

THE YEAR BOOK *of* DRUG THERAPY

(1958-1959 YEAR BOOK Series)

EDITED BY

HARRY BECKMAN, M.D.

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THE YEAR BOOK PUBLISHERS

INCORPORATED

200 EAST ILLINOIS STREET

CHICAGO 11

THE PRACTICAL MEDICINE YEAR BOOKS

This volume is one of the 15 comprising the Practical Medicine Series of Year Books founded in 1900 by G. F. Head, M.D., and C. J. Head, and published continuously since then. The complete list follows:

Medicine: *Infections*, edited by PAUL B. BEESON, M.D.; *The Chest*, by CARL MUSCHENHEIM, M.D.; *The Blood and Blood-Forming Organs*, by WILLIAM B. CASTLE, M.D.; *The Heart and Blood Vessels and Kidney*, by TINSLEY R. HARRISON, M.D.; *The Digestive System*, by FRANZ J. INGELFINGER, M.D.; *Metabolism*, by PHILIP K. BONDY, M.D.

General Surgery edited by MICHAEL E. DEBAKEY, M.D., with a section on *Anesthesia*, by STUART C. CULLEN, M.D.

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Endocrinology edited by GILBERT S. GORDAN, M.D.

Pathology and Clinical Pathology edited by WILLIAM B. WARTMAN, M.D.

Cancer edited by RANDOLPH LEE CLARK, JR., M.D., and RUSSELL W. CUMLEY, Ph.D.

Dentistry

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INTRODUCTION

Precise count is not kept of the number of journals seen and articles read in making selections for the YEAR BOOK. I do not want to know what these numbers are, as a matter of fact, for they might convict me of some sort of compulsive quirk. Suffice it to say that in the present volume there are 493 articles from 23 countries and 108 journals. Perhaps some users of the book will enjoy seeing the following partial* list of hospitals, clinics, universities and other institutions in which some of the original work, presented in brief essence herein, was done.

Aarhus Amtssygehus, Aarhus, Denmark
Albert Einstein Medical Center, Philadelphia, Pa.
A. N. Brady Hospital, Albany, N. Y.
Ashford Hospital, Middlesex, England
Baptist Memorial Hospital, Memphis, Tenn.
Battley State Hospital, Rome, Ga.
Baylor University, Houston, Texas
Bellevue Medical Center, New York, N. Y.
Beth Israel Hospital, Boston, Mass.
Birmingham Accident Hospital, Birmingham, England
Botleys Park Hospital, London, England
Bowman Gray School of Medicine, Winston-Salem, N. C.
Brooklyn Jewish Hospital, Brooklyn, N. Y.
Carlo Forlanini Institute, Rome, Italy
Cedars of Lebanon Hospital, Los Angeles, Cal.
Charing Cross Hospital, London, England
Charity Hospital of Louisiana, New Orleans, La.
Children's Hospital, Michigan & Wayne State Universities, Detroit, Mich.
City General Hospital, Sheffield, England
Cleveland Clinic, Cleveland, Ohio
College of Medical Evangelists, Loma Linda, Cal.
Columbia University, New York, N. Y.
Cook County Institutions, Chicago, Ill.
Cornell University, New York, N. Y.
County Central Hospital, Örebro, Sweden
Department of Health, New York, N. Y.
District of Columbia General Hospital, Washington, D. C.
Euclid-Glenville Hospital, Euclid, Ohio
Evans Memorial & Massachusetts Memorial Hospital, Boston, Mass.
Facultad de Med., Montevideo, Uruguay
Forest Hills Nursing & Rehabilitation Center, New York, N. Y.
Francis Delafield Hospital, New York, N. Y.
Franklin Square Hospital, Baltimore, Md.

*It is not always possible to identify precisely, from the article published in the journal, the place of origin of some investigations. Therefore, the list, of necessity, is not as complete as it might otherwise be.

Freedman's Hospital, Washington, D. C.
 Georgetown University, Washington, D. C.
 George Washington University, Washington, D. C.
 Gjøvik Fylkessykehus, Gjøvik, Norway
 Gloucestershire Royal Hospital, England
 Grand View Hospital, Sellersville, Pa.
 Grasslands Hospital, Valhalla, N. Y.
 Hahnemann Medical College, Philadelphia, Pa.
 Harlem Hospital, New York, N. Y.
 Harvard University, Boston, Mass.
 Hebrew University, Jerusalem, Israel
 High Carley Hospital, England
 Hosp. Del Rey Para Enfermedades Infecciosas, Madrid, Spain
 Howard University, Washington, D. C.
 Hudson River State Hospital, Poughkeepsie, N. Y.
 Indiana University, Indianapolis, Ind.
 Institute of Biology, Montpellier, France
 Jackson Clinic, Madison, Wis.
 Jersey City Medical Center, Jersey City, N. J.
 Jewish Hospital, Cincinnati, Ohio
 Johns Hopkins University, Baltimore, Md.
 Karolinska Sjukhuset, Stockholm, Sweden
 Kings County Hospital, Brooklyn, N. Y.
 Lebanon Hospital, New York, N. Y.
 Letterman Army Hospital, San Francisco, Cal.
 Liber-Institute of American Foundation for Tropical Medicine, Harbel,
 Liberia
 London Chest Hospital, London, England
 London Hospital, London, England
 Long Island College Hospital, Brooklyn, N. Y.
 Louisiana State University, New Orleans, La.
 Manchester Royal Infirmary, Manchester, England
 Marcy State Hospital, Marcy, N. Y.
 Marquette University, Milwaukee, Wis.
 Martin Luther University, Halle-Wittenberg, Germany
 Massachusetts Eye & Ear Infirmary, Boston, Mass.
 Massachusetts General Hospital, Boston, Mass.
 Mayo Clinic, Rochester, Minn.
 Medical College, Agra, India
 Medical College, Amritsar, India
 Medical College of Virginia, Richmond, Va.
 Medical Corps, U. S. Army
 Meharry Medical College, Memphis, Tenn.
 Montefiore Hospital, New York, N. Y.
 Montreal General Hospital, Montreal, Canada
 Montreal Hebrew Old People's Home, Montreal, Canada
 Michael Reese Hospital, Chicago, Ill.
 Middlesex Hospital, England
 Mount Sinai Hospital, New York, N. Y.
 National Cancer Institute, Bethesda, Md.
 National Institute of Allergy & Infectious Diseases, Bethesda, Md.
 National Institutes of Health, Bethesda, Md.
 National Jewish Hospital, Denver, Colo.
 Newark Beth Israel Hospital, Newark, N. J.
 New End Hospital, London, England
 New England Deaconess Hospital, Boston, Mass.
 New York Hospital, New York, N. Y.

New York Medical College, New York, N. Y.
New York Polyclinic Medical School, New York, N. Y.
New York University-Bellevue Medical Center, New York, N. Y.
New York University Post-Graduate Medical School, New York, N. Y.
Northwestern University, Chicago, Ill.
Ohio State University, Columbus, Ohio
Okayama University, Japan
Oklahoma State Penitentiary, McAlester, Okla.
Oregon State Hospital, Salem, Ore.
Otago University, Otago, New Zealand
Palo Alto Medical Clinic, Palo Alto, Cal.
Point Edward Hospital, Sydney, Nova Scotia, Canada
Postgraduate Medical School of London, England
Queens General Hospital, Jamaica, N. Y.
Rahway General Hospital, Rahway, N. J.
Report & Statistics Service Veterans Administration, Washington, D. C.
Royal Edinburgh Hospital, Edinburgh, Scotland
Royal Free Hospital, London, England
Royal Maternity & Women's Hospital, Glasgow, Scotland
Royal National Orthopaedic Hospital & Institute of Orthopaedics, London, England
Royal Victoria Hospital, Montreal, Canada
Runwell Hospital, Wickford, Essex, England
Sahlgrenska Sjukhuset, Göthenburg, Sweden
San Francisco Department of Health, San Francisco, Cal.
Saskatchewan Hospital, Weyburn, Saskatchewan, Canada
St. Anne's Maternity Hospital, Los Angeles, Cal.
St. Barnabas Medical Center, Newark, N. J.
St. Bartholomew's Hospital, London, England
St. Francis General Hospital, Pittsburgh, Pa.
St. James' Hospital, Leeds, England
St. Louis Hospital, Paris, France
St. Louis University, St. Louis, Mo.
St. Luke's Hospital, New York, N. Y.
St. Mary's Hospital, London, England
St. Peter's Hospital, Albany, N. Y.
St. Thomas's Hospital, London, England
Sefton General Hospital, Liverpool, England
Sheffield Centre, Sheffield, England
South Carolina State Hospital, Columbia, S. C.
State University of New York at Brooklyn
State University of New York at Syracuse
Sylhet Medical School, East Pakistan
Syracuse University, Syracuse, N. Y.
Temple University, Philadelphia, Pa.
Topeka State Hospital, Topeka, Kan.
Tufts University, Boston, Mass.
United Birmingham Hospitals, Birmingham, England
University Department of Clinical Medicine, London, England
U. S. Naval Hospital, Great Lakes, Ill.
U. S. Naval Hospital, Jacksonville, Fla.
U. S. Naval Hospital, Portsmouth, Va.
U. S. Naval Hospital, St. Albans, N. Y.
U. S. Naval Training Center, Bainbridge, Md.
University of Alabama, Birmingham, Ala.
University of Basel, Basel, Switzerland
University of Birmingham, Birmingham, England

University of Buffalo, Buffalo, N. Y.
 University of California, San Francisco, Cal.
 University of Chicago, Chicago, Ill.
 University of Cincinnati, Cincinnati, Ohio
 University of Colorado, Denver, Colorado
 University of Durham, Durham, England
 University of Edinburgh, Edinburgh, Scotland
 University of Frankfurt, Frankfurt, Germany
 University of Geneva, Geneva, Switzerland
 University of Glasgow, Glasgow, Scotland
 University of Gothenburg, Gothenburg, Sweden
 University of Guadalajara, Jalisco, Mexico
 University of Helsinki, Helsinki, Finland
 University of Illinois, Chicago, Ill.
 University of Iowa, Iowa City, Iowa
 University of Kansas, Kansas City, Kan.
 University of Malaya
 University of Maryland, Baltimore, Md.
 University of Melbourne, Melbourne, Australia
 University of Miami, Miami, Fla.
 University of Michigan, Ann Arbor, Mich.
 University of Minnesota, Minneapolis, Minn.
 University of North Carolina, Chapel Hill, N. C.,
 University of Oxford, Oxford, England
 University of Pennsylvania, Philadelphia, Pa.
 University of Puerto Rico, San Juan, Puerto Rico
 University of Rochester, Rochester, N. Y.
 University of Rome, Rome, Italy
 University of St. Andrews, St. Andrews, Scotland
 University of Sheffield, Sheffield, England
 University of South Dakota, Vermillion, S. Dak.
 University of Southern California, Los Angeles, Cal.
 University of Texas, Galveston, Texas
 University of Tennessee, Memphis, Tenn.
 University of Wisconsin, Madison, Wis.
 Vanderbilt University, Nashville, Tenn.
 Veterans Administration Hospital, Brooklyn, N. Y.
 Veterans Administration Hospital, Coral Gables, Fla.
 Veterans Administration Hospital, Fort Howard, Md.
 Veterans Administration Hospital, Phoenix, Ariz.
 Veterans Administration Hospital, Oakland, Cal.
 Veterans Administration Hospital, Palo Alto, Cal.
 Veterans Administration Hospital, Oteen, N. C.
 Veterans Administration Hospital, Sunmount, N. Y.
 Veterans Administration Hospital, New York, N. Y.
 Veterans Administration Hospital, West Haven, Conn
 Victoria Infirmary, Glasgow, Scotland
 Wadsworth Hospital, Los Angeles, Cal.
 Wake Forest College, Winston-Salem, N. C.
 Walter Reed Army Hospital, Washington, D. C.
 Washington University, St. Louis, Mo.
 Wellcome Laboratory Tropical Medicine, London, England
 West London Hospital, London, England
 Western Pennsylvania Hospital, Pittsburgh, Pa.
 Western Reserve University, Cleveland, Ohio
 Yale University, New Haven, Conn

ALLERGIC DISORDERS

Hydroxyzine (Atarax®) in Chronic Urticaria and in Allergic Manifestations: Clinical Observations in Man and Experimental Studies on Asthma in Guinea Pigs Produced by Several Agents. Alan R. Feinberg, Jacob J. Pruzansky, Samuel M. Feinberg and Eimer W. Fisherman¹ (Northwestern Univ.) tried Atarax in 60 patients with various allergic manifestations. Treatment was usually started with 10 mg. 3 times a day. In the absence of appreciable relief, this was often increased to 25 mg. 3 or 4 times daily. If results were obtained with 10 mg., lowering of the dose was attempted to determine the minimum necessary for relief.

Most striking results were seen in patients with chronic idiopathic urticaria. Of 17 patients, 15 obtained complete relief and 2 had fair to good relief. There were no complete failures. In several patients, however, relief lasted only a few weeks, then the drug appeared to lose its effectiveness. A number of the patients who maintained relief were able to take 10 mg. as seldom as every 24-72 hours. In some patients with chronic urticaria, Pyribenzamine® gave good relief from itching but not so much from swellings; however, the effect of each dose lasted only 4-6 hours. In contrast to chronic urticaria patients, only 1 of 4 with acute urticaria had significant relief. One who failed to obtain relief had a serum sickness type of urticaria from penicillin. Of 13 patients with asthma, 7 had fair to good relief and no effect was noted in 6. Better results were obtained in patients with dermatographism: 1 had excellent relief and 2 had good relief. One patient with a physical hypersensitivity to cold, who had had only slight relief with antihistamines, obtained excellent results with Atarax. In no case in which good therapeutic results were obtained was it necessary to discontinue this drug because of side effects.

Indirect evidence points to the possibility that there is a mediating mechanism in chronic urticaria besides the possible ones of histamine, acetylcholine or serotonin. Experimental studies in the guinea pig indicate that Atarax is a

(1) J. Allergy 29:358-361, July, 1958.

long-acting, potent, antianaphylactic, antihistamine, anti-serotonin and antiacetylcholine agent. Most other tranquilizing or antihistamine drugs have only part or none of these effects.

Treatment of Eosinophilic Lung (Tropical Eosinophilia) with Diethylcarbamazine (Hetrazan®) was studied by T. J. Danaraj² (Univ. of Malaya) in 110 patients. The salient features that distinguished eosinophilic lung from other respiratory disorders associated with eosinophilia were massive eosinophilic leukocytosis (over 3,000 eosinophils/cu. mm.), shadows in the chest x-rays and elevated erythrocyte sedimentation rate. Most patients were ill under 6 months.

The dosage of diethylcarbamazine was initially 4 mg./kg. body weight 3 times daily for 4 days. Later, 2 larger dosages were tried: 6 mg. and 10 mg./kg. body weight given thrice daily for 5 days to groups of 57 and 7 patients respectively. Average total adult dose for each of the 3 schedules was 3,200, 6,000, and 10,000 mg. respectively. The drug was given after meals in 50-mg. tablets, the syrup being used for children. Except for 11 who exhibited severe bronchial spasm and were treated with antispasmodics as well, the patients were given only diethylcarbamazine.

The patients were observed 2-4 weeks before treatment began, and up to 14 months thereafter to note any recurrence of symptoms or rise in the eosinophil count. Improvement in symptoms was noted in 107 patients 2-4 days after beginning treatment, while the drug was still being taken, and progressed steadily until, by the end of the 1st week, 59 had complete relief and 48 a residual cough only. Coincident with symptomatic improvement was a general clearing of abnormal lung signs and in most the lungs were clear by the 7th day after start of treatment.

In 98 patients, the leukocyte count showed a marked decrease in eosinophils on the 3d day of treatment; in 12, an increase was noted on the 3d day, followed by a similar rapid decrease, which was apparent on the 5th day.

The erythrocyte sedimentation rate reverted to normal in 19 patients 1 week after completing the diethylcarbamazine course and in 22, 2 weeks later. Although the rates in the other patients were still abnormal, they had decreased from

(2) Quart. J. Med. 27:243-263, April, 1958.

their original high levels and over the period of observation continued to decrease, becoming normal in a further 33; in 25, they were still above normal at the end of the observation period

Chest x-rays taken 1 week after end of treatment showed distinct improvement in 109 patients in that the striations became less prominent and the pulmonary mottling cleared. Mild toxic effects, which did not require reducing the dosage or discontinuing the treatment, were noted in 12 patients.

The eosinophil response did not vary with the 3 dosage schedules used, a satisfactory decrease in circulating eosinophils occurring with all dosages. Based on this study, the dosage recommended is 6 mg./kg. body weight 3 times a day for 5 days.

► [This is an important contribution since it apparently establishes Hetrazan as less toxic and quite as effective as the organic arsenicals in this disease, which was established as a clinical entity in the tropical Far East about 20 years ago. Most patients improve steadily under arsenotherapy, but some experience exacerbations after the initial treatment, a fairly high proportion suffer relapses (reinfections?), the therapeutic regimen is necessarily a protracted one, and arsenical encephalopathy is a much-feared reaction, in East Indians particularly.—Ed.]

Clinical Evaluation of New Long-Acting Preparation in Allergic Disorders. The antihistamines available until now have been limited by the severity of the side reactions, particularly depression of the central nervous system, drowsiness and short duration of action. Sandostene Spacetabs® is a new long-acting antiallergic drug with chemical structure that differs from most histamine antagonists. It has potent antihistaminic, anticholinergic and antipermeability activity, and local anesthetic properties. This drug is especially effective in allergic dermatitis.

Jerome Miller³ (Temple Univ.) gave Sandostene Spacetabs to 185 patients (63 males, 122 females) aged 9 months to 73 years. They were observed over 3 months, including the grass hay-fever season, and were seen at least once weekly. Each patient was to take or be given 1 tablet in the morning and 1 in the evening, and the dose was adjusted when necessary according to response and, in children, according to age. Of the 185 patients, 150 (81%) benefited and 63% obtained pronounced relief; results were unsatisfactory in only 35 (19%). The therapeutic response was reported as occurring

(3) *Ann. Allergy* 16:135-142, Mar.-Apr., 1958.

within at least 30 minutes. Seasonal and perennial hay-fever groups responded especially well, with excellent results in 81 (84.4%). The antipruritic effect was particularly helpful in those with marked itching of the eyes, ears, nose and roof of the mouth. Rhinorrhea and sneezing were modified and nasal blocking was lessened. Of 29 patients with bronchial asthma, 19 (65.5%) were favorably influenced, regardless of cause. Dyspnea and wheezing were abolished. Side effects were reported by 42 patients, but most were so slight and transient that they were no problem; many subsided while medication was continued. In only 5 patients was drowsiness severe enough to require discontinuance of therapy and in only 2 was dryness of the mouth of such severity.

Proper management of allergies calls for removal of the offending allergen from the diet or the environment. If impossible, specific hyposensitization is indicated. When these measures fail, other methods must be used. Sandostene Spacetabs is the most effective agent presently available for symptomatic treatment of allergies.

► [It is entertaining that L. LaMantia *et al.* (Ann. Allergy 5:506, 1957) found Sandostene relatively ineffective but Sandostene with calcium quite effective and well tolerated in treatment of chronic asthma; best results were achieved in elderly patients with complicating cardiac dysfunction.

D. A. Adams and S. Perry have described (J.A.M.A. 167:1207, July 5, 1958) 3 cases of agranulocytosis that occurred in patients who were taking Sandostene.—Ed.]

Prevention of Nonhemolytic Blood Transfusion Reactions with Antihistamine, Chlorpheniramine: Report of 6,131 Cases is presented by Frederick M. Offenkrantz and George Babcock, Jr.⁴ (Rahway, N. J., Gen'l Hosp.). In a control series of 3,346 patients, there were 47 allergic reactions, 100 pyrogenic, 21 combined allergic and pyrogenic, and 1 hemolytic reaction. In 2,785 patients in whom 10 mg. chlorpheniramine maleate (Chlor-Trimeton® maleate) was added to the blood before transfusion, there were 2 allergic reactions, 15 pyrogenic, 1 combined reaction and 1 hemolytic. For multiple transfusions, 10 mg. was added every 6 hours. Allergic reactions were thus reduced from 1.40% to 0.07% pyrogenic from 3.01% to 0.54% and combined allergic and pyrogenic reactions from 0.60% to 0.03%. Incidence of hemolytic reactions was 0.03% in both groups.

There were no undesirable sequelae attributable to the an-

(4) A.M.A. Arch. Surg. 76:379-383, March, 1958.