

## 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.

### Failure of Prophylaxis for Bacterial Endocarditis: American Heart Association Registry

To the Editor:

The American Heart Association (AHA) recognizes that its current recommendations for antibiotic prophylaxis are necessarily empiric.<sup>1</sup> This situation has arisen because important clinical information on the efficacy of antibiotic prophylaxis of bacterial endocarditis is lacking. The present recommendations are therefore based upon secondary sources of information such as the relative propensity of various procedures to cause bacteremia, in vitro studies of bacteria recovered from the blood, the effect of antibiotics on bacteremias, the susceptibility of various heart lesions to infection, anecdotal case reports, and study of experimental models.

Although over 30 individual cases of apparent prophylaxis failure have been recorded in the literature, many of our colleagues have rightly pointed out that the evidence indicating that a significant number of prophylaxis failures



actually occur is inconclusive. This question is of considerable medical and medicolegal importance because of the frequency with which measures to prevent endocarditis are called for, and because of the serious consequences of failure to prevent the disease.

In an attempt to accumulate useful epidemiologic data, the AHA Committee has established a Registry to record cases of apparent failure of antibiotic prophylaxis of bacterial endocarditis. We are now soliciting case reports. Notification may be made on a simple pre-printed postcard, which will require only identification of the patient and the name, address, and telephone number of the person referring the case. These postcards will be made available to physicians and dentists and to any other person or organization requesting them from the AHA or from one of us. Alternatively, a case may be reported directly to one of us, at the address or telephone number

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For UTI in their  
sexually active years...

## Macrochantin<sup>®</sup> (nitrofurantoin macrocrystals)

Capsules: 25 mg, 50 mg, 100 mg

**INDICATIONS:** Macrochantin is indicated for the treatment of urinary tract infections when due to susceptible strains of *Escherichia coli*, enterococci, *Staphylococcus aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses), and certain susceptible strains of *Klebsiella* species, *Enterobacter* species, and *Proteus* species.

**NOTE:** Specimens for culture and susceptibility testing should be obtained prior to and during drug administration.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 40 ml per minute) are contraindications to therapy with this drug. Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of the drug. For the same reason, this drug is much less effective under these circumstances.

The drug is contraindicated in pregnant patients at term as well as in infants under one month of age because of the possibility of hemolytic anemia due to immature enzyme systems (glutathione instability).

The drug is also contraindicated in those patients with known hypersensitivity to Macrochantin, Furadantin<sup>®</sup> (nitrofurantoin), and other nitrofurantoin preparations.

**WARNINGS:** Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin products. If these reactions occur, the drug should be withdrawn and appropriate measures should be taken.

An insidious onset of pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) in patients on long-term therapy warrants close monitoring of these patients.

There have been isolated reports giving pulmonary reactions as a contributing cause of death. (See Hypersensitivity reactions.)

Cases of hemolytic anemia of the primaquine sensitivity type have been induced by Macrochantin. The hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Negroes and a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Any sign of hemolysis is an indication to discontinue the drug. Hemolysis ceases when the drug is withdrawn.

*Pseudomonas* is the organism most commonly implicated in superinfections in patients treated with Macrochantin.

**PRECAUTIONS:** Peripheral neuropathy may occur with Macrochantin therapy; this may become severe or irreversible. Fatalities have been reported. Predisposing conditions such as renal impairment (creatinine clearance under 40 ml per minute), anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**Usage in Pregnancy:** The safety of Macrochantin during pregnancy and lactation has not been established. Use of this drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

**ADVERSE REACTIONS: Gastrointestinal reactions:** Anorexia, nausea and emesis are the most frequent reactions; abdominal pain and diarrhea occur less frequently. These dose-related toxicity reactions can be minimized by reduction of dosage, especially in the female patient. Hepatitis occurs rarely.

**Hypersensitivity reactions:** Pulmonary sensitivity reactions may occur, which can be acute, subacute, or chronic.

Acute reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution may be dramatic.

In subacute reactions, fever and eosinophilia are observed less often. Recovery is somewhat slower, perhaps as long as several months. If the symptoms are not recognized as being drug related and nitrofurantoin is not withdrawn, symptoms may become more severe.

Chronic pulmonary reactions are more likely to occur in patients who have been on continuous nitrofurantoin therapy for six months or longer. The insidious onset of malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations. Roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both are also common manifestations. Fever is rarely prominent.

The severity of these chronic pulmonary reactions and the degree of their resolution appear to be related to the duration of therapy after the first clinical signs appear. Pulmonary function may be permanently impaired even after cessation of nitrofurantoin therapy. This risk is greater when pulmonary reactions are not recognized early.

**Dermatologic reactions:** Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other sensitivity reactions:** Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

**Hematologic reactions:** Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurologic reactions:** Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous reactions:** Transient alopecia. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

**References:** 1. Center for Disease Control: *National Nosocomial Infections Study Report*, Annual Summary 1976, issued February 1978. Washington, DC, U.S. Department of Health, Education, and Welfare, p 8. 2. Cooper J, et al: Diagnostic and chemoprophylactic importance of perineal microbial carriage, in Siegenthaler W, Luthy R (eds): *Current Chemotherapy*. Washington, DC, American Society for Microbiology, 1978, vol 1, pp 198-200. 3. Buckley RM, McGuckin M, MacGregor RR: Urine bacterial counts after sexual intercourse. *N Engl J Med* 298:321-324, 1978. 4. PMR Bacteriologic Report, Summer Series, 1978; a national bacteriologic monitoring service for 200 acute-care hospitals of 100 beds or more.

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Manati, Puerto Rico 00701

Address medical inquiries to:  
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Norwich, New York 13815

## Valium® (diazepam/Roche)

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors, psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation, symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal, adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.

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listed below. After notification, one of us will follow up with a telephone call, in order to gather sufficient information to evaluate the case. All such information will be confidential.

Although there are obvious disadvantages to any retrospective evaluation such as this, the practical impossibility of conducting a prospective trial of different modes of prophylaxis has caused us to seek alternative means of gathering data. We hope that a useful body of information may be accumulated, which may influence future recommendations for prophylaxis of endocarditis.

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## References

1. American Heart Association Committee on Rheumatic Fever and Bacterial Endocarditis: Prevention of bacterial endocarditis. *Circulation* 56:139A, 1977

## Indications for Urine Culture To the Editor:

In the first problem of the April "Self-Assessment in Family Practice" I disagree with the answer which calls for "repetition of the urine culture and simultaneous administration of ampicillin" to a five-year-old girl with dysuria and a positive urine culture. In the discussion of this question it is stated that "one or two confirmatory cultures should be performed to document the infection."

A repeat urine culture will cost the patient's family or third-party payor between \$15 and \$40, and seems somewhat superfluous in this patient. In addition, a follow-up urinalysis might suffice to confirm the efficacy of therapy within one week after antibiotics were begun. Repetition of a urine culture two to seven days after antibiotic therapy is stopped is appropriate.

We in medicine, and especially in family practice, must be constantly aware of ways in which we can decrease the cost of care without compromising the care of our patients.

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