

Treating nocturnal asthma poses challenges

Nocturnal asthma occurs commonly in patients with asthma.¹ Potential causes include exposure to dust mites and a late-phase reaction to this exposure; the effects of posture or sleep stage on airway tone and airway cooling; reflux-mediated bronchospasm; increased nocturnal vagal tone; impaired ciliary clearance; and circadian changes in the levels of circulating hormones.² Treating nocturnal asthma is difficult, a point well taken in the study by Dr Brown and colleagues, featured on page 321 in this issue of *JAOA*. Although their study comprises a small population, the protocol is uniform and the patient population well defined. These researchers convincingly demonstrate—through chronobiologic techniques—that patients often continue to have reductions in nocturnal airflow despite long-term treatment with inhaled beta-agonists alone or in combination with theophylline.

Moreover, in this study population, patients who were treated with beta-agonists alone more frequently needed nocturnal rescue therapy with isoproterenol. As expected, the need for rescue therapy correlated with greater day-night variability in the peak expiratory flow rate (PEFR). An important finding, this correlation between greater day-night variability in PEFR and the need for rescue beta-agonist therapy emphasizes the importance of daily PEFR measurements. Ideally, this measurement should be taken in the morning and afternoon. Fluctuations in the PEFR measurement of greater than 20% indicate a suboptimal level of asthma control; more aggressive therapy is warranted in such instances.

Optimal treatment for nocturnal asthma has not yet been established; however, nocturnal oral dosing of sustained-release (SR) theophylline appears more effective than conventional therapy.³⁻⁵ Nocturnal oral dosing of SR-albuterol also provides effective therapy.⁶ Recent reports indicate that the use of inhaled corticosteroids,^{7,8} anticholinergic agents,⁹ and cromolyn sodium¹⁰ may also play a role in some patients. Until definitive studies are conducted, patients who still have nocturnal asthma despite the use of inhaled beta-agonists should be given nocturnal oral doses of either SR-theophylline

or SR-albuterol on a trial basis. If this therapy fails or is not tolerated, then anti-inflammatory therapy with inhaled steroids or cromolyn might be effective.

THOMAS E. MORLEY, DO

Associate Professor of Clinical Medicine
University of Medicine and Dentistry of New
Jersey—School of Osteopathic Medicine
Stratford, NJ

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Outcomes assessment: 'Buzz words' in medical education whose time has come

Outcomes assessment have become the new "buzz words" not only in healthcare delivery but also in

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NAPROSYN[®]

(NAPROXEN) 500 mg tablets

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 BOTH 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 alcohol 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, colitis, GI bleeding and/or perforation, hematemesis, jaundice, melena, peptic ulceration with bleeding and/or perforation, vomiting. Renal: glomerular nephritis, hematuria, hyperkalemia, interstitial nephritis, nephrotic syndrome, renal disease, renal failure, renal papillary necrosis. 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: aseptic meningitis, cognitive dysfunction. Dermatologic: epidermal necrolysis, erythema multiforme, photosensitivity reactions resembling porphyria cutanea tarda and epidermolysis bullosa, 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. A few patients have had seizures. 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.

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



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

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medical education. Drs Cope and Baker address this issue in their article, beginning on page 353 in this issue of *JAOA*. They write that outcomes assessment is the process of collecting information about the attainment of an outcome of an academic endeavor. Outcomes assessment is contrasted with techniques that review the structure and process.

Historically, when evaluating healthcare and medical education, we have focused on structure and process. Now, with outcomes assessment, we are focusing on the *results* of the process and procedures. This emphasis is good; it should be this way.

Drs Cope and Baker describe the West Virginia School of Osteopathic Medicine (WVSOM) assessment program in detail, including the assessment levels for students, curriculum, faculty, and post-graduate endeavors. The authors also detail one of the first initiatives in this assessment program: identifying the characteristics of the "ideal" post-graduate, including his or her osteopathic medical orientation, skills, and abilities. The experience of WVSOM's assessment program will be of interest to all of the colleges of osteopathic medicine and the graduate medical education programs in general.

In the near future, clinical competence evaluation will be conducted at various levels of undergraduate and graduate medical education. Although the traditional measures of process have essential value, the objective assessment of medical students' and physicians' competence is clearly a concept whose time has come.

THOMAS WESLEY ALLEN, DO
Editor in Chief