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## Minocycline for acne

*First line antibacterial treatment of acne should be with tetracycline or oxytetracycline*

See p 169

Acne is sometimes severe enough to cause psychological and physical scars, but for the most part it is a physiological inconvenience and few would risk their lives to be free from it. The drugs generally used to treat it should not, therefore, cause serious adverse effects. Minocycline has been promoted as a useful drug for treating acne because it is well absorbed, even when taken with food, and it need be taken only once or twice a day. However, there is increasing evidence that it can sometimes produce severe adverse effects.

The series of seven patients reported by Gough *et al* (p 169) provides more evidence that minocycline causes an unusual form of drug induced liver disease, in which hepatitis, sometimes with the histological features of chronic active hepatitis, is associated with polyarthralgia and positive antinuclear antibodies.<sup>1</sup> As would be expected with drug induced systemic lupus erythematosus, tests for antibodies to DNA were negative or only weakly positive, and the patients recovered within three months of stopping treatment with minocycline. Drug induced chronic active hepatitis is rare. It has been reported with the laxative oxyphenisatin (which is no longer widely used) and with nitrofurantoin, methyldopa, and diclofenac.<sup>2</sup> Most cases described in the literature have been in women.

The current series is augmented by data from spontaneous reports to Britain's Committee on Safety of Medicines of adverse reactions to minocycline, describing eight patients with systemic lupus erythematosus, 15 with hepatitis, and one suffering both reactions. Some of the adverse hepatic effects may have been due to fatty infiltration of the liver, similar histologically to that seen in Reye's syndrome and known to occur with high dosages of tetracyclines, especially in pregnancy. This reaction has previously been considered rare with minocycline.<sup>2</sup> One case report incriminated intravenous minocycline,<sup>3</sup> but cases have also been reported in association with oral minocycline.<sup>4</sup>

Minocycline has been implicated in another rare adverse reaction that is likely to have an immunological basis, eosinophilic pneumonitis. Patients develop dyspnoea, cough, and fever, and there is radiological evidence of pulmonary infiltrates, with eosinophilia in bronchoalveolar lavage fluid or peripheral blood.<sup>5-7</sup> This reaction seems to resolve within a few weeks of stopping minocycline.

Cases with mixed features have been reported. One patient suffered a febrile illness with pneumonitis, hepatitis, and a positive test for antinuclear antibody with each course of minocycline.<sup>8</sup> In another patient hepatitis was accompanied by eosinophilia.<sup>4</sup> A patient with pneumonitis and arthralgia, positive for antinuclear antibody, has also been described.<sup>9</sup>

Reports of immunological adverse effects with tetracycline and oxytetracycline are sparse or absent, though there is a suspicion that tetracycline can aggravate pre-existing systemic lupus erythematosus. Patients who have suffered

immunological reactions to minocycline can nevertheless be treated successfully with tetracycline<sup>8</sup> or oxytetracycline (unpublished observations). Other adverse effects specific to minocycline are blue-black hyperpigmentation affecting the skin, mucus membranes, nails, adult teeth, and internal organs, which is due to the deposition of black metabolites of the drug,<sup>10</sup> and dose dependent vestibular disturbance.<sup>11</sup>

All tetracyclines are contraindicated in pregnancy because they are deposited in the teeth and bones of the fetus. Benign intercranial hypertension is another potentially serious adverse effect of this class of antibacterial drug, and treatment should be withdrawn promptly if patients develop headache and signs of raised intracranial pressure.

Minocycline is widely used, and serious reactions are rare. However, its unusual propensity for causing immunologically mediated reactions may make it less safe than other tetracyclines, and this should be taken into account when treating essentially benign conditions such as acne. It is also very expensive, as Gough *et al* point out.<sup>1</sup> Tetracycline (or oxytetracycline) in a single or divided dose of 1 gram daily is effective and tolerable for most patients who require a systemic antibacterial agent to treat acne.<sup>12</sup> Absorption will be best if the tablets are taken with a glass of water at least half an hour before food. Prescribers should explain that the benefits will be seen only gradually, and treatment for several months is necessary. Tetracycline or oxytetracycline will be cheaper, and perhaps safer, than minocycline, which can be reserved for those patients who do not improve with one of the first line drugs.

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