

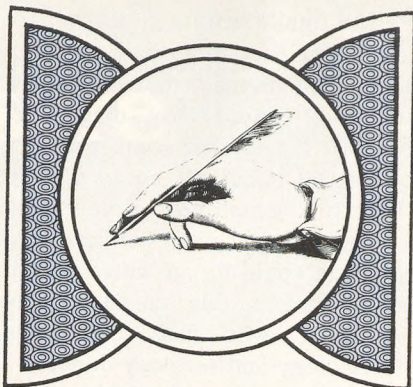
Letters to the Editor

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.

Diagnostic Tests for Infectious Mononucleosis

To the Editor:

The authors of "The Efficiency and Cost Effectiveness of Diagnostic Tests for Infectious Mononucleosis" (*English EC*,



Geyman JP. J Fam Pract 6:977, 1978) are to be complimented on their effort to determine the best approach to a problem commonly encountered in family practice. However, their findings and conclusions bring up several questions.

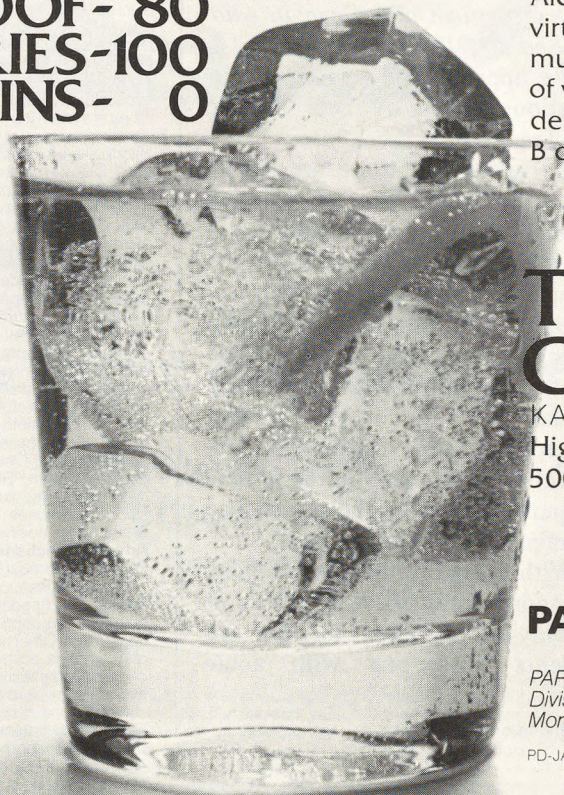
The first of these concerns the comparability of the two practice

populations studied. If the proportion of respiratory illness with adenopathy due to infectious mononucleosis was indeed higher in the student population as the article suggests, this could explain some or all of the increased "efficiency" and increased cost effectiveness ascribed by the authors to diagnostic Method II.

The second question concerns the method of calculation of the cost per positive test. The authors present no evidence that the WBC, differential, and smear done on the patients in Group I were intended to contribute in any way to the diagnosis of infectious mononucleosis. It would seem reasonable to consider the cost of the Monospot alone for patients in this group. If

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this is done, the cost per positive becomes \$107 for diagnostic Method I.

In studies of the cost effectiveness of screening tests, it is customary to consider the costs of the negative screening tests as well as those of the positives.¹ To do this for diagnostic Group II one would have to calculate the cost of WBCs, differentials, and blood smears on patients who were suspected clinically of having infectious mononucleosis but did not meet the hematologic criteria. Since the authors do not state the total number of patients screened by diagnostic Method II to yield 1,969 patients who meet the hematologic criteria, it is impossible to do precise calculations. However, a rough estimate of the size of this group is possible if one assumes that the incidence of infectious mononucleosis in the two populations is similar. Of patients in the first group who had clinically suspected infectious mononucleosis, 5.6 percent had a positive serological test. If this percent is applied to the second patient population one would need 9,875 patients with clinically suspected infectious mononucleosis in order to get 553 positive serological tests. Since only 1,969 patients met the hematologic criteria, this means that approximately 7,906 patients had a WBC, differential, and smear but did not go on to have a "monoscreen." If the cost of these additional 7,906 tests are added to the calculations, the cost per positive serological test for diagnostic Method II becomes \$202 compared with \$107 per positive test if the Monospot were done by itself on the patients in Group I who were suspected of having mononucleosis on clinical grounds.

The final question concerns the possibility that some patients who have infectious mononucleosis might be missed by diagnostic Method II, ie, that some patients who have infectious mono do not meet the hematologic criteria set down in the article. Perhaps this question could be answered by an analysis of the data on patients in Group I who had both the hematology and serology done.

Lorne A. Becker, MD

Donald F. Treat, MD

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Reference

1. Neuhauser D, Lewicki AM: What do we gain from the sixth stool guaiac? *N Engl J Med* 293:226, 1975

The preceding letter was referred to Drs. English and Geyman who respond as follows:

We appreciate the interest and questions raised by Drs. Becker and Treat.

We agree that there are differences in the two populations studied. A difference in prevalence of infectious mononucleosis as compared to diseases which resemble it would affect the efficiency of diagnosis. However, the most important factor, age, was similar in the two groups. Moreover, the diagnostic approaches discussed in the article are not affected by the prevalence of infectious mononucleosis.

With regard to the second question concerning the calculation of costs, the premise is that all patients presenting with acute

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Brief Summary

Indication: Hypertension. (See box warning.)
Contraindications: Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

Warnings:

These fixed combination drugs are not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton or Demi-Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adrenergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. If use of the drug is essential, the patient should stop nursing. **Precautions:** Antihypertensive therapy with these drugs should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with these agents two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** These drugs are generally well tolerated. The most frequent adverse reactions are anorexia, nausea, vomiting, gastric irritation, diarrhea, constipation, headache, dizziness, weakness, muscle cramps, nasal congestion, drowsiness and mental depression. Other potential side effects include skin rash, urticaria, ecchymosis; hyperglycemia and glycosuria (diabetics should be checked regularly), hyperuricemia and acute gout, and impotence. With chlorthalidone: restlessness, transient myopia; dysuria, orthostatic hypotension (may be potentiated by alcohol, barbiturates or narcotics), rare idiosyncratic reactions such as aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, purpura, necrotizing angitis and Lyell's syndrome (toxic epidermal necrolysis); pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged

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pharyngitis and adenopathy require a WBC and differential as part of their data base. If this is so, the cost of negative screening becomes irrelevant.

Concerning the adequacy of the hematologic screen and possibility of missing patients with infectious mononucleosis using Method II, we have been impressed by the lack of documentation of the validity of hematologic criteria which are generally used. A prospective study is underway using Epstein-Barr serology as well as agglutination tests to evaluate these hematologic criteria.

Eugenia C. English, MD

John P. Geyman, MD

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Seattle*

To the Editor:

I read with interest the article on serologic testing for infectious mononucleosis by Drs. English and Geyman in the May issue (*The efficiency and cost effectiveness of diagnostic tests for infectious mononucleosis. J Fam Pract 6:977, 1978*). While the article makes the important point that money is wasted in indiscriminate testing for mono, there are several problems with the paper.

The authors claim that hematologic preselection of patients for serologic study leads to a "five-fold increase in degree of accuracy of diagnosis." Unfortunately no data are presented to support this contention. To assess accuracy, one must rigidly define the disease being identified and determine with alternative measures the false positive, false negative, and reproducibility rates of the test under evaluation. What the authors

have in fact reported is a fivefold increase in the yield of serologic studies by preselection, a much different matter.

A terminology problem exists in dealing with infectious mononucleosis: since the work of Henle and co-workers, it has been known that the Epstein-Barr virus is the usual pathogen; some authors (English and Geyman apparently among them) have begun using the term "infectious mononucleosis" as a synonym for "Primary E-B virus infection," while others continue to use it as the name of a clinical syndrome (thus the existence of the term "heterophile-negative infectious mononucleosis" for the same syndrome when caused by CMV, Toxoplasma or hepatitis viruses). A clear statement of definition should be made early in any discussion of this sort.

Table 2 purports to show "Efficiency of Diagnosis." As in accuracy, one cannot know efficiency unless one knows the number of diagnoses missed by the method under study; such data are not presented. Some insight into this problem could be had by retrospective review of leukocyte counts and lymphocyte morphology in the patients evaluated by Method I. If virtually all of the positive heterophile titers were found in patients who would also have been selected for study by Method II, some support for claims of enhanced efficiency could be had. As the study stands, for all the reader knows the increased yield has been purchased with a large number of missed positives.

The real message of this paper is simple and useful: The more it looks like classical infectious mononucleosis, the more likely a case is to have positive mono

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DESCRIPTION Each yellow, scored tablet contains 4.50 mg. oxycodone HCl (WARNING: May be habit forming), 0.38 mg. oxycodone terephthalate (WARNING: May be habit forming), 224 mg. aspirin, 160 mg. phenacetin, and 32 mg. caffeine.

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCODAN®, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCODAN® is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCODAN® should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCODAN® may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCODAN® should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCODAN® should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or coagulation abnormalities.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

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Special risk patients PERCODAN® should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCODAN® may be additive with that of other CNS depressants. See WARNINGS.

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LETTERS TO THE EDITOR

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INDICATION: FASTIN is indicated in the management of exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate-to-severe hypertension, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states.

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

FASTIN may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: FASTIN is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of FASTIN should be kept in mind when evaluating the desirability of including a drug as part of weight-reduction program. Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Use of FASTIN by women who are or who may become pregnant, and those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: FASTIN is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing FASTIN for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of FASTIN and the concomitant dietary regimen.

FASTIN may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure. *Central Nervous System:* Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria. *Endocrine:* Impotence, changes in libido.

DOSAGE AND ADMINISTRATION: *Exogenous Obesity:* One capsule at approximately 2 hours after breakfast for appetite control. Late evening medication should be avoided because of the possibility of resulting insomnia.

Administration of one capsule (30 mg) daily has been found to be adequate in depression of the appetite for twelve to fourteen hours. FASTIN is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage with phentermine include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute phentermine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard. Acidification of the urine increases phentermine excretion. Intravenous phentolamine (REGITINE) has been suggested for possible acute, severe hypertension, if this complicates phentermine overdose.

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serology; indiscriminate serological testing probably wastes money. It is unfortunate that the authors did not report data to support the claim of increased diagnostic efficiency; that claim is probably true, and would add meaning to the enhanced cost effectiveness of Method II, if it were demonstrated.

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The preceding letter was referred to Drs. English and Geyman who respond as follows:

We thank Dr. Dale E. Hammerschmidt for his comments.

The point made that the evaluation reported is one of diagnostic yield rather than accuracy is well taken.

The definition of infectious mononucleosis seems quite clearly an Epstein-Barr infection as compared to the multiple etiologies of the clinical syndrome. The difficulty at the clinical level is the lack of availability and the cost of the more definitive viral tests. Because of this, we believe there is a need for further attention to optimizing and evaluating screening criteria, of which this study represents a first step.

Eugenia C. English, MD
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Orientation of Family Practice Residents

To the Editor:

I greatly appreciated reading Dr. John Dunn's article, "The First Month in Family Practice Resi-

dency Training," in the May 1978 issue of *The Journal of Family Practice* (6:1105, 1978). I believe that this should be required reading for all residency program directors and teachers in family medicine.

Dr. Dunn and the Air Force members at Scott Air Force Base have developed a program of training which should be widely copied. The idea of assigning to the resident during the first month of his residency families that he might follow through training is most commendable and gives a resident an opportunity to fulfill his/her role as "family doctor."

It has also been my experience in teaching at other locations that we often throw our resident into a very difficult service during his first month of residency, thereby causing feelings of inadequacy. He has not been properly introduced to the concepts of family practice or the model unit. Then, during his residency, the model unit becomes a foreign place to him and is a cause of discontent.

I do not feel that we should automatically expect a first year family practice resident to understand family practice and his role as family physician. As he struggles with the other subspecialists during his training program, he has a feeling of inadequacy and does not have the proper basis for refuting arguments toward subspecialization.

Again, I would recommend that family practice teachers communicate personally with Dr. Dunn concerning his approach as it is a most practical way of instructing family practice residents.

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