JUNE 1979

VOLUME 63
Number 6

ARTICLES

AMERICAN ACADEMY OF PEDIATRICS

EXPERIENCE AND REASON—BRIEFLY RECORDED

COMMENTARIES

PEDIAU 63(6) pp 825–965 (1979)

Pediatrics

AMERICAN ACADEMY OF PEDIATRICS EVANSTON ILLINOIS 60204

CORTISPORIN® OTIC SUSPENSION Sterile
(Polymyxin B-Neomycin-Hydrocortisone)
DESCRIPTION: Each cc contains:
Aerosporin®
(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%.
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.
PRECAUTIONS: 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.

CORTISPORIN® OTIC SOLUTION Sterile
(Polymyxin B-Neomycin-Hydrocortisone)
DESCRIPTION: Each cc contains:
Aerosporin®
(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 glycerin, hydrochloric acid, propylene glycol, purified water and potassium metabisulfite (preservative) 0.1%.
INDICATIONS: For the treatment of superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics.
PRECAUTIONS: This drug should be used with care when the integrity of the tympanic membrane is in question because of the possibility of ototoxicity caused by neomycin.
ADVERSE REACTIONS: Stinging and burning have been reported when this drug has gained access to the middle ear.

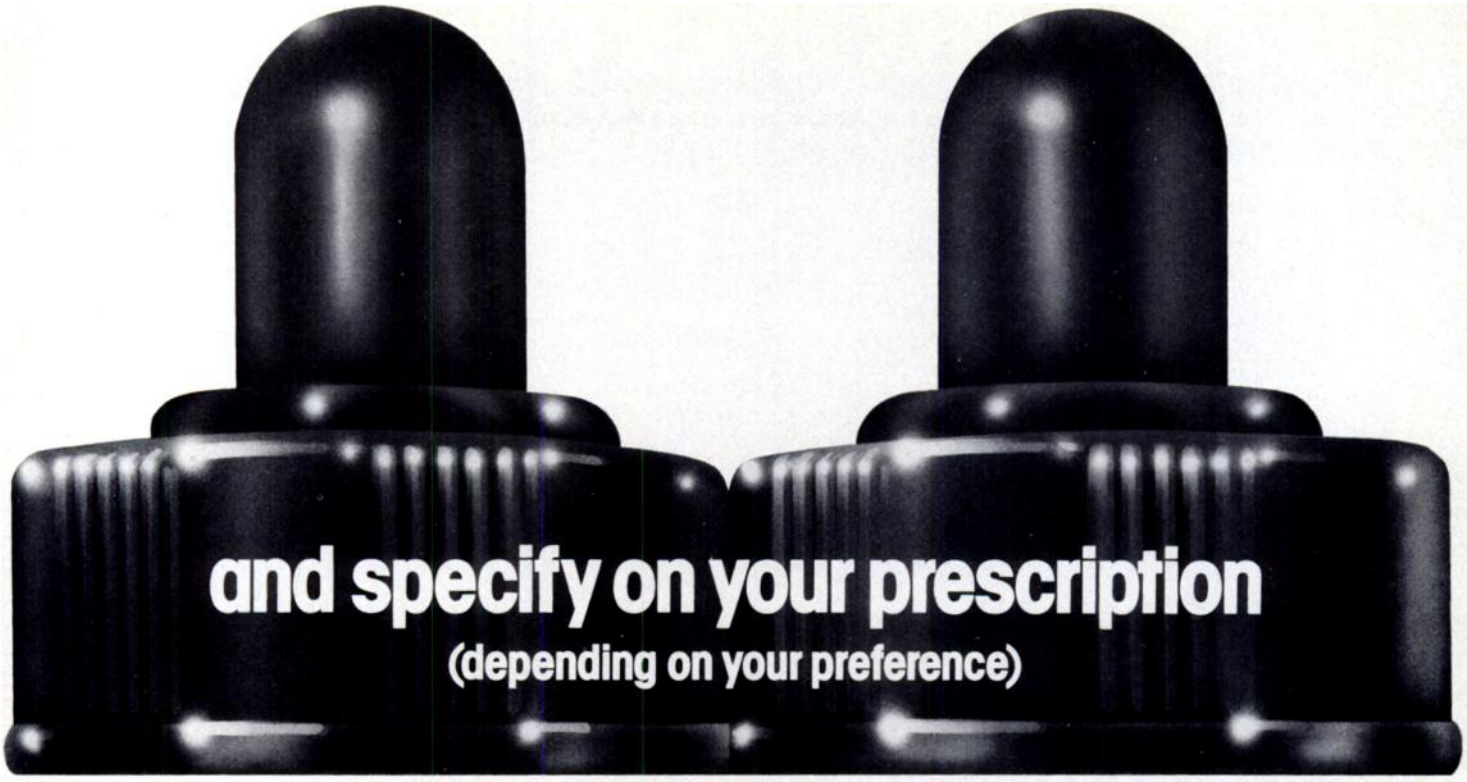
CONTRAINDICATIONS, WARNINGS, PRECAUTIONS AND ADVERSE REACTIONS COMMON TO BOTH PRODUCTS
CONTRAINDICATIONS: These products are contraindicated in those individuals who have shown hypersensitivity to any of the components, and in herpes simplex, vaccinia and varicella.
WARNINGS: As with other antibiotic 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.
When using neomycin-containing products to control secondary infection in the chronic dermatoses, such as chronic otitis externa, it should be borne in mind that the skin in these conditions is more liable than is normal skin to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.
PRECAUTIONS: If sensitization or irritation occurs, medication should be discontinued promptly. 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.
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.

Take your choice... of effective therapy for susceptible external ear infections

Solution or Suspension

Two otic products, giving you the assurance of:

- ☐ years of therapeutic success, clinical acceptance
- ☐ wide range of antibacterial activity, including many strains of *Pseudomonas aeruginosa,* the most common otic pathogen, as well as *Proteus* and staph
- ☐ direct anti-inflammatory action, relieving associated itching, swelling and pain
- ☐ acid pH to help restore normal acidity of the ear canal
- ☐ economy for your patients—usually less cost than with other comparable otics

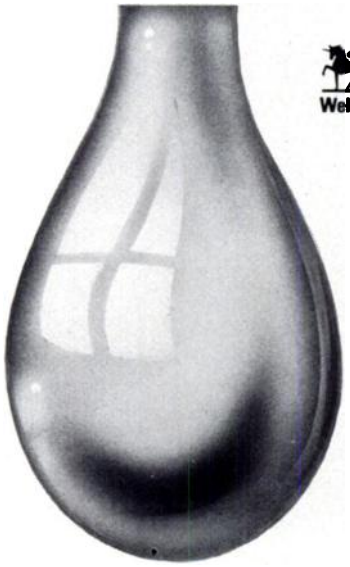


Cortisporin® Otic
SOLUTION Sterile
(polymyxin B-neomycin-hydrocortisone)

A clear solution (does not have to be shaken) providing clear visualization of field. Indicated for treatment of superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics. Stinging and burning have been reported when this drug has gained access to the middle ear.

Cortisporin® Otic
SUSPENSION Sterile
(polymyxin B-neomycin-hydrocortisone)

A white suspension for treating infections of mastoidectomy and fenestration cavities caused by organisms susceptible to the antibiotic as well as superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics.



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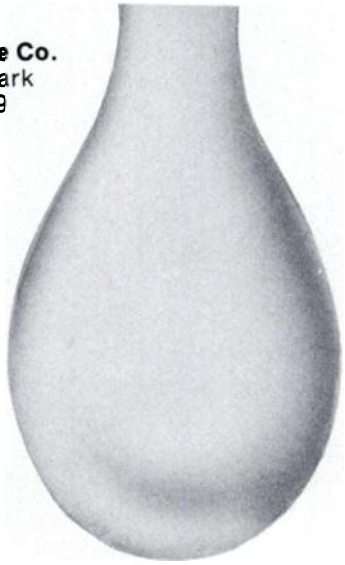

DDA9-DKL-APE5

Prescribing Information
Chloromycetin Sodium Succinate
(chloramphenicol sodium succinate for injection, USP)
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).

Each gram (10 ml of a 10% solution) of chloramphenicol sodium succinate contains approximately 52 mg (2.25 mEq) of sodium.

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. Base line 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-old 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 distention 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

N 0071-4057-3 (Steri-Vial® No. 57)
Chloromycetin Sodium Succinate (chloramphenicol sodium succinate for injection, USP) 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 milliliter (1 g/10 ml). Available in packages of 10 vials.

CHLOROMYCETIN, brand of chloramphenicol. Reg US Pat Off RJ

PD-JA-1281-2-P(12-77)

PARKE-DAVIS, Division of Warner-Lambert Company, Morris Plains, NJ 07950

PREPARATION OF MANUSCRIPTS

A CURRENT issue of PEDIATRICS should be consulted for general style. Three complete copies of the manuscript (including tables and illustrations) must be supplied. ALL material (including tables and references) should be double-spaced and typed on white 8½ × 11-inch bond paper with margins at least 1½ inches wide. Single-spaced material will be returned for retyping. Number pages consecutively.

Send all manuscripts to Jerold F. Lucey, M.D., Editor, Pediatrics Editorial Office, Mary Fletcher Hospital, Colchester Avenue, Burlington, VT 05401.

In view of the Copyright Revision Act of 1976, effective January 1, 1978, transmittal letters to the editor should contain the following language: "In consideration of the American Academy of Pediatrics taking action in reviewing and editing my submission entitled _____, also known as _____, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to the AAP in the event that such work in published by the AAP." We regret that transmittal letters not containing the foregoing language signed by all authors of the submission will delay review of the manuscripts.

Manuscripts should include a clear introductory statement of purpose; a historical review when desirable; a description of the technique and the scope of the experiments or observations (previously published procedures require only references to the original); a full presentation of the *Results* obtained; a brief *Comment or Discussion* on the significance of the findings and any correlation with those of other workers; a paragraph headed *Speculation and Relevance,* or *Implications;* and a *Summary,* in brief, logical résumé which may include conclusions.

The author's style will be respected; however, writing should conform to acceptable English usage and syntax. Titles should be concise and clear, subtitles avoided. Terminology should follow *Standard Nomenclature of Diseases and Operations.* Give authors' full names and professional degrees, principal author's address, and name of institution(s) where work was done; omit departmental appointments unless necessary for special reasons. Slang, medical jargon, obscure abbreviations, and abbreviated phrasing should be avoided. Mathematical terms, formulas, abbreviations, and units of measurement must conform to usage in PEDIATRICS, based on standards in *Science,* 120:1078, 1954. The metric system will be used; equivalent measurement in the English system may be included in parentheses. Name of chemical compounds—not formulas—should be given. Proprietary names, if unavoidable, will be indicated by capitalization of the first letter. Conversions to accepted standards and terms should be made before the manuscript is submitted.

References must be numbered consecutively according to order of appearance in the text. They must conform to the style employed in PEDIATRICS and be keyed in the text. Abbreviations for journals should be those listed in *Index Medicus.* References to books should contain the authors' names, title of book, volume, edition, and city and state, name of publisher, year of publication, and page numbers.

Authors are requested to furnish (in addition to the full title) a condensed title for the cover, not exceeding 60 spaces, and a running foot of not more than 35 spaces. Original articles should be accompanied by an Abstract, prepared by the author in 200 words or less, as well as up to five key words under which the paper should be indexed and an alphabetical list of any unusual abbreviations used, with meanings.

Illustrations—Photographs of line drawings and any other figure which is not composed simply of letters, numerals, and routine symbols must be furnished. Do not send original artwork or printed forms. A reasonable number of black-and-white illustrations will be printed from black-and-white glossies or film without cost, but the cost of color illustrations and other special processing is usually borne by the author. Manuscripts containing such materials will not be processed until arrangements for payment, on the basis of estimated prices, are made. Color work requires one month longer for production and authors will be expected to pay for the extra expenses involved.

Illustrations must be identified by number, author's name, and "top." They should be keyed in the text. If unessential, their omission may be requested. The prints should not be stapled, clipped together, mounted or trimmed. Details to be emphasized or crop marks should be indicated on a tissue overlay, not on the illustration itself. Illustrations of poor quality may be returned for improvement. Photographs of patients should be submitted *only* when parental permission has been obtained. It is the responsibility of the authors to obtain this permission and to keep it in their files. Use cardboard inserts to protect illustrations in the mail. Legends for figures are to be a separate sheet.

Tables must be comprehensible to the reader without reference to the text, typed (double-spaced) rather than photographed, and accompanied by headings. Care should be taken to make tables as concise and brief as possible.

Revised, December 1974

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Subscription price per year: U.S., Mexico, Canada, Central and South America, $21.00; other countries, $30.00. Special rates for medical students, hospital residents and fellows in full time training in U.S., Mexico, Canada, Central and South America, $13.00 per year. Renewal at special rate beyond two years will require a letter from an appropriate authority stating the individual's eligibility. Current single issue $3.00.

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Just a touch can transfer impetigo.

And just a touch of the right antibiotic can help clear it up.

Neosporin Ointment can help control minor cases of impetigo before other children catch it from your young patient, and it may be used as an adjunct to appropriate systemic therapy in more extensive disease. Neosporin Ointment provides broad, reliable antibiotic action against susceptible organisms—notably *Staphylococcus* and *Streptococcus*— with antibiotics that are 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 qs. In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

Warning: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

Precautions: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

Adverse Reactions: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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

Wellcome

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North Carolina 27709

JUNE 1979 VOL. 63 NO. 6

Pediatrics

OFFICIAL PUBLICATION OF THE AMERICAN ACADEMY OF PEDIATRICS

PUBLISHER
Arthur Retlaw and Associates, Inc.
1603 Orrington Avenue, Suite 2080
Evanston, IL 60201

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BPA Membership Applied for, November 1976

ARTICLES


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The four freedoms for young asthmatics...

- free of alcohol
- free of dye
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- free of potential additive-induced side effects

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Each tablespoonful (15 ml) contains theophylline (anhydrous) 150 mg and glyceryl guaiacolate (guaifenesin) 90 mg

Therapeutically equivalent to the Elixir it replaces... with these important benefits:

- Provides 100% free theophylline—its sole bronchodilator agent—for low dosage volume.
- Pleasant tasting to encourage patient acceptance and compliance in the young asthmatic.
- Controlled theophylline content for effective round-the-clock therapy.
- Contains glyceryl guaiacolate, a beneficial ingredient lacking in many other theophylline bronchodilators.

Indications: For the symptomatic relief of bronchospastic conditions such as bronchial asthma, chronic bronchitis, and pulmonary emphysema.
Dosage: Treatment should be initiated at 150 mg theophylline every 6 hours for adults and 4 mg/kg every 6 hours for children. The usual recommended dosages are *Adults:* 1-2 capsules or 1-2 tablespoons (15 ml) liquid every 6-8 hours. *Children 9 to 12:* 4-5 mg theophylline/kg bodyweight every 6-8 hours. *Children under 9:* 4-6 mg theophylline/kg bodyweight every 6-8 hours. When necessary, to achieve greater efficacy theophylline dosage may be cautiously adjusted upward. Serum theophylline determinations are helpful in monitoring therapeutic progress. When dosages exceed the usual recommended ranges serum determinations are essential. In the absence of side effects, the dosage may be titrated upward cautiously by increments of no more than 25% of previous dose, increasing the dose no more than every third day until the desired clinical response is obtained. If nausea, vomiting or other evidence of toxicity occurs, omit one dose and resume treatment at a lower dose.
Warnings: Do not administer more frequently than every 6 hours, or within 12 hours after rectal dose of any preparation containing theophylline or aminophylline. Do not give other compounds containing xanthine derivatives concurrently.

Precautions: Use with caution in patients with cardiac disease, hepatic or renal impairment. Concurrent administration with certain antibiotics, i.e., clindamycin, erythromycin, troleandomycin, may result in higher serum levels of theophylline. Plasma prothrombin and factor V may increase, but any clinical effect is likely to be small. Metabolites of guaifenesin may contribute to increased urinary 5-hydroxyindoleacetic acid readings, when determined with nitrosonaphthol reagent. Safe use in pregnancy has not been established. Use in case of pregnancy only when clearly needed.
Adverse Reactions: Theophylline may exert some stimulating effect on the central nervous system. Its administration may cause local irritation of the gastric mucosa, with possible gastric discomfort, nausea, and vomiting. The frequency of adverse reactions is related to the serum theophylline level and is not usually a problem at serum theophylline levels below 20 mcg/ml.
How Supplied: Capsules in bottles of 100 and 1000 and unit-dose packs of 100; Liquid in bottles of 1 pint and 1 gallon.
See package insert for complete prescribing information.

Mead Johnson PHARMACEUTICAL DIVISION

AMERICAN ACADEMY OF PEDIATRICS

1801 Hinman Avenue
Evanston, IL 60204

SCHEDULE OF MEETINGS

ANNUAL MEETINGS

1979
San Francisco Hilton
St. Francis Hotel
San Francisco
October 13 to 18

1980
Detroit Plaza Hotel
Detroit
October 25 to 30

1981
New Orleans
October 31 to Nov. 5

1982
New York Hilton
Americana Hotel
New York City
October 23 to 28

1983
San Francisco
October 22 to 27

Note: All Annual Meetings start on Saturday

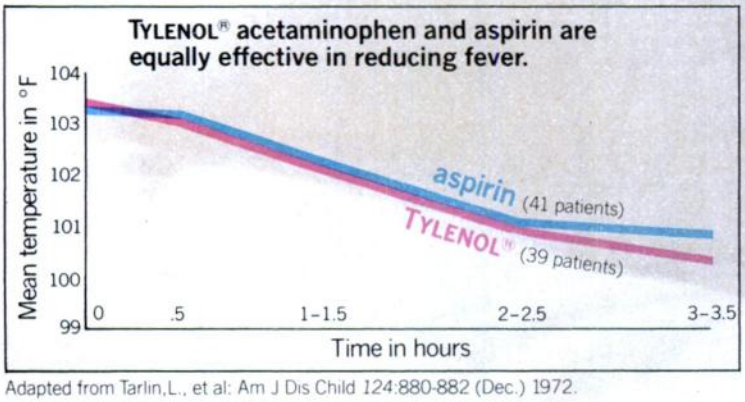
ARTICLES (CONTINUED)

AMERICAN ACADEMY OF PEDIATRICS

Fever's down fast with TYLENOL® safety

acetaminophen

Clinical evidence:



Adapted from Tarlin,L., et al: Am J Dis Child *124*:880-882 (Dec.) 1972.

your logical first choice for fever and pain

McNEIL

McNeil Consumer Products Company
Fort Washington, Pa. 19034

PEDICULOSIS.

THE ONLY DISEASE YOU CAN CURE IN FOUR MINUTES.

A single, four-minute lathering with Kwell Shampoo is generally all it takes to eliminate head and pubic lice fast–and completely![1] Just about 100% effective,[2] nonsensitizing and nonirritating to the skin, it's as easy to use as any ordinary shampoo.[1,2] For lice on less hirsute areas of the body, and for scabies, Kwell is also available in lotion form.

Available on prescription as Kwell Shampoo and Lotion in 2 and 16 fl. oz. bottles, and as Kwell Cream in 2 oz. and 1 lb. jars. Patient instruction pads in English and Spanish are available on request. See package insert for complete prescribing information.

REFERENCES: 1. Wexler, L.: Am. J. Nurs. 69:3, March, 1969. 2. Patient Care 7:94, Nov. 1, 1973.

WARNING: KWELL SHOULD BE USED WITH CAUTION ESPECIALLY IN INFANTS, CHILDREN AND IN PREGNANCY. GAMMA BENZENE HEXACHLORIDE PENETRATES HUMAN SKIN AND HAS THE POTENTIAL FOR CNS TOXICITY. STUDIES INDICATE THAT POTENTIAL TOXIC EFFECTS OF TOPICALLY APPLIED LINDANE ARE GREATER IN THE YOUNG. Seizures have been reported after the use of gamma benzene hexachloride but a cause and effect relationship has not been established. Simultaneous application of creams, ointments or oils may enhance the percutaneous absorption of gamma benzene hexachloride.

PRECAUTIONS: If accidental ingestion occurs, prompt institution of gastric lavage will rid the body of large amounts of the toxicant. However, since oils favor absorption, saline cathartics for intestinal evacuation should be given rather than oil laxatives. If central nervous system manifestations occur, they can be antagonized by the administration of pentobarbital, or phenobarbital.

If accidental contact with the eyes occurs flush with water. If irritation or sensitization occurs discontinue this product and consult a physician.

ADVERSE REACTIONS: Eczematous eruptions due to irritation from this product have been reported.

The unsurpassed standard for the treatment of pediculosis and scabies.

Kwell®

Gamma Benzene Hexachloride

SHAMPOO/LOTION/CREAM

Reed & Carnrick/Kenilworth, New Jersey 07033

AMERICAN ACADEMY
OF PEDIATRICS
1801 Hinman Avenue
Evanston, Illinois 60204

SCHEDULE OF MEETINGS

SPRING SESSIONS

1980
Las Vegas Hilton
Las Vegas
April 19 to 24

1981
Washington, D.C.
April 4 to 9

1982
Honolulu
March 20 to 25

Note: All Spring Sessions start on Saturday

In recurrent urinary tract infections

Septra® DS

Each tablet contains:
160 mg trimethoprim and 800 mg sulfamethoxazole

B.I.D.

where the action is.

In the kidney

Septra DS provides effective antibacterial action in the kidneys, via urine and blood, against susceptible strains of E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris and Proteus morganii.

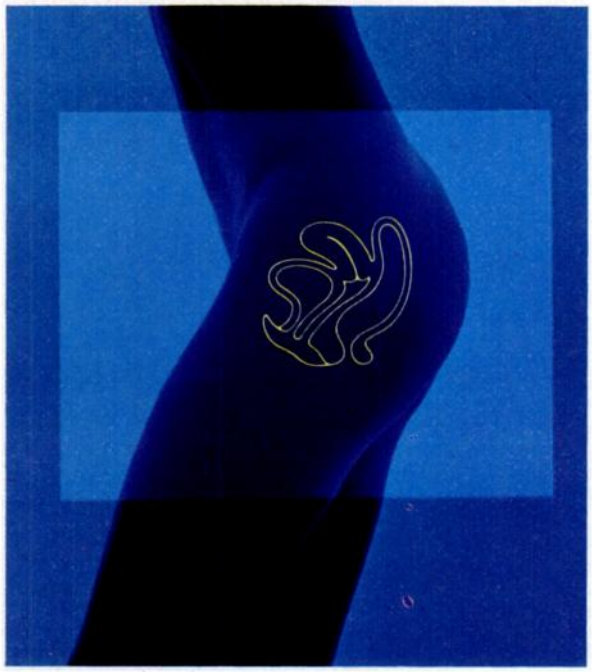
The high degree of efficacy of Septra DS was confirmed in a study of 59 patients with recurrent pyelonephritis. All patients had upper urinary tract disease as evidenced by fever $\geq$ 100.4° F and/or flank pain, and $\geq 10^5$ organisms/ml of urine. After two weeks' therapy and up to seven days post-therapy, Septra achieved bacteriologic cure ($\leq$ 10,000 organisms/ml of urine) in 91.5% of patients.[1]

And during the critical "recurrence" period from one to four weeks post-therapy, this excellent response rate was well maintained. Of the 53 patients evaluated at that time, 51 (96.2%) were still infection free.[1]

Unlike many other antibacterials for the treatment of urinary tract infections, Septra DS is administered on a convenient b.i.d. dosage schedule.

In the bladder

What makes Septra DS good for the tough areas—the kidneys—makes it good for the not-so-tough. Septra DS provides antibacterial action in the bladder, via urine and blood, against susceptible strains of major pathogens that cause recurrent cystitis.



And along the route to recurrence

During therapy, Septra DS diffuses into vaginal fluid[2] and into the bowel.[3,4] By eliminating potential uropathogens from the fecal flora, and bathing the periurethral area in an "antibacterial" vaginal fluid, Septra DS helps block the most common route to reinfection in women.

Maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination during therapy. Septra is contraindicated in children under two months old.

Please see prescribing information on next page.

Wellcome | **Burroughs Wellcome Co.**
Research Triangle Park
North Carolina 27709

Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

Septra® DS Tablets Double Strength
Septra® Tablets
Septra® Suspension

INDICATIONS AND USAGE:
URINARY TRACT INFECTIONS: **For the treatment of urinary tract infections due to susceptible strains of the following organisms:** *Escherichia coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris, Proteus morganii.* **It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.**

NOTE: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

ACUTE OTITIS MEDIA: **For the treatment of acute otitis media in children due to susceptible strains of** *Haemophilus influenzae* **or** *Streptococcus pneumoniae* **when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to** *Haemophilus influenzae* **resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.**

SHIGELLOSIS: **For the treatment of enteritis caused by susceptible strains of** *Shigella flexneri* **and** *Shigella sonnei* **when antibacterial therapy is indicated.**

PNEUMOCYSTIS CARINII **PNEUMONITIS: For the treatment of documented** *Pneumocystis carinii* **pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.**

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.

Clinical studies have documented that patients with Group A β-hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

PRECAUTIONS: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

ADVERSE REACTIONS: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood Dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, 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:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *C.N.S. Reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *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 to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

DOSAGE AND ADMINISTRATION: Not recommended for use in infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Children: The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose —every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 (5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

PNEUMOCYSTIS CARINII **PNEUMONITIS:**
The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose —every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 (5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

HOW SUPPLIED: TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

ORAL SUSPENSION, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.

REFERENCES:
(1) Data on file, Burroughs Wellcome Co. (2) Stamey TA, Condy M: The diffusion and concentration of trimethoprim in human vaginal fluid, in *Trimethoprim/Sulfamethoxazole: A Compilation of Clinical and Pharmacodynamic Studies in Chronic and Recurrent Urinary Tract Infections.* Science & Medicine Publishing Co, 1975, p 13. (3) Näff H: *Pathol Microbiol* 37:1, 1971. (4) Moorhouse EC, Farrell W: *J Med Microbiol* 6:249, 1973.

Wellcome | **Burroughs Wellcome Co.**
Research Triangle Park
North Carolina 27709

It's what's left out that's important.

We left out cow's milk *and* corn derivatives—because corn sensitivity is also a common cause of feeding problems in infants. In fact, NEO-MULL-SOY® formula is the *only* leading formula that is both milk-free *and* corn-free.

And, to help reduce the infant's environmental exposure to lead, we left lead solder out of the NEO-MULL-SOY cans. Last year, Syntex introduced seamless 14-oz cans made without lead solder for both the concentrate and ready-to-use forms of NEO-MULL-SOY formula. And now we have a new can made with pure tin solder—not lead—in the convenient quart size of our ready-to-use formula.

So, the next time you want to place an infant on a soy formula, consider what we left out—cow's milk, corn derivatives and lead solder—and recommend NEO-MULL-SOY formula. It's available in food and drugstores everywhere.

QUART CANS ARE BACK!

NEO-MULL-SOY®
SOY FORMULA

SYNTEX

SYNTEX LABORATORIES, INC.
NUTRITIONAL PRODUCTS DIVISION
PALO ALTO, CALIFORNIA 94304

Child care expert

Today's most widely used children's aspirin

Since 1899, aspirin has provided dependable antipyresis, analgesia and anti-inflammatory activity—compiling a record of clinical efficacy and versatility that no drug in its class can match.

In that time, millions upon millions of children have enjoyed its numerous benefits while experiencing remarkably few side effects. Also, in that time, much has been learned about the long-term use of aspirin. Far less is known about the long-term safety and efficacy of other commonly used pediatric analgesics/antipyretics.

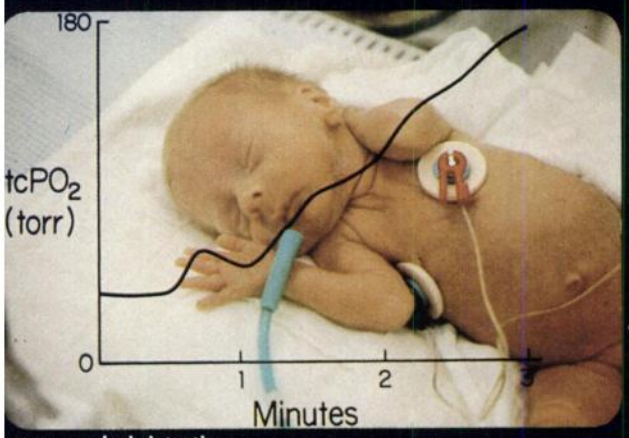
Today, of all pediatric aspirin, Bayer® Children's Chewable Aspirin is the most widely used. Bayer is the original name in aspirin—a name synonymous with aspirin purity, quality and stability. Each orange flavored Bayer Children's Chewable Aspirin tablet contains 1¼ grains of aspirin. Tablets can be chewed or will disintegrate easily in water, juice or milk.

So for the reduction of fever and relief of aches and pains of childhood colds and flu in your practice, rely on the expert...rely on experience...rely on Bayer Children's Chewable Aspirin!

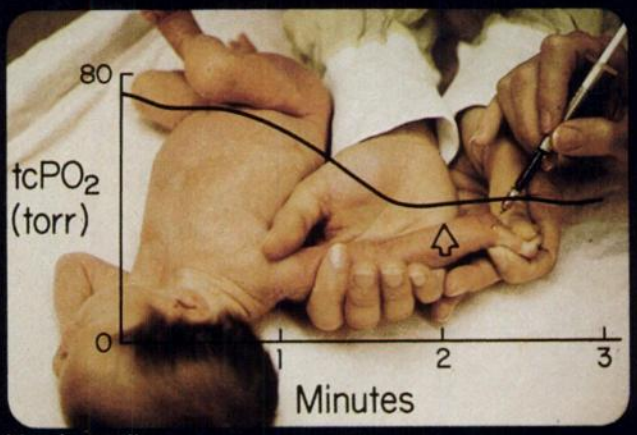
Bayer® Children's Chewable Aspirin

The Bayer Company
Glenbrook Laboratories, Division of Sterling Drug Inc.
90 Park Avenue, New York, New York 10016

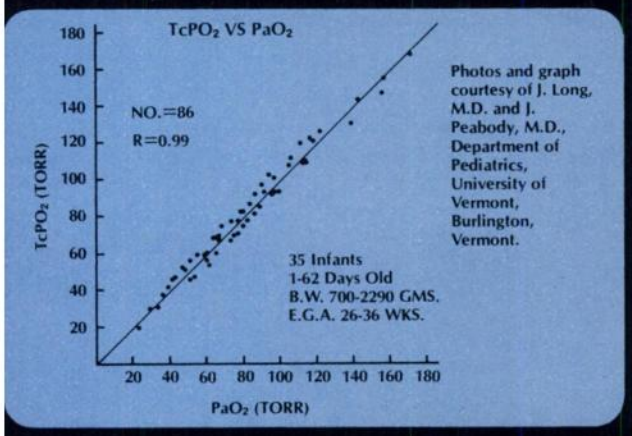
Oxymonitor™ = Non-Invasive



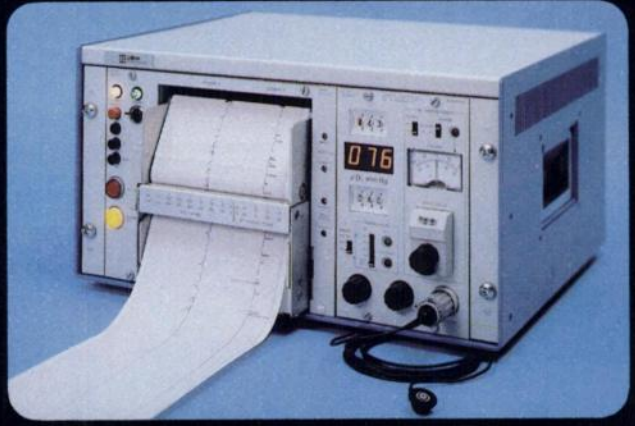
oxygen administration



blood sampling



Photos and graph courtesy of J. Long, M.D. and J. Peabody, M.D., Department of Pediatrics, University of Vermont, Burlington, Vermont.



With the Litton Oxymonitor, you can precisely and continuously monitor PO_2 levels... transcutaneously. The Oxymonitor is a valuable device to prevent hypoxemia and hyperoxemia. And, a perfusion channel reports the status of peripheral perfusion. The simple-to-use Huch Transoxode,™ placed on the skin, gives instant data with a very high correlation to blood gas readings...plus accurate and continuous trend data. Correlations of r=.9 or better are reported in infants. And, it is extensively referenced...over 5,000 case experiences have been published in world medical literature. The Litton Oxymonitor ...reliable, stable, proven!

Another high technology contribution by

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Medical Electronics

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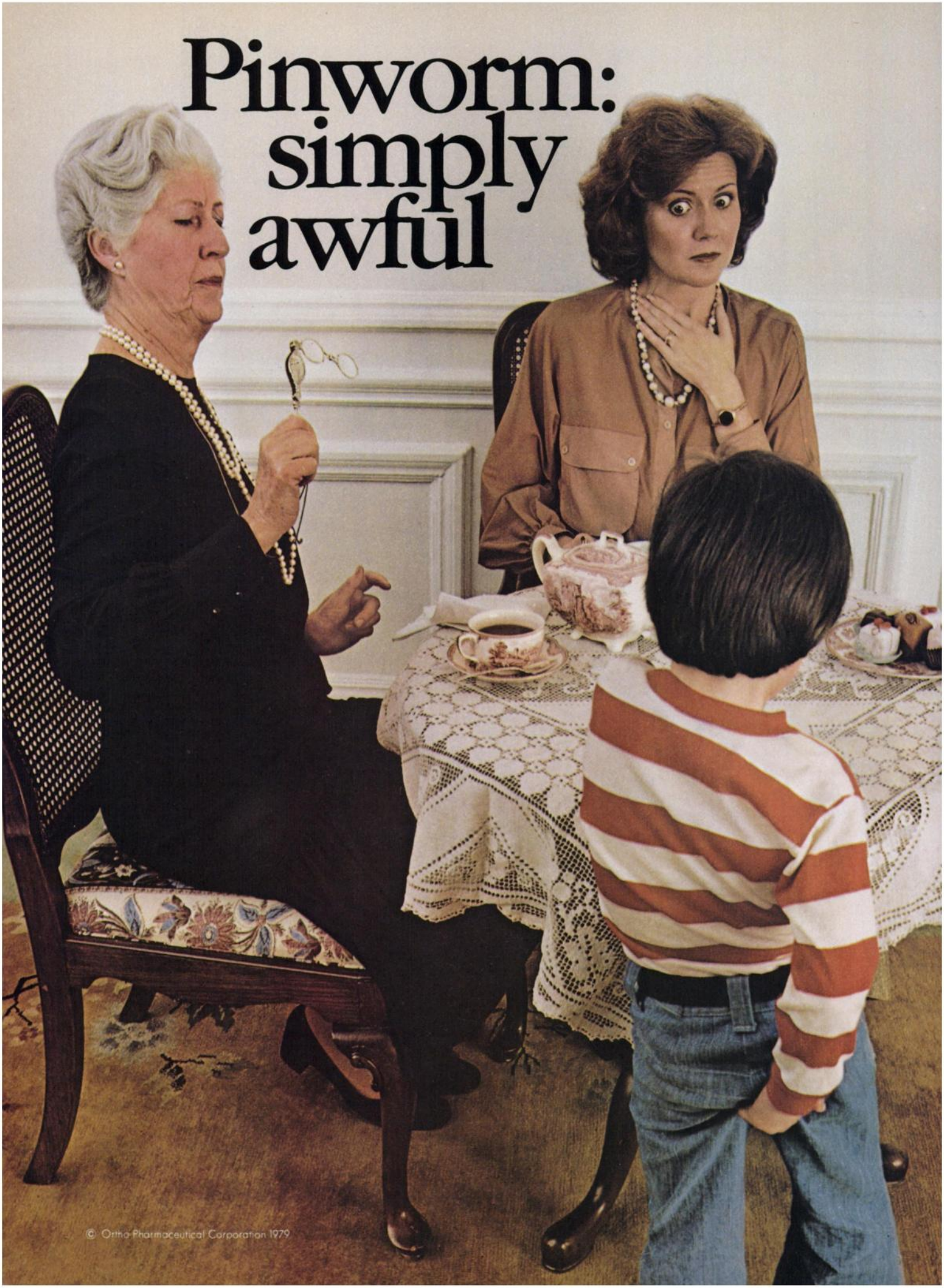
Please: Send literature on the Oxymonitor.™
Ask a Litton representative to call me.

Name _____
Title _____
Hospital _____
Address _____
City _____ State _____ Zip _____
Phone No. _____


Pinworm:
simply
awful
© Ortho Pharmaceutical Corporation 1979

Vermox: awfully simple

No dosage calculation

one dose single VERMOX 100 mg tablet is the treatment for pinworm in both adults and children* of all body weights; no dosage calculations or confusion

one time the VERMOX tablet may be taken any time that is convenient, so that normal routines won't be interrupted; convenient schedule encourages compliance

one tablet chewable, orange-flavored VERMOX tablet may also be crushed and mixed or simply swallowed; no messy liquid to spill and no dye to stain

95% cure mean cure rate in clinical studies was 95% (range: 90%-100%) after treatment with one VERMOX tablet; in cases of reinfection, a second tablet is advised

* Because Vermox has not been extensively studied in children under two years of age, the relative benefit/risk should be considered before treating these children. Vermox is contraindicated in pregnancy (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Vermox® chewable tablets (mebendazole)

TRADEMARK

Description VERMOX (mebendazole) is methyl 5-benzoylbenzimidazole-2-carbamate.

Actions VERMOX exerts its anthelmintic effect by blocking glucose uptake by the susceptible helminths, thereby depleting the energy level until it becomes inadequate for survival.

In man, approximately 2% of administered mebendazole is excreted in urine as unchanged drug or a primary metabolite. Following administration of 100 mg of mebendazole twice daily for three consecutive days, plasma levels of mebendazole and its primary metabolite, the 2-amine, never exceeded 0.03 μg/ml and 0.09 μg/ml, respectively.

Indications VERMOX is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections. Efficacy varies in function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains.

Contraindications VERMOX is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Precautions *PREGNANCY:* VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to children and adults. The tablet may be chewed, swallowed or crushed and mixed with food.

For the control of pinworm (enterobiasis), a single tablet is administered orally, one time.

For the control of roundworm (ascariasis), whipworm (trichuriasis), and hookworm infection, one tablet of VERMOX is administered, orally, morning and evening, on three consecutive days.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

How supplied VERMOX is available as chewable tablets, each containing 100 mg of mebendazole, and is supplied in boxes of twelve tablets.

VERMOX (mebendazole) is an original product of Janssen Pharmaceutica, Belgium, and co-developed by Ortho Pharmaceutical Corporation.

ORTHO

ORTHO PHARMACEUTICAL CORPORATION
Raritan, New Jersey 08869

OJ-1511

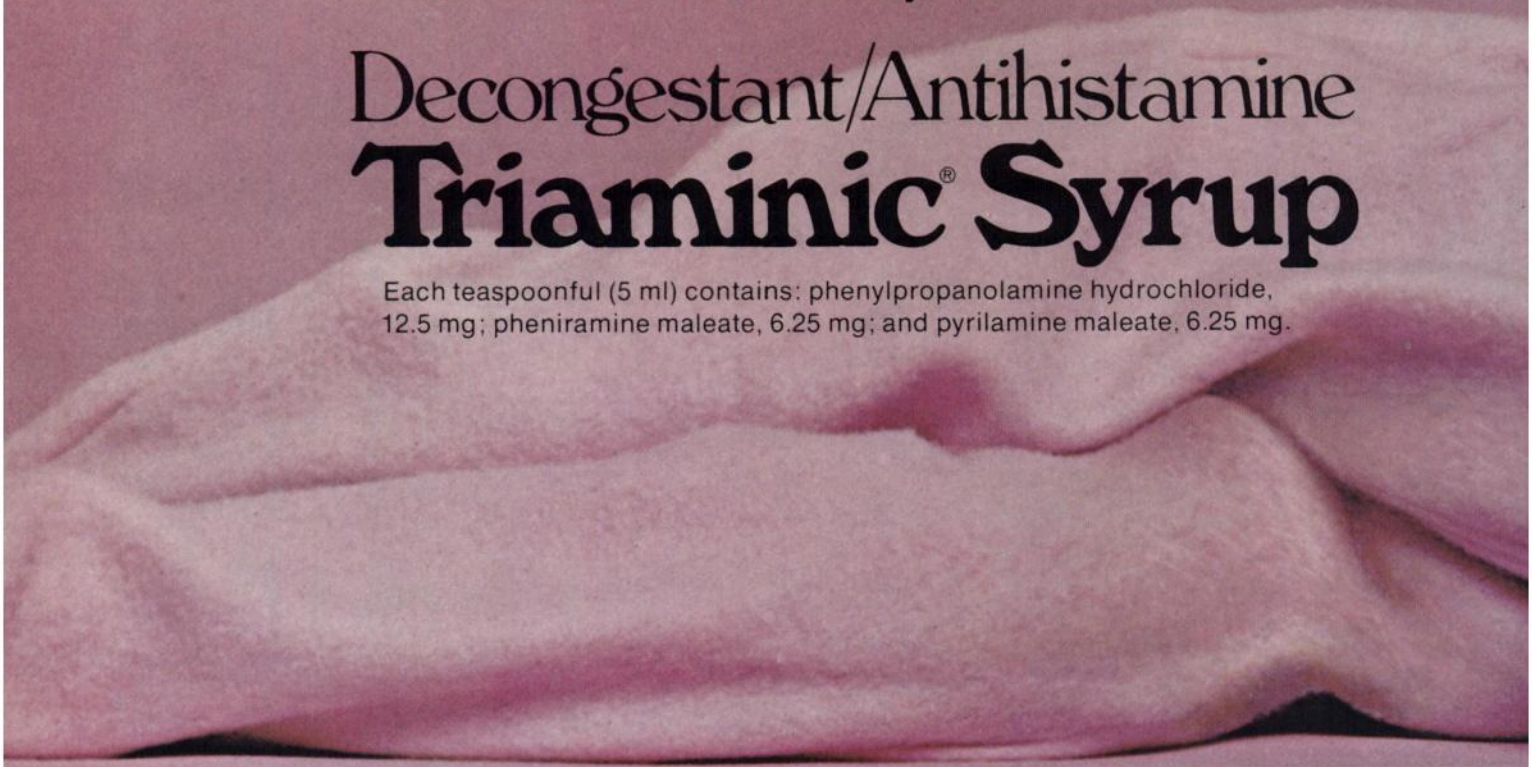
The Orange Medicine feel in the *Pink*

No R_x Required

- Saves your valuable time
- Costs less when you recommend
- Relieves stuffed and runny noses, postnasal drip
- Good-tasting ORANGE flavor that children accept
- Contains no tartrazine dye, no alcohol

Decongestant/Antihistamine
Triaminic® Syrup

Each teaspoonful (5 ml) contains: phenylpropanolamine hydrochloride, 12.5 mg; pheniramine maleate, 6.25 mg; and pyrilamine maleate, 6.25 mg.



29780

helps your little patients

One of the Recommendables® line of products from

Dorsey
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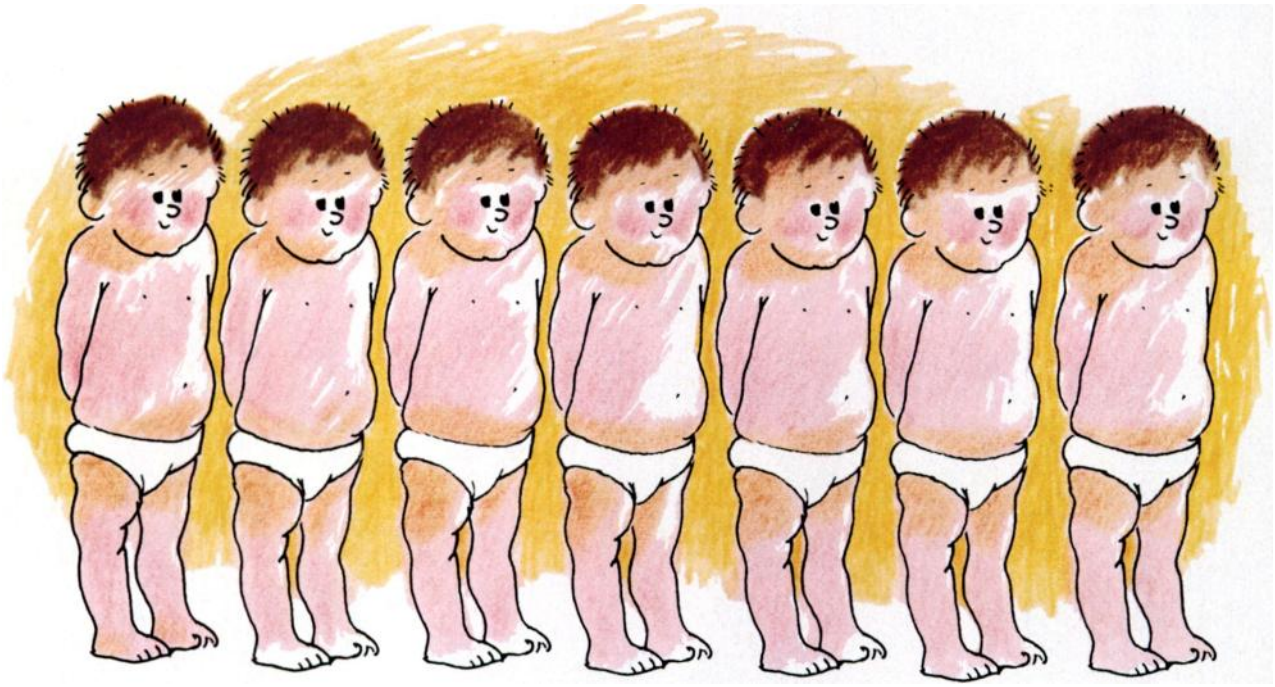
LINCOLN, NEBRASKA 68501

PREALLERGIC?



One is going to develop atopic allergy. Phadebas IgE PRIST® helps to identify which one!

(Paper Radio Immuno Sorbent Test)
The test to predict atopic allergies in children

"In children with a double parental history of atopic disease the incidence of such disease was higher than in children with a single such heredity in whom, however, the incidence was higher than in children without any parental history of atopic disease".

Determination of serum IgE with the Phadebas IgE PRIST® technique has been shown to provide a valuable means for predicting future atopic manifestations and may be used as a screening procedure especially in children of atopic parents.

Kjellman, N-I Max: Immunoglobulin E and Atopic Allergy in Children. Linkoping University Medical Dissertations 36, 1976

Pharmacia Diagnostics AB
Uppsala, Sweden

Pharmacia Diagnostics

Argentina: Lab. Dr. Gador y Cia., BUENOS AIRES, tel. 01-32-6333
Australia: Pharmacia (South Seas) Pty. Ltd., NORTH RYDE N.S.W., tel. 02-888-3622
Austria: Schoeller-Pharma GmbH, Wien, tel. 222-743641
Belgium: N.V. Pharmacia Belga S.A., BRUSSELS, tel. 02-6486490
Brazil. Emp. Medimex Importação e Comércio Ltda., RIO DE JANEIRO, tel. 021-223-2564
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Eastern Europe: Pharmacia GmbH, WIEN, tel. 222-855289
Finland: Pharmacia OY, ESBO, tel. 90-461766
France: Pharmacia France S.A., LE CHESNAY, tel. 01-9549060
German Federal Republic: Deutsche Pharmacia GmbH, FREIBURG, tel. 0761-41011
Great Britain: Pharmacia (Great Britain) Ltd., HOUNSLOW, tel. 01-5727321
Italy: Importex Chimici Farmaceutici S.p.A., TRIESTE, tel. 40-820521
Japan: Pharmacia (Japan) K.K., TOKYO 150, tel. 03-4064995
Mexico: Instrumental Teknion S.A., MEXICO, tel. 05-564-84-21
the Netherlands: Pharmacia Nederland B.V., DEN HAAG, tel. 070-210251
Norway: Norsk Pharmacia A/S, OSLO, tel. 02-209735
Portugal: J.A. Baptista D'Almeida Lda., LISBOA, tel. 19-534151
Spain: Atom, BARCELONA, tel. 03-2135002
Sweden: Pharmacia Norden AB, Avd. Diagnostika, UPPSALA, tel. 018-156040
Switzerland: Pharmacia – pdf – (Schweiz) A.G., ZURICH, tel. 01-556077
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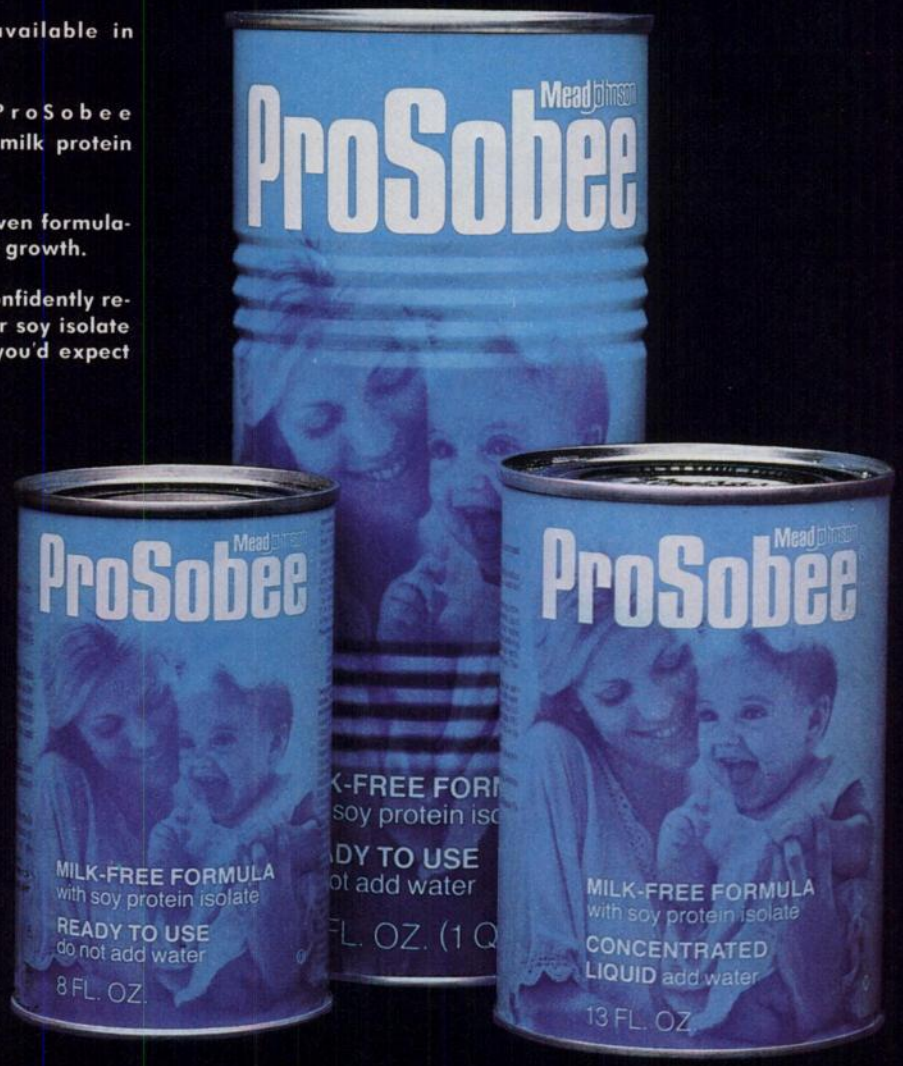

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ProSobee®

ProSobee® milk-free formula with soy isolate.

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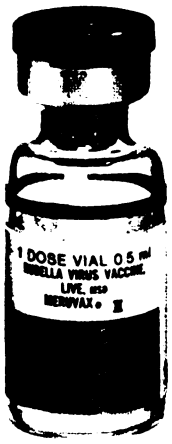
MERCK SHARP & DOHME ANNOUNCES STILL ANOTHER DEVELOPMENT IN IMMUNOLOGY

vaccines containing a new rubella virus strain*

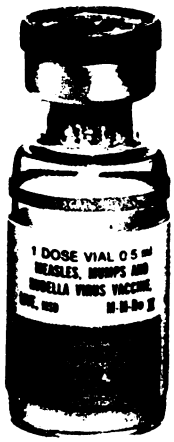
*Wistar Institute RA 27/3 Strain prepared in WI-38 human diploid cells

Now these MSD rubella-containing vaccines offer even greater clinical advantages than other strains of rubella vaccine



NEW SINGLE-DOSE VIALS
MERUVAX® II
(Rubella Virus Vaccine, Live|MSD)

NEW SINGLE-DOSE VIALS
M-R-VAX® II
(Measles and Rubella Virus Vaccine, Live|MSD)



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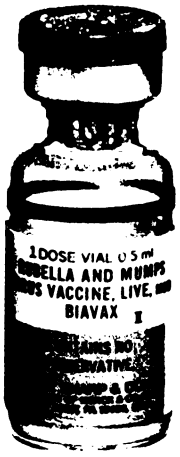
M-M-R® II
(Measles, Mumps and Rubella Virus Vaccine, Live|MSD)



NEW SINGLE-DOSE VIALS
BIAVAX® II
(Rubella and Mumps Virus Vaccine, Live|MSD)

- ☐ higher immediate postvaccination antibody levels
- ☐ broader profile of circulating antibodies
- ☐ more closely simulate immunity induced by natural disease
- ☐ greater resistance to subclinical reinfection with the wild virus

These vaccines are recommended for use at 15 months of age. (MERUVAX® II and BIAVAX® II may be given as early as 12 months if that offers greater convenience in scheduling.)

THE MSD VACCINE SYSTEM:
an integrated system of pediatric vaccines

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

MSD
MERCK SHARP & DOHME

Merck Sharp & Dohme rubella vaccines now contain a new virus strain

Indications: *ATTENUVAX® (Measles Virus Vaccine, Live, Attenuated, MSD)* — Active immunization against measles (rubeola) in children 15 months of age or older.
BIAVAX®-II (Rubella and Mumps Virus Vaccine, Live, MSD) — Simultaneous immunization against rubella and mumps in children 15 months of age to puberty. May be given as early as 12 months if that offers greater convenience in scheduling.
MERUVAX®-II (Rubella Virus Vaccine, Live, MSD) — Immunization against rubella (German measles) in children 15 months of age to puberty. May be given as early as 12 months if that offers greater convenience in scheduling. May be useful for adolescent and adult 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), agrees not to become pregnant for next three months (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®-II (Measles, Mumps and Rubella Virus Vaccine, Live, MSD) — Simultaneous immunization against measles, mumps, and rubella in children 15 months of age to puberty.
M-R-VAX®-II (Measles and Rubella Virus Vaccine, Live, MSD) — Simultaneous immunization against measles (rubeola) and rubella (German measles) in children 15 months of age to puberty.
MUMPSVAX® (Mumps Virus Vaccine, Live, MSD) — Immunization against mumps for children 15 months of age or older and adults. May be given as early as 12 months if that offers greater convenience in scheduling.

Contraindications: Pregnancy or the possibility of pregnancy within three months following vaccination (see special considerations for ATTENUVAX below); hypersensitivity to neomycin; any febrile respiratory illness or other active infection; for measles-containing vaccines, active untreated tuberculosis; therapy with ACTH, corticosteroids (except as replacement therapy, e.g., for Addison's disease), irradiation, alkylating agents, or antimetabolites; blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems; primary immunodeficiency states, including cellular immune deficiencies, hypogammaglobulinemic and dysgammaglobulinemic states.

Hypersensitivity to Eggs, Chicken, or Chicken Feathers: For measles- and/or mumps-containing vaccines, in patients hypersensitive to eggs, chicken, or chicken feathers, weigh benefits of immunization against potential risks of hypersensitivity reactions.

Pregnancy: *ATTENUVAX* — The effects of ATTENUVAX on fetal development are unknown at this time. Live attenuated measles virus vaccine should not be given to persons known to be pregnant; furthermore, pregnancy should be avoided for three months following vaccination. Reports have indicated that natural measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects, and prematurity have been observed subsequent to natural measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects for up to three months following vaccination.
Vaccine administration to postpubertal females entails a potential for inadvertent immunization during pregnancy. Theoretical risks involved should be weighed against the risks that measles poses to the unimmunized adolescent or adult. Advisory committees reviewing this matter have recommended vaccination of postpubertal females who are presumed to be susceptible to measles and not known to be pregnant. If a measles exposure occurs during pregnancy, one should consider the possibility of providing temporary passive immunity through the administration of immune serum globulin (human).

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 that ATTENUVAX, MUMPSVAX, and/or MERUVAX II may be administered simultaneously. BIAVAX II may be administered simultaneously with ATTENUVAX. Monovalent or trivalent poliovirus vaccine, live, oral, may be administered simultaneously with ATTENUVAX and/or MUMPSVAX. Vaccinations should be deferred for at least three months following blood or plasma transfusions or administration of more than 0.02 ml human immune serum globulin per pound of body weight. However, rubella vaccine may be given prior to discharge to susceptible postpartum patients who received blood products, provided that a repeat HI titer is drawn six to eight weeks after vaccination to insure seroconversion; similarly, although rubella vaccine may be given in the immediate postpartum period to those nonimmune women who have received anti-Rh_0 (D) immune globulin (human) without interfering with vaccine effectiveness, a follow-up postvaccination HI titer should also be determined.
Attenuated measles, mumps, and rubella virus vaccines, live, given separately, may result in a temporary depression of tuberculin skin sensitivity; therefore, if a tuberculin test is to be done, it should be administered before or simultaneously with any of these virus vaccines. Vaccination may not result in seroconversion in 100 percent of susceptible subjects.
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 nose and throat has occurred in the majority of susceptible individuals 7 to 28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, is not regarded as a significant risk.

Adverse Reactions: To date, clinical evaluation of the combination vaccines has revealed 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 previously received killed measles vaccine; the combination vaccines were not given under this condition in clinical trials.
Experience from more than 80 million doses of all live measles vaccines given in the U.S. through 1975 indicates that significant central nervous system reactions such as encephalitis and encephalopathy, 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." However, the data suggest the possibility that some of these cases may have been caused by measles vaccines. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with natural measles (one per thousand reported cases). There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of natural measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed, far less than the 5 to 10 cases of SSPE per million cases of natural measles.
Rubella-Containing Vaccines — Adverse reactions include malaise, sore throat, headache, fever, and rash; mild local reactions such as erythema, local pain, induration, tenderness, and regional lymphadenopathy; thrombocytopenia and purpura; allergic reactions such as urticaria; and arthritis, arthralgia that is infrequently associated with signs of inflammation, 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. In children, joint reactions are rare and of brief duration if they do occur. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0–3 percent; women: 12–20 percent), and the reactions tend to be more marked and of longer duration. Rarely, symptoms may persist for a matter of months. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35–45 years), these reactions are generally well tolerated and rarely interfere with normal activities.
Mumps-Containing Vaccines — Parotitis and orchitis. 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.

Shipment, Storage, and Reconstitution: During shipment, to insure that there is no loss of potency, the vaccine must be maintained at a temperature of 10 C (50 F) or less. 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. Use a separate sterile syringe and needle for each individual patient to prevent transmission of infectious agents from one person to another.
Color: The color of the vaccine when reconstituted is yellow. ATTENUVAX is acceptable for use only if clear.

How Supplied: *ATTENUVAX® (Measles Virus Vaccine, Live, Attenuated, MSD)* — Single-dose vials of lyophilized vaccine, containing when reconstituted not less than the equivalent of 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®-II (Rubella and Mumps Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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®-II (Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing not less than the equivalent of 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®-II (Measles, Mumps and Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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®-II (Measles and Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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 with a disposable syringe containing diluent and fitted with a 25-gauge, 5/8" needle, and as a box of 10 single-dose vials 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.

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WHEN INFECTION, AND ITS PAIN, ARE A MATTER OF FACT

RAPID RELIEF IS A MATTER OF

Coly-Mycin® S Otic

WITH NEOMYCIN AND HYDROCORTISONE

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- prompt relief of inflammation, pain, swelling and itching — Hydrocortisone Acetate
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plus, dosage versatility:
5 ml size—often sufficient therapy for unilateral infection; 10 ml size—may be preferable for more severe cases, or bilateral involvement.

See preceding page for prescribing information.

VOLUME 63 • JUNE 1979 • NUMBER 6

Pediatrics

ARTICLES

Liver Replacement for Pediatric Patients

Thomas E. Starzl, M.D., Ph.D., Lawrence J. Koep, M.D., Gerhard P. J. Schröter, M.D., Charles G. Halgrimson, M.D., Kendrick A. Porter, M.D., *and* Richard Weil III, M.D.

From the Departments of Surgery and Pediatrics, the University of Colorado Medical Center, Denver, and the Department of Pathology, St. Mary's Hospital Medical School, London

ABSTRACT. Between March 1963 and January 1978, 74 patients 18 years of age or younger have had liver replacements at the University of Colorado Medical Center, Denver. The most common cause of native liver failure was biliary atresia (48/74, 65%); the second most common cause was chronic aggressive hepatitis (12/74, 16%). Twenty-nine patients (39%) lived for at least one year, and 16 are still alive one to nine years after transplantation. Technical surgical problems, rejection, and infection were the main causes of death. Improved immunosuppression is needed; nevertheless, the quality of life in the long-term survivors has encouraged continuation of this difficult work. *Pediatrics* 63:825–829, 1979, *pediatric, liver, transplantation, surgery.*

Two medical groups have accumulated a preponderance of the world experience in orthotopic liver transplantation (liver replacement), our own, at the University of Colorado Medical Center,[1,2] and the English team headed by Calne and Williams that works at Cambridge University and Kings College in London.[3] The British group has treated very few children because they rarely have had pediatric donors. In addition, they have been fearful of the growth limitation and cosmetic deformity inherent in long-term steroid therapy. Consequently, most of the world experience with pediatric liver transplantation has been from the University of Colorado series. In this report, the results will be given for 74 pediatric recipients (18 years old or younger) who had liver replacement between March 1963 and January 1978. Thus, a minimum potential one-year follow-up is available in every case.

METHODS

Case Material and Indications

The reasons for proceeding are given in Table I. All 74 patients had chronic liver disease. Biliary atresia was the most common diagnosis, accounting for almost twice as many cases as all other diseases combined (Table I). Chronic aggressive hepatitis was the next most common diagnosis. Eight patients had inborn errors of metabolism, including α_1-antitrypsin deficiency, Wilson's disease, tyrosinemia, and type IV glycogen storage disease. It has been established that the enzyme specificity and protein synthetic phenotypes of liver homografts remain permanently those of the donor.[1,3] Thus, any liver-based inborn error of metabolism is potentially curable with liver transplantation.

The appropriate time to recommend liver transplantation required judgment. The predictable and tragic course of victims of biliary atresia usually made it easy to proceed relatively early. However, this situation has been made more ambiguous with the increasing number of patients with successful or partly successful portoenterostomy. In such cases, it has been a technical advantage to have the potential recipient grow

Received February 5; revision accepted for publication March 9, 1979.

ADDRESS FOR REPRINTS: (T.E.S.) Department of Surgery (C-305), University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80262.

preliminary descriptions and supply clinicians with the answers to the many questions that parents ask.

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ACKNOWLEDGMENTS

Jennifer Rathbun, M.D., and Isabel Paret, M.A., assisted in subject recruitment, data collection, and analysis. Thomas Bowe, M.A., assisted in data processing and statistical analysis. Eleanor Macoby, Ph.D., allowed us to use a cohort of her longitudinal study.

Partial support was received from the W. T. Grant Foundation, the Boys Town Center for Youth Development at Stanford, and the Robert Wood Johnson Foundation.

. . . Dr. Kane of Ciba-Geiby [was quoted] as saying that the Anturane Research Team used the *New England Journal of Medicine* as a "court of last resort" in deciding whether to continue their clinical study of the drug after initial results appeared to be so favorable . . . This seems to me to reflect a serious misunderstanding of the role of a scientific publication like the *New England Journal of Medicine* . . . We make no claim to editorial omniscience, nor do we guarantee that everything we publish will stand the test of time. Indeed, we know that much will not, for it is in the nature of medical progress that ideas are being continuously reshaped in the crucible of ongoing research and clinical experience.

Good journals try to facilitate this process by identifying noteworthy contributions from among the great mass of material that now overloads our scientific communications system. Everyone should understand, however, that this evaluating function is not quite the same thing as endorsement.

A.S. RELMAN

From the *New York Times*, March 19, 1978.

PAIN GONE

while the antibiotic gets going

An effective adjuvant to systemic antibiotic treatment, AURALGAN promptly relieves the pain and reduces the inflammation of acute otitis media, while the antibiotic of choice fights the infection.

AURALGAN contains the topical analgesic action of benzocaine and antipyrine plus glycerin dehydrated...a decongestant so hygroscopic that it "blots up" excess moisture through the tympanic membrane, for relief of pressure and pain in the middle ear.

BRIEF SUMMARY

OTITIS MEDIA (ACUTE): AURALGAN is indicated for relief of pain and reduction of inflammation in the congestive and serous stages of acute otitis media. It is effective adjuvant therapy when antibiotics or sulfonamides are administered systemically.

Administration: Otitis media (acute): Instill AURALGAN, permitting the solution to run along the wall of the canal until it is filled. Avoid touching ear with dropper. Then, moisten cotton pledget with AURALGAN and insert into the meatus. Repeat every one to two hours (or three or four times a day).

REMOVAL OF CERUMEN: AURALGAN facilitates the removal of excessive or impacted cerumen.

Administration for Removal of Cerumen: Instill AURALGAN three times daily for two days to help detach cerumen from wall of canal and facilitate removal of plug. Irrigate with warm water.

Note: Keep well closed. Do not rinse dropper after use.

SUPPLIED: No. 1000 – AURALGAN Otic Solution, in package containing 15 ml (1/2 fl oz.) bottle with separate dropper-screw cap attachment

...in acute otitis media

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Each ml contains	
Antipyrine	54.0 mg
Benzocaine	14.0 mg
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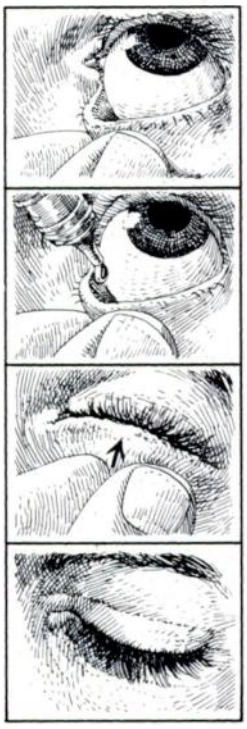
"Pouch" technique quadruples the amount of solution retained in the eye[1]

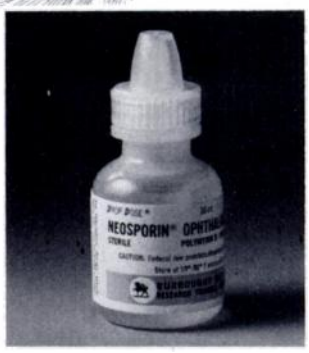


1
Have patient put head back. Gently pull lower eyelid away from eye to make a pouch. Have the patient look up.

2
Put one drop into the cul-de-sac (conjunctival pouch) without touching the eyelid or lashes.

3
Have the patient look down, then gently lift the lower eyelid and make contact with the upper lid.

4
Have patient keep eye closed for one or two minutes so blinking doesn't activate lacrimal pump.



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In a controlled study comparing a variety of common techniques, retention of eye drops on the eye during a five-minute interval went from 16% to 53% when the pouch technique was utilized in the 19- to 30-year-old age group. A 64% retention rate was achieved in the 50- to 60-year-old age group.

See adjacent page for brief prescribing information.

When dentition erupts . . . and discomfort occurs

THERE IS A SAFE AND EFFECTIVE MEDICATION FOR SYMPTOMATIC RELIEF — BABY ORA-JEL®

— a pediatric formulation for relief of teething discomfort.

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Reassurance and Baby Ora-jel

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The topical anesthetic action of Baby Ora-jel is achieved with benzocaine, the efficacy and safety of which has been demonstrated in decades of clinical use. A specially formulated water-miscible gel allows the anesthetic to be readily available to affected tissue. That's why Baby Ora-jel works so quickly and effectively to provide long-lasting relief. Unlike other teething preparations, Baby Ora-jel contains no alcohol or salicylates — ingredients which can irritate sensitive gum tissue.[2,3] And its incidence of sensitization is low.

You can recommend Baby Ora-jel with confidence. When baby feels better, so does mother.

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Div., Del Laboratories, Inc.
Farmingdale, L.I., New York 11735

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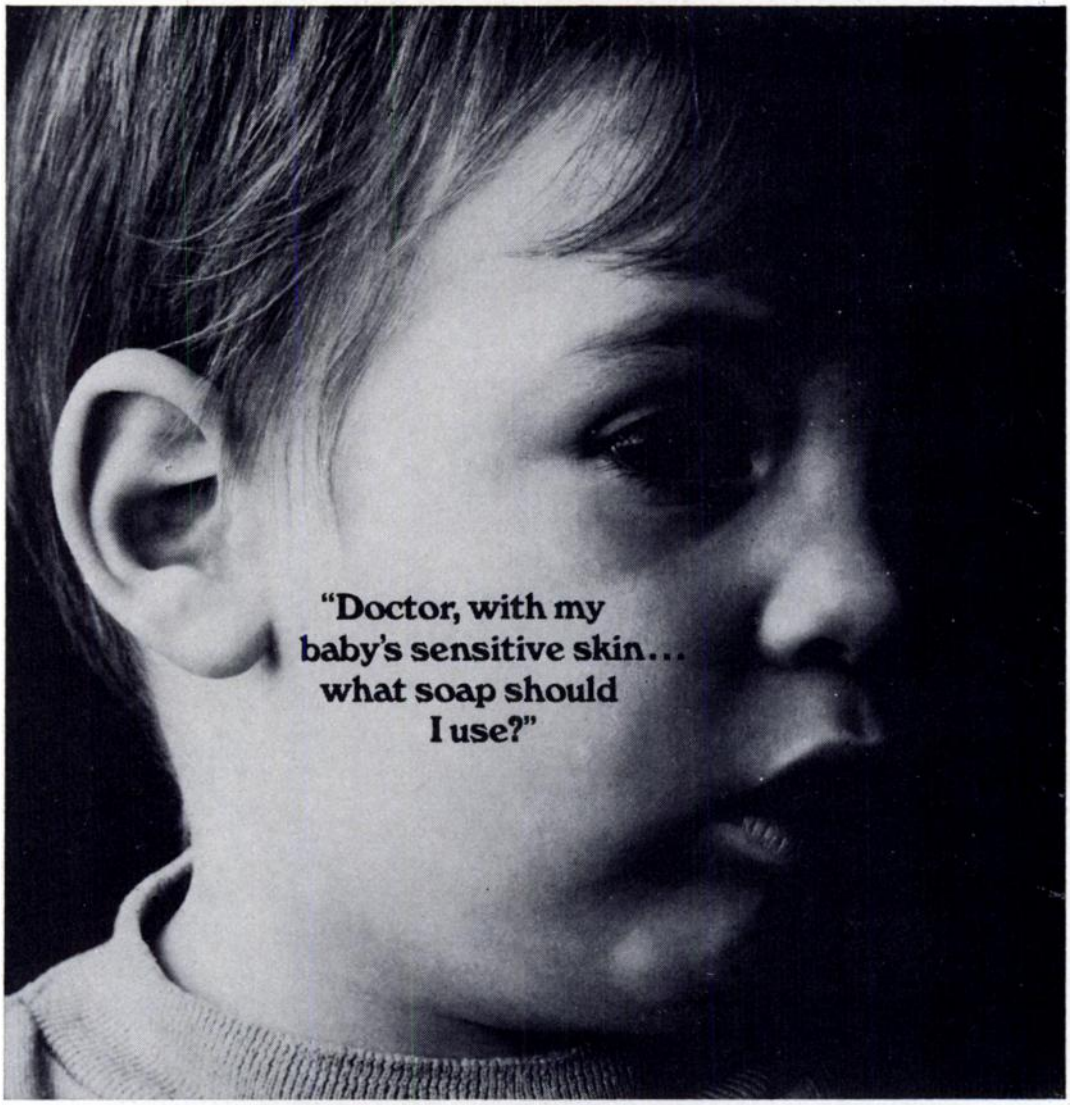

Pure mild Ivory is one of the safest possible soaps you can recommend for sensitive skin. More doctors recommend Ivory than any other soap.

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Most Physicians Have Patients Who Need a Bowel Retraining Program

Introducing the Fleet Bowel Retraining Program

For the Patient Who Needs Bowel Retraining: Immediate Results Without Systemic Involvement.

For the chronically constipated patient, a bowel retraining program may offer a solution to the problem of oral laxative dependence. The Fleet Bowel Retraining Program is excellent in its systematic and physiologic approach which includes the use of diet and exercise combined with the concurrent use of Fleet Enema for a short initial period.

The Fleet Bowel Retraining Program

- Take one Fleet® Enema daily, at intervals of two or three days, until normal defecation reflexes have been re-established. Fleet® Enema combats the oral laxative habit with its physiologic mode of action and lack of oral administration. The enema is known " . . . to cleanse only the distal colon and thus . . . it most nearly approximates, in its results, a normal bowel movement."[1]
- Establish dietary habits that will facilitate regularity. This includes increasing fluid intake and eating such foods as bran, whole grains, leafy vegetables and fruits.
- Increase exercise and activity level. Daily exercise is an important part of the program because it helps maintain good muscle tone throughout the body, including the intestinal tract.

As with any habit that has taken time to develop, chronic constipation can't be changed overnight. During the retraining period, Fleet Enema may be taken at intervals to combat any tendency to lapse back to oral laxatives until good bowel habits are re-established.

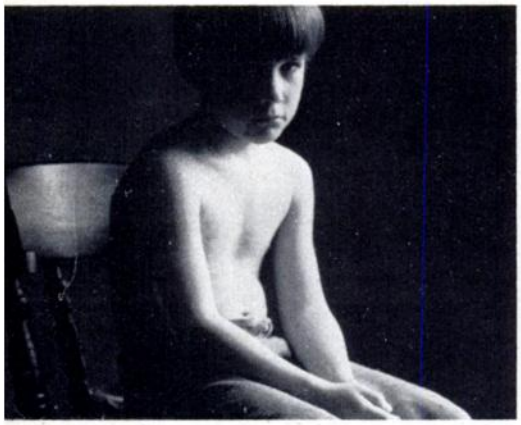
And for the Acute Patient with Immediate Needs: Avoid Oral Laxative Introduction.

When an acutely ill patient needs immediate relief from constipation, you can prescribe an oral laxative for him and his symptoms will be relieved promptly. But you may be needlessly setting him on the road to chronic laxative dependence by unnecessarily involving his whole system. Don't let him get started down that road in the first place.

Think, instead, of recommending a short-term solution. Prescribe Fleet Enema promptly for a short (3-day) period and provide immediate relief without the risk of oral laxative dependence. Fleet Enema now so he won't need retraining later.

- Physiologic Mode of Action
- Not Orally Administered
- No Systemic Involvement

[1]Steinberg H, Almy TP: *Drugs of Choice* 1964–1965, Modell (ed), Saint Louis, C V Mosby Co, 1964, p 351.



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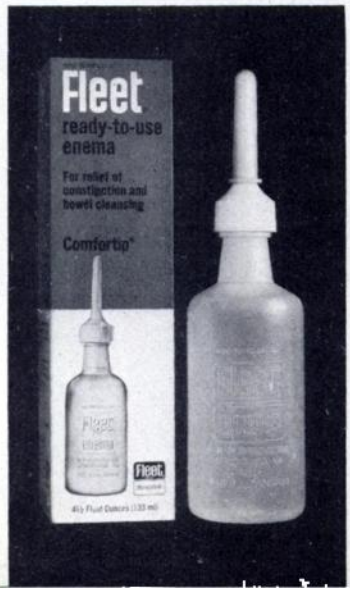

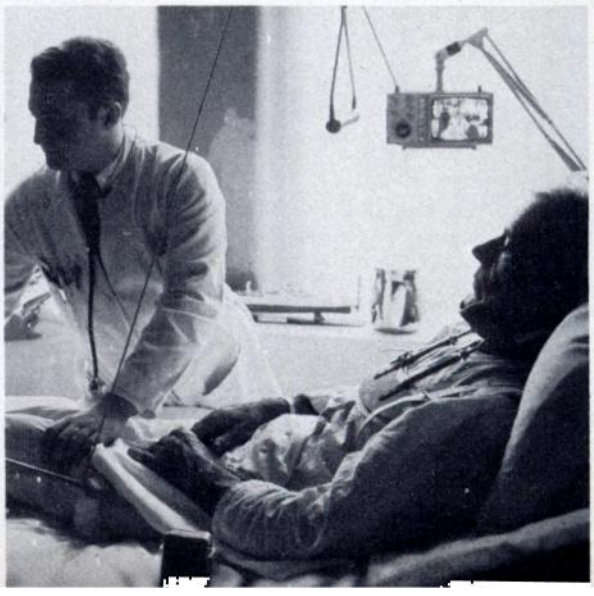

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ACKNOWLEDGMENTS

This research was funded by New York State Health Research Council, contract No. 784.

The authors are grateful to Ms. Jacquelyne Bayer for her help in the preparation of the manuscript, and to Dr. D. Moel and Dr. S. Castells for allowing us to examine their patients.

Therapeutics is the pouring of drugs of which one knows nothing into a patient of whom one knows less.

VOLTAIRE

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ACKNOWLEDGMENTS

Supported by USPHS grant GM 15253, Bureau of Community Health Service, Health Services Administration, Public Health Service, Department of Health, Education, and Welfare Project 913, and National Institutes of Health, grant HD 05961.

We are grateful to Cindy Dolan and Michael Donlan, M.D., Spokane, Washington, who assisted in the evaluation of Family 1, to Albert Schinzel, M.D., and Franz Real of Zürich, Switzerland for the information on Family 2, and to Jane Fowler for invaluable technical assistance.

. . . [There is] semantic confusion . . . [in] language symbols adopted from the medieval church hierarchy. Think of language holdovers like *Dean, Chancellor, Sabbatical, scholarship,* or university *service.* The Dean and the Chancellor not only have nothing to do with religion today; they may very well have nothing to do with scholarship, which in turn, often has nothing to do with intensive study. University service (known in the secular world as going to business meetings) hardly derives today from a faculty longing to serve. Yet despite the continuous erosion of the original meanings of these "old" words, the language remains, clouding the semantic environment of higher education with the image of the professor as public servant, motivated only by devotion to a higher cause, selflessly pursuing Truth—if not for the greater glory of God, then at least for the benfit of man. The professor still does not go off to *work* in the morning; he meets his classes or his seminar. He does not ask his boss for some *time off;* he sees his Dean to request a Sabbatical. It is this force in the semantic environment which has made the patched jacket or the unfashionable skirt the unique status symbol for the college professor.

NANCY M. MCCRACKEN
Submitted by Student

From McCracken NM: The Semantic Environment of Higher Education: Language in the Academic Shop. *Et cetera* 35:37, 1978.

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Keeping pace with advancing medical knowledge is a responsibility of every pediatrician. But scouring the literature for the information that is most relevant to *your* needs can be time-consuming and frustrating. What *you* need is a journal that offers regular information on the latest developments affecting general pediatrics, that emphasizes recognized areas of special interest, that organizes its content to coincide with subjects covered in an overall program of continuing education.

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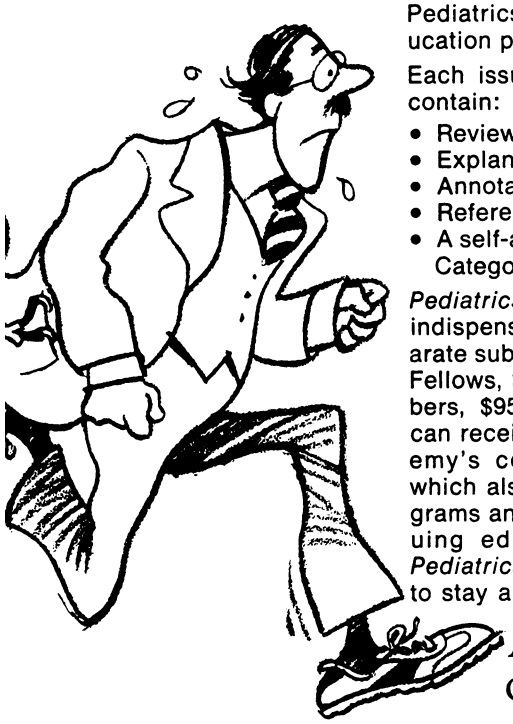

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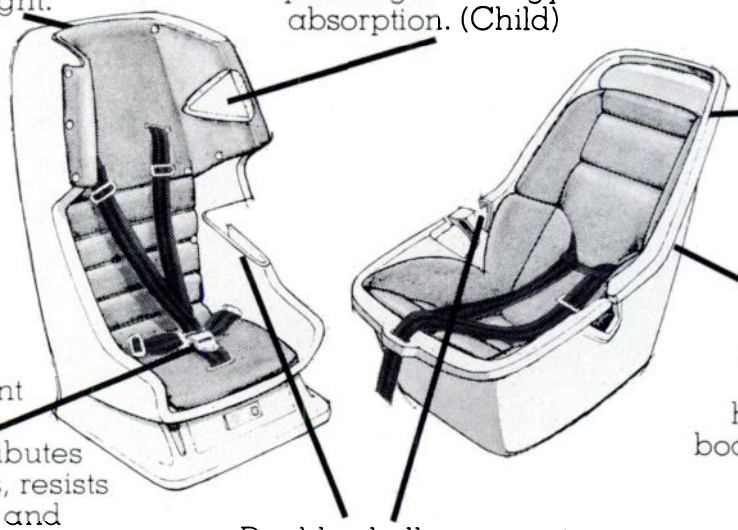

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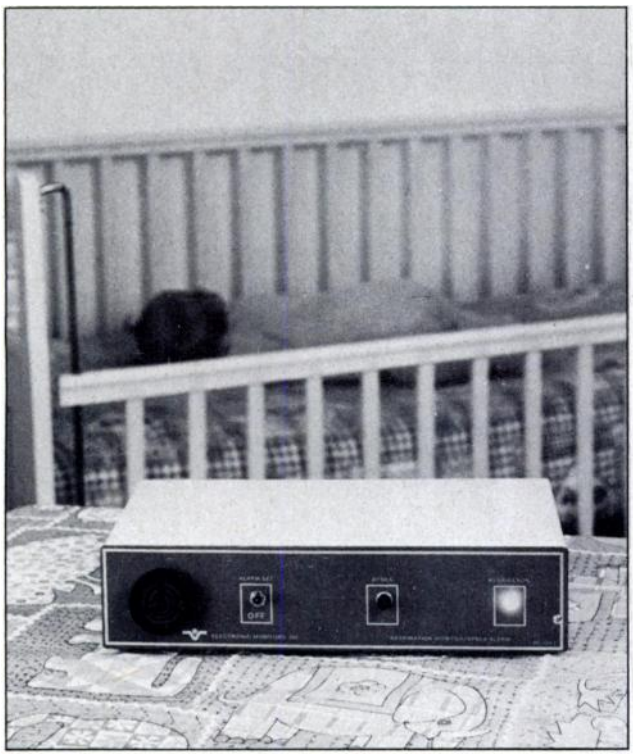

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FOR DEEP INTRAMUSCULAR INJECTION ONLY.

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 penicillin G benzathine.

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 penicillin G benzathine therapy is indicated as prophylaxis:

Rheumatic fever and/or chorea —Prophylaxis with penicillin G benzathine 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 penicillin G benzathine as active ingredient in aqueous suspension): 300,000 units per ml—10-ml multi-dose vial. Each ml 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-ml TUBEX® (sterile cartridge-needle unit) Wyeth, packages of 10.

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

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

2,400,000 units in 4-ml 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
BICILLIN® L-A
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GUESS WHAT PROTECTION HE'LL FORGET TO TAKE.

For rheumatic fever prophylaxis he can't forget:

Injection penicillin G benzathine is the recommended drug of choice* to prevent streptococcal infection and possible recurrence of rheumatic fever. One injection, once a month, of 1,200,000 units usually offers effective and continuous prophylaxis, virtually eliminating the problem of patient compliance.

*Commission on Rheumatic Fever and Bacterial Endocarditis of the Council on Cardiovascular Disease in the Young: "Rheumatic Fever Prevention," 71-006-B. American Heart Association, New York, (Sept.) 1976.

INJECTION
BICILLIN® L-A
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◀ See important information on preceding page.

Send pollen packing...

with effective relief from the symptoms of allergic rhinitis.

- tearing and weeping eyes
- uncomfortable itching around the eyes and nose
- uncontrolled sneezing and runny nose

There's hardly any symptom of allergic rhinitis that can't be helped significantly with Benadryl.

BENADRYL®
(diphenhydramine hydrochloride, USP)

Brief Summary of Prescribing Information

BENADRYL® (diphenhydramine hydrochloride)
INDICATIONS. Benadryl in the oral form is effective for the following indications:

Antihistaminic: For perennial and seasonal (hay fever) allergic rhinitis; vasomotor rhinitis; allergic conjunctivitis due to inhalant allergens and foods; mild, uncomplicated allergic skin manifestations of urticaria and angioedema; amelioration of allergic reactions to blood or plasma; dermatographism; as therapy for anaphylactic reactions *adjunctive* to epinephrine and other standard measures after the acute manifestations have been controlled.

Motion sickness: For active and prophylactic treatment of motion sickness.

Antiparkinsonism: For parkinsonism (including drug-induced extrapyramidal reactions) in the elderly unable to tolerate more potent agents; mild cases of parkinsonism (including drug-induced) in other age groups; in other cases of parkinsonism (including drug-induced) in combination with centrally acting anticholinergic agents.

CONTRAINDICATIONS. Use in Newborn or Premature Infants: This drug should *not* be used in newborn or premature infants.

Use in Nursing Mothers: Because of the higher risk of antihistamines for infants generally, and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Use in Lower Respiratory Disease: Antihistamines *should NOT* be used to treat lower respiratory tract symptoms including asthma.

Antihistamines are also contraindicated in the following conditions.

Hypersensitivity to diphenhydramine hydrochloride and other antihistamines of similar chemical structure.

Monoamine oxidase inhibitor therapy (See Drug Interactions section).

WARNINGS. Antihistamines should be used with considerable caution in patients with narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, bladder-neck obstruction.

Use in Children: In infants and children, especially, antihistamines in *overdosage* may cause hallucinations, convulsions, or death.

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

Use in Pregnancy: Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus.

Use with CNS Depressants: Diphenhydramine hydrochloride has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc).

Use in Activities Requiring Mental Alertness: Patients should be warned about engaging in activities requiring mental alertness such as driving a car or operating appliances, machinery, etc.

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

PRECAUTIONS. Diphenhydramine hydrochloride has an atropine-like action and, therefore, should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension.

DRUG INTERACTIONS. MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

ADVERSE REACTIONS. The most frequent adverse reactions are underscored.

1. *General:* Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat.
2. *Cardiovascular System:* Hypotension, headache, palpitations, tachycardia, extrasystoles.
3. *Hematologic System:* Hemolytic anemia, thrombocytopenia, agranulocytosis.
4. *Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.
5. *GI System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.
6. *GU System:* Urinary frequency, difficult urination, urinary retention, early menses.
7. *Respiratory System:* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

OVERDOSAGE. Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms, dry mouth; fixed, dilated pupils; flushing, and gastrointestinal symptoms may also occur.

If vomiting has not occurred spontaneously the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

If vomiting is unsuccessful gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or 1/2 isotonic saline is the lavage solution of choice.

Saline cathartics, as milk of magnesia, by osmosis draw water into the bowel and, therefore, are valuable for their action in rapid dilution of bowel content.

Stimulants should *not* be used.

Vasopressors may be used to treat hypotension.

HOW SUPPLIED. Supplied in (as) 50 and 25 mg capsules, and Elixir 12.5 mg/5 ml. **WF**

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PHASE II: MEDICAL UPDATE - CLINICAL ENCOUNTERS

Designed for health-care professionals who have extensive pediatric patient care involvement. Presenting a detailed examination of infant feeding practices and infant nutrition, and of the impact of infant nutrition on health in later life.

Phase II will focus specifically on the challenge of communicating effectively with parents.

The Phase II program will build on the data base developed in the earlier program, "Infant Nutrition: A Foundation for Lasting Health?" That program, also produced under an educational grant from Mead Johnson, consisted of pre- and post-program self-assessment tests, a symposium, a Visiting Faculty program, and a Dialogues in Infant Nutrition series.

PROGRAM COMPONENTS:

- Closed-circuit three-hour live televised symposium to be broadcast to physicians in 25 cities across the United States on Wednesday, September 26, 1979.
- Films and monographs based on the televised symposium.
- Visiting Faculty of professors to moderate local meetings using films and monographs.
- Volume II of a newsletter series entitled **Dialogues in Infant Nutrition.**
- **Practitioner's Clinical Viewpoint** — a series of newsletters designed to provide practical tips and information on various aspects of infant nutrition.
- Additional items to aid in communicating infant nutrition recommendations to parents.

PANEL PARTICIPANTS:

- L. J. Filer, Jr., M.D., Ph.D., Chairman
- Jo Anne Brasel, M.D.
- Charles J. Glueck, M.D.
- Malcolm A. Holliday, M.D.
- Barbara Korsch, M.D.
- George M. Owen, M.D.
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Approved by the Committee on Nutrition of the American Academy of Pediatrics.

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or, your Mead Johnson Nutritional Division Representative.

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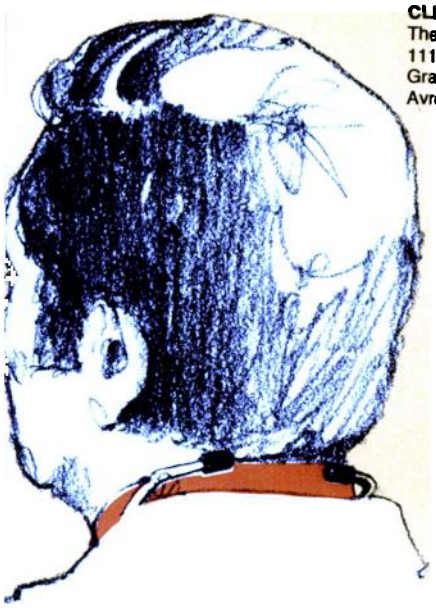
SYMPOSIUM LOCATIONS, MODERATORS, TIME (Wednesday, September 26, 1979)

EASTERN
3 p.m. Registration
4-7 p.m. Program

ATLANTA
Georgia World Congress
285 International Boulevard, N.W.
Rooms #309 and #310
Richard W. Blumberg, M.D.



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Pavilion Ballroom
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Grand Ballroom
Avroy A. Fanaroff, M.D.

DETROIT
Fairlane Manor
19000 Hubbard Drive
Dearborn, Michigan
The Manor Room
Charles F. Whitten, M.D.

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830 W. Market St.
The Ballroom
Floyd W. Denny, Jr., M.D.

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The Hartford Hilton
10 Ford Street
The Grand Ballroom
Robert Schwartz, M.D.

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3-6 p.m. Program

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The Great Hall
Joseph R. Christian, M.D.

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The Ballroom
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Exhibition Hall #3
Stanley Hellerstein, M.D.

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The Forum Ballroom
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The Presidential Room
John Lewy, M.D.

ST. LOUIS
The Breckinridge Pavilion
1 South Broadway
Pavilion Ballroom
James P. Keating, M.D.

MOUNTAIN
1 p.m. Registration
2-5 p.m. Program

DENVER
The Executive Tower Inn
1405 Curtis
The Ballroom
Donough O'Brien, M.D.

PACIFIC
12 Noon Registration
1-4 p.m. Program

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The PSA San Franciscan
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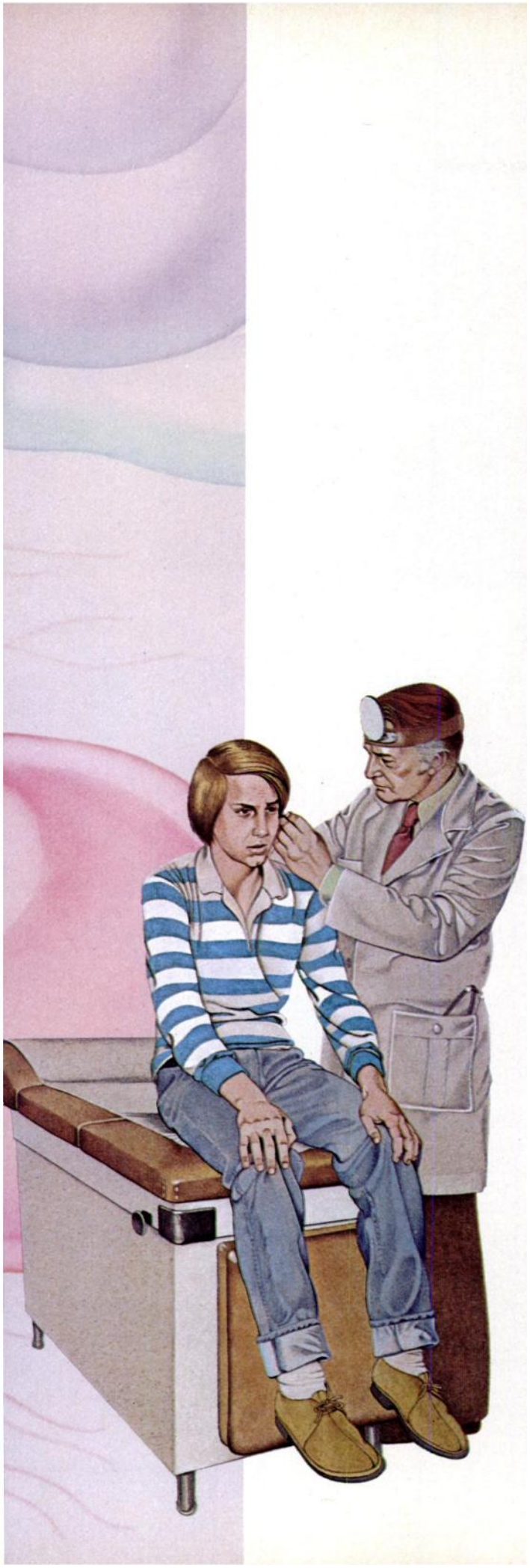
Nonantibiotic VōSoL® HC Otic Solution

(hydrocortisone 1%, acetic acid-nonaqueous 2%)

eliminates Pseudomonas* in otitis externa**

Artist's conception of pathogens most commonly isolated from cultures obtained in a controlled clinical study of acute otitis externa. Size and spatial relationships of organisms have no clinical significance and are not intended to reflect the incidence or virulence of any one organism relative to the others.



A frequent problem in children

"The warm, damp environment of this area (the child's external auditory canal) is conducive to the growth of *Pseudomonas aeruginosa* and other gram-negative bacteria."†

VōSoL HC as effective as Cortisporin®‡ Otic Solution

In a multicenter double-blind randomized study, VōSoL HC and Cortisporin Otic Solution achieved equivalent overall microbial cure rates* and equivalent overall clinical cure rates when *Pseudomonas aeruginosa*, other susceptible bacterial pathogens, *Candida* or *Aspergillus* were initially present, alone or in combination.**

VōSoL HC avoids the potential risks of neomycin and other antibiotics

There have been no reports of allergic cross-reactions with other anti-infective agents... no reports of overgrowth of nonsusceptible bacteria and fungi.

antibacterial/antifungal/anti-inflammatory

VōSoL® HC

(hydrocortisone 1%, acetic acid-nonaqueous 2%)

Otic Solution

*Based on absence of pathogens on repeat cultures, the overall microbial cure rates were 78.9% with VōSoL HC and 81.4% with Cortisporin Otic Solution. Usual duration of treatment was 10 days, but varied from 8 to 14 days.

†Reichelderfer, T.E., and Ziai, M.: The ears, in *Pediatrics*, ed. 2. (Ziai, M., Janeway, C.A., and Cooke, R.E. eds.): Boston, Little, Brown and Company, 1975, pp. 254-259.

‡Registered trademark of Burroughs Wellcome Co.; a combination of polymyxin B, neomycin and hydrocortisone.

**Data on file, Medical Department, Wallace Laboratories, Cranbury, New Jersey 08512.

VōSoL HC Otic Solution is a nonaqueous solution containing hydrocortisone (1%) and acetic acid (2%), in a propylene glycol vehicle containing propylene glycol diacetate (3%), benzethonium chloride (0.02%), sodium acetate (0.015%) and citric acid (0.2%).

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

Indications: For the treatment of superficial infections of the external auditory canal caused by organisms susceptible to the action of the antimicrobial, complicated by inflammation.

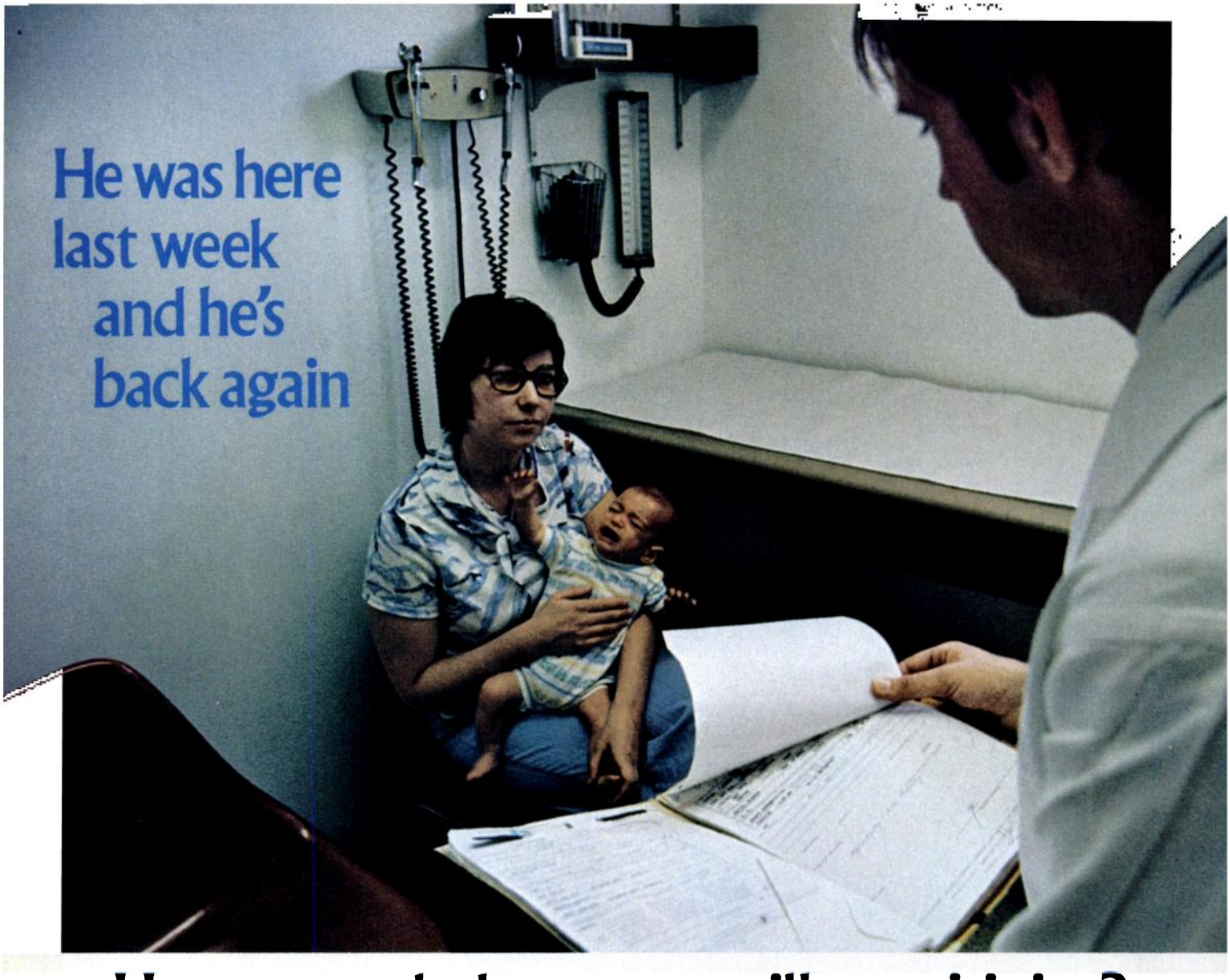
Contraindications: Hypersensitivity to any of the components; perforated tympanic membranes are frequently considered a contraindication. VōSoL HC is also contraindicated in vaccinia and varicella.

Precautions: 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, discontinue promptly.

How Supplied: VōSoL HC, in 10 ml measured-drop, safety-tip plastic bottle.

Issued 5/78

WALLACE LABORATORIES
Division of Carter-Wallace, Inc., Cranbury, New Jersey 08512 WJ 1679



Have you ruled out cow-milk sensitivity?

The physical symptoms are many and varied: diarrhea, colic, eczema, asthma, vomiting, bronchitis, rhinitis. They can be coupled with behavioral symptoms: repeated refusal of the nursing bottle . . . general fussiness.[1-3]

Alone or together, the manifestations of milk sensitivity are an unnecessary burden for the infant . . . and parents. More important, if unchecked the allergic syndromes can lead to failure to thrive and other serious health problems.[4]

With Isomil® Soy Protein Formula you can avoid the symptoms of milk sensitivity and help confirm your initial diagnosis.

Moreover, Isomil promotes normal growth.[2,5] It looks like milk, it pours like milk and has a pleasant aroma, which help insure acceptability. Unlike milk, Isomil is lactose free. It avoids the possibility of prolonged or recurring diarrhea caused by lactose intolerance.

Consider the possibility of milk sensitivity when associated symptoms are presented. "A high index of suspicion" is essential to its prompt detection.[2,6]

References: 1. Rapp, D. J.: Milk Allergy — From Birth to Old Age. Consultant 14:120, 1974. 2. Cowan, C.C., Brownlee, R.C., DeLoache, W.R., Jackson, H.P., and Matthews, J.P.: A Soy Protein Isolate Formula in the Management of Allergy in Infants and Children. South. Med. J. 62:389, 1969. 3. Clein, N.W.: Cow's Milk Allergy in Infants and Children. Int. Arch. Allergy. 13:245, 1958. 4. Goldman, A.S., Anderson, D.W., Sellars, W.A., Saperstein, S., Kniker, W.T., Halpern, S.R.: Milk Allergy. 1. Oral Challenge with Milk and Isolated Milk Proteins in Allergic Children. Ped. 32:425, 1963. 5. Jung AL, Carr SL: A soy protein formula and a milk-based formula. Clin.Ped. 16:982, 1977. 6. Frier, S. and Kletter, B.: Milk Allergy in Infants and Young Children. Clin. Ped. 9:449, 1970.

Switch first to ISOMIL®

Soy Protein Formula

when the baby can't take milk

ROSS LABORATORIES
COLUMBUS, OHIO 43216
Division of Abbott Laboratories, USA

208-B169

A neonatal monitor that begins its job right here.

It can help determine the survival of new life in distress. The 512 Neonatal Monitor is the only instrument available that can gather, display and record vital signs during the neonatal and intrapartum periods.

In your NICU, the 512 records NHR, long and short-term heart rate variability and arterial and central venous blood pressures. It records respiratory waveform with a unique breath-weighting circuit complementing the Apnea alarm system. It displays skin, core and ambient temperatures, allowing calculation of two delta temperatures.

Ordered with optional delivery room capability, the 512 additionally displays and records FHR. It also measures uterine activity and alerts for FHR bradycardia, tachycardia and decreased heart-rate variability.

The Corometrics 512 Neonatal Monitor. Like yourself, it gives your patient its undivided attention. For additional information contact: Corometrics Medical Systems, Inc., 61 Barnes Park Road North, Wallingford, Connecticut U.S.A. 06492, (203) 265-5631.

COROMETRICS MEDICAL SYSTEMS, INC. *Because new life can't tell you its problems.*

This label shows why 90% of pediatricians want Jimmy to eat a baby food like Beech-Nut®.

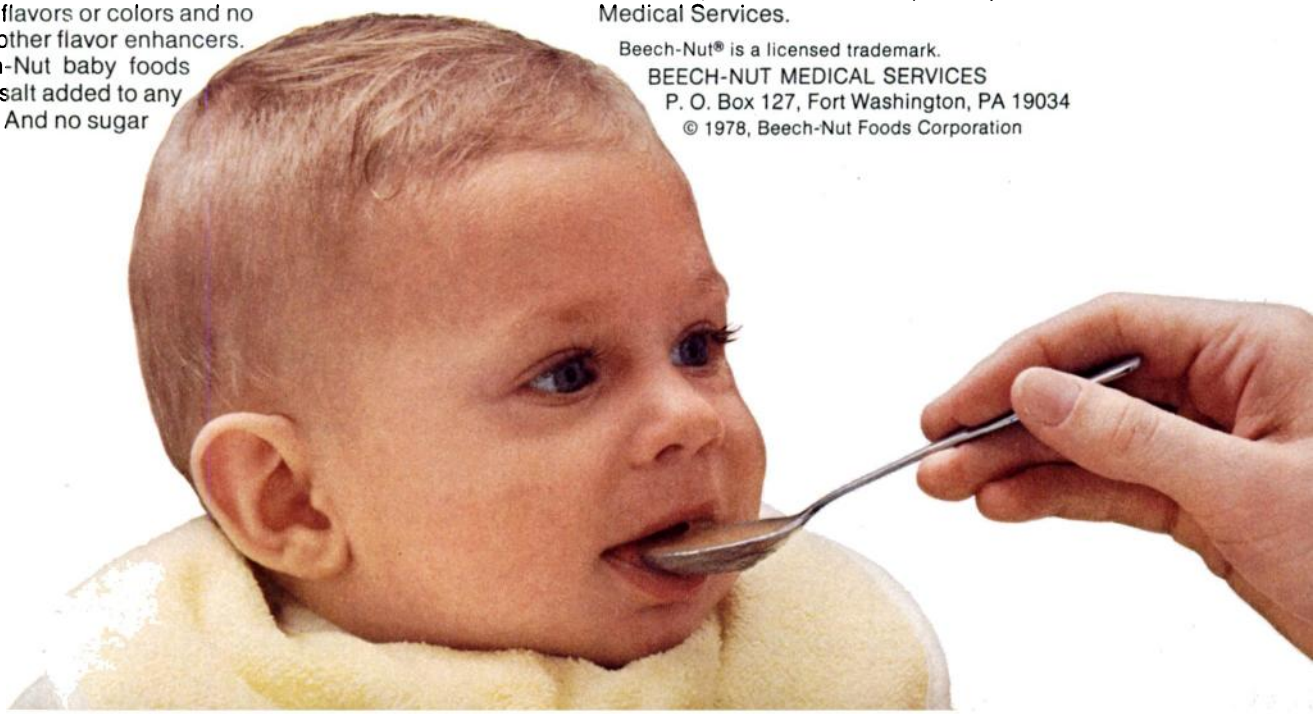
A recent national survey* was conducted to determine pediatricians' attitudes toward homemade and commercially prepared baby foods. *The results:* 9 out of 10 pediatricians preferred a baby food with no salt added—and no sugar added to most foods. These same pediatricians also preferred baby foods with no preservatives added, no artificial flavors or colors and no MSG or other flavor enhancers.

Beech-Nut baby foods have no salt added to any product. And no sugar added to most. And, of course, Beech-Nut contains no artificial colors, artificial flavors, MSG or other flavor enhancers.

No wonder 90% of pediatricians want Jimmy to eat a baby food like Beech-Nut.

*Survey results available upon request from Beech-Nut Medical Services.

BEECH-NUT MEDICAL SERVICES
P. O. Box 127, Fort Washington, PA 19034



NEW

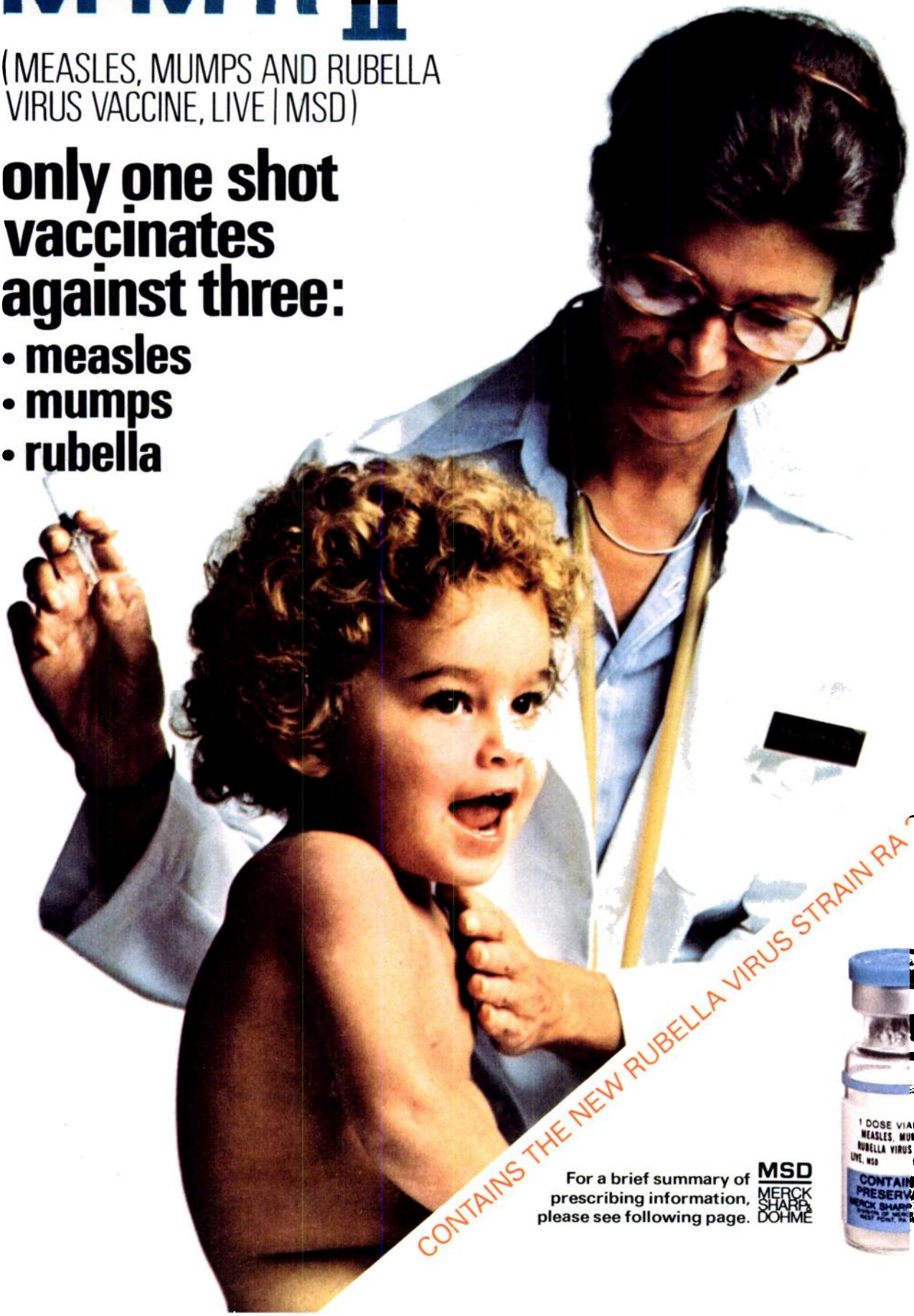
Single-Dose Vials

M-M-R® II

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

only one shot vaccinates against three:

- measles
- mumps
- rubella



CONTAINS THE NEW RUBELLA VIRUS STRAIN RA 27/3

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

MSD
MERCK SHARP & DOHME

Merck Sharp & Dohme rubella vaccines now contain a new virus strain

Indications: *ATTENUVAX® (Measles Virus Vaccine, Live, Attenuated, MSD)* — Active immunization against measles (rubeola) in children 15 months of age or older.

BIAVAX®II (Rubella and Mumps Virus Vaccine, Live, MSD) — Simultaneous immunization against rubella and mumps in children 15 months of age to puberty. May be given as early as 12 months if that offers greater convenience in scheduling.

MERUVAX®II (Rubella Virus Vaccine, Live, MSD) — Immunization against rubella (German measles) in children 15 months of age to puberty. May be given as early as 12 months if that offers greater convenience in scheduling. May be useful for adolescent and adult 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), agrees not to become pregnant for next three months (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®II (Measles, Mumps and Rubella Virus Vaccine, Live, MSD) — Simultaneous immunization against measles, mumps, and rubella in children 15 months of age to puberty.

M-R-VAX®II (Measles and Rubella Virus Vaccine, Live, MSD) — Simultaneous immunization against measles (rubeola) and rubella (German measles) in children 15 months of age to puberty.

MUMPSVAX® (Mumps Virus Vaccine, Live, MSD) — Immunization against mumps for children 15 months of age or older and adults. May be given as early as 12 months if that offers greater convenience in scheduling.

Contraindications: Pregnancy or the possibility of pregnancy within three months following vaccination (see special considerations for ATTENUVAX below); hypersensitivity to neomycin; any febrile respiratory illness or other active infection; for measles-containing vaccines, active untreated tuberculosis; therapy with ACTH, corticosteroids (except as replacement therapy, e.g., for Addison's disease), irradiation, alkylating agents, or antimetabolites; blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems; primary immunodeficiency states, including cellular immune deficiencies, hypogammaglobulinemic and dysgammaglobulinemic states.

Hypersensitivity to Eggs, Chicken, or Chicken Feathers: For measles- and/or mumps-containing vaccines, in patients hypersensitive to eggs, chicken, or chicken feathers, weigh benefits of immunization against potential risks of hypersensitivity reactions.

Pregnancy: *ATTENUVAX* — The effects of ATTENUVAX on fetal development are unknown at this time. Live attenuated measles virus vaccine should not be given to persons known to be pregnant; furthermore, pregnancy should be avoided for three months following vaccination. Reports have indicated that natural measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects, and prematurity have been observed subsequent to natural measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects for up to three months following vaccination.

Vaccine administration to postpubertal females entails a potential for inadvertent immunization during pregnancy. Theoretical risks involved should be weighed against the risks that measles poses to the unimmunized adolescent or adult. Advisory committees reviewing this matter have recommended vaccination of postpubertal females who are presumed to be susceptible to measles and not known to be pregnant. If a measles exposure occurs during pregnancy, one should consider the possibility of providing temporary passive immunity through the administration of immune serum globulin (human).

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 that ATTENUVAX, MUMPSVAX, and/or MERUVAX II may be administered simultaneously. BIAVAX II may be administered simultaneously with ATTENUVAX. Monovalent or trivalent poliovirus vaccine, live, oral, may be administered simultaneously with ATTENUVAX and/or MUMPSVAX. Vaccinations should be deferred for at least three months following blood or plasma transfusions or administration of more than 0.02 ml human immune serum globulin per pound of body weight. However, rubella vaccine may be given prior to discharge to susceptible postpartum patients who received blood products, provided that a repeat HI titer is drawn six to eight weeks after vaccination to insure seroconversion; similarly, although rubella vaccine may be given in the immediate postpartum period to those nonimmune women who have received anti-Rh_0 (D) immune globulin (human) without interfering with vaccine effectiveness, a follow-up postvaccination HI titer should also be determined.

Attenuated measles, mumps, and rubella virus vaccines, live, given separately, may result in a temporary depression of tuberculin skin sensitivity; therefore, if a tuberculin test is to be done, it should be administered before or simultaneously with any of these virus vaccines. Vaccination may not result in seroconversion in 100 percent of susceptible subjects.

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 nose and throat has occurred in the majority of susceptible individuals 7 to 28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, is not regarded as a significant risk.

Adverse Reactions: To date, clinical evaluation of the combination vaccines has revealed 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 previously received killed measles vaccine; the combination vaccines were not given under this condition in clinical trials.

Experience from more than 80 million doses of all live measles vaccines given in the U.S. through 1975 indicates that significant central nervous system reactions such as encephalitis and encephalopathy, 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." However, the data suggest the possibility that some of these cases may have been caused by measles vaccines. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with natural measles (one per thousand reported cases). There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of natural measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed, far less than the 5 to 10 cases of SSPE per million cases of natural measles.

Rubella-Containing Vaccines — Adverse reactions include malaise, sore throat, headache, fever, and rash; mild local reactions such as erythema, local pain, induration, tenderness, and regional lymphadenopathy; thrombocytopenia and purpura; allergic reactions such as urticaria; and arthritis, arthralgia that is infrequently associated with signs of inflammation, 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. In children, joint reactions are rare and of brief duration if they do occur. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0–3 percent; women: 12–20 percent), and the reactions tend to be more marked and of longer duration. Rarely, symptoms may persist for a matter of months. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35–45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

Mumps-Containing Vaccines — Parotitis and orchitis. 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.

Shipment, Storage, and Reconstitution: During shipment, to insure that there is no loss of potency, the vaccine must be maintained at a temperature of 10 C (50 F) or less. 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. Use a separate sterile syringe and needle for each individual patient to prevent transmission of infectious agents from one person to another.

Color: The color of the vaccine when reconstituted is yellow. ATTENUVAX is acceptable for use only if clear.

How Supplied: *ATTENUVAX® (Measles Virus Vaccine, Live, Attenuated, MSD)* — Single-dose vials of lyophilized vaccine, containing when reconstituted not less than the equivalent of 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®II (Rubella and Mumps Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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®II (Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing not less than the equivalent of 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®II (Measles, Mumps and Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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®II (Measles and Rubella Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, 0.5 ml when reconstituted as directed and containing 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.

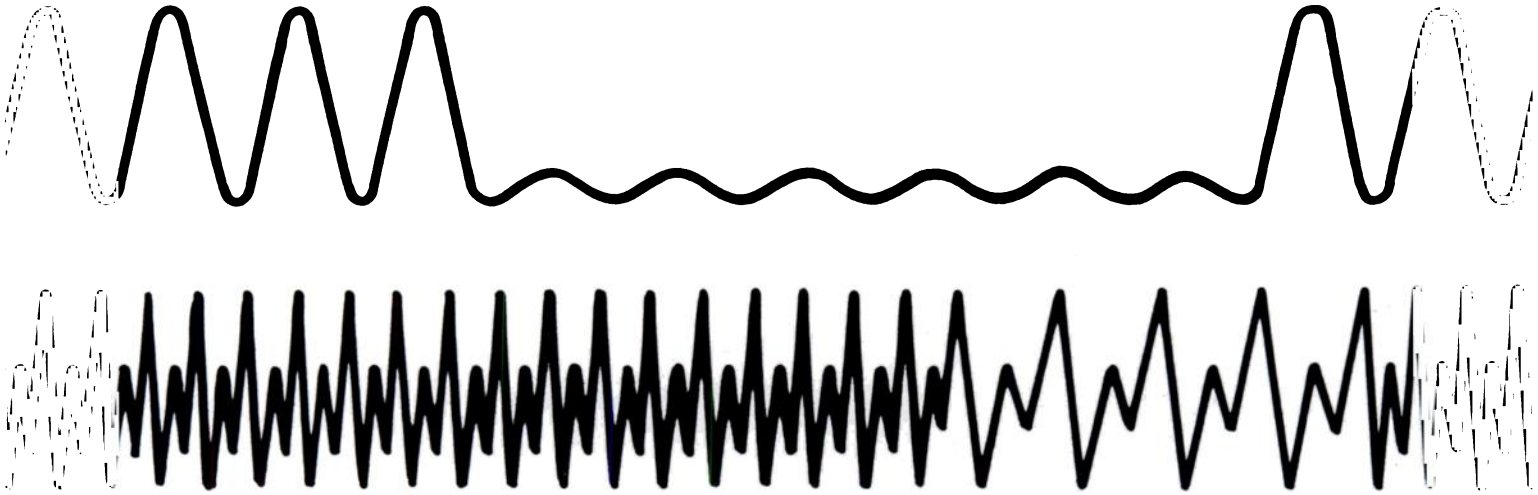
MUMPSVAX® (Mumps Virus Vaccine, Live, MSD) — Single-dose vials of lyophilized vaccine, containing when reconstituted not less than 5,000 $TCID_{50}$ of mumps virus vaccine expressed in terms of the assigned titer of the FDA Reference Mumps Virus, and approximately 25 mcg neomycin.

Each of these vaccines is supplied as a single-dose vial with a disposable syringe containing diluent and fitted with a 25-gauge, ⅝" needle, and as a box of 10 single-dose vials 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.

J7MM02R3

MSD
MERCK SHARP & DOHME



The PCG™ Pneumo-CardioGram Recording: An advanced technique for detecting and quantitating periods of apnea and/or bradycardia.

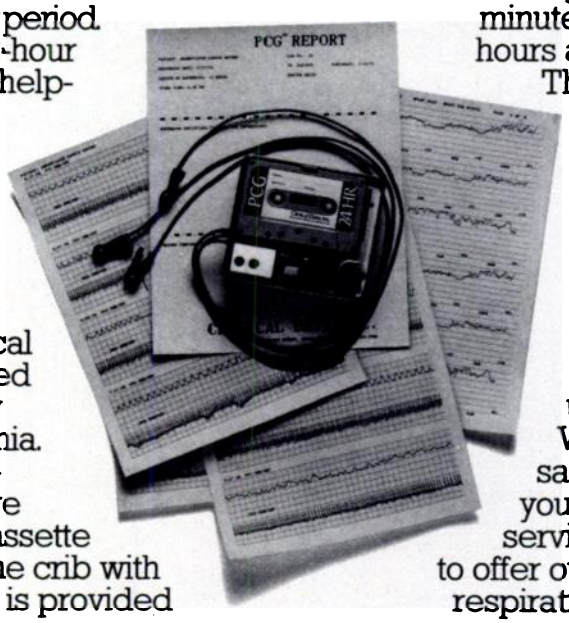
Two years ago Clinical Data introduced the Pediatric Pneumogram[1] – a continuous recording of respiration.

Now we introduce the Pneumo-CardioGram – an advanced technique for recording respiration and ECG simultaneously for a 12 or 24 hour period.

The timeliness of a 12-hour recording is especially helpful in evaluating and documenting the effectiveness of pharmacological intervention, such as theophylline or caffeine. A 24-hour recording provides more data to analyze the clinical significance of suspected apneic periods and any accompanying arrhythmia.

The recording is performed using a miniature battery-operated FM cassette recorder which sits in the crib with the infant. The recorder is provided at no capital expense, and provides continuous data over a 12 or 24 hour period.

To speed the processing of the data, we offer you a Telephone Transmission Unit (TTU™) which transmits the data to our reviewing and reporting center in minutes. Our facilities operate 24 hours a day, seven days a week. There, trained medical personnel using a proprietary computer-assisted playback system review the entire recording, and identify apneic episodes and arrhythmia. A verbal report is telephoned to you immediately and a printed report follows, usually within 24 hours. We'll gladly send you a sample PCG Report to show you how helpful this unique service can be. (We continue to offer our PPG™ recording for respiration only.) Call us toll free 800-225-9180.



Clinical Data, Inc.

1371 Beacon Street, Brookline, Massachusetts 02146

1. Stein IM, et al: The Pediatric Pneumogram: *A New Method for Detecting and Quantitating Apnea in Infants. Pediatrics 55: No. 5, 1975.*

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the quickest, easiest and safest way to circumcise newborns

Plastibell®
circumcision device

NO POST-OPERATIVE CARE. A sterile ligature seals off blood vessels, reducing possibility of hemorrhage and infection. No dressings or post-op care needed. Bell drops off naturally, usually after 5-8 days, leaving a clean, healed line of excision.

SAVES TIME AND MONEY. The entire procedure, properly performed, takes 3 minutes ...or less. Disposability of the device simplifies clean-up and eliminates a potential source of cross-infection.

The Plastibell device is now available also in a sterile, disposable tray that contains all necessary softgoods and instruments designed especially for infant circumcision.

Write for free samples, prices and literature.

HOLLISTER®

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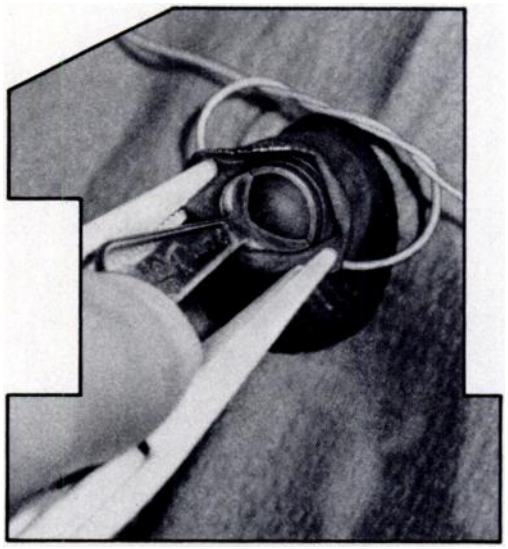
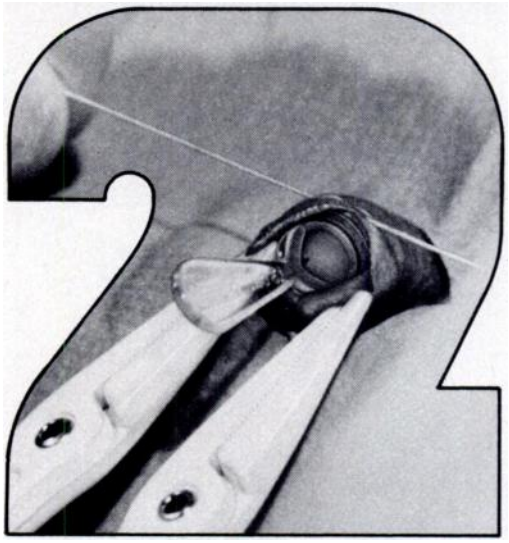


Make a short dorsal slit and free up adhesions. Place Plastibell device over glans inside foreskin.



Firmly tie ligature about the bell so it tightly compresses foreskin into groove.

Trim off excess foreskin distal to ligature. Break off handle.

To help you treat patients with multiple seizure types where absence occurs

Depakene®

Valproic Acid

Capsules 250 mg;
Syrup 250 mg/5 ml.

Add to your regimen in mixed seizures with absence

There's more to Depakene than just primary treatment for pure absence.

True, Depakene has worked gratifyingly well for such patients. The vast majority have seen a dramatic reduction in their seizures. Many have attained total freedom from seizures.

Nevertheless we urge you not to overlook the remarkable effectiveness of Depakene also in mixed seizures with absence.

Use in mixed grand mal or minor motor + absence

Depakene is indicated adjunctively in any multiple seizure type which includes absence.

Clinical opinion has been particularly encouraging among patients with generalized tonic-clonic attacks, or with minor motor seizures (e.g., myoclonic movements, akinetic seizures), where combined with absence or petit mal.

For example, in 16 studies[1] of patients with mixed grand mal and absence, 71% of all patients gained significant improvement.

1. Pinder, R.M., et al., *Drugs* 13:81, 1977.

How to add Depakene
(Valproic Acid)

Avoid high-dose side effects and improve control by adding Depakene, instead of pushing your usual starting agent to maximal levels. Observe recommendations for adjunctive use. Allow 6 weeks for evaluation.

After seizures are controlled, consider careful reduction of the other agent(s). Seek maintenance with lowest effective dosage and fewest drugs.

If side effects occur

Possible initial nausea is best managed by mealtime administration. Use of the syrup may help. Most instances are self-limiting and transient.

More serious problems are infrequent. Rise in liver enzymes has occurred. Fatal hepatic coma has been seen, usually in patients on concomitant agents; hence liver function should be tested regularly. Platelets should also be monitored: thrombocytopenia has been noted.

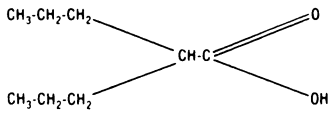
Of particular interest, Depakene has *not* been associated with hirsutism or gum hyperplasia. In some instances where Depakene has permitted phenytoin to be withdrawn, pre-existing gum overgrowth has remitted.

See overleaf for brief summary of prescribing information

9023309R

Depakene®
Valproic Acid

DESCRIPTION
DEPAKENE (valproic acid) is a carboxylic acid designated as 2-propylpentanoic acid. It is also known as dipropylacetic acid. DEPAKENE has the following structure:



Valproic acid (pKa 4.95) has a molecular weight of 144 and occurs as a colorless liquid with a characteristic odor. It is slightly soluble in water (1.3 mg/ml) and very soluble in organic solvents.

DEPAKENE is supplied as soft elastic capsules and syrup for oral administration.

CLINICAL PHARMACOLOGY
DEPAKENE is an anticonvulsant agent which is chemically unrelated to other drugs used to treat seizure disorders. It has no nitrogen or aromatic moiety characteristic of other anticonvulsant drugs. The mechanism by which DEPAKENE exerts its anticonvulsant effects has not been established. It has been suggested that its activity is related to increased brain levels of gamma-aminobutyric acid (GABA). The effect on the neuronal membrane is unknown.

DEPAKENE is rapidly absorbed after oral administration. Peak serum levels of valproic acid occur approximately one to four hours after a single oral dose of DEPAKENE. The serum half-life ($t_{1/2}$) of the parent compound is approximately eight to twelve hours. A slight delay in initial absorption occurs when the drug is administered with meals but this does not affect the total absorption.

A good correlation has not been established between daily dose, serum level and therapeutic effect. Valproic acid is rapidly distributed and the drug is strongly bound (90%) to human plasma proteins.

Elimination of DEPAKENE and its metabolites occurs principally in the urine, with minor amounts in the feces and expired air. Very little unmetabolized parent drug is excreted in the urine. The drug is primarily metabolized in the liver and is excreted as the glucuronide conjugate. Other metabolites in the urine are products of beta and omega oxidation (C-3 and C-5 position). The three major oxidative metabolites are 2-propyl-3-keto-pentanoic acid, 2-propyl-5-hydroxypentanoic acid, and 2-propyl-glutaric acid.

INDICATIONS
DEPAKENE (valproic acid) is indicated for use as sole and adjunctive therapy in the treatment of simple and complex absence seizures, including petit mal. DEPAKENE may also be used adjunctively in patients with multiple seizure types which include absence seizures.

In accordance with the International Classification of Seizures, simple absence is defined as very brief clouding of the sensorium or loss of consciousness (lasting usually 2-15 seconds), accompanied by certain generalized epileptic discharges without other detectable clinical signs. Complex absence is the term used when other signs are also present.

CONTRAINDICATIONS
DEPAKENE (valproic acid) is contraindicated in patients with known hypersensitivity to the drug.

WARNINGS
Liver dysfunction including hepatic failure resulting in fatalities has occurred in a few patients receiving DEPAKENE and concomitant anticonvulsant drugs. These incidences have occurred during the first six months of treatment with DEPAKENE. Although a causal relationship has not been established, liver function tests should be performed prior to therapy and every two months thereafter. Caution should be observed when administering DEPAKENE to patients with pre-existing hepatic disease.

Usage in Pregnancy: THE EFFECTS OF DEPAKENE IN HUMAN PREGNANCY ARE UNKNOWN. ANIMAL STUDIES HAVE DEMONSTRATED TERATOGENICITY.

Studies in rats demonstrated placental transfer of the drug. Doses greater than 65 mg/kg/day given to rats, mice and rabbits produced an increased incidence of skeletal abnormalities of the ribs, vertebrae and palate. In rats, there was a dose-related delay in onset of parturition. Postnatal growth and survival of the progeny was unaffected. Embryolethality or major developmental abnormalities occurred in rats and rabbits at doses of 350 mg/kg/day. Studies are being conducted to determine whether there are differences in the toxicity of DEPAKENE (valproic acid) in pregnant rabbits when compared to non-pregnant rabbits.

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

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic 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 major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

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

PRECAUTIONS
General: Because of rare reports of platelet aggregation dysfunction, thrombocytopenia and elevated liver enzymes, liver function tests, platelet counts and bleeding time determination are recommended before initiating therapy and at periodic intervals.

Since DEPAKENE (valproic acid) may interact with concurrently administered anticonvulsant drugs, periodic serum level determinations of concomitant anticonvulsant drugs are recommended during the early course of therapy. (See Drug Interactions).

DEPAKENE is partially eliminated in the urine as a ketone containing metabolite which may lead to a false interpretation of the urine ketone test.

Information For Patients: Since DEPAKENE may produce CNS depression, especially when combined with another CNS depressant (e.g., alcohol), patients should be advised not to engage in hazardous occupations, such as driving an automobile or operating dangerous machinery, until it is known that they do not become drowsy from the drug.

Drug Interactions: DEPAKENE may potentiate the CNS depressant activity of alcohol.

THERE IS EVIDENCE THAT DEPAKENE MAY CAUSE AN INCREASE IN SERUM PHENOBARBITAL LEVELS, ALTHOUGH THE MECHANISM OF THE INTERACTION IS UNKNOWN. ALL PATIENTS RECEIVING CONCOMITANT BARBITURATE THERAPY SHOULD BE CLOSELY MONITORED FOR NEUROLOGICAL TOXICITY, SERUM BARBITURATE DRUG LEVELS OBTAINED, IF POSSIBLE, AND THE BARBITURATE DOSAGE DECREASED, IF APPROPRIATE.

THERE IS CONFLICTING EVIDENCE REGARDING THE INTERACTION OF DEPAKENE WITH PHENYTOIN. IT IS NOT KNOWN IF THERE IS A CHANGE IN UNBOUND (FREE) PHENYTOIN SERUM CONCENTRATIONS. THE DOSAGE OF PHENYTOIN SHOULD BE ADJUSTED AS REQUIRED BY THE CLINICAL SITUATION.

THE CONCOMITANT USE OF VALPROIC ACID AND CLONAZEPAM MAY PRODUCE ABSENCE STATUS.

Caution is recommended when DEPAKENE (valproic acid) is administered with drugs affecting coagulation, e.g., aspirin and warfarin. (See ADVERSE REACTIONS).

Carcinogenesis, Mutagenesis: There has been insufficient study of the drug in animals to determine whether it has carcinogenic potential. Carcinogenicity studies in rats and mice are currently in progress.

Mutagenesis studies on DEPAKENE have been performed using bacterial and mammalian systems. These studies have provided no evidence of a mutagenic potential for DEPAKENE.

Pregnancy: See WARNINGS.

Nursing Mothers: DEPAKENE is excreted in breast milk. It is not known what effect this would have on a nursing infant. As a general rule, nursing should not be undertaken while a patient is receiving DEPAKENE.

Fertility: Chronic toxicity studies in juvenile and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at doses greater than 350 mg/kg/day in rats and greater than 90 mg/kg/day in dogs. THE EFFECT OF DEPAKENE (VALPROIC ACID) ON THE DEVELOPMENT OF THE TESTES AND ON SPERM PRODUCTION AND FERTILITY IN HUMANS IS UNKNOWN.

ADVERSE REACTIONS
Since DEPAKENE (valproic acid) has usually been used with other anticonvulsant drugs, it is not possible, in most cases, to determine whether the following adverse reactions can be ascribed to DEPAKENE alone, or the combination of drugs.

Gastrointestinal: The most commonly reported side effects at the initiation of therapy are nausea, vomiting and indigestion. These effects are usually transient and rarely require discontinuation of therapy. Diarrhea, abdominal cramps and constipation have been reported. Both anorexia with some weight loss and increased appetite with weight gain have also been reported.

CNS Effects: Sedative effects have been noted in patients receiving valproic acid alone but are found most often in patients receiving combination therapy. Sedation usually disappears upon reduction of other anticonvulsant medication. Ataxia, headache, nystagmus, diplopia, asterixis, "spots before eyes", tremor, dysarthria, dizziness, and incoordination have rarely been noted. Rare cases of coma have been noted in patients also on phenobarbital.

Dermatologic: Transient increases in hair loss have been observed. Skin rash and petechiae have rarely been noted.

Psychiatric: Emotional upset, depression, psychosis, aggression, hyperactivity and behavioral deterioration have been reported.

Musculoskeletal: Weakness has been reported.

Hematopoietic: Valproic acid inhibits the secondary phase of platelet aggregation. (See Drug Interactions). This may be reflected in altered bleeding time. Relative lymphocytosis and mild thrombocytopenia have also been noted in isolated cases. Leukopenia has been reported.

Hepatic: Increases in serum alkaline phosphatase and elevations of serum glutamic oxaloacetic transaminase (SGOT) have been noted. Isolated cases of severe hepatotoxicity have been reported. (See WARNINGS).

OVERDOSAGE
A single case of overdosage with valproic acid has been reported. After ingesting 36 grams in combination with phenobarbital and phenytoin, the patient presented in deep coma. An electroencephalogram recorded diffuse slowing, compatible with the state of consciousness. The patient made an uneventful recovery.

Since DEPAKENE is absorbed very rapidly, gastric lavage may be of limited value. General supportive measures should be applied with particular attention being given to the maintenance of adequate urinary output.

DOSAGE AND ADMINISTRATION
DEPAKENE (valproic acid) is administered orally. The recommended initial dose is 15 mg/kg/day increasing at one week intervals by 5 to 10 mg/kg/day, until seizures are controlled or side effects preclude further increases. The maximum recommended dosage is 30 mg/kg/day. If the total daily dose exceeds 250 mg, it should be given in a divided regimen.

The following table is a guide for the initial daily dose of DEPAKENE (valproic acid) (15 mg/kg/day):

Weight (kg)	Weight (lb)	Total Daily Dose (mg)	Number of Capsules or Teaspoonfuls of Syrup Dose 1	Dose 2	Dose 3
10 — 24.9	22 — 54.9	250	0	0	1
25 — 39.9	55 — 87.9	500	1	0	1
40 — 59.9	88 — 131.9	750	1	1	1
60 — 74.9	132 — 164.9	1,000	1	1	2
75 — 89.9	165 — 197.9	1,250	2	1	2

As the DEPAKENE dosage is titrated upward, blood levels of phenobarbital and/or phenytoin may be affected. (See PRECAUTIONS).

Patients who experience G.I. irritation may benefit from administration of the drug with food or by slowly building up the dose from an initial low level.

THE CAPSULES SHOULD BE SWALLOWED WITHOUT CHEWING TO AVOID LOCAL IRRITATION OF THE MOUTH AND THROAT.

HOW SUPPLIED
DEPAKENE (valproic acid) is available as orange-colored soft gelatin capsules of 250 mg valproic acid in bottles of 100 capsules (**NDC** 0074-5681-13), and as a red syrup containing the equivalent of 250 mg valproic acid per 5 ml as the sodium salt in bottles of 16 ounces (**NDC** 0074-5682-16).

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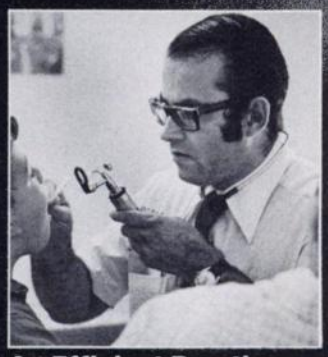

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