

Is Routine Influenza Immunization Indicated for People Over 65 Years of Age?

An Affirmative View

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The history of influenza is recorded in dramatic descriptions covering many centuries. Influenza epidemics arose explosively in a population and spread rapidly and widely over large geographical areas.¹ The comment has been made repeatedly in the literature that many became sick but few died, except the old and the infirm.

In recent years, numerous studies have examined the impact of influenza. This impact includes activity restriction,² excess emergency room utilization and absenteeism,³ hospitalizations, and mortality during an epidemic.⁴

The question of whether an attempt should be made to prevent or attenuate this illness in the elderly population in the environment of changing viruses needs to be answered affirmatively. Influenza usually begins with a sudden onset of fever, severe aching, pharyngitis, and cough. Its course is usually self-limiting to three or four days. Is the disease, however, always self-limiting in the elderly? This paper will examine influenza, its effects on the geriatric population, the case for immunization, and the current recommendations for immunization in the elderly.

INFLUENZA'S ONGOING CHANGE

Influenza is known to be transmitted by the respiratory route and characteristically spreads with unusual rapidity, commonly in an epidemic form. Influenza viruses are large ribonucleic acid (RNA) viruses belonging to the myxovirus group. Three major immunologically distinct groups exist among influenza viruses—influenza A, B, and C, as described by Horsfall et al in 1940.⁵ Influenza A and B are encountered most frequently and are the best

studied. On the basis of their hemagglutinative specificities, four major subgroups have been identified within the group A influenza viruses: influenza A swine, influenza A, influenza A1, and influenza A2. Minor antigenic variants of these prevalent types are frequently identified.

Excess mortality accompanies type A influenza outbreaks more commonly than B.^{6,7} This phenomenon is true for two reasons.⁸ First, type A appears to cause a more severe disease than type B in terms of associated symptoms and activity restriction, thus making a secondary bacterial infection more likely. The second reason is the age distribution. Type B occurs principally in the school-age group, and type A occurs in the older population, a group more at risk for lethal outcome.

The picture of influenza that emerges from epidemiologic studies is one of virtually continuous, minor antigenic drifting, punctuated approximately every 10 to 15 years by the appearance of a major antigenic variant against which the population has little or no protection.⁹ Minor changes or drifts can usually be planned for by including existing circulating strains as well as newer circulating wild strains in the influenza vaccine.

Major viral shifts did occur in the Great Pandemic of 1918, the Asian flu epidemic of 1957, and the Hong Kong flu epidemic of 1968. Because immunization with one of the type A subgroups provides little or no protection against heterologous subgroups, immunization with earlier A2 antigens, such as the A2/Japan/170/62 strain, provided little or no protection against the A2/Hong Kong/68 variant. It is apparent, therefore, that the inherent problem of antigenic variation is a critical consideration in the use of influenza vaccines.

Seventy-six countries now participate in the influenza surveillance program, and about 60 regularly send virus isolates to assist in identifying circulating strains. China, where many of the new virus subtypes are thought to arise, is one of the newer participating countries. The decision of what strains to include in the vaccine are made in late February of each year. The manufacturing process of the vaccine then takes approximately six months.¹⁰

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EFFECTS OF INFLUENZA IN THE ELDERLY

Barker and Mullooly¹¹ studied the impact of epidemic type A influenza during two periods of epidemic influenza (1968-1969 and 1972-1973), and 1970-1971 was studied as a nonepidemic reference year. The research population was the Kaiser-Permanente Health Care Program of Oregon, which represents 215,000 persons (approximately 15 to 20 percent of the metropolitan Portland population). The researchers found excess rates of hospitalizations of 150 to 172 per 100,000 persons without high-risk preexisting conditions and 476 to 636 per 100,000 with high-risk conditions in patients aged over 65 years.

A follow-up study on the same population focused on 39 deaths during the two epidemics.¹² This study revealed that more than 90 percent of the patients who died had underlying chronic conditions and that 67 percent were aged 65 years and over. Four persons who died during the 1968 epidemic had received influenza vaccine, but they had received H2N2 killed antigen, which was not protective against the H3N2 virus that became epidemic in Portland in 1968.

Although Frame¹³ stated that in the Barker and Mullooly study low-risk persons aged 65 years and over did not demonstrate a statistically significant decrease in deaths, a review of the Barker and Mullooly study¹⁴ itself does reveal that there were a total of four deaths in the unvaccinated, low-risk group as opposed to no deaths in the vaccinated, low-risk group. Also, there were no hospitalizations in the vaccinated, low-risk group for the 1972-1973 epidemic. Because of the small sample size, the low power prevented statistical significance from being obtained.

Frame did state that high-risk patients aged over 65 years did have a statistically significant decrease in deaths. On review of the definition for high risk in this study, the patient needed to have been seen only one or more times in the 12-month period prior to each study period for treatment of a high-risk condition, according to the Seventh Revision of the International Classification of Diseases, Adapted (ICDA).¹⁵ These conditions consisted of a large variety of cardiovascular, pulmonary, metabolic, and other diseases, which included illnesses such as hypertension and chronic bronchitis. The mean number of visits for high-risk patients in any year was only 1.3 to 1.4 per patient.

A study of the 38 pneumonia- and influenza-associated deaths in these two epidemics established a twofold to threefold excess in pneumonia- and influenza-associated mortality when compared with the nonepidemic years between 1969 and 1972.¹² More than one half of the deaths were attributed to the underlying chronic conditions, particularly cardiovascular disease, but 30 (79 percent) of these cases had prodromal illness characterized

by upper respiratory tract symptoms, fever, or both. The authors concluded that one half to two thirds of these deaths may have been prevented by providing influenza vaccination to all those persons at high risk.

ESTIMATED COSTS

Utilizing data from the National Hospital Discharge Survey (NHDS) of all influenza A epidemics from 1970 to 1978, excess hospitalization rates for persons aged 65 years and over were computed to be 370 per 100,000 persons.¹⁶ The age group of 65 years and over accounted for over 50 percent of the excess hospitalizations. There was a \$300,395,750 cost estimated for their care. The lack of a compensatory decreased rate of hospitalization during the postepidemic second quarter of the year indicated that the excess hospitalizations reported during the epidemics represented a true net increase.

REACTIONS TO INFLUENZA VACCINE

Reactions to influenza vaccine are most commonly limited to soreness, redness, and swelling at the vaccination site.¹⁷ In addition, there may be a fever, which is felt to be dose-related to the killed influenza virus, and, less often, headache. In recent years manufacturers have been able to reduce the amount of nonviral protein, and the frequency of severe reactions has thus been reduced.¹⁸⁻²⁰ Persons allergic to vaccine components or who have anaphylactic hypersensitivity to eggs, however, should not be given influenza vaccine.²¹

The reactions following influenza vaccine in an elderly population have been found to be of low order when compared with those of controls receiving sterile saline. Sutzker et al¹⁹ concluded that in such a population group the low incidence and mildness of side reactions should not adversely affect any influenza immunization program. Unlike the 1976 swine influenza vaccine, subsequent vaccines prepared from other viral strains have not been associated with an increased frequency of Guillain-Barré syndrome.²²

EFFECTIVENESS OF THE INFLUENZA VACCINE

Davenport²³ has published an excellent review of the historic development of influenza vaccines. When studies began with the first trial in 1943, the results exceeded the expectations of the investigators; an average protection ratio of 3.6 against influenza was found. In 1945 a trial

against influenza B proved to be equally effective (protection ratio 12.9). Data for 15 years (1943 to 1958) unequivocally established that vaccination against influenza A and B was effective when vaccines of proper constitution and potency were employed.

Barker and Mullooly¹⁴ found a significant reduction in pneumonia- and influenza-associated hospitalizations and deaths in elderly populations during the 1972 A/England/72 (H3N2) epidemic in Portland, Oregon. The vaccine used was derived from the A/Hong Kong/68 (H3N2) virus. The estimated reduction in hospitalizations was 72 percent (31 percent to 100 percent), and the reduction in mortality was 87 percent (52 percent to 100 percent).

INFLUENZA VACCINE IN THE ELDERLY

Research has shown that influenza vaccine can reduce the incidence and severity of influenza virus infections among the elderly and the chronically ill, which underscores the importance of vaccination programs for nursing home populations.²⁴ Unvaccinated residents are more likely than vaccinated residents to become ill (risk ratio 2.6; 95 percent confidence interval 1.8 to 3.6), and are more likely to become hospitalized (risk ratio 2.4; 95 percent confidence interval 1.2 to 4.8), to develop x-ray-documented pneumonia (risk ratio 2.9; 95 percent confidence interval 1.6 to 5.3), or to ultimately die (risk ratio 5.6; 95 percent confidence interval 1.2 to 9.1) from complications of influenza. In this study, the reduction in attack rates was only 28 to 37 percent between the vaccinated and unvaccinated nursing home residents. Influenza vaccine, therefore, may not totally prevent the illness in the elderly; however, the vaccine does appear to be effective in attenuating the complications of the illness as manifested in hospitalization rates, incidence of pneumonia, and even death rates attributable to influenza.

Influenza vaccine is considered by some to be one of the less satisfactory immunizing agents in common use today.⁹ Data from field trials only rarely have demonstrated greater than 80 percent effectiveness in the prevention of clinical influenza under conditions of epidemic challenge.^{1,23} From a more positive perspective, however, as much as 80 percent of the morbidity in influenza epidemics is preventable by immunization with the use of currently available vaccine preparations.

There have been some reports of the ineffectiveness of the vaccine. Residents in a Maryland nursing home were administered an influenza vaccine containing vaccine antigen closely related to the strain found in residents with an influenza illness, and this vaccine did not appear to offer protection to those residents who were vaccinated.²⁵ There were several problems with this study, the most

significant of which was that only six of the 76 identified influenza cases were confirmed by virus isolation or serological results. The authors cautioned that no general conclusions of the lack of efficacy of influenza vaccine should be drawn from this study.

Present Recommendations for Routine Immunization of the Elderly

The Immunization Practices Advisory Committee (ACIP)²¹ of the Centers for Disease Control has identified the elderly as a high-priority population for special vaccination programs. The goal of these programs should be to vaccinate at least 80 percent of each group at high risk. Looking specifically at the elderly groups in their recommendations, adults with chronic disorders of the cardiovascular or pulmonary systems severe enough to have required regular medical follow-up or hospitalization during the preceding year are considered to be at the greatest medical risk of influenza-related complications. The ACIP also included in its high-risk category residents of nursing homes and other chronic-care facilities. Groups considered at moderate risk of influenza-related complications are otherwise healthy individuals aged 65 years and older. This group also should be included in vaccination programs, according to the ACIP.

Need for Strong Immunization Programs

Several studies have reported that fewer than one fourth of adults with chronic disease are vaccinated against influenza in accord with annual recommendations.^{14,26} A study of 67 nursing homes in six states found the proportion of residents vaccinated ranged from 8 to 98 percent (mean 62 percent).²⁷ In one extended care facility of a large county hospital in Paramus, New Jersey, the immunization rate improved from 33 to 95 percent as the result of setting an institutional policy for administration of influenza vaccine.²⁸

Strategies for Implementing an Influenza Vaccine Program

Recommendations proposed by the Immunization Practices Advisory Committee of the Centers for Disease Control include giving vaccine at the time of regular medical follow-up in the autumn and notifying those not scheduled for regular medical appointments to come in specifically to receive the vaccine. Physicians responsible for the care of hospitalized patients should also consider administering influenza vaccine to high-risk patients before they are discharged.²⁹ The health care delivery system can administer

the vaccine when patients contact the system prior to the influenza season, and organized health care systems can facilitate vaccination programs, because their high-risk target populations can be identified.

SUMMARY

Influenza is usually a minor, self-limiting illness, but for the elderly, especially the elderly who have chronic illnesses, it may be a severe or fatal disease. During influenza epidemics this disease may not always be recognized clinically as influenza but may appear as an acute decompensation in a patient with a known chronic illness.^{16,30-32} The influenza vaccine is not perfect, but it has been shown to be effective in the elderly. Reactions to the vaccine are usually minor and administration costs are low.

Experience with influenza vaccine since the early 1940s has led to an improved, more pure vaccine formulation, has developed worldwide systems of tracking the dominant circulating viral strains, and has refined recommendations for vaccine usage based on clinical studies of its efficacy and cost effectiveness. Physicians should be aware of the present limitations of the existing studies and the imperfections of the vaccine, but in the elderly population, a proven intervention that will offer a substantial degree of protection during the influenza season should not be withheld. Most of the existing evidence suggests that the vaccine is effective and that physicians should be more stringent in their influenza immunization practices with the elderly. The elderly who are at high risk should be of high priority for receiving influenza vaccine, and the vaccine should also be recommended to healthy individuals aged 65 years and older because of its proven efficacy for reducing attack rates when appropriate viral strains are used.

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An Opposing View

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The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control¹ has recently updated and prioritized its recommendation for annual influenza vaccination to include the following statement: (1) The highest priority is to immunize all persons with chronic cardiovascular and pulmonary diseases and residents of chronic-care facilities; (2) health-care personnel having extensive contact with high-risk patients; and (3) all persons aged over 65 years and persons of any age with chronic metabolic disease. In 1979 The Canadian Task Force on the Periodic Health Examination² made a similar recommendation. The US Preventive Services Task Force³ has recently endorsed the ACIP recommendation, stating the quality of evidence for efficacy in the elderly is II-3 (evidence obtained from multiple time-series studies, with or without intervention or dramatic results in uncontrolled experiments). Thus, in 1987, the recommended standard of care is that all persons aged over 65 years should be immunized annually against influenza.

The purpose of this paper is to show that there is no evidence that the 60 percent of persons aged over 65 years who are healthy and without chronic disease⁴ benefit from influenza vaccination. In fact, there is evidence that vaccination provides little benefit for this age group.

ANTIGENIC SHIFT AND DRIFT

It has been appropriately said that "the only constant feature of influenza is inconstancy."⁵ Influenza is caused by a group of viruses that are constantly changing their antigenic makeup. Minor changes that are somewhat predictable are known as *antigenic drift*, while sudden, more dramatic changes are called *antigenic shift*. For reasons that are not entirely clear, once a new strain has emerged, older strains become less active. This constant change means that new influenza vaccines must be developed every year. Experts must decide even before the end of the current influenza season what components to include in next year's influenza vaccine.⁶ Manufacturers must then rush to complete development and testing of the vaccine before the fall season.

The swine influenza campaign of 1976 is vivid testimony that the experts are not always able to predict when

a major influenza epidemic will occur or what strain of influenza will be the cause.^{7,8}

In 1976, on the basis of a small epidemic at Fort Dix, New Jersey, experts feared a major epidemic in 1977 caused by a strain of influenza A similar to that which caused the 1918 pandemic. A national campaign was launched to immunize all adults against this strain. The program was suspended in December 1976, after the vaccine was found to be associated with a 1 in 100,000 incidence of Guillain-Barré syndrome. The cause of this association between the vaccine and Guillain-Barré syndrome has not been determined.⁹ Contrary to expectations, no major influenza epidemic occurred in 1977.

MORBIDITY AND MORTALITY OF INFLUENZA

The exact morbidity and mortality caused by influenza is difficult to measure. Influenza-virus identification is costly and difficult, and it is not available to most clinicians. The vast majority of influenza victims suffer a clinical syndrome that includes fever, headache, myalgia, and cough, lasting from a few days to a week, followed by spontaneous resolution. A few patients, especially those already compromised by chronic cardiovascular or pulmonary disease, have severe sequelae or even die, frequently of infection of the lower respiratory tract.

Lacking definitive identification of the influenza virus, experts usually estimate influenza morbidity and mortality by comparing rates of hospitalization and death from respiratory tract infection, including pneumonia and influenza, during epidemic and non-epidemic periods of time. Barker and Mullooly,⁴ using this type of analysis, reported an excess of 80 hospitalizations and 11 deaths per 100,000 population resulting from pneumonia or influenza syndrome during epidemic years. The rates for persons aged over 65 years were higher, 400 to 500 excess hospitalizations and 68 to 104 excess deaths.⁴

These figures probably overstate the morbidity from influenza and the potential benefit obtained from prevention through vaccination, as many of the cases of respiratory tract disease included are not caused by the influenza virus. Sabin¹⁰ reported that even at the peak of an influenza epidemic, only 20 to 25 percent of patients with

clinical influenza syndrome will have positive cultures for influenza A or B: "Most clinical influenza . . . is not caused by influenza viruses."¹⁰

EFFICACY OF INFLUENZA VACCINATION

Because most "clinical influenza" is not caused by influenza viruses, it is not surprising to find that even in epidemic years patients who have had influenza shots do not have fewer visits to physicians' offices for respiratory tract complaints.¹¹ Ironically, the prevention of colds, a major reason why elderly persons get influenza shots, is a false reason.

There are two ways to look at the efficacy of influenza vaccination. The first is to study how many vaccinated persons develop a significant antibody titer (HI titer > 1/40). The second, and more important measure, is the decrease in morbidity and mortality that results from vaccination.

Studies in young, healthy adults have demonstrated the development of protective antibody titers in 70 to 95 percent of persons vaccinated.^{12,13} Unfortunately, the antibody response of older adults, especially those with chronic diseases, is much lower.¹⁴ As reported by Riesenberg,¹⁵ a vaccine dose three times greater than currently used is needed to produce a hemagglutination-inhibition titer greater than 1/40 in 70 percent of elderly patients.

The best studies of influenza-vaccine efficacy in reducing morbidity and mortality in a controlled population are those reported by Barker and Mullooly from the Kaiser Permanente Health Plan of Portland, Oregon.^{4,11,16,17} They studied four influenza epidemics: 1968-1969, 1972-1973, 1975-1976, 1980-1981, as well as a reference year, 1970-1971, during which time there was little influenza. Comparable populations of vaccinated and unvaccinated health-plan members were retrospectively studied with regard to hospitalizations and deaths from "pneumonia and influenza."

In the reference year, 1970-1971, as expected, there was little influenza and no benefit from vaccination. In two of the epidemics, 1968-1969 and 1975-1976, the vaccine match was not good, and no decrease in hospitalizations or deaths could be demonstrated in the vaccinated group. Decreased hospitalizations and deaths were demonstrated among high-risk vaccinated patients during the 1972-1973 and 1980-1981 epidemics.¹¹

Analysis of Barker's data from the 1972-1973 epidemic shows that vaccination decreased hospitalizations and death from pneumonia and influenza only in persons who were at high risk because of concomitant chronic disease.¹⁶ These conditions included cardiovascular, pulmonary, renal, metabolic, neurologic, and neoplastic disease. Hy-

pertension alone did not increase a person's risk of morbidity from influenza.⁴ Vaccinated persons aged over 65 years who were not at high risk had no statistically significant reduction in hospitalizations or death. There is no controlled study in the literature that shows a reduction in morbidity or mortality from influenza vaccination of low-risk persons aged over 65 years.

Studies have shown vaccination to reduce clinical influenza-related hospitalizations and deaths in nursing-home populations during influenza epidemics. Patriarca et al¹⁴ report that vaccination reduced the influenza infection rate from 33 to 21 percent in a Michigan nursing-home population during the 1982-1983 epidemic. Deaths and hospitalizations were also reduced. These data, although statistically significant, are actually discouraging in that vaccination only reduced the incidence of influenza by 33 percent. As noted by Harper,¹⁸ "We need a vaccine that is more than 28 to 37 percent efficacious even when it is antigenically appropriate."

ADVERSE EFFECTS OF INFLUENZA VACCINATION

Although serious reactions to influenza vaccination are rare, minor side effects are common. One third of vaccinated persons will have local redness and induration at the vaccine site lasting one to three days. A few persons will have fever, malaise, and myalgia lasting one to two days.¹⁹ In 1976 there was an association of Guillain-Barré syndrome with influenza vaccination in 1 per 100,000 persons. This association would not have been detected had not an elaborate surveillance mechanism been instituted. Although the association is not known to have occurred since 1976, the cause of the association is still unknown.

SUMMARY

It is true that persons aged over 65 years have greater morbidity and mortality from influenza. This increased morbidity and mortality, however, is mostly the result of a higher prevalence of other chronic diseases in the elderly. There is no evidence that vaccination, even in epidemic years when the antigenic match of the influenza strain and the vaccine is good, benefits the 60 percent of the noninstitutionalized population over the age of 65 years who do not have other high-risk diseases. In fact, the grade II-3 evidence cited by the US Preventive Services Task Force actually supports not immunizing this population group.

Even among high-risk patients, the benefit from influenza vaccination is highly variable and difficult to demonstrate. In some years there will be little influenza, and little benefit will accrue; in other years the vaccine-influenza antigenic match will not be good, and little benefit will be obtained. In a few years (two of the 12 years during which Barker's studies were done), a reduction in morbidity can be demonstrated for high-risk elderly persons. Even then, vaccine efficacy is only about 33 percent.

Patients are telling physicians that they do not feel influenza vaccination is worthwhile. Less than 25 percent of high-risk persons are vaccinated annually. Many of those vaccinated do so because they falsely believe influenza vaccination will prevent the common cold.

In accordance with the ACIP recommendation, high-risk patients with concomitant chronic disease (priority 1) should be immunized, because at least some benefit can be demonstrated. Medicine should stop wasting its preventive energy and resources, however, trying to get healthy persons over the age of 65 years to have an annual influenza vaccination, and instead spend its resources more wisely on the important and proven business of preventing conditions such as heart disease and cancer.

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Primary Care Medicine: Office Evaluation and Management of the Adult Patient (2nd Edition). Allan H. Gorall, Lawrence A. May, Albert G. Mulley, Jr. J. B. Lippincott Company, Philadelphia, 1987, 1001 pp., \$49.50.

This book, the second edition of *Primary Care Medicine*, edited by Drs. Gorall, May, and Mulley, contains the presentations of 56 specialists in medicine and other health-related professions. Their contributions fulfill the editors' promise of a practical approach to the diagnosis and management of problems encountered in the everyday office practice of medicine.

The initial section, "Principles of Primary Care," sets the tone and delineates the tasks of the primary care physician. Although this book may be most useful as a reference, the reviewer recommends reading this section in its entirety.

The book reflects the resurgence of training in the ambulatory setting. The emphasis is on the personal and psychological support of all patients as well as the prevention of disease and maintenance care in a continuous manner.

The discussion of methods of clinical epidemiology and decision analysis shows ways by which the clinician and the patient can choose among a bewildering array of diagnostic and therapeutic options; the necessity for health education and self-help are likewise emphasized.

The authors offer explanations of the complexities associated with communicating information and dealing with patient expectations in an effort to improve compliance.

Physicians are encouraged to know their patients as human and social beings as well as symptom bearers. This book should broaden the perspective of students and residents whose teaching in the past emphasized mainly hospital care, and it

contains a synthesis of the best available information for management of the adult patient. The discussions are brief and practical. For further study the reader is provided with a key-annotated bibliography (including 2,000 new ones in this edition).

To improve the utility of the book for office-based care, chapters have been added in the second edition, such as the problems of AIDS, Alzheimer's disease, and eating disorders. The authors deal with the special problems of elderly, pregnant, and homosexual patients.

Guidance is given on sigmoidoscopy and office surgical procedures; difficult clinical problems (for example, asymptomatic complex ventricular irritability, persistent low-back pain, the use of estrogens, and chronic somatization) are discussed.

In all, the editors have organized sections that address 230 clinical problems, and the index and table of contents facilitate gaining access to the information.

In the opinion of this reviewer, the writers have met their ambitious goal. They have covered the breadth of adult primary care for the student and have provided sufficient depth in difficult areas to aid the experienced practitioner.

This book is a compact and welcome addition to the frequently used reference books on the desk of the student, the generalist, and, yes, the versatile subspecialist.

Mary A. Agna, MD
Wright State University
Dayton, Ohio

Manual of Cardiac Arrhythmias. Edward K. Chung. Yorke Medical Books, New York, 1986, 307 pp., \$30.00.

With the advent of new electrophysiologic techniques, an astonish-

ing number of new terms and medications have entered the area of cardiac arrhythmia medicine. Electrophysiologists and cardiologists alike use such terms as *accessory*, *orthodromic*, *antidromic*, *reciprocating*, and *reentrant*. To the uninitiated, such as myself, this field seems akin to descriptions of the solar system.

Into this whirlwind, Dr. Chung has attempted to write a guide to arrhythmias for use by noncardiologists. Toward this end Dr. Chung has constructed an overall design that is quite approachable, with separate chapters relating to sinus, atrial, atrioventricular junctional, and ventricular arrhythmias. Because of my confusion over Dr. Chung's use of terminology, however, I found the book difficult to approach. He never uses the term *paroxysmal supraventricular tachycardia*, and it remains unclear to me with what he has replaced this entity. Similarly, the frequent use of abbreviations, such as AV JER, can make for laborious reading.

The therapeutic section of the book is already somewhat out of date, as Dr. Chung recommends therapy for asymptomatic premature ventricular contractions if they are greater than 30 per hour. He also makes relatively sparing use of verapamil, at one point placing it in a category of new and unavailable agents. He does not mention flecainide when describing antiarrhythmic agents.

At this stage it would seem almost impossible to write a book about arrhythmias that is both comprehensible and up to date. Until the smoke clears, I would opt for perusing the literature for accessible review articles^{1,2} and hope that a new edition of Marriott's *Practical Electrocardiography*³ is on the horizon.

William Bayer, MD
Delhi, New York

continued on page 224

CURRENT

Medical Diagnosis & Treatment

Edited by Steven A. Schroeder, Marcus A. Krupp,
Lawrence M. Tierney, Jr.

1988

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About the Editors

Steven A. Schroeder, M.D. is Professor of Medicine and Chief, Division of General Internal Medicine at the University of California San Francisco. **Marcus A. Krupp**, M.D., is Clinical Professor of Medicine Emeritus at the Stanford University School of Medicine, and Director (Emeritus) of Research Institute, Palo Alto Medical Foundation. **Lawrence M. Tierney, Jr.**, M.D. is Professor of Medicine at the University of California San Francisco and Assistant Chief of Medical Services at the Veterans Administration Medical Center in San Francisco. In addition, 36 practicing physicians and educators have contributed to this text in areas of their specialty.

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continued from page 221

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A Synopsis of Endocrinology and Metabolism (3rd Edition). Ian Ramsay. *PSG Publishing Company, Littleton, Massachusetts, 1986, 210 pp., \$27.50 (paper).*

This book includes discussions about different endocrine disorders that vary from a half-page to 12 pages. The book does not include any references to the medical literature. It is written by British authors, and some of the drugs used are drugs available in the United Kingdom under a somewhat different name.

In the absence of references, it is difficult to agree with many of the statements made. For example, in the discussion of osteoporosis the authors state that "not all old ladies will accept this type of treatment [referring to estrogens and progesterones], and it may be necessary to give them anabolic steroids." They further state that a combination of fluoride, 60 to 75 mg/d, and calcium has been shown to reduce the occurrence of spinal fractures. Both of these statements are debatable and are not supported by enough discussion to clarify whether this is considered established treatment, experimental treatment, or something else.

On the other hand, the book is readable, the organization is good, the illustrations are adequate, and there are several helpful tables and outlines. It seems to me, however, that the endocrine section of one of the standard textbooks of family medicine or internal medicine, or one of the smaller textbooks of endocrinology such as Jubiz' book, might be more useful.

I am not clear as to where this book would be useful. If this book were in a family medicine library, the clinician might refer to it for a quick over-

view when working up an endocrine problem. It might also be useful for clinical students. A clinician might find the book helpful as a brief outline, but I would not recommend it for purchase over one of the above-mentioned references.

Charles Kent Smith, MD
Eastern Virginia Medical School
Norfolk

Encounters Between Patients and Doctors: An Anthology. John D. Stoeckle (ed). *The MIT Press, Cambridge, Massachusetts, 1987, 440 pp., \$35.00, \$17.50 (paper).*

Medical practice, with few exceptions, involves the face-to-face interaction of the physician with a patient. In this collection of readings, John Stoeckle has compiled a group of writings that provide a theoretical framework for developing an understanding of this clinical interaction. Written by seminal scholars in the field, this anthology will have its greatest appeal to individuals responsible for teaching medical students and residents about the process of "doctoring," especially as it involves interviewing, communication, and patient education. Because of its heavily theoretical nature, however, the use of this book as a classroom text is limited to students in the social sciences.

Beginning with an introduction that reviews the developments leading to the current state of the physician-patient encounter in the United States, these readings include papers that explore elements of structure and function in the interaction between physician and patient. Readers may find a favorite paper not included in this collection, but, overall, Dr. Stoeckle should be commended for his selection of readings.

I would strongly recommend this text to individuals in education or research activities that involve the physician-patient encounter. Reflecting my bias as a family physician, my only critique of this anthology is that it does not include any readings that specifically address the effects of the

family on the physician-patient relationship.

Sim S. Galazka, MD
University Hospitals Health Center
Cleveland, Ohio

Manual of Otolaryngology—Head and Neck Therapeutics. Arnold E. Katz (ed). *Lea & Febiger, Philadelphia, 1986, 531 pp., \$39.50 USA, \$52.50 Canada.*

The editor of this book emphasizes that the manual represents a meticulous approach to therapeutic problems of the head and neck, and that it presents a thorough and logical diagnostic and therapeutic evaluation of various diseases of the head and neck. I feel the book falls far short of these stated objectives.

The editor also felt that it should be useful for medical students and primary care physicians. He went on to mention that the 38 chapters deal with problems commonly seen by the internist, the pediatrician, the physician assistant, and the nurse practitioner. He does not include the family physician as a primary care physician who may benefit from this text: He is right!

The text is so superficial in its coverage of many commonly seen head and neck problems that it would be of little value to the actively practicing family physician. The manual is described as a book designed so that it could easily be carried in the house officer's coat pocket. The actual size and weight of this text makes that seem very unlikely. The book is far too large and heavy to be carried by anyone for quick reference.

The book is written in outline form so that the contents can be easily retrieved. Again, however, the superficial treatment that it gives to many topics precludes its use as a definitive reference text. Nevertheless, the book is complete in the number of topics covered and is readable, with concise statements regarding several specific disease entities.

The manual may be of interest to medical students and to first-year

head and neck residents, but I feel that it has limited attraction beyond that.

*Fran Larsen, MD
Ventura County Medical Center
Ventura, California*

Primary Care—Clinics in Office Practice: Office Laboratory Testing (Volume 13, Number 4). *Paul M. Fisher, Lois A. Addison (guest eds). W. B. Saunders Company, Philadelphia, 1986, 220 pp., \$16.95.*

This volume, which is one in a series of quarterly publications, focuses on a topic that has received a great deal of attention recently. Physicians have traditionally performed a variety of office laboratory testing, but technologic advances have increased both the number and variety of tests that can be performed outside full-service laboratories. With financial pressures transferring more testing from the hospital to the office laboratory, and the desire to provide rapid therapeutic decisions, knowledge of office laboratory testing will be important to the family physician.

This book includes 13 separate articles that are generally concise and well written, although several contain duplicate information. Photographs are rare. The numerous tables contain specific information on currently available tests and manufacturers and they are excellent resources.

Several articles address such relevant topics as personnel, quality audits, and regulatory programs for the office laboratory. Another group of articles deals effectively and in detail with reviews of traditional office testing (diagnosis of vaginitis and mono-

nucleosis) as well as the impact of more recently available tests (rapid testing for streptococcal pharyngitis, pregnancy, and urinary tract infection). Approximately one half of the book is devoted to the area of chemistry testing. The sections on therapeutic drug monitoring and laboratory evaluation of fluid, electrolyte, and acid-base disorders are particularly informative and provide an excellent review of pertinent aspects of physiology and pharmacology for the physician who chooses not to do in-office testing.

The practicing family physician would find this a stimulating review and consolidation of up-to-date topics in office laboratory testing. Certainly for the physician who is currently performing minimal office laboratory testing and wishes to expand those activities, this volume would be important reading. Selected articles on some of the practical aspects of laboratory tests are very appropriate for the allied health professional, medical student, and family practice resident.

*Kathryn M. Larsen, MD
University of California
Irvine Medical Center
Orange*

Clinical Electrocardiography: A Primary Care Approach. *Ken Grauer, R. Whitney Curry, Jr. Medical Economics Company, Oradell, New Jersey, 1987, 512 pp., \$24.95 (paper).*

This excellent paperback edition addresses the systematic analysis of electrocardiograms in the clinical setting. In that context it is quite useful to the family physician and other health care professionals who must

read electrocardiograms and manage their patients with cardiovascular and metabolic diseases. Electrocardiographic interpretation is approached in a step-by-step fashion, giving the clinician the opportunity to utilize the book as either a review or a reference text. The book is well organized with appropriate illustrations and has additional suggested reading at the end of each chapter.

The entire text is divided into four parts, the first of which covers the basic principles of electrocardiography. The second part develops clinical applications in both health and disease with special emphasis on atypical electrocardiograms in the asymptomatic patient.

The last two parts consist of review exercises and a detachable reference guide. Each chapter is problem oriented, allowing the beginning or advanced student of electrocardiography to evaluate the clinical question, highlighted in bold print, and confirm any conclusions by reading the answer and reference material that follows. The print is easy to read and the material as a whole is both straightforward enough for the student in clinical training and comprehensive enough for the clinician involved in the day-to-day management of patients with complex problems. It is written by primary care physicians with excellent knowledge in this field and should find wide application by family physicians. It is an excellent investment for the price.

*Robert L. Bass, MD
University of Nebraska
Medical Center
Omaha*

INFORMATION FOR AUTHORS

THE JOURNAL OF FAMILY PRACTICE is a peer-reviewed scientific journal specifically intended to meet the needs of the developing specialty of family practice. Manuscripts are considered in relation to their significance in the advancement and definition of the discipline of family medicine, the extent to which they represent original work, and their interest to the practicing family physician. High priority is given to clinical studies that have practical implications for improved patient care. Some papers that are accepted for publication will be selected for concurrent commentary by other invited authors addressing issues raised by the papers. Manuscripts are considered individually on the basis of content, originality, and relevance to the goal of this journal.

Contributions in the form of original articles, feature articles, and position papers are invited. All articles should include a careful compilation of bibliography. Letters to the Editor are also encouraged, including observations, opinion, corrections, and comment on topics under discussion in the journal. THE JOURNAL OF FAMILY PRACTICE publishes the following features:

Original Articles. Clinical aspects of family practice, representing the family physician's perspective on health, illness, and the family: family practice and health care delivery, addressing the relation of family practice to other clinical disciplines, allied health fields, and community resources; medicolegal matters, audit methods, or practice management; or changing patterns of health care; education in family practice; or research in family practice relating to any of the above broad areas.

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Family Practice Forum. Exchange of opinion on issues relating to the developing specialty of family practice. Limited to four double-spaced manuscript pages with supporting references.

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References. References will be critically examined at the time of editorial review. Personal communications should not be included. The journal abbreviation style of *Index Medicus* should be followed in preparing references. References should be numbered consecutively as they appear in the text and arranged in the order of citation, not alphabetically. References to a journal and a book are illustrated.

1. Fishbane M, Starfield B: Child health care in the United States: A comparison of pediatricians and general practitioners. *N Engl J Med* 1981; 305:552-556

2. Dubovsky SL, Weissberg MP: *Clinical Psychiatry in Primary Care*. Baltimore, Williams & Wilkins, 1978, p 46

Tables. Tables should be self-explanatory, clearly organized, and supplemental to the text of the manuscript. Each table should include a title, be typed on a separate sheet, and be numbered in order of its appearance in the text. Tables should be used to compare or classify information for easier understanding and should not duplicate data included in the text or figures.

Figures. Figures should be used only if they clearly increase understanding of the text. Figures include all material that cannot be set in type, such as graphs, charts, line drawings, and tracings. All figures must be professionally prepared (usually 5 × 7) and submitted in duplicate. Only black-on-white glossy prints and black ink drawings will be accepted. Photocopies of original figures will not substitute. All figures should be unmounted. Each should have a gummed label on the back listing the figure number, title of manuscript, and author(s), with an arrow indicating the top. Figures should be numbered and cited in the text, and each should have a legend.

Book Reviews. Each issue will include a section featuring reviews of books of interest. Books for review should be sent to: **Claire Griebbling, Assistant Editor, The Journal of Family Practice, Department of Family Medicine, RF 30, School of Medicine, University of Washington, Seattle, WA 98195.**

MONISTAT* Dual-Pak*

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MONISTAT* 3 Vaginal Suppositories

(miconazole nitrate 200 mg)

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(miconazole nitrate 2%)

INDICATIONS AND USAGE: MONISTAT 3 Vaginal Suppositories are indicated for the local treatment of vulvovaginal candidiasis (moniliasis). Effectiveness in pregnancy or in diabetic patients has not been established.

MONISTAT-DERM Cream—For topical application in the treatment of cutaneous candidiasis (moniliasis).

CONTRAINDICATIONS: MONISTAT 3 Vaginal Suppositories—Patients known to be hypersensitive to the drug.

MONISTAT-DERM Cream has no known contraindications.

PRECAUTIONS: MONISTAT 3 Vaginal Suppositories—General: Discontinue drug if sensitization or irritation is reported during use. The base contained in the suppository formulation may interact with certain latex products, such as that used in vaginal contraceptive diaphragms. Concurrent use is not recommended.

Laboratory Tests: If there is a lack of response to MONISTAT 3 Vaginal Suppositories, appropriate microbiological studies (standard KOH smear and/or cultures) should be repeated to confirm the diagnosis and rule out other pathogens.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies to determine carcinogenic potential have not been performed.

Fertility (Reproduction): Oral administration of miconazole nitrate in rats has been reported to produce prolonged gestation. However, this effect was not observed in oral rabbit studies. In addition, signs of fetal and embryo toxicity were reported in rat and rabbit studies, and dystocia was reported in rat studies after oral doses at and above 80 mg/kg. Intravaginal administration did not produce these effects in rats.

Pregnancy: Since imidazoles are absorbed in small amounts from the human vagina, they should not be used in the first trimester of pregnancy unless the physician considers it essential to the welfare of the patient.

Clinical studies, during which miconazole nitrate vaginal cream and suppositories were used for up to 14 days, were reported to include 514 pregnant patients. Follow-up reports available in 471 of these patients reveal no adverse effects or complications attributable to miconazole nitrate therapy in infants born to these women.

Nursing Mothers: It is not known whether miconazole nitrate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when miconazole nitrate is administered to a nursing woman.

MONISTAT-DERM Cream—If a reaction suggesting sensitivity or chemical irritation should occur, use of the medication should be discontinued. For external use only. Avoid introduction of MONISTAT-DERM Cream into the eyes.

ADVERSE REACTIONS: MONISTAT 3 Vaginal Suppositories—During clinical studies with the MONISTAT 3 Vaginal Suppository (miconazole nitrate, 200 mg) 301 patients were treated. The incidence of vulvovaginal burning, itching or irritation was 2%. Complaints of cramping (2%) and headaches (1.3%) were also reported. Other complaints (hives, skin rash) occurred with less than a 0.5% incidence. The therapy-related dropout rate was 0.3%.

MONISTAT-DERM Cream—There have been isolated reports of irritation, burning, maceration, and allergic contact dermatitis associated with application of MONISTAT-DERM.



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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.

STANDARDS FOR PRIMARY CARE

To the Editor:

Regarding the article by Hawler and Hosokawa (*Lawler FH, Hosokawa MC: Evaluation of standards of practice for primary care physicians using 12 hypothetical cases. J Fam Pract 1987; 24:377-383*), there are several points that should be made.

The results in the tables do not give the number of physicians who actually dealt with the given cases. From the methods section it is clear that one participating physician deals with six cases. For the pediatricians and internists it is obvious which cases, but it is not as clear for the family physicians. Further, what were the criteria in selecting three cases per specialty for the group of family physicians? Although the authors in their discussion write about minor differences in standards due to the specialties, it would have been appropriate to give the results specified by number of physicians and specialty. In this way it is also possible for readers to make up their minds regarding the interpretation of these data.

Of more importance is that there are at least two reasons why this study fails in providing standards for primary care. First of all, Norman and Feightner found in 1981 evidence that the effect of "cueing" severely weakened the validity of patient management problems (PMPs).¹ This reasoning has led most medical curriculum committees to drop the PMP as the most important assessment method of medical students and physicians. Nowhere in this study do the authors address this cueing phenomenon or the way it might have influenced the results. If the authors would have used an open-ended format, the validity of the results would have gained a great deal.²

Second, there is further evidence that seriously questions the written method of evaluating clinical practice management performance.^{3,4} The authors' defensive statement that those physicians who rated themselves as being more aggressive responded more aggressively on the 12 hypothetical cases is based on very weak reasoning, suggesting that being aggressive has something to do with the management of the cases—something I question severely.

It is true that establishing standards for primary care is an important issue in the debate of quality of care. It is my opinion, however, that the method used in this study (closed options and only 35 percent responding physicians) is not a valid approach for attaining such standards.

J. J. Rethans, MD
Department of Epidemiology
University of Limburg
The Netherlands

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3. Page GG, Fielding DW: Performance on PMPs and performance in practice: Are they related? *J Med Educ* 1980; 55:529-537
4. Rethans JJE, Boven van CPA: Simulated patients in general practice: A different look at the consultation. *Br Med J* 1987; 294: 809-812

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

We appreciate the interest Dr. Rethans has shown in our work. We shall address his comments in order.

continued on page 250

Nalfon® fenoprofen calcium

Brief Summary.

Consult the package literature for prescribing information.

Indications and Usage: Nalfon® (fenoprofen calcium, Dista) is indicated for relief of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management.

Nalfon 200 is indicated for relief of mild to moderate pain.

Controlled trials are currently in progress to establish the safety and efficacy of Nalfon in children.

Contraindications: Patients who have shown hypersensitivity to Nalfon, those with a history of significantly impaired renal function, or those in whom aspirin and other nonsteroidal anti-inflammatory drugs induce the symptoms of asthma, rhinitis, or urticaria.

Warnings: Use cautiously in patients with upper gastrointestinal tract disease (see Adverse Reactions). Gastrointestinal bleeding, sometimes severe (with fatalities having been reported), may occur as with other nonsteroidal anti-inflammatory drugs.

Patients with an active peptic ulcer should be on vigorous antiulcer treatment and be closely supervised for signs of ulcer perforation or severe gastrointestinal bleeding.

Genitourinary tract problems most frequently reported in patients taking Nalfon have been dysuria, cystitis, hematuria, interstitial nephritis, and the nephrotic syndrome. This syndrome may be preceded by fever, rash, arthralgia, oliguria, and azotemia and may progress to anuria. There may also be substantial proteinuria, and on renal biopsy, electron microscopy has shown foot process fusion and T-lymphocyte infiltration in the renal interstitium. Early recognition of the syndrome and withdrawal of the drug have been followed by rapid recovery. Administration of steroids and the use of dialysis have also been included in the treatment. Because this syndrome with some of these characteristics has also been reported with other nonsteroidal anti-inflammatory drugs, it is recommended that patients who have had these reactions with other such drugs not be treated with Nalfon. In patients with possibly compromised renal function, periodic renal function examinations should be done.

Precautions: Since Nalfon is eliminated primarily by the kidneys, patients with possibly compromised renal function (such as the elderly) should be closely monitored; a lower daily dosage should be anticipated to avoid excessive drug accumulation. Nalfon should be discontinued if any significant liver abnormalities occur.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (three times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with Nalfon. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with Nalfon as with other nonsteroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (eg, eosinophilia, rash, etc), Nalfon should be discontinued.

Administration to pregnant patients and nursing mothers is not recommended.

In patients receiving Nalfon and a steroid concomitantly, any reduction in steroid dosage should be gradual to avoid the possible complications of sudden steroid withdrawal.

Patients with initial low hemoglobin values who are receiving long-term therapy should have a hemoglobin determination at reasonable intervals.

Peripheral edema has been observed in some patients. Use with caution in patients with compromised cardiac function or hypertension. The possibility of renal involvement should be considered.

Eye examinations are recommended if visual disturbances occur.

Patients with impaired hearing should have periodic tests of auditory function during chronic therapy.

Nalfon decreases platelet aggregation and may prolong bleeding time.

Laboratory Test Interactions—Amelrex-M kit assay values of total and free triiodothyronine in patients receiving Nalfon have been reported as falsely elevated on the basis of a chemical cross-reaction that directly interferes with the assay. Thyroid-stimulating hormone, total thyroxine, and thyrotropin-releasing hormone response are not affected.

Adverse Reactions: The adverse reactions reported below were compiled during clinical trials of 3,391 arthritic patients, including 188 observed for at least 52 weeks of continuous therapy. During short-term studies for analgesia, the incidence of adverse reactions was markedly lower than in longer-term studies.

Incidence Greater Than 1%

Probable Causal Relationship—Digestive System: The most common adverse reactions were gastrointestinal and involved 14% of patients; in descending order of frequency, they included dyspepsia,* constipation,* nausea,* vomiting,* abdominal pain,* anorexia,* occult blood in the stool, diarrhea, flatulence, dry mouth. **Nervous System:** headache* and somnolence* occurred in 15% of patients; dizziness,* tremor, confusion, and insomnia were noted less frequently. **Skin and Appendages:** pruritus,* rash, increased sweating, urticaria. **Special Senses:** tinnitus, blurred vision, decreased hearing. **Cardiovascular:** palpitations,* tachycardia. **Miscellaneous:** nervousness,* asthenia,* dyspnea, fatigue, malaise.

Incidence Less Than 1%

Probable Causal Relationship—Digestive System: gastritis, peptic ulcer with or without perforation, and/or gastrointestinal hemorrhage. **Genitourinary Tract:** dysuria, cystitis, hematuria, oliguria, azotemia, anuria, interstitial nephritis, nephrosis, papillary necrosis. **Hematology:** purpura, bruising, hemorrhage, thrombocytopenia, hemolytic anemia, aplastic anemia, agranulocytosis, pancytopenia. **Miscellaneous:** peripheral edema, anaphylaxis.

Incidence Less Than 1%

Causal Relationship Unknown—Skin and Appendages: Stevens-Johnson syndrome, angioneurotic edema, exfoliative dermatitis, alopecia. **Digestive System:** aphthous ulcerations of buccal mucosa, metallic taste, pancreatitis. **Cardiovascular:** atrial fibrillation, pulmonary edema, electrocardiographic changes, supraventricular tachycardia. **Nervous System:** depression, disorientation, seizures, trigeminal neuralgia. **Special Senses:** burning tongue, diplopia, optic neuritis. **Miscellaneous:** personality change, lymphadenopathy, mastodynia, fever.

Usage and Administration: Rheumatoid Arthritis and Osteoarthritis—suggested dosage: 300 to 600 mg t.i.d. or i.d.

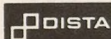
Mild to Moderate Pain—Nalfon 200 q. 4-5 h., as needed.

Do not exceed 3,200 mg per day.

*Incidence 3% to 9%.

PV 1026

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LETTERS TO THE EDITOR

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Each responding physician, whether internist, pediatrician, or family physician, dealt with six cases. The family physician sample was twice as large as the other two groups to enable family physicians as a group to cover all 12 cases.

We did comment in the discussion section that interspecialty differences were minor, but further discussion of that point was beyond the scope of the paper.

We were concerned with the "cueing" phenomenon associated with patient management problems cited by Dr. Rethans. We attempted to deal with this in several ways. First, a broad range of responses from "always used" to "never used" categories were given. Second, an option for "other approaches" was given for each case; this option was completed for less than 5 percent of responses, indicating that the respondents felt comfortable with the presented options. Third, the patient management problems (PMPs) cited have only a dichotomous response—ordering or not ordering—without any consideration as to the likelihood of a physician requesting that particular option. Since we provided a range of probabilities for requesting an option, we feel that our approach was more valid than the dichotomous approach to PMPs.

It is inconceivable that physicians are unable to rate themselves as to the style (aggressive or conservative) of their clinical approach compared to their peers. That this self-perception, both developed and refined in actual practice, is wholly invalid seems unreasonable.

Dr. Rethans is welcome to challenge the response rate and the validity of the method, issues pointedly raised in the discussion. Such difficulties with the present study merely bolster the need for further research.

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SOMATIZATION DISORDER

To the Editor:

deGruy et al, in their article (*deGruy F, Columbia L, Dickinson P: Somatization disorder in a family practice. J Fam Pract 1987; 25:45-51*), draw a number of conclusions that their data and analyses fail to support. In general, the authors over-extend statistical analyses and then draw conclusions inconsistent with the results.

Regarding Table 1, the chi-square statistic is not a "one-size-fits-all" for categorical data. There is no indication that the authors applied the Yates' correction for continuity, which is required when there is one degree of freedom.¹ Further, an assumption of the chi-square statistic with 1 *df* is that all expected frequencies must be five or more.^{1,2} From the data presented in Table 1, even the most liberal assumptions regarding expected frequencies³ indicate that 17 of the 18 chi-square statistics performed were inappropriate. The appropriate statistical technique for this data set is the Fisher's exact test,^{4,5} which is seldom covered in introductory statistical textbooks. The chi-square analyses, comparing definite and borderline somatization disorder patients to nonsomatization patients, contribute nothing to the stated purposes of the article (the prevalence or impact of the disorder), and the numbers in all of these analyses are so small that any analysis is suspect.

In Table 2 the authors set aside formal statistical tests but then proceed to interpret the data on face value, as if the differences were meaningful. In the abstract, perhaps the only part of a study read by the nonstatistically conversant reader, these data are listed in detail. The use of inferential statistics allows the researcher to make generalizations from a sample to a defined population. Without the use of inferential statistical methods, the authors have no basis for suggesting that patients with a somati-

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WARNINGS: Sympathomimetic amines should be used with caution in patients with hypertension, diabetes mellitus, heart disease, peripheral vascular disease, increased intraocular pressure, hyperthyroidism, or prostatic hypertrophy.

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Drug Interactions: Entex should not be used in patients taking monoamine oxidase inhibitors or other sympathomimetics.

Drug/Laboratory Test Interactions: Guaifenesin has been reported to interfere with clinical laboratory determinations of urinary 5-hydroxyindoleacetic acid (5-HIAA) and urinary vanilmandelic acid (VMA).

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Pediatric Use: Entex LA: Safety and effectiveness of Entex LA tablets in children below the age of 6 have not been established.

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LETTERS TO THE EDITOR

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zation disorder utilize medical services any differently than the general practice population.²

From data in Table 3, the authors conclude that somatization disorder is a "difficult problem for family physicians." While many or most family physicians may agree, the results of this study do not support this conclusion. The physicians rated these patients equally in treatment difficulty and problem management.

Statistics are designed to help researchers make decisions. The key point is, inappropriate use of statistics has led to inappropriate conclusions. Reinterpretation of the data given may clarify these issues or, if they do not support clinical impressions or opinions in family practice, may generate further research.

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2. Schor S, Karten I: Statistical evaluation of medical journal manuscripts. *JAMA* 1966; 195:145-150
3. Kuzma JW: Basic Statistics for the Health Sciences. Palo Alto, Calif, Mayfield, 1984, p 155

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

The concern of Drs. Replegle and Eicke have about the propriety of our statistical analyses and the inferences made therefrom is well taken. I appreciate the opportunity to describe the statistical dilemma this analysis presented.

Prior to the preparation of Table 1, the data were subjected to chi-square analysis with and without Yates' correction for continuity as well as the Fisher exact probability test by two different algorithms. The statistical significance of all compar-

isons was identical with two exceptions: when comparing household structure of those with definite somatization disorder (DSD) with those without, Yates' correction did not ascribe significance ($\chi^2 = 2.695$, $P > .10$, two-tailed); Fisher's exact test considered this comparison significant by one algorithm ($P = .050$), and not significant by another algorithm ($P = .061$).

Thus, we are dealing with similar conclusions irrespective of the statistical technique used, so the issue here is one of methods rather than results.

The Yates' correction for continuity is not required when there is one degree of freedom. It has been widely recommended when analyzing a 2×2 table, but this recommendation is controversial,^{1,2} and many statisticians argue compellingly that it should be abandoned altogether.³⁻⁵

For the chi-square to reliably test the independence of two variables, two criteria must be met: the data must be a random sample from a multinomial distribution, and the expected cell frequencies must not be too small. As noted by Drs. Replegle and Eicke, a minimum cell size of five is frequently recommended. Everitt,⁶ however, has demonstrated that this criterion is too stringent and can be relaxed. Expected cell frequencies of 2.5 to 3 are probably sufficient for a valid test of independence. In fact, Cochran⁷ recommends the chi-square as an appropriate statistic if the total sample N is greater than 40 and each cell has an expected frequency of at least one.

One could avoid this controversy altogether by using Fisher's exact probability test. This elegant test of significance is computed by adding the probability of finding the observed table to the probability of finding all hypothetical tables with the same marginals but "more extreme" cell frequencies. But herein lies our dilemma: there is no consensus on which cell should be decremented to zero for more extreme tables. Ordinarily the smallest cell is used, but when both marginal distributions are grossly unequal (as they are in Table 1), decrementing the smallest cell may

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