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## The continuing conundrum of varicocele

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Varicocele is an abnormal dilatation and tortuosity of the pampiniform venous plexus of the spermatic cord, chiefly affecting the internal spermatic vein and less commonly the cremasteric (external spermatic) vein. There are two types of varicocele: 1. the primary or idiopathic – the most common type, and 2 the secondary, due to kidney or retroperitoneal tumour, lymphadenopathy and hepatic congestion.

### How common is a varicocele?

Although rare in paediatric population, the prevalence of idiopathic varicocele markedly increases with pubertal development to approximately 15% by the late teenage years, a rate similar to that in adult population (1,2). If a varicocele does not develop during the adolescent years, that individual normally will not develop a varicocele later in life. Once present, varicoceles do not disappear spontaneously. On the other hand varicoceles are progressive lesions that may hinder testicular growth and function (spermatogenesis and steroidogenesis) over time. Approximately 40% of men with primary infertility have a varicocele (3) and the percentage may even double in men with secondary infertility (4). However, it should be remembered that more than 80% of varicoceles are not associated with infertility (5).

Approximately 80% of varicoceles are unilateral, left sided. Dubin and Amelar reported a 15% incidence of bilateral varicocele (3). But isolated right sided varicocele is rare.

### Why do men get varicocele?

Varicoceles are a consequence of man's upright posture, because they are rare in other species (6). The formation of varicocele and its preponderance on left side have been attributed predominantly to anatomic variances. Valve pathology (congenital absence of valves or incompetent valves) is not the sole cause; but it certainly contributes to varicocele formation and its severity (7,8).

Following are the causes for the preponderance of varicocele on the left side

- Left internal spermatic vein is 8 to 10 cm longer than the right because of its higher insertion into left renal vein and the lower position of the left testis, with a proportional increase in pressure head.
- Internal spermatic vein inserts perpendicularly into the left renal vein on the left and with an oblique angle into the inferior vena cava on the right. The inferior vena cava is thought to enhance drainage on the right because of a Venturi effect associated with its comparatively greater flow (9).
- Increased left renal vein pressure has been noted secondary to two nutcracker phenomenon mechanisms. The proximal nutcracker describes compression of the left renal vein as it passes between the aorta and superior mesenteric artery. The distal mechanism describes retrograde blood flow through the deferential (vasal) and external spermatic veins caused by the compression of the left common iliac vein as it course under the left common iliac artery (10).
- Adrenomedullin, a potent vasodilator expressed in adrenal and kidney tissues but not in the testes has been isolated in blood samples from the testicular veins of men with varicocele. Whether adrenomedullin plays a role in the formation of varicocele is questionable (11).

### What are the effects of varicocele?

Presence of clinically detectable varicocele is associated with testicular hypotrophy, an abnormal steroidogenesis and gonadotropin axis and abnormal spermatogenesis leading to subfertility. The most common findings in semen analysis are decreased sperm motility, decrease sperm density and increased number of pathologic sperm forms (12,13). There have been variable reports on serum testosterone level. Some studies found decreased levels where as others have found normal levels. LH levels are within normal limits except when

there is severe bilateral testicular atrophy. FSH may be normal or elevated depending on the severity of damage to the spermatogenesis (14).

How the varicocele exerts toxic effects on testis is not known precisely. Hyperthermia of the scrotum and testis is most widely accepted mechanism for testicular dysfunction. Varicocele disturbs the normal counter-current heat exchange between arterial blood and venous blood of pampiniform plexus. Heat on the testis can cause a direct effect on the germ cells leading to alerted metabolism and apoptosis and altered sertoli cell function (15,16). Production of increased nitric oxide, its active metabolites and reactive oxygen species in venous blood of varicocele is known to play a role in sperm dysfunction (17,18,19). Varicocele also reduces anti-oxygen defenses potentially adding to the localized oxidative stress (20). This proposed mechanism of testicular toxicity could explain why bilateral dysfunction is seen in many men with unilateral varicocele, because nitric oxide freely diffuses across membranes.

### Diagnosis

The diagnosis of varicocele should still be made on the basis of clinical findings.

The modes of presentation are

- Infertile men with varicocele (with or without symptoms)
- Adolescent or young adult with asymptomatic varicocele, detected during physical examination
- Men with symptomatic varicocele (testicular pain, fullness or heaviness)
- Varicocele diagnosed during the evaluation of scrotal mass

Patients should be examined in a warm room in standing and supine positions and with and without a Valsalva manoeuvre. Idiopathic varicocele is more prominent in upright position and disappears in supine position. Secondary varicocele especially on the right side can be caused by retroperitoneal tumour or lymphadenopathy and do not change size as noticeably in the supine position. Characteristic physical findings on examination include dilated veins behind and above the testis, usually on the left side, felt as a bag of worms and relative ipsilateral testicular volume loss.

Classically varicoceles are graded by an arbitrary scheme

- Subclinical: not palpable or visible either at rest or during Valsalva but demonstrable by special tests

- Grade 1: palpable only during a Valsalva manoeuvre
- Grade 2: palpable at rest but not visible
- Grade 3: visible and palpable at rest.

This grading scheme has been developed without validation. Hargreave compared the physical findings of two experienced clinicians and found disagreement in 26% of patients (21).

An important part of the physical examination in patients with varicocele is an accurate assessment of testicular consistency and volume. Although the assessment of testicular consistency is subjective, a careful simultaneous comparison of both testes may give the clinician additional qualitative information about the overall condition of the ipsilateral testis. A normal testis (in western studies) normally measures 4.5 × 3 × 2 cm with a volume of 20 - 25 ml. The methods available to measure the size of the testes are visual comparison, calipers, Prader orchidometer (comparative ovoids), Takahira orchidometer (disk elliptical rings) and ultrasound. Ultrasound should be considered the criterion standard for assessing testicular volume.

### Ultrasound scan

It can detect varicoceles missed on physical examination; many of these are clinically unimportant subclinical varicoceles. It can identify other pathological processes within the scrotum and give a more objective measurement of testicular size than physical examination and orchidometer.

### Venography

It is generally considered the best diagnostic test. However it is an invasive procedure with risk. Most clinicians who advocate venographic diagnosis recommend simultaneous treatment of the varicocele with either sclerotherapy or embolisation.

No diagnostic studies beyond physical examination are necessary unless the scrotal size and thickness or other pathology in the scrotum make the physical examination insufficient.

### Predictive factors for fertility

Following are the predictive factors for infertility

#### 1. Seminal parameters

In adults with varicocele the assessment of a semen sample is generally the first step in the evaluation. Chance of pregnancy is strongly influenced by motile sperm concentration. Varicocele repair improves the

seminal parameters in approximately 70% of patients with the improvement in motility being the most common (15,22). Patients with a total motile sperm count  $> 5 \times 10^6$  had a significant improvement in seminal parameters following treatment (23).

## 2. Varicocele size

Men with large varicoceles had poorer semen quality than with small varicocele (24). Larger varicoceles have a greater improvement in seminal parameters and a significant higher natural pregnancy initiation rate than men with small varicoceles after correction (25).

## 3. Testicular size

Preoperative testicular hypotrophy is associated with a significantly reduced total motile sperm count and high grade varicocele (26). A lack of testicular hypotrophy results in a higher postoperative pregnancy rate (27). Testicular volume greater than 30ml is an independent predictor of fertility following varix ligation (28).

## 4. Endocrine factors

GnRH stimulation test in adults is another predictor of varicocelectomy outcome. Patients with positive test 80.9% had post operative improvement of semen parameters and 67.4% initiated a pregnancy within 18 months. Patients with a negative test 18.7% had improvement in semen parameters and 9.3% initiated a pregnancy (29).

## Treatment

There has been no prospective study following a group of boys through puberty into manhood to determine the true natural history of varicocele. The mere presence of a varicocele is not, in general an indication for treatment. The goal of varicocele treatment (except in symptomatic varicocele) is to improve testicular function and seminal parameters and to increase the likelihood of the ultimate goal, increased pregnancy rate. Varicocelectomy gives improvement in seminal parameters in 60-80% of patients and natural pregnancy in 20-60% of couples (30).

The following indications are uncontroversial for surgical intervention in adults.

- Primary infertility with a grade 2/3 varicocele and abnormal semen parameters
- Secondary infertility with a grade 2/3 varicocele and abnormal semen parameters
- Presence of symptoms which are not relieved by conservative measures (analgesics and scrotal support)

In adolescences and young adults the following are uncontroversial indications for surgical intervention

- Presence of symptoms which are not relieved by conservative measures
- Grade 3 varicocele with testicular hypotrophy (Testicular volume discrepancy of more than 2 ml as assessed by ultrasonography)  
There is abundant literature confirming that varicocele is associated with testicular growth arrest in adolescent and varicocele repair results in testicular growth "catch up growth. Kass and Belman demonstrated that 16 of 20 patients had significant growth of the smaller affected ipsilateral testicle after surgery (31) Okuyama and his associates studied 40 patients with varicocele (11-17 years of age) of which 24 patients had surgery for the varicocele and 16 were uncorrected. During a follow up period of 15 to 64 months the surgical group at the end of the study had 71% of patients free of testicular hypotrophy (testicular growth failure) as compared with only 25% in the uncorrected group (32)
- Grade 3 varicocele with abnormal semen parameters even without testicular hypotrophy

## Treatment options

The treatment options include open surgical approaches, laparoscopic varicocele ligation and transvenous varicocele ablation (embolisation or sclerotherapy). Depending on the method, the recurrence of varicocele after treatment can occur in approximately 10%-15% of patients.

There are many open surgical approaches to correct varicocele

- Retroperitoneal approach / High ligation (Palomo procedure)  
This procedure was originally described by Alejandro Palomo in 1949. It involves of the whole of the vascular bundle, including the testicular artery at a site above the junction of vascular bundle and the vas to form the spermatic cord (just above the deep inguinal ring). Based on a review of the literature and the results of a survey of paediatric urologists in the United States, Paduch and Skoog found that the classic Palomo repair is the treatment of choice in adolescents (33). High ligation is quick and simple but the recurrence rate is high (34).
- The modified Palomo operation  
This is performed more than the original Palomo now. The authors have substantial experience in performing this procedure, where a short

segment of internal spermatic vein(s) is excised retroperitoneally (sparing the testicular artery) just above the level of the anterior superior iliac spine using a very short muscle splitting incision. Hargreave reports a recurrence rate after modified Palomo operation is approximately 5% and if reoperation is required the inguinal approach could be used (35). The main advantage is that the internal spermatic vein is more easily identified and usually there are only 1 or 2 vessels.

- Inguinal approach (Ivanissevich procedure)  
The proponents of this approach claim low recurrence rate. However the risk of injury to the testicular artery and subsequent testicular atrophy is greater with this approach (36,37). In the inguinal canal the dilated veins are usually 2-4mm in size. The testicular artery is 0.5 to 1mm in diameter. The lymphatics are smaller in diameter than the artery. Ramadan and his associates reported that identification of the internal spermatic artery in the inguinal canal was impossible without the use of the Doppler (38). Furthermore, classic inguinal approach is associated with a high rate of postoperative hydrocele formation.
- Microsurgical inguinal approach (Goldstein procedure) (39)  
Utilizing microsurgical artery and lymphatic sparing techniques, the recurrence rates are reduced to 1% and postoperative hydrocele and testicular atrophy virtually eliminated. Specifically microsurgical varicocelectomy provides three important benefits. First, it allows clear identification of small venous collaterals particularly the cremasteric vein, periarterial venous plexus, extraspermatic and gubernacular collaterals. These small venous collaterals if missed will dilate postoperatively with time leading to recurrence of varicocele. Second, testicular arteries are clearly identified under 10 to 25 x magnification and preserved. Finally, microsurgical varicocelectomy allows identification and preservation of the lymphatics, virtually eliminating postoperative hydrocele formation which is the most common complication of nonmicrosurgical varicocelectomy.
- Subinguinal approach  
It is similar to the inguinal approach; but the difference being the location of incision (below the external inguinal ring). It has the advantage of causing less pain than inguinal approach because less muscle cutting is involved.

- Scrotal approach  
This approach fell into disfavour as testicular artery damage and testicular atrophy were common.

#### Laparoscopic varicocele ligation

It is essentially an artery sparing high ligation; has the same disadvantages as modified Palomo and converts a retroperitoneal procedure with no intraabdominal risk, into an intraperitoneal procedure. The recurrence rate is in the range of 6-15%. The failure is usually due to preservation of the periarterial plexus of veins which have communication with larger internal spermatic vein. Dilated cremasteric vein another cause of varicocele recurrence cannot be identified during laparoscopy. Training for other laparoscopy procedures has been sighted as one of the benefits of laparoscopic varicocele ligation.

Transvenous varicocele ablation (percutaneous retrograde sclerotherapy / antegrade scrotal sclerotherapy / embolisation)

These procedures have the advantage of quick recovery and minimal pain. The success rate ranges from 89 – 95% with approximately 6% complication rate in addition to the issue of radiation exposure of the testis. Many urologists reserve these approaches for cases of surgical failure (40). Percutaneous retrograde sclero-therapy carried out by cannulation of femoral or basilic vein is used for varicocele ablation. However the method is hampered by a long operation and significant radiation exposure. The antegrade scrotal sclerotherapy described by Tauber and Johnsen is a simple surgical method and series in adults reported a low recurrence rate (41). For percutaneous embolisation transfemoral approach is used and tungsten coils are placed in the internal spermatic vein.

Varicocele is an entity about which there are several unanswered questions.

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