REVIEW Article

Gastrointestinal Disorders in The Dialysis Population

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EXTRACT

Gastrointestinal symptoms are among the commonest complaints in the dialysis population[1]. The causes and treatment of many gastrointestinal problems are similar in patients receiving the renal replacement therapy as in the general population. This review focuses on gastrointestinal disorders with special relevance to patients with end-stage renal disease (ESRD) receiving dialysis with some mention of patients, who have had kidney transplantation.

Key words : Gastrointestinal, dialysis, renal replacement

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INTRODUCTION

Gastrointestinal symptoms are among the commonest complaints in the dialysis population[1]. The causes and treatment of many gastrointestinal problems are similar in patients receiving the renal replacement therapy as in the general population. This review focuses on gastrointestinal disorders with special relevance to patients with end-stage renal disease (ESRD) receiving dialysis with some mention of patients, who have had kidney transplantation.

Anorexia

In the dialysis population, anorexia is common and is associated with significant morbidity[2]. Inadequate dialysis, post-hemodialysis fatigue, anemia and various comorbid, psychosocial and socioeconomic factors contribute to anorexia. Abdominal discomfort, the absorption of glucose and peritonitis also reduce appetite in the continuous peritoneal dialysis(CAPD) population.

Nausea and Vomiting

Nausea and vomiting occurs in up to two-thirds of patients on dialysis[3]. In new hemodialysis (HD) patients, nausea is a feature of the disequilibrium syndrome[4] due to rapid changes in BUN and subsequent transcellular water flux. Uremic toxins cause nausea and inadequate dialysis needs to be excluded. In addition, nausea can occur at the end of HD sessions in association with hypotension[5]. Excessive fluid removal and rapid changes in plasma osmolality contribute to the development of these symptoms as well. Less commonly, nausea is part of a reaction against

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cellulosic dialyzer membranes[6]. Changing to synthetic biocompatible membranes may be helpful. Intercurrent illness, medications (eg oral iron, digoxin toxicity) may be the cause in some cases. Gastrointestinal diseases including diabetic gastroparesis, constipation and gastritis need to be excluded and treated as appropriate.

UPPER GASTROINTESTINAL DISEASE

Oropharynx

Metallic taste, stomatitis, and less commonly, parotitis may occur in patients with chronic renal failure. Oral ulcers may be due to infections, connective tissue diseases or drugs. Herpes simplex and candidiasis may occur in the immunocompromized renal transplant recipients[7]. Antiviral or antifungal should be used as appropriate.

Esophagus

CAPD patients have increased gastroesophageal reflux symptoms[10]. In one study, symptomatic patients had higher reflux score based on 24 hour pH monitoring and decreased supine lower esophageal sphincter tone upon dialysate infusion compared to asymptomatic controls[9]. By contrast, other investigators found no differences in lower esophageal sphincters tone between symptomatic and asymptomatic patients[10]. In general, the diagnosis and treatment for gastroesophageal reflux in ESRD is similar to the general population[11]. Minimizing CAPD exchange volumes especially at night may be considered in some patients provided that clearance is not compromised.

Erosive esophagitis was found to be more prevalent in dialysis patients than the general population by some investigators[12] but not by others[3]. Patients with renal transplants are at increased risk from opportunistic infections e.g candida, CMV and herpes simplex[7]. In these cases, esophageal symptoms may be accompanied by odynophagia. Such patients should have the diagnosis confirmed by endoscopy and treated appropriately.

Gastritis and Duodenitis

Most endoscopic studies found a high prevalence of gastritis and duodenitis in the dialysis population[3,13-18]. Dyspeptic symptoms correlate poorly with the presence of pathology[3]. In one series of mostly asymptomatic HD subjects,macroscopic gastritis or duodenitis were present in 36% of patients and 24% had erosions[18]. In another study, the prevalence of histologic gastritis was 89% compared to 21 % in controls[15]. The relative prevalence of chronic superficial gastritis and atrophic gastritis appear to vary between studies[3,19,20].

Several factors likely contribute to the increases in gastritis in dialysis patients. Uremia per se may contribute. In undialyzed patients who died of uremia, hemorrhagic, ulcerative and pseudomembranous changes were found in the mucosal membranes at all levels of the digestive tract including the stomach[21]. In another autopsy study in dialyzed patients, frequent mucosal changes were seen, but these severe inflammatory features were absent[22].

Helicobacter pylori is a major cause of gastritis in the general population[23]. The increase in the availability of urea, a substrate for *H. pylori* metabolism might be expected to increase the prevalence of *H. pylori* infection in the dialysis population. However, the rate of seroprevalence of H. pylori in the HD[24-28] and transplant recipients[28,29], CAPD[29] population is 30-70%, which is comparable to the general population. Furthermore, there does not appear to be an increase in pathogenic strains of H. pylori (i.e.producing vacuolating cytotoxins or CagA-positive[30] in the dialysis population[31].

Studies on the role of acid secretion in uremic gastritis appear to be contradictory probably reflecting inadequate study size and the failure to distinguish dialysis subjects and predialysis subjects. Early studies found increased basal[32] and pentagastrin stimulated[33,34] gastric acid production. Gastrin levels are elevated in patients with renal failure[17,35-41], even up to levels comparable to those with gastrinomas[35,36]. In part, this increase may be due to the decreased renal clearance of gastrin[42], but enhanced gastrin synthesis may contribute[43]. The elevated gastrin levels have been proposed as an important stimulus for acid secretion in renal failure. However, other investigators did not find increases in pentagastrin response in dialysis patients[36,44]. Wide ranges for acid secretion have been found. A proportion of patients had hypochrohydria whereas another proportion had hyperchlorhydria[39]. Rather than being the cause of gastric hypersecretion, the elevated gastrin levels may be the consequence of a lack of negative feedback response to the undersecretion of acid, because of atrophic gastritis [40,41].

Several studies found an inverse correlation between gastrin levels and acid secretion in the dialysis population[18,41]. *H. pylori* infection may also account for hypergastrinemia in some patients since eradication of *H. pylori* is associated with the reduction in serum gastrin and reductions in gastric juice ammonia and pH levels[44].

Biliary reflux can worsen gastroduodenitis. Since gastrin decreases pyloric sphincter tone, high gastrin levels may lead to biliary reflux, thus worsen mucosal injury[45]. In the duodenum, impaired bicarbonate secretion[46-47] and increased pepsinogen release[19,46,48] may also contribute to mucosal inflammation.

In patients with gastritis, non-steroidal anti-inflammatory agents (NSAIDs) should be discontinued. Acid suppression with H2 receptor blockers or proton pump inhibitors should be initiated. Antacids containing magnesium or aluminium should be avoided[49]. Sucralfate is also associated with aluminum toxicity[50,51].

Peptic Ulcers

Between different studies, there is a large variation in the frequency of peptic ulcers in patients with chronic renal failure compared to non-uremic subjects. Early reports suggest an increase in incidence of peptic ulcer in the dialysis population[37,52]. However, more recent and larger studies found no increase in either gastric or duodenal ulcers[13,18,53]. These differences might be attributed to the differences in diagnostic method (radiology vs endoscopy), sample size and criteria for selection of patient and control groups as well as the use of antibiotics and H2 or proton pump inhibitors. Thus in a study 114 of unselected, asymptomatic and symptomatic dialysis patients, only 2% of patients were found to have endoscopic evidence of peptic ulcers, which was similar to the prevalence in the general population[18].

Similar to the general population, *H. pylori* should be identified and treated. The diagnosis of *H. pylori* is established by endoscopy by one of three methods: biopsy urease test, histology or less commonly, bacterial culture. However, ultrarapid urease test may be less sensitive and specific for *H. pylori* infection in dialysis subjects with elevated plasma urea concentrations[54]. Noninvasive strategies for diagnosis of *H. pylori* infection are also available [55]. These tests include stool antigen testing, isotope-urea breath test or serology. using ELISA technology for IgG or IgA. The 13C urea breath test relies on bacterial hydrolysis of isotope -labeled carbon dioxide after administration of isotope-labeled urea. Even when this test is performed after dialysis, it still has decreased specificity for *H. pylori* in uremic subjects[56]. In one study of ESRD patients using endoscopic biopsy specimen as the gold standard, stool antigen testing was over 97% sensitive and specific for the presence of *H. pylori* whereas Ig G screening was only 87% sensitive and 80% specific[57]. Moreover, stool antigen testing was 100 % sensitive and 97.5 % specific for detecting failure of *H. pylori* eradication whereas serology was only 22% specific.

As in the general population, eradication of *H. pylori* and cessation of NSAIDs and smoking and the acid suppression is the mainstay of treatment. Treatment of *H. pylori* infection is similar to the general population[23] except regimens containing bismuth may best be avoided to accumulation in ESRD[58]. These protocols appear to be effective in CAPD[59] and hemodialysis patients[60] with cure rates similar to non-uremic subjects.

Renal transplant recipients, however, have significantly increased risk of peptic ulcers with higher rates of complications[14,61]. Low dose aspirin, high dose steroid in treatment of acute rejection appear to be important risk factors, whereas the presence of *H. pylori* appears to be less important [62]. Opportunistic infections such as CMV also need to be considered as a cause of gastroduodenal ulceration in this population[7]. Pretransplant evaluation and perioperative H2 antagonists or proton pump inhibitors should be used to prevent post transplant gastroduodenal ulceration[63].

Gastric Emptying

Undialyzed, uremic patients frequently have delayed gastric emptying[64]. However, gastric emptying in both symptomatic or asymptomatic non-diabetic HD patients was found to be impaired by some investigators[65], but not by others[66,67]. Gastric motility is regulated by gastric myoelectrical activity. Increased abnormal myoelectrical activities in both fasting and fed state have been documented in renal failure[68,69]. HD decreased the normal gastric frequency in some studies[70], but not in others[69]. Instillation of peritoneal fluid may induce gastric dysrhythmia CAPD patients[69]. Abnormal gastric rhythm in CAPD subjects was associated with early satiety. Indeed, slower gas-

tric emptying has been documented in patients studied at the time of peritoneal fluid dwell period[71,72].

Gastric motility disorders however, are common in dialysis patients with diabetes mellitus[73]. Patients with gastroparesis had lower muscle mass and had 3 times as many days in hospital and one third median survival compared to diabetics on dialysis without gastroparesis. The importance of gastric motility dysfunction in dialysis subjects is underscored by the findings that, in patients with subclinical gastric emptying defects, treatment with prokinetic therapy increased the serum albumin[74,75].

Uremic toxins and electrolyte abnormalities may contribute to the development of gastric dysmotility in uremia. Some non-diabetic patients with renal failure have a degree of autonomic neuropathy[76]. In addition, the plasma concentrations of gastrointestinal hormones / peptides are elevated as a consequence of decreased renal and extra-renal clearance[37,77-81]. The fasting levels of gastrin, cholecystokinin, gastric inhibitory polypeptides, glucagon, vasoactive intestinal peptides, motilin are elevated but the appropriate postprandial increase is maintained. The serum levels revert back to normal after successful transplantation but are relatively unaffected by HD and CAPD[77-82]. These hormones at concentrations found in renal failure could affect GI motility (gastrin, motilin, cholecystekinin) or could regulate appetite and satiety (glucagon, cholecystokinin). However, the overall effects of the accumulation of gastrointestinal peptides on GI motility are unclear, since these hormones have complex synergistic and antagonistic interactions.

Prokinetic agents may be considered in the treatment of impaired gastric emptying with appropriate dose adjustment. In the non-uremic population, metoclopramide appeared to be as effective as domperidone, but was associated with higher extrapyramidal side effects[83]. Intravenous erythromicin has been used to kick start the stomach in severe gastric stasis[84] and intraperitoneal erythomycin (100mg/2L bag) has been used successfully in CAPD patients with severe uncontrolled vomiting[85]. Since potential complications include pseudomembranous colitis and GI toxicity, chronic use of erythromycin (oral) should be limited to those who do not respond to traditional therapies. Cisapride is a highly effective prokinetic agent. Unfortunately, the drug has been withdrawn from the US market because of several incidences of toursade de pointes and QT interval prolongation especially in patients with renal failure[86]. However, in a small retrospective analysis, Hentges et al was unable to demonstrate a significant effect on the QT interval after the administration of cisapride in stable HD patients[87]. The authors concluded that in ESRD patients with severe symptomatic gastroparesis unresponsive to other therapies, cisapride might be considered, provided that there is no underlying cardiac disease or concomitant use of drugs that inhibits the cytochrome P450 3A4 (eg erythromycin). Clearly these patients will require regular electrocardiogram monitoring for prolongation of the QT interval and other arrhythmias if cisapride is used.

LOWER GASTROINTESTINAL DISEASE

Small Bowel Function

In undialyzed severely uremic subjects, the small bowel may show mucosal edema, hemorrhage and even severe necrotizing ulcers[21]. In the dialyzed population, minor morphologic changes consisting of modest reduction of villus height, increased crypt depth and infiltration of lamina propia with inflammatory cells associated with normal d-xylose absorption and normal dipeptidases and disaccharidases activity are found[88]. If malabsorption is suspected, d-xylose absorption and d-xylose breath test appears to be an effective absorption test in this population[89]. In the transplant population, there is an increase in the incidence of small bowel lymphoma and carcinoma, however, the incidence of these rare malignancies is still low[90].

Ischemia

Patients with ESRD have accelerated atherosclerosis and a high prevalence of cardiomyopathy[91] that can result in increased risk of mesenteric ischemia and infarction. During HD, splanchnic blood flow is decreased even when blood pressure remains within the normal range[92]. This effect is usually transient but likely is more severe and more persistent if there is hypotension. Several studies cite hypotension occurring during HD as a precipitating event to ischemic bowel infarction[93-96]. Twenty-nine of 1,370 long term HD patients developed non-occlusive mesenteric infarction over a five year period[96]. Fifty-five percent had ischemia of the small bowel and the rest had ischemia of the colon. Overall mortality rate was 45%.

Indeed, mesenteric ischemia is one of the commonest causes for emergency bowel surgery in the dialysis population and is associated with high morbidity and mortality[97-99].

Constipation and Bowel Obstruction

Constipation is a common symptom in dialysis patients. Metabolic abnormalities associated with uremia and medications including aluminum, calcium carbonate and oral iron, constitute major risks to the development of constipation[100]. In CAPD patients, constipation can impair peritoneal fluid drainage. In treating constipation, predisposing medications should be stopped. Intravenous iron could be used instead of the oral form since they cause constipation three times less often[101]. Osmotic laxatives e.g. lactulose, stool softeners e.g. docusate sodium, and stimulants e.g. bisocodyl can be safely recommended. Soap suds, mineral oil or bisocodyl supositories can be used. GoLytely can be used for bowel preparations since the water and osmolyte content are not absorbed. Psyllium (Metamusil) fiber should be avoided because of the presence potassium and high fluid intake requirement. Magnesium containing laxatives should be avoided because of the danger of hypermagnesemia. Phosphate (Fleet) enema should be avoided because of excessive phosphate absorption[102].

Obstruction and pseudoobstruction occur more commonly in dialysis patients[103,104]. CAPD patients are at increased risk of developing hernias[105,106]. Occasionally, peritoneal dialysis catheter-related complications may present with bowel obstruction[107]. Sclerosing encapsulating peritonitis is a relatively uncommon cause of intestinal obstruction in CAPD patients[108-110]. Patients with this complication may present decreased peritoneal fluid clearance and weight loss in association with repeated peritonitis. Early recognition and conversion to HD is essential. Surgical procedures may be necessary but have high complication rates. Immunosupressive agents have been used in a small group of subjects with some beneficial effects[111].

Diverticular Disease

The prevalence of diverticulosis and diverticulitis is increased in patients with renal failure due to adult polycystic kidney disease but not due to other causes[112,113]. In this population, the diagnosis of diverticulitis can be confused with bleeding or infection of a cyst. The presence of diverticular disease may special impact on patients on renal replacement therapy. Active diverticulitis is a contraindication to CAPD. Although diverticular disease is not a contraindication to CAPD, the presence of multiple or large diverticula may increase the risk of developing peritonitis by enteric organisms[114]. Colonic complications after renal transplantation are uncommon, but have a high morbidity and mortality rate[115,116]. Perforation from diverticulosis may be increased in patients on high dose steroids, in whom symptoms and signs may be masked initially[117]. Thus dialysis patients with active diverticulitis may require surgical treatment prior to transplantation. Some have recommended colonic screening in patients over 50 years of age prior to transplantation to lessen the impact of colonic diverticular disease. However, in the absence of diverticulitis, it is not clear if this practice has clear impact on outcome[118] even in patients with adult polycystic kidney disease[119].

Clostridium Difficile Infection

Frequent antibiotic use, impaired immune function and decreased gastrointestinal motility predisposes dialysis patients to C difficile infection[120]. Hospitalized HD patients may have increased risk of Clostridium difficile infection[121]. Large outbreaks have been reported in dialysis centers[133]. Although often dialysis patients have severe symptoms, some can be asymptomatic. Because of the risk of spread in HD units, there should be a low threshold in testing for C difficile toxin in patients with diarrhea.

Ulceration and Perforation

Undialyzed, severely uremic subjects may have gross mucosal changes affecting the colon[21]. However, routine endoscopic studies of the colon in asymptomatic patients on maintenance dialysis showed few abnormalities[16]. In addition to the usual causes of intestinal perforation, including ischemia, obstruction and diverticular disease, less common causes of perforation have been reported in the dialysis population.

Bowel perforation has also been reported as a complication of indwelling peritoneal catheters in CAPD[123]. The use of sodium polystyrene (Kayexelate) in the treatment of hyperkalemia may result in bowel necrosis[124,125]. The risk appears to be higher in the perioperative period and during concurrent the administration of hypertonic sorbitol enema[126]. Thus

sorbitol enema should not be used and sodium polystyrene should be avoided in patients with bowel ileus.

Idiopathic colonic ulcers have been reported in dialysis patients[127,128] and may resent with bleeding, or peritonitis, and show a high mortality rate. Spontaneous idiopathic perforation[129-131] and segmental necrosis[132] of the ascending colon has also been described. The causes of these diseases are unknown, but may relate to the use of aluminum-based antacids, ischemia and impaired intestinal motility.

In CAPD patients, bowel perforation is suggested by the findings of unusual enteric[133] or mixed organisms[134]. Fecal material in the dialysate and diarrhea containing dialysate are uncommon. However, mixed organisms can be found even in absence of perforation or diverticulitis[135]. The diagnosis of bowel perforation in patients on CAPD can be delayed because of mild symptoms, and the absence of classical abdominal guarding and rigidity and confusion with the more typical staphylococcal peritonitis[136]. In addition, the presence of free air by plain x-ray occurs in up to 30% of patients on CAPD, irrespective of whether there is a perforated viscus[137]. The lack of free air on CT scan may have a greater negative predictive value than X-ray, but cannot rule out bowel rupture with absolute certainty[138].

Diseases Affecting Both Upper and Lower Tracts

Angiodysplasia

Angiodysplasia are composed of ectatic, dilated, thin walled vessels, that are lined by endothelium alone or by only small amounts of smooth muscle[139]. Angiodysplasia is a more frequent cause of gastrointestinal bleeding and recurrent bleeding in patients with chronic renal failure than in those with normal renal function[139-146]. They are often multiple and can be found throughout the entire GI tract, from the stomach to the large bowel. Their prevalence increases with the duration and severity of renal failure[146]. Renal failure is also a risk factor for the development of the watermelon stomach, another type of vascular malformation in the antral region of the stomach[147]. The causes for the increased prevalence of vascular malformations have been attributed to vascular calcification, constipation and chronic venous congestion from volume overload[139].

Angiodysplasia are usually diagnosed by endoscopy or angiography. ^{99m}Tc-labelled red cell scintigraphy can also be used to localize lesions[148]. Endoscopic therapy could be applied to bleeding lesions. Local instillation with vasopressin during angiography or embolization may be considered in patients with severe bleeding and surgical resection considered in patients with uncontrolled, life-threatening bleed. The management of angiodysplasia, which is not actively bleeding is less clear. In patients with angiodysplasia with previous hemorrhage or with otherwise unexplained occult blood loss, therapeutic ablation could be considered. The inaccessibility of some lesions, the multiplicity of angiodysplasia and potential complications associated with treatment could limit the success of local therapy.

Hormonal therapy with estrogen has been used to treat patients with angiodysplasia. The mechanism of action is unclear but treatment has been associated with improved bleeding times[149]. At present, randomized controlled trials are lacking in the dialysis population. In small uncontrolled studies, the combination of synthetic estrogen-progesterone[150] or estrogen[151], have been shown to beneficial in chronic renal failure patients with angiodysplasia[162]. In a prospective study, combined estrogen and progesterone or estrogen alone was given to non-uremic patients with recurrent GI bleed with angiodysplasia or an unknown bleeding source[163]. None of the 38 patients who were treated with combination hormonal therapy rebled as long as they continued their prescribed dosage. The role of progesterone is not clear but all five of the patients treated with estrogen alone had rebleeding episodes, but had no further bleeding after switching to combined therapy. Side effects occurred in 11 patients. However, not all studies have shown benefit for hormonal therapy[153]. Thus the potential benefits of hormonal therapy need to be balanced against their possible side-effects. More recently, octreotide has been used in a small number of patients with angiodysplasia[154]. The antifibrinolytic agent, tranexemic acid also been used during acute bleeding, and chronically to prevent rebleeds[155]. The use of these agents need to defined in the context a clinical trial

Amyloidosis

Although beta 2-microglobin amyloidosis typically affects the joints and bones, systemic deposition

can also occur in the gastrointestinal tract[156]. The presence of visceral beta 2-amyloid deposit is associated with longer duration on dialysis and should be considered in patients who have been on dialysis for over 10 years[157]. Amyloidosis can cause bleeding or massive diarrhea[158,159], intestinal infarcts[160], perforation[161] and pseudo-obstruction[162,163]. GI complaints have been reported even in the absence of overt joint complaints[163]. Definitive diagnosis is made by biopsy and staining with congo red and immunostaining for beta 2-microglobin[157]. Vascular histopathology range from mild focal thickening of vessel walls to massive vascular beta 2-microglobulin amyloid deposition with thrombosis and marked expansion of the submucosa. Currently, no specific treatment for visceral beta-2 amyloidosis can be recommended.

Gastrointestinal Bleeding

Dialysis patients have increased risk of gastrointestinal bleeding. Even in patients without overt symptoms, there appears to be 7-folds increase in GI blood loss[164]. This is due to the combination of the increased prevalence of angiodysplasia and gastritis and due to the coagulopathy associated with uremia and systemic heparinization[165]. Like the general population, peptic ulcers are among the most common causes of acute GI bleeding[12, 146]. Recurrent bleeding is also more likely. Upper gastrointestinal hemorrhage in dialysis subjects is associated with the use of ulcerogenic drugs such as steroids, iron and NSAIDs[166,167]. GI hemorrhage occurred in 13% of patients with acute renal failure despite the routine use of prophylactic H2 antagonist[168]. Upper GI disease with gastroduodenal erosions and ulcers account for over 50% of all acute bleeding episodes. The severity of the underlying illness and liver disease are major risk factors.

Because of the higher prevalence of angiodysplasia in patients with chronic renal failure, both upper and lower GI endoscopy is more appropriate than barium studies in evaluating GI bleeding. In the general population, intravenous omeprazole decreases rebleeding from active gastroduodenal ulcers[169] and may decrease this risk in patients with renal failure. During acute bleeding episodes, platelet defects should be corrected by maintaining adequate dialysis, administration of desmopressin (DDAVP 0.3 ug/kg iv), or cryoprecipitate[165]. Maintenance of adequate level of hematocrit and red cell mass with transfusion and erythropoeitin may also be beneficial. HD should be performed with no heparin and blood products may need to be administered during dialysis to avoid volume overload or electrolyte imbalance.

Colorectal Cancer Screening

The premise behind colorectal cancer screening is that malignancy develops from benign colonic polyps to cancer over several years[170]. The 2 principal screening tests, recommended in patients with average risks over the age of 50 are fecal occult blood testing (annually) and flexible sigmoidoscopy (every 5 years). For colorectal screening, the important studies showing improved survival with fecal occult bloods[171] and flexible sigmoidoscopy[172] show a lag time of 5 to 7 years before the survival effect is shown. Dialysis patients have a shorter life-expectancy than do patients of the same age without renal failure with the overall 7 year survival of only 30% for non-diabetic and 10% for diabetic patients[173]. Thus routine colorectal screening should be reserved for those with good prognosis

The incidence of GI malignancy does not appear to be consistently increased in dialysis patients[174]. The more frequent blood loss in patients with renal failure increases the prevalence of positive heme occult blood. In one small study, the rate of heme occult positive blood was 15% in dialysis population compared to 5% of controls[175]. Thus the incidence of colon cancer/polyp in heme occult positive blood was lower than the general population but some occult malignancies were identified[175,176]. Stool blood testing may still have a role in identifying potentially treatable, non-malignant GI lesions responsible for poor erythropoietin response[177]. In the transplant population, however, there is a three folds risk of colonic carcinoma[91]. The possible role for colonoscopy screening has been discussed for the general population at moderate risks[178], but the benefits of screening remains to be evaluated in the transplant population.

REFERENCES

1. Hammer J, Oesterreicher C, Hammer K, *et al*. Chronic gastrointestinal symptoms in hemodialysis patients. Wien Klin Wochenschr 1998; 110: 287-91.
2. Bergstrom J. Anorexia in dialysis patients. Semin Nephrol 1996; 16: 222-9.
3. Abu Farsakh NA, Roweily E, Rababaa M, *et al*. Brief report: evaluation of the upper gastrointestinal tract in uraemic patients undergoing haemodialysis. Nephrol Dial Transplant 1996; 11: 847-50.

4. Arieff AI. Dialysis disequilibrium syndrome: current concepts on pathogenesis and prevention [editorial]. Kidney Int 1994; 45: 629-35.
5. Henrich WL. Hemodynamic instability during hemodialysis [clinical conference]. Kidney Int 1986; 30: 605-12.
6. Daugirdas JT, Ing TS. First-use reactions during hemodialysis: a definition of subtypes. Kidney Int Suppl 1988; 24: S37-43.
7. Fishman JA, Rubin RH. Infection in organ-transplant recipients. N Engl J Med 1998; 338: 1741-51.
8. Anderson JE, Yim KB, Crowell MD. Prevalence of gastroesophageal reflux disease in peritoneal dialysis and hemodialysis patients. Adv Perit Dial 1999; 15: 75-8.
9. Kim MJ, Kwon KH, Lee SW. Gastroesophageal reflux disease in CAPD patients. Adv Perit Dial 1998; 14: 98-101.
10. Rossner S, Burkart J, Castell DO, *et al*. Effect of intraperitoneal fluid volume changes on esophageal pressures: studies in patients on continuous ambulatory peritoneal dialysis. Am J Kidney Dis 1991; 17: 307-10.
11. De Vault KR, Castell DO. Guidelines for the diagnosis and treatment of gastroesophageal reflux disease. Practice Parameters Committee of the American College of Gastroenterology. Arch Intern Med 1995; 155: 2165-73.
12. Zuckerman GR, Cornette GL, Clouse RE, *et al*. Upper gastrointestinal bleeding in patients with chronic renal failure. Ann Intern Med 1985; 102: 588.
13. Margolis DM, Saylor JL, Geisse G, *et al*. Upper gastrointestinal disease in chronic renal failure: a prospective evaluation. Arch Intern Med 1978; 138: 1214.
14. Franzin G, Musola R, Mencarelli R. Morphological changes of the gastroduodenal mucosa in regular dialysis uremic patients. Histopathology 1982; 6: 492.
15. Militio G, Taccone-Galluci M, Brancaleone C, *et al*. The gastroduodenal tract in uremic patients on longterm hemodialysis. Kidney Int 1985; 28(suppl 17): S157.
16. Wee A, Kang JY, HO MS, *et al*. Gastroduodenal mucosa in uremia: endoscopic and histological correlation and prevalence of helicobacter-like organisms. Gut 1990; 31: 1093.
17. Korman MG, LaverMC, Hansky J. Hypergastrinaemia in chronic renal failure. Br Med J 1972; 1: 209.
18. Kang JY, Wu AY, Sutherland IH, *et al*. Prevalence of peptic ulcer in patients undergoing maintenance hemodialysis. Dig Dis Sci 1988; 33: 774-8.
19. Tamura H, Tokushima H, Murakawa M, *et al*. Influences of *Helicobacter pylori* on serum pepsinogen concentrations in dialysis patients. Nephrol Dial Transplant 1999; 14: 113-7.
20. Moustafa FE, Khalil A, Abdel Wahab M, *et al*. *Helicobacter pylori* and uremic gastritis: A histopathologic study and a correlation with endoscopic and bacteriologi findings. Am J Nephrol 1997; 17: 165-71.
21. Jaffe RH, Laing DR. Changes of the digestive tract in uremia; pathologic anatomic study. Arch Intern Med 1934; 53: 851.
22. Vaziri ND, Dure-Smith B, Miller R, *et al*. Pathology of gastrointestinal tract in chronic hemodialysis patients: an autopsy study of 78 cases. Am J Gastroenterol 1985; 80: 608.
23. Howden CW, Hunt RH. Guidelines for the management of *Helicobacter pylori* infection. Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology. Am J Gastroenterol 1998; 93: 2330-8.
24. Shousha S, Arnout AH, Abbas SH, *et al*. Antral *Helicobacter pylori* in patients chronic renal disease. J Clin Pathol 1990; 43: 397.
25. Ali-Kaila K, Vaajalahti P, Karvonen AL, *et al*. Gastric Helicobacter and upper gastrointestinal symptoms in chronic renal failure. Ann Med 1991; 23: 403.
26. Gladziwa U, Haase G, Handt S, *et al*. Prevalence of *Helicobacter pylori* in patients with chronic renal failure. Nephrol Dial Transplant 1993; 8: 301.
27. Ozgur O, Boyacioglu S, Ozdogan M, *et al*. *Helicobacter pylori* infection in haemodialysis patients and renal transplant recipients. Nephrol Dial Transplant 1997; 12: 289-91.
28. Davenport A, Shallcross TM, Crabtree JE, *et al*. Prevalence of *Helicobacter pylori* in patients with end-stage renal failure and renal transplant recipients. Nephron 1991; 59: 597-601.
29. Antoniou S, Dimitriadis A, Kliridou M, *et al*. Prevalence of *Helicobacter pylori* antibodies in CAPD patients. Nephron 1997; 75: 358-9.
30. Van Doorn LJ, Figueiredo C, Sanna R, *et al*. Clinical relevance of the cagA, vacA, and iceA status of *Helicobacter pylori*. Gastroenterology 1998; 115: 58-66.
31. Fabrizi F, Martin P, Dixit V, *et al*. Epidemiology of *Helicobacter pylori* in chronic haemodialysis patients using the new RIBA *H. pylori* SIA. Nephrol Dial Transplant 1999; 14: 1929-33.
32. Shepherd Amm, Stewart WK, Wormsley KG. Peptic ulceration in chronic renal failure. Lancet 1973; 1: 1357.
33. MacConell JB, Stewart WK, Thjodleifsson B, *et al*. Gastric function in chronic renal failure: effects of maintenance hemodialysis. Lancet 1975; 2: 1121.
34. Venkatateswaran PS, Jeffers A, Hocken AG. Gastric acid secretion in chronic renal failure. Br Med J 1972; 4: 22.
35. Maxwell JG, Moore JG, Dixon J, *et al*. Gastrin levels in anephric patients. Surg Forum 1971; 127: 305.
36. Falcao HA, Wesdorp IC, Fischer JE. Gastrin levels and gastric acid secretion in anephric patients and in patients with chronic and acute renal failure. J Surg Res 1975; 18: 107.
37. Owyang C, Miller LJ, DiMagno EP, *et al*. Gastrointestinal hormone profile in renal insufficiency. Mayo Clin Proc 1979; 54: 760.
38. Doherty CC, Buchannan KD, Ardill J, *et al*. Git hormones and renal failure. Dial Transpl 1980; 9: 245.
39. Gold CH, Morley JE, Viljoen M, *et al*. Gastric acid secretion and serum gastrin levels in patients with chronic renal failure on regular hemodialysis. Nephron 1980; 25: 92.
40. Muto S, Murayama N, Asano Y, *et al*. Hypergastrinemia and achlrorhydria in chronic renal failure. Nephron 1985; 40: 143.
41. Ghonaimy E, Barsoum R, Soliman M, *et al*. Serum gastrin in chronic renal failure: morphological and physiological correlation. Nephron 1985; 39: 86.
42. Clendinnen BG, Davidson WO, Reeder DO, *et al*. Renal uptake and excretion of gastrin in the dog. Surg Gynecol Obstet 1971; 132: 1039.
43. Paronen I, Ala-Kaila K, Rantala I, *et al*. Gastric parietal,

chief, and G-cell densities in chronic renal failure. Scand J Gastroenterol 1991; 26: 696-700.
44. Tokushima H, Tamura H, Murakawa M, *et al*. Eradication of Helicobacter pylori restores elevation of serum gastrin concentrations in patients with end-stage renal disease. Intern Med 1998; 37: 435-9.
45. Fisher RS, Lipshutz W, Cohen S. The hormonal regulation of pyloric sphincter function. J Clin Invest 1973; 52: 1289.
46. Bartos V, Melichar J, Erben J. The function of the exocrine pancreas in chronic renal disease. Digestion 1970; 3: 33.
47. Dinoso VP Jr, Murphy SN, Saris AL, *et al*. Gastric and pancreatic function in patients with end-stage renal disease. J Clin Gastroenterol 1982; 4: 321.
48. Swamy AP, Mangla JC, Ceestero VM, *et al*. Serum pepsinogens and gastrins in chronic hemodilaysis patients. Biochem Med 1981; 25: 227.
49. Salusky IB, Foley J, Nelosn P, *et al*. Aluminium accumulation during treatment with aluminum hydroxide and dialysis in children and young adults with chronic renal disease. N Engl J Med 1991; 324: 527.
50. Robertson JA, Salusky IB, Goodman WH, *et al*. Sucralfate, intestinal aluminum absorption and aluminum toxicity in a patient on dialysis. Ann Intern Med 1989; 111: 179.
51. Mulla H, Peek G, Upton D, *et al*. Plasma aluminum levels during sucralfate prophylaxis for stress ulceration in critically ill patients on continuous venovenous hemofiltration: a randomized, controlled trial. Crit Care Med 2001; 29: 267-71.
52. Goldstein H, Murphy D, Sokol A, *et al*. Gastric acid secretion in patients undergoing chronic dialysis. Arch Intern Med 1967; 120: 645.
53. Musola R, Franzin G, Mora, *et al*. Prevalence of gastroduodenal lesions in uremic patients undergoing dialysis and after renal transplantation. Gastrointest Endosc 1984; 30: 343.
54. Misra V, Misra SP, Dwivedi M, *et al*. Decreased sensitivity of the ultrarapid urease test for diagnosing *Helicobacter pylori* in patients with chronic renal failure. Pathology 1999; 31: 44-6.
55. Vakil N, Rhew D, Soll A, *et al*. The cost-effectiveness of diagnostic testing strategies for *Helicobacter pylori*. Am J Gastroenterol 2000; 95: 1691-8.
56. Huang JJ, Huang CJ, Ruaan MK, *et al*. Diagnostic efficacy of (13)C-urea breath test for *Helicobacter pylori* infection in hemodialysis patients. Am J Kidney Dis 2000; 36: 124-9.
57. Wang YL, Sheu BS, Huang JJ, *et al*. Noninvasive stool antigen assay can effectively screen *Helicobacter pylori* Infection and assess success of eradication therapy in hemodialysis patients. Am J Kidney Dis 2001; 38: 98-103.
58. Gladwiza U, Koltz U. Pharmakokinetic optimization of treatment of peptic ulcer in patients with renal failure. Clin Pharmacokinet 1994; 27: 393-408.
59. Suleymanlar I, Tuncer M, Tugrul Sezer M, *et al*. Response to triple treatment with omeprazole, amoxicillin, and clarithromycin for *Helicobacter pylori* infections in continuous ambulatory peritoneal dialysis patients. Adv Perit Dial 1999; 15: 79-81.
60. Tamura H, Tokushima H, Murakawa M, *et al*. Eradication of *Helicobacter pylori* in patients with end-stage renal disease under dialysis treatment. Am J Kidney Dis 1997; 29: 86-90.
61. Kang JY. The gastrointestinal tract in uremia. Dig Dis Sci 1993; 38: 257.
62. Sarkio S, Rautelin H, Kyllonen L, *et al*. Should *Helicobacter pylori* infection be treated before kidney transplantation? Nephrol Dial Transplant. 2001; 16: 2053-7.
63. Skala I, Mareckova O, Vitko S, *et al*. Prophylaxis of acute gastroduodenal bleeding after renal transplantation. Transpl Int 1997; 10: 375-8.
64. McNamee PT, Moore, GW, *et al*. Gastric emptying in chronic renal failure. Br Med J 1985; 291: 310-11.
65. Kao CH, Hsu YH, Wang SJ. Delayed gastric emptying in patients with chronic renal failure. Nucl Med Commun 1996; 17: 164-7.
66. Wright RA, Clemente R, Wathen R. Gastric emptying in patients receiving hemodialysis. Arch Intern Med 1984; 144: 495.
67. Soffer EE, Geva B, Helman C, *et al*. Gastric emptying in chronic renal failure patients receiving hemodialysis. J Clin Gastroenterol 1987; 9: 651.
68. Lin X, Mellow MH, Southmayd L, *et al*. Impaired gastric myoelectrical activity in patients with chronic renal failure. Dig Dis Sci 1997; 42: 898-906.
69. Lee SW, Song JH, Kim GA, *et al*. Effect of dialysis modalities on gastric myoelectrical activity in end-stage renal disease patients. Am J Kidney Dis 2000; 36: 566-73.
70. Ko CW, Chang CS, Wu MJ, *et al*. Transient impact of hemodialysis on gastric myoelectrical activity of uremic patients. Dig Dis Sci 1998; 43: 1159-64.
71. Brown-Cartwright D, Smith HJ, Feldman M. Gastric emptying of an indigestible solid in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis. Gastroenterology 1988; 95: 49.
72. Bird NJ, Streather CP, O'Doherty MJ, *et al*. Gastric emptying in patients with chronic renal failure on continuous peritoneal dialysis. Nephrol Dial Transplant 1993; 9: 287-90.
73. Eisenberg B, Murata GH, Tzmaloukas AH, *et al*. Gastroparesis in diabetics on chronic dialysis; clinical and laboratory association and predictive features. Nephron 1995; 70: 296-3000.
74. Ross EA, Koo LC. Improved nutrition after the detection and treatment of occult gastroparesis in nondiabetic dialysis patients. Am J Kidney Dis 1998; 31: 62-6.
75. Silang R, Regalado M, Cheng TH, *et al*. Prokinetic agents increase plasma albumin in hypoalbuminemic chronic dialysis patients with delayed gastric emptying. Am J Kidney Dis 2001; 37: 287-93.
76. Vita G, Bellinghieri G, Trusso A, *et al*. Uremic autonomic neuropathy studied by spectral analysis of heart rate. Kidney Int 1999; 56: 232-7.
77. Sirinek KR, O'Dorisio TM, Gaskell HV, *et al*. Chronic renal failure hemodialysis on gastrointestinal hormone. Am J Surg 1984; 148: 732.
78. Hegbrant J, Thysell H, Ekman R. Plasma levels of gastrointestinal regulatory peptides in patients receiving maintenance hemodialysis. Scand J Gastroenterol 1991; 26: 599.
79. Doherty CC, Buchanan KD, Ardill J, *et al*. Elevations of

gastrointestinal hormones in chronic renal failure. P roc Eur Dial Transplant Assoc 1978; 15: 456-65.
80. Katz AI, Emmanouel DS. Metabolism of polypeptide hormones by the normal kidney and in uremia. Nephron 1978; 22: 69-80.
81. Haffner J, Linnestead P, Schrumpf E, *et al*. The immediate effect of human renal transplantation on basal and meal-stimulated levels of gastrointestinal hormones. Scand J Gastroenterol 1987; 22: 42-6.
82. Ravelli AM, Lederman SE, Trompeter RS, *et al*. Mechanisms of anorexia and vomiting in children with chronic renal failure II. Polypeptide hormones. Neurogastroenterol Mot 1994; 6: 176.
83. Patterson D, Abell T, Rothstein R, *et al*. A double-blind multicenter comparison of domperidone and metoclopramide in the treatment of diabetic patients with symptoms of gastroparesis. Am J Gastroenterol 1999; 94: 1230-4.
84. Janssens J, Peeters TL, Vantrappen G, *et al*. Improvement of gastric emptying in diabetic gastroparesis by erythromycin. Preliminary studies. N Engl J Med 1990; 322: 1028-31.
85. Gallar P, Oilet A, Vgil A , *et al*. Gastroparesis: an important cause of hospitalization in continuos ambulatory peritoneal dialysis patients and the role of erythromicin. Perit Dial Int 1993; 13 (Suppl 2): S183-6.
86. Wysowski DK, Corken A, Gallo-Torres H, *et al*. Postmarketing reportsof QT prolongation and ventricular arrhythmia in association with cisapride and Food and Drug Administration regulatory actions. Am J Gastroenterol 2001; 96: 1698-703.
87. Hentges MJ, Gunderson BW, Lewis MJ. Retrospective analysis of cisapride-induced QT changes in end-stage renal disease patients. Nephrol Dial Transplant 2000; 15(11): 1814-8.
88. Arvanitakis C, Nakos V, Kalekou-Greka H, *et al*. Small intestinal function and structure in patients with chronic renal failure. Clin Nephrol 1988; 29: 235-43.
89. Craig RM, Carlson S, Ehrenpreis ED. D-xylose kinetics and hydrogen breath tests in functionally anephric patients using the 15-gram dose. J Clin Gastroenterol 2000; 31: 55-9.
90. Kyllonen L, Salmela K, Pukkala E. Cancer incidence in a kidney-transplanted population. Transpl Int 2000; 13 (Suppl 1): S394-8.
91. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. J Am Soc Nephrol 1999; 10: 1606-15.
92. Jakob SM, Ruokonen E, Vuolteenaho O, *et al*. Splanchnic perfusion during hemodialysis: evidence for marginal tissue perfusion. Crit Care Med 2001; 29: 1393-8.
93. Diamond SM, Emmett M, Henrich WL. Bowel infarction as a cause of death in dialysis patients. JAMA 1986; 256: 2545.
94. Margolis DM, Etheredge EE, Garza-Garza R, *et al*. Ischemic bowel disease following bilateral nephrectomy or renal transplant. Surgery 1977; 82: 667.
95. Dahlberg PJ, Kisken WA, Newcomer KL, *et al*. Mesenteric ischemia in chronic dialysis patients. Am J Nephrol 1985; 5: 327.
96. John AS, Tuerff SD, Kerstein MD. Nonocclusive mesenteric infarction in hemodialysis patients. J Am Coll Surg 2000; 90: 84-8.
97. Wind P, Douard R, Rouzier R, *et al*. Abdominal surgery in chronic hemodialysis patients. Am Surg 1999; 65: 347-5.
98. Newman LA, Mittman N, Hunt Z, *et al*. Survival among chronic renal failure patients requiring major abdominal surgery. J Am Coll Surg 1999; 188: 310-4.
99. Toh Y, Yano K, Takesue F, *et al*. Abdominal surgery for patients on maintenance hemodialysis. Surg Today 1998; 28: 268-72.
100. Adams PL, Rutsky EA, Rostand SG, *et al*. Lower gastrointestinal tract dysfunction in patients receiving longterm hemodialysis. Arch Intern Med 1982; 142: 303.
101. Johnson DW, Herzig KA, Gissane R, *et al*. A prospective crossover trial comparing intermittent intravenous and continuous oral iron supplements in peritoneal dialysis patients. Nephrol Dial Transplant 2001; 16: 1879-84.
102. Knobel B, Petchenko P. Hyperphosphatemic hypocalcemic coma caused by hypertonic sodium phosphate. J Clin Gastroenterol 1996; 23: 217-9.
103. Townsend CM Jr, Remmers AR, Sarles HE, *et al*. Intestinal obstruction from mediation bezoar in patients with renal failure. N Engl J Med 1973; 288: 1058.
104. Welch JP, Schweitzer RT, Bartus SA. Management of antacid impactions in hemodialysis and renal transplant patients. Am J Surg 1980; 139: 561.
105. Bargman JM. Complications of peritoneal dialysis related to increased intraabdominal pressure. Kidney Int Suppl 1993; 40: S75-80.
106. O'Connor JP, Rigby RJ, Hardie IR, *et al*. Abdominal hernias complicating continuous ambulatory peritoneal dialysis. Am J Nephrol 1986; 6: 271-4.
107. Kanagasundaram NS, Fletcher S, Gupta S, *et al*. Acute small-bowel obstruction following mesenteric perforation by CAPD catheter. Nephrol Dial Transplant 1997; 12: 599-600.
108. Afthentopoulos IE, Passadakis P, Oreopoulos DG, *et al*. Sclerosing peritonitis in continuous ambulatory peritoneal dialysis patients: one center's experience and review of the literature. Adv Ren Replace Ther 1998; 5: 157-67.
109. Yokota S, Kumano K, Sakai T. Prognosis for patients with sclerosing encapsulating peritonitis following CAPD. Adv Perit Dial 1997; 13: 221-3.
110. Nomoto Y, Kawaguchi Y, Kubo H, *et al*. Sclerosing encapsulating peritonitis in patients undergoing continuous ambulatory peritoneal dialysis: a report of the Japanese Sclerosing Encapsulating Peritonitis Study Group. Am J Kidney Dis 1996; 28: 420-7.
111. Junor BJ, McMillan MA. Immunosuppression in sclerosing peritonitis. Adv Perit Dial 1993; 9: 187-9.
112.. Scheff RT, Zuckermann G, Harter H, *et al*. Diverticular disease in patients with chronic renal failure due to polycystic kidney disease. Ann Intern Med 1980 ;92: 202.
113. Lederman ED, McCoy G, Conti DJ, *et al*. Diverticulitis and polycystic kidney disease. Am Surg 2000; 66: 200-3.
114. Tranaeus A, Heimburger O, Granqvist S. Diverticular disease of the colon: a risk factor for peritonitis in continuous peritoneal dialysis. Nephrol Dial Transplant 1990; 5: 141-7.
115. Pirenne J, Lledo-Garcia E, Benedetti E, *et al*. Colon perforation after renal transplantation: a single-institution review.

Clin Transplant 1997; 11: 88-93.

116. Poris JJA, Barnes AD. Ileocolonic problems after cadaver renal transplantation. Br Med J 1972; 1: 99.
117. Canter JW, Shore, PE. Acute perforation of colonic diverticula associated with prolonged adrenocorticosteroid therapy. Am J Surg 1971; 121 :46.
118. McCune TR, Nylander WA, Van Buren H, *et al*. Colonic screening prior to renal transplantation and it's impact on post-transplant colonic complications. Clin Transplant 1992; 6: 91-6.
119. Dominguez Fernandez E, Albrecht KH, Heemann U, *et al*. Prevalence of diverticulosis and incidence of bowel perforation after kidney transplantation in patients with polycystic kidney disease. Transpl Int 1998; 11: 28-31.
120. Leung AC, Orange G, McLay A, *et al*. Clostidium difficile-associated colitis in uremic patients. Clin Nephrol 1985; 24: 242.
121. D'Agata EM, Mount DB, Thayer V, *et al*. Hospital-acquired infections among chronic hemodialysis patients. Am J Kidney Dis 2000; 35: 1083-8.
122. Barany P, Stenvinkel P, Nord CE, *et al*. Clostridium difficile infection- a poor prognostic sign in uremic patients? Clin Nephrol 1992; 38: 53.
123. Krebs RA, Burtis BB. Bowel perforation. A complication of peritoneal dialysis using a permanent peritoneal cannula. JAMA 1966; 198: 486.
124. Wooton FT, Rhodes DP, Lee WM, *et al*. Colonic necrosis with Kayexalate-sorbitol enemas after renal transplantation. Ann Intern Med 1989; 111: 947.
125. Roy-Chaudhury P, Meisels IS, Freedman S, *et al*. Combined gastric and ileocecal toxicity (serpiginous ulcers) after oral kayexalate in sorbital therapy. Am J Kidney Dis 1997; 30: 120-2.
126. Lillemoe KD, Romolo JL, Hamiltin SR, *et al*. Intestinal necrosis due to sodium polystyrene (Kayexalate) in sorbitol enemas: clinical and experimental support for the hypothesis. Surgery 1987; 101: 267.
127. Mills B, Zuckerman G, Sicard G. Discrete colon ulcers as a cause of lower gastrointestinal bleeding and perforation in end-stage renal disease. Surgery 1981; 89: 548.
128. Brown KM. Isolated ascending colon ulceration in a patient with chronic renal insufficiency. J Natl Med Assoc 1992; 84: 185.
129. Lipschutz DE, Easterling RE. Spontaneous perforation of the colon in chronic renal failure. Arch Intern Med 1973; 132: 758.
130. Bartolomeo RS, Calabrese PR, Taubin HL. Spontaneous perforation of the colon: A potential complication of chronic renal failure. Digestive Dis 1977; 22: 656.
131. Bischel MD, Reese T, Engel J. Spontaneous perforation of the colon in a hemodialysis patient. Am J Gastroenterol 1980; 74: 182-4.
132. Charra B, Cuche J, Ruffet M, *et al*. Segmental necrosis of ascending colon in haemodialysis patients. Nephrol Dial Transplant 1995; 10: 2281-5.
133. Harwell CM, Newman LN, Cacho CP, *et al*. Abdominal catastrophe: visceral injury as a cause of peritonitis in patients treated by peritoneal dialysis. Perit Dial Int 1997; 17: 586-94.
134. Tzamaloukas AH, Obermiller LE, Gibel LJ, *et al*. Peritonitis associated with intra-abdominal pathology in continuous ambulatory peritoneal dialysis patients. Perit Dial Int 1993; 13 (Suppl 2): S335-7.
135. Holley JL, Bernardini J, Piraino B. Polymicrobial peritonitis in patients on continuous peritoneal dialysis. Am J Kidney Dis 1992; 19: 162-6.
136. Carmeci C, Muldowney W, Mazbar SA, *et al*. Emergency laparotomy in patients on continuous ambulatory peritoneal dialysis. Am Surg 2001; 67: 615-8.
137. Kiefer T, Schenk U, Weber J, *et al*. Incidence and significance of pneumoperitoneum in continuous ambulatory peritoneal dialysis. Am J Kidney Dis 1993; 22: 30-5.
138. Lee FT Jr, Leahy-Gross KM, Hammond TG, *et al*. Pneumoperitoneum in peritoneal dialysis patients : significance of diagnosis by CT. J Comput Assist Tomogr 1994; 18: 439-42.
139. Poralla T. Angiodysplasia in the renal patient: how to diagnose and how to treat? Nephrol Dial Transplant 1998; 13: 2188-91.
140. Cunningham JT. Gastric telanjiectasias in chronic hemodialysis patients: a report of six cases. Gastroenterology 1981; 81: 1131.
141. Dave PB, Romeu J, Antonelli A, *et al*. Gastrointestinal telanjiectasias: a source of bleeding in patients receiving hemodialysis. Arch Intern Med 1984; 144: 1781.
142. Clouse RE, Cosatigan DJ, Mills BA, *et al*. Angiodysplasia as a cause of upper gastrointestinal bleeding. Arch Intern Med 1985; 145: 458.
143. Marcuard SP, Weinstock JV. Gastrointestinal angiodysplasia in renal failure. J Clin Gastroentrol 1988; 10: 482.
144. Navab F, Masters P, Subramani R, *et al*. Angiodysplasia in patients with renal insufficiency. Am J Gastroenterol 1989; 84: 1297.
145. Gheissari A, Rajuagur V, Kumashiro R, *et al*. Gastrointestinal hemorrhage in end-stage renal disease patients. Int Surg 1990; 75: 93.
146. Chalasani N, Cotsonis MA, Wilcox CM, *et al*. Upper gastrointestinal bleeding in patients with chronic renal failure; role of vascular ectasia. Am J Gastroenterol 1996; 91: 2329-32.
147. Gostout CJ, Viggiano TR, Ahlquist DA, *et al*. The clinical and endoscopic spectrum of the watermelon stomach. J Clin Gastroenterol 1992; 15: 256-63.
148. Oliveras A, Aubia J, Cao H, *et al*. 99mTc-labelled red blood cell scintigraphy for localization of gastrointestinal bleeding in chronic renal failure. Nephron 1998; 80: 76-8.
149. Shemin D, Elnour M, Amarantes B, *et al*. Oral estrogens decrease bleeding time and improve clinical bleeding in patients with renal failure. Am J Med 1990; 89: 436.
150. Bonner MH, Pate MB, Cunningham JT, *et al*. Estrogen-progesterone therapy for bleeding gastrointestinal telangiectasias in chronic renal failure: an uncontrolled trial. Ann Intern Med 1986; 105: 371.
151. Richardson JD, Lordon RE. Gastrointestinal bleeding caused by angiodysplasia: a difficult problem in patients with chronic renal failure receiving hemodialysis therapy. Ann Surg 1993; 59: 636.

152. Barkin JS, Ross BS. Medical therapy for chronic gastrointestinal bleeding of obscure origin. Am J Gastroenterol 1998; 93: 1250-4.
153. Lewis BS, Salomon P, Rivera-MacMurray S, *et al*. Waye JD Does hormonal therapy have any benefit for bleeding angiodysplasia? J Clin Gastroenterol 1992; 15: 99-103.
154. Rossini FP, Arrigoni A, Pennazio M. Octreotide in the treatment of bleeding due to angiodysplasia of the small intestine. Am J Gastroenterol 1993; 88: 1424-7.
155. Vujkovac B, Lavre J, Sabovic M. Successful treatment of bleeding from colonic angiodysplasias with tranexamic acid in a hemodialysis patient. Am J Kidney Dis 1998; 31: 536-8.
156. Campistol JM, Argiles A. Dialysis-related amyloidosis: visceral involvement and protein constituents. Nephrol Dial Transplant 1996; 11 (Suppl 3): 142-5.
157. Jimenez RE, Price DA, Pinkus GS, *et al*. Development of gastrointestinal beta2-microglobulin amyloidosis correlates with time on dialysis. Am J Surg Pathol 1998; 22: 729-35.
158. Maher ER, Hamilton Dutoit S, Baillod RA, *et al*. Gastrointestinal complications of diadlysis re;ated amyloidosis. Br Med J 1988; 297: 265.
159. Takahashi S, Morita, Koda Y, *et al*. Gastrointestinal involvement of dialysis-related amyloidosis. Clin Nephrol 1988; 30: 168.
160. Choi HS, Heller D, Picken MM, *et al*. Infarction of intestine with massive amyloid deposition in two patients on long-term hemodialysis. Gastroenterology 1989; 6: 230.
161. Campistol JM. Visceral involvement of dialysis amyloidosis. Am J Nephrol 1987; 7: 390-3.
162. Bruno MJ, van Dorp WT, Ferwerda J, *et al*. Colonic pseudo-obstruction due to beta2-microglobulin amyloidosis after long-term haemodialysis. Eur J Gastroenterol Hepatol 1998; 10: 717-20.
163. Kanai H, Kashiwagi M, Hirakata H, *et al*. Chronic intestinal pseudo-obstruction due to dialysis-related amyloid deposition in the propria muscularis in a hemodialysis patient. Clin Nephrol 2000; 53: 394-9.
164. Rosenblatt SG, Drake S, Fadem S, *et al*. Gastrointestinal blood loss in patients with chronic renal failure. Am J Kid Dis 1982; 1: 232.
165. Eberst ME, Berkowitz LR. Hemostasis in renal disease: pathophysiology and management. Am J Med 1994; 96: 168-79.
166. Alvarez L, Puleo J, Balian JA. Investigation of gastrointestinal bleeding in patients with end-stage renal disease. Am J Gastroenterol 1993; 88: 30.
167. Boyle JM, Johnston B. Acute upper gastrointestinal hemorrhage in patients with chronic renal disease. Am J Med 1983; 75: 409.
168. Fiaccadori E, Maggiore U, Clima B, *et al*. Incidence, risk factors, and prognosis of gastrointestinal hemorrhage complicating acute renal failure. Kidney Int 2001; 59: 1510-9.
169. Lau JY, Sung JJ, Lee KK, *et al*. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med 2000; 3:343(5): 310-6.
170. Beck LH. Screening and preventive health practices for the end-stage renal disease patient. Adv Ren Replace Ther 2000; 7: 195-201.
171. Mandel JS, Bond JH, Church TR, *et al*. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. N Engl J Med 1993; 328: 1365-71.
172. Muller AD, Sonnenberg A. Prevention of colorectal cancer by flexible endoscopy and polypectomy. A case-control study of 32,702 veterans. Ann Intern Med 1995; 123: 904-10.
173. Wolfe RA, Held PJ, Hulbert-Shearon TE, *et al*. A critical examination of trends in outcomes over the last decade. Am J Kidney Dis 1998; 32(Suppl 4): S9-15.
174. Maisonneuve P, Agodoa L, Gellert R, *et al*. Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. Lancet 1999; 354: 93-9.
175. Ajam M, Ramanujam LS, Gandhi VC, *et al*. Colon-cancer screening in dialysis patients. Artif Organs 1990; 14: 95.
176. Ito T, Tanaka I, Kadoya T, *et al*. Screening for gastroenterological malignancies in new and maintenance dialysis patients. J Gastroenterol 1999; 34: 35-4.
177. Akmal M, Sawelson S, Karubian F, *et al*. The prevalence and significance of occult blood loss in patients with predialysis advanced chronic renal failure (CRF), or receiving dialytic therapy. Clin Nephrol 1994;42 :198-202.
178. Lieberman DA, Rex DK. Feasibility of colonoscopy screening: Discussion of issues and recommendations regarding implementation. Gastrointest Endosc 2001; 54: 662-7.