

AM El-Tawil, MSc, MRCS, PhD, Series Editor

Idiopathic fistula-in-ano

Sherief Shawki, Steven D Wexner

Sherief Shawki, Steven D Wexner, Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, FL 33331, United States

Sherief Shawki, Department of Surgery, Suez Canal University, Ismailia 41225, Egypt

Correspondence to: Steven D Wexner, MD, FACS, FRCS, FRCS(Ed), Professor of Surgery, Cleveland Clinic Florida, 2950, Cleveland Clinic Boulevard, Weston, FL 33331, United States. wexners@ccf.org

Telephone: +1-954-659-5278 Fax: +1-954-659-5252

Received: February 21, 2011 Revised: July 6, 2011

Accepted: July 13, 2011

Published online: July 28, 2011

Abstract

Fistula-in-ano is the most common form of perineal sepsis. Typically, a fistula includes an internal opening, a track, and an external opening. The external opening might acutely appear following infection and/or an abscess, or more insidiously in a chronic manner. Management includes control of infection, assessment of the fistulous track in relation to the anal sphincter muscle, and finally, definitive treatment of the fistula. Fistulotomy was the most commonly used mode of management, but concerns about post-fistulotomy incontinence prompted the use of sphincter preserving techniques such as advancement flaps, fibrin glue, collagen fistula plug, ligation of the intersphincteric fistula track, and stem cells. Many descriptive and comparative studies have evaluated these different techniques with variable outcomes. The lack of consistent results, level I evidence, or long-term follow-up, as well as the heterogeneity of fistula pathology has prevented a definitive treatment algorithm. This article will review the most commonly available modalities and techniques for managing idiopathic fistula-in-ano.

© 2011 Baishideng. All rights reserved.

Key words: Anal fistula; Seton; Fistulotomy; Advancement flap; Fibrin glue; Fistula plug

Peer reviewer: Patricia Sylla, MD, General and Colorectal Surgery, Massachusetts General Hospital, WACC 460, 15 Parkman Street, Boston, MA 02114, United States

Shawki S, Wexner SD. Idiopathic fistula-in-ano. *World J Gastroenterol* 2011; 17(28): 3277-3285 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v17/i28/3277.htm> DOI: <http://dx.doi.org/10.3748/wjg.v17.i28.3277>

INTRODUCTION

Fistula-in-ano is a devastating problem which has been described since the "Corpus Hippocratum". Although the disease has been well described, no definitive mode of management has been established. The most widespread traditionally accepted treatment has been fistulotomy. Problems with management are due to the heterogeneity of fistulas, and to the potential adverse effects on continence arising from division of the involved anal sphincter. Because of a desire to maintain continence, a variety of therapeutic alternatives to fistulotomy have been described^[1]. The etiology includes idiopathic and iatrogenic fistulas, and fistulas secondary to other causes. This article will focus on idiopathic fistula-in-ano.

Idiopathic fistula-in-ano most commonly occurs in healthy subjects, with cryptoglandular infection being the most widely accepted etiologic factor. The anal crypt gland penetrates the anal sphincter to varying degrees. Once obstructed, infection will ensue and suppuration will follow the least resistant path, which accordingly determines the location of the abscess (perianal, ischioanal, inter-sphincteric) and the type of fistula. Therefore, understanding the anatomy is essential to manage this disease.

Based on the relationship with the anal sphincter muscles, fistulas are classified into 5 main types: (1) **submucosal**: the fistula track passes superficially beneath the submucosa and does not involve any sphincter muscle; (2) **intersphincteric** fistula: the track passes through the internal sphincter and continues in the inter-sphincteric plane to the perianal skin, not including the external anal sphincter;

(3) **trans-sphincteric fistula:** the track cross through the internal and external anal sphincter on its exit towards the perianal area. The amount of involved external anal sphincter further subdivides the type of fistula into low when up to one-third of the distal external anal sphincter or less is involved, and high if a larger area of the external sphincter is included; (4) **suprasphincteric fistula:** the fistulous tract passes through the internal sphincter but traverses the external sphincter below the puborectalis muscle; and (5) **extrasphincteric fistula:** the fistulous track may pass outside the sphincter complex through the ischio-rectal fossa to the perianal skin. In this case, the origin of the fistula is not from the dentate line but could be from a rectal, pelvic or supralelevator origin, usually secondary to an inflammatory or neoplastic process.

A fistula-in-ano can be “simple” or “complex”^[2,3]. Fistulas with multiple external openings, those involving more than 30%-50% of the anal sphincter (high transsphincteric fistulas), those lying above the sphincter (suprasphincteric), extrasphincteric, or have high blind extensions, or horseshoe tracts, or are anterior in a female patient are considered complex, with higher risk of continence disturbance posed by surgically managing these fistulas. Alternatively, an anal fistula in patients with a preexisting history of fecal incontinence, Crohn’s disease, or local irradiation are also considered complex. Submucosal and low intersphincteric (traversing less than 30% of anal sphincter muscle) as well as low transsphincteric fistulas are considered simple^[4].

The management of fistulas-in-ano includes 3 main goals: to cure the fistula, to prevent or minimize recurrence, and to retain continence. Regardless of the type of fistula, there are certain principles that lead to successful management: the infection/inflammatory process should be resolved, the source of pathology should be addressed, and when treating the fistula, the internal opening should be closed with least risk to continence. This goal can be achieved with care taken not to jeopardize the integrity of the anal sphincter complex. In a retrospective study of 404 male patients with fecal incontinence, the most common confounding factor in patients younger than 70 years was a surgical history of fistulectomy or hemorrhoidectomy^[5].

PREOPERATIVE ASSESSMENT AND PLANNING

Preoperative evaluation is very important. Medical history and physical examination are most important in the assessment phase. The patient’s continence is another important facet that needs to be included, as well as any history of anorectal surgery. Anal ultrasound with hydrogen peroxide is another important adjunct for preoperative evaluation. This procedure is simple, fast, may be done in the same office visit, and provides information about the fistula track, the type and complexity and whether the anal sphincter muscle is normal, scarred, or disrupted, as well as the presence of an abscess cavity^[6,7]. Anal ultrasound is operator-dependent; scars and defects may confuse sonographic interpretation and might render delineation of the

fistulous track difficult^[8].

Magnetic resonance imaging (MRI) has become an integral part of the assessment of fistula as it can distinguish between sepsis and granulation tissue from sphincter muscles^[9]. A prospective study compared the preoperative MRI assessment of the anal fistula and intraoperative findings. High concordance rates were reported in terms of recognizing the course of primary tracks (86%), demonstrating secondary tracks (91%), and horseshoe extension (97%), as well as identifying internal opening (80%)^[10]. Furthermore, MRI accurately detected previously missed secondary tracks when compared with the clinical examination, and correctly identified the level of the fistula with respect to the anal sphincters^[11]. An endocoil greatly increases tissue resolution and provides superior anatomical details^[12,13]. However, it has a limited field of view (about 2-3 cm from the coil) in which any fistulous extension in this zone might be missed, and is not widely available and is very uncomfortable for the patient^[14,15].

Although anal manometry may provide information about sphincter pressures, obtaining a fecal incontinence score will also yield clinically relevant information^[16]. Collectively, this information will help select the best choice for treatment, and allows the surgeon to counsel the patient about expectations and probabilities of success. Pescatori *et al*^[17] prospectively studied the impact of preoperative anal manometry for guiding the surgical approach, on functional outcomes of fistula surgery. In this study 96 patients underwent pre- and post-operative anal manometry and were compared with a control group of 36 patients who did not have anal manometry. Internal sphincterotomy was performed for effective drainage of the intersphincteric plane in less than 50% of both groups (45 and 15, respectively). While 24% (11/45 patients) from the anal manometry group had postoperative soiling, 53% (8/15 patients) of the control group did. As for recurrence, 3% and 13%, respectively, experienced recurrence. Another study of 45 patients assessed the clinical and manometric effects of fistulotomy for intersphincteric fistulas on anal sphincter function. Although there was a significant decrease in resting pressures throughout the distal 2 cm of the anal canal after surgery, the maximum squeeze pressures did not change. Continence problems arose in patients who had lower preoperative resting pressures^[18].

In the majority of patients with idiopathic fistulas-in-ano, a thorough history and physical examination may suffice for surgical planning. When in doubt or if a complex fistula is suspected, an ultrasound is justified for further evaluation. Complexity and or sepsis might require further magnetic resonance imaging assessment. Anal manometry is especially useful in patients in whom postoperative continence is a concern.

MANAGEMENT OF FISTULA-IN-ANO

Management may be achieved by one of the following methods: (1) **keep the track from closing around a remnant septic focus preventing further abscess formation using a non-cutting seton;** (2) **expose the track and let it**

heal secondarily heal following a fistulotomy; (3) **excise** the whole fistulous tract: fistulectomy; (4) **excise the internal opening** and cover the defect with healthy mucosa as an advancement flap; (5) **obliterate the fistulous track** with glue, or a collagen and fistula plug; (6) **ligate and disconnect** the fistula tract in the inter-sphincteric plane as a LIFT (ligation of the intersphincteric fistula tract) procedure; (7) **ablate the tract and induce scarring** with radiofrequency waves; and (8) **induce regeneration** in the tract with biologic agents or stem cells.

OPERATIVE APPROACH AND SURGICAL MANAGEMENT

Seton

One of the simplest modes of treating anal fistulas involves passing a thread through the anal fistula tract. The material used may be a non-absorbable suture, drain, rubber band, or even a vessel loop. Setons are a viable option for high trans-sphincteric fistulas, for those fistula involving more than half of the sphincter, and anterior fistulas in female patients^[19,20]. There are basically two types of setons used in treating anal fistulas. A cutting seton is used to slowly cut through the tissue allowing for healing from inside to outside thus minimizing the risk of incontinence. In this case, after identifying the external and internal openings of the fistula tract, the skin and anal mucosa overlying the sphincter are incised, and subsequently the seton is passed through and tightened. In a study conducted among 160 patients with a fistula-in-ano, 10% received seton placement for either high transsphincteric or suprasphincteric fistulas. The authors reported that all of the patients in whom a seton was placed had encountered temporary alterations in continence to gas only, for an unreported length of time^[20]. Parks and Stitz treated 80 patients with a seton for high transsphincteric fistulae ($n = 23$) and suprasphincteric fistula ($n = 57$), of whom a total of 30 (8 and 22, respectively) patients underwent division of residual external sphincter muscle at the time of seton removal. Sixty eight patients were available for functional assessment. The authors found that 17% of those patient who had a seton alone without muscle division complained of partial loss of continence as opposed to 39% of those who had muscle division, emphasizing the importance of conserving muscle as much as possible even if it necessitates a longer healing time^[21]. Thirty-four patients (aged between 20 and 57 years), of whom 31 patients had normal preoperative continence, were offered a 2-stage seton procedure for high anal fistulas (16 extrasphincteric and 18 trans-sphincteric). All trans-sphincteric fistulas healed and there were only 2 recurrences. Among 29 patients with preoperative normal fecal control who were available for follow-up, postoperative continence was normal in 12 patients; while 5 patients had no control over flatus, 11 were incontinent for liquid stool or flatus, and one had continued fecal leakage. The authors did not recommend the 2-stage seton technique for fistulas

with high anal or rectal openings^[22].

In a review of the literature, including 37 different studies on cutting setons, the average incontinence rate was 12%. The more proximal the location of the internal opening the higher was the incontinence rate. Among the studies which described alterations to continence, incontinence to liquid was most common followed by incontinence to flatus. The authors concluded that, when feasible, other sphincter-preserving techniques should be employed especially with high anal fistulas^[23]. The cutting seton requires further follow-up visits for subsequent tightening of the seton to achieve the desired effect. The time for a fistula to heal with this method ranged from 1 mo to more than a year^[24,25].

The second type of seton, the non-cutting seton, is used primarily for draining, especially in the acute setting, or where other modalities cannot be implemented or have failed previously, and in certain disease entities such as Crohn's disease, and HIV^[26,27]. In the acute setting it provides rapid and safe relief of the infection, with no compromise to the sphincter complex, providing time for the inflammation to resolve, and better assessment and decision-making. Furthermore, keeping the seton in place helps prevent abscess recurrence and can act as a guide to the internal and external opening for following treatment(s). A recent consensus conference on fistulas concluded that setons should be used as an initial method until there is no evidence of acute inflammation^[28].

Fistulotomy

Fistulotomy is considered to be the procedure of choice for low, single tract, anal fistulas, especially when submucosal, since the risk for incontinence or recurrence is very low^[29]. However, others use this procedure for low inter-sphincteric as well as for trans-sphincteric fistulas^[19,30]. According to the practice parameters for the treatment of perianal abscess and fistula-in-ano presented by Whiteford and colleagues (2005), fistulotomy may be used in the treatment of perianal simple anal fistulas in cryptoglandular disease^[30]. In this report, a simple fistula was defined as a single, non recurrent tract that crossed less than 30%-50% of the external anal sphincter, not the anterior sphincter in women, and was present in subjects with perfect continence and no history of Crohn's disease or pelvic radiation. Furthermore, the authors suggested the use of tract debridement and/or fibrin glue as these methods do not impose a risk on continence, and, despite the associated higher recurrence rate, still offer the opportunity for alternative treatment.

While some surgeons use fistulotomy only for submucosal fistulas^[29], others apply this technique to more complex fistulas, including recurrent, high trans-sphincteric, or extra-sphincteric fistulas^[31], in conjunction with sphincter reconstruction. To perform fistulotomy, the internal and external sphincters are divided, accessory tracts are excised, and eventually overlapping sphincter reconstruction is performed. Thirty five patients underwent fistulotomy with sphincter reconstruction for complex anal fistulas (high

transsphincteric = 30, suprasphincteric = 4, extrasphincteric = 1). Eleven patients reported preoperative fecal incontinence, and fistulas were recurrent in 16 patients (8 with preoperative incontinence). Mean follow-up was 32 mo (range, 24-42). Two patients suffered from recurrence at 3 and 6 mo, respectively. One presented with a recurrent fistula. While 3 (12.5%) of the preoperatively fully continent patients ($n = 19$) experienced minor alterations in incontinence in terms of control of flatus and soiling, all of the preoperatively incontinent patients demonstrated significant improvement in fecal control after surgery. The authors suggested that fistulotomy with sphincter reconstruction provides an effective resource in the management of complex fistula-in-ano^[31]. The same technique was applied to 16 recurrent complex fistulas (4 patients experienced at least 2 recurrences) with a mean follow-up of 40 mo. Seven of the 8 patients who had previous fecal incontinence significantly improved. One patient experienced recurrence after 6 mo and was offered the same procedure after 38 mo without recurrence^[32]. The same authors, in a randomized controlled study, compared the advancement flap ($n = 27$) to fistulotomy with sphincter reconstruction ($n = 28$) for managing primary complex fistula-in-ano, in terms of recurrence and anal function. Fistulas were classified as high transsphincteric fistula ($n = 44$) and suprasphincteric fistula ($n = 11$) which were comparable between groups. After a mean follow-up of 36 mo (range, 24-52), there were 2 recurrences in each group (7.4% and 7.1%, respectively). There was no significant difference between the 2 groups regarding continence either before or after surgery, as 77.8% of the flap group and 82.1% of the fistulotomy and reconstruction group were fully continent prior to surgery whereas 70.4% and 67.9%, respectively, maintained postoperative continence^[33].

The incontinence rate associated with fistulotomy varies from 0% to 40%^[34,35]. In a prospective randomized study among 148 patients with inter-sphincteric fistulas, age, gender, duration of disease, location of the internal orifice, and previous surgery were not found to be significant factors influencing postoperative incontinence^[36]. However, in the same study, low voluntary squeeze pressure and multiple prior drainage procedures were deemed as predisposing factors for postoperative incontinence. The authors recommended anal manometry prior to fistulotomy, and not to use this technique in patients with a past history of multiple drainage^[36]. Other authors found similar results^[34]. However, Garcia-Aguilar *et al.*^[37] reported that previous surgery, female gender, high internal orifice, type of surgery performed in high fistulas were all risk factors for developing postoperative incontinence following fistulotomy^[37].

Others have concluded that trans-sphincteric fistulas and the extent of external sphincter involvement are significant risk factors for post-fistulotomy incontinence^[35]. In this retrospective study, 64% of the population ($n = 110$) experienced at least occasional incontinence episode(s). Lifestyle restriction was found to be mild in 14% and moderate in 10%; mild and moderate depression were en-

Table 1 Results of endorectal advancement flap

Author	<i>n</i>	Follow-up months (mean)	Success rates (%)	Incontinence rates (%)
Dixon <i>et al.</i> ^[39]	29	5.7	69.0	0
Koehler <i>et al.</i> ^[40]	42	55	73.8	28.6
Ellis <i>et al.</i> ^[41]	58	22	62.9	NA
Gustafsson <i>et al.</i> ^[42]	83	12	57.0	NA
Perez <i>et al.</i> ^[33]	30	36	92.6	7.4
van der Hagen <i>et al.</i> ^[43]	103	72	36.6	9.8
Uribe <i>et al.</i> ^[44]	56	43.8	92.9	19.6
Zbar <i>et al.</i> ^[45]	11	20	81.8	18.2
Mitalas <i>et al.</i> ^[46]	87	15	66.7	3.4
Dubsky <i>et al.</i> ^[47]	54	53.2	75.9	28.9
Ortiz <i>et al.</i> ^[48]	91	24	82.4	12.1
van Koperen <i>et al.</i> ^[49]	80	67	73.8	NA
Abbas <i>et al.</i> ^[50]	36	27	76.0	12.0

NA: Not available; *n*: Number of patients

countered in 9% and 4%, respectively, with 5% of patients having moderate embarrassment^[35].

Endorectal advancement flaps

Advancement flaps were implemented as a sphincter-saving method since there is no division of the sphincter muscles, and are mainly used for complex or high fistula. Basically, an incision is made distal to the internal opening of the fistula, a flap of healthy tissue is elevated, the diseased part is excised, and the internal opening is closed followed by advancement of the flap to cover the closed internal opening, and is finally sutured in place. There are a few crucial points to help ensure an optimal outcome. Dissection is started in the submucosal level. As the dissection proceeds proximally, the thickness of the flap increases without injuring the sphincter. In addition, the wide base of the flap should ensure a tension-free flap with a good blood supply. Alternatively a curvilinear (semicircular) flap could be raised to avoid ischemia at the edges^[38]. Regardless of the incision used, it should not be very close to the anoderm to avoid ectropion. The healing rates, shown in Table 1, range from about 57% to more than 90% with an acceptable period of follow-up.

In a retrospective review of 91 patients who underwent flap repair for complex fistulas, the recurrence rate was 19% after a median follow-up of 42 mo (range, 24-65)^[48]. The authors noted in their cohort that the median time to relapse was 5 mo with no recurrences after 1 year.

Abbas and colleagues^[50] conducted a study to determine the long-term outcome of an endorectal advancement flap for complex anorectal fistulas in 36 patients. The primary success rate was 83%. Transient fecal incontinence was reported by 3 male patients, but this problem spontaneously resolved in all 3 patients in 2 mo. Transient and minor continence-related problems have been encountered in other studies^[8,29,43,44,51]. Long-term functional outcome was assessed among 179 patients after surgical treatment of cryptoglandular fistulas, 70 of whom received

advancement flaps. The 3-year recurrence rate was 21% soiling was reported in 40% of the patients^[54]. Fifty six patients underwent prospective clinical and manometric evaluation after receiving advancement flaps. Four (7.1%) patents had recurrence and were offered the same procedure with a successful outcome. After surgery, 78.6% of patients maintained their continence, 7 patients (12.5%) reported minor incontinence problems and 5 patients (9%) suffered from major continence disturbances. Three months after surgery there was an overall reduction in maximum resting and squeeze pressures. Age, gender, and previous fistula surgery did not affect outcome in multivariate analysis^[44].

Dubsky *et al*^[47] retrospectively compared full thickness flaps ($n = 20$) to partial thickness (mucosal) flaps ($n = 34$). Although incontinence was found in 5 (11.1%) patients, full transection of the rectal wall for flap creation did not pose a threat to continence as only one of the 5 patients belonged to the full thickness flap group. The overall recurrence rate was 24%, occurring mainly in patients who had undergone multiple prior fistula-related procedures. Similarly, one patient (5%) experienced recurrence from the full thickness flap group as opposed to 12 patients (35.3%) from the partial (mucosal) thickness group.

The endorectal advancement flap provides sphincter preservation, and is a relatively safe alternative for managing fistulas-in-ano, with acceptable outcomes. The associated fecal disturbance is temporary in the majority of cases, yet necessitates awareness during preoperative assessment, patient counseling and the operative procedure.

Fibrin glue

During World War I, fibrin glue was initially implemented in surgery for hemostasis. Later, the material was utilized in different fields of surgery mainly as a sealant^[52] till 1992 when Hjortrup and colleagues^[53] used it to seal anal fistulas. The fibrinogen, thrombin, and calcium mixture in the fibrin glue seal the fistulous track by virtue of inducing clot formation. The initial soluble clot results from cleavage of fibrinogen to fibrin, which transforms to a stable clot once thrombin and calcium activates factor XIII. This reaction takes about 30-60 s. Subsequently, the glue promotes the migration of fibroblasts and pluripotent cells to start healing the fistula by laying down collagen. Over the following 7-14 d, the initially formed fibrin clot starts to dissolve by the lysis action of the plasmin present in the surrounding tissues while the tract is filled with synthesized collagen fibers^[54].

For the procedure to be successful, both internal and external openings of the fistula tract need to be identified. Injecting hydrogen peroxide or methylene blue can help to identify the openings. A loaded double-barrel syringe is introduced into the tract till the tip is seen through the internal opening. The syringe is emptied allowing the components of the glue to mix then exit the syringe to fill the fistula tract while steadily withdrawing the syringe outwards with a simultaneous compression to fill the fistula tract from inside out avoiding any filling

Table 2 Results of fibrin glue

Author	<i>n</i>	Follow-up months (mean)	Success rates (%)
Patrlj <i>et al</i> ^[58]	69	28	74
Sentovich <i>et al</i> ^[59]	20	10	85
Lindsey <i>et al</i> ^[60]	42	4	63
Sentovich <i>et al</i> ^[61]	48	22	69
Zmora <i>et al</i> ^[62]	60	6	53
Gisbertz <i>et al</i> ^[55]	27	7	33
Dietz <i>et al</i> ^[63]	39	23	31
Adams <i>et al</i> ^[57]	36	3	61
Witte <i>et al</i> ^[64]	34	7	55
Parades <i>et al</i> ^[56]	30	12	50

n: Number of patients

deficiencies. The injection is followed by a ten minute wait to allow the reaction to stabilize the clot. While some authors advocate suturing the internal and external openings^[55], others found no benefits^[56,57]. The success rate varies, ranging from 31% to 85% as shown in Table 2.

Various reasons have been suggested to explain success or failure, which includes technical-related and post-operative care issues. Dislodgement of the fibrin plug has been one of the most common proposed reasons^[56]. Based upon this theory many surgeons instruct their patients to follow a sedentary lifestyle in the immediate post-operative period, and to avoid heavy lifting or any strenuous activity. Others prescribe stool softeners, or suggest that fistula tract preparation by mechanical curettage is a key to success, such that inadequate removal of granulation tissue could lead to failure of the glue^[54].

Postoperative infection and abscess formation are other causes of failure. These postoperative septic sequelae may be due to a technical, improper cleansing of the tract prior to instillation of the glue, or a non-resolved infection^[60,61]. The length of the fistula tract has also been related to success or failure. While some surgeons have demonstrated higher success rates when using fibrin glue in long tracts (> 3.5 cm)^[58,60], assuming that fibrin glue has greater liability to leak from shorter tracts, others have shown greater success rates in shorter tracts^[59,61,65].

As previously mentioned, the length of follow-up is an important facet in evaluating such new techniques. Sentovich *et al*^[59], in their initial study showed a success rate of 85% over a follow-up period of 10 mo. This rate became 69% after 22 mo of follow-up^[61]. Queraltó *et al*^[66], offered 34 patients with high cryptoglandular fistula synthetic glue. At 1 mo, the healing rate was 67.6%. This rate remained almost the same during a median follow-up period of 34 mo (range, 21-43), with no continence problems.

Despite the inconsistent success rates, the majority of studies showed that in properly selected patients, fibrin glue can achieve 30%-60% success rates. The technique is simple, less invasive to the anal sphincter complex, and in case of failure, it does not preclude the patient from receiving other methods of treatment.

Fistula plug

Another less invasive, sphincter preserving technique is the fistula plug. This biologic plug (Surgisis® Anal Fistula Plug, Cook Surgical, Belington, IN, USA) is manufactured from porcine small intestinal mucosa. The plug characteristically is resistant to infection, and ideally, does not induce a foreign body reaction. Furthermore, it invites host cells to populate it, promoting multiplication and ultimately filling the fistulous tract^[67].

Prior to usage, the plug should be rehydrated in 0.9% normal saline for 3-5 min. During this time the surgeon should have identified both the internal and external openings of the fistula tract in the usual manner. The plug should be inserted in the fistula tract through its internal opening. Once light resistance is encountered, the plug is trimmed if needed, and secured at the internal opening, since dislodgement is a primary cause of plug failure^[68]. Similarly, the excess at the external opening is trimmed at the skin level, but the external opening is left opened for drainage in an attempt to reduce the possibility of infection and failure of treatment. Similar to fibrin glue, the results of the anal fistula plug vary greatly as shown in Table 3.

Preoperative bowel preparation, perioperative antibiotics, and prone operative position of patient, are not mandatory but preferred by most surgeons^[80]. The prior use of a seton not only ensures the elimination of any inflammation or infection, but has been postulated to prepare the tract, making the wall more fibrotic, with an ultimate increase in success rates^[75,77]. Conversely, seton use has not been found to correlate with increased healing rates in other studies but seems to facilitate the procedure by identifying the fistula anatomy^[68,70].

Several authors have tried to assess predictors of success and to identify causes of failure. Following the previously mentioned technique, with mechanical bowel preparation, hydrogen peroxide irrigation of the fistula tract before plug insertion, strict postoperative limitation of activity, and topical metronidazole, Johnson *et al*^[69] reported an 87% success rate at 14 wk, and 83% at 12 mo^[68]. O'Connor *et al*^[70] achieved an 80% success rate with the addition of seton placement prior to plug insertion, while Garg^[71] reported a 71% success rate without using hydrogen peroxide, which is thought to clear the tract of all debris that might interfere with cell migration induced by the plug and hence prevent healing^[72].

An anal fistula plug has also been used for complex anal fistulas. Ellis *et al*^[81] retrospectively studied the long-term outcomes of an anal fistula plug in complex fistulas in patients who had at least 1 year of follow-up since their last treatment. Sixty three patients were identified, 51 of whom (81%) had had clinical healing of the fistula. When applying multivariate analysis, the authors noted that tobacco smoking, a history of prior plug failure, and a posterior fistula were all predictive factors for failure. This study concluded that the anal fistula plug is an effective method for long-term closure of complex anal fistulas^[81]. Similarly, Lenisa *et al*^[82] studied 60 consecutive pa-

Table 3 Results of anal fistula plug

Author	n	Follow-up months (mean)	Success rate (%)
Johnson <i>et al</i> ^[69]	25	3	87
Champagne <i>et al</i> ^[68]	46	12	83
O'Connor <i>et al</i> ^[70]	20	10	80
Ellis <i>et al</i> ^[41]	18	10	78
Garg <i>et al</i> ^[71]	21	10	71
Schwandner <i>et al</i> ^[72]	19	9.3	61
Ky <i>et al</i> ^[73]	45	6.5	55
Thekkinkattil <i>et al</i> ^[74]	43	11	44
Christoforidis <i>et al</i> ^[75]	47	6.5	43
van Koperen <i>et al</i> ^[76]	17	7	41
El-Gazzaz <i>et al</i> ^[77]	33	7.4	25
Lawes <i>et al</i> ^[78]	20	7.4	24
Safar <i>et al</i> ^[79]	35	4	14

n: Number of patients.

tients with complex fistulas through a prospectively maintained database. Eleven patients had multiple fistula tracts, 17 were located anteriorly in female patients, and the remaining were trans-sphincteric, while 38 tracts were recurrent in nature. At a mean follow-up of 13 mo, the success rate was 60% in all patients and 70% for the fistula tracts. The mean time for recurrence was 5.7 mo. Replugging successfully managed 2 recurrent patients, and 5 patients received successful post-plug fistulotomy. This resulted in a global healing rate of 72% with no continence impairment. The authors concluded that an anal fistula plug remains a safe option in treating complex anal fistulas and the reasons and risk factors for recurrence remain to be discovered.

The higher than expected recurrence rate with the glue and plug, and the associated risk of incontinence with other conventional methods prompted the search for other techniques to find an optimal treatment for fistula-in-ano.

Ligation of the intersphincteric fistula tract

Initially described by Rojanasakul^[83], Ligation of the intersphincteric fistula tract (LIFT) involves a small incision in the intersphincteric groove where the fistula tract crosses from the internal sphincter to the external sphincter. Dissection is carried out till the fistula tract is clearly identified, ligated, then divided. The initial report showed healing in 17 out of 18 patients by a mean time of 4 wk.

Bleier *et al*^[84], applied the technique in 39 patients, 74% of whom had undergone a median of 2 previous attempted repairs. Follow-up data on 35 patients at a median follow-up of 20 wk revealed a success rate of 57% (20/35) and a duration of failure of 10 wk (range, 2-38), with no subjective decrease in continence. Shanwani *et al*^[85], applied the same technique on 45 patients (transsphincteric = 33, complex = 12), with 5 patients presenting with recurrent fistula after prior surgical intervention. After a median follow-up of 9 mo (range, 2-16), the primary healing rate was 82% (37/35), with a median healing time of 7 wk

(range, 4-10). Recurrence was encountered in 8 patients over a period of 3 to 8 mo, with no significant morbidity.

Radiofrequency

Radiofrequency ablation of the fistula was used in an effort to reduce continence-related problems by limiting damage to the surrounding muscle. Gupta^[86,87] conducted a study among 100 patients with low anal fistulas comparing radiofrequency to conventional fistulotomy. The radiofrequency group was found to have less gas incontinence; 4% *vs* 12%.

Stem cells

Patients' adipose-derived stem cells have been used to treat complex fistulas, either cryptoglandular or Crohn's-related^[88]. In a separate procedure, and under complete aseptic techniques, adipose tissue was obtained from the patients, processed and centrifuged to provide adipose-derived stem cells. These cells were cultured, then in a second procedure, were injected into the fistula tract.

In a comparative study in 49 patients with cryptoglandular or Crohn's-related fistulas, the healing rate was 71% in the stem cell group in addition to fibrin glue *vs* 16% in the fibrin glue group, with no difference in adverse reactions among the groups. At 1 year follow-up, recurrence rate was 17.6 % in the stem cell group, with the earliest recurrence occurring at 7 mo, while no recurrences were observed in the control group. The authors concluded that this method was safe and had the potential of healing fistulas in complex disease^[88].

CONCLUSION

An anal fistula is a common disease which is devastating to the patients and imposes challenges to the surgeon. Proper management requires knowledge of the etiology and an understanding of the anatomy. So far, the available treatment methods have not achieved the main goals of preventing recurrence and preservation of continence. The lack of level I evidence, absence of long follow-up periods, inconsistent results, and varying methodology among published studies has resulted in the current lack of consensus. However, the higher than accepted recurrence rates, and fear of incontinence, has prompted a search for newer methods. Nevertheless, the variability in success and incontinence and/or recurrence rates could be related to surgeon expertise and/or technique and/or patient selection.

REFERENCES

- 1 **Malik AI**, Nelson RL. Surgical management of anal fistulae: a systematic review. *Colorectal Dis* 2008; **10**: 420-430
- 2 **Parks AG**, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. *Br J Surg* 1976; **63**: 1-12
- 3 **Vasilevsky CA**. Anorectal abscess and fistula. In: David E. Beck, Patricia L. Roberts, Theodore J. Saclarides, Anthony J. Senagore, Michael J. stamos, Steven D. Wexner, ed. The ASCRS Textbook of Colon and Rectal Surgery. second ed. New York: Springer; 2011:219-244

- 4 **Ellis CN**. Bioprosthetic plugs for complex anal fistulas: an early experience. *J Surg Educ* 2007; **64**: 36-40
- 5 **Kim T**, Chae G, Chung SS, Sands DR, Speranza JR, Weiss EG, Noguerras JJ, Wexner SD. Faecal incontinence in male patients. *Colorectal Dis* 2008; **10**: 124-130
- 6 **Cataldo PA**, Senagore A, Luchtefeld MA. Intrarectal ultrasound in the evaluation of perirectal abscesses. *Dis Colon Rectum* 1993; **36**: 554-558
- 7 **Sudol-Szopinska I**, Szczepkowski M, Panorska AK, Szopiński T, Jakubowski W. Comparison of contrast-enhanced with non-contrast endosonography in the diagnostics of anal fistulas. *Eur Radiol* 2004; **14**: 2236-2241
- 8 **Vasilevsky CA**, Gordon PH. Benign Anorectal: Abscess and Fistula. In: Wolff BG, Fleshman JW, Beck DE, Pemberton JH, Wexner SD, editors. The ASCRS Textbook of Colon and Rectal Surgery. New York: Springer, 2007: 192-214
- 9 **Halligan S**. Imaging fistula-in-ano. *Clin Radiol* 1998; **53**: 85-95
- 10 **Lunniss PJ**, Barker PG, Sultan AH, Armstrong P, Reznek RH, Bartram CI, Cottam KS, Phillips RK. Magnetic resonance imaging of fistula-in-ano. *Dis Colon Rectum* 1994; **37**: 708-718
- 11 **Van Beers B**, Grandin C, Kartheuser A, Hoang P, Mahieu P, Detry R, Vanheuverzwijn R, Pringot J. MRI of complicated anal fistulae: comparison with digital examination. *J Comput Assist Tomogr* 1994; **18**: 87-90
- 12 **Stoker J**, Hussain SM, van Kempen D, Elevelt AJ, Laméris JS. Endoanal coil in MR imaging of anal fistulas. *AJR Am J Roentgenol* 1996; **166**: 360-362
- 13 **deSouza NM**, Puni R, Kmiot WA, Bartram CI, Hall AS, Bydder GM. MRI of the anal sphincter. *J Comput Assist Tomogr* 1995; **19**: 745-751
- 14 **deSouza NM**, Kmiot WA, Puni R, Hall AS, Burl M, Bartram CI, Bydder GM. High resolution magnetic resonance imaging of the anal sphincter using an internal coil. *Gut* 1995; **37**: 284-287
- 15 **Myhr GE**, Myrvold HE, Nilsen G, Thoresen JE, Rinck PA. Perianal fistulas: use of MR imaging for diagnosis. *Radiology* 1994; **191**: 545-549
- 16 **Jorge JM**, Wexner SD. Etiology and management of fecal incontinence. *Dis Colon Retum* 1993; **36**: 77-97
- 17 **Pescatori M**, Maria G, Anastasio G, Rinallo L. Anal manometry improves the outcome of surgery for fistula-in-ano. *Dis Colon Rectum* 1989; **32**: 588-592
- 18 **Chang SC**, Lin JK. Change in anal continence after surgery for intersphincteral anal fistula: a functional and manometric study. *Int J Colorectal Dis* 2003; **18**: 111-115
- 19 **Townsend CBR**, Evers B, editors. 18th ed. Sabiston text book of surgery: the biological basis of modern surgical practice. Philadelphia: Saunders Elsevier, 2008: 1447-1449
- 20 **Vasilevsky CA**, Gordon PH. Results of treatment of fistula-in-ano. *Dis Colon Rectum* 1985; **28**: 225-231
- 21 **Parks AG**, Stitz RW. The treatment of high fistula-in-ano. *Dis Colon Rectum* 1976; **19**: 487-499
- 22 **Van Tets WF**, Kuijpers JH. Seton treatment of perianal fistula with high anal or rectal opening. *Br J Surg* 1995; **82**: 895-897
- 23 **Ritchie RD**, Sackier JM, Hodde JP. Incontinence rates after cutting seton treatment for anal fistula. *Colorectal Dis* 2009; **11**: 564-571
- 24 **Isbister WH**, Al Sanea N. The cutting seton: an experience at King Faisal Specialist Hospital. *Dis Colon Rectum* 2001; **44**: 722-727
- 25 **Hämäläinen KP**, Sainio AP. Cutting seton for anal fistulas: high risk of minor control defects. *Dis Colon Rectum* 1997; **40**: 1443-1146; discussion 1447
- 26 **Williams JG**, Rothenberger DA, Nemer FD, Goldberg SM. Fistula-in-ano in Crohn's disease. Results of aggressive surgical treatment. *Dis Colon Rectum* 1991; **34**: 378-384

- 27 **Person B**, Wexner SD. Management of Perianal Crohn's Disease. *Curr Treat Options Gastroenterol* 2005; **8**: 197-209
- 28 The Surgisis AFP anal fistula plug: report of a consensus conference. *Colorectal Dis* 2008; **10**: 17-20
- 29 **Tyler KM**, Aarons CB, Sentovich SM. Successful sphincter-sparing surgery for all anal fistulas. *Dis Colon Rectum* 2007; **50**: 1535-1539
- 30 **Whiteford MH**, Kilkenny J, Hyman N, Buie WD, Cohen J, Orsay C, Dunn G, Perry WB, Ellis CN, Rakinic J, Gregorczyk S, Shellito P, Nelson R, Tjandra JJ, Newstead G. Practice parameters for the treatment of perianal abscess and fistula-in-ano (revised). *Dis Colon Rectum* 2005; **48**: 1337-1342
- 31 **Perez F**, Arroyo A, Serrano P, Candela F, Perez MT, Calpena R. Prospective clinical and manometric study of fistulotomy with primary sphincter reconstruction in the management of recurrent complex fistula-in-ano. *Int J Colorectal Dis* 2006; **21**: 522-526
- 32 **Perez F**, Arroyo A, Serrano P, Candela F, Sanchez A, Calpena R. Fistulotomy with primary sphincter reconstruction in the management of complex fistula-in-ano: prospective study of clinical and manometric results. *J Am Coll Surg* 2005; **200**: 897-903
- 33 **Perez F**, Arroyo A, Serrano P, Sánchez A, Candela F, Perez MT, Calpena R. Randomized clinical and manometric study of advancement flap versus fistulotomy with sphincter reconstruction in the management of complex fistula-in-ano. *Am J Surg* 2006; **192**: 34-40
- 34 **van Koperen PJ**, Wind J, Bemelman WA, Bakx R, Reitsma JB, Slors JF. Long-term functional outcome and risk factors for recurrence after surgical treatment for low and high perianal fistulas of cryptoglandular origin. *Dis Colon Rectum* 2008; **51**: 1475-1481
- 35 **Cavanaugh M**, Hyman N, Osler T. Fecal incontinence severity index after fistulotomy: a predictor of quality of life. *Dis Colon Rectum* 2002; **45**: 349-353
- 36 **Toyonaga T**, Matsushima M, Kiriu T, Sogawa N, Kanyama H, Matsumura N, Shimojima Y, Hatakeyama T, Tanaka Y, Suzuki K, Tanaka M. Factors affecting continence after fistulotomy for intersphincteric fistula-in-ano. *Int J Colorectal Dis* 2007; **22**: 1071-1075
- 37 **Garcia-Aguilar J**, Belmonte C, Wong WD, Goldberg SM, Madoff RD. Anal fistula surgery. Factors associated with recurrence and incontinence. *Dis Colon Rectum* 1996; **39**: 723-729
- 38 **Ozuner G**, Hull TL, Cartmill J, Fazio VW. Long-term analysis of the use of transanal rectal advancement flaps for complicated anorectal/vaginal fistulas. *Dis Colon Rectum* 1996; **39**: 10-14
- 39 **Dixon M**, Root J, Grant S, Stamos MJ. Endorectal flap advancement repair is an effective treatment for selected patients with anorectal fistulas. *Am Surg* 2004; **70**: 925-927
- 40 **Koehler A**, Risse-Schaaf A, Athanasiadis S. Treatment for horseshoe fistulas-in-ano with primary closure of the internal fistula opening: a clinical and manometric study. *Dis Colon Rectum* 2004; **47**: 1874-1882
- 41 **Ellis CN**, Clark S. Fibrin glue as an adjunct to flap repair of anal fistulas: a randomized, controlled study. *Dis Colon Rectum* 2006; **49**: 1736-1740
- 42 **Gustafsson UM**, Graf W. Randomized clinical trial of local gentamicin-collagen treatment in advancement flap repair for anal fistula. *Br J Surg* 2006; **93**: 1202-1207
- 43 **van der Hagen SJ**, Baeten CG, Soeters PB, van Gemert WG. Long-term outcome following mucosal advancement flap for high perianal fistulas and fistulotomy for low perianal fistulas: recurrent perianal fistulas: failure of treatment or recurrent patient disease? *Int J Colorectal Dis* 2006; **21**: 784-790
- 44 **Uribe N**, Millán M, Minguez M, Ballester C, Asencio F, Sanchiz V, Esclapez P, del Castillo JR. Clinical and manometric results of endorectal advancement flaps for complex anal fistula. *Int J Colorectal Dis* 2007; **22**: 259-264
- 45 **Zbar AP**. Experience with staged mucosal advancement anoplasty for high trans-sphincteric fistula-in-ano. *West Indian Med J* 2007; **56**: 446-450
- 46 **Mitalas LE**, Gosselink MP, Zimmerman DD, Schouten WR. Repeat transanal advancement flap repair: impact on the overall healing rate of high transsphincteric fistulas and on fecal continence. *Dis Colon Rectum* 2007; **50**: 1508-1511
- 47 **Dubsky PC**, Stift A, Friedl J, Teleky B, Herbst F. Endorectal advancement flaps in the treatment of high anal fistula of cryptoglandular origin: full-thickness vs. mucosal-rectum flaps. *Dis Colon Rectum* 2008; **51**: 852-857
- 48 **Ortiz H**, Marzo M, de Miguel M, Ciga MA, Oteiza F, Armendariz P. Length of follow-up after fistulotomy and fistulectomy associated with endorectal advancement flap repair for fistula in ano. *Br J Surg* 2008; **95**: 484-487
- 49 **van Koperen PJ**, Wind J, Bemelman WA, Slors JF. Fibrin glue and transanal rectal advancement flap for high trans-sphincteric perianal fistulas; is there any advantage? *Int J Colorectal Dis* 2008; **23**: 697-701
- 50 **Abbas MA**, Lemus-Rangel R, Hamadani A. Long-term outcome of endorectal advancement flap for complex anorectal fistulae. *Am Surg* 2008; **74**: 921-924
- 51 **Golub RW**, Wise WE Jr, Kerner BA, Khanduja KS, Aguilar PS. Endorectal mucosal advancement flap: the preferred method for complex cryptoglandular fistula-in-ano. *J Gastrointest Surg* 1997; **1**: 487-491
- 52 **Swinscoe MT**, Ventakasubramaniam AK, Jayne DG. Fibrin glue for fistula-in-ano: the evidence reviewed. *Tech Coloproctol* 2005; **9**: 89-94
- 53 **Hjortrup A**, Moesgaard F, Kjaergård J. Fibrin adhesive in the treatment of perineal fistulas. *Dis Colon Rectum* 1991; **34**: 752-754
- 54 **Hammond TM**, Grahn MF, Lunniss PJ. Fibrin glue in the management of anal fistulae. *Colorectal Dis* 2004; **6**: 308-319
- 55 **Gisbertz SS**, Sosef MN, Festen S, Gerhards MF. Treatment of fistulas in ano with fibrin glue. *Dig Surg* 2005; **22**: 91-94
- 56 **de Parades V**, Far HS, Etienney I, Zeitoun JD, Atienza P, Bauer P. Seton drainage and fibrin glue injection for complex anal fistulas. *Colorectal Dis* 2010; **12**: 459-463
- 57 **Adams T**, Yang J, Kondylis LA, Kondylis PD. Long-term outlook after successful fibrin glue ablation of cryptoglandular transsphincteric fistula-in-ano. *Dis Colon Rectum* 2008; **51**: 1488-1490
- 58 **Patrlj L**, Kocman B, Martinac M, Jadrijevic S, Sosa T, Sebecic B, Brkljacic B. Fibrin glue-antibiotic mixture in the treatment of anal fistulae: experience with 69 cases. *Dig Surg* 2000; **17**: 77-80
- 59 **Sentovich SM**. Fibrin glue for all anal fistulas. *J Gastrointest Surg* 2001; **5**: 158-161
- 60 **Lindsey I**, Smilgin-Humphreys MM, Cunningham C, Mortensen NJ, George BD. A randomized, controlled trial of fibrin glue vs. conventional treatment for anal fistula. *Dis Colon Rectum* 2002; **45**: 1608-1615
- 61 **Sentovich SM**. Fibrin glue for anal fistulas: long-term results. *Dis Colon Rectum* 2003; **46**: 498-502
- 62 **Zmora O**, Neufeld D, Ziv Y, Tulchinsky H, Scott D, Khaikin M, Stepansky A, Rabau M, Koller M. Prospective, multi-center evaluation of highly concentrated fibrin glue in the treatment of complex cryptogenic perianal fistulas. *Dis Colon Rectum* 2005; **48**: 2167-2172
- 63 **Dietz DW**. Role of fibrin glue in the management of simple and complex fistula in ano. *J Gastrointest Surg* 2006; **10**: 631-632
- 64 **Witte ME**, Klaase JM, Gerritsen JJ, Kummer EW. Fibrin glue treatment for simple and complex anal fistulas. *Hepato-gastroenterology* 2007; **54**: 1071-1073
- 65 **Cintron JR**, Park JJ, Orsay CP, Pearl RK, Nelson RL, Sone JH, Song R, Abcarian H. Repair of fistulas-in-ano using fibrin adhesive: long-term follow-up. *Dis Colon Rectum* 2000; **43**: 944-999
- 66 **Queralto M**, Portier G, Bonnaud G, Chotard JP, Cabarrot

- P, Lazorthes F. Efficacy of synthetic glue treatment of high cryptoglandular fistula-in-ano. *Gastroenterol Clin Biol* 2010; **34**: 477-482
- 67 **Ueno T**, Pickett LC, de la Fuente SG, Lawson DC, Pappas TN. Clinical application of porcine small intestinal submucosa in the management of infected or potentially contaminated abdominal defects. *J Gastrointest Surg* 2004; **8**: 109-112
- 68 **Champagne BJ**, O'Connor LM, Ferguson M, Orangio GR, Schertzer ME, Armstrong DN. Efficacy of anal fistula plug in closure of cryptoglandular fistulas: long-term follow-up. *Dis Colon Rectum* 2006; **49**: 1817-1821
- 69 **Johnson EK**, Gaw JU, Armstrong DN. Efficacy of anal fistula plug vs. fibrin glue in closure of anorectal fistulas. *Dis Colon Rectum* 2006; **49**: 371-376
- 70 **O'Connor L**, Champagne BJ, Ferguson MA, Orangio GR, Schertzer ME, Armstrong DN. Efficacy of anal fistula plug in closure of Crohn's anorectal fistulas. *Dis Colon Rectum* 2006; **49**: 1569-1573
- 71 **Garg P**. To determine the efficacy of anal fistula plug in the treatment of high fistula-in-ano: an initial experience. *Colorectal Dis* 2009; **11**: 588-591
- 72 **Schwandner O**, Stadler F, Dietl O, Wirsching RP, Fuerst A. Initial experience on efficacy in closure of cryptoglandular and Crohn's transsphincteric fistulas by the use of the anal fistula plug. *Int J Colorectal Dis* 2008; **23**: 319-324
- 73 **Ky AJ**, Sylla P, Steinhagen R, Steinhagen E, Khaitov S, Ly EK. Collagen fistula plug for the treatment of anal fistulas. *Dis Colon Rectum* 2008; **51**: 838-843
- 74 **Thekkinkattil DK**, Botterill I, Ambrose NS, Lundby L, Sagar PM, Buntzen S, Finan PJ. Efficacy of the anal fistula plug in complex anorectal fistulae. *Colorectal Dis* 2009; **11**: 584-587
- 75 **Christoforidis D**, Etzioni DA, Goldberg SM, Madoff RD, Mellgren A. Treatment of complex anal fistulas with the collagen fistula plug. *Dis Colon Rectum* 2008; **51**: 1482-1487
- 76 **van Koperen PJ**, D'Hoore A, Wolthuis AM, Bemelman WA, Slors JF. Anal fistula plug for closure of difficult anorectal fistula: a prospective study. *Dis Colon Rectum* 2007; **50**: 2168-2172
- 77 **El-Gazzaz G**, Zutshi M, Hull T. A retrospective review of chronic anal fistulae treated by anal fistulae plug. *Colorectal Dis* 2010; **12**: 442-447
- 78 **Lawes DA**, Efron JE, Abbas M, Heppell J, Young-Fadok TM. Early experience with the bioabsorbable anal fistula plug. *World J Surg* 2008; **32**: 1157-1159
- 79 **Safar B**, Jobanputra S, Sands D, Weiss EG, Noguera JJ, Wexner SD. Anal fistula plug: initial experience and outcomes. *Dis Colon Rectum* 2009; **52**: 248-252
- 80 **Rizzo JA**, Naig AL, Johnson EK. Anorectal abscess and fistula-in-ano: evidence-based management. *Surg Clin North Am* 2010; **90**: 45-68, Table of Contents
- 81 **Ellis CN**, Rostas JW, Greiner FG. Long-term outcomes with the use of bioprosthetic plugs for the management of complex anal fistulas. *Dis Colon Rectum* 2010; **53**: 798-802
- 82 **Lenisa L**, Espin-Basany E, Rusconi A, Mascheroni L, Escoll-Rufino J, Lozoya-Trujillo R, Vallribera-Valls F, Mégevand J. Anal fistula plug is a valid alternative option for the treatment of complex anal fistula in the long term. *Int J Colorectal Dis* 2010; **25**: 1487-1493
- 83 **Rojanasakul A**, Pattanaarun J, Sahakitrungruang C, Tantiphlachiva K. Total anal sphincter saving technique for fistula-in-ano; the ligation of intersphincteric fistula tract. *J Med Assoc Thai* 2007; **90**: 581-586
- 84 **Bleier JI**, Moloo H, Goldberg SM. Ligation of the intersphincteric fistula tract: an effective new technique for complex fistulas. *Dis Colon Rectum* 2010; **53**: 43-46
- 85 **Shanwani A**, Nor AM, Amri N. Ligation of the intersphincteric fistula tract (LIFT): a sphincter-saving technique for fistula-in-ano. *Dis Colon Rectum* 2010; **53**: 39-42
- 86 **Gupta PJ**. Anal fistulotomy with radiofrequency. *Dig Surg* 2004; **21**: 72-73
- 87 **Gupta PJ**. Radiosurgical fistulotomy; an alternative to conventional procedure in fistula in ano. *Curr Surg* 2003; **60**: 524-528
- 88 **Garcia-Olmo D**, Herreros D, Pascual I, Pascual JA, Del-Valle E, Zorrilla J, De-La-Quintana P, Garcia-Arranz M, Pascual M. Expanded adipose-derived stem cells for the treatment of complex perianal fistula: a phase II clinical trial. *Dis Colon Rectum* 2009; **52**: 79-86

S- Editor Sun H L- Editor Cant MR E- Editor Ma WH