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Surgery Illustrated – Surgical Atlas
Mainz pouch continent cutaneous diversion

Joachim W. Thüroff, Hubertus Riedmiller*, Margit Fisch†, Raimund Stein, Christian Hampel and Rudolf Hohenfellner

*Department of Urology, University Medical Center, Johannes Gutenberg University, Mainz; *Department of Urology and Paediatric Urology, University Hospital Würzburg, Würzburg, †Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

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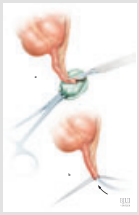
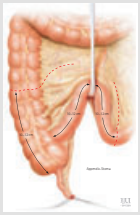
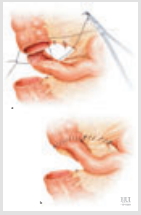
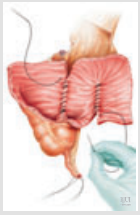
INTRODUCTION

Since the early 1980s, the ileocaecal segment has been used in the Mainz pouch technique not only for continent cutaneous urinary diversion but also for orthotopic bladder substitution [1–4]. Initially, the ileal intussusception nipple was the standard continence mechanism for the catheterizable efferent segment [1–3]. Since 1990, the submucosally embedded appendix, when available and useable, has become the standard catheterizable continent efferent segment [5] and the intussusception nipple remains a reserve technique after appendectomy. Both techniques are described in this article. Other catheterizable continent conduits have been developed [6] but are not described herein. The Mainz pouch offers a low-pressure reservoir with good capacity [7]. To date, >1500 procedures have been performed at our institution.



PLANNING AND PREPARATION

INDICATIONS

The main indication for continent cutaneous diversion by the Mainz pouch technique is bladder cancer, when orthotopic bladder substitution after radical cystoprostatectomy (cystectomy in females) is not the patient's choice or not advisable. The latter is the case if urothelial cancer extends into the prostate (in females beyond the bladder neck), or if in frozen sections the surgical margins are positive for cancer, so that urethrectomy is required. In other cases, pre-existing sphinteric urinary incontinence (e.g. after

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radical prostatectomy) would make orthotopic bladder substitution unlikely to be functional. Females after orthotopic bladder substitution require in up to one third of cases intermittent catheterization for neobladder emptying. Some of them prefer continent cutaneous urinary diversion for the ease of catheterization through the umbilicus rather than through the urethra. Other indications are benign conditions with and without urinary incontinence, such as hyperreflexive neurogenic bladder or interstitial cystitis, when urinary diversion is required or is the patient's wish.

Patient selection is critical for the functional success of the procedure. In patients aged >75 years or in patients with a lack of motivation or manual dexterity (hemiplegics, tetraplegics) to perform transumbilical clean intermittent self-catheterization (CISC), an incontinent type of urinary diversion might be preferable.

SPECIFIC INSTRUMENTS AND MATERIALS

- Optical loupes (×2.5–3.5, 50 cm focal length)
- Headlight
- Allis clamps
- 4/0 glyconate monofilament absorbable sutures on a 1/2 needle (HR22) for ileoascendostomy, pouch suturing
- 4/0 polydioxanone monofilament absorbable sutures on a straight 60 mm needle for pouch suturing
- 4/0 polyglytone monofilament rapidly absorbable sutures on a 1/2 needle (CV-23) for fixation of stents, pouchostomy
- 4/0 polypropylene monofilament nonabsorbable sutures on a 1/2 needle (RB-1) for closing the caecal seromuscularis over the embedded appendix
- 3/0 polypropylene monofilament nonabsorbable sutures on a 1/2 needle (RB-1) for securing the base of the intussusception nipple and for fixation of the pouch against the abdominal peritoneum
- 2/0 polyglactin braided absorbable sutures on a 3/8 needle (UR-6) for fixation of the afferent segment to the abdominal fascia
- 4/0 polydioxanone monofilament uncoloured absorbable sutures on a cutting 3/8 needle (FS-2S) for anastomosis of the efferent segment with the umbilical skin
- 6/0 and 5/0 glyconate monofilament absorbable sutures on a 1/2 needle (HR13) for ureteric anastomosis
- 6 F and 8 F polyurethane/polypropylene ureteric stents
- 10 F pigtail pouchostomy catheter
- TA 55 stapler with 4.8 mm metal staples (green magazine)

To exclude a pathology of the bowel segments required for pouch formation, preoperative evaluation must include imaging of the colon by conventional retrograde double-contrast colonography, colonoscopy or preferably CT-colonography. Colonic diverticulae are rare in the caecum and ascending colon and, if present, are not a contraindication to perform the procedure. However, polyps should be removed preoperatively by colonoscopy to obtain a histological diagnosis.

The day before surgery the bowel is cleansed by administering 3 L of polyethylene glycol solution. During surgery antibiotics (ampillicin/clavulanic acid and metronidazol) are administered and continued for 7–10 days.

The patient is placed supine on the table with about 15° of overextension.

INTRAOPERATIVE DECISION MAKING

APPENDIX STOMA OR INTUSSUSCEPTION NIPPLE?

In general, an appendix stoma would be the first choice, if the appendix is of normal size and calibre. However, even if the appendix looks normal, this should be checked as a first step by appendiceal calibration and dilatation (Fig. 2) before decisions about length of bowel resection for pouch formation are made (Figs 3 and 11). The reason is that a normal looking appendix might (rarely) reveal obliteration upon calibration.

Moreover, patients have to be informed preoperatively, that an appendix stoma has excellent continence results but higher rates of stoma stenosis due to its smaller calibre as compared with an ileal intussusception nipple. If an appendix stoma is possible and reflects the patient's wish, bowel resection can be started and requires only resection of 20–25 cm of terminal ileum (Fig. 3). If the appendix is not useable as the continence mechanism, is absent, or if it is the patient's wish, an ileal intussusception valve is an alternative continence mechanism. However, it requires 12 more centimetres of ileum resection (Fig. 11). The proximal 12 cm of ileum required for creation of the intussusception nipple must remain intact when all the other bowel segments are opened antimesenterically for spherical reconfiguration and pouch formation (Fig. 12).

Figure 1

A midline abdominal incision is made with left-sided semi-circumcision of the umbilicus. The length of the abdominal incision depends on whether continent urinary diversion is performed with or without cystectomy (e.g. in neurogenic bladder). In any case, it should allow complete mobilization of the right colon beyond the right colonic flexure.

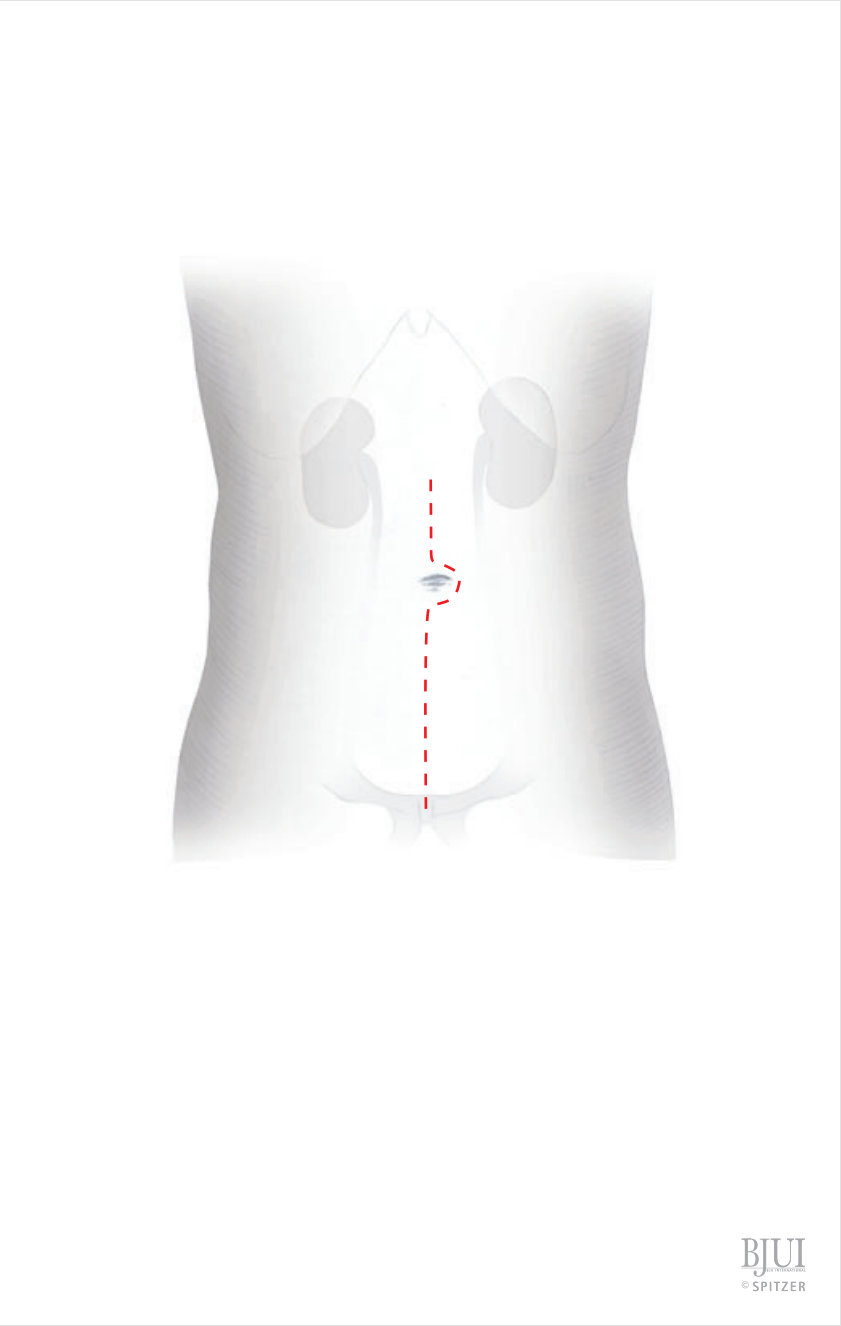


Figure 2

If an appendix of normal size and length is present, its usability as a continent outlet should be determined before any decisions on the length of bowel resection are made. For this, the appendix is opened at its tip, calibrated and stepwise dilated with metal sounds of increasing diameter. Dilatation should allow insertion of at least a 16 F catheter in adults and a 14 F catheter in children. If the appendix is too narrow to accommodate catheters of a reasonable size, emptying of the pouch may be cumbersome due to a low flow and plugging of the catheter by mucous. If this is the case, the appendix should rather be resected and an ileum intussusception nipple (Fig. 11ff) be considered as continent outlet.

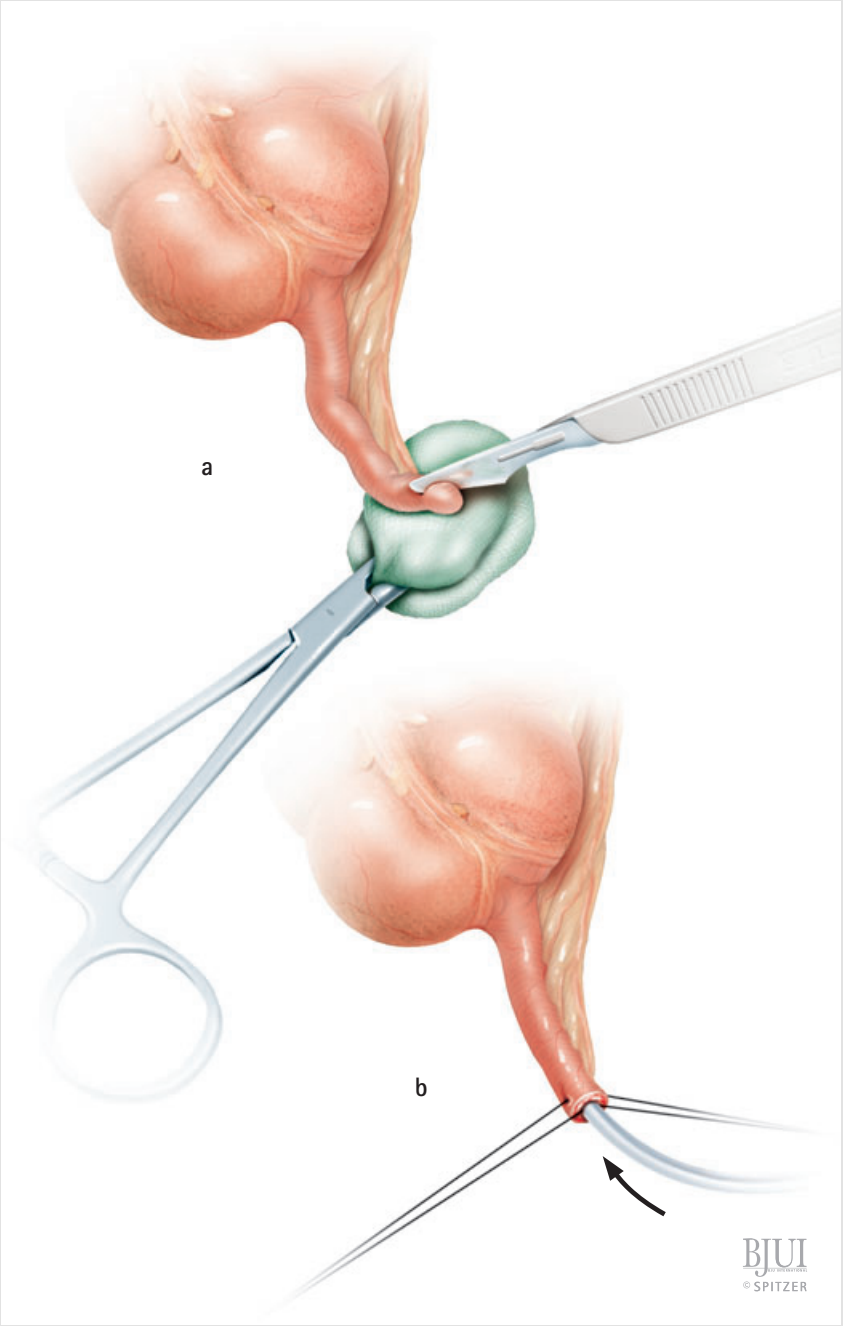


Figure 3

Caecum and ascending colon are mobilized beyond the right colonic flexure from the right abdominal wall. For an ileocaecal pouch with appendix stoma, 10–12 cm of caecum and ascending colon and 20–25 cm of distal ileum are marked by stay sutures at the intended resection lines. The mesentery of the ascending colon is divided between the right colonic and the ileocolic arteries, where usually only one vascular arcade close to the bowel has to be transected. The mesentery of the ileum is divided using the 'back-light' technique for identification of the vascular supply. In this technique, a focal light (e.g. fibre optic cold light) is directed onto the mesentery at the opposite side of the surgeon's view for transillumination so that, with the room lights dimmed, the vessels in the mesentery can be seen. Usually two to a maximum of three vascular arcades have to be divided.

For additional intraoperative cleansing of the isolated ileocaecal segments, a 20 F Foley balloon catheter is inserted proximally into the ileum and secured, and the bowel segments are rinsed with saline using a bowel sucker in the ascending colon for removing the fluid. With a 100-mL syringe, these segments are rinsed repeatedly until the outflow becomes clear.

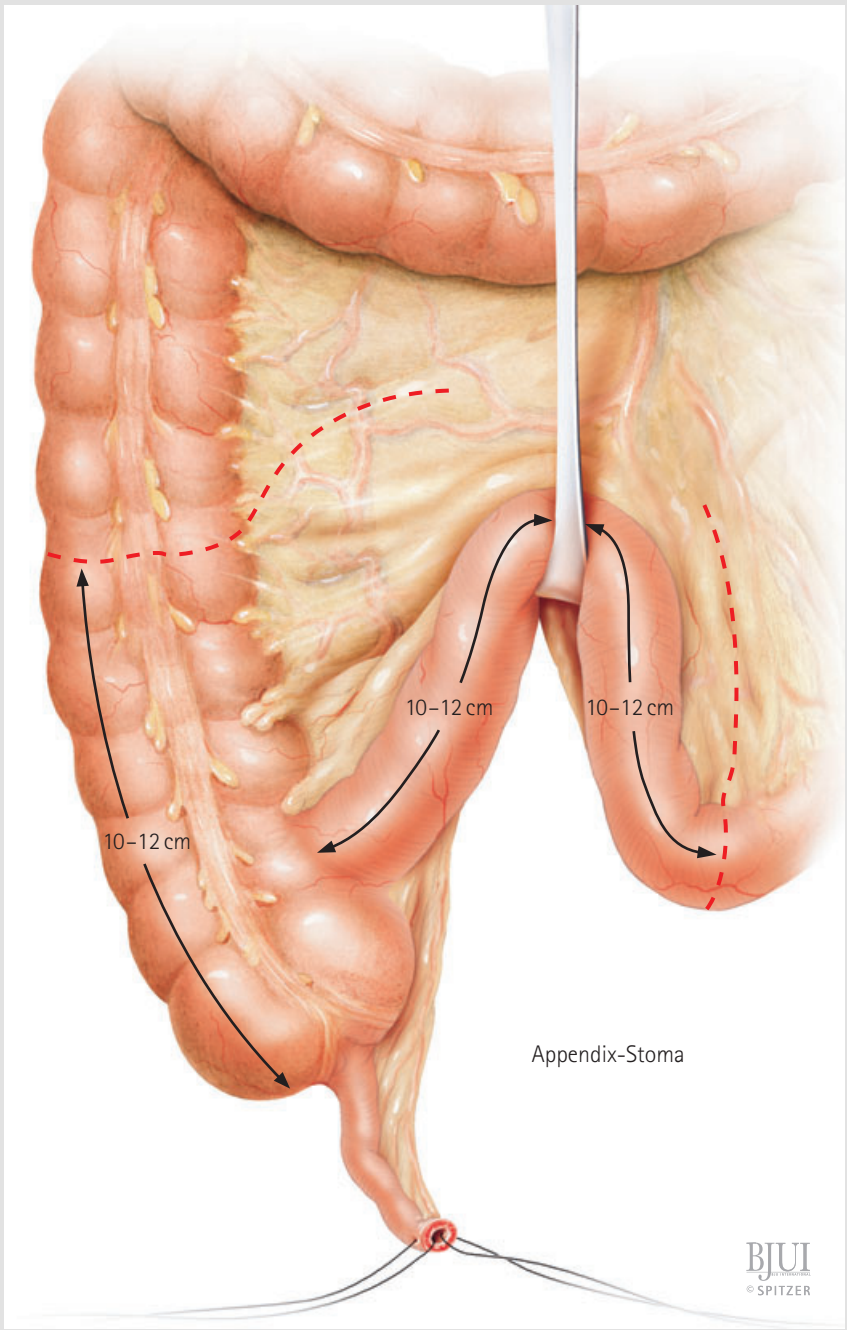


Figure 4

After the proximal end of ileum and the distal end of ascending colon have been mechanically cleaned by using several gauze swabs, bowel continuity is restored. Ileoascendostomy is accomplished in standard technique as a sutured single-row, dual-layer (seromuscularis), running end-to-end anastomosis. For adjustment of differences in bowel diameter, the ileum is spatulated antimesenterically. For the running bowel sutures of the posterior and anterior walls, 4/0 polyglyconate monofilament absorbable sutures are used. The same suture material is used to close the mesenteric gap with another running suture.

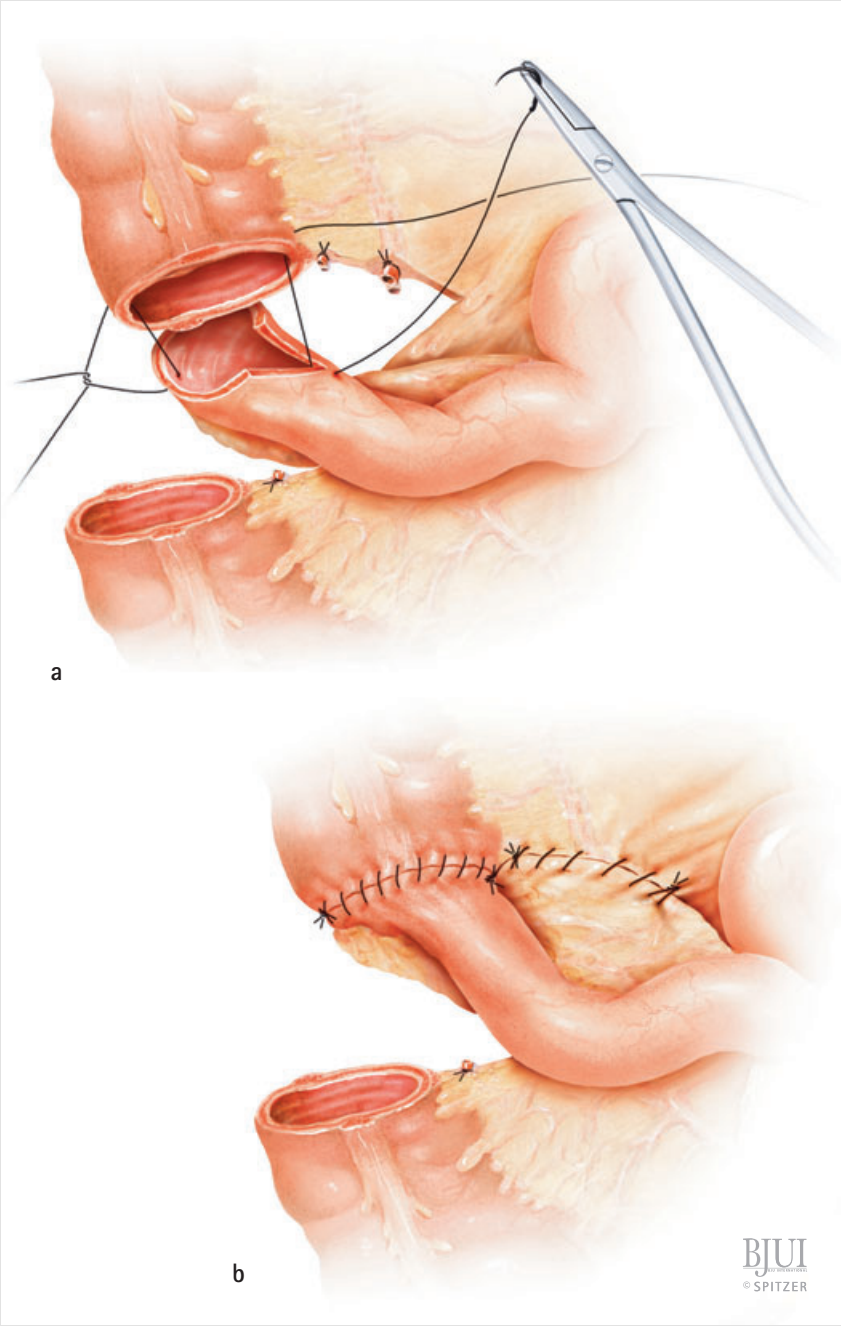


Figure 5

For spherical reconfiguration of the bowel segments into the pouch, ileum and ascending colon are split open at their antimesenteric borders (dotted line), but the caecum must remain intact to create the continence mechanism, which requires embedding of the appendix into the anterior taenia.

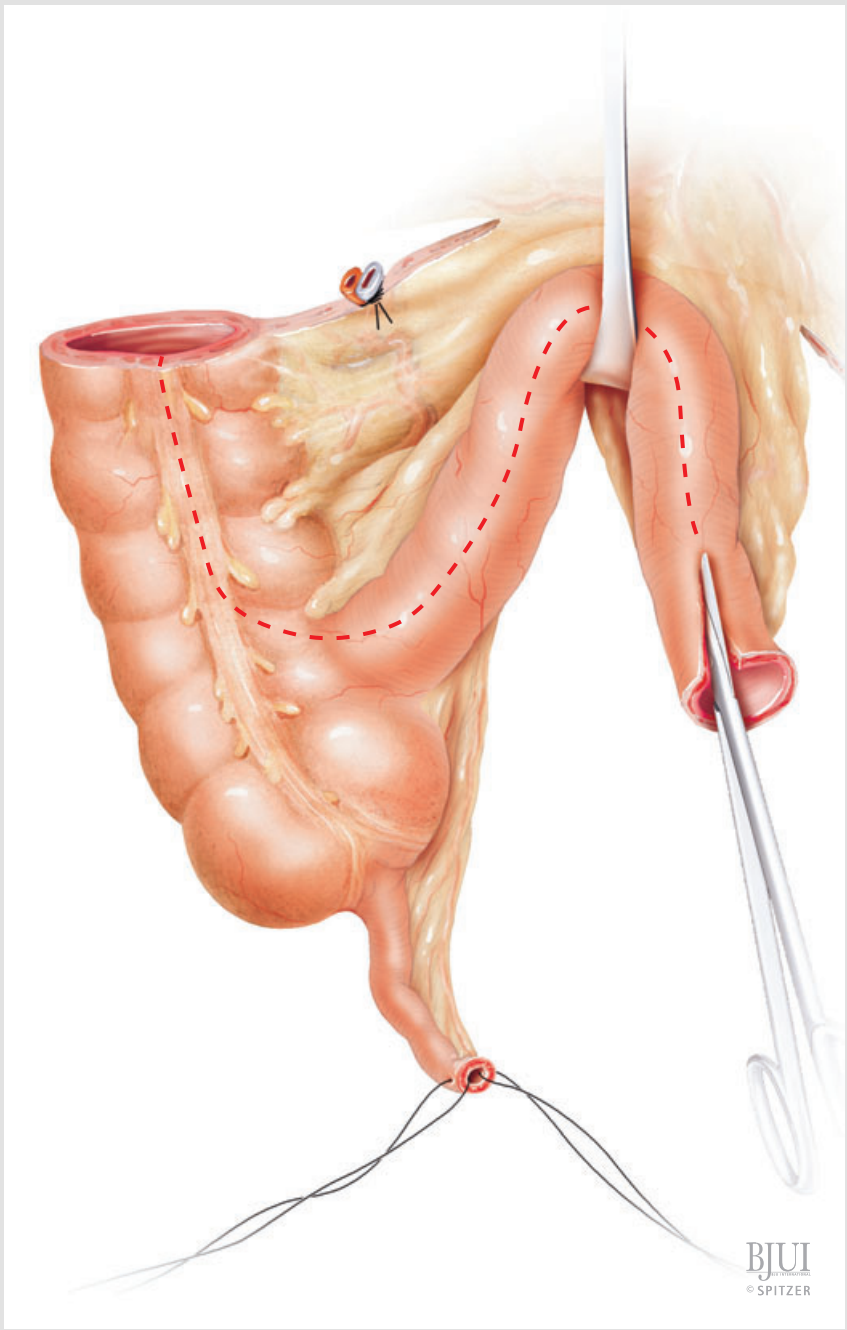


Figure 6

The posterior wall of the pouch is established by side-to-side anastomosis of the ascending colon with the terminal ileal loop and of the latter with the next proximal ileal loop. The anastomoses are made by single-row, all-layer running sutures of 4/0 polydioxanone monofilament absorbable sutures on a straight needle. The straight needle allows faster hand suturing than a curved needle with a needle holder. However, each of the long running sutures should at least be interrupted once in half of the suture line.

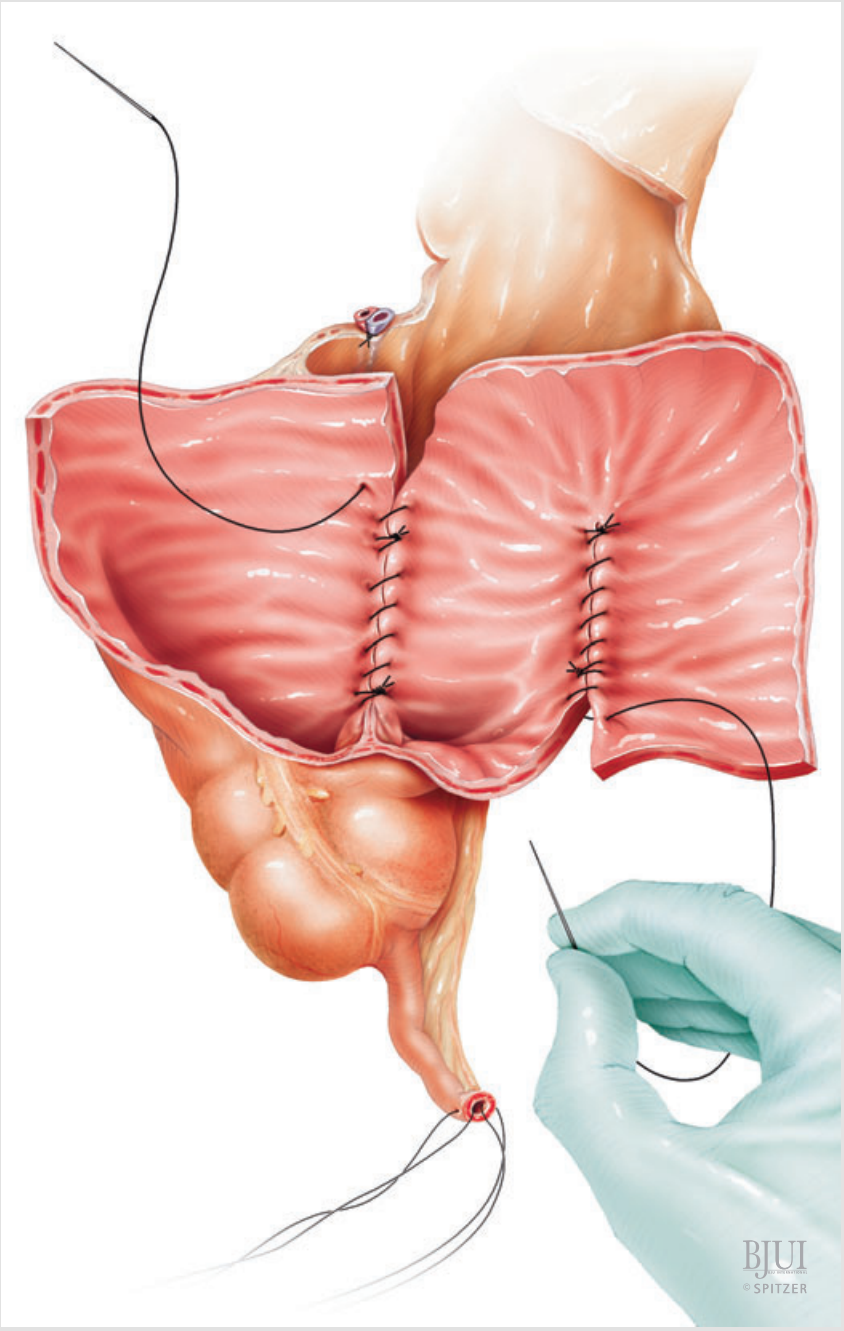


Figure 7

Antirefluxive ureteric implantation by creating a 3–4 cm submucosal tunnel is performed in the 'open end technique', in which the submucosal tunnel is established from the margin of the transected ascending colon. For establishing the tunnel, two stay sutures must be placed on either side of the tunnel. The tunnel is established by dividing the mucosa from the muscularis with scissors by sharp and blunt dissection, starting from the margin of the transected ascending colon (**A**). This procedure is eased if the bowel is stretched well between the stay sutures and if the tunnel is established along one of the longitudinal taeniae rather than at the haustra. If the mobilization of the mucosa is difficult, previous submucosal injection of saline along the intended tunnel length is helpful to separate mucosa from muscularis.

The ureter is spatulated ventrally over 2–3 mm and should be freed from excessive connective tissue outside its vascular supply layer over the tunnel length. On a stay suture, the ureter is pulled with a curved clamp into the tunnel (**B**).

The ureteric orifice is anchored at its distal end by a 5/0 glyconate absorbable monofilament suture through the seromuscularis and mucosa of the bowel. The neo-orifice of the spatulated ureter is completed by 6/0 polyglyconate absorbable monofilament uretero-mucosal sutures (**C**). At the entrance of the ureter into the tunnel, the ureter is anchored by another 6/0 polyglyconate suture between seromuscularis of the bowel and adventitia of the ureter.

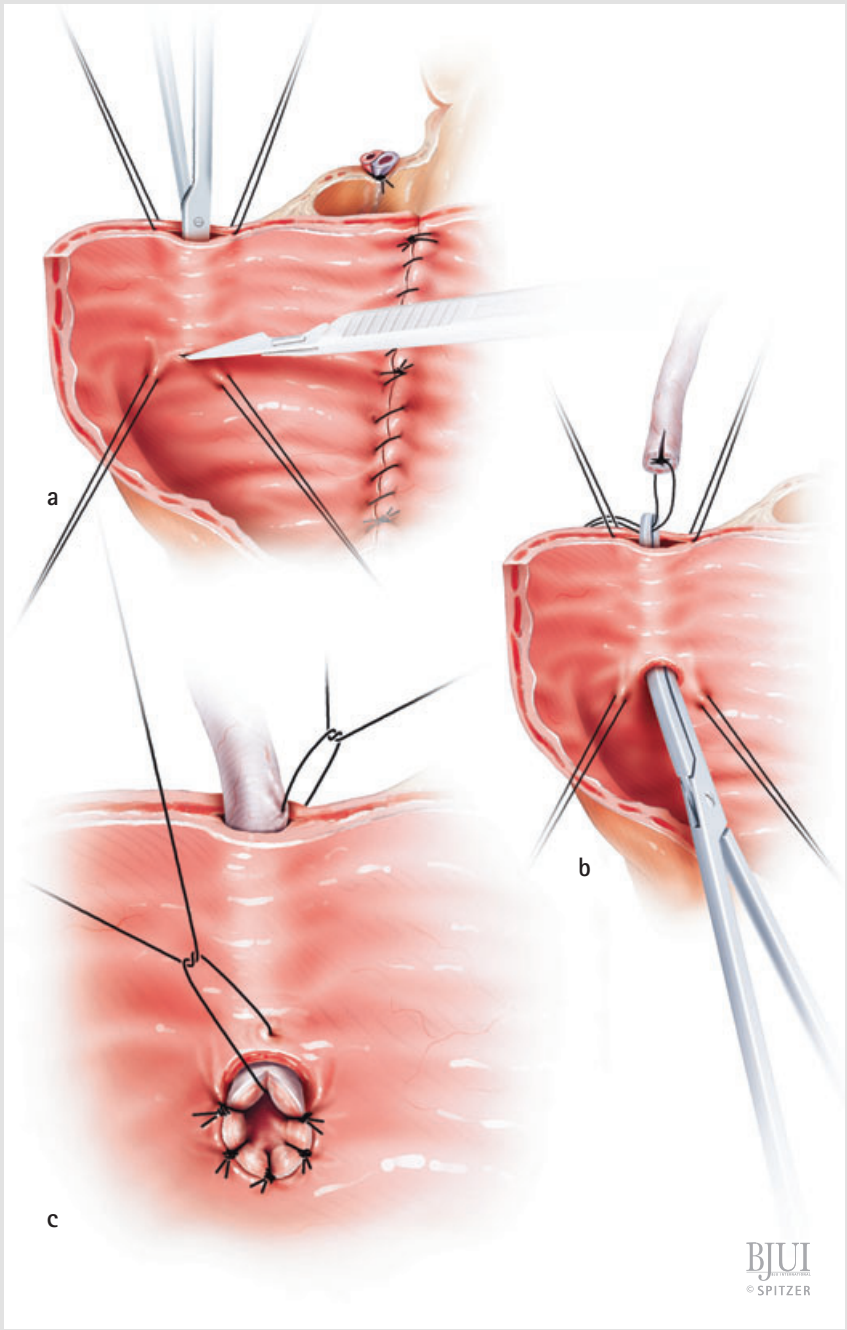


Figure 8

The left ureter is brought into the right retroperitoneum behind the mesentery of the descending colon and in front of the large abdominal vessels. This should be accomplished above the inferior mesenteric artery to avoid compression of the ureter between the inferior mesenteric artery and the aorta ('ureteric nutcracker phenomenon'). The ureters are intubated with 6 F stents (8 F stents for dilated ureters), which are secured to the mucosa by 4/0 polyglytone rapidly absorbable monofilament sutures and brought out on the right side through the bowel wall where they are secured again with the same rapidly absorbable sutures. For creation of the continence mechanism of the appendix, a submucosal tunnel at the lower caecal pole is established for embedding the appendix. The seromuscularis of the anterior taenia of the lower caecal pole is incised down to the mucosa over a length of ≈5 cm. If during this preparation, the mucosa is inadvertently damaged, the hole may be closed by a 6/0 polyglyconate absorbable monofilament suture without expecting any problems from this.

For preserving the blood supply to the appendix, incisions of the serosa (dotted lines) between the perpendicular vessels of the lowest arcade of the appendicular artery are performed using the back-light technique to create openings in the mesenteriolum.

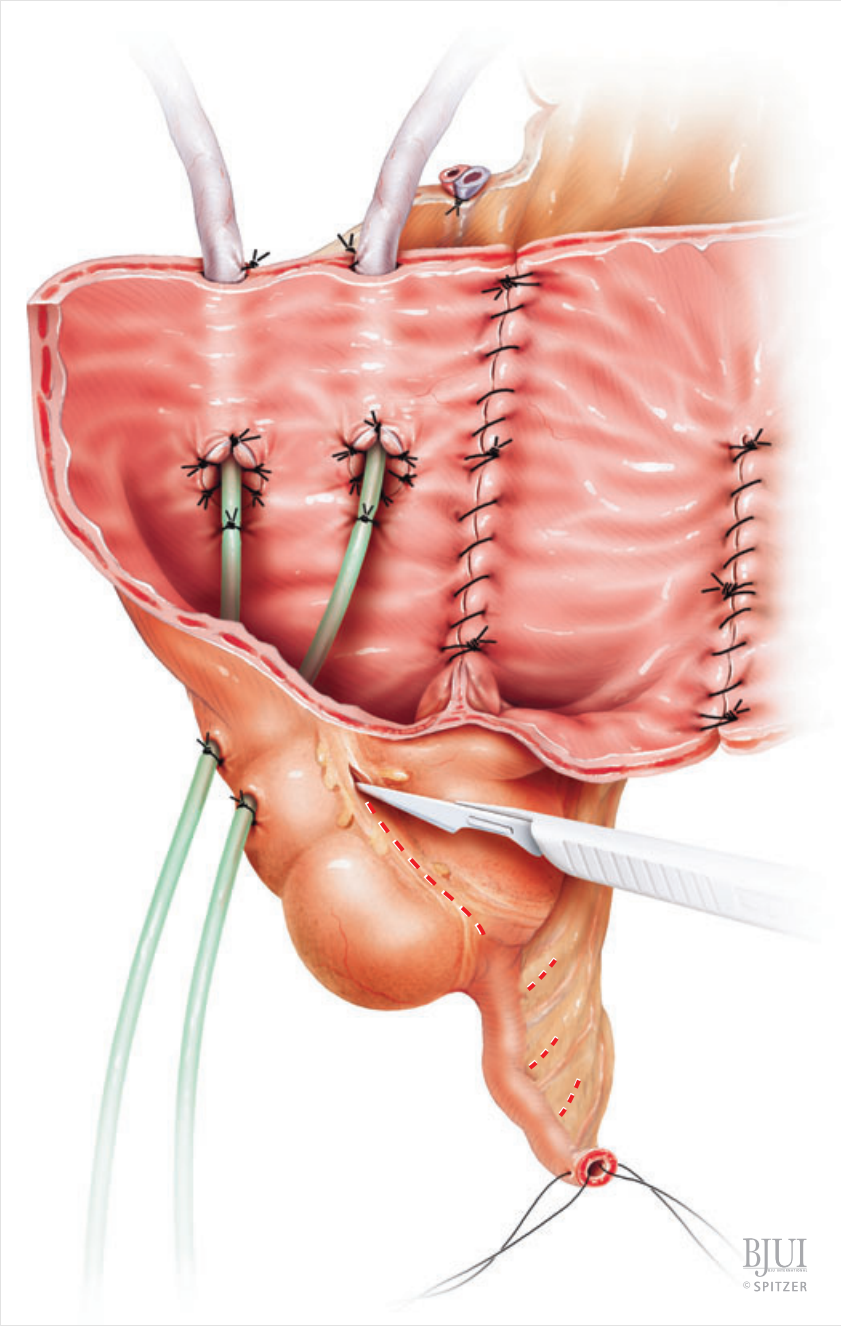


Figure 9

A, shows the completed caecal mucosal bed after longitudinal splitting of the anterior taenia down to the mucosa for submucosal embedding of the appendix. Furthermore, the windows in the mesenteriolum between the perpendicular blood supply are seen. **B**, the appendix is intubated with the Foley balloon catheter for pouch drainage and flipped over into the submucosal bed. The seromuscularis of the caecal pole is closed through the windows in the mesenteriolum by several 4/0 polypropylene nonabsorbable monofilament sutures.

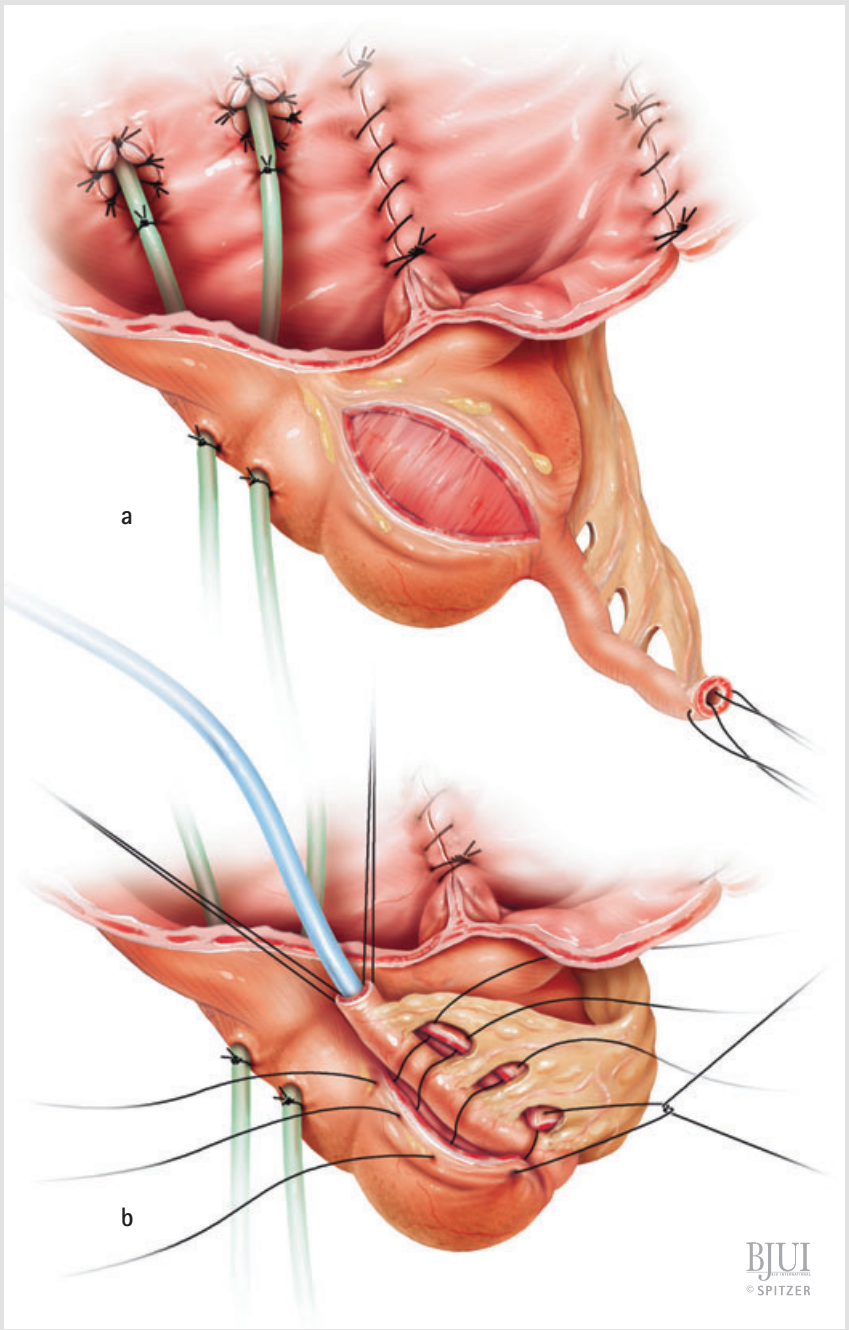


Figure 10

The pouch has been completed by closing the anterior wings of the pouch plate with several running 4/0 polydioxanone monofilament absorbable sutures. Note single interrupted sutures at the entrance of the ureters into their respective submucosal tunnels to prevent compression of the ureters at these sites. In addition to the two ureteric stents, which had been brought out through the right lateral pouch wall, a 10 F pigtail pouchostomy drainage is brought out through the pouch wall and secured with a 4/0 polyglytone rapidly absorbable monofilament suture.

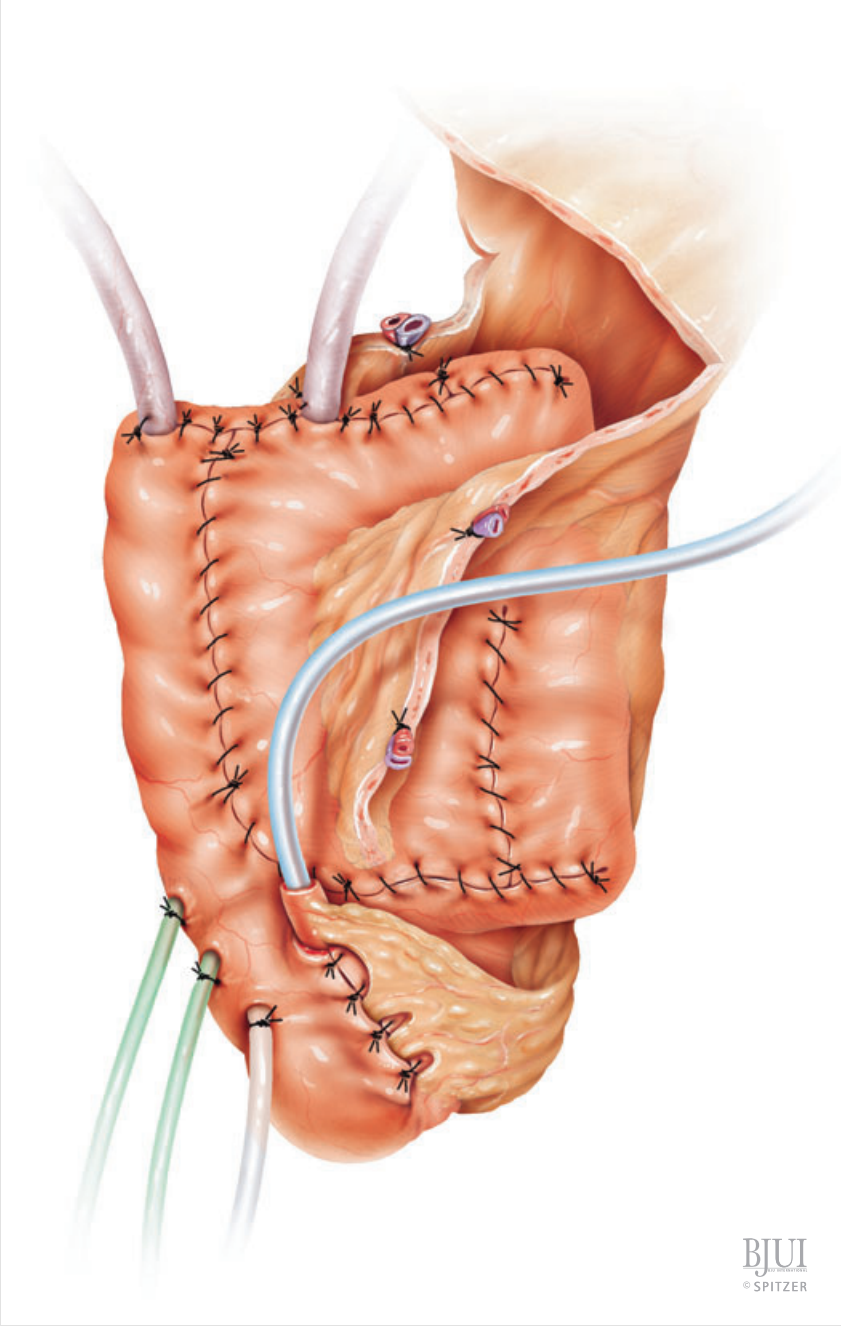


Figure 11

If the appendix is not useable as the continence mechanism or absent and an ileum intussusception nipple is to be constructed, bowel resection has to comprise 12 more centimetres of ileum proximally for constructing the intussusception nipple.

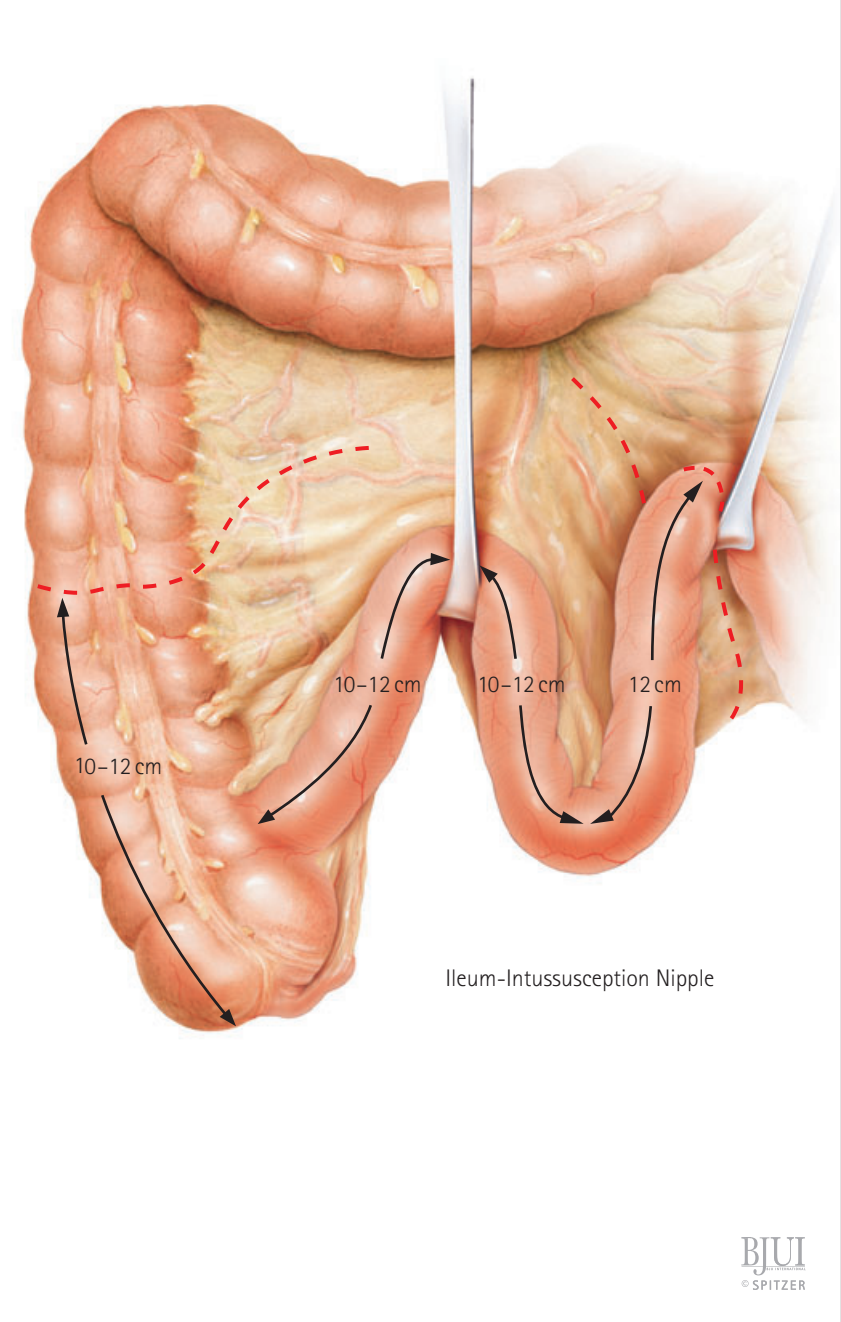


Figure 12

The ileoascendostomy for reconstitution of bowel continuity has been completed, the ascending colon and the terminal to ileal loops have been opened for spherical pouch reconfiguration and the posterior wall of the pouch has been established by side-to-side anastomoses. Note that the proximal 12 cm of ileum in continuity to the pouch remain unopened for construction of the intussusception nipple. The mesentery of the proximal intact ileal segment is beyond the first arcade divided from the ileum over a distance of 5 cm to ease the intussusception.

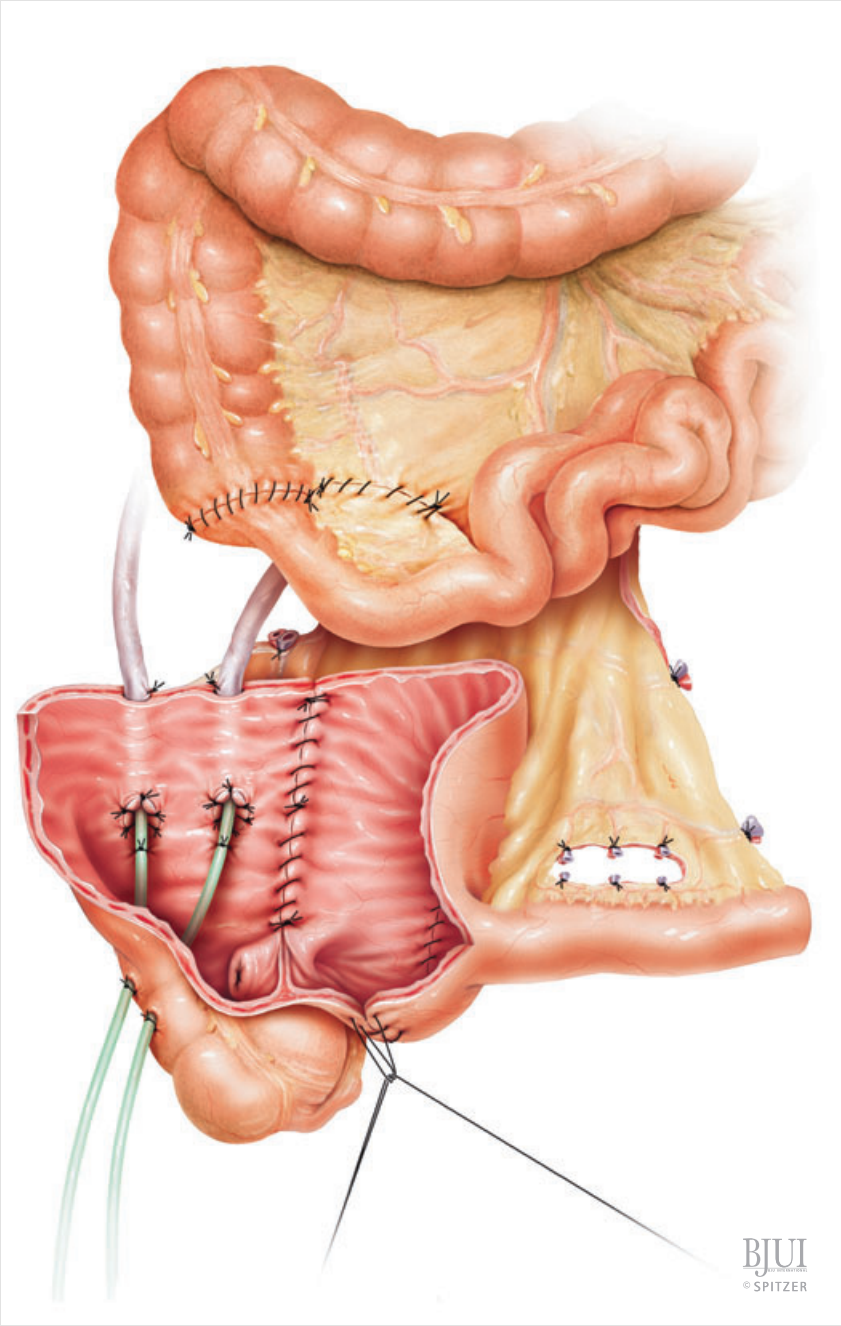


Figure 13

A, shows the dimensions of the segments used for the intussusception nipple. The length of the mesenterial exclusion is 5 cm over the tip of the nipple. B will be the tip of the nipple, A–B will be the outer layer and B–C the inner layer of the nipple. The proximal 2 cm are for anastomosis with the umbilicus. **B**, two Allis clamps have been inserted through the ileocaecal valve into the proximal segment of ileum and have grasped the ileal wall at opposite sides of B for establishing the isoperistaltic intussusception nipple.

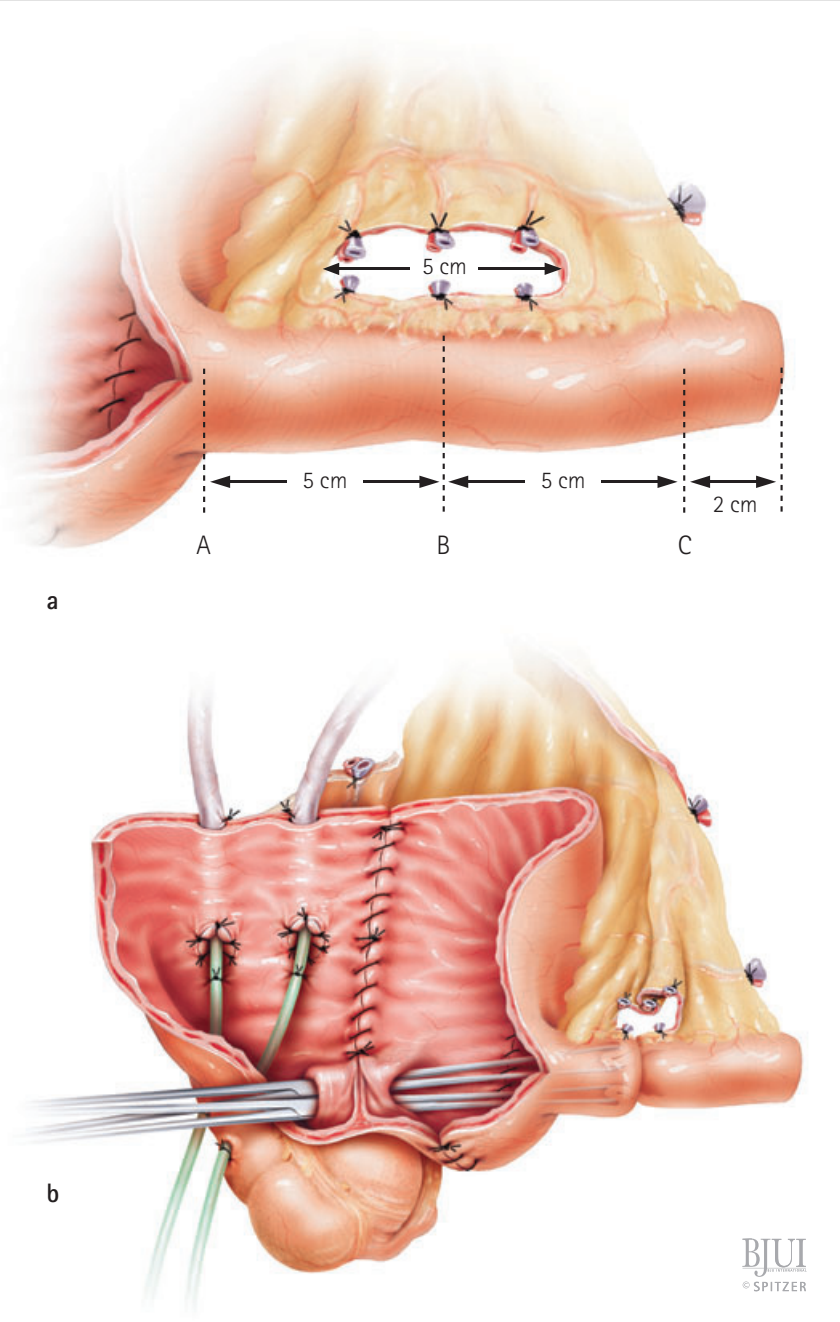


Figure 14

The isoperistaltic intussusception nipple of 5 cm is completed and pulled by two Allis clamps through the ileocaecal valve.

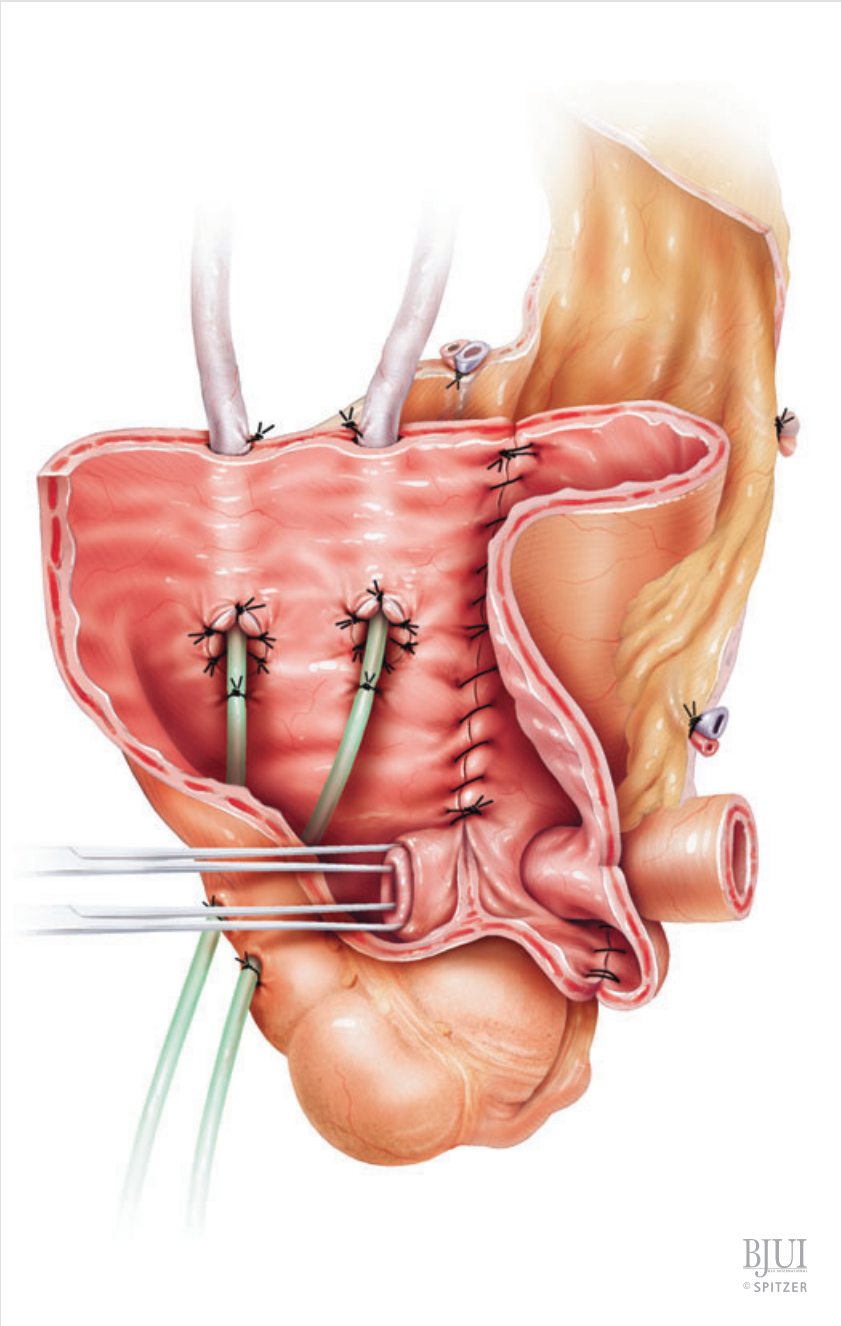
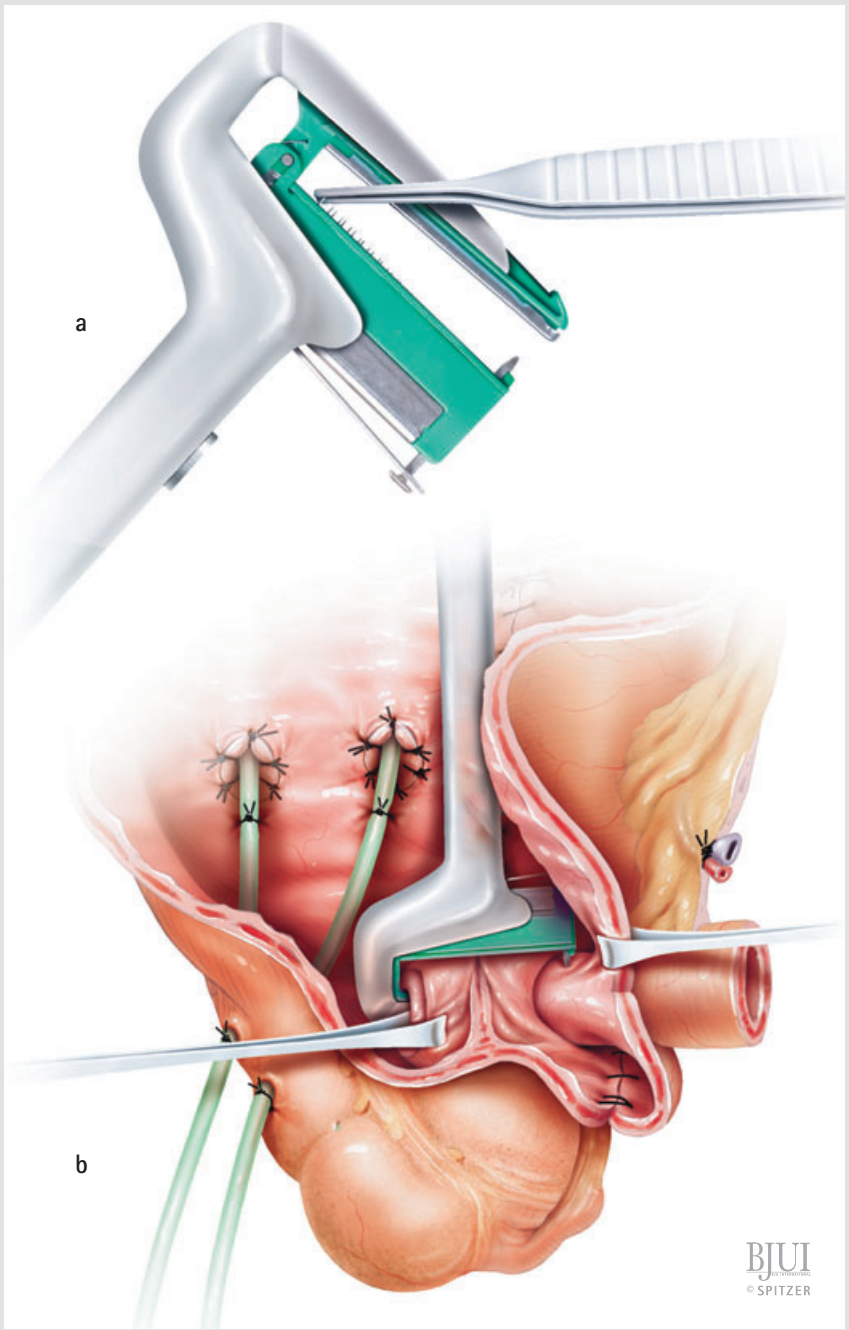


Figure 15



The ileal intussusception nipple is stabilized and fixed to the ileocaecal valve by three rows of staples, two rows of which are applied from inside the pouch and one further from outside.

For the two staple rows applied from inside the pouch, three staples, which would be located at the tip of the nipple but are not required for nipple stabilization and fixation, are removed from the magazine to avoid exposure of these staples to urine and encrustation (**A**). For this, a TA55 magazine with 4.8 mm staples (green magazine) is inserted only three-quarters into the magazine holder to allow asymmetrical closure. With the magazine closed at this position, the release handle is slowly and gradually advanced only so far, so that the most inner staples would appear at this mode of asymmetrical release. This allows removal of some of the staples at the inner part of the magazine, which later on would be at the tip of the nipple, without advancing all the other staples of the magazine.

However, before application to the nipple the magazine is now completely inserted into the magazine holder and inserted into the nipple within the ileocaecal valve (**B**). The magazine is closed, its position and the correct alignment of the pin at the tip of the magazine are checked and it is released. As the magazine staples three layers of bowel (two layers of intussusception valve and the ileocaecal valve), there is crushing of the mucosa, which is of no concern. Moreover, the three-layer stapling process produces deep insertion of the staples with later healing of the crushed mucosa over the metal staples, so ideally no metal staples will be exposed to urine when healed. The pin of the magazine, necessary for exact alignment of the staples, produces a pinhole at the base of the nipple through all bowel layers, which must be closed to avoid a fistula at this site.

Figure 16

A, shows the closure of the pinhole from the first stapler application by a 4/0 polyglyconate absorbable monofilament suture in a figure-of-eight fashion. Furthermore, the second row of staples is applied in an identical way as the first one in Fig. 15.

B, shows the closure of the pinhole from the second stapler application by a figure-of-eight 4/0 polyglyconate absorbable monofilament suture. Furthermore, the third stapler application from the outside of the pouch is shown. For this application, no staples must be removed from the magazine. The stapler is inserted into the serosal slit between the inner and outer layer of the nipple and slit down to the tip of the nipple. Thus, it encompasses only two layers: the outer layer of the nipple and the lower pouch wall with the ileocaecal valve. This row of staples attaches the nipple to the wall of the pouch to prevent dislodgement of the nipple from its intended position (nipple sliding).

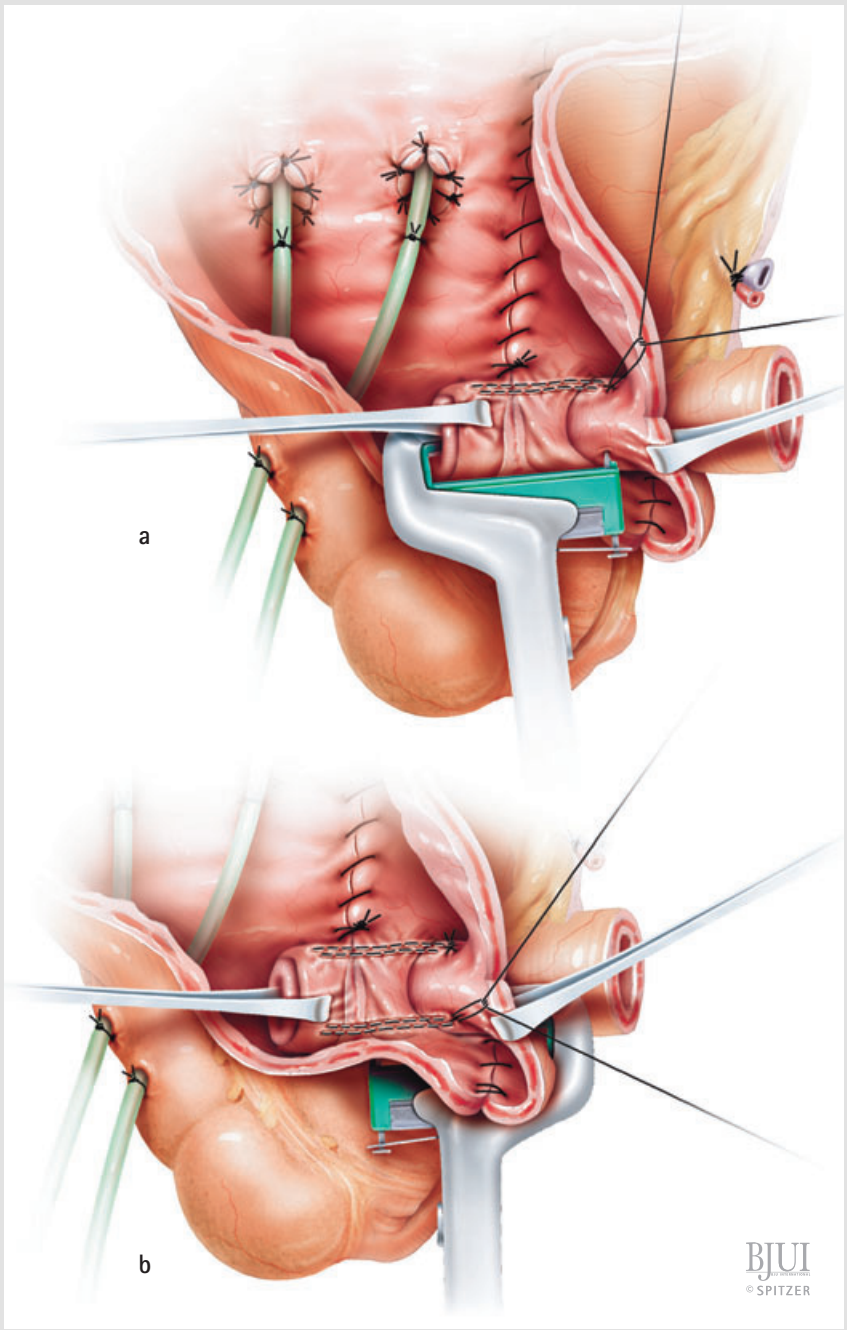


Figure 17

A, shows the closure of the pinhole from the third stapler application for fixation of the nipple to the pouch wall by a figure-of-eight 4/0 polyglyconate absorbable monofilament suture. Furthermore, the tip of the nipple is secured to the ileocaecal valve by several 4/0 polyglyconate absorbable monofilament sutures.

B, the mesenterial slit of the intussusception nipple is closed by several 3/0 polypropylene nonabsorbable monofilament sutures.

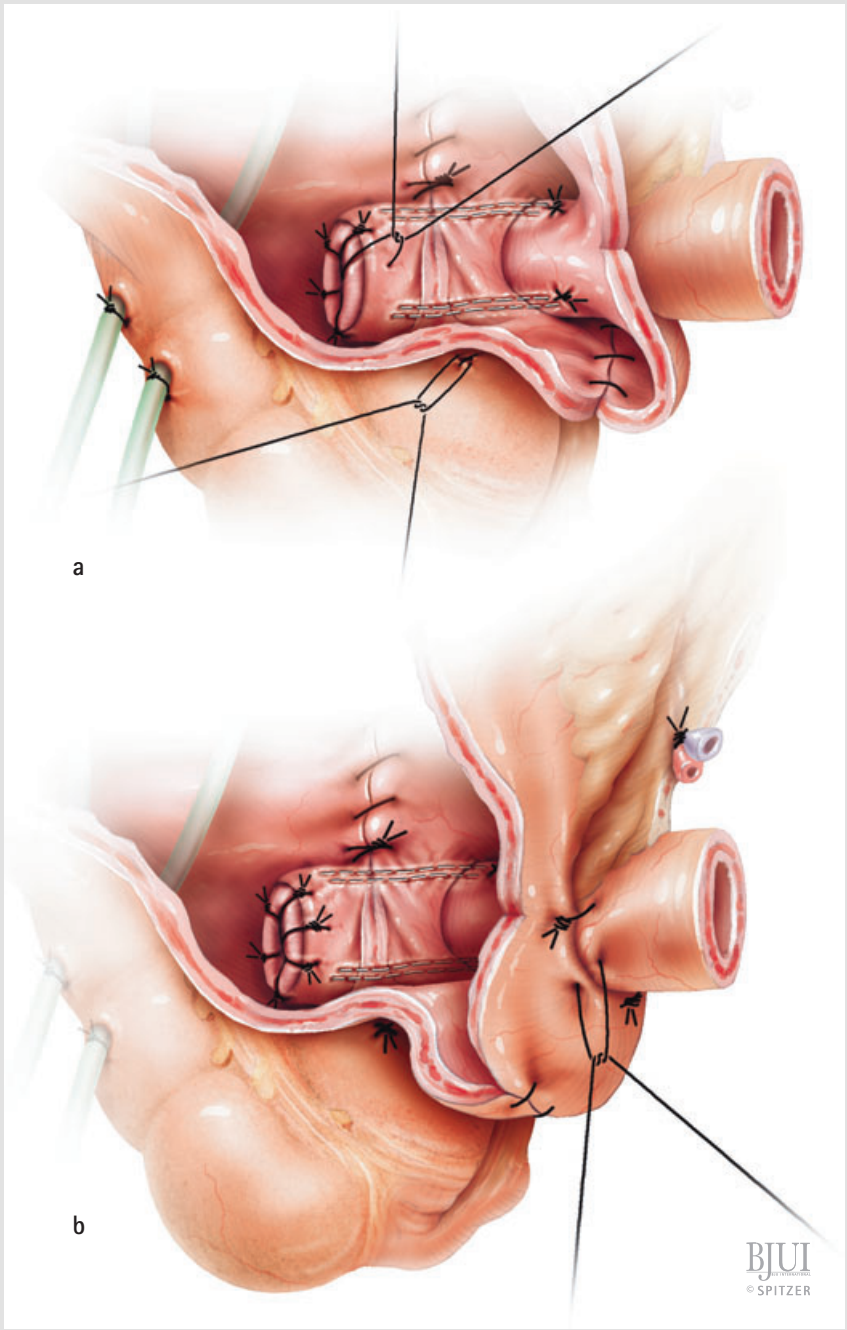


Figure 18

The pouch has been completed by closing the anterior wings of the pouch plate with several running 4/0 polydioxanone monofilament absorbable sutures. Note the single interrupted sutures at the entrance of the ureters into their respective submucosal tunnels to prevent compression of the ureters at these sites. In addition to the two ureteric stents, which had been brought out through the right lateral pouch wall, a 10 F pigtail pouchostomy drainage is brought out through the pouch wall and secured with a 4/0 polyglytone rapidly absorbable monofilament suture.

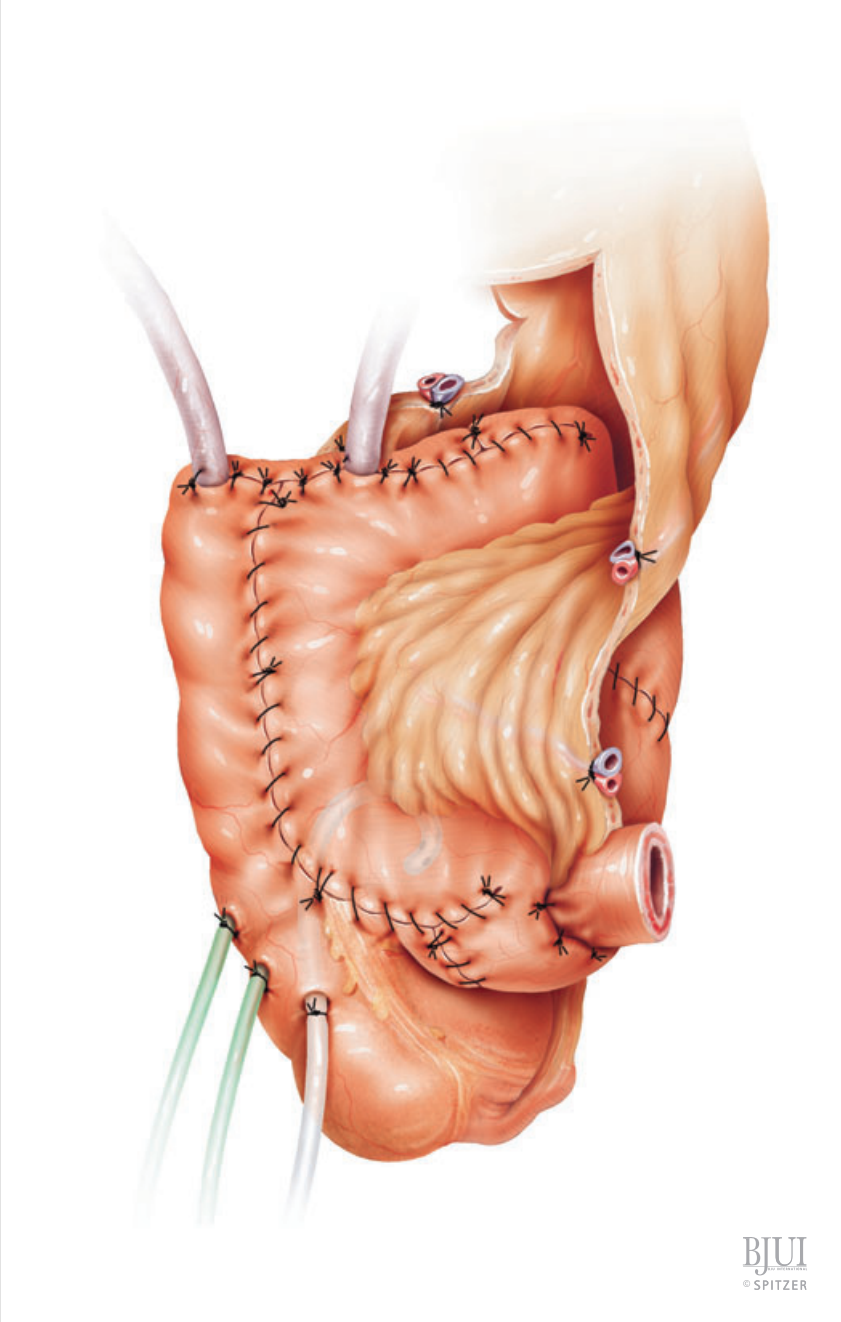


Figure 19

For the creation of the umbilical stoma, the skin funnel of the umbilicus is separated from the abdominal fascia and opened at its tip (**A**). This is easily accomplished by access from the side at the abdominal incision. The abdominal fascia and the peritoneum are incised crosswise and both, the skin of the umbilicus and the efferent segment of the pouch (ileum nipple or appendix) are spatulated at opposite sides (**A**: dotted lines and **B**).

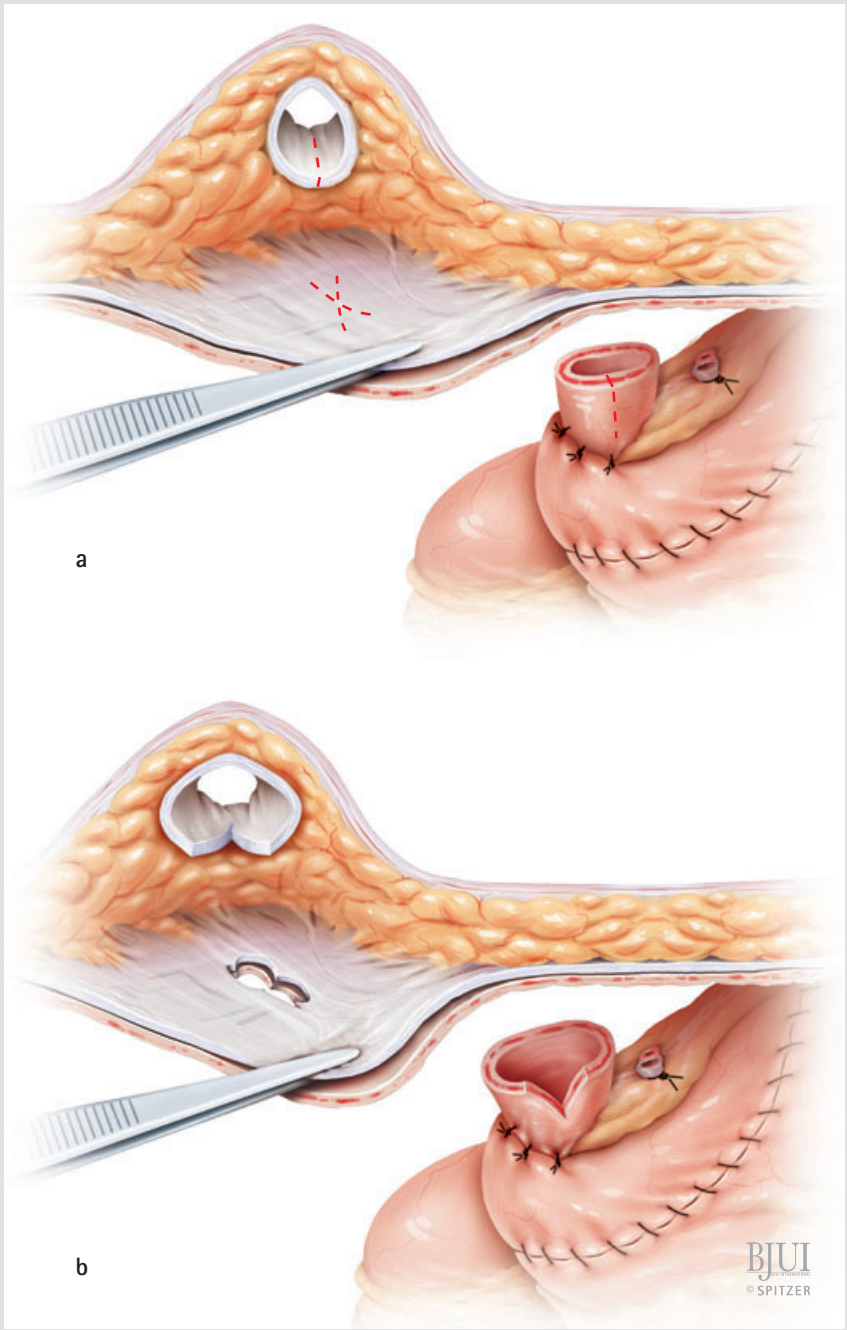


Figure 20

The efferent segment (ileum nipple or appendix) is pulled through the abdominal wall incision with Allis clamps and secured to the abdominal fascia with several 2/0 polyglycolic acid braided absorbable sutures (**A**). The skin of the umbilicus and the efferent segment are anastomosed with 3/0 polydioxanone uncoloured monofilament absorbable sutures on a cutting needle (**B**). The right (posterior) side of the anastomosis is completed first, followed by the left (anterior) side, which is readily accessible from the abdominal incision.

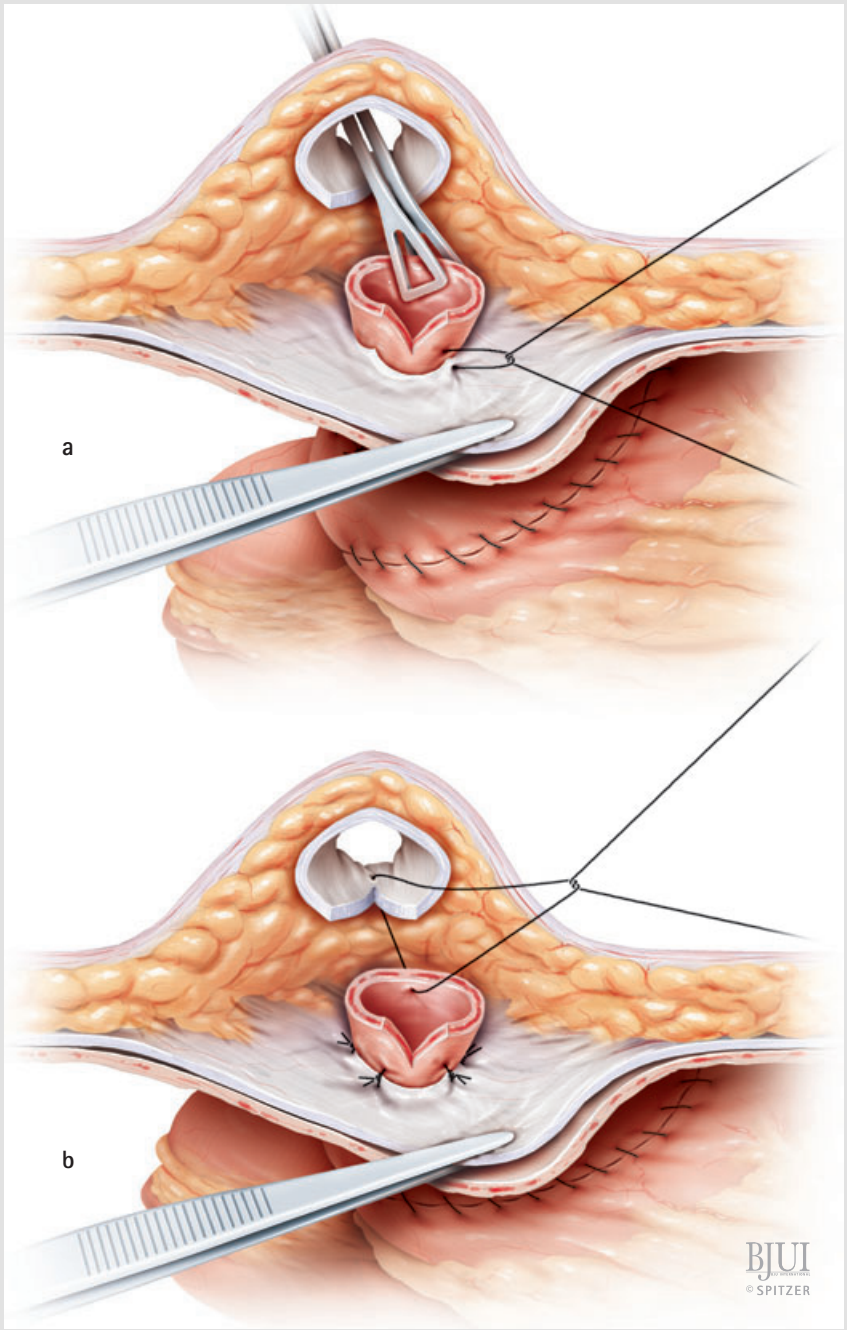


Figure 21

A, The medial aspect of the umbilical stoma is being completed. An 18 F Foley balloon catheter is inserted through the umbilical stoma and the ileal intussusception nipple into the pouch. Note that in the appendix stoma, the previously before creation of the submucosal tunnel of the appendix inserted Foley balloon catheter (Fig. 9b) must not be removed and antegradely reinserted, but should be retrogradely pulled out through the abdominal incision and the umbilicus before the stoma is established as shown in Fig. 20. Inside the abdomen, the reservoir is sutured against the adjacent peritoneum with several 3/0 polypropylene sutures (**B**).

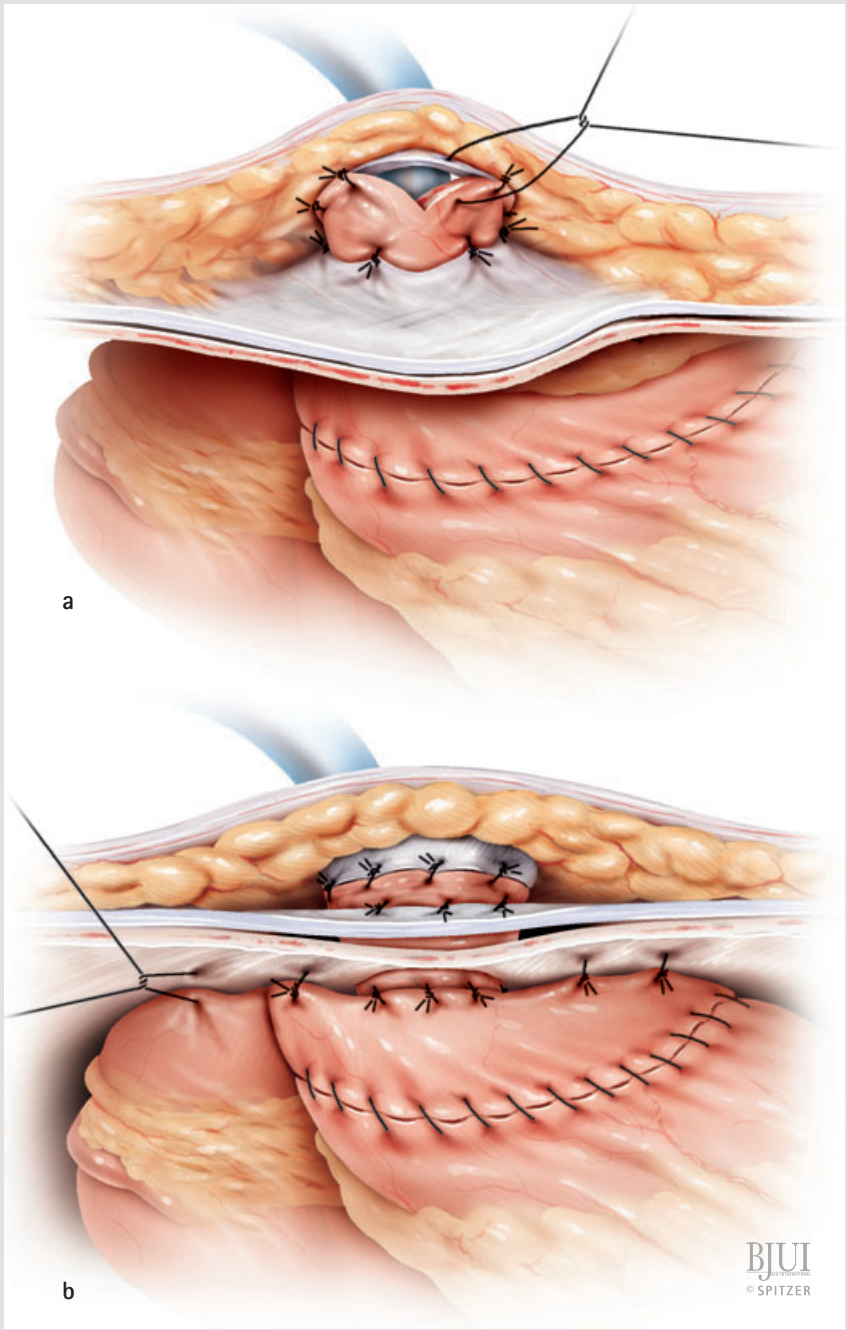
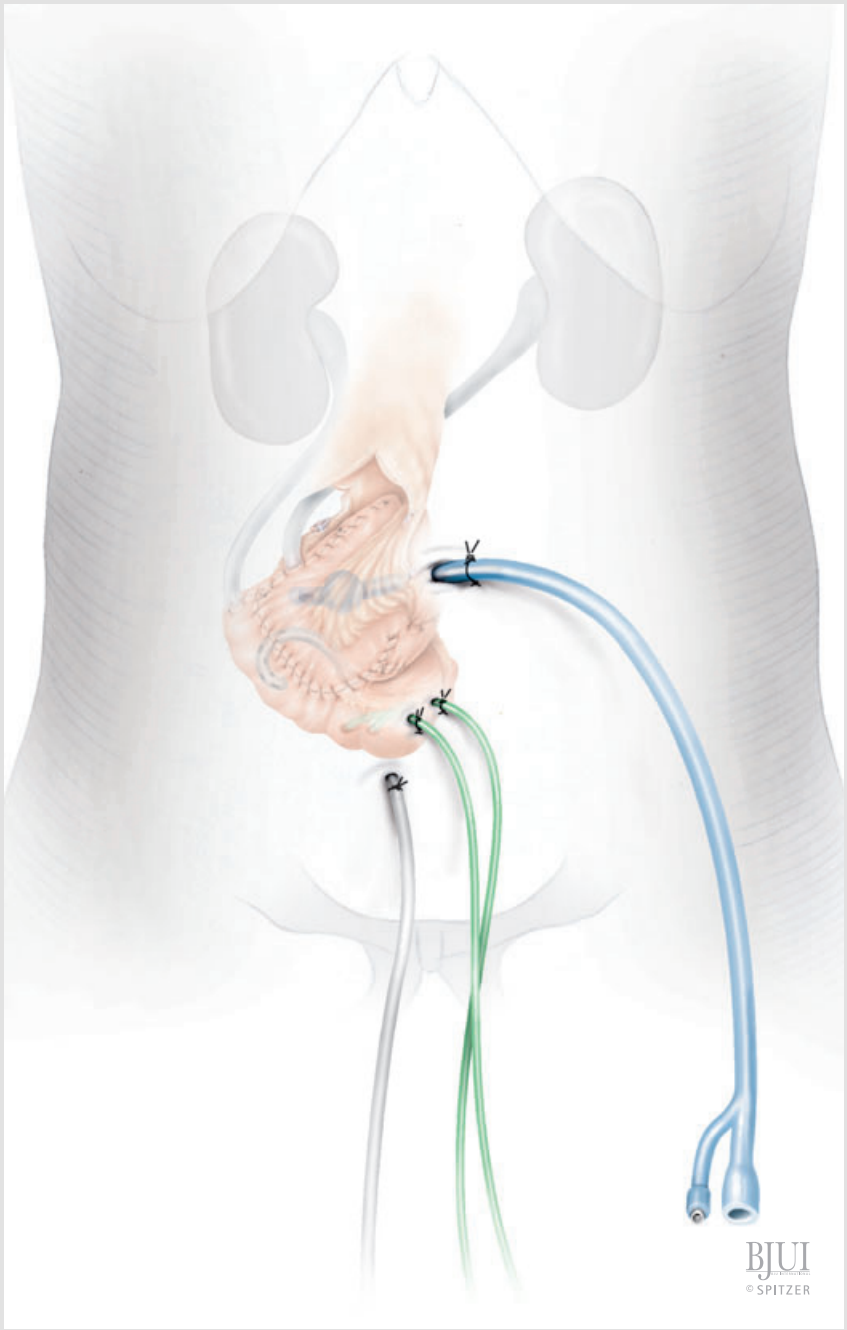


Figure 22

At completion of the surgery, the pouch is drained by a transumbilical Foley catheter and an additional transcutaneous pigtail pouchostomy catheter. The stents of both ureters are also brought out transcutaneously and all catheters are secured to the skin.



POSTOPERATIVE CARE

Medication. Antibiotics (ampillicin/clavulanic acid and metronidazole) are started before surgery and continued for 5–7 days afterwards. For postoperative drainage of the stomach, we prefer intraoperative insertion of a 12 F balloon gastrostomy catheter rather than a nasogastric tube for patients' comfort. Patients are mobilized as early as the first day after surgery.

Drains are placed behind the pouch and into the small pelvis if cystectomy was performed. The gravity drains are removed as soon as the drainage is <50 mL/24 h. The ureteric stents are removed at days 9 and 10, at which time the rapidly absorbable polyglytone sutures for fixation of the stents are generally partially dissolved and breakable. The upper tracts are imaged the day thereafter by IVU or ultrasound.

At discharge from the hospital, the pigtail pouchostomy catheter and the Foley catheter are left indwelling on continuous drainage for 3 weeks and patients are instructed to irrigate the pouch with 50 mL of saline on a daily basis. After 3 weeks, a pouchogram is performed to exclude extravasation and the pigtail pouchostomy catheter is removed. The day thereafter, the transumbilical Foley balloon catheter is removed and the patient is instructed to perform transumbilical CISC of the pouch.

SURGEON TO SURGEON

The procedure requires special attention to ureteric implantation and construction of the continence mechanism of the efferent segment. If during the preparation of the submucosal tunnels for antirefluxive ureter implantation or for embedding of the appendix as a continent outlet, a hole in the colonic mucosa is made, this can be closed with a 6/0 or 7/0 polyglyconate absorbable monofilament suture without expecting adverse sequelae.

In the ileal intussusception nipple valve, placement of the three rows of metal staples generally turns the colour of the nipple mucosa into blue because of impaired perfusion, specifically venous drainage. This is normal and perfusion will recover after all oedema and swelling have subsided.

If previously undiagnosed polyps of the colon are incidentally found when opening the caecum and ascending colon, they should be excised and submitted to frozen-section analysis. Usually they are benign, so there is no reason to abandon the planned procedure.

If postoperatively, a ureteric stent is inadvertently lost, this is usually without sequelae. However, the upper tract should be checked by ultrasound and, if extravasation is to be excluded, by IVU or CT. If the pigtail pouchostomy catheter is lost, this has generally also no adverse sequelae. However, upon discharge the patient must be instructed to adhere precisely to the irrigation intervals of the transumbilical Foley balloon catheter, as the second drainage of the pouch for the case of a blocked catheter is lost.

If the transumbilical Foley catheter is lost postoperatively, reinsertion is usually not a problem if an ileal intussusception nipple is the continent outlet. However, a submucosally embedded appendix stoma can be difficult to re-catheterize before it has healed with some fibrosis in its exact position. For this reason, reinsertion of a transumbilical catheter is recommended to be done under fluoroscopic control with a coaxial technique. In this technique, a guidewire (preferably of the Terumo type) is inserted first, over which a 6 F open-end ureteric catheter is passed into the pouch. If successful insertion of the guidewire remains questionable or is impossible, it should be done under direct vision using a 9–10 F rigid or flexible ureteroscope. After removal of the guidewire from the ureteric catheter, contrast dye is injected through the ureteric catheter to ensure a correct position in the pouch. The ureteric catheter is now used as a guide for coaxial placement of an open-end balloon catheter (Integral® nephrostomy silicone catheter; Uromed, Oststeinbek, Germany) of the same size, which had been lost.

If there is extravasation from the pouch and associated symptoms after removal of the transumbilical catheter at 3 weeks, this might be from the opening of the pouchostomy catheter. Usually the problem is solved by reinserting the transumbilical Foley catheter for about another 10 days. Leakage from the site of the ureteric anastomosis usually requires percutaneous nephrostomy drainage with or without antegrade ureteric stenting. If antegrade stenting is not possible, this will most probably result in a stricture at the implantation site, requiring later surgical revision.

REFERENCES

1 **Thüroff JW, Alken P, Engelmann U, Riedmiller H, Jacobi GH, Hohenfellner R.** The Mainz pouch (mixed augmentation ileum and cecum) for bladder augmentation and continent urinary diversion. *Eur Urol* 1985; **11**: 152–60
2 **Thüroff JW, Alken P, Riedmiller H, Engelmann U, Jacobi GH, Hohenfellner R.** The Mainz pouch (mixed augmentation ileum and cecum) for bladder augmentation and continent urinary diversion. *J Urol* 1986; **136**: 17–26
3 **Thüroff JW, Alken P, Riedmiller H, Jacobi GH, Hohenfellner R.** The Mainz pouch for augmentation or substitution of the bladder and continent diversion. *Semin Urol* 1987; **5**: 69–79
4 **Thüroff JW, Franzaring L, Gillitzer R, Wöhr M, Melchior S.** Simplified orthotopic ileocaecal pouch (Mainz pouch) for bladder substitution. *BJU Int* 2005; **96**: 443–65
5 **Riedmiller H, Bürger R, Müller S, Thüroff J, Hohenfellner R.** Continent appendix stoma: a modification of the Mainz pouch technique. *J Urol* 1990; **143**: 1115–7
6 **Lampel A, Hohenfellner M, Schultz-Lampel D, Thüroff JW.** *In situ* tunneled bowel flap tubes: 2 new techniques of a continent outlet for Mainz pouch cutaneous diversion. *J Urol* 1995; **153**: 308–15
7 **Thüroff JW, Alken P, Riedmiller H, Jacobi GH, Hohenfellner R.** 100 cases of Mainz pouch: continuing experience and evolution. *J Urol* 1988; **140**: 283–8

Correspondence: Joachim W. Thüroff, Department of Urology, University Medical Center, Johannes Gutenberg University, Langenbeckstrasse 1, 55131 Mainz, Germany.
e-mail: joachim.thueroff@unimedizin-mainz.de