



Management of adolescent varicocele

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ABSTRACT

Varicocele is defined as an abnormal dilation and tortuosity of the internal spermatic veins found within the pampiniform plexus. It is a common finding in adolescents and adult men alike, however its diagnosis in the adolescent population poses different dilemmas in regard to indications for treatment than in adults. Failed Paternity is a clear-cut indication for repair in adult men attempting to father children. In adolescents, the physicians, family and patients must consider potential for future fertility problems which may or may not actually become of concern. Assessing the degree of negative effect of the varicocele on an adolescent's testicular health can also be difficult as teenagers typically are not asked to provide semen for analysis and thus surrogate markers for testicular health such as testicular size differentials must be used. Treatment options for the adolescent varicocele are similar to options in adult populations. While risks and benefits of various techniques can be considered, the gold standard for varicocele repair in adolescents has not been clearly defined.

We aim to discuss diagnosis of varicocele, considerations for initiating treatment of varicocele in the adolescent, and techniques for management.

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Introduction

With an incidence of approximately 15%, left-sided varicoceles are a common urologic anomaly in the adolescent male.¹ The enlargement of the pampiniform venous plexus in the scrotum is believed to be due to suboptimal drainage of blood on the left side. Three factors are discussed to play a role. Cadaver studies have shown that valves are missing in approximately 1/3 of testicular veins.² Secondly, the left testicular vein drains into the left renal vein with what is believed to be an unfavorable angle.³ The third reason is believed to be the impingement of the left renal vein between the aorta and the superior mesenteric artery also known as nutcracker syndrome.⁴ Rarely, varicoceles can be caused by an intraabdominal or retroperitoneal tumor which compresses the testicular vessels. This entity should be ruled out in right sided varicoceles. Routine abdominal ultrasound to rule out associated malignancy in left sided varicoceles is not mandatory as the risk is very low.⁵

Varicoceles are typically identified by the adolescent or found on routine examinations. They are graded as published by Dubin and Amelar into 4 Grades (Table 1).⁶

Ultrasound is often used as a diagnostic tool to assess venous diameter, peak flow and testicular volume (Fig. 1.). Ultrasound was found to be more accurate in estimating testicular size differentials than the examination with the Prader orchidometer.⁷ There is however great inter-institutional and inter-radiologist variability.⁸ Volume differences should therefore be evaluated both clinically and radiologically and findings need to be interpreted carefully when making surgical decisions. Repair of varicoceles with a higher preoperative spermatic venous diameter has been associated with more improvement in postoperative semen parameters. Schiff et al. correlated preoperative ultrasound findings with postoperative semen parameters in 68 infertile men. The greatest improvement was seen when the preoperative spermatic venous diameter exceeded 3 mm and reversal of spermatic venous flow on valsalva was demonstrated.⁹ The value of the peak retrograde flow as a prognostic factor and guide for surgical decision-making has yet to be identified, but there are data suggesting that a high peak flow (>38 cm/sec) has predictive value for persistent or worsening testicular asymmetry.¹⁰

Indications for repair of varicocele

In the adult population, the primary indication to repair a varicocele is straightforward: failed paternity. Apart from the occasional presentation for pain due to varicocele, the pediatric population

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Table 1
Grading of varicoceles as published by Dubin and Amelar.⁶

Grade 0	subclinical, only identified on ultrasound
Grade I	Palpable only with the patient standing and performing a Valsalva maneuver
Grade II	Palpable with the patient standing and without Valsalva maneuver
Grade III	Visible through the scrotal skin, as well as palpable with the patient standing

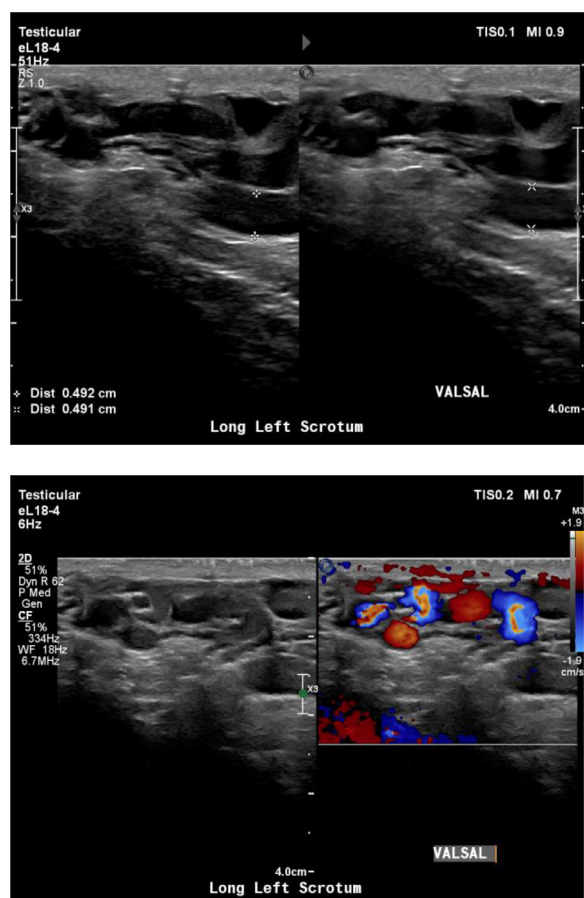


Fig. 1. Findings on ultrasound in patient with varicocele. Dilated veins can be seen with retrograde flow during Valsalva.

presents a different challenge: teenagers are not typically attempting to father children and the indications for repair center around future fertility preservation and testicular health. Thus, the indications for treatment are much less clear cut. This is especially true knowing that most adult patients with varicocele are able to father children. A population-based study showed 85% of adults with varicocele are fathers.¹¹ In addition, there are ethical considerations regarding interventional management in adolescents and because they are minors, the importance of clear-cut indications for surgery is high. Testicular size asymmetry and semen analysis parameters can be used to guide indications for proceeding with varicocele repair, however the data regarding these parameters is sometimes conflicting and semen analysis can be challenging to obtain in adolescents. Nonetheless, given the clear connection between varicocele repair in adult population and improvement in sperm parameters and fertility rate, as well as the newly defined improvement in hormonal milieu with varicocele repair, a discussion regarding varicocele repair between the urologist and adolescent and his family is appropriate and warranted^{12–14}. Currently the recommendation from the American Society of Reproductive Medicine states that adolescent males who have unilateral or bi-

lateral varicoceles and objective evidence of reduced testicular size ipsilateral to the varicocele may be considered candidates for varicocele repair, otherwise the adolescents with varicoceles should be followed with annual objective measurements of testis size and/or semen analyses to detect the earliest sign of varicocele-related testicular injury. The recommendation further states that varicocele repair may be offered on detection of testicular size or semen abnormalities, as catch up growth and reversal of semen abnormalities can occur. However, data are lacking regarding the impact on future fertility.¹⁵ The decision to treat a young man with varicocele continues to be a topic of debate and several factors must be considered as our understanding of and the recommendations for management of this condition evolve.

Pain

Testicular discomfort is a subjective indication to treat a varicocele. As most people practicing urology have experienced, adolescent males often present with testicular pain, which can be idiopathic or related to other conditions such as trauma, constipation, voiding dysfunction, sexually transmitted disease and intermittent testicular torsion. When considering treatment of the adolescent varicocele for pain, an attempt should be made to identify other causes which could be responsible for the pain and address them. A varicocele repair can certainly be undertaken for pain that seems to be related to the varicocele, however one must carefully counsel patients undergoing a procedure for this indication, as they may not see the pain resolve or even improve and it can lead to patient dissatisfaction.

Fertility

In the adult population the effect of repair of varicoceles on fertility is now commonly accepted. A recent literature review found an improvement in sperm concentration and overall motility with repair of all grades of varicocele.¹⁶ In the adolescent population intervention for this reason is more difficult to justify, as the relationship between varicocele repair in adolescence and future fertility preservation is still poorly defined. Furthermore, it is unknown if early varicocele repair during adolescence versus repair if and when the patient desires fertility is beneficial. Bogaert et al. contacted patients >30 years of age who were diagnosed with a grade II or III varicocele during adolescence to evaluate paternity. Effective paternity was 85% (61/72) in the non-repaired group and 79% (67/86) in the treatment group ($p > 0.05$) with similar distribution of varicocele grades and similar rate of testicular asymmetry among the groups. This study thus suggests that varicocele repair had no influence on paternity rate.¹⁷ However, the incidence of testicular asymmetry in this study was lower than other studies, making comparison difficult and potentially underestimating the effect of varicoceles on asymmetric testicles. In addition, the varicoceles in this study were treated angiographically with no objective verification of resolution and thus the success rate of only this modality can really be concluded upon from this study.

Androgen deficiency and hypogonadism

Another consideration to repair varicoceles in adolescents is the potential for preservation of testicular health. Varicoceles can have an effect on sperm, as well as Sertoli and Leydig cells within the testicle. Clinically, Sertoli cell dysfunction can be observed by a decreased responsiveness to follicle stimulating hormone (FSH), and by alterations in androgen binding protein (ABP), transferrin, and inhibin. In the setting of varicocele, some men present with elevated FSH and decreased testosterone production, and 48%–76%

have improvement in one or both of these parameters following varicocelectomy.^{18,19} Inhibin B levels also often improve after varicocelectomy, suggesting a reversible Sertoli cell defect.²⁰

A 2007 study by Tanrikut et al. showed a significantly lower serum testosterone level in men with varicocele (412.2 ng dl⁻¹) than in men without (462.6 ng dl⁻¹). A follow-up study by the same group in 2011 showed a significant increase (178 ng dl⁻¹) in serum testosterone levels after varicocele repair irrespective of varicocele grade, laterality or patient age, more strongly implicating varicocele as a risk factor for androgen deficiency or hypogonadism.¹⁴

A large study by the World Health Organization was performed in 1992 and evaluated 9034 men who presented for fertility evaluation. Men with varicocele and fertility problems who were older than 30 years of age had significantly lower testosterone levels than men who were under 30. This trend is not observed in the infertile patients without varicocele which implicates varicoceles in the effect on testosterone.²¹

Several studies such as one by Hsiao et al. in 2011 have examined the effect of varicocele on testosterone and showed normalization of testosterone following varicocele repair indicating reversible effects. In this study, young men <30 years of age were studied and did show an increase in testosterone with repair.²² The clinical significance of this is difficult to interpret given that these patients did not have hypogonadism. There are no studies to show the effect of varicocele repair on testosterone in adolescence. During adolescence and young adulthood, the effects of varicocele may thus not be impactful enough to cause true hypogonadism, however the potential for long term effect on testosterone should be considered and further studies to aid with proper counseling.

Testicular size asymmetry

In the adolescent, testicular size asymmetry is used as a surrogate for testicular dysfunction and suggestion of possible fertility issues in the future. Testicular growth is in part utilized due to the issues surrounding obtaining a semen analysis in a teenager. Furthermore, normal semen analysis parameters are defined based on analysis from men 17 years and older and may not be applicable to younger adolescent patients. The parameter of testicular size asymmetry can be difficult to use in guidance of varicocele correction given that adolescents may have asymmetrical growth of the testicles unrelated to varicocele, however it may be the best way to approximate testicular health in the adolescent boy.

Varicocele has been shown to progressively decrease sperm motility and vitality in 17–19 year old patients with varicoceles that have not yet been treated.²³ A correlation between increasing testicular volume differentials and abnormal semen parameters has also been identified by Diamond et al. Their study included 57 boys and identified that those with testicular volume differentials of 10–20% had an 11% chance of having a subnormal total motile sperm count. Patients with testicular volume differential greater than 20% had abnormal total motile sperm count 59% of the time.²⁴

In the setting of the testicular asymmetry, varicocele repair appears to result in “catch-up” testicular growth as well as improvement in sperm count.²⁵ A large 2012 meta-analysis encompassing 14 studies and 1475 patients evaluating the effect of varicocelectomy on testicular catch-up growth in adolescents with testicular volume discrepancy showed a significant reduction in volume differential after varicocelectomy.²⁶

Studies have attempted to show correlation between gonadotropin levels and testicular function in order to suggest a better indicator for varicocele repair than testicular size asymmetry. Guarino et al. correlated testicular size, gonadotropin levels, and semen parameters in adolescents, finding higher gonadotropin levels in patients with abnormal semen parameters and no correlation

with testicular size measurements.²⁷ In a more recent study, Deshpande et al. evaluated the reliability of testicular catch-up growth as a marker of normal testicular function in men 18–27 years old who underwent laparoscopic varicocelectomy between 11 and 16 years old.²⁸ In this study, they were not able to show correlation between elevated FSH and testicular size. Lower serum inhibin B levels have also been observed in adolescents with varicocele relative to controls in a small study of 16 adolescent males with varicocele and 13 controls.²⁹ In this study, no differences in testosterone, luteinizing hormone or FSH were observed between groups. Thus, testicular size differential remains an important parameter to be utilized as indication for varicocele repair, however with further studies and larger patient populations, other indicators may become of greater importance such as gonadotropin levels.

A difference in testicular volume exceeding 20% at diagnosis or an increasing volume difference during follow-up has been accepted as an indication to treat in many practices.

Common practice of the authors is to treat boys with a testicular size difference of more than 20% on both palpation and ultrasound. If the size difference is 20% or less, we follow the patient half-yearly or yearly. If the adolescent presents with complaints of pain but no testicular size difference, we make an attempt to identify other causes of pain such as voiding dysfunction, constipation or infection and properly address them. Once such causes have been addressed or ruled out, we counsel the patient appropriately and often find that once the patient is given information and education, anxiety related to the condition subsides and pain often resolves. If however the adolescent expresses pain credibly, especially if the description of the pain is consistent with pain typically associated with varicocele such as dull ache associated with heavy feeling in scrotum, treatment is offered.

Treatment options

Numerous techniques with many modifications are used to treat varicoceles but there is no consensus on which should be considered the gold standard.^{30,31} Conflicting reports have been published with data likely affected by heterogeneous cohorts and differing definitions of successful treatment. Sperm samples are often not available and paternity is usually not desired for years, thus these are not adequate end points for studies. Surrogate parameters need to be defined and studies comparing various treatment modalities need to meticulously analyze normalization of scrotal veins or downgrading of varicoceles, testicular catch-up growth, change in hormonal status, peri-operative complications, recurrence and hydrocele formation.

Questionnaire studies inquiring pediatric urologists in different locations about their preferred method for repair of varicocele show geographically grouped preferences. The subinguinal microsurgical approach is found to be more commonly used in e.g. Korea³² whereas the laparoscopic approach is the favored technique in the United States.^{33,34} Procedures by interventional radiology, though not the most commonly used method overall, seem to be widespread in Europe.³⁵ Due to these evidently local preferences, few randomized controlled trials comparing different techniques exist. In summary, due to a lack of comparative data, it is currently impossible to determine the best treatment modality.³⁰ Practitioners should be encouraged to take into consideration their own experience, and risks and benefits of various treatment modalities should be discussed with patients and their families when indicated.

High (retroperitoneal) ligation of the vasa spermatica: Palomo technique

The high, retroperitoneal (and therefore suprainguinal) ligation of the vasa spermatica (mass ligation of artery and vein) as a

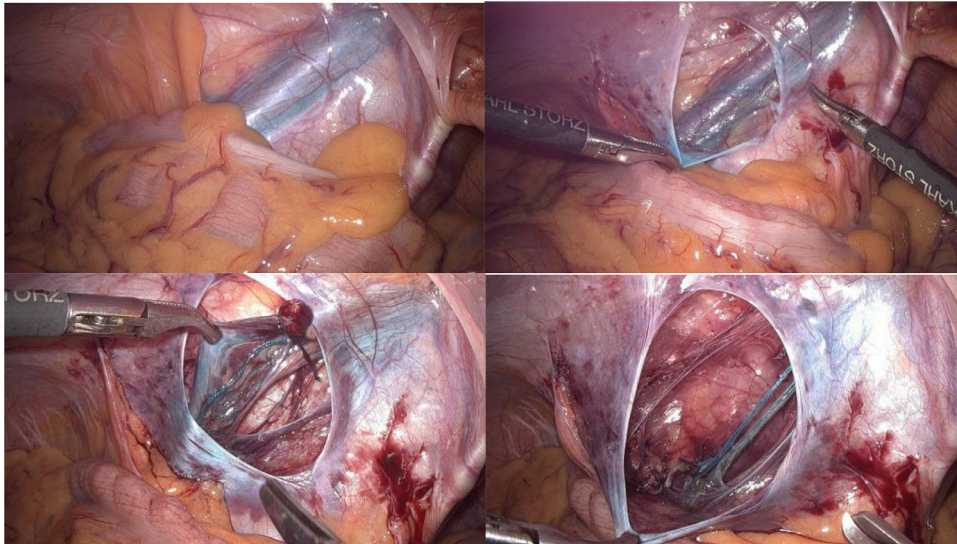


Fig. 2. Intraoperative situs during laparoscopic lymph-sparing mass ligation (Palomo) A: 10 min after scrotal infection of isofluran blue, B: after opening the peritoneum, C: after ligation of the testicular artery, D: spared lymphatics after ligation of both artery and vein. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

treatment option for varicoceles was first published by Palomo in 1949.³⁶ As the testicle's blood supply has three sources: the testicular artery, the deferential artery and the cremasteric artery, the testicle should still be adequately vascularized even if the gonadal artery of the testicle is ligated. This theory has been proven correct. Even though testicular atrophy after ligation of the vasa spermatica has been described in the literature, none of the recent meta-analyses found evidence of any recent cases.³¹ The mass ligation of the artery and vein remain popular because of the low recurrence rate of varicocele, ease of performing the technique, and low rate of testicular atrophy.³⁷ Opponents criticize it because of its most common complication: the formation of postoperative hydroceles. The reported incidence varies greatly between 2% and 40%.^{38,39} This variability may in part be due to differing criteria for the diagnosis of postoperative hydroceles. As previously published, a grading of those would increase uniformity. We suggested the following: grade I: only detectable by ultrasound, not palpable, grade II: detectable by ultrasound, soft hydrocele on palpation, mild volume difference, no discomfort; grade III: firm hydrocele, testes not palpable within the fluid collection, skin folds elapsed, patient reports discomfort.⁴⁰

Since the 1990s, laparoscopic and retroperitoneoscopic Palomo procedures have been performed. In 2002, Podkamenev et al. analyzed a large cohort of patients and found that the success rate was identical (98.6%) to open, however the laparoscopic approach was associated with significantly fewer hydroceles and wound complications. Hospital stay in their open cohort was an average of seven days.⁴¹ Due to its invasiveness and related complications, as well as the other available treatment modalities, the open Palomo technique is rarely performed today.

Single-incision laparoscopic Palomo procedure has been documented as safe and efficient without detailed analysis of long-term results. Evidence for the latter is dispensable as it can be assumed that they will not differ from conventional laparoscopy. This approach may provide some benefits in cosmesis.

Modified Palomo technique

Artery sparing = supra-inguinal (Ivanissevich)

Due to an understandable fear of testicular artery ligation and the theoretical advantage of artery preservation, the Palomo tech-

nique was modified to spare the artery and ligate only the veins in the retroperitoneal space. This technique was described by Ivanissevich in 1960: the suprainguinal ligation of the testicular vein.^{42,43} The commonly used name remains "modified Palomo technique", although admittedly Ivanissevich's modification was a novel technique of its own. Consecutive studies in adolescents have suggested that the rate of hydrocele formation is lower but recurrence rate of varicocele is higher (around 15%) when using the artery sparing technique^{44–47}. Zampieri et al. found the same (higher) recurrence rate, but reported better semen analysis parameters in their artery sparing group.⁴⁸ This somewhat surprising data could not be confirmed in other (adult) studies.⁴⁹

The fewer hydroceles might be explained by the greater likelihood of lymph vessel preservation if the vasa spermatica are dissected. In an effort to improve upon these two approaches, pediatric urologists introduced the lymphatic sparing classic Palomo procedure.

Lymphatic sparing classic Palomo procedure

The use of blue dyes to better visualize lymph vessels has been used for decades. Injecting 2 ml of isosulfan blue between the tunica vaginalis and the tunica albuginea leads to a successful mapping of the lymph vessels in 70–90%.⁵⁰ Fig. 2 shows intraoperative findings after isosulfan blue infection. Some authors regard it necessary to gently manipulate the testis and scrotum afterwards for a couple of minutes, but there is no evidence supporting the need for this maneuver. Esposito et al. achieved a 100% mapping by injecting an additional 0.5 ml of isosulfan blue into the body of the testis⁵¹. However data exist that intratesticular injection of dyes produces pathological changes and Makari et al. suggests that these injections should therefore be abandoned⁵². Hydrocele formation was demonstrated to decrease significantly in studies comparing lymph-sparing to non-lymph-sparing techniques.^{53,54}

Lymph- and artery sparing techniques resulted in fewer hydroceles, but more recurrences of varicoceles than the only lymph-sparing approach in a study by Yehay et al. (10 vs. 1.25%).⁵⁵

Indocyanine green fluoresce injected into the testicle (2 ml) has also been shown to result in a detectable staining of the lymph vessels in 100% of patients.⁵⁶ Adverse effects of this intratesticular injection will need to be analyzed further.

Inguinal (Bernardi) and subinguinal vein ligation – with or without magnification

The rationale of approaching the veins at different location is anatomical. Ivanissevich argued that with a supra-inguinal approach, it was likely to encounter a single venous trunk, which would reduce the risk of missing collaterals thus reducing the risk of recurrences. The counterargument is the existence of numerous collaterals between testicular veins with those of the colon and the contralateral side⁵⁷ thus allowing collateral drainage after high ligation.³

The microsurgical subinguinal approach has become the gold standard for the adult population. "Microsurgical" refers to the use of magnification during surgery but the applied magnification varies between microscopes (8 to 15x) or loops (2.5–4.5x). There is not enough evidence to transfer the superiority of the subinguinal approach to adolescent patients.³⁵ Existing studies have specified their research questions to subsections and left some outcomes parameters unmentioned: Cayan et al. compared different types of magnification with no magnification and found the rate of hydroceles and recurrence increased when no magnification was used. Both inguinal and subinguinal approaches were included in their study and not differentiated in the analysis.⁵⁸ Another study found similar rates of catch-up growth when comparing inguinal and subinguinal approaches, the authors saw no recurrences in either group but one hydrocele in the subinguinal approach. As the study population only included 13 patients per group, it is too small to draw valid conclusions.⁵⁹ A study published by Lurvey et al. analyzed a large data set from the faculty practice solutions center database in the US. They found fewer re-treatments and hydroceles in the open approach group compared to laparoscopic or radiological groups.⁶⁰ However, the data did not specify if the open approach was carried out subinguinally or inguinally (or retroperitoneally), with or without magnification, or whether the artery was spared.

Ambiguity also exists as to whether the testis should be delivered and collaterals be ligated during the inguinal or subinguinal approach. Spinelli et al. found fewer recurrences in the delivery group⁶¹ whereas Choi et al. found more recurrences in this group.¹³

A study comparing ligation of the veins at the level of the external inguinal ring to the retroperitoneal ligation of artery and vein (both lymph-sparing and both with magnification) found more recurrences in the inguinal/subinguinal than in the retroperitoneal approach.⁶² They did not expose the testis in their inguinal/subinguinal approach.

Percutaneous embolization by interventional radiology

Embolization techniques have been used since the 1970s and can be separated into sclerotherapy and antegrade or retrograde embolization. They all have the selective venous occlusion and sparing of the artery in common and reports emphasize the low risk of perioperative complications with utilization of these techniques. Technical feasibility (access to the veins) is reported to be around 96 to 98%.⁶³ Successful embolization is repeatedly found to be around 93%, but early recurrence is reported in up to 13%.^{64,65} Hydrocele formation is reported as a complication, but rarely. Galvano et al. noticed that the success rate is dependent on the practitioner's experience.⁶⁶ Many authors utilize embolization techniques after failure of other techniques.⁶⁷

Summary

Indications for varicocele repair in teenagers include pain and poor testicular growth, as well as poor semen analysis parameters

when this data is available. Recent data in adult populations suggests varicocele repair improves not only fertility, but also the hormonal milieu. The implications of varicocele on hormonal status of adolescents are poorly understood. Further studies about long term implications of varicocele on fertility and hormone status may help pediatric practitioners to make decisions about timing of varicocele repair in adolescence.

The evidence suggests that the laparoscopic lymphatic-sparing Palomo procedure and the microsurgical subinguinal approach are associated with the lowest recurrence rates and lowest hydrocele formation rates. There is not enough evidence to decide which technique is superior. Comparable data for catch-up growth, semen quality and pregnancy rates are also lacking.

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