



1983
YEAR BOOK OF
**DRUG
THERAPY**

HOLLISTER
LASAGNA

The YEAR BOOK of

Drug Therapy[®]

1983

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Acta Medica Scandinavica
Acta Neurochirurgica
Acta Neurologica Scandinavica
Acta Psychiatrica Scandinavica
Acta Radiologica (Diagnosis)
American Family Physician
American Heart Journal
American Journal of Cardiology
American Journal of Clinical Nutrition
American Journal of Diseases of Children
American Journal of Epidemiology
American Journal of Gastroenterology
American Journal of the Medical Sciences
American Journal of Medicine
American Journal of Obstetrics and Gynecology
American Journal of Ophthalmology
American Journal of Psychiatry
American Journal of Surgery
American Review of Respiratory Disease
Anaesthesia and Intensive Care
Anesthesia Progress
Anesthesiology
Annals of Allergy
Annals of Emergency Medicine
Annals of Internal Medicine
Annals of Neurology
Annals of Ophthalmology
Annals of Rheumatic Diseases
Annals of Surgery
Annals of Thoracic Surgery
Archives of Dermatology
Archives of Disease in Childhood
Archives of General Psychiatry
Archives of Internal Medicine
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Australian and New Zealand Journal of Medicine
Blood
British Heart Journal
British Journal of Anaesthesia
British Journal of Clinical Pharmacology
British Journal of Diseases of the Chest
British Journal of Obstetrics and Gynaecology
British Journal of Pharmacology
British Journal of Psychiatry

British Journal of Surgery
 British Medical Journal
 Canadian Journal of Surgery
 Canadian Medical Association Journal
 Cancer
 Cancer Treatment Reports
 Chest
 Circulation
 Clinical Nephrology
 Clinical Pharmacology and Therapeutics
 Comprehensive Psychiatry
 Critical Care Medicine
 Cutis
 Diabetes
 Digestion
 Digestive Diseases and Sciences
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 Hospital Practice
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 Hypertension
 International Journal of Cardiology
 International Journal of Dermatology
 Johns Hopkins Medical Journal
 Journal of Affective Disorders
 Journal of Allergy and Clinical Immunology
 Journal of the American Academy of Child Psychiatry
 Journal of the American Academy of Dermatology
 Journal of the American Geriatrics Society
 Journal of the American Medical Association
 Journal of Bone and Joint Surgery (American vol.)
 Journal of Clinical Gastroenterology
 Journal of Clinical Investigation
 Journal of Clinical Pharmacology
 Journal of Clinical Psychiatry
 Journal of Laryngology and Otology
 Journal of the National Cancer Institute
 Journal of Neurology
 Journal of Neurology, Neurosurgery, and Psychiatry
 Journal of Neurosurgery
 Journal of Occupational Medicine
 Journal of Otolaryngology
 JPEN. Journal of Parenteral and Enteral Nutrition
 Journal of Pediatrics
 Journal of Pharmaceutical Sciences
 Journal of Surgical Research
 Journal of Urology
 Klinische Wochenschrift
 Lancet
 Life Sciences
 Lung
 Mayo Clinic Proceedings
 Medical Care
 Medical Journal of Australia

Medicine and Sciences in Sports and Exercise
Metabolism
Nature
Neurology
Neurosurgery
New England Journal of Medicine
New York State Journal of Medicine
Obstetrics and Gynecology
Ophthalmology
Pain
Pediatrics
Pharmacology
Postgraduate Medicine
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Psychopharmacology
Review of Infectious Diseases
Scandinavian Journal of Gastroenterology
Schweizerische Medizinische Wochenschrift
Science
Southern Medical Journal
Stroke
Surgery
Surgical Neurology
Therapeutic Drug Monitoring
Yale Journal of Biology and Medicine

1. General Information

1-1 **Pharmacology and Aging** is discussed by Robert F. Vestal (Univ. of Washington). The elderly are a more heterogeneous group than younger people. Rates of deterioration of organs and enzyme systems differ greatly with age; therefore, effective, safe use of drug therapy for old people is a matter of individual prescribing.

A patient should be given the least number of necessary drugs. However, elderly patients often have multiple diseases requiring multiple drugs. Evidence of adverse drug reactions increases with the number of drugs administered. Many elderly patients are improperly medicated and overmedicated. Although compliance with therapeutic regimens is not necessarily worse in the elderly than in younger age groups, the consequences of errors in self-medication may be more severe.

Basic principles in prescribing for geriatric patients are as follows: establish a diagnosis before treatment, obtain a careful drug history, know the pharmacology of drugs prescribed, titrate dosage with patient response, use smaller doses for the elderly, simplify therapeutic regimens (which includes explaining the treatment plan to the patient and a friend or relative, giving concise written directions, and choosing a dosage form appropriate for the patient), regularly review drugs in the treatment plan and discontinue those not needed, and remember that drugs may cause illness. Often the relationship of the clinician with the patient is more important than the drugs prescribed.

Epidemiologic studies using standard methodology, such as the Defined Daily Dose, are needed to compare drug use in the elderly among countries and regions. Evidence indicates that age-related alterations in the physiology of drug distribution, drug elimination, and drug action are the substrata upon which disease-related alterations in drug disposition and response are superimposed.

In geriatric clinical pharmacologic studies, study populations and the selection criteria should be carefully described. Greater attention to environmental factors, such as smoking and diet, and protocol design is also necessary. Research protocols should try to simulate clinical use of the drug studied, which often means conducting studies at steady state after multiple dosing. In data analysis, it must be remembered that an apparent effect of age may possibly be accounted for by age-related variables, rather than by age per se.

► [Several years ago, the National Institute on Aging found that relatively little was known about the effects of drugs in the elderly. A modest program of grant support was initiated to encourage interest in this area. Interest was predictably encouraged, with a vast increase in the amount of knowledge about how drugs act in the elderly.

Robert Vestal was one of the pioneers in this field, his efforts antedating the current explosion. The above paper, in a slightly different version, also appeared in *Pharmacology* (30:191–200, 1982). Other review articles on the subject have appeared in the *New England Journal of Medicine* (306:1081–1088, 1982), the *Annals of Internal Medicine* (95:711–722, 1981), and the *Southern Medical Journal* (75:522–528, 1982). All are worth reading. The main point is that elderly patients differ quite a bit in body composition and their ability to eliminate drugs as compared with younger persons. Besides pharmacokinetic differences, which are relatively easy to document, they also show pharmacodynamic differences, which are somewhat more difficult to prove. In general, these differences mean that initial doses of drugs in the elderly should be lower and that augmentations of dose should be slower than in younger patients. The old adage for treating elderly patients still holds: "Start low; go slow."—L.E.H.] ◀

- 1–2 **Will All New Drugs Become Orphans?** "Orphan" drugs are those not pursued or brought to market because their total sales would prove insufficient to justify their research and development (R&D) costs. Originally, the term referred to drugs intended to treat diseases afflicting very small numbers of patients or diseases endemic in the Third World, where there are many patients but there is little purchasing power. Louis Lasagna (Univ. of Rochester) suggests that regulatory and economic developments now force consideration of a broader definition to include drugs that would have justified capital investment 20 years ago but may no longer do so.

In 1980, U.S. firms spent an estimated \$70 million to bring each new drug to market. Of 119 drugs introduced during 1967–1976, 25% had sales of almost 3 million prescriptions per year, whereas 75% averaged less than 500,000. Pharmaceutical prices have lagged behind other producer prices for at least a decade: since 1970, producer prices and industrial commodities have increased almost 150% and the medical care index has increased 120%, whereas pharmaceutical prices have risen only 55%–57%. It is estimated that it will take most new drugs more than 20 years to generate accumulated sales as large as the R&D investment cost to bring them to market.

Economic theory predicts that this scenario will reduce the rate of flow of resources into the pharmaceutical industry. Because R&D costs have been rising and drug prices declining (relatively), the percentage of sales dollars devoted to R&D fell from 10% in 1961 to 6.6% in 1978. Another indicator of trouble is diversification of effort away from human prescription drugs. A third sign of possible trouble is the decrease in number of independent firms adding drugs to the market: there were 51 such firms during 1954–1958 but only 40 during 1972–1976.

There are several disincentives for industry. Because of delays in marketing, attributable to the increased amount of time spent in pre-clinical testing, in clinical trials, in preparing a New Drug Application, and in obtaining FDA approval, and because of the speedier issuing of patents, about half of the theoretical 17-year patent protection is lost before a new drug is able to generate income. Most drugs are introduced abroad before being marketed in the United States. The time lag between satisfying the regulations of a foreign country

(1–2) Clin. Pharmacol. Ther. 31:285–289, March 1982.