KEY WORDS OF MODERN ANTIFUNGAL THERAPY

CYTOCHROME P450

OR WHAT'S IN A NAME...

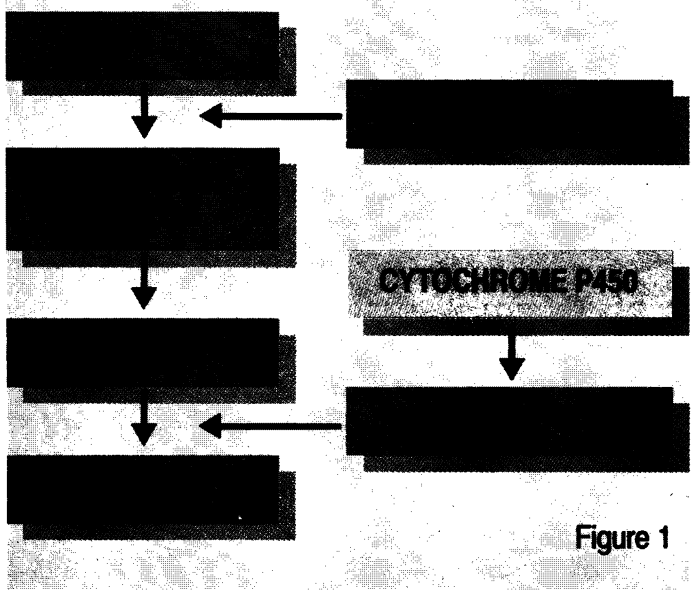

Figure 1

The metabolism of fungi is almost identical to that of other eukaryotic organisms, such as humans. Therefore, trying to design a systemic drug that kills fungi without harming their human host means searching for infinitesimal differences in metabolic pathways.

Selective precision for the metabolic pathways in fungi, as distinct from those in humans, remains the key determinant for any systemic antimycotic, regardless of its point of biochemical interaction. This precision has been achieved to an exceptional degree with itraconazole, alias Sporanox*, because it selectively inactivates the fungal cytochrome P450 only.

Figure 1 is a simplified illustration of one of the pathways for the enzymatic ergosterol synthesis in fungal cell membranes. (Ergosterol is essential for the structural cohesion of these membranes). Pharmacologically one can disrupt this process at two distinct points. The first is where squalene is made into an oxide. Alternatively, one can interfere where lanosterol is converted into ergosterol, by inactivating **cytochrome P450** – a chemical catalyst that performs a vital function in the enzymatic reaction. The broadest research experience to date has been gathered with the latter approach. Importantly, in view of the close similarities between the enzymatic processes in fungi and humans, either approach must be highly selective in disrupting the fungal enzyme systems only.

Sporanox* itraconazole

SHORT AND SIMPLE ORAL THERAPY

standard dose in dermatomycoses: 1 capsule (100 mg) once daily for 15 days
standard dose in vaginal candidosis: 2 x 2 capsules (400 mg) for 1 day only

*** Trademarks: SPORANOX, SEMPERA, SISTIZOL, TRISPORAL.**

JANSSEN PHARMACEUTICA
2340 Beerse, Belgium
expertise in antimycotic research

Properties: Sporanox (itraconazole), a triazole derivative, is orally active against infections with dermatophytes (*Trichophyton* spp., *Microsporum* spp., *Epidermophyton floccosum*), yeasts (*Candida* spp., *Pityrosporum* spp.), *Aspergillus* spp. and various other yeasts and fungi. **Indications:** Sporanox (itraconazole) is indicated for vulvovaginal candidosis, pityriasis versicolor, dermatophytoses, fungal keratitis and oral candidosis. **Dosage and administration:** Vulvovaginal candidosis: 2 capsules (200 mg) morning and evening for 1 day, Pityriasis versicolor: 2 capsules (200 mg) once daily for 7 days. - Tinea corporis, tinea cruris, tinea pedis, tinea manus: 1 capsule (100 mg) daily for 15 days; highly keratinized regions, as in plantar tinea pedis and palmar tinea manus, require 1 capsule (100 mg) daily for 30 days. - Oral candidosis: 1 capsule (100 mg) daily for 15 days. - Fungal keratitis: 2 capsules (200 mg) once daily for 21 days. **Contra-indications:** Sporanox (itraconazole) is contra-indicated during pregnancy. **Warnings and precautions:** Although clinically Sporanox (itraconazole) has not been associated with hepatic dysfunction, it is advisable not to give this drug to patients with a known history of liver disease. **Nursing mothers:** It is recommended not to breast feed whilst taking Sporanox (itraconazole). **Drug interactions:** Sporanox (itraconazole) should not be given concomitantly with rifampicin.

Full prescribing information is available on request.

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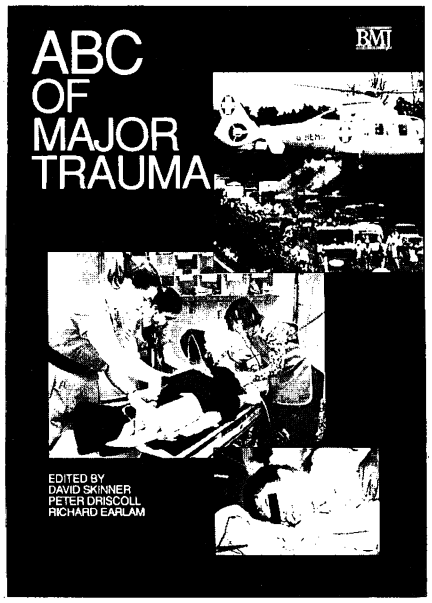


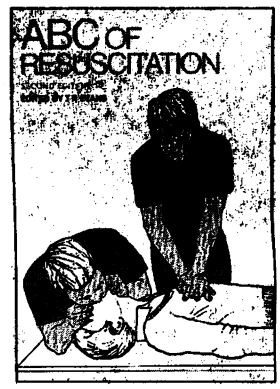
Suddenly it happens: can you cope?

Injury is an enormous problem in Western society. It is the commonest cause of death among those aged under 35, and about 100 people die each week in road traffic accidents in Britain. Hospital staff have to manage about 500,000 patients with injury who are admitted each year, often with multiple injuries requiring urgent treatment.

The *ABC of Major Trauma* is a comprehensive guide to the early management of the multiply injured patient. All immediately life threatening problems are dealt with, the chapters being written by experts in all of the relevant specialties and by doctors who have day to day experience of treating patients with major injuries in the accident and emergency department. Also covered are the handling of accident victims and their transport to hospital and how to deal with major accidents. Practical guidance is clear and dogmatic to avoid delay in urgent treatment and is relevant to all medical, paramedical, and nursing staff who are concerned with the management of patients from the moment of injury to eventual discharge.

March 1991

UK £12.95; Abroad £15.00 (BMA members £11.95 or £14.00)



The second edition of the *ABC of Resuscitation* incorporates the latest standards and guidelines for cardiopulmonary resuscitation issued by the Resuscitation Council (UK) in 1989. The are three new chapters—one on trauma, one on resuscitation in late pregnancy, and one on avoiding HIV infection—and throughout, recommendations have been updated where necessary and other revisions have been made in view of current theory and practice. Written by members of the Resuscitation Council (UK) and other invited experts, the new edition of *ABC of Resuscitation* offers the most up to date information and advice on this vital aspect of health care.

Review of the first edition

"This book represents a major achievement on the part of the Resuscitation Council and the *British Medical Journal* and must be essential reading for every practising doctor, and especially those in the 'front-line' of pre-hospital care." *BASICS, Journal of the Association for Immediate Care*

Second edition 1990

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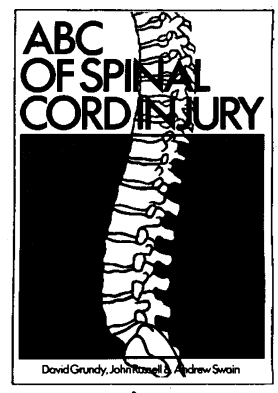

In spinal cord injury correct management from the outset is vital to prevent further damage. But what is the correct management? The *ABC of Spinal Cord Injury* sets it out step by step: how the injured patient should be moved from the scene of the accident; the assessment of his injuries; transfer to a spinal treatment centre; immediate medical problems and later complications; and the specialised nursing, physiotherapy, and occupational therapy that are essential in helping the patient and his family adjust to what may be a lifetime of disability. A valuable introduction to a topic that non-specialists need to know more about.

Third impression 1990

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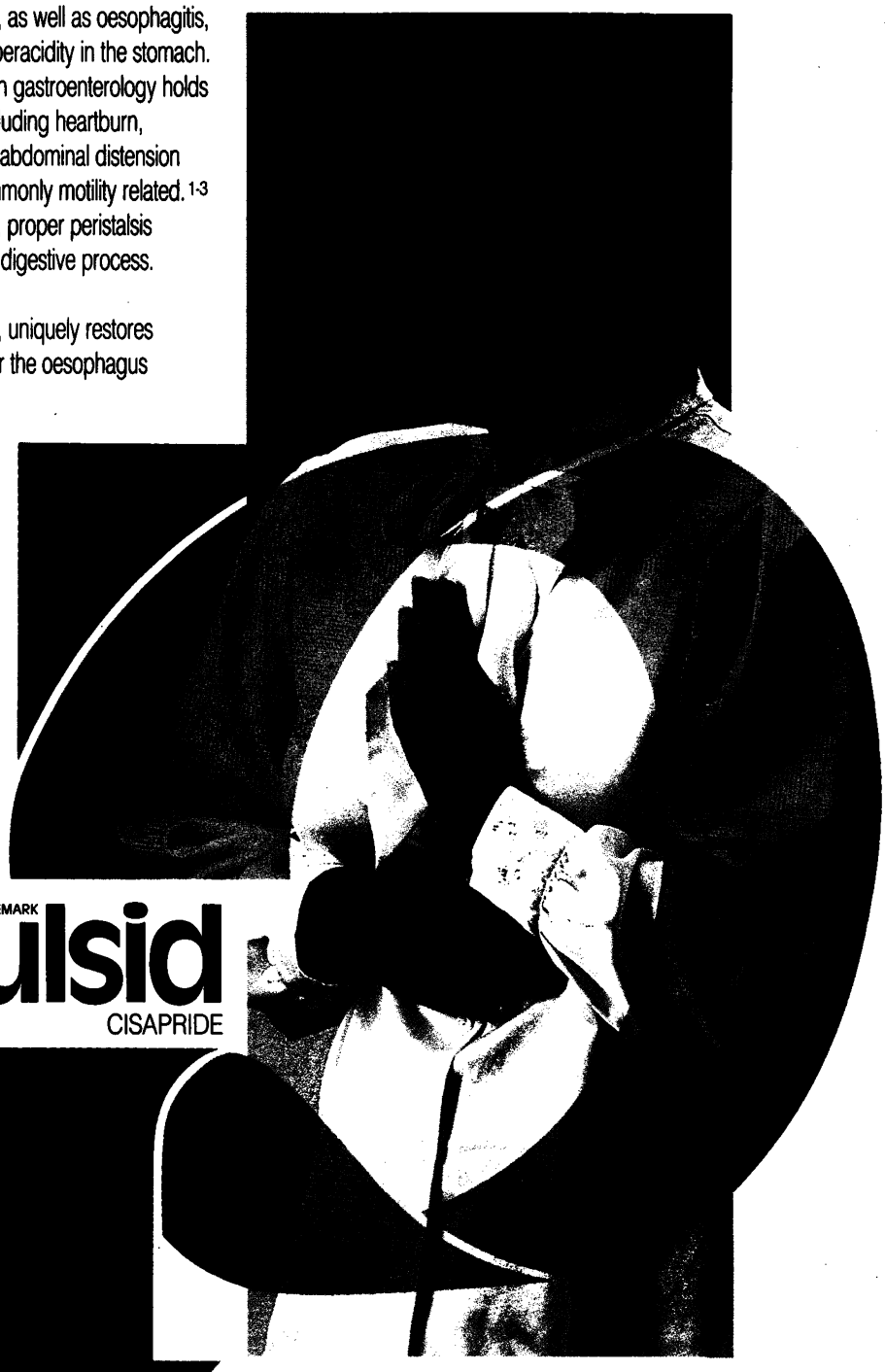
gastric distress & oesophagitis
hyperacidity or dysmotility?

Most complaints of gastric distress, as well as oesophagitis, are conventionally attributed to hyperacidity in the stomach. However, the contemporary view in gastroenterology holds that most upper G.I. problems, including heartburn, postprandial fullness, early satiety, abdominal distension and epigastric discomfort, are commonly motility related.[1-3] And this stands to reason. After all, proper peristalsis is a physiological necessity for our digestive process.

Prepulsid, the novel G.I. prokinetic, uniquely restores healthy peristalsis to efficiently clear the oesophagus and empty the stomach.[4-6]



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restores upper G.I. motility like no other agent.

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expertise in digestive motility

References: 1. Knuff J.E. et al. Dig. Dis. Sci. 29: 194 (1984). 2. Kahrilas J.P. et al. Gastroenterology 91: 897 (1986). 3. Malagelada J.R. et al. Gastroenterol. 88: 1223 (1985). 4. Ceccatelli P. et al. Gut 29: 631 (1988). 5. Collins B.J. et al. Hepato-Gastroenterol. 34: 113 (1987). 6. Jian R. et al. Dig. Dis. Sci. 34: 657 (1989).

Prescribing information - Prepulsid (cisapride) is a gastro-intestinal prokinetic agent. Prepulsid enhances and co-ordinates gastro-intestinal propulsive motility, thereby preventing stasis and reflux. **Therapeutic indications:** 1. Gastroparesis. 2. Symptoms of X-ray or endoscopy negative upper digestive discomfort. 3. Gastro-oesophageal reflux disorders, including oesophagitis. 4. Intestinal pseudo-obstruction. **Contra-indications:** No absolute contra-indications are known. **Precautions:** *Pregnancy:* Although, in animals, there is no effect on primary fertility, no primary embryotoxic and no teratogenic effect, the anticipated therapeutic benefits should be weighed against the potential hazards before Prepulsid is given during pregnancy, especially during the first trimester. *Nursing mothers:* Although the excretion in breast milk is minimal, nursing mothers are advised not to breast feed while taking Prepulsid. *Driving and machine-operating ability:* Prepulsid does not affect psychomotor function and does not induce sedation or drowsiness. Prepulsid may, however, accelerate the absorption of central nervous system depressants, such as barbiturates and alcohol. Caution should therefore be exercised when Prepulsid is administered with these drugs. **Interactions:** - The acceleration by Prepulsid of gastric emptying may affect the rate of absorption of drugs: absorption of drugs from the stomach may be diminished, whereas absorption of drugs from the small bowel may be accelerated (e.g. benzodiazepines, anticoagulants, paracetamol, H_2-blockers). - In patients receiving anticoagulants, the coagulation times may somewhat increase. It is advisable to check the coagulation time one week after the start of Prepulsid treatment to adapt the anticoagulant dose if necessary. - The effects of Prepulsid on gastro-intestinal motility are, for the most part, antagonized by anticholinergic drugs. - In hepatic and renal insufficiency, it is recommended to halve the initial daily dose. Subsequently, this dose can be adapted, depending on the therapeutic effects or possible side-effects. - In the elderly, steady-state plasma levels are generally higher, due to a moderate prolongation of the elimination half-life. Therapeutic doses, however, are similar to those used in younger patients. - In the case of drugs that require individual titration, it may be useful to monitor plasma levels of such drugs when Prepulsid is associated. **Adverse reactions:** In line with the pharmacological activity of Prepulsid, transient abdominal cramping, borborygmi and diarrhoea may occur. Mild and transient headache or lightheadedness have been reported occasionally. When diarrhoea occurs in babies or infants, the dose should be reduced. There have been isolated reports of convulsive seizures without clearcut relationship to Prepulsid. **Dosage:** - Adults: according to the severity of the condition, 5 or 10 mg of Prepulsid, 2 to 4 times daily, to be taken as tablets or as oral suspension (the full plastic 5-ml spoon contains 5 mg). As a rule the following doses have proven adequate • less severe conditions: 5 mg t.i.d. (dose can be doubled) • severe conditions (gastroparesis, oesophagitis, refractory constipation): 10 mg t.i.d. to 10 mg q.i.d. (before the 3 main meals and before retiring). - Infants and children: on the average 0.2 mg/kg per intake, 3 to 4 times daily. For the suspension,intakes are indicated on the dosing pipet as a function of body weight.

Full prescribing information available on request.

Note : Prepulsid (cisapride) is not yet available in all countries and not all indications have been approved everywhere.