

THE YEAR BOOK *of* MEDICINE

(1961-1962 YEAR BOOK *Series*)

EDITED BY

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YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

200 EAST ILLINOIS STREET • CHICAGO 11

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THE PRACTICAL MEDICINE YEAR BOOKS

► There are fifteen YEAR BOOKS in various fields of medicine and one in dentistry. Publication of these annual volumes has been continuous since the first one appeared in 1900. The YEAR BOOKS make available in detailed abstract form the working essence of the cream of recent international medicoscientific literature. Selection of this material on vital advances in clinical management and research is made by distinguished editors who critically review each year more than 120,000 articles published in the world's foremost journals. The source of each abstract is included, and all volumes are indexed, by subject and author. The YEAR BOOKS and their editors are:

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The Digestive System

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INFECTIONS



PAUL B. BEESON, M.D.

INFECTIOUS DISEASES, 1950-1960

ANTIMICROBIAL THERAPY

In the fifties we were not quite able to match the spectacular developments in antimicrobial therapy seen in the thirties (sulfonamides) or the forties (penicillin, streptomycin, chlortetracycline and chloramphenicol). Nevertheless, we can record two important additions to our catalogue of antimicrobial agents: *amphotericin B*, the first really effective agent for treatment of systemic mycoses, and *isoniazid*, a significant advance in the management of tuberculosis. There was, of course, a continuing vast effort directed toward discovery and testing of new antimicrobial agents, but nearly all of them proved either ineffective clinically or too toxic. Certain preparations had some usefulness and deserve mention. *Erythromycin* is comparatively nontoxic and is effective in infections due to gram-positive cocci, but the chief defect lies in the readiness with which most pathogens become resistant to it. *Tetracycline*, a modification of chlortetracycline and oxytetracycline, appears to be an improvement, being just as effective and somewhat better tolerated. *Novobiocin* is effective against the same bacteria as penicillin but is only indicated when penicillin resistance is encountered. Its principal defect is frequent provocation of allergic manifestations (fever and skin eruption). *Vancomycin*, *Kanamycin* and *Ristocetin* were all introduced for use in infections caused by penicillin-resistant staphylococci. Beneficial clinical results were obtained, but these drugs cause serious toxic side effects and are likely to have little use in the future. The recent partial synthesis of a new penicillin, known in this country by the trade name *Staphicillin*, appears to have provided us with the best treatment for infections due to penicillin-resistant staphylococci. *Griseofulvin* should be mentioned also for its effectiveness in treatment of superficial fungus infections.

Interest in the phenomena of *antibiotic synergism and antagonism* has slackened. Indubitably there is a synergistic action of penicillin and streptomycin in enterococcal infections, and there are situations where use of a second antibiotic helps to delay the development of bacterial resistance to an agent of primary value; for example, the adjunctive use of tetracycline delays streptomycin-resistance in infections of the urinary tract. Antibiotic antagonism, although easily demonstrable in laboratory experiments, can rarely if ever be discerned as antibiotics are used clinically, perhaps because of the excessive doses of antimicrobial compounds given.

The *emergence of resistant bacterial populations as a result of widespread clinical use of antimicrobial agents* has raised certain serious problems. Most notable is the situation resulting from penicil-

lin treatment of staphylococcal infections. Since 1943 there has been a steady increase in prevalence of penicillin-resistant staphylococci, due to the gradual selection of penicillinase producers. These organisms first began to be encountered frequently in hospital patients and personnel but are now often carried by healthy members of all communities where penicillin treatment has been extensive. All evidence points to the nasal cavity as the most important site for carriage and dissemination of staphylococci. Since the majority of hospital personnel have these organisms in their noses, and since the same bacteria can also be demonstrated in dust, laundry, eating utensils, etc., attempts to block all possible avenues of cross-infection have proved tedious, costly and only moderately successful. The advent of Staphicillin provides us once again with a practical and comparatively safe drug for treatment of staphylococcal infections. Time will tell whether strains resistant to this will become more numerous.

A comparable problem seems to have developed in regard to certain gram-negative bacilli: the coliforms, pseudomonas and proteus species. Evidence has appeared that hospital patients are colonized by an unusually high proportion of enteric organisms resistant to commonly used antimicrobial agents, and spread of these from patient to patient, particularly in urologic wards, now constitutes a serious hazard. In this connection we should note a revival of interest in an old controversy regarding the hazard of catheterization and other urethral instrumentation. There is reason to argue that a significant proportion of urinary tract infections are caused by such procedures.

The *major misuse of antibiotics* is their employment in prophylaxis of bacterial infection. They continue to be administered widely to patients with the common cold or other respiratory infection, despite complete lack of evidence justifying such use. Several well-conducted clinical investigations have been carried out in hospital patients with such diseases as measles, poliomyelitis, heart failure, cerebrovascular accidents, etc., and in all of these the results show no benefit, but instead a higher incidence of bacterial respiratory infection in patients who received the treatment. The lesson appears to be clear: people are safest with their normal flora; "prophylactic" antimicrobial therapy is only likely to upset the equilibrium and facilitate colonization by antibiotic-resistant micro-organisms.

It is regrettable that despite nearly two decades of research we still have only fragmentary knowledge of the mechanisms by which antimicrobial agents interfere with bacterial reproduction.

NEWLY RECOGNIZED EXPRESSIONS OF DISEASE BY WELL-KNOWN PATHOGENS

Epidemiologic, clinical and laboratory investigations of several outbreaks of severe pneumonia have shown that *histoplasmosis* is

capable of causing this syndrome. Epidemics have involved persons engaged in excavations, exploration of caves or cleaning silos or chicken roosts.

After years of masquerading in laboratories as a filterable virus, the causative agent of *Fort Bragg fever*, or pretibial fever, was discovered to be a leptospire.

European clinicians have shown that *toxoplasmosis* can present features somewhat like those of infectious mononucleosis in young adults.

Many factors have combined to set the stage for more frequent occurrence of *disseminated fungus infections*, particularly moniliasis, in debilitated persons who might previously have succumbed to their primary diseases.

A major contribution has been the demonstration that certain types of beta hemolytic streptococcus are more likely to induce *acute glomerulonephritis* than others. These, notably types 12, 4, 19, 25 and Red Lake, are spoken of as nephritogenic types.

Use of antimicrobial drugs has, of course, caused great changes in the prevalence of many infectious diseases. Among serious infections in hospitals, there has been a marked decline in bacteremia due to pneumococcus and hemolytic streptococcus but an increased incidence of staphylococcal and enterococcal bacteremia. Even more impressive has been the greater relative importance of gram-negative bacteremia, due to *Escherichia coli*, proteus, pseudomonas and *Aerobacter aerogenes*.

NEWLY RECOGNIZED DISEASES

In the Korean War, *hemorrhagic fever*, a disease characterized by fever, purpura, circulatory collapse and renal shutdown, presented a serious challenge to medical officers of the United Nations forces. The disease was assumed to be of viral or rickettsial origin but intensive investigation failed to disclose the etiologic agent, and with cessation of hostilities little further news has been forthcoming.

Cat-scratch disease came to be recognized as a common entity during the last decade. Although it usually takes the form of an ulceroglandular disorder somewhat resembling tularemia, it is believed also to appear in other forms, such as Parinaud's oculoglandular syndrome, meningitis or mesenteric adenitis. The etiologic agent has not yet been demonstrated, but a skin test using heat-treated exudative material helps to establish the diagnosis.

Many small outbreaks of a prolonged disabling disease now called *benign myalgic encephalomyelitis* were recognized during the past decade. Other names given to this were Iceland disease and epidemic neuromyasthenia. Most of the persons involved have been young women. The usual clinical picture is an acute febrile illness

associated with muscular weakness or paralysis, which clears completely within weeks. A small proportion of affected persons, however, continue to complain of vague symptoms like those of severe neurasthenia, which may go on for months or years. No etiologic agent has been demonstrated but the epidemiologic characteristics strongly suggest an infectious disease.

A peculiar epidemic occurred at Ardmore, Oklahoma, in 1955 and was named *Ardmore disease*. It had clinical features resembling infectious mononucleosis, infectious hepatitis and epidemic pleurodynia. Several physicians, nurses and orderlies who cared for the patients were also stricken. Most remarkable was the very long period of disability, averaging 2 to 5 months. No clue to etiology was obtained.

VIRUS DISEASES

Notable advances were made during the past decade in identification of filterable viruses capable of causing human infection. The principal enabling factors were improvements in tissue culture technics and the use of suckling mice as test animals. Four new categories of viruses were found widely prevalent in man: the adenoviruses, the Coxsackie viruses, the ECHO viruses and the parainfluenza (hemadsorption) viruses. The adenoviruses cause certain kinds of respiratory disease and pharyngoconjunctival fever. Members of the Coxsackie group are responsible for herpangina, aseptic meningitis, Bornholm disease and myocarditis. The ECHO viruses give rise to lymphocytic meningitis and febrile disease with exanthem. The parainfluenza agents seem to play a part in respiratory infections of children, particularly croup.

A serious worldwide epidemic of Asian influenza occurred in 1957-1958.

A few dogged workers have continued to search for causative agents of the common cold. Recently encouraging results were obtained, by the use of tissue culture technics and adjusting acidity of the medium as well as temperature of incubation. It seems likely that we will have much better knowledge of the etiology of the common cold within a few years.

Tissue culture technics also enabled workers to isolate the virus of measles and to begin work on a vaccine against it.

Perhaps the "biggest news" in the entire infectious disease field during the past decade involved attempts to prevent poliomyelitis. First came a large-scale test of passive protection with gamma globulin. The results were encouraging, but further work was dropped owing to the advent of the Salk vaccine. Suggestive evidence of protection against poliomyelitis had been obtained in small-scale trials before the much publicized national trial and evaluation in 1954-1955. Despite a serious accident wherein one of the lots of vaccine under