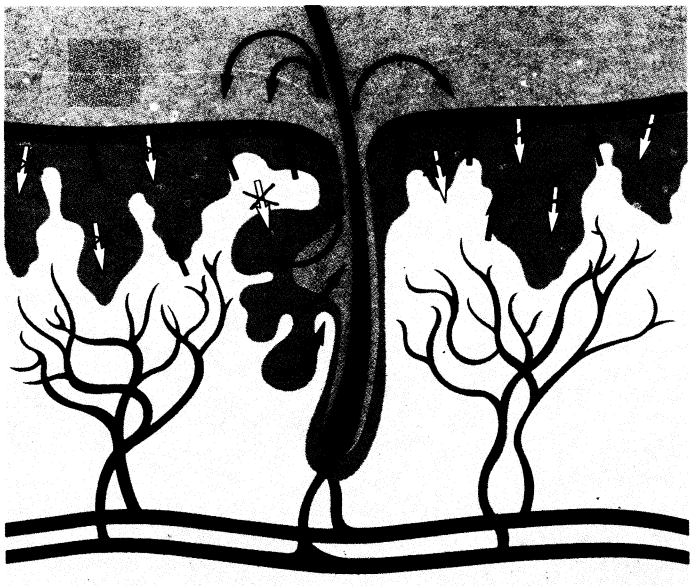
KEY WORDS OF MODERN ANTIFUNGAL THERAPY

THE REASSURING FACTOR:

NO REDISTRIBUTION...



After oral intake, itraconazole is delivered to the skin: **1.** by excretion via the sebaceous glands and **2.** by passive diffusion from the blood into the keratinocytes in the epidermis. Its antifungal activity in the epidermis continues for a full epidermal cycle (4 weeks) after the end of therapy, as its lipophilic structure prevents redistribution via the bloodstream.

Fungi and yeasts are notorious for their ability to entrench themselves in what may be called *the outside:* the skin, nails, hair and mucosa.
As for antifungal therapy, an effective way to reach all parts of that outside is via *the inside,* i.e. by the systemic route.

Ideally, an oral antimycotic should quickly disappear from the bloodstream and firmly establish itself in keratinous and mucosal tissues. And preferably, having reached its destination, *it should remain in those tissues and not be released back into the bloodstream.*

This is precisely what happens with itraconazole (Sporanox). Because of its lipophilic structure, it is strongly attracted to the epithelial cells, from where it will only be eliminated — *and only towards the outside* — as those cells gradually desquamate. During all that time its antifungal activity continues.

In fact, this strong fixation to — and inside — the outside tissues is what now permits the use of short, fixed, oral antifungal treatment schedules.

Sporanox *

ITRACONAZOLE 100 mg

SHORT AND SIMPLE ORAL THERAPY

(See prescribing information below)
Basic dose in dermatology: 1 capsule (100 mg) once daily for 15 days
Standard dose in vaginal candidosis: 2 x 2 capsules (400 mg) for 1 day only

Note: This product is not yet available in all countries.

*** Trademarks: SPORANOX, SEMPERA, TRISPORAL**

JANSSEN PHARMACEUTICA
B-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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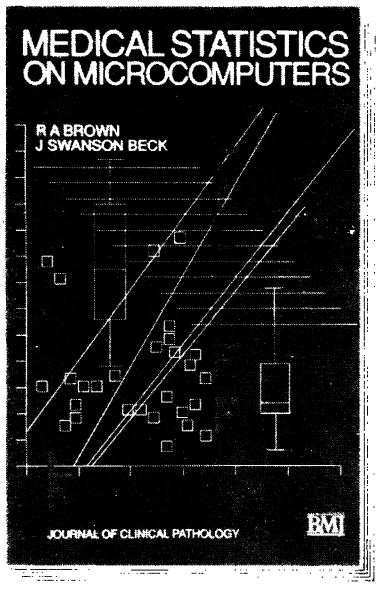

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- Analysis of categorical data
- Statistical methods for diagnostic tests.

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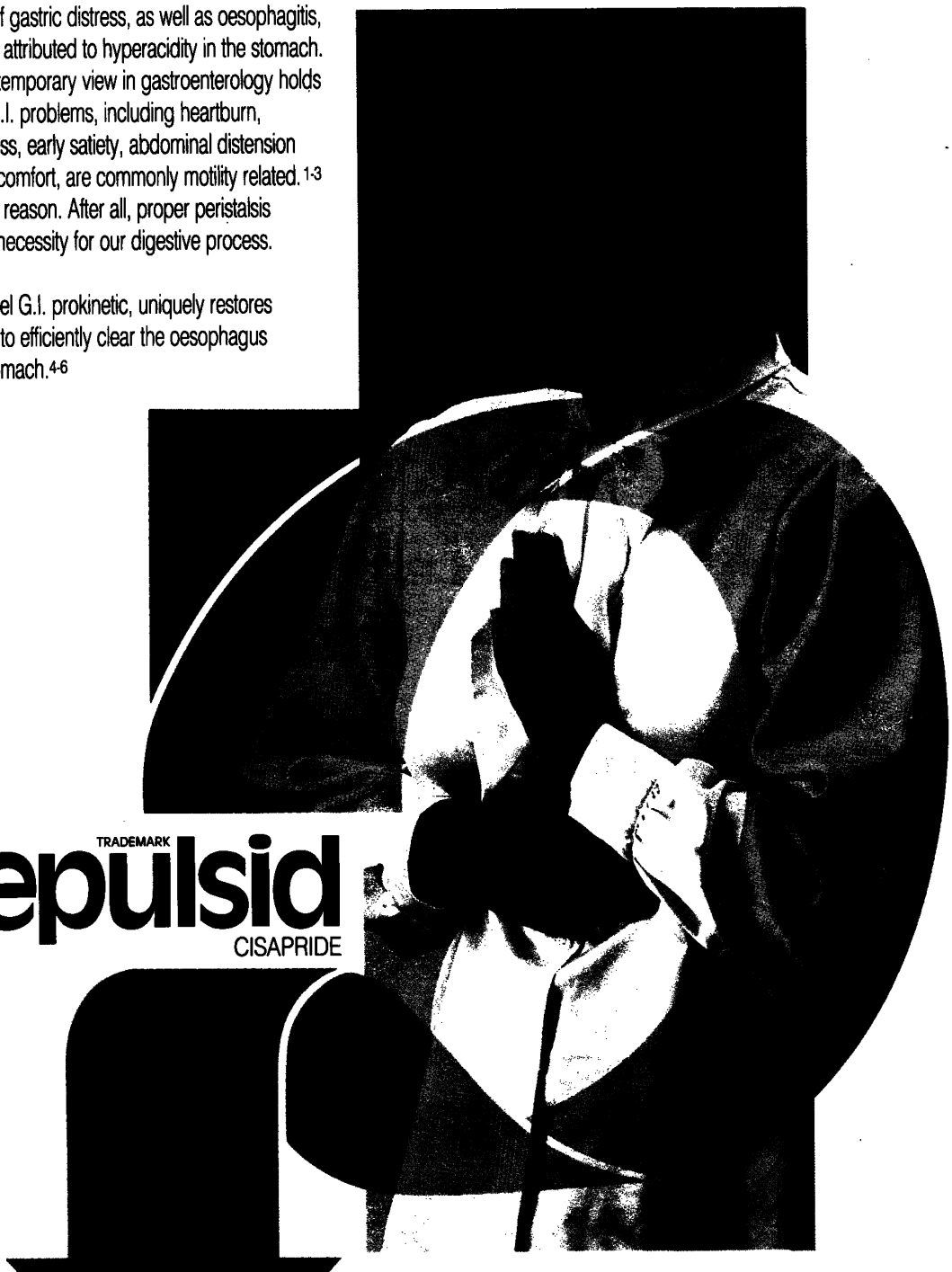
gastric distress & oesophagitis
hyperacidity or dysmotility?

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]



TRADEMARK
Prepulsid
CISAPRIDE

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

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PHARMACEUTICA
B-2340 Beerse, Belgium

expertise in digestive motility

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. Anticoagulants: the coagulation time may somewhat 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, H2-blockers). - In hepatic and renal insufficiency, it is recommended to titrate the levels of such drugs when Prepulsid is associated. Adverse reactions: In line 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 patients without clear-cut relationship to Prepulsid. **Dosage:** - Adults: according to the 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 batches or interrs. the dose should be reduced. There have been isolated reports of convulsions (gastroparesis, oesophagitis, refractory constipation): 10 mg t.i.d. to 10 mg q.i.d. (before the 3 main meals and before 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.