Colonic Adenomatous Polyposis Syndromes: Clinical Management

C. Neal Ellis, M.D.[1]

ABSTRACT

Colorectal cancer is one of the major causes of cancer deaths in both men and women. It is estimated that 5 to 10% of patients with colorectal cancer have an inherited germline mutation that predisposes them to cancer. Hereditary colorectal cancer syndromes can be divided into those associated with colonic polyposis – familial adenomatous polyposis (FAP), attenuated familial adenomatous polyposis (aFAP), and *MYH* associated polyposis (MAP), and those not associated with colonic polyposis – hereditary nonpolyposis colon cancer (HNPCC). The hereditary polyposes are usually easier to diagnose than HNPCC, but their higher penetrance and variable phenotype pose some difficult problems in management and surveillance. The timing and type of surgical intervention, the management of desmoid risk, the treatment of rectal or pouch neoplasia, and the management of duodenal neoplasia are all questions that must be addressed in patients with FAP or MAP.

KEYWORDS: Familial adenomatous polyposis, attenuated familial polyposis, MYH-associated polyposis, desmoids

Objectives: Upon completion of this article, the reader should be familiar with the characteristics of inherited colorectal cancer syndromes and their treatment options.

Clinically, hereditary colorectal cancer syndromes can be divided into those associated with colonic polyposis (familial adenomatous polyposis [FAP], attenuated familial adenomatous polyposis [aFAP], and MYH-associated polyposis [MAP]) and those not associated with colonic polyposis (hereditary nonpolyposis colon cancer [HNPCC]). Treatment options for these patients include multiple aggressive screening regimens, chemopreventive medications, and prophylactic surgery. Selection of the appropriate management approach is best made using information obtained from the patient's clinical examination, the family medical history, and genetic evaluation.

CLINICAL–PATHOLOGIC FEATURES

Familial Adenomatous Polyposis and Attenuated Familial Adenomatous Polyposis

Classical FAP is defined by the presence of over 100 synchronous colorectal adenomas. Review of the family medical history will usually reveal an autosomal dominant pattern of inheritance, although up to 30% of patients appear to develop the disease from a new adenomatous polyposis coli (*APC*) mutation.[1] Although all areas of the colon are involved in the fully developed syndrome, there appears to be a predilection for the rectum and left colon. Adenomatous polyps are present

[1]Department of Surgery, University of South Alabama College of Medicine, Mobile, Alabama.

Address for correspondence and reprint requests: C. Neal Ellis, M.D., Department of Surgery, University of South Alabama College of Medicine, 2451 Fillingim St., MSTN 721, Mobile, AL 36617 (e-mail: nellis@ usouthal.edu).

Polyps and Polyposis Coli; Guest Editor, Janice F. Rafferty, M.D.

Clin Colon Rectal Surg 2008;21:256–262.
DOI 10.1055/s-0028-1089940. ISSN 1531-0043.

in 15% of FAP by 10 years of age, 50% at age 15 years, and 75% by 20 years of age. The lifetime risk of colorectal malignancy in untreated patients with FAP is near 100% with a median age of 39 years. However, 7% of affected patients will develop cancer before age 21 years.[2–5]

In contrast to patients with FAP, those with attenuated FAP have less than 100 synchronous adenomas (an average of 30) with the polyps more likely to be right-sided. The onset is also later with the polyps developing after 25 years of age.[6] Like FAP, the lifetime risk of colorectal malignancy in untreated patients with aFAP is near 100%, but the median age of cancer diagnosis is 59 years.[2,7] Also like FAP, the family medical history will usually reveal an autosomal dominant pattern of inheritance.

MYH-Associated Polyposis

It is usually impossible to distinguish MAP from FAP and aFAP clinically in an individual patient. On evaluation of the family medical history however, the distinction is usually obvious. Although FAP and aFAP have an autosomal dominant pattern of inheritance, MAP is inherited in an autosomal recessive manner. The number of polyps in MAP is variable, having a reported range of 5 to 750, with a median of ~50 polyps, and 36% of patients having over 100 polyps.[8,9] To date, patients with MAP have been diagnosed at a median age of 48 years with a range of 13 to 65 years. Colorectal cancer has been present at diagnosis in 48% at a mean age of 50 years and a range of 30 to 65 years. The cancers are usually left-sided, with multiple colorectal cancers present in 24% of the patients at diagnosis.[9]

Extracolonic Manifestations

Any APC mutation can result in FAP or one of its clinical variants. The variants of FAP are distinguished by the number of polyps (aFAP) or by the extracolonic manifestations (Gardner's syndrome, Turcot's syndrome). The clinical significance of the extracolonic manifestations can range from a benign asymptomatic marker (congenital hypertrophy of the retinal pigmented epithelium [CHRPE]), to a cosmetic problem (osteomas), to a lesion with significant malignant potential or morbidity (gastroduodenal adenomas, desmoids) as shown in Table 1.

Duodenal adenomatous polyps develop in 80 to 90% of patients with FAP with a 12% risk of duodenal or periampullary cancer, which will occur an average of 16 years after the diagnosis of FAP.[10–14] Adenomas can also develop in the jejunum and ileum, but the malignant potential of these lesions is low.[15]

Gastric polyps are also present in the majority of patients with FAP. Most commonly these are small sessile lesions that on histologic evaluation are composed of dilated fundic glands. These polyps are considered to be hamartomas with no malignant potential.[16–20] Gastric adenomas are found in 10% of patients with FAP, but there seems to be regional differences in the incidence of the lesions with these neoplasms being much more common in Japanese compared with non-Japanese patients.[11,16,21]

Desmoid tumors are tumors of fibroaponeurotic tissue with an incidence of 12 to 38% in patients with FAP.[22–25] An increased risk of desmoids has been described in premenopausal women, and during pregnancy, or following abdominal trauma or surgery.[26–31] Desmoids usually present within 2 to 3 years of the precipitating event and are located intraabdominally in 80% of patients, within the abdominal wall in 18% of patients, or extraabdominally in 2% of patients.[30,32] There are multiple desmoids in 5 to 38% of patients.[31–33] In contrast to sporadic desmoids, those associated with FAP have a variable clinical course. Although 47% will remain stable or grow slowly after diagnosis, 10% will regress completely, 29% will undergo cycles of growth and regression and 10% will grow rapidly.[32] Symptoms related to intraabdominal desmoids can include abdominal pain, obstruction of the small intestine or ureters, or occlusion of the mesenteric blood vessels with resultant intestinal ischemia, perforation, and sepsis. Surgery for a desmoid-related complication will be required in 27% of patients with an intraabdominal desmoid.[34,35]

Extracolonic manifestations have also been associated with *MYH* mutations and include 2 reported cases

Table 1 Extracolonic Manifestations of Adenomatous Polyposis Coli (APC) Mutations

	Incidence	Significance
Duodenal adenomas	80–90%	12% Risk of malignancy
Gastric hamartomas	50–70%	Must exclude gastric adenoma
Desmoids	12–35%	27% Risk of complications
Hepatoblastoma	1%	Most common before age 2 years
Osteomas	80%	Usually <1 cm in size
CHRPE	60%	Marker for screening purposes
Thyroid cancer (papillary)		Predilection for women

CHRPE, congenital hypertrophy of the retinal pigment epithelium.

Table 2 Screening Recommendations for Patients at Risk for a Polyposis Syndrome

For the patient whose family medical history suggests FAP or whose *APC* mutation is between codons 200–2500	Flexible sigmoidoscopy or colonoscopy begin at puberty, then flexible sigmoidoscopy annually
For the patient whose family medical history suggests aFAP or MAP, or whose *APC* mutation is before codon 157 or after codon 2500	Colonoscopy beginning at age 18–21 years; Every 1–2 years
For all patients with a known or suspected *APC* mutation	Esophagogastroduodenoscopy every 1–5 years according to Spigelman stage, beginning at 20 years

FAP, familial adenomatous polyposis; APC, adenomatous polyposis coli; aFAP, attenuated familial adenomatous polyposis; MAP, *MYH* associated polyposis.

of gastric cancer (1 at 17 years of age) and 2 cases of duodenal polyps. Congential hypertrophy of the retinal pigment epithelium (CHRPE) and osteomas have also been reported.[9,36,37]

MANAGEMENT

The initial management of a suspected inherited cancer syndrome is genetic counseling. Subsequent management options include aggressive screening regimens, chemoprevention, and prophylactic surgery. Regardless of the initial treatment modality chosen, a lifetime of surveillance is needed.

Screening

FAMILIAL ADENOMATOUS POLYPOSIS

Endoscopy is the screening method most commonly chosen for patients at risk for a polyposis syndrome (Table 2). For individuals whose family history or *APC* gene mutation suggests FAP, the initial examination should be performed at 10 to 12 years of age. Complete colonoscopy has been recommended by some, whereas others, given the predilection for rectal and left colonic polyps in FAP, have recommended flexible proctosigmoidoscopy.[1] Annual flexible proctosigmoidoscopy is the method of choice for subsequent examinations. Screening should be continued until adenomas are diagnosed. If no polyps have been identified by age 25 years in patients at risk for FAP by family history and whose genetic status is unknown, it is reasonable to conclude that their chance of inheriting an *APC* mutation is slim and the frequency of screening can be reduced.

ATTENUATED FAMILIAL ADENOMATOUS POLYPOSIS

For individuals whose family history or APC mutation suggests aFAP, complete colonoscopy is the screening procedure of choice because of the predominance of right colonic polyposis in aFAP.[1,6] Screening should begin at age 20 years and be performed every 1 to 2 years. There is no consensus on when to discontinue screening examinations, but given the natural history of aFAP, it would seem that screening of the healthy individual should continue into the eighth decade of life.

MYH-ASSOCIATED POLYPOSIS

No guidelines for the screening of patients with MAP have been proposed. However, given the clinical features of MAP, it would seem appropriate to follow a screening protocol similar to that used for aFAP.

Extracolonic Manifestations

Once a patient is known to have a polyposis syndrome by either the clinical findings of colon polyps or by genetic testing, the possibility of extracolonic manifestations must be considered. All patients should have esophagogastroduodenoscopy starting at age 20 years and continuing at intervals determined by the findings of the previous examination. The findings in the duodenum are expressed according to the Spigelman Staging System (Table 3), which integrates adenoma size, number, histology, and degree of dysplasia. Patients with stage 0 or I disease can be reexamined in 5 years. Patients with stage II disease need a 3-year follow-up; stage III demands a 1-year exam. Stage IV disease is an indication for strong consideration of duodenectomy.[13]

There is no consensus regarding screening for desmoid tumors. However, it is appropriate to consider their potential presence when a polyposis syndrome is identified. Patients with an increased risk for desmoids include those with an APC mutation 5′ of codon 1400,

Table 3 Spigelman Staging for Duodenal Adenomatosis

Score*	1	2	3
No. polyps	1–4	5–20	>20
Size (mm)	1–4	5–10	>10
Histologic type	Tubular	Tubulovillous	Villous
Dysplasia	Mild	Moderate	Severe

*Spigelman stage I, score 1–4; stage II, score 5–6; stage III, score 7–8; stage IV, score 9–12.

those with >30% affected family members suffering from desmoids, those having reoperative surgery, and those with an extraabdominal desmoid already.

Desmoid tumors can be staged according to clinical characteristics.[38] Stage I desmoids are asymptomatic, small (<10 cm in maximum dimension) and found incidentally during laparotomy or on computed tomography (CT) scan. It is unlikely that these tumors will enlarge and cause problems. Management options include observation, or nonsteroidal antiinflammatory drugs (NSAIDs). If a stage I desmoid is found incidentally at surgery and it is easily resectable without the removal of a significant amount of bowel, resection is appropriate.[39,40]

Stage II desmoids are symptomatic, 10 cm or less in greatest diameter, and have no evidence of enlargement. Symptomatic desmoids require treatment. If they are resectable with minimal sequelae, then resection is best. If the tumor is unresectable, the addition of tamoxifen or raloxifene to a NSAID offers the possibility of a quicker and more consistent response with low risk of side effects.[41,42]

Stage III desmoids are symptomatic and 11 to 20 cm in maximum dimension, or asymptomatic and slowly increasing in size (<50% increase in diameter in 6 months). Management options for these lesions include NSAID, tamoxifen, raloxifene, and vinblastine/methotrexate. Antisarcoma chemotherapy (adriamycin/dacarbazine) can be given if the tumor continues to grow despite the less toxic agents.[43–45]

Stage IV desmoids are symptomatic, >20 cm maximum diameter, or demonstrate rapid growth (>50% increase in diameter within 6 months). Antisarcoma chemotherapy and radiation are usually employed in the management of these tumors. Desmoids that cause life-threatening complications such as sepsis, perforation, or hemorrhage are also classified as stage IV tumors. Management usually requires emergent, major exenterative surgery likely to result in significant loss of bowel and long-term morbidity.[46,47]

Chemoprevention

Several clinical trials have shown that the NSAIDS, sulindac, celecoxib, and aspirin can reduce the number and size of colorectal adenomas in patients with FAP.[48–51] It is unclear, however, if suppression of the polyps will prevent colorectal cancer. Given the case reports of cancer occurring in patients with FAP whose polyps were suppressed with sulindac,[52] chemoprevention cannot be recommended as primary therapy for intestinal polyposis. It can be considered for special circumstances, where surgical therapy has been declined or has an unacceptably high risk of complications, or when polyposis develops in an ileal pouch and surgery means an end ileostomy.

Surgery

Surgery, preferably prophylactic, is the best way of managing the large intestine in patients with colonic polyposis syndromes. The timing and the choice of surgery must take into account the manifestations of the disease in the patient and their family, and the site of the mutation (if known) (Table 4). *APC* mutations between codons 1250–1464 are associated with profuse polyposis that always demands a total proctocolectomy. The risk of cancer for patients with more than 1000 adenomas is twice that of patients with fewer polyps.[53] In contrast, patients with aFAP (less than 100 synchronous adenomas) can be safely managed with colectomy and ileorectal anastomosis, preserving the rectum for the functional benefits it offers.

With these considerations, it has been recommended that surgery be performed at age 12 to 15 years for patients with severe disease by clinical exam. Surgery can be delayed until ages 18 to 21 for those with less severe disease. For patients whose family medical history or genetic test results reveal an increased risk of desmoid disease, or who are found to have a desmoid tumor on clinical evaluation, surgery should be delayed until they have an increasing number and size of polyps, which cannot be managed endoscopically, or develop polyps with severe dysplasia.

Surgical options include total abdominal colectomy with ileorectostomy (TAC), proctocolectomy with ileal pouch anal reconstruction (IPAA), and total proctocolectomy with Brooke ileostomy (TPC). The indications for each are shown in Table 5.

The advantages of a TAC include a single-stage procedure with a low risk of surgical complications, preservation of bowel continuity with superior functional results when compared with the other surgical options, and the avoidance of a proctectomy with its potential for damage to the pelvic nerves, decreased fertility, and urinary and sexual dysfunction.[53–59] Bowel function is influenced by the length of the remaining rectum.

Table 4 Factors Determining Timing of Surgery

Presentation	Timing
Symptomatic disease	Next available time
Severe disease by family history	Soon after diagnosis
Mild disease, asymptomatic	When convenient, ages 16–18 years
Attenuated disease by family history Phenotype or genotype	21–25 years
High risk of desmoids by family history, clinical exam, or genetic test results	Defer as long as is safe
Discovery of a polyp that cannot be removed endoscopically or with severe dysplasia; cancer	Immediately

Table 5 Surgical Options for Polyposis Syndromes

Procedure	Indications
Abdominal colectomy with ileorectostomy	aFAP by family history, clinical exam, or genetic testing; mild disease (FAP or MAP) as manifested by fewer than 20 polyps in the rectum and less than 1000 overall
Proctocolectomy with ileal-pouch anal anastomosis	Severe disease (FAP or MAP) by family history, clinical exam, or genetic test results; cancer in the colon or mid-upper rectum; risk of desmoid tumor by personal or family history or *APC* mutation between codons 1403–1578.
Proctocolectomy with ileostomy	When ileal-pouch anal anastomosis contraindicated because of anal sphincter dysfunction or technical problems; low rectal cancer which precludes sphincter preservation.

aFAP, attenuated familial adenomatous polyposis; FAP, familial adenomatous polyposis; MAP, *MYH* associated polyposis; *APC*, adenomatous polyposis coli.

Longer rectal remnants are associated with better bowel function, but an increased risk of subsequent rectal neoplasia.[60] It appears that 15 cm of remaining rectum is the optimal remnant, having an adequate reservoir capacity and low risk of subsequent neoplasia. The risk of subsequent malignancy with 10 to 12 cm of remaining rectum has been reported to be 25 to 37% over 20 years and is the major disadvantage of TAC.[60,61] Clinical and genetic factors can be used to predict the likelihood a cancer will develop in the rectal remnant. The presence of over 20 polyps in the rectum or more than 1000 polyps in the colon, a rectal polyp >3 cm in size, or a cancer anywhere in the colon are clinical findings associated with an increased risk of subsequent malignancy in the remaining rectum.[62]

Given the risk of rectal neoplasia after TAC, many surgeons recommend IPAA for patients with severe (>1000 adenomas) polyposis. With preservation of the anal transition zone, bowel function after IPAA can be similar to that after TAC,[59,63,64] but the risk of subsequent neoplasia in the anal transition zone is reported to be as high as 30%.[54,65] Complete rectal mucosectomy will decrease this risk by half, but is associated with significantly worse bowel function and an increased surgical complication risk.[66–68]

The 20 to 40% risk of surgical complications is a major disadvantage of IPAA.[69–73] Proctectomy is associated with a risk of damage to the pelvic autonomic nerves resulting in impotence and retrograde ejaculation in 2% and 6% of males, respectively.[74] Damage to the pelvic autonomic nerves will result in vaginal dryness and dyspareunia in 25 to 30% of women.[75,76] Furthermore, IPAA is associated with a drop of 50% in a woman's ability to conceive, a drop not seen with ileorectal anastomosis (IRA).[77] Despite these disadvantages, IPAA is the procedure of choice for patients with an unacceptably high risk of rectal cancer after TAC. Although TPC does not have the risk of subsequent neoplasia that is associated with TAC and IPAA with preservation of the anal transition zone, it is almost never performed as the initial procedure for the management of polyposis because of the permanent stoma.[76] However, with preoperative counseling, proper selection of a stoma site, and postoperative teaching, a patient with an ileostomy can lead a full and active life. Currently, TPC is reserved for patients with a contraindication to sphincter preservation such as a low rectal cancer, those with poor sphincter function from previous anorectal conditions or obstetric trauma, or for technical problems that prevent an ileal pouch from reaching the anus.

Postoperative Surveillance

Regardless of the surgical procedure chosen, postoperative surveillance of the rectal remnant after TAC, the ileal pouch after IPAA, and the ileostomy after TPC, and screening for the extracolonic manifestations is essential for the remainder of the patient's life. Endoscopy of the rectal remnant or ileal pouch should be performed annually with polyps <5 mm followed and larger polyps removed without fulguration and examined histologically to exclude dysplasia. For patients who underwent TAC, proctectomy with IPAA can be considered for an increasing number or size of polyps or the development of severe dysplasia.[78–80] Although the significance of polyps in an ileal pouch is uncertain, it has been suggested that these can be managed with the NSAIDS sulindac or celecoxib.

REFERENCES

1. Church JM, Lowry A, Simmang C. Practice parameters for the identification and testing of patients at risk for dominantly inherited colorectal cancer – supporting documentation. Dis Colon Rectum 2001;44:1404–1412
2. Guillen JG, Smith AJ, Calle JP, Ruo L. Gastrointestinal polyposis syndromes. Curr Probl Surg 1999;36(4):217–323
3. Petersen JM, Slack J, Nakamura Y. Screening guidelines and premorbid diagnosis of familial adenomatous polyposis using linkage. Gastroenterology 1991;100:1658–1664
4. Berk T, Cohen Z, Bapat B, et al. Negative genetic test results in familial adenomatous polyposis: clinical screening implications. Dis Colon Rectum 1999;42(3):307–310
5. Church JM, McGannon E, Burke C, Clark B. Teenagers with familial adenomatous polyposis: what is their risk for colorectal cancer?. Dis Colon Rectum 2002;45:887–889
6. Hernegger GS, Moore HG, Guillem JG. Attenuated familial adenomatous polyposis: and evolving and poorly understood entity. Dis Colonl Rectum 2002;45:127–134

7. Giardiello FM, Brensinger JD, Luce MC, et al. Phenotypic expression in adenomatous polyposis families with mutations in the 5′ region of the adenomatous polyposis coli gene. Ann Intern Med 1997;126:514–519
8. Sampson JR, Dolwani S, Jones S, et al. Autosomal recessive colorectal polyposis due to inherited mutations of MYH. Lancet 2003;362:39–41
9. Lipton L, Tomlinson I. The multiple colorectal adenoma phenotype and MYH, a base excision repair gene. Clin Gastroenterol Hepatol 2004;2(8):633–638
10. Church JM. Non-cytotoxic drug therapy for intra-abdominal desmoids tumor in patients with familial adenomatous polyposis. Dis Colon Rectum 1992;35:29–33
11. Bulow S, Alm T, Fausa O, et al. Duodenal adenomatosis in familial adenomatous polyposis. DAF project group. Int J Colorectal Dis 1995;10:43–46
12. Wallace MH, Phillips RKS. Upper gastrointestinal disease in patients with familial adenomatous polyposis. Br J Surg 1993;85(6):742–750
13. Groves CJ, Saunders BP, Spigelman AD, et al. Duodenal cancer in patients with familial adenomatous polyposis (FAP); results of a 10 year prospective study. Gut 2002;50: 634–636
14. Burke C, Church J, Beck G. The natural history of upper gastrointestinal adenomas in untreated patients with familial polyposis. Gastrointest Endosc 1999;49:358–364
15. Spigelman AD, Phillips RKS. The upper gastrointestinal tract. In: Phillips RKS, Spigelman AD, Thompson JPS, eds. Familial Adenomatous Polyposis and Other Polyposis Syndromes. London: Edward Arnold; 1994:106–127
16. Jarvinen H, Nyberg M, Pettokailio P. Upper gastrointestinal tract polyps in familial adenomatous coli. Gut 1983;24:333–339
17. Park JG, Park KJ, Ahn Yo, et al. Risk of gastric cancer among Korean familial adenomatous polyposis patients. Dis Colon Rectum 1992;35:996–998
18. Iwama T, Mishima Y, Utsunomiya J. The impact of familial adenomatous polyposis on the tumorigenesis and mortality at several organs; its rational treatment. Ann Surg 1993;217: 101–108
19. Offerhaus GJ, Giardiello FM, Krush AJ, et al. The risk of gastrointestinal cancer in familial adenomatous polyposis. Gastroenterology 1992;102:1980–1982
20. Burt RW. Polyposis syndromes. In: Yamada T, Alpers DH, Oywang C, Powell DW, Silerstein FE, eds. Textbook of Gastroenterology. 2nd ed. Philadelphia, PA: JB Lippincott; 1995
21. Watanabe H, Enjoli M, Yoa T, et al. Gastric lesions in familial adenomatous coli, their incidence and histologic analysis. Hum Pathol 1978;9:269–283
22. Eccles DM, VanderLuijt R, Breukel C, et al. Hereditary desmoid disease due to a frame-shift mutation at codon 1924 of the APC gene. Am J Hum Genet 1996;59:1193–1201
23. Sorvia C, Berk T, McLeod RS, et al. Desmoid disease in patients with familial adenomatous polyposis. Dis Colon Rectum 2000;43:363–369
24. Scott RJ, Froggat NJ, Trembath RC, et al. Familial infiltrative fibromatosis (desmoid tumors) caused by a recurrent APC gene mutation. Hum Mol Genet 1996;5: 1921–1924
25. Clark SK, Neale KF, Landgrebe JC, et al. Desmoid tumors complicating familial adenomatous polyposis. Br J Surg 1999; 86:1185–1189
26. Kinzbrunner B, Ritter S, Domingo J, Rosenthal CJ. Remission of rapidly growing desmoid tumors after tamoxifen therapy. Cancer 1983;52:2201–2204
27. Clark SK, Phillips RKS. Desmoids in familial adenomatous polyposis. Br J Surg 1996;83:1494–1504
28. Reitamo JJ, Scheinin TM, Hayry P. The desmoid syndrome; new aspects in the cause, pathogenesis and treatment of the desmoid tumor. Am J Surg 1986;151:230–237
29. Bus PJ, Verspaget HW, Van Krieken JH, et al. Treatment of mesenteric desmoid tumors and the anti-osteogenic agent toremifene: case histories and an overview of the literature. Eur J Gastroenterol Hepatol 1999;11:1179–1183
30. Rodriguez-Bigas MA, Mahoney MC, Karakousis CP, et al. Desmoid tumors in patients with familial adenomatous polyposis. Cancer 1994;74:1270–1274
31. Einstein DM, Taglinbue JR, Desai RK. Abdominal desmoids; CT findings in 25 patients. AJR Am J Roentgenol 1991;157:275–279
32. Church JM. Familial adenomatous polyposis; a review. Perspect Colon Rectal Surg 1995;8:203–225
33. Gurbuz AK, Giardiello FM, Peterson FM, et al. Desmoid tumors in familial adenomatous polyposis. Gut 1994;35:377–381
34. Doi K, Iida M, Kohrogi N, et al. Large intra-abdominal desmoid tumors in a patient with familial adenomatous coli; their rapid growth detected by computerized tomography. Am J Gastroenterol 1993;88:595–598
35. Penna C, Phillips RK, Tiret E, et al. Surgical polypectomy of duodenal adenomas in familial adenomatous polyposis; experience of two European centers. Br J Surg 1993;80: 1027–1029
36. Jones S, Emmerson P, Maynard J, et al. Biallelic germline mutations in MYH predispose to multiple colorectal adenomas and somatic G:C (right arrow)T:A mutations. Hum Mol Genet 2002;11:2961–2967
37. Venesio T, Molatore S, Catteno F, et al. High frequency of MYH mutations in a subset of patients with familial adenomatous polyposis. Gastroenterology 2004;126:1681–1685
38. Church J, Berk T, Boman B, et al. Staging intra-abdominal desmoid tumors in familial adenomatous polyposis: a search for a uniform approach to a troubling disease. Dis Colon Rectum 2005;48:1528–1534
39. Tsukada K, Church JM, Jagelman DG, et al. Non-cytotoxic drug therapy for intra-abdominal desmoid tumor in patients with familial adenomatous polyposis. Dis Colon Rectum 1992;35:29–33
40. Poon R, Smits R, Li C, et al. Cyclooxygenase-two (COX-2) modulates proliferation in aggressive fibromatosis (desmoid tumor). Oncogene 2001;20:451–460
41. Hansmann A, Adolph C, Vogel T, Unger A, Moslein G. High-dose tamoxifen and sulindac as first-line treatment for desmoid tumors. Cancer 2004;100:612–620
42. Tonelli F, Ficari F, Valanzano R, Brandi ML. Treatment of desmoids and mesenteric fibromatosis in familial adenomatous polyposis with raloxifene. Tumori 2003;89:391–396
43. Azzarelli A, Gronchi A, Bertulli R, et al. Low-dose chemotherapy with methotrexate and vinblastine for patients with advanced aggressive fibromatosis. Cancer 2001;92: 1259–1264
44. Okuno SH, Edmonson JH. Combination chemotherapy for desmoid tumors. Cancer 2003;97:1134–1135
45. Poritz LS, Blackstein M, Berk T, Gallinger S, McLeod RS, Cohen Z. Extended follow-up of patients treated with

cytotoxic chemotherapy for intra-abdominal desmoid tumors. Dis Colon Rectum 2001;44:1268–1273
46. Tzakis AG, Tryphonopoulos P, Faria W, et al. Partial abdominal evisceration, ex vivo resection, and intestinal autotransplantation for the treatment of pathologic lesions of the root of the mesentery. J Am Coll Surg 2003;197:770–776
47. Nuyttens JJ, Rust PF, Thomas CR Jr, Turrisi AT III. Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: a comparative review of 22 articles. Cancer 2000;88:1517–1523
48. Hawk E, Lubert R, Limburg P. Chemoprevention in hereditary colorectal cancer syndromes. Cancer 1999;86: 2551–2563
49. Cruz-Carreira M, Hylind LM, Romans KE, et al. Long-term treatment with sulindac in familial adenomatous polyposis: a prospective cohort study. Gastoenterology 2002;124:641–645
50. Steinbach G, Lynch PM, Phillips RK, et al. The effect of celecoxib, a cyclooxygenase – 2 inhibitor in familial adenomatous polyposis. N Engl J Med 2000;342:1946–1952
51. Tonelli F, Valanzano R, Messerini L, et al. Long-term treatment with sulindac in familial adenomatous polyposis: is there an actual efficacy in prevention or rectal cancer. J Surg Oncol 2000;74:15–20
52. Lynch HT, Thorson AG, Smyrk T. Rectal cancer after prolonged sulindac chemoprevention: a case report. Cancer 1995;75:936–938
53. Van Duijvendijk P, Slors JF, Taat CW, et al. Quality of life after total colectomy with ileorectal anastomosis or proctocolectomy and ileal pouch-anal anastomosis for familial adenomatous polyposis. Br J Surg 2000;87:590–596
54. Church JM, Fazio VW, Lavery IC, et al. Quality of life after prophylactic colectomy and ileorectal anastomosis in patients with familial adenomatous polyposis. Dis Colon Rectum 1996;39:1404–1408
55. Bulow C, Vasen H, Jarvinen H, et al. Ileorectal anastomosis is appropriate for a subset of patients with familial adenomatous polyposis. Gastroenterology 2000;119:1454–1460
56. Bussey HJ, Eyers AA, Ritchie SM, Thompson JP. The rectum in adenomatous polyposis: the St. Mark's policy. Br J Surg 1985;72:529–531
57. Madden MV, Neale KF, Nicholls RJ, et al. Comparison of morbidity and function after colectomy with ileorectal anastomosis or restorative proctocolectomy for familial adenomatous polyposis. Br J Surg 1991;78:789–792
58. Jagelman DG. Choice of operation in familial adenomatous polyposis. World J Surg 1991;15:47–49
59. Ambroze WL, Dozois RR, Pemberton GH, et al. Familial adenomatous polyposis: results following ileal-pouch anal anastomosis and ileorectostomy. Dis Colon Rectum 1992; 35:12–15
60. DeCosse JJ, Bulow S, Neale K, et al. Rectal cancer risk in patients treated for familial adenomatous polyposis. Br J Surg 1992;79(12):1372–1375
61. Heiskanen I, Harvinen HJ. Fate of the rectal stump after colectomy and ileorectal anastomosis for familial adenomatous polyposis. Int J Colorectal Dis 1997;12:9–13
62. Church JM, Burke C, McGannon E, et al. Predicting polyposis severity by proctoscopy: how reliable is ti? Dis Colon Rectum 2001;44:1249–1254
63. Kartheuser AH, Parc R, Penna CP, et al. Ileal pouch-anal anastomosis as the first choice operation in patients with familial adenomatous polyposis: a ten year experience. Surgery 1996;119:615–623
64. Van Duijvendijk P, Vasen HF, Bertario L, et al. Cumulative risk of developing polyps or malignancy at the ileal pouch-anal anastomosis in patients with familial adenomatous polyposis. J Gastrointest Surg 1999;3:325–330
65. Remzi FH, Church JM, Bast J, et al. Mucosectomy vs staples ileal pouch-anal anastomosis in patients with familial adenomatous polyposis: functional outcome and neoplasia control. Dis Colon Rectum 2001;44:1590–1596
66. Fazio VW, Tjandra JJ. Transanal mucosectomy. Ileal pouch advancement for anorectal dysplasia or inflammation after restorative proctocolectomy. Dis Colon Rectum 1994;37: 1008–1011
67. Ziv Y, Fazio VW, Church JM, et al. Stapled ileal pouch-anal anastomosis are safer than hand sewn anastomosis in patients with ulcerative colitis. Am J Surg 1996;171:320–323
68. Tuckson W, Lavery I, Fazio V, et al. Manometric and functional comparison of ileal pouch-anal anastomosis with and without anal manipulation. Am J Surg 1991;161: 90–95
69. Fazio VW, Ziv Y, Church JM, et al. Ileal pouch-anal anastomosis: complications and function in 1005 patients. Ann Surg 1995;222:120–127
70. Kollmorgen CF, Nivatvongs S, Dean PA, et al. Long-term cause of death following ileal pouch-anal anastomosis. Dis Colon Rectum 1996;39:525–528
71. Setti-Carraro P, Ritchie JK, Wilkinson KH, Nicholls RJ, Hawley RR. The first 10 years experience of restorative proctocolectomy for ulcerative colitis. Gut 1994;35:1070–1075
72. Keighley MR, Ogunbiyi OA, Korsgen S. Pitfalls and outcome in ileo anal pouch surgery for ulcerative colitis. Neth J Med 1997;5:23–27
73. Mikkola K, Lukkonene P, Harvinene HJ. Long-term results of restorative proctocolectomy for ulcerative colitis. Int J. Colorectal Dis 1995;10:10–14
74. Oresland T, Palmblad S, Ellstrom M, et al. Gynecological and sexual functions related to anatomical changes in the female pelvis after restorative proctocolectomy. Int J Colorectal Dis 1994;9:77–81
75. Barnbrick M, Fazio VW, Hull TL, et al. Sexual function following restorative proctocolectomy in women. Dis Colon Rectum 1996;39:610–614
76. McLeod RS, Baxter NN. Quality of life of patients with inflammatory bowel disease after surgery. World J Surg 1998; 22:375–381
77. Olsen KO, Juul S, Bulow S, et al. Female fecundity before and after operation for familial adenomatous polyposis. Br J Surg 2003;90:227–231
78. Feinberg SM, Jagelman DG, Sarre RG, et al. Spontaneous resolution of rectal polyps in patients with familial polyposis following abdominal colectomy and ileorectal anastomosis. Dis Colon Rectum 1988;31:169–175
79. Nicholls RJ, Springall RG, Gallager P. Regression of rectal adenomas after colectomy and ileorectal anastomosis for familial adenomatous polyposis. BMJ 1988;296:1707–1708
80. Penna C, Tiret E, Parc R, et al. Operation and abdominal desmoid tumors in familial adenomatous polyposis. Surg Gynecol Obstet 1993;177:263–268