Infectious Diseases: Epidemiology and Clinical Practice

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PREFACE TO SECOND EDITION

Samuel Pepys had no daughter. Susan, who fell 'sick with the meazles, or at least of a scarlett feavour' was a maid in his house, not a daughter of his blood. That I mistook the relationship in my first edition is inexcusable, for an author may be wrong in his opinions, but should be right in his facts. I was admonished by two readers, one in Geneva and one in Edinburgh; their kindly manner allayed the shame I might otherwise have felt at putting in print an error which could have been avoided by turning over a few pages in a man's diary. But indeed, I have been greatly touched by the kindness of the comments which have been made about my book, by friends and colleagues, and also by many whom I have never met, but who have written to me from many parts of the world. They have made me feel that to some extent I may have succeeded in what I tried to do, namely to present the subject of infectious disease as a study to which a man may devote his time with profit and great pleasure.

It is relatively easy to produce a first edition. All that one needs is a measure of self-discipline, a few sheets of paper and a long-suffering wife. A second edition requires something more. In the first place, one has to read the whole of the first edition. This demands endurance of a high degree, and one must be prepared for surprises. Certainly, while reading through the text, some statements have leapt at me from the pages which have made me wonder what the author was about when he made them. These I have tried to temper and correct, but never by sacrificing the unorthodox if I believed it to be true. The most difficult part of the task, however, has been in keeping mentally afloat in spite of the torrent of publications that keeps pouring from so many diverse medical sources. A man, said Johnson, may turn over half a library to make one book. Dr Johnson never wrote a medical text-book, but I feel he knew what the task would involve.

Readers, and especially reviewers, are apt to forget that the date of publication is not the date on which the text was written. If that is kept in mind, it may not seem strange that in the first edition of this book no mention was made of Australia or SH antigen. Hundreds, if not thousands, of articles have since appeared on this subject. I have not read them all, but from those I have read I have selected over 60 which seem significant and have added these to my list of references. I have tried, within my limits as a clinician, to assess the present situation as

regards the significance of the antigen and its subtypes, the relationship of antigen-antibody complexes and of thymus-dependent lymphocyte function to clinical manifestations, and the nature of the core and the envelope of the large Dane particles. My assessment will doubtless be overtaken by the pace of research on this subject. I have tried to cover in some detail the clinical and epidemiological aspects of the relationship between Epstein-Barr (EB) virus and infectious mononucleosis: titration of VCA and EA antibodies and the demonstration of the transforming effect of EB virus on leucocytes seem to me important advances which may lead in time to a better understanding of Paul-Bunnell-positive and Paul-Bunnell-negative mononucleosis syndromes. The life cycle of *Toxoplasma gondii* has perhaps become clearer with the detection of sexual forms in the cat intestine, but the main worry with toxoplasmas at the moment is taxonomy. I have tried to tread carefully here, but who can keep in step with the taxonomists? I am not sure if toxoplasmas are still toxoplasmas, but *Bedsoniae* seem to have changed into *Chlamydiae*. I have done my best to give an accurate outline of leptospiral classification, and, not without a pang, I have adopted *Clostridium perfringens* in place of *Clostridium welchii*.

Much of the chapter on pyogenic meningitis has been rewritten to take account of the increasing resistance of meningococci to sulphonamides and also of the constantly changing epidemic pattern of these organisms. Vaccines may replace drugs in the prevention of meningococcal meningitis and I have referred to encouraging trials of polysaccharide antigen vaccines in military units. Immunization is the most important aspect of the rubella problem, and I find it odd to read my very cautious remarks on rubella vaccines in the first edition. Both in the chapter on rubella and in the expanded immunization chapter in this new edition I have tried to look at every aspect. The possible teratogenic effect of vaccine virus is, of course, the main problem, and with this are linked the problems of vaccination or reinfection during pregnancy, the duration of vaccine immunity and the best age at which to give the vaccine. Measles immunization is scarcely less important, especially in tropical countries where the disease can be so severe: it is now clear that measles virus will not readily surrender its grip on a community, and a very high immunization rate is necessary to keep this disease under control. Encephalitis is a minor risk after measles vaccine, but against this must be balanced the probable role of measles virus in subacute sclerosing encephalitis and its possible role in multiple sclerosis: both these subjects are alluded to in the chapter on measles. Two of the problems of poliomyelitis vaccine campaigns are the difficulty of obtaining good seroconversion rates in tropical countries and the worry of vaccine-associated poliomyelitis: both these prob'ems are discussed in chapter 17. The influenza virus with its shifts and drifts continues to tantalize virologists, but we may be within sight of a vaccine that will forestall the virus in its not unlimited capacity to mutate. This and the prospects for other respiratory viral vaccines are

discussed in the chapter on acute respiratory infections. I have discussed the possible reasons for the poor results of whooping cough vaccine in the past in Britain: there are as yet no reports on the effect of the more potent vaccines in use more recently. Mumps vaccine appears to be an effective prophylactic in Russia, but elsewhere it has been mainly neglected. T.A.B. vaccine continues, in my opinion, to be a rather poor vaccine: the protection it gives depends perhaps on the dose of typhoid or paratyphoid bacilli which the vaccinee swallows, and I have considered in some detail the volunteer experiments carried out by Hornick and his colleagues on this problem. Although results of trials so far are disappointing, live oral typhoid vaccines which should stimulate intestinal IgA may yet displace parenteral T.A.B. vaccines. Live oral shigella vaccines are more effective and should find their place in the control of endemic institutional dysentery. There are few infectious diseases for which vaccines have not been prepared; Q fever, leptospirosis and botulism to give examples. The difficulty is how and where to use them: pentavalent botulinum toxoid is available but could be used rationally only in laboratory workers who handle the organism. The great gap in our array of vaccines is, of course, the absence of a vaccine against the hepatitis virus or viruses. If this book ever goes into a third edition it might well have a section on hepatitis immunization.

Food poisoning has not declined in recent years. *Bacillus cereus* and *Vibrio parahaemolyticus* have joined the salmonellae, the clostridia and the staphylococci as causes of outbreaks in Britain and elsewhere. At least five staphylococcal enterotoxins have been identified, and these can be identified in the laboratory without the use of animals, though the technique is laborious. Transferable drug resistance is a major hazard in intestinal infections: chloramphenicol resistance has already been transferred to *S. typhi* under epidemic conditions. I have enlarged the section on this subject, a difficult one for a clinician, but I hope my remarks are in essence accurate. Travellers' diarrhoea is one of the main epidemic diseases of this century and I have tried to give a balanced account of its probable aetiology.

Eradication of smallpox seems nearer than when I wrote the first edition. The emphasis in the campaign has moved from mass vaccination to surveillance along with contact or village vaccination. The possibility of a reservoir of smallpox in nature has to be considered, and monkeypox and related poxviruses are important in this connection. I am greatly indebted to Professor A. W. Downie for helping me to understand the virological background of these problems. Routine infant vaccination has been given up in Britain and the United States, but vaccination of travellers to endemic smallpox areas is still an essential part of the eradication programme. The chapter on zoster has been enlarged to take account of treatment with idoxuridine and other drugs: much of the material is based on Juel-Jensen and MacCallum's excellent monograph. The chapter on herpes simplex has also benefited from the monograph: a good deal has been added on genital and congenital infections, on

the types of simplex viruses and on antibody response to the infection.

In preparing the second edition I have frequently consulted Dr G. C. Turner, Director of the Public Health Laboratory Service, Liverpool: his laboratory is now in the grounds of Fazakerley Hospital. I am deeply indebted to him for his help at all times, especially for his lucid explanation of microbiological problems which I have sometimes found baffling. His colleague Dr G. B. Bruce-White has also helped me on points of virological detail. But although I have benefited greatly from their help, neither of them is responsible for anything I have written and any mistakes are entirely my own. My colleague Dr H. E. Parry has again helped me with the index, a formidable task due to the many changes and additions in this edition. My secretary Mrs Darby has again helped me with the typing, but the main typing burden has been borne by my wife who, being self-taught, has not found the task a light one.

A book, said Disraeli, may be as great a thing as a battle, and certainly the disorder in my study might give the impression that something more than a second edition was taking place. Dr Johnson meant much the same thing when he remarked that what is written without effort is in general read without pleasure. Should anyone derive pleasure from reading this book, I would regard all my efforts as more than amply repaid.

A. B. CHRISTIE

Liverpool, 1973

PREFACE TO FIRST EDITION

A good book, it has been said, should be opened with expectation and closed with profit, and probably no writer has ever begun his task without hoping that in both respects his work will satisfy his readers. He can never be sure, for expectation often fails, perhaps 'most oft there, where most it promises'. But if the reader fails to profit from this book, it is not true of the writer for, in the years that he has devoted to the task, he has derived great profit and much pleasure from studying the work of other men and trying to see it in the light of his own. In the intellectual history of mankind there are, happily, periods when the energies of many minds run together and the filament of human thought lights up and who can doubt that, in the field of epidemiology and infectious diseases, the middle twentieth century has been such an age? 'Of making many books there is no end', but, in such an exciting period, much study can hardly be a weariness of the flesh.

When I qualified in medicine I had not heard of sulphonamides. This must have been partly due to my lack of application as a student for, in 1935, they had certainly been discovered, though their use in medicine was still only tentative. I first learned about them at the London School of Hygiene and Tropical Medicine, where I had the good fortune to study under Professors Topley and Wilson, and to catch a spark from their inspiration which led me to choose for my career the study of infectious diseases, and to apply for a post in a London fever hospital. The employing authority was still known as the Metropolitan Asylums Board, but although most of its hospitals had a Victorian cast about them, the work that went on inside was up-to-date. I met Dr Goodall there and Drs Rolleston and Ronaldson, all famous writers on infectious diseases and clinicians of vast bedside experience. But my first chief was Maurice Mitman, a great clinician, and also a man alert to the scientific advances that were taking place in related fields. With Dr Harries, whom I also knew, he wrote the well-known text-book which embodied those advances and which, though the last edition was published in 1951, still provides an exact foundation for the clinical study of infectious diseases.

It was in a period of transition, then, that I began my studies in infectious diseases: transition from an era in which the doctor in a fever hospital had unlimited clinical material to study, with limited help from the laboratory and scarcely any from the pharmaceutical

industry, to an era in which, although the number of his patients may have dwindled, he requires all his energies to keep abreast of the knowledge coming unceasingly from these two sources. I spent seven years of this period in Southend-on-Sea, working under my friend and colleague Dr J. Stevenson Logan: he drilled me in the public health aspects of infectious diseases, a discipline which I hope is reflected in my book. For over twenty years I have worked in Liverpool: the University Department of Bacteriology has been for most of the time under Professor A. W. Downie and the Public Health Laboratory Service under Professor D. T. Robinson, and no infectious diseases physician could hope to work in a more stimulating atmosphere.

I have tried in this book to write down what I have learned. At the bedside of my patients I have learned most, and I have tried to put into words what I have seen there. In reviewing the work of other men I have sought to put down plainly what they had to say, and to relate this to my theme, which is to present the subject of infectious diseases as one of the more liberal studies to which a medical man can devote himself. I have never seen my patients as a collection of interesting cases: a diseased body, in itself, I have always found repulsive. I have, instead, seen them as human beings caught up in that ceaseless conflict between different forms of life of which their illness is one aspect only. The study of infectious diseases begins, or perhaps ends, at the bedside but plague comes many a long mile.

With regard to the content of the book I have not included any introductory chapters on immunology or other sciences. I believe that, in a general text-book, such chapters are usually skipped by the reader who, if he wants specialized information, prefers a specialized text-book. I have instead gone straight into the subject of which I have some experience—the epidemiological and clinical practice of infectious diseases. I have adhered to no strict plan for my chapters, but have allowed each one to take its form according to the content of its subject. One chapter may have a long section on epidemiology and almost nothing on treatment; the next may have nothing on epidemiology and several pages on treatment. I have not hesitated to alter the sequence of sections where I have thought it best: in the chapter on rubella, I have described the clinical aspects first because I think one must grasp these before one can understand the epidemiology. Some of the chapters may appear too long, others too short. There are over sixty references to Q fever, nearly eighty to rabies and just over thirty to chickenpox. This does not mean that I regard Q fever and rabies as commoner diseases than chickenpox although, if one includes their incidence in animals as well as in man, they may well be. The number of references and the size of chapters are contolled by the interest of the subject and the work in progress, not by the frequency of the disease in man. The common cold occupies less than a page but it is the commonest disease described in the book.

In preparing this book I have read widely, and my sources are

acknowledged in the lists of references. Where I have not myself read an article, this is indicated as being a quoted reference: the titles of some of these are not given, but I have thought it helpful, nevertheless, to include the journal references. I have referred in nearly every chapter to Topley and Wilson's *Principles of Bacteriology and Immunity* and to Horsfall and Tamm's *Viral and Rickettsial Infections of Man*, and without these two, this text-book could hardly have been written. I have repeatedly quoted from the *Bulletin of Hygiene*, known from 1968 as *Abstracts on Hygiene*. A man might, with great application, keep abreast of all the literature on infectious disease, but he could not write a text-book at the same time: the *Bulletin of Hygiene* has enabled me at least to keep in touch. Bloomfield's *A Bibliography of Internal Medicine: Communicable Diseases* is a remarkable source book to which I have frequently referred. As far as text-books on infectious diseases by other authors are concerned, I have tried to use them as little as possible while writing my own but, where I have, they are given in the list of references. I have, of course, read most of the standard books in the past and, like every student, I am aware that my own knowledge is founded on them.

I have been greatly helped in my work by Mr Lee and the staff of the Liverpool Medical Institution Library, as well as by the staff of the Harold Cohen Library in the University of Liverpool, and the Librarian of the Liverpool School of Tropical Medicine. My secretary, Mrs Kneale, has also helped me to check references, and has had the monumental task of typing the work, often from an almost illegible script. In the last rush, my wife has also taken to typing, but her main contribution has been in bearing the disarray in my study and the irregular hours of my life in the last six years. Most of the illustrations in the book are from photographs taken by Mr Gordon Wilkins, photographer at Fazakerley Hospital, and I am greatly indebted to him for his enthusiasm and skill. My deputy, Dr H. E. Parry, has taken much routine work off my shoulders and I have had countless discussions with him on the scope of the book: he has read each chapter for me as it has been typed and has shared with me the task of compiling the index. Professor D. T. Robinson was my patient while I was writing the book and he gave a great deal of time, when convalescent, to reading it chapter by chapter: his criticism was always meticulous, but kindly, and it has been one of my pleasures in writing to have had his expert help. The book, however, remains my own: all its faults are certainly mine. I am indebted to my publishers for help and encouragement throughout my task, and for precise editing of my manuscript and references.

I have tried to write for fellow physicians, for Medical Officers in the Public Health field and for postgraduate students. I hope that general practitioners may find the book useful too, for they see more infections in their practices than I do in my hospital. I also hope that bacteriologists and virologists may find a place for it on their shelves, if only to remind

them of the clinician's point of view. No book could cover all these requirements; no book is ever without faults, for 'there is always a man behind it'.

A. B. CHRISTIE

Liverpool, 1969

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CHAPTER ONE

THE EPIDEMIOLOGIST AND THE CLINICIAN

Man is a creature composed of countless millions of cells: a microbe is composed of only one, yet throughout the ages the two have been in ceaseless conflict. Epidemiology is the study of that conflict which, in spite of the numbers on one side, is by no means a one-sided affair. Man and his microbes are both involved in the struggle for existence, both must adapt to their environment, and successful adaptation is the secret of survival. Man is constantly battling with the elements of his environment, with time and space, and with motion and speed. Microbes too have environmental problems, but the adaptations they make are often simpler and less taxing. Man pays for his with the stress diseases, but a microbe may resolve its struggles by changing into a spore, or by taking up an indolent parasitic position inside a human host cell. 'All subsists by elemental strife', but it is doubtful whether man or microbe has the better weapons.

The history of epidemics is the history of wars and wanderings, of famine and drought and of man's exposure to inhospitable surroundings. When man has travelled rough, micro-organisms have always been ready to take advantage of his discomfitures. But epidemics have also occurred when man has *not* been off his guard. Poliomyelitis has been a killing disease where standards of hygiene are highest, and many diseases, such as measles and the common cold, flourish in the most civilized communities. Man's attempts to manipulate his resources have often brought him infection. The most homely examples come from his contact with domestic animals: he got bovine tuberculosis from his cattle, brucellosis from his goats, and 'Q' fever from his sheep. His commercial ventures brought him some exotics: he imported smallpox in bales of cotton, anthrax in cargoes of hides or bones, psittacosis in parrots and innumerable salmonellae have crossed the oceans in his ships. Other diseases have threatened him through no fault of his own. Rabies is basically a disease of smaller animals such as mongooses, polecats, martens and skunks: only when it builds up and breaks through into foxes, wolves and dogs is man threatened, though in some areas of the world the disease is carried by bats to cattle and to man himself. The whole animal kingdom is engaged in bacteriological warfare, with man not always the most successful contestant.

At the bedside of his patient, the physician sees a very small part of a very large scene. He is often able to destroy the infectious agent by

treating its victim with an antimicrobial drug, but, although this may represent one of the wonders of modern medicine, it is really quite a feeble contribution to the solution of the problems of competition between man and microbe, and the latter has already found one answer in infectious drug resistance. Vaccines provide a more intelligent approach for, if the host can be made resistant, the parasite cannot invade and, if it is dependent on that one host only, the parasite must give up the competition completely and cease to exist. But unicellular organisms have a tenacious hold on life and direct attack may not be their only approach. Viruses seem capable of hybridization or of causing the cells of other species to hybridize. They are possibly able to stimulate tumour formation. There appear to be infectious agents smaller still than viruses as in scrapie of sheep, and many diseases of man not regarded as infectious may yet prove to be caused by infectious agents. The clinician at the bedside, the epidemiologist in the field, the bacteriologist and the virologist in the laboratory have much to concern them. None of them should work in isolation.

CHAPTER TWO

FOOD POISONING: SALMONELLOSIS

The Old English word 'foda' meant sustenance for man and beast. It has come down to us as 'food' for man, and 'fodder' for beast. All three are good, plain words with no emotional significance other than simple contentment or satisfaction. 'Drink' comes straight from the Old English 'drincan': it meant originally just what it said but it has gathered sophistication on the way down to us so that it now has an emotional charge which may vary considerably according to what is being drunk. But the etymological landslide has been reserved for its Latin synonym. 'Potion', from potare, originally meant just something to drink but it grew more specialized and came to mean the kind of drink prescribed by an apothecary; as such, it might be unpleasant, but was usually intended to be beneficial. Sometimes, however, the intention was less benevolent and, when this was so, the word altered both in form and connotation and, still from the same root, 'potion' became 'poison'. The word 'poison' used by itself is not lacking in emotional overtones, but when it is accompanied by the homely word 'food', these overtones are thrown into a startling jangle, and the uncomfortably dissonant sound 'food poisoning' is produced. There can hardly be a more striking contradiction in terms than this combination of the basic and the outlandish—food, which sustains life, and poison, which destroys it. Yet, contradictory though it may be in the terminological sense, food poisoning is in fact a hazard of man's very existence. Man must eat to live, but he is not provided in nature with ready-made sustenance: he must instead plunder and manipulate his environment, often in competition with other forms of life which find the same fare agreeable and indeed, in both the most primitive and the most civilized society, man's quest for food is his most constant occupation. It is a quest that takes him far and wide, from a hole in the ice to an abattoir, and it is not surprising that he incurs risks on the way, both seen and unseen, and that when he is at last ready to sit down and eat, the food before him, from some hazard of the chase, is already unfit for human consumption.

Definition

From the clinical or the epidemiological point of view, 'food poisoning' is not a wholly satisfactory term. It may cover an aetiological field that is at once too wide and too narrow. Thus if a man eats food

contaminated by pesticides he may develop symptoms due to the poison[1]: if he eats potatoes with green buds on them[2] or apples stewed in a galvanized pan,[3, 4] a poisonous toadstool in mistake for an edible mushroom[5] or ortho-tricresyl phosphate in mistake for cooking oil[3, 16] or if he eats food that has been contaminated by *Clostridium botulinum* from the soil or by *Clostridium perfringens* or staphylococci from some human carrier, in all these cases he may develop symptoms of considerable diversity, yet the illness in each case may quite properly be diagnosed as food poisoning. On the other hand, the illnesses due to infection with members of the salmonella or shigella group of organisms may be clinically indistinguishable: moreover each may, on occasion, be caused by exactly the same set of circumstances involving food and food-handlers, yet the salmonella infection is labelled food poisoning, but the shigella infection is dysentery.

Typhoid fever is invariably conveyed by some article of food or drink,[7, 8] but the nature and severity of the symptoms are usually distinct from those of other salmonella infections, and it is not normally included under the heading of food poisoning. *Salmonella paratyphi B* may, on the other hand, cause an illness with clinical features indistinguishable from the enteritis due to any other member of the salmonella group: yet, though bacteriologists may sometimes report an outbreak of paratyphoid infection as a variety of food poisoning,[9] more often it is regarded by the administrator, and certainly by the public, as something quite distinct and much more menacing. Diarrhoea caused by salmonellae is more often labelled 'enteritis' than 'food poisoning'. The former term is much less alarming than the latter, and is often preferred for this reason; but epidemiologically this is quite unsound, for although an illness may be clinically trivial, investigation may prove it to be due to circumstances that are hygienically quite intolerable.

Sometimes the urgency of the symptoms or the number of people involved may determine which diagnostic label is used. Thus an occasional bout of mild diarrhoea in some elderly person in a home for the aged may be put down to a 'touch of enteritis' or even ascribed to 'something you have eaten' without, in the latter case, any real appreciation of the accuracy of the diagnosis or of its implications: but when all the inmates are seized with sudden, severe diarrhoea and one or two die,[11] 'food poisoning' is at once diagnosed and investigation follows as a matter of extreme urgency. It is, of course, difficult to strike a balance. To label every sporadic case of diarrhoea as food poisoning may only cause alarm without leading to any satisfactory epidemiological results, for often, as will be seen later, the origin of sporadic cases of food poisoning may be hopelessly lost in the tangle of modern food distribution: yet, on the other hand, careful investigation of cases spread over wide and apparently quite unconnected areas of consumption may sometimes show that such cases are not sporadic at all, but are, in fact, parts of a widespread yet closely linked epidemic.

Inexact, loose and, at times, illogical as the use of the term 'food