THE YEAR BOOK *of* MEDICINE

1971

THE YEAR BOOK *of* MEDICINE 1971

EDITED BY

DAVID E. ROGERS, M.D.

CARL MUSCHENHEIM, M.D.

PAUL HELLER, M.D.

T. JOSEPH REEVES, M.D.

NORTON J. GREENBERGER, M.D.

PHILIP K. BONDY, M.D.

FRANKLIN H. EPSTEIN, M.D.

YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

35 EAST WACKER DRIVE CHICAGO

THE PRACTICAL MEDICINE YEAR BOOKS

Medicine: DAVID E. ROGERS, M.D.; CARL MUSCHENHEIM, M.D.; PAUL HELLER, M.D.; T. JOSEPH REEVES, M.D.; NORTON J. GREENBERGER, M.D.; PHILIP K. BONDY, M.D.; FRANKLIN H. EPSTEIN, M.D.

Surgery: SEYMOUR I. SCHWARTZ, M.D.; JOHN S. NAJARIAN, M.D.; ERLE E. PEACOCK, JR., M.D.; G. TOM SHIRES, M.D.; WILLIAM SILEN, M.D.; FRANK C. SPENCER, M.D.

Anesthesia: JAMES E. ECKENHOFF, M.D.

Drug Therapy: DALE G. FRIEND, M.D.

Obstetrics & Gynecology: J. P. GREENHILL, M.D.

Pediatrics: SYDNEY S. GELLIS, M.D.

Radiology: WALTER M. WHITEHOUSE, M.D.; HOWARD B. LATOURETTE, M.D.

Ophthalmology: WILLIAM F. HUGHES, M.D.

Ear, Nose & Throat: JOHN A. KIRCHNER, M.D.

Neurology & Neurosurgery: RUSSELL N. DE JONG, M.D.; OSCAR SUGAR, M.D.

Psychiatry & Applied Mental Health: FRANCIS J. BRACELAND, DOUGLAS D. BOND, M.D.; M.D.; DANIEL X. FREEDMAN, M.D.; ARNOLD J. FRIEDHOFF, M.D.; LAWRENCE C. KOLB, M.D.; REGINALD S. LOURIE, M.D.

Dermatology: FREDERICK D. MALKINSON, M.D.; RODGER W. PEARSON, M.D.

Urology: JOHN T. GRAYHACK, M.D.

Orthopedics & Traumatic Surgery: H. HERMAN YOUNG, M.D.

Plastic & Reconstructive Surgery: NEAL OWENS, M.D.; KATHRYN STEPHENSON, M.D.

Endocrinology: THEODORE B. SCHWARTZ, M.D.

Pathology & Clinical Pathology: WILLIAM B. WARTMAN, M.D.

Nuclear Medicine: JAMES L. QUINN, III, M.D.

Cancer: RANDOLPH LEE CLARK, M.D.; RUSSELL W. CUMLEY, Ph.D.

Cardiovascular Medicine & Surgery: EUGENE BRAUNWALD, M.D.; W. PROCTOR HARVEY, M.D.; JOHN W. KIRKLIN, M.D.; ALEXANDER S. NADAS, M.D.; OGLESBY PAUL, M.D.; ROBERT W. WILKINS, M.D.; IRVING S. WRIGHT, M.D.

Printed in U.S.A.

Library of Congress Catalog Card Number: CD 38-25

DEPARTMENTS *of the* YEAR BOOK *of* MEDICINE

Infections

DAVID E. ROGERS, M.D.

Professor of Medicine, Vice President and Dean, The Johns Hopkins University School of Medicine; Medical Director, The Johns Hopkins Hospital, Baltimore, Md.

The Chest

CARL MUSCHENHEIM, M.D.

Clinical Professor of Medicine, Cornell University Medical College, New York, N.Y.

The Blood and Blood-Forming Organs

PAUL HELLER, M.D.

Senior Medical Investigator, Veterans Administration West Side Hospital; Chief, Hematology Section, Department of Medicine, and Professor of Medicine, University of Illinois, Abraham Lincoln School of Medicine, Chicago

The Heart and Blood Vessels

T. JOSEPH REEVES, M.D.

Professor and Chairman, Department of Medicine, and Associate Professor of Physiology, University of Alabama in Birmingham, School of Medicine

The Digestive System

NORTON J. GREENBERGER, M.D.

Professor of Medicine and Director, Division of Gastroenterology, Ohio State University College of Medicine

Metabolism

PHILIP K. BONDY, M.D.

C. N. H. Long Professor of Medicine and Chairman of the Department of Internal Medicine, Yale University School of Medicine; Physician-in-Chief, Yale-New Haven Hospital

Kidney, Water and Electrolytes

FRANKLIN H. EPSTEIN, M.D.

Professor of Medicine, Yale University School of Medicine

There are twenty YEAR BOOKS in various fields of medicine and one in dentistry. Publication of these annual volumes has been continuous since 1900. The YEAR BOOKS make available in detailed abstract form the working essence of the cream of recent international medicoscientific literature. Selection of the material is made by distinguished editors who critically review each year more than 500,000 articles published in the world's foremost journals.

TABLE OF CONTENTS

The material covered in this volume represents literature reviewed up to April, 1971.

PART I

INFECTIONS

PART II

THE CHEST

PART III

THE BLOOD AND BLOOD-FORMING ORGANS

PART IV

THE HEART AND BLOOD VESSELS

INFECTIONS

DAVID E. ROGERS, M.D.

INTRODUCTION

Again, it has been a good re-education to put the YEAR BOOK "to bed." The world of biomedical research and clinical research and the practice of medicine remain just as stimulating and challenging as ever.

I have, as I did last year, relied heavily on my friend, associate and keeper, Dr. M. Glenn Koenig, in selecting articles for this year's YEAR BOOK. He is closer to the bedside than I am, but he keeps me on my intellectual and clinical toes. However, I have explained to him that anything that is good about the section I will take credit for, and any omissions or errors of fact or judgment I will cheerfully blame on him. A splendid example of the democracy in academe!

DAVID E. ROGERS

PART I

INFECTIONS

SUGGESTIVE NEW ETIOLOGIC RELATIONSHIPS

Possible Role of Mycoplasma Fermentans in Pathogenesis of Rheumatoid Arthritis. The inflamed joint in rheumatoid arthritis is the site of an active immunologic process. The factors causing the change in host IgG that provokes antiglobulin formation have not been identified. Mycoplasma fermentans was previously found in 31 of 79 synovial fluids from rheumatoid arthritic patients and in 3 of 37 from subjects without rheumatoid arthritis. Usual serologic tests for mycoplasma antibodies did not clearly differentiate rheumatoid arthritic patients from control subjects.

M. H. Williams, Jonathan Brostoff and I. M. Roitt[1] (Middlesex Hosp. Med. School, London) studied 43 patients with established rheumatoid arthritis, 19 with osteoarthritis and 21 healthy control subjects. Mycoplasma antigens were prepared, and preparation of antiglobulins was done in rabbits using antigen in complete Freund's adjuvant. The passive hemagglutination test was carried out. Leukocyte migration was estimated, and the indirect macrophage migration test was performed.

The leukocyte migration inhibition test in the presence of M. fermentans membrane preparations at a protein concentration of 0.5 mg./ml. was unequivocally positive in 67% of the patients with seropositive rheumatoid arthritis. No positive reactions were noted in the osteoarthritic patients or normal subjects. Positive results persisted over a 6-month period. Three of twelve indirect tests for the production of migration inhibitory factor were positive, and one gave a borderline result.

Mycoplasma fermentans appeared to take up IgG from the medium and bind it firmly to or into its membrane. Urea treatment greatly reduced the ability of mycoplasma membranes to sensitize red blood cells to hyperimmune rabbit antiserum. Studies with isolated rheumatoid factors gave evidence that rabbit antiserums reacted with IgG. Urea treatment of the membranes released IgG reactant into the supernatant.

The leukocyte migration inhibition test clearly differentiates patients with seropositive rheumatoid arthritis from healthy subjects and those with osteoarthritis. The test appears to be indicative of a state of cell-mediated (delayed-type) hypersensitivity.

It seems that patients with rheumatoid arthritis uniquely exhibit hypersensitivity to the antigens of M. fermentans, an organism recovered with some regularity from the joints of affected persons. Sensitivity appears to be directed against membrane components other than

(1) Lancet 2:277-280, Aug. 8, 1970.

bound IgG. The membrane immunoglobulin, however, is clearly modified in structure in the sense that it can react readily with rheumatoid factor and might therefore be the stimulus for production of the antiglobulin factors that are a prominent feature of the disease and which may contribute to the inflammatory changes occurring in synovial effusions.

Gold salts and antimalarial drugs strongly inhibit the growth of M. fermentans. The findings provide encouragement for new chemotherapeutic approaches to rheumatoid arthritis.

► [This is an interesting way of approaching the question of what is the relationship of mycoplasma to rheumatoid arthritis. Many have been intrigued with the possible role of mycoplasma in this disease because of their striking propensity to cause arthritis in animals. Sharp and Riggs have noted that of 17 known mycoplasma infections in animals, 13 are associated with arthritis (Mycoplasmas and Rheumatic Disease, Rheumatologie 1:51, 1967).

Although some have reported that inhibition of leukocyte migration does not necessarily measure classic tuberculin-type delayed hypersensitivity, most believe that it does, and it is obvious from the results reported here that it measures something that is characteristic of patients with rheumatoid arthritis. If these results are confirmed and mycoplasma are consistently shown to be present in the synovial tissues of patients with rheumatoid arthritis, the question of what do they mean will remain. Are they responsible for, or secondary to, the inflammatory changes that are characteristic of this disease? For a nice discussion of the problem, see the article by Smith, C. B., and Ward, J. R. (Chronic Infectious Arthritis· Role of Mycoplasmas, J. Infect. Dis. 123:313, 1971).

For another "difference" in rheumatoid synovial cells, see the following article. – Ed.]

Rubella Infection of Synovial Cells and Resistance of Cells Derived from Patients with Rheumatoid Arthritis. Rubella infection commonly causes an acute but limited polyarthritis in man. Arthur I. Grayzel and Carolyn Beck[2] (Montefiore Hosp., New York) studied the effects of rubella virus on monolayer cultures of cells from explants of human synovial membranes.

METHOD. – Synovial biopsies were taken from patients with definite or classic rheumatoid arthritis who were having reconstructive surgery and from those with chronic synovitis of known cause or without inflammatory disease. Confluent monolayers of fibroblasts were grown from synovial membrane explants in modified Eagle's medium with added calf serum. Strain F-8 rubella virus was used to infect synovial cultures. Virus was titered by the hemadsorption-negative particle assay using a strain of human pleural fibroblasts. Interferon was induced in nonrheumatoid synovial cells using the synthetic polynucleotide poly I:C, and was detected by challenging Vero cells with rubella or synovial cells with vesicular stomatitis virus.

Cells from explants of synovial membranes in all 28 nonrheumatoid conditions showed marked cytopathic effects at 12-14 days, whereas none of the 21 rheumatoid synovial membranes were visibly affected even after several subcultures. Infectious rubella virus could be recovered from nonrheumatoid cultures, in titers of $0.5\text{-}1\times10^6$ hemadsorption-negative particles per ml. No virus was found in Vero cells or by hemadsorption-negative assay in rheumatoid cultures. Human convalescent antiserums known to contain neutralizing antibody against rubella prevented cytopathic effects in nonrheumatoid cells. Interferon played no role in protecting the rheumatoid cells. Rubella virus could not be recovered from lysates of infected rheumatoid cells 2, 10 or 28 days after infection.

---

(2) J. Exper. Med. 131:367-375, February, 1970.

Rubella virus can infect nonrheumatoid synovial cells. The findings increase the likelihood that rubella synovitis represents viral multiplication within synovial cells rather than a secondary immune response. The possibility that resistance of rheumatoid cells may reflect the acquisition of genetic information through a latent or defective virus rather than some change in metabolic or immune function as a result of the disease is raised.

► [These are clear-cut results. The authors could not show that the resistance of rheumatoid synovial cells was interferon mediated; indeed, rheumatoid cells have proved poor producers of interferon. That this resistance may be more general is suggested by similar findings by Smith and Hamerman using Newcastle disease virus (Arthritis & Rheumat., 1971). The explanation that most readily enters my simple mind is that the cells are already infected (mycoplasma?) and thus resistant to secondary infection. – Ed.]

Sarcoidosis, Another Disease Associated with Serologic Evidence for Herpes-Like Virus Infection. Serologic data have associated herpes-like virus (HLV) with Burkitt's lymphoma, carcinoma of the posterior nasal space and infectious mononucleosis. Yashar Hirshaut, Philip Glade, Luiz Octavio B.D. Vieíra, Eugene Ainbender, Bozena Dvorak and Louis E. Siltzbach[3] identified a fourth disease, sarcoidosis, associated with antibody to HLV. Serums were taken from patients with characteristic clinical and biopsy specimen features of sarcoidosis, including a positive Kveim test. Anti-HLV antibody was determined by immunofluorescence, using a culture of the Jijoye cell line as a source of antigen and fluorescein-conjugated goat antihuman IgG. Leukocyte cultures were prepared, and immunoglobulins were quantitated by the single radial diffusion technic.

All 131 sarcoidosis patients studied had detectable serum anti-HLV antibody at a dilution of 1:10 or higher (table). The prevalence in 93 normal adults was 76%. Titers of 1:640 or higher were found in 79% of the patients and 24% of the healthy subjects. Patients with chronic disease had a 77% prevalence of high titers, compared with 46% for those with subacute disease and 81% for those with inactive disease. Immunoglobulins were elevated in 74% of 125 serums from patients. No striking correlation with anti-HLV titers was found, but anti-HLV titers of 1:640 or above were more prevalent with high IgG levels.

Three of 12 attempts to isolate long-term lymphoid cell cultures from patients with sarcoidosis were successful. Two lines were isolated from patients with chronic disease and one, from a patient with subacute illness. Only the latter lymphoid cell line harbored HLV on immunoflu-

ANTI-HERPES-LIKE VIRUS ANTIBODY IN NORMAL SUBJECTS AND IN PATIENTS WITH SARCOIDOSIS

DIAGNOSIS	NO. OF SUBJECTS TESTED	NO. WITH DETECTABLE* ANTIBODY	% WITH DETECTABLE ANTIBODY	NO. OF TITERS ≥ 1:640	% OF POSITIVE TITERS ≥ 1:640
Normal	93	71	76	17	24
Sarcoidosis	131	131	100	103	79

*At dilution of 1:10.

(3) New England J. Med. 283:502-506, Sept. 3, 1970.

orescence and electron microscopy. Lymphoid suspension cultures could not be established from the peripheral blood of any of 25 normal subjects.

The diseases associated with HLV may increase susceptibility to HLV infection. Herpes-like virus may produce a benign or undetected latent primary infection, which is reactivated by stress. It is also possible that the disease stimulates the entire humoral antibody mechanism in a relatively nonspecific manner. Earlier conclusions on the pathogenic nature of HLV must be viewed with caution. The unequivocal assignment of HLV to a candidate disease ultimately depends on the induction of the disease in a suitable animal host with the use of purified, infectious HLV.

► [This says it well. Thus, there now appear to be four diseases (infectious mononucleosis, Burkitt lymphoma, carcinoma of the posterior nasal space and sarcoid) associated with serologic evidence of HLV infection. Infectious mononucleosis now seems closely linked to EBV infection. The high anti-HLV antibody titers in sarcoid, Burkitt lymphoma and carcinoma of the posterior nasal space may, in part, reflect enhanced antibody responsiveness in these diseases rather than intensity of viral infection per se.—Ed.]

↓ Here's a new "disease of technical progress" (DOTP). The following editorial suggests that we may see it in consumers; the article by Belin *et al.* indicates that it has been.—Ed.

Sensitization to Enzymes in Detergents is discussed by Lawrence M. Lichtenstein, I. Leonard Bernstein, Francis C. Lowell, Jordan N. Fink, David A. Levy, Solbert Permutt, Raymond G. Slavin, Sidney Leskowitz, Merrill W. Chase and Jerry Dolovich.[4] Enzymes, proteinaceous extracts of Bacillus subtilis, have been added to household laundry detergents in the United States since 1967. The products are presently supplied as dust-producing powders; some manufacturers recently began supplying enzyme in a beaded form to reduce dust exposure. Exposed workers have acquired sensitization and respiratory disease. As many as half of highly exposed workers appear to become sensitized to B. subtilis proteins. There is dyspnea with wheezing and fatigue, and with high exposure an attack resembling acute asthma may occur. Typically episodes start at night after a day's work. Malaise is prominent but fever is rare. Symptoms may take months to clear when exposure ceases. Eosinophilia of 5-15% is seen. Lung function tests have most often shown obstructive changes; diffusion defects may also occur. Changes in air flow and carbon monoxide transfer have lasted for over a year in persons moved to areas of "low" exposure. Patients invariably have immediate wheal-and-flare reactions when challenged with appropriate skin tests.

The pathogenesis of the condition is unclear. It has been termed an "allergic alveolitis." In sensitized persons, the exposure needed to elicit disease typically encompasses a wide range. Consumers are being exposed to this material daily. It is expected that consumers will become sensitized in the course of normal home use of enzyme-containing detergents. These facts warrant careful attention by physicians, the detergent industry and federal regulatory agencies.

► [The disturbing feature is the persistence of obstructive and diffusion defect changes after removal from exposure. For a report on the disease as seen in factory workers, see the article by Franz, T., McMurrain, K. D., Brooks, S., and Bernstein, L. (Clinical, Immunologic

---

(4) J. Allergy 47:53-55, January, 1971.

and Physiologic Observations in Factory Workers Exposed to B. Subtilis Enzyme Dust, J. Allergy 47:170, 1971).—Ed.]

Enzyme Sensitization in Consumers of Enzyme-Containing Washing Powder. The immunogenic potency of inhaled enzyme powders became more apparent when washing powders containing proteolytic enzyme obtained by cultivation of Bacillus subtilis were marketed. A fairly high frequency of respiratory disturbances has been found in workers producing these washing powders, and skin and provocative tests have indicated that immunologic mechanisms are involved. L. Belin, E. Falsen, J. Hoborn and J. André[5] (Univ. of Göteborg) studied 3 users of an enzyme-containing washing powder (Alcalase) who had respiratory complaints. Analysis was made of the Alcalase dry powder, and antiserum was produced in a rabbit.

Woman, 44, with no personal or family history of allergy, had had periods of cough after colds for several years, accompanied by tightness in the chest. Violent coughing attacks occurred with slight wheezing after the patient switched to using Alcalase. She became worse when she did the laundry. The symptoms subsided when another powder was used, and the patient has been free from symptoms for over 6 months during which she has used simple detergent washing powder. She recalled having a violent attack after visiting friends who lived in a trailer where the Alcalase had just been used. Spirometry was normal and circulating eosinophils were 4%. Skin tests with standard allergens were negative.

These female domestic users had local atopic-type reactions to Alcalase washing powder. Prick tests resulted in immediate skin reactions to test enzyme solutions. Circulating IgE antibodies to the enzyme were demonstrated. Immunization studies in a rabbit indicated that the allergen is immunogenic and identical with the main active fractions obtained by gel filtration and electrophoresis. The danger of sensitization to enzyme-containing washing powders is apparently not restricted to workers manufacturing the powders, but may arise in consumers in situations where the enzymes may be present as dust particles.

► [Unfortunately, the article does not indicate whether defects persisted in the 3 patients. It does provide unequivocal evidence of sensitization to the enzyme.—Ed.]

EPIDEMIOLOGY OF INTRAHOSPITAL INFECTIONS

► It is quite apparent that hospital-acquired infections, particularly those caused by gram-negative bacilli, pose a tough problem for our hospitalized patients. Required reading in this area is a recent article by David. S. Feingold (New England J. Med. 283:1384, 1970), in which he reviews the problem, discusses preventive measures and offers some intriguing approaches which might be used to deal with prevention and treatment of nosocomial infections in the future.

This chapter and the one that follows deal with two important facets of the hospital infection problem: epidemiology and source of infection.—Ed.

Antibiotic Usage in Seven Community Hospitals located throughout the United States was studied by William E. Schreckler and John V. Bennett[6] (Nat'l Communicable Dis. Center, Atlanta, Ga.). A total of 24 prevalence studies was done in these hospitals during 1967-69 to de-

(5) Lancet 2:1153-1157, Dec. 5, 1970.
(6) J.A.M.A. 213:264-267, July 13, 1970.

ANTIBIOTIC USAGE AND RECORDED EVIDENCE OF INFECTIONS BY HOSPITAL SERVICE*

Service	No. Patients Studied	Patients Receiving Antibiotics			Of Those Receiving Antibiotics, % With Any Clinical Infection	
		No.	% Overall	% Range†	% Overall	% Range†
Medicine	534	127	24	18-32	51	30-81
General surgery	449	170	38	20-63	32	0-70
Orthopedics	109	43	39	21-68	30	0-60
Urology	30	26	87	75-100	42	0-100
Gynecology	88	28	32	13-50	7	0.100
Obstetrics	108	14	13	0-24	0	0
Newborn	137	4	3	0-14	0	0
Pediatrics	82	42	51	0-88	64	0-75
Total	1,537	454	29.5	20-44	38	25-76

*Includes seven community hospitals, January through June, 1969.
†Range among individual hospitals.

termine presence of active nosocomial infections and the antibiotics in use at the time. Charts of 95% of patients in the hospital were usually available for review. All institutions are acute-care general hospitals with 190-350 beds.

Of 5,256 patients whose charts were reviewed, 30.6% were receiving 2,094 antibiotics, for an average of 1.3 per treated patient. About 4 of every 5 patients were receiving a single agent. There was a wide range of usage in the same hospital at different times and among the different hospitals. The most commonly used antibiotics were ampicillin, tetracycline and penicillin, comprising about half of all those given. The next most commonly used agents were sulfonamides and cephalosporins. During the study, there was a relative decrease in use of penicillin, streptomycin and chloramphenicol and increase in use of cephalosporins and ampicillin. A marked drop in use of chloramphenicol was noted at each hospital.

The differences in usage by service with regard to definite evidence of infection were striking (table). Antibiotic usage was greatest in surgical patients without evidence of definite infection. Of the patients receiving antibiotics, 62% had no definite evidence of any infection. Fewer than 30% of the patients given penicillin, sulfonamides, methicillin or streptomycin had evidence of infection. Two of the 5 patients given chloramphenicol in 1969 did not have documented evidence of infection.

These data may serve as a baseline for comparisons to be made by hospital infection committees in fulfilling their obligations to patients and their hospital communities.

► [It is startling to realize that 31% of hospitalized patients receive antimicrobials. It is even more startling and disturbing to find out that 62% of patients receiving these drugs had no definite evidence of infection as judged by information available in their charts. All hospitals should probably collect such data. This might lead to better physician education and more rational use of antibiotics. Though not definitely proved, many infectious disease specialists feel that antimicrobial overuse has been one of the factors contributing to our intrahospital infection problem.

Another nice article dealing with nosocomial infection and antibiotic usage was published by Adler and Shulman (South. M. J. 63:102, 1970).—Ed.]

↓ The following article compares the recent incidence and pattern of infection seen on a surgical service with that observed in 1957.—Ed.