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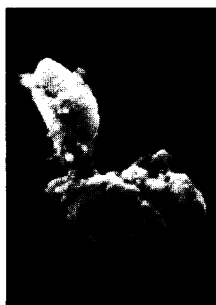
Goodman, L.S. and Gilman, A. (eds) (1975). *The Pharmacological Basis of Therapeutics*, 5th Ed, New York; MacMillan.

in vivo Results

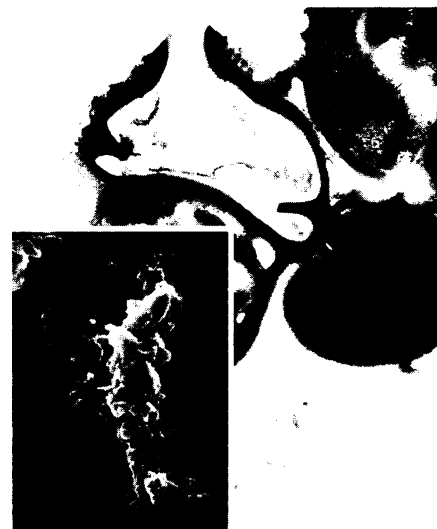
Staphylococcus aureus after 3 days treatment with Erythrocin 500. Intracellular dissolution almost total. Surface defects consistent with protein synthesis inhibition.



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Beta-haemolytic streptococcus after 5 days treatment with Erythrocin 500. Dissolution of cellular integrity is almost total and cellular debris can be seen quite clearly.



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Pictures taken from an *in vivo* co-operative study by Merle Balbirsingh *et al* (in Press)

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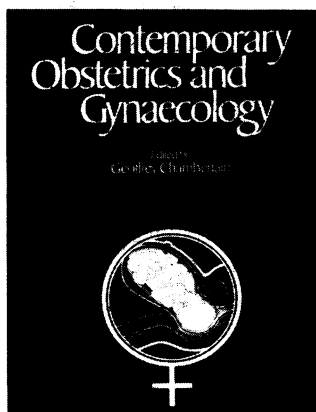
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Prothiaden

What's the significance of the new 75mg tablet?

Presentation Prothiaden is dothiepin hydrochloride, an antidepressant of the tricyclic group.

Prothiaden is available as sugar-coated tablets, each containing 75mg of dothiepin hydrochloride. The tablets are red in colour and bear the overprint 'P 75' in white. It is also available in hard gelatin capsules, each containing 25mg of dothiepin hydrochloride. The capsules are red/brown in colour with the overprint 'P25' in white.

Uses Prothiaden is indicated in the treatment of depression and the anxiety frequently associated with depressive illness.

Dosage and Administration Prothiaden should be given in a dosage of 75 to 150mg daily. The following dosage schemes are suggested:

Mild to moderate depression, 25mg three times daily or 75mg at night.
Moderate to severe depression, 150mg daily in divided doses, or as a single dose at night. (If the latter regimen is adopted, it is preferable to use a smaller dose for the first few days).

In certain circumstances, i.e. in hospital use, Prothiaden has been given at dosages up to 225mg daily. No dietary restrictions are necessary during treatment with Prothiaden.

Contra-indications. Warnings, etc. Prothiaden has anticholinergic properties; therefore, it may precipitate urinary retention in susceptible individuals and its use should be avoided in patients with existing or potential urinary retention. Patients with closed-angle glaucoma should not be given Prothiaden and the occurrence of a painful red eye in a patient receiving the drug may indicate acute closed-angle glaucoma; this requires urgent treatment. In patients with chronic simple glaucoma, the risk of Prothiaden causing a rise in intraocular pressure is relatively small provided adequate anti-glaucoma therapy is being used. Caution is advised when treating epileptic patients and those with cardiovascular disorders. From studies in animals, it was concluded that Prothiaden had no teratogenic effects in the species tested. Nevertheless, as with any relatively new drug, the use of Prothiaden during pregnancy should be avoided if possible.

Use with other drugs: Prothiaden should not be given concurrently with MAO inhibitors; nor should it be given within 14 days of ceasing treatment with an MAO inhibitor. Prothiaden may alter the pharmacological effects of some concurrently administered drugs: CNS depressants, including alcohol and narcotic analgesics, will be potentiated, as will the effects of adrenaline and noradrenaline (it should be borne in mind that some local anaesthetic preparations contain these sympathomimetics). The hypotensive effect of certain antihypertensive agents (e.g. bethanidine, debrisoquine, guanethidine) may be reduced.

Side-effects: Generally, the side-effects associated with Prothiaden have been mild and controlled by reduced dosage. The following have been reported—dryness of mouth, constipation, disturbed accommodation, lassitude, dizziness, orthostatic hypotension, palpitations, somnolence, tremor, headache.

Overdosage: The symptoms of overdosage with Prothiaden may include sedation, dry mouth, blurring of vision, tachycardia, tremor, sweating, nausea, vomiting, confusion. The main dangers from overdosage arise from unconsciousness, convulsions, abnormal cardiac rhythms, hypotension and depression of respiration. The smallest dose of Prothiaden alone which resulted in the death of an adult was reported to be 0.75–1.0g (30 to 40 x 25mg capsules). The largest dose from which recovery took place was reported to be 5.0g (200 x 25mg capsules). In view of the many factors which influence the outcome of an overdose, these figures should not be considered in isolation.

Treatment of overdosage: Gastric lavage; in the unconscious patient or where the cough reflex is depressed, the lungs should be protected by a cuffed endotracheal tube. Repeated gastric/intestinal aspiration may remove drug and metabolites excreted into the gut via the bile. General support of the circulation with continuous ECG monitoring is advised. Abnormalities of cardiac rhythm and epileptic convulsions may occur and should be treated accordingly. Forced diuresis and haemodialysis are not recommended. Bed-rest is advisable, even after clinical recovery.

Pharmaceutical Precautions—Recommended storage conditions 5°C to 20°C.

Legal Category POM.

Package Quantities—Prothiaden Tablets (75mg) 100, 500. **Prothiaden Capsules (25mg)** 100, 600.

Basic NHS Prices: 100 x 25mg £1.57 600 x 25mg £9.03
100 x 75mg £4.52 500 x 75mg £21.70

Product Licence Number Prothiaden capsules PL 0096/5007. Prothiaden Tablets PL 0096/0046.

The Crookes Laboratories Ltd., Basingstoke, Hants.

References: 1. Pearce, J. B. & Linford Rees, W. J., *Int. Med. Res.* 1974, **2**, 12.
2. Rees, J. A. & Cryer, P. C. *Curr. Med. Res. Opin.* 1976, **4**, 416.

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more effective, better tolerated
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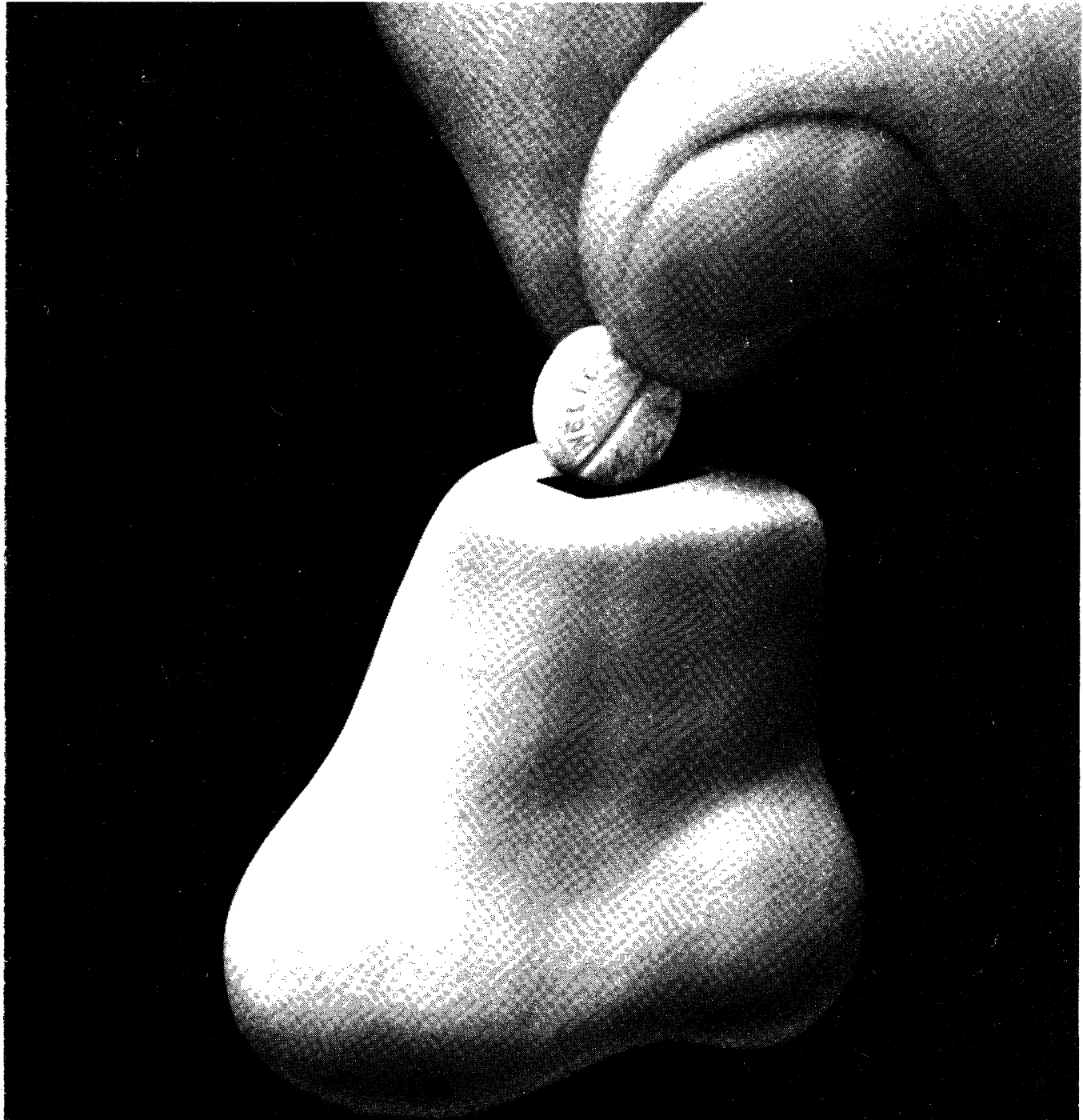
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... A single daily dose of dothiepin (Prothiaden) has been shown to produce a better clinical response and to be better tolerated than a divided daily dose regimen. 1

... with dothiepin both the incidence and severity of side-effects were much less than with amitriptyline.

2

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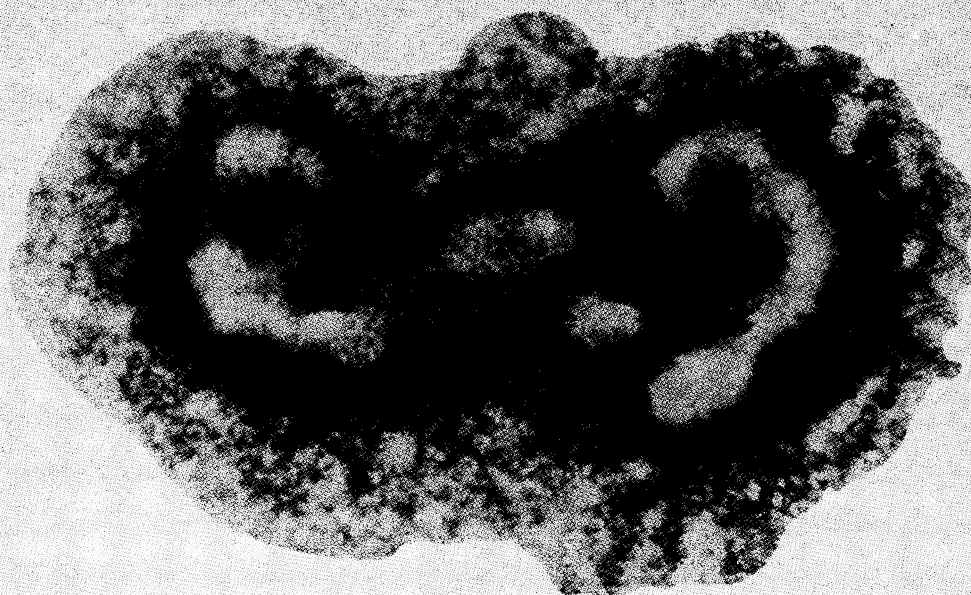
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