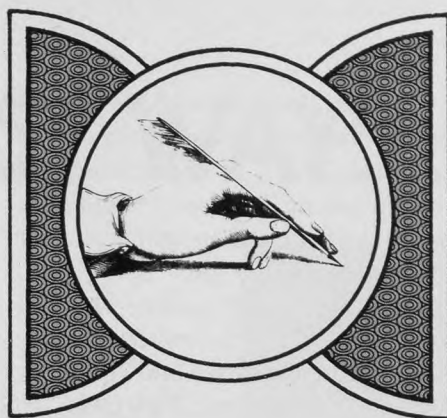


Letters to the Editor

The Journal welcomes Letters to the Editor; if found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with journal style.



Cimetidine Drug Interactions

To the Editor:

In the June 1983 issue of *The Journal of Family Practice*, in an article reviewing cimetidine drug interactions, Greene, Self, and Levinson¹ state that:

The interaction with diazepam and chlordiazepoxide results in clinically appreciable increased sedation, and there appears to be no interaction with oxazepam or lorazepam. On this basis it is recommended that when a benzodiazepine is needed in combination with cimetidine, oxazepam or lorazepam should be considered as agents of first choice.

This is not completely accurate. A number of reports and comments have appeared in the literature regarding the interaction between benzodiazepines and cimetidine.²⁻¹⁶ For the most part, these have been pharmacokinetic studies, with little or no attention paid to clinical effects. In fact, of the older studies, only Klotz and Reimann^{3,5} and Patwardhan¹¹ mention clinical effects. Klotz and Reimann note that after a single intravenous dose of diazepam (Valium), “. . . five of six patients experienced pronounced sedation and slept for one to three hours when pretreated with cimetidine.” Patwardhan et al, on the other hand, found that after a single intravenous dose of chlordiazepoxide (Librium) “. . . all subjects remained asymptomatic during the

course of the investigation.”

It appears that an interaction between cimetidine and benzodiazepines does occur. However, the important fact is that *no significant clinical effects* have been demonstrated to date, a fact further demonstrated by the recently published study by Gough et al.¹⁵

Dr. David Greenblatt has conducted a study titled “Clinical Implication of a Cimetidine-Diazepam Interaction.” The study has been completed, and although the statistics are not in final form, he has stated the following based on preliminary observation (personal communication, December 13, 1982):

Coadministration of cimetidine to patients receiving diazepam causes an increase in steady-state plasma concentrations of diazepam and desmethyl-diazepam, but this causes no detectable change in the therapeutic effects of diazepam; nor is there any unwanted drowsiness or excessive sedation. Our study shows that the diazepam-cimetidine pharmacokinetic interaction is not clinically important.

Good medical practice dictates that patients receiving prescription drugs (either singly or in combination), including the drugs in question, be closely monitored.

Finally, it is important to note that indications for the various benzodiazepines do vary, and choice, therefore, cannot be made based

on a pharmacokinetic interaction alone. Only some are indicated in alcohol withdrawal, as adjunctive therapy in convulsive disorders, and only one as adjunctive therapy in muscle spasm.

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Thaddeus E. Sudol, RPh
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Treatment of Giardiasis

To the Editor:

We would like to make additional comments concerning the treatment of giardiasis in children, prompted by a communication, "Giardia Lamblia: A Clinical-Epidemiological Case Report," by Sim S. Galazka (*J Fam Pract* 15:1165, 1982). This article stated that quinacrine is the drug of choice for giardiasis in both adults and children, with metronidazole as a second-line agent. We would like to expand on the treatment options based on a review of recent literature.

While quinacrine has been chosen as the drug of choice by many experts,^{1,2} with 90 to 95 percent cure rates, its use has been accompanied by many side effects including nausea, vomiting, diarrhea, bitter taste, and yellow skin discoloration, particularly in young children.^{1,3} In adults it is generally well tolerated and most effective. The product is available as a tablet only.

Metronidazole is 85 to 90 percent effective in conventional doses. Its use is limited by frequent nausea, vomiting, and metallic taste. It is generally better tolerated than quinacrine in children, though its potential teratogenicity has not been resolved. Liquid suspensions for pediatric use are available only outside the United States.

Furazolidone is available in both tablet and suspension forms. It is reported to be 77 to 92 percent effective in young children,^{1,3} and it is better tolerated than quinacrine or metronidazole in this age group. Its usefulness for routine therapy in young children is limited by relatively frequent nausea and vomiting, local availability, and high cost.

Other effective treatments not currently available in the United States include tinidazole, ornidazole, and nimorazole.

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Allan Ellsworth, PharmD

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Hospital Privileges for Family Physicians

To the Editor:

In his article about hospital privileges for family physicians in the July 1983 issue (*Pugno PA: Hospital privileges for family physicians: Rights, rationale, and resources. J Fam Pract* 17:77, 1983), Dr. Pugno omitted an important restrictor of hospital privileges—state law. On moving from Michigan to New York, I was distressed to discover that under New York state law, "physicians permitted to perform all types of obstetric procedures and deliveries shall be limited to qualified obstetricians. . . . physicians permitted to perform deliveries of a normal, uncompli-

Continued on page 202

Ilosone® (erythromycin estolate)

Brief Summary.

Consult the package literature for prescribing information.

WARNING

Hepatic dysfunction with or without jaundice has occurred, chiefly in adults, in association with erythromycin estolate administration. It may be accompanied by malaise, nausea, vomiting, abdominal colic, and fever. In some instances, severe abdominal pain may simulate an abdominal surgical emergency. If the above findings occur, discontinue Ilosone promptly. Ilosone is contraindicated for patients with a known history of sensitivity to this drug and for those with preexisting liver disease.

Indications: *Streptococcus pyogenes* (Group A Beta-Hemolytic)—Upper and lower respiratory tract, skin, and soft-tissue infections of mild to moderate severity.

Injectable penicillin G benzathine is considered by the American Heart Association to be the drug of choice in the treatment and prevention of streptococcal pharyngitis and in long-term prophylaxis of rheumatic fever.

When oral medication is preferred for treating the above-mentioned conditions, penicillin G or V or erythromycin is the alternate drug of choice.

The importance of the patient's strict adherence to the prescribed dosage regimen must be stressed when oral medication is given. A therapeutic dose should be administered for at least ten days.

Alpha-Hemolytic Streptococci (Viridans Group)—Although no controlled clinical efficacy trials have been conducted, oral erythromycin has been suggested by the American Heart Association and American Dental Association for use in a regimen for prophylaxis against bacterial endocarditis in patients hypersensitive to penicillin who have congenital and/or rheumatic or other acquired valvular heart disease when they undergo dental procedures and surgical procedures of the upper respiratory tract.¹ Erythromycin is not suitable for such prophylaxis prior to genitourinary or gastrointestinal tract surgery.

Note: When selecting antibiotics for the prevention of bacterial endocarditis, the physician or dentist should read the full joint statement of the American Heart Association and the American Dental Association.¹

Staphylococcus aureus—Acute infections of skin and soft tissue which are mild to moderately severe. Resistance may develop during treatment.

S. (Diplococcus) pneumoniae—Infections of the upper respiratory tract (e.g., otitis media, pharyngitis) and lower respiratory tract (e.g., pneumonia) of mild to moderate severity.

Mycoplasma pneumoniae (Eaton Agent, PPLD)—Respiratory tract infections due to this organism.

Haemophilus influenzae—May be used concomitantly with adequate doses of sulfonamides for upper respiratory tract infections of mild to moderate severity. Not all strains of this organism are susceptible at the erythromycin concentrations ordinarily achieved (see appropriate sulfonamide labeling for prescribing information).

Treponema pallidum—As an alternate treatment for primary syphilis in penicillin-allergic patients. In primary syphilis, spinal-fluid examinations should be done before treatment and as part of follow-up after therapy.

Corynebacterium diphtheriae—As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

C. minutissimum—In the treatment of erythrasma.

Entamoeba histolytica—For intestinal amebiasis only. Extra-intestinal amebiasis requires treatment with other agents.

Listeria monocytogenes—Infections due to this organism.

Legionnaires' Disease—Although no controlled clinical efficacy studies have been conducted, in vitro and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' disease.

Contraindication: Known hypersensitivity to this antibiotic.

Warnings: (See Warning box above.) The administration of erythromycin estolate has been associated with the infrequent occurrence of cholestatic hepatitis. Laboratory findings have been characterized by abnormal hepatic function test values, peripheral eosinophilia, and leukocytosis. Symptoms may include malaise, nausea, vomiting, abdominal cramps, and fever. Jaundice may or may not be present. In some instances, severe abdominal pain may simulate the pain of biliary colic, pancreatitis, perforated ulcer, or an acute abdominal surgical problem. In other instances, clinical symptoms and results of liver function tests have resembled findings in extrahepatic obstructive jaundice.

Initial symptoms have developed in some cases after a few days of treatment but generally have followed one or two weeks of continuous therapy. Symptoms reappear promptly, usually within 48 hours after the drug is readministered to sensitive patients. The syndrome seems to result from a form of sensitization, occurs chiefly in adults, and has been reversible when medication is discontinued.

Usage in Pregnancy—Safety of this drug for use during pregnancy has not been established.

Precautions: Caution should be exercised in administering the antibiotic to patients with impaired hepatic function.

Recent studies of erythromycin reveal that its use in patients who are receiving high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. In such a case, the dose of theophylline should be reduced while the patient is receiving concomitant erythromycin therapy.

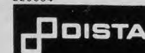
Surgical procedures should be performed when indicated.

Adverse Reactions: The most frequent side effects are gastrointestinal (e.g., abdominal cramping and discomfort) and are dose related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses.

During prolonged or repeated therapy, overgrowth of nonsusceptible bacteria or fungi is possible. If such infections arise, the drug should be discontinued and appropriate therapy instituted.

Mild allergic reactions, such as urticaria and other skin rashes, have occurred. Serious allergic reactions, including anaphylaxis, have been reported.


¹ American Heart Association. Prevention of Bacterial Endocarditis. Circulation. 56:139A, 1977. [093086]



Address medical inquiries to:
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Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patient to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, e.g., excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

LETTERS TO THE EDITOR

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cated nature shall be required to hold consultations with a qualified obstetrician under the conditions listed below; and, such physicians shall transfer responsibility to a qualified obstetrician for those procedures which are not encompassed in their privileges" (NY Hosp Code, title 10, chap V, §405.8). There follows a list of 12 specific situations, including use of oxytocin and labors longer than 12 hours, to which these restrictions apply. This indeed is a case for the action of organized family practice.

David M. Newman, MD
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Bacterial Contamination of Sheathed Thermometers

To the Editor:

A variety of infectious diseases may be transmitted to patients by cross-contamination from oral secretions and oral lesions. One mode of transmission may be facilitated by medical instruments or materials.

Mercury-in-glass thermometers are commonly used in medical practice and often remain contaminated or are recontaminated before they are reused.¹ In 1972, a thermometer sheath was marketed to reduce cross-contamination. The current annual distribution of this sheath (according to Steridyne Corporation) is estimated at over 50 million units. Litsky² reported that the thermometer sheath is effective in preventing cross-contamination when utilized for taking rectal temperatures. Later, Valenti and Takacs³ reported the thermometer sheath is frequently perforated when used for taking oral temperatures. However, in this latter study the oral placement time was not standardized, the presence

or absence of teeth was not reported, and contamination of the thermometer was not evaluated.

We conducted a study to evaluate mercury-in-glass sheathed thermometers for bacterial contamination after being used for taking 6-minute and 11-minute oral temperatures. One hundred mercury-in-glass thermometers were sterilized in buffered glutaraldehyde (Cider) for 24 hours. Using sterile technique, the thermometers were packaged individually in Steritemp Thermometer Sheaths. A control group of 25 thermometers were evaluated to determine whether they remained sterile after the packaging procedures. Results showed that all 25 thermometers from the control group remained sterile after the packaging procedures.

In a second group, the outer surfaces of 25 Steritemp Sheaths were evaluated for sterility and their permeability to oral bacteria from whole saliva in vitro. Results showed that the outer surfaces of all 25 sheaths were sterile and that each sheath was impermeable to oral bacteria when tested in vitro.

A third group of 25 sheathed thermometers were evaluated for contamination after being used for 11-minute oral temperatures from dentulous patients. Results showed that 80 percent of the thermometers (20/25) were contaminated.

A fourth group of 25 sheathed thermometers were evaluated for contamination after being used for taking 6-minute oral temperatures. Results showed that 80 percent of the thermometers (20/25) were contaminated.

The findings from this study indicate that the thermometer sheath does not prevent bacterial contamination of the mercury-in-glass

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Roche Products Inc.
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thermometer when used for taking oral temperatures from dentulous patients. Patients tend not to comply with the request to avoid tooth contact with the sheathed-thermometer. Results showed that 80 percent of the sheaths had been perforated by the dentition and that all the respective thermometers were contaminated. Therefore, if the thermometer is not effectively sterilized after each use, the potential for cross-contamination may be as high as 80 percent.

In consideration of this potential for cross-contamination, we recommend that all sheathed thermometers be resterilized after each use using chlorine, iodophor, buffered glutaraldehyde preparations, or ethylene oxide.^{1,2,4,5,6}

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Drug Interactions With Furosemide

To the Editor:

In the March 1983 issue of *The Journal of Family Practice*, we re-

ported a case of an interaction between furosemide and indomethacin resulting in decreased effectiveness of furosemide.¹ In the discussion we pointed out that "diflunisal apparently causes no deleterious effect on the action of furosemide."

Recent work has been done, however, to dispute this fact. Favre et al² studied the effects of diflunisal (in addition to indomethacin) on the action of furosemide, hydrochlorothiazide, triamterene, and spironolactone. Results of those studies indicate that diflunisal may indeed have an effect on furosemide similar to that of indomethacin, ie, an inhibitory effect on the action of furosemide. Further, it appears from this study that hydrochlorothiazide and triamterene are not significantly affected by indomethacin or diflunisal. This is in contrast to previous reports.³

It is not uncommon to see conflicting reports to the medical literature. This emphasizes the need to be especially cautious using drug combinations and to interpret the literature very carefully. The combination of any nonsteroidal anti-inflammatory drug and diuretic deserves careful monitoring and follow-up.

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