

ZARONTIN® (Ethosuximide Capsules, USP)

Before prescribing, please consult full prescribing information. A brief summary follows:

Indication: Zarontin is indicated for the control of absence (petit mal) epilepsy.

Contraindication: Ethosuximide should not be used in patients with a history of hypersensitivity to succinimides.

Warnings: Blood dyscrasias, including some with fatal outcome, have been reported to be associated with the use of ethosuximide; therefore, periodic blood counts should be performed.

Ethosuximide is capable of producing morphological and functional changes in the animal liver. In humans, abnormal liver and renal function studies have been reported.

Ethosuximide should be administered with extreme caution to patients with known liver or renal disease. Periodic urinalysis and liver function studies are advised for all patients receiving the drug.

Cases of systemic lupus erythematosus have been reported with the use of ethosuximide. The physician should be alert to this possibility.

Usage in Pregnancy: The effects of Zarontin in human pregnancy and nursing infants are unknown.

Recent reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause-and-effect relationship. There are intrinsic methodological problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, eg, genetic factors or the epileptic condition itself, may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants. It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

The prescribing physician will wish to weigh these considerations in treating or counseling epileptic women of childbearing potential.

Hazardous Activities: Ethosuximide may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a motor vehicle or other such activity requiring alertness; therefore, the patient should be cautioned accordingly.

Precautions: Ethosuximide, when used alone in mixed types of epilepsy, may increase the frequency of grand mal seizures in some patients.

As with other anticonvulsants, it is important to proceed slowly when increasing or decreasing dosage, as well as when adding or eliminating other medication. Abrupt withdrawal of anticonvulsant medication may precipitate absence (petit mal) status.

Adverse Reactions

Gastrointestinal System: Gastrointestinal symptoms occur frequently and include anorexia, vague gastric upset, nausea and vomiting, cramps, epigastric and abdominal pain, weight loss, and diarrhea.

Hemopoietic System: Hemopoietic complications associated with the administration of ethosuximide have included leukopenia, agranulocytosis, pancytopenia, aplastic anemia, and eosinophilia.

Nervous System: Neurologic and sensory reactions reported during therapy with ethosuximide have included drowsiness, headache, dizziness, euphoria, hiccups, irritability, hyperactivity, lethargy, fatigue, and ataxia. Psychiatric or psychological aberrations associated with ethosuximide administration have included disturbances of sleep, night terrors, inability to concentrate, and aggressiveness. These effects may be noted particularly in patients who have previously exhibited psychological abnormalities. There have been rare reports of paranoid psychosis, increased libido, and increased state of depression with overt suicidal intentions.

Integumentary System: Dermatologic manifestations which have occurred with the administration of ethosuximide have included urticaria, Stevens-Johnson syndrome, systemic lupus erythematosus, and pruritic erythematous rashes.

Miscellaneous: Other reactions reported have included myopia, vaginal bleeding, swelling of the tongue, gum hypertrophy, and hirsutism.

YC

Letters to the Editor



Pediatric Health Screening

To the Editor:

The article by Eggertsen et al, "An Updated Protocol for Pediatric Health Screening," (*Eggertsen SC, Schneeweiss R, Bergman JJ. J Fam Pract 10:25, 1980*), is in general an excellent analysis of pediatric screening. However, I would like to take issue with two points.

First, the authors point out that we do not even know how to define pediatric hypertension much less what to do with it if we find it. Hypertension, defined by adult standards, is rare under age ten but rises in incidence during adolescence and presumably carries with it risk of significant morbidity.¹ In support of screening for hypertension at ages 4 and 6, the authors cite "authorities," not evidence. I contend screening for hypertension should be category III in children under age 10 and should be category I in adolescents. I would be most interested in hearing of evidence to support screening for hypertension in younger children.

Secondly, although the authors mention screening for several conditions by specific parts of the physical examination, eg, cardiac auscultation and tests for strabismus, no specific mention is made in

the article of screening for congenital hip dislocation; (it does appear on one of the flow sheets, Figure 1). This disease is common (incidence between 1 in 400 to 2,000 children), asymptomatic, and easily detected. If treated early, it is usually curable. If undetected, it leads to serious morbidity. Screening for congenital hip dislocation should be included several times in the first six months of life as a category I procedure.

Paul S. Frame, MD
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References

1. Lauer RM, Connor WE, Leaverton PE, et al: Coronary heart disease risk factors in school children: The Muscatine study. *J Pediatr 85:697, 1975*

To the Editor:

Drs. Eggertsen, Schneeweiss, and Bergman's recent article in January, "An Updated Protocol for Pediatric Health Screening" (*J Fam Pract 10:25, 1980*), is an excellent attempt at rational preventive care. However, I was quite dismayed at one glaring omission. De-

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Age	Concentration of Fluoride in Drinking Water (ppm)		
	<0.3	0.3-0.7	>0.7
2 weeks-2 years	0.25	0	0
2-3 years	0.50	0.25	0
3-16 years	1.00	0.50	0

†2.2 mg sodium fluoride contains 1 mg fluoride
 Table reprinted with permission from the American Academy of Pediatrics, Committee on Nutrition: Fluoride supplementation: Revised dosage schedule. *Pediatrics* 63:151, 1979. Copyright American Academy of Pediatrics, 1979

spite the unequivocal evidence favoring fluoride supplementation as prevention of dental caries, there is no mention of this in their protocol. Even though most cities now have fluoridated water supplies, a large segment of our prac-

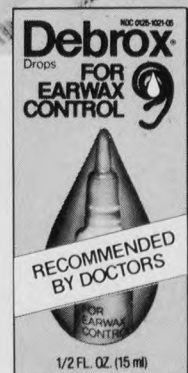
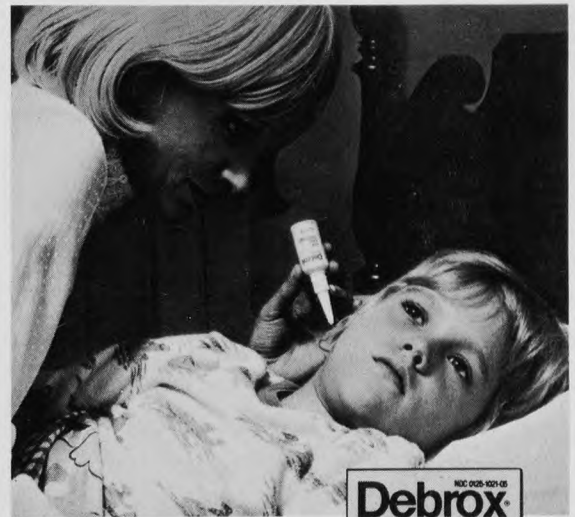
tice in the rural Upper Peninsula of Michigan obtains its water supply from wells with little or no natural fluoride. Since oral fluoride supplementation can lead to a 50 percent decrease in the number of dental caries, it is essential that these

children do receive oral fluoride supplements. The dosage schedule approved by the Committee on Nutrition of the American Academy of Pediatrics is listed in Table 1.

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Macrochantin®

(nitrofurantoin macrocrystals)

Capsules: 25, 50, 100mg

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® (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.

Hepatitis, including chronic active hepatitis, has been observed rarely. Fatalities have been reported. The mechanism appears to be of an idiosyncratic hypersensitive type.

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 child-bearing 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 hypersensitivity reactions: Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, hepatitis, including chronic active hepatitis, 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.

Neurological 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.

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LETTERS TO THE EDITOR

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Greater awareness by family physicians of the need for fluoride supplementation would greatly reduce the time and expense our children will spend in one of our own least favorite spots—the dentist's chair.

John Hickner, MD

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Michigan State University

College of Human Medicine

Escanaba, Michigan

The preceding letters were referred to Drs. Schneeweiss, Eggertsen, and Bergman who respond as follows:

Dr. Frame's thoughtful letter touches on the controversies surrounding the area of health screening and is exactly the kind of response we hoped to elicit with our article.

At this time evidence does not exist in support of screening for hypertension in the pediatric age group. However, on the other hand, there is no evidence to the converse. For that reason we have chosen to put hypertension screening in Category II (uncertain benefit) and hope that future studies will elucidate this point.

The issue of cost-benefit including the risks and cost of working-up false-positive cases will have to be addressed.

Dr. Frame has appropriately pointed out the importance of examining carefully for congenital dislocation of the hip and it is indeed a specific part of the recommended physical examination as implied in Figures 3 and 4. We absolutely endorse the routine but careful exclusion of this problem by repeated examinations in the first year of life.

Dr. Hickner's point regarding the significance of fluoride supplementation in the prevention of dental caries, in those areas where the water supply is unfluoridated, is well taken. It is chastening to note that we ourselves had overlooked this issue since we work in a city where water supplies are fluoridated!

As the Committee on Nutrition of the American Academy of Pediatrics has indicated, there remains some controversy regarding the optimum ages for fluoride supplementation.¹ Some physicians do not initiate treatment under the age of six months to reduce problems with mild fluorosis. In addition, the development of the permanent tooth crowns, excluding the third molar, which is more variable, is complete by ages 10-12 years. It is not clear whether there is benefit in continuing with fluoride supplements beyond this age.

Ronald Schneeweiss, MD

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James J. Bergman, MD

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Reference

1. American Academy of Pediatrics: Fluoride supplementation: Revised dosage schedule. *Pediatrics* 63:150, 1979