REVIEW ARTICLE

Urinary Diversion—Approaches and Consequences

Raimund Stein, Markus Hohenfellner, Sascha Pahernik, Stephan Roth, Joachim W. Thüroff, Herbert Rübber

SUMMARY

Background: Bladder cancer is not a rare disease: In 2010, there were more than 70 000 affected patients in the United States. Radical cystectomy for the treatment of muscle invasive bladder cancer necessitates urinary diversion.

Methods: We present the current options for urinary diversion and their different indications on the basis of a selective search for pertinent literature in PubMed and our own clinical experience.

Results: When bladder cancer is treated with curative intent, continence-preserving orthotopic urinary bladder replacement is preferred. For heterotopic urinary bladder replacement, a reservoir is fashioned from an ileal or ileocecal segment. Urine is diverted to the rectum by way of the sigmoid colon. When bladder cancer is treated with palliative intent, non-continence-preserving cutaneous urinary diversion is usually performed: The creation either of a renal-cutaneous fistula or a self-retaining ureteral stent is a purely palliative procedure. In these interventions, the resorptive surface of the bowel segment used can no longer play its original physiological role in the gastrointestinal tract, even though its absorptive and secretory functions are still intact. This has metabolic consequences, because the diverted urine here comes into contact with a large area of bowel epithelium. Early preventive treatment must be provided against potentially serious complications such as metabolic acidosis and loss of bone density. The resection of ileal segments can also lead to malabsorption. The risk of secondary malignancy is elevated after either continence-preserving anal urinary diversion (>2%) or bladder augmentation (>1%).

Conclusion: There are four options for urinary diversion after cystectomy that can be performed when surgery is performed with either curative or palliative intent. There are also a number of purely palliative interventions.

► Cite this as:

Stein R, Hohenfellner M, Pahernik S, Roth S, Thüroff JW, Rübber H: Urinary diversion—approaches and consequences. *Dtsch Arztebl Int* 2012; 109(38): 617–22. DOI: 10.3238/arztebl.2012.0617

In 2010 a total of 70 530 persons in the United States developed bladder cancer, and 14 680 patients died from their cancer (1). These numbers are an indication that a substantial prevalence can also be assumed for this cancer in Germany. Cystectomy with curative intent is the accepted treatment, especially in patients with invasive, but not yet metastasized, tumors. Cystectomy with palliative intent can become necessary with voiding disorders or in case of local complications such as fistulization or life-threatening hemorrhage, for example as a result of the tumor or trauma.

In addition to the oncological result, patients' quality of life plays an important part when defining the differential indication. The choice of urinary diversion surgery is discussed with each patient individually and depends on the patient's wishes, age, and comorbidities, as well as the tumor's oncological characteristics. The notable increase in the use of continent diversion methods has meant that postoperative follow-up care has become an increasingly important issue in general practice too.

Methods

We conducted a selective literature search in PubMed from 2000 through 2010, using the following search terms: "urinary diversion", "bladder substitution", "urinary reconstruction". The studies we identified were primarily retrospective cohort studies and review articles; randomized studies with high evidence levels on this topic are rare (2–4). Furthermore, we used our own experience.

Continent orthotopic bladder substitution (neobladder)

Implantation of an artificial bladder—for example, a silicone bladder—has not found its way into clinical practice, particularly because of the rapid incrustation. Continent orthotopic bladder replacement (neobladder) is the treatment of choice in patients with an indication for cystectomy with curative intent. This option comes closest to the natural bladder's urine storage and voiding function. The reservoir, which as a rule consists of 50 to 70 cm of ileum, is situated in the pelvis minor and is voided by increasing intra-abdominal pressure. Continence is achieved through the patient's own sphincter (*Figure 1*).

Clinic and Polyclinic for Urology, University Hospital Mainz:
Prof. Dr. med. Stein, Prof. Dr. med. Thüroff

Clinic and Polyclinic for Urology, University Hospital Heidelberg:
Prof. Dr. med. Hohenfellner, PD Dr. med. Pahernik

Department of Urology, HELIOS Hospital Wuppertal: Prof. Dr. med. Roth

Clinic and Polyclinic for Urology, University Hospital Essen:
Prof. Dr. med. Dr. h. c. Rübber

Orthotopic bladder replacement (neobladder)
with access to the urethra and bladder voiding through the normal channels

FIGURE 1

FIGURE 2

Heterotopic continent bladder replacement (pouch);
continence is achieved, for example, by submucosal embedding of the appendix, which is then channeled on to the skin; voiding takes place via self-catheterization

Contraindications include renal failure (glomerular filtration rate [GFR] <50 mL/min) because patients with renal failure can only minimally compensate for metabolic acidosis; liver function disorders; and chronic inflammatory bowel disease. Similarly, continent orthotopic bladder replacement is not an option in patients in whom urethrectomy is indicated because of their cancer, or in women whose bladder neck is affected by the tumor.

Urinary continence during the day is reported to exceed 90%, but the nocturnal incontinence rate is higher. Impaired emptying of the reservoir has been observed in 10% to 15% of patients and is treated by using a sterile one-off catheter (5–7). A specific issue is mucus production in the reservoir, which needs to be removed by using forced diuresis and, if required, intermittent irrigation of the reservoir by using self-catheterization.

Complications that are specific to urinary diversion include stenosis of the ureterointestinal anastomosis, metabolic acidosis, vitamin B-12 deficiency, cholegenic diarrhea (ileum-specific), urinary tract infections, and voiding disorders of the reservoir, which require close monitoring for life (8, 9).

Heterotopic continent bladder replacement (pouch)

This form of urinary diversion is used if the reservoir cannot be connected to the urethra—for example, if the urethra is affected by tumor growth, neurogenic func-

tional disorders, congenital malformations, and disorders of the lower urinary tract (incontinence). However, it is essential for patients to be intellectually and physically able to catheterize the reservoir. Contraindications include renal failure, liver function disorders, and intestinal disorders.

Usually, a reservoir is created from an ileal or ileocecal segment, which is emptied by self-catheterization through a permanent naval stoma. The continence mechanism usually relies on a submucosally embedded appendix, an ileum invagination nipple, or a Yang-Monti channel (Figure 2) (10).

Complications that are specific to urinary diversion that should be mentioned include formation of calculi (lithogenesis) in the reservoir (10% to 14%) (ileum invagination nipple), voiding impairments of the reservoirs subsequent to stoma stenosis (7% to 11%) (appendix nipple), and stenosis of the ureteral anastomosis (7% to 8%) (11). Incontinence requiring revision surgery is rare, at <5%. Since the terminal ileum is used to form the reservoirs, patients may develop metabolic acidosis, as well as vitamin B12 deficiency and cholegenic diarrhea (12, 13).

Urinary diversion via the rectum

Ureterosigmoidostomy is a procedure whereby the ureters are implanted in an antirefluxive manner into the rectosigmoid colon. The result is a mixture of urine and feces. The anal sphincter preserves continence.

FIGURE 3

Ureterocutaneous-
tomy, a simple uri-
nary diversion tech-
nique with a low
complication rate, is
used primarily in
the palliative setting
or in patients with
many comorbidities

FIGURE 4

Ileal conduit as
standard urinary
diversion in pa-
tients who are not
suitable for conti-
nent urinary diver-
sion

Contraindications for urinary diversion via the rectum are renal failure, pathology of the rectosigmoid colon (sigma diverticulosis), and completed or planned radiotherapy of the pelvis minor and an incompetent anal sphincter. The competence of the anal sphincter should be evaluated before the surgery.

The benefits are the avoidance of a stoma, excellent continence, and the short duration of the procedure.

Specific complications include stenosis of the ureteral anastomosis (7% to 22%), recurring ascending urinary tract infections (some 16%), and severe metabolic acidosis (0% to 4%) (14–16). Incontinence is rare but requires conversion to a different type of urinary diversion. Urinary diversion through the rectum carries an increased risk of developing an adenocarcinoma at the site of the ureterointestinal implant. For this reason, follow-up examinations after the fifth postoperative year should include annual colonoscopy (14–17).

Non-continent cutaneous urinary diversion

Implantation of the ureters into the skin (ureterocutaneousostomy) (Figures 3 and 4) is the simplest form of urinary diversion, which can be done without bowel surgery. The high complication rate, especially ureteral stenosis, is a problem, so that patients usually require ureteral catheterization. Indications for ureterocutaneousostomy include palliative treatment, serious comorbidities, reduced life expectancy, previous or intended radiotherapy of the intestine, or other pathologies of the bowel (ulcerative colitis, Crohn's disease) that mean that the use of bowel segments should be avoided (18). The ileal conduit is the most commonly used type of urinary diversion (33% to 63%) (11, 19, 20). An ileal segment of about 15 cm is detached and laterally

brought out as a stoma from the lower abdomen. The ureters are anastomosed into the ileum segment in a reflexive manner; the urine can flow back into the kidney from the conduit. Creating an ileal conduit is technically more straightforward and the procedure takes less time than a continent bladder substitution system. Furthermore, less of the bowel is resected when an ileal conduit is created. Complications reported in the long term (15 years) include deterioration in renal function (up to 80% after 15 years), problems with the stoma (prolapse, hernia, stomatitis) (up to 24%), recurring urinary tract infections (up to 23%), ureteral stenosis (14%) with development of renal atrophy and urolithiasis (21). An ileal conduit can be created even in patients with severe renal failure (serum creatinine >2 mg/dL) and unsatisfactory compliance on the patient's part. On the background of worse functional outcomes in continent urinary diversions in older patients as well as before planned radiotherapy of the pelvis minor, ileal conduit should also be the intervention of choice in patients with limited life expectancy.

Differential indication in cystectomy with curative intent

The differential indication depends on a patient's age, comorbidities, wishes, and general condition, as well as on the surgeon's experience and medical and oncological aspects. Providing the patient with detailed and comprehensive information is obligatory. It is important that the patient is prepared to undergo close and lifelong aftercare.

Creating a ureterocutaneousostomy (anastomosis of the ureter to the skin), which avoids bowel surgery, is indicated in a palliative setting and in patients with poor

general health and substantial comorbidities; it is done in 1% to 10% of patients. However, as a rule, creating an ileal conduit as non-continent urinary diversion should be the preferred option in view of the risk of ureteral stenosis after ureterocutaneostomy, which occurs as a consequence of 33% to 63% of these patients. The main disadvantage of non-continent urinary diversion are the stoma and impaired body image.

Contraindication to continent orthotopic and heterotopic as well as rectal urinary diversions, which constitute about 60% of all urinary diversion procedures, are renal failure, liver function impairments, and bowel disorders. In large case series, the risk for developing a local recurrence in orthotopic urinary diversion was reported to be 4% to 6% (22). An oncological contraindication is a tumor of the urethra/prostatic urethra in men and the bladder outlet in women. A locally advanced or metastasized urothelial carcinoma is principally not a contraindication to orthotopic urinary diversion (8).

Urinary diversion in cancer treatment with palliative intent

The question of whether urinary diversion improves the affected patient's quality of life is easy to answer if pain is present. It needs to be identified whether the pain is the result of the urinary stasis or of the extravasation or anastomosis. Urinary stasis usually develops slowly and mostly asymptotically as a tumor-related compression. Even extravasation related to the anastomosis is more a problem of quality of life and only rarely causes pain. An exception to the rule is tumor-related urinary extravasation in the perineal or pelvic regions with fistula-related chronic dermatitis or decubitus ulcer development.

In our opinion, urinary diversion is not required in patients with advanced tumor disease and limited life expectancy whose renal function is intact or only mildly impaired and who are not showing any signs of infection, who have asymptomatic renal engorgement or renal decompression.

In patients with renal engorgement and unexplained raised body temperature, sonographically guided diagnostic puncture is recommended. The puncture specimen can be examined immediately for possible infection, and a nephrostomy can be created at the same time. In more than 50% of patients thus punctured, creation of a urinary diversion was unnecessary in view of the sterility of the urine obtained by puncture.

If patients present for consultation in the emergency setting then the question is which type of urinary diversion should be used. The mean survival period of patients in palliative care, in whom urinary diversion is undertaken, varies between three and nine months and depends on the metastatic load. Three criteria can be used to define prognostic groups, whose 6-month survival differs significantly, at 69% (favorable prognosis) versus 24% (intermediate prognosis) versus 2% (poor prognosis). Criteria for a poor prognosis included

- pre-interventional albumin in serum (≤ 3 mg/dL),
- low-grade urinary stasis (grade 1 and 2), and
- $\geq$ three metastasis-related events.

In our experience, the dying process in patients with incurable disease who are receiving palliative care, have the shortest life expectancy, and whose uremia is treated appropriately, entails increasing fatigue and impaired consciousness without pain, apnea, and convulsions.

Techniques of palliative urinary diversion

Among the multitude of options for palliative urinary diversion the dominant interventions—independently of the question of whether a transurethral or suprapubic catheter should be used—are the creation of a percutaneous renal fistula and endoscopic insertion of a self-retained internal ureteral stent (the so called double J stent). Both lead to decompression of the kidney and thus treat obstructions and, if present, infections, at the same time.

If a patient's life expectancy is sufficiently long and in order to avoid percutaneous urinary diversion, an alloplastic subcutaneous bypass from the kidney to the bladder can be placed in selected cases, which has a good success rate and low tendency to incrustate (23). Renal fixation is simple, whereas the vesical end needs to be attached intraluminally through a small incision. In selected patients, subcutaneous urinary diversion improves quality of life more than nephrostomy (23).

Metabolic disorders after urinary diversion

If individual segments are removed from bowel continuity and used for urinary diversion, the resorption area of the used bowel segment is lost to the physiological function of the gastrointestinal tract. Furthermore, the bowel segment retains its absorbing and secreting characteristics even after incorporation into the urinary tract (12, 13).

This may result in changes to the absorption of food components such as vitamin B12 and reabsorption of bile acids in the small bowel and large bowel. Each bowel segment has particular, specific characteristics from which the typical metabolic consequences result. The extent of metabolic problems depends on the length and type of bowel segments used as well as on atrophy of the bowel mucosa subsequent to chronic urinary diversion, a patient's renal and liver function, his/her age, and prior radiotherapy or chemotherapy as well as comorbidities (12).

Electrolyte imbalances

In contrast to patients with non-continent urinary diversion, changes to the electrolyte balance are common in patients after continent urinary diversion. The type of electrolyte change depends on the bowel segment that is used:

- In rare cases, gastric tissue is used for the purpose of bladder augmentation in patients at risk of postoperative short bowel syndrome and/or renal failure. Owing to the high acid content of the

continuing gastric secretions there is no risk of acidosis in this context. Gastrocystoplasty can cause hypochloremic, hypokalemic metabolic alkalosis, which can be life threatening (24). The severity of the metabolic alkalosis correlates with the gastrin concentration—the higher the serum gastrin level, the more severe the metabolic alkalosis.

- If jejunal segments are used then hyponatremic, hypochloremic, hyperkalemic acidosis may develop. A relevant loss of NaCl results in water loss with subsequent dehydration.
- If segments of the ileum or colon are used the patient may develop hypokalemic acidosis, which is treated with alkalizing medication. If Na^+/K^+ citrate is given prophylactically when the base excess is below -2.5 mmol/L, then clinically evident acidosis can be avoided in more than 95% of patients (25).

Clinical consequences of metabolic acidosis

Chronic acidosis can lead to a reduction in bone density and osteomalacia, owing to the buffering mechanisms of bone. Data in children are contradictory. By correcting the acidosis, bone remineralization can be achieved independently of the type of urinary diversion (e1).

Vitamin B12

Resecting more than 60 cm of the ileum is associated with a risk of clinically relevant vitamin B12 malabsorption; in children, this applies if more than 45 cm are resected (e2, e3).

A cobalamin concentration of 200 pg/mL is commonly regarded as the threshold below which substitution should be given.

Vitamin B12 concentrations are measured from the seventh postoperative year and are measured annually. Substitution can be given orally (2 mg/d) or as an injection into the muscle (1 mg/month) (e4).

Dysfunction of the gastrointestinal tract

If ileum is resected the risk of malabsorption of bile acids increases in tandem with the length of bowel segment that is resected. If more than 60 to 100 cm of ileum are resected, malabsorption is inevitable. Subsequent to an increase in bile acid concentration, water, and sodium in the colon, chologenic diarrhea may occur.

In addition to dietary advice, drug treatment with cholestyramine for postoperative diarrhea reduces free bile acids in the colon. Cholestyramine binds bile acids and thus reduces the frequency of bowel movements after the resection of ileum segments (e5). Long-term intake of cholestyramine can, however, result in reduced absorption of vitamins A, D, and K, which are fat-soluble.

Secondary malignancies

After bladder augmentation, a secondary malignancy was observed in 4.5% (7/153) of patients after a follow-

up period of 27 years. Risk factors include nicotine misuse and immunosuppression; furthermore, patients with bladder exstrophy seem to be at a higher risk for developing secondary malignancies (e6). When gastric tissue is used the risk seems to be even higher than that, and the tumors developed earlier (e7, e8). The risk of secondary malignancy is notably lower for heterotopic and orthotopic urinary diversion (17).

After ureterosigmoidostomy the median latency period for the development of benign tumors is 20 years (2 to 48 years) and for malignant tumors 26 years (6 to 27 years) in patients with benign underlying disease. Patients with a primary malignancy develop secondary tumors far earlier: The mean latency period for developing an adenoma is 10 years (1 to 21 years), that for developing a carcinoma 13 years (6 to 27 years) (e9).

Lifelong follow-up is therefore vital. Endoscopic examination in patients with a primary malignancy should be started three to five years postoperatively and in patients with benign underlying disease after 10 years (e9).

Acknowledgement

The authors thank Dr Oliver Schmelz, head of the palliative care department at the HELIOS Hospital Wuppertal, for his comments and additions to our manuscript.

Conflict of interest statement

Professor Stein has received honoraria for acting as an adviser from Grachtenhaus Apotheke and Bayer vital, as well as reimbursement for travel and accommodation expenses, and honoraria into a third-party account for conducting commissioned clinical studies from Mainz University Medical Center. Professor Thüroff has received honoraria for acting as an adviser from Pfizer and honoraria into a third-party account for conducting commissioned clinical studies and research projects from Mainz University Medical Center. Professor Rübber has received honoraria for acting as an adviser from Astellas, Innovacell, and Fresenius. Professor Hohenfellner and Dr Pahernik declare that no conflict of interest exists.

Manuscript received on 26 October 2011, revised version accepted on 27 March 2012.

Translated from the original German by Dr Birte Twisselmann.

REFERENCES

1. Jemal A, Siegel R, Xu J, Ward E: Cancer statistics 2010. *CA: a cancer journal for clinicians* 2010; 60: 277–300.
2. Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS: Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. *Eur Urol* 2010; 57: 196–201.
3. Osman Y, Abol-Enein H, El-Mekresh M, Gad H, Elhefnawy A, Ghoneim M: Comparison between a serous-lined extramural tunnel and T-limb ileal procedure as an antireflux technique in orthotopic ileal substitutes: a prospective randomized trial. *BJU Int* 2009; 104: 1518–21.
4. Skinner EC, Skinner DG: Does reflux in orthotopic diversion matter? A randomized prospective comparison of the Studer and T-pouch ileal neobladders. *World J Urol* 2009; 27: 51–5.
5. Simon J, Bartsch G Jr., Kufer R, Gschwend JE, Volkmer BG, Hautmann RE: Neobladder emptying failure in males: incidence, etiology and therapeutic options. *J Urol* 2006; 176: 1468–72; discussion 72.
6. Finley DS, Lee U, McDonough D, Raz S, deKernion J: Urinary retention after orthotopic neobladder substitution in females. *J Urol* 2011; 186: 1364–9.

KEY MESSAGES

- If the intent is curative, the usual procedure is orthotopic bladder replacement (neobladder) with a reservoir fashioned from ileal segments.
- If the reservoir cannot be connected to the urethra, heterotopic bladder replacement is indicated.
- Urinary diversion via the rectum allows the urine to flow out through the rectosigmoid colon and maintains continence.
- If the intent is palliative, non-continent cutaneous urinary diversion is the usual procedure.
- The physiological characteristics of bowel tissue remain the same after the procedure. For this reason, prophylactic measures need to be taken to prevent metabolic sequelae, such as acidosis and reduced bone density.

- Gupta NP, Ansari MS, Nabi G: National survey on orthotopic neobladder. *Int Urol Nephrol* 2007; 39: 143–8.
- Hautmann RE, de Petroni R, Gottfried HW, Kleinschmidt K, Mattes R, Paiss T: The ileal neobladder: complications and functional results in 363 patients after 11 years of follow-up [see comments]. *J Urol* 1999; 161: 422–7; discussion 7–8.
- Stenzl A, Colleselli K, Poisel S, Feichtinger H, Pontasch H, Bartsch G: Rational and technique of nerve sparing radical cystectomy before an orthotopic neobladder procedure in women. *J Urol* 1995; 154: 2044–9.
- Ardelt PU, Woodhouse CR, Riedmiller H, Gerharz EW: The efferent segment in continent cutaneous urinary diversion: a comprehensive review of the literature. *BJU Int* 2012; 109: 288–97.
- Somani BK, Nabi G, Wong S, Lytle M, Atiemo K, McPherson G, N'Dow J: How close are we to knowing whether orthotopic bladder replacement surgery is the new gold standard?—evidence from a systematic review update. *Urology* 2009; 74: 1331–9.
- McDougal WS: Metabolic complications of urinary intestinal diversion. *J Urol* 1992; 147: 1199–208.
- Stein R, Schroder A, Thuroff JW: Bladder augmentation and urinary diversion in patients with neurogenic bladder: Non-surgical considerations. *J Pediatr Urol* 2012; 8: 145–52.
- D'Elia G, Pahernik S, Fisch M, Hohenfellner R, Thuroff JW: Mainz Pouch II technique: 10 years' experience. *BJU Int* 2004; 93: 1037–42.
- Tollefson MK, Elliott DS, Zincke H, Frank I: Long-term outcome of uretersigmoidostomy: an analysis of patients with > 10 years of follow-up. *BJU Int* 2010; 105: 860–3.
- Pahernik S, Beetz R, Schede J, Stein R, Thuroff JW: Rectosigmoid pouch (Mainz Pouch II) in children. *J Urol* 2006; 175: 284–7.
- Kalble T, Hofmann I, Riedmiller H, Vergho D: Tumor growth in urinary diversion: a multicenter analysis. *Eur Urol* 2011; 60: 1081–6.
- Yoshimura K, Maekawa S, Ichioka K, et al.: Tubeless cutaneous ureterostomy: the Toyoda method revisited. *J Urol* 2001; 165: 785–8.
- Lowrance WT, Rumohr JA, Clark PE, Chang SS, Smith JA Jr., Cookson MS: Urinary diversion trends at a high volume, single American tertiary care center. *J Urol* 2009; 182: 2369–74.
- Hautmann RE, Abol-Enein H, Hafez K, et al.: Urinary diversion. *Urology* 2007; 69: 17–49.
- Madersbacher S, Schmidt J, Eberle JM, Thoeny HC, Burkhard F, Hochreiter W, Studer UE: Long-term outcome of ileal conduit diversion. *J Urol* 2003; 169: 985–90.
- Stenzl A, Sherif H, Kuczyk M: Radical cystectomy with orthotopic neobladder for invasive bladder cancer: a critical analysis of long term oncological, functional and quality of life results. *Int Braz J Urol* 2010; 36: 537–47.
- Ubrig B, Lazica M, Waldner M, Roth S: Extraperitoneal bilateral cutaneous ureterostomy with midline stoma for palliation of pelvic cancer. *Urology* 2004; 63: 973–5.
- Gosalbez R Jr., Woodard JR, Broecker BH, Warshaw B: Metabolic complications of the use of stomach for urinary reconstruction. *J Urol* 1993; 150: 710–2.
- Tanrikut C, McDougal WS: Acid-base and electrolyte disorders after urinary diversion. *World J Urol* 2004; 22: 168–71.

Corresponding author

Prof. Dr. med. Dr. h. c. Herbert Rübber
 Director of the Clinic and Polyclinic for Urology
 University Hospital Essen
 Hufelandstr. 55
 45122 Essen
herbert.ruebben@uni-duisburg-essen.de

@ For eReferences please refer to:
www.aerzteblatt-international.de/ref3812

REVIEW ARTICLE

Urinary Diversion—Approaches and Consequences

Raimund Stein, Markus Hohenfellner, Sascha Pahernik, Stephan Roth, Joachim W. Thüroff, Herbert Rübben

eReferences

- e1. Kawakita M, Arai Y, Shigeno C: Bone demineralization following urinary intestinal diversion assessed by urinary pyridinium cross-links and dual energy x-ray absorptiometry. *J Urol* 1996; 156: 355–9.
- e2. Valman HB, Roberts PD: Vitamin B12 absorption after resection of ileum in childhood. *Arch Dis Child* 1974; 49: 932–5.
- e3. Filipsson S, Hultén L, Lindstedt G: Malabsorption of fat and vitamin B12 before and after intestinal resection for Crohn's disease. *Scandinavian Journal of Gastroenterology* 1978; 13: 529–36.
- e4. Kuzminski AM, Del Giacco EJ, Allen RH, Stabler SP, Lindenbaum J: Effective treatment of cobalamin deficiency with oral cobalamin. *Blood* 1998; 92: 1191–8.
- e5. Jacobsen O, Hojgaard L, Hylander Møller E, et al.: Effect of enterocoated cholestyramine on bowel habit after ileal resection: a double blind crossover study. *Br Med J (Clin Res Ed)* 1985; 290: 1315–8.
- e6. Husmann DA, Rathbun SR: Long-term follow up of enteric bladder augmentations: the risk for malignancy. *J Pediatr Urol* 2008; 4: 381–5; discussion 6.
- e7. Vemulakonda VM, Lendvay TS, Shnorhavorian M, et al.: Metastatic adenocarcinoma after augmentation gastrocystoplasty. *J Urol* 2008; 179: 1094–6; discussion 7.
- e8. Castellan M, Gosalbez R, Perez-Brayfield M, Healey P, McDonald R, Labbie A, Lendvay T: Tumor in bladder reservoir after gastrocystoplasty. *J Urol* 2007; 178: 1771–4; discussion 1774.
- e9. Austen M, Kalble T: Secondary malignancies in different forms of urinary diversion using isolated gut. *J Urol* 2004; 172: 831–8.