COMPENDIUM OF PHARMACEUTICALS AND SPECIALTIES 1984

NINETEENTH EDITION 1984

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Editorial Staff
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PREFACE

The *Compendium of Pharmaceuticals and Specialties* (CPS) is a publication editorially compiled and produced by the staff of the Canadian Pharmaceutical Association for the benefit of all health professionals.

In CPS '84, the format of previous editions has been retained and the policy of making improvements has been continued. The 1983 edition introduced the Blue Pages. This section has been enlarged in response to user comments. The monograph section contains a new category, Medical Devices. Included are devices which are for human use and contain a drug component. Monographs of significant new therapeutic agents introduced in the '84 edition include aminoglutethimide, atenolol, diflunisal, diltiazem HCl, gemfibrozil, human biosynthetic insulin, inosiplex, isotretinoin, and terfenadine. New products released during 1983 are indicated by the designation "New Product 1983". Monographs which have been either reviewed by the CPS staff or the CPS Advisory Panel are designated "Reviewed 1984".

As an added service to the users of the CPS, those products which have been discontinued since publication of the 1982 and 1983 editions are listed after the monographs of Medical Devices.

Acknowledgments

The editors express their thanks to all manufacturers and distributors who have cooperated by supplying information, offering suggestions and reading proofs. We extend an appreciation to the users of the CPS who forwarded constructive suggestions for amendments to the text and revisions in the format. We acknowledge the active interest of the Canadian Medical Association, the Canadian Hospital Association, the Canadian Society of Hospital Pharmacists and the Pharmaceutical Manufacturers' Association of Canada. The assistance of the Ottawa Valley Regional Drug Information Services and Jeannine Wolfe is greatly appreciated.

The financial support of the following companies is gratefully acknowledged:

Abbott; Adria; Allen & Hanburys; Ancalab; Anca Pharma; Apotex; Astra; Ayerst; Beecham; Boehringer; Bristol; Burroughs Wellcome; Calmic; Canderm; Charton; Ciba; Connaught; Cooper; CooperVision; Cowling & Braithwaite; Cutter; Desbergers; Doak; Dormer; Dow; Du Pont; Efamol Research; Elder; Ferring; Fisons; Flint; Frosst; Geigy; Glaxo; Hoechst; Hoffmann-La Roche; Horner; Hynson, Westcott & Dunning; I.A.F.; ICI Pharma; ICN; Institut Rosell; Interpharm; Jamieson; Jan Distributing; Janssen; Jouveinal; Kenral; K-Line; Lederle; Leo; Lilly; McNeil; McNeil Consumer Products; Mead Johnson; Merck Sharp & Dohme; Merrell; Miles; Nadeau; Nordic; Norwich Eaton; Novopharm; Ohio; Organon; Ortho; Parke-Davis; Pennwalt; Pentagone; Pfizer; Pharmacia; Pharmascience; Purdue Frederick; Reed & Carnrick; Rh Institute; Rhône-Poulenc; Riker; Robins; Rorer; Ross; Rougier; Roussel; Roxane; Roy; Sabex; Sandoz Pharma; Schering; Searle; Servier; Smith Kline & French; Spraylab; Squibb; Sterling; Stiefel; Syntex; Trans-Canada Dermapeutics; Travenol; Unimed; Upjohn; USV; Welcker-Lyster; Westwood; Winthrop; Wyeth.

EDITORIAL ADVISORY PANEL

GENERAL CONSIDERATIONS

The inclusion of monographs of a company's products in the CPS does not imply that the editors or the CPS Editorial Advisory Panel accept, endorse or recommend these preparations as being clinically superior to similar products of any other firm.

The monographs are based upon information received from the manufacturers and the Health Protection Branch (HPB). They include those products available for use to meet the needs of professional practice. Products registered under the Food and Drug Regulations, Division 10, which are offered to the public for self-medication, have not been included.

Products that have been introduced on the Canadian market are designated " *New Product 1983*". Monographs that have been reviewed by the CPS editorial staff and/or the CPS Advisory Panel are designated "Reviewed . . ." and the year during which this occurred.

In the monograph section, when appropriate (and not including the general monographs), products are alphabetically listed by names which are registered trademarks of the company whose name, in full or in abbreviated form, immediately follows it. In these cases, the appropriate designation ® or ™ appears beside the product name. CPS users are cautioned regarding the unauthorized use of any listed name. The monographs are intended to present unbiased, factual information on drugs in a format that will be useful to health care practitioners. For additional product information, readers are referred to the pertinent scientific and professional literature, to the descriptive literature of the company concerned, or to its professional personnel.

Great care has been taken to ensure the accuracy and completeness of the information contained in the CPS. However, the editors and publishers cannot be responsible for errors in publication or any consequences whatsoever arising from the use of the information published herein.

Comments concerning the CPS '84, its usefulness to the practitioners of the various health professions, and suggestions for the improvement of future editions are welcomed.

ERRATA POLICY

Serious dosage errors, or errors which threaten the patient's safety, or those which could have serious consequences will be considered for an errata. In this event, an immediate letter of correction or an appropriate insert will be sent to all known subscribers of the CPS. Minor errors, which do not have an impact on health care, will be corrected in the next edition of the CPS. In some cases, such appropriate journals as the *Canadian Pharmaceutical Journal* and the *Canadian Medical Association Journal* will be used to convey changes which are not urgent or serious.

EDITORIAL POLICY

The CPS contains information about products intended for human use. Products are alphabetically listed by names which are the registered trademarks of the company whose name, in full or abbreviated form, immediately follows the trademark. General product monographs are shown in the monograph section under the nonproprietary or proper name of the active moiety.

The CPS is not intended to be exhaustive in terms of drug products available in Canada. The CPS editorial staff compile, edit and distribute appropriate monographs which have been submitted by the manufacturer for inclusion in the book.

The CPS contains information with respect to proprietary and nonproprietary products intended for human use.

The information provided in the CPS monographs is based on the Official Product Monograph prepared by the pharmaceutical manufacturers and accepted by the Health Protection Branch. Product information as published in the CPS is a direct equivalent of the prescribing information contained and described in Section 2(a) through (j), Part 1, of the Health Protection Branch Guidelines for Product Monographs (1979). Editorial adjustments are limited to those required for consistency of style, clarity and presentation.

Information published in various literature sources may be valuable to CPS users and the CPS Editorial Advisory Panel may recommend additional information.

The general nonproprietary monographs are developed by the CPS editorial staff and are based upon information available from the originator's Official Product Monograph and independent literature sources. The CPS Editorial Advisory Panel reviews the monographs for accuracy and appropriateness with respect to current medical practice.

Prescribing information for products marketed prior to the publication of the Trade Information Letter, No. 302, June 6, 1968, is periodically reviewed in cooperation with the appropriate pharmaceutical manufacturer, the Health Protection Branch and the CPS Editorial Advisory Panel.

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

Generic Monographs

The following is a list of generic monographs which appear in the white pages of the CPS. The monographs have been compiled by the CPS editorial staff and reviewed by the CPS Editorial Advisory Panel.

Acetaminophen
ACTH
Albumin Human
Allergens and Specific Desensitization Extracts
Allopurinol ℞
Aluminum Hydroxide
Aminophylline
Amitriptyline ℞
Ammonium Chloride
Amoxicillin ℞
Ampicillin ℞
Antihemophilic Factor (Human)
Anti-Rust Tablets
ASA
Ascorbic Acid
Atropine
Bacitracin
Barium Sulfate
Benzalkonium Chloride
Benztropine Mesylate
Bisacodyl
Calcium Salts
Camphorated Opium Tincture B.P.®
Carbachol
Cetrimide
Chloral Hydrate ℞
Chloramphenicol ℞
Chlordiazepoxide HCl ℞
Chlorpheniramine Maleate
Chlorpromazine HCl ℞
Chlorpropamide ℞
Chlorthalidone ℞
Chorionic Gonadotropin For Injection USP ℞
Chymotrypsin
Clofibrate ℞
Cloxacillin Sodium ℞
Codeine Phosphate®
Colchicine
Corticosteroids, Topical ℞
Cortisone Acetate ℞
Cyclopentolate HCl
Dehydrocholic Acid
Dexamethasone ℞
Dextromethorphan HBr
Diazepam ℞
Dicyclomine HCl
Diethylpropion HCl◈
Digoxin
Dihydrostreptomycin ℞
Dimenhydrinate
Diphenhydramine HCl
Docusate Sodium
Dyphylline
Ephedrine
Epinephrine
Ergonovine Maleate ℞
Erythromycin ℞
Estradiol ℞
Estrogens-Conjugated / Esterified ℞
Ethambutol HCl ℞
Factor IX Complex (Human) Dried
Ferrous Fumarate and other Iron Salts
Fluorescein Sodium
Fluorouracil ℞
Fluoxymesterone ℞
Fluphenazine HCl ℞
Folic Acid
Furosemide ℞
Glutamic Acid HCl
Glyburide ℞
Guaifenesin
Guanethidine Sulfate ℞
Halothane
Heparin Sodium
Hexachlorophene ℞
Homatropine
Hydrochlorothiazide ℞
Hydrocodone Bitartrate®
Hydrocortisone ℞
Hydroxocobalamin
Imipramine HCl ℞
Immune Serum Globulin (Human)
Influenza Virus Vaccines (Trivalent, Types A & B)
Ipecac Syrup
Isoniazid ℞
Isoproterenol ℞
Levothyroxine Sodium ℞
Lidocaine HCl Local
Lidocaine HCl Parenteral
Lithium Carbonate ℞
Magnesium Hydroxide
Magnesium Sulfate
Mannitol
Meprobamate ℞
Methaqualone HCl◈
Methenamine Mandelate
Methyldopa ℞
Methylphenidate HCl◈
Metronidazole ℞
Morphine®
Naphazoline HCl
Neomycin ℞
Niacin
Niacinamide
Nitrofurantoin ℞
Nitroglycerin
Nylidrin HCl
Opium Tincture®
Oxytocin
Pantothenic Acid
Paraldehyde ℞
PAS
Penicillin G ℞
Penicillin V ℞
Pentaerythritol Tetranitrate
Pentobarbital Sodium◈
Perphenazine ℞
Pethidine HCl®
Phenazopyridine HCl
Phenobarbital◈
Phentermine◈
Phenylbutazone ℞
Phenylephrine HCl
Phenytoin ℞
Pilocarpine
Piperazine
Potassium Salts
Prednisolone ℞
Prednisone ℞
Primidone ℞
Probenecid
Procyclidine HCl
Progesterone ℞
Promazine HCl ℞
Promethazine HCl
Propantheline Bromide
Proparacaine HCl
Propoxyphene ®
Propranolol ℞
Propylthiouracil ℞
Pseudoephedrine HCl
Pyridoxine
Pyrvinium Pamoate
Quinidine
Quinine Sulfate
Reserpine ℞
Riboflavin
Rifampin ℞
Saccharin, Saccharin Sodium
Secobarbital Sodium◈
Selenium Sulfide
Sodium Bicarbonate
Sodium Chloride
Sodium Fluoride
Sodium Sulfacetamide ℞
Stilbestrol ℞
Streptomycin ℞
Sulfadiazine ℞
Sulfamethoxazole ℞
Sulfapyridine ℞
Sulfasalazine ℞
Sulfisoxazole ℞
Testosterone ℞
Methyltestosterone ℞
Tetanus Immune Globulin (T.I.G.) (Human)
Tetanus Toxoid, Adsorbed
Tetracaine HCl
Tetracyclines ℞
Theophylline
Thiamine
Thimerosal
Thioridazine HCl ℞
Tolbutamide ℞
Trifluoperazine HCl ℞
Trihexyphenidyl HCl
Tubocurarine Chloride
Vaccinia Immune Globulin (V.I.G.) (Human)
Vitamin A
Vitamin B_{12}
Vitamin D
Vitamin E
Vitamin K
Warfarin Sodium ℞

. . . The GREEN PAGES link the trade names of drug products with their active chemical constituent.

Monographs of Pharmaceuticals and Specialties

A-200 PYRINATE

A-200 PYRINATE – See A-"TWO HUNDRED" PYRINATE.

AAD PATCH TEST KIT

— see Medical Devices Section.

A and D OINTMENT *Schering*

Vitamins A & D—Lanolin Compound

Emollient

Indications: Diaper rash, minor skin irritations, chafing, mild sunburn, minor burns, scalds, abrasions and skin dryness.

Dosage: Apply liberally, as needed to affected skin area. Cover with suitable dressing if required.

Supplied: Each g contains: vitamin A 1,500 I.U and vitamin D 213 I.U. in a lanolin petrolatum base. Available in 25 and 75 g tubes and 450 g jars.

ABDEC® *P.D.*

Multivitamins ***Dietary Supplement***

For prescribing information, refer to "Vitamin Compounds – Oral – Liquid" and "Solid Dosage Forms".

ACCELERASE® *Organon*

Pancrelipase Compound

Enzymes—Digestant

Supplied: Each gray capsule contains: pancrelipase equivalent to 4,000 USP Lipase units, 15,000 USP Amylase units, 15,000 USP Protease units, mixed conjugated bile salts 65 mg, cellulase 2 mg. Tartrazine free. Bottles of 60 and 1,000 capsules.

(Shown in Product Recognition Section)

ACCUTANE™ ROCHE® ℞ *Roche*

Isotretinoin ***Acne Therapy***

Pharmacology: The mechanism of action of isotretinoin is unknown. Vitamin A is important for functional integrity of the skin and is known to affect the keratinization process. In acne patients, improvement occurs in association with a reduction in sebum secretion. The decrease in sebum secretion is temporary and is related to either the dose or duration of isotretinoin administration and reflects a reduction in sebaceous gland size and an inhibition of sebaceous gland differentiation.

Following oral administration of 80 mg, peak plasma concentrations ranged from 167 to 459 ng/mL with a mean time to peak of 3.2 hours in volunteers, while in acne patients peak plasma concentrations ranged from 98 to 535 ng/mL with a mean time to peak of 2.9 hours. Isotretinoin is 99.9% protein bound in human plasma, almost exclusively to albumin. The mean terminal elimination half-life of isotretinoin in volunteers and patients ranged from 9 to 22 hours. Following oral administration of ^{14}C-isotretinoin, ^{14}C activity in blood declined with a mean half-life of 90 hours. Approximately equal amounts of radioactivity were recovered in the urine and feces, with 65 to 83% of the dose recovered.

The major metabolite identified in blood and urine was 4-oxo-isotretinoin. Tretinoin and 4-oxo-tretinoin were also observed. The apparent half-life for elimination of the 4-oxo-isotretinoin ranged from 11 to 50 hours with a mean of 28 hours. Following 80 mg of isotretinoin administered orally, maximum plasma concentrations of the 4-oxo-isotretinoin was 87 to 399 ng/mL and maxima were observed between 6 and 20 hours. The blood concentration of the major metabolite generally exceeded that of isotretinoin after 6 hours. The data suggest that both isotretinoin and the major metabolite are excreted in the bile and reabsorbed.

The mean minimum steady-state blood concentrations of isotretinoin were 160 ng/mL in 10 patients receiving 40 mg twice daily. After single and multiple doses, the mean ratio of areas under the curves of 4-oxo-isotretinoin to isotretinoin was between 3 and 3.5.

Indications: The treatment of cystic acne, conglobate acne and severe acne which has failed to respond to an adequate course of systemic antimicrobial.

Contraindications: Patients who are pregnant or likely to become pregnant. **Major fetal abnormalities associated with isotretinoin administration during pregnancy have been reported. These include hydrocephalus, microcephaly and abnormalities of the external ear (micropinna, small or absent external auditory canals). Patients who are sensitive to parabens or with known hypersensitivity to retinoids.**

Warnings: Patients who intend to become pregnant while undergoing treatment should not receive isotretinoin (see Contraindications).

Precautions: Women of childbearing potential should not take isotretinoin unless the use of an effective form of contraception is established prior to treatment, continued throughout treatment, and for at least the first month after treatment (see Contraindications).

Liver function and blood lipids (triglycerides and cholesterol) should be monitored at the start of treatment, after the first 2 weeks of administration and thereafter bi-weekly until the effect of maintenance dose therapy upon these tests is determined. Some patients have developed a slight to moderate decrease in high density lipoproteins, which were reversible upon cessation of therapy. Patients with increased tendency to develop hypertriglyceridemia may be at greater risk of developing hypertriglyceridemia while taking isotretinoin. Some patients have been able to reverse triglyceride elevations by weight reduction and restriction of dietary fat and alcohol while continuing to take isotretinoin.

The cardiovascular consequences of hypertriglyceridemia are not well understood, but may increase the patients risk status. In addition, elevation of serum triglycerides in excess of 800 mg/dL has been associated with acute pancreatitis.

Because of the relationship of isotretinoin to vitamin A, patients should be advised against taking vitamin preparations and health food supplements containing vitamin A to avoid additive toxic effects.

It is not known whether this drug is excreted in human milk. Due to isotretinoin's potential for tumorigenicity in rats, a decision should be made whether to postpone therapy during nursing, taking into account the importance of the drug to the mother.

The long-term safety for use of isotretinoin in prepubertal children has not been established.

Adverse Effects: Most of the clinical side-effects are dose-related and are usually well tolerated at the recommended dosages. The side-effects may recede during continued treatment and in all cases were reversible with reduction of dosage or discontinuation of therapy.

The most common side-effects are mucocutaneous. These include: cheilitis (96%), facial dermatitis (55%), dry nose (51%), desquamation (50%), pruritus (30%), dry skin (22%), conjunctivitis (19%), joint pain (13%), alopecia (13%), irritation of the eyes (11%). Dryness of the nasal mucosa may be associated with mild epistaxis. Mild-to-moderate conjunctivitis may be alleviated by use of an ophthalmic ointment.

Rash, peeling of palms and soles, skin infections, increased susceptibility to sunburn, changes in skin pigment, urticaria, bruising, erythema nodosum, paronychia, pyogenic granuloma, non-specific urogenital symptoms, non-specific gastrointestinal symptoms, inflammatory bowel disease (including regional ileitis), mild gastrointestinal bleeding, rectal bleeding, headache, disseminated herpes, edema, hair problems (other than thinning), respiratory infections, fatigue, visual disturbances, weight loss, paresthesias, corneal opacities, dizziness, and abnormal menses have been reported infrequently.

Cases of pseudotumor cerebri have been reported, usually associated with concomitant tetracycline therapy. This disorder usually includes headache, visual disturbances and papilledema. Headaches and visual disturbances have been reported as isolated events with isotretinoin therapy.

In investigations of the use of isotretinoin in skin disorders other than acne, in which high doses were administered for longer periods of time, x-ray evidence of bone abnormalities such as: diffuse idiopathic skeletal hypertrophy (D.I.S.H.) (17 patients), severe cervical spine degeneration (2 patients), premature epiphyseal closure (2 patients) and corneal opacities (5 patients) were observed. The relationship between the development of these conditions and the administration of isotretinoin had not been determined.

Isotretinoin therapy induces changes in the serum lipids in a significant number of treated subjects. These changes consisted of: elevationof serum triglycerides, mild to moderate decreases in serum high density lipoprotein (HDL), and minimal elevations of serum cholesterol. Abnormalities of serum triglycerides, HDL and cholesterol were reversible upon cessation of therapy.

A rise in serum levels of liver enzymes may occur, especially with higher dosages. Although the changes have usually been within the normal range, and may return to baseline levels despite continued treatment, significant increases have occurred in a few cases, necessitating dosage reduction or discontinuation of isotretinoin. An elevated erythrocyte sedimentation rate may also occur.

Other less commonly reported laboratory abnormalities were: decreases in red blood cell parameters and white blood cell counts, elevated platelet counts, white cells in the urine, proteinurea, red blood cells in the urine, elevated fasting blood sugar, elevated creatinine phosphokinase (CPK) or hyperuricemia.

Most adverse effects appear to be dose-related, with the more pronounced effects occurring at doses above 1 mg/kg/day. Adverse effects were generally reversible when therapy was discontinued.

Overdose: Symptoms and Treatment: There has been no experience, to date, with acute overdoses of isotretinoin. Signs and symptoms of overdosage with isotretinoin would probably be similar to acute vitamin A toxicity, severe headaches, nausa or vomiting, drowsiness, irritability and pruritis. They would be expected to be reversible and to subside without need for treatment. Gastric lavage may be worthwhile in the first few hours after ingestion.

Elevated intracranial pressure has been reported with both acute and chronic vitamin A overdoses. It is therefore possible that the same effect may be present with an isotretinoin overdosage.

Dosage: The therapeutic response to isotretinoin is dose-related and varies between patients. Individual adjustments of dosage according to the response of the condition and the patient's tolerance of the drug are necessary. In most cases complete or near-complete suppression of acne is achieved with a single 12 to 16 week course of therapy. If a second course of therapy is needed, it can be initiated 8 or more weeks after completion of the first course, since experience has shown that patients may continue to improve while off the drug.

Initial Therapy: The initial dose should be individualized according to the patient's weight and severity of the disease: 0.5 mg/kg daily for a period of 2 to 4 weeks, when responsiveness to the drug will usually be apparent. Transient exacerbation of acne is occasionally seen during this initial period.

The daily dosage should be taken with food in the nearest number of whole capsules, either as a single dose or in 2 divided doses during the day, whichever is more convenient.

Maintenance Therapy: Between 0.1 and 1 mg/kg daily and, in exceptional instances, up to 2 mg/kg daily, depending upon individual patient response and tolerance to the drug.

A complete course of therapy consists of 12 to 16 weeks.

Patients may show additional improvement for up to several months after a course of treatment. With effective treatment, appearance of new lesions will not normally be evident for a period of at least 3 to 6 months.

Supplied: Each opaque, oval-shaped, soft gelatin capsule contains: isotretinoin 10 mg (light pink, imprinted ACCUTANE 10 ROCHE) or 40 mg (yellow, imprinted ACCUTANE 40 ROCHE). Bottles of 30 capsules.

Protect from light at all times. Dispense with information for the consumer.

(Shown in Product Recognition Section)

New Product 1983

ACET-AM® Preparations *Organon*

Theophylline Preparation ***Bronchodilator***

Supplied: Liquid: Each 5 mL contains: theophylline sodium glycinate 100 mg (equivalent to theophylline 50 mg). Alcohol 20%. Tartrazine free. Available in 250 mL bottles.

Tablets: Each white compressed tablet contains: theophylline calcium glycinate 325 mg (equivalent to 165 mg of anhydrous theophylline). Tartrazine free. Bottles of 100, 500 and 1,000 tablets.

(Shown in Product Recognition Section)

ACET-AM® ELIXIR Preparations

Organon

Theophylline-Sodium Glycinate-Ephedrine

Bronchodilator

Supplied: Acet-Am Elixir: Each 5 mL of elixir contains: theophylline sodium glycinate 100 mg, (equivalent to theophylline 50 mg), ephedrine HCl 3.5 mg, diphenhydramine HCl 12.5 mg. Alcohol 20%. Tartrazine free. Available in 250 mL bottles.

Acet-Am Elixir Plus: Each 5 mL contains: same components as Acet-Am Elixir plus guaifenesin 100 mg. Tartrazine free. Available in 250 mL bottles.

ACET-AM® EXPECTORANT

Organon

Theophylline Sodium Glycinate—Guaifenesin

Bronchodilator - Expectorant

Supplied: Each 5 mL of expectorant contains: theophylline sodium glycinate 100 mg (equivalent to theophylline 50 mg), guaifenesin 100 mg, alcohol 20%. Tartrazine free. Available in 250 mL bottles.

ACETAMINOPHEN

Paracetamol ***Analgesic—Antipyretic***

Pharmacology: Acetaminophen is the major metabolite of phenacetin and acetanilid. Animal and clinical studies have shown acetaminophen to have antipyretic and analgesic activity equal to that of ASA.

Unlike the salicylates, acetaminophen does not interfere with tubular secretion of uric acid, nor does it affect acid base balance in normal therapeutic doses. Acetaminophen does not interfere with hemostasis and does not inhibit platelet aggregation.

Acetaminophen is rapidly and completely absorbed from the gastrointestinal tract. Approximately 85% of a 1 g dose is recovered from the urine in 24 hours. About 3% is excreted unchanged, the balance being conjugated principally to the glucuronide or sulfate. Peak plasma concentrations of the free and conjugated drug are achieved ½ to 1 hour after administration. The plasma half life of the unchanged drug is about 2 hours.

Allergic reactions are rare with acetaminophen but have occurred. This drug may be useful in asthmatic patients sensitive to salicylates; however, patients with salicylate induced urticaria or angioedema can suffer cross reactivity with acetaminophen.

Small amounts of acetaminophen are normally converted to a highly reactive metabolite by hepatic microsomal enzymes. At therapeutic doses, the small amounts of the active metabolite so formed are rapidly inactivated by hepatic glutathione and removed by renal excretion. However, where hepatic glutathione has been rapidly depleted by a large dose of acetaminophen, covalent binding of the metabolite to liver-cell macromolecules occurs and is presumed to be responsible for the hepatic cell necrosis. Prompt administration of acetylcysteine is indicated to prevent acetaminophen induced hepatic necrosis (see Overdose section).

Indications: The treatment of mild to moderate pain and the reduction of fever.

Contraindications: Hypersensitivity to acetaminophen.

Adverse Effects: The incidence of gastrointestinal upset is less than after salicylate administration.

Hepatic toxicity has been associated with acetaminophen overdose. Phenobarbital increases the activity of microsomal enzymes which produce a toxic metabolite and therefore acetaminophen's hepatotoxicity may be enhanced. Thus, concomitant ingestion of phenobarbital may increase the likelihood of liver necrosis in acetaminophen overdose. The chronic ingestion of alcohol may be implicated in the increasing potential for hepatic toxicity. Abnormal liver function has been associated with therapeutic doses ranging from 3 to 8 g per day. In patients with compromised liver function, acetaminophen could exacerbate liver insufficiency.

Renal papillary necrosis has been reported following prolonged acetaminophen administration of up to 19 g per day. There have been no authenticated reports of renal papillary necrosis with therapeutic doses of acetaminophen alone. Renal insufficiency may occur as an effect secondary to liver failure.

Anemia has been reported in patients with gastrointestinal bleeding who were often analgesic abusers, had chronic gastric ulcers or where gastrointestinal bleeding was already present. Neutropenia, methemoglobinemia and thrombocytopenia have rarely occurred.

Rarely, asthmatic attacks have been precipitated by acetaminophen.

Skin rashes and fixed dermatitis with pruritis have been rarely reported.

Overdose: In adults, hepatotoxicity may occur after ingestion of a single dose of 10 to 15 g (200 to 250 mg/kg) of acetaminophen; a dose of 25 g or more is potentially fatal.

Reports have indicated hepatic necrosis with a single dose of 6 g and death occurring with a single dose of 13 g. Non fatal overdoses of 12.5 to 31.5 g have also been reported. However, it is generally agreed that consumption of more than 50% of the toxic dose, e.g., 7.5 g in adults and 140 to 150 mg/kg in children could initiate liver damage.

Symptoms: The earliest symptoms of overdose with acetaminophen are nausea, vomiting, sweating and pallor. This initial period is frequently followed by an asymptomatic phase of 24 to 48 hours after which hepatic damage may become evident. Elevation in hepatic enzymes, SGOT, SGPT are noted. BUN remains low. Hepatic function is altered as measured by bilirubin and prothrombin time. The liver enlarges with marked right upper quadrant pain and tenderness.

After 3 to 5 days, jaundice, hypoglycemia, encephalopathy, cardiomyopathy, renal failure, hepatic coma and death may occur.

Factors contributing to an accurate evaluation of toxicity include: the amount of drug ingested and more significantly, the serum acetaminophen concentration measured optimally, after 4 hours of ingestion.

When serum determinations of acetaminophen are above 150 μg/mL at 4 hours, or above 40 μg/mL at 12 hours following the estimated time of ingestion, the patient is at risk of liver damage and antidotal therapy should be instituted immediately.

An additional reliable indicator of possible hepatic injury is the serum half life. The normal half life of acetaminophen in a healthy adult is 2 hours. If the serum half life exceeds 4 hours, it can be assumed that hepatic necrosis will occur; if the half life exceeds 12 hours hepatic coma is a likely possibility.

Treatment of acetaminophen overdosage includes ipecac induced emesis or gastric lavage which should, when possible, commence within 4 hours of drug ingestion. Activated charcoal is effective only when given within 1 to 2 hours of the alleged overdose. Prior to antidotal treatment with acetylcysteine (Mucomyst) residual activated charcoal must be removed by gastric lavage with water.

Acetylcysteine is effective orally. A loading dose of 140 mg/kg is given as a single dose. A maintenance dose of 70 mg/kg is then given every 4 hours for 17 doses. If nausea and vomiting occurs within 1 hour of the loading or maintenance dose, the entire dose should be repeated. If nausea and vomiting persist, a nonphenothiazine antiemetic e.g. dimenhydrinate, may be administered. Acetylcysteine 20% solution may be diluted to a 5% concentration with a soft drink or fruit juice to make it more palatable. This mixture should be consumed within 1 hour of preparation.

The use of i.v. acetylcysteine is recommended when oral therapy is not feasible or practical. A loading dose, 150 mg/kg of sterile Mucomyst 20% is infused in 200 mL D5w over 15 mins., followed by an infusion of 50 mg/kg in 500 ml D5w over 4 hours, and finally 100 mg/kg in 1000 ml D5w during the next 16 hours. The total dose is 300 mg/kg administered over 20 hours.

Dosage: Adults: 650 to 1,000 mg every 4 to 6 hours, not to exceed 4,000 mg/24 hours.

Children: 10-15 mg/kg every 4 to 6 hours, not to exceed 65 mg/kg/24 hours.
or the following, 4 to 5 times daily.

Age	Single Dose
Newborn to under 4 months	40 mg
4 months to under 12 months	80 mg
12 months to under 2 years	120 mg
2 and 3 years	160 mg
4 and 5 years	240 mg
6, 7 and 8 years	320 mg
9 and 10 years	400 mg
11 and 12 years	480 mg
13 years and older	640 mg

Note: Acetaminophen drops are approximately 5 times as concentrated as the elixir or syrup form. Care must be taken to ensure that this is taken into account when doses are expressed in mL.

Reviewed 1982

ACETAMINOPHEN SUPPOSITORIES

Beecham

Paracetamol ***Analgesic — Antipyretic***

Pharmacology: Acetaminophen is the major metabolite of phenacetin and acetanilid. Animal and clinical studies have shown acetaminophen to have antipyretic and analgesic activity equal to that of ASA. Acetaminophen lacks anti-inflammatory effects.

Unlike the salicylates, acetaminophen does not interfere with tubular secretion of uric acid nor does it affect acid-base balance if taken in therapeutic doses. Acetaminophen does not interfere with hemostasis and, in particular does not inhibit platelet aggregation. Allergic reactions are rare and thus the drug is useful in patients who cannot tolerate salicylates and those with an allergic diathesis, including bronchial asthmatics. A small portion of the administered acetaminophen is converted by hepatic microsomal enzymes to a reactive metabolite. At therapeutic doses this minor metabolite is rapidly inactivated by conjugation with glutathione and eliminated by renal excretion. However, where hepatic glutathione has been depleted, covalent binding of the reactive metabolite to liver-cell macromolecules occurs and hepatic cell necrosis ensues. It has been shown that glutathione precursors such as N-acetylcysteine, cysteine, cysteamine and methionine can decrease experimental acetaminophen-induced hepatic necrosis when administered promptly after a toxic dose of acetaminophen. Rectal absorption of acetaminophen, as with most rectally administered drugs, is more erratic than absorption following oral administration. Absorption rate is generally slower. Peak blood levels of free acetaminophen are not reached until 1.5 to 3 hours following rectal administration and the peak concentration in the blood is approximately 50% of that observed following an equivalent oral dose. The percentage of a rectal dose of acetaminophen absorbed also varies giving wide variances in the bioavailability. In view of these observations higher rectal doses or more frequent administration may be required to achieve and/or maintain blood concentrations of acetaminophen comparable to those obtained following oral administration.

Indications: For the treatment of mild to moderate pain and the reduction of fever.

Contraindications: Hypersensitivity to acetaminophen.

Warnings: Acetaminophen poisoning can result in severe hepatic damage.

Precautions and Adverse Effects: When used as directed, acetaminophen is virtually free of severe toxicity or side effects. The incidence of gastrointestinal upset is less than after salicylate administration. If a rare sensitivity reaction occurs, discontinue the drug.

Hypersensitivity to acetaminophen is usually manifested by a rash or urticaria.

Regular use of acetaminophen has been shown to produce a slight increase in prothrombin time in patients receiving oral anticoagulants but the clinical significance of this effect is not clear.

Overdose: Symptoms: In adults hepatotoxicity may occur after ingestion of a single dose of 10 to 15 g (200 to 250 mg/kg) of acetaminophen; a dose of 25 g or more is potentially fatal.

In adults, nonfatal overdoses (ranging from 12.5 to 31.5 g have been reported and 1 death after 30 g of acetaminophen had been ingested. A 13 year old child is reported to have died after ingesting 15 g.

Symptoms during the first 2 days of acute poisoning by acetaminophen do not reflect the potential seriousness of the intoxication. Nausea, vomiting, anorexia and abdominal pain occur during the initial 24 hours and may persist for a week of more. Liver injury may become manifest the second day, initially by elevation of serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of prothrombin time. Alkaline phosphatase activity and serum albumin concentration may remain normal. The hepatotoxicity may progress to encephalopathy, coma and death. Liver biopsy reveals centrilobular necrosis with sparing of the periportal area. In nonfatal cases, the hepatic lesions are reversible over a period of weeks or months. Transient azotemia is apparent in most patients and acute renal failure occurs in some. Hypoglycemia may occur, but glycosuria and impaired glucose tolerance have also been reported. Both metabolic acidosis and metabolic alkalosis have been noted, cerebral edema and non-specific myocardial depression have also occurred. Since acetaminophen is metabolized primarily by the liver, in cases of acute poisoning, prolongation of the plasma half life beyond 3 hours may be indicative of liver injury. Hepatic necrosis should be anticipated if the half life exceeds 4 hours, and hepatic coma is likely if the half life is greater than 12 hours. A single determination of serum acetaminophen concentration is a less reliable predictor of hepatic injury. However, only minimal liver damage has developed when the serum concentration was below 120 μg/mL at 4 hours or less than 50 μg/mL at 12 hours after ingestion of the drug. Encephalopathy should also be anticipated if serum bilirubin concentration exceeds 4 mg/100 mL during the first 5 days.

Treatment: Early diagnosis is vital. Vigorous supportive therapy is essential when intoxication is severe. Procedures to limit continuing absorption of the drug must be initiated promptly. When the oral route of administration is used induction of vomiting or gastric lavage should be performed and should be followed by oral administration of activated charcoal (50 g). Hemodialysis, if it can be initiated within the first 12 hrs., has been advocated for all patients with a plasma concentration of acetaminophen greater than 120 μg/mL 4 hours after drug ingestion. If administered within the first few hours after ingestion of acetaminophen, sulphydryl compounds, which replete glutathione, have been shown effectively to prevent or reduce the hepatotoxic effects of acetaminophen. N-acetylcysteine, has been shown to be particularly effective and well tolerated when given orally as a 5% solution diluted with cola, fruit juice, or water. The accepted treatment regime is a loading dose of 140 mg/kg followed by 70 mg/kg every 4 hours for 17 doses or until plasma concentrations of acetaminophen are indicative of a low risk of hepatotoxicity.

Dosage: Method of Use: First remove wrapper and moisten the suppository with water. Lie down on side and insert the suppository pushing it well up into the rectum with finger.

Adults: One suppository (650 mg) 4 to 6 times daily as necessary and after each bowel movement.

Children: Under 2 years, as recommended by the physician. 2 to 6 years, one suppository (120 mg) 4 times daily. 6 to 12 years, two suppositories (240 mg) 4 times daily.

A physician should be consulted for treatment regimens lasting longer than 5 days. The inherancy in the rectal route of administration of an erratic absorption, lower blood concentrations and the possibility of lower bioavailability in some patients relative to the oral route of administration makes more frequent rectal administration acceptable when deemed necessary by the prescriber.

Although no direct evidence is available, pharmacokinetic studies would suggest that the susceptibility to hepototoxicity of acetaminophen by the rectal route would be lower than that by the oral route.

Supplied: Suppositories are available in adult and child strengths containing 650 and 120 mg of acetaminophen respectively. No tartrazine. Suppositories are individually sealed in plastic moulds and available in boxes of 12. Réfrigerate suppositories.

Reviewed 1982

ACETAZOLAM Ⓡ *ICN*

Acetazolamide ***Carbonic Anhydrase Inhibitor***

Indications: To decrease ocular aqueous humor secretion in glaucoma (chronic, simple and secondary types). Also used as an adjunct in the treatment of selected cases of epilepsy. To alkalinize the urine in selected cases of salicylate overdosage.

Contraindications: Depressed sodium and/or potassium blood levels, in renal failure, adrenal gland failure, metabolic acidosis, and some cases of hepatic cirrhosis, severe glaucoma due to peripheral anterior synechias or in hemorrhagic glaucoma. Longterm use in chronic noncongestive angle closure glaucoma is contraindicated.

Studies on acetazolamide in mice and rats have consistently demonstrated embryocidal and teratogenic effects at doses in excess of 10 times the human dose. There is no evidence of these effects in humans; however, acetazolamide should not be used in pregnancy, unless the anticipated benefits outweigh these potential hazards and are not attainable in other ways.

Precautions: Increasing the dose does not increase and may often decrease the diuresis and may yet produce drowsiness and/or paresthesia.

Adverse Effects: Metabolic acidosis and hypokalemia may occur during prolonged acetazolamide therapy.

Adverse reactions common to all sulfonamide derivatives including fever, rash, crystalluria, renal calculus, bone marrow depression, thrombocytopenic purpura, hemolytic anemia, leukopenia, pancytopenia and agranulocytosis may occur. If such reactions occur, discontinue therapy and institute appropriate measures.

Untoward effects during short term therapy are said to be minimal. Those noted include paresthesias, some loss of appetite, polyuria and occasional instances of drowsiness and confusion. Other occasional adverse reactions include urticaria, melena, hematuria, glycosuria, hepatic insufficiency, flaccid paralysis and convulsions.

Transient myopia has been reported. This condition invariably subsided upon the diminution or discontinuation of the medication.

Dosage: Chronic simple (open angle) glaucoma: 250 mg 1 to 4 times daily. A complementary effect has been noted when acetazolamide was used with miotics or mydriatics as the case demanded. Secondary glaucoma and preoperative treatment of some cases of acute congestive (closed angle) glaucoma: 250 mg every 4 hours. Epilepsy: 8 to 30 mg/kg (375 to 1 000 mg) daily in divided doses. To alkalinize the urine: 250 mg every 4 to 6 hours.

Supplied: Each white, scored, compressed tablet contains: acetazolamide USP 250 mg. Bottles of 100 and 500 tablets.

ACETEST® *Ames*

Sodium Nitroprusside Reagent

Ketonuria Diagnostic Aid

Indications: Detection of acetone and acetoacetic acid in urine, serum, plasma or whole blood.

Precautions: Bromsulphalein or high concentrations of phenylketones will cause color reactions with Acetest tablets.

Method of Use: Place tablet on a clean sheet of paper and add 1 drop of urine, serum, plasma or whole blood to tablet. For urine testing, wait 30 seconds to compare reaction with color chart provided. Trace, moderate or strongly positive reactions are indicated by color range of lavender to deep purple. For serum or plasma, compare color to color chart at 2 minutes after application of specimen. For whole blood, 10 minutes after application of specimen, remove clotted blood from tablet and compare color of tablet to color chart.

Overdose: Symptoms: If accidentally ingested, symptoms are those of borate poisoning.

Treatment: Gastric lavage.

Supplied: Reagent tablets containing: sodium nitroprusside, sodium borate, disodium phosphate, glycine and lactose. Bottles of 100 and 250 reagent tablets.

ACETOPHEN® *Frosst*

ASA ***Analgesic—Antipyretic—Anti-inflammatory***

Pharmacology: See ASA monograph.

Indications: The relief of pain, fever and inflammation in a variety of conditions such as influenza, common cold, low back and neck pain, dysmenorrhea, headache, toothache, sprains and strains, fractures, myositis, neuralgia, synovitis, arthritis, bursitis, burns, injuries, following surgical and dental procedures.

Contraindications: Salicylate sensitivity, active peptic ulcer.

Warnings: ASA is one of the most frequent causes of accidental poisoning in toddlers and infants. Therefore, keep salicylates well out of children's reach.

Precautions: Administer salicylates cautiously to patients with asthma and other allergic conditions, a history of gastrointestinal ulcerations, bleeding tendencies, significant anemia, or hypoprothrombinemia.

Patients taking 2 to 3 g of ASA daily are at an increased risk of developing severe gastrointestinal bleeding following the ingestion of alcohol.

If possible, uncoated ASA tablets should not be swallowed whole but should be well chewed and followed with an adequate volume of water or crushed into a fine powder and taken as a suspension in orange juice.

Since salicylates interfere with maternal and infant blood clotting and lengthen the duration of pregnancy and parturition time, they should not be administered during the last trimester of pregnancy unless the need outweighs the potential risks.

Caution is necessary when salicylates and anticoagulants are prescribed concurrently, as salicylates can depress the concentration of prothrombin in the plasma.

Patients receiving concurrent salicylate hypoglycemic therapy should be monitored closely, and reduction of the hypoglycemic drug dosage may be necessary.

Although salicylates in large doses are uricosuric agents, smaller amounts may depress uric acid clearance and thus decrease the uricosuric effects of probenecid, sulfinpyrazone, oxyphenbutazone and phenylbutazone.

Exercise caution when corticosteroids and salicylates are used concurrently.

Acute hepatitis has been reported rarely in patients with systemic lupus erythematosus and juvenile rheumatoid arthritis with plasma salicylate concentrations above 25 mg/100 mL. Patients have recovered upon cessation of therapy.

Restrict salicylate ingestion in patients receiving indomethacin (and perhaps other nonnarcotic analgesics) for conditions such as rheumatoid arthritis.

Salicylates can produce changes in thyroid function tests.

Sodium excretion produced by spironolactone may be decreased by salicylate administration.

Concomitant ingestion of salicylates and aminosalicylic acid (PAS) or aminobenzoic acid (PABA) in normal dose may lead to increased toxicity and salicylism.

Salicylates reportedly displace sulfonylureas, penicillins and methotrexate from their binding sites on plasma proteins. Salicylates also retard the renal elimination of methotrexate.

Adverse Effects: Gastrointestinal: nausea, vomiting, diarrhea, gastrointestinal bleeding and/or ulceration.
Ear: tinnitus, vertigo, hearing loss.
Hematologic: leukopenia, thrombocytopenia, purpura.
Dermatologic and hypersensitivity: urticaria, angioedema, pruritus, skin eruptions, asthma, anaphylaxis.
Miscellaneous: acute, reversible hepatotoxicity; mental confusion, drowsiness, sweating, thirst.

Overdose: Symptoms: In mild overdosage these may include rapid and deep breathing, nausea, vomiting (leading to alkalosis), hyperpnea, vertigo, tinnitus, flushing, sweating, thirst and tachycardia. (High ASA blood concentrations lead to acidosis). Severe cases may show fever, hemorrhage, excitement, confusion, convulsions or coma, and respiratory failure.

Treatment is essentially symptomatic and supportive. Administer water, activated charcoal and remove by cautious gastric lavage or emesis. Force fluids and replace sodium loss. If the patient is unable to retain fluids orally, the alkalosis can be treated by i.v. hypertonic saline. If salicylism acidosis is present, i.v. sodium bicarbonate is preferred because it increases the renal excretion of salicylates. Vitamin K is indicated if there is evidence of hemorrhage. Dialysis has been used with success.

Use general supportive measures for depressed respiration e.g. oxygen and artificial respiration. Convulsions may best be treated by the administration of succinylcholine and artificial ventilation with oxygen. Do not use CNS depressant agents. Hyperthermia and dehydration are immediate threats to life and initial therapy must be directed to their correction and to the maintenance of adequate renal function. External cooling with cool water or alcohol should be provided quickly to any child who has a rectal temperature over 40° C.

Dosage: Adults—Analgesic/antipyretic: 650 mg 4 to 6 times a day as necessary.
Anti-inflammatory: 1 g 4 to 6 times a day, up to 10 g daily.
Usual dosage range: 325 mg to 10 g daily.
Children—Analgesic/antipyretic: 11 mg/kg or 250 mg/m² of body surface, 6 times a day to 16 mg/kg or 375 mg/m² of body surface, 4 times a day. Maximum daily dose is 3.6 g.
Anti-inflammatory: 16 mg/kg 6 times a day or 25 mg/kg 4 times a day initially (up to 125 mg/kg/day). After complete relief of symptoms in the absence of signs of toxicity, reduce the dose to 10 mg/kg 6 times a day or 15 mg/kg 4 times a day (up to 100 mg/kg/day).

Supplied: Each white tablet engraved with F symbol contains: ASA 325 mg. Bottles of 1,000 tablets.

(Shown in Product Recognition Section)

ACETOPHEN® COMPOUNDS *Frosst*

Tablets of ACETOPHEN® (ASA) and various combinations—e.g. 217, 222, 282, 292, 283, 692, etc., refer to Monographs of Numbered Specialties located at the end of the white pages.

ACETOXYL® 2.5% and 5% GEL
ACETOXYL® 10% and 20% GEL Ⓡ *Stiefel*

Benzoyl Peroxide Compound

Acne Vulgaris Therapy

Indications: Topical treatment of acne vulgaris.

Contraindications: Known hypersensitivity to any of the components, presence of eczema or seborrheic dermatitis. Use on patients with very blond (albino) skin is not recommended.

Precautions: Keep away from eyes or mucous membranes. Transitory stinging or burning sensation on initial application invariably disappears on continued use. May cause irritation on neck, circumoral and other sensitive areas. If excessive dryness, irritation or sensitivity occurs, discontinue use temporarily. Acetoxyl may bleach hair and colored fabrics.

Radiation from ultraviolet and cold quartz sources as well as abrasion may add to the desquamative effect produced by benzoyl peroxide and, therefore, should be reduced in intensity and/or frequency during treatment.

Very fair individuals should always be started with a single application of Acetoxyl 2.5 at bedtime.

Adverse Effects: Allergic contact dermatitis and severe erythema with crusting have been reported with topical benzoyl peroxide. Do not confuse a strong irritant reaction with allergic sensitivity. Patch testing should be employed to confirm sensitivity.

Dosage: Apply once daily to affected areas as prescribed. For best results, wash face with a detergent soap prior to application.

Supplied: Each plastic tube contains benzoyl peroxide 2.5% (Acetoxyl 2.5), 5% (Acetoxyl 5), 10% (Acetoxyl 10) or 20% (Acetoxyl 20) in an acetone gel base. Available in 60 g tubes. Store at room temperature.

ACETYLSALICYLIC ACID

See ASA

ACHROCIDIN® Ⓡ *Lederle*

Tetracycline-Salicylamide Compound

Antibiotic—Analgesic

Indications: The treatment of tetracycline sensitive bacterial infection which may complicate vasomotor rhinitis, sinusitis and other allergic diseases of the upper respiratory tract, and for the concomitant symptomatic relief of headache and nasal congestion.

Contraindications, Precautions and Adverse Effects: As for Achromycin. Patients should be cautioned not to operate vehicles or hazardous machinery until their response to the drug has been determined. Since the depressant effects of antihistamines are additive to those of other drugs affecting the CNS, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, pyschotherapeutic agents or other drugs with CNS depressant effects during antihistamine therapy.

Dosage: Adults, 2 tablets, with water at onset of symptoms, then 2 tablets 3 or 4 times daily for 3 to 5 days. Children, dosage is determined by the tetracycline content on the basis of 22 to 44 mg tetracycline/kg per day.

Oral forms of tetracycline should be given 1 hour before or 2 hours after meals. Antacids, containing aluminum, calcium or magnesium and iron salts impair absorption and should not be given to patients taking oral tetracyclines. Foods and some dairy products also interfere with absorption.

Supplied: Each yellow, round, film coated tablet contains: tetracycline HCl 125 mg, caffeine 30 mg, salicylamide 300 mg, chlorothen citrate 25 mg. Calories: 1 per tablet. Tartrazine-free. Bottles of 100 and 500 tablets.

ACHROMYCIN® Preparations Ⓡ

Lederle

Tetracycline HCl — ***Antibiotic***

Pharmacology: see tetracycline monograph.

Indications: Many strains of bacteria have been shown to be resistant to the tetracyclines. These include certain strains of streptococci, staphylococci, pneumococci, gonococci, and many other gram negative organisms. Therefore, culture and sensitivity testing are advised to determine the susceptibility of the infecting organisms to tetracyclines. Chemotherapy should not be initiated until all the necessary bacteriological investigations have been started.

Microorganisms that have become insensitive to one tetracycline invariably exhibit cross resistance to other tetracyclines.

Some cross resistance between the tetracyclines and chloramphenicol for gram negative organisms but not for gram positive ones has been reported. Tetracycline resistant organisms are most likely to be acquired from other individuals in a population where tetracycline has been widely used.

The tetracyclines are indicated in infections caused by the following microorganisms:

Rickettsiae (Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, tick fevers). M. pneumoniae (PPLO, Eaton agent), agents of psittacosis and ornithosis, agents of L. venereum and G. inguinale, and the spirochetal agent of relapsing fever (B. recurrentis).

The following gram negative organisms: H. ducreyi (chancroid), P. pestis and P. tularensis, B. bacilliformis, Bacteroides, V. comma and V. fetus, and Brucella organisms (in conjunction with streptomycin).

The following gram negative organisms, when bacteriologic testing indicates appropriate susceptibility to the drug: E. coli, E. aerogenes, Shigella, Mima, Herellea, H. influenzae (respiratory infections), and Klebsiella infections (respiratory and urinary).

The following gram positive organisms when bacteriologic testing indicates appropriate susceptibility to the drug: anaerobic streptococci, S. pyogenes (For upper respiratory infections due to Group A beta hemolytic streptococci, penicillin is the drug of choice including prophylaxis of rheumatic fever), S. pneumoniae, and S. aureus. The frequency of resistance to tetracyclines in hemolytic streptococci is highest in strains from infections of the ear, wounds and skin. Tetracyclines should not be prescribed for acute throat infections; also, they are not the drug of choice in any staphylococcal infection.

When penicillin is contraindicated, tetracyclines are alternative drugs in the treatment of infections due to: N. gonorrhoeae, T. pallidum and T. pertenue (syphilis and yaws), L. monocytogenes, Clostridia, B. anthracis, Fusobacterium (Vincent's infection), and Actinomyces.

In acute intestinal amebiasis, the tetracyclines may be a useful adjunct to amebicides. In severe acne the tetracyclines may be useful adjunctive therapy.

Tetracyclines are indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.

Inclusion conjunctivitis may be treated with oral tetracyclines or with a combination of oral and topical agents.

Because tetracycline tends to accumulate in certain neoplastic cells and to exhibit a brilliant, yellowish gold fluorescence when exposed to ultraviolet light, it may be useful in experienced hands for the diagnosis of malignancy.

Contraindications: Hypersensitivity to any of the tetracyclines; severe renal or hepatic disease.

Pregnant or lactating women unless potential benefit to patient outweighs risk to fetus or child.

Therapy of common infections in children under 12. Any condition in which bactericidal effect is essential (bacterial endocarditis).

Avoid prophylactic administration to surgical cases, if possible.

Precautions: The use of tetracyclines during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent tooth discoloration (yellow, gray, brown). This reaction is more common during long term use of the tetracyclines, but has been observed following short term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.

Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

Tetracyclines are present in the milk of lactating women who are taking a drug in this class.

If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and, if therapy is prolonged, serum level determinations of the drug may be advisable.

The antianabolic action of the tetracycline may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired function, higher serum levels of tetracycline may lead to azotemia, hyperphosphatemia, and acidosis. Consequently, increasing levels of BUN may not accurately reflect changes in renal function; the serum creatinine will provide a more reliable index.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients should be warned to avoid exposure to direct sunlight and/or ultraviolet light while under treatment with tetracycline drugs, and treatment should be discontinued at the first evidence of skin discomfort.

Tetracyclines form a stable calcium complex in any bone forming tissue. A decrease in the fibula growth rate has been observed in prematures given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued.

Tetracycline administration may result in overgrowth of nonsusceptible organisms. Superinfections due to staphylococci and other organisms may occur during oral but rarely during parenteral administration.

C. albicans can produce effects at three levels: proliferation in the mouth can cause disturbances ranging from simple soreness to frank and extensive thrush, which may spread to the pharynx and possibly the bronchi; in the bowel, it can be manifested by diarrhea; also, pruritus ani occurs frequently.

Proteus and Pseudomonas species resistant to tetracyclines may become predominant in the bowel and diarrhea is common. Periodic microbiologic examination of materials, such as stool and sputum, during tetracycline therapy may alert one to changes in flora indicating bacteriologic superinfection in time to avert progression to clinical disease.

If superinfections are encountered, tetracyclines should be discontinued and appropriate therapy started. Superinfection of the bowel by staphylococci may be life threatening.

Adhere closely to expiration dates; ingestion of deteriorated tetracyclines has produced kidney damage corresponding clinically to the acute Fanconi syndrome (nausea, vomiting, albuminuria, glycosuria, aminoaciduria, hypophosphatemia, hypokalemia, and acidosis). Such damage is usually reversed slowly after withdrawal of the deteriorated tetracycline, although fatal reactions have been reported.

Before treating gonorrhea, a darkfield examination should be made from any lesion suggesting concurrent syphilis. Serological tests for syphilis should be made for at least 4 months afterwards.

Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage. Interference with vitamin K synthesis by microorganisms in the gut has been reported.

Concurrent use of methoxyflurane and tetracyclines has been reported to impair renal function seriously leading in some cases to death. Such use of these two drugs is therefore not recommended unless the benefits outweigh the risks.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline in conjunction with penicillin.

During long term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal and hepatic studies should be performed.

All infections due to Group A beta hemolytic streptococci should be treated for at least 10 days.

Since sensitivity reactions are more likely to occur in persons with a history of allergy, asthma, hay fever, or urticaria, the preparations should be used with caution in such individuals. Cross-sensitization among the various tetracyclines is extremely common.

When it is essential to administer any of the tetracyclines i.v., the blood level should not be permitted to exceed 15 μg/mL and, if possible, other potentially hepatotoxic drugs should be avoided. Presumably, large doses may be expected to have comparable toxicity by either the i.m. or oral route if renal or hepatic insufficiency is present.

Adverse Effects: Gastrointestinal: anorexia, epigastric distress, nausea, vomiting, diarrhea, bulky loose stools, stomatitis, sore throat, glossitis, black hairy tongue, dysphagia, hoarseness, enterocolitis, and inflammatory lesions (with candidal overgrowth) in the anogenital region, including proctitis and pruritus ani. These reactions have been caused by both the oral and parenteral administration of tetracyclines but are less frequent after parenteral use.

Skin: maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Onycholysis and discoloration of the nails have been reported rarely. Photosensitivity has occurred (see Precautions).

Renal toxicity: rise in BUN has been reported and is apparently dose related (see Precautions).

Hepatic cholestasis has been reported rarely, and is usually associated with high dosage levels of tetracycline. Hepatic toxicity, associated with pancreatitis in some cases, has been attributed to the long term use of doses larger than those recommended in patients with renal insufficiency or to the concomitant administration of other potentially hepatotoxic drugs. This serious reaction has occurred most often in pregnant or postpartum patients with pyelonephritis.

Hypersensitivity reactions: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus, and serum sickness like reactions, as fever, rash, and arthralgia. When given over prolonged periods, tetracyclines have been reported to produce brownish black microscopic discoloration of thyroid glands. No abnormalities of thyroid function studies are known to occur.

Bulging fontanels have been reported in young infants following full therapeutic dosage. This sign disappeared rapidly when the drug was discontinued.

Blood: anemia, hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, neutropenia and eosinophilia have been reported.

Dosage: Oral: Adults should receive an average daily dose of 250 mg 4 times a day. Higher dosages, such as 500 mg 4 times a day may be required for severe infections.

Antacids, containing aluminum, calcium or magnesium and iron salts impair absorption and should not be given to patients taking oral tetracyclines. Foods and some dairy products also interfere with absorption. Oral forms of tetracycline should be given 1 hour before or 2 hours after meals.

Parenteral: I.V. or I.M. administration should be employed only when the oral route is not practical.

I.M. —Add 2 mL of sterile water for injection USP (or sodium chloride injection USP) to the 250 mg vial. The resulting solution may be stored at room temperature and should not be used after 24 hours. Inject deeply, either into the gluteal region or the anterior thigh. Inadvertent injection into the s.c. or fat layers may cause mild pain and induration, which can be relieved by applying an ice pack.

Infants and children: 10 mg/kg (4.5 mg/lb.) per day in divided doses. Adults: Average dose range: 200 to 300 mg daily in divided doses or a single 250 mg vial per day. In severe infections: 100 mg every 4 to 6 hours or one 250 mg vial every 12 hours.

I.V. —The vials may be initially reconstituted by adding 10 mL of sterile water for injection to the 500 mg vial. After the solution has been prepared, it should be further diluted prior to administration to at least 100 mL (up to 1,000 mL) with any of the following diluents: sterile water for injection USP; sodium chloride injection USP; dextrose injection USP; dextrose and sodium chloride injection USP; Ringer's injection USP; Lactated Ringer's injection USP; protein hydrolysate injection; low sodium USP 5%, 5% with dextrose 5%, 5% with invert sugar 10%.

The initial reconstituted solutions are stable at room temperature for 12 hours without significant loss of potency. The final dilution for administration should be administered without delay. The use of solutions containing calcium should be avoided as these tend to form precipitates (especially in neutral to alkaline solution) and, therefore, should not be used unless necessary. However, Ringer's injection, USP and Lactated Ringer's injection USP can be used with caution since the calcium ion content in these diluents does not normally precipitate tetracycline in an acid media.

The rate of infusion should not exceed 100 mL per 5 minutes. Tetracycline i.v. infusion may precede or follow, but should not accompany, a blood transfusion. The i.v. route should not be used unless the oral route is not feasible.

Usual dose is 500 mg at 12 hour intervals which should not ordinarily be exceeded unless the physician, because of the severity of the disease, wishes to increase it to a maximum of 500 mg every 6 hours. The suggested parenteral pediatric dosage for newborn and young children is 10 to 15 mg/kg/day, given in 2 doses. Because of insufficient experience in the treatment of infants under 1 month of age, caution should be exercised in administering the drug to patients in this age group.

Topical Ointment: Apply directly to the involved area preferably on sterile gauze, one or more times daily as the condition indicates. In severe local infections, systemic therapy may become necessary as prescribed.

Ophthalmic Ointment: Apply to the infected eye every 2 hours or oftener as the condition and response indicate. Severe or stubborn infections may require oral antibiotic administration in addition to local treatment.

Supplied: Injectables: I.M.: Each vial contains: tetracycline HCl 250 mg, procaine HCl 40 mg, magnesium chloride 46.84 mg, ascorbic acid 275 mg; tartrazine-free. Available in boxes of 12 vials.

I.V.: Each vial contains: tetracycline HCl 500 mg, ascorbic acid 1,250 mg; tartrazine-free. Available in boxes of 12 vials.

Topical Ointment: Each g contains: tetracycline HCl 30 mg in a wool fat petrolatum base; tartrazine-free. Available in 30 g tubes.

Ophthalmic Ointment: Each 3.5 g tube contains: 1% tetracycline HCl in a wool fat petrolatum base; tartrazine-free.

. . . The physician should carefully weigh the anticipated therapeutic benefit from any drug against all potential adverse effects.

ACHROMYCIN® V Ⓡ *Lederle*

Tetracycline HCl *Antibiotic*

Supplied: Each blue and yellow, hard shell capsule printed "Lederle A3" and "Lederle 250 mg" contains: tetracycline HCl 250 mg. Calories: 1 per capsule. Tartrazine-free. Bottles of 500 capsules.

For prescribing information, refer to Achromycin monograph.

ACID MANTLE® *Miles*

Aluminum Acetate *Dermatitis Therapy*

Indications: To restore and maintain the protective acidity of the skin. Treatment of irritated skin due to soaps, detergents, chemicals, alkalis. Useful for the treatment of diaper rash, winter eczema, and dry, rough, scaling skin.

Precautions: Limited compatibility and stability with vitamin A, neomycin and water sensitive antibiotics.

Dosage: Prophylactically after each washing of skin surface. Therapeutically as required.

Supplied: Available in cream or lotion form: formulated with buffered aluminum acetate in a water miscible base. Acid pH. Availability: **Cream:** 30 mL tubes, 120 mL jars. **Lotion:** 110 mL squeeze bottles. Store below 30°C. Avoid freezing.

ACIDOBYL® *Desbergers*

Biles Salts-Homatropine Compound
Choleretic—Antispasmodic

Indications: Dyspepsia due to biliary deficiency. Biliary dyskinesia. Adjunct in management of infective states of gallbladder and hepatobiliary ducts.

Contraindications: Biliary tract obstruction, acute hepatitis, glaucoma, advanced renal or hepatic disease, prostatic hypertrophy, hypersensitivity to any of the components.

Precautions: Observe longterm patients periodically for signs of increased intraocular pressure.

Adverse Effects: Diarrhea, dry mouth, blurred vision and difficult urination may occur.

Overdose: Symptoms: Diarrhea, dry mouth.

Treatment: Delay absorption of ingested drug by giving water, milk or activated charcoal and then remove by gastric lavage or Ipecac Syrup USP emesis followed by catharsis. As a physiologic antidote, physostigmine may be given to reverse the central and peripheral effects of homatropine.

Dosage: 1 or 2 tablets after each meal.

Supplied: Each yellow round, biconvex, coated tablet contains: dehydrocholic acid 120 mg, bile salts 120 mg, docusate sodium 60 mg, homatropine methylbromide 500 μg. Bottles of 50 and 500 tablets.

(Shown in Product Recognition Section)

ACIDOBYL® with CASCARA *Desbergers*

Bile Salts-Homatropine-Cascara Compound
Choleretic—Laxative—Antispasmodic

Indications: Treatment of functional gastrointestinal disorders associated with hepatobiliary stasis (chronic constipation, dyspepsia).

Contraindications, Precautions, Adverse Effects: As for Acidobyl.

Overdose: Symptoms: Diarrhea, dry mouth, pigmentation of the rectal mucosa, melena.

Treatment: As for Acidobyl.

Dosage: 1 or 2 tablets after each meal.

Supplied: Each brown, round, biconvex, coated tablet contains: dehydrocholic acid 60 mg, bile salts 120 mg, casanthranol 20 mg, docusate sodium 50 mg, homatropine methylbromide 500 μg. Bottles of 50 and 500 tablets.

(Shown in Product Recognition Section)

ACIDULIN® *Lilly*

Glutamic Acid HCl *Gastric Acidifier*

Supplied: Each No. 1, pink Pulvule capsule contains: glutamic acid hydrochloride 340 mg which is equivalent to about 10 minims of Diluted Hydrochloric Acid, NF or to about 16.8 mL of 0.1 N hydrochloric acid. Bottles of 100 Pulvules.

Identi-Code: F 31.

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ACI-JEL® *Ortho*

Acetic-Boric Acid Compound
Vaginal Acidifier

Indications: In cases where the restoration and maintenance of vaginal acidity is desirable as in the treatment of nonspecific vaginal infection and in the milder forms of simple cervicitis. Also useful prophylactically after courses of more specific therapy.

Dosage: In the average case, one applicatorful intravaginally in the morning and upon retiring. In those cases where there is a tendency to vaginal discharge or leakage, a vulvar pad is recommended. The frequency of application and duration of treatment depends upon the type of case and the degree of progress.

Supplied: Jelly: Contains: acetic acid 0.92%, oxyquinoline sulfate 0.025%, ricinoleic acid 0.7%, boric acid 3% and glycerin 5%, compounded with tragacanth, acacia, propylparaben, potassium hydroxide, stannous chloride, egg albumen, potassium bitartrate, perfume and water. Available in 85 g tubes with or without applicator.

ACNAVEEN® BAR *Cooper*

Colloidal Oatmeal-Sulfur Salicylic Acid Compound *Acne Therapy*

Indications: For the treatment of acne.

Contraindications: Sensitivity to any of the components.

Precautions: If irritation or rash persists or increases, discontinue use.

Drug Interactions: None reported.

Dosage: Wet face thoroughly and massage into skin vigorously to produce lather. Allow lather to remain on skin for several minutes. Rinse thoroughly. Repeat 2 or 3 times daily or as required.

Supplied: Each 100 g bar contains: colloidal oatmeal, 2% sulfur and 2% salicylic acid, in a sudsing soap-free base containing a mild surfactant.

ACNE-AID® GEL *Stiefel*

Sulfur-Resorcinol Compound *Acne Therapy*

Indications: In acne vulgaris, and where a mild keratolytic, antiseborrheic and antimicrobial agent is required.

Contraindications: Do not apply to diffuse, acutely inflamed areas.

Precautions: Keep away from eyes and off eyelids. Should excessive dryness or irritation develop, discontinue use.

Dosage: Wash the affected part with cleanser recommended by the physician. Dry thoroughly without rubbing. Apply gel with the fingertips, allowing a thin film to remain.

Supplied: Each 15 or 50 g tube of gel contains: sulfur 2.5%; resorcinol 1.25%; chloroxylenol 0.375% with microporous cellulose in a flesh colored, gel base.

ACNE-AID® SOAP *Stiefel*

Acne Therapy

Indications: To cleanse oily skin; open clogged pores; a shampoo for the oily scalp.

Dosage: Using warm water, massage lather on affected areas, with fingers, cloth or facial brush as indicated. Rinse warm, then cold. Repeat if skin is very oily. Dry and apply medication, if any.

Supplied: Each 100 g cake consists of a hypoallergenic blend of neutral soap and surfactant.

ACNOMEL® *SK&F*

Resorcinol-Sulfur Compound *Acne Therapy*

Indications: Treatment of acne: basic topical medication for acne. The cake may be used by patients who desire a medicated preparation to mask lesions during the day and by those with sensitive skin.

Contraindications: Should not be applied to diffuse, acutely inflamed areas. Keep out of eyes and off eyelids.

Precautions: Moderate erythema and scaling are normal and expected results of therapy. However, should these reactions become excessive, the patient should apply the product less frequently or discontinue until they subside.

Pharmaceutical Compatibility: Should not be diluted or compounded with other drugs. Dispense in the original container.

Overdose: Involves the skin primarily.

Symptoms: Moderate erythema and scaling are normal and expected results of therapy. Overdosage is marked by excessive drying and erythema or by burning and itching.

Treatment: Switch the patient to one half strength Acnomel cake. In severe cases, discontinue medication and apply a bland ointment or cold cream.

Accidental ingestion: In case of accidental ingestion by children, the amount which the child succeeds in swallowing would be expected to be small, and symptoms would generally consist merely of mild gastrointestinal disturbance. Treatment consists of general measures such as inducing emesis; gastric lavage; catharsis; and forcing fluids.

Dosage: Before application, wash affected areas with soap and water, then dry.

Cake: Apply with moist sponge or finger tips, 2 or 3 times daily, as required, to treat and mask individual lesions.

Cream: Apply a thin coating with fingers. Stroke on lightly; do not rub in. One or two applications daily are usually adequate. Patients with oily skin may apply more frequently.

Supplied: Cake (Half strength): resorcinol 1%, sulfur 4%, in a washable, flesh tinted cake base. Available in 25 g plastic compacts.

Cream (Standard strength): resorcinol 2%, sulfur 8%, in a stable, greaseless, flesh tinted base. Available in 25 and 40 g tubes.

Vanishing Cream (Standard strength): resorcinol 2%, sulfur 8% in a water-washable, greaseless, vanishing cream base. Available in 25 g tubes.

ACRIFLEX® *Glaxo*

Aminacrine HCl *Topical Antiseptic*

Indications: As a first aid antiseptic application to minor superficial wounds, minor burns, cuts, abrasions, scratches and as an emollient for chapped skin, sunburn, diaper rash and minor superficial skin infections.

Supplied: A non staining cream containing: aminacrine HCl 1:1,000. Available in 30 g tubes.

ACTH

Corticotropin
Adrenocorticotropic Hormone

Indications: Diagnostic testing of adrenocortical function.

Corticotropin injections have limited therapeutic value in conditions responsive to corticosteroid therapy; however, corticosteroid therapy is considered to be the treatment of choice. Accordingly, corticotropin injections may be employed in the following disorders:

Rheumatic disorders: As adjunctive therapy for short term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, acute and subacute bursitis, acute nonspecific tenosynovitis, acute gouty arthritis.

Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus, systemic dermatomyositis (polymyositis), acute rheumatic carditis.

Dermatologic diseases: pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, severe psoriasis.

Allergic states: Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment—seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness.

Ophthalmic diseases: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as allergic conjunctivitis, keratitis, herpes zoster ophthalmicus, iritis, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia.

Respiratory diseases: symptomatic sarcoidosis, Loeffler's syndrome not manageable by other means, berylliosis.

Hematologic disorders: acquired (autoimmune) hemolytic anemia.

Neoplastic diseases: palliative management of adult leukemias and lymphomas, acute leukemia of childhood.

Edematous state: To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

Miscellaneous: tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy, trichinosis of neurologic or myocardial involvement.

Contraindications: Scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, hypertension, sensitivity to proteins of porcine origin.

Treatment of conditions listed within the "Indications" section when they are accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction.

Administration of i.v. corticotropin is contraindicated for treatment of conditions listed within the "Indications" section.

Precautions: Chronic corticotropin administration may lead to irreversible adverse effects. Corticotropin may only suppress symptoms and signs of chronic disease without altering the natural course of the disease. Do not administer corticotropin for treatment until adrenal responsiveness has been verified with the route of administration which will be utilized during treatment. A rise in urinary