MAY 1986

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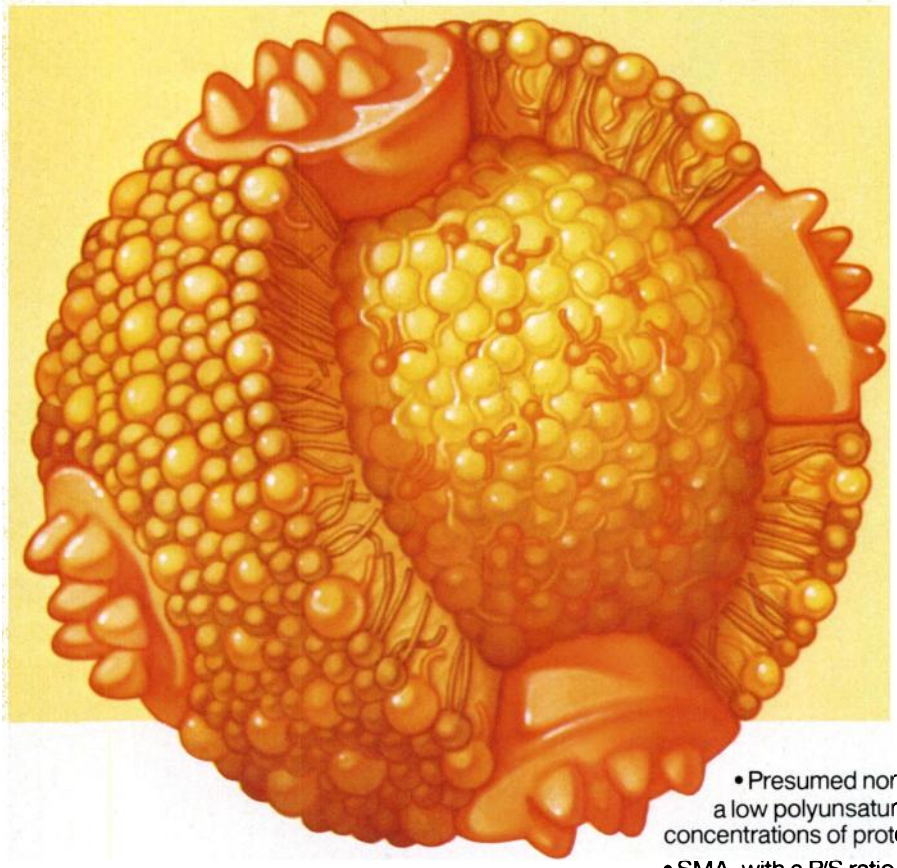
Pediatrics

AMERICAN ACADEMY OF PEDIATRICS ELK GROVE VILLAGE ILLINOIS 60007

HDL: the protective lipoprotein

HDL (high-density lipoprotein) has been called the "good" lipoprotein because unlike LDL (low-density lipoprotein), which promotes fatty deposits in the blood vessels, HDL helps eliminate cholesterol from the body. Because of this, researchers have noted that persons with higher levels of HDL have a lower rate of heart disease.



Medical artist's visualization of HDL as it might appear while circulating in blood or plasma.

Clinical study: SMA® produces high HDL levels virtually identical to breast milk.

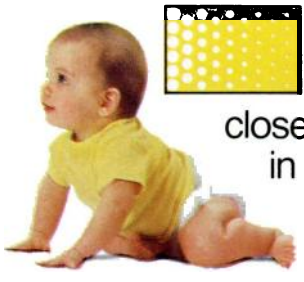
- Presumed normolipemic infants fed human milk with a low polyunsaturated to saturated (P/S) fat ratio had high concentrations of protective HDL cholesterol.[1]
- SMA, with a P/S ratio virtually identical to breast milk, maintained the high level of HDL cholesterol closest to that of human milk.
- Infant formula with a high P/S ratio significantly lowered the level of HDL cholesterol compared with human milk and SMA.

Reference:
1. Carlson SE, DeVoe PW, Barness LA: Effect of infant diets with different polyunsaturated to saturated fat ratios on circulating high-density lipoproteins. J Pediatr Gastroenterol Nutr 1:303-309, 1982.

Important Notice. Breast milk is best for babies. Infant formula is intended to replace or supplement breast milk when breast-feeding is not possible or is insufficient, or when mothers elect not to breast-feed.

Good maternal nutrition is important for the preparation and maintenance of breast-feeding. Extensive or prolonged use of partial bottle-feeding, before breast-feeding has been well established, could make breast-feeding difficult to maintain. A decision not to breast-feed could be difficult to reverse.

Professional advice should be followed on the need for and proper method of use of infant formula and on all matters of infant feeding. Infant formula should always be prepared and used as directed. Unnecessary or improper use of infant formula could present a health hazard. Social and financial implications should be considered when selecting the method of infant feeding.



SMA® INFANT FORMULA

closest to breast milk in all nutritional components

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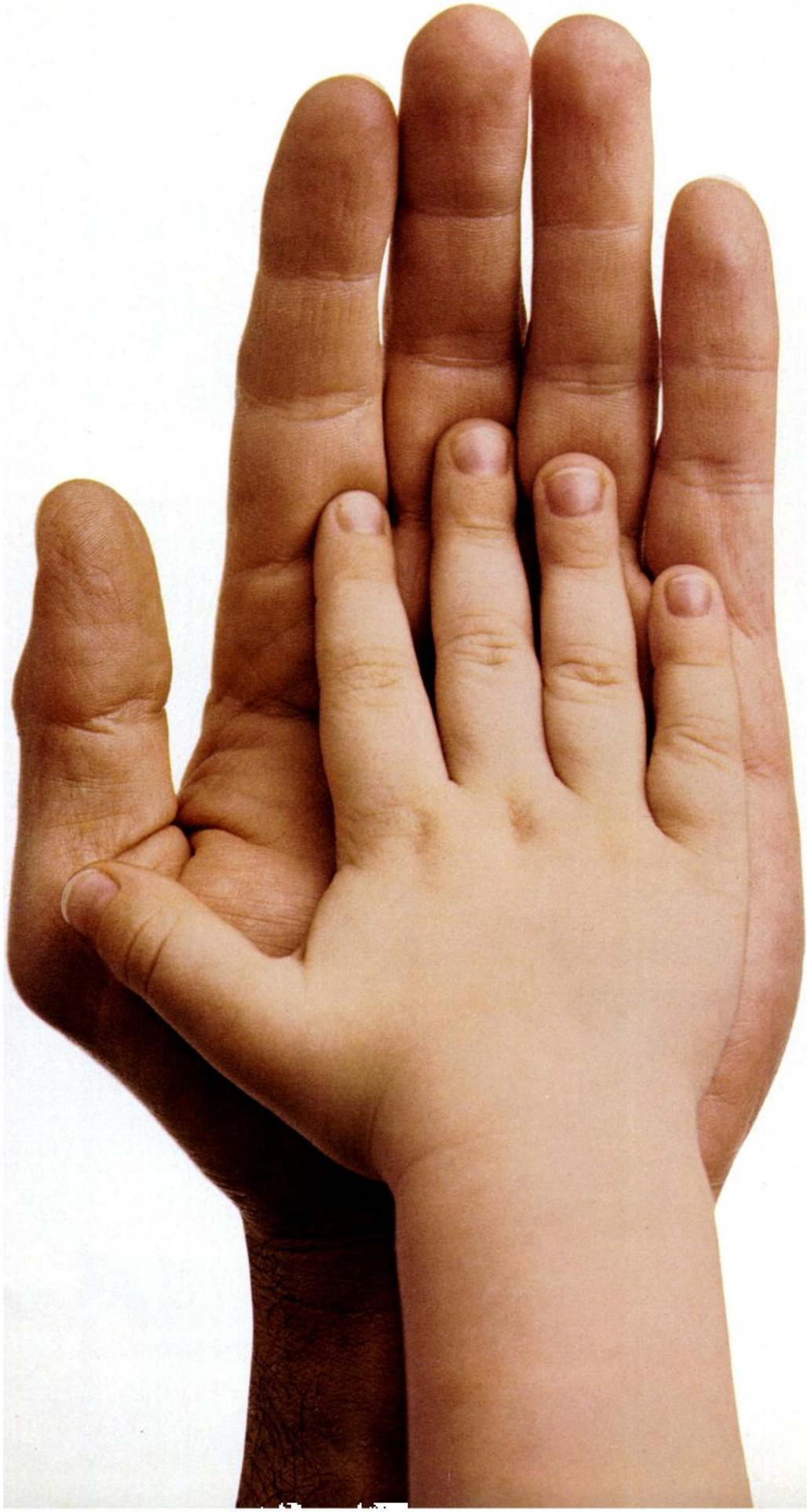
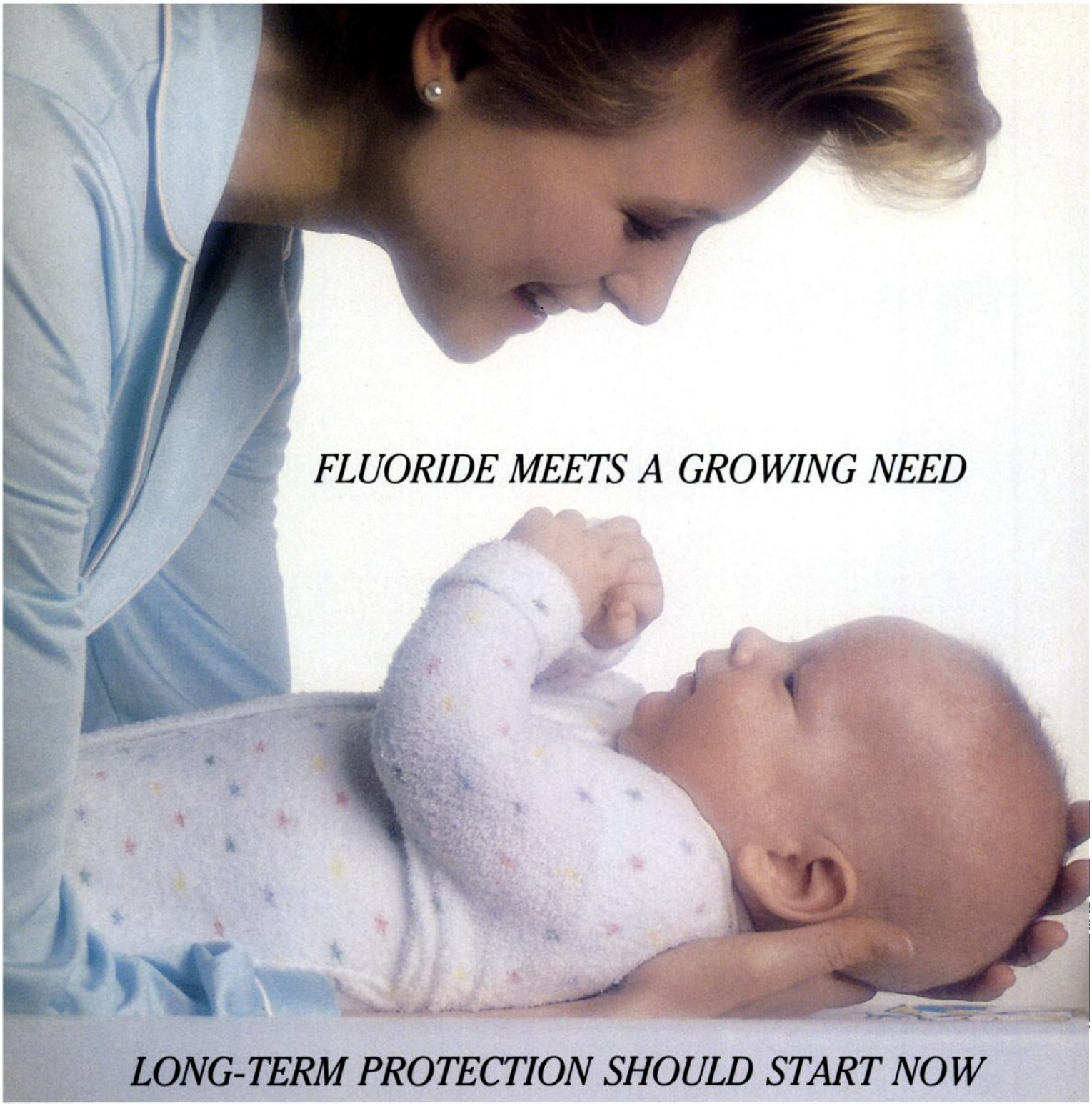
Philadelphia, PA 19101
Pioneers in Infant Nutrition™





Developing primary and permanent teeth supplied with systemic fluoride are so much stronger that caries can be reduced 50-80% during childhood.[1,2]

Since pre-eruptive teeth incorporate fluoride more easily than erupted teeth,[3] systemic fluoride is recommended every day from birth.

Breast milk and Ready-To-Use (RTU) formulas contain only trace amounts of fluoride.

So, even if a nursing mother drinks fluoridated water, a fluoride supplement for baby is needed when breast milk or RTU formulas are baby's main food sources.

Provide the fluoride infants need.

Prescribe Vi-Flor® vitamin-fluoride supplements soon after birth.

See accompanying full prescribing information.

Mead Johnson
NUTRITIONAL DIVISION

REFERENCES:
[1]Aasenden R and Peebles T: Effects of fluoride supplementation from birth on human deciduous and permanent teeth. Arch Oral Biol 1974; 19:321.
[2]Hambert L: Controlled trial of fluoride in vitamin drops for prevention of caries in children. Lancet 1971 Feb. 27; p 442.
[3]Newbrun E: How Fluoride Works: Topical vs. Systemic Action, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants, Children and Young Adults, Chicago, Pragmaton®, 1985, p 7.

Releasing the human potential for growth

PROTROPIN® (somatrem for injection):
For children who need growth hormone

In the past, the limited supply of pituitary-derived growth hormone meant that only the most profoundly growth hormone-deficient children were treated.[1,2]

Today, the recombinant DNA technology of Genentech ensures a virtually limitless supply of pure Protropin growth hormone for the treatment of all children lacking adequate endogenous growth hormone. Clinical studies of Protropin growth hormone, the most complete studies conducted for any growth hormone product, confirm its safety and efficacy in the treatment of this disorder.[3]

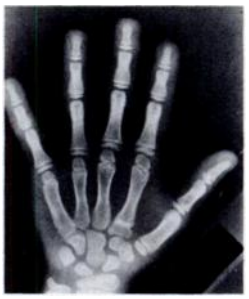
Some important clinical guidelines for patient identification

- Record height at all routine pediatric examinations.[4]
- Compare with cross-sectional data on a standard growth chart.[4]
- Careful, consistent technique for measuring children's height is critical.[4]
- Growth rates of less than 5 centimeters (2 inches) per year before age five, or less than 4.5 centimeters (1.8 inches) per year after age five, are cause for concern and may warrant further evaluation.[5]
- Progressive deviation from a normal growth curve may become apparent at any time during childhood.[5]
- Measurements made over four to six months, that show a decline in growth rate, may signal the need to refer the child for further evaluation.[6]

Early intervention: Time to grow

- Early diagnosis of children lacking adequate endogenous growth hormone is desirable because younger children typically demonstrate better responses to treatment and better long-term results than older children.[6]

For further information,
please call toll free 1-800-821-8590
or 1-800-551-2231



X-ray child aged 8

Protropin®
[somatrem for injection]

A Pure Product of Biotechnology

Genentech, Inc.

Please see Protropin® (somatrem for injection) brief summary on adjacent page.

References: 1. Oberfield SE, Levine LS. The child with short stature. *NY State J Med*. Essays in pediatrics, Jan 1986, 15-21 **2.** Growth hormone in the treatment of children with short stature. Report of Ad Hoc Committee on Growth Hormone Usage, the Lawson Wilkins Pediatric Endocrine Society and Committee on Drugs AAP. *Pediatrics* 1983, 72 891-94 **3.** Glasbrenner K. Technology spurt resolves growth hormone problem, ends shortage. *JAMA*, 1986, 255 (5) 581-587 **4.** Rosenfeld RG, Hintz RL. Diagnosis and management of growth disorders, *Drug Therapy*, May 1983, 61-76 **5.** Growth and growth hormone. Disorders of the anterior pituitary, in Kaplan SA. *Clinical Pediatric and Adolescent Endocrinology* WB Saunders Co, 1982 **6.** Underwood LE, Rosenfeld RG, Hintz RL. *Human Growth and Growth Disorders. An Update*, University of North Carolina School of Medicine and Stanford University School of Medicine, October 1985

Brief summary of prescribing information

PROTROPIN® (somatrem for injection)
INDICATIONS AND USAGE Protropin (somatrem for injection) is indicated only for the long term treatment of children who have growth failure due to a lack of adequate endogenous growth hormone secretion. Other etiologies of short stature should be excluded.
CONTRAINDICATIONS Protropin (somatrem for injection) should not be used in subjects with closed epiphyses. Protropin growth hormone should not be used when there is evidence of any progression of underlying intracranial lesion. Intracranial lesions must be inactive and antitumor therapy complete prior to instituting therapy. Protropin growth hormone should be discontinued if there is evidence of recurrent tumor growth. Protropin growth hormone, when reconstituted with Bacteriostatic Water for Injection, USP (Benzyl Alcohol Preserved) should not be used in patients with a known sensitivity to benzyl alcohol.
WARNINGS Benzyl alcohol as a preservative in Bacteriostatic Water for Injection has been associated with toxicity in newborns. When administering Protropin to newborns, reconstitute with Water for Injection, USP. USE ONLY ONE DOSE PER VIAL AND DISCARD THE UNUSED PORTION.
PRECAUTIONS Protropin (somatrem for injection) should be used only by physicians experienced in the diagnosis and management of patients with pituitary growth hormone deficiency. Patients with growth hormone deficiency secondary to an intracranial lesion should be examined frequently for progression or recurrence of the underlying disease process. Because Protropin growth hormone may induce a state of insulin resistance, patients should be observed for evidence of glucose intolerance. Concomitant glucocorticoid therapy may inhibit the growth promoting effect of Protropin growth hormone. Patients with coexisting ACTH deficiency should have their glucocorticoid replacement dose carefully adjusted to avoid an inhibitory effect on growth. Hypothyroidism may develop during Protropin treatment. Untreated hypothyroidism prevents optimal response to Protropin growth hormone. Therefore, patients should have periodic thyroid function tests and should be treated with thyroid hormone when indicated. See WARNINGS for use of Bacteriostatic Water for Injection, USP (Benzyl Alcohol Preserved) in newborns.
ADVERSE REACTIONS
A. Protropin (somatrem for injection) Approximately 30 percent of all Protropin treated patients developed persistent antibodies to growth hormone. In patients who had been previously treated with pituitary-derived growth hormone, one of twenty-two subjects developed persistent antibodies to growth hormone in response to Protropin therapy. In children not previously treated with any exogenous growth hormone approximately 40 percent developed persistent antibodies to growth hormone. In general, the growth hormone antibodies are not neutralizing and do not interfere with the growth response to Protropin growth hormone. One of eighty-four subjects treated with Protropin growth hormone for 6 to 36 months developed antibodies associated with high binding capacities and failed to respond to treatment with Protropin growth hormone. In addition to an evaluation of compliance with treatment program and thyroid status, testing for antibodies to human growth hormone should be carried out in any patient who fails to respond to therapy. Additional short term immunologic and renal function studies were carried out in a group of patients after approximately two years of treatment to detect other potential adverse effects of antibodies to growth hormone. The antibody was determined to be of the IgG class, no antibodies to growth hormone of the IgE class were detected. Testing included immune complex determination, measurement of total hemolytic complement and specific complement components, and immunochemical analyses. No adverse effects of growth hormone antibody formation were observed. These findings are supported by a toxicity study conducted in a primate model in which a similar antibody response to growth hormone was observed. Protropin (somatrem for injection), administered to monkeys by intramuscular injection at doses of 125 and 625 µg/kg t i w., was compared to pituitary-human growth hormone at the same doses and with placebo over a period of 90 days. Most monkeys treated with high-dose Protropin growth hormone developed persistent antibodies at week four. There were no biologically significant drug related changes in standard laboratory variables. Histopathologic examination of the kidney and other selected organs (pituitary, lungs, liver and pancreas) showed no treatment related toxicity. There was no evidence of immune complexes or immune complex toxicity when the kidney was also examined for the presence of immune complexes and possible toxic effects of immune complexes by immunohistochemistry and electron microscopy.
B. Bacteriostatic Water for Injection, USP (Benzyl Alcohol Preserved) Toxicity in newborns has been associated with benzyl alcohol as a preservative (see WARNINGS).
OVERDOSAGE The recommended dosage of up to 0.1 mg (0.2 IU) per kg body weight three times per week should not be exceeded due to the potential risk of side effects.
DOSAGE AND ADMINISTRATION The Protropin (somatrem for injection) dosage must be individualized for each patient. A dosage and schedule of up to 0.1 mg/kg (0.2 IU/kg) body weight administered three times per week (t i w.) by intramuscular injection is recommended. After the dose has been determined, reconstitute each 5 mg vial with 1-5 mL of Bacteriostatic Water for Injection, USP (Benzyl Alcohol Preserved) only. For use in newborns see WARNINGS. The pH of Protropin after reconstitution is approximately 7.8. To prepare the Protropin solution, inject the Bacteriostatic Water for Injection, USP (Benzyl Alcohol Preserved) into the vial of Protropin growth hormone, aiming the stream of liquid against the glass wall. Then swirl the product vial with a GENTLE rotary motion until the contents are completely dissolved. DO NOT SHAKE. It is recommended that Protropin growth hormone be administered using sterile, disposable syringes and needles. After reconstitution, vial contents should be clear, without particulate matter. If solution is cloudy or contains particulate matter the contents MUST NOT be injected. Before and after injections the septum of the vial should be wiped with an antiseptic solution to prevent contamination of the contents after repeated needle insertions. The syringes should be of small enough volume that the prescribed dose can be drawn from the vial with reasonable accuracy. The needle should be of sufficient length (usually 1 inch or more) to ensure that the injection reaches the muscular layer.

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PEDS

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The author's style will be respected; however, writing should conform to acceptable English usage and syntax, and American Medical Association style preferences will be observed. 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.

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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.

References must be numbered consecutively according to their citation in the text. Abbreviations for journals should be those listed in *Index Medicus*. The following reference style (a modified form of that shown in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals") will appear in the journal effective with volume 71 (January 1983 issue):

Journal (list first three authors then et al):

1. Starzl TE, Klintmalm GBG, Porter KA, et al: Liver transplantation with use of cyclosporin A and prednisone. *N Engl J Med* 1981; 305:266–269

Book

1. Kavet J: Trends in the utilization of influenza vaccine: An examination of the implementation of public policy in the United States, in Selby P (ed): *Influenza: Virus, Vaccines, and Strategy*. New York, Academic Press Inc, 1976, pp 297–308

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Revised, July 1985

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(polymyxin B-neomycin-gramicidin)

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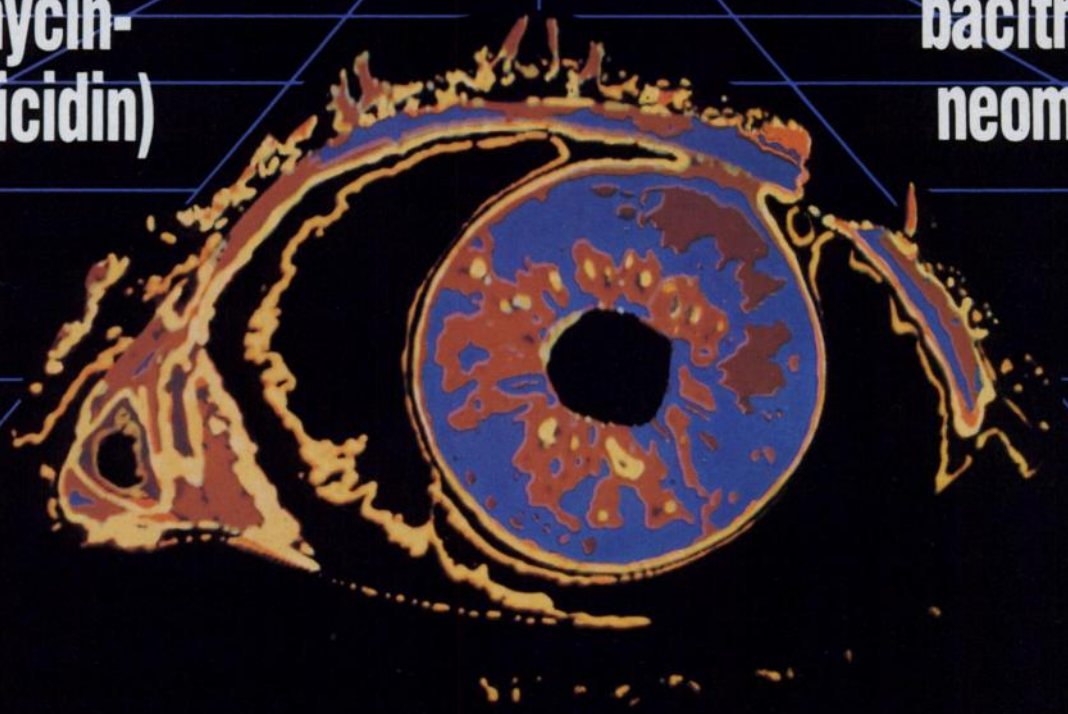
(polymyxin B-bacitracin-neomycin)



Clears up bacterial hot spots *in a hurry.*

The following is a Combined Brief Summary. For complete prescribing information, please consult the full prescribing information in B.W. Co.* literature or the PDR: **NEOSPORIN*** OPHTHALMIC OINTMENT Sterile (Polymyxin B Sulfate-Bacitracin Zinc-Neomycin Sulfate). **DESCRIPTION:** Each gram contains: Aerosporin* (polymyxin B sulfate) 10,000 units, bacitracin zinc 400 units, neomycin sulfate equivalent to 3.5 mg neomycin base and special white petrolatum, qs. **HOW SUPPLIED:** Tube of ⅛ oz with ophthalmic tip. (NDC-0081-0732-86) Store at 15°-30°C (59°-86°F). **NEOSPORIN*** OPHTHALMIC SOLUTION Sterile (Polymyxin B Sulfate-Neomycin Sulfate-Gramicidin). **DESCRIPTION:** Each ml contains: Aerosporin* (polymyxin B sulfate) 10,000 units, neomycin sulfate equivalent to 1.75 mg neomycin base and gramicidin 0.025 mg. The vehicle contains alcohol 0.5%, thimerosal 0.001% (added as a preservative) and the inactive ingredients propylene glycol, polyoxyethylene polyoxypropylene compound, sodium chloride and water for injection. **HOW SUPPLIED:** Drop Dose® of 10 ml (plastic dispenser bottle). (NDC-0081-0728-69) Store at 15°-30°C (59°-86°F) and protect from light. The information below applies to both the ointment and the solution. **INDICATIONS AND USAGE:** For the short term treatment of superficial external ocular infections caused by organisms susceptible to one or more of the antibiotics contained therein. **CONTRAINDICATIONS:** This product is contraindicated in those individuals who have shown hypersensitivity to any of its components. **WARNINGS:** The manifestations of sensitization to neomycin are usually itching, reddening and edema of the conjunctiva and eyelid. 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 subside quickly on withdrawing the medication. Neomycin-containing applications should be avoided for the patient thereafter. **PRECAUTIONS:** General: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms including fungi. Appropriate measures should be taken if this occurs. 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. Information for Patients: If redness, irritation, swelling or pain persists or increases, discontinue use and contact your physician. Avoid contaminating the ointment applicator tip or the solution dropper with material from the eye, fingers, or other source. This caution is necessary if the sterility of the product is to be preserved. **ADVERSE REACTIONS:** Neomycin Sulfate may cause cutaneous and conjunctival sensitization. A precise incidence of hypersensitivity reactions (primarily skin rash) due to topical neomycin is not known.

Wellcome

Burroughs Wellcome Co.,
Research Triangle Park, NC 27709

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Pediatrics

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ARTICLES

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Routine VI-FLOR®
supplementation

to help you guard appropriate patients against caries risk and nutritional risk.

INDICATIONS AND USAGE: Prophylaxis of vitamin deficiencies and dental caries in children and adults when fluoride of water supply does not exceed 0.7 ppm.[1,2,3] And, in the case of TRI-VI-FLOR® 0.25 mg Drops with Iron and POLY-VI-FLOR® Drops and Chewable Tablets with Iron, prophylaxis against iron deficiencies. Note: VI-FLOR Drops do not contain folic acid because the vitamin is not stable in liquid form.

PRECAUTIONS: Do not exceed recommended dose or give concurrently with other medications containing significant amounts of fluoride. Prolonged excessive fluoride intake may cause dental fluorosis. All VI-FLOR® with Iron products: as with all products containing iron, parents should be warned against excessive dosage. The bottle should be kept out of reach of children.

Keep all VI-FLOR with Iron products tightly closed and away from direct light.

VI-FLOR Drops should be dispensed in the original plastic container, since contact with glass leads to instability and precipitation.

ADVERSE REACTIONS: Allergic rash has rarely been reported.

DOSAGE AND ADMINISTRATION:

Supplemental Fluoride Dosage Schedule (mg/day)*

Age	Concentration of Fluoride in Drinking Water (ppm)		
	<0.3	0.3-0.7	>0.7
2 wk-2 yr**	0.25	0	0
2-3 yr	0.5	0.25	0
3-16 yr	1.0	0.5	0

*From the American Academy of Pediatrics Committee on Nutrition statement, Fluoride Supplementation: Revised Dosage Schedule. Pediatrics 63(1):150-152, 1979.

**The Committee favors initiating fluoride supplementation shortly after birth in breast-fed infants (0.25 mg F/day). In formula-fed infants, fluoride supplementation should be according to the fluoride content of the water used to prepare formula.

PRODUCT	FORM	SIZE	FLUORIDE mg/dose
POLY-VI-FLOR 0.25 mg	Drops	50 ml Bottle	0.25
POLY-VI-FLOR 0.25 mg with Iron	Drops	50 ml Bottle	0.25
POLY-VI-FLOR 0.5 mg	Drops	50 ml Bottle	0.5
POLY-VI-FLOR 0.5 mg with Iron	Drops	50 ml Bottle	0.5
POLY-VI-FLOR 0.5 mg	Tablets	Bottle of 100	0.5
POLY-VI-FLOR 0.5 mg with Iron	Tablets	Bottle of 100	0.5
POLY-VI-FLOR 1.0 mg	Tablets	Bottle of 100	1.0
POLY-VI-FLOR 1.0 mg with Iron	Tablets	Bottle of 100	1.0
TRI-VI-FLOR 0.25 mg	Drops	50 ml Bottle	0.25
TRI-VI-FLOR 0.25 mg with Iron	Drops	50 ml Bottle	0.25
TRI-VI-FLOR 0.5 mg	Drops	50 ml Bottle	0.5
TRI-VI-FLOR 1.0 mg	Tablets	Bottle of 100	1.0

REFERENCES:

1. Hennon DK, Stookey GK and Muhler JC: The Clinical Anticariogenic Effectiveness of Supplementary Fluoride-Vitamin Preparations—Results at the End of Four Years. J Dentistry for Children 34:439-443 (Nov) 1967.
2. Hennon DK, Stookey GK and Muhler JC: The Clinical Anticariogenic Effectiveness of Supplementary Fluoride-Vitamin Preparations—Results at the End of Five and a Half Years. Pharmacology and Therapeutics in Dentistry 1:1-6 (Oct) 1970.
3. Hennon DK, Stookey GK and Muhler JC: Prophylaxis of Dental Caries: Relative Effectiveness of Chewable Fluoride Preparations With and Without Added Vitamins. J Pediatrics 80:1018-1021 (June) 1972.

VI-SOL®/VI-FLOR® products are the nation's most prescribed children's vitamin and fluoride-vitamin supplements.

(For complete details, please consult full prescribing information.)

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NUTRITIONAL DIVISION

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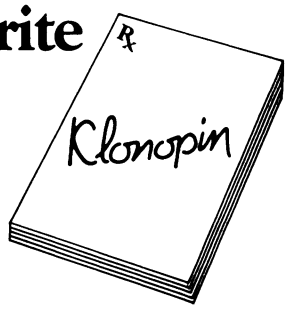

Klonopin™ Ⓥ

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the same product... a different spelling

Possible confusion of our product name with clonidine, an antihypertensive medication, prompts us to take this action.

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SCHEDULE OF MEETINGS

ANNUAL MEETINGS

1986
Washington, DC
November 1-6

1987
New Orleans
October 31-November 5

1988
San Francisco
October 22-27

1989
Chicago
October 21-26

1990
Boston
October 6-11

1991
New Orleans
October 26-31

1992
San Francisco
October 10-15

SPRING SESSIONS

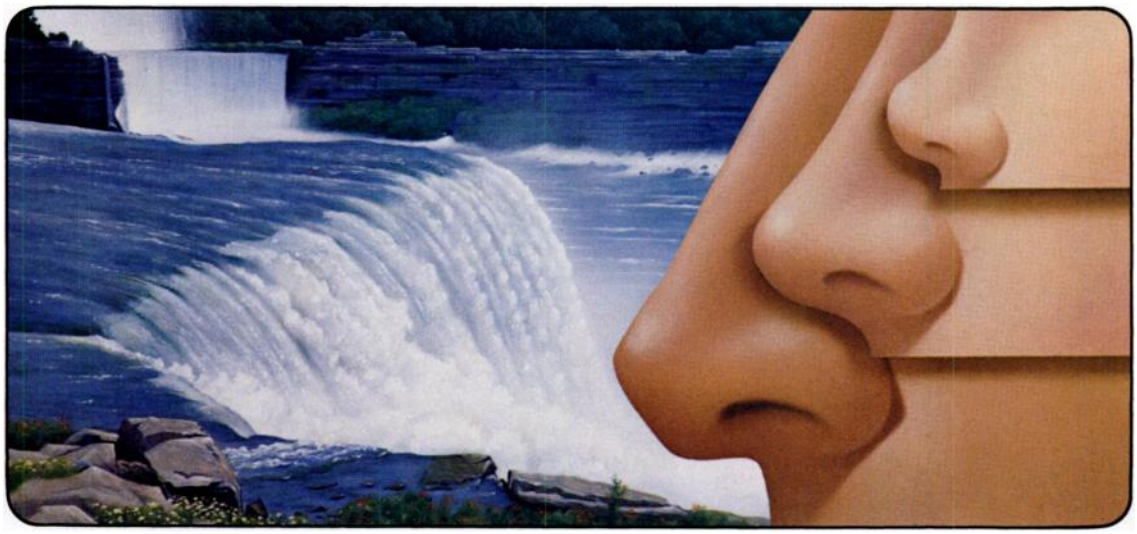
1987
San Francisco
May 9-14

1988
New York City
May 14-19

Recommend NāSal™ Saline

Nasal Moisturizing Solution

From the makers of Neo-Synephrine®



When moisture is all they really need

NāSal provides soothing, gentle relief from dry, irritated nasal passages due to allergic rhinitis, chronic sinusitis, colds and low humidity.

Unlike homemade preparations, NāSal is a specially-formulated, buffered saline solution containing 0.65% sodium chloride adjusted with phosphate buffers to the proper tonicity and pH. This special formulation soothes and moisturizes nasal passages without nasal irritation.

And NāSal is non-habit-forming. It can be used with a decongestant. NāSal is safe no matter how often it's used.

NāSal™ (Nay-sal)

for the dry noses
you see...
even the littlest ones

Available in spray and monodrops

Winthrop Consumer Products
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A personal foul took Tom out of the action...

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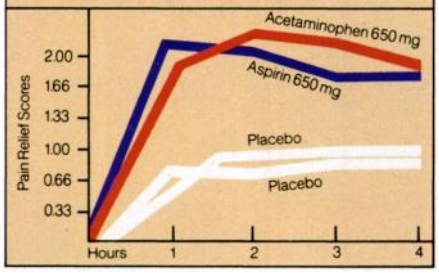
and while he's feeling the pain, his pediatrician knows how to effectively treat it—with local therapy and Junior Strength TYLENOL® acetaminophen.

Tom's pediatrician prefers to treat minor injuries with local therapy* for the inflammation, and TYLENOL for the pain.

One reason Tom's pediatrician chooses TYLENOL first for pain relief is that clinical studies have proven it to be, milligram for milligram, every bit as effective as aspirin.[1]

Composite time-effect curves of two studies of a total of 177 patients with pain following oral surgery. Patients took either acetaminophen, aspirin or placebo.[1]



And just as important, with TYLENOL there are few side effects such as GI irritation or allergic reactions—side effects associated with aspirin use.[2]

TYLENOL also offers a dosage form that's right for every patient. For Tom, and other children between the ages of 6 and 14, 160 mg Junior Strength TYLENOL is often recommended. Children need only half as many Junior Strength TYLENOL tablets as chewables, and they're easy to swallow.

So patients get effective pain relief without aspirin side effects, in a dosage form that is just right. Next time children in your practice are in pain, recommend Junior Strength TYLENOL to help put them back in the action.

*Local therapy often encompasses rest, ice, compression and elevation.

References: 1. Cooper SA. *Arch Intern Med* 141:282, 1981. **2.** Aspirin or paracetamol? *Lancet* II:287, 1981.

McNEIL McNeil Consumer Products Company
Fort Washington, PA 19034

JUNIOR STRENGTH

TYLENOL®

160 mg acetaminophen

SWALLOWABLE TABLETS

first choice for pain in the 6-14 year old

AMERICAN ACADEMY OF PEDIATRICS

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SCHEDULE OF CONTINUING EDUCATION COURSES

1986

Infectious Diseases
Vancouver, British Columbia
June 1–3

Connective Tissue Disease, Pulmonology, and Intensive Care
Hilton Head, South Carolina
June 12–14

Pediatric Advances
New York, New York
September 12–14

Advances in Pediatric, ENT, Allergy and Infectious Diseases
San Francisco, California
September 26–28

1987

2nd Annual Vail Infectious Disease Seminar
Vail, Colorado
January 8–11

Pediatric Advances
San Diego, California
February 6–8

Pediatric Advances
Maui, Hawaii
March 5–7

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PEDS

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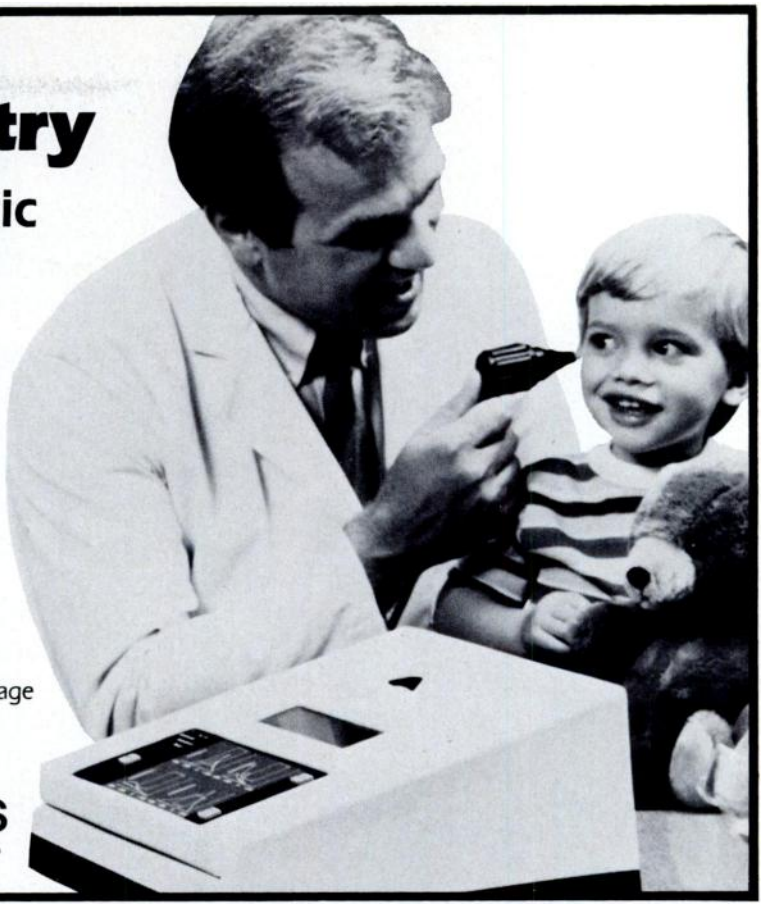
Get accuracy automatically with the TA-7A Automatic Impedance Meter, only from Teledyne Avionics.



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UNIVERSITY STUDY WITH MYCITRACIN® TYPE ANTIBIOTIC REVEALS:

Helps keep small hurts from becoming big infections.

Chance of infection cut 68.4% for children with minor skin injuries.

A doctors' study conducted at a leading university used a first aid ointment with a formula such as found in triple antibiotic Mycitracin. It was applied to a variety of minor skin injuries among a group of boys and girls age two to five.

The result? The group using the ointment developed 68.4% fewer incidences of skin infections than a group that did not. Or: those children who did not use the ointment were more than three times as likely to become infected. When minor cuts, scrapes and burns occur, use soothing Mycitracin.

BOOKS RECEIVED

The Skin in Diabetes. J. E. Jelinek. Philadelphia, Lea & Febiger, 1986, $33.50 (U.S.), $44.50 (Canada), 237 pp.

Child Health in the Tropics. R. E. Eeckles, O. Randome-Kuti, and C. C. Kroonenberg. The Netherlands, Martinus Nijhoff Publishers, 1985, $69.50, 347 pp.

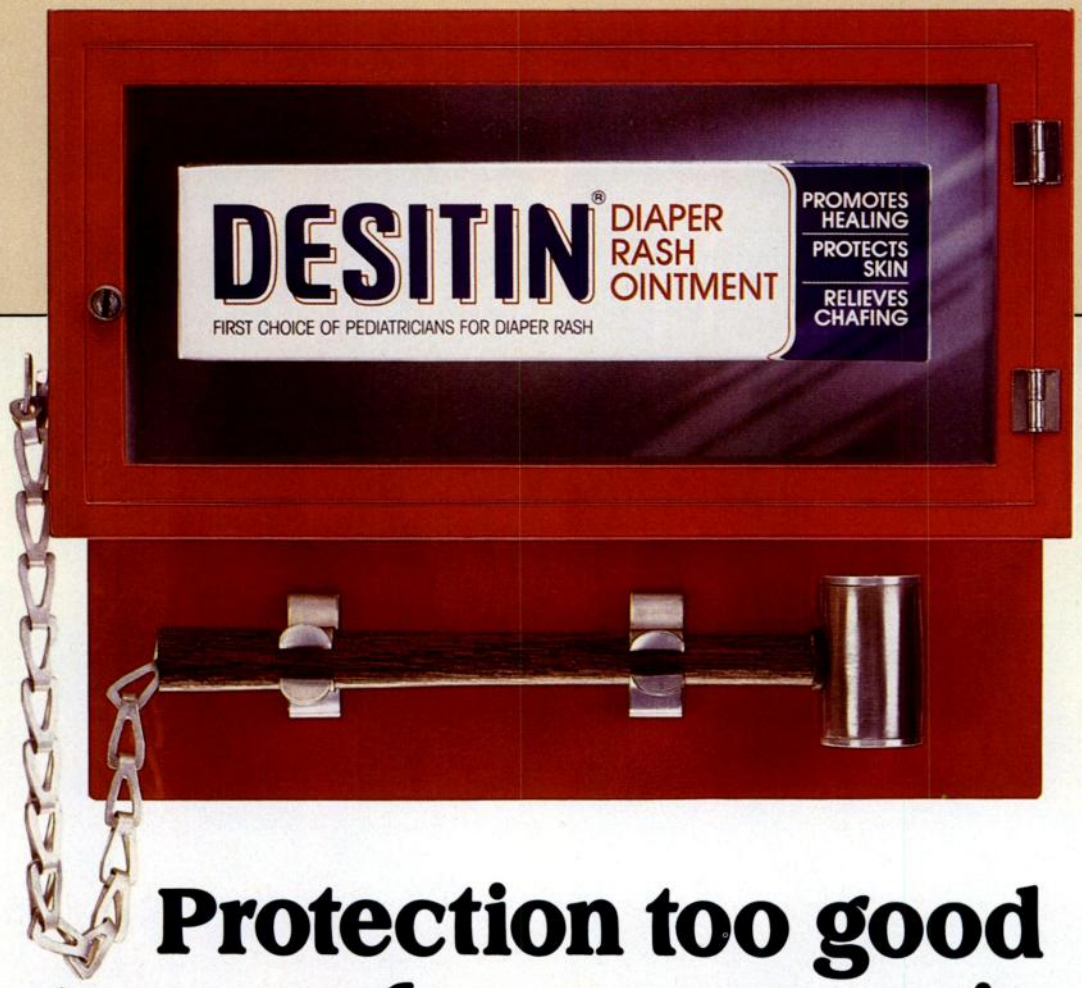
Legal Issues in Pediatrics and Adolescent Medicine, ed 2. A. Roddey Holder. New Haven, CT, Yale University Press, 1986, $35, 357 pp.

Drug Therapy During Pregnancy. T.K.A.B. Eskes and M. Finster. London, Butterworths, 1985, $79.95, 230 pp.

A Pocket Guide to Differential Diagnosis, ed 2. R. D. Eastham. Littleton, MA, PSG Publishing Co, 1985, $17.50, 532 pp.

Infant Care and Feeding in the South Pacific. Food and Nutrition in History and Anthropology, vol 3. L. B. Marshall. New York, Gordon and Breach. $58, 355 pp.

PEDIATRICS IN REVIEW: July 1986 Contents



Protection too good to save for emergencies.

Desitin.® So effective, it makes sense from the start.

In the treatment of diaper rash, more Pediatricians recommend Desitin more often than any other brand. It makes sense. Desitin is effective because it was formulated to be effective.

Desitin has zinc oxide to dry and soothe, natural vitamins A & D (from Norwegian cod liver oil) to help promote granulation and the formation of epithelium plus high-quality talc, lanolin and petrolatum.

So, to protect babies before diaper rash starts, doesn't it make sense to recommend protection that has healing built-in. That's Desitin...protection that can help prevent diaper rash...because two emollients, lanolin and petrolatum, combine with the zinc oxide in Desitin to form a long-lasting protective barrier against wetness and ammonia compounds that can cause diaper rash.

DESITIN®

The recommendation that stands for efficacy.


Announcing
a new age in
bronchodilator therapy...
TWO AND OLDER

New!

VENTOLIN® SYRUP

(ALBUTEROL SULFATE/GLAXO) 2mg/5ml

New Ventolin Syrup for children two and older...

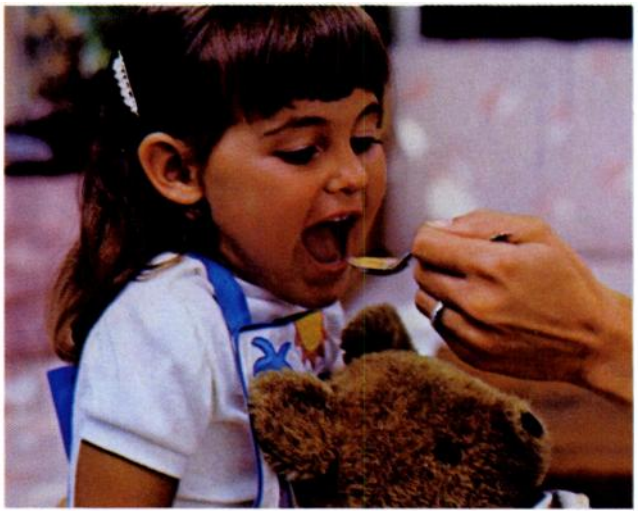
The only β_2-adrenergic bronchodilator recommended for children as young as two years old. New VENTOLIN Syrup extends the benefits of VENTOLIN therapy to pediatric patients:

- **Rapid, effective relief of bronchospasm within 30 minutes**
- **Control for up to six hours**
- **Continued effectiveness with long-term use**
- **A simple dosage regimen**
- **Side effects reported with VENTOLIN Syrup are similar to those of other sympathomimetic amines**

Strawberry flavor enhances compliance

Strawberry flavor is favored by children. And VENTOLIN Syrup is free of sugar, alcohol, tartrazine dye (yellow dye #5) and bisulfites.

Please see brief summary of Prescribing Information on following page



Glaxo a world leader in respiratory care
Glaxo Inc., Research Triangle Park, NC 27709

VENTOLIN® SYRUP
(ALBUTEROL SULFATE/GLAXO) 2mg/5ml

Brief summary of prescribing information

INDICATIONS AND USAGE: VENTOLIN® Syrup is indicated for the relief of bronchospasm in adults and in children 2 years of age and older with reversible obstructive airway disease.

In controlled clinical trials in patients with asthma, the onset of improvement in pulmonary function, as measured by maximal midexpiratory flow rate (MMEF) and forced expiratory volume in one second (FEV_1), was within 30 minutes after a dose of VENTOLIN (albuterol sulfate) Syrup. Peak improvement of pulmonary function occurred between two to three hours. In a controlled clinical trial involving 55 children, clinically significant improvement (defined as maintenance of mean values over baseline of 15% to 20% or more in the FEV_1 and MMEF, respectively) continued to be recorded up to six hours. No decrease in the effectiveness was reported in one uncontrolled study of 32 children who took VENTOLIN Syrup for a three-month period.

CONTRAINDICATIONS: VENTOLIN® Syrup is contraindicated in patients with a history of hypersensitivity to any of its components.

PRECAUTIONS: General: Although albuterol *usually* has minimal effects on the beta$_2$-adrenoceptors of the cardiovascular system at the recommended dosage, *occasionally* the usual cardiovascular and CNS stimulatory effects common to all sympathomimetic agents have been seen with patients treated with albuterol, necessitating discontinuation. Therefore, albuterol should be used with caution in patients with cardiovascular disorders, including coronary insufficiency and hypertension, in patients with hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis. Additionally, albuterol and other beta-agonists, when given intravenously, may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of VENTOLIN® Syrup is unknown.

Information for Patients: The action of VENTOLIN Syrup may last up to six hours and therefore it should not be taken more frequently than recommended. Do not increase the dose or frequency of medication without medical consultation. If symptoms get worse, medical consultation should be sought promptly.

Drug Interactions: The concomitant use of VENTOLIN Syrup and other oral sympathomimetic agents is not recommended since such combined use may lead to deleterious cardiovascular effects. This recommendation does not preclude the judicious use of an aerosol bronchodilator of the adrenergic stimulant type in patients receiving VENTOLIN Syrup. Such concomitant use, however, should be individualized and not given on a routine basis. If regular coadministration is required, then alternative therapy should be considered.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a 2-year study in the rat, at doses corresponding to 2, 9, and 46 times the maximum human (child weighing 21 kg) oral dose. In another study this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Teratogenic Effects: *Pregnancy Category C:* Albuterol has been shown to be teratogenic in mice when given subcutaneously in doses corresponding to 0.2 times the maximum human (child weighing 21 kg) oral dose. There are no adequate and well controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice with albuterol showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg. None were observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses at 50 mg/kg corresponding to 46 times the maximum human (child weighing 21 kg) oral dose of albuterol sulfate.

Labor and Delivery: Oral albuterol has been shown to delay preterm labor in some reports. There are presently no well controlled studies which demonstrate that it will stop preterm labor or prevent labor at term. Therefore, cautious use of VENTOLIN Syrup is required in pregnant patients when given for relief of bronchospasm so as to avoid interference with uterine contractibility. Use in such patients should be restricted to those patients in whom the benefits clearly outweigh the risks.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children below the age of 2 years have not yet been adequately demonstrated.

ADVERSE REACTIONS: The adverse reactions to albuterol are similar in nature to those of other sympathomimetic agents. The most frequent adverse reactions to VENTOLIN® Syrup in adults and older children were tremor, 10 of 100 patients; nervousness and shakiness, each 9 of 100 patients. Other reported adverse reactions were headache, 4 of 100 patients; dizziness and increased appetite, each 3 of 100 patients; hyperactivity and excitement, each 2 of 100 patients; tachycardia, epistaxis, irritable behavior, and sleeplessness, each 1 of 100 patients. The following adverse effects occurred in less than 1 of 100 patients each: muscle spasm, disturbed sleep, epigastric pain, cough, palpitations, stomach ache, irritable behavior, dilated pupils, sweating, chest pain, and weakness.

In young children 2 to 6 years of age, some adverse reactions were noted more frequently than in adults and older children. Excitement was noted in approximately 20% of patients and nervousness in 15%. Hyperkinesia occurred in 4% of patients, insomnia, tachycardia, and gastrointestinal symptoms in 2% each. Anorexia, emotional lability, pallor, fatigue, and conjunctivitis were seen in 1%.

In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as hypertension, angina, vomiting, vertigo, central stimulation, unusual taste, and drying or irritation of the oropharynx.

The reactions are generally transient in nature, and it is usually not necessary to discontinue treatment with VENTOLIN Syrup. In selected cases, however, dosage may be reduced temporarily, after the reaction has subsided, dosage should be increased in small increments to the optimal dosage.

Glaxo

Manufactured for Glaxo Inc.
Research Triangle Park, NC 27709 by
Schering Corporation, Kenilworth, NJ 07033

August 1985

Caring for the Young Athlete

As children and adolescents become more active in sports, you need a guide that has answers to common and special sports medicine problems.

The American Academy of Pediatrics' book, *Sports Medicine: Health Care for Young Athletes,* provides you with this needed information—with guidelines on care.

The book discusses prevention and management of sports-related illness and injuries. Other chapters deal with nutrition, stress reduction, and the role of the athletic trainer.

This book is for every physician who has been or will be involved in sports medicine. As an advisor to parents. As a team physician. As the parent of a young athlete from elementary school through high school.

American Academy of Pediatrics

American Academy of Pediatrics (AAP)
Publications Department
P.O. Box 927, Elk Grove Village, IL 60007

Please send me _____ copies of *Sports Medicine: Health Care for Young Athletes* @ $20.00 each.
☐ Payment of $_____ enclosed.
☐ Bill me. Formal purchase order required.
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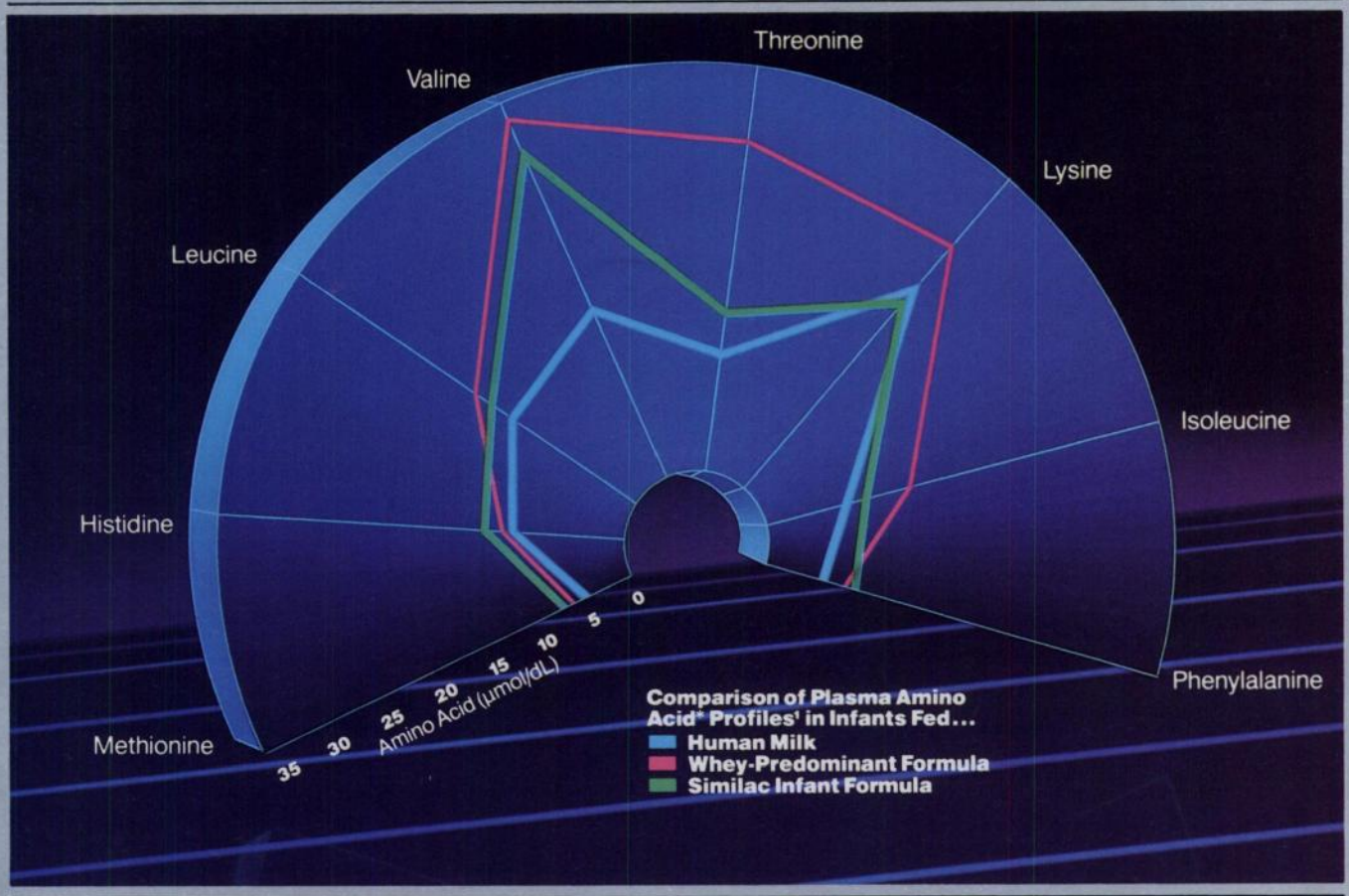
The closer you look, the closer we look.



Plasma amino acid* profile closest to mother's milk.

Clinical evidence establishes that the plasma amino acid profile of infants fed Similac is closest to that of breast-fed infants.[1,2]

For optimal development, amino acid metabolism of the formula-fed infant should be as close as possible to that of the breast-fed infant, the nutritional norm.[3]

*Essential amino acids

in vivo performance...

SIMILAC®
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INFANT FORMULAS

Closest to mother's milk.

References

1. Janas LM, Picciano MF, Hatch TF: Indices of protein metabolism in term infants fed human milk, whey-predominant formula or cow's milk formula. *Pediatrics* 75:775-784, 1985.

2. Järvenpää A-L, et al: Milk protein quantity and quality in the term infant: II. Effects on acidic and neutral amino acids. *Pediatrics* 70:221-230, 1982.

3. Pardridge W: Brain amino acids metabolism, in Wurtman RJ, Wurtman JJ (eds): *Nutrition and the Brain:* New York: Raven Press, 1977.

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Playing hard can be hard on the skin. To reduce bacteria on skin, SAFEGUARD provides the highest levels of TCC (triclocarban) in an OTC soap. The active ingredient TCC is effective *in vitro* against a wide range of gram-positive bacteria. In fact, SAFEGUARD reduces resident bacteria on skin by 94%.*

And, SAFEGUARD produces mounds of rich lather—more than any other leading OTC antibacterial soap—a feature patients like. For excellent antibacterial efficacy plus unsurpassed mildness...recommend the gentle strength of SAFEGUARD.

*Data on file

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SGQ-718/85

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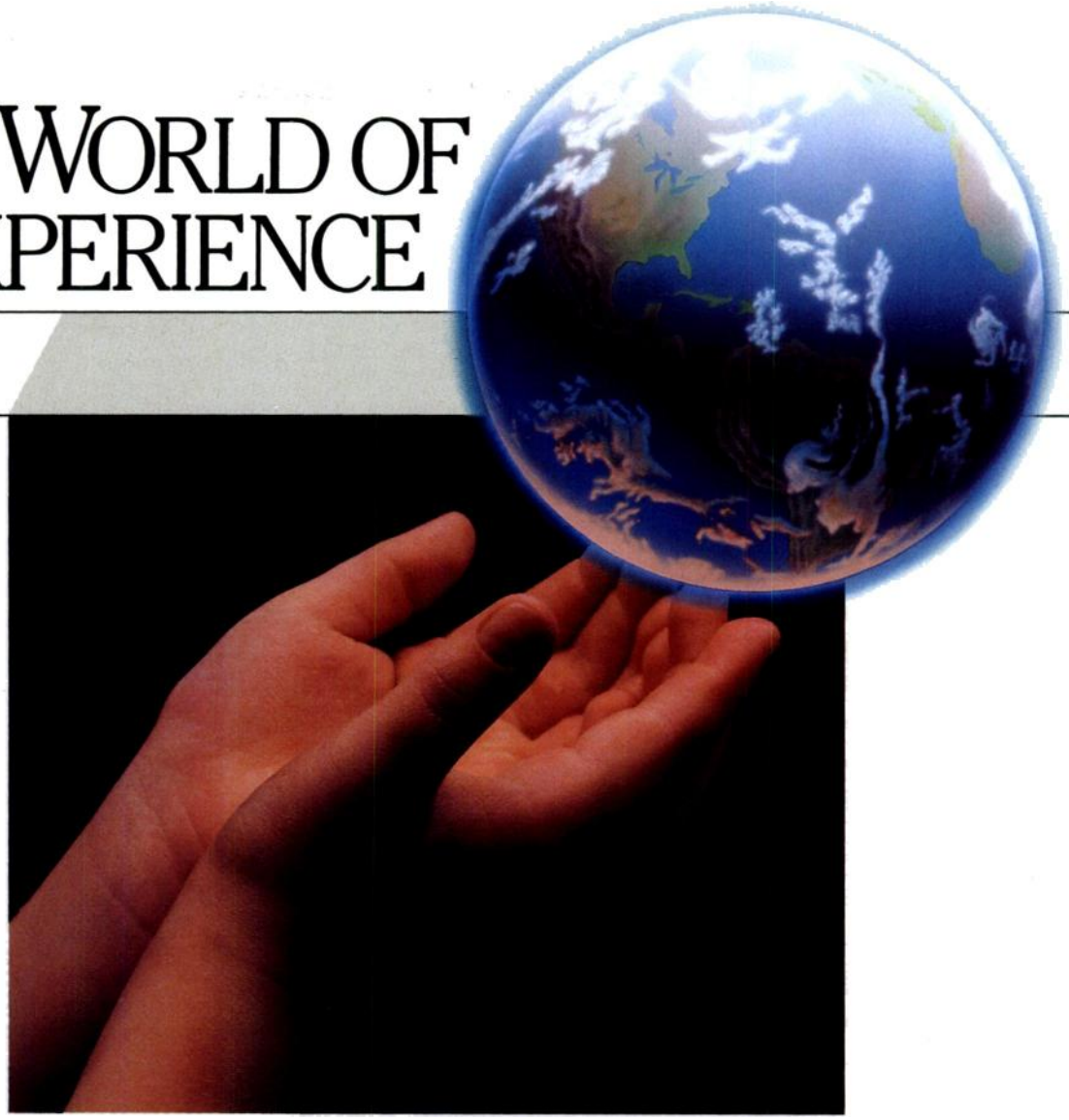


b-Capsa™ I VACCINE

(Haemophilus b Polysaccharide Vaccine)

During the first six months of clinical use, more than two million doses of *b*-CAPSA I VACCINE have been administered to children 2- to 6-years of age...substantiating clinical expectations.[1]

Based on more than fourteen million patient-months of experience, *b*-CAPSA I is confirming a protective efficacy profile of 90% against *Haemophilus influenzae* type b (Hib) disease, while also demonstrating an excellent record of minimal (less than 2%) side effects and adverse reactions.[1,2]

b-CAPSA I VACCINE: a world of experience to depend on

Manufactured by:
PRAXIS BIOLOGICS
Distributed by:
Mead Johnson
NUTRITIONAL DIVISION

LK-192R-04-86

See references and brief summary on following page.

b-Capsa™ I VACCINE

(Haemophilus b Polysaccharide Vaccine)

BRIEF SUMMARY

DESCRIPTION

b-CAPSA I VACCINE (Haemophilus b Polysaccharide Vaccine) is a sterile, lyophilized vaccine for subcutaneous administration. It is the capsular polysaccharide purified from the bacterium, *Haemophilus influenzae* type b, strain Eag and is a polymer of ribose, ribotol, and phosphate.[1]

Lactose is included in the vaccine at a concentration of 2.5 mg per 0.5 ml dose to improve product stability.[2] The lyophilized vaccine contains 25 μg of purified Haemophilus b polysaccharide per dose. The reconstituted vaccine contains thimerosal (mercurial derivative) 1:10,000 and sodium chloride for isotonicity. When reconstituted, *b*-CAPSA I VACCINE is a clear, colorless liquid.

CLINICAL PHARMACOLOGY

Haemophilus influenzae type b is the most common cause of bacterial meningitis and a leading cause of serious, systemic bacterial diseases in young children in the United States. This vaccine will not stimulate protection against other types of *Haemophilus influenzae* or other microorganisms that cause meningitis or septic disease.

Several population-based studies conducted within the last 10 years in the U.S. indicate that a child's cumulative risk of developing systemic *Haemophilus influenzae* b (Hib) disease at some time during the first 5 years of life is about 1 in 200.[3] About 60% of the children have meningitis and 40% other systemic diseases, such as cellulitis, epiglottitis, pericarditis, pneumonia, sepsis, or septic arthritis.[3] In these U.S. studies, about 35-40% of systemic Hib disease has occurred in children 18 months of age or older. In contrast, a recent prospective, five-year analysis of all children in Finland indicated that 60% of bacteremic Hib disease occurred in children 18 months of age or older and 45% in those 2 or more years of age.[4]

The incidence of systemic Hib disease is increased in certain children, e.g., Eskimo[5] and American Indian[6] children, patients with asplenia, sickle cell disease,[7] and antibody deficiency syndromes.[8] Recent studies also indicate that *Haemophilus influenzae* b can cause outbreaks of systemic disease among previously healthy children attending nursery school or day care, and that attendance at day care significantly increases the risk of developing systemic Hib disease.[9-11] Furthermore, the risk of acquiring systemic Hib disease for a child in intimate contact with one who has developed such a disease is up to 400 times that of a child in the general population.[9]

Hib diseases usually can be treated successfully. Even with appropriate antibiotic therapy, however, the mortality rate of Hib meningitis[12] and other bacteremic diseases can be 5%, and serious, long-term neurologic sequelae have been observed in 19-45% of survivors of meningitis.[3, 13] Up to 20% of *Haemophilus influenzae* b isolated in the USA from patients with systemic disease are resistant to ampicillin,[12, 14] and the mortality rate of meningitis is significantly greater when it is caused by ampicillin-resistant than by ampicillin-sensitive *Haemophilus influenzae* b.[12] Moreover, resistance to chloramphenicol and to multiple antibiotics has emerged.[14] When properly administered, rifampin can prevent bacteremic Hib disease among contacts at risk,[15] and its use for this purpose has been recommended by health authorities.[15, 16] Implementation of those recommendations can be difficult, however, especially in the setting of a large group. Thus, the strategy of controlling Hib disease by antibiotics has deficiencies.

The capsular polysaccharide of *Haemophilus influenzae* b (Haemophilus b polysaccharide) is its principal virulence factor. Anti-Haemophilus b polysaccharide antibody mediates complement-dependent bacteriolysis and opsonization *in vitro* and protects experimentally infected animals. Hyperimmune animal serum was used successfully to treat invasive human Hib diseases in the pre-antibiotic era, and antibody to the capsular polysaccharide was reported to be the protective component of that serum.[17]

For these reasons, Haemophilus b polysaccharide has been purified for use as a vaccine to prevent Hib diseases. More than 60,000 children and several hundred adults have been vaccinated with Haemophilus b polysaccharide in studies conducted in multiple centers.[4, 18-23] Adverse reactions have been mild and transient. Adults and older children uniformly produce a long-lived, non-boostable antibody response.[4, 18-20] Children respond variably according to their age: infants respond less frequently with less antibody.[4, 18-22] The percent of responding individuals increases significantly between 12 and 24 months of age.[4, 18, 20, 22] Approximately 90% of children 24 months of age or older produce a significant antibody response to Haemophilus b polysaccharide vaccination, and most of the non-responders have high pre-vaccination titers.[4] The amount of antibody produced by children is also affected by the molecular size of the vaccine: vaccines containing high molecular weight capsular polysaccharide generate more antibody than those with low molecular weight polysaccharide.[24]

The precise protective level of anti-Haemophilus b polysaccharide antibody has not been established. Titers associated with protection of agammaglobulinemic children[18, 20] and experimentally infected animals by passively administered gamma globulin suggest that 0.15 μg/ml is protective. In a controlled field trial, levels ≥1 μg/ml in 3 week post-vaccination serum were correlated with clinical protection[20]; approximately 75% of tested 18-23 month old and 85% of 24-29 month old children achieved that level following Haemophilus b polysaccharide vaccination.[23] These Finnish data can be compared to those obtained with *b*-CAPSA I (see Table 1).

The efficacy of Haemophilus b polysaccharide vaccine was evaluated in a double-blind, controlled field trial conducted in Finland in children 3 months to 5 years of age.[4, 23] Approximately 98,000 children, half of whom received Haemophilus b polysaccharide vaccine, were followed for 4 years. The Haemophilus b polysaccharide vaccine for that study was prepared by the scientific founders of Praxis Biologics. The results indicated that the vaccine was highly protective for children of 18 months to 5 years of age: a single dose reduced the overall attack rate of bacteremic Hib disease by 90%. Of more than 4,000 children who were 18-23 months old when vaccinated, *none* who received Haemophilus b polysaccharide developed bacteremic Hib disease during the four years of follow-up. However, the number of cases of bacteremic Hib disease in the control group was too small to permit a meaningful assessment of Haemophilus b polysaccharide vaccine efficacy in that age group. Children younger than 18 months of age had little immunologic response to the vaccine and were not protected.

Based on the results of their field trial, the Finnish investigators recommended universal vaccination with Haemophilus b polysaccharide for children of ≥18 months of age and suggested the potential need for a booster dose for children who received their primary Haemophilus b polysaccharide vaccination at 18-23 months of age.[4] An analysis of U.S. epidemiological data by clinical investigators at the USPHS Centers for Disease Control supported such use of Haemophilus b polysaccharide vaccine.[3]

Considerable evidence correlates the immunogenicity of bacterial polysaccharide vaccines with their physicochemical properties and the side effects with trace contaminants, especially endotoxin. The properties of *b*-CAPSA I VACCINE are equivalent to those of the Haemophilus b polysaccharide vaccine used in the Finnish field trial. The unique protein-free, chemically defined bacterial growth medium and purification procedures used in the preparation of *b*-CAPSA I VACCINE minimize the content of protein, nucleic acids, and endotoxin and guarantee a large molecular weight.

Table 1 summarizes the antibody responses to *b*-CAPSA I VACCINE.

TABLE 1
ANTIBODY RESPONSES TO VACCINATION WITH *b*-CAPSA I VACCINE

Age (mos.)	No. of Children	Geometric Mean Titer (μg/ml) Pre	Post*	Percent of Children with Post-Vaccination Titers ≥1 μg/ml
18-20	34	0.63	1.88	76
24-29	161	0.37	4.30	96
≥30	72	0.24	12.11	100
ALL	267	0.35	5.06	95

**Approximately 3 weeks post-vaccination.*

A limited number of children have been reported to have received DTP and Haemophilus b polysaccharide vaccines at the same time.[22, 24, 25, 27] No impairment of the immune response to individual antigens occurred. The incidence and type of associated reactions[22, 24, 25, 27] approximated those reported for DTP vaccine.[28]

INDICATIONS AND USAGE

b-CAPSA I VACCINE is indicated for immunization of children of 24 months to six years of age against diseases caused by *Haemophilus influenzae* b.

Children of 24 months of age and older have a high rate of seroconversion, and clinical studies indicate that they will be protected against bacteremic Hib diseases following a single vaccination with *b*-CAPSA I VACCINE.

b-CAPSA I VACCINE may be given to children 18-23 months of age known to be at high-risk of systemic Hib disease, e.g., children who attend day care. A controlled field trial suggested that many children in this age group will be protected by a single vaccination, although the rate of seroconversion is not as high as with older children. Parents should be informed that the vaccine is not likely to be completely effective in this age group.

Studies are ongoing to determine the need and timing for revaccination, particularly for children vaccinated at 18-23 months of age.

b-CAPSA I VACCINE *will not protect children younger than 18 months of age and will not protect against* Haemophilus influenzae *other than type b or other microorganisms that cause meningitis or septic disease.*

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including thimerosal.

WARNINGS

If the vaccine is used in persons deficient in producing antibody, whether due to genetic defect or to immunosuppressive therapy, the expected immune response may not be obtained.

PRECAUTIONS

General

As with the injection of any biological material, epinephrine injection (1:1000) should be available for immediate use should an anaphylactoid reaction occur.

Any febrile illness or active infection is reason for delaying use of *b*-CAPSA I VACCINE.

The vaccine should not be injected intradermally or intravenously, since the safety and efficacy of these routes of administration have not been evaluated. The vaccine should be given *subcutaneously*.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis viruses and other infectious agents from one person to another.

Pregnancy

Pregnancy Category C

Animal reproductive studies have not been conducted with *b*-CAPSA I VACCINE. It is not known whether *b*-CAPSA I VACCINE can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Data are not available to support the use of this product during pregnancy at this time, regardless of benefits.

Nursing Mothers

There is no indication for using this product in nursing mothers.

Pediatric Use

b-CAPSA I VACCINE is not recommended for infants younger than 18 months of age. See comments above about vaccine use in children older than 18 months of age.

ADVERSE REACTIONS

Different preparations of Haemophilus b polysaccharide produced by different procedures and administered at different doses have been evaluated in several field studies. Objectively observed side effects, e.g., erythema and induration at the injection site and fever, have generally been minor and lasted 24 hours or less.[18, 21-23] The incidence of local side effects reported in the Finnish field trial was 51%. In all other reported trials, the incidence of these reactions was 4-9%.[18, 21, 22] Temperatures >38.3°C (101°F) at 24 hours post-vaccination have occurred in up to 13% of vaccinated children. In the Finnish field trial, one child had a possible anaphylactoid reaction; following an injection of epinephrine, the child recovered rapidly and without complications.

The side effects associated with the use of *b*-CAPSA I VACCINE in children are summarized in Table 2. At 24 hours post-vaccination, local reactions were observed in 1.5% of vaccinated children, and temperature >38.3°C (101°F) in 0.75%.

TABLE 2
SIDE EFFECTS AT 24 HOURS ASSOCIATED WITH VACCINATION OF CHILDREN (18-60 MOS.) WITH *b*-CAPSA I VACCINE

No. of Children	Temperature >38.3°C (101°F)	Objective Local Reaction Swelling	Erythema
267*	2	4	4

**161 of these children were 24-29 months at vaccination.*

DO NOT INJECT INTRAVENOUSLY.

The immunizing dose is a single injection of 0.5 ml of reconstituted b-CAPSA I VACCINE given subcutaneously.

b-CAPSA I VACCINE is manufactured by Praxis Biologics, Inc., Rochester, New York 14623 and distributed by Mead Johnson Nutritional Division, Evansville, Indiana 47721.

For information contact: MEAD JOHNSON NUTRITIONAL DIVISION at (812) 429-7480.

Reference list will be supplied by Mead Johnson upon request.

REFERENCES

(TO TEXT ON PRECEDING PAGE)

1. Data on File, Praxis Biologics.
2. Package insert.

Manufactured by
PRAXIS BIOLOGICS

Distributed by
Mead Johnson
NUTRITIONAL DIVISION

Some mommies don't know about waterproof

SUNDOWN®
SUNBLOCK

Some parents don't know that SUNDOWN® Sunblock SPF 15 keeps their children "covered" for at least 80 minutes when they play in the water.[1]

SUNDOWN is waterproof to withstand splashing or sweating. And it effectively blocks ultraviolet radiation with a three-sunscreen formulation.* So SUNDOWN helps prevent sunburn, and may help prevent the development of more serious sun-related problems such as premature aging of the skin and skin cancer.[1,2]

So don't keep SUNDOWN—and your patients—under wraps. Recommend it for the children in your practice.

References: 1. FDA Advisory Review Panel on Sunscreen Products for Over-the-Counter Human Use: *Federal Register* 43(166): 38206-38269, 1978. **2.** Pathak MA, et al: in Petersdorf RG, et al (eds): *Harrison's Principles of Internal Medicine*, ed 10. New York, McGraw-Hill Book Co, 1983, pp 273-282.

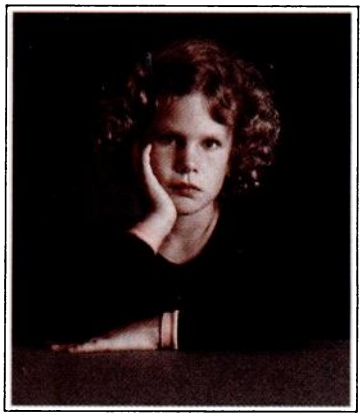
*Octyl dimethyl PABA, oxybenzone and octyl methoxycinnamate.

†Refer to package labeling; contraindicated in patients sensitive to any ingredient contained in this product.

Effective protection for every patient under the sun†

Johnson & Johnson

New safety appraisal of valproate...



A recent report by the AMERICAN ACADEMY OF PEDIATRICS' Committee on Drugs:

"...valproate seems to be relatively free of many adverse neuropsychologic effects..."[1]

"Valproate added to preexisting therapy had no effect on paired associate learning tasks, and its use produced minimal adverse effects in patients performing a series of psychologic tests."[1]

PRIMARY BEHAVIORAL AND COGNITIVE SIDE EFFECTS OF ANTICONVULSANT AGENTS*

DRUG	BEHAVIORAL EFFECTS	COGNITIVE EFFECTS
Phenobarbital	Hyperactivity, fussiness, lethargy, disturbed sleep, irritability, disobedience, stubbornness, depressive symptoms	Deficits on neuropsychologic tests, impaired short-term memory and memory concentration tasks
Phenytoin	Unsteadiness, involuntary movements, tiredness, alteration of emotional state	Deficits on neuropsychologic tests, impaired attention, problem solving and visuomotor tasks
Carbamazepine	Difficulty sleeping, agitation, irritability, emotional lability	Impaired task performance
Valproic acid	Drowsiness (especially when used in combination with barbiturates)	Minimal adverse effects on psychosocial tests

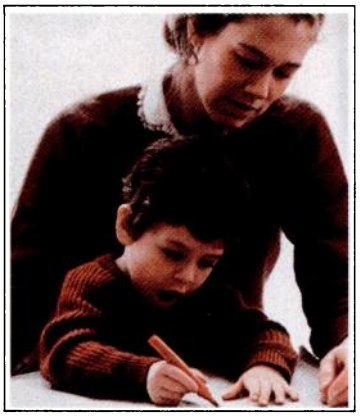
*Adapted from American Academy of Pediatrics' Committee on Drugs. Behavioral and Cognitive Effects of Anticonvulsant Therapy. *Pediatrics*, 76: 644-649, 1985.

NOTE: Large doses of virtually all anticonvulsant medications can affect mental function. See full prescribing information for reported side effects of Depakote (divalproex sodium), especially the boxed warning concerning hepatotoxicity and the necessity for monitoring liver function.

DEPAKOTE®

Presented on April 30, 1986 at the Annual Meeting of the American Academy of Neurology.[2] A comprehensive, retrospective review of reported cases of hepatic fatalities between 1978 & 1984 in the U.S:

- No hepatic fatalities in patients above the age of ten receiving valproate as monotherapy. (This group represents about 36% of the 400,000 patients treated with valproate during this period.)
- Risk of hepatic fatality is very low in patients on monotherapy (1 per 37,000).
- Primary risk of hepatic fatality is in patients aged 0-2 years treated with polytherapy (1 per 500), but is substantially lower in patients above the age of two treated with polytherapy (1 per 12,000).



Restores control
and quality of life

DEPAKOTE® Enteric-Coated Tablets
divalproex sodium

If you would like additional information about the above studies, please contact Abbott Laboratories, Pharmaceutical Products Division, Dept. 426, North Chicago, IL 60064.

REFERENCES:

1. American Academy of Pediatrics Committee on Drugs, Behavioral and Cognitive Effects of Anticonvulsant Therapy. *Pediatrics* 76:644-649, 1985.
2. Dreifuss, F. E. and Santilli, N., Valproic Acid Hepatic Fatalities: Analysis of U.S. Cases. *Neurology* 36(4, Suppl. 1): 1986.

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DEPAKOTE®
divalproex sodium
Enteric-Coated Tablets

Restores control and quality of life

Three dosage strengths:
125mg tablet; 250mg tablet;
and 500mg tablet

WARNING:
HEPATIC FAILURE RESULTING IN FATALITIES HAS OCCURRED IN PATIENTS RECEIVING VALPROIC ACID AND ITS DERIVATIVES. EXPERIENCE HAS INDICATED THAT CHILDREN UNDER THE AGE OF TWO YEARS ARE AT A CONSIDERABLY INCREASED RISK OF DEVELOPING FATAL HEPATOTOXICITY, ESPECIALLY THOSE ON MULTIPLE ANTICONVULSANTS, THOSE WITH CONGENITAL METABOLIC DISORDERS, THOSE WITH SEVERE SEIZURE DISORDERS ACCOMPANIED BY MENTAL RETARDATION, AND THOSE WITH ORGANIC BRAIN DISEASE. WHEN DEPAKOTE IS USED IN THIS PATIENT GROUP, IT SHOULD BE USED WITH EXTREME CAUTION AND AS A SOLE AGENT. THE BENEFITS OF SEIZURE CONTROL SHOULD BE WEIGHED AGAINST THE RISKS. ABOVE THIS AGE GROUP, EXPERIENCE HAS INDICATED THAT THE INCIDENCE OF FATAL HEPATOTOXICITY DECREASES CONSIDERABLY IN PROGRESSIVELY OLDER PATIENT GROUPS.

THESE INCIDENTS USUALLY HAVE OCCURRED DURING THE FIRST SIX MONTHS OF TREATMENT. SERIOUS OR FATAL HEPATOTOXICITY MAY BE PRECEDED BY NON-SPECIFIC SYMPTOMS SUCH AS LOSS OF SEIZURE CONTROL, MALAISE, WEAKNESS, LETHARGY, FACIAL EDEMA, ANOREXIA AND VOMITING. PATIENTS SHOULD BE MONITORED CLOSELY FOR APPEARANCE OF THESE SYMPTOMS. LIVER FUNCTION TESTS SHOULD BE PERFORMED PRIOR TO THERAPY AND AT FREQUENT INTERVALS THEREAFTER, ESPECIALLY DURING THE FIRST SIX MONTHS.

DESCRIPTION: Divalproex sodium is a stable co-ordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship and formed during the partial neutralization of valproic acid with 0.5 equivalent of sodium hydroxide. Chemically it is designated as sodium hydrogen bis(2-propylpentanoate).

Divalproex sodium has a molecular weight of 310.41 and occurs as a white powder with a characteristic odor.

DEPAKOTE is an oral antiepileptic supplied as enteric-coated tablets in three dosage strengths containing divalproex sodium equivalent to 125 mg, 250 mg or 500 mg of valproic acid.

Inactive Ingredients

125 mg tablets: cellulosic polymers, diacetylated monoglycerides, FD&C Blue No. 1, FD&C Red No. 40, povidone, pregelatinized starch (contains corn starch), silica gel, talc, titanium dioxide, vanillin and other ingredients.

250 mg tablets: cellulosic polymers, diacetylated monoglycerides, FD&C Yellow No. 6, iron oxide, povidone, pregelatinized starch (contains corn starch), silica gel, talc, titanium dioxide, vanillin and other ingredients.

500 mg tablets: cellulosic polymers, diacetylated monoglycerides, D&C Red No. 30, FD&C Blue No. 2, iron oxide, povidone, pregelatinized starch (contains corn starch), silica gel, talc, titanium dioxide, vanillin and other ingredients.

CLINICAL PHARMACOLOGY: DEPAKOTE is an antiepileptic agent which is chemically related to valproic acid. It has no nitrogen or aromatic moiety characteristic of other antiepileptic drugs. The mechanism by which DEPAKOTE exerts its antiepileptic 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. DEPAKOTE dissociates into valproate in the gastrointestinal tract.

Because of the enteric coating of DEPAKOTE, absorption is delayed one hour following oral administration. Thereafter, DEPAKOTE is uniformly and reliably absorbed, as shown by studies in normal volunteers. Peak serum levels of valproate occur in 3 to 4 hours. Bioavailability of divalproex sodium tablets was found to be equivalent to that of DEPAKENE® (valproic acid) capsules. Concomitant administration with food would be expected to slow absorption but not affect the extent of absorption. The serum half-life of valproate is typically in the range of six to sixteen hours. Half-lives in the lower part of the above range are usually found in patients taking other antiepileptic drugs capable of enzyme induction.

Enteric-coated divalproex sodium may reduce the incidence of the irritative gastrointestinal effects of valproate as compared to valproic acid capsules.

Valproate is rapidly distributed and at therapeutic drug concentrations, drug is highly bound (90%) to human plasma proteins. Increases in dose may result in decreases in the extent of protein binding and increased valproate clearance and elimination.

Elimination of DEPAKOTE 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, omega-1, and omega oxidation (C-3, C-4 and C-5 positions). The major oxidative metabolite in the urine is 2-propyl-3-keto-pentanoic acid; minor metabolites are 2-propyl-glutaric acid, 2-propyl-5-hydroxypentanoic acid, 2-propyl-3-hydroxypentanoic acid and 2-propyl-4-hydroxypentanoic acid.

INDICATIONS AND USAGE: DEPAKOTE (divalproex sodium) is indicated for use as sole and adjunctive therapy in the treatment of simple (petit mal) and complex absence seizures. DEPAKOTE 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.

SEE "WARNINGS" SECTION FOR STATEMENT REGARDING FATAL HEPATIC DYSFUNCTION.

CONTRAINDICATIONS: DEPAKOTE (DIVALPROEX SODIUM) SHOULD NOT BE ADMINISTERED TO PATIENTS WITH HEPATIC DISEASE OR SIGNIFICANT DYSFUNCTION.

DEPAKOTE is contraindicated in patients with known hypersensitivity to the drug.

WARNINGS: Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid. These incidents usually have occurred during the first six months of treatment. Serious or fatal hepatotoxicity may be preceded by non-specific symptoms such as loss of seizure control, malaise, weakness, lethargy, facial edema, anorexia and vomiting. Patients should be monitored closely for appearance of these symptoms. Liver function tests should be performed prior to therapy and at frequent intervals thereafter, especially during the first six months. However, physicians should not rely totally on serum biochemistry since these tests may not be abnormal in all instances, but should also consider the results of careful interim medical history and physical examination. Caution should be observed when administering DEPAKOTE to patients with a prior history of hepatic disease. Patients on multiple anticonvulsants, children, those with congenital metabolic disorders, those with severe seizure disorders accompanied by mental retardation, and those with organic brain disease may be at particular risk. Experience has indicated that children under the age of two years are at a considerably increased risk of developing fatal hepatotoxicity, especially those with the aforementioned conditions. When DEPAKOTE is used in this patient group, it should be used with extreme caution and as a sole agent. The benefits of seizure control should be weighed against the risks. Above this age group, experience has indicated that the incidence of fatal hepatotoxicity decreases considerably in progressively older patient groups.

The drug should be discontinued immediately in the presence of significant hepatic dysfunction, suspected or apparent. In some cases, hepatic dysfunction has progressed in spite of discontinuation of drug.

The frequency of adverse effects (particularly elevated liver enzymes) may be dose-related. The benefit of improved seizure control which may accompany the higher doses should therefore be weighed against the possibility of a greater incidence of adverse effects.

Usage in Pregnancy: ACCORDING TO PUBLISHED AND UNPUBLISHED REPORTS, VALPROIC ACID MAY PRODUCE TERATOGENIC EFFECTS IN THE OFFSPRING OF HUMAN FEMALES RECEIVING THE DRUG DURING PREGNANCY.

THERE ARE MULTIPLE REPORTS IN THE CLINICAL LITERATURE WHICH INDICATE THAT THE USE OF ANTIEPILEPTIC DRUGS DURING PREGNANCY RESULTS IN AN INCREASED INCIDENCE OF BIRTH DEFECTS IN THE OFFSPRING. ALTHOUGH DATA ARE MORE EXTENSIVE WITH RESPECT TO TRIMETHADIONE, PARAMETHADIONE, PHENYTOIN, AND PHENOBARBITAL, REPORTS INDICATE A POSSIBLE SIMILAR ASSOCIATION WITH THE USE OF OTHER ANTIEPILEPTIC DRUGS. THEREFORE, ANTIEPILEPTIC DRUGS SHOULD BE ADMINISTERED TO WOMEN OF CHILDBEARING POTENTIAL ONLY IF THEY ARE CLEARLY SHOWN TO BE ESSENTIAL IN THE MANAGEMENT OF THEIR SEIZURES.

THE INCIDENCE OF NEURAL TUBE DEFECTS IN THE FETUS MAY BE INCREASED IN MOTHERS RECEIVING VALPROATE DURING THE FIRST TRIMESTER OF PREGNANCY. THE CENTERS FOR DISEASE CONTROL (CDC) HAS ESTIMATED THE RISK OF VALPROIC ACID EXPOSED WOMEN HAVING CHILDREN WITH SPINA BIFIDA TO BE APPROXIMATELY 1 TO 2%.[1] THIS RISK IS SIMILAR TO THAT FOR NONEPILEPTIC WOMEN WHO HAVE HAD CHILDREN WITH NEURAL TUBE DEFECTS (ANENCEPHALY AND SPINA BIFIDA).

ANIMAL STUDIES ALSO HAVE DEMONSTRATED VALPROIC ACID INDUCED TERATOGENICITY. Studies in rats and human females demonstrated placental transfer of the drug. Doses greater than 65 mg/kg/day given to pregnant rats and mice produced skeletal abnormalities in the offspring, primarily involving ribs and vertebrae; doses greater than 150 mg/kg/day given to pregnant rabbits produced fetal resorptions and (primarily) soft-tissue abnormalities in the offspring. In rats a dose-related delay in the onset of parturition was noted. Postnatal growth and survival of the progeny were adversely affected, particularly when drug administration spanned the entire gestation and early lactation period.

Antiepileptic drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

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

PRECAUTIONS: *Hepatic Dysfunction:* See "Boxed Warning," "Contraindications" and "Warnings" sections.

General: Because of reports of thrombocytopenia, inhibition of the secondary phase of platelet aggregation, and abnormal coagulation parameters, platelet counts and coagulation tests are recommended before initiating therapy and at periodic intervals. It is recommended that patients receiving DEPAKOTE (divalproex sodium) be monitored for platelet count and coagulation parameters prior to planned surgery. Evidence of hemorrhage, bruising or a disorder of hemostasis/coagulation is an indication for reduction of DEPAKOTE dosage or withdrawal of therapy.

Hyperammonemia with or without lethargy or coma has been reported and may be present in the absence of abnormal liver function tests. If clinically significant elevation occurs, DEPAKOTE should be discontinued.

Since DEPAKOTE (divalproex sodium) may interact with concurrently administered antiepileptic drugs, periodic serum level determinations of concomitant antiepileptic drugs are recommended during the early course of therapy. (See "Drug Interactions" section).

Valproate is partially eliminated in the urine as a keto-metabolite which may lead to a false interpretation of the urine ketone test.

There have been reports of altered thyroid function tests associated with valproate. The clinical significance of these is unknown.

Information for Patients: Since DEPAKOTE 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: Valproic acid may potentiate the CNS depressant activity of alcohol.

The concomitant administration of valproic acid with drugs that exhibit extensive protein binding (e.g., aspirin, carbamazepine, and dicumarol) may result in alteration of serum drug levels.

THERE IS EVIDENCE THAT VALPROIC ACID CAN CAUSE AN INCREASE IN SERUM PHENOBARBITAL LEVELS BY IMPAIRMENT OF NONRENAL CLEARANCE. THIS PHENOMENON CAN RESULT IN SEVERE CNS DEPRESSION. THE COMBINATION OF VALPROIC ACID AND PHENOBARBITAL HAS ALSO BEEN REPORTED TO PRODUCE CNS DEPRESSION WITHOUT SIGNIFICANT ELEVATIONS OF BARBITURATE OR VALPROATE SERUM LEVELS. ALL PATIENTS RECEIVING CONCOMITANT BARBITURATE THERAPY SHOULD BE CLOSELY MONITORED FOR NEUROLOGICAL TOXICITY. SERUM BARBITURATE LEVELS SHOULD BE OBTAINED, IF POSSIBLE, AND THE BARBITURATE DOSAGE DECREASED, IF APPROPRIATE.

Primidone is metabolized into a barbiturate and, therefore, may also be involved in a similar or identical interaction.

THERE HAVE BEEN REPORTS OF BREAKTHROUGH SEIZURES OCCURRING WITH THE COMBINATION OF VALPROIC ACID AND PHENYTOIN. MOST REPORTS HAVE NOTED A DECREASE IN TOTAL PLASMA PHENYTOIN CONCENTRATION. HOWEVER, INCREASES IN TOTAL PHENYTOIN SERUM CONCENTRATION HAVE BEEN REPORTED. AN INITIAL FALL IN TOTAL PHENYTOIN LEVELS WITH SUBSEQUENT INCREASE IN PHENYTOIN LEVELS HAS ALSO BEEN REPORTED. IN ADDITION, A DECREASE IN TOTAL SERUM PHENYTOIN WITH AN INCREASE IN THE FREE VS. PROTEIN BOUND PHENYTOIN LEVELS HAS BEEN REPORTED. 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.

There is inconclusive evidence regarding the effect of valproate on serum ethosuximide levels. Patients receiving valproate and ethosuximide, especially along with other anticonvulsants, should be monitored for alterations in serum concentrations of both drugs.

Caution is recommended when DEPAKOTE (divalproex sodium) is administered with drugs affecting coagulation, e.g., aspirin and warfarin. (See "Adverse Reactions" section).

Carcinogenesis: Valproic acid was administered to Sprague Dawley rats and ICR (HA/ICR) mice at doses of 0, 80 and 170 mg/kg/day for two years. Although a variety of neoplasms were observed in both species, the chief findings were a statistically significant increase in the incidence of subcutaneous fibrosarcomas in high dose male rats receiving valproic acid and a statistically significant dose-related trend for benign pulmonary adenomas in male mice receiving valproic acid. The significance of these findings for man is unknown at present.

Mutagenesis: Studies on valproic acid have been performed using bacterial and mammalian systems. These studies have provided no evidence of a mutagenic potential for DEPAKOTE.

Fertility: Chronic toxicity studies in juvenile and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at doses greater than 200 mg/kg/day in rats and greater than 90 mg/kg/day in dogs. Segment I fertility studies in rats have shown doses up to 350 mg/kg/day for 60 days to have no effect on fertility. THE EFFECT OF DEPAKOTE (DIVALPROEX SODIUM) ON THE DEVELOPMENT OF THE TESTES AND ON SPERM PRODUCTION AND FERTILITY IN HUMANS IS UNKNOWN

Pregnancy: Pregnancy Category D: See "Warnings" section.

Nursing Mothers: Valproate is excreted in breast milk. Concentrations in breast milk have been reported to be 1-10% of serum concentrations. It is not known what effect this would have on a nursing infant. Caution should be exercised when DEPAKOTE is administered to a nursing woman.

ADVERSE REACTIONS: Since valproic acid and its derivatives have usually been used with other antiepileptic drugs, it is not possible, in most cases, to determine whether the following adverse reactions can be ascribed to valproic acid 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. The administration of enteric-coated divalproex sodium may result in reduction of gastrointestinal side effects in some patients.[2]

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 antiepileptic medication. Tremor has been reported in patients receiving valproate and may be dose-related. Ataxia, headache, nystagmus, diplopia, asterixis, "spots before eyes," dysarthria, dizziness, and incoordination have rarely been noted. Rare cases of coma have been noted in patients receiving valproic acid alone or in conjunction with phenobarbital.

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

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

Musculoskeletal: Weakness has been reported.

Hematologic: Thrombocytopenia has been reported. Valproic acid inhibits the secondary phase of platelet aggregation. (See "Drug Interactions" section). This may be reflected in altered bleeding time. Petechiae, bruising, hematoma formation, and frank hemorrhage have been reported. (See "Precautions" section). Relative lymphocytosis and hypofibrinogenemia have been noted. Leukopenia and eosinophilia have also been reported. Anemia and bone marrow suppression have been reported.

Hepatic: Minor elevations of transaminases (e.g., SGOT and SGPT) and LDH are frequent and appear to be dose related. Occasionally, laboratory test results include, as well, increases in serum bilirubin and abnormal changes in other liver function tests. These results may reflect potentially serious hepatotoxicity. (See "Warnings" section).

Endocrine: There have been reports of irregular menses and secondary amenorrhea, and rare reports of breast enlargement and galactorrhea occurring in patients receiving valproic acid and its derivatives.

Abnormal thyroid function tests have been reported. (See "Precautions" section).

Pancreatic: There have been reports of acute pancreatitis, including rare fatal cases, occurring in patients receiving valproic acid and its derivatives.

Metabolic: Hyperammonemia. (See "Precautions" section).

Hyperglycinemia has been reported and has been associated with a fatal outcome in a patient with preexistent nonketotic hyperglycinemia.

Other: Edema of the extremities has been reported.

OVERDOSAGE: Overdosage with valproic acid may result in deep coma.

Since DEPAKOTE tablets are enteric-coated, the benefit of gastric lavage or emesis will vary with the time since ingestion. General supportive measures should be applied with particular attention being given to the maintenance of adequate urinary output.

Naloxone has been reported to reverse the CNS depressant effects of valproate overdosage. Because naloxone could theoretically also reverse the antiepileptic effects of DEPAKOTE it should be used with caution.

DOSAGE AND ADMINISTRATION: DEPAKOTE 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 60 mg/kg/day. If the total daily dose exceeds 250 mg, it should be given in a divided regimen.

Conversion from DEPAKENE to DEPAKOTE: In patients previously receiving DEPAKENE (valproic acid) therapy, DEPAKOTE should be initiated at the same total daily dose and dosing schedule.[3] After the patient is stabilized on DEPAKOTE, a twice-a-day or three-times-a-day schedule may be instituted in selected patients.

The frequency of adverse effects (particularly elevated liver enzymes) may be dose-related. The benefit of improved seizure control which may accompany higher doses should therefore be weighed against the possibility of a greater incidence of adverse reactions.

A good correlation has not been established between daily dose, serum level and therapeutic effect. However, therapeutic valproate serum levels for most patients will range from 50 to 100 mcg/ml. Occasional patients may be controlled with serum levels lower or higher than this range.

As the DEPAKOTE dosage is titrated upward, blood levels of phenobarbital and/or phenytoin may be affected. (See "Precautions" section).

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.

HOW SUPPLIED: DEPAKOTE (divalproex sodium enteric-coated tablets) are supplied as:

125 mg salmon pink-colored tablets:	
Bottles of 100	(NDC 0074-6212-13)
250 mg peach-colored tablets:	
Bottles of 100	(NDC 0074-6214-13)
Abbo-Pac® unit dose packages of 100	(NDC 0074-6214-11).
500 mg lavender-colored tablets:	
Bottles of 100	(NDC 0074-6215-13)
Abbo-Pac® unit dose packages of 100	(NDC 0074-6215-11).

REFERENCES

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2. Wilder, B.J., et al, Gastrointestinal Tolerance of Divalproex Sodium, *Neurology* 33:808-811, June, 1983.
3. Wilder, B.J., et al, Twice-Daily Dosing of Valproate with Divalproex, *Clin Pharmacol Ther* 34(4): 501-504, 1983.

Revised: Jan., 1986

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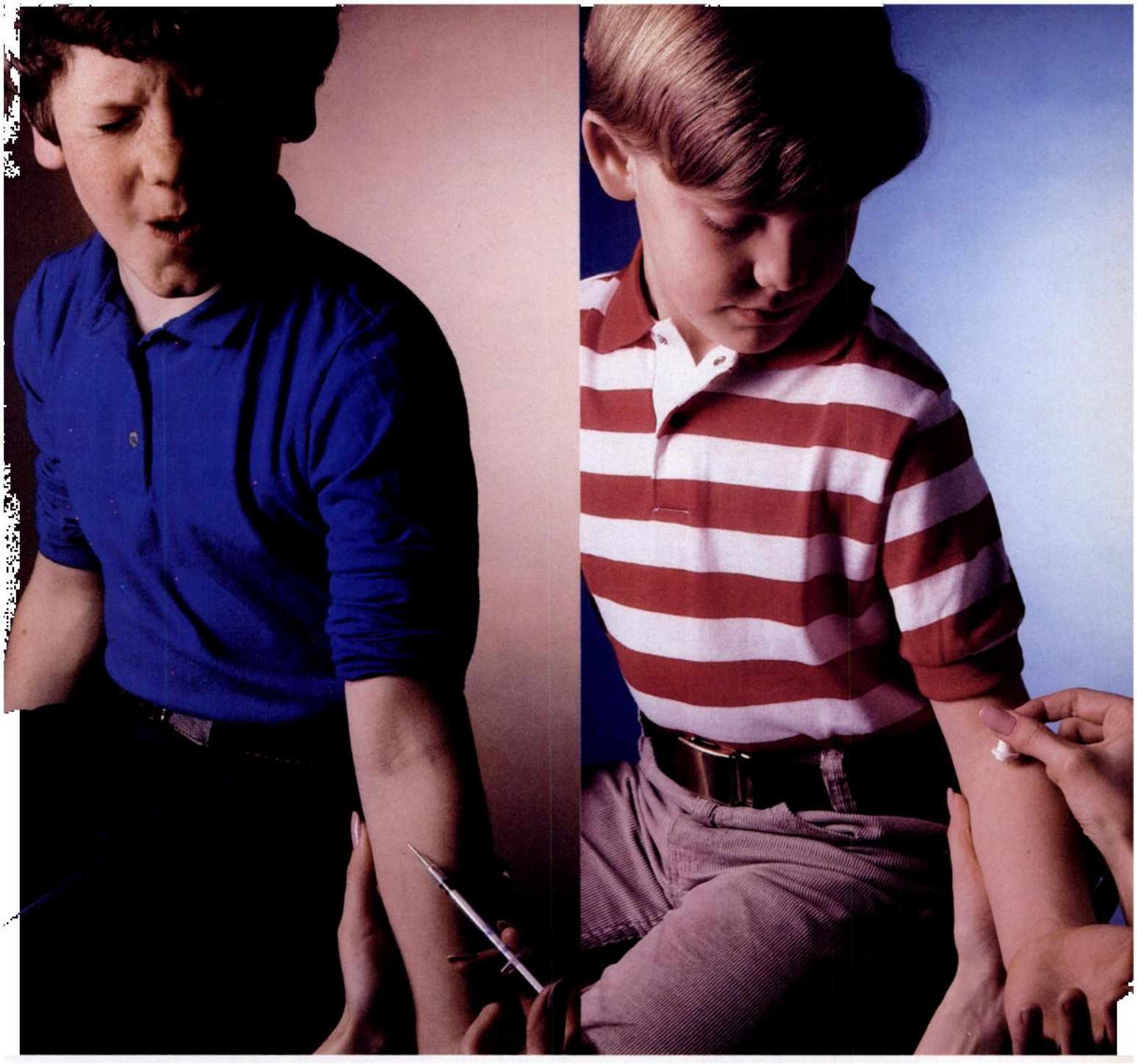

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*Report on clinical evaluation of multiple puncture devices for administration of tuberculin. U.S. Dept. of Health & Human Services. March 31, 1983. (As compared with duplicate Mantoux Tests.)

Please see following page for brief summary of prescribing information.

Tuberculin, Old,
TINE TEST®
Tuberculin purified protein derivative
TINE TEST® PPD

Lederle Biologicals, A Division of American Cyanamid Company, Wayne, New Jersey 07470

Tuberculin, Old, TINE TEST®
Tuberculin Purified
Protein Derivative
TINE TEST® PPD

Brief Summary
Please see package insert for full prescribing information.

INDICATIONS: For screening for tuberculosis.

PRECAUTIONS: Use with caution in persons with acute tuberculosis (activation of quiescent lesions is rare); and in patients with known allergy to acacia. Reactivity to the test may be suppressed in those receiving corticosteroids or immunosuppressive agents, or those who have recently been vaccinated with live virus vaccine such as measles, mumps, rubella, polio, etc. With a positive reaction, further diagnostic procedures must be considered, ie, chest x-ray, microbiologic examinations of sputum and other specimens, confirmation of positive tine test (except vesiculation reactions) by Mantoux method. When vesiculation occurs, the reaction is to be interpreted as strongly positive and a repeat test by the Mantoux method must not be attempted. If a patient has a history of occurrence of vesiculation and necrosis with a previous tuberculin test by any method, tuberculin testing should be avoided. Similar or more severe vesiculation with or without necrosis is likely to occur.

Pregnancy Category C: Animal reproduction studies have not been conducted; whether these tuberculin tests can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity is unknown. Tuberculin, Old, TINE TEST or Tuberculin, Purified Protein Derivative TINE TEST PPD should be given to a pregnant woman only if clearly needed. During pregnancy, known positive reactors may demonstrate a negative response.

ADVERSE REACTIONS: Vesiculation, ulceration, or necrosis may appear at test site in highly sensitive persons. Pain, pruritus and discomfort at test site may be relieved by cold packs or by topical glucocorticoid ointment or cream. Any transient bleeding at puncture site is not significant.

Rev. 3/86

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IF YOU'RE TELLING YOUR PATIENTS TO AVOID COLD CUTS, YOU'RE NOT TALKING TURKEY.

The next time you prescribe a lower-fat diet, you ought to talk Louis Rich. Because Louis Rich™ turkey products are so naturally lean, they're up to 95% fat free.

So, instead of beef or pork bologna, now your patients can sink their teeth into bologna made from turkey with 34% fewer calories and 20% less sodium. And it tastes like the bologna they grew up on. The same goes for the taste of Louis Rich ham, hot dogs, and all their cold cuts. In fact, Louis Rich makes all sorts of turkey products—like their fully cooked Breast of Turkey and full line of Fresh Turkey Cuts. Many are leaner than chicken, salmon, or even flounder. Whether it's Louis Rich smoked sausage for breakfast, cold cuts for lunch, or Breast of Turkey for dinner, you'll never run out of ways to serve it. So when your patients have to cut back on fat, give them some good news and talk turkey.

It took Louis Rich™ to make turkey so right.

Comparative nutritional claims are based on data from *Agricultural Handbook No. 8-7 Composition of Foods, Sausages, and Luncheon Meats, United States Department of Agriculture, September, 1980.*

Premature Formula Mineral Levels...

[1] Bhatia J, Fomon S: Pediatrics 72:37-40, 1983.

[2] Chan G, Moyer L, Shino J, Hansen JW: Ped Res, April 18, 1984/Part 2:192A.

[3] Gross S: New England Journal of Medicine 308:237-241, February 3, 1983.

[4] Based on reference standards of fetal calcium retention reported by Ziegler EE, O'Donnell AM, Nelson SE, Fomon SJ: Growth 40:329-341, 1976.

 L-K157-4-84

What Does the Evidence Support?

Extensive research studies and thorough clinical validation show that ENFAMIL® Premature Formula (117 mg calcium/100 kcal):

Delivers Calcium & Phosphorus More Reliably

A study of mineral delivery concludes that Enfamil Premature Formula is more stable with respect to calcium and phosphorus suspension than a premature formula with higher mineral levels.[1]

The same study shows that, following infusion pumping, Enfamil Premature Formula delivered higher average calcium and phosphorus levels than any other premature infant formula.

Supports Appropriate Bone Density

Bone density studies prove that no advantage is gained by increasing the mineral content of Enfamil Premature Formula.[2] In these studies, one group of premature infants was fed Enfamil Premature Formula and another group was fed Enfamil Premature Formula fortified with additional minerals. After four weeks, the bone density of the infants fed the currently marketed Enfamil Premature Formula was the same as the bone density of those infants fed the fortified product.

Also, both groups of infants had comparable serum alkaline phosphatase levels averaging 250-400 I.U. per liter.

Maintains Normal Serum Biochemistry

A study of serum biochemistry documents that Enfamil Premature Formula maintains serum calcium and serum phosphorus at appropriate levels for the preterm infant.[3]

The study also shows that serum alkaline phosphatase levels are significantly lower in infants fed Enfamil Premature Formula than those fed either preterm or mature human milk.

Provides Calcium Retention Similar to *In Utero* Accretion

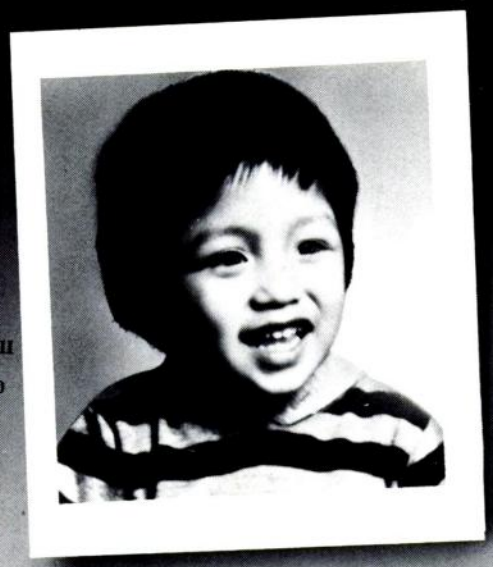
Metabolic balance studies demonstrate that calcium retention of infants fed Enfamil Premature Formula is similar to that of normal *in utero* accretion rates.[4]

Proven in Millions of Feedings

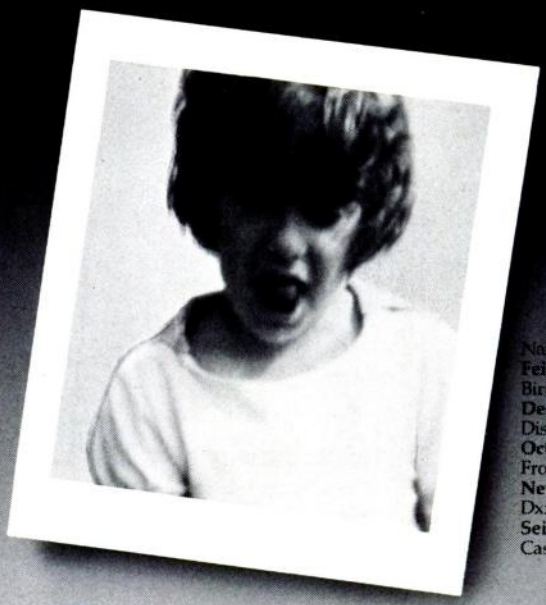
Finally, the appropriateness of Enfamil Premature Formula mineral levels has been proven in 10 million feedings; there have been no reports of rickets among infants consuming appropriate quantities of formula.

The Evidence Supports ENFAMIL® Premature Formula

Mead Johnson NUTRITIONAL DIVISION

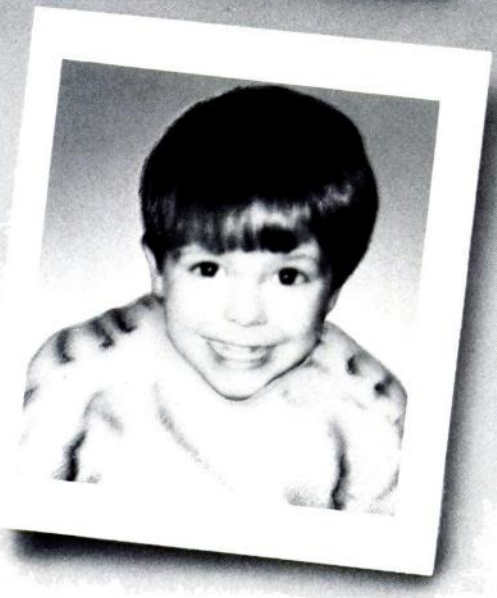


Name:
Roland Spencer III
Birthdate:
September 3, 1980
Disappeared:
May 25, 1984
From:
Wapato, WA
Dx:
Epilepsy
Case# 3484 s



Name:
Feige Freeman
Birthdate:
December 14, 1970
Disappeared:
October 9, 1983
From:
New York, NY
Dx:
Seizure Disorder
Case# 2467 p

Name:
Tiahease Jackson
Birthdate:
October 5, 1972
Disappeared:
August 13, 1983
From:
Staten Island, NY
Dx:
Bright's Disease; Allergies
Case# 3032 s



Name:
Joshua Carter
Birthdate:
June 9, 1978
Disappeared:
August 1983
From:
Huntington, WV
Dx:
Asthma
Case# 2812 p

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*Please see brief summaries of product information on adjoining page.

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Combined Brief Summary

Triaminic® Cold Syrup/Triaminic® Cold Tablets/ Triaminic-12® Tablets/Triaminic® Oral Infant Drops

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

DESCRIPTION: Each teaspoonful (5 ml) of TRIAMINIC Cold Syrup and each TRIAMINIC Cold Tablet contains: phenylpropanolamine hydrochloride 12.5 mg and chlorpheniramine maleate 2 mg. Each TRIAMINIC-12 Tablet contains: phenylpropanolamine hydrochloride 75 mg and chlorpheniramine maleate 12 mg. TRIAMINIC Oral Infant Drops: Each ml contains phenylpropanolamine hydrochloride 20 mg, pheniramine maleate 10 mg, pyrilamine maleate 10 mg.

INDICATIONS AND USAGE: For temporary relief from such symptoms as nasal congestion, and postnasal drip associated with colds, allergies, sinusitis and rhinitis. Also for the relief of symptoms associated with allergic rhinitis such as sneezing, rhinorrhea, pruritus and lacrimation.

CONTRAINDICATIONS: These products are contraindicated in patients exhibiting hypersensitivity to any of the components. Antihistamines are contraindicated in patients receiving monoamine oxidase inhibitors since these agents prolong and intensify the anticholinergic effects of antihistamines (see Drug Interactions). Antihistamines should not be used to treat lower respiratory tract symptoms. Sympathomimetic preparations are contraindicated in patients with severe hypertension, severe coronary artery disease and in patients receiving MAO inhibitor therapy due to potentiation of the pressor effects of phenylpropanolamine.

WARNINGS: Sympathomimetics should be used with caution in patients with hypertension, hyperthyroidism, diabetes mellitus and cardiovascular disease. Antihistamines should be used with caution in patients with narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy and bladder neck obstruction.
Antihistamines have addictive effects with other CNS depressants (hypnotics, sedatives, tranquilizers, alcohol, etc.). Warn mothers that drowsiness may occur. When prescribing antihistamine preparations, patients should be cautioned against mechanical activity requiring alertness.

PRECAUTIONS:

General: Use with caution in patients with hypertension, hyperthyroidism, diabetes mellitus, cardiovascular disease, bronchial asthma, increased intraocular pressure (see WARNINGS).

Information for Patients: Mothers should be informed of the potential for sedation or drowsiness. Antihistamines may also cause excitability especially in children.

Drug Interactions:

(1) Monamine oxidase inhibitors: MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines and potentiate the pressor effects of sympathomimetics.

(2) Alcohol and CNS depressants: These agents potentiate the sedative effects of antihistamines.

(3) Certain antihypertensives: Sympathomimetics may reduce the antihypertensive effects of methyldopa, mecamylamine, reserpine and veratrum alkaloids.

Pediatric Use: TRIAMINIC Oral Infant Drops have been formulated to provide safe and effective symptomatic relief for infants and small children. Precise dosage (on a body weight basis) is facilitated through the use of the plastic squeeze bottle with attached dropper tip (see DOSAGE AND ADMINISTRATION). It is important to note the variability of response infants and small children exhibit to antihistamines and sympathomimetics. As in adults, the combination of an antihistamine and sympathomimetic can elicit either mild stimulation or mild sedation in children. In the young child, mild stimulation is the response most frequently seen. In infants and children, overdosage of antihistamines may cause hallucinations, convulsions or death. (See Dosage and Administration section for further information.)

ADVERSE REACTIONS: The most frequent adverse reactions are underlined.

(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, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions, CNS depression, hallucinations.

(5) *GI System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

(6) *GU System:* Urinary frequency, difficult urination, urinary retention.

(7) *Respiratory System:* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

DOSAGE AND ADMINISTRATION: TRIAMINIC Cold Syrup—Adults—2 teaspoonfuls every 4 hours. Children 6-12—1 teaspoonful every 4 hours. Children 2-6 years—½ teaspoonful every 4 hours. The suggested dosage in pediatric patients 3 months to 2 years of age is 4 to 5 drops per kilogram of body weight administered every four hours. TRIAMINIC Cold Tablets—Adults: 2 tablets every 4 hours. Children 6-12 years: 1 tablet every 4 hours. TRIAMINIC-12 Tablets: Adults and children over 12 years of age—1 tablet every 12 hours. TRIAMINIC-12 Tablets are not recommended for children under the age of 12 years. TRIAMINIC Oral Infant Drops: 1 drop per 2 pounds of body weight administered orally four times daily. The prescribed number of drops may be put directly into child's mouth or on a spoon for administration.

HOW SUPPLIED: TRIAMINIC Cold Syrup (orange) in 4 fl oz and 8 fl oz. TRIAMINIC Cold Tablets (orange) in blister packs of 24 and 48. TRIAMINIC-12 Tablets (orange) in blister packs of 10 and 20. TRIAMINIC Oral Infant Drops in 15 ml plastic squeeze bottles which deliver approximately 24 drops per ml.

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Diarrhea, vomiting, eczema, rhinitis, wheezing, irritability...classic symptoms that may call for a change in infant diet. Nursoy® soy protein formula can help relieve these distressing symptoms by eliminating:

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- Lactose—a problem for infants with congenital or temporary lactase deficiency.
- Cow milk protein—the most common food offender for the newborn.

In addition, Nursoy has the lowest sodium level of all available soy formulas, and contains a physiologic fat blend. Nursoy® puts the symptoms to rest while meeting the nutritional needs of the milk-sensitive infant.

Breast milk is the preferred feeding for newborns. Nursoy® milk-free formula is intended to meet the nutritional needs of infants and children who are allergic to cow milk proteins or intolerant to lactose. It should not be used in infants and children allergic to soybean protein. Professional advice should be followed.

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milk-free nutrition without corn syrup solids

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TOBREX®
tobramycin 0.3%
ophthalmic solution and ointment

When you see that conjunctivitis is the problem, it's time to focus on TOBREX.

TOBREX produces outstanding clinical results in pediatric superficial eye infections; and it exhibits excellent bactericidal *in vitro* activity against virtually all significant ocular pathogens, including *H. influenzae,* the most frequent cause of pediatric conjunctivitis.[1-3]

Furthermore, TOBREX has an exceptional safety record; in fact, no side effects were observed in a study of children with external ocular infections. And you and your young patients will appreciate the superior comfort TOBREX offers — which can lead to better compliance.[1,3]

TOBREX® (tobramycin 0.3%)
OPHTHALMIC SOLUTION/OINTMENT

DESCRIPTION: TOBREX® (tobramycin 0.3%) is a sterile topical ophthalmic solution prepared specifically for topical therapy of external infections. This product is also supplied in an ointment form.

Each ml of solution contains: Tobramycin 0.3% (3 mg/ml), Boric Acid, Sodium Sulfate, Sodium Chloride, Tyloxapol, Sodium Hydroxide and/or Sulfuric Acid (to adjust pH), Purified Water, and Benzalkonium Chloride (0.01%) as a preservative. DM-00

Each gram of ointment contains: Tobramycin 0.3% (3 mg/g), Mineral Oil, Petrolatum Base, and Chlorobutanol (0.5%) as a preservative. DM-00

Tobramycin is a water-soluble aminoglycoside antibiotic active against a wide variety of gram-negative and gram-positive ophthalmic pathogens.

CLINICAL PHARMACOLOGY: *In Vitro Data: In vitro* studies have demonstrated tobramycin is active against susceptible strains of the following microorganisms:

Staphylococci, including *S. aureus* and *S. epidermidis* (coagulase-positive and coagulase-negative), including penicillin-resistant strains.

Streptococci, including some of the Group A — beta-hemolytic species, some nonhemolytic species, and some *Streptococcus pneumoniae. Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis* (indole-negative) and indole-positive *Proteus* species. *Haemophilus influenzae* and *H. aegyptius, Moraxella lacunata,* and *Acinetobacter calco-aceticus (Herellea vaginicola)* and some *Neisseria* species. Bacterial susceptibility studies demonstrate that in some cases microorganisms resistant to gentamicin retain susceptibility to tobramycin. A significant bacterial population resistant to tobramycin has not yet emerged; however, bacterial resistance may develop upon prolonged use.

INDICATIONS AND USAGE: TOBREX is a topical antibiotic indicated in the treatment of external infections of the eye and its adnexa caused by susceptible bacteria. Appropriate monitoring of bacterial response to topical antibiotic therapy should accompany the use of TOBREX.

CONTRAINDICATIONS: TOBREX Ophthalmic Solution and Ointment are contraindicated in patients with known hypersensitivity to any of their components.

WARNINGS: Not for injection into the eye. Sensitivity to topically applied aminoglycosides may occur in some patients. If a sensitivity reaction to TOBREX occurs, discontinue use.

PRECAUTIONS: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated.
Ophthalmic ointments may retard corneal wound healing.
Pregnancy Category B. Reproduction studies in three types of animals at doses up to thirty-three times the normal human systemic dose have revealed no evidence of impaired fertility or harm to the fetus due to tobramycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Nursing Mothers: Because of the potential for adverse reactions in nursing infants from TOBREX, a decision should be made whether to discontinue nursing the infant or discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE REACTIONS: The most frequent adverse reactions to TOBREX Ophthalmic Solution and Ointment are localized ocular toxicity and hypersensitivity, including lid itching and swelling, and conjunctival erythema. These reactions occur in less than three of 100 patients treated with TOBREX. Similar reactions may occur with the topical use of other aminoglycoside antibiotics. Other adverse reactions have not been reported from TOBREX therapy; however, if topical ocular tobramycin is administered concomitantly with systemic aminoglycoside antibiotics, care should be taken to monitor the total serum concentration.

In clinical trials, TOBREX Ophthalmic Ointment produced significantly fewer adverse reactions (3.7%) than did Garamycin Ophthalmic Ointment (10.6%).

OVERDOSAGE: Clinically apparent signs and symptoms of an overdose of TOBREX Ophthalmic Solution or Ointment (punctate keratitis, erythema, increased lacrimation, edema and lid itching) may be similar to adverse reaction effects in some patients.

DOSAGE AND ADMINISTRATION: Solution: In mild to moderate disease, instill one or two drops into the affected eye(s) every four hours. In severe infections, instill two drops into the eye(s) hourly until improvement, following which treatment should be reduced prior to discontinuation.

Ointment: In mild to moderate disease, apply a half-inch ribbon into the affected eye(s) two or three times per day. In severe infections, instill a half-inch ribbon into the affected eye(s) every three to four hours until improvement, following which treatment should be reduced prior to discontinuation.

Clinical studies have shown tobramycin to be safe and effective for use in children.

HOW SUPPLIED: STERILE solution in 5 ml Drop-Tainer® dispenser (NDC 0065-0643-05), containing tobramycin 0.3% (3 mg/ml) and STERILE ointment in 3.5 g ophthalmic tube (NDC 0065-0644-35), containing tobramycin 0.3% (3 mg/g).

References: 1. Timewell RM, Rosenthal AL, Smith JP, et al: Safety and efficacy of tobramycin and gentamicin sulfate in the treatment of external ocular infections of children. *J Pediatr Ophthalmol Strabismus* 20:22-26, 1983. **2.** Hammerschlag MR: Conjunctivitis in infancy and childhood. *Pediatr Rev* 5:285-290, 1984. **3.** Data on file, Alcon Laboratories, Inc.

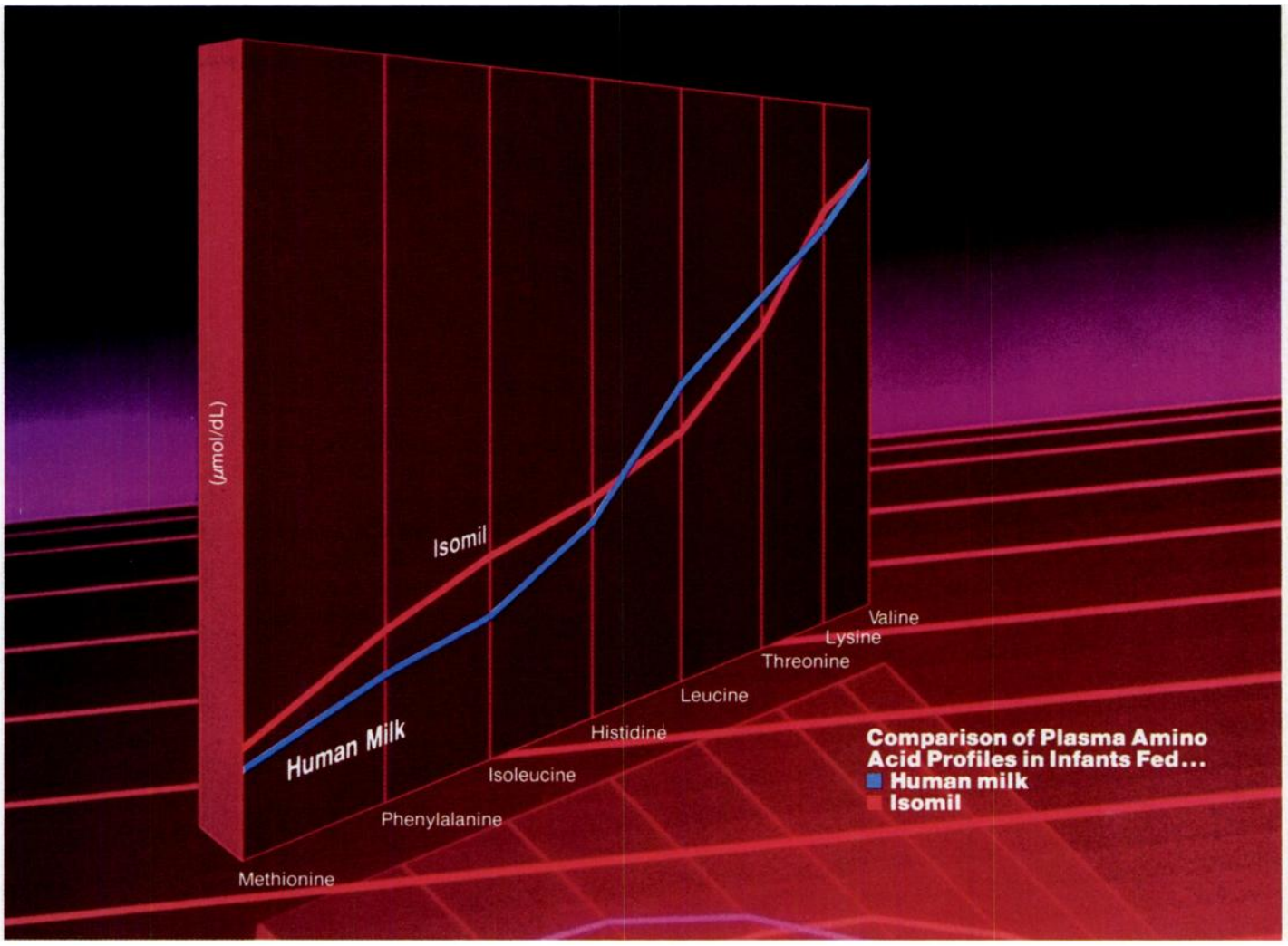
Alcon

Alcon Laboratories Inc., Fort Worth, Texas 76134

 860232A

in vivo performance...

Plasma amino acid* profile — similar to that of breast-fed babies.



Recent clinical evidence demonstrates that the plasma amino acid profile of infants fed Isomil is similar to that of breast-fed infants.[1]

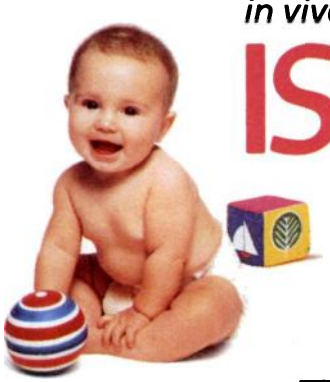
For optimal development, amino acid metabolism of the formula-fed infant should be as close as possible to that of the breast-fed infant, the nutritional norm.[2-5]

*Essential amino acids.

Meeting the standard of *in vivo* performance...

ISOMIL®

Soy Protein Formula With Iron



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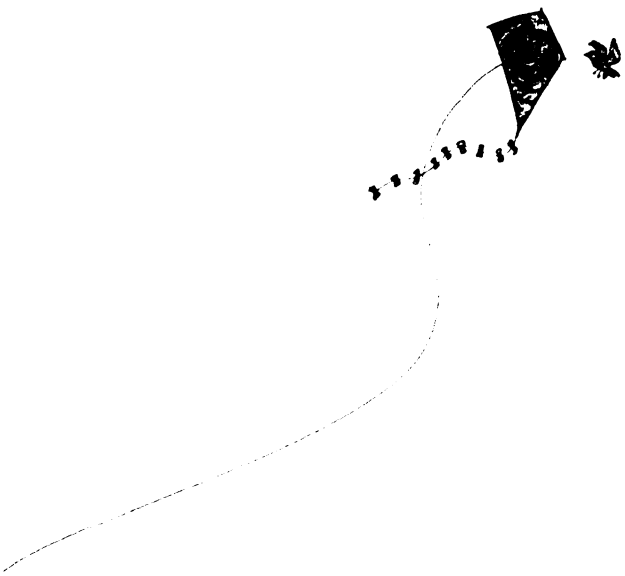

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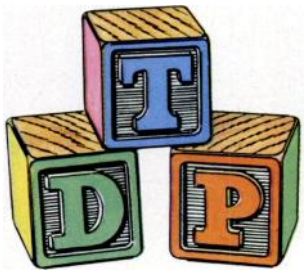

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CL91-JA-86

Issued: February, 1986

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P-586

ILLITERATE SCIENCE STUDENTS

. . . distressingly many [students who have had an abundance of mathematics and science instruction are] unable to read discursive texts critically. . . . Many more students are hardly able to write a single paragraph of grammatically correct English that says what they intend it to say. . . .

If our lives are not to be controlled by chemicals and computers, our schools had better get on with what is their overwhelmingly most important task: teaching their charges to express themselves clearly and with precision in both speech and writing; in other words leading them toward mastery of their own language. Failing that, all their instruction in mathematics and science is a waste of time.

Submitted by Student

From Joseph Weizenbaum, Professor of Computer Science, MIT. *The New York Times*, Dec 15, 1985.

MOTHER'S OPINIONS AFTER 20 YEARS OF EXPERIENCE

I have recently had occasion to interview 15 mothers of 17 severely mentally handicapped young adults aged between nineteen and twenty-five years. This was a pilot study for a survey on the subject of service provision for this group of the severely disabled. At the conclusion of the interviews, I asked the mothers whether, with the experience they now had, they thought that infants born severely handicapped "should receive all possible medical treatment to enable them to survive or should they be permitted to die in peace".

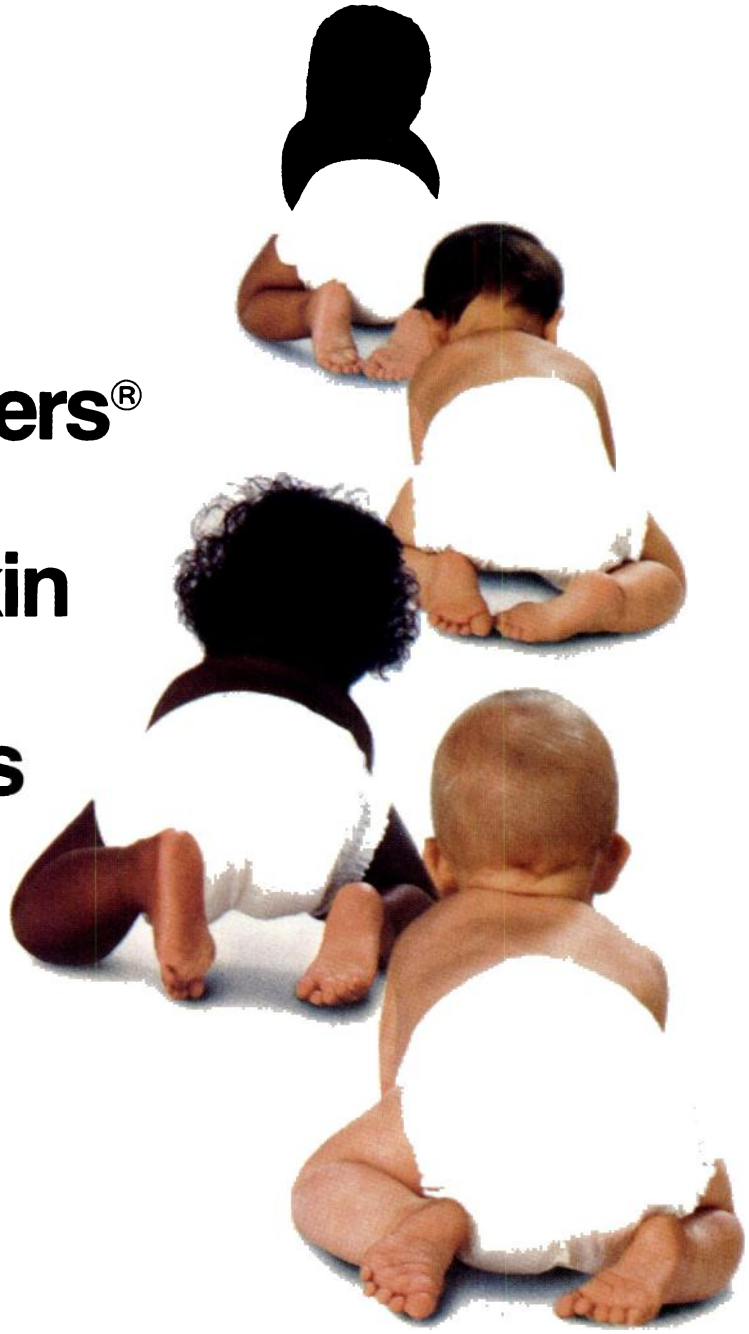
3 mothers thought all medical means should be used to keep such infants alive, though 1 had reservations about using a life-support machine and another observed "only if they will enjoy their lives". 12 mothers took the opposite view.

This is only a pilot study and the numbers are too small to enable us to draw any more general conclusions. It is clear, however, that most of these mothers do not look upon a lifetime spent caring for the severely mentally handicapped as time well spent, even though they love their children, have compassion for them, and want to do the best for them that they can. Those who have had twenty years' experience caring for young people classified as severely mentally handicapped have views that perhaps deserve to be heard more than most.

Submitted by Student

From Simms M: Surgery for retarded infants. *Lancet* Nov 2, 1985.

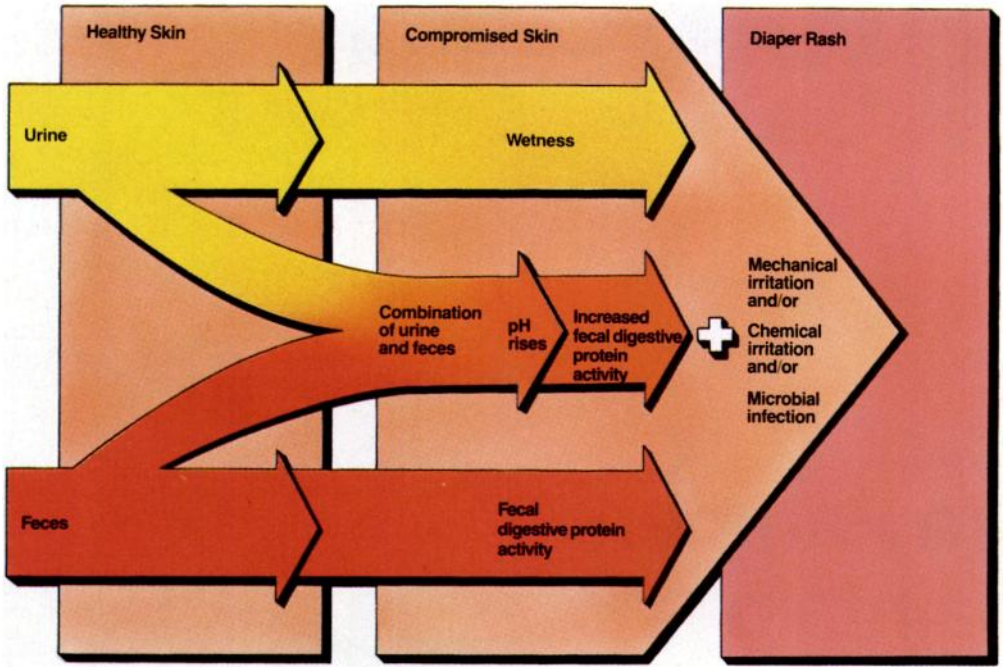
Announcing a breakthrough in diaper technology...



New Ultra Pampers® helps maintain healthy infant skin by interrupting the rash process

NEW Ultra Pampers®

Helps interrupt the rash process...



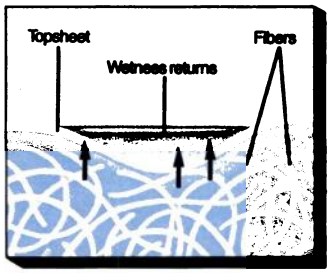
by locking urine away from skin and feces

New research links wetness and fecal digestive protein activity to diaper rash

New research confirms that wet skin is more susceptible to irritation, and it also reveals that the combination of urine and feces is even more damaging to skin than wetness alone. When urine combines with feces, ammonia is released from the urine and pH rises. The elevated pH increases fecal digestive protein activity—a major cause of diaper rash. Skin compromised by wetness or digestive protein is more vulnerable to rash-causing factors: mechanical and chemical irritation, and microbial infection. This rash model demonstrates the importance of keeping wetness away from skin and feces.

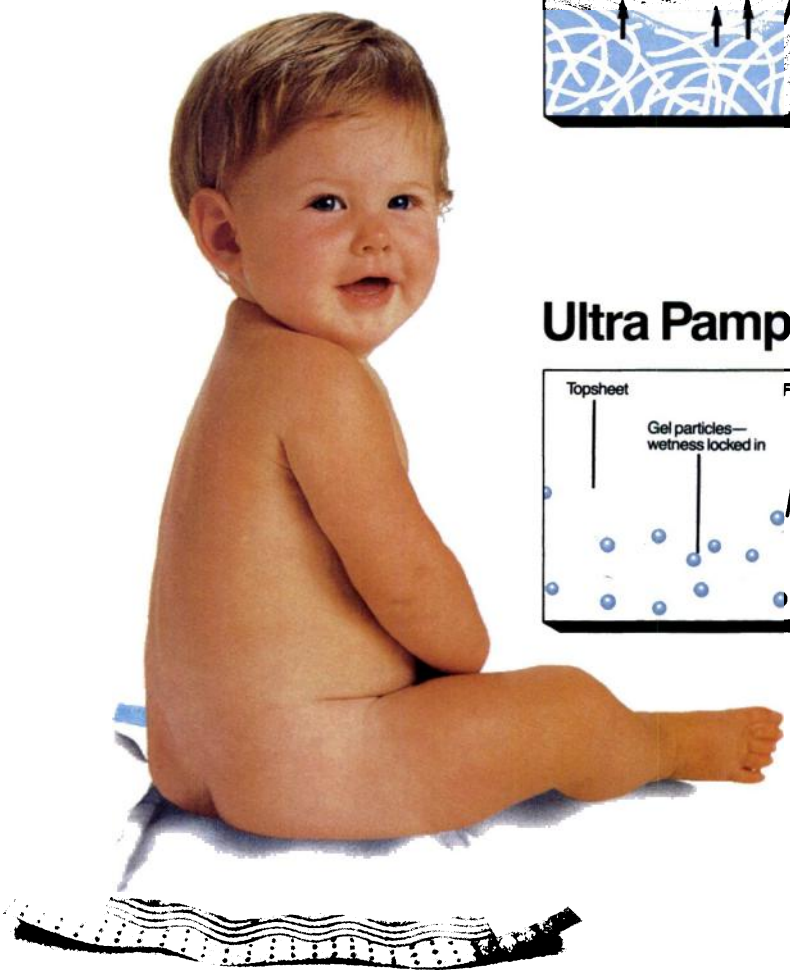
Only Ultra Pampers has unique absorbent gelling materials which reduce skin wetness and decrease urine/feces interaction. Locking away urine helps control pH and minimizes fecal digestive protein activity.

Another leading diaper allows wetness return



Ordinary diapers work like a sponge. Wetness is absorbed into the diaper but can be squeezed back against baby's skin and into feces by pressure of baby's body.

Magnified cross section of diaper core
Artist's representation: Comparison of effect of baby's body pressure on diaper's ability to help prevent wetness from returning.



Ultra Pampers helps lock wetness away from baby's skin

Absorbent gelling materials combine with urine to form a gel in the diaper's core. Wetness that is locked away can't be squeezed back against baby's skin or mix with feces. The rash process is interrupted.

Ultra Pampers is a premium diaper provided by Procter & Gamble at the regular Pampers price.

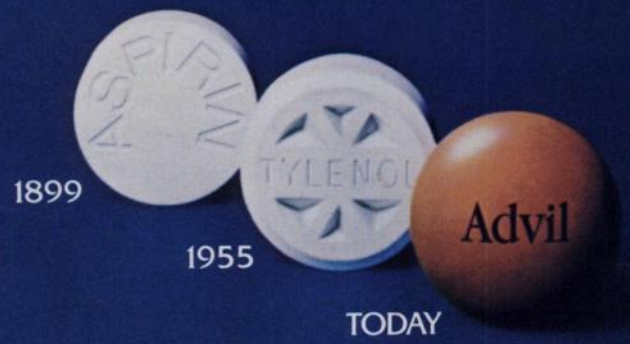
Extensive testing and in-use experience with Ultra Pampers

Clinical evaluations versus cloth and conventional disposables confirmed Ultra Pampers superiority in keeping baby's skin closer to normal pH and in keeping baby's skin drier by locking away irritating wetness. Further experience includes observations by 36 private practice pediatricians of more than 4,000 infants wearing Ultra Pampers. Positive in-use experience has also been reported with approximately 23,000 babies at home and in 39 hospital nurseries.

If you have any questions or comments about Ultra Pampers, please call toll-free (800) 358-8707; in Ohio (800) 346-9101.

Ultra Pampers. The leader in helping maintain healthy infant skin.

PAQ 002 86



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FOR ADOLESCENTS:

A NEW STANDARD FOR OTC ANALGESIA™

Many adolescents 12 years and older tend to stay with their pediatricians. When these patients or their parents describe these symptoms, that's one time when your recommendation for ADVIL is particularly appropriate. However, please remind parents that ADVIL should not be given to children under 12 without the advice and supervision of a doctor.

Please advise patients and parents to read and follow product labeling. Patients should not take this product if they have had a severe allergic reaction to aspirin.

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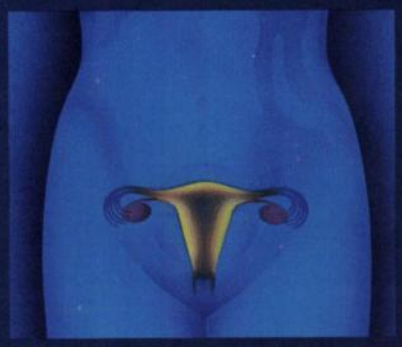
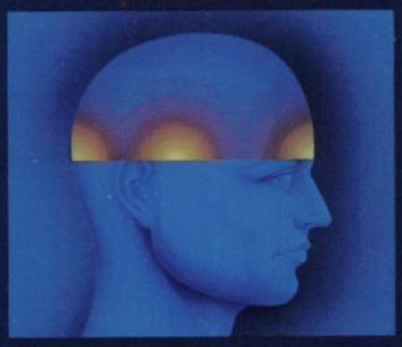
A HEALTH CARE DIVISION OF
AMERICAN HOME PRODUCTS CORPORATION

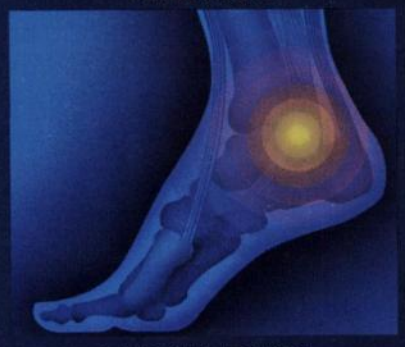
FEVER



DYSMENORRHEA



HEADACHE



MUSCLE ACHES

They need a form that fits.

A form that protects them day and night with convenient q12h dosing.

Unlike many adults, children are rapid metabolizers of theophylline. This means that many theophylline products have to be dosed three or four times a day to maintain stable serum concentrations in children.

Theo-Dur Sprinkle produces smooth serum concentrations for a full 12 hours with convenient twice-daily dosing. Children are protected through the day and night, eliminating the need to medicate during school and bedtime hours.

A form that allows precise titration in small increments.

Children may be more sensitive than adults to changes in theophylline dosage. Children may exhibit dose-dependent saturation of metabolic pathways, which can lead to disproportionate increases in theophylline concentrations and increase the risk of toxicity.[1] Theo-Dur Sprinkle minimizes the risk of toxicity because it is available in 50, 75, 125 and 200 mg strengths, allowing for precise titration in 25 mg increments.

A form that's easy to swallow.

Unlike adults, children often have trouble swallowing tablets. Theo-Dur Sprinkle overcomes this problem because it is designed to be sprinkled onto a small amount of a child's favorite soft food. Each dose is easy and pleasant to swallow. Unlike theophylline liquids, which are often bitter tasting, Theo-Dur Sprinkle is completely tasteless and odorless. And unlike many theophylline elixirs, Theo-Dur Sprinkle contains no alcohol. In addition, it contains no placebo beads, dyes or preservatives.

The safety and effectiveness of Theo-Dur Sprinkle in children under 6 years of age have not been established. Patients should take Theo-Dur Sprinkle at least one hour before or two hours after a full meal to minimize the effect of food on drug absorption.

THEO-DUR® SPRINKLE®

(theophylline anhydrous)

Sustained Action Capsules

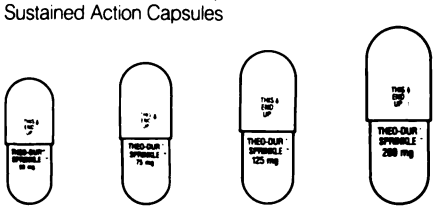
The first form of theophylline designed especially for children.

Please see next page for brief summary of prescribing information.

THEO-DUR® SPRINKLE

(theophylline anhydrous)

Sustained Action Capsules



DESCRIPTION:
THEO-DUR SPRINKLE sustained action capsules contain anhydrous theophylline, a bronchodilator, in a sustained release formulation with no color additives.

CLINICAL PHARMACOLOGY:
Theophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator and smooth muscle relaxant. The drug also produces other actions typical of the xanthine derivatives: coronary vasodilator, cardiac stimulant, diuretic, cerebral stimulant, and skeletal muscle stimulant. The actions of theophylline may be mediated through inhibition of phosphodiesterase and a resultant increase in intracellular cyclic AMP. Apparently, no development of tolerance occurs with chronic use of theophylline.

INDICATIONS:
THEO-DUR SPRINKLE is indicated for relief and/or prevention of symptoms of bronchial asthma and for reversible bronchospasm associated with chronic bronchitis and emphysema.

CONTRAINDICATIONS:
THEO-DUR SPRINKLE is contraindicated in individuals who have shown hypersensitivity to theophylline or any of the capsule components.

WARNINGS:
Excessive theophylline doses may be associated with toxicity; serum theophylline levels should be monitored to insure maximum benefit with minimum risk. Incidence of toxicity increases at serum levels greater than 20 mcg/ml. High blood levels of theophylline resulting from conventional doses are correlated with clinical manifestation of toxicity in: patients with lowered body plasma clearances, patients with liver dysfunction or chronic obstructive lung disease, and patients who are older than 55 years of age, particularly males. There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may occur in up to 50% of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity. Many patients who have higher theophylline levels exhibit tachycardia. Theophylline products may worsen pre-existing arrhythmias.

PRECAUTIONS:
THEO-DUR SPRINKLE CAPSULES SHOULD NOT BE CHEWED OR CRUSHED. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, in the elderly (especially males) and in neonates. In particular, great caution should be used in giving theophylline to patients with congestive heart failure. Frequently, such patients have markedly prolonged theophylline serum levels with theophylline persisting in serum for long periods following discontinuation of the drug. Use theophylline cautiously in patients with history of peptic ulcer. Theophylline may occasionally act as a local irritant to the G.I. tract although gastrointestinal symptoms are more commonly centrally mediated and associated with serum drug concentrations over 20 mcg/ml.

Drug-Food Interactions:
Theo-Dur Sprinkle has not been adequately studied to determine whether its bioavailability is altered when given with food.
Available data suggest that drug administration at the time of food ingestion may influence the absorption characteristics of some or all theophylline controlled-release products resulting in serum values different from those found after administration in the fasting state.
A drug-food effect, if any, would likely have its greatest clinical significance when high theophylline serum levels are being maintained and/or when large single doses (greater than 13 mg/kg or 900 mg) of a controlled-release theophylline product are given. The influence of the type and amount of food on performance of controlled-release theophylline products is under study at this time.

Usage in Pregnancy:
Animal reproduction studies have not been conducted with theophylline. It is not known whether theophylline can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Xanthines should be given to a pregnant woman only if clearly needed.

Nursing Mothers:
It has been reported that theophylline distributes readily into breast milk and may cause adverse effects in the infant. Caution must be used if prescribing xanthines to a mother who is nursing, taking into account the risk-benefit of this therapy.

Pediatric Use:
Safety and effectiveness of THEO-DUR SPRINKLE in children under 6 years of age have not been established.

ADVERSE REACTIONS:
The most consistent adverse reactions are usually due to overdose and are:
Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, diarrhea.
Central nervous system: headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
Cardiovascular: palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, ventricular arrhythmias.
Respiratory: tachypnea.
Renal: albuminuria, increased excretion of renal tubular and red blood cells, potentiation of diuresis.
Others: rash, hyperglycemia and inappropriate ADH syndrome.

HOW SUPPLIED:
THEO-DUR SPRINKLE 50, 75, 125 and 200 mg sustained action capsules are available in bottles of 100.

CAUTION:
Federal law prohibits dispensing without prescription.
For full prescribing information, see package insert.

Revised 09/84

Reference
1 Weinberger M, Ginchansky E: *J Pediatr* 1977;91:820-824

Key Pharmaceuticals, Inc.
Miami, Florida 33137

KY TS-1202


TINEA KNOWS NO AGE BARRIERS.
NEITHER DOES
GRIFULVIN V
TRADEMARK
(griseofulvin microsize)
• The only griseofulvin available in an oral suspension
• Especially suitable for pediatric use
• Also available in 250 and 500 mg tablets
A TREATMENT FOR ALL AGES
Please see next page for brief summary of Prescribing Information.
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Grifulvin V
(griseofulvin microsize)
Suspension

GRIFULVIN V
TRADEMARK

(griseofulvin microsize)
Tablets/Suspension

Indications
Major indications for GRIFULVIN V griseofulvin microsize are

Tinea capitis	Tinea unguium
Tinea corporis	Tinea cruris
Tinea pedis	Tinea barbae

GRIFULVIN V (griseofulvin microsize) inhibits the growth of those genera of fungi that commonly cause ringworm infections of the hair, skin, and nails, such as

Trichophyton rubrum	Microsporum audouini
Trichophyton tonsurans	Microsporum canis
Trichophyton mentagrophytes	Microsporum gypseum
Trichophyton interdigitalis	Epidermophyton floccosum
Trichophyton verrucosum	Trichophyton megnini
Trichophyton sulphureum	Trichophyton gallinae
Trichophyton schoenleini	Trichophyton crateriform

Note: Prior to therapy, the type of fungi responsible for the infection should be identified. The use of the drug is not justified in minor or trivial infections which will respond to topical antifungal agents alone.

It is *not* effective in

Bacterial infections	Coccidioidomycosis
Candidiasis (Moniliasis)	North American Blastomycosis
Histoplasmosis	Cryptococcosis (Torulosis)
Actinomycosis	Tinea versicolor
Sporotrichosis	Nocardiosis
Chromoblastomycosis	

Contraindications
This drug is contraindicated in patients with porphyria, hepatocellular failure, and in individuals with a history of hypersensitivity to griseofulvin.

Warnings
Usage in Pregnancy: Safe use of GRIFULVIN V (griseofulvin microsize) in pregnancy has not been established.

Prophylactic Usage: Safety and efficacy of prophylactic use of this drug has not been established.

Chronic feeding of griseofulvin, at levels ranging from 0.5-2.5% of the diet, resulted in the development of liver tumors in several strains of mice, particularly in males. Smaller particle sizes result in an enhanced effect. Lower oral dosage levels have not been tested. Subcutaneous administration of relatively small doses of griseofulvin once a week during the first three weeks of life has also been reported to induce hepatomata in mice. Although studies in other animal species have not yielded evidence of tumorigenicity, these studies were not of adequate design to form a basis for conclusions in this regard.

In subacute toxicity studies, orally administered griseofulvin produced hepatocellular necrosis in mice, but this has not been seen in other species. Disturbances in porphyrin metabolism have been reported in griseofulvin-treated laboratory animals. Griseofulvin has been reported to have a colchicine-like effect on mitosis and cocarcinogenicity with methylcholanthrene in cutaneous tumor induction in laboratory animals.

Reports of animal studies in the Soviet literature state that a griseofulvin preparation was found to be embryotoxic and teratogenic on oral administration to pregnant Wistar rats. Rat reproduction studies done thus far in the United States and Great Britain have been inconclusive in this regard, and additional animal reproduction studies are underway. Pups with abnormalities have been reported in the litters of a few bitches treated with griseofulvin.

Suppression of spermatogenesis has been reported to occur in rats but investigation in man failed to confirm this.

Precautions
Patients on prolonged therapy with any potent medication should be under close observation. Periodic monitoring of organ system function, including renal, hepatic and hemopoietic, should be done.

Since griseofulvin is derived from species of penicillin, the possibility of cross sensitivity with penicillin exists, however, known penicillin-sensitive patients have been treated without difficulty.

Since a photosensitivity reaction is occasionally associated with griseofulvin therapy, patients should be warned to avoid exposure to intense natural or artificial sunlight. Should a photosensitivity reaction occur, lupus erythematosus may be aggravated.

Patients on warfarin-type anticoagulant therapy may require dosage adjustment of the anticoagulant during and after griseofulvin therapy. Concomitant use of barbiturates usually depresses griseofulvin activity and may necessitate raising the dosage.

Adverse Reactions
When adverse reactions occur, they are most commonly of the hypersensitivity type such as skin rashes, urticaria and rarely, angioneurotic edema, and may necessitate withdrawal of therapy and appropriate countermeasures. Paresthesias of the hands and feet have been reported rarely after extended therapy. Other side effects reported occasionally are oral thrush, nausea, vomiting, epigastric distress, diarrhea, headache, fatigue, dizziness, insomnia, mental confusion and impairment of performance of routine activities.

Proteinuria and leukopenia have been reported rarely. Administration of the drug should be discontinued if granulocytopenia occurs.

When rare, serious reactions occur with griseofulvin, they are usually associated with high dosages, long periods of therapy, or both.

Our Commitment is to Skin Care & Dermatology

DERMATOLOGICAL DIVISION
ORTHO PHARMACEUTICAL CORPORATION
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NOW... The standard ADD medication in once-a-day dosage

One 20-mg sustained-release Ritalin-SR tablet given at breakfast provides a therapeutic effect equivalent to that of the standard 10-mg tablet given twice daily.[1]

Eliminates the need to take medication in school

"The availability of a sustained-release (SR) formulation of methylphenidate would greatly improve patient compliance and lessen school-related dosing problems...."[1]

Improves compliance... affords greater convenience and greater privacy

Ritalin is indicated as adjunctive therapy to other remedial measures (psychological, educational, social) for ADD in children. Drug treatment is not indicated for all children with ADD. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis.

Also available: Regular tablets of 5, 10 and 20 mg.

Before prescribing, please consult Brief Summary of Prescribing Information on next page.

RITALIN-SR®

methylphenidate

20-mg sustained-release tablets

 174-2492-A

CIBA

Now— a standard therapy for ADD becomes more convenient... more simple... more private...

RITALIN-SR®C
methylphenidate
20-mg sustained-release tablets

Reference

1. Whitehouse D, Shah U, Palmer FB: *J Clin Psychiatry* 1980 (Aug); 41(8):282-285.

Part of the ADD management team— only when medication is indicated

C85-55 (Rev. 11/85)
665615

Ritalin® hydrochloride
methylphenidate hydrochloride
tablets USP

C II

Ritalin-SR®
methylphenidate hydrochloride USP
sustained-release tablets

C II

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE INSERT)

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Ritalin, since the drug may aggravate these symptoms. Ritalin is contraindicated also in patients known to be hypersensitive to the drug, in patients with glaucoma, and in patients with motor tics or with a family history or diagnosis of Tourette's syndrome.

WARNINGS

Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.

Sufficient data on safety and efficacy of long-term use of Ritalin in children are not yet available. Although a causal relationship has not been established, suppression of growth (*ie*, weight gain, and/or height) has been reported with the long-term use of stimulants in children. Therefore, patients requiring long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin. Clinical experience suggests that in psychotic children, administration of Ritalin may exacerbate symptoms of behavior disturbance and thought disorder.

Ritalin should not be used for the prevention or treatment of normal fatigue states.

There is some clinical evidence that Ritalin may lower the convulsive threshold in patients with prior history of seizures, with prior EEG abnormalities in absence of seizures, and, very rarely, in absence of history of seizures and no prior EEG evidence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. In the presence of seizures, the drug should be discontinued.

Use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

Symptoms of visual disturbances have been encountered in rare cases. Difficulties with accommodation and blurring of vision have been reported.

Drug Interactions

Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors.

Human pharmacologic studies have shown that Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy

Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence

Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

Drug treatment is not indicated in all cases of this behavioral syndrome and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe Ritalin should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his/her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with Ritalin is usually not indicated.

Long-term effects of Ritalin in children have not been well established.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. There have been rare reports of Tourette's syndrome. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the needs and responses of the patient.

Adults

Tablets: Administer in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

SR Tablets: Ritalin-SR tablets have a duration of action of approximately 8 hours. Therefore, Ritalin-SR tablets may be used in place of Ritalin tablets when the 8-hour dosage of Ritalin-SR corresponds to the titrated 8-hour dosage of Ritalin. Ritalin-SR tablets must be swallowed whole and never crushed or chewed.

Children (6 years and over)

Ritalin should be initiated in small doses, with gradual weekly increments. Daily dosage above 60 mg is not recommended.

If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

Tablets: Start with 5 mg twice daily (before breakfast and lunch) with gradual increments of 5 to 10 mg weekly.

SR Tablets: Ritalin-SR tablets have a duration of action of approximately 8 hours. Therefore, Ritalin-SR tablets may be used in place of Ritalin tablets when the 8-hour dosage of Ritalin-SR corresponds to the titrated 8-hour dosage of Ritalin. Ritalin-SR tablets must be swallowed whole and never crushed or chewed.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

OVERDOSAGE

Signs and symptoms of acute overdosage, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. If signs and symptoms are not too severe and the patient is conscious, gastric contents may be evacuated by induction of emesis or gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate *before* performing gastric lavage.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for Ritalin overdosage has not been established.

HOW SUPPLIED

Tablets 5 mg — round, yellow
(imprinted CIBA 7)
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Bottles of 500 ..... NDC 0083-0007-35
Bottles of 1000 ..... NDC 0083-0007-40

Tablets 10 mg — round, pale green, scored
(imprinted CIBA 3)
Bottles of 100 ..... NDC 0083-0003-30
Bottles of 500 ..... NDC 0083-0003-35
Bottles of 1000 ..... NDC 0083-0003-40
Accu-Pak® Unit Dose (blister pack)
Box of 100 (strips of 10) ..... NDC 0083-0003-32

Tablets 20 mg — round, pale yellow, scored
(imprinted CIBA 34)
Bottles of 100 ..... NDC 0083-0034-30
Bottles of 1000 ..... NDC 0083-0034-40

Protect from light.
Dispense in tight, light-resistant container (USP).

SR Tablets 20 mg — round, white, coated
(imprinted CIBA 16)
Bottles of 100 ..... NDC 0083-0016-30

Note: SR Tablets are color-additive free.

Do not store above 86°F (30°C). Protect from moisture.
Dispense in tight, light-resistant container (USP).

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XVIII International Congress of Pediatrics
Honolulu, Hawaii
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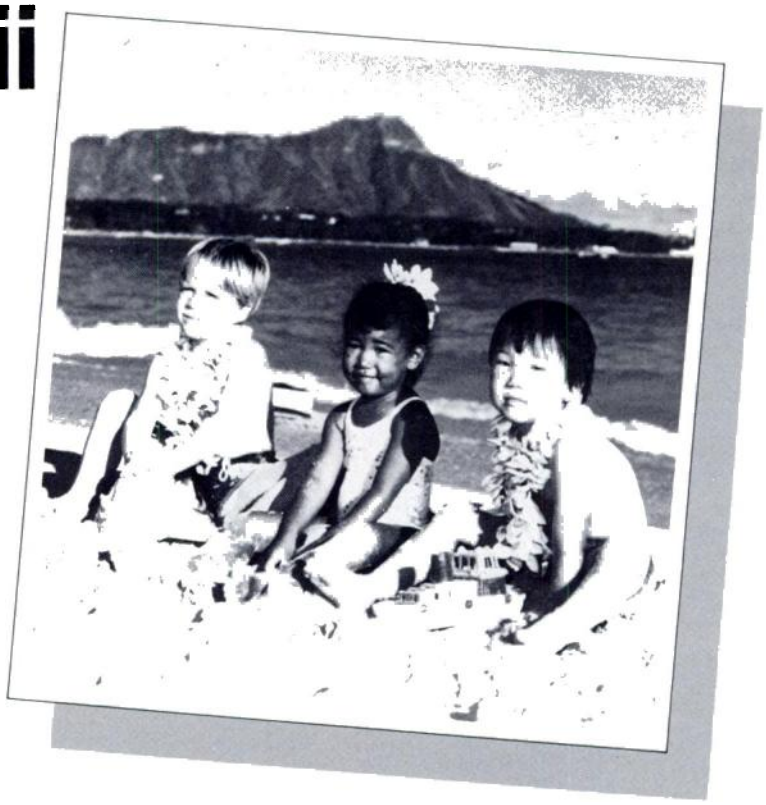

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STRIP SEARCHES OF INFANTS UPHELD IN PRISON VISITS

The need for security during visits with prison inmates outweighs an infant's right to privacy, a Federal appeals court has ruled in rejecting a prisoner's complaint about the strip search of his diapered son.

The United States Court of Appeals for the Fourth Circuit last week upheld a lower court's dismissal of a 1983 lawsuit that contended that the removal and search of a diaper violated the child's Fourth Amendment protection against unreasonable search.

Submitted by Student

From *The New York Times*, Dec 30, 1985.

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Biotechnology is the *first* instance where the people who *did* the [basic scientific] research decided to form companies themselves.... In my day, Professors would be horrified at the thought. Now we've raised a generation of scientists who are into making money.

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From Commoner B: Tinkering with genetics. *Pacific Sun*, Dec 13, 1985.

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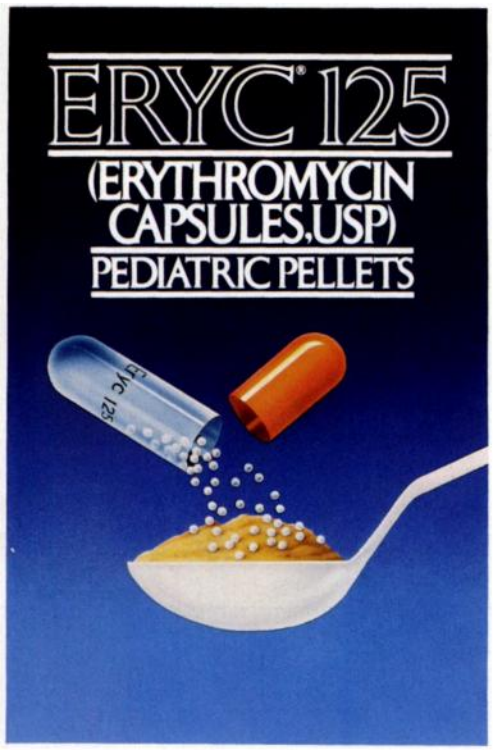

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Before prescribing, please see full prescribing information. A brief summary follows.

INDICATIONS AND USAGE: ERYC 125 is indicated in children and adults for the treatment of the following conditions: Upper respiratory tract infections of mild to moderate degree caused by *Streptococcus pyogenes* (group A beta hemolytic streptococci); *Streptococcus pneumoniae (Diplococcus pneumoniae)*; *Haemophilus influenzae* (when used concomitantly with adequate doses of sulfonamides, since not all strains of *H influenzae* are susceptible at the erythromycin concentrations ordinarily achieved). (See appropriate sulfonamide labeling for prescribing information.)

Lower respiratory tract infections of mild to moderate severity caused by *Streptococcus pyogenes* (group A beta hemolytic streptococci); *Streptococcus pneumoniae (Diplococcus pneumoniae)*.

Respiratory tract infections due to *Mycoplasma pneumoniae* (Eaton's agent).

Skin and skin structures infections of mild to moderate severity caused by *Streptococcus pyogenes* and *Staphylococcus aureus* (resistant staphylococci may emerge during treatment).

Pertussis (whooping cough) caused by *Bordetella pertussis*. Erythromycin is effective in eliminating the organism from the nasopharynx of infected individuals, rendering them noninfectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

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

Erythrasma—In the treatment of infections due to *Corynebacterium minutissimum*.

Intestinal amebiasis caused by *Entamoeba histolytica* (oral erythromycins only). Extraenteric amebiasis requires treatment with other agents.

Infections due to *Listeria monocytogenes*.

Erythromycin is indicated for treatment of the following infections caused by *Chlamydia trachomatis*: conjunctivitis of the newborn, pneumonia of infancy and urogenital infections during pregnancy. When tetracyclines are contraindicated or not tolerated, erythromycin is indicated for the treatment of uncomplicated urethral, endocervical, or rectal infections in adults due to *Chlamydia trachomatis*.

When tetracyclines are contraindicated or not tolerated erythromycin is indicated for the treatment of nongonococcal urethritis caused by *Ureaplasma urealyticum*.

Primary syphilis caused by *Treponema pallidum*. Erythromycin (oral forms only) is an alternative choice of treatment for primary syphilis in patients allergic to the penicillins. In treatment of primary syphilis, spinal fluid should be examined before treatment and as part of the follow-up after therapy.

Legionnaires' Disease caused by *Legionella pneumophila*. Although no controlled clinical efficacy studies have been conducted, in vitro and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' Disease.

Prevention of Initial Attacks of Rheumatic Fever—Penicillin is considered by the American Heart Association to be the drug of choice in the prevention of initial attacks of rheumatic fever (treatment of group A beta-hemolytic streptococcal infections of the upper respiratory tract, e.g. tonsillitis or pharyngitis).

Erythromycin is indicated for the treatment of penicillin-allergic patients. A therapeutic dose should be administered for ten days.

Prevention of Recurrent Attacks of Rheumatic Fever—Penicillin or sulfonamides are considered by the American Heart Association to be the drugs of choice in the prevention of recurrent attacks of rheumatic fever.

In patients who are allergic to penicillin and sulfonamides, oral erythromycin is recommended by the American Heart Association in the long-term prophylaxis of streptococcal pharyngitis (for the prevention of recurrent attacks of rheumatic fever).

Prevention of Bacterial Endocarditis—Although no controlled clinical efficacy trials have been conducted, oral erythromycin has been recommended by the American Heart Association for prevention of bacterial endocarditis in penicillin-allergic patients with prosthetic cardiac valves, most congenital cardiac malformations, surgically constructed systemic-pulmonary shunts, rheumatic or other acquired valvular dysfunction, idiopathic hyperthrophic subaortic stenosis (IHSS), previous history of bacterial endocarditis and mitral valve prolapse with insufficiency when they undergo dental procedures and surgical procedures of the upper respiratory tract.

CONTRAINDICATION: ERYC 125 is contraindicated in patients with known hypersensitivity to this antibiotic.

WARNING: There have been a few reports of hepatic dysfunction, with or without jaundice, occurring in patients receiving erythromycin ethylsuccinate, base, estolate and stearate products.

PRECAUTIONS: Caution should be exercised when erythromycin is administered to patients with impaired hepatic function (see CLINICAL PHARMACOLOGY and WARNING section).

Prolonged or repeated use of erythromycin may result in an overgrowth of nonsusceptible bacteria or fungi. If superinfection occurs, erythromycin should be discontinued and appropriate therapy instituted. When indicated, incision and drainage or other surgical procedures should be performed in conjunction with antibiotic therapy.

Laboratory Tests: Erythromycin interferes with the fluorometric determination of urinary catecholamines.

Drug Interactions: Erythromycin use in patients who are receiving high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. In case of theophylline toxicity and or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving concomitant erythromycin therapy.

Erythromycin administration in patients receiving carbamazepine has been reported to cause increased blood levels of carbamazepine with subsequent development of signs of carbamazepine toxicity.

Pregnancy Category B—Reproduction studies have been performed in rats, mice and rabbits using erythromycin and its various salts and esters, at doses which were several times the usual human dose. No evidence of impaired fertility or harm to the fetus that appeared related to erythromycin was reported in these studies. There are, however, no adequate well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery—The effect of ERYC 125 on labor and delivery is unknown.

Nursing Mothers—Erythromycin is excreted in milk (see CLINICAL PHARMACOLOGY).

Pediatric Use—See INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION.

ADVERSE REACTIONS: The most frequent side effects of oral erythromycin preparations are gastrointestinal and are dose-related. They include nausea, vomiting, abdominal pain, diarrhea and anorexia. Symptoms of hepatic dysfunction and/or abnormal liver function test results may occur (see WARNING).

Mild allergic reactions such as rashes with or without pruritus, urticaria, bullous fixed eruptions, and eczema have been reported with erythromycin. Serious allergic reactions, including anaphylaxis, have been reported.

There have been isolated reports of reversible hearing loss occurring chiefly in patients with renal insufficiency and in patients receiving high doses of erythromycin.

DOSAGE AND ADMINISTRATION: The entire contents of an ERYC 125 Capsule should be sprinkled on a small amount of applesauce immediately prior to ingestion. SUBDIVIDING THE CONTENTS OF A CAPSULE IS NOT RECOMMENDED. If desired ERYC 125 Capsule may be swallowed whole.

Optimum and uniform serum levels of erythromycin are obtained when ERYC 125 is administered in the fasting state (at least 1 hour before meals).

ADULTS: The usual dose is 250 mg every 6 hours. If twice-a-day dosage is desired, the recommended dose is 500 mg every 12 hours. Dosage may be increased up to 4 grams per day, according to the severity of infection. Twice-a-day dosing is not recommended when doses larger than 1 gram daily are administered.

CHILDREN: Age, weight, and severity of the infection are important factors in determining the proper dosage. The usual dosage is 30-50 mg/kg/day in equally divided doses. For the treatment of more severe infections this dosage may be doubled.

In the treatment of group A beta-hemolytic streptococcal infections of the upper respiratory tract (eg tonsillitis or pharyngitis) a therapeutic dosage of erythromycin should be administered for ten days.

The American Heart Association suggests a dosage of 250 mg of erythromycin orally twice a day in long-term prophylaxis of streptococcal upper respiratory tract infections for the prevention of recurrent attacks of rheumatic fever in patients allergic to penicillin and sulfonamide.

In prophylaxis against bacterial endocarditis (see Indications), the oral regimen for penicillin-allergic patients is erythromycin 1.0 g one hour before the procedure followed by 500 mg six hours later.

Conjunctivitis of the newborn caused by *Chlamydia trachomatis*: Oral erythromycin syrup 50 mg/kg/day in four divided doses for at least two weeks.

Pneumonia of infancy caused by *Chlamydia trachomatis*. Although the optimal duration of therapy has not been established, the recommended therapy is oral erythromycin syrup 50 mg/kg/day in four divided doses for at least three weeks.

Urogenital infections during pregnancy due to *Chlamydia trachomatis*: Although the optimal dose and duration of the therapy have not been established, the suggested treatment is erythromycin 500 mg, by mouth, four times a day on an empty stomach for at least seven days. For women who cannot tolerate this regimen, a decreased dose of 250 mg, by mouth, four times a day should be used for at least fourteen days.

For adults with uncomplicated urethral, endocervical, or rectal infections caused by *Chlamydia trachomatis* in whom tetracyclines are contraindicated or not tolerated: 500 mg, by mouth, four times a day for at least seven days.

For patients with nongonococcal urethritis caused by *Ureaplasma urealyticum* in whom tetracyclines are contraindicated or not tolerated: 500 mg, by mouth, four times a day for at least seven days.

Primary syphilis: 30-40 grams given in divided doses over a period of ten to fifteen days.

Intestinal amebiasis: 250 mg four times daily for ten to fourteen days for adults. 30 to 50 mg/kg/day in divided doses for ten to fourteen days for children.

Legionnaires' Disease: Although optimal doses have not been established, doses utilized in reported clinical data were those recommended above (1 to 4 grams daily in divided doses).

Pertussis: Although optimum dosage and duration of therapy have not been established, doses of erythromycin utilized in reported clinical studies were 40-50 mg kg/day, given in divided doses for five to fourteen days.

Caution—Federal law prohibits dispensing without prescription.

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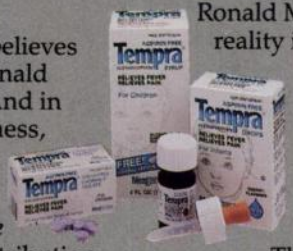

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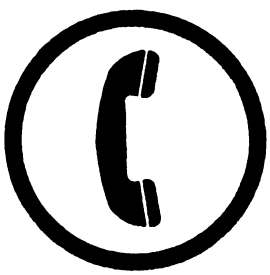

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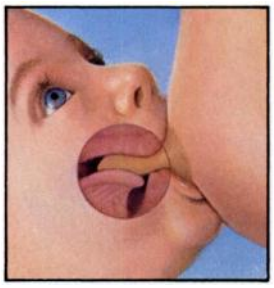

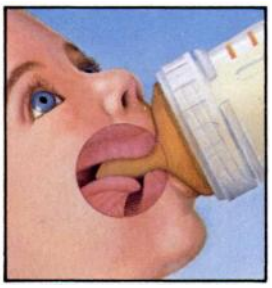

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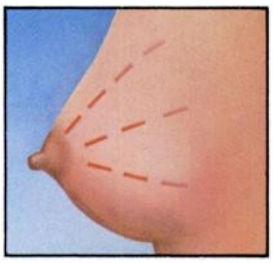

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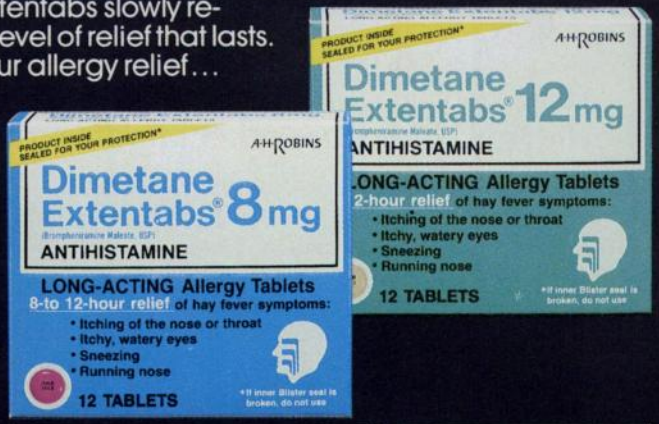

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