

borne in mind as the primary physician considers the clinical conundrum of thyroid disease and when he or she is called upon to evaluate the patient with myasthenic symptoms.

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A Four-Year Experience with Hemocult Testing Kits in a Family Medicine Center

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The importance of screening for colorectal cancer is widely accepted and has been reviewed in this journal.¹ The Hemocult* slide test is perhaps the best screening method for colon cancer. It is also used to determine whether gastrointestinal blood loss is occurring in symptomatic patients. This report presents four years of experience using prepared kits given to patients in a family practice clinic.

Methods

A standardized method of Hemocult screening was introduced in the Family Medical Center at the University of Washington in June 1978. The population served at this residency training site (18 residents, 10 faculty) includes 7,100 patients, most of whom live in the surrounding university community of middle-class predominance. Thirty-two percent of the active registered patients are over the age of 35 years, with a female-to-male ratio of 1 to 6. Forty percent of total patient visits (1982) were from patients over the age of 35 years, with a female-to-male ratio of 2 to 1. The clinic screening protocol for adults over the age of 40 years includes Hemocult testing every one to two years. Kits are prepared that contain three Hemocult cards, applicators, instructions (including a recommended diet), and a return envelope. Attached

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to each kit is a card for the initial recording of the patient's name. These kits are stored with a data book in the clinic laboratory. When the physician orders a Hemocult test, the nurse records the patient's name and date on the removable card, files it, and gives the kit to the patient. The laboratory technician transcribes the information from the card into the data book.

As envelopes are returned, the laboratory technician records the appropriate information and notifies the physician of the result. From June 1978 through October 1982 a total of 1,207 kits were given to patients.

The clinic Hemocult log was reviewed, and for every positive test the corresponding chart was reviewed according to availability (43 of 45 charts). Documentation of the positive test was confirmed and the subsequent evaluation, diagnostic findings, and treatment were tabulated for each case.

Results

Of the 1,207 kits distributed, 964 Hemocult cards (80 percent) were returned, of which 51 (5.3 percent of total returned) contained at least one positive slide. These 51 positive slides came from a total of 45 patients, and the charts of 43 of the patients were reviewed. Although the intent had been to use these kits for screening for colorectal cancer, they were also used to evaluate symptoms and to document bleeding.

In patients under 40 years of age, Hemocult cards were used to determine whether gastrointestinal blood loss was continuing after a history of bleeding was given (10 patients) as well as to evaluate symptoms in five patients. While physicians usually elected not to work up positive tests in this age group, of the 6 that were evaluated, 3 patients demonstrated hemorrhoids, and 3 patients remained undiagnosed.

Twenty-eight patients over 40 years of age had positive tests. Screening was the indication for Hemocult testing in 15 patients. Three of these had no further workup. One had a sigmoidoscopy performed, which was negative, and no further

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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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testing. For seven patients the evaluation included a barium enema but not a colonoscopy; one of these patients had a carcinoma. Four patients had a workup including colonoscopy after a suspicious or positive barium enema; all of these patients had villoadenomatous polyps, which were removed.

Thirteen patients aged over 40 years had Hemocult testing to evaluate symptoms. One patient was found to have cecal adenocarcinoma. Diverticulosis was found in two of those with abdominal pain. There were no new diagnoses made on the basis of a bowel evaluation in the remaining ten patients.

Thus, as a result of all Hemocult testing and further evaluation in this clinic over a four-year period, carcinoma was diagnosed in two patients and villoadenomatous polyps in four patients. Table 1 displays the causes found for positive Hemocult testing.

A random sample of 60 patients with negative tests was obtained to evaluate the possibility that those with positive Hemocult tests were not representative of the total population tested. Screening was the indication for testing in 61 percent of those with negative tests, compared with 37 percent of those with positive tests. Seventeen percent of the sample with negative tests were younger than 40 years old, compared with 35 percent of all those with positive tests being younger than 40 years of age.

Discussion

Frame and Kowulich² recently presented results following a five-year experience screening patients 40 years of age and older. Unlike that series from a solo practice setting, this report examines the results of introducing a standardized Hemocult testing kit into a multiphysician training clinic where individual physicians elected to use the kit for screening and evaluating patients with selected histories.

In addition to reporting the four-year experience with Hemocult at this clinic, this study presents two areas that should be considered for improvement. One is that Hemocults were obtained even though the result was unlikely to

Table 1. Causes of Positive Hemocult Tests

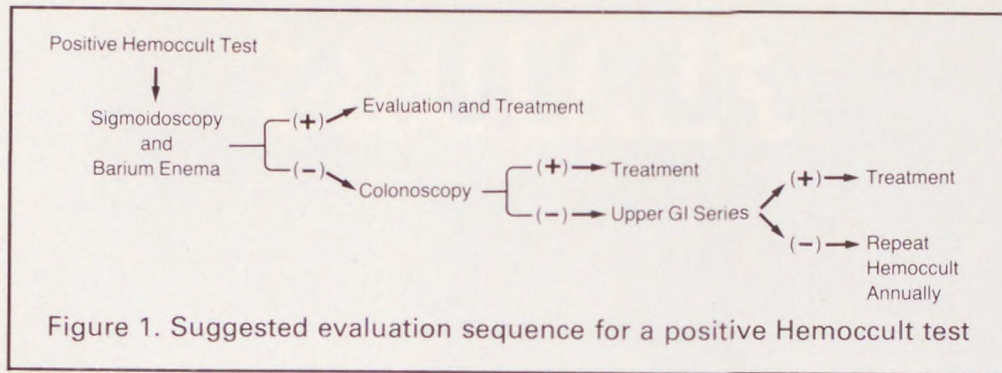
Etiology	Number of Patients
None found	10
Villoadenomatous polyp	4
Diverticulosis	4
Hemorrhoids	3
Presumed upper gastrointestinal bleeding	3
Colon adenocarcinoma	2
Anti-inflammatory agents	2
Not evaluated	15

influence subsequent evaluation and treatment. This was the case with most patients younger than 40 years. In those patients older than 40 years, if the decision was made not to evaluate a positive result because of complicating illnesses, one can argue that the test should not have been done in the first place. The other area of concern was inadequate evaluation of a positive result. A complete evaluation in those over 40 years old may include colonoscopy (Figure 1), and only four of 26 patients aged over 40 years (two patients had definitive surgery after a barium enema) with positive tests underwent colonoscopy.

Conclusions

In order to correct the problems noted, clinic physicians have been informed of the poor yield of significant disease and the minimal influence on subsequent evaluation and treatment that a positive result has on those less than 40 years of age. Physicians were encouraged not to order the test unless they had clearly considered how a positive result would change the patient's treatment. In addition, a protocol (Figure 1) similar to those presented elsewhere^{3,4} has been adopted for those over 40 years of age. It has been re-emphasized that a single positive test is sufficient justification for further evaluation.

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The use of Hemocult screening is valuable in detecting colorectal cancer. It is clear that in the clinic setting, the cost effectiveness of this screening approach can be improved if physicians use this test with more care both in terms of to whom it is given and in terms of more effort being given to appropriate follow-up.

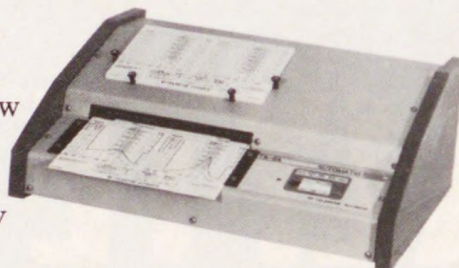
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