diminished gradually as it extended upwards. Pampiniform varicosity occurred in 25 patients.

At operation, pampiniform varices were distinguished from cremasteric ones in that (a) they covered the testicular back and not the front as occurs in cremasteric varices, (b) they were under cover of the internal fascial tube, and (c) they were larger.

The vasal venous plexus was not varicosed in any patient, and in the inguinal canal, no varicosities whether cremasteric, pampiniform, or vasal could be detected.

Microscopic study of the pampiniform veins showed the intima thrown into folds in some specimens and with papillary formations in others (Fig. 14). The tunica media was greatly thickened due to muscular hypertrophy; in some specimens it was hyalinized (Fig. 15) and in others it was fragmented in its outer aspect. The adventitia was slightly thickened. In hugely dilated and tortuous veins septa could be demonstrated transecting, partially or completely, the venous lumen (Fig. 16). They consisted of hypertrophied muscle bundles

Fig. 15. Photomicrograph of a varicosed pampiniform vein showing hyalinization of the media: *a* intima; *b* media. Hematoxylin and eosin, × 62. (From Shafik and Olfat [14])

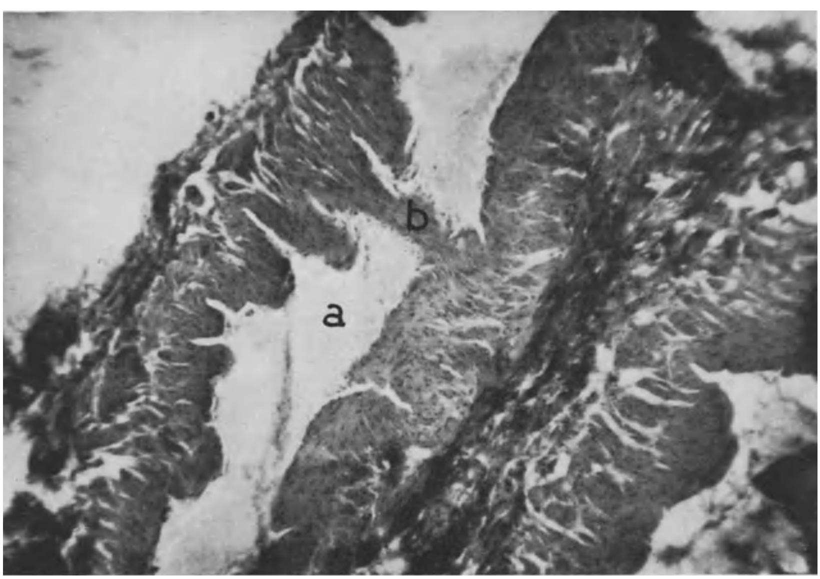

Fig. 16. Photomicrograph of a varicosed pampiniform vein showing a complete septum transecting the venous lumen: *a* venous lumen; *b* complete septum. Hematoxylin and eosin, × 62. (From Shafik and Olfat [14])

continuous with those of the media, and were lined with intimal endothelium.

The cremasteric veins had regular intima, while the media was hypertrophied, with hyalinized areas. The vasal veins were microscopically normal.

Pathological Staging of Varicocele

Whatever the primary etiological factor of varicocele may be, venous hypertension in the cord veins is a constant feature and is responsible for the different pathological changes which occur in both the cord veins and the testicle (Fig. 17) [13]. In varicocele development, the increased venous pressure leads to hypertrophy of the media. In the early stage, the veins are thickened but not dilated. Venous stasis does not occur, because the venous pumping mechanism efficiency is augmented due to the medial hypertrophy.

With further increase of venous tension, there is increased medial hypertrophy and venous pumping power until the muscle bundles overstretch

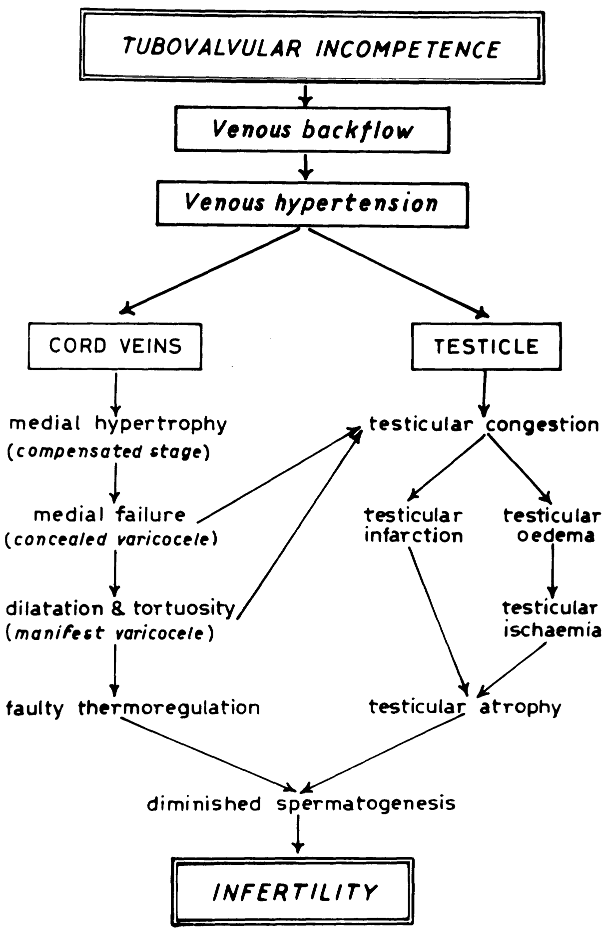

Fig. 17. Mechanism of varicocele formation

and fail. During this stage, the pumping mechanism efficiency is reduced and blood stagnates. This results in more venous tension which burdens the already failing pumping mechanism. A vicious circle which leads to cord vein congestion is thus created. With prolonged venous hypertension, degenerative changes as evidenced by hyalinization and fragmentation affect the venous wall. Later on, atrophy and fibrosis lead to tortuosity and sacculation of the veins.

The development of septa in the hugely dilated veins seems to be a mechanism provided by nature to fractionate the large, heavy blood column within these veins in an attempt to augment the efficiency of the venous pumping mechanism and to minimize venous stasis [14]. The mechanism of septa formation is mysterious. It could be that kinking of the veins due to tortuosity results in the formation of projections within the venous lumen. The blood backflow and venous hypertension exert their effects on these projections leading to their hypertrophy and incomplete septa formation. These septa may fuse with denuded intimal areas in the venous wall, with a resulting complete septa formation. The septa seem to protect the testicle as much as possible from the detrimental effect of the venous backflow and hypertension which occur in advanced varicocele.

Thus, three pathological stages can be identified in varicocele: hypertrophy, failure, and dilatation [14].

Hypertrophy (Compensated Stage). The earliest stage of varicocele is hypertrophy. The veins are thickened. There is no blood stasis as the venous return is kept normal by the compensatory medial hypertrophy. No testicular congestion or spermatogenic depression occurs at this stage. Clinically, the patient is symptomless, and cord veins are not dilated.

Failure (Concealed Varicocele). The continuous rise of venous tension results in medial failure and venous stasis. At this stage, there is cord and testicular congestion, although the cord veins are clinically not varicose. Palpable thickening of the veins may be detected. I call this stage "concealed varicocele" [15]. It is of special clinical interest since there is testicular congestion and possible spermatogenic depression although varices are clinically undetectable. "Concealed varicocele" could thus be responsible for idiopathic infertility in some patients in whom no varicocele can be detected by clinical examination.

Dilatation (Manifest Varicocele). With prolonged and sustained venous hypertension, degeneration and atrophy of cord veins result in dilatation and varicosity. This is the stage of "manifest varicocele" in which testicular congestion and spermatogenic depression are maximal. Clinically, the cord veins present the classical varicocele picture.

Anatomical Staging of Varicocele

With venous hypertension and medial failure, congestion and dilatation manifest primarily in the cremasteric plexus, being the least supported. When this plexus is fully engorged, the pampiniform veins are the next to congest and dilate. Vasal plexus varicosity occurs only late, as the plexus is well supported.

Accordingly, a varicocele has three anatomical stages: cremasteric, pampiniform, and vasal [14]. They are not separate types, but different stages in one process of venous congestion.

Cremasteric Varicosity (Stage I Varicocele). In the earliest stage of varicocele, the cremasteric is the first plexus to react to venous hypertension in the cord veins because (a) it is less supported, owing to its location outside the rigid internal spermatic tube; (b) its veins are poorly muscularized [4]; and (c) the communicating veins between the cremasteric and other venous plexuses, being numerous, transmit the high venous tension from inside to outside the internal spermatic tube [4].

Pampiniform Varicosity (Stage II Varicocele). With maximal cremasteric plexus dilatation and continuously increasing venous tension, the pampiniform plexus starts to congest and dilate. The pampiniform veins can absorb high venous pressure for long periods because (a) they are numerous with ample collaterals; (b) they are well muscularized and thus effect appreciable resistence to venous tension [4]; and (c) they are adequately supported, being enclosed within the internal spermatic tube.

Vasal Varicosity (Stage III Varicoceles). Vasal varicosity occurs late in varicocele. Being well supported by the ductus deferens and by its location inside the narrow vasal compartment, the vasal plexus requires a rather high venous tension to varicose. For this reason, vasal varicosity was not encountered in a series of 28 varicocele patients [14]. It seems to occur in secondary varicocele owing to testicular vein obstruction by a tumor; this would create venous tension high enough to overcome the extra support provided to the vasal veins.

The Bilateral Effect of Varicocele

The cause of the bilateral effect of varicocele, leading to infertility, is not known. A recent study [13] excludes the possibility of the effect being caused by a contralateral venous reflux and hypertension, since venous tension on the nonvaricose sides of the infertile patients was found normal or negligibly elevated. However, it could be the difference in venous tension between both sides that allows the blood to flow across the rich communicating veins, carrying toxic metabolites from the varicose high-tension side to the other lower-tension side [13]. Furthermore, it seems that these metabolites should reach a certain concentration to induce a contralateral inhibitory effect. This would explain the disordered spermatogenesis with infertility in some cases of varicocele, and normal semen quality with adequate fertility in others.

Tunica Dartos in Varicocele

The surgical anatomy of the dartos was studied in both normal and varicocele subjects [6]. Normally, the muscle bundles are arranged separately and not in fasciculi. They decussate in a crisscross pattern, and the blood vessels occupy the spaces between the decussating bundles. Each scrotal compartment has its own dartos, and both muscles share in the scrotal septum formation.

In varicocele, the scrotal skin is thinner on the affected side than on the control side, and the dartos is attenuated and acquires a more superficial position. The spaces between the decussating bundles are wide and contain dilated and thin-walled vessels.

Role of Dartos in Testicular Thermoregulation

The dartos muscle bundles, being arranged in a crisscross "plywood" pattern, constitute potential "sphincters" around the blood vessels between their decussations [6]. When the muscle contracts, the intervening vessels are constricted, resulting in diminished scrotal blood flow, a mechanism which minimizes heat loss (Fig. 18). Meanwhile, the testicle is elevated close to the warm body surface. With dartos relaxation, the potential sphincters relax, leading to increased blood circulation and heat radiation (Fig. 18). The testicle is drawn away from the body surface by the scrotal ligament.

Another mechanism is provided by the dartos meshwork arrangement: Mesh obliteration by dartos contraction helps to preserve the intrascrotal temperature, while the opening up of meshes encourages heat loss.

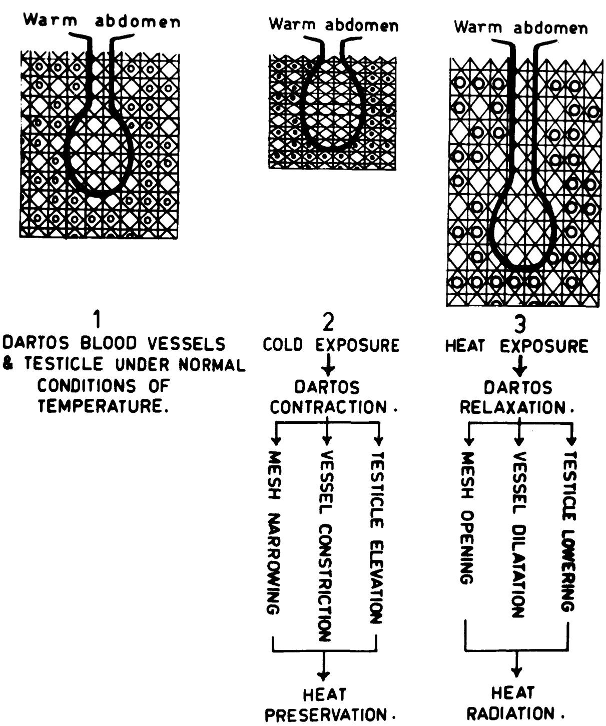

Fig. 18. Mechanism of thermoregulatory function of dartos. (From Shafik [6])

Role of the Dartos in Varicocele

The histologic changes in the scrotal skin and dartos in varicocele indicate a thermoregulatory function in adaptation to the increased intrascrotal temperature. The thinning of the scrotal skin, the opening up of dartos meshes, and blood vessel dilatation all encourage heat radiation. Furthermore, dartos relaxation pulls the testicle, through the scrotal ligament, away from the warm abdomen.

Cremasterico-Darto-Venous Complex

The testicle possesses a "thermoregulatory apparatus" which maintains a constant scrotal-rectal temperature difference. It consists of the cremasterico-darto-venous complex which includes the m. cremaster and the dartos, as well as the cord and scrotal vessels [8]. The complex is structurally adapted to serve as a thermostat for the testicle. Its components work collectively and spontaneously in reaction to changes in environmental temperature. The cremasterico-dartos component, through its sphincteric action, regulates the amount and rate of blood flow within the cord and scrotal vessels. In addition, it changes the exposed surface areas of both the scrotal skin and spermatic cord. Thus, on exposure to heat, cremasterico-dartos relaxation increases the cord and scrotal blood flow and exposed surface area, factors which encourage heat radiation. Conversely, cremasterico-dartos contraction preserves testicular temperature by diminishing the cord and scrotal blood flow and surface area.

The aeration induced by the dartos meshes or "windows" [6], and the heat radiated from the warm abdominal wall are accessory factors to the cremasterico-darto-venous complex. Closure of the dartos windows on dartos contraction transforms the scrotum into a thermoisolated cavity; the testicles, being high in the scrotum, gain warmth from the abdominal wall. Opening of the dartos windows by dartos relaxation, while the testicles are in a lowered position, helps testicular aeration and heat radiation.

Weight-Bearing Mechanism of the Testicle and Varicocele

Under normal temperature conditions, the testicular weight is carried by the fasciomuscular tube, especially its cremasteric component, and not by the dartos or the spermatic cord [6]. With variations in scrotal sac temperature, the dartos goes into action. Thus, on exposure to cold, both the dartos and the m. cremaster contract, carrying the testicle in close proximity to the warmer abdominal surface. Under the influence of heat, both muscles relax, the testicle being carried by the m. cremaster only, the dartos functioning to pull the testicle away from the abdomen by the scrotal ligament [10]. With excessive scrotal elongation, as in varicocele, the testicular weight is taken off the m. cremaster by the spermatic cord, which thus becomes stretched. The scrotal pain in varicocele is attributable to overstretching of both the m. cremaster and the spermatic cord because of excessive scrotal elongation [6].

Plication Operation in the Treatment of Varicocele

Previous studies [4–6, 19] have shown that the fasciomuscular tube of the spermatic cord plays a significant role in the venous pumping mechanism of the cord and that it is consistently subluxated in varicocele. Accordingly, the plication operation [3] has been devised to correct the subluxated tube and the disordered pumping mechanism. The technique has by now been performed in 380 varicocele patients.

Technique

The spermatic cord, within its tube, and the testicle are brought out through a transverse scrotal incision. The tunica vaginalis is everted. The fasciomuscular tube is plicated by multiple purse-string stitches, 0.5 in. apart, starting close to the testicle and continuing up to one finger's breadth below the superficial inguinal ring (Fig. 19). The stitches, 3/0 silk placed by an atraumatic needle, should include the whole tubal thickness, and in the lower part of the cord, the everted tunica as well. They are cautiously tightened to afford support, but overcorrection is avoided. If the tube is too capacious, as occurred in 83 cases, a

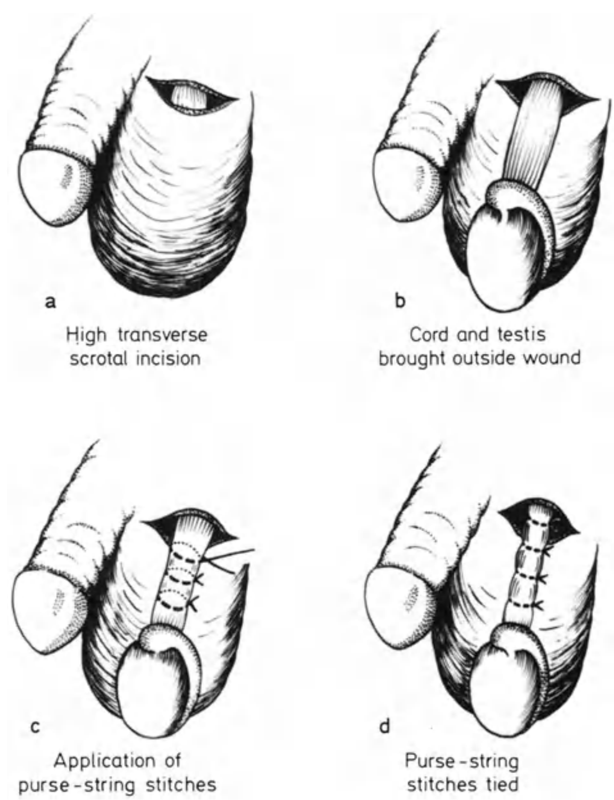

Fig. 19. Plication operation for varicocele. The spermatic cord is plicated with multiple purse-string stitches. (From Shafik [3])

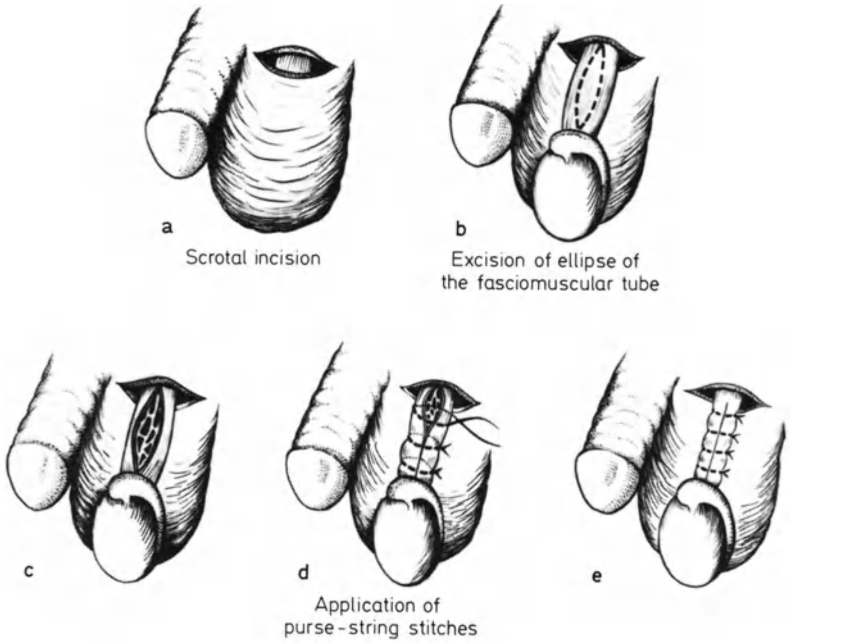

Fig. 20. Plication operation. Excision of longitudinal strip of the fasciomuscular tube prior to application of purse-string stitches. (From Shafik [3])

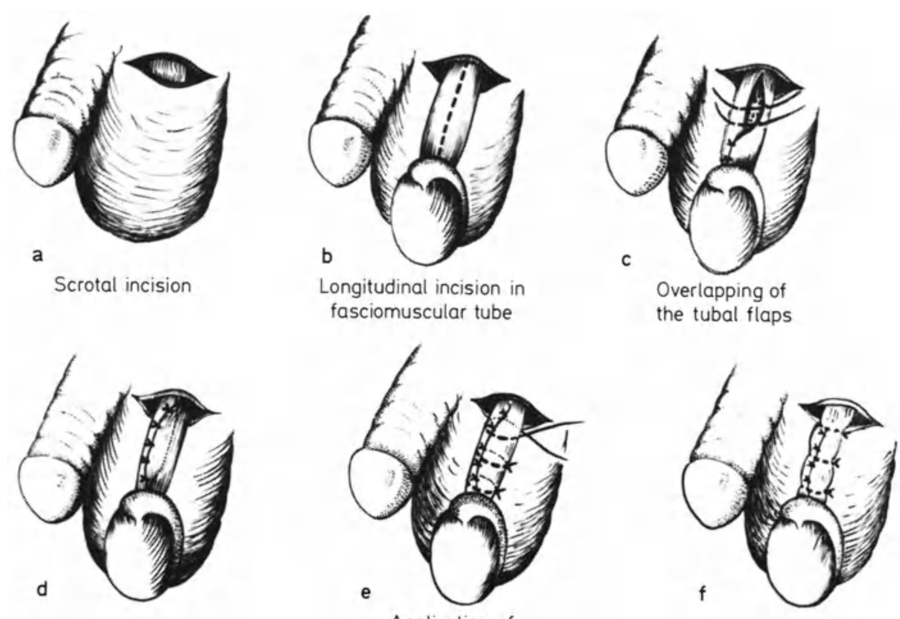

Fig. 21. Plication operation. Incision and overlapping of the fasciomuscular tube prior to application of purse-string stitches. (From Shafik [3])

longitudinal strip is excised prior to the application of the purse-string stitches (Fig. 20). In another 62 cases the capacious tube was incised longitudinally and its two flaps were overlapped before the purse-string stitches were applied (Fig. 21). The testicle is then replaced into the scrotum, and the wound closed with drainage. The operated scrotal compartment is suspended to the abdominal wall by a silk stitch for 48 h.

Results

The convalescent period was uneventful. Intrascrotal hematoma did not occur in any patient. Of the 380 patients operated on, 348 were followed up for periods varying between 1.5 and 5 years. No testicular atrophy was encountered. Recurrence of varicocele occurred in four patients (1.1%).

Pre- and postoperative measurement of the venous tension in the right and left cord veins was performed in 38 patients of the series [12]. All patients showed preoperative venous hypertension and reflux in the left cord veins (Table 1). The readings with the patients at rest varied from 70 to 92 mm Hg with an average of 81.8 mm Hg, and during Valsalva's maneuver from 76 to 96 mm Hg with an average of 85.8 mm Hg. Venous tension in the right cord veins

Table 1. Preoperative venous tension in 38 infertile varicocele patients

	Venous tension (mm Hg)			
	Left side		Right side	
	At rest	During Valsalva's maneuver	At rest	During Valsalva's maneuver
Mean	81.8	85.8	60.5	61.7
SD	± 5.1	± 5.2	± 5.3	± 5.8
Range	70–92	76–96	52–74	54–80

SD = Standard deviation
$p \leqq 0.05$

Table 2. Postoperative venous tension in 38 patients

	Venous tension (mm Hg)			
	Left side		Right side	
	At rest	During Valsalva's maneuver	At rest	During Valsalva's maneuver
Mean	60.8	62.5	59.5	60.4
SD	± 1.8	± 1.82	± 5.1	± 5.5
Range	55–64	58–66	52–74	53–78

SD = Standard deviation
$p \leqq 0.05$

was within normal range in all patients (Table 1) with the exception of four who showed venous hypertension despite absence of both cord varicosities and reflux.

Postoperatively, venous tension on the left side normalized in all patients, with disappearance of both varicosities and reflux. With the patient at rest, venous tension varied between 55 and 64 mm Hg with an average of 60.8 mm Hg, while it varied between 58 and 66 mm Hg with an average of 62.5 mm Hg during Valsalva's maneuver (Table 2). In the right cord veins, postoperative venous tension remained at normal levels (Table 2). The four patients with bilateral venous hypertension showed left venous tension normalization, but no change in the right venous tension. Subsequent right-sided plication operation corrected venous hypertension on the right side, too.

Merits of the Operation

Plication aims at the correction of tubal subluxation in order to reestablish an efficient fasciomuscular pump [3]. The improvement which follows the operation may be attributed to (a) the better support of the cord venous plexuses, preventing their dilatation and improving the pumping mechanism efficiency; and (b) venous decongestion, which is achieved early by the support of the purse-string stitches and later by the fibrosis induced by them.

The effectiveness of the operation was demonstrated in the present series by the disappearance of both varicosities and reflux, and by normalization of venous tension. The operation does not disturb the cord contents, especially the arterial supply to the testicle and epididymis. It is worth mentioning that the different operations devised for varicocele therapy have always been directed towards the treatment of the mechanical effects of varicosity rather than towards the primary abnormality. In this respect, the plication operation may be regarded as an attempt to correct a basic factor responsible for varicocele formation.

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Induced Varicocele in an Animal Model and Comparisons With Clinical Patients

R. M. Harrison and R. W. Lewis

Many tests that need to be conducted to provide data concerning the causal factors of infertility associated with varicocele cannot be ethically conducted in human patients. In 1975 we began efforts to establish an animal model that would present clinical patterns similar to those seen in humans with varicocele. Our model is the monkey, *Macaca fascicularis,* and the varicocele is induced by placing a Silastic device around the left renal vein between the insertion of the left testicular vein and the vena cava. The device restricts the renal vein by about 60%, but due to in flexibility this restriction varies from 50% to 75%. Dilation of the left spermatid vein is almost immediate.

The animals stadied to date include controls and restricted groups. In the control groups mon reys were either sham restricted only or sham restricted with left adrenalectomy in the restricted group the monkeys were restricted only or restricted with left drenalectomy. No differences have been seen within the control group or within the restricted group, i.e., adrenalectomy has not affected the results found tɔ date.

At six months, ultcastructure changes are seen in the left testes of restricted monkeys. These changes include delamination and thinning of the basal lamina, enlargement of the spaces between the basal cells, cytoplasmic vacuolation and swelling of endoplasmic reticulum in Sertoli cells and spermatogonia, and some swelling and vasculation of the nuclear membrane. There are no degenerative changes seen in the control animals or in the right testes of restricted animals at six months. At 18 months, there is more extensive damage to spermatids in the left testes of restricted animals, and the right testes at this point exhibit changes similar to those seen on the left one year earlier. These findings [2] are similar to those reported in clinical patients by Cameron et al. [1] and Okuyama et al. [3].

Testosterone levels at 52 weeks after varicocele induction range from 3.3 to 19.7 ng/ml in the restricted animals. These values are well within the episodic variation of this species and varicocele does not, at this time, appear to influence testosterone values in peripheral blood. This parallels our findings in clinical patients and those reported by Rege et al. [4].

Our intratesticular thermistor probe and contact scrotal thermography readings have shown excellent agreement but the differences in left testicular temperatures have not been significant. There is an increase in left testicular temperature of about 0.17° C at one year.

The finding that monkeys with varicocele induction concomitant with left adrenalectomy develop the same patterns as those with varicocele induction and

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intact adrenals suggests that adrenal metabolites refluxed into the testicular venous system do not influence the changes seen in varicocele patients.

Five monkeys with varicoceles and decreased motility of sperm were subjected to high ligation of the left testicular vein at one year after induction. Three months later, three had shown increases in the percentage of motile sperm and in the grade of motility. This is similar to the general response seen in clinical cases.

Biochemical analysis of semen has included assays for maltase, fructose, lactate dehydrogenase, acid phosphatase, citric acid, and total protein. No significant differences have been found between the control groups and the restricted groups.

The results of semen analysis show no significant changes in sperm concentration. There have been decreases in sperm motility in varicocele monkeys, as well as increases in abnormal sperm morphology.

Our studies indicate that the animal model we have developed is an excellent one, closely paralleling human clinical cases. Varicocele is present in all restricted animals but the degenerative changes are not equal in all monkeys. The testicular changes are progressive, beginning on the left and continuing to the right, as has also been reported in pubertal boys by Okuyama et al. [3]. There is no clear relationship between varicocele and peripheral blood testosterone levels, also as described in humans [4, 6]. There are no changes in seminal biochemical markers; this agrees with studies reported in humans by Rodrigues-Netto and de Castro [5].

The close agreement of data obtained from this animal model and those obtained from clinical patients indicates that this model may provide the tool to determining why varicocele may cause infertility, whether the condition is progressive to a point of irreversible damage, and how a varicocele patient is best treated for optimal prognosis.

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Histological and Enzyme-Histochemical Studies on Varicocele Orchiopathy

N. Hofmann, B. Hilscher, D. Passia, S. G. Haider, and W. Hilscher

Biopsy material from infertility patients, suffering from varicocele orchiopathy as diagnosed by clinical and spermatological analysis, was processed for histological and enzyme-histochemical examinations.

The patients showed various degrees of varicocele (from subclinical to third degree) with different degrees and durations of damage (early varicocele up to "burnt out" cases) [10]. The venous reflux was determined and confirmed with Valsalva's maneuver, ultrasonic Doppler investigations and phlebographic methods.

However, venous reflux does not necessarily indicate a varicocele orchiopathy. Our investigations on autopsy testicular material, employing effusion objects prepared by pouring Plastogen G (A. Schmidt Co, Mainz, Germany) into v. testicularis and v. ductus deferens as well as into v. cremasterica (unpublished results) have revealed that there is an extensive network of peritesticular phlebostomoses. In some cases this network creates crosses, that is drainage veins, through which the pathological reflux can be drained out [6, 7].

Results

Observations on Blood Vessels, Tunica Albuginea and Boundary Tissue of Seminiferous Tubules

The formation of intratesticular varicosities was demonstrated in varicocele orchiopathy with the help of ATPase reaction (Fig. 1). Generally the venous blood vessels increased in number with an enlargement of the lumen. The walls of the venous blood vessels were thickened, and marked by hyalin deposition. Similarly, the number of intratesticular lymph spaces and capillaries increased. These changes are well known.

Similar changes in the blood vessels of tunica albuginea and tunica vasculosa have not been reported till now. The vascular band of tunica vasculosa, which is normally thin (Fig. 2), was markedly enlarged by multiplication and enlargement of veins, with degeneration signs in the sheath structures; multiplication and enlargement of lymph capillaries; and pronounced tissue oedema (Fig. 3).

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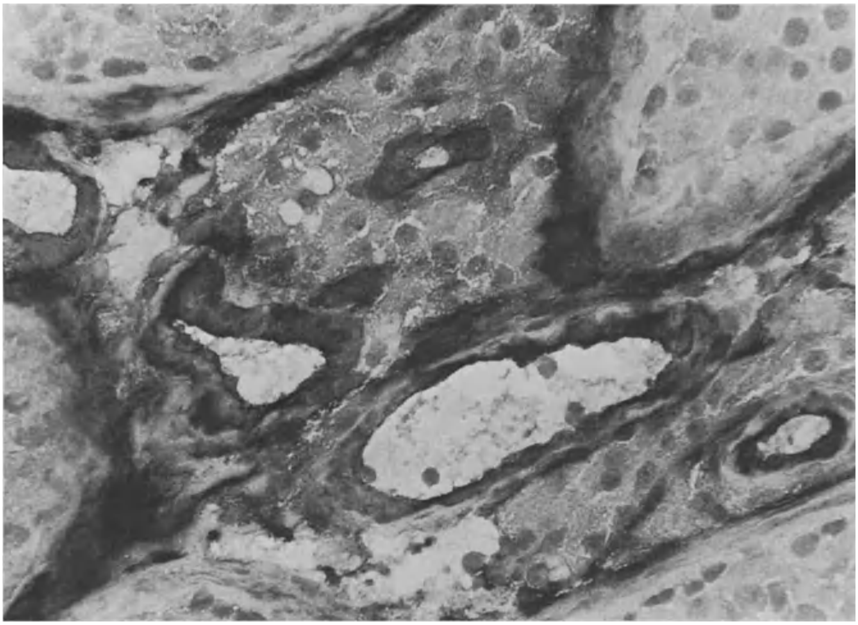

Fig. 1. Intratesticular varicosity in a case of varicocele orchiopathy. ATPase, acetone-prefixed cryostate section, × 25

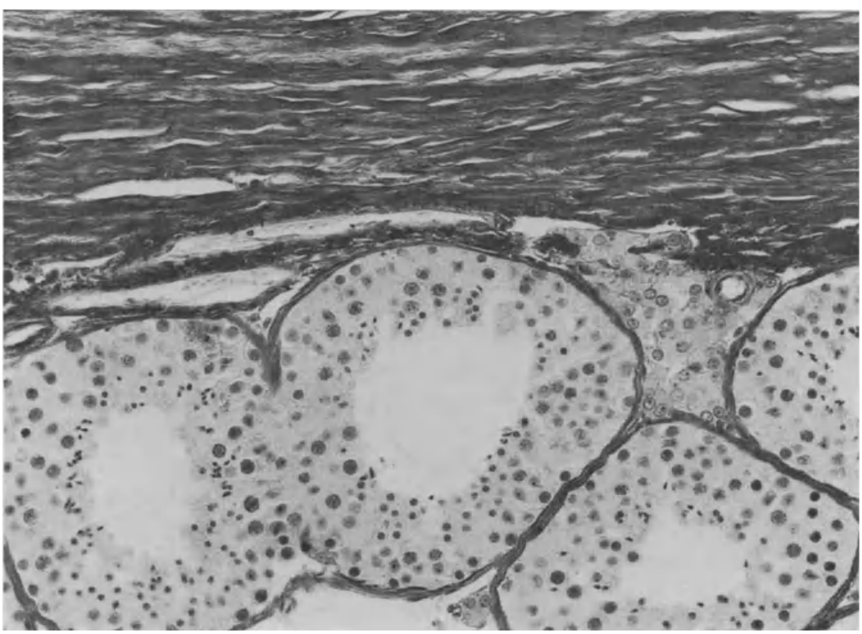

Fig. 2. Normal tunica albuginea and tunica vasculosa. Bouin's fluid fixation, van Gieson's stain × 10

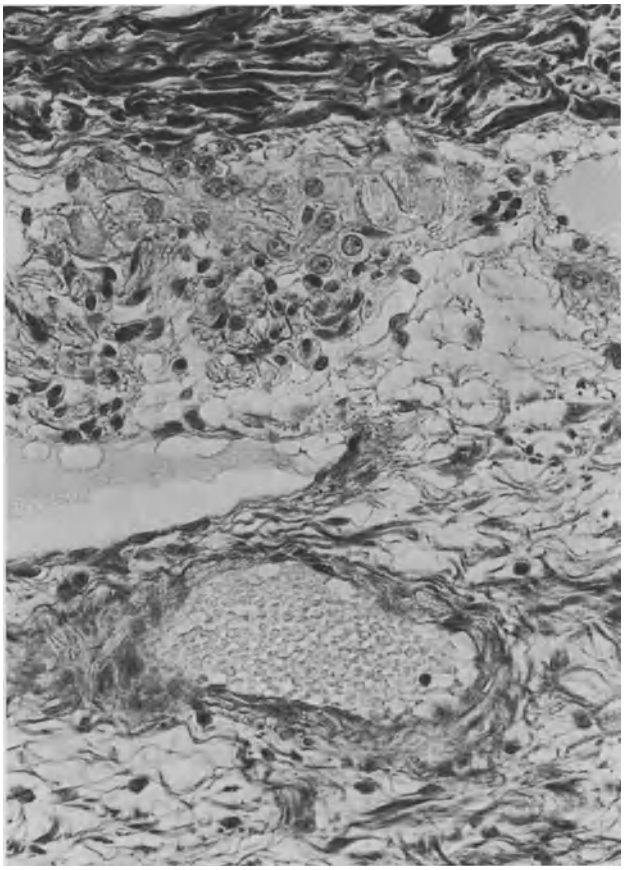

Fig. 3. Tunica vasculosa in a case of varicocele orchiopathy. Bouin's fluid fixation, van Gieson's stain × 25

Noteworthy were the Leydig cells in the vicinity of lymph capillaries with a normal morphological appearance (Fig. 4). The tunica albuginea was thick and had spread owing to the increased number of muscle fibres; it contained Leydig cells. In cases of advanced varicocele orchiopathy, enlarged lymph capillaries were observed within the tunica albuginea.

From these findings we conclude that increases in the number of muscle fibres and intratunical Leydig cells are compensation mechanisms which occur when the contractile function of tunica albuginea is affected in varicocele orchiopathy. We interpret the enlarged intratunical lymph capillaries observed in the later stages of the disease as a sign of decompensation.

Another marked finding in the tunica vasculosa is the presence of throttle veins ("Drosselvenen") (Fig. 5) and arteries, which have not so far been studied in detail, and seem to be multiplied in this disease [4]. Neuroendocrine corpuscles are present in their neighbourhood (Fig. 6).

Arterioles and small arteries were also involved in the varicocele orchiopathy. The changes were characterized by a swollen intima and a stenosis

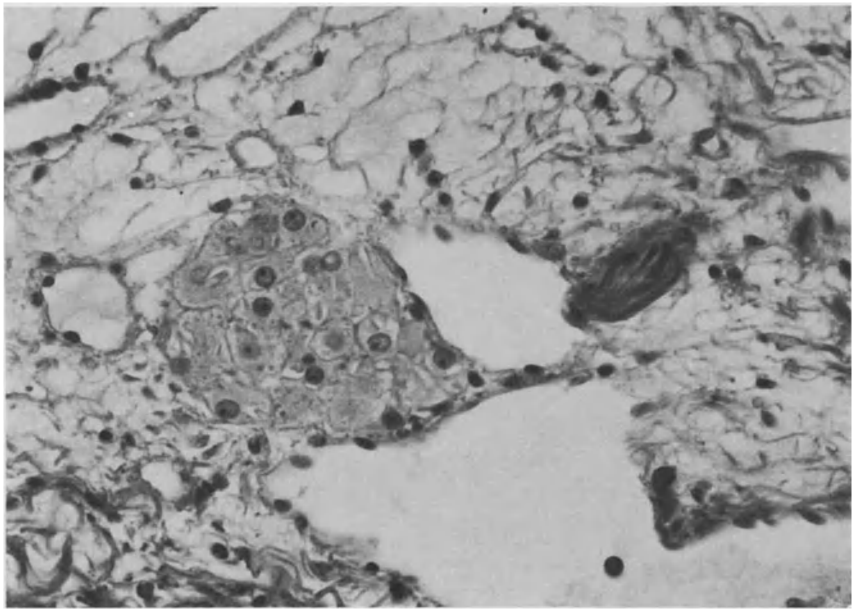

Fig. 4. Leydig's cells in the vicinity of lymph capillaries, tunica vasculosa. Bouin's fluid fixation, van Gieson's stain × 25

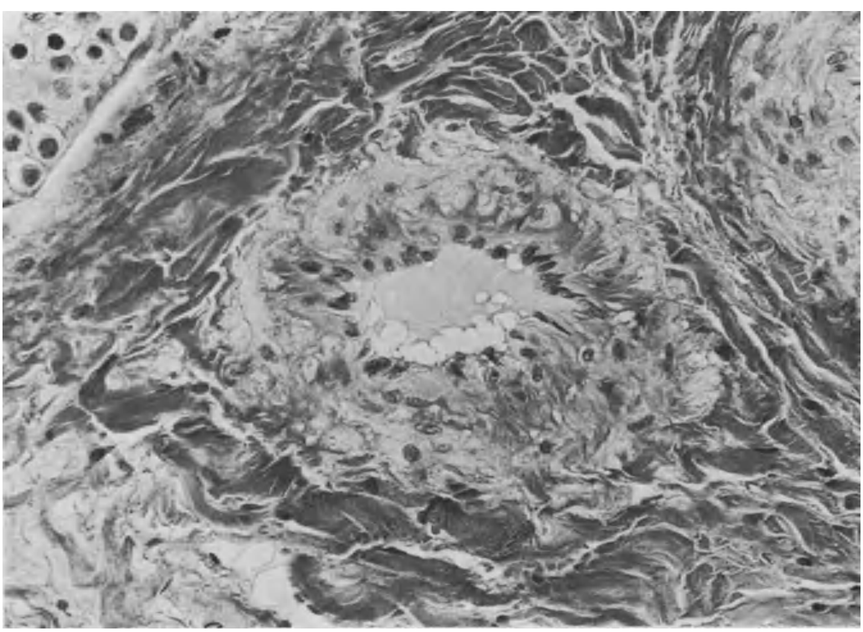

Fig. 5. Throttle vein in tunica vasculosa. Bouin's fluid fixation, van Gieson's stain × 63

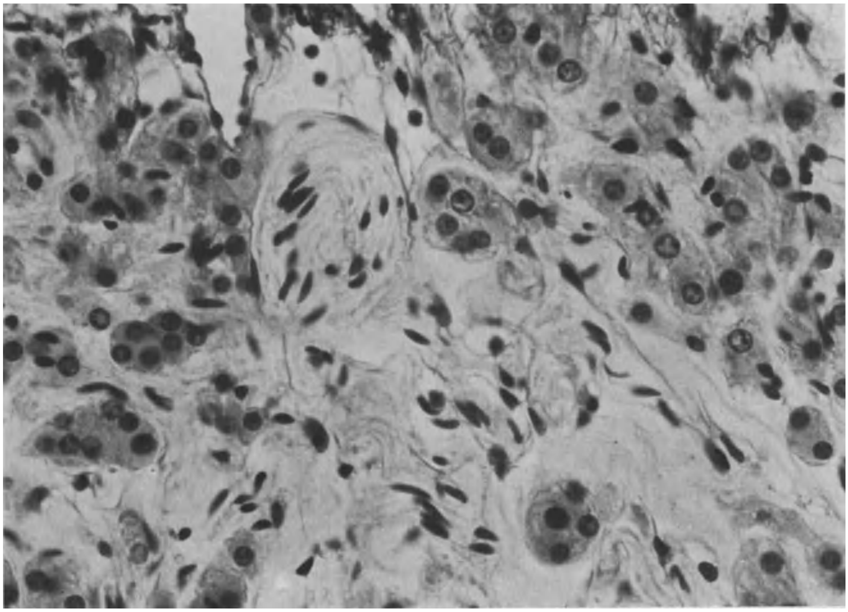

Fig. 6. Neuroendocrine corpuscle in the vicinity of throttle veins and a throttle artery. Bouin's fluid fixation, orcein, × 25

of lumen, which were more important than the hyalinosis of tunica adventitia. This finding was more distinct in the operated, but spermatologically unrecovered cases [1].

The boundary tissue of the seminiferous tubules was dispersed and expanded. Hyalin was deposited in the basal membrane in cases of advanced varicocele orchiopathy. The impairment of this compartment is evident from the discontinuous enzyme-histochemical reaction of ATPase [8]. The change in the activity correlates with the decrease in LDH activity.

Observations on Spermatogenesis

The characteristic pathological changes of varicocele orchiopathy were concerned with the adluminal compartment of seminiferous tubules; they may be described as Sertoli cell asthenia and in advanced cases as Sertoli cell insufficiency [2]. Sertoli cell asthenia is marked by a slight exfoliation of individual germ cells. The Sertoli cell insufficiency is characterized by a heavier exfoliation and formation of "puff" in the lumen of seminiferous tubules; the puff is formed as the Sertoli cells and the germ cells are dislocated and pushed towards the lumen.

These changes in the Sertoli cells can be studied with the help of the enzyme-histochemical reaction of thiamine pyrophosphatase [8]. The reaction zones of this enzyme are located in the Golgi apparatus and in the surrounding endoplasmatic reticulum, in cape-like formations. In cases of varicocele orchiopathy the enzyme activity was mostly in smaller areas, while in advanced cases, the activity showed a heterogenous reaction pattern.

On the basis of present knowledge it is difficult to determine at which stage of varicocele orchiopathy the basal compartment is markedly affected [3]. During the early stages of the disease we have observed a proliferation of the A-pale spermatogonia, which coincides with the increased spermatozoa count in semen analyses [5]. Apparently, this phenomenon is the result of compensation mechanisms of spermatogenesis.

In the later stages the number of A-dark spermatogonia decreased, perhaps simultaneously with the appearence of the changes in arterioles mentioned above. However, it must be emphasized that this is only a preliminary observation which must be studied further.

The decrease in the number of A-dark spermatogonia is not so pronounced as in other testicular disorders [5], likewise the occurrence of nuclear alterations of spermatogonia [3].

Observations on Leydig Cells

The Leydig cells exhibited a typical enzymatic pattern, characterized by decrease of thiamine pyrophosphatase activity in varying degrees. The activity for hydroxy steroid dehydrogenase (3-β-HSDH) was reduced, indicating decreased steroid synthesis. However, the activities of 17-beta-hydroxybutyric acid dehydrogenase, an enzyme for steroid precursors, and alcohol dehydrogenase were found at normal intensity.

The histological and enzyme-histochemical studies reported here lead to the conclusion, that two different lines of pathogenesis exist for varicocele orchiopathy:

1. An intrastesticular line, which starts in the intratesticular blood vessels, proceeds via interstitium to the boundary tissue and finally reaches the germinal epithelium. During the course of this line Leydig cells are major targets for damage.
2. A peripheral line of pathogenesis, which involves the tunica vasculosa and tunica albuginea: the contractility of tunica albuginea is impaired leading to the disturbances of the output and transport of tubular fluid, which is secreted by the Sertoli cells. This disorder of tunica albuginea can thereby cause congestion of tubular fluid and thus hamper the Sertoli cell function.

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Ultrastructural Study of Human Testicular Biopsies in Varicocele

A. Terquem and J. P. Dadoune

The mechanism by which a varicocele affects testicular function is controversial. Three principal arguments have been proposed: (1) disturbance of thermoregulation, (2) hypoxia of germinal tissue, and (3) reflux of toxic substances (see [10] for review). Light microscope studies have shown the extreme variability of spermatogenetic changes and have pointed out the bilaterality of the lesions despite frequent left unilateral localization of the varicocele [1, 11]. There have been scattered reports of lesions in the peritubular sheath, the Leydig cells, and the blood vessels.

In order to evaluate the nature of the changes in the seminal epithelium, the role of the blood-testis barrier, and the state of the blood vessels, an ultrastructural study of bilateral testicular biopsies from 30 patients with varicocele was performed. Several of the biopsies were also studied using ultrastructural tracers and freeze-fracture techniques on fixed samples. The control group consisted of six patients with obstructive azoospermia in whom the seminal epithelium was normal.

The changes in spermatogenesis – which we found always to be decreased in patients with varicocele (Fig. 1) – can, in the extreme, lead to germinal aplasia. Necrotic primary spermatocytes are not considered significant, as they are also observed in the control series; however, the germinal cell exfoliation constantly seen in our series is an important sign of testicular modification in varicocele. Large dilatations in the endoplasmic reticulum of Sertoli cells can be seen without any modification of the arrangement of thick filaments around the ends of spermatids (Fig. 2). The presence of fragments of Sertoli cell cytoplasm coupled with germinal cell desquamation suggests a cleavage of saccular dilatations of Sertoli cells and not a problem of defective anchorage filaments as has recently been proposed [3]. The dilatations of endoplasmic reticulum are not restricted to the cell apex but are distributed throughout the entire Sertoli cell.

Regardless of the importance of the vacuolization, the intercellular space remains unchanged. The Sertoli-Sertoli junctions seem intact, thus preventing the diffusion of colloidal lanthanum as has already been demonstrated [2]. Examination of the replicas shows the extent of the junctional complexes, made up of parallel networks (Fig. 3), sometimes anastomosed or branched, of lines of particles or short segments characterizing occlusive junctions [7]. It should also be pointed out that in the center of this network punctuate or linear gap junctions are found (Fig. 4). Thus, the structural integrity of the blood testis

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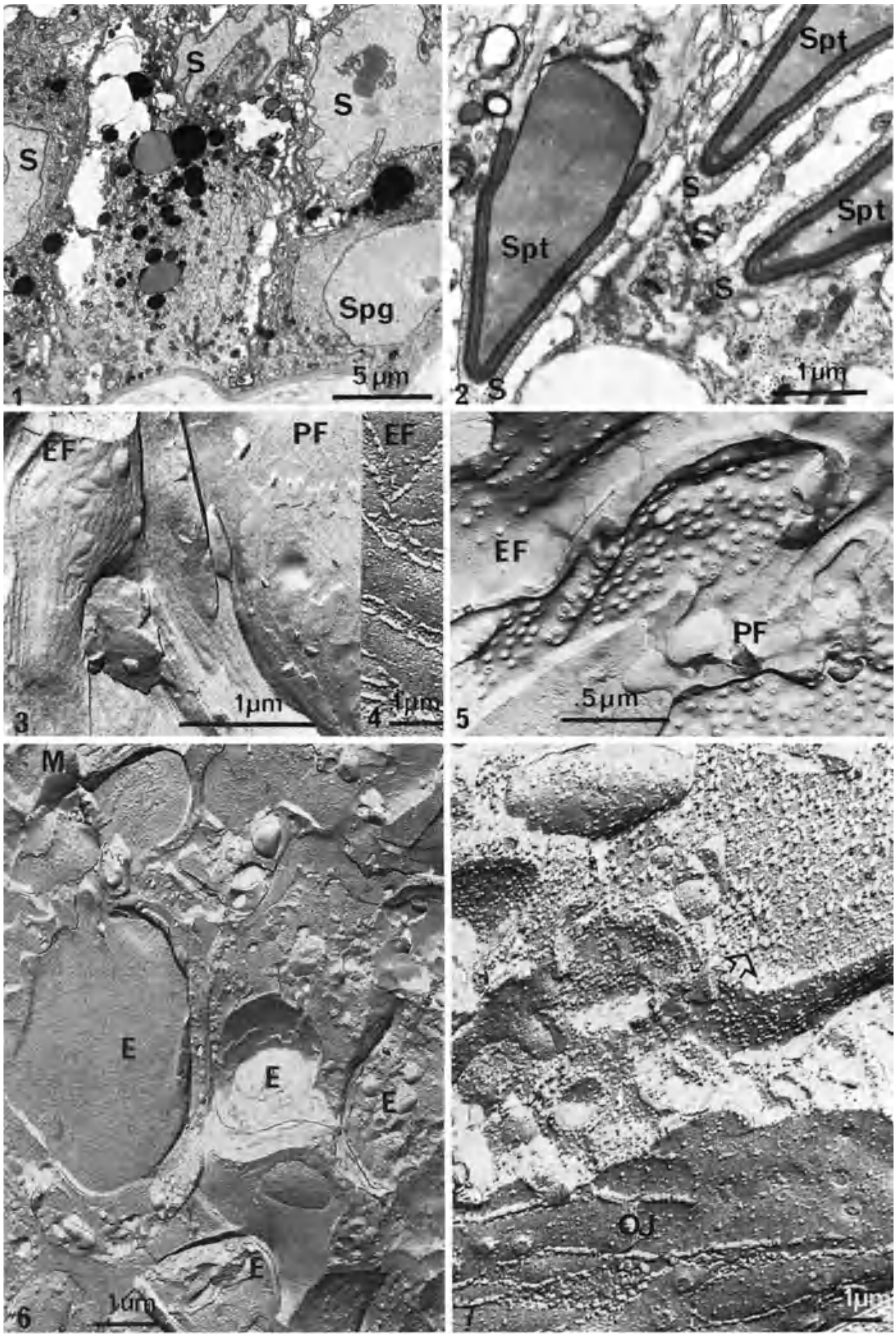
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Figs. 1–7

barrier supports the theory that the modifications in spermatogenesis are due to functional changes in the Sertoli cells, which are known to be sensitive to various injuries [4].

Besides the peritubular sheath which is sometimes fibrotic, and the Leydig cells which seem to be morphologically active, attention should be paid to the blood vessels in the interstitial spaces. Although the aspect of the veins was similar in the group with varicocele and in the control group, the capillaries in the varicocele group had a thickened endothelium (0.70 μm vs. 0.50 μm; $0.05 > P > 0.02$) with a great number of pinocytotic vesicles (Fig. 5). The arterioles were constricted bilaterally in the varicoceles group and relaxed in the control group. The lumina of the arterioles were reduced, with protrusion of endothelial cells which had salient bundles of microfilaments (Fig. 6). This proliferation of microfilaments (Fig. 7), also seen in other tissues, has been interpreted as a defense or adaptive mechanism [9].

Our observations during this study underscore the constant association of Sertoli cell changes with modifications of the germinal cells. In particular, we noted the modifications of the capillary and arteriolar walls which demonstrate the vascular effect of varicocele in both testicles. If one accepts that the catecholamine level is increased in the spermatic venous blood of patients with varicocele [5], it can be assumed that the vascular modifications are due to a reflux of these vasoconstrictors. The theory of tissular hypoxia has been disproved [6], thus, the catecholamines would seem to have a direct toxic effect on the Sertoli cells, as is suggested by experimental data [8].

Fig. 1. Seminiferous tubule from varicocelar biopsy; spermatogenesis is decreased. Numerous vacuoles can be seen in the Sertoli cell cytoplasm. *S,* Sertoli cell; *Spg,* spermatogonium

Fig. 2. Elongated spermatids (*Spt*) surrounded by cytoplasmic expansions of the apical portion of Sertoli cells (*S*) in which numerous dilatations of the endoplasmic reticulum and normal disposition of filaments can be seen

Fig. 3. Freeze fracture of the basal part of a seminiferours tubule. Lines of particles principally seen on the expolasmic face (*EF*) form a network characterizing occlusive junctions. *PF,* protoplasmic face

Fig. 4. Stretched gap junction seen in the network of occlusive junctions

Fig. 5. Freeze fracture of capillary endothelium. Numerous plasmalemmal vesicles can be seen on both faces of the fracture

Fig. 6. Spastic arteriole. The lumen is reduced and deformed by the protrusion of the endothelial cells (E) *M,* myocyte

Fig. 7. Detail of an endothelial cell in cross fracture. Numerous filaments are seen in the hyaloplasm (*arrow*). *OJ,* endothelial occlusive junction

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Physiopathology of Testicular Dysfunction in Varicocele: Does Varicocele Exist Without Reflux in the Internal Spermatic Vein?

F. H. Comhaire, M. Kunnen, and M. Simons

The physiopathological mechanisms involved in epididymal testicular dysfunction in some patients with varicocele are not yet clear. However, it is our opinion that no varicocele exists without reflux in the internal spermatic vein. In the present paper we will try to support this statement and will propose a possible physiopathological mechanism.

Material

Our study included 500 pubertal adolescents and adult men consulting for infertility (the majority of cases), sexual inadequacy, or local discomfort. In a few cases the varicocele was asymptomatic and detected during school examination. These adolescents were treated only if signs of impaired testicular development were found.

In all of the men included, the presence of varicocele was confirmed by means of a clearly abnormal scrotal thermogram, either telethermogram or contact thermogram using Thermostrips, and/or Doppler tracing. In the Doppler examination a bidirectional registration should unequivocally disclose the presence of reflux during Valsalva's manoeuvre.

Methods

The final criterion for the presence or absence of reflux in the spermatic vein was retrograde venography [1]. This examination was performed by Dr. Kunnen whose experience is based on over 500 explorations performed during the last 8 years.

During retrograde venography, the left and right renal veins are first injected. The patient is lifted to an almost vertical position by means of the tilting table. He is requested to perform a forceful Valsalva's manoeuvre during the injection of contrast medium. The presence or absence of reflux in the internal spermatic vein is studied by both television screen amplification and radiographic registration.

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Results

Using this technique, the left spermatic venous outlet is always visualized. However, not less than 14% of patients with left-side varicocele present competent valves near the spermatic venous outlet in the renal vein, and no reflux occurs into the superior segment of this vein. Collateral bypasses, however, do connect the spermatic vein with the renal vein and reflux occurs through these [3]. The collaterals generally end in the extrarenal segment of the renal vein but may also be connected to the intrarenal ramifications of the renal vein. Retrograde opacification of the spermatic vein and of the pampiniform plexus through such collaterals can only be determined if the collaterals are carefully searched for.

Nonetheless, reflux could not be demonstrated radiologically in 1.5% of cases with clinical varicocele. Five such cases were further explored by means of ascending phlebography which was performed during surgical ligation of the varicocele (Department of Urology, Chief Prof. Dr. de Sy). In four cases, left-side varicocele was found to be filled by reflux in the pampiniform plexus occurring through a greatly aberrant collateral connecting the perirenal venous plexus with the gonadal veins. The spermatic vein itself appeared normal. In the fifth patient, right-side varicocele was due to reflux in an enlarged right spermatic vein which entered the caval vein at its usual anatomical site.

Furthermore, we studied a group of 25 men consulting for recurrence or persistence of varicocele after either surgical or transcatheter embolisation treatment. In all cases reflux in the spermatic vein or in an aberrant renal-gonadal vein was demonstrated. Most commonly, only one ramification of the spermatic vein was found to be ligated, leaving another branch patent to reflux.

In one case, the left spermatic vein was found to be completely obstructed, but reflux persisted through the right spermatic vein. Right-to-left shunts at the retropubic level caused engorgement of the left pampiniform plexus.

Finally, one patient presented a complete obstruction of the spermatic vein after transcatheter embolization, but left-side varicocele persisted through adrenogonadal collaterals which were not visualized during the retrograde venography.

Physiopathological Considerations

In 1974 we [2] suggested chronic constriction of the intratesticular arterioles to be involved in the physiopathological of epididymal testicular dysfunction. Recently, Terquem and Dadoune [4] have demonstrated the presence of vasoconstriction in electron microscopic studies of testicular biopsies of varicocele patients. Further support of this hypothesis is given by the study of testicular perfusion using a bolus injection of technetium 99m pertechnate. Indeed, arterial perfusion through the affected testicle is sometimes clearly reduced as compared to the contralateral testis. Not longer than 12 h after

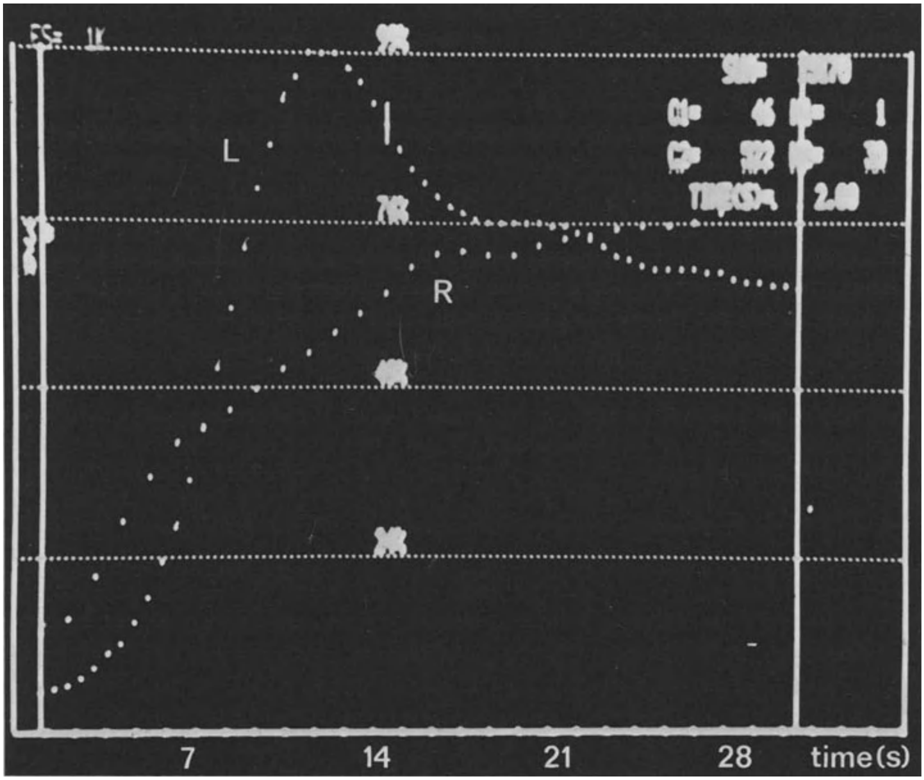

Fig. 1. Dynamic registration of radioactivity over left (*L*) and right (*R*) region of interest in a patient with large clinical varicocele and oligozoospermia before treatment. Notice the important venous stasis, together with decreased arterial perfusion on the left side

successful transcatheter embolization of the spermatic vein with interruption of reflux, the arterial blood supply returns to normal (Figs. 1, 2).

Arterial vasoconstriction is thought to result from reflux of vaso-active cathecholamines into the pampiniform plexus. Measurement of the cathecholamine concentration by radioimmunoassay (Dr. E. Moerman, Heymans Institute for Pharmacology) on blood aspirated from the spermatic vein during retrograde venography indeed indicated the noradrenaline concentration to be clearly increased over that in peripheral blood, as soon as the patient was in an upright position. The mean concentration of noradrenaline in spermatic venous blood was 42 ng/ml as compared to a mean concentration in peripheral blood of 17 ng/ml ($n = 23$).

The origin of the elevated concentration of noradrenaline is hard to determine. It is possible that adrenal venous blood is forced into the spermatic vein due to the so-called nutcracker phenomenon, which squeezes the left renal vein between the aorta and the mesenteric artery. Renal venous flow may then

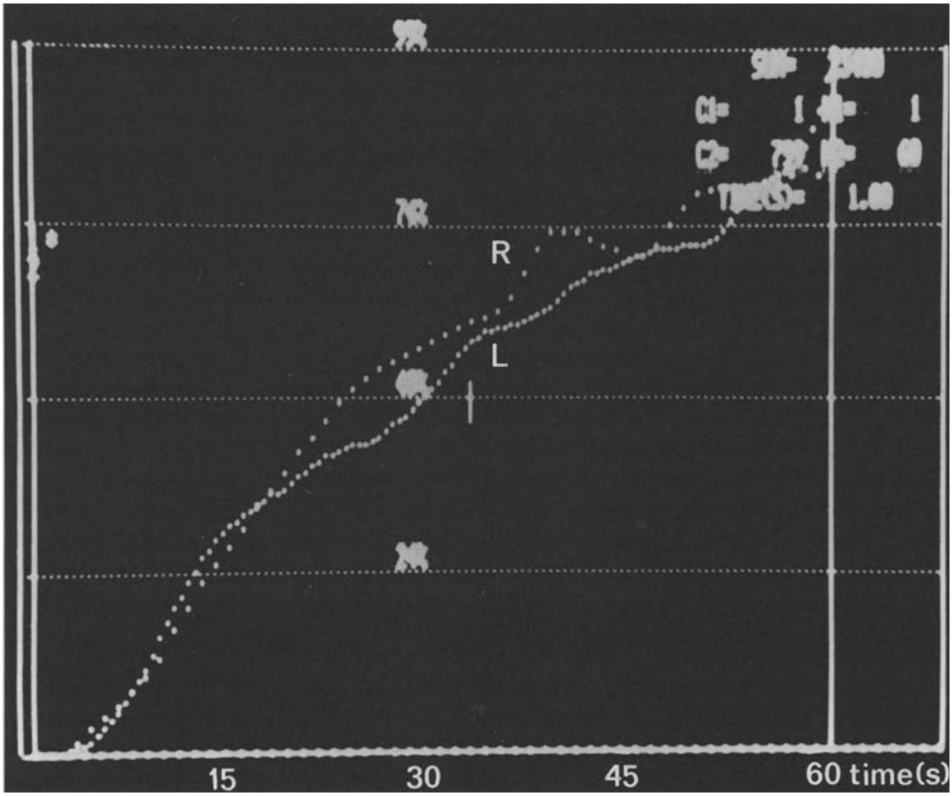

Fig. 2. Dynamic registration of radioactivity in the left (*L*) and right (*R*) region of interest in the same patient as in Fig. 1, 12 h after transcatheter embolization of the internal spermatic vein using bucrylate. Venous stasis has completely disappeared; moreover, arterial perfusion is completely symmetrical

be hindered and adrenal venous blood may cross the renal vein to enter the spermatic vein.

In other cases a direct connection between the adrenal and the pampiniform plexus is visualized (Fig. 3); in such cases the pampiniform plexus is filled with blood refluxing from the adrenal, via the perirenal venous plexus into the spermatic vein. Radiological data suggest such reflux to be more common than suspected. Many retrograde venograms disclose the presence of an outlet of an adrenogonadal vein in the spermatic vein near the iliac crest. This ramification is not completely opacified because of the presence of valves which hamper blood flow in the gonadoadrenal direction, but permit downward flow from the adrenal to the gonad.

Conclusion

Our data support the statement that varicocele is always due to venous reflux, either in the internal spermatic vein or, though less common, in aberrant

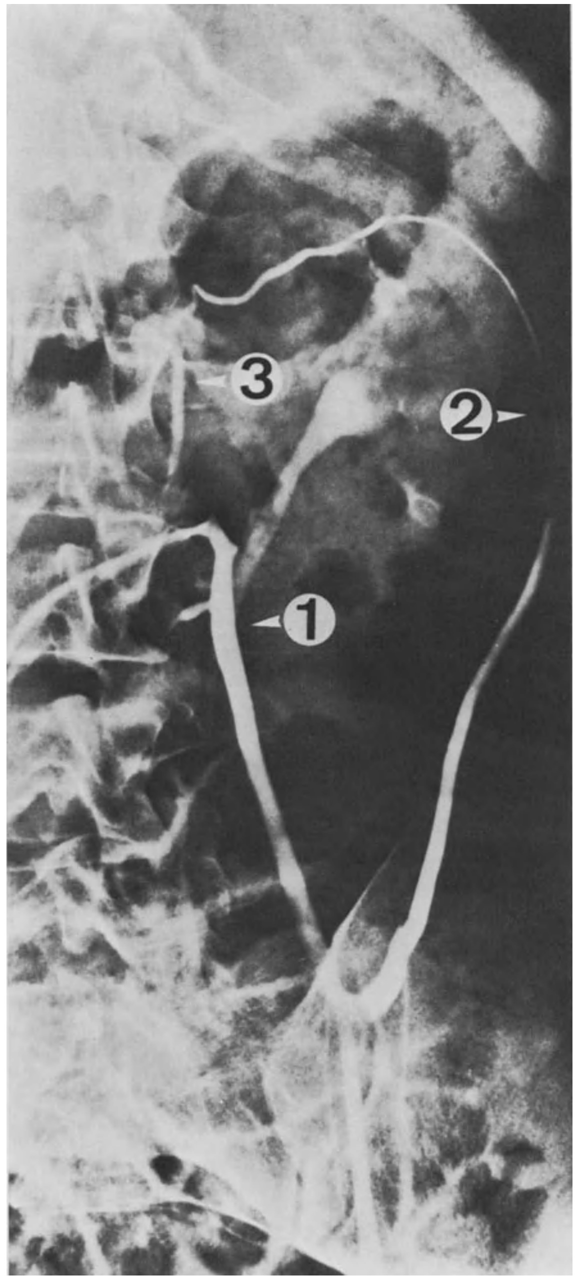

Fig. 3. Retrograde venogram of the internal spermatic vein showing an adrenogonadal bypass directly connecting the adrenal with the spermatic vein. *1*, internal spermatic vein; *2*, bypass connecting the adrenal via the perirenal complex to the spermatic vein; *3*, adrenal vein ending in the renal vein

renal-gonadal bypasses. Possible inversion of blood flow in the deferential, hypogastric and cremasteric veins is a secondary phenomenon, resulting from dilatation of these veins due to prolonged overloading. Venous reflux of vaso-active substances (such as noradrenaline) which are counter-current exchanged at the pampiniform plexus, cause chronic arterioconstriction at the testicular level and may be responsible for epididymal testicular dysfunction in some patients with varicocele.

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Are There Different Types of Varicocele?

A. Hirsh and J. P. Pryor

The description 'a tumour of veines dilated and woven with a various and mutuall implication about the testicle and codde, and swelling with a grosse and melancholy bloud' was applied by Ambroise Paré to the term Circocele [7]. It would satisfy 20th century medicine as describing varicocele, and a contemporary French medical dictionary indicates the terms are synonymous [8].

A distinction between varicocele and circocele is evident from Sir Percivall Pott [9] in 'Practical remarks on the hydrocele or watry rupture': "The varicocele is a dilatation of the vessels of the scrotum . . . but [they] are seldom so much enlarged as to be troublesome, unless they are the consequence of some disorder of the testicle or spermatic cord: when this is the case the original disease is what engages our attention, and not this simple effect of it: and therefore considered abstractedly, the varicocele is of little or no importance". "The circocele is a varicous enlargement, and distension of the spermatic vein, and whether considered on account of the pain it so sometimes occasions, or a wasting of the glandular part of the testicle which sometimes follows it, may truly be called a disease". This difference was later verified by Benjamin Bell [1] and suggests two different pathological entities although the precise details are no clearer than those in Sir Percivall Pott's original text.

The reported incidence of varicocele in patients who are attending infertility clinics varies considerably, but it is more common in those patients with oligozoospermia [2]. The recognition of a palpable or visible collection of varicosities of the spermatic cord depends upon their size and upon the experience and thoroughness of the clinician. This makes the clinical diagnosis of small varicoceles unreliable and may explain the variation in the reported incidence of the condition. There are few studies in which a comparison has been made by the same clinician between the incidence of varicocele in fertile and subfertile men. Russell [10] found an incidence of 9.2% in infertile and of 2% in fertile patients. More recent studies of infertile patients show an incidence of 20%–40% [4]. This report attempts to eliminate observer error by comparing the incidence of varicocele in men of proven fertility and in the male partners of infertile marriages as detected by a single observer.

Methods and Patients

Male partners of infertile marriages – 240, average age 31.3 years – attending an infertility clinic, and 190 men of proven fertility presenting for vasectomy,

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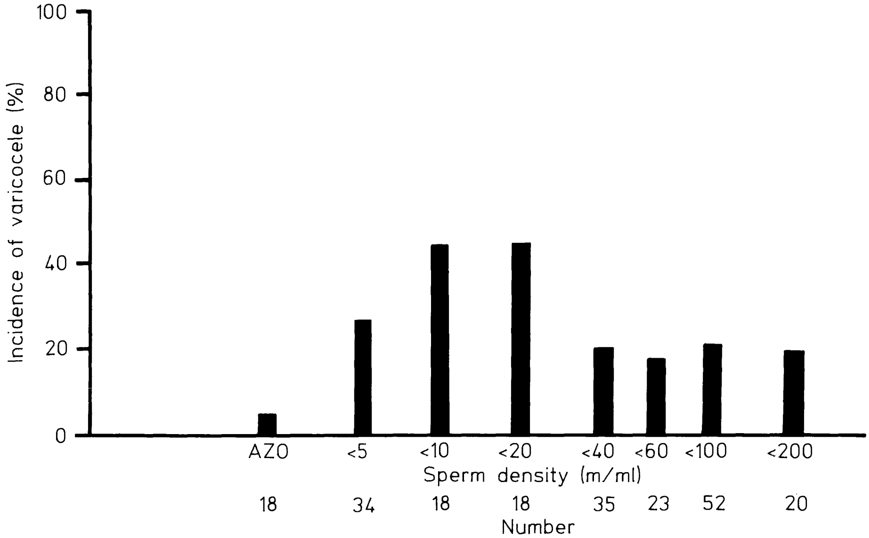

Fig. 1. The incidence of varicocele as detected on clinical examination by a single observer, in a group of 218 infertile men whose semen quality was subsequently assessed. *AZO,* azoospermia

average age 34.3 years, were examined by the same observer (AVH) between 1976 and 1980. Each patient was examined standing, at room temperature (20° C), and naked below the waist. The scrotum was inspected under adequate illumination and both spermatic cords were palpated. The diagnosis of a varicocele was established by the presence of a visible or palpable collection of tortuous veins of the spermatic cord during quiet respiration. Seminal analysis was done for 218 of the male partners of infertile marriages, and the geometric means of the sperm densities from all samples from each patient were divided into cohorts as shown in Fig. 1. The other parameters of the semen analysis were determined by standard techniques using arithmetic methods of statistical assessment.

Results

Table 1 shows that the incidence of varicocele in patients of proven fertility and in the male partners of barren marriages was 26.3% and 23.8% respectively, almost identical. All patients had left-sided varicoceles, and bilateral varicoceles were present in two of the infertile and five of the fertile patients. No patient was found with a unilateral, right-sided varicocele. Figure 1 shows an incidence of varicocele of 35.7% in the infertile group of men with a sperm density of less than 20 million/ml. Only one of the 18 men with azoospermia had a varicocele (6%). This increased incidence of varicocele in men with oligozoospermia was significant (Table 2). In the infertile group, within each cohort of sperm density there was no significant difference between the motility, progression, morphology or semen volume in patients with or without varicocele.

Table 1. Incidence of varicocele detected by a single observer on clinical examination of 190 allegedly fertile and 240 allegedly infertile men

Category	Number	Mean age (years)	Incidence
Fertile	190	34.3	26.3%
Infertile	240	31.3	23.8%

p = n.s.

Table 2. Incidence of varicocele relative to sperm density in 218 allegedly infertile men

Category	Number	Incidence	Significance
AZO	18	5.6%	$\chi^2 = 9.79$
< 20 m/ml	70	35.7%	$p < 0.01$
> 20 m/ml	130	20.0%	

AZO, azoospermia

Discussion

Although these results do not prove a direct relationship between infertility and the presence of a varicocele, it is well known that in male infertility clinics patients presenting with oligozoospermia have a high incidence of varicocele [4]. It is also evident that patients of proven fertility (including some with obvious varicocele) usually have excellent semen quality, and that the proportion of these with a sperm density below 20 million/ml is small [3].

As an explanation for the contradictory findings it is postulated that there may be different types of varicocele, and scientific evidence has accumulated in support of this. It has been demonstrated by Doppler studies that varicoceles have different venous flow characteristics, and not all are associated with elevation of scrotal temperature, internal spermatic vein reflux, or with reduction of left testicular size [5, 6]. The presence of very obvious varicoceles in patients of proven fertility, as well as the fact that there is no single accepted cause for the infertility associated with other varicoceles, has led to continued debate over the aetiology of the infertility in the latter [11].

It is certainly possible that Sir Percivall Pott knew the difference between those varicoceles which caused testicular atrophy and pain, and those which were of little consequence. He called the former circoceles and the latter varicoceles, and with modern technological advances we may be missing something in the clinical examination of the patient of which our predecessors were aware. It is thus apparent that modern medical science should attempt to distinguish between the circocele and varicocele by examination or technology, in order to obtain a better understanding of the relationship between the varicocele (or circocele) and male infertility.

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II. Diagnosis

The Doppler Assessment of Varicoceles

A. Hirsh and J. P. Pryor

The relationship between varicocele and male subfertility remains uncertain and new techniques are being used in an attempt to improve our understanding of this condition. The use of ultrasonic Doppler equipment has become an accepted method for the evaluation of peripheral vascular conditions. The technique is non-invasive, and convenient for the clinician, and portable equipment is available. This presentation summarises our experience using the Doppler technique to assess varicoceles in both fertile and infertile men.

Diagnosis of Varicoceles

In a previously published study [1] it was found that the pocket Doppler apparatus was highly sensitive to Valsalva-induced venous flow within the spermatic cord. Positive results were found too frequently in the normal spermatic cord (approaching 80%) for investigation to be meaningful in the evaluation of a varicocele. This simple qualitative test was therefore abandoned in favour of more sensitive directional Doppler equipment.

Spontaneous Venous Activity

A Sonicaid BV380 directional Doppler velocimeter (8 Hz) was coupled to a chart recorder. The Doppler examination was carried out with the patient standing and breathing quietly at room temperature. The Doppler probe was applied with gel contact to the skin of the scrotum above the testes. Satisfactory tracings were obtained from the chart recorder indicating spontaneous venous activity (Fig. 1). Further exploration with the Doppler probe was made on both sides over the inguinal canal, the upper quadrant of the scrotum and the lower pole of the testis. It can be seen that in the presence of a varicocele on the left side, spontaneous venous activity could be detected in all three sites. It is evident from Fig. 1 that spontaneous venous activity was absent on the control side (right), even though a response to Valsalva's manoeuvre was recorded. In the absence of any spontaneous venous flow it was possible to locate a vein by scanning with the probe for the testicular artery or gently squeezing the cord to induce venous flow. Examination of a larger series of venous velocity wave forms showed seven different types of wave-form characteristics. These are

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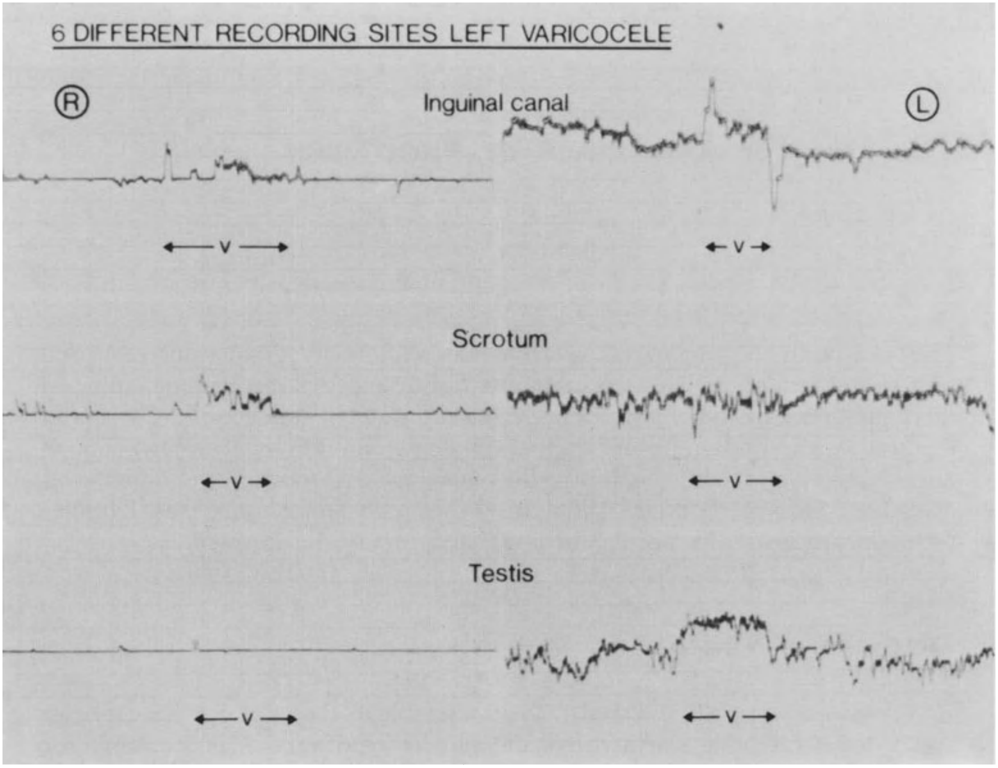


Fig. 1. Wave-forms recorded by a directional Doppler velocimeter during quiet respiration while standing and also during Valsalva's manoeuvre (V) over the right and left spermatic cords at three levels

shown in Fig. 2. It was confirmed that the majority of varicoceles were associated with spontaneous venous activity. Few patients without clinically detectable varicoceles were found to have subclinical spontaneous venous activity, and in some of the varicoceles of infertile patients this phenomenon was not detectable.

Grading of Varicoceles

When the response to Valsalva's manoeuvre was excluded from the evaluation of the venous velocity wave-form characteristics a method of grading varicoceles on spontaneous venous activity alone was found to be possible. No spontaneous venous activity (venous stasis) was detected in grade I varicocele. Intermittent spontaneous venous activity was detected in grade II varicoceles, and in grade III varicoceles continuous venous activity was present (Fig. 3). The clinical implications of these grades are still unclear, but some correlations with other observations have been found [2]. The higher grades of varicoceles were found to be associated with greater diameter of the spermatic cord (i.e., larger

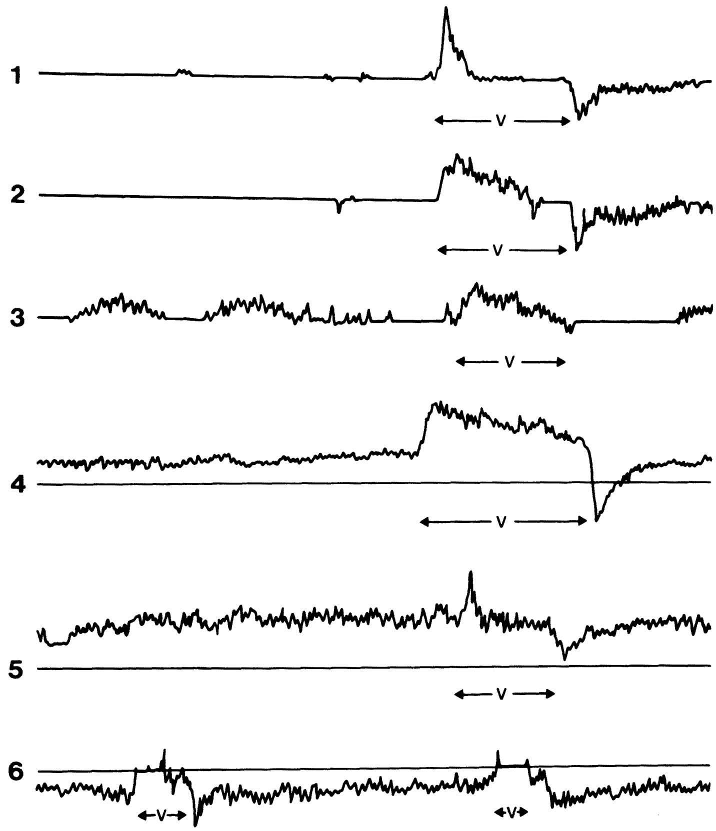


Fig. 2. Examples of the six different wave-form patterns that have been recorded over the veins in the spermatic cord

DOPPLER GRADING OF VARICOCELES

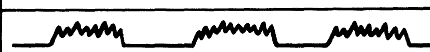
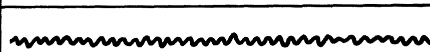
	Audible signal from Pocket Unit	Chart recording from directional apparatus
Grade I	No spontaneous venous activity	
Grade II	Intermittent venous reflux	
Grade III	Continuous venous reflux	

Fig. 3. The grading system of venous reflux is based on the presence or absence of flow during quiet respiration while standing

Table 1. Comparison of the Doppler grades recorded over 51 left varicoceles and varicocele size, as estimated by the difference in spermatic cord diameters (excludes one patient with bilateral varicoceles)

	Wave-form	Number	Difference (cm) Mean ± SD	
Grade I	0–2	4	0.4 ± 0.3	
Grade II	3	28	0.4 ± 0.2	$p < 0.001$ (II vs III)
Grade III	4–5	19	0.7 ± 0.3	

Table 2. Relationship between the diameter of the internal spermatic vein (ISV) measured at operation and the preoperative Doppler findings recorded over the inguinal canal (44 operations)

	Wave-form	Number	Diameter ISV (mm) Mean ± SD	Range (mm)	Significance
Grade I	0–2	12	4 ± 2	2–7	I vs II p = n.s.
Grade II	3	20	4 ± 1	2–7	II vs III $p < 0.001$ $t = 5.48$
Grade III	4–5	12	6 ± 1	4–8	III vs I $p < 0.01$ $t = 3.10$

Table 3. Comparison of left internal spermatic vein testosterone concentrations and peripheral testosterone values found at 37 left-varicocele operations (nmol/l)

Doppler grade	Number	Testicular side range of values	Peripheral vein geom. mean (range)	Renal side geom. mean (range)
I	3	400+ –2,000+	15.6 (8.8–25.5)	30.7 (10.8– 76.9)
II	21	372.5– 412×10^3	13.1 (3.3–24.0)	119.3 (8.0–2,797.2*)
III	13	360.2– 17×10^3	13.0 (5.5–25.0)	25.9 (5.1– 299.8*)

* $p < 0.01$; $t = 3.117$

varicoceles) as shown in Table 1, with greater diameter of the internal spermatic vein (as measured directly at operation in the inguinal canal) shown in Table 2, and with reduction in the concentration of testosterone within the internal spermatic vein as sampled at operation (Table 3). The latter may be due to the diluting effect of increased venous reflux in the vein.

Doppler grades have not been found to correlate with sperm density, reduction in testicular size or impairment of testicular histological appearance as measured by the Johnsen scoring method.

Table 4. Postoperative Doppler study

Preoperative	Number	Postoperative wave-forms			Doppler recurrence	Clinical recurrence
		0–2	3	4–5		
Grade II	15	12	3	0	20%	0
Grade III	11	4	5	2	64%	1

Postoperative Evaluation Using the Doppler Technique

Table 4 shows the postoperative results of ligation of the internal spermatic vein in the inguinal canal; the higher the grade preoperatively, the greater the incidence of Doppler recurrence postoperatively. These findings raise the possibility that the inguinal approach might not be fully effective in eliminating venous reflux, or that venous incompetence in alternative systems may have been responsible for the varicocele.

Conclusion

Doppler equipment may be too sensitive for the evaluation of Valsalva-induced venous reflux. However, the Doppler may be used to detect spontaneous venous activity, which appears to be a more reliable method of identifying and grading varicoceles in the andrology clinic.

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Doppler Test and Scrotal Thermography in Varicocele

D. Fontana, S. D. Bianchi, D. F. Randone, M. Bellina, L. Rolle, and G. Fasolis

Varicocele is most likely the result of an incompetent spermatic vein or veins with retrograde flow of blood into the scrotum; this retrograde flow may cause a significant increase in scrotum temperature. The Doppler test and scrotal thermography have been widely employed in the past few years not only to confirm clinical diagnosis but also to detect infraclinical varicoceles in subfertile patients. We have attempted, therefore, to make a comparison of these two examination methods by checking their practical usefulness and reliability.

Materials and Methods

We subjected 120 patients, aged 17–35 years, suffering from oligoterato-asthenospermia (OTA) (50 with and 70 without clinically palpable left varicocele) to the Doppler test (Directional Doppler 1010 Parks El. Lab.) and scrotal thermography (AGA Thermovision 680). All 50 patients with varicocele underwent inguinal or suprainguinal section of the spermatic vein or veins. Postoperative controls (physical examination, semen analysis, Doppler test and thermography) were carried out 1, 3, 6, and 12 months after surgery.

Of 70 patients without clinically palpable varicocele, seven showed alterations in Doppler test and/or thermography results. In these patients a retrograde selective phlebography of the spermatic vein was carried out to confirm the suspicion of an infraclinical varicocele. The patients with infraclinical varicocele were operated on and followed up for up to 1 year (Fig. 1).

Results

In all patients with OTA plus left varicocele, the Doppler test performed on the veins of the spermatic cord showed a steady increase of the flow rate in basal conditions, a further increase being observed after Valsalva's manoeuvre, which provokes a stop of the venous flow in normal subjects. Scrotal thermography showed a temperature difference between left and right scrotum higher than 1.5° C in all patients.

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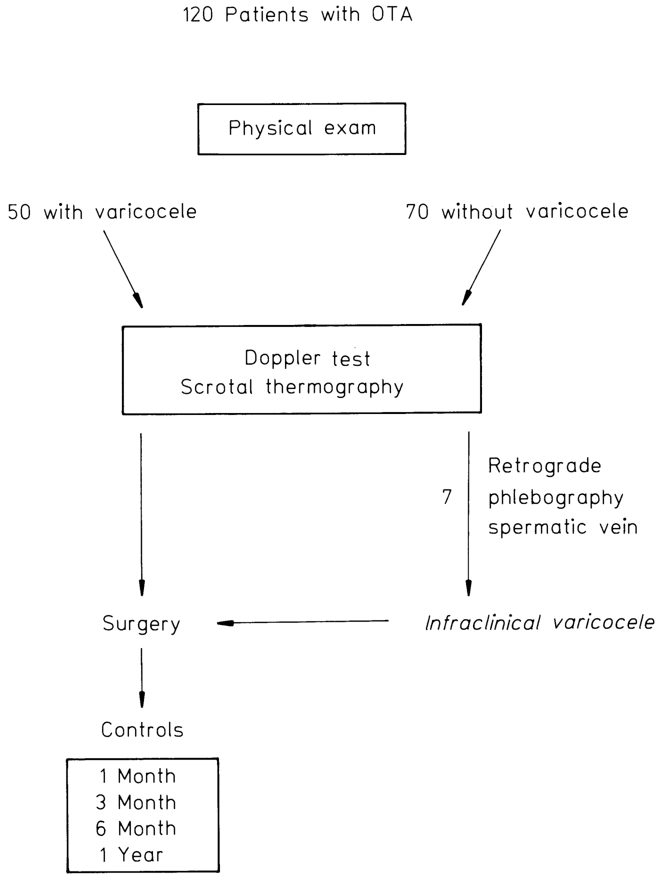

Fig. 1. Results of Doppler test and thermography in 120 patients with oligoteratoasthenospermia *(OTA)*

In 63 patients with OTA but without varicocele, Doppler test and thermography were normal; in seven a pathological Doppler recording was present, and three of them also had a scrotal thermic gradient of 1°–1.5° C. A pathological thermogram associated with a normal Doppler recording was never observed.

The seven patients suspected of having a reno-spermatic reflux according to the Doppler test were subjected to retrograde selective phlebography of the spermatic vein, which confirmed the presence of reflux in all cases. An infraclinical varicocele was therefore diagnosed in these patients (Fig. 2).

In 51 of 57 patients operated on, the Doppler test results returned to normal on the day of surgery; the decrease and then the disappearance of the thermic gradient was much slower (1–3 months). One year after surgery the Doppler test and thermography showed two cases of persistent and four of recurring varicocele, the physical examination of the scrotum, however, being completely normal in three of these patients (Fig. 3).

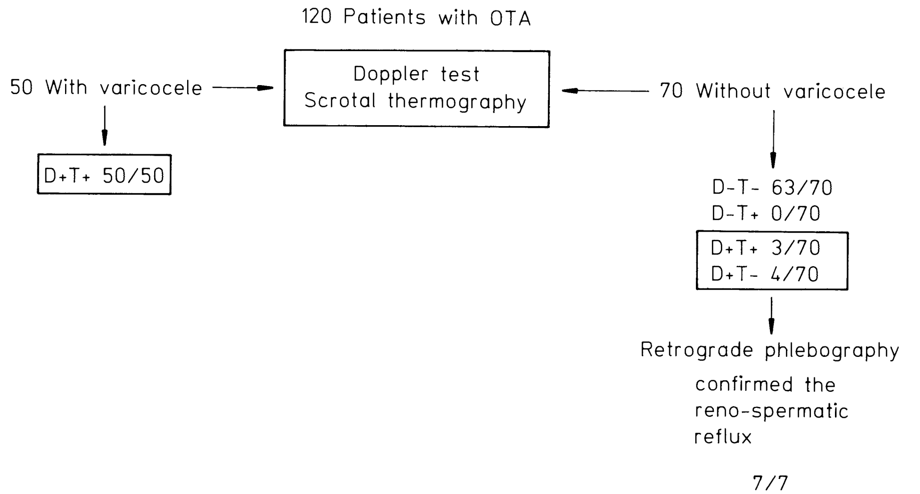

Fig. 2. Confirmation of reflux by retrograde phlebography. D−, +: Doppler examination. Negative and positive results, respectively; T−, +: Thermography. Negative and positive results, respectively

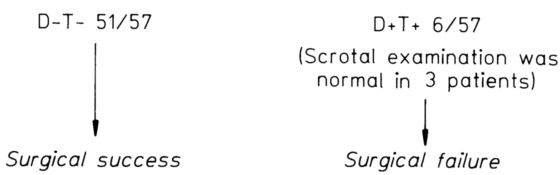

Fig. 3. Postoperative follow-up of 57 patients 1 year after surgery. D−, +: Doppler examination. Negative and positive results, respectively; T−, +: Thermography. Negative and positive results, respectively

Discussion

In patients with OTA and varicocele the diagnostic usefulness of the Doppler test and scrotal thermography is limited; nevertheless, we think that these examinations should be carried out, as they represent a basis of comparison with postoperative controls.

In patients with OTA but without clinically palpable varicocele the Doppler test seems the safest way to detect a reno-spermatic reflux, i.e., infraclinical varicocele. The Doppler test has always been confirmed by spermatic phlebography, a more invasive technique, not suitable for diagnostic screening purposes. Scrotal thermography, in our experience, is less reliable than the Doppler test.

In postoperative controls the Doppler test and scrotal thermography have proved useful in detecting persistent or recurring varicocele, not always revealed by physical examination of the scrotum.

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Scrotal Scintigraphy Vs Scrotal Thermography: A Comparison of Scrotal Imaging Techniques for the Diagnosis of Varicocele

D. Nicolaij, W. Coucke, G. Lamberigts, O. Steeno, A. van Steen, M. De Roo, and P. Devos

In otherwise normal and healthy young men the most frequent cause of subfertility is varicocele. As this is also the cause most easy to cure, correct diagnosis of varicocele is extremely important.

Several invasive and non-invasive techniques are used to visualize scrotal phlebectases in subfertile men when the clinical examination does not provide enough information for a definite diagnosis. Telethermography requires expensive apparatus and much technical skill for correct interpretation of the results. The Doppler stethoscope has the disadvantage of false positive results, frequently provoked by contraction of the cremaster muscles; its results are not easily reproduced from one examiner to the next, and it does not provide an image of the varicocele. Contact thermography, recently commercialized, is a simple inexpensive alternative to telethermography which seems very promising for the future. These three are non-invasive techniques. Phlebographic techniques (retrograde or antiretrograde) are invasive and reserved for selected cases; they are not screening procedures.

The use of radioisotopes for the diagnosis of scrotal lesions was described by Nadel in 1973 [10]. He and other authors [2, 7, 12] visualized the scrotal blood pool and detected hypervascularity (abcesses, inflammatory processes, tumours and traumata), and hypo- or avascularity (torsio testis, hydrocele and spermatocele).

Since 1978, four papers have appeared [4, 6, 11, 18] concerning the use of technetium 99m for the diagnosis of varicocele. Vandeweghe and Comhaire [18]

Table 1. Results of Vandeweghe and Comhaire [18] and Freund et al. [4] using forms of technetium 99m in diagnosis of varicocele

	No. of positive scans (%)	No. of marginal scans (%)
Vandeweghe and Comhaire	(Free pertechnetate)	
Normal men	0/26 (0)	
Clinically suspect	2/12 (16.7)	
Varicocele	9/13 (69.2)	
Freund et al.	(^{99m}Tc-labelled erythrocytes)	
Normal men	10/41 (24.4)	10/41 (24.4)
Clinically suspect	3/13 (23.1)	5/13 (38.5)
Varicocele	26/29 (89.7)	

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used free pertechnetate; Nahoum et al. [11] used technetium-labelled human serum albumin; Freund et al. [4] and Harris et al. [6] used in vivo-labelled erythrocytes to visualize the scrotal blood contents.

The results of Vandeweghe and Comhaire [18] and those of Freund et al. [4] are summarized in Table 1. The sensitivity of the technique is much higher in the hands of Freund et al. [4], either because he uses other clinical criterial or because he uses another technique; the latter seems less probable to us.

Methods

After peroral administration of sodium perchlorate (500 mg), to block thyroidal uptake, the patients were positioned in front of a Searle LFOV gamma camera, with a parallel hole high resolution collimator. The patients were examined upright, the legs slightly abducted to reduce thigh background, the penis fixed to the abdominal wall. An intravenous injection of 185 MBq (5 mCi) of technetium-labelled human serum albumin (5 mg), was given in an antecubital vein. Immediately after injection four views of 100,000 counts each were taken, the first representing the flow phase. One view of 100,000 counts was recorded during Valsalva's reflux manoeuvre, and one view of 500,000 counts was taken 15 min after injection, after equilibration of the tracer in the general circulation.

Results

In the absence of a varicocele (Fig. 1), symmetrical tracer distribution is seen during all phases of the examination. A spot of hyperactivity is seen at the base of the penis, and the bladder is visualized as an area of hypoactivity on the early images (Fig. 1A–D) and on the view taken during Valsalva's manoeuvre (Fig. 1E). On the view taken after equilibration of the tracer, the bladder contains radioactive urine; therefore the patient should be asked to void his bladder before the image is taken (Fig. 1F).

A varicocele is characterized by three kinds of images:

1. A hot spot at the base of the scrotum or in the trajectory of the spermatic cord (Fig. 2A)
2. A global asymmetry of the scrotal blood pool (Fig. 2B)
3. A clear, nearly anatomical visualization of the pampiniform plexus and the distal part of the testicular vein (Fig. 2C), also visible on the view taken at equilibrium (Fig. 2D)

Seventy-six patients were examined scintigraphically; they were divided into four groups, according to the clinical criteria of Steeno [15], a combination of those of Uehling [17] and Dubin and Amelar [3]. The decisive criterion for the diagnosis of varicocele is venous reflux during Valsalva's reflux manoeuvre (Table 2).

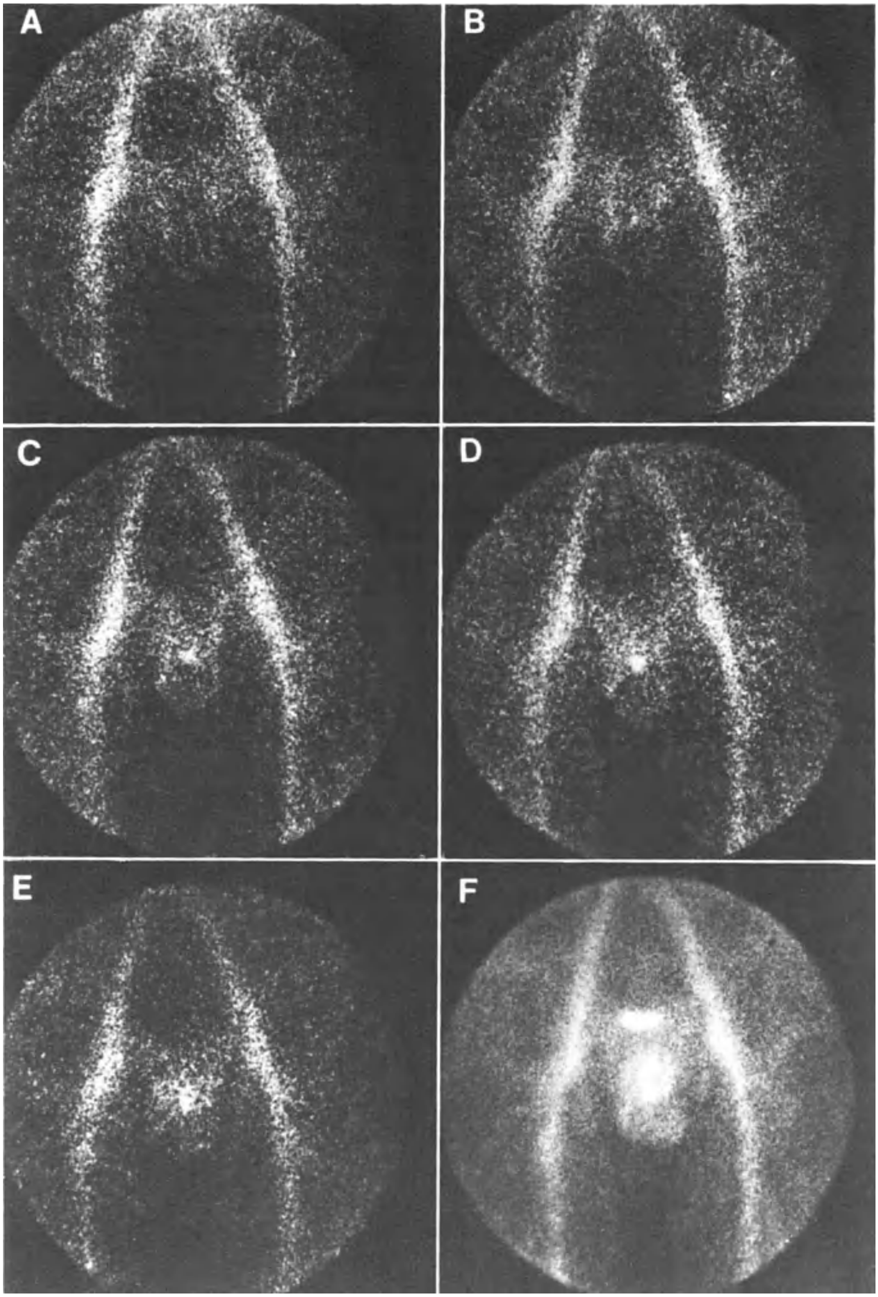

Fig. 1A–F. Normal scrotal scintigrams. **A–D** are early images; **E** is an image made during Valsalva's manoeuvre; **F** is an image made after equilibration of tracer

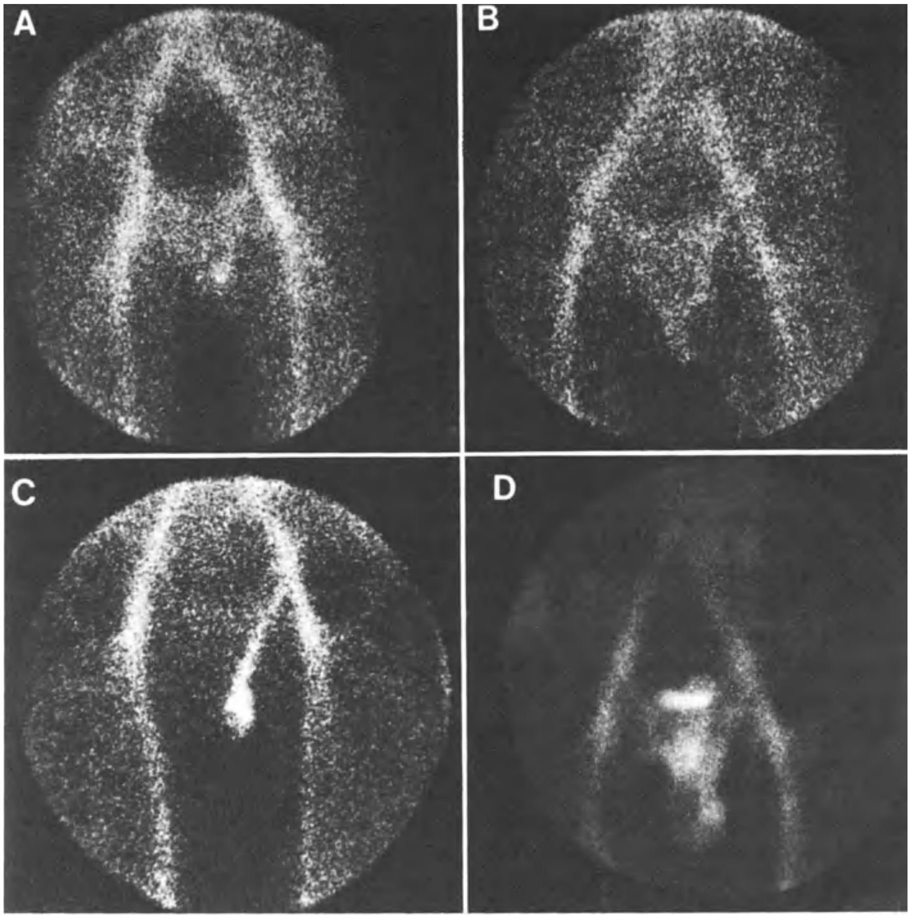

Fig. 2A–D. Pathological scrotal scintigrams. **A** shows a hot spot; **B** illustrates global asymmetry; **C** and **D** illustrate the "string" sign in an early image (**C**) and after equilibration (**D**)

Scintigraphic results are summarized in Table 3. The more obvious the clinical diagnosis of varicocele becomes, the more sensitive scintigraphy becomes, resulting in 0% sensitivity for a normal group and 100% sensitivity for second- and third-degree varicoceles.

In clinically normal, but subfertile men (Table 4), thermography detected subclinical varicoceles in four of eight patients who were all scintigraphically normal.

In individuals clinically suspected of having a varicocele (Table 5) thermography was also obviously more sensitive than scintigraphy, however, when we analyse the results for this group we see that thermography was less specific. One varicocele was detected scintigraphically and missed by thermography. Of the five right-sided positive thermographies, only one was concordant with the clinically suspected right varicocele. The other four were of patients

Table 2. Diagnostic criteria of Steeno et al. [15]

A. Normal
No distended vein
No reflux on Valsalva's manoeuvre
Symmetrical testicular volume
Symmetrical testicular consistency

B. Clinically suspected
Distended vein, less than 1 cm
No reflux on Valsalva's manoeuvre
Asymmetrical testicular volume
Asymmetrical testicular consistency

C. Grade I varicocele
Palpable scrotal varicosity of less than 1 cm in diameter and with reflux during Valsalva's manoeuvre

D. Grade II varicocele
Pronounced varicocele mass with a diameter of 1–2 cm

C. Grade III varicocele
The venous mass fills the hemiscrotum, is easily visible at a distance and has a diameter greater than 2 cm at the time of positive pressure reflux

Table 3. Results of scrotal scintigraphy

	Group			
	A	B	C	D
Normal	100% (13)	70.4% (19)	23.1% (6)	0% (0)
Left +	0% (0)	29.6% (8)	73.1% (19)	100% (10)
Right +	0% (0)	0 % (0)	3.8% (1)	0% (0)
Bilateral +	0% (0)	0 % (0)	0 % (0)	0% (0)
Total	(13)	(27)	(26)	(10)

Table 4. Comparison of scintigraphy and thermography in Group A

	Scintigraphy	Thermography
Normal	100% (8)	50% (4)
Left +	0% (0)	50% (4)
Right +	0% (0)	0% (0)
Bilateral +	0% (0)	0% (0)
Total	(8)	(8)

Table 5. Comparison of scintigraphy and thermography in Group B

	Scintigraphy	Thermography
Normal	68% (17)	28% (7)
Left +	32% (8)	48% (12)
Right +	0% (0)	20% (5)
Bilateral +	0% (0)	4% (1)
Total	(25)	(25)

Table 6. Comparison of scintigraphy and thermography in Group C

	Scintigraphy	Thermography
Normal	22.7% (5)	13.6% (3)
Left +	72.7% (16)	77.3% (17)
Right +	4.5% (1)	4.5% (1)
Bilateral +	0 % (0)	4.5% (1)
Total	(22)	(22)

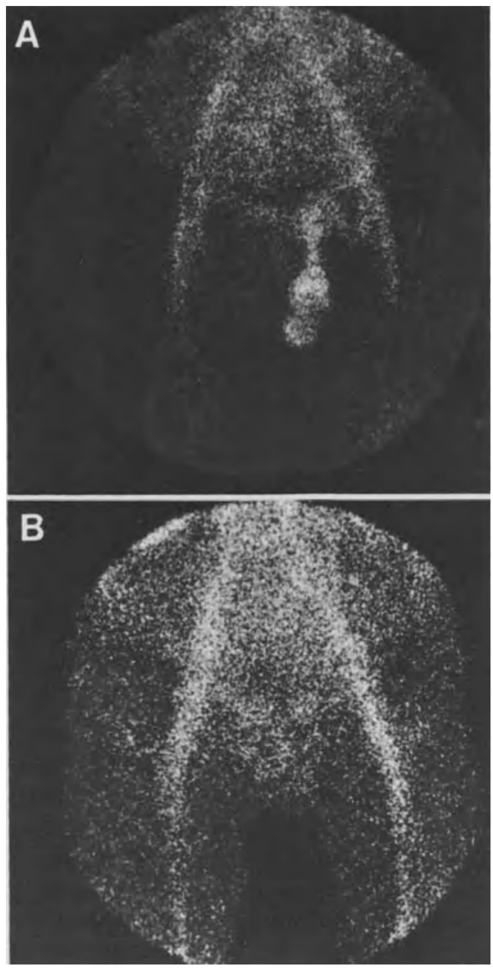

Fig. 3A, B. Scintigrams of second-degree varicocele. **A** preoperative, **B** postoperative scan

suspected of having left-sided varicoceles; two of them were detected by scintigraphy. The bilaterally positive thermography was from a patient with a suspicion of left-sided varicocele only.

In patients with an obvious first-degree varicocele (Table 6), the sensitivity of both techniques was comparable. However, further analysis showed one negative thermography in a patient with left-sided varicocele, detected clinically and scintigraphically; a negative scintigraphy in a patient with clinically and thermographically proven varicocele was encountered three times. Temperature difference in these three cases, however, was not greater than 2° C. One right-sided positive thermography was in discordance with the left-sided positive clinical examination and scintigraphy, and the right-sided positive scintigraphy also remains unexplained. The bilaterally positive thermography is from a patient with a clinically and scintigraphically documented left varicocele.

Three patients with second- or third-degree varicoceles underwent both examinations: in all three cases concordant positive information was obtained.

Three patients were also examined before and after surgical treatment: preoperatively (Fig. 3A) all three showed an obvious „string sign"; postoperatively (Fig. 3B) in all three cases, scrotal asymmetry had disappeared.

Discussion

We think there is a need for visualization of varicocele in two instances:
1. If a subfertile male, clinically normal or only slightly suspected of having a varicocele, has a spermiogram suggestive of varicocele and a normal FSH level, a subclinical varicocele must be excluded, because this diagnosis offers the opportunity for simple surgical treatment with a good perspective for improvement of semen.
2. In a patient with a clinically diagnosed varicocele, an objective document can be important for comparison with postoperative results should semen disturbances persist.

Scrotal blood-pool imaging with radionuclides, in our experience and in that of others, is less sensitive than scrotal telethermography. However, there are cases in which the two techniques offer conflicting results, the scintigraphy often being more concordant with the clinical findings. This can be explained by a different physiological base for both procedures: thermography visualizes venous reflux, scintigraphy visualizes blood stasis in the scrotum.

Conclusion

We conclude that scrotal scintigraphy is less sensitive than thermography, but possible more specific. While it cannot be considered the screening procedure of first choice, it offers complementary information, especially when the results of thermography are at variance with those of clinical examination, and it can help the andrologist in selecting cases for surgical (high vasoligation) or non-surgical (embolization) treatment, offering a good chance for the restoration of male fertility.

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Detection of Varicocele by Isotopic Angiography

J. Leclere, P. Thouvenot, R. Mizrahi, P. Genton,
J. Robert, and D. Regent

The relationship between varicocele and infertility in men is still under debate, but numerous reports seem to demonstrate the pathogenic role of venous abnormalities in the impairment of spermatogenesis [10]. Thus the diagnosis of a varicocele is an important stage in the assessment of male infertility. Others suggest that there is no relationship between the importance of the venous abnormality and the degree of impairment of spermatogenesis, which makes the identification of subclinical varicoceles a key problem.

Available diagnostic procedures include phlebography [1], thermography [2] and Doppler ultrasound [3, 5]. Phlebography remains the standard procedure, but is invasive, causes significant irradiation, and may be technically difficult on the right side where the anatomy of the spermatic vein varies. Telethermography seems to ignore discrete subclinical lesions. Doppler ultrasound requires very well-trained personnel, and early enthusiasm for this method has somewhat mitigated lately.

The use of radioactive tracers has not been much investigated [4, 6–9], and their usefulness has been disclaimed. In the wake of preliminary work [9], we attempt here, by means of a personal technique, to assess the value of dynamic scrotal scanning (DSS) in the early diagnosis of varicoceles.

Material and Methods

We studied 240 patients with impaired spermatogenesis. All genital abnormalities, infectious ones in particular, had been sorted out, with the exception of clinically diagnosed varicoceles. Thus our 240 patients had either varicocele or so-called idiopathic oligozoospermia.

At the beginning we injected ^{99m}Tc-labelled serum albumin, but results were disappointing, and we subsequently preferred free ^{99m}Tc pertechnetate.

A 10-mCi bolus of ^{99m}Tc was administered intravenously, the subject standing with his penis upright and taped to the abdominal wall. A gamma camera (OPTICAMERA, CGR, France) gave pictures of scrotal radioactivity at 15-s intervals for 5 min (Fig. 1). Radioactivity levels of each half of the scrotum were compared to those obtained on vascular areas of both thighs. A dynamic curve of radioactivity could thus be computed automatically (using a computer from Informatek Co., France) in four standard areas: left and right iliofemoral

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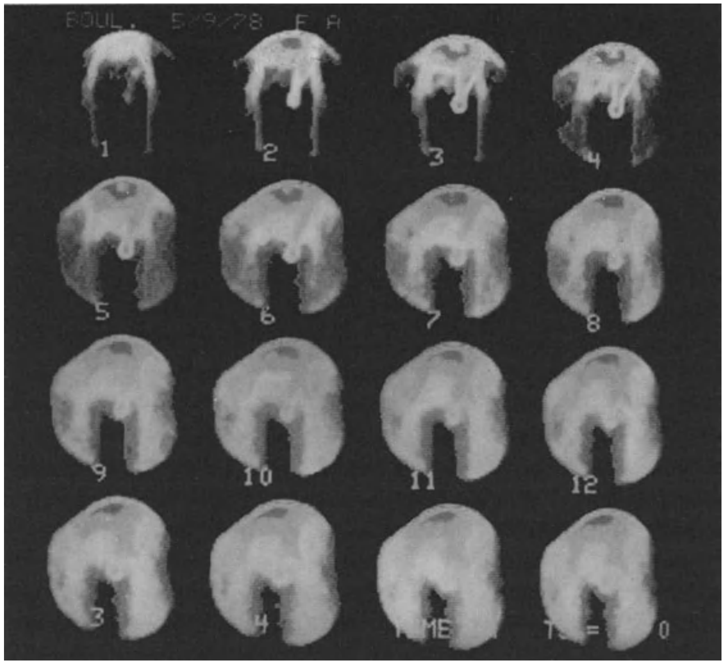

Fig. 1. Scrotal scans obtainet at 15-s intervals after $^{99m}Tc\ 04^{-}$ i.v.

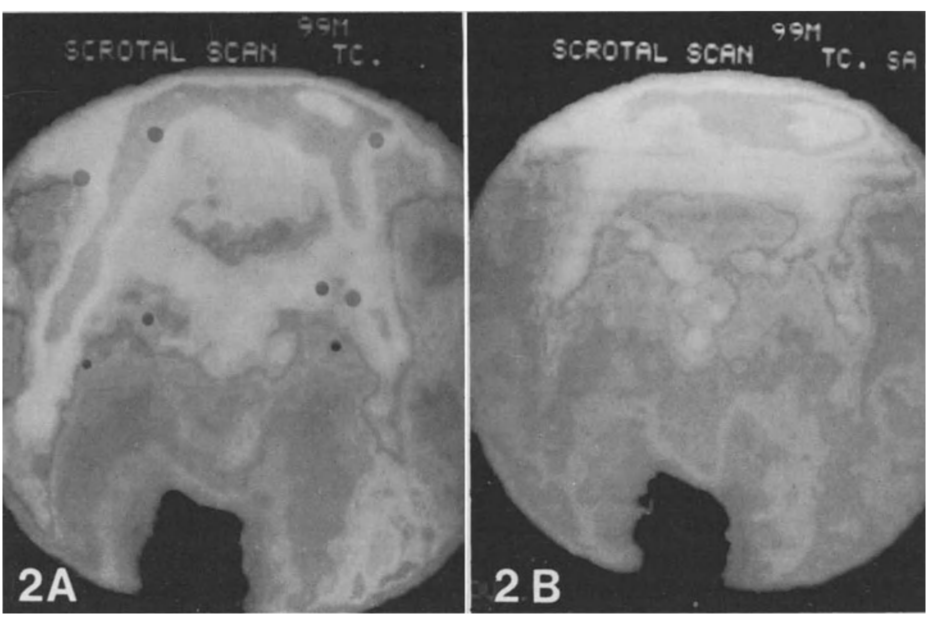

Fig. 2. Patient with scrotal asymmetry as revealed by $^{99m}Tc\ 04^{-}$, **A**; but not by ^{99m}Tc-labelled serum albumin, **B**

blood vessels, left and right hemiscrotum. Towards the end of the procedure a standard scintigraphic scan was performed to show whether this less sophisticated procedure might have been sufficient. The scrotal scintigram and the DSS were read "blindly", i.e., without previous knowledge of clinical or phlebography data. The diagnostic value of the isotopic procedure was established in comparison to retrograde phlebography as described by Comhaire and Kunnen [1].

Results

After our initial experience with ^{99m}Tc-labelled serum albumin we abandoned that technique, for positive results were obtained mainly in clinically evident cases of varicocele. The quick diffusion of ^{99m}Tc pertechnetate into the extracellular space may enhance abnormal findings. The advantages of the latter tracer as compared to the former are clearly shown in Fig. 2 (same patient as in Fig. 1).

Scrotal Scanning

As previously described [4], the study of scrotal scans obtained 5 min after i.v. injection of the tracer shows three types of pictures (Fig. 3): normal (very low,

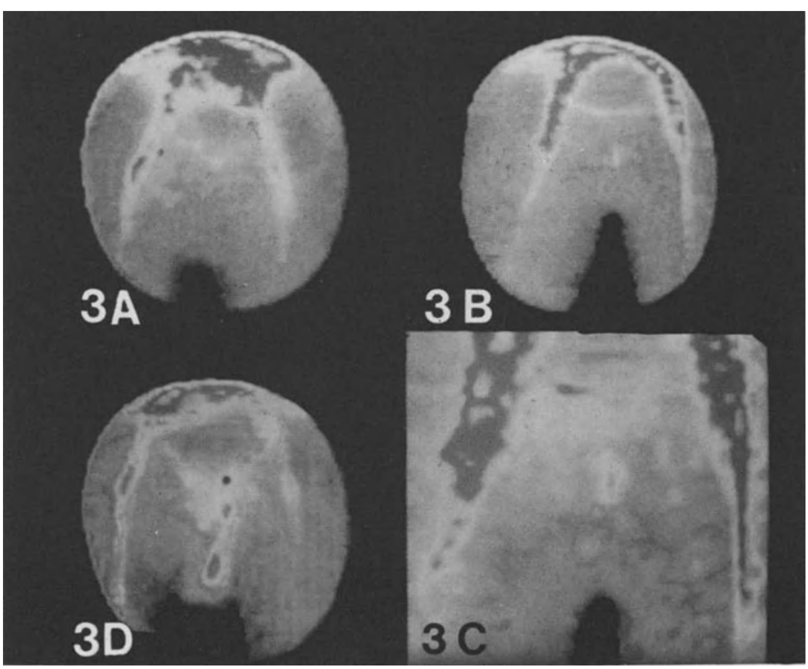

Fig. 3. Scrotal scans 15 min after 10 mCi ^{99m}Tc 04^{-}; normal **A** vs. asymmetrical scan **B,** (blow up, **C**); varicocele **D**

symmetrical radioactivity), asymmetrical (radioactivity at a moderate level, intensified on one side), typical varicocele (high radioactivity with evident venous pattern).

Of 240 patients, 104 showed normal and 60 asymmetrical scans, while 76 had typical varicocele. However, it may be difficult to differentiate between normal and asymmetrical scans. Correlations between clinical and "blind" scintigraphic diagnosis did not seem satisfactory: in 39 clinically diagnosed cases only 25 scans were positive and 14 were considered normal – a reliability of 64.1%, inferior to that of telethermography.

Dynamic Scrotal Scanning

Given the disappointing result detailed above, we chose to study the dynamic curve of the radioactive flow in each half-scrotum. Three different types of curves can be obtained (Fig. 4):

1. Normal; low, early maximum radioactivity that remains stable or rises only very slowly
2. Type 2; fast-growing, high radioactivity, above the iliofemoral level; the static scan generally shows a typical varicocele, which is also clinically detectable
3. Type 1; radioactivity rises progressively – sometimes only slightly above normal levels – and regularly, and tends to reach iliofemoral levels during the late measurements. Often there is also asymmetry on the (static) scan, but the curve allows better discrimination.

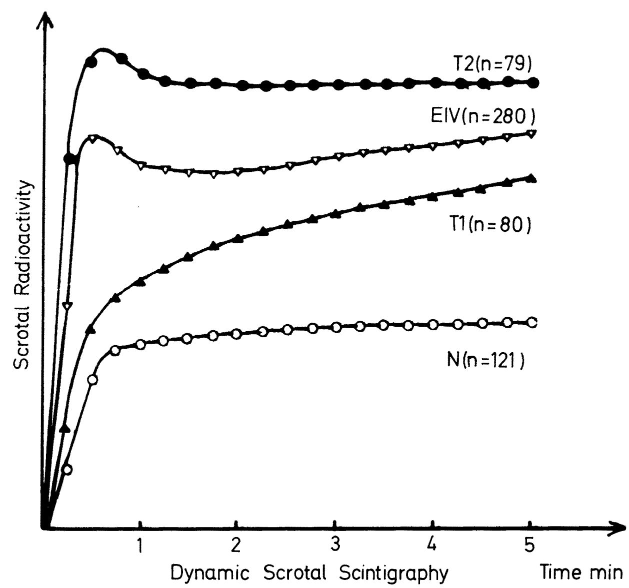

Fig. 4. Dynamic curves of scrotal vs. iliofemoral radioactivity as seen in 140 patients: *EIV,* external iliac vessel; *N,* normal curve; *T1,* type 1 curve; *T2,* type 2 curve; (*n* =), number of cases. Each hemiscrotum is singled out, giving a total of 280 for 140 patients

Table 1. Comparison of dynamic scrotal scanning with clinical findings (*n* =140)

Clinical status	Dynamic curves		
	Normal	Type 1	Type 2
Normal (*n* = 70)	88	30	22
Unilateral varicocele (*n* = 57)	6 (+23)*	15 (+23)*	36 (+11)*
Bilateral varicocele (*n* = 13)	4	12	10

* Contralateral varicocele

Table 2. Comparison of static scrotal scanning and DSS with phlebography in patients with clinically diagnosed varicocele (*n* = 39)

	Scrotal scans	Scrotal curves (DSS)	Phlebography
Normal	14	2	2
Abnormal	25	Type 1 = 16 > 37 Type 2 = 21	37

Table 3. Comparison of static scrotal scanning and DSS with phlebography in patients with no clinical varicocele (*n* = 40)

	Scrotal scans	Scrotal curves	Phlebography		
			Normal	Insufficience	Varicocele
Normal	26	12	10	2	
Abnormal	14	Type 1 = 17 > 28 Type 2 = 11		16	1 11

The performance of DSS has been compared with clinical evaluation and the results are shown in Table 1; two important findings must be stressed. First, curves were abnormal in 52 patients with no clinically diagnosed varicocele, i.e., 37.1% of cases (52 abnormalities in 140 patients). Second, 32 curves were abnormal contralateral to clinically diagnosed varicocele. A normal curve was found in 12% of clinically diagnosed varicoceles, i.e., in 83 cases (57 unilateral, 13 bilateral, i.e., 26 hemiscrota).

In order to study the significance of our findings, we established a correlation with phlebography in 79 patients. The rather small number of patients is explained, at least partly, by the failure of right-side catheterization (30% in our experience), which led us to exclude several patients. Comparative results are summarized in Tables 2 (patients with clinical varicocele) and 3 (no clinically diagnosed varicocele).

Discussion

Our results clearly show that static scintiscanning has but limited usefulness. It can visualize 64.1% of clinically detectable varicoceles and reveals only 46% of subclinical venous abnormalities. On the other hand, dynamic scrotal scanning correlates closely with phlebography. In clinical varicocele the overlapping is complete (37 abnormal curves and 37 normal phlebographies). In subclinical varicocele, DSS is faulty in only 5% of cases (two curves having been contradicted in 40 phlebographies). Comparisons between phlebographic findings and the type of abnormal curve show that there is no fundamental difference between curves seen in mere reflux and curves seen in true varicocele. This might explain the lack of correlation between the extent of the venous abnormality and the degree of impairment of spermatogenesis.

The abnormal gathering of radioactivity in the scrotum is still unaccounted for. Abnormal venous permeability caused by the reflux appears to be an explanation, but still has to be proven.

This procedure nevertheless seems to constitute an important step in the assessment of male infertility. A normal DSS proves the absence of venous abnormalities – with 95% certitude. The presence of high radioactivity contralateral to a clinical varicocele suggests the presence of subclinical venous abnormalities. Finally, a control DSS may detect a subclinical varicocele recurring after surgery.

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Comparison of Four Different Methods for the Diagnosis of Varicocele

F. H. Comhaire, M. Kunnen, M. Vandeweghe, and M. Simons

While the diagnosis of large varicoceles should not cause any problems, small varicoceles are often more difficult to detect on clinical palpation. Besides, some patients do present reflux in the internal spermatic vein without palpable distension of the pampiniform plexus [1]. Four objective techniques are available to diagnose such subclinical reflux. Scrotal thermography, Doppler blood-flow measurement and testicular perfusion analysis using radioisotopes are non-invasive, and useful for routine patient screening, whereas retrograde venography of the internal spermatic vein should be reserved for selected cases.

We have evaluated the usefulness of the three screening methods in relation to the following questions:

1. What is the value of the method for the selection of patients to undergo retrograde venography?
2. What is the accuracy of the method for the recognition of the side on which the reflux occurs?

Findings

Comparison Between Measurement of Scrotal Perfusion Using a Radioisotope and Telethermography

After intravenous injection of a bolus of 10 mCi sodium pertechnate with the patient standing erect, the radioactivity occurring over the pelvic region and scrotum was recorded by means of a gamma camera. Summation of radioactivity occurring during the period from 30 to 120 s after injection was registered on a polaroid film [3–5]. Comparative study was performed in 51 men consulting for infertility. The scrotal thermography was abnormal in 12 of 13 cases with clinically palpable varicocele, but in only nine was the technetium perfusion abnormal. Seven of 12 patients suspected of having varicocele presented a positive thermogram, as against only two with a positive perfusion study. Finally, of 26 cases clinically not suspected of having varicocele, four had an abnormal thermographic registration, whereas the technetium scan was not disturbed in any [2]. Computerized registration together with quantitative curve analysis in regions of interest does not improve the sensitivity of the method.

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Indeed, using this more sophisticated equipment, six of 14 patients recently examined for the detection of clinical or subclinical varicocele still had a falsely negative scrotal scan.

Technetium scanning results in a rather large number of falsely negative registrations. Such patients present spermatic venous reflux, but no stasis of blood occurs in the pampiniform plexus. Reflux is probably compensated through increased collateral efflux along the cremasteric and the deferential veins.

Comparison of Palpation, Doppler Flow Measurement, Telethermography and Venography

The next comparative study concerns 81 patients in whom a retrograde venogram of the internal spermatic vein was made. Patients were selected on the basis of clinical findings or as a result of the screening methods.

The venography revealed a retrograde opacification of the internal spermatic vein in 90% of cases. Two retrograde venograms were falsely negative: the reflux did not occur through the spermatic vein proper, but through a collateral connecting the perirenal venous plexus directly to the pampiniform plexus.

Clinical examination had correctly detected the varicocele in 56 of 81 cases (69%), in another nine cases (11%) reflux was suspected and confirmed by venography. In the remaining 16 cases (20%) the clinical examination had failed to detect reflux, which could however, be demonstrated on the venogram. In 18% of cases, clinical examination overlooked simultaneous right-side reflux occurring in a patient with left-side varicocele.

Doppler flow measurement correctly detected reflux in 82% of cases. In a further 8% of cases the Doppler result was falsely negative, and in 10% of cases the Doppler examination suggested reflux which could not be confirmed by venography.

As far as the localization of reflux is concerned, the Doppler registration was fully correct in only 58% of cases, falsely positive left-side predictions and falsely negative right-side predictions being particularly common.

Scrotal thermography correctly indicated the presence of reflux in 83% of cases. False-positive recordings occurred in 14%, false-negative results in 3% of cases. The prediction of the localization of reflux was correct in 73%.

Discussion

Our data indicate that scrotal thermography is slightly more reliable than the other methods applied for screening of spermatic venous reflux. Good results with the Doppler flow method can only be obtained under specific conditions: all examinations should be performed by the same person who has assessed the patient clinically. Strict diagnosis criteria should be observed and registrations should be performed using an apparatus for bidirectional measurement. Clear-cut reflux-efflux should be documented in both recumbent and erect position. If the examination is performed only with the Doppler stethoscope the results of this method are particularly poor.

New Developments

A most interesting development in the field of thermography has occurred with the development of flexible strips for contact thermography (Thermostrip, Bayer). Indeed, telethermography requires expensive equipment whereas contact thermography using a rigid plate is rather inadequate because of the difficulty in adjusting the scrotum against the plate.

A set of three Thermostrips allows for rapid and adequate assessment of the temperature of the scrotal skin. After the patient has been left 5–10 min in a cool room with the genital region uncovered, strips of 34°, 33°, and 32° C are sequentially applied. With the strip showing the best colour-contrast in place, possible differences in the temperature of the scrotal skin are carefully looked for (Fig. 1).

In a study comparing the aspect of scrotal tele- and contact thermography including over 100 patients, a perfect correlation between the two methods was demonstrated.

The Thermostrips are relatively cheap and, if manipulated with care, they can be used for up to 50 examinations.

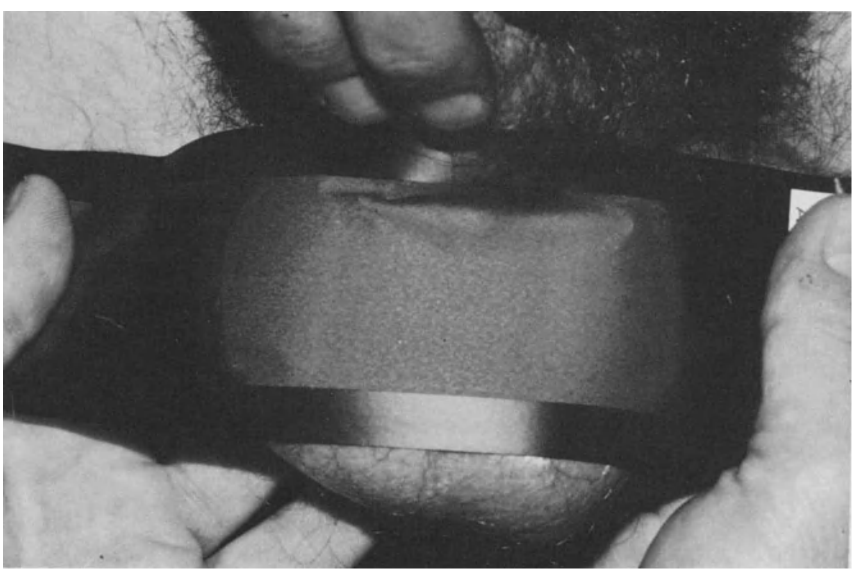

Fig. 1. Contact thermogram using Thermostrip (32° C) in a patient with clinically unpalpable reflux (subclinical varicocele). The strip is carefully folded around the scrotum whilst the patient holds up his penis. The cool skin of the right hemiscrotum changes the thermosensitive crystals of the strip to a brown colour. The zone with warmer skin temperature in the upper left hemiscrotum induces a green-to-blue colour

Conclusions

Study of the testicular perfusion with technetium pertechnate is more of academic interest than of practical significance for the screening of varicocele. The Doppler method yields satisfactory results only when a machine allowing for directional registration is used by a trained examiner. Scrotal thermography is the most reliable screening method. Thanks to the availability of flexible, multiple-use strips for contact thermography, this technique has become with us the method of choice in routine screening of infertility patients for varicocele.

The method may also be applied systematically in the follow-up of patients treated either surgically or by non-surgical methods.

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Varicoceles Combined With Other Fertility Disturbances: The Use of Kallikrein as a Diagnostic Test

N. Hofmann and L. Ebert

Due to the frequent appearance of varicocele, it can be expected that this disease is combined with other extratesticular and testicular fertility disorders. Such combinations were observed in 24.6% of our patients with varicocele and significant reflux [1].

Among the extratesticular diseases, the chronic non-specific genital infections, which are often subclinical, are of particular diagnostic importance, not only because of the frequency but also for the therapeutic steps, as the genital infections should be treated before the varicocele operation or percutaneous occlusion is performed.

As far as the combination with other testicular diseases is concerned, we have observed congenital as well as early-acquired testicular disorders, for example undescended testis. In these cases, the pathogenesis of the damage can be assessed; therapy and prognosis are predictable. However, the diagnosis of acquired testicular damages may be difficult where the anamnesis does not give any indication. In some cases unfortunately, only the postoperative results lead to the diagnosis.

In such circumstances, the kallikrein test has proved to be a useful diagnostic tool [4]. According to our studies, reported elsewhere [3, 5], there are three types of results:

1. A positive effect with improved spermatological findings
2. A negative effect with impaired spermatological findings, especially of spermatozoa motility
3. No changes

The positive effect was observed in disturbances of epididymal function of spermatozoa maturation, disturbances of spermiogenesis, for example Sertoli cell asthenia, characterized by exfoliation of spermatids, and disturbances of spermatozoa output.

As these disorders are characteristic for early varicocele orchiopathy (Hofmann et al., this vol., p. 32), we have employed the kallikrein test for this disease.

The kallikrein dosage was 200 units orally three times a day – independent of meals – for 5 weeks. The spermatological control tests were performed in the 6th week. Tables 1 and 2 show the results of tests in patients with varicocele and varicocele orchiopathy and in patients with varicocele in combination with other testicular diseases.

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Table 1. Results of tests with kallikrein (K) in 29 patients with varicocele and early varicocele-orchiopathy

		m	SD	*t*-value	2-tail probability
Spermatozoa count (million/ml)	Before K After K	30.86 41.58	31.14 37.30	3.01	0.005
Motility (%)	Before K After K	43.10 52.41	16.33 11.54	3.39	0.002
Progressive motility (classes acc. to Eliasson [2])	Before K After K	2.10 1.48	0.90 0.57	−4.59	0.000
Normal morphology (%)	Before K After K	33.83 36.83	17.26 16.24	1.25	0.220

Table 2. Results of tests with kallikrein (K) in 20 cases of varicocele in combination with other testicular diseases

		m	SD	*t*-value	2-tail probability
Spermatozoa count (million/ml)	Before K After K	13.70 16.00	20.41 18.07	1.32	0.202
Motility (%)	Before K After K	34.75 38.50	14.73 18.14	1.20	0.244
Progressive motility (classes acc. to Eliasson [2])	Before K After K	2.95 2.35	0.88 1.04	−3.04	0.007
Normal morphology (%)	Before K After K	23.44 29.50	13.37 15.88	2.16	0.046

The individual analysis of the second group showed varying results, positive, indifferent, and negative. Positive results were found in the cases in which varicocele orchiopathy was the determining disease, indifferent results in cases of advanced varicocele orchiopathy and in cases in which the other testicular disease was determining, and negative results in the "inflammatory" but noninfectious testicular disorders.

The negative results were of some significance: as kallikrein/kinine are substances promoting inflammatory reactions, kallikrein enhanced the pathological "inflammatory" testicular processes; the spermatological results, and particularly the spermatozoa motility, were found to be impaired. Such results were observed in the testicular disorders with peritubular and perivascular round-cell infiltrates with increased mast-cell formations, and in those with only increased formations of mast cells. According to the autopsy results of Suoranta [6], these findings are not so rare as generally may be expected.

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III. Therapy

A Short Historical Review and Comparative Results of Surgical Treatment for Varicocele

M. Glezerman

Historical Review

Surgery of varicocele dates back to the first century A. D.; Hotchkiss [18] reports on Celsus, who seems to have performed the first documented ligation and cauterization of a varicocele. In 1541, Ambroise Paré [30] described a condition of "compact groups of vessels [in the scrotum] filled with melancholic blood". If one interpretes "melancholic" as "quiet, slow" then one might assume that Paré was aware of blood stasis in varicocele veins. For centuries, varicocele was treated solely in order to relieve the dragging weight and pain (Table 1). In 1833, Bumstead and Taylor [5] described several of the approaches then used for treatment and palliation. Rather popular was a complicated suspensory for the testes which exerted pressure on the varicocele and had to be attached to an abdominal belt. The surgical method described by these authors, the so-called Woods operation centred on the scrotal contents and consisted of passing wire loops under tension around the vessels in the scrotum and leaving them in place until they eventually cut themselves out. Obviously, abscess formation and ulceration of the scrotal skin was the rule. R. F. Weir [cited in 16] later modified the procedure by introducing a spring steel clamp to apply tension and removing the wires before they cut themselves out of the scrotum. Another surgical tool was the so-called Andrew's varicocele clamp [15]. This instrument was used to remove the dilated vessels together with the scrotal skin which

Table 1. Milestones in the surgical treatment of varicocele

Author	Year	Procedure
Wood [cited in 16]	18th century	Wire looping of dilated plexus
Weir [cited in 16]	1800	Spring steel clamping of plexus
Andrew [cited in 15]		In toto clamping of plexus and excision
Ivanissevich [21]	1918	High ligation of spermatic vein
Palomo [29]	1949	High ligation of spermatic vein and artery
Ribeiro [31]	1956	Tunneling of separated pampiniform plexus
Ishigami et al. [19]	1970	Vascular anastomosis between great saphenous vein and distal stump of spermatic vein or pampiniform plexus
Skafik [34]	1972	Plication of the fasciomuscular tube of the spermatic cord

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covered them. Later, the classical operation for varicocele was introduced, involving the division, ligation, and excision of the pampiniform plexus, or part of it, by the inguinal or scrotal route. The high recidivation rate, severance of endarteries, and postoperative infections prompted Ivanissevich in 1918 to introduce his "high ligation of the internal spermatic vein" by a retroperitoneal approach [21]. In 1960, Ivanissevich summarized his personal experience in 4,470 operative cases [20]. The complication and recidivation rate was astonishingly low.

In 1949, Palomo [29] presented his technique of high ligation of both spermatic vein and artery. However, Baumgärtel et al. [1] reported later degenerative changes in the testes of rabbits following this procedure, and Fiedler and Rost [9] confirmed this observation.

In 1965, Ribeiro [31] proposed a "tunneling operation", burying the separated pampiniform plexus in a tunnel constructed from the aponeurosis of the obliquus abdominis externus muscle. Physical effort then causes compression of the plexus.

Microsurgical techniques were applied to the treatment of varicocele by Ishigami et al. [19] in an attempt to preserve the venous circulation through the spermatic vein after its high ligation and division. Anastomoses were performed between the saphenous vein and either the distal part of the severed spermatic vein or the pampiniform plexus.

Shafik [34] believes that varicocele formation is basically due to an inefficient fasciomuscular pump and has proposed a plication operation of the fasciomuscular tube of the spermatic cord, regardless of whether the affected plexus is

Table 2. Results of surgical correction of varicocele in infertile men

Author	Year	No. of cases	Seminal impr. (%)	Pregnancy rate (%)
Tulloch [36]	1955	30	66	30
Scott [32]	1961	93	78	29
Charny [6]	1962	36	64	38
Hanley and Harrison [14]	1962	78	68	28
Scott and Young [33]	1962	142	70	30
MacLeod [25]	1965	77		41
Fritjofsson and Ahren [10]	1967	35	62	17
Klosterhalfen et al. [23]	1968	58	61	19
Charny and Baum [7]	1968	104	61	24
Brown et al. [4]	1968	185	60	43
MacLeod [26]	1969	108	74	40
Kaufmann et al. [22]	1974	80	85	26
Gunter [13]	1975	60	83	52
Brown [3]	1976	251	58	41
Dubin and Amelar [8]	1977	986	70	53
Lome and Ross [24]	1977	80	78	51
Homonnai et al. [17]	1980	238	50	40
Newton et al. [28]	1980	149	55	34
Glezerman et al. [12]	1980	99	47	40
Total		2,889	65.5	42.1

dilated due to insufficiency of the spermatic vein or the cremasteric vein (see page 5, this volume).

To date, the most widely used surgical method for correction of varicocele is based on the technique originally proposed by Ivanissevich and Gregorini [21].

The association between varicocele and infertility was suggested for the first time by Bennet in 1889 [2]. Forty years later, Macomber and Sanders [27] reported on restoration of fertility in a patient operated on for correction of varicocele. The next case of restored fertility after surgical treatment for varicocele appeared in 1952 [35]. Since then numerous reports have substantiated this beneficial effect of surgery (Table 2). Data compiled on nearly 3,000 infertile men operated on for varicocele revealed improved seminal parameters in some 65% and an average pregnancy rate in their female partners of 42%.

Our Own Experience

Methods

We have performed the Ivanissevich procedure in 99 men in whom oligozoospermia, asthenospermia, and/or teratospermia coincided with a left varicocele. Spermiograms were compared preoperatively, at 3-month intervals after the operation for the first year, and thereafter according to the availability of the patient for up to 32 months. The patients were asked to refrain from sexual intercourse for 4 days before every semen analysis. The main parameters of the spermiogram, that is absolute sperm count (volume of semen times concentration of sperm cells), sperm motility, and sperm morphology (percentage of normally configurated sperm cells) were classified empirically into six grades (Table 3). The parameters of the spermiogram were classified with a three-digital index, thereby making it possible to determine changes (only changes of two grades were considered). The diagnosis of varicocele was determined by clinical examination. Size and degree of varicocele were determined using a classification presented earlier [11].

Table 3. Classification of sperm analysis

Grade	Total count	Motility (%)	Morphology (%)
1	$\leq 10 \times 10^6$	$\leqslant 10$	$\leqslant 30$
2	$11-29 \times 10^6$	11–19	31–39
3	$30-49 \times 10^6$	20–29	40–49
4	$50-74 \times 10^6$	30–39	50–59
5	$75-99 \times 10^6$	40–59	60–69
6	$> 100 \times 10^6$	$\geqslant 60$	$\geqslant 70$

Table 4. Pregnancy rate related to changes in seminal parameters following high ligation of varicocele

Parameters	No. of cases	Pregnancies	Pregnancy rate (%)
Improved	71	33	46.5
Unchanged	25	4	16.0
Unknown	3	3	
Total	99	40	40.4

Table 5. Seminal fluid analysis after high ligation and division of left spermatic vein

	Total count		Motility		Morphology	
	n	%	*n*	%	*n*	%
Improvement	57	59.4	46	47.9	38	46.9
Deterioration	3	3.1	7	7.3	8	9.9
Unchanged	31	32.3	30	31.3	30	37.0
Normal values before surgery	5	5.2	13	13.5	5	6.1
Subtotal	96	100	96	100	81	99.9
Unknown	3		3		18	
Total	99		99		99	

Results

Thirty-three pregnancies were reported by 71 patients in whom seminal parameters improved (46.5%), while in the partners of 25 males with unchanged seminal parameters after surgery only four pregnancies occurred (16%); the difference was statistically highly significant (Table 4). Following surgery, the improvements in total count, motility, and morphology were comparable (Table 5). In 59.4% of the patients the total count was higher, in 47.9% the percentage of motile sperm cells was higher, and in 46.9% the percentage of normally configurated sperm cells increased. Of those cases in whom seminal parameters eventually improved, 33.8% showed improvement in one parameter, 33.8% in two parameters, and 32.4% in all three parameters (Table 6).

When the incidence of reported conceptions was related to the improvements occurring in the three parameters, it appeared that increase in total sperm count had little impact on subsequent pregnancy rates (Table 7). Only three pregnancies were reported by ten men in whom the the sperm cell content was the only parameter to increase following surgery. However, the wives of five of seven men in whom the percentage of motile sperm cells increased conceived.

Improvement in seminal parameters was related to the time since surgery (Fig. 1). Improvement occurred first in motility, then in total sperm count, and

Table 6. Combination of seminal parameters improved following high ligation of varicocele

Parameters improved	*n*	%
One	24	33.8
Two	24	33.8
Three	23	32.4
Total	71	100

Table 7. Improvement in seminal parameters following high ligation of varicocele and related pregnancy rates

Improvement	*n*	Pregnancies	Pregnancy rate (%)
Total count	10	3	30.0
Total count + motility	16	6	37.5
Total count + morphology	8	3	37.5
Total count + motility + morphology	23	12	52.2
Morphology	7	4	57.1
Motility	7	5	71.4

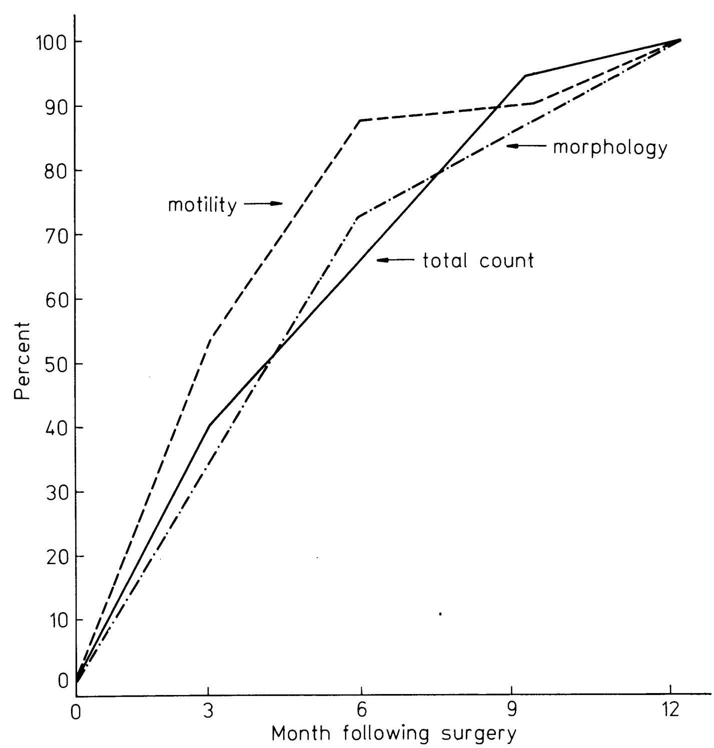

Fig. 1. Motility, morphology, and total count of sperm cells after high ligation of the spermatic vein: follow-up of patients in whom seminal parameters improved following surgery

finally in morphology. In 64 of the 71 men in whom seminal parameters improved this occurred within 12 months of surgery, in seven improvement was observed 13–19 months after operation.

Conclusion

During the past three decades much evidence has accumulated which strongly suggests a deleterious effect of varicocele on male fertility. To date, the main therapeutic approach for correction of varicocele is surgery, but nonsurgical modalities have in recent years gained wide acceptance. However, it seems too early to state that the surgical era has passed; both surgical and nonsurgical therapy will probably remain in the armamentarium. Treatment results, as far as fertility is concerned, should be assessed for 1 year following intervention, primarily monitored by repeated semen analysis. If no improvement in seminal parameters occurs within this period, management should be reevaluated.

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Treatment of Varicocele by Transcatheter Embolization With Bucrylate

F. Comhaire and M. Kunnen

Treatment of varicocele aims at the complete interruption of reflux in the internal spermatic vein or veins. In recent years a non-surgical cure by means of intraluminal obliteration has been applied as an alternative to surgical ligation and division of these veins.

Techniques for treating sclerosis of the veins have been described in previous papers; we will report on a new technique, i.e., transcatheter embolization using the tissue adhesive isobutyl 2-cyanoacrylate (registered name Bucrylate, manufactured by Ethicon).

Methods

The embolization is performed using specially designed coaxial catheters. The outer catheter is cobra-shaped and is used first for diagnostic venography.

The venography has to be performed carefully in order to demonstrate all accompanying connecting or collateral veins. The ideal site for occlusion is inferior to the lowest anastomosis between the spermatic vein and the renal vein or perirenal venous plexus.

Immediately after the selective venography has been performed, a thin inner catheter fitted with a suitable guide wire is pushed through the diagnostic cobra catheter into the spermatic vein. After the guide wire is removed, the few millilitres of 60% Isopaque are injected by hand in order to control the exact localization of the catheter tip. The patient is brought to an almost horizontal position, chosen to stop the blood circulation in the spermatic vein. This precludes accidental thrombosis of the renal vein and injection of the testicular veins.

An aliquot of 0.3–0.6 ml Bucrylate, opacified with 60% Isopaque is injected into the spermatic vein through the inner catheter. In contact with blood, the Bucrylate polymerizes immediately to form a stable thrombus. The inner catheter is immediately withdrawn, and 10 min later a control venography is performed, using the cobra catheter which was left in place.

The advantage of this method is that even larger veins can be embolized without problems. It is also possible to pass through several competent valves and to successfully embolize the insufficient caudal part of the spermatic vein connected by insufficient collateral veins to the perirenal plexus.

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Since the Bucrylate embolus can be localized with extreme precision, the drug never enters the blood circulation and does not reach the testicular veins. The embolus is stable and recanalization has not been observed even after 3 years' follow-up. Coaxial catheterization only once provoked vessel dissection. Pain, thrombophlebitis, extravasation and fever never occurred in our patients. None of them developed hydrocele and no lung embolism was recorded. The method thus proved to be safe and indeed successful [1].

Results

Changes in epididymal-testicular function were followed by repeated measurements of serum testosterone and semen characteristics.

The mean testosterone concentration before treatment was 519 ng/dl, after treatment 560 ng/dl. However, patients with a clearly subnormal pretreatment testosterone concentration (< 450 ng/dl) presented a rapid normalization.

In a follow-up of 80 patients during 3 months or more after treatment the following changes in sperm characteristics were noticed:

1. Sperm count clearly increased in two-thirds of the cases, the mean concentration doubling within 3–6 months after treatment. Two patients with pretreatment azoospermia produced spermatozoa in their ejaculates; however, the post-treatment sperm count did not exceed 5 million/ml and no pregnancies ensued.
2. The mean percentage of spermatozoa with rapid progressive motility tended to increase as well. As a result the number of motile spermatozoa per millilitre (so-called motile sperm count) significantly increased in 80% of the patients.
3. Sperm morphology is known to be the most difficult characteristic to influence by any treatment. In our patients the mean pretreatment percentage of ideal spermatozoa was only 8%; it increased to a mean value of 17% after treatment. Significant improvement occurred in slightly more than half of the cases.

Effect of Varicocele Embolization With Bucrylate on Fertility

During the 2-year period from January 1979 to December 1980, 78 patients were treated by means of embolization. Follow-up data are available on 72 cases; of these 51 were treated for infertility. All of these men presented abnormal semen characteristics in at least two semen analyses performed with a 1-month-or-more interval. In eight patients the infertility was secondary; whereas in 43 it was primary. Using the cascade method of Morucci et al. [2] the following results were obtained.

Treatment was considered a technical failure in one case with persistent reflux due to the presence of a adrenogonadal bypass. In all other cases complete interruption of reflux was proven by disappearance of abnormal findings on clinical examination, together with normalization of Doppler blood flow examination and scrotal thermography.

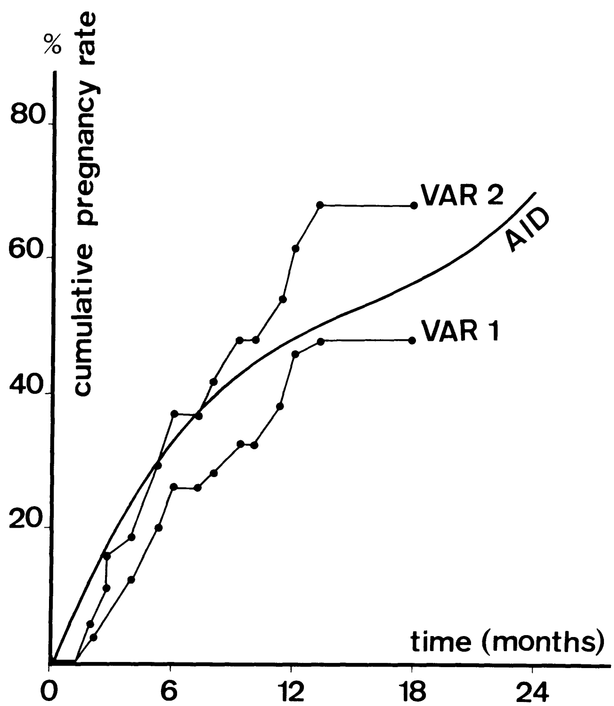

Fig. 1. Life table of results obtained in artificial insemination with donor sperm (AID); all infertility cases (*VAR 1*) and selected infertility cases (*VAR 2*) were treated by means of transcatheter embolization with Bucrylate. [From Comhaire F (1981) Evaluation of the effect of varicocele embolization with Bucrylate in fertility. In: Proceedings of the Third World Congress of Human Reproduction, Berlin (West), 22–26 March, 1981. Excerpta Medica, Amsterdam]

Five patients decided to switch to artificial insemination with donor semen since no pregnancy was achieved for 6 months or longer after embolization. Of these cases, one presented azoospermia together with elevated FSH in peripheral blood. Of the remaining patients, 11 did not achieve pregnancy despite the presumably normal fertility of their female partners. Three men whose partners' fertility status was unknown did not achieve pregnancy (one of these males was azoospermic). The fertility of the female partners of 13 men not achieving pregnancy was impaired (endometriosis, two cases; immunological factor, one case; hyperprolactinemia, two cases; ovulation disturbances, eight cases).

Sixteen men reported pregnancies; three of these pregnancies ended in early abortion, 13 progressed well and ended in the uneventful delivery of a normal child. Using Morucci's et al. [2] cascade method the overall pregnancy rate thus was 32%.

In evaluating the effect of treatment, however, the time factor should be considered. It was therefore decided to express treatment results using the statistical method of life tables as described by Schwartz and Mayaux [3], applying the computerized modification developed by Trounson et al. [4]. Furthermore, we elected to compare the life-table cumulative pregnancy rate obtained after treatment for varicocele with the life-table cumulative pregnancy rate obtained with artificial insemination with donor semen as calculated on the results obtained during the same 2-year period. Thirteen months after embolization a cumulative pregnancy rate of 45% was reached; this is identical to the cumulative pregnancy rate after artificial insemination with deep-frozen donor semen. Except for the sixteen pregnancies detailed above no further conception was reported by the group of men treated for varicocele. In the group of patients treated with donor sperm by artificial insemination, the cumulative success rate continued to increase after 13 months.

Since treatment of one patient technically failed and varicocele persisted, it is justified to eliminate this case from the statistics. Furthermore it is known that varicocele together with azoospermia has a poor fertility prognosis. In particular, if serum FSH is increased such patients should not be offered treatment. Finally, it is difficult to evaluate the effect of treatment on the male if the fertility status of the female is disturbed. Most studies on the effect of treatment in the male exclude couples in which the female partner presents any abnormality impairing her chances to conceive.

If we reconsider our data including only infertile relationships of at least 1-year duration, in which the male partner presents abnormal semen analysis but no azoospermia, and in which the female partner does not present evident abnormalities impairing her fertility, a cumulative pregnancy rate of 68% is obtained within 13 months after technically successful embolization. This cumulative success rate corresponds with the success rate for artificial insemination with donor semen obtained over 24 months.

Conclusion

Treatment of varicocele by means of transcatheter embolization of the internal spermatic vein with the tissue adhesive Bucrylate is a safe and highly effective method resulting in a 45% cumulative pregnancy rate within 13 months. Treatment should be offered to the male partners of infertile couples presenting either clinical or subclinical varicocele concommitant with subnormal semen quality. Treatment of men with azoospermia or with normal semen quality is not indicated. Care should be taken to fully explore the fertility status of the female, since the fertility prognosis after treatment of the male may be hampered by adverse factors in the female.

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Percutaneous Sclerosation of the Testicular Vein Using a Balloon Catheter

P. Riedl

Since the first description of testicular vein obliteration by Jaccarino in 1977, many other methods have been described for preventing reflux into the pampiniform plexus [4, 5, 8, 9, 11–14]. At the University of Vienna Medical School since 1979 a coaxial catheter-balloon catheter system has been used for sclerosing, in order to minimize the risk of sclerosant reflux into the renal vein [8].

Material and Method

In 87 patients the testicular vein was sclerosed with 2–3 cm^3 4% hydroxy-polyethoxydodecane (Aethoxysklerol, Kreussler Co.) via a balloon catheter system. The technique has been reported elsewhere [8, 9]. Patients were aged between 13 and 48 years (mean age, 27.3 years). In about 50% testicular vein obliteration was performed for infertility (duration: 5 months to 14 years); in the remaining cases, obliteration was indicated for other reasons (accidental detection of varicocele on general check-up, pains, or increasing size of varicocele).

Prior to obliteration, then 1 week and 1, 3, 6, and 12 months after treatment, the patients underwent clinical examination, contact thermography, and spermatologie analysis.

Results

Of the 214 patients undergoing selective vein phlebography, 106 were scheduled for obliteration, which was successful in 87 cases (82.1%). Failures were due to anatomical factors in 13 cases and to other causes (e.g., collapse of the patient, fluoroscopy time exceeding self-imposed limits) in six.

In 72 cases (82.75%) varicoceles completely disappeared following treatment. Six of the 15 patients with persistent or only slightly smaller varicoceles underwent repeat phlebography and reobliteration, with complete disappearance of the variococele in five cases.

Improved spermiograms were seen in 71.3% of all cases; in 18.4% spermiograms were unchanged, and in 10.3% of cases spermiograms deterio-

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rated. The female partners of 14 of 45 patients who had wanted children have meanwhile conceived.

Transitory scrotal vein thrombosis was palpated in 15 instances, but disappeared in all cases within some months. Perivascular infiltration of the radiopaque substance in the area of the proximal spermatic vein was found to be present in five cases; nine patients complained of transitory low-grade pain. Serious complications of longer duration were not noted.

Discussion

Transfemoral testicular vein obliteration with a sclerosing agent via a balloon catheter constitutes an alternative to surgical ligation. The failure rate in this study (11.5%) is comparable to that of surgical treatment [6, 7, 10]. In experienced hands the procedure takes 15–30 min. The obliteration is done on an outpatient basis, and the patient is able to leave the hospital immediately after the procedure. Complications and success rates in terms of qualitative improvement of the spermiogram and the occurrence of pregnancy are also comparable to postoperative results [1, 2].

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Effects of Varicocelectomy on Spermatogenesis

H. Y. Lee, H. B. Shim, and K. S. Lee

Varicocele has been considered one of the most common causes of male infertility, based mainly on the following three factors:
1. The incidence of varicocele has been shown to be higher in infertile males (12%–39%) than in the general population (8%–23%).
2. Varicocele has been associated with abnormalities in semen quality and testicular histology in 20%–50% of patients.
3. Varicocelectomy has been shown to result in improvement in semen quality (50%–80%) and pregnancy rate (20%–50%).

However, considerable controversy concerning the detrimental effects of varicocele on male reproductive function has appeared in the literature. Many patients with varicocele have normal semen quality and fertility; semen quality is not always improved by varicocelectomy (20%–50% of varicocelectomized patients); and pregnancy may occur in partners of patients whose semen quality does not improve after varicocelectomy (30% of patients without improvement) [1, 5, 6].

We wish here to present our clinical experience in evaluating the effects of varicocelectomy on semen quality and fertility in patients with left-sided varicocele.

Materials and Methods

A random selection of 37 patients with left-sided varicocele who had been referred to our infertility clinic were studied during the 5-year period from 1975 to 1979. They were 20–40 years of age (mean age, 29 years), and the duration of infertility ranged from 1 to 15 years (mean, 3 years) (Table 1). The mean values of seminal parameters analyzed in at least two semen samples from each patient were:

volume, 2.9 ml (range: 0.5–5.1 ml)
count, 26 × 10^6/ml (range: 0–275 × 10^6/ml)
motility, 34% (range: 0%–80%)
normal shape, 68% (range: 0%–85%)

There were no significant differences in semen parameters between age groups, except for a significantly higher sperm count ($p < 0.01\%$) in the group of patients 21–25 years of age (Table 1).

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Table 1. Mean values for seminal parameters in patients with varicocele according to age group

Age group	No. of cases	pH	Volume (ml)	Count ($\times 10^6$/ml)	Motility (%)	Morphology (%)
20 (−)	3	7.3	3.7	34	47	79
21−25	7	7.4	3.4	59*	39	65
26−30	13	7.4	2.4	25	39	71
31−35	11	7.4	2.5	10	27	65
36 (+)	3	7.7	4.3	7	13	71
Mean of total	37	7.4	2.9	26	34	68

* $p < 0.01$

Table 2. Mean testicular volume and plasma hormone levels in relation to size of varicocele

Varicocele		Testicular volume		FSH (IU/l)	LH (IU/l)	Testosterone (ng/ml)
Grade	No. of cases	Left (ml)	Right (ml)			
I	8	18*	20*	7.06*	7.94*	6.13*
II	18	17	18	6.37	6.23	5.70
III	11	16	18	5.64	6.08	6.37
Mean of total	37	17	18	6.39	6.25	5.97

* $p > 0.1$

Patients were divided into three grades according to the size or the severity of the varicocele: grade I, varicocele detectable during Valsalva's maneuver (eight cases); grade II, palpable varicocele (18 cases); grade III, visible varicocele (11 cases) (see Table 2). The mean volume of the testes, measured by means of an orchidometer, was 17 ml (range: 15−25 ml) on the left side and 18 ml (range: 12−30 ml) on the right side (Table 2).

Mean levels of plasma FSH (6.39 IU/l with a range of 2.02−13.00 IU/l), LH (6.25 IU/l with a range of 2.20−11.15 IU/l), and testosterone (5.97 ng/ml with a range of 3.00−9.75 ng/ml) measured by radioimmunoassay were within normal ranges. There were no significant differences in size of testicle between left and right sides and among the grades of varicocele. There were also no significant differences in hormonal levels among the grades of varicocele ($p > 0.1$) (Table 2).

There were no significant differences in parameters of semen analysis such as pH, volume, motility, and morphology among the three grades of varicocele ($p > 0.1$) (Table 3).

Azoospermia was noted in three cases, oligospermia of less than 20×10^6/ml was found in 21 cases, and a sperm count of more than 21×10^6/ml was found in 13 cases (Table 4). Six subjects with sperm counts of more than 41×10^6/ml (mean volume, 2.5 ml; count, 90×10^6/ml; motility, 63%; normal shape, 79%) were assigned to a control group which was not submitted to varicocelectomy

Table 3. Mean sperm quality in relation to size of varicocele

Varicocele		pH	Volume (ml)	Count ($\times 10^6$/ml)	Motility (%)	Morphology (%)
Grade	No. of cases					
I	8	7.6*	2.7*	49	24*	72*
II	18	7.4	2.9	25	38	72
III	11	7.3	3.0	11	33	60
Mean of total	37	7.4	2.9	26	34	68

* $p > 0.1$

Table 4. Mean sperm count in relation to size of varicocele

Varicocele		Sperm counts of 10^6/ml				
Grade	No. of cases	0	1–10	11–20	21–40	41 (+)
		No. of cases				
I	8	0	5	1	0	2
II	18	1	3	4	7	3
III	11	2	5	3	0	1
Total	37	3	13	8	7	6

and the remaining 31 patients with sperm counts of less than 40×10^6/ml underwent varicocelectomy.

Testicular biopsies performed on three azoospermic patients before varicocelectomy revealed hypospermatogenesis with peritubular fibrosis in two cases, and Sertoli-cell-only syndrome in one case.

Four patients with sexual impotence and one patient with idiopathic microscopic hematuria were found among the 37 patients with varicocele.

The sexual impotence might have had psychological origins, since the hormone levels of FSH, LH, and testosterone were within normal limits in these patients, and the findings of the Minnesota Multiphasic Personality Inventory applied to them revealed depression, anxiety disorders, and psychophysiological sexual disorders [7]. The idiopathic hematuria might have been caused by renal vein compression since evaluations of the patient's urinary tract were normal [8].

Varicocelectomy was done by means of high ligation and division of the internal spermatic vein at the left inguinal (Poupart) ligament via the suprainguinal approach using a modified Ivanissevich technique [9] (Fig. 1). Follow-up studies were carried out monthly or bimonthly for more than 12 months after varicocelectomy.

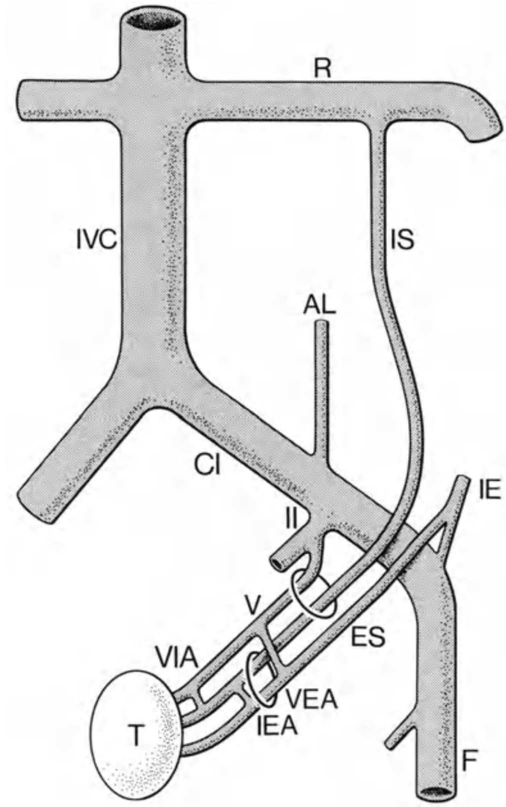

Fig. 1. Left venous drainage of testis. *IVC,* inferior vena cava; *R,* renal vein; *IS,* internal spermatic vein; *AL,* ascending lumbar vein; *CI,* common iliac vein; *II,* internal iliac vein; *IE,* inferior epigastric vein; *ES,* external spermatic vein; *V,* vasal vein; *F,* femoral vein; *T,* testis; *VIA,* vasal vein-internal spermatic vein anastomosis; *VEA,* vasal vein-external spermatic vein anastomosis; *IEA,* internal spermatic vein-external spermatic vein anastomosis

Results

Sperm appeared in one of the three azoospermic patients after varicocelectomy. However, these azoospermic patients had been treated with HCG and clomiphene citrate for more than 6 months in addition to undergoing varicocelectomy. Mean total sperm counts increased from 61×10^6/ml to 91×10^6/ml only in the grade II varicocele group after varicocelectomy. The mean fertility index (total counts × motility × morphology ÷ 10^6) increased from 19 to 33 only in the grade II varicocele group following varicocelectomy (Table 5).

In connection with general semen parameters, mean sperm counts increased from 14×10^6/ml to 21×10^6/ml, and fertility index increased from 12 to 18 after varicocelectomy. No significant changes were observed in pH, volume, motility, and morphology after the varicocelectomy ($p > 0.1$) Table 6).

Regarding preoperative sperm counts, 3% of patients with sperm counts of less than 10×10^6/ml, but 26% of patients with sperm counts of more than 10×10^6/ml showed improvement after varicocelectomy when judged by the arbitrary rise of the fertility index by one or more points (Table 7). By the same criterion,

Table 5. Semen quality before and after varicocelectomy in relation to size of varicocele

Grade of varicocele (no. of cases)	Total count ($\times 10^6$)		Motility (%)		Morphology (%)		Fertility index	
	Before	After	Before	After	Before	After	Before	After
I (6)	22.5	24.0	0	0	80	80	1.8	1.9
	15.0	17.5	5	10	56	60	0.4	1.1
	15.0	20.0	3	5	70	80	0.3	0.8
	6.0	7.5	20	25	70	65	0.8	1.2
	50.0	20.0	5	0	65	72	1.6	0.1
	30.0	22.0	12	15	70	70	2.5	2.3
Mean	23.1	18.5	8	9	69	71	1.2	1.2
II (15)	50.0	100.0	40	60	70	70	14.0	42.0: I
	70.0	60.0	60	65	75	80	31.5	31.2: P
	100.0	187.5	70	65	80	80	56.0	97.5: I
	15.0	16.0	15	20	84	80	1.9	2.6
	18.0	44.0	8	8	75	75	1.1	2.6: I
	50.0	225.0	60	65	80	80	24.0	117.0: I,P
	75.0	80.0	40	30	70	70	21.0	16.8
	0	0	0	0	0	0	0	0
	94.6	114.0	34	40	80	78	25.7	35.6: I,P
	42.0	39.2	30	28	72	69	9.1	7.6
	24.0	18.0	20	25	63	70	3.0	3.2
	178.5	240.0	28	30	75	72	37.5	51.8: I
	89.6	144.0	30	40	82	78	22.0	44.0: I,P
	30.0	22.5	60	65	80	80	6.2	4.7
	75.0	80.0	26	30	79	70	36.0	41.2: I
Mean	60.8	91.3	35	38	71	70	19.3	33.2
III (10)	0	3.0	0	0	0	75	0	0.2
	0	0	0	0	0	0	0	0
	15.0	32.0	60	70	70	70	6.3	0.5
	48.0	39.0	60	60	70	75	20.0	17.6: P
	45.0	44.8	28	20	77	79	9.7	7.1
	18.0	20.0	40	45	70	70	2.5	3.3
	9.0	10.5	60	65	68	70	7.3	9.1: I
	63.0	40.0	30	22	78	80	14.7	7.0: P
	10.0	8.0	10	20	77	79	0.8	1.3
	37.2	30.0	15	20	70	75	3.9	4.5
Mean	24.5	22.7	30	32	58	68	6.5	5.1
Total mean of 31 cases	41.8	55.2	28	30	66	69	11.7	18.0

I, improvement; P, pregnancy; Fertility index = total count $\times$ motility $\times$ morphology $\div$ 10^6

improvement was observed in nine (29%) of the 31 varicocelectomized patients following the operation (Tables 5 and 8).

Six (19%) of the 31 varicocelectomized patients impregnated their wives 1–31 months after varicocelectomy (Tables 5 and 8), and two subjects (33%) of the six cases in the control group impregnated their wives during the same period. No recurrence was found after varicocelectomy in the present series

Table 6. Mean semen quality before and after varicocelectomy

Varicocele Grade	No. of cases	Varico-celectomy	pH	Volume (ml)	Count ($\times 10^6$/ml)	Motility (%)	Mor-phology (%)	Fertility index
I	6	Before	7.6	2.7	9	8	69	1.2
		After	7.4	2.4	9	9	71	1.2
II	15	Before	7.4	2.9	20	35	71	19.3
		After	7.5	2.6	34	38	70	33.2
III	10	Before	7.3	3.1	8	30	58	6.5
		After	7.5	3.0	8	32	68	5.1
Mean of total	31	Before	7.4[a]	2.9[a]	14	28[a]	66[a]	11.7
		After	7.7	2.7	21	30	69	18.0

[a] $p > 0.1$

Table 7. Changes in sperm counts after varicocelectomy based on preoperative counts

Changes[a]	Preoperative sperm counts $< 10 \times 10^6$/ml No. of cases	%	$> 10 \times 10^6$/ml No. of cases	%	Total No. of cases	%
Increased	1	3	8	26	9	29
Unchanged	12	39	2	6	14	45
Decreased	3	10	5	16	8	26
Total	16	52	15	48	31	100

[a] Changes of more than one point in the fertility index (total counts × motility × morphology ÷ 10^a)

Table 8. Effect of varicocelectomy on sperm count and pregnancy rate

Varicocele Grade	No. of cases	Sperm count (fertility unit)[a] Decreased No. of cases	%	Unchanged No. of cases	%	Increased No. of cases	%	Pregnancy rate No. of cases	%
I	6	2	6	4	13	0	0	0	0
II	15	3	10	4	13	8	26	4	13
III	10	3	10	6	19	1	3	2	6
Total	31	8	26	14	45	9	29	6	19

[a] Changes of more than one point in the fertility index (total counts × motility × morphology ÷ 10^6)

[10–12]. Sexual impotence disappeared in three of the four presenting patients after varicocelectomy [7].

Conclusion

No significantly beneficial effects have been observed on semen quality and fertility after varicocelectomy in our present study. This is in contrast to other studies [2–4] reporting improvement in seminal parameters in 50%–80% of cases and pregnancy rats up to 50% following surgery for varicocele.

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Varicocele: Changes in the Anatomy of Venous Reflux After Ligation

J. P. Pryor, J. T. Hill, and A.V. Hirsh

In 1977 Hill and Green [1] published the results of a venographic study of the varicoceles of 26 infertile men, of nine men requesting vasectomy, and of 13 patients requiring surgery for a variety of scrotal conditions. Ascending venography was performed in all 48 patients, retrograde renal venography in 26 patients and cremasteric venography in 12 patients. On this basis they classified varicoceles as due to testicular vein insufficiency in 18 patients, due to cremasteric vein insufficiency in 15, and mixed in 10; the five remaining patients were unclassified. The relevance of this work is that it emphasises that varicoceles may be of more than one type. This paper reports venographic changes that follow ligation of a varicocele.

Method

Ascending scrotal venography was performed in 24 men with clinical varicoceles requiring surgery (18 of whom were subfertile). The procedure was performed with the patient under a general anaesthetic and his head elevated 30°. A vein in the pampiniform plexus was cannulated near the testis; 20 ml 45% Hypaque was injected and a radiograph taken. The cannula was left in situ and the testicular and cremasteric veins were ligated at the level of the internal inguinal. Following this, a further 20 ml of contrast was injected through the cannula, which had remained in the vein of the pampiniform plexus, and a further radiograph taken. The subsequent fate of these patients over the ensuing 18 months has been studied.

Results

The pattern of venous drainage demonstrated is shown in Table 1. The testicular (internal spermatic) vein was demonstrated in only 67% of patients and the superficial external pudendal vein was demonstrated in an almost equal number. There was a wide variation in venous drainage. The repeat venograms following ligation of the veins showed that the pattern of venous drainage was unchanged in nine patients and diverted in 15. On subsequent examination it was found that there was no recurrence in those patients where the venous drainage appeared

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Table 1. Pattern of venous drainage of the pampiniform plexus in 24 varicocele patients before and after ligation of the cremasteric and testicular veins (patients' heads elevated 30°)

Vein	Preligation venogram		Postligation venogram	
	Number	%	Number	%
Testicular	17	71	9	38
Superficial external pudendal	15	63	15	63
Cremasteric	12	50	11	46
Vein of ductus deferens	8	33	8	33
Contralateral communications	6	25	9	38
Obturator	4	17	4	17
Superficial circumflex iliac	1	4	1	4

Table 2. Change in venous drainage following ligation of cremasteric and testicular veins and recurrence of varicocele

Venous drainage	Number	Recurrence	
		Clinical	Doppler
Diverted	15	4	5
Unchanged	9	–	1

Table 3. Clinical data of 11 infertile men whose pattern of venous drainage changed following venous ligation

Ascending venography TV opacification		Retrograde venography TV reflux	Recurrence of varicocele	Semen changes			Conception
Preligation	Postligation			Volume	Sperm density	Motility	
+	+	+	0	–	↓	–	
+	+	+	+	↑	↑	↑	
+	0	+	0	↓	–	↑	
+	0	+	+	↑	↑	↑	
+	0		0	–	–	–	*
+	0		0	–	↓	–	
+	0		(+)	–	↓	↑	
0	0	+	0	↓	↓	–	*
0	0	+	0	↑	(↑)	↑	
0	0	0	0	–	↓	–	
0	0		0	↑	–	↑	

unchanged but there were four clinical recurrences (five diagnosed by Doppler examination) in the 15 cases where the blood had been diverted (Table 2).

Where the operation had been carried out for subfertility, only two of the 18 patients had partners who conceived in the subsequent 18-month follow-up

Table 4. Clinical data of seven infertile men whose pattern of venous drainage was unchanged

Ascending venography TV opacification		Retrograde venography TV reflux	Recurrence of varicocele	Semen changes			Con-ception
Preligation	Postligation			Vol-ume	Sperm density	Motility	
+	+	+	(+)	–	–	–	0
+	+	0	0	$\uparrow$	$\uparrow$	$\uparrow$	0
+	+	0	0	–	–	$\uparrow$	0
+	+		0	–	–	–	0
+	+		0	–	–	$\uparrow$	0
+	+		0	–	–	$\uparrow$	0
0	0	+	0	–	–	–	0

period. In both these patients the pattern of venous drainage had changed but there had been no improvement in the semen quality. Table 3 shows the findings on ascending venography, retrograde venography (when performed), recurrence of varicocele, changes in semen quality, and incidence of conception by partners occurring in the subsequent 18 months for the 11 patients whose pattern of venous drainage was changed by the varicocele ligation. Table 4 gives the results when there was no change in the pattern of venous drainage (seven patients). These tables emphasize the variable haemodynamic findings in patients with varicocele and illustrate why it is very difficult to generalize about the changes that may occur following varicocele treatment.

Discussion

The fact that the testicular vein was not shown on ascending venography in two-thirds of the patients may have been due to the reflux of blood towards the testis which occurred when the patient was placed with his head elevated 30°. This is certainly possible in those patients in whom the retrograde renal venogram showed testicular vein reflux. In those patients where the testicular vein did not fill on retrograde renal venography it is more likely that competent valves prevented reflux.

This study has shown that the venous drainage of a varicocele takes place through many veins and that ligation of the cremasteric and testicular veins at the internal inguinal ring is not effective in stopping antegrade flow through these veins. Recurrence of the varicocele did not occur when the pattern of venous drainage was unchanged; and the effects of the operation on semen quality and fertility were extremely variable.

An example of this variability in the effects of a varicocele is the size of the left testis in patients with varicocele. Table 5 compares the sizes of the left and right testes in 69 men with small, medium or large varicoceles. The size of the left

Table 5. Difference in testicular lengths in varicocele ($n = 69$)

Size of varicocele	Number of cases	Size of left testis as compared with right testis (cm)				
		−1.0	−0.5	0	+0.5	+1.0
Small	35	12%	11%	57%	14%	6%
Medium	24	25%	21%	46%	8%	–
Large	10	50%	40%	10%	–	–

testis was reduced in only 22% of patients with small varicoceles, in 46% of those with medium varicoceles, but in 90% of patients with large varicoceles.

Finally, an article by Mulcahy entitled "As Others See Us" [2] included a map of the British Isles drawn from the biased viewpoints of different nationalities. We have similar differences of opinion on varicoceles; some feel that treatment of varicocele is of great benefit in improving either semen quality or fertility, while others believe that ligation of a varicocele has no effect whatsoever on fertility. No true map of the British Isles resulted from the varying biases, and at present we are still searching for the true relationship of varicocele to infertility.

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The Value of HCG After Varicocelectomy in Severely Oligospermic Men

I. Samberg, A. Zilberman, and M. Sharf

The high ligation procedure has become one of the most popular operations performed for male infertility. Amelar and Dubin [1] have reported that 39% of infertile males have varicocele.

This operation has gradually been mustering greater support over the years. There have even been some suggestions that because varicocele is such a progressive disease, prophylactic varicocelectomy might be advisable when first diagnosed on routine examination.

Most authors [2–5] note a 70% improvement in semen analysis 3–6 months after the operation, with subsequent pregnancies in up to 50% of cases. In cases of severe oligospermia (under 10 million/ml), the prognosis is poor, even when high ligation is performed.

Treatment with gonadotropins is indicated in hypogonadism. The clinical term "hypogonadism", as most often used, refers to failure in interstitial cell function that results in decreased production or absence of male sex hormones. However, seminiferous tubular failure is often associated with decreased Leydig cell function and may also occur without significant changes in testicular hormonal production.

In gonadotropin therapy to the male patient, no guidelines such as chemical and biological expressions are available. Nor, for that matter, is the correlation between steroid biosynthesis and germ cell maturation as well established for the testis as it is for the human ovary.

We treated 54 men with varicocele, who had undergone high ligation of the left spermatic vein, by administration of HCG. At least two semen analyses were performed by standard dilution techniques.

The levels of FSH, LH and testosterone were measured. A total of 48,000 units of HCG were given intramuscularly, in 16 divided doses over a 12-week

Table 1. HCG dosage schedule; units per injection = 3,000

Week	No. of injections
1	3
2	2
3	2
4–12	1
Total	16 × 3,000 units = 48,000 units

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Table 2. Seminal and endocrinological parameters of 54 patients, measured before and after administration of HCG (Mean values)

	Before	After
Sperm count (× 10^6/ml)	7	23
Sperm motility (%)	42	59
FSH (mIU/ml)	19	11
LH (mIU/ml)	12	7
Testosterone (ng/dl)	511	577

period starting 1 week after operation in accordance with the dosage schedule shown in Table 1.

Of 54 patients who had undergone internal spermatic vein ligation, 19 showed no improvement in sperm count. The remaining 35 men showed improvement, a response rate of 64%. Table 2 shows the seminal parameters before and after treatment with HCG. Of the 35 patients showing improvement, 21 achieved pregnancy, a rate of 39%.

Discussion

Since after completion of meiotic division spermiogenesis and epididymal function are androgen-dependent, the sperm pathology and histologic disturbances found in men with varicocele could be explained by disturbed Leydig cell function, resulting in decreased testicular androgen production.

Dubin and Amelar [1] reported improvement in semen quality and pregnancy rate in oligospermic men with varicocele treated with human chorionic gonadotropin. They suggested a relation between Leydig cell dysfunction and disturbed spermatogenesis in patients with varicocele. Treatment with HCG in this particular group of severely oligospermic men improved the results after high ligation.

Although chemically HCG is clearly different from HLH, it is considered to resemble the latter in its Leydig cell stimulation effect. Futterweit et al. [6] reported that in men administration of HCG is followed by increased plasma levels of testosterone. We have also found testosterone elevation in response to HCG.

The testosterone response to HCG i.m. injections seems to be biphasic. A first peak is observed 2 h after the injection, the second at 48 h; this response is dose-dependent and can last for 6 days [7]. This effect could be attributed to (a) the long circulatory half-life ($t_{1/2}$ – 30 h) of the i.m.-administered hormone and (b) the probability that the half-life of HCG at the cellular level might be longer than its circulatory half-life, thus inducing a prolonged biological effect at the Leydig cell level. It is thought that this increase in Leydig cell activity provides a local stimulus to the seminiferous tubules. The decrease in levels of FSH after the administration of HCG is due to a total inhibition of endogenous release of FSH.

In this study there was a 64% response rate and a 39% pregnancy rate, compared with 72% and 45% respectively in the study by Cheval et al. [8]. There have been no side effects from the HCG and no patient's condition became significantly worse as a result of therapy. The study provides evidence for a cause-effect relationship between varicocele, Leydig cell dysfunction, and impairment of semen quality.

Conclusion

In patients with severe oligospermia, high ligation does not always result in significant improvement of semen quality or fertility. Based on our study, we believe that a combination of surgery and medical treatment with human chorionic gonadotropin can improve testicular androgen production in patients with varicocele and testicular dysfunction.

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The Influence of Superimposed Male and Female Factors of Infertility on the Prognosis of Spermatic Vein Ligation in Varicocele

Y. Soffer, R. Ron-El, D. Pace-Shalev, J. Sayfan, and E. Caspi

Surgical treatment of patients with varicocele and impaired semen quality has been widely investigated [1]. However, the studies were performed on selected patients, excluding those couples with superimposed or associated infertility factors.

There is a paucity of information on the impact of high ligation in couples with multiple factors of infertility, who actually constitute the majority of varicocele cases. This study analyses the semen quality and pregnancy rate following operation in patients with varicocele and associated infertility factors.

Material and Methods

Among infertile couples referred to the Infertility Clinic between January 1976 and May 1979, 219 cases of varicocele were diagnosed. Both partners of each couple underwent a thorough infertility work-up. Clinical examination of the male included careful evaluation of scrotal content and accessory glands. Bacterial culture of semen and sperm analysis [2] were performed. The latter included sperm count, motility, viability, morphology, seminal volume, pH, fructos, *myo*-inositol [3] and Zn^{2+}. Functional evaluation of pituitary-testicular axis and testicular biopsy were performed in cases of oligozoospermia below 5×10^6/ml. Clinical examination of the female covered menstrual cycle evaluation and mechanical factors. When necessary, hysterosalpingography and laparoscopy were performed.

Ten azoospermic patients and 34 patients demonstrating normal seminal parameters were excluded. The remaining 175 cases included oligozoospermia (sperm counts below 20×10^6/ml), teratozoospermia (normal forms below 60%) and/or asthenozoospermia (2 h motility index – percent × grade – below 150). These cases were divided into four groups:

Group I, patients with varicocele and impaired semen quality without any other male or female infertility factor
Group II, cases of varicocele demonstrating impaired semen quality and prostatovesiculitis [4]
Group III, cases of varicocele with impaired semen quality and demonstrating a severe degree of testicular failure [5]

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Group IV, cases of varicocele with impaired semen quality and concomitant female infertility factors

A high ligation of the left spermatic vein was performed on 147 patients according to the method of Palomo [6]. The surgical procedure was refused by 28 patients. Postoperative follow-up began 3 months after surgery and examinations were repeated quarterly and semi-annually.

Results

Good postoperative anatomical results were obtained in 129 patients. In 18 cases a postoperative recurrent venous reflux was demonstrated; these cases were excluded from the study. In group I, a significant improvement of only the motility index was recorded following surgery, while no significant changes were observed in other seminal parameters. In all other groups, no change in any sperm variables was observed following operation.

Postoperative fertility rate results were as follows:

Group I: Cumulative pregnancy rate was 51% within 6 months and 62% within 12 months after surgery. No pregnancy was recorded during the second year of follow-up (Fig. 1). These results are significant improvement compared with a control group followed up for 6 months without operation. This control group consisted of 19 patients who declined operation and 17 from group I in whom high ligation took place more than half a year after their referral. In these 36 patients the cumulative pregnancy rate was 14% ($p < 0.005$ as compared with group I).

Group II: One pregnancy was recorded out of 16 cases within the first postoperative 6 months of follow-up, 25% cumulative pregnancy rate within 1

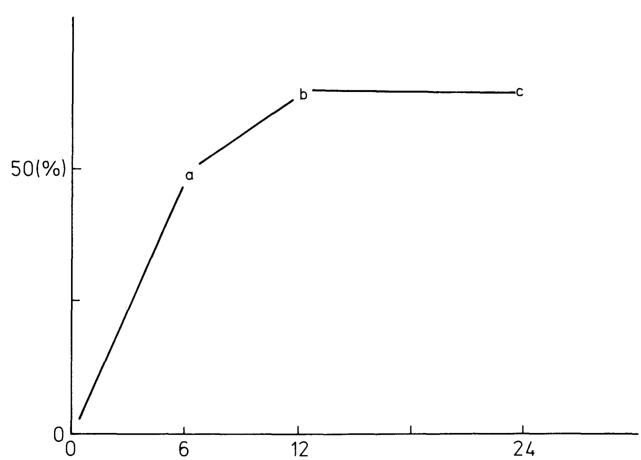

Fig. 1. Cumulative pregnancy rate following high ligation in group of 55 patients with varicocele only. *a*, 28 cases (51%); *b*, 34 cases (62%); *c*, no additional cases

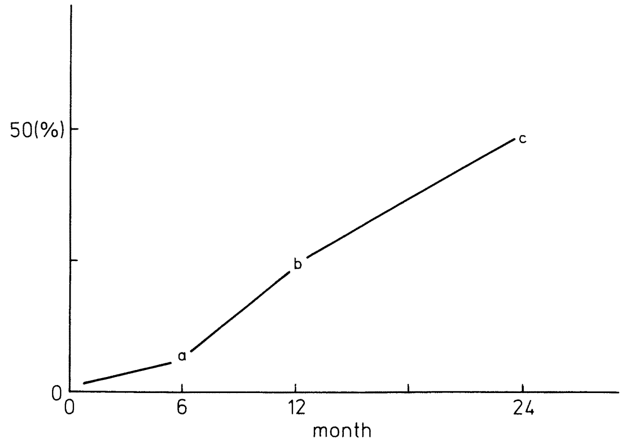

Fig. 2. Cumulative pregnancy rate following high ligation in group of 16 patients with varicocele and prostatovesiculitis. *a,* one case (6%); *b,* four cases (25%); *c,* eight cases (50%)

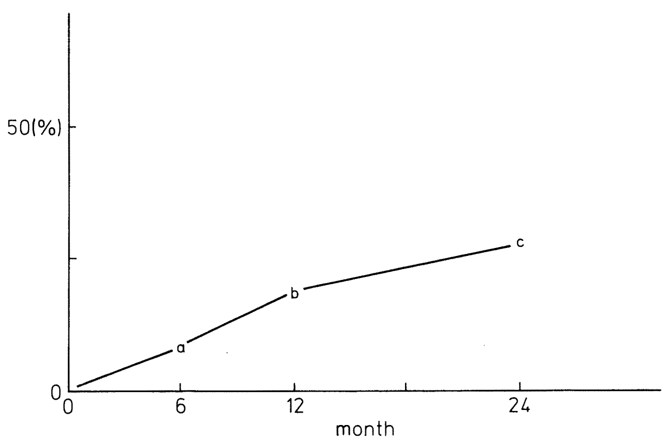

Fig. 3. Cumulative pregnancy rate following high ligation in group of 16 patients with varicocele and testicular failure. *a,* one case (6%); *b,* three cases (19%); *c,* five cases (31%)

year and 50% within 2 years. In this group, additional treatment was given when necessary (Fig. 2).

Group III: The cumulative pregnancy rate within the first 6 months was 6%, 19% within 1 year and 31% within 2 years. These results are significantly lower than those of group I (Fig. 3).

Group IV: Cumulative pregnancy rate following surgery was significantly low compared with group I – 2.4% within the first 6 months, 9.5% within 1 year and 31% within 2 years (Fig. 4).

Figure 5 summarizes the cumulative pregnancy rate following surgery in all four groups: 60 pregnancies in 129 couples were recorded, yielding an overall pregnancy rate of 47%.

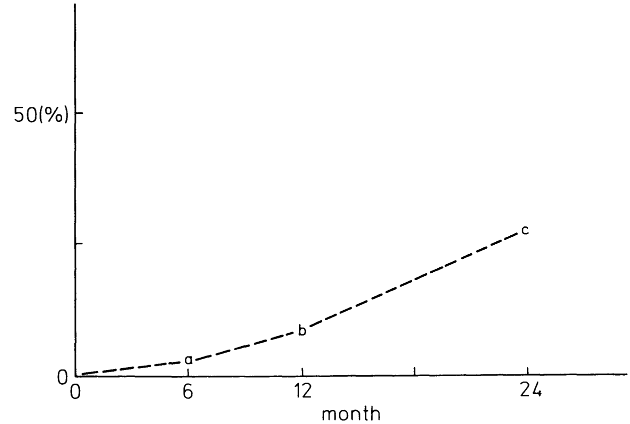

Fig. 4. Cumulative pregnancy rate following high ligation in group of 42 couples presenting varicocele and female factors. *a,* one case (2.4%); *b,* four cases (9.5%); *c,* 13 cases (31%)

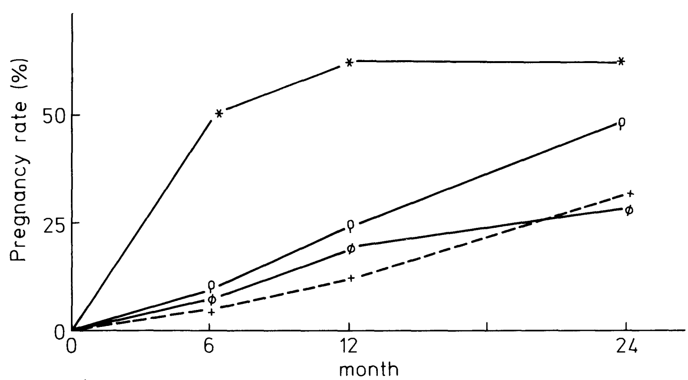

Fig. 5. Comparison of cumulative pregnancy rates following high ligation from Figs. 1–4. *———*, varicocele only; p———p, varicocele with prostatovesiculitis; ϕ———ϕ, varicocele with testicular failure; +———+, varicocele with female factors (From Soffer Y, Ron-El R, Sayfan J, Caspi E: Spermatic vein ligation in varicocele: prognosis and associated male and female infertility factors. *Fertil Steril* 40: 353, 1983. Reproduced with permission of the publisher, The American Fertility Society)

In conclusion, surgical treatment of varicocele produces best results in those cases where no other infertility factors are found. Semen quality as measured by sperm motility index improves, and is associated with a greater percentage of pregnancies within a shorter period. With severe testicular failure or female infertility factors, the prognosis worsens. The presence of prostatic pathology requires additional treatment and results similar to those in group I are eventually obtained. A re-evaluation of the fertility status of both partners should be carried out if pregnancy fails to occur within 6 months to 1 year following surgery.

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Multicenter-Compiled Results of Pregnancies After Non-surgical Cure of Varicocele

F. Comhaire, E. W. Jecht, L. Schwarzstein, and G. Van Maele

One of the major difficulties in evaluating the effect of varicocele treatment is the lack of uniformity in patient selection, follow-up, treatment techniques, criteria for success and statistical methods. The number of patients treated by each center may be relatively small and the data from control groups are scarce and contradictory.

In evaluating the success of treatment either the overall success rate or the cumulative success rate can be calculated. The latter makes use of the life-table technique which takes into account the time factor. The time factor is of primary importance in the evaluation of treatment particularly when events are not defined by the all-or-nothing principle. The great majority of patients treated for varicocele do not have infertile semen, in terms of azoospermia, but the potential fertilizing capacity of their ejaculate is to some extent decreased. The chances of conception being reduced, the time necessary to possibly achieve a pregnancy is increased. Any treatment which decreases this time, therefore, is to be considered effective, even if the total number of pregnancies (overall pregnancy rate) is not different from that in a matched control group.

Furthermore, the lapse of time which has passed between the treatment and the evaluation of the effect will influence the results in terms of overall success rate. The use of the life-table method overcomes these difficulties since the cumulative success rate is calculated in relation to the number of patients still under follow-up.

Methods and Subjects

The results of three centers involved with non-surgical treatment have been compiled. For each case the following information was requested:

1. Status at the moment of the last control: pregnant; still followed-up without pregnancy; lost to follow-up; switched to alternative treatment such as artificial insemination with donor semen; treatment failure due to persistence or recurrence of the varicocele
2. Number of months elapsed between the date of treatment and the date of last control or presumed date of conception
3. Information about the fertility potential of the female partner: apparently undisturbed, impaired or unknown, i.e., not explored

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Results were evaluated by means of the life-table method described by Schwartz et al. [1] using a computerized programme elaborated by Trounson et al. [2].

Full data were obtained on a total of 230 cases:
111 from the Erlangen-Nurnberg group, Drs. Jecht and Zeitler; 68 from the Argentine group in Rosario, centralized by Dr. Schwarzstein; and 51 from the clinic in Ghent.

Results

The mean duration of follow-up tended to be longer in the material from Rosario; it was similar in the cases seen in Erlangen and in Ghent. This difference should not influence the results, however, since the life-table calculation corrects for such differences.

As far as the fate of patients whose female partners did not conceive is concerned, there are some striking differences between the groups (Table 1). Indeed, 44% of the Erlangen cases were lost to follow-up, while 5% switched to another treatment. No treatment failures were observed.

In Rosario only 15% of cases were lost to follow-up; 5% switched to another treatment, but 13% were considered treatment failures. In Ghent the lost-to-follow-up rate was the lowest, only 3% of cases were considered treatment failures and 10% switched to another treatment.

As far as the fertility potential of the female partner is concerned, some differences are prominent (Table 2). In Erlangen, 28% of patients treated had a subfertile partner, but information on 47% is lacking. In Rosario not more than 2% of the men had subfertile partners; information is missing on 16% of cases. In Ghent, 28% of the men had a subfertile partner and the situation of the female is unknown in 10% of cases.

Table 1. Outcome of cases not obtaining pregnancy

	n	Lost to F. U.	Other treatment	Failure
Erlangen	111	44	5	0
Rosario	68	15	5	13
Ghent	51	4	10	3

Table 2. Fertility potential of partner

	n	Impaired	Unknown
Erlangen	111	28	47
Rosario	68	2	16
Ghent	51	28	10

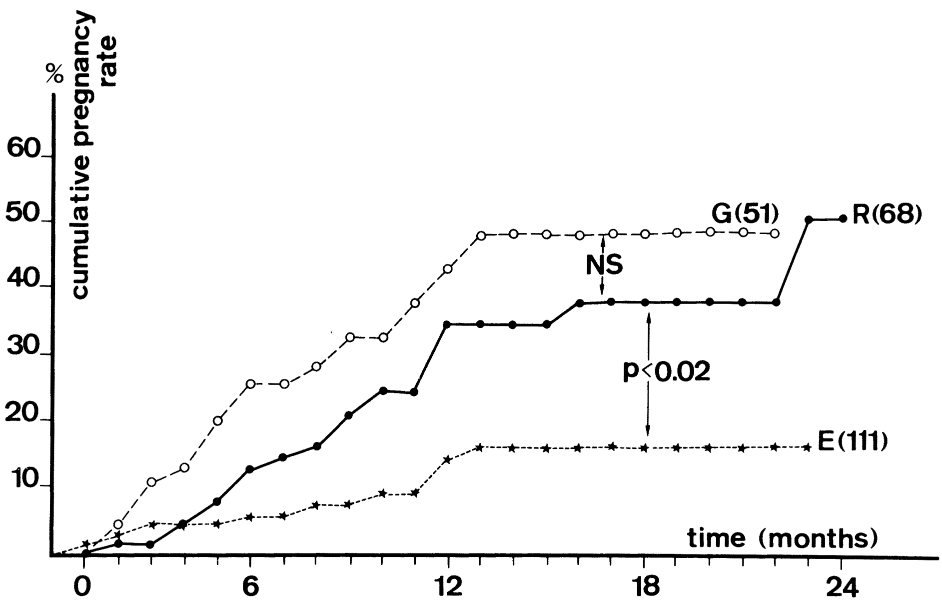

Fig. 1. Pregnancies occurring after non-surgical cure of varicocele. Shown are the life-table curves of 111 cases treated in Erlangen (*E*), of 68 cases treated in Rosario (*R*), and of 51 cases treated in Ghent (*G*). *NS,* not significant

Pregnancy Rates

The cumulative pregnancy rates and the life-table curves from Rosario and Ghent are similar, not statistically different (Fig. 1). At both centers pregnancies occurred primarily between the second and 12th month after treatment. Only a few pregnancies occurred after that time, contrasting with the clearly higher pregnancy rate during the first 12 months. Considering the higher percentage of technical failures in the patients treated in Rosario, both life-tables should be considered identical.

Treatment in the Erlangen group seems to be significantly less successful, since both the life-table aspects and cumulative pregnancy rates are much lower. Since no technical failures are reported, the difference must be due to either different selection of patients or lack of sufficient data. Considering that almost half of the Erlangen cases were lost to follow-up and/or data on the fertility potential of the female was lacking, insufficient data on treatment results seems to be the more likely explanation.

Discussion

This study demonstrates the usefulness and limitations of collaborative, multicenter evaluation of treatment protocols. The statistical methods are applicable, though clear differences in patient material and adequacy of follow-up certainly interfere. Further extension of this project through the inclusion of matched controls and surgically treated patients is suggested.

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