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# Family Practice Grand Rounds

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## Upper Gastrointestinal Bleeding in the Elderly

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DR. JIM WILSON (*Associate Professor, Department of Family Practice*): Our focus this morning is on hemorrhage in the upper gastrointestinal tract in an elderly patient, centering on a patient who was hospitalized recently on the family practice service with massive upper gastrointestinal bleeding (UGIB) secondary to duodenal ulcers. We will review some epidemiological data on this problem in the elderly that was gathered from recent literature, and we will also discuss its management, especially with reference to fiberoptic esophagogastroduodenoscopy (EGD).

DR. EDWIN POWELL (*Second-year family practice resident*): Admitted to the University of South Alabama Medical Center for the first time, this 72-year-old white retired grandfather from Mobile had been well until one week prior to admission, when he developed vague, viral-like symptoms and signs, including nausea, vomiting, and

occasional diarrhea. During that time, he noticed one episode of hematochezia and subsequent melena. The patient also reported a 5-lb weight loss over the last two to three months and recently had become anorexic. He denied any changes in daily bowel habits or consistency of stools. He also denied a history of peptic ulcer disease. He was seen at the Family Practice Center on the day of admission.

The patient stated that he had been healthy most of his life. He had a tonsillectomy at the age of 16 years, but had not seen a physician regularly since. His last visit to a physician had occurred several years prior to admission. He was taking no prescribed medication and had taken no over-the-counter medication on a regular basis. He was allergic only to tetanus toxoid. His family history revealed that his mother had a history of pseudo-diverticulosis coli and died at age 82 of congestive heart failure. His father had diabetes and died of a stroke. The patient gave a smoking history of greater than 50 pack-years and claimed only occasional ethanol use. His review of systems was noncontributory.

On physical examination he was noted to be a thin, frail-looking man in no acute distress who appeared to be his stated age. His temperature was

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97° F, pulse was 105 beats/min, respirations were 12/min, blood pressure was 100/60 mmHg without postural changes. Examination of the head, ears, eyes, nose, and throat yielded benign results except that the mucous membranes were pale. Examination of the cardiovascular and respiratory systems was normal and the abdominal examination was unremarkable. Rectal examination revealed an enlarged prostate and black stool, which was positive for occult blood. There were no masses in the rectum. The remainder of the physical examination was unremarkable.

Admission electrocardiogram and chest roentgenogram were within normal limits. Admission complete blood count revealed a hemoglobin level of 7.9 g/dL, hematocrit of 23 percent, and a normal white cell count and differential. The only blood chemistry abnormalities were alkaline phosphatase, which was elevated to 471 U/L, and gamma-glutamyltranspeptidase elevated to 294 U/L. The initial diagnostic impression was UGIB probably secondary to peptic ulcer disease, but gastrointestinal neoplasm was also considered. Upon admission the patient was given a transfusion with two units of packed cells. On the morning following admission an upper gastrointestinal series showed multiple antral ulcers. Later that same day the patient was given another two units of packed red blood cells. The following day EGD revealed active duodenal peptic ulcer disease and marked pyloroduodenal deformity with partial obstruction. Gastric acid analysis and serum gastrin determinations were obtained and later were reported as normal. Antacid and cimetidine therapy was recommended.

The patient's condition stabilized until the sixth hospital day. At morning rounds the nurses mentioned that he had fallen earlier that morning in his room. He was noted to be less talkative and less alert than usual. He was found to be hypotensive with a blood pressure of 80/50 mmHg. A hematocrit determination was 17 percent. He was transferred to the medical intensive care unit, transfused with more blood, and monitored hemodynamically using a Swan-Ganz catheter. He was transferred to the surgery service with plans for operative intervention as soon as his condition was stabilized.

At operation an exploratory celiotomy with truncal vagotomy, antrectomy, and Billroth II gastrojejunostomy was performed. During the proce-

dures, periodic hypotension was manifest, but responded well to fluid administration. Incidental splenectomy was required because of intraoperative trauma, and generalized tissue friability was observed during the operation.

In spite of these difficulties the immediate postoperative course was uneventful, and a water-soluble contrast upper gastrointestinal series on the fourth postoperative day showed no extravasation from the anastomosis. However, the drain in the subhepatic space continued to have greater than expected amounts of bilious drainage, and a duodenocutaneous fistula was diagnosed on the ninth postoperative day. The fistula was the major factor that prolonged this patient's hospitalization. Total parenteral nutrition was instituted early in the postoperative course and was continued until the patient's oral intake was adequate and the fistula healed. He was transferred from the surgical intensive care unit to the floor on the 12th postoperative day.

On the 47th hospital day he was discharged to an extended-care facility to recuperate for another two weeks. Following this he was discharged to the home of his daughter, where his recovery has been gradual but steady. After several months he has regained his prehospital status.

**DR. WILSON:** Upper gastrointestinal bleeding is a commonly encountered problem in clinical practice. Although technological advances have improved our ability to monitor patients and to provide medical and surgical intensive care, overall mortality, reported at approximately 10 percent, has remained unchanged. Why should this be so? Has the condition changed or has the patient population changed?

In England, Schiller et al<sup>1</sup> studied during a 15-year period 2,149 emergency admissions to hospitals due to hematemesis or melena. During that time no major changes were noted in the sex ratio, age distribution, or diagnostic categories encountered. A number of factors, however, including the age of the patient and the underlying diagnosis, affected the patient's prognosis. The mortality rate remained unchanged during the study period.

In another study reported from England, Allan and Dykes<sup>2</sup> reviewed a series of articles on UGIB reported in the European literature since 1900. A striking and steady increase in the proportion of older patients was noted in these studies. In addi-

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**Table 1. Clinical Prognostic Factors in Upper Gastrointestinal Bleeding From the National American Society of Gastrointestinal Endoscopy Survey of Patients Aged 2 to 96 Years (n = 2,225)**

Mortality	Percentage
Overall	10.8
Patients less than 60 years	8.7
Patients greater than 60 years	13.4
Patients who bled before admission	7.1
Patients who bled during hospitalization	13.4
Patients with clear nasogastric aspirate and brown stools	8.0
Patients with red nasogastric aspirate and red blood in stools	30.0

From Silverstein et al<sup>3</sup>

tion, these authors conducted a prospective study of 300 patients admitted for hematemesis or melena. They found that the risk for developing a hemorrhage from the upper gastrointestinal tract was greater for the older age group (60 years and older), and that mortality was greater in the older population (4 deaths in 157 patients younger than 60 years vs 25 deaths in 143 patients over 60 years).

In the United States a study was recently conducted by the American Society of Gastrointestinal Endoscopy (ASGE).<sup>3</sup> From May 1978 through October 1979, 269 members of that organization were surveyed and submitted information on at least five consecutive patients referred to them for evaluation of UGIB. A large volume of data on 2,225 patients was collected, some of which is shown in Table 1. Mortality for patients older than 60 years was significantly higher than for patients younger than 60 years. A dramatic increase in mortality was also noted as the number of disease categories per patient increased. Congestive heart failure and cardiac arrhythmias were associated with increased mortality, whereas hypertension and angina were not. Encephalopathy, stroke,

**Table 2. Endoscopic Findings in 2,097 Patients From the National American Society of Gastrointestinal Endoscopy Survey\***

Finding	Percentage
Gastric erosion	29.6
Duodenal ulcer	22.8
Gastric ulcer	21.9
Varices	15.4
Esophagitis	12.8
Erosive duodenitis	9.1
Mallory-Weiss syndrome	8.0
Other	15.6

\*Some patients had more than one type of lesion  
From Silverstein et al<sup>3</sup>

liver disease, renal disease, chronic obstructive pulmonary disease, and pneumonia were also associated with increased mortality. A listing of the diagnoses found at EGD and frequencies of each are shown in Table 2.

The ASGE data were collected on patients of all age groups. In searching the literature, only a few studies of UGIB dealing specifically with the elderly were discovered. Antler and colleagues<sup>4</sup> prospectively evaluated 136 consecutive patients with UGIB during July 1976 and October 1978. For purposes of comparison, this group of patients was divided into three age groups: young (23 to 34 years), middle aged (40 to 54 years), and elderly (55 years and older). The site of bleeding was determined by EGD. Among the differences noted were the more common occurrence of peptic ulcer disease in the group of elderly patients (duodenal ulcer was twice as common in the elderly compared with the young) and the more common occurrence of hemorrhagic gastritis in the group of young patients. Although the mortality rate for the older group of patients was substantially higher, the difference was not statistically significant. Mortality rates with respect to the bleeding site also revealed some interesting differences. For example, there was a 41 percent mortality rate among the patients in the elderly group who had gastric ulcer, where-

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## Motrin® Tablets (ibuprofen)

**Contraindications:** Anaphylactoid reactions have occurred in individuals hypersensitive to Motrin Tablets or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin, iodides, or other nonsteroidal anti-inflammatory agents.

**Warnings:** Peptic ulceration and GI bleeding, sometimes severe, have been reported. Ulceration, perforation and bleeding may end fatally. An association has not been established. Use Motrin Tablets under close supervision in patients with a history of upper gastrointestinal tract disease, after consulting ADVERSE REACTIONS. In patients with active peptic ulcer and active rheumatoid arthritis, try nonulcerogenic drugs, such as gold. If Motrin Tablets are used, observe the patient closely for signs of ulcer perforation or GI bleeding.

Chronic studies in rats and monkeys have shown mild renal toxicity with papillary edema and necrosis. Renal papillary necrosis has rarely been shown in humans treated with Motrin Tablets.

**Precautions:** Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin Tablets and the patient should have an ophthalmologic examination, including central visual fields and color vision testing.

**Fluid retention and edema** have been associated with Motrin Tablets; use with caution in patients with a history of cardiac decompensation or hypertension. In patients with renal impairment, reduced dosage may be necessary. Prospective studies of Motrin Tablets safety in patients with chronic renal failure have not been done.

Motrin Tablets can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, skin rash, weight gain, or edema.

Patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin Tablets are added.

The antipyretic, anti-inflammatory activity of Motrin Tablets may mask inflammation and fever.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Meaningful elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other nonsteroidal anti-inflammatory drugs. If liver disease develops or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), Motrin should be discontinued.

**Drug interactions.** Aspirin: used concomitantly may decrease Motrin blood levels.

Coumarin: bleeding has been reported in patients taking Motrin and coumarin.

**Pregnancy and nursing mothers:** Motrin should not be taken during pregnancy or by nursing mothers.

**Adverse Reactions:** The most frequent type of adverse reaction occurring with Motrin is gastrointestinal of which one or more occurred in 4% to 16% of the patients.

### Incidence Greater than 1% (but less than 3%)—Probable Causal Relationship

**Gastrointestinal:** Nausea,\* epigastric pain,\* heartburn,\* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence); **Central Nervous System:** Dizziness,\* headache, nervousness; **Dermatologic:** Rash\* (including maculopapular type), pruritus; **Special Senses:** Tinnitus; **Metabolic/Endocrine:** Decreased appetite; **Cardiovascular:** Edema, fluid retention (generally responds promptly to drug discontinuation; see PRECAUTIONS).

### Incidence less than 1%—Probable Causal Relationship\*\*

**Gastrointestinal:** Gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, gastritis, hepatitis, jaundice, abnormal liver function tests; **Central Nervous System:** Depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma; **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome, alopecia; **Special Senses:** Hearing loss, amblyopia (blurred and/or diminished vision, scotomata, and/or changes in color vision) (see PRECAUTIONS); **Hematologic:** Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs positive), thrombocytopenia with or without purpura, eosinophilia, decreases in hemoglobin and hematocrit; **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure, palpitations; **Allergic:** Syndrome of abdominal pain, fever, chills, nausea and vomiting; anaphylaxis; bronchospasm (see CONTRAINDICATIONS); **Renal:** Acute renal failure in patients with pre-existing significantly impaired renal function, decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria; **Miscellaneous:** Dry eyes and mouth, gingival ulcer, rhinitis.

### Incidence less than 1%—Causal Relationship Unknown\*\*

**Gastrointestinal:** Pancreatitis; **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities, pseudotumor cerebri; **Dermatologic:** Toxic epidermal necrolysis, photoallergic skin reactions; **Special Senses:** Conjunctivitis, diplopia, optic neuritis; **Hematologic:** Bleeding episodes (e.g., epistaxis, menorrhagia); **Metabolic/Endocrine:** Gynecomastia, hypoglycemic reaction; **Cardiovascular:** Arrhythmias (sinus tachycardia, sinus bradycardia); **Allergic:** Serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis; **Renal:** Renal papillary necrosis.

\*Reactions occurring in 3% to 9% of patients treated with Motrin. (Those reactions occurring in less than 3% of the patients are unmarked.)

\*\*Reactions are classified under "Probable Causal Relationship (PCR)" if there has been one positive rechallenge or if three or more cases occur which might be causally related. Reactions are classified under "Causal Relationship Unknown" if seven or more events have been reported but the criteria for PCR have not been met.

**Overdosage:** In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine so alkaline diuresis may be beneficial.

**Dosage and Administration:** Rheumatoid arthritis and osteoarthritis. Suggested dosage is 300, 400, or 600 mg t.i.d. or q.i.d. Do not exceed 2400 mg per day. Mild to moderate pain: 400 mg every 4 to 6 hours as necessary.

**Caution:** Federal law prohibits dispensing without prescription.

## UPPER GASTROINTESTINAL BLEEDING

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as in the younger population the mortality rate for this condition was only 14 percent. Hemorrhagic gastritis in the young group had a mortality rate of 35 percent, whereas in the elderly the mortality rate for this condition was only 20 percent. In this study, however, the numbers were relatively small, and no statistically significant differences were noted.

Chang et al<sup>5</sup> reported an analysis of UGIB in 66 patients between the ages of 60 and 90 years, and in France Lamy et al<sup>6</sup> reported a similar study involving 165 patients aged 65 years or older. Although a greater frequency of portal hypertension was found in the patients from France (23 percent), these two groups of elderly patients were similar with respect to the high frequency of the diagnosis of peptic ulcer disease in each (71 percent and 44 percent, respectively).

The mortality rate in UGIB has not decreased during the past 40 years despite many technological advances. One of the most important has been the development and refinement of the fiberoptic endoscope. In recent years many clinicians and investigators have advocated an early, aggressive approach to the diagnosis and management of UGIB. In such an approach the use of the endoscope plays a prominent role. Many have argued that aggressive treatment results in better treatment outcomes. Others have refuted such arguments. Early EGD does yield a correct diagnosis more frequently than other techniques, but this does not seem to significantly affect the overall management or the eventual outcome of the acute bleeding episode.<sup>7</sup>

DR. CHARLES RODNING (*Assistant Professor, Departments of Surgery and Anatomy*): I think Dr. Wilson has clearly identified the gravity of the problem of acute upper gastrointestinal bleeding in a patient of advanced age. My goal is to discuss the diagnostic evaluation and the non-operative therapeutic intervention available to manage patients with such problems. In my opinion, the mainstay of diagnostic evaluation is esophagogastroduodenoscopy. During the past two decades the flexible fiberoptic endoscope, employing the physical principle of light transmitted along fiberoptic bundles, has been used extensively in clinical care. With the endoscope it is also possible to insufflate air and aspirate liquid from the upper gastrointestinal tract, which is important

in obtaining adequate visualization. In addition, such diagnostic instruments as biopsy forceps, cytologic brushes, and snares can be inserted through the instrument to perform various diagnostic and therapeutic procedures. EGD can be performed in almost any patient; however, it does require a cooperative patient, and written consent must be obtained, since it is an invasive procedure. The patient must be hemodynamically stable before endoscopy can be performed, since it is necessary to administer narcotic and soporific medications to achieve adequate relaxation and sedation. A knowledgeable assistant must be available to administer supplemental medications and to assist with various maneuvers. With the endoscope the region from the oral cavity to the fourth part of the duodenum can routinely be visualized, and a variety of pathologic entities, such as hiatal hernia, esophageal varices, foreign bodies, neoplasia, and peptic ulcers, are readily identifiable using this technique. In addition to the diagnostic capability, the endoscope is useful for performing several therapeutic procedures, such as the use of electrocoagulation to control ulcer-induced hemorrhage, extraction of foreign bodies, and injection of sclerosing agents into esophageal varices. The morbidity and mortality associated with EGD is negligible.

Does emergency EGD produce better results in the management of acute UGIB? Patients with vigorous hemorrhage are most likely to require emergency surgery; therefore, early identification of the bleeding site will be most helpful to the surgeon in planning and performing additional therapeutic intervention. Also, early EGD is extremely beneficial to the surgeon in prescribing appropriate therapy.

Sugawa et al<sup>8</sup> retrospectively analyzed the early therapeutic results associated with EGD in 183 patients. This procedure was successful in 97 percent of those patients, but was impossible or unsatisfactory in 3 percent for such reasons as a lack of patient cooperation, acute alcohol intoxication, massive hemorrhage precluding adequate visualization, or hemodynamic instability. The most common diagnoses were similar to those mentioned by Dr. Wilson. Another important observation was the identification of more than one bleeding site in more than one half of the patients investigated. This information is important and desirable for the surgeon when planning operative

intervention, since it may significantly alter the therapeutic approach.

The diagnostic accuracy of EGD has been shown to exceed that of radiography. Allen et al<sup>9</sup> studied 260 patients who underwent EGD and reported an accuracy greater than 90 percent; the rate of accuracy using upper gastrointestinal radiography was approximately 30 percent. If endoscopy was delayed 48 hours or longer, the ability to make a positive diagnosis was substantially reduced, presumably because of the remarkable regenerative capacity of the gastrointestinal epithelium.

Some investigators, however, have refuted the argument for early EGD. Sandlow et al<sup>10</sup> prospectively evaluated 150 patients in whom UGIB was aggressively managed with early EGD and radiography. They observed an overall mortality rate of 7.5 percent of the patients who were aggressively managed compared with 8.5 percent of conservatively managed patients. Consequently, they argued that early EGD was not necessary. They also observed that continuous and recurrent hemorrhage was more frequent in the patients who underwent this procedure on an emergency basis, that emergency surgery was required more often, and that the hospitalization was more protracted. My interpretation of those data is that the more aggressively managed patients were more profoundly ill than the conservatively managed group. This is supported by examining the overall mortality of patients in that study. The operative mortality for the aggressively managed patient was 16 percent, whereas the operative mortality of the conservatively managed patient population who ultimately required operation was 40 percent. Therefore, I would conclude that their argument against early EGD was not supported.

Dronfield et al,<sup>11</sup> who also refuted the need for early EGD, prospectively analyzed 318 patients who were divided into a group receiving this procedure early and another group receiving radiography. The demographic data of the two groups of patients were similar, although the authors did not indicate the exact hemoglobin levels or the number of transfusions required by the patients in either group. The number of patients investigated early in their hospitalization was similar, and the diagnostic accuracy of EGD exceeded that of radiography. In a number of examinations the

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**References:**

1. Stone PH, Turi ZG, Muller JE: Efficacy of nifedipine therapy for refractory angina pectoris. *Am Heart J* 104:672-681, September 1982.
2. Antman E, Muller J, Goldberg S, et al: Nifedipine therapy for coronary-artery spasm: Experience in 127 patients. *N Engl J Med* 302:1269-1273, June 5, 1980.

**BRIEF SUMMARY  
PROCARDIA® (nifedipine) CAPSULES**

For Oral Use

**INDICATIONS AND USAGE: I. Vasospastic Angina:** PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

**II. Chronic Stable Angina (Classical Effort-Associated Angina):** PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in those patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

**CONTRAINDICATIONS:** Known hypersensitivity reaction to PROCARDIA.

**WARNINGS: Excessive Hypotension:** Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out. In PROCARDIA treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for PROCARDIA to be washed out of the body prior to surgery.

**Increased Angina:** Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PROCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

**Beta Blocker Withdrawal:** Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

**Congestive Heart Failure:** Rarely, patients, usually receiving a beta blocker, have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

**PRECAUTIONS: General: Hypotension:** Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See Warnings.)

**Peripheral edema:** Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

**Drug interactions:** Beta-adrenergic blocking agents: (See Indications and Warnings.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis: Administration of PROCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PROCARDIA to avoid possible over- or under-digitalization.

Carcinogenesis, mutagenesis, impairment of fertility: When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose.

Pregnancy: Category C. Please see full prescribing information with reference to teratogenicity in rats, embryotoxicity in rats, mice and rabbits, and abnormalities in monkeys.

**ADVERSE REACTIONS:** The most common adverse events include dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antianginal medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, diarrhea, constipation, inflammation, joint stiffness, shakiness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, and sexual difficulties. Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

**Laboratory Tests:** Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted, and a single incident of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PROCARDIA therapy is uncertain. These laboratory abnormalities have rarely been associated with clinical symptoms. Cholestasis, possibly due to PROCARDIA therapy, has been reported twice in the extensive world literature.

**HOW SUPPLIED:** Each orange, soft gelatin PROCARDIA CAPSULE contains 10 mg of nifedipine. PROCARDIA CAPSULES are supplied in bottles of 100 (NDC 0069-2600-66), 300 (NDC 0069-2600-72), and unit dose (10x10) (NDC 0069-2600-41). The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

More detailed professional information available on request.

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bleeding site could not be precisely determined, but this was comparable in both groups. The number of patients undergoing surgery, the mortality rates, and the duration of hospitalization were also similar in the two groups. On the basis of their analysis these authors concluded that early EGD was not mandatory and not efficacious. A criticism of their analysis, in an otherwise well-designed study, is that they did not precisely define the magnitude of the hemorrhage. The number of transfusions required or the degree of hemorrhage was not specified. I would presume that most of the patients experienced slight to moderate hemorrhage. In the context of the magnitude of hemorrhage, two other papers are relevant. Helmers and Ihre<sup>12</sup> evaluated severely hemorrhaging patients, comparing aggressive management (EGD, radiography, intensive care, electrocoagulative therapy, and early surgical intervention) with conservative management. Diagnostic accuracy was greater with the aggressive approach, and surgery within the first 48 hours occurred more frequently. Patients managed conservatively required an average 17 pints of blood vs 7 pints per patient in the other group. Surgical mortality was 47 percent in the conservatively managed patients and 11 percent in the aggressively managed patients. The authors argued that aggressive management of patients with severe UGIB substantially decreased morbidity and mortality. Hival et al<sup>13</sup> reported similar results. Mortality in a group of patients requiring less than 6 units of blood in a 24-hour period was 2.1 percent, but if transfusion requirements were greater than 10 units in a 24-hour period, the mortality rate was almost 50 percent. These authors also argued that multimodality intervention substantially reduced morbidity and mortality.

In addition to antacid and cimetidine therapy for the treatment of UGIB, there are other therapeutic maneuvers that should be considered prior to EGD and surgery. One effective means of evacuating the stomach before diagnostic evaluation or therapeutic intervention is a technique described by Atkinson and Nyhus<sup>14</sup> employing the insertion of an 18 F Levine tube through the nose and a 24 F Harris tube through the nose or by mouth for the instillation of an iced-saline solution and simultaneous gravity syphonage. This is an extremely effective method for evacuating blood from the gas-

tric lumen because it permits contraction of the stomach and may be effective in eliminating ongoing hemorrhage from this region.

Douglass<sup>15</sup> advocated the use of intraperitoneal or intraluminal instillation of levarterenol bitartrate in patients with UGIB. This was administered in a nonrandom and uncontrolled fashion in an attempt to control UGIB in a group of desperately ill patients with widely disseminated malignancies. Levarterenol bitartrate (16 mg) in 200 mL of isotonic saline was instilled by nasogastric tube into the gastric lumen, which was aspirated after 15 minutes and repeated two to four times until the bleeding had ceased. This technique was successful in controlling UGIB in this group of patients.

Papp<sup>16</sup> reviewed a series of 4,000 patients who underwent EGD over a five-year period. Massive hemorrhage was noted in 245 of those patients. In 38 patients active hemorrhage was noted prior to the procedure, and endoscopic electrocoagulation was 95 percent effective in achieving immediate cessation of hemorrhage. A similar experience was noted by Gaisford,<sup>17</sup> who observed a 97 percent success rate in achieving hemostasis within one or two sessions utilizing electrocoagulation techniques. It is difficult to categorically attribute causality between this technique and cessation of hemorrhage, since many other therapeutic maneuvers were used that may have contributed to the high success rate; nevertheless, it is certainly a technique that is available, and the data suggest it may be very effective.

The use of angiography to demonstrate the site of hemorrhage, to delineate vascular anatomy, and to permit infusion of embolic material or vasoconstrictive agents is another diagnostic and therapeutic option. Goldman et al<sup>18</sup> and Katzen et al<sup>19</sup> reported that injection of Gelfoam powder, Gelfoam sponge, or isobutyl-2-cyanoacrylate were effective in achieving occlusion of major vessels responsible for UGIB.

DR. MAX H. BERNIS (*Associate Professor, Department of Family Practice*): What about the use of endoscopy in the elderly who have many diseases?

DR. RODNING: It is even more important in that context to arrive at an early definitive diagnosis. When the homeostatic capabilities of a patient are compromised, as in the elderly, ongoing hemorrhage is poorly tolerated. The necessity of being aggressive from both a diagnostic and a

therapeutic perspective is well substantiated.<sup>12,13</sup> If the patient is cooperative, the stomach must be evacuated of all blood, and the patient must be hemodynamically stable before this diagnostic procedure is performed. I would argue even more vigorously for the use of early EGD in the elderly patient with UGIB.

DR. JOSEPH TRONCALE (*Assistant Professor, Department of Family Practice*): Once endoscopy is performed and you find severe variceal bleeding, what is the treatment of choice?

DR. RODNING: The immediate control of UGIB secondary to esophageal varices can be accomplished by the insertion of a multiple-lumen tube (Sengstaken-Blakemore, Edlich-Leonard, Linton-Nachlas, etc) to provide tamponade of the esophagogastric region.<sup>20-22</sup> In addition, the systemic intravenous infusion of vasopressin, which decreases portal venous pressure by 30 percent, can be effective in controlling hemorrhage secondary to portal venous hypertension.<sup>23-25</sup> These maneuvers are employed in addition to blood component therapy and replacement of extracellular fluid volume. Once the patient has been hemodynamically stabilized and the hemorrhage has ceased, additional therapeutic intervention is determined by the patient's status and course. If the patient has evidence of hepatocellular dysfunction, I would favor the use of sclerotherapy, injecting sclerosing agents around the esophagogastric varices as a temporizing measure to control hemorrhage.<sup>26-28</sup> If the patient's hepatocellular function can be improved substantially in the course of days to weeks, then consideration must be given to the use of a portosystemic shunt for more definitive control of the portal hypertension.<sup>29</sup>

DR. WOODROW POLEWODA (*Family Physician*): How do you account for the friability of the tissues other than his advanced age?

DR. WILSON: The patient's nutritional status was poor prior to hospitalization. This elderly man had been living alone and eating when and what he wanted. He had been anorexic and had lost weight prior to admission. I believe that the use of total parenteral nutrition, which this patient received, was one of the most important aspects of his recovery. Because of the duodenocutaneous fistula that developed, it was necessary to restrict oral alimentation for most of his hospital stay.

DR. RODNING: I agree with that assessment. I

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think the patient was profoundly catabolic at the time he was admitted, and we were operating upon him under emergency circumstances. We did not have the opportunity to improve his nutritional status prior to surgery.

DR. GORDON E. CARROLL (*Family Physician*): Could you comment on the choice of the operative procedure? Why was that particular choice made?

DR. RODNING: The patient had two problems identified before and during the operation, namely, acute massive UGIB and partial gastric outlet obstruction as a consequence of acute and chronic peptic ulcer disease. Truncal vagotomy with some type of decompressive procedure—pyloroplasty, gastrojejunostomy, or antrectomy with gastrojejunostomy—was considered.<sup>30,31</sup> Significant pyloro-antral deformity precluded the technical performance of a pyloroplasty. Considering this patient's status at the time of surgery, one could argue in favor of a gastrojejunostomy. The surgical team concluded that this patient's peptic ulcer diathesis was significant, and elimination of the gastrin-secreting portion of the stomach was therefore desirable. Consequently, an antrectomy and gastrojejunostomy were performed.

DR. WILSON: If there are no further questions, I would like to close by thanking you for your participation.

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