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AMERICAN ACADEMY OF PEDIATRICS EVANSTON ILLINOIS 60204

Pediatrics

When they find moondust, and you find allergic rhinitis...*

When engaged in extra-vehicular activity, susceptible young space explorers can encounter allergens... and develop allergic rhinitis.* For effective, symptomatic relief, prescribe ACTIFED®... the oral antihistaminic-decongestant carried by astronauts on their Apollo space flights. Each dose lasts up to 8 hours for a convenient, easy-to-remember regimen—at breakfast, after school, at bedtime.

INDICATIONS: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

*"Probably" effective: For the symptomatic treatment of seasonal and perennial allergic rhinitis and vasomotor rhinitis.

Final classification of the less-than-effective indications requires further investigation.

PRECAUTIONS: Although pseudoephedrine hydrochloride is virtually without pressor effect in normotensive patients, it should be used with caution in patients with hypertension. In addition, even though triprolidine hydrochloride has a low incidence of drowsiness, appropriate precautions should be observed.

ADVERSE REACTIONS: The great majority of patients will exhibit no side effects. However, certain patients may exhibit mild stimulation or mild sedation—no serious side effects have been noted.

*for symptomatic relief in allergies**

Actifed® *tablets syrup*

Each scored tablet contains Actidil® (triprolidine hydrochloride) 2.5 mg. and Sudafed® (pseudoephedrine hydrochloride) 60 mg.

Each 5 cc. teaspoonful of syrup contains Actidil (triprolidine hydrochloride) 1.25 mg. and Sudafed (pseudoephedrine hydrochloride) 30 mg.

Complete literature available on request from Professional Services Dept. PML.

Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Consider it as first-aid for ears.

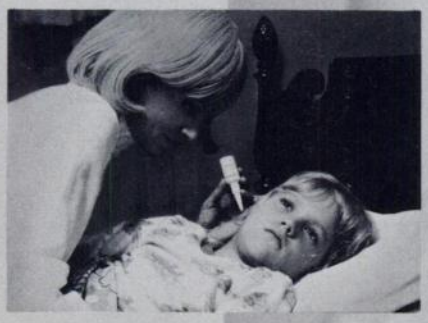
Many of your patients suffer from ear problems from time to time. Often during the night. They can be painful and frightening. Naturally, you want to see them as soon as possible.

In the interim, suggest soothing Debrox® Drops. Debrox is a safe otic solution . . . a cleansing, antiseptic way to temporarily ease discomfort. *No traumatizing or allergenic reactions have been reported in millions of patient-uses.*

Debrox is indicated as adjunctive therapy in the management of ceruminosis, otitis externa and exudative otitis media.

Encourage parents to keep Debrox on hand in the medicine cabinet along with other first-aid items. It's a pharmacologically safe, clinically effective, chemically *stable* solution for many minor ear ailments.[1] In fact, regular use of Debrox helps promote good ear hygiene for every member of the family.

Available without prescription in economical ½ ounce plastic applicator bottles at pharmacies everywhere. Contains carbamide peroxide 6.5% in specially prepared anhydrous glycerol.



Debrox®
DROPS

International Pharmaceutical Corporation, Warrington, Pennsylvania 18976

1. DICKSTEIN, B. *A Simplified Approach to Cerumenolysis.* E.E.N.T. DIGEST 26:49-51, January, 1964. DBJM-1175

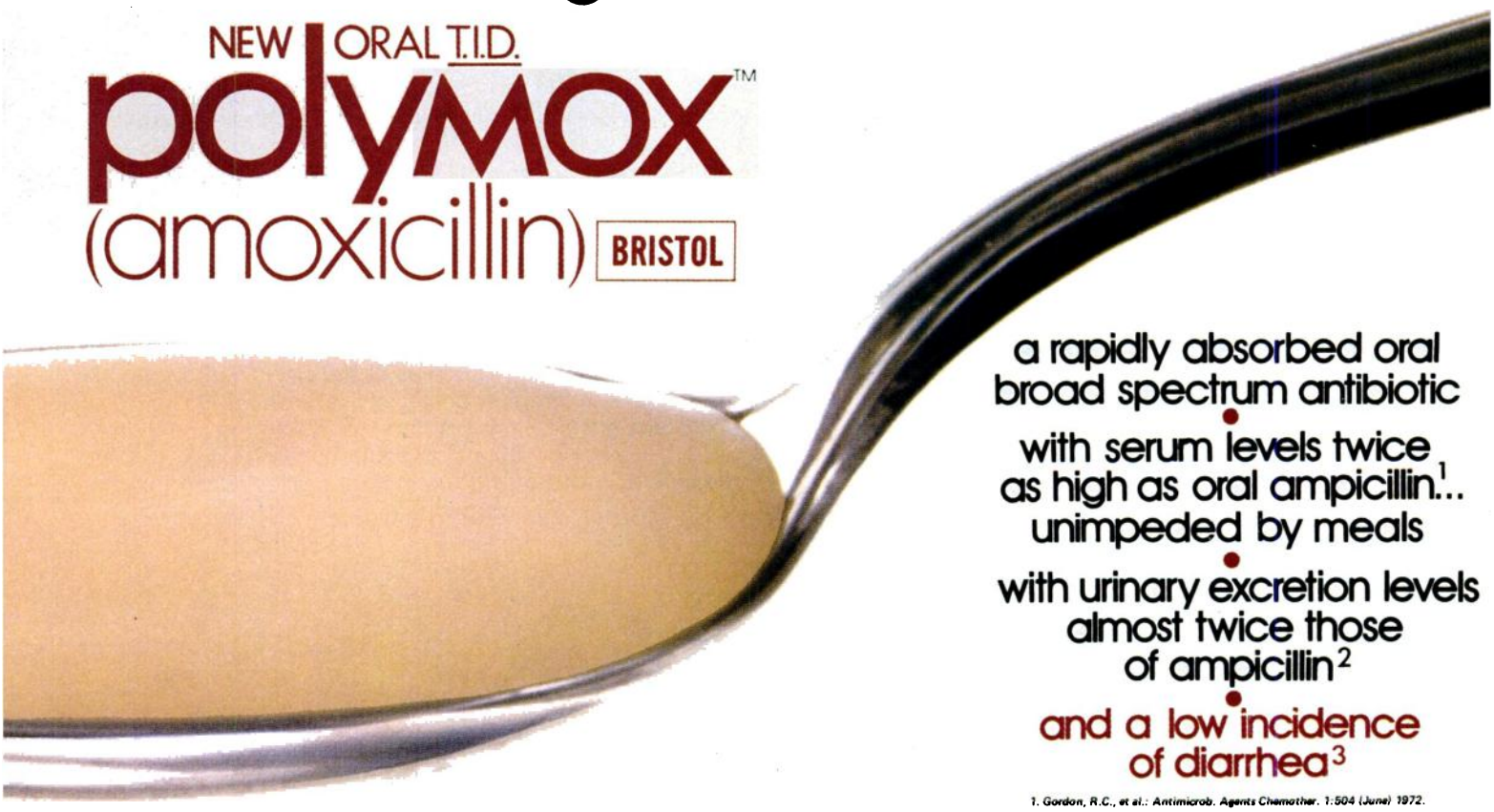
When outpatient therapy requires inpatient blood levels...

introducing

NEW ORAL T.I.D.

polymox™

(amoxicillin) BRISTOL



a rapidly absorbed oral broad spectrum antibiotic

•

with serum levels twice as high as oral ampicillin[1]... unimpeded by meals

•

with urinary excretion levels almost twice those of ampicillin[2]

•

and a low incidence of diarrhea[3]

1. Gordon, R.C., et al.: *Antimicrob. Agents Chemother.* 1:504 (June) 1972.
2. Gordon, Ibid.
3. Croydon, E.A.P.: Chemotherapy 18: 112, 1973

PLEASE SEE NEXT PAGE FOR PRESCRIBING INFORMATION

The new high absorption ampicillin analog that can be mixed with the flavors children like best!

Pleasant tasting oral suspension may be added to milk, fruit juice, ginger ale and other cold drinks on a per-dose basis

Available in 250 and 500 mg. capsules; 125 mg./5 ml. and 250 mg./5 ml. oral suspension; 50 mg./ml. pediatric drops

BRIEF SUMMARY OF PRESCRIBING INFORMATION
(2) 8/20/74
POLYMOX™ CAPSULES, ORAL SUSPENSION AND PEDIATRIC DROPS
(amoxicillin)

For complete information, consult Official Package Circular.

INDICATIONS:
Polymox™ (amoxicillin) is similar to ampicillin in its bactericidal action against susceptible strains of Gram-negative organisms—**H. influenzae, E. coli, P. mirabilis** and **N. gonorrhoeae;** and Gram-positive organisms—Streptococci (including **Streptococcus faecalis**), **D. pneumoniae** and nonpenicillinase-producing staphylococci. Culture and sensitivity studies should be obtained. Indicated surgical procedures should be performed.

CONTRAINDICATIONS:
A history of a previous hypersensitivity reaction to any of the penicillins is a contraindication.

WARNING:
Anaphylaxis may occur, particularly after parenteral administration and especially in patients with an allergic diathesis. Check for a history of allergy to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, discontinue amoxicillin and institute appropriate treatment. Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids and airway management.

Usage in Pregnancy
Safety for use in pregnancy is not established.

PRECAUTIONS:
Mycotic or bacterial superinfections may occur. Cases of gonorrhea with a suspected primary lesion of syphilis should have darkfield examinations before receiving treatment. In all other cases where concomitant syphilis is suspected, monthly serological tests should be performed for a minimum of 4 months. Assess renal, hepatic and hematopoietic function intermittently during long-term therapy.

ADVERSE REACTIONS:
Untoward reactions include: glossitis, black "hairy" tongue, nausea, vomiting and diarrhea, skin rashes, urticaria, exfoliative dermatitis, erythema multiforme and anaphylaxis (usually with parenteral administration). Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been noted, are usually reversible and are believed to be hypersensitivity phenomena. Moderate elevations in SGOT have been noted.

USUAL DOSAGE:
Adults—250 to 500 mg. orally q. 8h. (depending on infection site and offending organisms). Children—20-40 mg/kg./day orally q. 8h. (depending on infection site and offending organisms). Children over 20 Kg. should be given adult dose.
Gonorrhea, acute uncomplicated—3 Gms. as a single oral dose (see PRECAUTIONS).
Serious infections, such as meningitis or septicemia, should be treated with parenteral antibiotics.

SUPPLIED:
Capsules—250 mg. in bottles of 100's and 500's.
500 mg. in bottles of 50's and 100's.
Oral Suspension—125 mg./5 ml. and 250 mg./5 ml. in 80 ml. and 150 ml.
Pediatric Drops—50 mg./ml. in 15 ml. bottles with marked dropper.

NEW ORAL T.I.D.
polyMOX™
(amoxicillin) BRISTOL

BRISTOL LABORATORIES — Div. Bristol-Myers Company, Syracuse, New York 13201

SEPTEMBER 1975 VOL. 56 NO. 3

CONTENTS

Pediatrics

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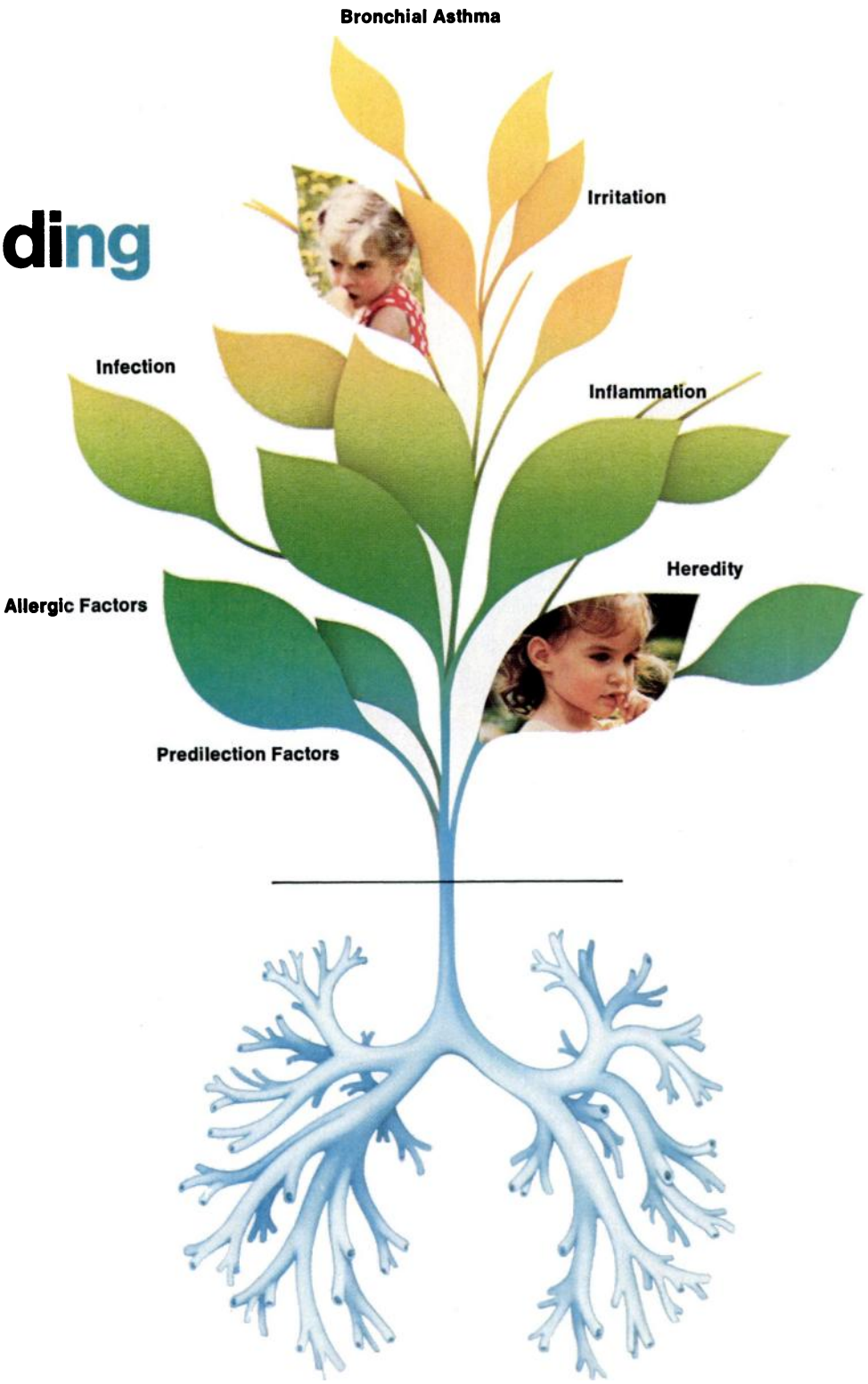
COMMENTARIES

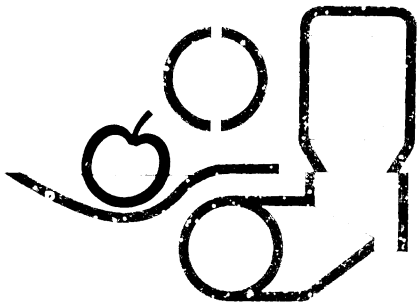
ARTICLES

For the budding asthmatic



Alupent

The only single-entity bronchodilator available in tablet, aerosol and syrup



New Alupent® Syrup

(metaproterenol sulfate) 10mg/5ml

Alupent Syrup works. In 11 controlled studies of bronchospastic patients, FEV_1 increased to clinically significant levels (more than 15% above baseline).[1]

Helps offset exercise-induced bronchospasm. The administration of Alupent Syrup before exercise can help to protect against bronchospasm induced by exercise.

Improves school attendance. In helping to decrease airway obstruction and relieve dyspnea associated with bronchospasm, Alupent Syrup can help to improve a bronchial asthmatic child's school attendance.

Generally well tolerated. In 37 studies involving 961 patients, the vast majority pediatric, Alupent Syrup was generally well tolerated.[1] Its adverse reactions are similar to those of other sympathomimetic drugs (see Brief Summary).

A single entity that works as well as combination products. Alupent Syrup contains only Alupent as its therapeutic entity... no sedatives, no tranquilizers.

Single dose works up to four hours. Duration of a single dose of Alupent Syrup (the period in which there is at least a 15% increase in mean FEV_1) is up to four hours.

Good-tasting...and virtually no sugar. New Alupent Syrup's rich cherry flavor is well accepted by children and adults. No tartrazine, and it's virtually sugar-free.

[1] Data on file, Boehringer Ingelheim Ltd.

Alupent® Syrup
(metaproterenol sulfate)
10 mg/5 ml

Indications: Bronchial asthma and reversible bronchospasm which may occur in association with bronchitis and emphysema.

Contraindications: Cardiac arrhythmias associated with tachycardia.

Precautions: Use extreme care when administering additional sympathomimetic drugs. Sufficient time should elapse before administering another sympathomimetic agent. Use great caution with metaproterenol sulfate and other sympathomimetics in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism and diabetes, or when there is sensitivity to sympathomimetic amines.

Usage in Pregnancy: Safety in pregnancy has not been established. Do not use except with caution, weighing patient benefit against potential risk to fetus. Studies in mice, rabbits and rats have shown no significant teratogenic effects at oral doses up to 50 mg/kg (310 times the recommended daily human inhalational dose and 31 times the recommended daily human oral dose). In rabbits, fetal loss and teratogenic effects have been observed at and above oral doses of 50 and 100 mg/kg, respectively.

Adverse Reactions: Adverse reactions such as tachycardia, hypertension, palpitations, nervousness, tremor, nausea and vomiting have been reported. These reactions are similar to those noted with other sympathomimetic agents.

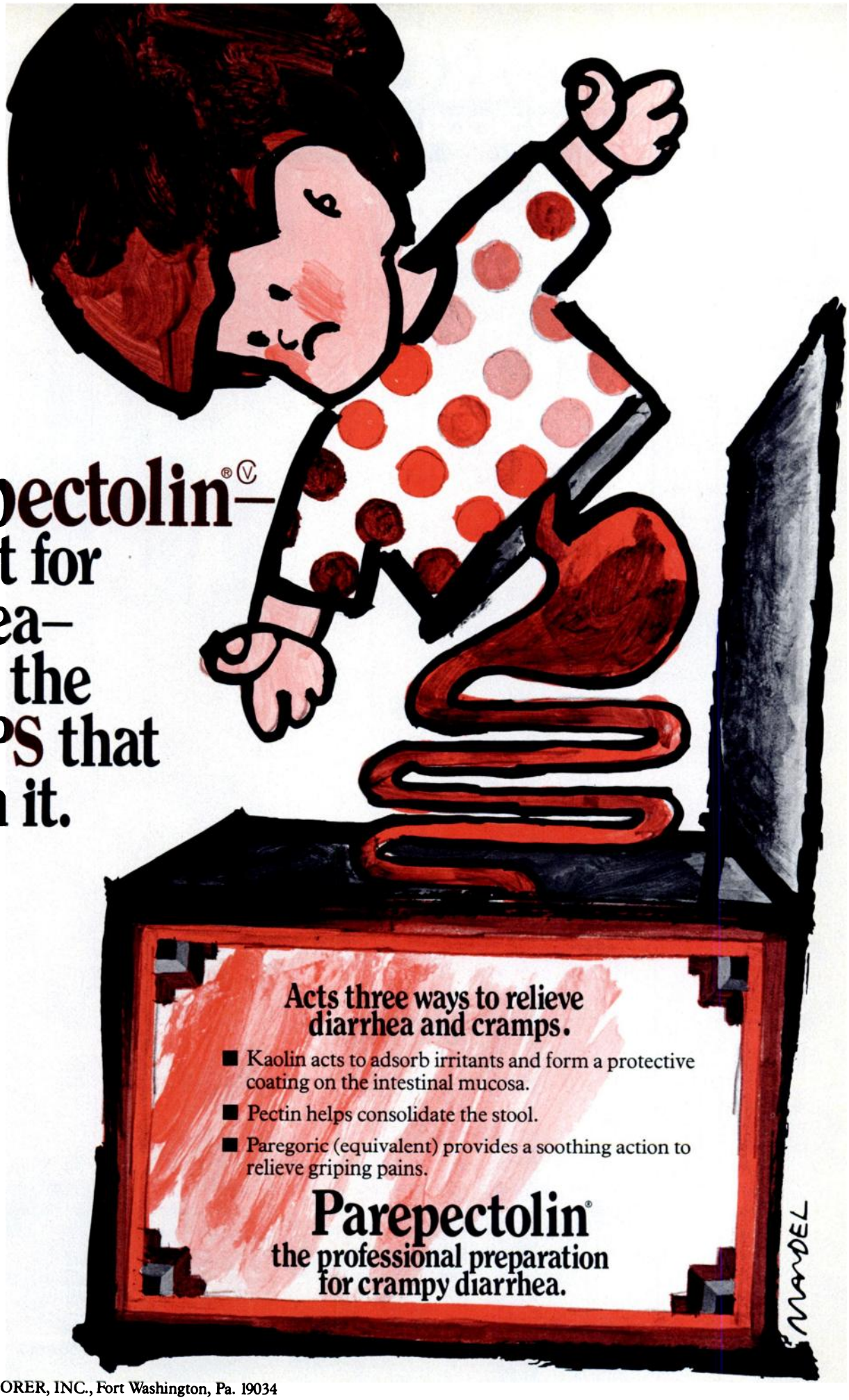
Symptoms of Overdosage: The symptoms of overdosage are those of excessive beta-adrenergic stimulation listed under Adverse Reactions.

How Supplied: Cherry-flavored syrup, 10 mg per teaspoon (5 cc), in 16 oz bottles.

Also available as 20 mg tablets in bottles of 100 and as a micronized powder in a 15 cc metered dose inhaler.

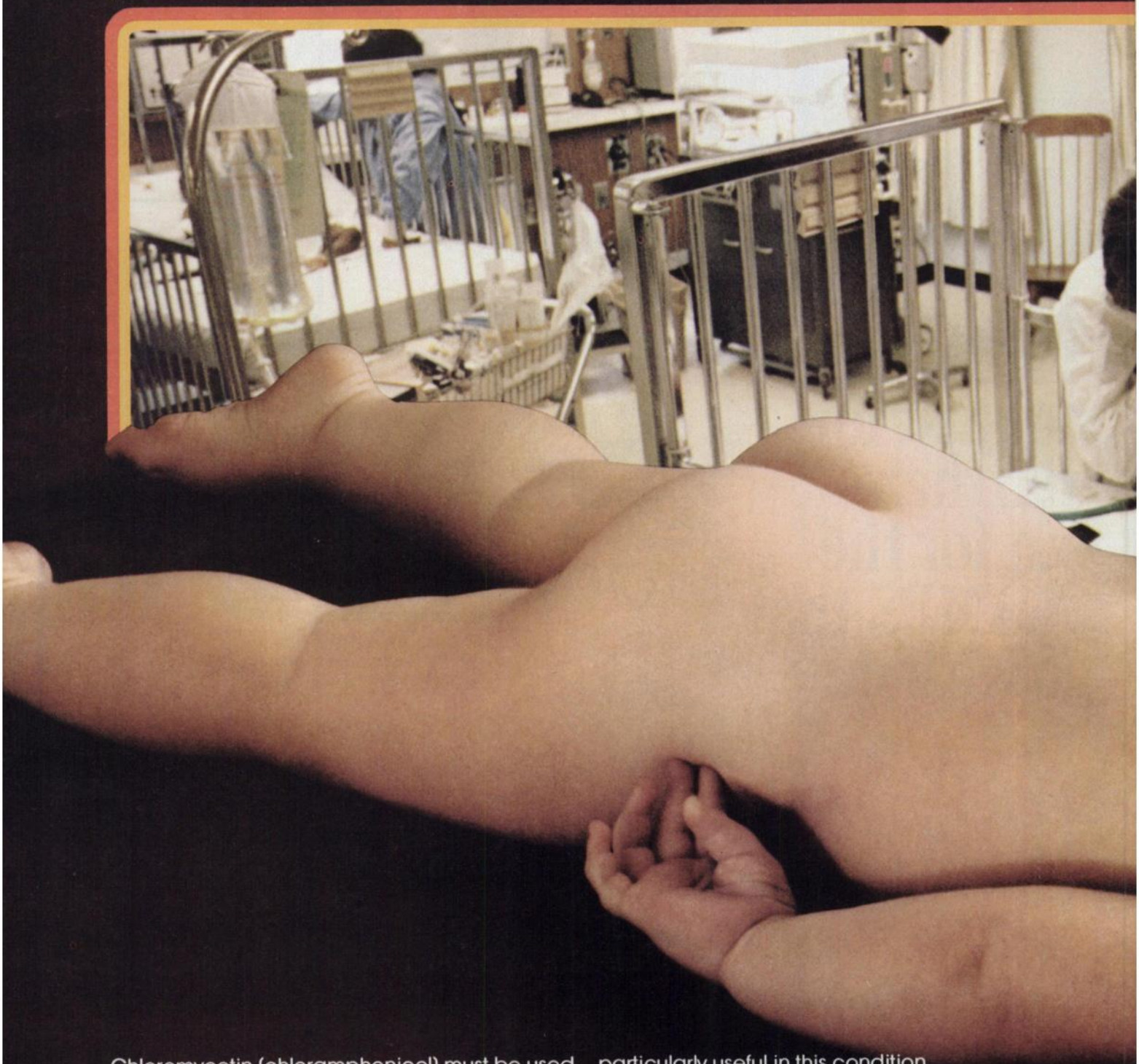
For complete details, please see the full prescribing information.

Boehringer Ingelheim
Boehringer Ingelheim, Ltd.
Elmsford, New York 10523



WILLIAM H. RORER, INC., Fort Washington, Pa. 19034

CHLOROMYCETIN®
(chloramphenicol) Sodium Succinate



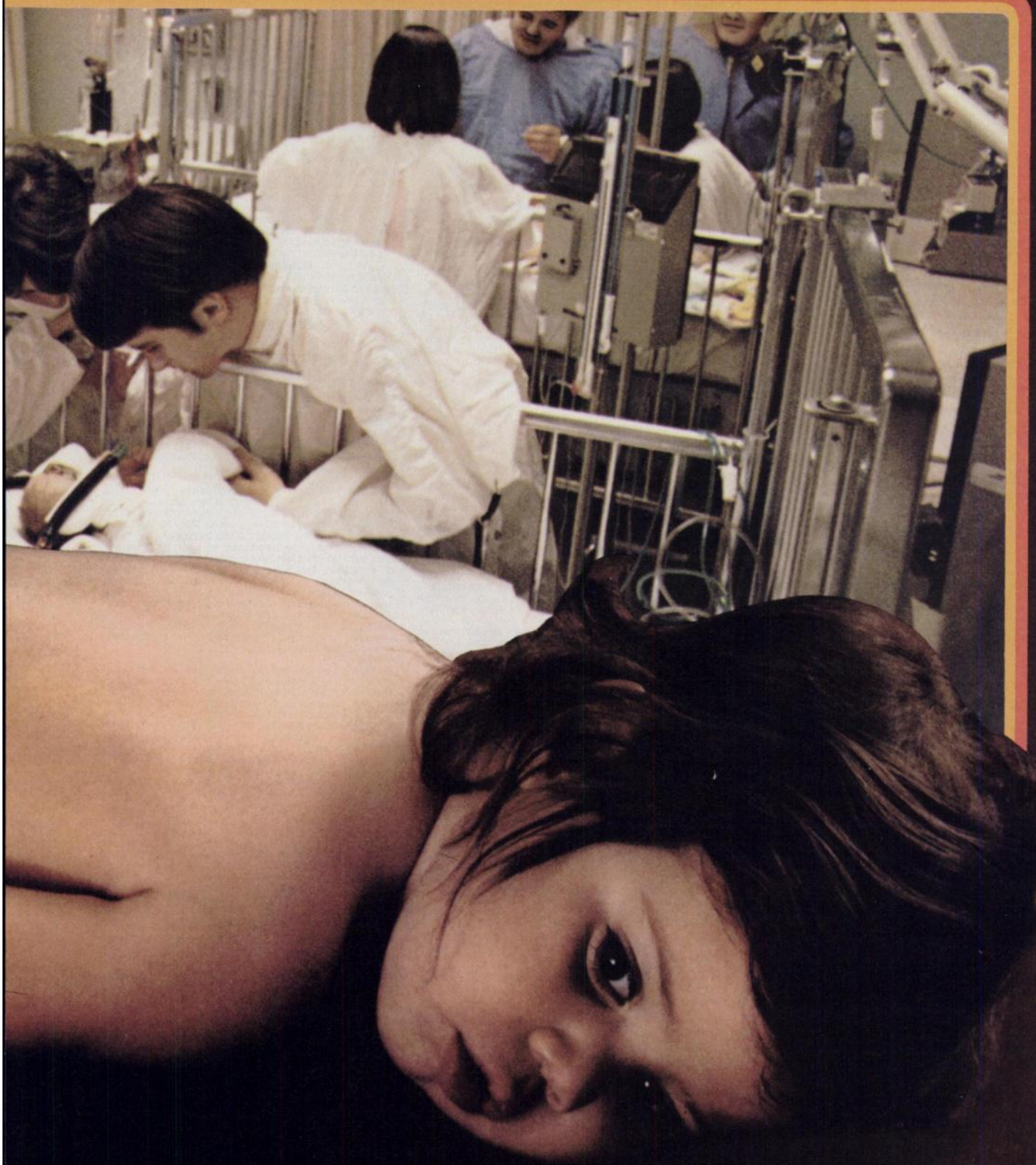
Chloromycetin (chloramphenicol) must be used only in those serious infections for which less potentially dangerous drugs are ineffective or contraindicated. However, Chloromycetin may be chosen to initiate antibiotic therapy on the clinical impression that *Hemophilus influenzae* meningitis is believed to be present.

Among diseases of the central nervous system *H influenzae* meningitis is one of the most severely threatening. Chloromycetin can be particularly useful in this condition.

- With Chloromycetin there has been no reported resistance in the treatment of *H influenzae* meningitis.*
- Chloromycetin may be used in the treatment of *H influenzae* meningitis when the patient has known—or suspected—allergy to penicillin.

*When administered in accordance with recommended dosage and routes of administration.

for H influenzae meningitis



Please see next page for full prescribing information.

PARKE-DAVIS

Prescribing Information—Chloromycetin® (chloramphenicol) Sodium Succinate For intravenous administration

WARNING

Serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia) are known to occur after the administration of chloramphenicol. In addition, there have been reports of aplastic anemia attributed to chloramphenicol which later terminated in leukemia. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. Chloramphenicol must not be used when less potentially dangerous agents will be effective, as described in the Indications section. It must not be used in the treatment of trivial infections or where it is not indicated, as in colds, influenza, infections of the throat; or as a prophylactic agent to prevent bacterial infections.

Precautions: It is essential that adequate blood studies be made during treatment with the drug. While blood studies may detect early peripheral blood changes, such as leukopenia, reticulocytopenia, or granulocytopenia, before they become irreversible, such studies cannot be relied on to detect bone marrow depression prior to development of aplastic anemia. To facilitate appropriate studies and observation during therapy, it is desirable that patients be hospitalized.

IMPORTANT CONSIDERATIONS IN PRESCRIBING INJECTABLE CHLORAMPHENICOL SODIUM SUCCINATE

CHLORAMPHENICOL SODIUM SUCCINATE IS INTENDED FOR INTRAVENOUS USE ONLY. IT HAS BEEN DEMONSTRATED TO BE INEFFECTIVE WHEN GIVEN INTRAMUSCULARLY.

1. Chloramphenicol sodium succinate must be hydrolyzed to its microbiologically active form and there is a lag in achieving adequate blood levels compared with the base given intravenously.
2. The oral form of chloramphenicol is readily absorbed and adequate blood levels are achieved and maintained on the recommended dosage.
3. Patients started on intravenous chloramphenicol sodium succinate should be changed to the oral form as soon as practicable.

DESCRIPTION

Chloramphenicol is an antibiotic that is clinically useful for, and should be reserved for, serious infections caused by organisms susceptible to its antimicrobial effects when less potentially hazardous therapeutic agents are ineffective or contraindicated. Sensitivity testing is essential to determine its indicated use, but may be performed concurrently with therapy initiated on clinical impression that one of the indicated conditions exists (see Indications section).

ACTIONS AND PHARMACOLOGY

In vitro chloramphenicol exerts mainly a bacteriostatic effect on a wide range of gram-negative and gram-positive bacteria and is active *in vitro* against rickettsias, the lymphogranuloma-psittacosis group, and *Vibrio cholerae*. It is particularly active against *Salmonella typhi* and *Hemophilus influenzae*. The mode of action is through interference or inhibition of protein synthesis in intact cells and in cell-free systems.

Chloramphenicol administered orally is absorbed rapidly from the intestinal tract. In controlled studies in adult volunteers using the recommended dosage of 50 mg/kg/day, a dosage of 1 g every six hours for eight doses was given. Using the microbiological assay method, the average peak serum level was 11.2 mcg/ml one hour after the first dose. A cumulative effect gave a peak rise to 18.4 mcg/ml after the fifth dose of 1 g. Mean serum levels ranged from 8 to 14 mcg/ml over the 48-hour period. Total urinary excretion of chloramphenicol in these studies ranged from a low of 68% to a high of 99% over a three-day period. From 8% to 12% of the antibiotic excreted is in the form of free chloramphenicol; the remainder consists of microbiologically inactive metabolites, principally the conjugate with glucuronic acid. Since the glucuronide is excreted rapidly, most chloramphenicol detected in the blood is in the microbiologically active free form. Despite the small proportion of unchanged drug excreted in the urine, the concentration of free chloramphenicol is relatively high, amounting to several hundred mcg/ml in patients receiving divided doses of 50 mg/kg/day. Small amounts of active drug are found in bile and feces. Chloramphenicol diffuses rapidly, but its distribution is not uniform. Highest concentrations are found in liver and kidney, and lowest concentrations are found in brain and cerebrospinal fluid. Chloramphenicol enters cerebrospinal fluid even in the absence of meningeal inflammation, appearing in concentrations about half of those found in the blood. Measurable levels are also detected in pleural and in ascitic fluids, saliva, milk, and in the aqueous and vitreous humors. Transport across the placental barrier occurs with somewhat lower concentration in cord blood of newborn infants than in maternal blood.

INDICATIONS

IN ACCORD WITH THE CONCEPTS IN THE WARNING BOX AND THIS INDICATIONS SECTION, CHLORAMPHENICOL MUST BE USED ONLY IN THOSE SERIOUS INFECTIONS FOR WHICH LESS POTENTIALLY DANGEROUS DRUGS ARE INEFFECTIVE OR CONTRAINDICATED. HOWEVER, CHLORAMPHENICOL MAY BE CHOSEN TO INITIATE ANTIBIOTIC THERAPY ON THE CLINICAL IMPRESSION THAT ONE OF THE CONDITIONS BELOW IS BELIEVED TO BE PRESENT; *IN VITRO* SENSITIVITY TESTS SHOULD BE PERFORMED CONCURRENTLY SO THAT THE DRUG MAY BE DISCONTINUED AS SOON AS POSSIBLE IF LESS POTENTIALLY DANGEROUS AGENTS ARE INDICATED BY SUCH TESTS. THE DECISION TO CONTINUE USE OF CHLORAMPHENICOL RATHER THAN ANOTHER ANTIBIOTIC WHEN BOTH ARE SUGGESTED BY *IN VITRO* STUDIES TO BE EFFECTIVE AGAINST A SPECIFIC PATHOGEN SHOULD BE BASED UPON SEVERITY OF THE INFECTION, SUSCEPTIBILITY OF THE PATHOGEN TO THE VARIOUS ANTIMICROBIAL DRUGS, EFFICACY OF THE VARIOUS DRUGS IN THE INFECTION, AND THE IMPORTANT ADDITIONAL CONCEPTS CONTAINED IN THE WARNING BOX ABOVE:

1. Acute infections caused by *S typhi**
   It is not recommended for the routine treatment of the typhoid carrier state.
2. Serious infections caused by susceptible strains in accordance with the concepts expressed above:
   a) *Salmonella* species
   b) *H influenzae*, specifically meningeal infections
   c) Rickettsia
   d) Lymphogranuloma-psittacosis group
   e) Various gram-negative bacteria causing bacteremia, meningitis, or other serious gram-negative infections
   f) Other susceptible organisms which have been demonstrated to be resistant to all other appropriate antimicrobial agents
3. Cystic fibrosis regimens

*In the treatment of typhoid fever, some authorities recommend that chloramphenicol be administered at therapeutic levels for 8 to 10 days after the patient has become afebrile to lessen the possibility of relapse.

CONTRAINDICATIONS

Chloramphenicol is contraindicated in individuals with a history of previous hypersensitivity and/or toxic reaction to it. It must not be used in the treatment of trivial infections or where it is not indicated, as in colds, influenza, infections of the throat; or as a prophylactic agent to prevent bacterial infection.

PRECAUTIONS

1. Baseline blood studies should be followed by periodic blood studies approximately every two days during therapy. The drug should be discontinued upon appearance of reticulocytopenia, leukopenia, thrombocytopenia, anemia, or any other blood study findings attributable to chloramphenicol. However, it should be noted that such studies do not exclude the possible later appearance of the irreversible type of bone marrow depression.
2. Repeated courses of the drug should be avoided if at all possible. Treatment should not be continued longer than required to produce a cure with little or no risk of relapse of the disease.
3. Concurrent therapy with other drugs that may cause bone marrow depression should be avoided.
4. Excessive blood levels may result from administration of the recommended dose to patients with impaired liver or kidney function, including that due to immature metabolic processes in the infant. The dosage should be adjusted accordingly or, preferably, the blood concentration should be determined at appropriate intervals.
5. There are no studies to establish the safety of this drug in pregnancy.
6. Since chloramphenicol readily crosses the placental barrier, caution in use of the drug is particularly important during pregnancy at term or during labor because of potential toxic effects on the fetus (gray syndrome).
7. Precaution should be used in therapy of premature and full-term infants to avoid gray syndrome toxicity. (See Adverse Reactions.) Serum drug levels should be carefully followed during therapy of the newborn infant.
8. Precaution should be used in therapy during lactation because of the possibility of toxic effects on the nursing infant.
9. The use of this antibiotic, as with other antibiotics, may result in an overgrowth of nonsusceptible organisms, including fungi. If infections caused by nonsusceptible organisms appear during therapy, appropriate measures should be taken.

ADVERSE REACTIONS

1. Blood Dyscrasias

The most serious adverse effect of chloramphenicol is bone marrow depression. Serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia) are known to occur after the administration of chloramphenicol. An irreversible type of marrow depression leading to aplastic anemia with a high rate of mortality is characterized by the appearance weeks or months after therapy of bone marrow aplasia or hypoplasia. Peripherally, pancytopenia is most often observed, but in a small number of cases only one or two of the three major cell types (erythrocytes, leukocytes, platelets) may be depressed.

A reversible type of bone marrow depression, which is dose related, may occur. This type of marrow depression is characterized by vacuolization of the erythroid cells, reduction of reticulocytes, and leukopenia, and responds promptly to the withdrawal of chloramphenicol.

An exact determination of the risk of serious and fatal blood dyscrasias is not possible because of lack of accurate information regarding (1) the size of the population at risk, (2) the total number of drug-associated dyscrasias, and (3) the total number of nondrug-associated dyscrasias.

In a report to the California State Assembly by the California Medical Association and the State Department of Public Health in January 1967, the risk of fatal aplastic anemia was estimated at 1:24,200 to 1:40,500 based on two dosage levels.

There have been reports of aplastic anemia attributed to chloramphenicol which later terminated in leukemia.

Paroxysmal nocturnal hemoglobinuria has also been reported.

2. Gastrointestinal Reactions

Nausea, vomiting, glossitis and stomatitis, diarrhea and enterocolitis may occur in low incidence.

3. Neurotoxic Reactions

Headache, mild depression, mental confusion, and delirium have been described in patients receiving chloramphenicol. Optic and peripheral neuritis have been reported, usually following long-term therapy. If this occurs, the drug should be promptly withdrawn.

4. Hypersensitivity Reactions

Fever, macular and vesicular rashes, angioedema, urticaria, and anaphylaxis may occur. Herxheimer reactions have occurred during therapy for typhoid fever.

5. "Gray Syndrome"

Toxic reactions including fatalities have occurred in the premature and newborn; the signs and symptoms associated with these reactions have been referred to as the gray syndrome. One case of gray syndrome has been reported in an infant born to a mother having received chloramphenicol during labor. One case has been reported in a 3-month infant. The following summarizes the clinical and laboratory studies that have been made on these patients:

a) In most cases, therapy with chloramphenicol had been instituted within the first 48 hours of life.
b) Symptoms first appeared after three to four days of continued treatment with high doses of chloramphenicol.
c) The symptoms appeared in the following order:
   (1) abdominal distension with or without emesis;
   (2) progressive pallid cyanosis;
   (3) vasomotor collapse, frequently accompanied by irregular respiration;
   (4) death within a few hours of onset of these symptoms.
d) The progression of symptoms from onset to exitus was accelerated with higher dose schedules.
e) Preliminary blood serum level studies revealed unusually high concentrations of chloramphenicol (over 90 mcg/ml after repeated doses).
f) Termination of therapy upon early evidence of the associated symptomatology frequently reversed the process with complete recovery.

ADMINISTRATION

Chloramphenicol, like other potent drugs, should be prescribed at recommended doses known to have therapeutic activity. Administration of 50 mg/kg/day in divided doses will produce blood levels of the magnitude to which the majority of susceptible microorganisms will respond.

AS SOON AS FEASIBLE, AN ORAL DOSAGE FORM OF CHLORAMPHENICOL SHOULD BE SUBSTITUTED FOR THE INTRAVENOUS FORM BECAUSE ADEQUATE BLOOD LEVELS ARE ACHIEVED WITH CHLORAMPHENICOL BY MOUTH.

The following method of administration is recommended:

Intravenously as a 10% (100 mg/ml) solution to be injected over at least a one-minute interval. This is prepared by the addition of 10 ml of an aqueous diluent such as water for injection or 5% dextrose injection.

DOSAGE

Adults

Adults should receive 50 mg/kg/day in divided doses at six-hour intervals. In exceptional cases, patients with infections due to moderately resistant organisms may require increased dosage up to 100 mg/kg/day to achieve blood levels inhibiting the pathogen, but these high doses should be decreased as soon as possible. Adults with impairment of hepatic or renal function or both may have reduced ability to metabolize and excrete the drug. In instances of impaired metabolic processes, dosages should be adjusted accordingly. (See discussion under Newborn Infants.) Precise control of concentration of the drug in the blood should be carefully followed in patients with impaired metabolic processes by the available microtechniques (information available on request).

Children

Dosage of 50 mg/kg/day divided into four doses at six-hour intervals yields blood levels in the range effective against most susceptible organisms. Severe infections (eg, bacteremia or meningitis), especially when adequate cerebrospinal fluid concentrations are desired, may require dosage up to 100 mg/kg/day; however, it is recommended that dosage be reduced to 50 mg/kg/day as soon as possible. Children with impaired liver or kidney function may retain excessive amounts of the drug.

Newborn Infants

(See section titled Gray Syndrome under Adverse Reactions.)

A total of 25 mg/kg/day in four equal doses at six-hour intervals usually produces and maintains concentrations in blood and tissues adequate to control most infections for which the drug is indicated. Increased dosage in these individuals, demanded by severe infections, should be given only to maintain the blood concentration within a therapeutically effective range. After the first two weeks of life, full-term infants ordinarily may receive up to a total of 50 mg/kg/day equally divided into four doses at six-hour intervals. These dosage recommendations are extremely important because blood concentration in all premature infants and full-term infants under two weeks of age differs from that of other infants. This difference is due to variations in the maturity of the metabolic functions of the liver and the kidneys.

When these functions are immature (or seriously impaired in adults), high concentrations of the drug are found which tend to increase with succeeding doses.

Infants and Children with Immature Metabolic Processes

In young infants and other children in whom immature metabolic functions are suspected, a dose of 25 mg/kg/day will usually produce therapeutic concentrations of the drug in the blood. In this group particularly, the concentration of the drug in the blood should be carefully followed by microtechniques. (Information available on request.)

HOW SUPPLIED

NDC 0071-1089-01 (Steri-Vial® No. 57)
Chloromycetin (chloramphenicol) Sodium Succinate is supplied as a dried powder in Steri-Vials (rubber-diaphragm-capped vials). When reconstituted as directed, each vial contains a sterile solution equivalent to 100 mg of chloramphenicol per ml (1 g/10 ml). Available individually and in packer units of 10 tens, NSN 6505-00-754-0280

CHLOROMYCETIN, brand of chloramphenicol, Reg US Patent Office MK

PD-JA-1281-1-P 8/74

PARKE, DAVIS & COMPANY, Detroit, Michigan 48232

GENERAL INFORMATION

PEDIATRICS publishes papers on original research or observations and special feature or review articles in the field of pediatrics as broadly defined. Papers on material pertinent to pediatrics will also be included from related fields such as nutrition, surgery, dentistry, public health, child health services, human genetics, animal studies, psychology, psychiatry, education, sociology and nursing.

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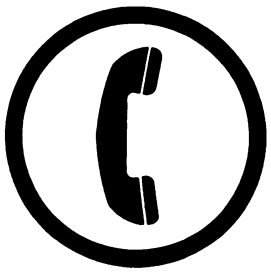

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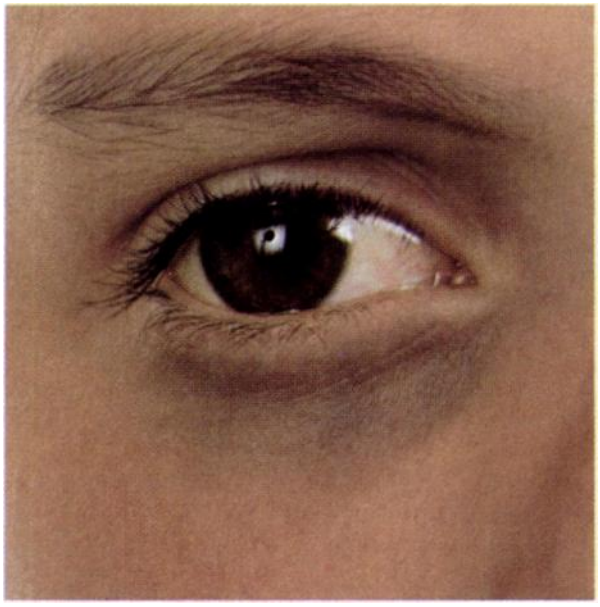
cold or allergy?



Maybe his mother's 'diagnosis' is right. It could be a cold. But that black eye looks like an 'allergic shiner,' and strongly suggests one of the various types of allergic rhinitis. Or perhaps allergic rhinitis complicated by a cold.

If a complete history and examination confirm your suspicion of allergic rhinitis, this young fellow will be mighty lucky his 'cold' was brought to your attention. Without long-term management, including identification of the offending allergens, he would, of course, run a much higher risk than necessary of developing serious complications, perhaps even asthma, as he grows older.

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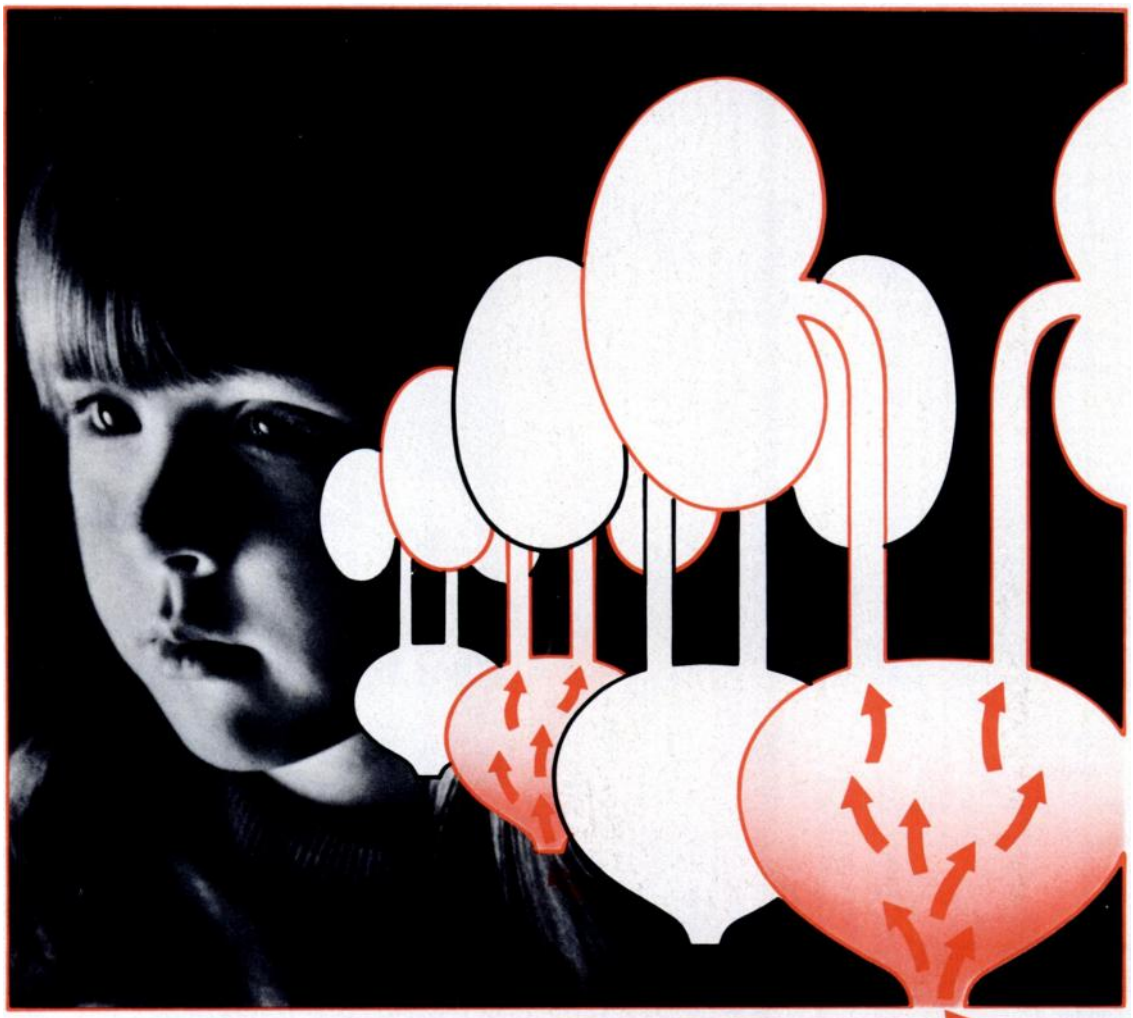

Children at Risk

In nonobstructive but recurrent pediatric UTI, a rapidly developing rationale favors long-term suppressive therapy with nitrofurantoin.[1,2,3]

For long-term or short-term therapy
of pediatric infections of the urinary tract*

*Cystitis, pyelitis or pyelonephritis due to susceptible organisms. See information concerning susceptible organisms under Indications in prescribing information.

Furadantin®
(nitrofurantoin)
Oral Suspension

25 mg per 5 cc, in bottles of 60 and 473 cc

Advantage of nitrofurantoin vs sulfonamide "...is best explained by the almost complete absence of effects (of nitrofurantoin) on the physiological bacterial reservoirs."[3]

A large-scale study of pediatric UTI in young girls "...suggests that, when no resistant strains are present in the gut at the onset of treatment, sulfonamide promotes colonization of the gut with resistant bacteria from the environment, while nitrofurantoin does not do so to any appreciable extent...sulfonamide influenced the resistance of the periurethral flora markedly, but nitrofurantoin very little so."[3]

"The disappearance of the resident intestinal *E. coli* and their replacement by sulfonamide resistant bacteria, either enterococci or *E. coli*, within a few days of sulfonamide therapy, can explain the high frequency of recurrences caused by such bacteria....This selective effect of sulfonamide is serious. Because of the high frequency of multiple resistant bacteria in the feces...it may result in therapeutic problems in future recurrences."[3]

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For children too young to take capsules or tablets, and for fractional dosage in infants
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- Specific antibacterial action is concentrated in one tract only... the urinary tract.
- It does not foster resistant flora in the bowel which may cycle urinary reinfection.
- Dosage can, and should, be reduced to lowest effective maintenance level in long-term suppressive therapy, so long as urine sterility is maintained.

References: 1. FAIR WR, GOVAN DE, FRIEDLAND GW, et al: West J Med 121:366-373, 1974
2. GOVAN DE, FAIR WR, FRIEDLAND GW, et al: West J Med 121:382-389, 1974
3. WINBERG J, BERGSTROM T, LINCOLN K, et al: Clin Nephrol 1:142-148, 1973

Furadantin Oral Suspension
(nitrofurantoin)
Indications: Indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus, some strains of Klebsiella-Aerobacter and Proteus, or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Not indicated for the treatment of renal cortical or perinephric abscesses, systemic infections, prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis or cystitis.
Contraindications: Anuria, oliguria, or extensive impairment of renal function, infants under one month, pregnant patients at term, known hypersensitivity.
Warnings: May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency (found in 10% of Negroes and in a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Such patients should be closely observed while receiving nitrofurantoin). Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to Pseudomonas.
Safety not established during pregnancy and lactation. Should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.
Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.
Adverse Reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion, and eosinophilia have been reported. Other possible reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy.
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"But we still have some medicine from his last strep throat!"

Some patients just won't complete the full course of prescribed oral therapy. This is becoming an all too common occurrence.* Especially in strep pharyngitis† when patients can be asymptomatic after only 5 days.

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Bicillin® C-R produces initial high, followed by long lasting, penicillin blood levels. Given in adequate doses, Bicillin C-R usually controls pharyngitis, tonsillitis and other common susceptible streptococcal infections in children.†

*Green, J.L. *et al.* Recurrence rate of streptococcal pharyngitis related to oral penicillin, J. Pediat. 75:292 (Aug.) 1969. Howie, V.M. and Ploussard, J.H.: Compliance dose-response relationships in streptococcal pharyngitis. Am. J. Dis. Child. *123*:18 (Jan.) 1972.

INJECTION

BICILLIN® C-R

(benzathine penicillin G and procaine penicillin G suspension)

Wyeth Laboratories
Philadelphia, Pa 19101

FOR DEEP INTRAMUSCULAR INJECTION ONLY

This product is not indicated for continuous prophylaxis of rheumatic fever or in the treatment of venereal diseases.

† **Indications:** The treatment of moderately severe infections due to penicillin-G susceptible micro-organisms susceptible to serum levels common to this dosage form. Therapy should be guided by bacteriological studies (including susceptibility testing) and by clinical response. NOTE: When high-sustained serum levels are required, sodium or potassium penicillin G either IM or IV should be used. This drug should **not** be used in the treatment of venereal diseases including syphilis, gonorrhea, yaws, bejel, and pinta.

The following infections usually respond to adequate dosages of this drug: **Streptococcal infections** (group A—without bacteremia). Moderately severe to severe infections of the upper respiratory tract, skin and soft tissue infections, scarlet fever and erysipelas. To prevent rheumatic fever or glomerulonephritis, in most instances, a measurable blood concentration of penicillin must be maintained for at least 10 days. NOTE: Streptococci in groups A, C, G, H, L and M are very sensitive to penicillin G. Other groups, including group D (enterococci) are resistant. Sodium or potassium penicillin G is recommended for streptococcal infections with bacteremia. **Pneumococcal infections.** Moderately severe pneumonia and otitis media. NOTE: Severe pneumonia, empyema, bacteremia, pericarditis, meningitis, peritonitis and arthritis of pneumococcal etiology are better treated with sodium or potassium penicillin G during acute stage.

Contraindications: Previous hypersensitivity reaction to any penicillin or to procaine.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported. Although anaphylaxis is more frequent following parenteral therapy it has occurred with oral penicillins. Reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens. Reports of individuals with a history of penicillin hypersensitivity reactions who have had severe hypersensitivity reactions when treated with a cephalosporin have been well documented. Before penicillin therapy, inquire carefully concerning previous hypersensitivity reactions to penicillins, cephalosporins and other allergens. If allergic reaction occurs, drug should be discontinued and patient treated with the usual agents, e.g., pressor amines, antihistamines and corticosteroids.

Precautions: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma. Care should be taken to avoid intravenous or intraarterial administration or injection into or near major peripheral nerves or blood vessels, since such injections may produce neurovascular damage. In streptococcal infections, therapy must be sufficient to eliminate the organism; otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following completion of treatment to determine whether streptococci have been eradicated. A small percentage of patients are sensitive to procaine. If there is a history of sensitivity make the usual test: Inject intradermally 0.1 cc of a 1 to 2 percent procaine solution. Development of an erythema, wheal, flare or eruption indicates procaine sensitivity. Sensitivity should be treated by the usual methods, including barbiturates, and procaine penicillin preparations should not be used. Antihistaminics appear beneficial in treatment of procaine reactions. The use of antibiotics may result in overgrowth of nonsusceptible organisms. Constant observation of the patient is essential. If new infections due to bacteria or fungi appear during therapy, the drug should be discontinued and appropriate measures taken. Whenever allergic reactions occur, penicillin should be withdrawn unless, in the opinion of the physician, the condition being treated is life threatening and amenable only to penicillin therapy. In prolonged therapy with penicillin, and particularly with high dosage schedules, periodic evaluation of the renal and hematopoietic systems is recommended.

Adverse Reactions: Penicillin is a substance of low toxicity but does possess a significant index of sensitization. The following hypersensitivity reactions have been reported: skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria, serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").

Composition: 300,0000 units (150,000 units benzathine penicillin G and 150,000 units procaine penicillin G) per cc in a stabilized aqueous suspension with sodium citrate buffer and approx. 6 mg. lecithin, 3 mg. povidone, 1 mg. carboxymethylcellulose, 0.5 mg. sorbitan monopalmitate, 0.5 mg. polyoxyethylene sorbitan monopalmitate, 1.2 mg. methylparaben and 0.14 mg. propylparaben per cc. 10-cc multi-dose vials.

600,000 units (300,000 units benzathine penicillin G and 300,000 units procaine penicillin G) in 1-cc Tubex® (sterile cartridge-needle unit) Wyeth (packages of 10 and 50).

1,200,000 units (600,000 units benzathine penicillin G and 600,000 units procaine penicillin G) in 2-cc. Tubex (packages of 10 and 50) and 2-cc. single-dose disposable syringes (packages of 10).

2,400,000 units (1,200,000 units benzathine penicillin G and 1,200,000 units procaine penicillin G) in 4-cc. single-dose disposable syringes (packages of 10).

In addition to stated penicillin units in a stabilized aqueous suspension, each Tubex or disposable syringe also contains sodium citrate buffer and as w/v approx. 0.5% lecithin, 0.55% carboxymethylcellulose, 0.55% povidone, 0.1% methylparaben and 0.01% propylparaben.

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VOLUME 56 • SEPTEMBER 1975 • NUMBER 3

Pediatrics

COMMENTARIES

Let's stop looking over our shoulders

Of course, I am biased, but I think the place I work is one of the best children's hospitals in the country. We are both a community hospital, where physicians admit their own private patients, and a university-affiliated hospital with a substantial teaching program, a sometimes tense, but generally beneficial combination. We also have an all-women governing board, which is a blessing for a children's hospital. Their ultimate yardstick on tough decisions is to do what's best for the kids. I'm not smug. My colleagues will testify that I perpetually carry a yard-long laundry list of suggested improvements. Overall, though, I'm proud of our hospital and think we're on the right track.

Unfortunately, this idyllic view does not permeate the hospital. Chilling winds of changes are blowing down the corridors, creating a mood of pessimism and frustration among the medical staff and board of trustees. The cause is the proliferating number of individuals and agencies expressing interest in making judgments on how we provide care. Ordinarily, I would welcome the assistance of any and all parties interested in improving the health of children, but these folks enter with guns in hand, which doesn't make for relaxed dialogue. Such groups as the Joint Commission on Accreditation of Hospitals, the Professional Standards Review Organization (PSRO), and our state's new Hospital Rate Commission all state their desire to "help" the hospital provide (I hate the term "deliver") quality care. The catch is the threat of some form of sanction if their particular concept of quality does not coincide with ours. Thus, the question being asked at our committee meetings is changing from "What do we think is best for the kids?" to "What do we think THEY want us to do?"

JOINT COMMISSION INSPECTION

An inspector from the Joint Commission recently spent several days reviewing the operation of our hospital. At the conclusion of his visit, most of his recommendations dealt with improving our procedures for auditing. He urged us to establish quality standards for different diseases, and then, through review of charts, demonstrate (supposedly to the satisfaction of outside authorities) that the standards were being met. It added up to many more doctors spending much more time pouring over a lot of written documents.

I asked if the Commission had any suggestion for standards of caring for infants with failure to thrive due to neglect; he said the Commission did not suggest the standards, that was our job. Continuing on that tack, I asked whether in the course of his inspection, he interviewed children or parents on whether they were satisfied with our institution. The answer was no. Finally, I asked when the Commission investigated children's hospitals, whether points were given for a warm atmosphere, adequate playrooms, and evidence of the children being cuddled by the nurses. Convinced that he was dealing with a nut, the very pleasant inspector replied that they hadn't gotten into that area.

AMERICAN ACADEMY OF PEDIATRICS

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SCHEDULE OF MEETINGS

ANNUAL MEETINGS

1975–Forty-Fourth October 18 to 23
The Washington Hilton, Washington, D.C.

1976–Forty-Fifth October 16 to 21
Palmer House, Chicago

1977–Forty-Sixth November 5 to 10
New York Hilton and Americana Hotel, New York City

1978–Forty-Seventh October 21 to 26
Palmer House, Chicago

1979–Forty-Eight October 13 to 18
San Francisco Hilton St. Francis Hotel, San Francisco

1980–Forty-Ninth October 24 to 30
Detroit Plaza Hotel, Detroit, Michigan

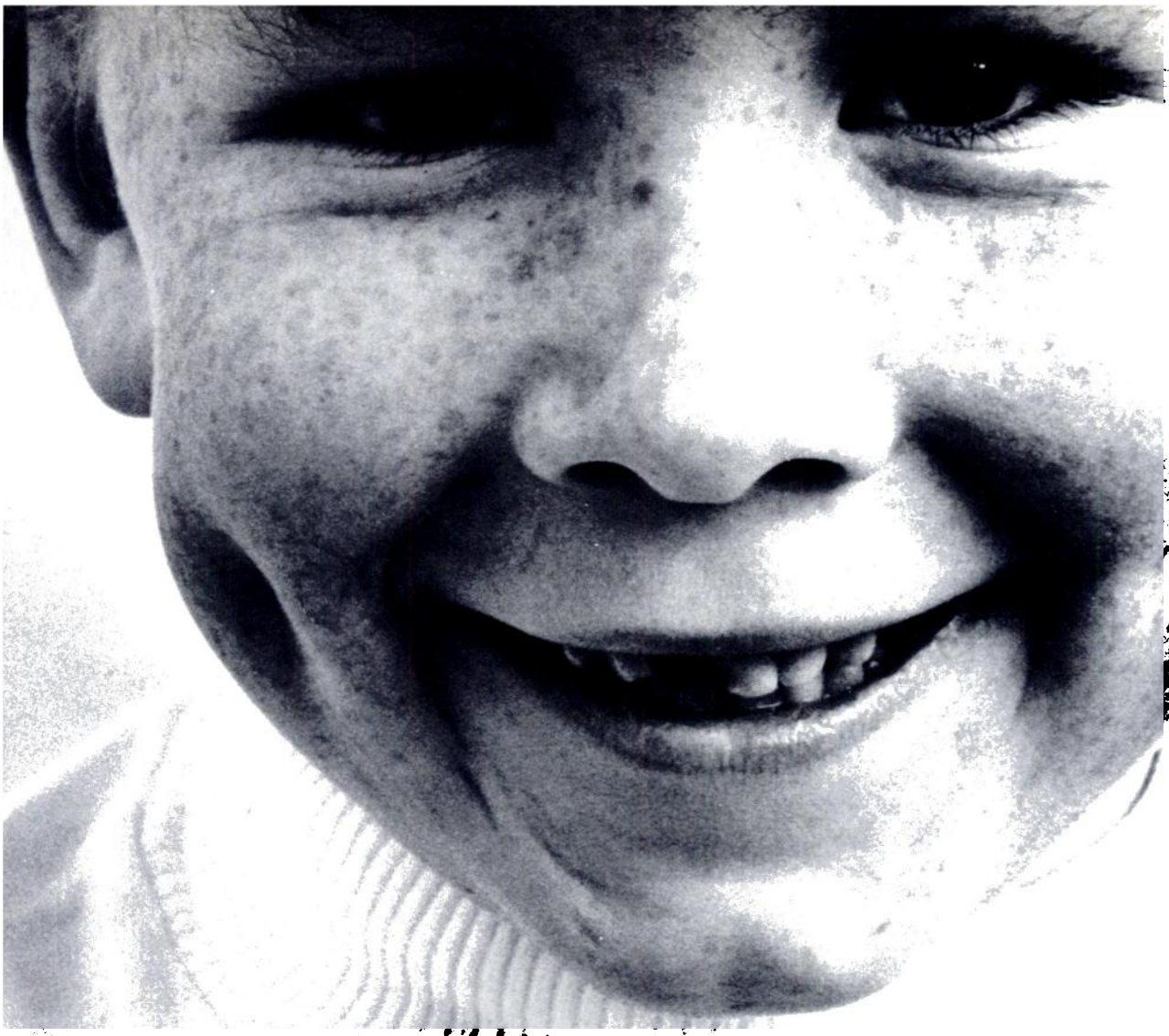
SPRING SESSIONS

1976–Bellevue Stratford April 12 to 15
Philadelphia, Pennsylvania

1977–New Orleans Marriott April 18 to 21
New Orleans, Louisiana

1978–Century Plaza April 10 to 13
Los Angeles, California

Note: All Annual Meetings start on Saturday
All Spring Sessions start on Monday



When otitis externa makes them unhappy, Cortisporin® Otic Drops helps them smile (from ear to ear).

Otitis externa. Itchy. Painful. Swollen. And you know what that does to kids. But Cortisporin® Otic Drops helps put them back in a good mood because it relieves the symptoms and gets to the cause of most superficial bacterial external otitis.

Helping kids smile may be one reason that Cortisporin Otic Drops is prescribed more than any other agent of its kind. And here are other reasons:

- antibacterial against a broad range of susceptible pathogens in superficial otitis externa, especially *Pseudomonas* and staphylococci.
- anti-inflammatory for effective relief of itching, swelling and pain caused by inflammation.
- acid pH helps restore skin's normal acid mantle.
- economical for your patients.

CONTRAINDICATIONS: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components, and in herpes simplex, vaccinia and varicella.

WARNINGS: As with other antibiotic preparations, prolonged treatment may result in overgrowth of nonsusceptible organisms and fungi.

If the infection is not improved after one week, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether therapy should be changed.

Patients who prefer to warm the medication before using should be cautioned against heating the solution above body temperature, in order to avoid loss of potency.

PRECAUTIONS: If sensitization or irritation occurs, medication should be discontinued promptly.

This drug should be used with care in cases of perforated eardrum and in longstanding cases of chronic otitis media because of the possibility of ototoxicity caused by neomycin.

Treatment should not be continued for longer than ten days.

Allergic cross-reactions may occur which could prevent the use of any or all of the following antibiotics for the treatment of future infections: kanamycin, paromomycin, streptomycin, and possibly gentamicin.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. There are articles in the current literature that indicate an increase in the prevalence of persons sensitive to neomycin.

HOW SUPPLIED: Bottles of 5 cc and 10 cc with sterile droppers.

Cortisporin® Otic Drops Sterile

(polymyxin B-neomycin-hydrocortisone)

Each cc contains: Aerosporin® brand Polymyxin B Sulfate 10,000 Units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); hydrocortisone 10 mg (1%). The vehicle contains the inactive ingredients cetyl alcohol, propylene glycol, polysorbate 80, purified water and thimerosal (preservative) 0.01%.

Complete literature available on request from Professional Services Dept. PML.

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By now she should

Rheumatic fever prevention and the noncompliant patient.

Patients on oral penicillin for prevention of recurrent rheumatic fever usually don't ignore their daily dosage regimen deliberately. But since patients are only human, doses *are* missed occasionally—through simple lapse of memory, lack of time or insufficient drug on hand.

Prolonged penicillin blood levels to obviate need for daily dosage.

A single injection of benzathine penicillin G (1.2 million units) once a month provides continuous prophylaxis in most patients. Which is why it's recommended as the method of choice* to prevent streptococcal infection and possible recurrence of rheumatic fever.

A method of choice in treatment of strep pharyngitis, too.*

In therapy of mild to moderate Group A streptococcal pharyngitis without bacteremia, just one injection of 600,000 to 900,000 units usually maintains penicillin serum concentrations in children for the 10 days necessary to eradicate the infecting organisms.† In adults, 1.2 million units are required.

*Rheumatic Fever Committee of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association

have taken all of them.

FOR DEEP INTRAMUSCULAR INJECTION ONLY.

Indications: In treatment of infections due to penicillin G-sensitive microorganisms susceptible to the low and very prolonged serum levels common to this dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and clinical response.

The following infections usually respond to adequate dosage of IM benzathine penicillin G.

Streptococcal infections (Group A — without bacteremia). Mild to moderate upper respiratory infections (e.g., pharyngitis).

Venereal infections — Syphilis, yaws, bejel, and pinta.

Medical Conditions in which Benzathine Penicillin G Therapy is indicated as Prophylaxis:

Rheumatic fever and/or chorea — Prophylaxis with benzathine penicillin G has proven effective in preventing recurrence of these conditions. It has also been used as followup prophylactic therapy for rheumatic heart disease and acute glomerulonephritis.

Contraindications: Previous hypersensitivity reaction to any penicillin.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported. Anaphylaxis is more frequent following parenteral therapy but has occurred with oral penicillins. These reactions are more apt to occur in individuals with history of sensitivity to multiple allergens. Severe hypersensitivity reactions with cephalosporins have been well documented in patients with history of penicillin hypersensitivity. Before penicillin therapy, carefully inquire into previous hypersensitivity to penicillins, cephalosporins and other allergens. If allergic reaction occurs, discontinue drug and treat with usual agents, e.g., pressor amines, antihistamines and corticosteroids.

Precautions: Use cautiously in individuals with histories of significant allergies and/or asthma.

Carefully avoid intravenous or intraarterial use or injection into or near major peripheral nerves or blood vessels, since such injection may produce neurovascular damage.

†In streptococcal infections, therapy must be sufficient to eliminate the organism, otherwise the sequelae of streptococcal disease may occur. Take cultures following completion of treatment to determine whether streptococci have been eradicated.

Prolonged use of antibiotics may promote overgrowth of non-susceptible organisms including fungi. Take appropriate measures if superinfection occurs.

Adverse Reactions: Hypersensitivity reactions reported are skin eruptions (maculopapular to exfoliative dermatitis), urticaria and other serum sickness-like reactions, laryngeal edema and anaphylaxis. Fever and eosinophilia may frequently be only reaction observed. Hemolytic anemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are infrequent and usually associated with high parenteral doses.

As with other antisyphilitics, Jarisch-Herxheimer reaction has been reported.

Composition: (units benzathine penicillin G as active ingredient in aqueous suspension):
300,000 units per cc. — 10-cc. multi-dose vial. Each cc. also contains sodium citrate buffer, approximately 6 mg. lecithin, 3 mg. povidone, 1 mg. carboxymethylcellulose, 0.5 mg. sorbitan monopalmitate, 0.5 mg. polyoxyethylene sorbitan monopalmitate, 1.2 mg. methylparaben and 0.14 mg. propylparaben.

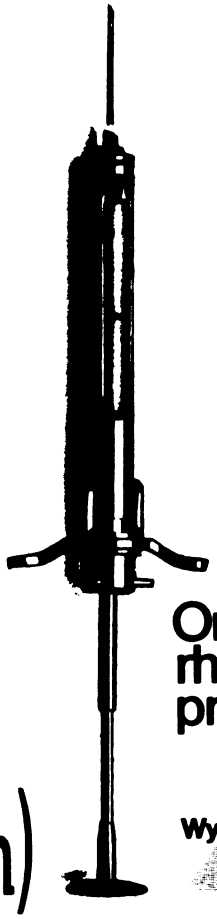
600,000 units in 1-cc. TUBEX® (sterile cartridge-needle unit) Wyeth, packages of 10.

900,000 units, 1.5-cc. fill in 2-cc. TUBEX, packages of 10.

1,200,000 units in 2-cc. TUBEX, packages of 10, and in 2-cc. single-dose disposable syringe, packages of 10.

2,400,000 units in 4-cc. single-dose disposable syringe, packages of 10.

Each TUBEX or disposable syringe also contains sodium citrate buffer and, as w/v, approximately 0.5% lecithin, 0.6% carboxymethylcellulose, 0.6% povidone, 0.1% methylparaben and 0.01% propylparaben.



INJECTION

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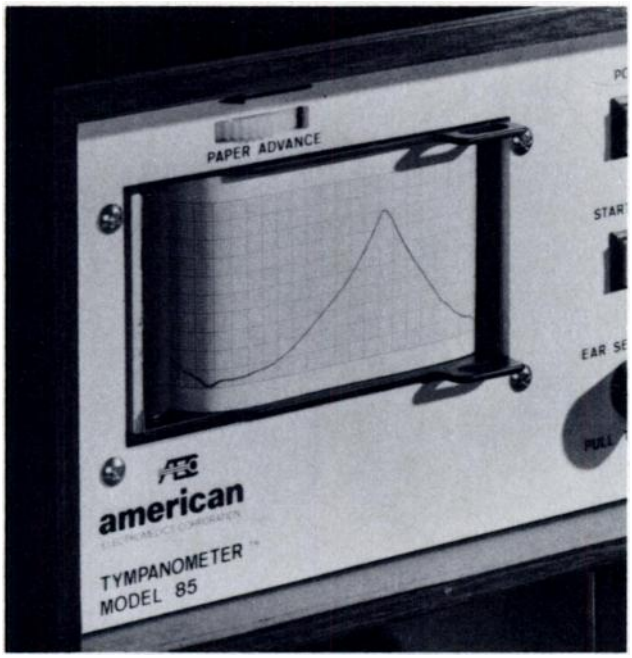

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The new Tympanometer™ Model AE 85 permits rapid and accurate diagnosis of middle ear pathology in children. The child's subjective response is eliminated...the Tympanometer™ is quick and easy to operate...printout is automatic ...compact and lightweight.

For the pediatrician, the Tympanometer™ aids in the positive identification of secretory otitis media especially when not obvious on otoscopy. It measures middle ear pressure and may be used to track the course of secretory otitis media from onset to complete resolution. The Tympanometer™ also allows identification of perforated tympanic membranes which may be missed with otoscopy. The test is valid whether or not the ear is clear, providing that the outer canal is not totally occluded with wax.

Time consuming behavioral tests are no longer necessary to identify middle ear disease.

For further details return the coupon below:

american
ELECTROMEDICS CORPORATION
"the impedance people"

145 Palisade Street • Dobbs Ferry, New York 10522

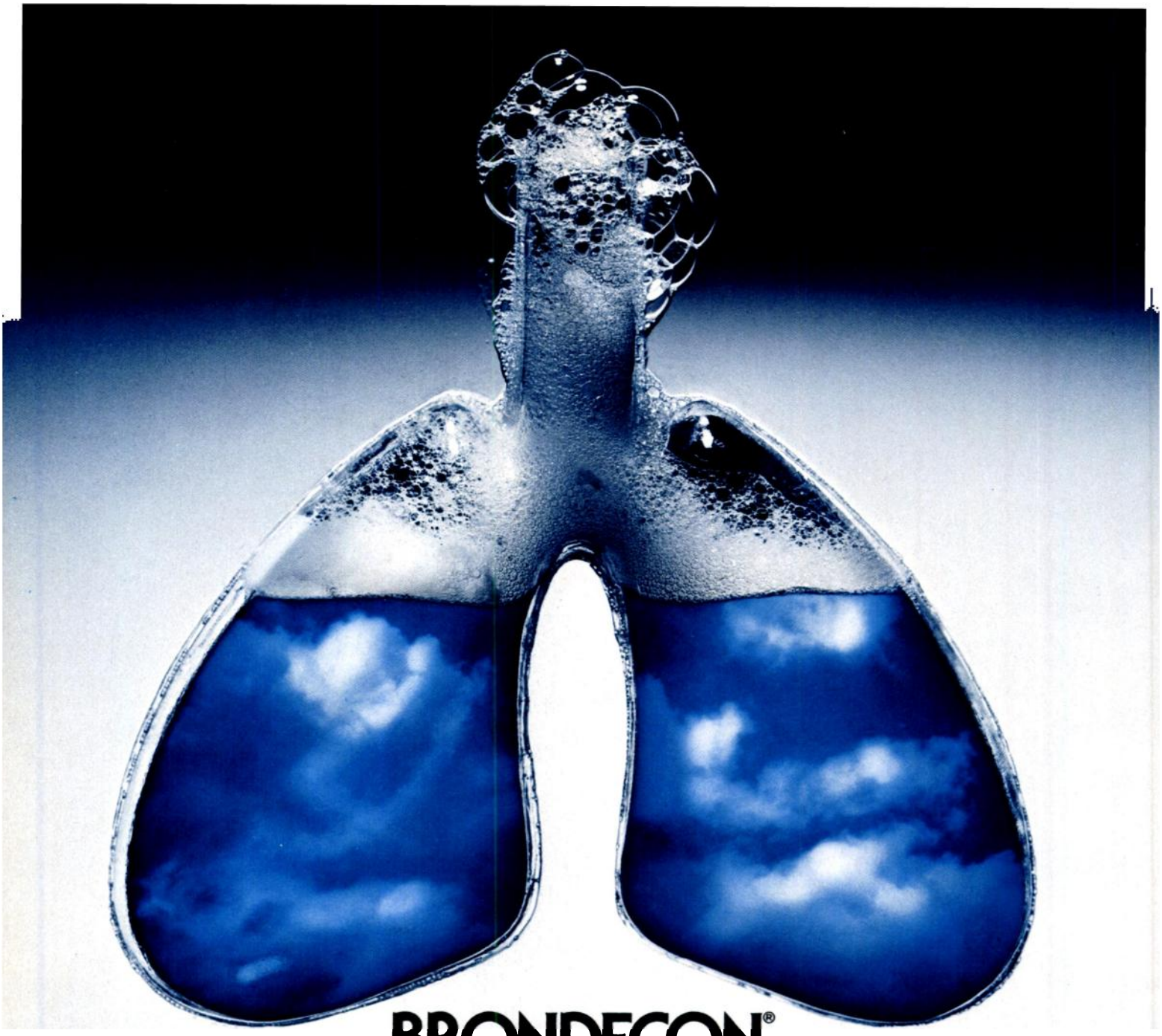
- Please provide me with further information on the Tympanometer™

Name.....

Address.....

City.....State.....Zip.....

Telephone.....



BRONDECON®

(oxtriphylline and guaifenesin)

MAKES ROOM FOR AIR FLOW in obstructive lung disease

Brondecon. The combination of oxtriphylline – the effective bronchodilator – and the time-tested expectorant, guaifenesin. To help relieve bronchospasm and help thin tenacious mucus in patients with obstructive lung disease. For freer breathing and more productive coughs.

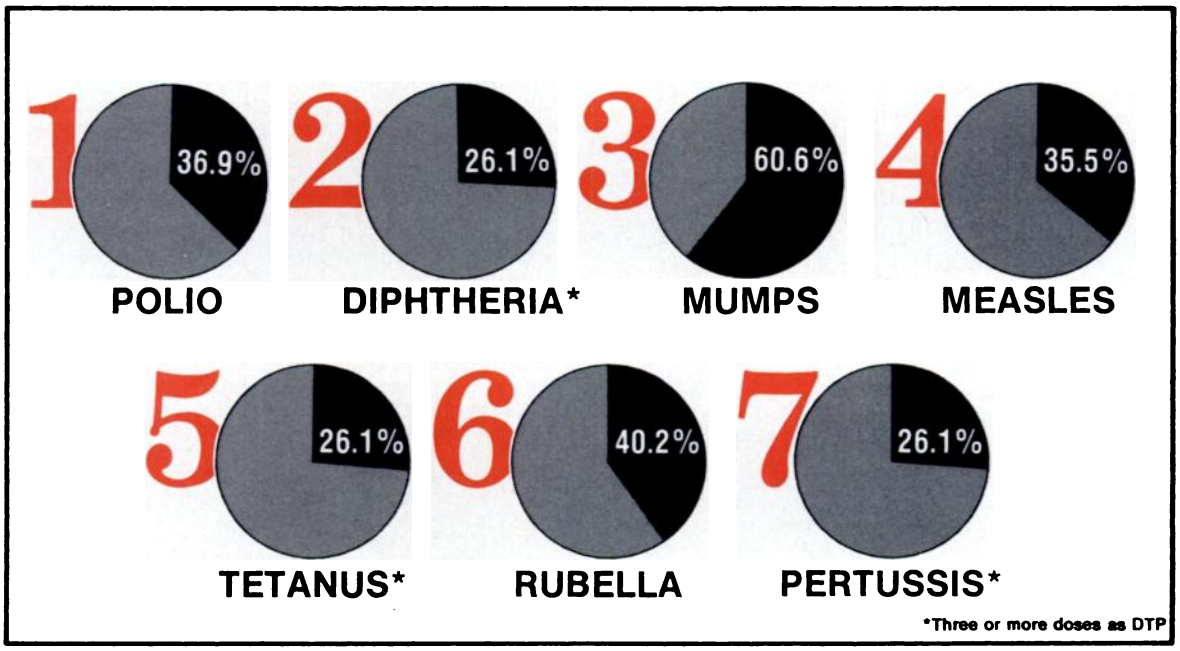
BRONDECON® Tablets/Elixir Each tablet or 10 ml elixir contains 200 mg oxtriphylline and 100 mg guaifenesin. Each 5 ml teaspoonful of elixir contains 100 mg oxtriphylline and 50 mg guaifenesin; alcohol 20%. CAUTION: Federal law prohibits dispensing without prescription. **Indications:** Brondecon is an adjunct in the management of bronchitis, bronchial asthma, asthmatic bronchitis, pulmonary emphysema, and similar chronic obstructive lung disease. It is indicated when both relaxation of bronchospasm and expectorant action are desirable. **Precautions:** Concurrent use of other xanthine preparations may lead to adverse reactions, particularly CNS stimulation in children. **Adverse Reactions:** Gastric distress and, occasionally, palpitation and CNS stimulation have been reported. **Dosage:** Tablets—over 12 years of age: one tablet, 4 times a day. Elixir—over 12 years of age: two teaspoonfuls, 4 times a day; from 2 to 12 years: one teaspoonful per 60 lb body weight, 4 times a day. **Supplied:** Salmon-pink tablets in bottles of 100 (N 0047-0200-51). Dark red, cherry flavored elixir in 237 ml (8 fl oz) (N 0047-0201-08) and 474 ml (16 fl oz) (N 0047-0201-16) bottles. Full information is available on request.

BR-GP-51-2/C

WARNER/CHILCOTT
Div. Warner-Lambert Company
Morris Plains, N.J. 07950

7 GOOD REASONS FOR IMMUNIZATION ACTION MONTH: OCTOBER 1975

PERCENT OF 1-TO 4-YEAR OLDS NOT ADEQUATELY VACCINATED IN 1974[1,2]



*Three or more doses as DTP

Too many parents are still not bringing in their preschool children for routine vaccinations. As a result, many more preschoolers than is generally realized are contracting preventable diseases.

During Immunization Action Month, a widespread TV, radio, and newspaper campaign will help you carry out your vaccination programs by alerting parents to the dangers of these diseases and motivating them to have their children adequately vaccinated.

It should be remembered that no vaccine is 100% effective and no vaccine is 100% free of risks. However, informed medical opinion and the United States Public Health Service have concluded that widespread vaccination of 1- to 4-year olds is medically and epidemiologically advisable.

iAM
IMMUNIZATION ACTION MONTH

MSD
MERCK SHARP & DOHME

1. Based on: *Summary of immunization status for polio, dtp, measles, and rubella, United States, 1974.* Preliminary data obtained from U.S. Immunization Survey, 1974, USPHS Center for Disease Control.
2. USPHS, Center for Disease Control, United States Immunization Survey: 1974.

For a brief summary of the prescribing information of MSD vaccines please see the following page.

pediatric vaccines from Merck Sharp & Dohme

Indications: *ATTENUVAX® (Measles Virus Vaccine, Live, Attenuated, MSD)*—Active immunization against measles (rubeola) in children one year of age or older.

BIAVAX® (Rubella and Mumps Virus Vaccine, Live, MSD)—Simultaneous immunization against rubella and mumps in children one year of age to puberty.

MERUVAX® (Rubella Virus Vaccine, Live, MSD)—Immunization against rubella (German measles) in children one year of age to puberty. May be useful for postpubertal males to prevent or control rubella outbreaks in circumscribed population groups. In postpubertal females vaccination must not be undertaken unless the woman is not pregnant, is susceptible to rubella (as shown by Hemagglutination Inhibition test), understands it is imperative not to become pregnant for next three months and will follow a medically acceptable method for pregnancy prevention (also in immediate postpartum period), and is informed of frequent occurrence of self-limited arthralgia and possible arthritis beginning two to four weeks after vaccination.

M-M-R® (Measles, Mumps and Rubella Virus Vaccine, Live, MSD)—Simultaneous immunization against measles, mumps, and rubella in children one year of age to puberty.

M-R-VAX® (Measles and Rubella Virus Vaccine, Live, MSD)—Simultaneous immunization against measles (rubeola) and rubella (German measles) in children one year of age to puberty.

MUMPSVAX® (Mumps Virus Vaccine, Live, MSD)—Immunization against mumps for all ages over one year.

Contraindications: Pregnancy or the possibility of pregnancy within three months following vaccination; infants less than one year old, except that measles-containing vaccines may be administered during the first year of life in certain populations (infants vaccinated under such conditions should be revaccinated after 12 months of age); sensitivity to eggs, chicken, chicken feathers, or neomycin, and, for rubella-containing vaccines, duck, or duck eggs or feathers; any febrile respiratory illness or other active infection; for measles-containing vaccines, active untreated tuberculosis; therapy with ACTH, corticosteroids, irradiation, alkylating agents, or antimetabolites; blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems; gamma globulin deficiency, i.e., agammaglobulinemia, hypogammaglobulinemia, and dysgammaglobulinemia.

Precautions: Administer subcutaneously; *do not give intravenously.* Epinephrine should be available for immediate use should an anaphylactoid reaction occur. Should not be given less than one month before or after immunization with other *live* virus vaccines, with the exception of monovalent or trivalent poliomyelitis vaccine, live, oral, which may be administered simultaneously. Vaccinations should be deferred for at least three months following blood transfusions or administration of human plasma or more than 0.02 ml immune serum globulin (human) per pound of body weight, and for MERUVAX (Rubella Virus Vaccine, Live, MSD) following anti-Rh_o (D) immune globulin (human).

Attenuated live virus measles, mumps, and rubella vaccines, given separately, may temporarily depress tuberculin skin sensitivity; therefore, if a tuberculin test is to be done, it should be scheduled before vaccination, to avoid the possibility of a false negative response.

Measles-Containing Vaccines—Due caution should be employed in children with a history of febrile convulsions, cerebral injury, or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur 5 to 12 days after vaccination. The occurrence of thrombocytopenia and purpura has been extremely rare.

Rubella-Containing Vaccines—Excretion of live attenuated rubella virus from the throat has occurred in the majority of susceptible individuals administered rubella vaccine. There is no definitive evidence to indicate that such virus is contagious to susceptible persons who are in contact with vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, has not been regarded as a significant risk.

MERUVAX (Rubella Virus Vaccine, Live, MSD)—If given to postpubertal females, patient must not be already pregnant at the time of vaccination, and adequate medical information should be provided to prevent conception for at least three months. (See **Indications**.)

Adverse Reactions: To date, clinical evaluation of the combination vaccines has revealed only those adverse reactions expected to follow administration of the monovalent vaccines given separately.

Measles-Containing Vaccines—Occasionally, moderate fever (101-102.9 F); less commonly, high fever (above 103 F); rarely, febrile convulsions. Infrequently, rash, usually minimal without generalized distribution. Reactions at injection site. Local reactions characterized by marked swelling, redness, and vesiculation at the injection site of attenuated live measles virus vaccines have occurred in children who received killed measles vaccine previously; the combination vaccines were not given under this condition in clinical trials.

Experience from more than 44 million doses of all live measles vaccines given in the U.S. by mid-1971 indicates that significant central nervous system reactions such as encephalitis, occurring within 30 days after vaccination, have been temporally associated with measles vaccine approximately once for every million doses. In no case has it been shown that reactions were actually caused by vaccine. The Center for Disease Control has pointed out that "a certain number of cases of encephalitis may be expected to occur in a large childhood population in a defined period of time even when no vaccines are administered. A survey conducted in New Jersey in 1965 showed that 2.8 cases of encephalitis (of unknown cause) occurred per million children, ages 1-9 years per 30-day period." † However, the Center for Disease Control has analyzed the reported reactions following measles vaccines and pointed out that "the clustering of cases in the period 6 through 13 days after inoculation as well as the recovery of measles virus (probably the vaccine strain) from the CSF of one patient does suggest that some of these cases may have been caused by the vaccine." The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis with measles (one per thousand reported cases).

Rubella-Containing Vaccines—Adverse reactions may include fever and rash; mild local reactions such as erythema, induration, tenderness, and regional lymphadenopathy; thrombocytopenia and purpura; allergic reactions such as urticaria; and arthritis, arthralgia, and polyneuritis.

Moderate fever (101-102.9 F) occurs occasionally, and high fever (103 F) occurs less commonly. Rash occurs infrequently and is usually minimal without generalized distribution. Encephalitis and other nervous system reactions have occurred very rarely.

Transient arthritis, arthralgia, and polyneuritis vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. Symptoms relating to joints (pain, swelling, stiffness, etc.) and to peripheral nerves (pain, numbness, tingling, etc.) occurring within approximately two months after vaccination should be considered as possibly vaccine related. These symptoms need not be associated with other features of rubella, such as fever, rash, and lymphadenopathy. In prepubertal children, the symptoms have generally been mild and of no more than three days' duration, with an incidence of less than 1 percent for reactions that would interfere with normal activity or necessitate medical attention. In teen-age girls, the rates of reactions are somewhat higher but probably do not exceed 5 to 10 percent. In women, the rates are greater and may exceed 30 percent; the symptoms in older females tend to be more prominent and of longer duration, rarely persisting for a matter of months, but have not generally interfered with normal activity. There is, at present, no evidence that the joint involvement or neuritis accompanying infection with either natural rubella or the attenuated viruses predisposes to any of the known chronic arthritic or neurologic diseases. Transient arthralgia and arthritis in nonimmune postpubertal males may occur; however, as in the natural disease, the incidence is expected to be lower than in women.

Mumps-Containing Vaccines—Parotitis. Rarely, purpura and allergic reactions such as urticaria. Very rarely, encephalitis and other nervous system reactions. With the monovalent mumps vaccine, mild fever occurs occasionally, and fever above 103 F is uncommon.

Storage and Reconstitution: Before reconstitution, store vaccines at 2-8 C (35.6-46.4 F) and *protect from light.* Use only diluent supplied to reconstitute vaccines. If not used immediately, store reconstituted vaccines in a dark place at 2-8 C (35.6-46.4 F), and discard if not used within eight hours.

How Supplied: *ATTENUVAX® (Measles Virus Vaccine, Live, MSD)*—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus vaccine expressed in terms of the assigned titer of the FDA Reference Measles Virus, and approximately 25 mcg neomycin.

BIAVAX® (Rubella and Mumps Virus Vaccine, Live, MSD)—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ of rubella virus vaccine, live, and 5,000 $TCID_{50}$ of mumps virus vaccine, live, expressed in terms of the assigned titer of the FDA Reference Rubella and Mumps Viruses, and approximately 25 mcg neomycin.

MERUVAX® (Rubella Virus Vaccine, Live, MSD)—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ of rubella virus vaccine expressed in terms of the assigned titer of the FDA Reference Rubella Virus, and approximately 25 mcg neomycin.

M-M-R® (Measles, Mumps and Rubella Virus Vaccine, Live, MSD)—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ of measles virus vaccine, live, attenuated, 5,000 $TCID_{50}$ of mumps virus vaccine, live, and 1,000 $TCID_{50}$ of rubella virus vaccine, live, expressed in terms of the assigned titer of the FDA Reference Measles, Mumps, and Rubella Viruses, and approximately 25 mcg neomycin.

M-R-VAX® (Measles and Rubella Virus Vaccine, Live, MSD)—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ of measles virus vaccine, live, attenuated, and 1,000 $TCID_{50}$ of rubella virus vaccine, live, expressed in terms of the assigned titer of the FDA Reference Measles and Rubella Viruses, and approximately 25 mcg neomycin.

MUMPSVAX® (Mumps Virus Vaccine, Live, MSD)—Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 5,000 $TCID_{50}$ of mumps virus vaccine expressed in terms of the assigned titer of the FDA Reference Mumps Virus, and approximately 25 mcg neomycin.

Each of these vaccines is supplied as a single-dose vial packed with a disposable syringe containing diluent and fitted with a 25-gauge, ⅝" needle, and as a box of 10 single-dose vials in a pop-out tray with an accompanying box of 10 diluent-containing disposable syringes with affixed needles.

For more detailed information, consult your MSD representative or see full prescribing information.

Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486.

†National Communicable Disease Center, Encephalitis Surveillance Report, 1965 Annual Supplement, July 1, 1966.

MSD
MERCK SHARP & DOHME

IMPORTANT

NAME CHANGE ANNOUNCEMENT

Larotid™
(amoxicillin)

is the new name for Larocin... the oral broad spectrum antibiotic from Roche

ROCHE

Please see following page for a summary of product information.

IMPORTANT
NAME CHANGE ANNOUNCEMENT

Larotid™ (amoxicillin) is the new name for Larocin

Why we changed the name: Since its introduction in March of 1974, Larocin has been prescribed more than a million times by physicians in the United States. In several of these instances, written prescriptions for Larocin have been confused with Lanoxin, Burroughs Wellcome Company's brand of digoxin. Although the reported incidence of such confusion has been extremely low, Roche Laboratories has changed the name of its product to LAROTID (amoxicillin). We believe this action is in the best interest of the patient and of everyone concerned.

Everything else remains the same: Virtually complete absorption ▪ Convenient *t.i.d.* dosage ▪ Blood, tissue and urine levels twice as high as ampicillin at equivalent doses ▪ Excellent response in infections due to susceptible bacteria ▪ Low incidence of diarrhea and other side effects to date.

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

Indications: Infections due to susceptible strains of the following gram-negative organisms: *H. influenzae, E. coli, P. mirabilis* and *N. gonorrhoeae;* and gram-positive organisms: streptococci (including *Streptococcus faecalis*), *D. pneumoniae* and nonpenicillinase-producing staphylococci. Therapy may be instituted prior to obtaining results from bacteriological and susceptibility studies to determine causative organisms and susceptibility to amoxicillin.

Contraindications: In individuals with history of allergic reaction to penicillins.

WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH MORE FREQUENT FOLLOWING PARENTERAL THERAPY, ANAPHYLAXIS HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. MORE LIKELY IN INDIVIDUALS WITH HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. BEFORE THERAPY, INQUIRE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS OR OTHER ALLERGENS. IF ALLERGIC REACTION OCCURS, INSTITUTE APPROPRIATE THERAPY AND CONSIDER DISCONTINUANCE OF AMOXICILLIN. **SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. ADMINISTER OXYGEN, INTRAVENOUS STEROIDS AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, AS INDICATED.**

Usage in Pregnancy: Safety in pregnancy not established.

Precautions: As with any potent drug, assess renal, hepatic and hematopoietic function periodically during prolonged therapy. Keep in mind possibility of superinfections with mycotic or bacterial pathogens; if they occur, discontinue drug and/or institute appropriate therapy.

Adverse Reactions: As with other penicillins, untoward reactions will likely be essentially limited to sensitivity phenomena and more likely occur in individuals previously demonstrating penicillin hypersensitivity and those with history of allergy, asthma, hay fever or urticaria. Adverse reactions reported as associated with use of penicillins: *Gastrointestinal:* Nausea, vomiting, diarrhea. *Hypersensitivity Reactions:* Erythematous maculopapular rashes, urticaria. *NOTE:* Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Discontinue amoxicillin unless condition is believed to be life-threatening and amenable only to amoxicillin therapy. *Liver:* Moderate rise in SGOT noted, but significance unknown. *Hemic and Lymphatic Systems:* Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, agranulocytosis. All are usually reversible on discontinuation of therapy and believed to be hypersensitivity phenomena.

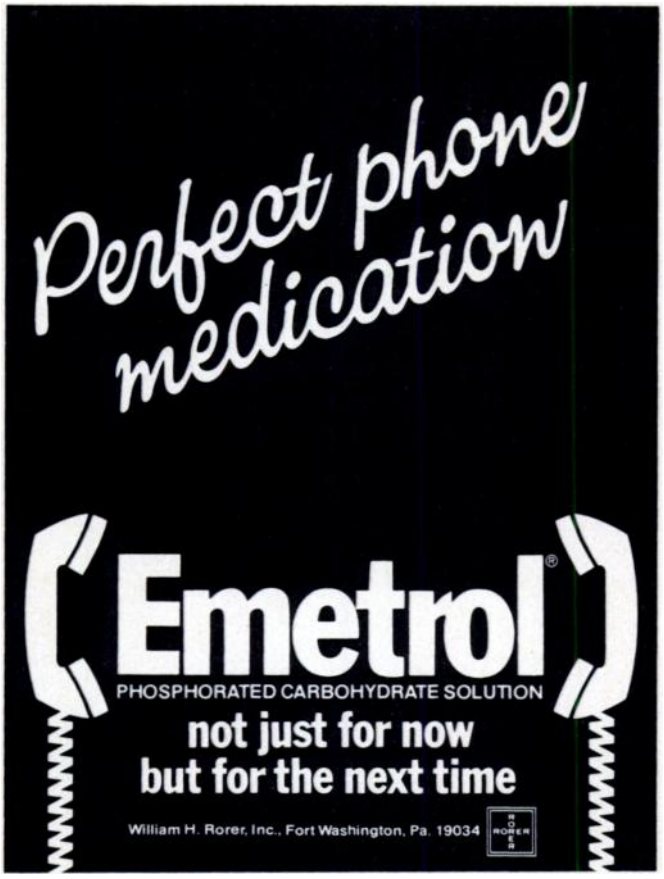
Dosage: Ear, nose, throat, genitourinary tract, skin and soft tissue infections—Adults: 250 mg every 8 hours. Children: 20 mg/kg/day in divided doses every 8 hours; under 6 kg, 0.5 ml of Pediatric Drops every 8 hours; 6-8 kg, 1 ml of Pediatric Drops every 8 hours. Lower respiratory tract infections and severe infections or those caused by less susceptible organisms—Adults: 500 mg every 8 hours. Children: 40 mg/kg/day in divided doses every 8 hours; under 6 kg, 1 ml of Pediatric Drops every 8 hours; 6-8 kg, 2 ml of Pediatric Drops every 8 hours. Gonorrhea (acute uncomplicated anogenital and urethral infections)—Males and females: 3 grams as a single oral dose. NOTE: Children weighing more than 8 kg should receive appropriate dose of oral suspension 125 mg or 250 mg/5 ml. Children weighing 20 kg or more should be dosed according to adult recommendations.

Note: In gonorrhea with suspected lesion of syphilis, perform darkfield examinations before amoxicillin therapy and monthly serological tests for at least four months. In chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller than recommended doses should not be used. In stubborn infections, several weeks' therapy may be required. Except for gonorrhea, continue treatment for a minimum of 48-72 hours after patient is asymptomatic or bacterial eradication is evidenced. Treat hemolytic streptococcal infections for at least 10 days to prevent acute rheumatic fever or glomerulonephritis.

Supplied: Amoxicillin as the trihydrate: Capsules, 250 mg and 500 mg; oral suspension, 125 mg/5 ml and 250 mg/5 ml; pediatric drops, 50 mg/ml.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



Columbia University, College of Physicians & Surgeons and the Department of Pediatrics-Babies Hospital, The Children's Medical and Surgical Center presents a three day course Pediatrics PM 3 - Infectious Diseases of Infants & Children under the direction of Dr. Michael Katz, Director, Division of Infectious Diseases, Babies Hospital, December 10, 11, and 12, 1975.

For information and application write
Jose M. Ferrer, M.D.,
Associate Dean,
630 West 168th Street,
New York, N.Y. 10032
or phone 212 579-3682.

Fee $175.
interns and residents $100.

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13μg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

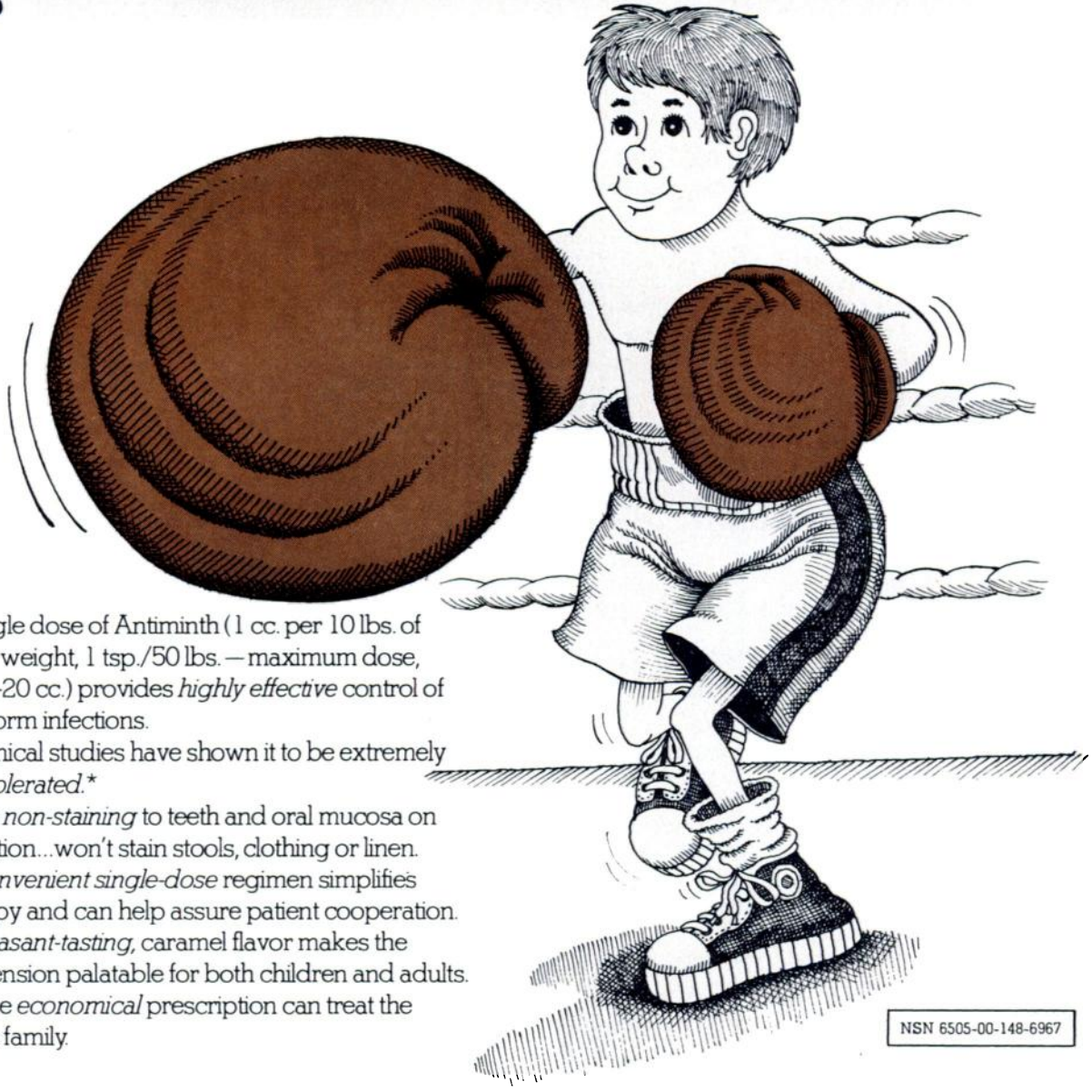
Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Knock out pinworms



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs.—maximum dose, 4 tsp.-20 cc.) provides *highly effective* control of pinworm infections.

Clinical studies have shown it to be extremely *well tolerated.**

It is *non-staining* to teeth and oral mucosa on ingestion...won't stain stools, clothing or linen.

Convenient single-dose regimen simplifies therapy and can help assure patient cooperation.

Pleasant-tasting, caramel flavor makes the suspension palatable for both children and adults.

One *economical* prescription can treat the entire family.

NSN 6505-00-148-6967

with a single, non-staining dose of

ANTIMINTH®

(pyrantel pamoate)

equivalent to 50 mg. pyrantel/ml.

ORAL SUSPENSION

*Data on file at Roerig

Please see prescribing information on facing page

ROERIG Pfizer

A division of Pfizer Pharmaceuticals

New York, New York 10017

In external otitis.

When the ear is "hot"...

VōSoL HC contains hydrocortisone, which reduces inflammation, and
(hydrocortisone 1%, acetic acid nonaqueous 2%)
VōSoL, which acts to stop infection...but avoids antibiotic risks.
(acetic acid-nonaqueous)

VōSoL (acetic acid-nonaqueous) is potent against bacteria

Rapidly effective against cultures of Pseudomonas, Proteus, staphylococci and other pathogens encountered in otitis externa.[1]

VōSoL is potent against fungi

Rapidly effective against cultures of *Candida albicans*, *Nocardia asteroides*, *Cryptococcus neoformans* and other fungi.[1]

VōSoL potency proved in double-blind study

In a randomized, double-blind study, VōSoL and VōSoL HC achieved a higher overall percentage of microbial and clinical cures after seven days of treatment when compared with respective control preparations of acetic acid solutions and an aqueous acetic acid suspension containing neomycin, colistin and hydrocortisone.[2] No side effects were reported.

Free of major problems

which may be encountered with antibiotics, such as:

- Risk of sensitization
- Fungal overgrowth
- Development of bacterial resistance

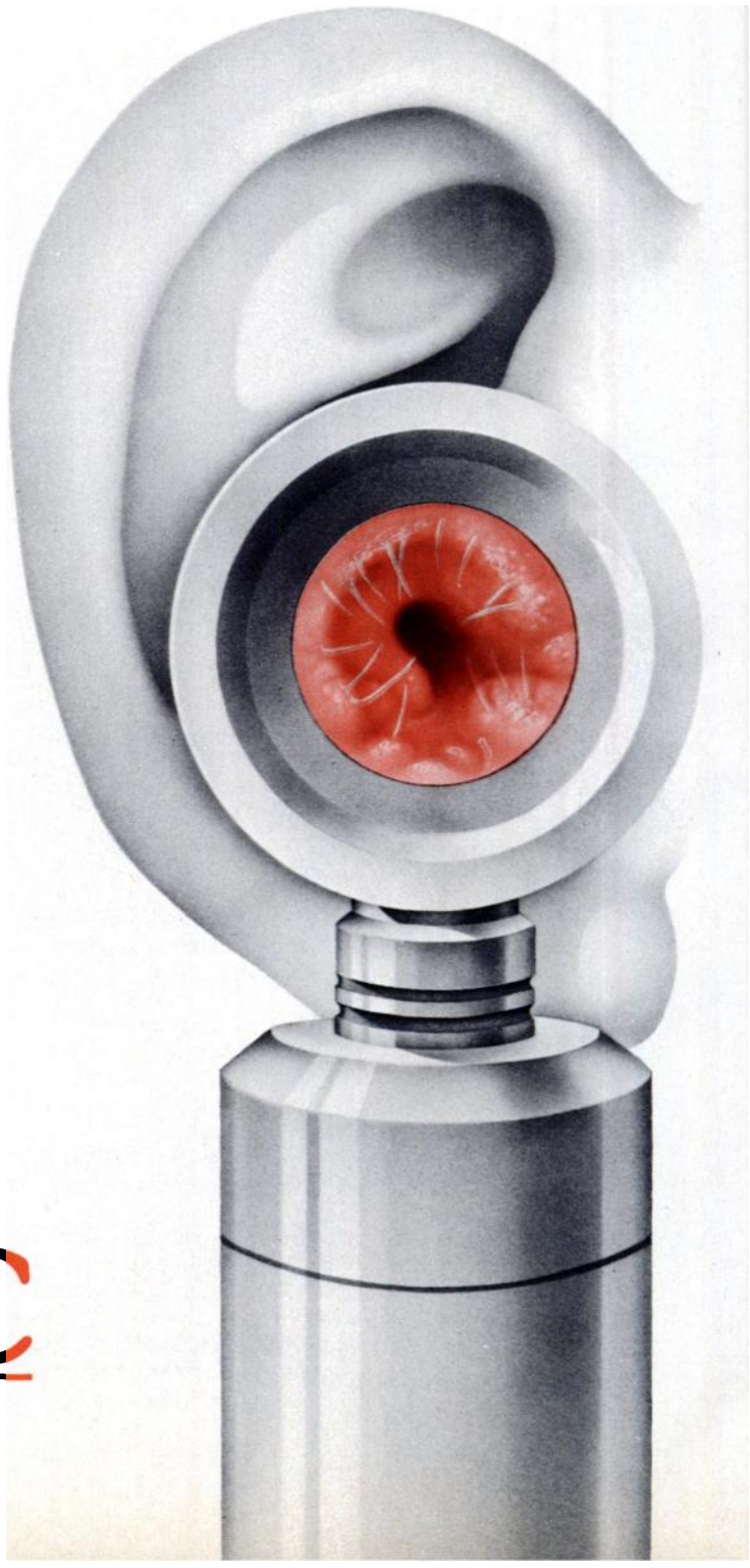
VōSoL pH and ear pathogens

There is evidence that external ear infection is associated with ear canal pH above 6.3, and that restoration of a lower pH helps fight infection.[3] VōSoL, which has a pH of 3, reduces the pH to between 4 and 5 in the ear canal[3]... restores and maintains the skin's normal "acid barrier."

1. Seneca, H., and Avakian, S.: Antimicrob. Agents Chemother.: 807-810 (May) 1961.
2. Dadagian, A.J., et al.: Curr. Ther. Res. *16*:431-436 (May) 1974.
3. Goffin, F.B.: N. Engl. J. Med. *268*:287-289 (February 7) 1963.

AVAILABLE IN DEPOT-VōSoL 6505-00-111-7864/VōSoL HC 6505-00-111-7865

WALLACE LABORATORIES
Division of Carter-Wallace, Inc.
Cranbury, New Jersey 08512



VōSoL® HC

(hydrocortisone 1%, acetic acid nonaqueous 2%)

OTIC SOLUTION for external otitis with inflammation

and when it's not

For extending therapy* after VōSoL HC has done its job, or in cases when HC is not indicated,

(hydrocortisone 1%, acetic acid nonaqueous 2%)

VōSoL makes sense: It's antibacterial without antibiotics.

(acetic acid-nonaqueous)

The need for extended therapy

External otitis often recurs... a history of relapse or reinfection is common in "swimmer's ear," for example. That is why it is frequently desirable to extend therapy beyond the few days usually needed to control an acute infection.

The logic of VōSoL (acetic acid-nonaqueous)

While otic antibiotic preparations are generally limited to short courses of treatment, VōSoL antimicrobial therapy may be prolonged without the threat of fungal overgrowth or development of bacterial resistance, and with virtually no likelihood of sensitization. (No cases of fungal overgrowth, bacterial resistance or sensitization have been reported to date.)

To help discourage bacterial and fungal infection, VōSoL also helps dry the surface of the ear canal, and restores and maintains the skin's normal "acid barrier."

Action: VōSoL is antibacterial, antifungal, hydrophilic, has an acid pH and a low surface tension.
VōSoL HC is, in addition, anti-inflammatory and antipruritic.

* **Indications:** (VōSoL only) Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
Effective: For the treatment of superficial infections of the external auditory canal caused by organisms susceptible to the action of the antimicrobial.
"Possibly" effective: For prophylaxis of otitis externa in swimmers and susceptible subjects.
Final classification of the less-than-effective indication requires further investigation.

Indications: (VōSoL HC only) For the treatment of superficial infections of the external auditory canal caused by organisms susceptible to the action of the antimicrobial, complicated by inflammation.
Contraindications: These products are contraindicated in those individuals who have shown hypersensitivity to any of their components; perforated tympanic membranes are frequently considered a contraindication to the use of external ear canal medication. VōSoL HC is contraindicated in vaccinia and varicella.
Precautions: VōSoL HC: As safety of topical steroids during pregnancy has not been confirmed, they should not be used for an extended period during pregnancy. Systemic side effects may occur with extensive use of steroids. If sensitization or irritation occurs, medication should be discontinued promptly.
How Supplied: VōSoL Otic Solution, in 15 ml. measured-drop, safety-tip plastic bottle. VōSoL HC Otic Solution, in 7½ ml. measured-drop, safety-tip plastic bottle.

VōSoL®

(acetic acid-nonaqueous)

OTIC SOLUTION for extended use against recurrent otitis externa

May be the start of a better life for the epileptic

About nine out of ten epileptics suffer their first seizure in childhood.[1] Certain physical and psychic postseizure evidence—a badly bitten tongue, broken or dropped objects, amnesia, exhaustion—may suggest grand mal. Once the diagnosis of epilepsy has been established, *MYSOLINE (primidone) may mean the start of a seizure-free life.*

Early therapy for control of grand mal, focal and psychomotor epilepsy. Used alone or as concomitant therapy, MYSOLINE may reduce the frequency and severity of major motor seizures—or even eliminate them. Based on years of clinical success, MYSOLINE has earned the reputation of being an *excellent* drug for control of grand mal epilepsy.[2-4] But its usefulness is not confined to this type alone: MYSOLINE has proved to be valuable for control of psychomotor[2,3] and focal epilepsy[5] as well.

Improves response to concomitant therapy. When other anticonvulsants prove to be inadequate, adding MYSOLINE to the regimen can improve seizure control in grand mal and psy-

chomotor epilepsy. A double-blind comparative study[6] shows that the combined use of phenobarbital, diphenylhydantoin, and MYSOLINE may have additive anticonvulsant effects without additive side effects.

Effective changeover therapy. Unsatisfactory performance or important side effects may force discontinuation of the patient's existing anticonvulsant therapy. For more effective control, MYSOLINE may be added to the patient's present regimen, then gradually substituted for the original medication. The changeover to MYSOLINE is frequently warranted when grand mal is refractory to phenobarbital, with or without diphenylhydantoin.[7]

Mysoline®
(primidone)

See last page of advertisement for prescribing information.

Ayerst®

AYERST LABORATORIES
New York, N.Y. 10017

Mysoline® (primidone)
May be the start of a better life for the epileptic

initial and maintenance therapy for grand mal, psychomotor and focal epilepsy

BRIEF-SUMMARY

(For full prescribing information, see package circular.)

MYSOLINE® Brand of **PRIMIDONE**
Anticonvulsant

ACTIONS: MYSOLINE acts on the central nervous system to raise seizure threshold or alter seizure pattern. The mechanism(s) of action of anticonvulsant drugs is not known.

Primidone has anticonvulsant activity *per se*. In addition, its two metabolites possess anticonvulsant qualities. The major metabolite is phenylethylmalonamide (PEMA); the other is phenobarbital. In addition to its own anticonvulsant potential, PEMA potentiates phenobarbital.

INDICATIONS: MYSOLINE, either alone or used concomitantly with other anticonvulsants, is indicated in the control of grand mal, psychomotor, and focal epileptic seizures. It may control grand mal seizures refractory to other anticonvulsant therapy.

CONTRAINDICATIONS: Primidone is contraindicated in: 1) patients with porphyria and 2) patients who are hypersensitive to phenobarbital (see ACTIONS).

WARNINGS: The abrupt withdrawal of antiepileptic medication may precipitate status epilepticus.

The therapeutic efficacy of a dosage regimen takes several days before it can be assessed.

Use in pregnancy: Recent reports strongly 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. Reference has been made to primidone in several cases in which it was used *in combination* with other anticonvulsants; but its teratogenicity has not been conclusively demonstrated. The possibility exists that other factors, *e.g.*, genetic factors or the epileptic condition, may contribute to the higher incidence of birth defects. The data also indicate that the great majority of mothers receiving anticonvulsant medication deliver normal infants.

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 risk to both mother and the unborn child.

When the nature, frequency, and severity of the seizures do not pose a clear threat to the patient, good medical practice requires that the physician weigh the expected therapeutic benefit of anticonvulsant therapy against possible risk on an individual basis.

Neonatal hemorrhage, with a coagulation defect resembling vitamin K deficiency, has been described in newborns whose mothers were taking primidone and other anticonvulsants. Pregnant women under anticonvulsant therapy should receive prophylactic vitamin K_1 therapy for one month prior to, and during, delivery.

The physician should weigh all of the foregoing considerations when treating and counseling epileptic women of childbearing potential.

PRECAUTIONS: The total daily dosage should not exceed 2 Gm. Since MYSOLINE therapy generally extends over prolonged periods, a complete blood count and a sequential multiple analysis-12 (SMA-12) test should be made every six months.

In nursing mothers: There is evidence that in mothers treated with primidone, the drug appears in the milk in substantial quantities. Since tests for the presence of primidone in biological fluids are too complex to be carried out in the average clinical laboratory, it is suggested that the presence of undue somnolence and drowsiness in nursing newborns of MYSOLINE-treated mothers be taken as an indication that nursing should be discontinued.

ADVERSE REACTIONS: The most frequently occurring early side effects are ataxia and vertigo. These tend to disappear with continued therapy, or with reduction of initial dosage. Occasionally, the following have been reported: nausea, anorexia, vomiting, fatigue, hyperirritability, emotional disturbances, sexual impotency, diplopia, nystagmus, drowsiness, and morbilliform skin eruptions. Occasionally, persistent or severe side effects may necessitate withdrawal of the drug. Megaloblastic anemia may occur as a rare idiosyncrasy to MYSOLINE (primidone) and to other anticonvulsants. The anemia responds to folic acid, 15 mg. daily, without necessity of discontinuing medication.

DOSAGE AND ADMINISTRATION: The average adult dose is 0.75 to 1.5 Gm. per day. The initial dose is 250 mg. Increments of 250 mg. are added, usually at weekly intervals, to tolerance, or therapeutic effectiveness, up to daily doses not exceeding 2.0 Gm. A typical dosage schedule for the introduction of MYSOLINE is as follows:

Adults and Children Over 8 Years of Age

1st Week 250 mg. daily at bedtime	*2nd Week* 250 mg. b.i.d.
3rd Week 250 mg. t.i.d.	*4th Week* 250 mg. q.i.d.

In children under 8 years of age, maintenance levels are established by a similar schedule, but at one-half the adult dosage. It is best to begin with 125 mg., with gradual weekly increases of 125 mg. a day, to a daily total usually between 500 mg. and 750 mg.

In patients already receiving other anticonvulsants: MYSOLINE (primidone) should be gradually increased as dosage of the other drug(s) is maintained or gradually decreased. This regimen should be continued until satisfactory dosage level is achieved for combination, or the other medication is completely withdrawn. When therapy with this product alone is the objective, the transition should not be completed in less than two weeks.

MYSOLINE 50 mg. Tablet can be used to practical advantage when small fractional adjustments (upward or downward) may be required, as in the following circumstances:

- for initiation of combination therapy
- during "transfer" therapy
- for added protection in periods of stress or stressful situations that are likely to precipitate seizures (menstruation, allergic episodes, holidays, etc.)

HOW SUPPLIED: MYSOLINE *Tablets*—No. 430—Each tablet contains 250 mg. of primidone (scored), in bottles of 100 and 1,000. Also in unit dose package of 100. No. 431—Each tablet contains 50 mg. of primidone (scored), in bottles of 100 and 500. MYSOLINE *Suspension*—No. 3850—Each 5 cc. (teaspoonful) contains 250 mg. of primidone, in bottles of 8 fluidounces.

References: 1. Livingston, S., and Pruce, I.: Pediatr. Ann. 2:10 (Aug.) 1973. 2. Livingston, S., and Pruce, I. M.: Drug Therapy for Epilepsy, Springfield, Ill., Charles C Thomas, 1966, p. 23. 3. Scholl, M. L., in Conn, H. F.: Current Therapy 1973, Philadelphia, Saunders, 1973, pp. 675-7. 4. Metrick, S.: C.M.D. 37:49 (Jan.) 1970. 5. Forster, F. M.: Med. Clin. North Am. 47:1579 (Nov.) 1970. 6. White, P. T.: Wis. Med. J. 68:178 (Apr.) 1969. 7. Millichap, J. G.: Drug Ther. 1:15 (Oct.) 1971.

AYERST LABORATORIES
New York, N.Y. 10017 **Ayerst®**

When the "drug vacation" shows that the child with MBD still needs medication, consider

Cylert®

C IV

(PEMOLINE)

ABBOTT

Cylert (pemoline) offers these benefits

- **Single daily dose administration**
- **Minimal cardiovascular effects**
- **No evidence of tolerance**

If you wish to switch a child to Cylert:

Many clinicians recommend that drug-free periods be scheduled periodically to observe if there is still a need for drug therapy. These drug-free periods are the logical time to introduce Cylert if symptoms return. Because the serum half-life of other drugs (methylphenidate and d-amphetamine) used for MBD is very short, if abnormal behavior returns, it is usually within a day or two.

Dosage and administration

Cylert is given as a single oral dose each morning.

The recommended starting dose is 37.5 mg. per day. This daily dosage should be gradually increased at one week intervals using increments of 18.75 mg. until the desired clinical response is obtained.

The mean daily effective dose ranges from 56.25 to 75 mg. per day. The maximum recommended daily dose of Cylert is 112.5 mg.

Using the recommended schedule of dose titration, significant benefits may not be seen until the third or fourth week of drug therapy. Side effects may be seen prior to optimum clinical results.

Cylert can be taken with meals

You can prescribe Cylert a.c., p.c., or with meals. Although the speed of absorption is slightly slowed by food, the total absorption is not affected.

Name _____ Age _____

Address _____ Date _____

℞ Cylert 37.5 mg.
Disp. #50
Sig: tabs I q AM
Call Dr. in one week

Refill _____ Times _____

DEA No. _____ Dr. _____

The 3 dosage strengths

Cylert 18.75 mg.
(yellow-colored, grooved)

Cylert 37.5 mg.
(orange-colored, grooved)

Cylert 75 mg.
(tan-colored, grooved)

Tablets Shown Actual Size

Please see last page of this advertisement for Prescribing Information.

Physicians', teachers', and parents' ratings demonstrated Cylert (pemoline) to be effective[1,2]

Description of Clinical Studies

Multi-clinic design
21 investigators from 10 states and two provinces in Canada.

Double-blind, placebo control
413 patients randomly assigned to Cylert or placebo groups. 238 patients met all criteria for evaluation of efficacy.

Patient selection
Strict criteria were established: ages 6 to 12; intelligence, a WISC score of 90 or above; good health with no significant personal or family psychopathology; one or more of the general indicators of MBD; and a combined (parent and teacher) "hyperkinesis index" rating of 36 or more.

Physical examination
Included determination that vision and hearing were within normal limits to preclude their being major factors in disorder.

Laboratory tests
Obtained at beginning and end of study: hemoglobin, hematocrit, WBC differential and platelet estimate, BUN, alkaline phosphatase, SGOT, SGPT (or LDH), bilirubin, uric acid and urinalysis.

Length of study
Nine weeks.

Results of Clinical Studies

Measurement of results
Global (overall) ratings by teachers, parents and physicians were performed at weeks 0, 3, 6 and 9.

Overall results
Roughly two out of three patients were significantly improved by treatment with Cylert as reflected by global ratings.

Behavioral changes
Parents and teachers reported in general that, compared with the control group, children on Cylert:

- Got along better with others
- Were less subject to temper tantrums
- Showed less tendency to leave things unfinished
- Engaged in less fighting
- Seemed more mature

Psychological tests
Children on Cylert had statistically significantly higher scores than those on placebo on these psychological tests:

- The Wechsler Intelligence Scale for Children (WISC) and its performance IQ Sub-Component
- The Wide Range Achievement Test (WRAT) (reading and arithmetic)

- The Lincoln-Oseretsky Motor Performance Test Factor II

Laboratory tests
No abnormalities attributed to Cylert.

1. *Conners, C. K., ed.*, Clinical Use of Stimulant Drugs in Children, *Excerpta Medica, 1974, p. 98.*
2. *Page, J. G., et al., J. Learning Disabilities, 7:498, Oct., 1974.*

Cylert (pemoline) single daily dosage benefits both child and adults

For the adults:		For the child:
Control of medication stays with parents	⟷	No drug in child's possession while at school
Obviates need for nurse or teacher to supervise taking of mid-day doses	⟷	Avoids situation in which child is repeatedly singled out as being "different"
Helps assure that the prescribed dosage is being given each day	⟷	Helps prevent possible variations in effect caused by missed, forgotten or delayed doses

Cylert, alone among CNS stimulants used to treat MBD, is inherently long-acting, permitting once-daily dosage.

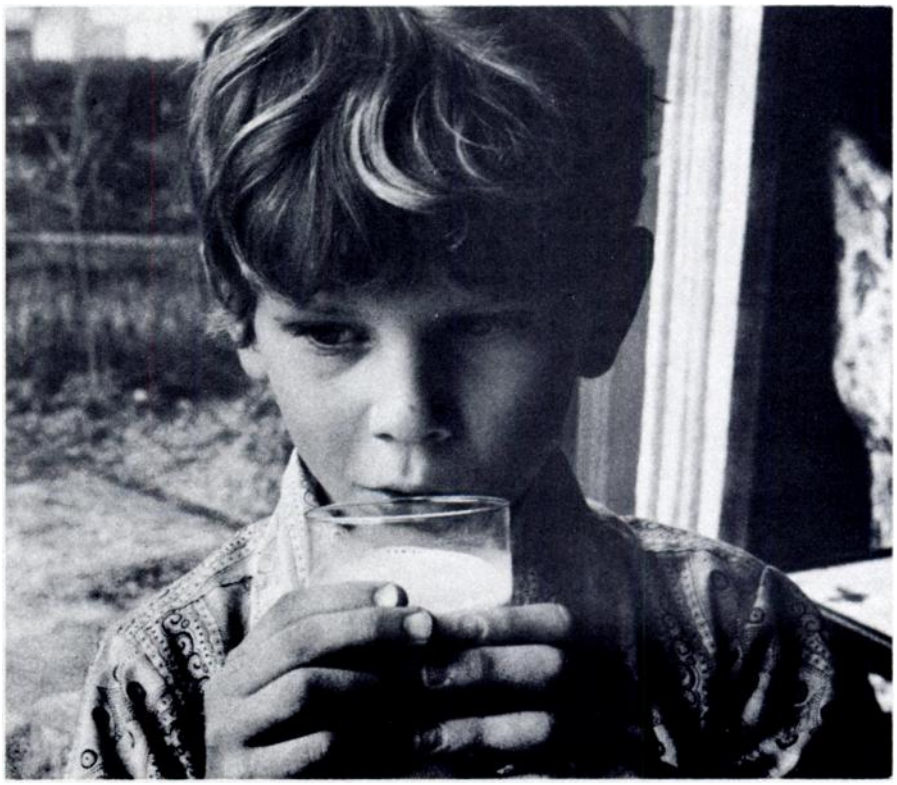
When *not* to use Cylert

Cylert should not be used for (and will not be effective in) simple cases of overactivity in school-age children.

Neither should it be used in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis.

The physician should rely on a complete history of the child and a thorough description of symptoms from both parents and teacher before postulating a diagnosis of MBD.

Please see last page for Prescribing Information.



Cylert (pemoline) has an impressive safety profile

From Multi-Clinic Studies (9 weeks); safety data analyzed on 407 patients

No significant difference between Cylert and placebo groups—

—in blood pressure

—in pulse

—in laboratory tests

—in neurological status

Other criteria:

Adverse reactions	Insomnia and anorexia were the most frequently seen side effects and often improved with continuation of treatment or reduction of dosage. (For other side effects, please see Prescribing Information on last page.)
Weight loss	Mean weight loss of 1.1 lbs. was demonstrated in Cylert group during early weeks of treatment; long-term studies have shown that by 3-6 months, most children return to the normal rate of weight gain for their age group.

From Additional Studies (Long-Term) on Cylert (up to two years and continuing)

Mean dosage	Essentially unchanged on mg./kg. basis from original effective dosage.
Blood pressure	No significant changes attributed to Cylert.
Pulse rate	No significant changes attributed to Cylert.
Laboratory examination	Mild to moderate increase in transaminase (SGOT and SGPT) levels in 1-2% of patients (no clinical symptoms); levels returned to normal on withdrawal of medication. No clinically significant abnormalities in the other tests.

Cylert (pemoline)

Ⓒ IV

Prescribing Information

Description: Cylert (pemoline) is a white, tasteless, odorless powder which is relatively insoluble (less than 1 mg/ml) in water, chloroform, ether, acetone, and benzene. In 95% ethyl alcohol, the solubility of pemoline is 2.2 mg/ml.

Actions: Cylert (pemoline) is a central nervous system stimulant. The pharmacologic activity of pemoline is similar to that of other known stimulants but with minimal sympathomimetic effects. Pemoline is structurally dissimilar from the amphetamines and methylphenidate. Although the exact mode of pharmacodynamic action is undetermined in man, pemoline has been reported to increase the rate of synthesis of dopamine in rat brain.

In human subjects, Cylert produces peak blood levels within 2-4 hours. The serum half-life is approximately 12 hours. Multiple dose studies in adults at several dose levels indicate that serum levels plateau in approximately three days. Cylert and its metabolites are primarily excreted by the kidneys with approximately 75% of an oral dose appearing in the urine within a 24-hour period. Approximately 43% of pemoline is excreted unchanged. Metabolites include pemoline dione, conjugated pemoline and mandelic acid.

Cylert (pemoline) has a gradual onset of action in children with minimal brain dysfunction. Using the recommended schedule of dosage titration, significant clinical benefit may not be evident until the third or fourth week of drug administration.

Indications: MINIMAL BRAIN DYSFUNCTION IN CHILDREN—as adjunctive therapy to other remedial measures (psychological, educational, social).

Special Diagnostic Considerations: Specific etiology of minimal brain dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis includes the use not only of medical but of psychological, educational, and social resources.

Characteristics commonly reported include: A chronic history of moderate to severe hyperactivity, short attention span, distractibility, emotional lability, and impulsivity. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics.

Drug treatment is not indicated for all children with MBD. In the primary therapy of MBD, appropriate educational placement is essential and psychosocial intervention is generally necessary. When these measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis.

Contraindication: Cylert (pemoline) is contraindicated in patients with known hypersensitivity or idiosyncrasy to the drug. (See PRECAUTIONS)

Warnings: Cylert is not recommended for children under six years of age since safety and efficacy in this age group have not yet been established.

Since Cylert (pemoline) and its metabolites are excreted primarily by the kidneys, caution should be observed in administering the drug to children with significantly impaired renal function.

Sufficient data on safety and efficacy of Cylert administration for periods beyond two years duration in children with minimal brain dysfunction are not yet available. Although a definite causal relationship has not been established, some temporary suppression of predicted growth pattern(i.e., weight and/or height) has been reported with the long-term use of stimulants in children. Therefore, patients requiring long-term therapy should be carefully monitored.

Drug Interactions: Interactions between Cylert and other drugs have not been studied in humans. As with most other drugs, concurrent administration with other agents, especially drugs with central nervous system activity, should be carefully monitored.

Usage in Pregnancy: Safety for use in pregnancy has not been established. Standard studies of fertility, teratology and reproduction were conducted in rats and rabbits. Daily oral doses of pemoline of 18.75 and 37.5 mg/kg beginning at conception produced no abnormalities in the fetuses and did not affect viability at birth. Further studies using similar dose levels with drug administration beginning 14 days before conception demonstrated an increased incidence of stillbirths in these animals.

Drug Dependence: Studies of the drug abuse potential of Cylert (pemoline) in primates have not demonstrated a potential for self-administration. However, the pharmacologic similarities between Cylert and other CNS stimulants with known abuse liability suggest that drug dependence of the stimulant type might occur. There have been isolated reports of transient psychotic symptoms in adults following long-term misuse of pemoline taken orally in excessive quantities. Therefore, caution should be observed in emotionally unstable patients considered to have a psychological potential for drug dependence.

Precautions: Delayed hypersensitivity reactions involving the liver have been reported in 1-2% of the patients receiving Cylert usually after several months of therapy. No clinical symptomatology has been observed, but mild to moderate increases in transaminase (SGOT and SGPT) levels have occurred in these cases. These effects appear to be completely reversible when drug treatment is discontinued. Transaminase levels should be determined periodically during therapy with Cylert to detect any such reactions.

Adverse Reactions: The most frequently reported adverse reaction with Cylert is insomnia. Insomnia has been observed prior to optimum therapeutic response and in the majority of cases was transient in nature or responded to dosage reduction. Anorexia with weight loss during the first few weeks of therapy has also been reported. With continuing therapy, a return to a normal weight curve usually occurred within three to six months. Other adverse reactions reported include stomachache, skin rash, irritability, mild depression, nausea, dizziness, headache, drowsiness, and hallucinations. Mild adverse reactions appearing early in treatment often remit with continuing therapy. If adverse reactions are of a significant or protracted nature, dosage reduction or discontinuation should be considered.

Dosage and Administration: Cylert (pemoline) is administered as a single oral dose each morning. The recommended starting dose is 37.5 mg per day. This daily dosage should be gradually increased at one week intervals using increments of 18.75 mg until the desired clinical response is obtained. The mean daily effective dose ranges from 56.25 to 75 mg per day. The maximum recommended daily dose of pemoline is 112.5 mg.

Clinical improvement with Cylert is gradual. Using the recommended schedule of dosage titration, significant benefit may not be evident until the third or fourth week of drug administration. Drug administration should be interrupted occasionally to determine if behavioral symptoms sufficient to require continuing therapy recur.

Overdosage: Cylert overdosage has been reported to produce symptoms of tachycardia, hallucinations, agitation, or restlessness. The treatment of acute massive overdosage with pemoline is essentially the same as that for overdosage with any drug having CNS stimulatory effects. Management is largely symptomatic and may include induction of emesis, gastric lavage or other measures as appropriate.

How Supplied: Cylert (pemoline) is supplied as monogrammed, grooved tablets in three dosage strengths:

18.75 mg. tablets (yellow-colored) in bottles of 100 (**NDC** 0074-6025-13)

37.5 mg. tablets (orange-colored) in bottles of 100 (**NDC** 0074-6057-13)

75 mg. tablets (tan-colored) in bottles of 100 (**NDC** 0074-6073-13)

ABBOTT

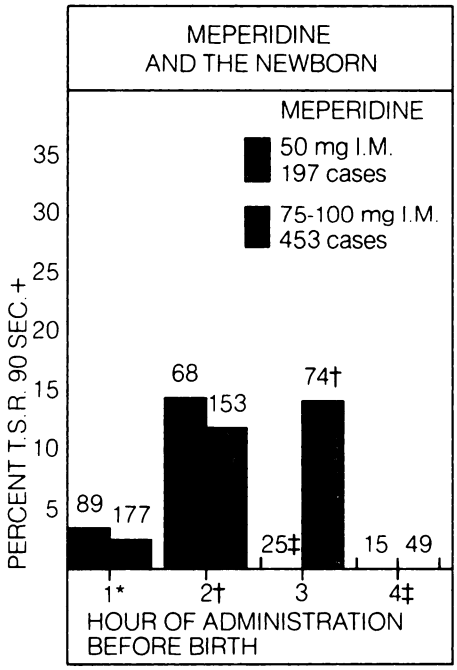
508097

Whenever you suspect
neonatal narcotic depression
due to maternal analgesia

NARCAN® NEONATAL
(naloxone HCl)

CAN HELP ENSURE A MORE RESPONSIVE BEGINNING

While it's widely known that narcotics given during labor can cause overt depression in the newborn, recent more sensitive techniques have shown subtle respiratory and neurobehavioral changes[1-3] —changes that, in the past, would have gone undetected or not been recognized as narcotic related.



Correlation between time of meperidine administration and neonatal depression – according to time to sustained respiration (T.S.R.)[4]

* incidence of depression not statistically significant compared to control group

† significantly higher incidence of depression

‡ no apparent effect

without causing depression of its own...

without augmenting non-narcotic depression

NARCAN® NEONATAL (naloxone hydrochloride) reverses narcotic effects—including all degrees of narcotic-induced respiratory depression.

NARCAN® is an Endo registered U.S. trademark U.S. Pat. 3,254,088

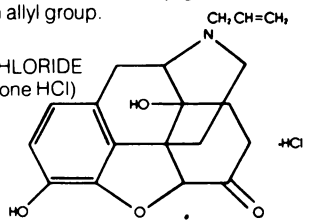
Endo Laboratories, Inc.
Subsidiary of E.I. du Pont de Nemours & Co. (Inc.)
Garden City, New York 11530
DUPONT

Whenever you suspect neonatal narcotic depression due to maternal analgesia

NARCAN®
NARCAN® NEONATAL
(naloxone HCl)

DESCRIPTION NARCAN® (naloxone hydrochloride), a narcotic antagonist, is a synthetic congener of oxymorphone. In structure it differs from oxymorphone in that the methyl group on the nitrogen atom is replaced by an allyl group.

NALOXONE HYDROCHLORIDE
(N-allyl-nor-oxymorphone HCl)



Naloxone hydrochloride occurs as slightly off-white crystals, and is soluble in water, slightly soluble in alcohol and practically insoluble in ether.

NARCAN® (naloxone hydrochloride) Injection is available in two concentrations, 0.02 mg and 0.4 mg of naloxone hydrochloride per ml. Each ml of either strength contains 8.6 mg of sodium chloride; and 2.0 mg of methylparaben and propylparaben as preservatives in a ratio of 9 to 1. pH is adjusted with hydrochloric acid.

ACTIONS NARCAN® (naloxone hydrochloride) is an essentially pure narcotic antagonist, i.e., it does not possess the "agonistic" or morphine-like properties characteristic of other narcotic antagonists; NARCAN® (naloxone hydrochloride) does not produce respiratory depression, psychotomimetic effects or pupillary constriction. In the absence of narcotics or agonistic effects of other narcotic antagonists it exhibits essentially no pharmacologic activity.

In the presence of physical dependence on narcotics NARCAN® (naloxone hydrochloride) will produce withdrawal symptoms; it has not been shown to produce tolerance nor to cause physical or psychological dependence.

When NARCAN® (naloxone hydrochloride) is administered intravenously the onset of action is generally apparent within two minutes; the onset of action is only slightly less rapid when it is administered subcutaneously or intramuscularly. The duration of action is dependent upon the dose and route of administration of NARCAN® (naloxone hydrochloride). Intramuscular administration produces a more prolonged effect than intravenous administration. The requirement for repeat doses of NARCAN® (naloxone hydrochloride), however, will also be dependent upon the amount, type and route of administration of the narcotic being antagonized.

INDICATIONS NARCAN® (naloxone hydrochloride) is indicated for the complete or partial reversal of narcotic depression, including respiratory depression, induced by natural and synthetic narcotics, propoxyphene and the narcotic-antagonist analgesic pentazocine. NARCAN® (naloxone hydrochloride) is also indicated for the diagnosis of suspected acute opiate overdosage.

CONTRAINDICATIONS NARCAN® (naloxone hydrochloride) is contraindicated in patients known to be hypersensitive to it.

WARNINGS NARCAN® (naloxone hydrochloride) should be administered cautiously to persons including newborns of mothers who are known or suspected to be physically dependent on opioids. In such cases an abrupt and complete reversal of narcotic effects may precipitate an acute abstinence syndrome.

The patient who has satisfactorily responded to NARCAN® (naloxone hydrochloride) should be kept under continued surveillance and repeated doses of NARCAN® (naloxone hydrochloride) should be administered, as necessary, since the duration of action of some narcotics may exceed that of NARCAN® (naloxone hydrochloride).

NARCAN® (naloxone hydrochloride) is not effective against respiratory depression due to non-opioid drugs.

Usage in Pregnancy Safe use of NARCAN® (naloxone hydrochloride) during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or other embryotoxic effects (See ANIMAL PHARMACOLOGY AND TOXICOLOGY). However, NARCAN® (naloxone hydrochloride) should be administered to pregnant patients only when, in the judgment of the physician, the potential benefits outweigh the possible hazards.

PRECAUTIONS In addition to NARCAN® (naloxone hydrochloride), other resuscitative measures such as maintenance of a free airway, artificial ventilation, cardiac massage, and vasopressor agents should be available and employed when necessary to counteract acute narcotic poisoning.

In an isolated report two patients with pre-existing ventricular irritability requiring lidocaine, and either isoproterenol or epinephrine for hypotension following cardiopulmonary bypass procedures, developed ventricular tachycardia or fibrillation when given NARCAN® (naloxone hydrochloride) I.V. at 9 and 14 hours, respectively, postoperatively for persistent unresponsiveness. Although a direct cause and effect relationship has not been established, NARCAN® (naloxone hydrochloride) should be used with caution in patients with cardiac irritability.

ADVERSE REACTIONS In rare instances nausea and vomiting have been reported in postoperative patients receiving NARCAN® (naloxone hydrochloride) in doses higher than that recommended; a cause and effect relationship has not been established.

DOSAGE AND ADMINISTRATION NARCAN® (naloxone hydrochloride) may be administered intravenously, intramuscularly, or subcutaneously. The most rapid onset of action is achieved by intravenous administration and it is recommended in emergency situations.

Since the duration of action of some narcotics may exceed that of NARCAN® (naloxone hydrochloride) the patient should be kept under continued surveillance and repeated doses of NARCAN® (naloxone hydrochloride) should be administered, as necessary.

USAGE IN ADULTS Narcotic Overdose—Known or Suspected The usual initial adult dose is 0.4 mg (1 ml) NARCAN® (naloxone hydrochloride) administered I.V., I.M. or S.C. If the desired degree of counteraction and improvement in respiratory function is not obtained immediately following I.V. administration, it may be repeated intravenously at 2 to 3 minute intervals. Failure to obtain significant improvement after 2 or 3 doses suggests that the condition may be due partly or completely to other disease processes or non-opioid drugs.

Post Operative Narcotic Depression For the partial reversal of narcotic depression following the use of narcotics during surgery, smaller doses of NARCAN® (naloxone hydrochloride)—are usually sufficient. The dose of NARCAN® (naloxone hydrochloride) should be titrated according to the patient's response. Excessive dosage of NARCAN® (naloxone hydrochloride) may result in significant reversal of analgesia and increase in blood pressure. Similarly, too rapid reversal may induce nausea, vomiting, sweating or tachycardia.

For the initial reversal of respiratory depression, NARCAN® (naloxone hydrochloride) should be injected in increments of 0.1 to 0.2 mg intravenously at two to three minute intervals to the desired degree of reversal i.e., adequate ventilation and alertness without significant pain or discomfort.

Repeat doses of NARCAN® (naloxone hydrochloride) may be required within one to two hour intervals depending upon the amount, type (i.e., short or long acting) and time interval since last administration of narcotic. Supplemental intramuscular doses have been shown to produce a longer lasting effect.

USAGE IN CHILDREN Narcotic Overdose—Known or Suspected The usual initial child dose is 0.01 mg/kg body weight given I.V., I.M. or S.C. This dose may be repeated in accordance with the adult administration guideline. If necessary, NARCAN® (naloxone hydrochloride) can be diluted with sterile water for injection.

USAGE IN NEONATES Narcotic-induced depression The usual initial dose is 0.01 mg/kg body weight administered I.V., I.M. or S.C. This dose may be repeated in accordance with adult administration guidelines.

HOW SUPPLIED 0.4 mg/ml of NARCAN® (naloxone hydrochloride) for intravenous, intramuscular and subcutaneous administration.

Available in 10 ml vials; and 1 ml ampuls in boxes of 10 and 100.

0.02 mg/ml of NARCAN® (naloxone hydrochloride) NEONATAL INJECTION for intravenous, intramuscular and subcutaneous administration.

Available in 2 ml ampuls in boxes of 10 and 100 ampuls.

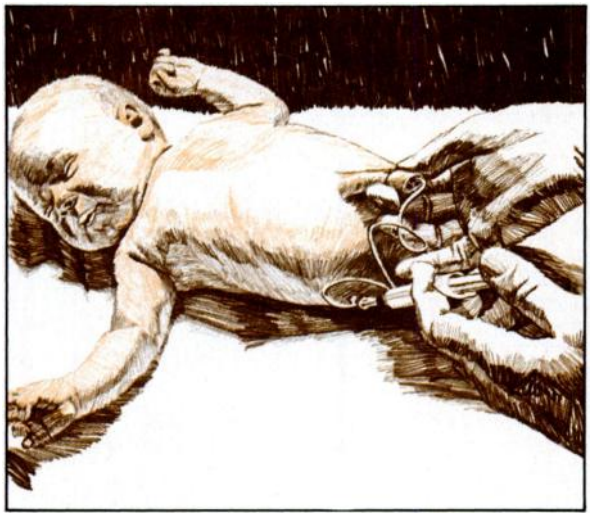
ANIMAL PHARMACOLOGY AND TOXICOLOGY In the mouse and rat the intravenous LD_{50} is 150 ±5 mg/kg and 109 ±4 mg/kg respectively. In acute subcutaneous toxicity studies in newborn rats the LD_{50} (95% CL) is 260 (228-296) mg/kg. Subcutaneous injection of 100 mg/kg/day in rats for 3 weeks produced only transient salivation and partial ptosis following injections; no toxic effects were seen at 10 mg/kg/day for 3 weeks.

Reproductive studies including fertility, general reproductive performance, embryotoxicity, teratogenicity, and lactation did not show any abnormality in mice and rats at 10 mg/kg/day.

Endo Laboratories, Inc.
Subsidiary of E.I. du Pont de Nemours & Co. (Inc.)
Garden City, N.Y. 11530

DUPONT

EDO-3080



You'll find that NARCAN® NEONATAL (naloxone hydrochloride) acts rapidly —generally within two minutes following I.V. administration, and only slightly longer with I.M. or subcutaneous use. Duration of action depends upon dose and route of administration—I.M. produces a more prolonged effect than I.V. The usual dose is 0.01 mg/kg body weight.

Because NARCAN® NEONATAL has no narcotic-like activity, you can repeat it I.V. at 2 to 3 minute intervals if the initial dose doesn't give the desired degree of narcotic counteraction and improvement in respiratory function.

Following satisfactory response to NARCAN® NEONATAL, the infant should be observed carefully and given repeat doses if necessary, since the duration of action of some narcotics may exceed that of NARCAN® NEONATAL.

NARCAN® NEONATAL should be administered cautiously to an infant whose mother is known or suspected to be physically dependent on narcotics. In such cases an abrupt and complete reversal of narcotic effects may precipitate acute withdrawal symptoms.

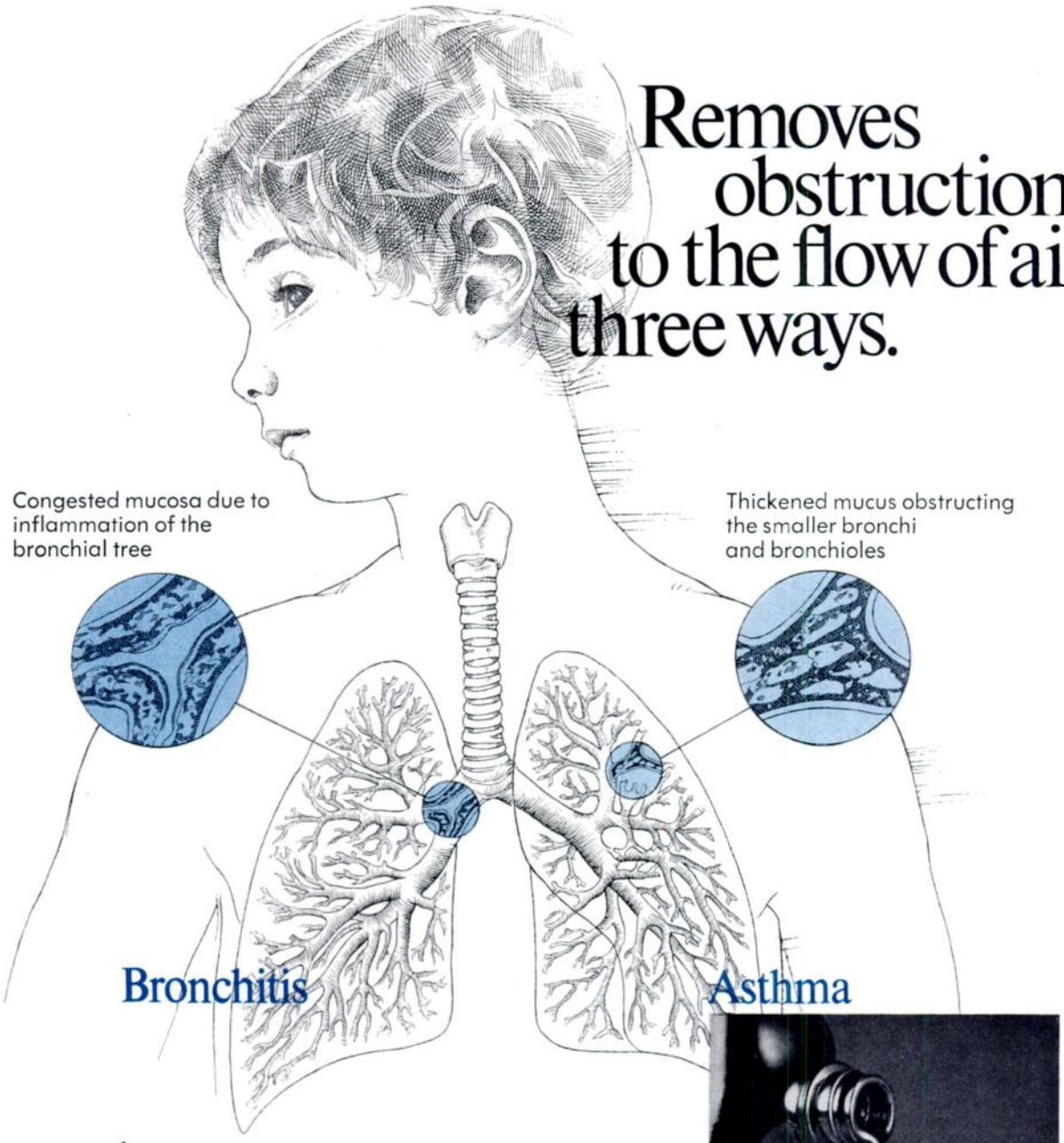
Please see next page for complete prescribing information.

References
1. Brackbill Y. *et al: Anesthesiology 40:* 116-120. Feb 1974. **2.** Brackbill Y. *et al: Am J Obstet Gynecol 40:* 377-384. Feb 1. 1974. **3.** Koch G. Wendel H. *Acta Obstet Gynecol Scand 47:* 27-37. 1968. **4.** Shnider SM. Moya F. *Am J Obstet Gynecol 89:* 1009-1015. Aug 15. 1964.

narcotic antagonist

NARCAN® NEONATAL
(naloxone HCl)

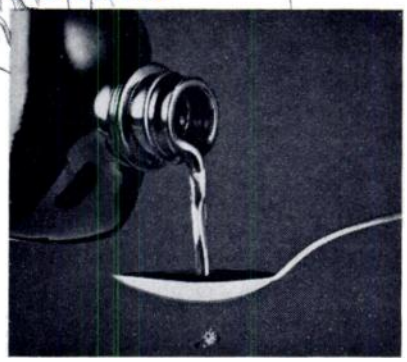
Removes obstruction to the flow of air three ways.



1 Dilates air passages
ephedrine and theophylline relax bronchospasm and ephedrine decongests bronchial mucosa to open airways and keep them open

2 Provides expectorant action
glyceryl guaiacolate helps liquefy viscid mucus to permit the child to expel it

3 Decreases anxieties
phenobarbital (4 mg.) (Warning: may be habit-forming) provides mild calming action to help control anxiety



Bronkolixir®

dependable liquid formulation for asthma/bronchitis

Each 5 ml teaspoonful contains ephedrine sulfate 12 mg; glyceryl guaiacolate 50 mg; theophylline 15 mg; phenobarbital 4 mg (warning: may be habit-forming).
Precautions: Sympathomimetic side effects are minimal, and there are none of the problems associated with steroid therapy. However, frequent and prolonged use may cause nervousness, sleeplessness, or restlessness.

Bronkolixir should be used with caution in the presence of heart disease, hypertension, diabetes or hyperthyroidism. Drowsiness may occur. Ephedrine may cause urinary retention, especially in the presence of partial obstruction, as in prostatism.
Usual Dosage: Children over 6, 1 tsp. q.i.d. Under 6, as directed by physician. Adults, 2 tsp. three to four times daily, depending on individual requirements. Dosage should be adjusted to severity of the condition and response of the individual patient.
Supplied: Bottles of 16 oz.

BREON **BREON LABORATORIES INC.**
90 Park Avenue
New York, New York 10016

AMERICAN ACADEMY OF PEDIATRICS

Breathing Exercises for Asthmatic Children

A physician or therapist must show the asthmatic child the correct breathing technique, but he cannot be present for the child's daily exercises. With the aid of this booklet, which was written to help asthmatic children institute and maintain correct breathing patterns, the child can practice the exercises by himself. The booklet is well illustrated, and the text is printed in big, bold letters for easy reading by young children. There is a chart on which the child can record his exercises to encourage him to use the booklet daily.

Prepared by the Section on Allergy of the American Academy of Pediatrics.
Prices: $1.00 each; six or more, 30¢ each.

AMERICAN ACADEMY OF PEDIATRICS
P. O. Box 1034
Evanston, Illinois 60204

Catching impetigo is easy

Neosporin Ointment, used as an adjuvant to appropriate systemic therapy, can help you control impetigo before other children catch it from your young patient. Neosporin Ointment provides topical antibiotic action against susceptible organisms, notably *Staphylococcus* and *Streptococcus*—broad and reliable action from antibiotics seldom used systemically.

Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and 1/32 oz. (approx.) foil packets.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical aftercare, and pyogenic dermatoses.

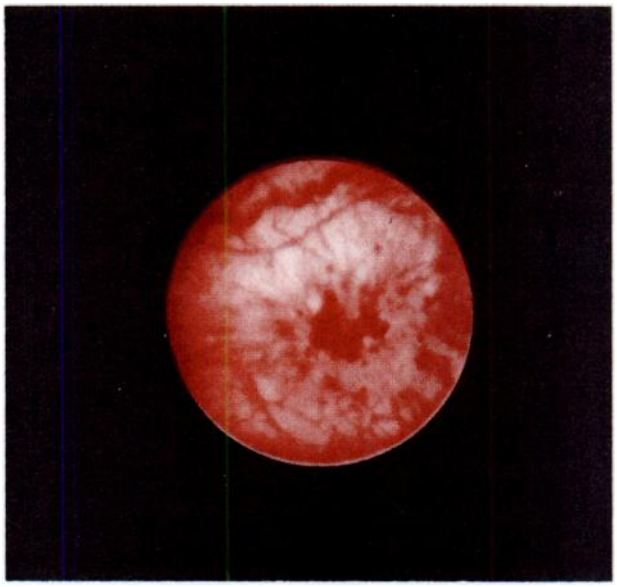
Contraindications: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

Wellcome

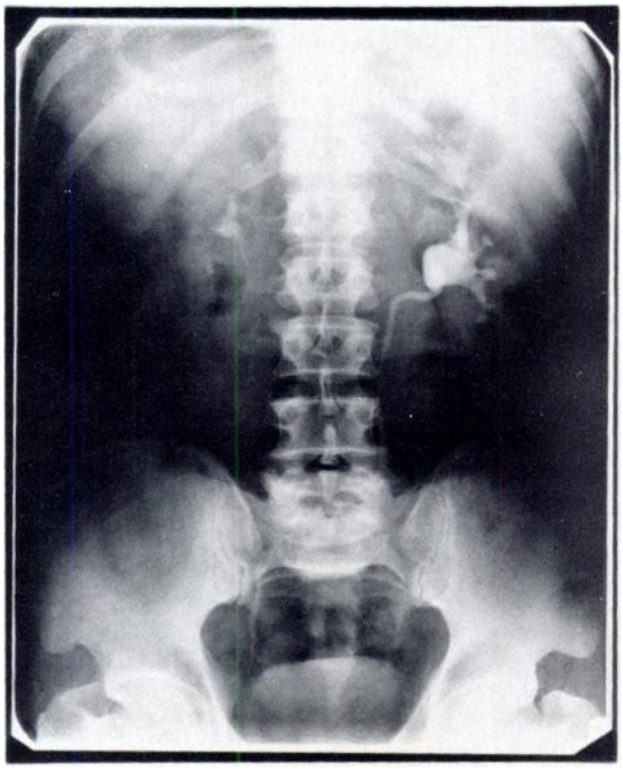
Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709



Cystoscopic view of bladder of preschool child with cystitis.

Urinary tract infection inadequately treated at age 4...

may mean pyelonephritis at 24.



Pyelogram showing unilateral (right) pyelonephritic changes in young adult.

The choice of therapy

Urinary tract infection originating in childhood may be responsible for progressive disease and pyelonephritis. Once a girl has bacteriuria, she is apparently at high risk years later with marriage and pregnancy. Early detection, treatment and careful follow-up are required to protect the growing kidney from potential damage. When the diagnosis is unobstructed urinary tract infection, Gantrisin Pediatric Suspension is a good choice of medication. Not only is it effective, but it is also noted for its relative safety. It is economical as well. Appealing flavor makes it readily acceptable by young patients, helping assure their finishing the full course of therapy.

Gantrisin®
acetyl sulfisoxazole/Roche®
Pediatric Suspension

Broad range of efficacy in unobstructed urinary tract infections Gantrisin is effective against the most common susceptible urinary tract pathogens: *E. coli, Klebsiella-Aerobacter, Staph. aureus, Proteus mirabilis* and, less frequently, *Proteus vulgaris*. Action is prompt, therapeutic urine/blood levels are reached within two to three hours of ingestion.

Established safety Gantrisin is rapidly absorbed and excreted. Its high solubility minimizes the threat of crystalluria and possible renal damage. While side effects are few, during any sulfonamide therapy adequate fluid intake should be maintained, and urinalysis with careful microscopic examination should be performed frequently.

Economical Few antibacterials are as inexpensive as Gantrisin. The suspension costs only about 12¢ per teaspoonful.

10-14 days' therapy While symptoms may disappear in 2 or 3 days, the full course may be necessary for adequate therapy.

Good-tasting flavors The rich raspberry flavor of the Pediatric Suspension and the chocolate flavor of the Syrup are readily acceptable to children.

Usual pediatric dosage (0.5 Gm/5-ml teasp.)	
stat	q.4 h.
1¼ teasp./20 lbs	½ teasp./20 lbs

Please consult complete product information, a summary of which follows:

Indications: Nonobstructed urinary tract infections (mainly cystitis, pyelitis, pyelonephritis) due to susceptible organisms. **IMPORTANT NOTE: *In vitro* sensitivity tests not always reliable; must be coordinated with bacteriological and clinical response. Add aminobenzoic acid to follow-up culture media. Increasing frequency of resistant organisms limits usefulness of antibacterial agents, especially in chronic and recurrent urinary infections.** Maximum safe total sulfonamide blood levels, 20 mg/100 ml; measure levels as variations may occur.

Contraindications: Hypersensitivity to sulfonamides; infants less than 2 months of age; pregnancy at term and during the nursing period.

Warnings: Safety in pregnancy not established. Do not use for group A beta-hemolytic streptococcal infections, as sequelae (rheumatic fever, glomerulonephritis) are not prevented. Deaths reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. CBC and urinalysis with careful microscopic examination should be performed frequently.

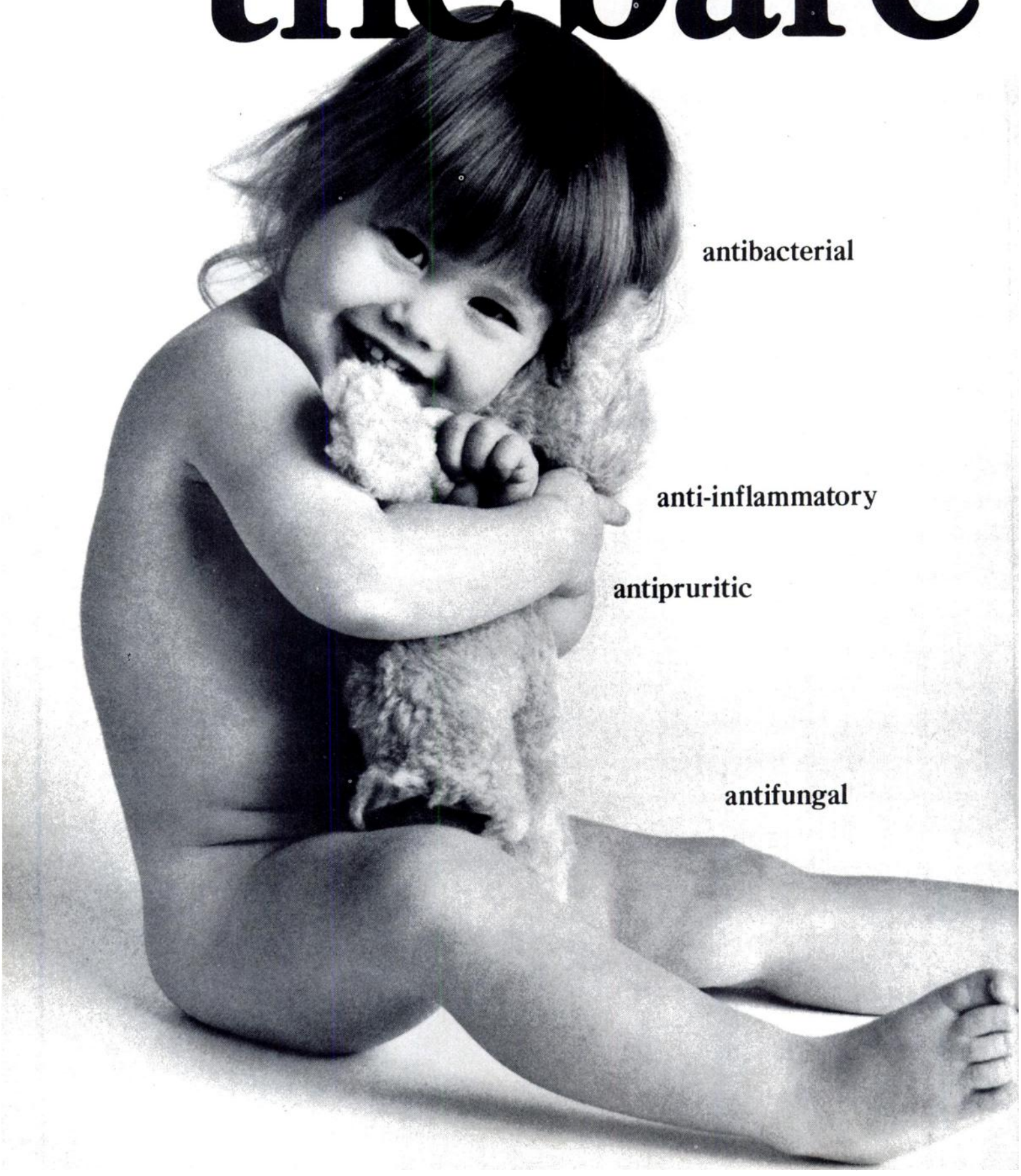
Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy or bronchial asthma. Hemolysis, frequently dose-related, may occur in glucose-6-phosphate dehydrogenase-deficient patients. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *Allergic reactions:* Erythema multiforme (Stevens-Johnson syndrome), generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *Gastrointestinal reactions:* Nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; *Miscellaneous reactions:* Drug fever, chills and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L.E. phenomenon have occurred. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Supplied: Pediatric Suspension and Syrup containing the equivalent of 0.5 Gm sulfisoxazole per teasp.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

the bare



antibacterial

anti-inflammatory

antipruritic

antifungal

facts...

The condition is pediatric – but the problem it poses is often full-sized.

For even a child needs more than an ordinary topical steroid to clear a dermatitis infected with fungi or bacteria.

Vioform-Hydrocortisone combines the antibacterial, antifungal actions of Vioform with the anti-inflammatory and antipruritic actions of hydrocortisone – provides the kind of comprehensive therapy many common dermatoses* require.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. *Lotion,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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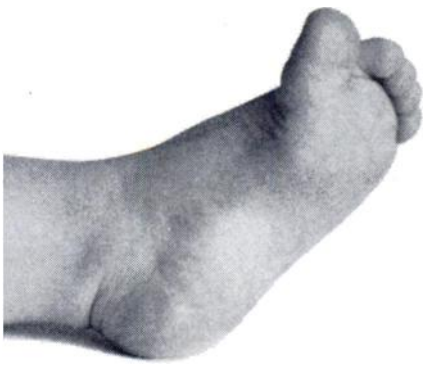
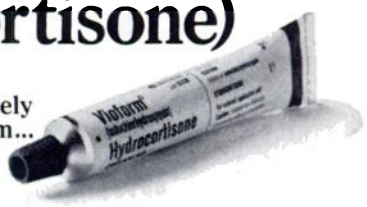


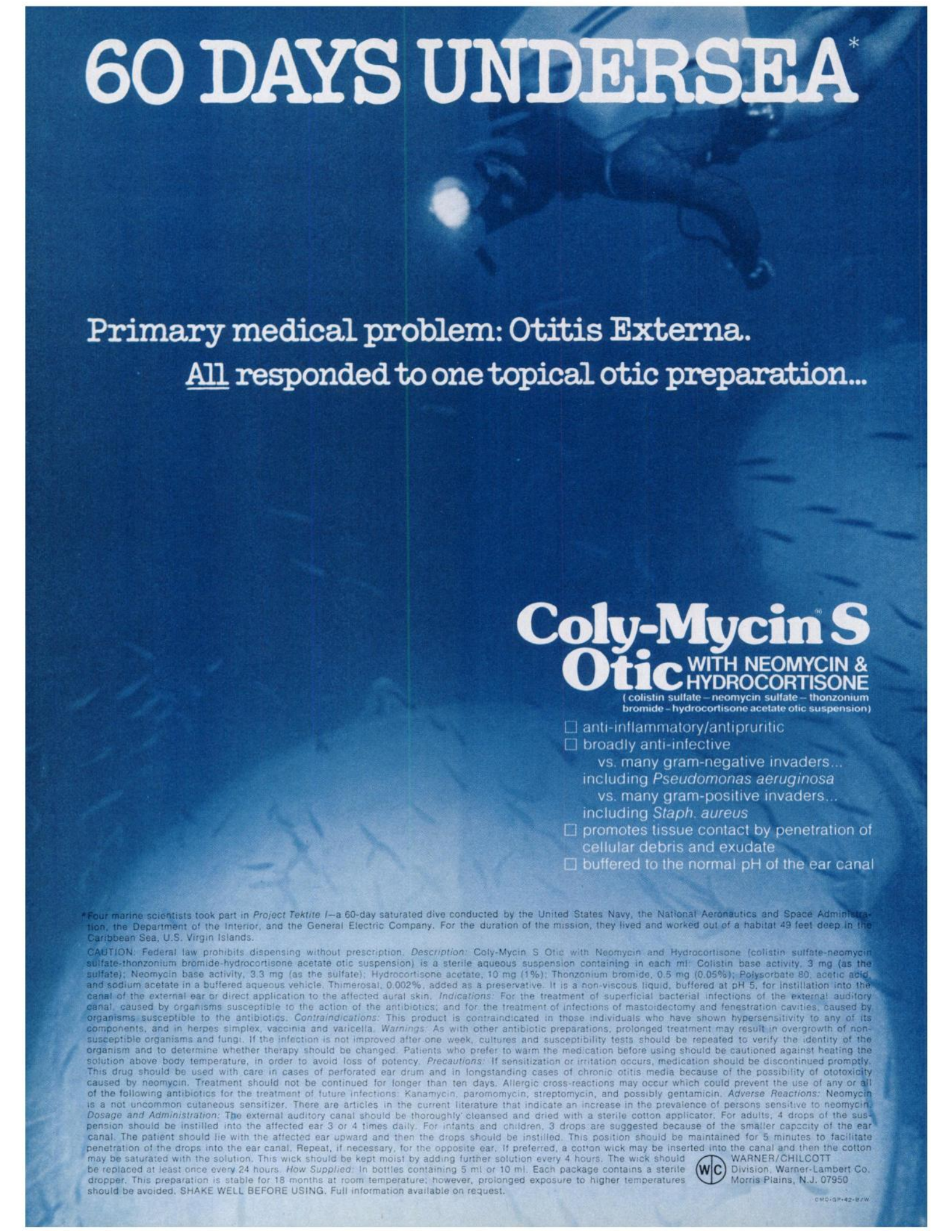
Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

Another fact... the most widely prescribed form... 20 Gm Cream



CIBA

60 DAYS UNDERSEA*



Primary medical problem: Otitis Externa.
All responded to one topical otic preparation...

Coly-Mycin® S Otic

WITH NEOMYCIN & HYDROCORTISONE

(colistin sulfate – neomycin sulfate – thonzonium bromide – hydrocortisone acetate otic suspension)

- ☐ anti-inflammatory/antipruritic
- ☐ broadly anti-infective
  - vs. many gram-negative invaders... including *Pseudomonas aeruginosa*
  - vs. many gram-positive invaders... including *Staph. aureus*
- ☐ promotes tissue contact by penetration of cellular debris and exudate
- ☐ buffered to the normal pH of the ear canal

*Four marine scientists took part in *Project Tektite I*—a 60-day saturated dive conducted by the United States Navy, the National Aeronautics and Space Administration, the Department of the Interior, and the General Electric Company. For the duration of the mission, they lived and worked out of a habitat 49 feet deep in the Caribbean Sea, U.S. Virgin Islands.

CAUTION: Federal law prohibits dispensing without prescription. *Description:* Coly-Mycin S Otic with Neomycin and Hydrocortisone (colistin sulfate-neomycin sulfate-thonzonium bromide-hydrocortisone acetate otic suspension) is a sterile aqueous suspension containing in each ml: Colistin base activity, 3 mg (as the sulfate); Neomycin base activity, 3.3 mg (as the sulfate); Hydrocortisone acetate, 10 mg (1%); Thonzonium bromide, 0.5 mg (0.05%); Polysorbate 80, acetic acid, and sodium acetate in a buffered aqueous vehicle. Thimerosal, 0.002%, added as a preservative. It is a non-viscous liquid, buffered at pH 5, for instillation into the canal of the external ear or direct application to the affected aural skin. *Indications:* For the treatment of superficial bacterial infections of the external auditory canal, caused by organisms susceptible to the action of the antibiotics; and for the treatment of infections of mastoidectomy and fenestration cavities, caused by organisms susceptible to the antibiotics. *Contraindications:* This product is contraindicated in those individuals who have shown hypersensitivity to any of its components, and in herpes simplex, vaccinia and varicella. *Warnings:* As with other antibiotic preparations, prolonged treatment may result in overgrowth of non-susceptible organisms and fungi. If the infection is not improved after one week, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether therapy should be changed. Patients who prefer to warm the medication before using should be cautioned against heating the solution above body temperature, in order to avoid loss of potency. *Precautions:* If sensitization or irritation occurs, medication should be discontinued promptly. This drug should be used with care in cases of perforated ear drum and in longstanding cases of chronic otitis media because of the possibility of ototoxicity caused by neomycin. Treatment should not be continued for longer than ten days. Allergic cross-reactions may occur which could prevent the use of any or all of the following antibiotics for the treatment of future infections: Kanamycin, paromomycin, streptomycin, and possibly gentamicin. *Adverse Reactions:* Neomycin is a not uncommon cutaneous sensitizer. There are articles in the current literature that indicate an increase in the prevalence of persons sensitive to neomycin. *Dosage and Administration:* The external auditory canal should be thoroughly cleansed and dried with a sterile cotton applicator. For adults, 4 drops of the suspension should be instilled into the affected ear 3 or 4 times daily. For infants and children, 3 drops are suggested because of the smaller capacity of the ear canal. The patient should lie with the affected ear upward and then the drops should be instilled. This position should be maintained for 5 minutes to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear. If preferred, a cotton wick may be inserted into the canal and then the cotton may be saturated with the solution. This wick should be kept moist by adding further solution every 4 hours. The wick should be replaced at least once every 24 hours. *How Supplied:* In bottles containing 5 ml or 10 ml. Each package contains a sterile dropper. This preparation is stable for 18 months at room temperature; however, prolonged exposure to higher temperatures should be avoided. SHAKE WELL BEFORE USING. Full information available on request.

WARNER/CHILCOTT
Division, Warner-Lambert Co.
Morris Plains, N.J. 07950

CMO-GP-42-B/W

American Academy of Pediatrics

CONTINUING EDUCATION COURSE

NUMBER 2

CHILD DEVELOPMENT

COSPONSOR

St. Christopher's Hospital for Children

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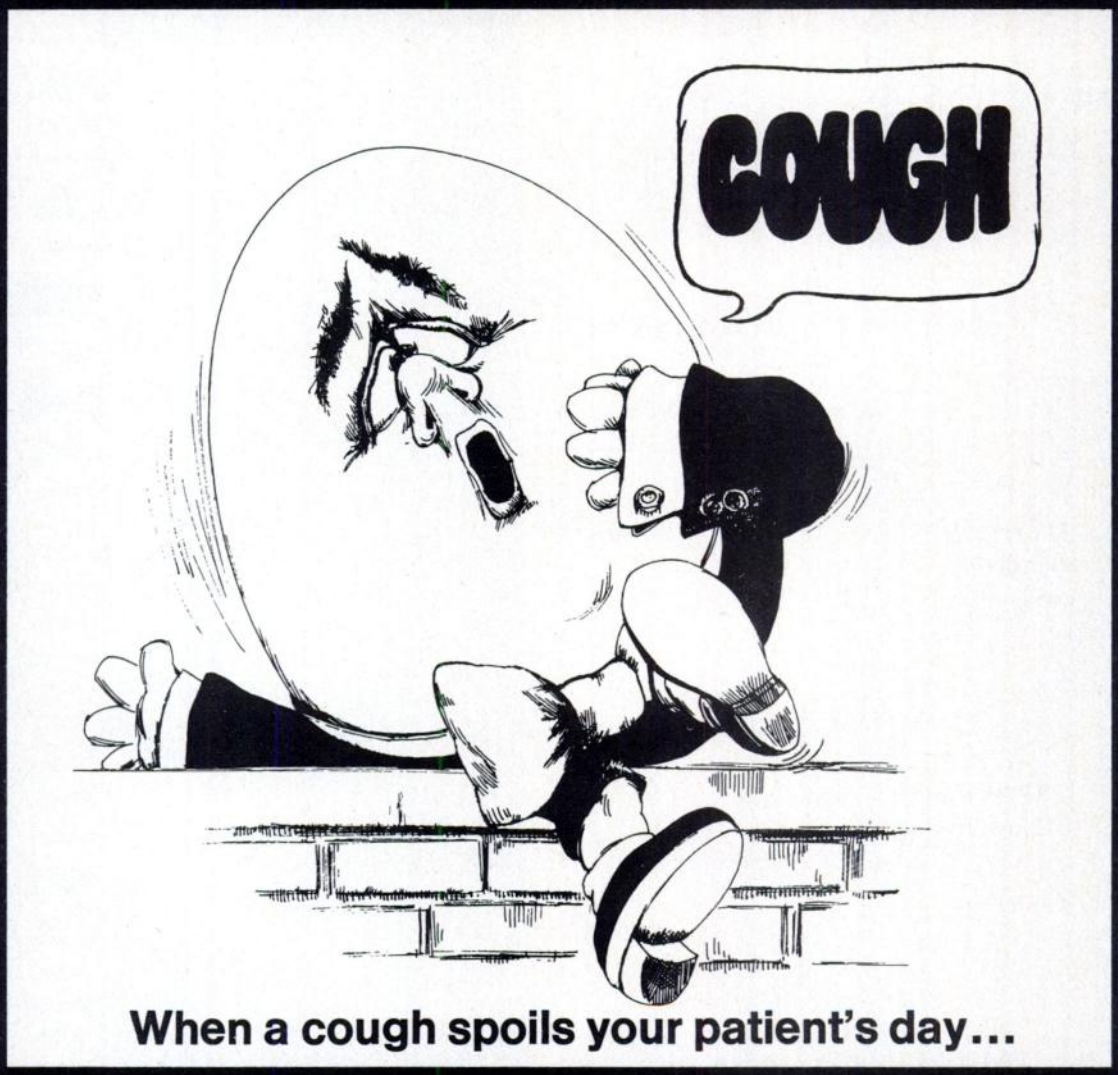
TOPICS TO INCLUDE

Developmental Examinations
Social Developments of Infants and Children
Methods of Changing Behavior of Children and Parents
Language Development and Utilization of Resources for Handicapped Children

Complete details will be mailed to all Fellows. For further information contact:

Gerald E. Hughes, M.D.
DEPARTMENT OF EDUCATIONAL AFFAIRS
P. O. Box 1034
Evanston, Illinois 60204



Triaminic® Expectorant

Each teaspoonful (5 ml.) contains:

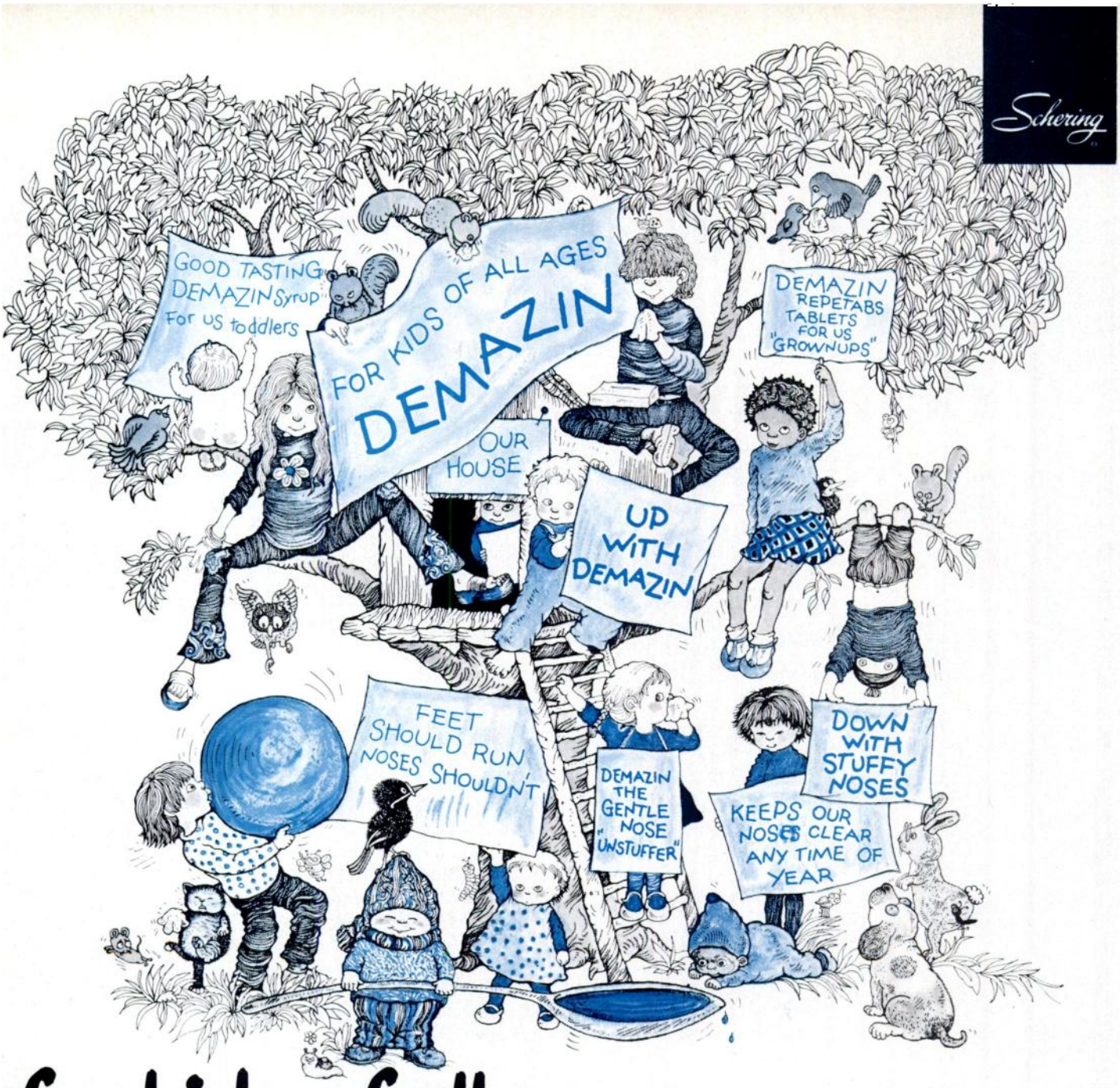
Triaminic, 25 mg. (phenylpropanolamine hydrochloride, 12.5 mg.; pheniramine maleate, 6.25 mg.; pyrilamine maleate, 6.25 mg.); glyceryl guaiacolate, 100 mg.; alcohol, 5%.

Available in 8-oz. Family Size and 4-oz.
No Rx needed—recommend over the phone.

For Children's Unproductive Coughs

Dorsey Laboratories/Division of Sandoz, Inc./Lincoln, Nebraska 68501

DY-EB



for kids of all ages

The decongestant designed for children

DEMAZIN® REPETABS® Tablets

brand of chlorpheniramine maleate 2 mg., U.S.P., and phenylephrine 10 mg. brand of repeat-action tablets

A special form for very young patients–even babies

DEMAZIN® Syrup

brand of chlorpheniramine maleate 1 mg., U.S.P., and phenylephrine hydrochloride 2.5 mg., U.S.P., alcohol (approx.) 7.5% by volume in each 5 ml.

Clinical Considerations:
INDICATIONS DEMAZIN REPETABS **Tablets** and **Syrup** are indicated for the relief of nasal congestion accompanying respiratory allergic conditions, sinusitis or the common cold. The **Syrup** is primarily intended for pediatric respiratory disorders. The **Syrup** is also indicated in the unproductive cough of allergic bronchitis and in bronchial asthma. Its use in edematous nasal obstruction often makes topical nasal instillation unnecessary; thus, it is invaluable in relieving nasal congestion associated with the common cold, hay fever or vasomotor rhinitis and summer colds. In the runny nose frequently seen in the 2 to 6 year-old group who have adenoidal hypertrophy or allergic rhinitis, its use dries up the discharge. DEMAZIN REPETABS **Tablets** and **Syrup** are also suggested for use in skin allergies. In allergic skin conditions, the sympathomimetic agents are a time-honored therapy and their complementary action with antihistamines in urticaria, neurodermatitis, poison ivy, allergic eczema, and contact dermatitis is of value. **PRECAUTIONS** Sympathomimetic drugs such as phenylephrine and phenylephrine hydrochloride should be used with caution in patients with cardiovascular disease, thyrotoxicosis or diabetes. Since drowsiness may occur with chlorpheniramine maleate, caution patients against engaging in mechanical operations requiring alertness, such as driving an automobile, until their response has been determined. **ADVERSE REACTIONS** Slight to moderate drowsiness occurs relatively infrequently with chlorpheniramine maleate. Other possible side effects include restlessness, dry mouth, dizziness, weakness, anorexia, nausea, headache, nervousness, polyuria, heartburn, diplopia, sweating, dysuria, and very rarely dermatitis.
For more complete details, consult package insert or Schering literature available from your Schering Representative or Professional Services Department, Schering Corporation, Kenilworth, New Jersey 07033. 010 OCTOBER 1971

 SLS-039

APLITEST
(tuberculin purified protein derivative)
MULTIPLE PUNCTURE DEVICE

Description Aplitest (tuberculin PPD) is a sterile, single-use, multiple-puncture-type device for use in determining the tuberculin sensitivity status of individuals. The convenient, disposable devices are especially useful in mass tuberculosis screening programs. The product packaging also facilitates the use of Aplitest units for testing of individual patients in office, ward, or clinic settings.

Each Aplitest unit consists of a cylindrical plastic holder bearing four equally spaced stainless steel tines at one end. The tines have been coated by dipping in a solution of tuberculin PPD and dried.

These devices are designed so that the narrow (tine-bearing) end of each unit fits into the hollow, handle portion of the adjacent unit (or into a protective cap) to protect the tines and maintain their sterility.

The purified tuberculin protein fraction is isolated from culture filtrates of human-type strains of *Mycobacterium tuberculosis* by the method of Florence B. Seibert.[1,2] Purified tuberculin protein solution is prepared from a single master lot (No. 975302) to eliminate lot-to-lot variation.

The tuberculin solution which is applied to the tines is buffered with potassium and sodium phosphates and contains approximately 0.5% phenol as a preservative.

Tuberculin PPD is employed as the diagnostic reagent because it has been demonstrated to be more specific than Old Tuberculin.[3]

Aplitest units have been standardized by clinical studies in human subjects to give reactions equivalent to 5 TU* of PPD-S administered intradermally in the Mantoux test. This close correlation can be expected to minimize the incidence of false-positive reactions. However, all multiple-puncture-type devices should be regarded as screening tools and appropriate diagnostic procedures (eg, Mantoux test with tuberculin PPD diluted, Aplisol®) should be employed for retesting doubtful reactors.

Indication Aplitest is indicated to detect tuberculin-sensitive individuals. Aplitest units are also useful in programs to establish priorities for additional testing (ie, chest x-rays) and in epidemiological surveys to identify areas with high levels of infection.

Regular periodic (annual)[4] testing of tuberculin-negative persons is recommended and is especially valuable because the conversion of a reactor from negative to positive is highly indicative of recent tuberculosis infection. Repeated testing of the uninfected individual does not sensitize to tuberculin. In persons with waning sensitivity to homologous or heterologous mycobacterial antigens, however, the stimulus of a tuberculin test may "boost" or increase the size of reaction to a second test, even causing an apparent development of sensitivity in some instances.[3]

*US (International) Tuberculin Units

Precautions A separate, sterile unit must be used for each individual patient and disposed of after use.

As with any biological product, epinephrine should be immediately available in case an anaphylactoid or acute hypersensitivity reaction occurs.

Sensitivity may decrease or disappear temporarily during or immediately following severe febrile illness; measles and other exanthemas; live virus vaccination; sarcoidosis; overwhelming miliary or pulmonary tuberculosis; and the administration of corticosteroids or immunosuppressive drugs. Severe malnutrition may also have a similar effect.

A positive tuberculin reaction does not necessarily signify the presence of active disease. Further diagnostic procedures should be carried out before a diagnosis of tuberculosis is made.

Adverse Reactions In highly sensitive individuals, strongly positive reactions including vesiculation, ulceration, or necrosis may occur at the test site. Cold packs or topical steroid preparations may be employed for symptomatic relief of the associated pain, pruritus, and discomfort.

Minimal bleeding may be experienced at a puncture site. This occurs infrequently and does not affect interpretation of the test.

Dosage and Administration Each Aplitest (tuberculin PPD, multiple puncture device) unit provides for the intradermal administration of one test dose of tuberculin PPD clinically equivalent to 5 TU administered by the Mantoux test.

Method of Application. 1. The preferred site of the test is the flexor surface of the forearm about four inches below the elbow. Other suitable skin sites, such as the dorsal surface of the forearm, may be used. Areas without adequate subcutaneous tissue, such as over a tendon, should be avoided.

2. The skin at the test site should be cleansed with 70% alcohol or other suitable agents, and allowed to dry thoroughly.

3. To expose the four impregnated tines, grasp the device (top one if stacked) and twist to break the perforated label seal. To prevent loss of sterility of the other units in a stack, the top unit must always be removed first and the remaining ones in sequence. Care should be taken to avoid breaking the seals on the remaining units when the end unit is removed.

4. Grasp the patient's forearm firmly to stretch the skin taut at the test site and to prevent any jerking motion of the arm that could cause scratching with the tines.

5. Apply the Aplitest unit firmly and without twisting to the test area for approximately one second. Sufficient pressure should be exerted to assure that all four tines have penetrated the skin of the test area.

6. Dispose of used units in a manner to avoid accidents. Do not re-use.

Interpretation of Response Reading of reactions should be made during the period from 48 to 72 hours after application of Aplitest and should be conducted under good lighting conditions. Induration only should be considered in interpreting the test. Erythema should be disregarded. The diameter of the induration of the greatest response at any of the four puncture points should be determined by visual inspection and palpation. If there is coalescence of reaction, the largest diameter of coalescent induration should be measured and recorded.

Prior to the development of Aplitest for determining sensitivity to tuberculin, the American Thoracic Society[3] recommended that all multiple-puncture, tuberculin-skin-test devices be interpreted as follows. If vesiculation is present, the test may be interpreted as positive. If vesiculation is not present, induration of 2 mm or more is considered as a doubtful reaction and should be confirmed by Mantoux testing. Induration of less than 2 mm and/or erythema of any size is a negative test and there is no need for retesting.

In clinical studies with Aplitest, it has been determined that coalescence of the induration at around two or more puncture sites corresponds to 10 mm or more of induration in the same individual tested by Mantoux at the 5-TU level with PPD-S.† On the basis of this correlation, a reaction may be considered to be "positive" if either vesiculation or coalescence is present. Thus the following criteria of interpretation have been established.

Vesiculation—Positive Reaction. The test should be interpreted as positive and the management of the subject is the same as that for one classified as positive by Mantoux test.

Coalescence of induration from two or more puncture points—Positive Reaction. The test may be interpreted as positive and equivalent to a reaction of 10 mm or more of induration with PPD-S (5 TU) administered by Mantoux test. Management of the subject is the same as for those showing vesiculation at the test site.

2 mm or more of induration without coalescence—Doubtful Reaction. Reactions of this size range reflect sensitivity that can result from infection with either atypical mycobacteria or *M tuberculosis*; hence they are classified as doubtful. A standard Mantoux test should be done on all subjects in this group. Management should be based on the reaction to the Mantoux test as well as other clinical considerations.

Less than 2 mm of induration—Negative Reaction. There is no need for retesting unless the individual is a contact to a case of tuberculosis or there is clinical evidence suggestive of the disease.

Selection of the appropriate criteria for interpretation of response to the tuberculin PPD Aplitest should be made in accordance with the objectives of the specific testing program and with consideration of the history and clinical status of the individuals.[4]

How Supplied NDC 0071-1589-01 (Bio 1589) 25-test package; five stacks of five Aplitest units. NDC 0071-1590-01 (Bio 1590) 25-test package; 25 individually capped Aplitest units in a dispensing package.

Aplitest (tuberculin PPD, multiple puncture device) units should be stored at no warmer than 30 C (86 F).

†Purified Protein Derivative (Seibert). Lot No. 49608, the standard adopted by the World Health Organization in 1952 as International PPD Tuberculin and used to prepare the official US Public Health Service 5-TU solution of tuberculin for skin testing known as PPD-S.

References 1. Seibert FB: *Am Rev Tuberc* **30**: 713, 1934. 2. Seibert FB, and Glenn JT: *Am Rev Tuberc* **44**:9, 1941. 3. Comstock GW et al: The Tuberculin Skin Test, *Am Rev Resp Dis* **104**, No. 5, Nov 1971, pp 769-775 (Supplement to Diagnostic Standards and Classification of Tuberculosis-revision of pp 59-66 of Chap 5, 1969 ed). 4. Report of the Committee on the Control of Infectious Diseases: American Academy of Pediatrics, 1970. **PK**

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit, Michigan 48232
PD-JA-1397-1-B (5-75) Printed in USA

Now there's a better way to plug the holes in tuberculin screening

new APLITEST®

(tuberculin purified protein derivative)
Multiple Puncture Device

APLITEST is standardized...
clinically equivalent to 5 TU of PPD-S administered in the Mantoux test.

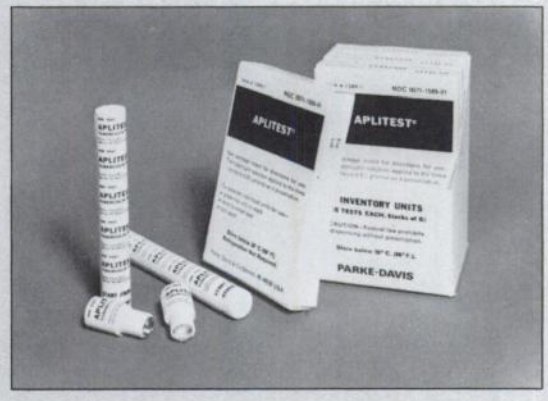
APLITEST uses tuberculin purified protein derivative (PPD) because it is demonstrably more specific than Old Tuberculin.

APLITEST can save time, effort, and money by elimination of much retesting

APLITEST tines are arranged in a special design to
- minimize bleeding
- reduce possibility of tuberculin washout after application

See next page for complete prescribing information.

APLITEST is convenient
- Stacks of 5s take little storage space
- No refrigeration required
- 5-Stacks are easy to handle – ideal for mass screening programs as well as for office use
- Two-year expiration date



- **Packages of 25 singles also available**

PARKE-DAVIS

I would like information on:

- ☐ Aplitest® (tuberculin PPD) Introductory Special Offers
- ☐ Aplitest Measuring Device
- ☐ Aplitest Wall Chart (Typical Test Reactions)

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PD-JA-1397-1-B (5-75)

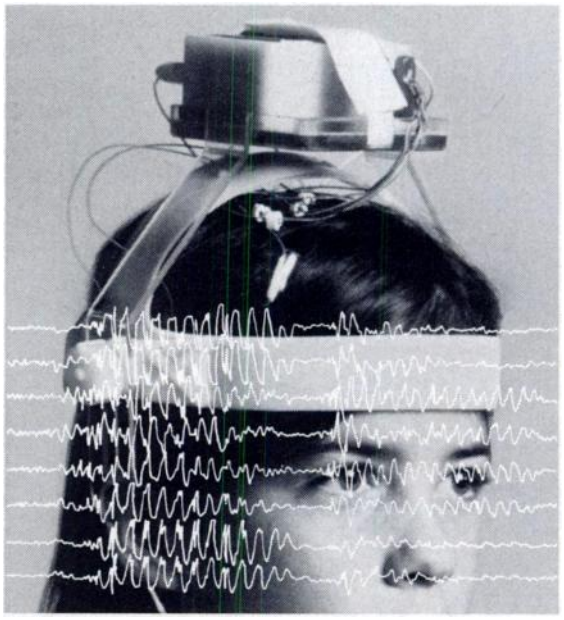
Printed in USA

ROCHE Now available from Roche Laboratories

Clonopin® (clonazepam) IV a new, oral anticonvulsant

The management of many patients with minor motor seizures has always presented a challenge to physicians responsible for their care. Now, ongoing research into the basic benzodiazepine molecule at Roche Laboratories has resulted in the development of Clonopin...a new and specific oral agent with potent anticonvulsant properties.

Clonopin is indicated alone or as an adjunct in the treatment of akinetic, myoclonic and petit mal variant seizures (Lennox-Gastaut syndrome); it may also be useful in petit mal when succinimide therapy has failed. A clinical profile of Clonopin is presented on the following pages.



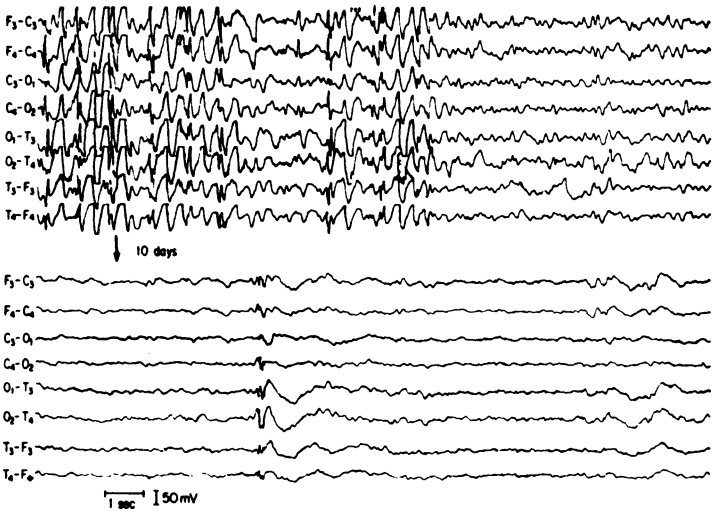
Noninvasive EEG telemetry device, used to monitor patients in studies evaluating Clonopin.

Please see last page of this advertisement for complete product information.

Clonopin®(clonazepam) EEG studies demonstrate specific anticonvulsant effect

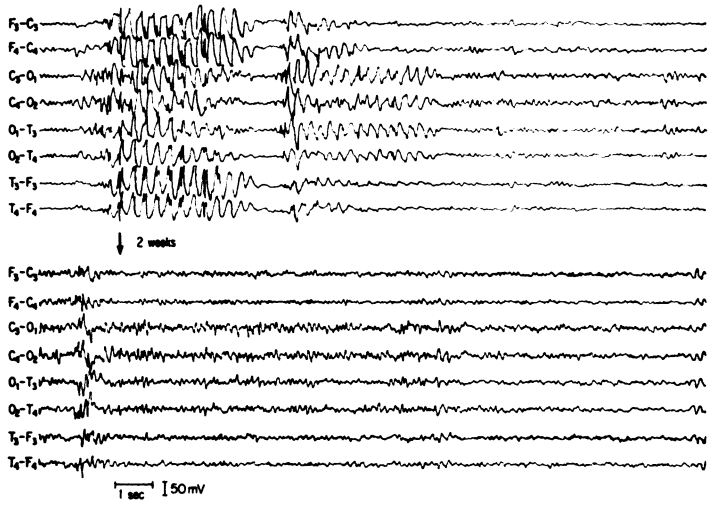
EEG studies were performed to determine the effect of Clonopin on patients suffering from various seizure types. In some cases, patients were continuously monitored for periods as long as 12 hours after administration of Clonopin. This was made possible by the use of a new telemetry technique which allows the patient freedom of activity. Typical results are illustrated at the right.

In minor motor seizures, Clonopin (clonazepam) decreased frequency, amplitude, duration and spread of discharge*



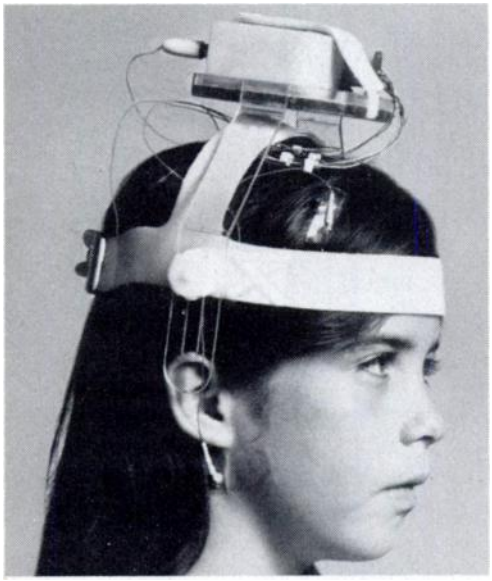
EEG of retarded 18-month-old boy having frequent massive myoclonic jerks *(top)*. After 10 days on clonazepam, patient was having only 0-1 seizure per day *(bottom)*. Three months later patient was still much improved, although seizures had increased to two or three per day.

In petit mal, Clonopin (clonazepam) suppressed spike and wave activity*



EEG of 10-year-old girl with petit mal, 500 attacks per day *(top)*. Same patient after two weeks on clonazepam is free of seizures *(bottom)*. Leads in this and figure above are as follows: F_3 left frontal, F_4 right frontal, C_3 left central, C_4 right central, O_1 left occipital, O_2 right occipital, T_3 left mid-temporal, T_4 right mid-temporal.

*Hanson RA, Menkes JH: *Dev Med Child Neurol* 14: 3-14, Feb 1972



Clonopin® (clonazepam)

a new, oral anticonvulsant from Roche Laboratories

Please see last page of this advertisement for complete product information.

Clonopin®(clonazepam) clinical studies show patient improvement

The effect of Clonopin alone or adjunctively on seizure frequency and severity has been evaluated clinically in an ongoing multiclinic study. Clonopin was shown to significantly reduce both seizure frequency and severity in patients with akinetic, myoclonic, petit mal variant (Lennox-Gastaut) and absence seizures. (See charts on the right.)

In some studies, up to 30% of the patients have shown a loss of anticonvulsant effect within three months of initiating therapy. In certain of these cases, efficacy was successfully reestablished by dosage adjustment.

During the clinical evaluation of Clonopin, the side effects encountered were generally dose-related and were often extensions of pharmacologic effects, such as drowsiness and ataxia. Abnormal behavioral effects were found to occur more often in patients with extensive preexisting brain damage and/or mental retardation. Some adverse reactions could be controlled by dosage adjustment; others required the termination of therapy with Clonopin.

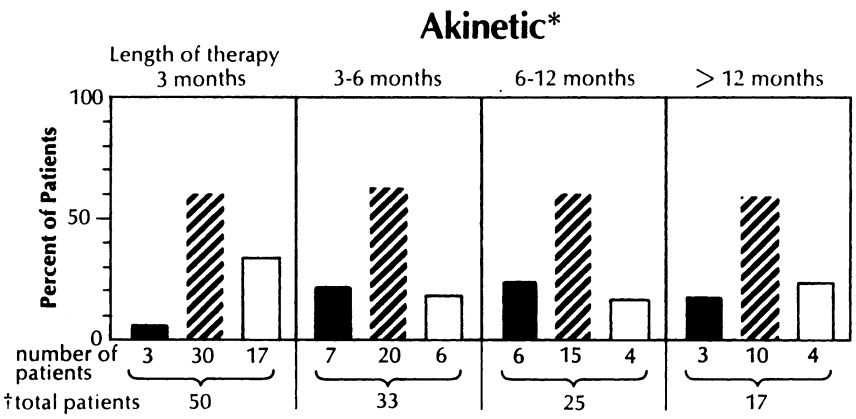
How to institute therapy

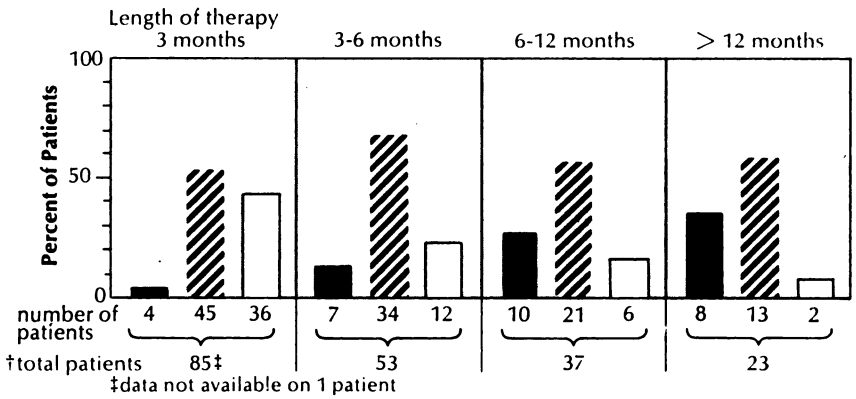
Clonopin (clonazepam) is usually effective in small doses. The initial dose for infants and children (up to 10 years of age or 30 kg of body weight) should be between 0.01 and 0.03 mg/kg/day, not to exceed 0.05 mg/kg/day, given in two or three divided doses. Dosage should be increased by no more than 0.25 to 0.5 mg every three days until a daily maintenance dose of 0.1 to 0.2 mg/kg has been reached, unless seizure control has been achieved at a lower daily dose or side effects preclude increase.

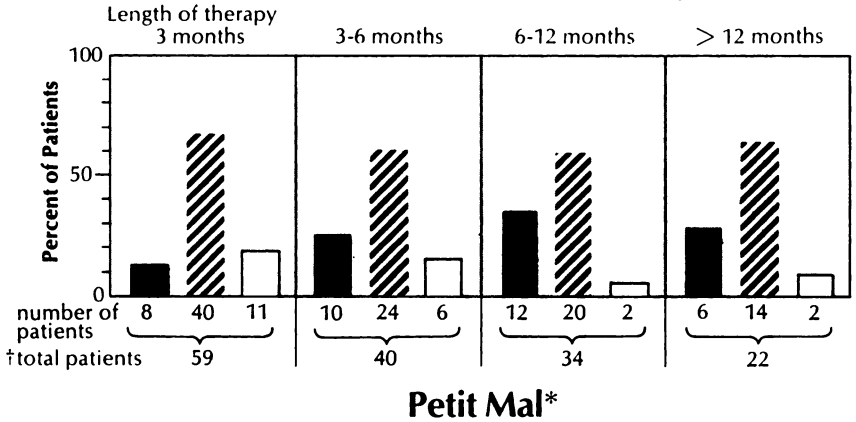
The initial dose for adults should not exceed 1.5 mg/day divided into three doses, increased in increments of 0.5 to 1 mg every three days until seizures are adequately controlled. *Maintenance dosage must be individualized for each patient depending upon response.* Maximum recommended daily dose is 20 mg.

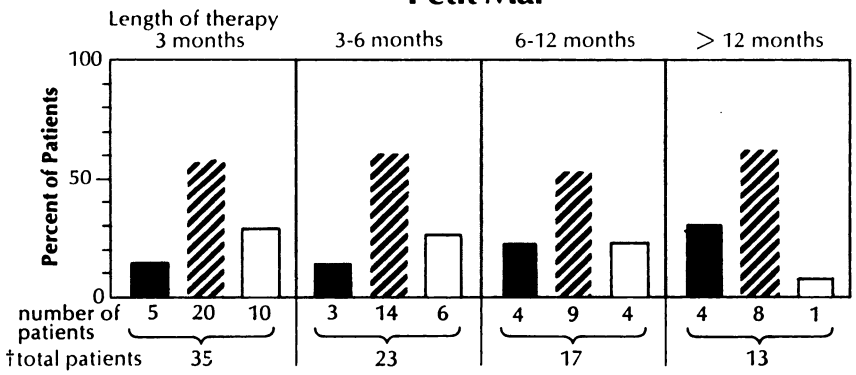
Clonopin is supplied as scored tablets in three strengths: 0.5 mg, 1 mg, 2 mg.

Effect of Clonopin (clonazepam) on seizure frequency









*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

†Patients dropped from the study for a variety of reasons as well as those treated for less than 12 months account for the decrease in total patient population.

■ Seizures 100% controlled
▨ Seizures better than 50% reduced in frequency
□ Seizures uncontrolled

A new, oral anticonvulsant

Clonopin® (clonazepam)

Complete Product Information:

Description: Chemically, clonazepam is 5-(2-chlorophenyl)-1,3-dihydro-7-nitro-2H-1, 4-benzodiazepin-2-one. It is a light yellow crystalline powder. It has a molecular weight of 315.7.

Actions: In laboratory animals, Clonopin exhibits several pharmacologic properties which are characteristic of the benzodiazepine class of drugs. Convulsions produced in rodents by pentylenetetrazol or electrical stimulation are antagonized, as are convulsions produced by photic stimulation in susceptible baboons. A taming effect in aggressive primates, muscle weakness and hypnosis are likewise produced by Clonopin. In humans it is capable of suppressing the spike and wave discharge in absence seizures (petit mal) and decreasing the frequency, amplitude, duration and spread of discharge in minor motor seizures.

Single oral dose administration of Clonopin to humans gave maximum blood levels of drug, in most cases, within one to two hours. The half-life of the parent compound varied from approximately 18 to 50 hours, and the major route of excretion was in the urine. In humans, five metabolites have been identified. In general, the biotransformation of clonazepam followed two pathways: oxidative hydroxylation at the C-3 position and reduction of the 7-nitro function to form 7-amino and/or 7-acetyl-amino derivatives.

Indications: Clonopin is useful alone or as an adjunct in the treatment of the Lennox-Gastaut syndrome (petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (petit mal) who have failed to respond to succinimides, Clonopin may be useful.

In some studies, up to 30% of patients have shown a loss of anticonvulsant activity, often within three months of administration. In some cases, dosage adjustment may re-estaolish efficacy.

Contraindications: Clonopin should not be used in patients with a history of sensitivity to benzodiazepines, nor in patients with clinical or biochemical evidence of significant liver disease. It may be used in patients with open angle glaucoma who are receiving appropriate therapy, but is contraindicated in acute narrow angle glaucoma.

Warnings: Since Clonopin produces CNS depression, patients receiving this drug should be cautioned against engaging in hazardous occupations requiring mental alertness, such as operating machinery or driving a motor vehicle. They should also be warned about the concomitant use of alcohol or other CNS-depressant drugs during Clonopin therapy (see Drug Interactions).

Usage in Pregnancy: The effects of Clonopin 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 diphenylhydantoin 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 methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, e.g., 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 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 mild seizures do not pose some hazards to the developing embryo or fetus.

These considerations should be weighed in treating or counseling epileptic women of childbearing potential.

Use of Clonopin in women of childbearing potential should be considered only when the clinical situation warrants the risk. Mothers receiving Clonopin (clonazepam) should not breast feed their infants.

In a two-generation reproduction study with Clonopin given orally to rats at 10 or 100 mg/kg/day, there was a decrease in the number of pregnancies and a decrease in the number of offspring surviving until weaning. When Clonopin was administered orally to pregnant rabbits at 0.2, 1.0, 5.0 or 10.0 mg/kg/day, a nondose-related incidence of cleft palates, open eyelids, fused sternebrae and limb defects was observed at the 0.2 and 5.0 mg/kg/day levels. Nearly all of the malformations were seen from one dam in each of the affected dosages.

Usage in Children: Because of the possibility that adverse effects on physical or mental development could become apparent only after many years, a benefit-risk consideration of the long-term use of Clonopin is important in pediatric patients.

Physical and Psychological Dependence: Withdrawal symptoms similar in character to those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepine drugs. These symptoms include convulsions, tremor, abdominal and muscle cramps, vomiting and sweating. Addiction-prone individuals, such as drug addicts or alcoholics, should be under careful surveillance when receiving benzodiazepines because of the predisposition of such patients to habituation and dependence.

Precautions: When used in patients in whom several different types of seizure disorders coexist, Clonopin may increase the incidence or precipitate the onset of generalized tonic-clonic seizures (grand mal). This may require the addition of appropriate anticonvulsants or an increase in their dosages.

Periodic blood counts and liver function tests are advisable during long-term therapy with Clonopin.

The abrupt withdrawal of Clonopin, particularly in those patients on long-term, high-dose therapy, may precipitate status epilepticus. Therefore, when discontinuing Clonopin, gradual withdrawal is essential. While Clonopin is being gradually withdrawn, the simultaneous substitution of another anticonvulsant may be indicated. Metabolites of Clonopin are excreted by the kidneys; to avoid their excess accumulation, caution should be exercised in the administration of the drug to patients with impaired renal function.

Clonopin may produce an increase in salivation. This should be considered before giving the drug to patients who have difficulty handling secretions. Because of this and the possibility of respiratory depression, Clonopin should be used with caution in patients with chronic respiratory diseases.

Adverse Reactions: The most frequently occurring side effects of Clonopin are referable to CNS depression. Experience to date has shown that drowsiness has occurred in approximately 50% of patients and ataxia in approximately 30%. In some cases, these may diminish with time; behavior problems have been noted in approximately 25% of patients. Others, listed by system, are:

Neurologic: Abnormal eye movements, aphonia, choreiform movements, coma, diplopia, dysarthria, dysdiadochokinesis, "glassy-eyed" appearance, headache, hemiparesis, hypotonia, nystagmus, respiratory depression, slurred speech, tremor, vertigo.

Psychiatric: Confusion, depression, forgetfulness, hallucinations, hysteria, increased libido, insomnia, psychosis, suicidal attempt (the behavior effects are more likely to occur in patients with a history of psychiatric disturbances).

Respiratory: Chest congestion, rhinorrhea, shortness of breath, hypersecretion in upper respiratory passages.

Cardiovascular: Palpitations.

Dermatologic: Hair loss, hirsutism, skin rash, ankle and facial edema.

Gastrointestinal: Anorexia, coated tongue, constipation, diarrhea, dry mouth, encopresis, gastritis, hepatomegaly, increased appetite, nausea, sore gums.

Genitourinary: Dysuria, enuresis, nocturia, urinary retention.

Musculoskeletal: Muscle weakness, pains.

Miscellaneous: Dehydration, general deterioration, fever, lymphadenopathy, weight loss or gain.

Hematopoietic: Anemia, leukopenia, thrombocytopenia, eosinophilia.

Hepatic: Transient elevations of serum transaminases and alkaline phosphatase.

Drug Interactions: The CNS-depressant action of the benzodiazepine class of drugs may be potentiated by alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antianxiety agents, the phenothiazines, thioxanthene and butyrophenone classes of antipsychotic agents, monoamine oxidase inhibitors and the tricyclic antidepressants, and by other anticonvulsant drugs.

Overdosage: Symptoms of Clonopin overdosage, like those produced by other CNS depressants, include somnolence, confusion, coma and diminished reflexes. Treatment includes monitoring of respiration, pulse and blood pressure, general supportive measures and immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of levarterenol or metaraminol. Methylphenidate or caffeine and sodium benzoate may be given to combat CNS depression. Dialysis is of no known value.

Dosage and Administration: *Infants and Children:* Clonopin is administered orally. In order to minimize drowsiness, the initial dose for infants and children (up to 10 years of age or 30 kg of body weight) should be between 0.01 to 0.03 mg/kg/day but not to exceed 0.05 mg/kg/day given in two or three divided doses. Dosage should be increased by no more than 0.25 to 0.5 mg every third day until a daily maintenance dose of 0.1 to 0.2 mg/kg of body weight has been reached unless seizures are controlled or side effects preclude further increase. Whenever possible, the daily dose should be divided into three equal doses. If doses are not equally divided, the largest dose should be given before retiring.

Adults: The initial dose for adults should not exceed 1.5 mg/day divided into three doses. Dosage may be increased in increments of 0.5 to 1 mg every three days until seizures are adequately controlled or until side effects preclude any further increase. Maintenance dosage must be individualized for each patient depending upon response. Maximum recommended daily dose is 20 mg.

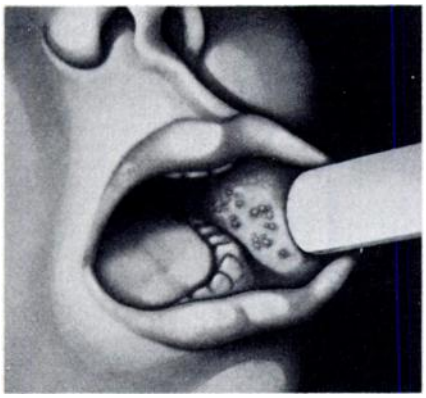
The use of multiple anticonvulsants may result in an increase of depressant adverse effects. This should be considered before adding Clonopin (clonazepam) to an existing anticonvulsant regimen.

How Supplied: Scored tablets—0.5 mg, orange; 1 mg, blue; 2 mg, white—Prescription Paks of 100.

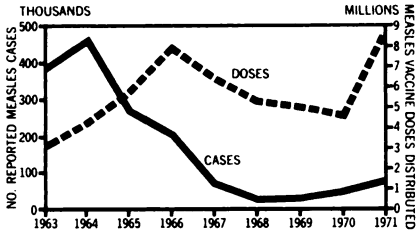
ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Measles, mumps, and rubella are "simple" childhood diseases...

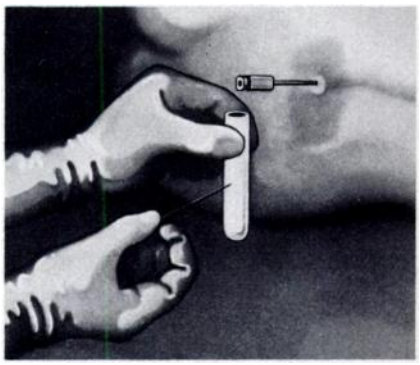
until serious complications develop



The complications that can result from measles. Bronchopneumonia, middle ear infection, and encephalitis are complications that frequently make measles a severe disease. From 1966 through 1971 the average annual rate of occurrence of reported encephalitis was 95.7 per 100,000 cases of measles.[1] Death from measles occurs primarily in children under five years of age, with about one half the fatalities occurring in children under two years.[2]



Measles has by no means been eradicated. Although the incidence of measles has been greatly reduced within the last decade, the disease has not been eradicated. Persisting incidence of measles must be regarded as significant, especially in view of the potential for complications. The decline in incidence which occurred after the introduction of live measles virus vaccine (1963) was interrupted in 1969, and by 1971 there was a nationwide resurgence of the disease. This upswing in incidence correlates with a steadily declining use of vaccine between 1966 and 1970.[2] Widespread use of vaccine for susceptible children is urged in the effort to reduce further the incidence of measles.



Mumps can have serious, even fatal, consequences. In 1971, 310 cases of encephalitis associated with mumps were reported in the United States, and 288 cases were reported in 1970.[1] One half of the reported cases from 1967 through 1970 occurred in children 5 to 9 years old.[3] According to yearly reports from 1960 to 1969, there was a relatively constant incidence of 2 to 4 cases of mumps encephalitis in every 1,000 cases of mumps. From 1960 to 1968, the case fatality ratio likewise showed relative constancy, with a range of 1.6 to 3.8 deaths per 10,000 reported cases of mumps.[3]

Congenital defects that may result from maternal rubella. The risk of congenital defects, such as deafness, congenital heart disease, cataract, and psychomotor retardation, is greatest following maternal rubella infection during the first four months of pregnancy.[4] In one study, multiple defects occurred in almost all affected infants.[5] Furthermore, infants infected *in utero* may shed rubella virus in pharyngeal secretions for weeks or months. They remain infective for susceptible persons during this period.[4]

You can vaccinate against all three with just one injection...

M-M-R®

(MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE|MSD)

Single-Dose Vials

M-M-R, a single injection, simplifies your routine vaccination program for susceptible children age one to puberty. Given at 12 months of age, M-M-R provides for vaccination early in life against measles, mumps, and rubella. (Clinical experience with live attenuated measles, mumps, and rubella virus vaccines given individually indicates that encephalitis and other nervous system reactions have occurred very rarely. These might occur also with M-M-R. See brief summary on following page for a more complete discussion.)

In 715 triple seronegative children age 7 months to 8 years receiving M-M-R, antibodies were induced against measles in 96 percent, against rubella in 94 percent, and against mumps in 95 percent. It is expected that antibody levels produced by M-M-R will be as durable as those produced by administration of the single vaccines given separately.

The adverse clinical reactions associated with the use of M-M-R are those expected to follow administration of the monovalent vaccines given separately. These may include fever and rash; mild local reactions such as erythema, induration, tenderness, and regional lymphadenopathy; parotitis; thrombocytopenia and purpura; allergic reactions such as urticaria; and arthritis, arthralgia, and polyneuritis. Moderate fever (101-102.9 F) occurs occasionally, and high fever (above 103 F) occurs less commonly. On rare occasions, children developing fever may exhibit febrile convulsions. Rash occurs infrequently and is usually minimal without generalized distribution.

Combination measles, mumps and rubella virus vaccine, live, is recommended for use by the Committee on Infectious Diseases of the American Academy of Pediatrics (AAP)[6] and the United States Public Health Service (USPHS) Advisory Committee on Immunization Practices.[2,7]

1. USPHS, Center for Disease Control, Neurotropic Viral Diseases Surveillance, Encephalitis, July 1973.
2. USPHS, Center for Disease Control, Immunization Against Disease—1972.
3. USPHS, Center for Disease Control, Mumps Surveillance Report No. 2, Sept 1972.
4. Cooper LZ et al: Rubella: Clinical manifestations and management, Am J Dis Child *118*:18, July 1969.
5. Peterson DR, Chinn N: Rubella-induced congenital defects and rubella immunization, Northwest Med *70*:169, March 1971.
6. AAP Newsletter, Sept 15, 1971.
7. USPHS, Center for Disease Control, MMWR, Vol. 21, No. 25—Supplement, June 24, 1972.

MSD
MERCK SHARP & DOHME

For a brief summary of prescribing information, please see following page.

vaccinate against measles, mumps, and rubella with just one injection

M-M-R®

(MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE|MSD)

Single-Dose Vials

Contraindications: Pregnancy or possibility of pregnancy within three months following vaccination; infants less than one year old; sensitivity to chicken or duck, chicken or duck eggs or feathers, or neomycin; any febrile respiratory illness or other active febrile infection; active untreated tuberculosis; therapy with ACTH, corticosteroids, irradiation, alkylating agents, or antimetabolites; blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems; gamma globulin deficiency, i.e., agammaglobulinemia, hypogammaglobulinemia, and dysgammaglobulinemia.

Precautions: Administer subcutaneously; *do not give intravenously.* Epinephrine should be available for immediate use should an anaphylactoid reaction occur. Should not be given less than one month before or after immunization with other live virus vaccines, with the exception of monovalent or trivalent poliovirus vaccine, live, oral, which may be administered simultaneously; vaccination should be deferred for at least three months following blood transfusions or administration of more than 0.02 ml immune serum globulin (human) per pound of body weight, or human plasma.

Due caution should be employed in children with a history of febrile convulsions, cerebral injury, or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur 5 to 12 days after vaccination.

Excretion of the live attenuated rubella virus from the throat has occurred in the majority of susceptible individuals administered the rubella vaccine. There is no definitive evidence to indicate that such virus is contagious to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, has not been regarded as a significant risk.

Attenuated live virus measles, mumps, and rubella vaccines, given separately, may temporarily depress tuberculin skin sensitivity; therefore, if a tuberculin test is to be done, it should be scheduled before vaccination, to avoid the possibility of a false negative response.

Before reconstitution, refrigerate vaccine at 2-8 C (35.6-46.4 F) and *protect from light.* Use only diluent supplied to reconstitute vaccine. If not used immediately, return reconstituted vaccine to refrigerator at 2-8 C (35.6-46.4 F), and discard after eight hours.

Adverse Reactions: To date, clinical evaluation has not revealed any adverse reactions peculiar to the combination.

Fever, rash; mild local reactions such as erythema, induration, tenderness, regional lymphadenopathy; parotitis; thrombocytopenia and purpura; allergic reactions such as urticaria; arthritis, arthralgia, and polyneuritis.

Occasionally, moderate fever (101-102.9 F); less commonly, high fever (above 103 F); rarely, febrile convulsions.

Encephalitis and other nervous system reactions that have occurred very rarely with the individual vaccines may also occur with the combined vaccine. Experience from more than 44 million doses of all live measles vaccines given in the U.S. by mid-1971 indicates that significant central nervous system reactions such as encephalitis, occurring within 30 days after vaccination, have been temporally associated with measles vaccine approximately once for every million doses. In no case has it been shown that reactions were actually caused by vaccine. The Center for Disease Control has pointed out that "a certain number of cases of encephalitis may be expected to occur in a large childhood population in a defined period of time even when no vaccines are administered. A survey conducted in New Jersey in 1965 showed that 2.8 cases of encephalitis (of unknown cause) occurred per million children, ages 1-9 years per 30-day period." However, the Center for Disease Control has analyzed the reported reactions following measles vaccines and pointed out that "the clustering of cases in the period 6 through 13 days after inoculation as well as the recovery of measles virus (probably the vaccine strain) from the CSF of one patient does suggest that some of these cases may have been caused by the vaccine." The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis with measles (one per thousand reported cases).

Transient arthritis, arthralgia, and polyneuritis are features of natural rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. Such reactions have been reported with live attenuated rubella virus vaccines. Symptoms relating to joints (pain, swelling, stiffness, etc.) and to peripheral nerves (pain, numbness, tingling, etc.) occurring within approximately two months after immunization should be considered as possibly vaccine related. Symptoms have generally been mild and of no more than three days' duration. The incidence in prepubertal children would appear to be less than 1% for reactions that would interfere with normal activity or necessitate medical attention.

How Supplied: Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus vaccine, live, attenuated, 5,000 $TCID_{50}$ of mumps virus vaccine, live, and 1,000 $TCID_{50}$ of rubella virus vaccine, live, expressed in terms of the assigned titer of the FDA Reference Measles, Mumps, and Rubella Viruses, and approximately 25 mcg neomycin, with a disposable syringe containing diluent and fitted with a 25-gauge, ⅝" needle. Also in boxes of 10 single-dose vials nested in a pop-out tray with a separate box of 10 diluent-containing syringes.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486.

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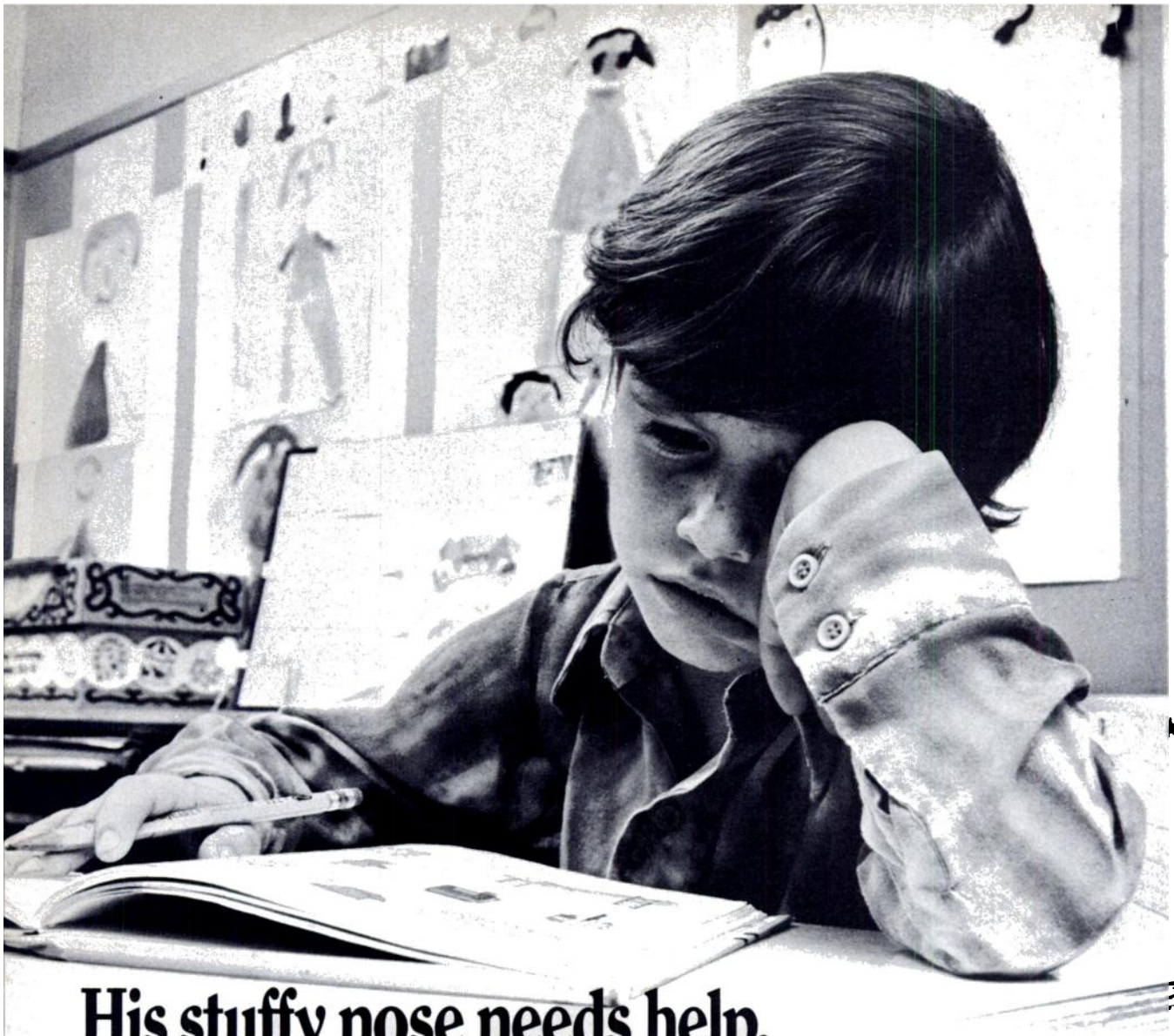

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SUDAFED decongests nasal passages, eustachian tubes, paranasal sinuses and bronchi.

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Precaution: Although pseudoephedrine is virtually without pressor effect in normotensive patients, it should be used with caution in hypertensive patients.
Side Effects: While the great majority of patients will experience no side effects, those particularly sensitive to sympathomimetic drugs may note mild stimulation.
Supplied: Syrup—30 mg./5 cc., bottles of 4 fl. oz. and 1 pt.
Also available as tablets—60 mg., bottles of 100 and 1000 and 30 mg. in vials of 24 and bottles of 100 and 1000.

Sudafed® syrup
(pseudoephedrine hydrochloride)

Complete literature available on request from Professional Services Dept. PML.

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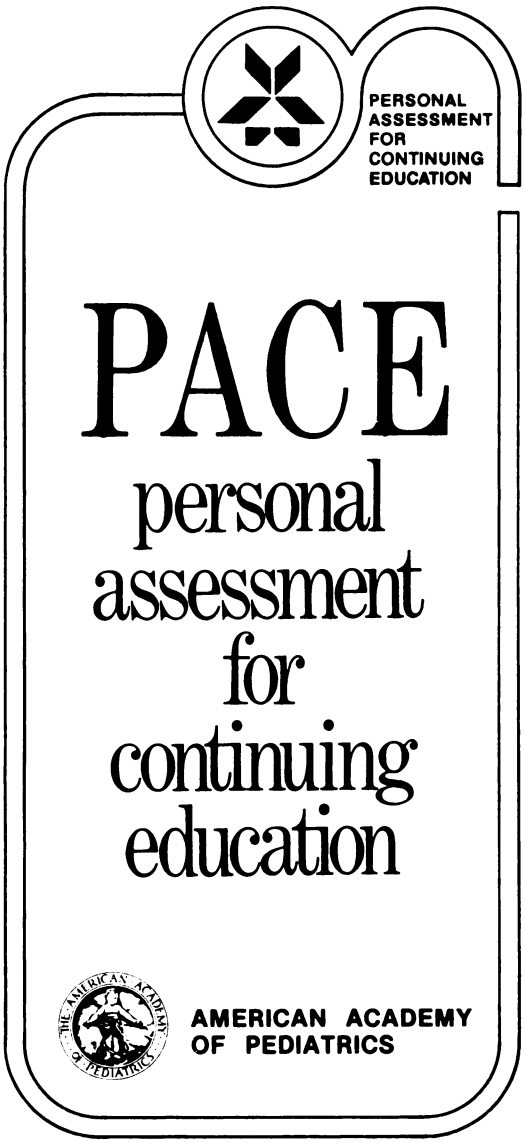

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