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THE JOURNAL OF THE AMERICAN OSTEOPATHIC ASSOCIATION

ORIGINAL CONTRIBUTION

CLINICAL PRACTICE

SPECIAL COMMUNICATION

MEDICAL PRACTICE

continued on page **100**

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THE JOURNAL OF THE AMERICAN OSTEOPATHIC ASSOCIATION

CASE REPORTS

LETTERS

EDITORIALS

DEPARTMENTS

COVER

In the study beginning on page **139**, Michael B. Clearfield, DO, Steve Fedorko, PhD, and Mark E. McKinney, PhD, assess physician awareness of an elevated serum cholesterol level among patients at a university-affiliated, 200-bed community hospital. Criteria for awareness included any notation in the patient's chart indicating the physician's recognition of the abnormal cholesterol level or prescribing dietary or pharmacologic therapeutic intervention. (The test tube lipid precipitate is rendered as an airbrushed painting after slide 2, "Risk Factors for Coronary Heart Disease," from *Hypertension, Cholesterol, and Coronary Heart Disease: Comprehensive Slide/Lecture Guide*, written by Antonio M. Gotto, Jr, MD, DPhil, and produced through an education grant from Pfizer Laboratories.) *Cover design by Barry and Wayne Lau of Design Two, Ltd.*

IN CHRONIC OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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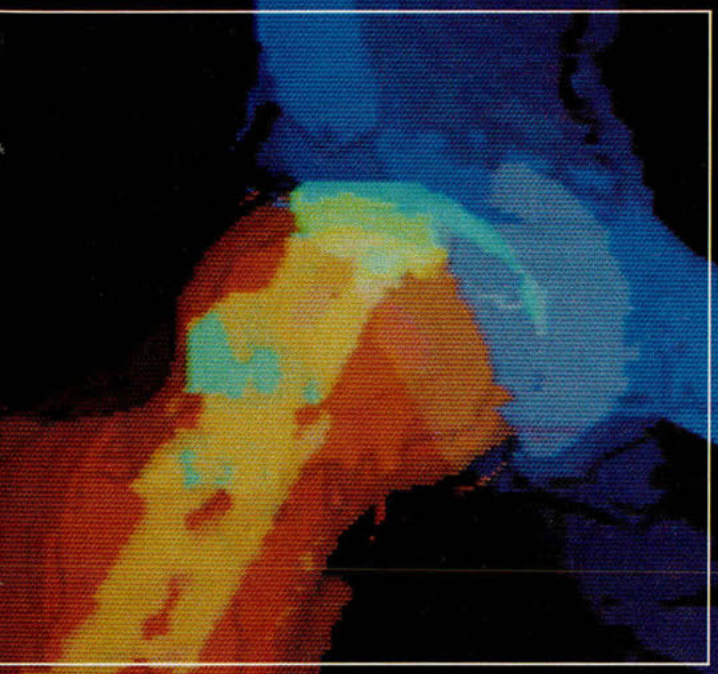

3-D MRI of osteoarthritic hip showing osteonecrosis with core decompression. Supplied by David W. Stoller, MD, Philipp Lang and Dimensional Medicine, Inc.

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*The most frequent complaints are gastrointestinal. See "Warnings" and "Precautions" sections of prescribing information.
**As with other NSAIDs, rare hepatic and renal reactions have been reported. Please see "Precautions" section of prescribing information. †It is prudent to use the lowest effective dose in the elderly.

Please see adjacent page for brief summary of prescribing information and references.

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1. Naprosyn prescribing information. **2.** Geczy M, Peltier L, Wolbach R: Naproxen tolerability in the elderly: A summary report. *J Rheumatol* 1987;14:348-354. Data on file, Syntex Laboratories, Inc., Document #90669-2. **3.** Corwin HL, Bonventre JV: Renal insufficiency associated with nonsteroidal anti-inflammatory agents. *Am J Kidney Dis* 1984;4:147-152. **4.** Turner R: Hepatic and renal tolerability of long-term naproxen treatment in patients with rheumatoid arthritis. *Semin Arthritis Rheum* 1988;17(3)(suppl 2):29-35. ††Leading industry audits for 12 months ending December 1988. Data available upon request from Syntex Laboratories, Inc., Document #90669-A. ‡Leading industry audits for 12 months ending February 1989. Pharmacy sales of naproxen in the U.S. Data available upon request from Syntex Laboratories, Inc., Document #90669-B. ‡‡Leading industry audit. A representative sample of 50 U.S. rheumatologists and 100 U.S. orthopaedic surgeons were asked which NSAID they prescribe most often. In 1988 Naprosyn was named by 57% of rheumatologists and 28% of orthopaedic surgeons in this survey, which is conducted annually by an independent market research firm. Data available upon request from Syntex Laboratories, Inc., Document #90669-C.

Brief Summary:
Contraindications: Patients who have had allergic reactions to NAPROSYN, ANAPROX or ANAPROX DS or in whom aspirin or other NSAIDs induce the syndrome of asthma, rhinitis, and nasal polyps. Because anaphylactic reactions usually occur in patients with a history of such reactions, question patients for asthma, nasal polyps, urticaria, and hypotension associated with NSAIDs before starting therapy. If such symptoms occur, discontinue the drug. **Warnings:** Serious GI toxicity such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated chronically with NSAIDs. Remain alert for ulceration and bleeding in such patients even in the absence of previous GI tract symptoms. In clinical trials, symptomatic upper GI ulcers, gross bleeding or perforation appear to occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. Inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur. Studies have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Except for a prior history of serious GI events and other risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (e.g., age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well than others and most spontaneous reports of fatal GI events are in this population. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity. **Precautions:** DO NOT GIVE **NAPROSYN®** (NAPROXEN) CONCOMITANTLY WITH **ANAPROX®** (NAPROXEN SODIUM) OR **ANAPROX® DS** (NAPROXEN SODIUM) SINCE THEY CIRCULATE IN PLASMA AS THE NAPROXEN ANION. Acute interstitial nephritis with hematuria, proteinuria, and nephrotic syndrome has been reported. Patients with impaired renal function, heart failure, liver dysfunction; patients taking diuretics, and the elderly are at greater risk of overt renal decompensation. If this occurs, discontinue the drug. Use with caution and monitor serum creatinine and/or creatinine clearance in patients with significantly impaired renal function. Use caution in patients with baseline creatinine clearance less than 20 mL/minute. Use the lowest effective dose in the elderly or in patients with chronic alcoholic liver disease or cirrhosis. 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. Elevations of SGPT or SGOT occurred in controlled clinical trials in less than 1% of patients. Severe hepatic reactions, including jaundice and fatal hepatitis, have been reported rarely. If liver disease develops 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 periodically for patients with initial values of 10 grams or less who receive long-term therapy. Peripheral edema has been reported. Therefore, use with caution in patients with fluid retention, hypertension or heart failure. The drug's antipyretic and anti-inflammatory activities may reduce fever and inflammation, diminishing their diagnostic value. Conduct ophthalmic studies if any change or disturbance in vision occurs. For patients with restricted sodium intake, note that the suspension contains 8 mg/mL of sodium. **Information for Patients:** Side effects of NSAIDs can cause discomfort and, rarely, there are more serious side effects, such as GI bleeding, which may result in hospitalization and even fatal outcomes. Physicians may wish to discuss with patients the potential risks and likely benefits of NSAID treatment, particularly when they are used for less serious conditions where treatment without NSAIDs may be an acceptable alternative. Patients should use caution for activities requiring alertness if they experience drowsiness, dizziness, vertigo or depression during therapy. **Laboratory Tests:** Because serious GI tract ulceration and bleeding can occur without warning symptoms, follow chronically treated patients for signs and symptoms of these and inform them of the importance of this follow-up. **Drug Interactions:** Use caution when giving concomitantly with coumarin-type anticoagulants; a hydantoin, sulfonamide or sulfonylurea; furosemide; lithium; beta-blockers; probenecid; or methotrexate. **Drug/Laboratory Test Interactions:** The drug may decrease platelet aggregation and prolong bleeding time or increase urinary values for 17-ketogenic steroids. Temporarily stop therapy for 72 hours before doing adrenal function tests. The drug may interfere with urinary assays of 5HIAA. **Carcinogenesis:** A 2-year rat study showed no evidence of carcinogenicity. **Pregnancy:** Category B. Do not use during pregnancy unless clearly needed. Avoid use during late pregnancy. **Nursing Mothers:** Avoid use in nursing mothers. **Pediatric Use:** Single doses of 2.5-5 mg/kg, with total daily dose not exceeding 15 mg/kg/day, are safe in children over 2 years of age. **Adverse Reactions:** In a study, GI reactions were more frequent and severe in rheumatoid arthritis patients on 1,500 mg/day than in those on 750 mg/day. In studies in children with juvenile arthritis, rash and prolonged bleeding times were more frequent, GI and CNS reactions about the same, and other reactions less frequent than in adults. Incidence Greater Than 1%; Probable Causal Relationship: GI: The most frequent complaints related to the GI tract: constipation,* heartburn,* abdominal pain,* nausea,* dyspepsia, diarrhea, stomatitis. CNS: headache,* dizziness,* drowsiness,* light-headedness, vertigo. Dermatologic: itching (pruritus),* skin eruptions,* ecchymoses,* sweating, purpura. Special Senses: tinnitus,* hearing disturbances, visual disturbances. Cardiovascular: edema,* dyspnea,* palpitations. General: thirst. Incidence Less Than 1%; Probable Causal Relationship: GI: abnormal liver function tests, GI bleeding and/or perforation, hematemesis, jaundice, melena, peptic ulceration with bleeding and/or perforation, vomiting. Renal: glomerular nephritis, hematuria, interstitial nephritis, nephrotic syndrome, renal disease. Hematologic: agranulocytosis, eosinophilia, granulocytopenia, leukopenia, thrombocytopenia. CNS: depression, dream abnormalities, inability to concentrate, insomnia, malaise, myalgia and muscle weakness. Dermatologic: alopecia, photosensitive dermatitis, skin rashes. Special Senses: hearing impairment. Cardiovascular: congestive heart failure. Respiratory: eosinophilic pneumonitis. General: anaphylactoid reactions, menstrual disorders, pyrexia (chills and fever). Causal Relationship Unknown: Hematologic: aplastic anemia, hemolytic anemia. CNS: cognitive dysfunction. Dermatologic: epidermal necrolysis, erythema multiforme, Stevens-Johnson syndrome, urticaria. GI: non-peptic GI ulceration, ulcerative stomatitis. Cardiovascular: vasculitis. General: angioneurotic edema, hyperglycemia, hypoglycemia. **Overdosage:** May have drowsiness, heartburn, indigestion, nausea, vomiting. Empty stomach and use usual supportive measures. In animals 0.5 g/kg of activated charcoal reduced plasma levels of naproxen. **Caution:** Federal law prohibits dispensing without prescription. See package insert for full Prescribing Information.

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*Incidence of reported reaction 3%-9%. Where unmarked, incidence less than 3%.

U.S. patent nos. 3,904,682, 3,998,966 and others.

SYNTEX

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