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materials; well under 10% of total housekeeping costs are for the products used for cleaning and/or disinfecting floors.

If disinfectant-containing products were not used in floor cleaning, it is likely that wet mops would become so contaminated during a work-shift that there might be increased rather than decreased microbial contamination after "cleaning" (and we recommend additionally that the mops be laundered and thoroughly dried daily). Some references cited in our paper "Housekeeping in operating suites," *AORN Journal* 21:213-220, 1975, indicate that disinfectant-containing products are more effective in reducing microbial contamination than detergents and water alone (T.S. Gable, *Hospitals*, 40:107-111, February 16, 1966; G.A.J. Ayliffe, B.J. Collins, E.J.L. Lowbury, *Br Med J* 2:442-445, 1966; W.D. Foster, *Lancet*, 1:670-673, 1960; and J.S. Kuipers, *J Hygiene*, 66:625-631, 1968).

Apparently, use of two cleaning products (one with a disinfecting ingredient and the other with a detergent only) is suggested by Dr. Daschner based on European experience. This policy might increase labor costs of housekeepers and their supervisors because of decisions that would have to be made on how and when a disinfectant-detergent floor cleaning would be justified and dispatched. In my view, such a special cleaning for known presence of potentially infectious material would likely cost more than if a disinfectant-detergent were used for routine cleaning.

In summary, I believe that it is not a cost disadvantage to use disinfectant-detergent products for all floors in patient-care areas of hospitals.

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## Detection of Bacteremia: Technical Aspects of the Blood Culture

### To the Editor:

In the article "Detection of Bacteremia: Technical aspects of the blood

culture" (2:399-400, 1981), I would like to respectfully disagree with Dr. Weinstein's statement on subcultures. He comments that subcultures are routine at 7 or 14 days before the blood culture is discarded. While this practice may currently be the case in many hospitals, this practice should now be abandoned. In the past two years, several studies have been done which indicate that the terminal subculture does not detect previously unsuspected bacteremia. Those terminal subcultures that are positive usually appear from patients where other blood cultures were positive earlier. These studies have been documented in standard blood culture media involving over 14,000 blood cultures in a study by Campbell and Washington<sup>1</sup> and in 2,780 cultures by Gill.<sup>2</sup> In a study using the BACTEC radiometric blood culture media, Araj et al could not demonstrate any significant value of terminal subcultures in 5,354 blood culture bottles.<sup>3</sup> This laboratory practice should be abandoned. The aforesaid, however, does not denigrate the value of subcultures within the first 24 hours.

### REFERENCES

1. Campbell J, Washington JA Jr: Evaluation of the necessity for routine terminal subcultures of previously negative blood cultures. *J Clin Microbiol*, 12:576-578, 1980.
2. Gill VJ: Lack of clinical relevance in routine terminal subculturing of blood cultures. *J Clin Microbiol*, 14:116-118, 1981.
3. Araj GF, Hopfer RL, Wenglar M, et al: Value of terminal subcultures from negative BACTEC blood culture bottles. *J Clin Microbiol*, 14:589-590, 1981.

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*Dr. Melvin Weinstein responds to Dr. Gross' comments below.*

Dr. Gross correctly points out that three recent studies have demonstrated no advantage to routine terminal subculture after seven days incubation.<sup>1-3</sup> One study reported observations made during a three-week study period<sup>1</sup> and another examined results during a three-month time span.<sup>3</sup> These somewhat limited evaluations may not be adequate to support Dr. Gross' conclusion that the practice of performing terminal subcultures be

abandoned completely. Indeed, Araj et al<sup>3</sup> concluded their report by recommending that laboratories review their terminal subculture results before making changes in blood culture policy. In at least one institution where this recommendation was followed, the microbiologist decided to continue performing terminal subcultures.<sup>4</sup>

Campbell and Washington suggest that seven days incubation of blood cultures is probably adequate for general hospitals but that a second week of incubation is indicated in suspected endocarditis, persistent or recurrent infection, and in laboratories which serve referral centers.<sup>1</sup> Reller also has recommended a two-week incubation of blood cultures in suspected endocarditis.<sup>5</sup> To my knowledge there are no published data on the value of terminal subcultures at the end of a two-week incubation period. During a 21-month period (1975-1977) at the University of Colorado Health Sciences Center (UCHSC), more than 15,000 blood cultures were obtained of which 1069 (7%) were positive for microorganisms which represented true bacteremia as determined clinically by members of the Infectious Disease Service (Weinstein MP, Reller LB, unpublished data). Fifty-three microorganisms, representing 5% of all clinically important isolates, were detected only by the terminal subculture at 14 days. Since 1977 the clinical microbiology laboratory at UCHSC has continued to identify 5% of clinically important isolates, in particular gonococci, cryptococci, and *Candida spp.*, only by the terminal subculture (Reller LB, personal communication). While the yield is limited, the accompanying table shows that the microorganisms isolated represent a broad spectrum of human pathogens.

Is the limited yield worth the extra cost and effort? Laboratory directors hopefully in consultation with interested clinicians, will have to judge the relative value of terminal subcultures in their institutions. At our teaching hospital all blood cultures are incubated for 14 days, and terminal subcultures are and will continue to be performed.

Lastly, Dr. Gross' letter confuses data from two of the studies he quotes. Campbell and Washington<sup>1</sup> evaluated

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An important first:

# NIZORAL<sup>®</sup> TABLETS

(ketoconazole)

Safe and effective and offers a number of distinct advantages over nystatin in treating severe oral thrush

## Saves time and trouble for patients and staff

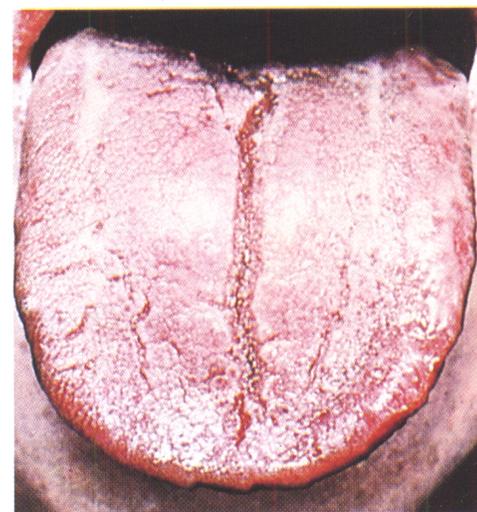
- Simple one-tablet-a-day regimen fosters compliance, facilitates ambulatory and outpatient therapy
- No need for patients to suck on suppositories or swish around nystatin preparations several times a day
- Cost of therapy significantly less than nystatin treatment

## Systemic action can reach remote Candida lesions

- In contrast to the topical action of nystatin, NIZORAL<sup>®</sup> (ketoconazole) can reach asymptomatic lesions in the esophagus or GI tract
- Excellent overall effectiveness... one week clinical cures seen in over 50 percent of patients
- SAFE: Can be administered for prolonged periods; well tolerated. Since possible idiosyncratic hepatocellular dysfunction has been reported, it is desirable to perform appropriate liver function tests before and during treatment, particularly in patients on long-term therapy.

Please see revised brief summary of Prescribing Information on next page.

Jones, Mary	126-34-4439
Date	Doctor's orders
9/12/81	1. Ambulatory as desired
	2. Regular diet
	3. Nizoral 200mg p.o., q.d.



**Top:** Severe oral thrush before therapy.  
**Bottom:** After 7 days, 200 mg per day oral NIZORAL.

world leader in antimycotic research



**JANSSEN**  
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# NIZORAL<sup>®</sup> TABLETS

(ketoconazole)

Before prescribing, please consult complete prescribing information, of which the following is a brief summary.

## INDICATIONS AND USAGE

NIZORAL<sup>®</sup> is indicated for the treatment of the following systemic fungal infections: candidiasis, chronic mucocutaneous candidiasis, oral thrush, candiduria, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis. NIZORAL<sup>®</sup> should not be used for fungal meningitis because it penetrates poorly into the cerebral-spinal fluid.

For the initial diagnosis, the infective organism should be identified; however, therapy may be initiated prior to obtaining laboratory results.

## CONTRAINDICATIONS

NIZORAL<sup>®</sup> is contraindicated in patients who have shown hypersensitivity to the drug.

## WARNINGS

Several cases of possible idiosyncratic hepatocellular dysfunction have been reported during NIZORAL<sup>®</sup> treatment. It is important to recognize that liver disorders may occur with NIZORAL<sup>®</sup> therapy. The rare occurrences of liver disorders could be potentially fatal unless properly recognized and managed.

It is desirable to perform liver function tests, such as SGPT, alkaline-phosphatase, SGPT, SGOT and bilirubin, before treatment and at periodic intervals during treatment (monthly or more frequent), particularly in patients who will be on prolonged therapy or who have a history of liver disease. Instances of minor elevations of liver enzyme levels in patients on NIZORAL<sup>®</sup> have been shown to normalize during therapy and may not necessitate discontinuation of treatment. However, if liver function tests are significantly elevated or other signs and symptoms are suggestive of hepatocellular dysfunction, ketoconazole should be discontinued.

In female rats treated three to six months with ketoconazole at dose levels of 80 mg/kg and higher, increased fragility of long bones, in some cases leading to fracture, was seen. The maximum "no-effect" dose level in these studies was 20 mg/kg (2.5 times the maximum recommended human dose). The mechanism responsible for this phenomenon is obscure. Limited studies in dogs failed to demonstrate such an effect on the metacarpals and ribs.

## PRECAUTIONS

**General:** In four subjects with drug-induced achlorhydria, a marked reduction in NIZORAL<sup>®</sup> absorption was observed. NIZORAL<sup>®</sup> requires acidity for dissolution. If concomitant antacids, anticholinergics, and H<sub>2</sub>-blockers are needed, they should be given at least two hours after NIZORAL<sup>®</sup> administration. In cases of achlorhydria, the patients should be instructed to dissolve each tablet in 4 ml aqueous solution of 0.2 N HCl. For ingesting the resulting mixture, they should use a glass or plastic straw so as to avoid contact with the teeth. This administration should be followed with a cup of tap water.

**Information for Patient:** Patient should be instructed to report any signs and symptoms which may suggest liver dysfunction so that appropriate biochemical testing can be done. Such signs and symptoms may include unusual fatigue, nausea or vomiting, jaundice, dark urine or pale stools (see WARNINGS).

**Drug Interactions:** There is no evidence for clinically significant interaction with oral anticoagulant or oral hypoglycemic agents.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** The dominant lethal mutation test in male and female mice revealed that single oral doses of NIZORAL<sup>®</sup> as high as 80 mg/kg produced no mutation in any stage of germ cell development. The Ames' *Salmonella* microsomal activator assay was also negative.

**Pregnancy:** Teratogenic effects: Pregnancy Category C. NIZORAL<sup>®</sup> has been shown to be teratogenic (syndactylia and oligodactylia) in the rat when given in the diet at 80 mg/kg/day, (10 times the maximum recommended human dose). However, these effects may be related to maternal toxicity, evidence of which also was seen at this and higher dose levels.

There are no adequate and well controlled studies in pregnant women. NIZORAL<sup>®</sup> should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nonteratogenic effects:** NIZORAL<sup>®</sup> has also been found to be embryotoxic in the rat when given in the diet at doses higher than 80 mg/kg during the first trimester of gestation.

In addition, dystocia (difficult labor) was noted in rats administered NIZORAL<sup>®</sup> during the third trimester of gestation. This occurred when NIZORAL<sup>®</sup> was administered at doses higher than 10 mg/kg (higher than 1.25 times the maximum human dose).

It is likely that both the malformations and the embryotoxicity resulting from the administration of NIZORAL<sup>®</sup> during gestation are a reflection of the particular sensitivity of the female rat to this drug. For example, the oral LD<sub>50</sub> of NIZORAL<sup>®</sup> given by gavage to the female rat is 166 mg/kg, whereas in the male rat the oral LD<sub>50</sub> is 287 mg/kg.

**Nursing Mothers:** Since NIZORAL<sup>®</sup> is probably excreted in the milk, mothers who are under NIZORAL<sup>®</sup> treatment should not breast-feed the child.

**Pediatric Use:** Safety in children under two years of age has been documented in a limited number of cases.

## ADVERSE REACTIONS

NIZORAL<sup>®</sup> is usually well tolerated. Most adverse reactions reported have been mild and transient and have only rarely required withdrawal of therapy.

The most frequent adverse reactions were nausea and/or vomiting, which occurred in approximately 3% of patients. Abdominal pain was reported in approximately 1.2% of patients; pruritus in approximately 1.5% of patients. The following have been reported in less than 1% of patients: headache, dizziness, somnolence, fever and chills, photophobia, diarrhea, jaundice and gynecostasia.

Transient increases in serum liver enzymes have been observed. In the majority of cases, these increases have normalized during therapy or shortly after drug has been discontinued. However, several cases of idiosyncratic hepatocellular dysfunction have been reported (see WARNINGS).

## OVERDOSAGE

In the event of accidental overdosage, supportive measures, including gastric lavage with sodium bicarbonate, should be employed.

## DOSE AND ADMINISTRATION

**Adults:** The recommended starting dose of NIZORAL<sup>®</sup> is a single daily administration of 200 mg (one tablet). In very serious infections or if clinical responsiveness is insufficient within the expected time, the dose of NIZORAL<sup>®</sup> may be increased to 400 mg (two tablets) once daily.

## Children:

Children weighing 20 kg or less: ..... 50 mg (¼ tablet) once daily  
 Children weighing 20-40 kg: ..... 100 mg (½ tablet) once daily  
 Children weighing over 40 kg: ..... 200 mg (1 tablet) once daily

Generally, treatment should be continued until all clinical and laboratory tests indicate that active fungal infection has subsided. Inadequate periods of treatment may yield poor response and lead to early recurrence of clinical symptoms. Minimum treatment for candidiasis is one or two weeks. Patients with chronic mucocutaneous candidiasis usually require maintenance therapy. Minimum treatment for the other indicated systemic mycoses is six months.

## HOW SUPPLIED

NIZORAL<sup>®</sup> is available as white, scored tablets containing 200 mg of ketoconazole debossed "JANSSEN" and on the reverse side debossed "K" and "200." They are supplied in bottles of 60 tablets and in blister packs of 10 x 10 tablets. Rev. Feb. 1982

U.S. Patent Pending  
 NDC 50458-220-01 (10 x 10 tablets-blisters)  
 NDC 50458-220-06 (60 tablets)

Manufactured by:  
 Janssen Pharmaceutica n.v.  
 B-2340 Beerse, Belgium

For:  
 Janssen Pharmaceutica Inc.  
 New Brunswick, New Jersey 08903 USA

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## TABLE MICROORGANISMS ISOLATED ONLY BY TERMINAL SUBCULTURE AT UCHSC July 1975—April 1977

Microorganism	No.
Staphylococcus aureus	7
Staphylococcus epidermidis	2
Escherichia coli	3
Klebsiella pneumoniae	1
Enterobacter cloacae	1
Proteus mirabilis	1
Citrobacter sp.	1
Serratia marcescens	1
Pseudomonas aeruginosa	1
Pseudomonas sp.	1
Acinetobacter calcoaceticus	1
Haemophilus influenzae	1
Neisseria gonorrhoeae	1
Peptostreptococcus sp.	3
Peptococcus sp.	2
Eubacterium sp.	3
Clostridium sp.	2
Bacteroides fragilis group	2
Bacteroides melaninogenicus	2
Bacteroides sp.	2
Veionella sp.	1
Candida albicans	5
Candida spp.	4
Cryptococcus neoformans	3
Torulopsis glabrata	2

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1385 blood cultures rather than 14,000 as indicated by Dr. Gross. The study by Gill<sup>2</sup> evaluated over 14,000 bottles from 7579 blood cultures.

## REFERENCES

- Campbell J, Washington JA Jr: Evaluation of the necessity for routine terminal subcultures of previously negative blood cultures. *J Clin Microbiol*, 12:576-578, 1980.
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