

Before we do so, however, two points made in the paper should be clarified. First of all, 30 to 45 per cent figure for morbidity associated with hysterectomy cited by Dr. Donahue consists mainly of low-grade fever and urinary-tract infection. Secondly, most of the studies on "post-hysterectomy depression" dealt with patients having a medical indication for operation. The validity of extending such findings to women seeking hysterectomy for birth control and cancer prophylaxis can be seriously questioned.

One argument in favor of elective hysterectomy is provided by the recent reports associating increased risk of endometrial carcinoma with menopausal and postmenopausal estrogen therapy.^{1,2} Hysterectomy removes this risk. Thus, any woman having undergone a hysterectomy need not be denied the generally acknowledged benefits of a continued youthful appearance and a delay of osteoporosis that are attributed to estrogen replacement.³

Cancer of the cervix (in situ), corpus uteri, cervix (invasive) and ovary rank third, fourth, fifth and seventh, respectively, in cancer incidence among women in the United States.⁴ Furthermore, ovarian cancer has a poor survival rate owing to difficulties in early detection. Clearly, hysterectomy and ovariectomy are efficacious in cancer prophylaxis since there is no dispute that cancer cannot occur in organs that have been removed. A substantial reduction in cancer incidence and mortality among women can be effected by routine removal of the uterus and ovaries after childbearing age.

Dr. Cole's economic analysis of the costs and savings of elective hysterectomy led him to conclude that the objective benefits of cancer prophylaxis are insufficient to justify the costs. Although we recognize the conceptual difficulty entailed in assessment of the subjective benefits of the procedure, it is not a valid reason to discount their importance. Associated with routine gynecologic care is the repeated embarrassment and indignity of the pelvic examination; with each Papanicolaou smear is the fear and anxiety of cancer, and most of all with each case of cancer is the unspeakable pain and suffering of the patient and the prolonged anguish and sorrow in the family, neither of which is reflected in the \$15,000 cost of treatment.

We wish to emphasize Dr. Bunker's point that the overall benefits of hysterectomy, as perceived by a woman, may well offset the attendant costs and risks. The high rate of hysterectomies among a group of informed consumers of medical care — physicians' wives — provides strong support for this conclusion. To deny women an efficacious method of cancer prophylaxis because it is not economically justifiable, or to say that improvements in the quality of life are not sufficient grounds for "medical necessity," appears to be at odds with our values and system of medical care. Indeed, tubal ligation and vasectomy appear to be even more medically "unnecessary." Generally, there are no abnormalities of the fallopian tubes or vas deferens. Yet the procedures are sought, and their associated morbidity accepted, merely for personal preference. The ultimate costs of all surgical procedures are borne by the members of society, over half of whom are women. In our opinion, the woman, not the epidemiologist or the cost analyst, should make the informed decision whether or not to avail herself of this mode of disease prevention.

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1. Zeil HK, Finkle WD: Increased risk of endometrial carcinoma among users of conjugated estrogens. *N Engl J Med* 293:1167-1170, 1975
2. Smith DC, Prentice R, Thompson DJ, et al: Association of exogenous estrogens and endometrial carcinoma. *N Engl J Med* 293:1164-1167, 1975
3. Weiss NS: Risks and benefits of estrogen use. *N Engl J Med* 293:1200-1202, 1975
4. Levin DL, Devessa SS, Godwin JD II, et al: *Cancer Rates and Risks* (DHEW Publication No. [NIH] 76-691). Second edition. Bethesda, MD, National Cancer Institute, 1974, p 13

To the Editor: Referring to the symposium, "Elective Hysterectomy: Pro and con" (*N Engl J Med* 295:264, 1976), perhaps at the 1976 meeting of the American Academy of Obstetrics and Gynecology

another popularity contest could be held for elective hysterectomy. Let's also invite anesthesiologists, pathologists and hospital administrators — and, indeed, all the remaining intact ladies.

Now we add one new rule: There will be no third-party payments.

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The above letters were referred to Dr. Cole, who offers the following reply:

To the Editor: Dr. Pasch's first point is correct and was accommodated in my statement of preference, which began, "In my opinion..."

As implied by Drs. Ing and Roth, most women who are going to use exogenous estrogens in high dose for a long period probably should have a hysterectomy. The need for such an operation is an adverse effect of these drugs and should be evaluated, along with their controversial benefits, before their use is initiated or continued. I do not think the rank order of the cancers prevented is pertinent, nor is the fact that they can be prevented unless it is evaluated in relation to costs. Most persons would agree with Drs. Ing and Roth that a woman, and her physician, should make an "informed decision" regarding hysterectomy. The facts, costs and benefits of elective hysterectomy on which a truly informed decision can be based are only beginning to be recognized.

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Letters to the Editor should be typed double-spaced (including references) with conventional margins. The length of the text is limited to 1½ manuscript pages.

RANDOMIZED CLINICAL TRIALS

To the Editor: Byar et al. (*N Engl J Med* 295:74, 1976) are quite right to say that randomized clinical trials are not outmoded. But I believe they are wrong to be ambiguous about technics that can improve on plain randomization. (I say "ambiguous" because their paper seems to support the approach at one point and to oppose it at another.) To an investigator who has had more than his share of randomized trials end with disquieting differences in important base-line variables, their quotation of Fisher is not reassuring. Our department is now using the Taves intriguing "minimization" technic (whose paper the authors do not cite), and we recommend it to others.

They are also correct in saying that "some questions cannot be answered by randomized clinical trials," but miss the most important question for therapeutics: how will a drug actually perform in clinical practice? There are many differences between controlled trials and what I have termed "naturalistic" circumstances,² and society sorely needs to develop methodology for post-marketing surveillance of both the good and the harm that drugs do.

There is one extremely interesting ethical implication of recent FDA policy, which has required at least two positive American controlled trials, regardless of how many impeccable foreign trials exist. How does one justify to an ethicist (or a patient) doing a second trial when a clearly positive one exists? As Byar et al. state, "no patient [should] receive a therapy that is known to be inferior to another." The key word here is "known." When is something "known"? The dilemma is clear and serious: science is based on repeatability of results, but ethics and the law may suggest other-

wise, accusing the scientist of placing the corporate public weal above individual rights.

I wish the authors had commented further on the practice of parceling out subgroups of patients who allegedly are specifically benefited (or hurt) by treatment, despite the absence of statistical differences between the total groups. This has occurred in both the UGDP and Coronary Drug Projects. The probability calculations are by no means clear in such cases, and one would have thought that the statisticians of the world would have rallied round the flag and decried such tactics as anything other than a source of hypotheses to be tested prospectively in new controlled trials. What we have seen, instead, is the use of such subanalyses to come to conclusions in which regulatory decisions are proposed. "Curiouser and curiouser," said the ghosts of both Lewis Carroll and Sir Ronald Fisher.

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1. Taves DR: Minimization: a new method of assigning patients to treatment and control groups. *Clin Pharmacol Ther* 15:443-453, 1974
2. Lasagna L: A plea for the "naturalistic" study of medicines. *Eur J Clin Pharmacol* 7:153, 1974

BOOK REVIEWS

The Biological and Clinical Basis of Infectious Diseases. By Guy P. Youmans, M.D., Ph.D.; Philip Y. Paterson, M.D.; and Herbert M. Sommers, M.D. 813 pp., illustrated. Philadelphia: W.B. Saunders Company, 1975. \$17.50 — cloth; \$12.95 — paper.

A spin-off of the student's request for relevance and meaning on campuses in the late 1960's was the collaboration of basic scientists and clinicians in teaching medicine in segments organized by organ system or other common denominators. In infectious disease this approach resulted in the formidable task of integrating the role of the lac operon with the host's immune response. In most institutions, this alliance involved the pathologist, the microbiologist and clinicians with an interest in infectious disease. This book is admittedly the product of a collective approach. Intended as a comprehensive textbook, but limited in its scope to students and house staff, it has both faults and strengths.

The faults are, in part, organizational and pictorial. For example, phagocytosis is not covered in depth, nor is there a section on anaerobic infections, rubella or nosocomial infections. On page 125 there is a diagram with instructions on the technic of translaryngeal tracheal aspiration; then, on page 282 the topic is again covered with a picture, but neither picture stands well by itself. Many of the figures are line drawings and require studied spatial orientation before the message comes across; the x-ray reproductions suffer from the lack of arrows.

One of the strengths of the book is that, by and large, all the data are there. If the problem is common and it occurs in the United States, the authors have dealt with it and included the information from their experience and the literature. The case histories and discussions are helpful: however, controversial areas or the cases in which care was not optimal are not commented on. For example, on page 440 is the case of a patient with *Escherichia coli* bacteremia treated parenterally for four days. This is probably what happened on the ward, but some note should be made of the validity of this practice. The historical notes, which exist almost nowhere else, are particularly fascinating and give the reader a perspective of the way infectious diseases were perceived and managed in the preantibiotic era.

On balance, the book is worthwhile, and accurately depicts the state of the art and basic scientific findings that underlie infectious disease, as it is understood in the United States in 1976. The contemporary references and the modest price make this book a best buy for the medical student.

ARNOLD L. SMITH, M.D.

Toxicology of Pesticides. By Wayland J. Hayes, Jr., M.D., Ph.D. 580 pp., illustrated. Baltimore: Williams and Wilkins, 1975. \$39.50.

This textbook, the first of its kind in the field of toxicology, outlines in considerable detail the basic principles of toxicology and provides information on pesticides that would permit the reader to make a rational decision about safety. This volume is directed partly to the practicing physician, enabling him, in an emergency, to diagnose and treat poisoning and advise his patients about the safe use of pesticides. It will be equally useful to county agents, health officers, manufacturers, legal experts and formulators and applicators of pesticides, and is an excellent textbook for students of toxicology.

This volume is not primarily concerned with individual compounds, but, rather, deals with the general conditions of exposure, the observed effects of this exposure on human health, the problems of diagnosis and treatment, the means of preventing injury and, briefly, with the impact of pesticides on domestic animals and wildlife. It is written with the goal of showing how the modern, quantitative science of toxicology can help to achieve a rational approach to environmental chemicals.

The book is dedicated to Paracelsus, whose famous statement about the importance of dosage in determining poisoning was published at least as early as 1564. Dr. Hayes emphasizes that the importance of dosage cannot be fully appreciated except in association with a quantitative study of all factors bearing on toxicity. Those whose responsibility it is to judge the safety of a chemical compound must have an appreciation for the importance of the dose-response relation if they are to avoid ambiguous decisions.

The author recommends that, whenever possible, clinicians should be provided with information on tolerated doses or blood levels of pesticides, as well as on doses or blood levels that have caused illness or fatalities. Differences in exposure can explain how a compound that is dangerous to workers may be safe for the general population, and vice versa. Only through quantitative toxicology will it be possible to reach justifiable decisions and correct diagnoses in cases of suspected poisoning.

This book is recommended highly to all who have an interest in toxicology, but particularly to those who must reach rational decisions based on toxicologic data.

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NOTICES

SYMPOSIUM ON CANCER MANAGEMENT

The American Cancer Society, Massachusetts Division, and the Greater Boston Medical Society are presenting a symposium entitled "Successes in Cancer Management Today" on Wednesday, December 15 at the Sheraton-Boston Hotel. The program has been approved for 5 hours of continuing-education credit by the American Medical Association and is acceptable for 5 prescribed hours by the American Academy of Family Physicians. The deadline for registration is December 1.

Further information may be obtained from Dr. Sheldon Binder, American Cancer Society, 247 Commonwealth Avenue, Boston, Massachusetts 02116, or by telephone to (617) 267-2650.

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS JUNIOR FELLOWSHIP LECTURE SERIES

The American College of Obstetricians and Gynecologists and the Ortho Pharmaceutical Corporation will sponsor a lecture series in the Countway Library Auditorium, 10 Shattuck Street, Boston on the following Tuesdays: "Menopausal Hormonal Therapy: Risks vs. Benefits" on January 11; and "Hirsutism: Diagnosis and Treatment" on February 8.

Further information may be obtained from Dr. Philip D. Darney, Department of Obstetrics-Gynecology, Boston Hospital for Women, Harvard Medical School, 221 Longwood Avenue, Boston, Massachusetts 02215, or by telephone to (617) 734-5300.