

## CLINICAL CAPSULES

**Antibiotic Prescribing Reviewed**

Appropriate interventions in hospitals and doctors' offices can improve antibiotic prescribing and may reduce drug resistance, according to two new Cochrane reviews.

The first, by Peter Davey, M.D., of the University of Dundee, and his colleagues, looked at 66 studies involving hospitals. Of these, 51 studies showed a significant improvement in at least one antibiotic prescribing outcome. Of 16 that reported microbiological outcomes, 12 showed significant improvement. Interventions such as lectures and seminars to educate and/or

persuade staff to change prescribing behaviors were less effective than approaches that involved imposing restrictions via guidelines and orders (Cochrane Database Syst. Rev. 2005;CD003543).

In a review of 39 studies of doctors' offices, attitudes toward prescribing were changed the most by interventions that incorporated information about local circumstances into education of patients and physicians. One-on-one meetings with physicians, small group discussions, and combined approaches had a more powerful effect on prescribing patterns than less

complex approaches, such as handing out printed materials or holding lectures without discussion time, Sandra Arnold, M.D., of the University of Tennessee, Memphis, and Sharon E. Straus, M.D., of Mt. Sinai Hospital, Toronto, reported (Cochrane Database Syst. Rev. 2004;CD003539).

**Treating Invasive Aspergillosis**

Salvage therapies in patients with invasive aspergillosis have little efficacy, so it is imperative to choose an effective initial therapy, a study led by Thomas F. Patterson, M.D., of the University of Texas, suggests.

Of 144 patients treated initially with voriconazole, 36% were switched to an-

other licensed antifungal therapy before completion of the initial therapy, and 48% of those responded. Of 133 patients initially treated with amphotericin B, 80% were switched to another antifungal, and 38% of those responded. Switches were made because of intolerance or insufficient response in 24% of voriconazole patients, compared with 70% of amphotericin B patients (Clin. Infect. Dis. 2005;41:1448-52).

Salvage therapy response rates were poorest with lipid formulations of amphotericin B, particularly when they were used after failed amphotericin B therapy. The overall response rate to such formulations was 30%, but the response rate in those who switched due to poor response to amphotericin B was 12%.

**Candidemia Treatment Options**

Voriconazole is safer than, and as effective as, the common regimen of amphotericin B followed by fluconazole for treatment of candidemia in non-neutropenic patients, a randomized noninferiority trial suggests.

A total of 422 patients were randomized to receive voriconazole or the amphotericin B and fluconazole regimen, and 41% of those in the intention-to-treat population in both groups had successful outcomes in the primary efficacy analysis. At the last evaluable follow-up, 65% of those in the voriconazole group, and 71% in the amphotericin B group had a successful outcome; the difference was not statistically significant, reported B. J. Kullberg, M.D., of University Nijmegen (the Netherlands) Medical Centre, and colleagues.

Voriconazole cleared blood cultures as quickly as the amphotericin B regimen, but serious adverse events and renal toxicity occurred more frequently in the amphotericin B regimen group, the investigators noted (Lancet 2005;366:1435-42).

The authors concluded that voriconazole, which can be given as an initial intravenous treatment or as an oral step-down agent, is an important treatment option for candidemia as it has a broader spectrum and better safety than amphotericin B.

**Gatifloxacin Risk**

Gatifloxacin is associated with potentially deadly glucose homeostasis abnormalities, particularly in patients with diabetes, according to Richard Frothingham, M.D., of Duke University, Durham, N.C.

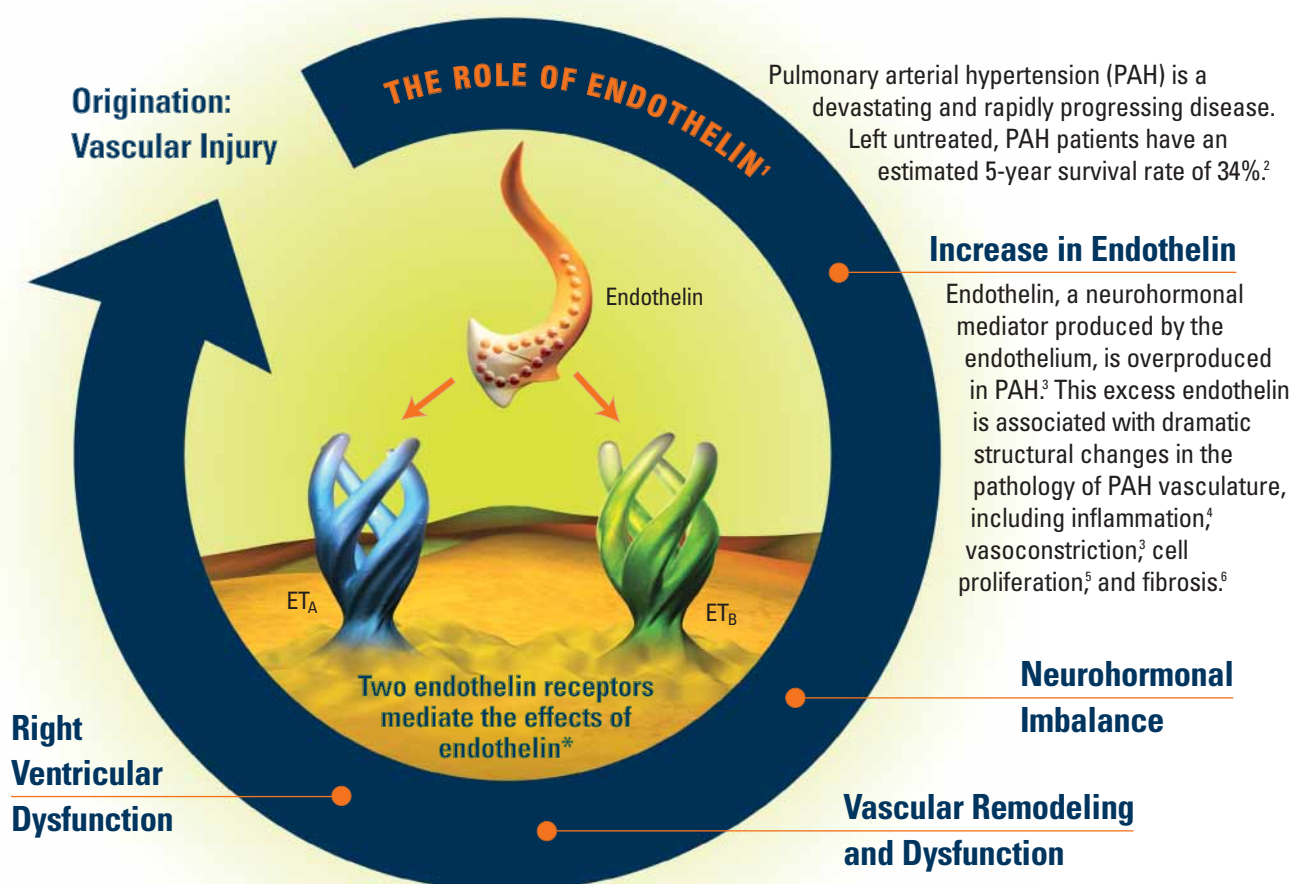
Spontaneous adverse event reports over 6 years show that gatifloxacin was associated with 80% of 568 glucose homeostasis abnormality adverse event reports and 68% of 25 such events involving fatality that were associated with the use of ciprofloxacin, levofloxacin, moxifloxacin, or gatifloxacin. Of all the adverse event reports associated with gatifloxacin, 24% were glucose homeostasis abnormalities, compared with less than 2% of those associated with the other drugs.

Older patients and those being treated for diabetes had the greatest risk of these types of adverse events, Dr. Frothingham noted (Clin. Infect. Dis. 2005;41:1269-76).

Gatifloxacin should be avoided in diabetics, and the dosage in other patients should not exceed 400 mg/day. In patients with creatinine clearance of less than 40 mL/min and probably also in persons over age 65 years, the dosage should be reduced to 200 mg/day, he concluded.

—Sharon Worcester

# Endothelin's Role in the Rapid Progression of Pulmonary Arterial Hypertension



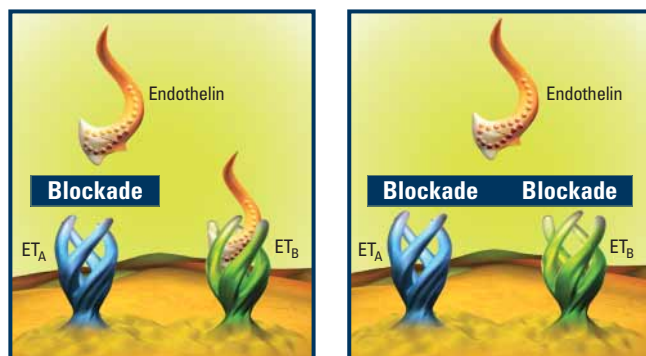
## Blockade of Both ET<sub>A</sub> and ET<sub>B</sub> Receptors Is Critical

**ET<sub>A</sub> Activity in PAH\***

Cell proliferation<sup>5</sup>  
Vasoconstriction<sup>3</sup>  
Inflammation<sup>4</sup>

**ET<sub>B</sub> Activity in PAH\***

Cell proliferation<sup>5</sup>  
Vasoconstriction<sup>3</sup>  
Inflammation<sup>4</sup>  
Fibrosis<sup>6</sup>  
Hypertrophy<sup>6</sup>



To learn more about the effects of endothelin in pulmonary arterial hypertension, please visit [www.endothelinscience.com](http://www.endothelinscience.com)



\*Statements are based on observations reported from in vitro or animal trials.

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