

GLOSSARY

OSTEOCLASTS

Large multinuclear cells associated with the absorption and removal of bone

'BLACK BOX' WARNING

Text boxes containing prescribing contraindications are highlighted by a prominent black border in the *Physician's Desk Reference*, the most commonly used source of drug labeling information in the US

Animal study shows antiresorptive agent has novel mechanism of action

Researchers from Japan and the US have developed a novel antiresorptive drug, reveromycin A, which inhibits bone resorption by inducing apoptosis in OSTEOCLASTS. In osteoporosis, excessive bone resorption and bone loss is mediated by osteoclasts. The two main classes of antiresorptive drugs that are currently available, bisphosphonates and calcitonin, either cannot be used in combination with other common agents or decrease in effectiveness over time.

In a rodent model, Woo *et al.* showed that reveromycin A caused cell death only in mature, bone-resorbing osteoclasts, and not in osteoclast progenitors, osteoblasts or inactive osteoclasts. Reveromycin A caused apoptosis by blocking the aminoacylation activity of isoleucyl-transfer-RNA synthetase (thereby blocking protein synthesis), and by inducing cytochrome c release and caspase 3 activation. Apoptosis and inhibition of bone resorption were demonstrated both *in vivo* and *in vitro*.

The authors suggest that reveromycin A's specificity for osteoclasts might be the result of the acidic extracellular microenvironment of osteoclasts, which increased the ability of reveromycin A to permeate these cells. Their results indicate that reveromycin A has a very different mechanism of action to bisphosphonates or calcitonin, and will not have the same limitations on its use.

Katherine Sole

Original article Woo J-T *et al.* (2006) Reveromycin A, an agent for osteoporosis, inhibits bone resorption by inducing apoptosis specifically in osteoclasts. *Proc Natl Acad Sci USA* 12: 4729–4734

How can we avoid the prescription of contraindicated drugs?

Adverse events caused by prescribing drugs in violation of a 'BLACK BOX' WARNING are thankfully rare—occurring in <1% of those who receive a contraindicated drug, according to results of an observational study of records from 51 outpatient practices in the greater Boston area. Despite this encouraging finding, the number

of patients at risk is large; and adverse drug events are thought to cause ~100,000 deaths annually in the US alone.

Lasser *et al.* report that 10% of adult outpatients given prescription medication received a drug bearing a black box warning; warning violations occurred in 7% of cases (2,354 of 33,778 patients). Seven drugs accounted for almost three-quarters of violations. The authors reviewed a randomly selected sample of 575 medical records, and identified 92 cases in which the warning violation could have resulted in an adverse effect, and four cases in which an adverse event actually occurred. All four were deemed preventable.

Clinical practice guidelines often contain different information to black box warnings, say the authors, and the latter can be vague and difficult to interpret. Compliance could be improved by devising a searchable online database of consistent, clear and simple warnings. With the increasing use of electronic health records, say Lasser *et al.*, the potential of online alerts to support prescribing decisions, especially for drugs with the most commonly violated warnings, or those with the greatest potential to cause harm, should be explored.

Caroline Barranco

Original article Lasser KE *et al.* (2006) Adherence to black box warnings for prescription medications in outpatients. *Arch Intern Med* 166: 338–344

Psoriatic arthritis can be difficult to distinguish from rheumatoid arthritis

Psoriatic arthritis is a heterogeneous disease that shares many characteristics with rheumatoid arthritis (RA). Tests for rheumatoid factor (RF) can help to distinguish between the two conditions, as patients with psoriatic arthritis are usually (although not always) RF-negative. The specificity of RF for RA can be improved by additional testing for antibodies to cyclic citrullinated peptide (CCP); a cross-sectional study in Sweden, therefore, investigated the prevalence of anti-CCP antibodies in patients with psoriatic arthritis. Alenius *et al.* found that the presence of both RF and anti-CCP antibodies in a patient with psoriatic arthritis predicted the development of RA.