

Letters to the Editor

The Journal welcomes Letters to the Editor; if found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with journal style.



Education of Medical Students

To the Editor:

The Association of American Medical Colleges has embarked on a project to appraise the status of The General Professional Education of the Physician and College Preparation for Medicine. An 18-member panel, chaired by Dr. Steven Muller, President of The Johns Hopkins University, after its first year of deliberation, has identified four concerns that will challenge faculties responsible for selecting and educating medical students:

- The rapid growth of knowledge applicable to the care of patients and the treatment of disease
- The ascendancy of complex technology and procedures in the diagnosis and treatment of patients with overt or potential disease
- The coalescence of physicians, other health professionals, and hospitals into complex systems, which is paralleled by a concentration of the financial support for medical care in government and private agencies
- The mounting evidence that physicians are having difficulty coping with the rapid progress in medical care and in adapting to demands placed upon them by their

patients and by the profession

To gather information and ideas, the panel is holding regional hearings where faculty, students, practicing physicians and other individuals interested in and concerned about medical education can express their views. The hearing schedule is:

University of Texas, Houston,
February 24-25, 1983

Northwestern University, Chicago,
March 24-25

New York Academy of Medicine,
May 5-6, 1983

For more information, contact Mary H. Littlemeyer, Project Coordinator, Association of American Medical Colleges, 1 Dupont Circle, Washington, DC 20036.

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Association of

American Medical Colleges

Washington, DC

Depression: Symptom or Syndrome?

To the Editor:

The recent response to the position taken in our letter, "Use of

Depression Inventories" (*J Fam Pract* 14:454, 1982), by Seller, Blascovich, and Lenkei (*J Fam Pract* 14:456, 1982) apparently misunderstands our main concern and perpetuates a pervasive clinical and research error in family medicine that we believe should be remedied.

We do not find fault with the use of either Beck's Depression Inventory¹ or our own² as measures of severity of depressive symptomatology. Both instruments are sound, although the short forms of both may be preferable in family medicine settings.

What Seller et al³ and other authors in family medicine have failed to recognize is the difference between depression as a symptom and depression as a syndrome or diagnosis. This lack of conceptual clarity is analagous to assuming that every patient with symptoms of pharyngitis has strep throat.

No existing depression inventory can make a diagnosis of a depressive syndrome, and Beck¹ has appropriately cautioned readers that his inventory should be used for screening purposes. It therefore can be useful in detecting patients who may fulfill the criteria for a diagnosis of depression, but it alone cannot make a diagnosis. For example, neither instrument documents the two-week duration of symptoms required in standard psychiatric diagnosis, nor do they question bizarre behavior or mood-incongruent delusions or hallucinations, both of which are key factors in differential diagnosis.

Schizophrenic patients often score very high on symptoms like social withdrawal, distortion of body image, irritability, and indecision. Beck's inventory would then indicate severe depressive symptomatology, despite the ab-

sence of a depressive syndrome. When physicians are prepared to prescribe penicillin for every sore throat, then it will be time to prescribe antidepressants for everyone scoring high on a depression inventory.

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and*

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Alcohol Education for Family Practice Residents

To the Editor:

The disease of alcoholism is an important part of the family physician's practice experience, both in the hospital and in the office. Attitudes, especially negative ones, toward the alcoholic patient cause the physician considerable difficulty in effectively treating his patients. Many studies of family physician experiences show minimal awareness of the disease of alcoholism and suggest that when alcoholics are treated by family physicians, their conditions may be significantly underdiagnosed.¹

Studies of attitude development suggest that physicians' negative attitudes toward the alcoholic and alcoholism begin early in the

medical education and generally worsen as experience with alcoholics becomes more burdensome.¹ Recognition of the disease process of alcoholism has not permeated the physician's view of this disorder. Several studies found that courses in medical school tended to hamper the physician's total view of his alcoholic patients and in fact increased negative attitudes toward alcoholics.¹⁻³ Chavetz⁴ many years ago felt that personal relationships were very important from the outset in determining the treatment potential for the alcoholic. A good interpersonal relationship and working together to deal with the problem produced the best chances for the physician to effectively treat the alcoholic. If positive relationships did not develop, no positive treatment could be developed for the alcoholic.⁴

Given this problem, a special program was developed at the Sundown M Alcoholism Treatment Center in White Swan, Washington. This program was designed not only to change attitudes of family physicians but also to have them experience a close relationship with recovering alcoholics. These physicians were given an attitude questionnaire before and after their program at Sundown to see if the program could effectively change their opinions regarding alcoholics and alcoholism.

The program consisted of four 7-hour days at Sundown M Ranch. The family physicians were expected to follow the regular treatment program during these four days and were presented with lecture topics and engaged in large and small group discussions. They were involved on a one-to-one basis with recovering alcoholics, exposed their own views, and were exposed to the views of the recovering alco-

holic. The final day of their four-day experience they were involved at the local community alcohol center, where they were exposed to outpatient education and follow-up programs with recovering alcoholics.

The results of this program showed that physicians can be well educated in the area of alcoholism. The questionnaires given before and after the experience indicated major changes in attitude. Prior to the experience the physicians believed that alcoholism was related to a personality or mental disorder; this view was changed in over 90 percent of the physicians tested. The disease concept of alcoholism was accepted, and the view that alcoholism is a moral weakness or character disorder was rejected. The belief that alcoholism is primarily a condition, affecting men and lower socioeconomic groups that has a very poor prognosis, was changed considerably. An awareness of the value of Alcoholics Anonymous also accounted for a major shift in attitude.

Sundown M's relationship with family physicians continues as a regular part of the family practice residency program. We feel this is an exciting program. It has made major changes in attitudes and education of young physicians. We would hope that this program can be instituted in other areas so that physicians can enhance their understanding of and care-giving capacity toward the alcoholic patient.

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References

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4. Chavetz ME: A procedure for establishing therapeutic contact with the alcoholic. *Q J Stud Alcohol* 22:325, 1961

Cervical Cytology

To the Editor:

In July 1981¹ we published the results of a study comparing the adequacy of cervical cytologic preparations utilizing the standard Ayre spatula and cotton-tipped applicator with a newer extended tip spatula (Surgipath Medical). In that article it was shown that the yield of endocervical cells on cervical Pap smears was significantly greater when the extended tip spatula was used by family practice residents and faculty in the Family Practice Center of the Department of Family Medicine of the University of Cincinnati College of Medicine.

In the published study only the Ayre spatula and cotton-tipped applicator or the extended tip spatula were made available to the study group of physicians. They were not aware of the study in progress, nor were they especially trained in cervical cell harvesting. The applicance used to harvest cervical cells was used because it was, at that time, the only one available. It was found that under those circumstances 58 percent of 100 Pap smears from premenopausal women prepared from the Ayre spatula and cotton swab revealed endocervical cells. The presence of endocervical cells was used as our criterion for an adequate smear. Seventy-seven percent of 54 pairs of slides in which

the extended tip spatula was used were found to have endocervical cells.

So that laboratory bias would be minimized in that study, the cytotechnologists screening the slides were not informed of the study. The chief cytotechnologist, who was involved in the study, reviewed the specially coded slides in order to verify the screening cytotechnologist interpretation. Questionable slides were further reviewed by the physician cytopathologist of the Department of Pathology. Because of the efforts to minimize use and interpretation biases, it was felt that the results obtained reflect a basic difference in the mechanical efficiency of harvesting endocervical cells by Ayre spatula and cotton swab and the extended tip spatula.

In order to further evaluate our methods and results, we continued our study of endocervical cell harvesting following the publication of our first paper on the subject. Faculty and resident colleagues in the Department of Family Medicine were apprised of the research activity and were asked to use the cervical cell harvesting appliances that they preferred to obtain gynecologic Pap smears. In the past several months we have studied 258 additional pairs of cervical Pap smears obtained from premenopausal women examined at the Family Practice Center.

One hundred pairs of slides were made with the Ayre spatula and cotton-tipped applicator and 158 from the extended tip spatula. In that group 66 percent (66/100) of the Ayre Pap smears revealed endocervical cells and again 77 percent (122/158) of the extended tip spatula slides combined endocervical cells.

In total we have studied the

cervical Pap smears from 412 premenopausal women. Overall we have obtained endocervical cells in 77 percent of the extended tip spatula examinations and 62 percent of the Ayre spatula and cotton swab examinations. We feel that these findings support the concept that a spatula which can be placed within the cervical os with its surface contiguous to the cervical canal is a highly effective instrument in obtaining endocervical cells for cytologic evaluation. It is our opinion that the extended tip of the spatula is much more likely to come into direct contact with the squamocolumnar junction than is the cotton-tipped applicator. The increased harvest of cells may well tend to have a salutary effect on decreasing the number of false-negative Pap smears now obtained using less thorough methods. In view of the current guidelines of the American Cancer Society for cervical cytology, this could well be an important factor for many women.

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and
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Reference

1. Colón VF, Linz LE: The extended tip spatula for cervical cytology. *J Fam Pract* 13: 37, 1981

Toxic Epidermal Necrolysis

To the Editor:

This letter reports the case of a 74-year-old black man with seven

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(erythromycin ethylsuccinate)

INDICATIONS: *Streptococcus pyogenes* (Group A beta hemolytic streptococcus): Upper and lower respiratory tract, skin, and soft tissue infections of mild to moderate severity.

Injectable benzathine penicillin G is considered by the American Heart Association to be the drug of choice in the treatment and prevention of streptococcal pharyngitis and in long-term prophylaxis of rheumatic fever.

When oral medication is preferred for treatment of the above conditions, penicillin G, V, or erythromycin are alternate drugs of choice.

When oral medication is given, the importance of strict adherence by the patient to the prescribed dosage regimen must be stressed. A therapeutic dose should be administered for at least 10 days.

Alpha-hemolytic streptococci (viridans group): Although no controlled clinical efficacy trials have been conducted, oral erythromycin has been suggested by the American Heart Association and American Dental Association for use in a regimen for prophylaxis against bacterial endocarditis in patients hypersensitive to penicillin who have congenital heart disease, or rheumatic or other acquired valvular heart disease when they undergo dental procedures and surgical procedures of the upper respiratory tract. Erythromycin is not suitable prior to genitourinary or gastrointestinal tract surgery. **NOTE:** When selecting antibiotics for the prevention of bacterial endocarditis the physician or dentist should read the full joint statement of the American Heart Association and the American Dental Association.

Staphylococcus aureus: Acute infections of skin and soft tissue of mild to moderate severity. Resistant organisms may emerge during treatment.

Streptococcus pneumoniae (Diplococcus pneumoniae): Upper respiratory tract infections (e.g., otitis media, pharyngitis) and lower respiratory tract infections (e.g., pneumonia) of mild to moderate degree.

Mycoplasma pneumoniae (Eaton agent, PPO): For respiratory infections due to this organism.

Hemophilus influenzae: For upper respiratory tract infections of mild to moderate severity when used concomitantly with adequate doses of sulfonamides. (See sulfonamide labeling for appropriate prescribing information). The concomitant use of the sulfonamides is necessary since not all strains of *Hemophilus influenzae* are susceptible to erythromycin at the concentrations of the antibiotic achieved with usual therapeutic doses.

Treponema pallidum: Erythromycin is an alternate choice of treatment for primary syphilis in patients allergic to the penicillins. In treatment of primary syphilis, spinal fluid examinations should be done before treatment and as part of follow-up after therapy. **Corynebacterium diphtheriae:** As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

Corynebacterium minutissimum: For the treatment of erythrasma.

Entamoeba histolytica: In the treatment of intestinal amebiasis only. Extraenteric amebiasis requires treatment with other agents.

Listeria monocytogenes: Infections due to this organism.

Bordetella pertussis: Erythromycin is effective in eliminating the organism from the nasopharynx of infected individuals, rendering them non-infectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

Legionnaires' Disease: 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.

CONTRAINDICATIONS: Erythromycin is contraindicated in patients with known hypersensitivity to this antibiotic.

PRECAUTIONS: Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. There have been reports of hepatic dysfunction, with or without jaundice occurring in patients receiving oral erythromycin products.

Areas of localized infection may require surgical drainage in addition to antibiotic therapy.

Recent data from studies of erythromycin reveal that its use in patients who are receiving high doses of theophylline may be associated with an increase of 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.

Usage during pregnancy and lactation: The safety of erythromycin for use during pregnancy has not been established.

Erythromycin crosses the placental barrier. Erythromycin also appears in breast milk.

ADVERSE REACTIONS: The most frequent side effects of erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses.

During prolonged or repeated therapy, there is a possibility of overgrowth of nonsusceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted.

Allergic reactions ranging from urticaria and mild skin eruptions to anaphylaxis have occurred.

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



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recurrences of toxic epidermal necrolysis. *Episode 1* (1947): Without any known exposure to drugs or chemicals, the patient developed a swollen face and sloughed his skin within two days. *Episode 2* (1965): An upper respiratory tract infection was treated with penicillin. Denuded areas appeared on both upper extremities. Oral corticosteroids helped to achieve complete recovery. *Episode 3* (1967): Self-treatment with penicillin and aspirin for a toothache resulted in intense pruritus and multiple bullae with denuded areas. A skin biopsy showed full thickness epidermal necrolysis with underlying early epidermal regeneration. *Episode 4* (1970): The day following a left cataract extraction, multiple bullae appeared, and topical steroids were given with slow improvement. *Episode 5* (1971): The postoperative course to a right cataract extraction was marked by widespread, multiple vesicles with resulting denuded areas. Topical steroids were used with slow healing. *Episode 6* (1973): Within one day after a temporal artery biopsy, an intensely pruritic, diffuse papular eruption appeared with areas of sloughing. Oral steroids were used. In 1974, oral steroids were given before a traumatized right eye was repaired, and only mild pruritus developed. *Episode 7* (1977): The day after a bilateral orchiectomy was performed because of prostatic carcinoma, extensive sloughing appeared. A skin biopsy showed extensive epidermal necrosis; pemphigus antibody was negative. Oral prednisone was tapered as healing progressed.

In a review of the English medical literature,¹⁻⁹ only one other patient survived seven recurrences.⁷

In Rowell and Thompson's 1961 review of 27 patients, 6 had had recurrences.⁸ However, no multiple recurrences were cited. The high recurrence rate is unusual in that 25 to 50 percent of patients succumb to the initial episode. A careful analysis of the drugs given perioperatively (episodes 4-7) indicate that barbiturates were the most consistently given drug. Barbiturates have long been known to produce toxic epidermal necrolysis.⁹

The most important lesson to draw from these events is the importance of old records. Every resident, intern, and practicing physician dreads the thought of reviewing the records of a multi-problem patient during the course of the initial workup. In 1974 preoperative steroids and careful attention to all drugs given thwarted the manifestation of toxic epidermal necrolysis. Analysis of the patient's old records alerted the staff physicians. How many times has the careful review, albeit tedious, of old records revealed an important, interesting finding that had direct bearing on the outcome of the current problems!

Eric S. Miller, MD
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Pediazole[®]

erythromycin ethylsuccinate
and sulfisoxazole acetyl
for oral suspension

BRIEF SUMMARY:
Please see package enclosure for full prescribing information.

Indication
Treatment of ACUTE OTITIS MEDIA in children caused by susceptible strains of *Hemophilus influenzae*.

Contraindications
Known hypersensitivity to either erythromycin or sulfonamides.
Infants less than 2 months of age.

Pregnancy at term and during the nursing period, because sulfonamides pass into the placental circulation and are excreted in human breast milk and may cause kernicterus in the infant.

Warnings
Usage in Pregnancy (SEE ALSO: CONTRAINDICATIONS): The safe use of erythromycin or sulfonamides in pregnancy has not been established. The teratogenic potential of most sulfonamides has not been thoroughly investigated in either animals or humans. However, a significant increase in the incidence of cleft palate and other bony abnormalities of offspring has been observed when certain sulfonamides of the short, intermediate and long-acting types were given to pregnant rats and mice at high oral doses (7 to 25 times the human therapeutic dose).

Reports of deaths have been associated with sulfonamide administration from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. The presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts should be done frequently in patients receiving sulfonamides.

The frequency of renal complications is considerably lower in patients receiving the most soluble sulfonamides such as sulfisoxazole. Urinalysis with careful microscopic examination should be obtained frequently in patients receiving sulfonamides.

Precautions
Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. There have been reports of hepatic dysfunction, with or without jaundice occurring in patients receiving oral erythromycin products.

Recent data from studies of erythromycin reveal that its use in patients who are receiving high doses of theophylline may be associated with an increase of 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.

Surgical procedures should be performed when indicated.
Sulfonamide therapy should be given with caution to patients with impaired renal or hepatic function and in those patients with a history of severe allergy or bronchial asthma. In the presence of a deficiency in the enzyme glucose-6-phosphate dehydrogenase, hemolysis may occur. This reaction is frequently dose-related. Adequate fluid intake must be maintained in order to prevent crystalluria and renal stone formation.

Adverse Reactions
The most frequent side effects of oral erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose-related. Nausea, vomiting and diarrhea occur infrequently with usual oral doses. During prolonged or repeated therapy, there is a possibility of overgrowth of nonsusceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted. The overall incidence of these latter side effects reported for the combined administration of erythromycin and a sulfonamide is comparable to those observed in patients given erythromycin alone. Mild allergic reactions such as urticaria and other skin rashes have occurred. Serious allergic reactions, including anaphylaxis, have been reported with erythromycin.

The following untoward effects have been associated with the use of sulfonamides:

Blood dyscrasias: Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprotrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme (Stevens-Johnson syndrome), generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis.

Gastrointestinal reactions: Nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis.

CNS reactions: Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia.

Miscellaneous reactions: Drug fever, chills and toxic nephrosis with oliguria or anuria. Periarteritis nodosa and L.E. phenomenon have occurred.

The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Goiter production, diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents.

Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

Dosage and Administration
PEDIAZOLE SHOULD NOT BE ADMINISTERED TO INFANTS UNDER 2 MONTHS OF AGE BECAUSE OF CONTRAINDICATIONS OF SYSTEMIC SULFONAMIDES IN THIS AGE GROUP.

For Acute Otitis Media in Children: The dose of Pediazole can be calculated based on the erythromycin component (50 mg/kg/day) or the sulfisoxazole component (150 mg/kg/day to a maximum of 6 g/day). Pediazole should be administered in equally divided doses four times a day for 10 days. It may be administered without regard to meals.

The following approximate dosage schedule is recommended for using Pediazole:

Children: Two months of age or older.	
Weight	Dose—every 6 hours
Less than 8 kg	Adjust dosage by
(less than 18 lb)	body weight
8 kg (18 lb)	½ teaspoonful (2.5 ml)
12 kg (26 lb)	1 teaspoonful (5 ml)
16 kg (35 lb)	1½ teaspoonfuls (7.5 ml)
24 kg (53 lb)	2 teaspoonfuls (10 ml)
Over 45 kg (over 100 lb)	

How Supplied
Pediazole Suspension is available for teaspoon dosage in 100-ml (NDC 0074-8030-13), 150-ml (NDC 0074-8030-43) and 200-ml (NDC 0074-8030-53) bottles, in the form of granules to be reconstituted with water. The suspension provides erythromycin ethylsuccinate equivalent to 200 mg erythromycin activity and sulfisoxazole acetyl equivalent to 600 mg sulfisoxazole per teaspoonful (5 ml).

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Diuretic Induced Hypokalemia To the Editor:

The article by Robert P. Navarro et al, "Diuretic Induced Hypokalemia in the Elderly," which appeared in the April 1982 issue (*J Fam Pract* 14:685, 1982) appears to have a major design flaw in the study that invalidates the results. The study was a retrospective chart audit of patients on four diuretics—hydrochlorothiazide, hydrochlorothiazide-triamterene, furosemide, and chlorthalidone. The study found that the potassium level did not fall below 3.0 regardless of the diuretic used and that none of the patients became symptomatic. Therefore, it was concluded that no clinical significance exists among the four diuretics in regard to production of hypokalemia.

The possible flaw in the design of the study was to apparently exclude all patients from the study who were on potassium supplements. Since all patients in the study had at least one potassium level determined, it is safe to assume that those who did develop low potassium were placed on supplements, whereas those who

did not significantly drop their potassium levels were not. This study appears to look only at the latter. If this is correct, the only conclusion that can be reached from the study is that elderly patients on diuretic therapy who do not significantly decrease their potassium levels, regardless of the diuretic, do not need potassium supplements.

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The preceding letter was referred to Dr. Navarro, who responds as follows:

I appreciate Dr. Milhorn's interest in our paper. However, I do not believe the possible flaw he suggests regarding study bias occurred. I apologize for the lack of clarity in the original article regarding data collection. It is true that the data was collected retrospectively. However, each patient was followed prospectively; that is, regardless of when the diuretic was started, all patients were followed from that day forward (assuming potassium supplementation was not started prophylactically prior to checking the serum potassium). If patients were eventually given potassium supplementation, they could have been included in the study prior to supplementation, and the potassium value (responsible for the institution of supplementation) would have been reported in the study.

In summary, we began collecting data on patients from the day di-

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ACTIFED-C[®] EXPECTORANT C[®]

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

"Lacking substantial evidence of effectiveness as a fixed combination" for the symptomatic relief of cough in conditions such as: the common cold, acute bronchitis, allergic asthma, bronchiolitis, croup, emphysema, tracheobronchitis.

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

CONTRAINDICATIONS:

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

Use in Nursing Mothers: Because of the higher risk of antihistamines, codeine and sympathomimetic amines for infants generally and for newborn and premature in particular, Actifed-C Expectorant therapy is contraindicated in nursing mothers.

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

Actifed-C Expectorant is also contraindicated in the following conditions:

Hypersensitivity to: 1) triprolidine hydrochloride and other antihistamines of similar chemical structure; 2) sympathomimetic amines including pseudoephedrine; and/or 3) any of the other ingredients.

Monoamine oxidase inhibitor therapy (see Drug Interactions Section).

WARNINGS: Actifed-C Expectorant should be used with considerable caution in patients with:

Increased intraocular pressure (Narrow angle glaucoma)	Hypertension
Stenosing peptic ulcer	Diabetes mellitus
Pyloroduodenal obstruction	Ischemic heart disease
Symptomatic prostatic hypertrophy	Hyperthyroidism
Bladder neck obstruction	

Sympathomimetics may produce central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

Codeine can produce drug dependence of the morphine type, and therefore has the potential of being abused.

Use in Children: As in adults, the combination of an antihistamine and sympathomimetic amine can elicit either mild stimulation or mild sedation in children.

While it is difficult to predict the result of an *overdosage* of a combination of triprolidine, pseudoephedrine, and codeine the following is known about the individual components:

In infants and children especially, antihistamine in overdosage may cause hallucination, convulsion or death. Large doses of pseudoephedrine are known to cause weakness, lightheadedness, nausea and/or vomiting. An overdosage of codeine may cause CNS depression with muscular twitching and convulsion, weakness, disturbed vision, dyspnea, respiratory depression, collapse and coma.

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

Use with CNS Depressants: Triprolidine and codeine phosphate have additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.)

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

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation and hypotension in elderly patients. Overdosages of sympathomimetics in this age group may cause hallucinations, convulsions, CNS depression, and death.

PRECAUTIONS: Actifed-C Expectorant should be used with caution in patients with: history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension.

DRUG INTERACTIONS: MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines and overall effects of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects of methyldopa, decamylamine, reserpine, and veratrum alkaloids.


The CNS depressant effect of triprolidine hydrochloride and codeine phosphate may be additive with that of other CNS depressants.

ADVERSE REACTIONS:

- General:** Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and throat.
- Cardiovascular System:** Hypotension, headache, palpitations, tachycardia, extrasystoles.
- Hematologic System:** Hemolytic anemia, thrombocytopenia, agranulocytosis.
- 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, hallucination.
- G.I. System:** Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.
- G.U. System:** Urinary frequency, difficult urination, urinary retention, early menses.
- Respiratory System:** Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

NOTE: Guaifenesin has been shown to produce a color interference with certain clinical laboratory determinations of 5-hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).

HOW SUPPLIED: Bottles of 1 pint, 1 gallon and 4 oz Unit of Use Bottle with Child Resistant Cap.

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

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retic therapy was started by reviewing chart notes and laboratory reports. Some subjects eventually received supplementation. However, they were included in the study if they had potassium values reported prior to receiving supplementation. Therefore, we believe patients who eventually developed "low" serum potassium were not selected out.

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To the Editor:

I very much enjoyed the article by Robert P. Navarro et al, "Diuretic Induced Hypokalemia in the Elderly" (*J Fam Pract* 14:685, 1982). There are several references that might be included in future work dealing with this area. Those presenting with ischemic heart disease or ventricular dysrhythmias may be a unique population deserving further study. Solomon and Cole noted an increased incidence of ventricular dysrhythmias in acute myocardial infarction patients whose plasma potassium levels were between 3.1 and 3.5 mEq/L.¹ This increased frequency of ventricular dysrhythmias was corroborated in another group of patients who did not have organic heart disease.²

Further work in this area might profitably focus on morbidity outcomes in elderly patients with plasma potassium values in this range.

Was this study designed to utilize serum, as opposed to plasma, potassium? As a medical technologist, I was taught that potassium is released from leukocytes and platelets during the process of clotting and retraction. Therefore plasma

potassium is more stable and reproducible.

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References

- Solomon RJ, Cole AG: Importance of potassium in patients with acute myocardial infarction. *Acta Med Scand Suppl* 647:87, 1981
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Subclavian Lines and Venous Thrombosis

To the Editor:

In a recent article on subclavian lines (*Placement of subclavian lines. J Fam Pract* 12:543, 1981), Dr. Duane S. Bietz indicated that venous thrombosis could occur after long-term usage. We have recently had a patient with subclavian vein thrombosis that developed after only 48 hours of placement.

The patient was a 52-year-old male alcoholic who experienced a gastrointestinal bleed. He had a subclavian line placement without difficulty and was discharged 72 hours after admission. He was later readmitted because of swelling of his right upper extremity. Contrast venogram revealed thrombosis of the vessels leading to the subclavian vein and multiple collaterals.

The patient was treated with anticoagulation and elevation with total resolution of his problem. Subclavian vein catheterization for diagnosis and therapy carries with it the complication of thrombosis.

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

Indications: Management of anxiety disorders, or short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not as sole therapy).

The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

The clearance of Valium and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Anxiety disorders, symptoms of anxiety, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

How Supplied: For oral administration, Valium scored tablets—2 mg, white; 5 mg, yellow; 10 mg, blue—bottles of 100* and 500.* Prescription Paks of 50, available in trays of 10.* Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25¹ and in boxes containing 10 strips of 10.¹

*Supplied by Roche Products Inc., Manati, Puerto Rico 00701

¹Supplied by Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, New Jersey 07110

- References:** 1. Tallman JF *et al:* *Science* 207:274-281, Jan 18, 1980. 2. Bunney WE Jr: *Psychiatr Ann* 11:11-15, Jan 1981. 3. Davis JM *et al:* *J Clin Psychiatry* 42(11) Sec 2:4-14, Nov 1981. 4. Study RE, Barker JL: *JAMA* 247: 2147-2151, Apr 16, 1982. 5. Braestrup C, Nielsen M, Olsen CE: *Proc Natl Acad Sci USA* 77:2288-2292, Apr 1980. 6. Bosmann HB, Case KR, DiStefano P: *FEBS Lett* 82:368-372, Oct 1977. 7. Braestrup C, Albrechtsen R, Squires RF: *Nature* 269:702-704, Oct 20, 1977. 8. Snyder SH: *Psychosomatics* 22:986-989, Nov 1981. 9. Rickels K: *J Clin Psychiatry* 42(11) Sec 2:40-44, Nov 1981. 10. Haefely WE: *Br J Psychiatry* 133:231-238, Sep 1978.

This accounts for only 2 to 3 percent of all deep vein thromboses, but prevalence may be increasing because of increasing utilization of the procedure.

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Choice of Sterilization Procedure

To the Editor:

The article "The Choice of Sterilization Procedure Among Married Couples" by Markham and Frankel in the January 1982 issue (*J Fam Pract* 14:27, 1982) was quite interesting; however, there was an absence of data that would have enhanced its usefulness and perhaps altered the results and conclusions.

The sample analyzed was limited to the 86 patients (29 vasectomy and 57 tubal ligation) who returned questionnaires handed out to all patients for the two procedures. No analysis was made, however, of the patients who did not return the questionnaires. In the absence of this data, primarily demographic, one is left with an unanswered question: Are young, white, well-educated, moderately affluent, maritally stable patients most likely to return questionnaires? Although this is factitious, it does serve to make one question the validity and applicability of the conclusions beyond the small sample analyzed.

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