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# Family Practice Grand Rounds

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## Colonic Polyps and Colon Cancer

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DR. R. PRASAAD STEINER (*Assistant Professor, Department of Family Practice*): The family physician has the opportunity to use multiple diagnostic aids to screen patients for colonic lesions. Increased knowledge about risk factors and conditions associated with colonic cancer, as well as new or revised procedures for detecting colonic pathology, has led to earlier detection and decreased mortality. How to best use these new advances to provide optimal care for patients is the subject of this Grand Rounds.

Dr. Donna Roberts will present two brief case summaries for discussion by our panel.

DR. DONNA ROBERTS (*Second-year resident, Department of Family Practice*): R.W. is a 69-year-old black woman with multiple problems including anemia, alcoholism, and traumatic rib fractures. There is no family history of bowel carcinoma. During the evaluation of her anemia, stools were negative for occult blood. An air-contrast barium enema revealed a 1.2-cm polyp in the rectal region and a polypoid lesion proximal to the hepatic flexure. The patient was admitted to the hospital for colonoscopy. Three polyps were identified, all of which were pedunculated

and regular in surface appearance. All polyps were excised, but only two were retrieved.

Another patient, J.R., a 44-year-old black woman, presented with complaints of intermittent rectal bleeding first noted 18 months ago. Blood was almost always mixed with the stool. At times she had diarrhea associated with lower abdominal pain. Recently she felt that her stool was being pushed through a narrowed area. She denied other symptoms. There was no family history of colonic cancer. Physical examination revealed tenderness in the left lower quadrant of the abdomen. Pelvic and rectal examinations were normal, but a stool test for occult blood was positive. An outpatient barium enema showed a polypoid lesion in the midsigmoid colon. The patient was admitted to the hospital for colonoscopy, which showed a broad-based polypoid lesion in the distal sigmoid colon approximately 19 to 20 cm from the anus. Biopsies of the lesion were taken. As the lesion was large and sessile, endoscopic polypectomy was not feasible. Colonoscopy was performed proximal to the lesion, but was electively stopped at the splenic flexure because of severe pain. The patient underwent a sigmoid colectomy with primary anastomosis. The postoperative course was unremarkable.

DR. STEINER: These two cases represent contrasting presentations of colonic polyps. Both cases involve women aged over 40 years with no family history of cancer. The first patient had no

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bowel complaints and negative tests for occult blood in the stool. A barium enema revealed multiple pedunculated polyps that were resectable with colonoscopy. The second patient had bowel symptoms and gross and occult rectal bleeding, and a single large sessile mass in the distal colon was demonstrated on barium enema that could not be removed by colonoscopy. Pathology reports from these two cases revealed differing histologies, as will be discussed later.

DR. KENNETH HOLTZAPPLE (*Chairman, Department of Family Practice*): Polyp, from the Greek *polypous* meaning "many footed," refers to any mass of tissue that projects from a mucosal surface. It is a general term used to describe many colonic abnormalities noted at the time of contrast or endoscopy studies. The vast majority of individuals with colonic polyps are asymptomatic. Polyps can, however, cause signs and symptoms of bowel dysfunction—abdominal discomfort, change in bowel habit, change in character of stool, gross or occult bleeding, and intussusception. Rarely, a villous adenoma can cause diarrhea from massive amounts of mucous secretion. This excessive mucous secretion may lead to hypokalemia, hypoproteinemia, and even hypovolemia.<sup>1</sup> Realizing that all the foregoing symptoms and signs can be distressing to a patient, the most bothersome issue to clinicians and to patients is the relationship of polyps to cancer of the colon.

Excluding nonmelanoma skin cancer and carcinomas in situ, cancer of the colon is the third most common cancer in adult men, exceeded only by cancer of the lung and prostate. It is the second most common carcinoma in women, being exceeded in incidence only by breast carcinoma. The expected incidence in 1983 for cancer of the colon totals 126,000 new cases with 87,000 cases expected in the colon and 39,000 cases of carcinoma expected in the rectum.<sup>2</sup> Over the past 30 years, the distribution of colonic carcinoma has progressed proximally so that fewer carcinomas occur in the rectum and more carcinomas occur in the cecum.<sup>3</sup> Recent studies show that 12 to 15 percent of colonic cancers are in the rectum, 38 to 42 percent in the rectosigmoid and sigmoid, and the remainder in the more proximal segments of the colon.<sup>4</sup> It is obvious from this distribution that the time-honored methods of rectal examination and rigid sigmoidoscopy for early detection of bowel carcinoma would miss a large number of lesions.

**Table 1. Hereditary Patterns of Colon Cancer**

Polyposis Group	Nonpolyposis Group
Familial polyposis (AD)*	Cancer family syndrome (AD)
Gardner's syndrome (AD)	Site-specific colon cancer (AD)
Turcot's syndrome (AR)**	Gastrocolonic cancer (AD)
Peutz-Jeghers syndrome (AD)	Torres' or Muir's syndrome (AD)
Juvenile polyposis (?)	Sporadic colon cancer (suggested inheritance)
*AD—Autosomal dominant **AR—Autosomal recessive	

The advent of the 35-cm flexible sigmoidoscope and the 60-cm sigmoidoscope has provided means for increasing the detection rate of these tumors.

There appears to be little question that early detection and proper treatment leads to a prolonged five-year survival. From 1970 to 1973, at the time of diagnosis, about 44 percent of patients with colonic cancer had localized lesions (Duke's stage A or B), 26 percent had regional lymph node involvement, and 25 percent had distant metastasis.<sup>2</sup> The five-year survival rate is about 70 percent for localized carcinoma for both men and women, but it decreases sharply as the staging of the disease advances.<sup>5</sup>

An aid to early detection of colonic carcinoma is the identification of populations at greater risk for the disease. Heredity is clearly a significant risk factor. It has been suggested that 20 to 30 percent of colon carcinomas may have a familial basis. The hereditary pattern of colon cancer can be divided into two main groups according to the presence or absence of colonic polyps (Table 1).<sup>6</sup>

The polyposis group consists of often-cited but rare syndromes. If patients with familial polyposis are left untreated, 95 percent develop carcinoma of the colon. Gardner's syndrome is characterized by bone and soft-tissue tumors, colonic polyps, and the occurrence of carcinoma of the colon at an early age. Central nervous system tumors, in association with adenomatous and villous polyps of the colon and a greater than expected incidence

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## NITRO-BID® Ointment (nitroglycerin 2%) BRIEF SUMMARY

**INDICATIONS:** This drug product has been conditionally approved by the FDA for the prevention and treatment of angina pectoris due to coronary artery disease. The conditional approval reflects a determination that the drug may be marketed while further investigation of its effectiveness is undertaken. A final evaluation of the effectiveness of the product will be announced by the FDA.

**CONTRAINDICATIONS:** In patients known to be intolerant of the organic nitrate drugs.

**WARNINGS:** In acute myocardial infarction or congestive heart failure, nitroglycerin ointment should be used under careful clinical and/or hemodynamic monitoring.

**PRECAUTIONS:** Symptoms of hypotension, particularly when suddenly arising from the recumbent position, are signs of overdosage. When they occur, the dosage should be reduced.

**ADVERSE REACTIONS:** Transient headaches are the most common side effect, especially at higher dosages. Headaches should be treated with mild analgesics, and nitroglycerin ointment continued. Only with untreatable headaches should the dosage be reduced. Although uncommon, hypotension, an increase in heart rate, faintness, flushing, dizziness, and nausea may occur. These all are attributable to the pharmacologic effects of nitroglycerin on the cardiovascular system, but are symptoms of overdosage. When they occur and persist, the dosage should be reduced. Occasionally, contact dermatitis has been reported with continuous use of topical nitroglycerin. Such incidence may be reduced by changing the site of application or by using topical corticosteroids.

**DOSAGE AND ADMINISTRATION:** When applying the ointment, place the specially designed Dose Measuring Applicator supplied with the package printed side down and squeeze the necessary amount of ointment from the tube or pouch onto the applicator. Then place the applicator with the ointment side down onto the desired area of skin, usually the chest (although other areas can be used). Spread the ointment over a 6x6-inch (150x150-mm) area in a thin, uniform layer using the applicator. Cover the area with plastic wrap which can be held in place by adhesive tape. The applicator allows the patient to measure the necessary amount of ointment and to spread it without its being absorbed through the fingers while applying it to the skin surface.

The usual therapeutic dose is 2 inches (50 mm) applied every eight hours, although some patients may require as much as 4 to 5 inches (100 to 125 mm) and/or application every four hours.

**TUBE:** Start at ½ inch (12.5 mm) every eight hours and increase the dose by ½ inch (12.5 mm) with each successive application to achieve the desired clinical effects. The optimal dosage should be selected based upon the clinical response, side effects, and the effects of therapy upon blood pressure. The greatest attainable decrease in resting blood pressure which is not associated with clinical symptoms of hypotension, especially during orthostasis, indicates the optimal dosage. To decrease adverse reactions, the dose and frequency of application should be tailored to the individual patient's needs.

Keep the tube tightly closed and store at room temperature 59° to 86°F (15° to 30°C).

**FOIL POUCH:** The 1-gram foil pouch is approximately equivalent to one inch as squeezed from a tube and is designed to be used in increments of one inch. Apply the ointment by squeezing the contents of the pouch onto a specially designed Dose Measuring Applicator supplied with the package printed side down.

**PATIENT INSTRUCTIONS FOR APPLICATION:** Information furnished with Dose Measuring Applicators.

**HOW SUPPLIED:** NITRO-BID® Ointment is available in 20-gram and 60-gram UNI-Rx® Paks (six tubes per pack); in individual 20-gram, 60-gram, and 100-gram tubes; and in Unit Dose Identification Paks of 100 1-gram foil pouches.

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## COLONIC POLYPS AND CANCER

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of carcinoma of the colon, characterizes Turcot's syndrome. The Peutz-Jeghers syndrome is now believed to be associated with an increased number of adenomatous polyps as well as a greater than expected incidence of carcinoma of the colon. Juvenile polyposis, also once thought to be relatively benign, is now believed to predispose to an increased incidence of carcinoma of the colon.

The nonpolyposis group contains common syndromes, and every family physician will undoubtedly encounter patients in this group. The cancer family syndrome is characterized by a high incidence of adenocarcinoma of the proximal colon, endometrial carcinoma, and multiple other carcinomas. Carcinomas occur at a young age in this group. Site-specific colon cancer refers to the occurrence of proximal bowel carcinoma, again occurring at a young age. Gastrocolonic syndrome refers to the occurrence of adenocarcinoma of the stomach and colon in the same family. Torres' syndrome is the occurrence of multiple sebaceous cysts and adenocarcinomas in the same patient. Sporadic colon cancer is the entity family physicians most frequently encounter. The risk of colon cancer developing in a first-degree relative of an individual with known colon cancer is three times greater than the risk in the general population.

Other risk factors believed to play a role in cancer of the colon include an age of 40 years or over; dietary factors including a high fat, high animal protein, and low fiber content; and a high concentration of bile salts in the gut lumen and the bacterial flora of the gut. Occupational exposure to asbestos, presence of ulcerative colitis or other inflammatory bowel disease, and a previous history of adenoma or cancer of the colon all increase risk for the development of cancer of the colon.<sup>7</sup>

**DR. STEINER:** Dr. Peterson, please review the x-ray examinations of the two cases and comment on the radiologic issues in detection and evaluation of colonic masses.

**DR. GARY PETERSON, MD** (*Associate Professor, Department of Diagnostic Radiology*): These two patients had different types of colon examination. R.W. had a good-quality, double-contrast study that revealed three colonic polyps. Two of these were fairly large, in the range of 1.5 cm. The third was quite small. The two larger polyps were not sessile and had no direct signs of malignancy.



The second patient, J.R., was examined at another hospital using the conventional, full-column technique. A large, broad-based sigmoid mass was seen only on the early spot films taken during fluoroscopy. None of the overhead films, obtained after the colon was filled, showed any abnormality. The mass had extensive surface irregularity, suggesting a villous component.

In these patients, both types of examinations demonstrated the pathology, but this is not always the case. Most radiologists now agree that the double-contrast barium enema is far superior for detection of polyps and cancer of the colon, as well as inflammatory bowel disease. In one comparative study,<sup>8</sup> the detection rate of polyps 1.0 cm or larger was 60 percent using full-column techniques. This rate rose to 96 percent with double-contrast examinations.

Regardless of the examination performed, the single most important factor is the adequacy of patient preparation. The radiologist must assume the responsibility for bowel preparation for his patients. Our department uses a combination of senna (X-Prep) and castor oil, which produces a rather unpleasant but thorough catharsis. Maximum hydration of the patient is especially important to improve effectiveness of the preparation and to compensate for water loss. We also insist that patients be placed on a clear liquid diet from no later than noon the day before the study. Compliance with this regimen significantly increases the quality of the examination by reducing false-positive and false-negative results caused by fecal debris.

While the location of the polyp is of little clinical value, its appearance can sometimes help in predicting the likelihood of its being malignant.<sup>9</sup> Polyps on a stalk are far more likely to be benign than cancerous, but they must be removed for confirmation. Occasionally, a polyp or polypoid lesion will show evidence of dimpling or actual invasion of the colonic wall. This is an ominous sign and is suggestive of malignancy. Size is the most important factor, as increasing polyp size is known to increase malignant potential.

The air-contrast barium enema requires more time from the radiologist, more radiation exposure, more patient discomfort, and about \$15 additional expense compared with the full-column barium enema. The results of any radiologic examination are operator dependent so that the training and expertise of the radiologist is one important

aspect of an air-contrast barium enema. A frequently neglected item concerning air-contrast barium enemas is the requirement that the patient be cooperative and moveable. Too often, the elderly, disabled patient is sent for an air-contrast barium enema for the evaluation of rectal bleeding when a full-column barium enema would actually serve the patient's purpose much better. Community physicians should always strive to match the requested procedure with the suspected diagnosis with an eye to the particular limitations of the patient.

DR. ROBERT P. KRAFT, JR (*Gastroenterologist*): The American Cancer Society recommends that patients over the age of 50 years have a sigmoidoscopy performed every three years to screen for cancer of the distal colon and rectum. Patients who are in high-risk groups may need to be screened on a more frequent basis from an earlier age. A barium enema examination is essential to rule out possible neoplasm of the proximal colon in those patients who are in a high-risk group or those who have a stool that is positive for occult blood along with a negative sigmoidoscopic examination. Colonoscopy is not used as a screening procedure in most patients; rather, it is used to gain more information on a lesion suggested by barium enema or in selected individuals at high risk for colonic neoplasms. Some of the indications for colonoscopy are as follows: follow-up examination of patients who have a lesion seen on barium enema, biopsy, or removal of colonic polyps; evaluation of inflammatory bowel disease; evaluation of diarrhea; localizing the source of either occult or gross bleeding; follow-up examination of patients with prior colonic surgery for neoplasms; and evaluation of patients with abdominal symptoms suggesting colorectal disease.

To perform an optimal examination of the colon, the bowel must be clean and empty. If the patient is poorly prepared, the ability of the endoscopist to visualize the colon is limited, and advancement of the colonoscope becomes both difficult and risky for the patient. The patient may be prepared as if he were having a barium enema. A newer and more rapid technique for cleansing the bowel includes the use of a lavage solution administered orally in adequate volumes to induce diarrhea. Currently, the most accepted solution is called Go-Lytely.<sup>10</sup> This solution contains sodium

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# NAPROSYN<sup>®</sup>

(naproxen) available in 250 mg, 375 mg, 500 mg tablets.

COLONIC POLYPS AND CANCER

**Brief Summary: Contraindications:** The drug is contraindicated in patients who have had allergic reactions to NAPROSYN<sup>®</sup> (naproxen) or to ANAPROX<sup>®</sup> (naproxen sodium). Do not give to patients in whom aspirin or other nonsteroidal anti-inflammatory/analgesic drugs induce the syndrome of asthma, rhinitis, and nasal polyps. Both types of reactions have the potential of being fatal. **Warnings:** Gastrointestinal bleeding, sometimes severe, and occasionally fatal, has been reported in patients receiving the drug. Among 960 patients treated for rheumatoid arthritis or osteoarthritis, 16 cases of peptic ulceration were reported. More than half were on concomitant corticosteroid and/or salicylate therapy and about a third had a prior history of peptic ulcer. Gastrointestinal bleeding, including nine potentially serious cases, was also reported. These were not always preceded by premonitory gastrointestinal symptoms. Although most of the patients with serious bleeding were receiving concomitant therapy and had a history of peptic ulcer disease, the drug has the potential for causing gastrointestinal bleeding on its own. Administer to patients with active gastric and duodenal ulcers only under close supervision. **Precautions: General: NAPROSYN<sup>®</sup> [NAPROXEN] SHOULD NOT BE USED CONCOMITANTLY WITH THE RELATED DRUG ANAPROX<sup>®</sup> [NAPROXEN SODIUM] SINCE THEY BOTH CIRCULATE IN PLASMA AS THE NAPROXEN ANION.** Because anaphylactic reactions usually occur in patients with a history of such reactions, question patients for such things as asthma, nasal polyps, urticaria, and hypotension associated with NSAIDs before starting therapy. If such symptoms occur, discontinue the drug. In chronic studies in laboratory animals, the drug has caused nephritis. Glomerular nephritis, interstitial nephritis and nephrotic syndrome have been reported. Use with great caution in patients with significantly impaired renal function. Monitoring of serum creatinine and/or creatinine clearance is advised in these patients. Certain patients, including those with compromised renal blood flow and some elderly in whom impaired renal function may be expected, should have renal function assessed before and during therapy. Consider reducing daily dosage in these patients. With NSAIDs borderline elevations of liver tests may occur in up to 15% of patients. They may progress, remain unchanged, or be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Elevations (3 times the upper limit of normal) of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Evaluate patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, for evidence of more severe hepatic reaction. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported rarely. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia or rash), discontinue therapy. If steroid dosage is reduced or eliminated during therapy, do so slowly and observe patients closely for adverse effects, including adrenal insufficiency and exacerbation of arthritis symptoms. Determine hemoglobin values frequently for patients with initial values of 10 grams or less who receive long-term therapy. Peripheral edema has been observed in some patients. Each tablet contains approximately 25 mg (1 mEq) sodium, which should be considered in patients whose overall intake of sodium must be markedly restricted. Use with caution in patients with fluid retention, hypertension or heart failure. The antipyretic and anti-inflammatory activities of the drug may reduce fever and inflammation, thus diminishing their utility as diagnostic signs. Conduct ophthalmic studies soon after starting therapy and at periodic intervals if the drug is used for an extended period. **Information for Patients:** Caution should be exercised by patients whose activities require alertness if they experience drowsiness, dizziness, vertigo or depression during therapy. **Drug Interactions:** Naproxen anion may displace other albumin-bound drugs from their binding sites and could likewise be displaced itself. Studies failed to show that the drug significantly affects prothrombin times when administered to individuals on coumarin-type anticoagulants, but use caution since interactions have been seen with other nonsteroidal agents of this class. Observe patients receiving the drug and a hydatantoin, sulfonamide or sulfonylurea for signs of toxicity to these drugs. Some drugs of this class inhibit the natriuretic effect of furosemide. Increased plasma lithium due to inhibition of renal lithium clearance has been reported. This drug and other NSAIDs can reduce the antihypertensive effect of beta-blockers. Probenecid given concurrently increases naproxen anion plasma levels and extends its plasma half-life significantly. **Drug/Laboratory Test Interactions:** The drug may decrease platelet aggregation and prolong bleeding time. The drug may result in increased urinary values for 17-ketogenic steroids because of an interaction between the drug and/or its metabolites with m-dinitrobenzene used in this assay. Temporarily discontinue therapy with the drug for 72 hours before adrenal function tests are performed. The drug may interfere with some urinary assays of 5-hydroxy indoleacetic acid (5-HIAA). **Carcinogenesis:** A two-year study in rats to evaluate the carcinogenic potential of the drug showed no evidence of carcinogenicity. **Pregnancy:** Teratogenic Effects: Pregnancy Category B. Do not use during pregnancy unless clearly needed. Avoid use during late pregnancy. Non-teratogenic Effects: In rats, pregnancy was prolonged when the drug was given before the onset of labor; labor was protracted when the drug was given after labor had begun. **Nursing Mothers:** Avoid use in nursing mothers. **Pediatric Use:** Pediatric indications and dosage recommendations have not been established. **Adverse Reactions: Incidence Greater Than 1%: Gastrointestinal:** The most frequent complaints related to the gastrointestinal tract: constipation,\* heartburn,\* abdominal pain,\* nausea,\* dyspepsia, diarrhea, stomatitis. **Central Nervous System:** Headache,\* dizziness,\* drowsiness,\* lightheadedness, vertigo. **Dermatologic:** Itching (pruritus),\* skin eruptions,\* ecchymoses,\* sweating, purpura. **Special Senses:** Tinnitus,\* hearing disturbances, visual disturbances. **Cardiovascular:** Edema,\* dyspnea,\* palpitations. **General:** Thirst. \*Incidence of reported reaction 3%-9%. Reactions seen in less than 3% of the patients are unmarked. **Incidence Less Than 1%: Probable Causal Relationship:** The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions: Abnormal liver function tests, gastrointestinal bleeding, hematemesis, jaundice, melena, peptic ulceration with bleeding and/or perforation, vomiting, glomerular nephritis, hematuria, interstitial nephritis, nephrotic syndrome, renal disease, eosinophilia, granulocytopenia, leukopenia, thrombocytopenia, depression, dream abnormalities, inability to concentrate, insomnia, malaise, myalgia and muscle weakness, alopecia, skin rashes, hearing impairment, congestive heart failure, anaphylactoid reactions, menstrual disorders, pyrexia (chills and fever). **Causal Relationship Unknown:** Other reactions have been reported in circumstances in which a causal relationship could not be established. However, in these rarely reported events, the possibility cannot be excluded. Therefore these observations are being listed to serve as alerting information to the physicians: agranulocytosis, aplastic anemia, hemolytic anemia, urticaria, angioneurotic edema, hyperglycemia, hypoglycemia. **Overdosage:** Threatening dose is not known. If patient ingests many tablets, empty stomach and employ usual supportive measures. Animal studies suggest that the prompt administration of 5 grams of activated charcoal would tend to reduce markedly drug absorption. It is not known if the drug is dialyzable. **Caution:** Federal law prohibits dispensing without prescription. See package insert for full prescribing information. August 1983 Rev. 24

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salts, magnesium chloride, and polyethylene glycol, is isotonic, and because polyethylene glycol is a nonabsorbable solute, causes no flux of water either into or out of the intestinal lumen. The solution is administered at the rate of 1,000 mL/h and is continued until the patient has developed diarrhea; the infusion is stopped when the diarrhea becomes clear. Metaclopramide may be given with Go-Lytely to accelerate gastric emptying of the solution. Residual fluid, which commonly remains in the colon after this preparation, can be removed with the colonoscope. This bowel preparation is not suitable for barium enemas as fluid retention will dilute the barium within the colon.

Colonoscopy is a procedure best performed in the hospital but may be done on an outpatient basis. The patient is usually placed in the left lateral decubitus position with the knees and hips flexed. This position, rather than the prone knee-chest position used in standard rigid sigmoidoscopy, is preferred for performing colonoscopy.

The diagnostic yield of fiberoptic sigmoidoscopy has been compared with both rigid sigmoidoscopy and barium enema.<sup>11</sup> Using the long (60 cm) flexible fiberoptic sigmoidoscope, the diagnosis rate is approximately three times that of the rigid 25-cm sigmoidoscope. The detection rate for both benign polyps and malignancies is increased by using the long flexible sigmoidoscope. The amount of time for the procedure using the long scope is only slightly longer than procedure time using the rigid proctosigmoidoscopy. Polls of patient preference indicate that the flexible sigmoidoscopic examination is more comfortable than that using the rigid 25-cm sigmoidoscope.

The flexible sigmoidoscope and colonoscope afford the physician the opportunity to perform electrosurgical polypectomy. Visualization of masses is superior with the flexible instrument, and lesions beyond the 25-cm mark can be successfully removed. Any pedunculated polyp the size of which is less than that of the snare can be successfully removed with the colonoscope. Larger lesions, obviously, must be surgically removed. There is present controversy over whether large sessile polyps should be endoscopically removed in a piecemeal fashion or removed by colectomy.

The complication rate with colonoscopy is low. A poll of members of the American Society for Gastrointestinal Endoscopy showed a morbidity



rate of 0.32 percent and a mortality rate of 0.008 percent with the use of colonoscope for diagnostic purposes.<sup>12</sup> Surgical procedures with the colonoscope raised morbidity to 1.0 to 2.5 percent, with complications such as hemorrhage being slightly more common than that of perforation. The risk to the patient is considerably higher with untrained endoscopists. Most complications will occur during the training period of the endoscopist, especially during the first 40 to 50 procedures. Potential complications include hematoma of the intestine and explosion. Explosion may occur in patients who have been inadequately prepared, causing methane gas to be retained in the colon. The use of bowel preparations containing mannitol may also increase the methane content within the bowel.

The development of the fiberoptic sigmoidoscopy and colonoscopy has improved the detection and treatment of diseases of the lower gastrointestinal tract. Family practice residency programs should encourage proper training sessions for the residents and faculty in the use of the fiberoptic sigmoidoscope.

DR. STEINER: The family physician should be aware that there are many classifications of colonic polyps. Polyps can be classified as neoplastic and nonneoplastic. The nonneoplastic group consists of hyperplastic polyps, inflammatory pseudopolyps, hamartomas, and lipomas. The neoplastic polyps are customarily grouped into mainly adenomatous and mainly villous types. Although most cancers of the colon arise as adenomas, it should be remembered that the majority of adenomas never develop into cancer.<sup>13</sup>

DR. HERBERT DICKSTEIN (*Clinical Associate Pathologist*): The biopsy specimen from the second patient, J.R., shows a polyp composed of adenomatous glands that become tortuous and show cellular changes regarded as atypical. The specimen from the colon resection was a 2.5×2.0-cm pedunculated polyp. Microscopic examination demonstrates that elongated villous areas are present in addition to the adenomatous glands. The stalk shows no invasion. This polyp was classified as a villous and glandular adenoma with atypia.

The biopsy from R.W., the first patient, shows a polyp composed of hyperplastic columnar mucosal glands. There is no infiltration of the lamina propria.

Histopathologic features of polyps are useful in

the assessment of the malignant potential of a lesion.<sup>14</sup> The hyperplastic mucosal polyp, composed of colonic mucosal glands, is benign, and is sometimes found in association with carcinoma in other areas of the bowel. The adenomatous polyp, with its tortuous glandular configuration, is generally benign. If severe atypia is found, the pathologist may interpret changes as carcinoma in situ. If the stalk shows no invasion, then the prognosis after removal is excellent. However, there are occasional reports of adenomatous polyps with carcinoma with no invasion of the stalk associated with metastasis to a regional lymph node.<sup>15</sup> Polyps with a villous component have a high malignant potential, with the pure villous adenomas having the highest incidence of becoming malignant. It is estimated that 40 to 50 percent of mainly villous polyps will become malignant.

In summary, the first patient, R.W., has a benign lesion and should have an excellent prognosis. However, the second patient, J.R., has a good prognosis as the present lesion was completely removed, but because of the presence of villous features, the patient should be followed closely.

DR. HOLTZAPPLE: Having identified groups at greater risk for carcinoma of the colon, we then need a sensitive and specific screening tool to identify premalignant lesions such as polyps and early cancers. It was noted earlier that rectal examination will detect relatively few lesions. Rigid sigmoidoscopy, while capable of detecting a greater number of lesions, has never gained wide acceptance with either physicians or patients as a screening tool. It should be mentioned, however, that in populations where it has been used, there has been a significant reduction in mortality from carcinoma of the rectosigmoid.<sup>16</sup>

Since the late 1960s detection of occult blood in the stool has been touted as a screening tool for early detection of colorectal carcinoma and premalignant lesions. The best controlled studies of screening for colorectal cancer with stool occult blood suggest the following: (1) testing for occult blood in stool is more likely to detect cancer than precancerous lesions such as adenomas, although the latter do frequently produce occult bleeding when greater than 2.0 cm in size, (2) cancers detected by occult blood testing are more often localized (Duke's stage A and B) than not, and (3) occult blood testing and proctosigmoidoscopy are

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# SINEQUAN® (doxepin HCl)

COLONIC POLYPS AND CANCER

Reference: 1. Barranco SF, Thrash ML, Hackett E, Frey J, et al (Pfizer Pharmaceuticals, Pfizer Inc., New York, N.Y.): Early onset of response to doxepin treatment. *J Clin Psychiatry* 40:265-269, 1979.

## BRIEF SUMMARY

### SINEQUAN® (doxepin HCl) Capsules/Oral Concentrate

**Contraindications.** SINEQUAN is contraindicated in individuals who have shown hypersensitivity to the drug. Possibility of cross sensitivity with other dibenzoxepines should be kept in mind.

SINEQUAN is contraindicated in patients with glaucoma or a tendency to urinary retention. These disorders should be ruled out, particularly in older patients.

**Warnings.** The once-a-day dosage regimen of SINEQUAN in patients with intercurrent illness or patients taking other medications should be carefully adjusted. This is especially important in patients receiving other medications with anticholinergic effects.

**Usage in Geriatrics:** The use of SINEQUAN on a once-a-day dosage regimen in geriatric patients should be adjusted carefully based on the patient's condition.

**Usage in Pregnancy:** Reproduction studies have been performed in rats, rabbits, monkeys and dogs and there was no evidence of harm to the animal fetus. The relevance to humans is not known. Since there is no experience in pregnant women who have received this drug, safety in pregnancy has not been established. There are no data with respect to the secretion of the drug in human milk and its effect on the nursing infant.

**Usage in Children:** The use of SINEQUAN in children under 12 years of age is not recommended because safe conditions for its use have not been established.

**MAO Inhibitors:** Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Therefore, MAO inhibitors should be discontinued at least two weeks prior to the cautious initiation of therapy with SINEQUAN. The exact length of time may vary and is dependent upon the particular MAO inhibitor being used, the length of time it has been administered, and the dosage involved.

**Usage with Alcohol:** It should be borne in mind that alcohol ingestion may increase the danger inherent in any intentional or unintentional SINEQUAN overdose. This is especially important in patients who may use alcohol excessively.

**Precautions.** Since drowsiness may occur with the use of this drug, patients should be warned of the possibility and cautioned against driving a car or operating dangerous machinery while taking the drug. Patients should also be cautioned that their response to alcohol may be potentiated.

Since suicide is an inherent risk in any depressed patient and may remain so until significant improvement has occurred, patients should be closely supervised during the early course of therapy. Prescriptions should be written for the smallest feasible amount.

Should increased symptoms of psychosis or shift to manic symptomatology occur, it may be necessary to reduce dosage or add a major tranquilizer to the dosage regimen.

**Adverse Reactions. NOTE:** Some of the adverse reactions noted below have not been specifically reported with SINEQUAN use. However, due to the close pharmacological similarities among the tricyclics, the reactions should be considered when prescribing SINEQUAN.

**Anticholinergic Effects:** Dry mouth, blurred vision, constipation, and urinary retention have been reported. If they do not subside with continued therapy, or become severe, it may be necessary to reduce the dosage.

**Central Nervous System Effects:** Drowsiness is the most commonly noticed side effect. This tends to disappear as therapy is continued. Other infrequently reported CNS side effects are confusion, disorientation, hallucinations, numbness, paresthesias, ataxia, and extrapyramidal symptoms and seizures.

**Cardiovascular:** Cardiovascular effects including hypotension and tachycardia have been reported occasionally.

**Allergic:** Skin rash, edema, photosensitization, and pruritus have occasionally occurred.

**Hematologic:** Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression manifesting as agranulocytosis, leukopenia, thrombocytopenia, and purpura.

**Gastrointestinal:** Nausea, vomiting, indigestion, taste disturbances, diarrhea, anorexia, and aphthous stomatitis have been reported. (See anticholinergic effects.)

**Endocrine:** Raised or lowered libido, testicular swelling, gynecomastia in males, enlargement of breasts and galactorrhea in the female, raising or lowering of blood sugar levels have been reported with tricyclic administration.

**Other:** Dizziness, tinnitus, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice, alopecia, and headache have been occasionally observed as adverse effects.

**Dosage and Administration.** For most patients with illness of mild to moderate severity, a starting daily dose of 75 mg is recommended. Dosage may subsequently be increased or decreased at appropriate intervals and according to individual response. The usual optimum dose range is 75 mg/day to 150 mg/day.

In more severely ill patients higher doses may be required with subsequent gradual increase to 300 mg/day if necessary. Additional therapeutic effect is rarely to be obtained by exceeding a dose of 300 mg/day.

In patients with very mild symptomatology or emotional symptoms accompanying organic disease, lower doses may suffice. Some of these patients have been controlled on doses as low as 25-50 mg/day.

The total daily dosage of SINEQUAN may be given on a divided or once-a-day dosage schedule. If the once-a-day schedule is employed the maximum recommended dose is 150 mg/day. This dose may be given at bedtime. **The 150 mg capsule strength is intended for maintenance therapy only and is not recommended for initiation of treatment.**

Anti-anxiety effect is apparent before the antidepressant effect. Optimal antidepressant effect may not be evident for two to three weeks.

## Overdosage.

### A. Signs and Symptoms

1. Mild: Drowsiness, stupor, blurred vision, excessive dryness of mouth.
2. Severe: Respiratory depression, hypotension, coma, convulsions, cardiac arrhythmias and tachycardias.

Also: urinary retention (bladder atony), decreased gastrointestinal motility (paralytic ileus), hyperthermia (or hypothermia), hypertension, dilated pupils, hyperactive reflexes.

### B. Management and Treatment

1. Mild: Observation and supportive therapy is all that is usually necessary.
2. Severe: Medical management of severe SINEQUAN overdose consists of aggressive supportive therapy. If the patient is conscious, gastric lavage, with appropriate precautions to prevent pulmonary aspiration, should be performed even though SINEQUAN is rapidly absorbed. The use of activated charcoal has been recommended, as has been continuous gastric lavage with saline for 24 hours or more. An adequate airway should be established in comatose patients and assisted ventilation used if necessary. EKG monitoring may be required for several days, since relapse after apparent recovery has been reported. Arrhythmias should be treated with the appropriate antiarrhythmic agent. It has been reported that many of the cardiovascular and CNS symptoms of tricyclic antidepressant poisoning in adults may be reversed by the slow intravenous administration of 1 mg to 3 mg of physostigmine salicylate. Because physostigmine is rapidly metabolized, the dosage should be repeated as required. Convulsions may respond to standard anticonvulsant therapy, however, barbiturates may potentiate any respiratory depression. Dialysis and forced diuresis generally are not of value in the management of overdose due to high tissue and protein binding of SINEQUAN.

More detailed professional information available on request.

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complementary screening procedures.<sup>16</sup> Slides impregnated with guaiac are most commonly used for the detection of occult blood in the stool. Most physicians are familiar with the product Hemoccult.

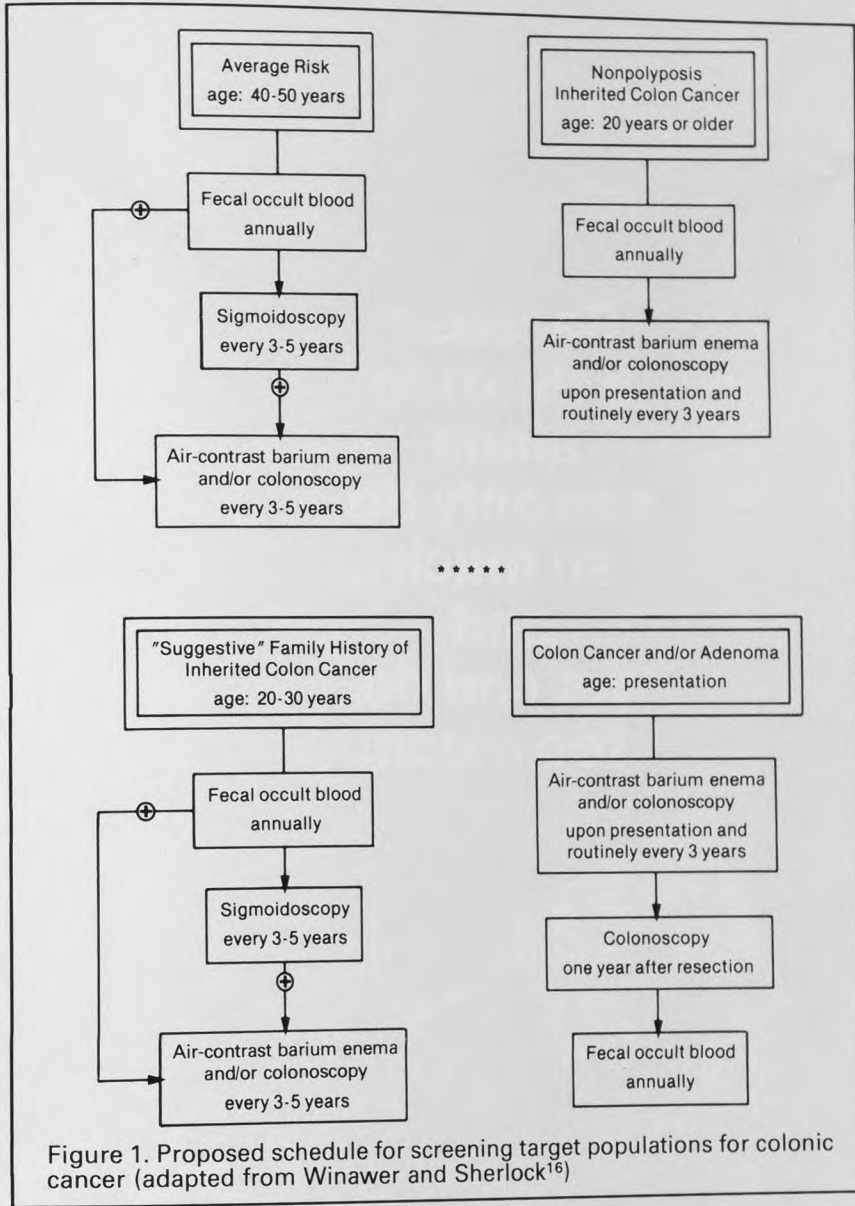
Using recent evidence regarding the value of a low-peroxidase diet,<sup>17</sup> an optimal protocol for stool occult blood screening is as follows: before collecting the first stool specimen, adherence to a diet for 24 to 48 hours that contains no red meat, but permits chicken, pork, ham, bacon, or white fish; no uncooked fruit, except for oranges or strawberries; no uncooked vegetables; and no vitamin C supplements. The use of bran cereals or Metamucil to increase fiber content should be encouraged. This diet should be continued until the patient has prepared two slides from the stools on each of three consecutive days. All slides should be rehydrated, as this significantly improves yield. All bluish reactions are interpreted as positive; all others as negative. A single positive slide has the same significance as multiple positive slides.

Linking the information about populations at risk with our current knowledge of screening tools, the protocols charted in Figure 1<sup>16</sup> are recommended for the early detection of premalignant or malignant lesions of the colon.

DR. STEINER: The panel members have provided a comprehensive and up-to-date presentation on many aspects of colonic polyps, colonic cancer, and colonoscopy. The family physician should be aware that family history of cancer and colonic lesions is an important factor for selecting appropriate screening procedures. These protocols should help eliminate much of the low-yield repetition and cost of some screening tests while maintaining high early detection rates in the at-risk population. Training family physicians to use the fiberoptic sigmoidoscope will help provide optimal care for patients.

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