Infectious Diseases: Epidemiology and Clinical Practice

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Preface to Third Edition

I have always felt sorry for Charles Lamb. Ever haunted by a sense of his incapacity for business it was nevertheless his lot to waste the golden years of his life in the irksome confinement of an office.[1] For six and thirty years he took his seat at his desk in Mincing Lane, London for eight, nine and sometimes ten hours a day attendance at a counting-house. Time, he said, reconciles us to anything, yet when he was asked to accept a pension for life instead of work he felt as if he, a man formerly so poor in Time, was suddenly lifted up into a vast revenue of it. He needed, he said, some judicious bailiff to manage his estates in Time. He could scarcely trust himself with it. But as he got used to it he felt that a man could never have too much Time or too little to do. Man was out of his element, he concluded, as long as he was operative.

That has not been my experience. A life-time spent in the study of infectious diseases is not, of course, the same as working in a counting-house. It is perhaps wrong to regard it as work at all: it is more of a pleasant occupation. And it does not stop with retirement. I have, in fact, always felt sorry for other medical men, surgeons and anaesthetists, for example, when they retire: if they wish to remain employed they have to carry on working, whereas I remain pleasantly occupied, as I have been all my life. But in another world. I have forsaken the academic colonnades, if the wards of my Liverpool I.D. hospital can be so described, and have gone out into the field, sometimes into the bush. It has been my pleasure and privilege to find that if I have acquired any understanding of infectious diseases during what I must call my working life, I have been able to enlarge it in a world that is still developing. I have been in villages in Indonesia and in shanty towns in Peru, as well as in overcrowded capitals in the new world and in the old. I have learned a great deal. I have met several very old diseases that were nevertheless new to me, plague, typhus and cholera, for example: dread diseases, but full of microbiological and ecological interest. I have written a chapter on each of the three for this new edition and I hope I have conveyed in them some of that interest. But diarrhoea is the great plague of the developing world, and I have tried in the relevant chapters to bring science down to village level: to the health centre or health post and into the village hut: for I have worked in Asian and South American villages and it is in the village that problems must be solved. I have not, I hope, neglected the scientific aspects. There are two chapters on gastroenteritis in this third edition in place of only one in the first two: this I have found necessary in order to cope with the flurry of microbiologists chasing campylobacters, rotaviruses and other exciting new pathogens in the intestinal field. Compared with these newcomers *B. cereus* is almost an old fashioned bacillus but I have nevertheless rewritten the section on it, and I have also tried to update information on how salmonellae and clostridia act in the intestinal tract. Pig bel is a clostridial disease I saw in Papua New Guinea and I have given a short account of it and of the promise of a vaccine to protect against it. Intestinal pathogens never fail to move in new and unexpected ways and we find shigellae turning up in work-trains in Labrador, on pleasure rafts on the Colorado and in cruise ships in the Carribean. Salmonellae have spread in chocolate and, once or twice, in medical products. It is not clear if salmonellae are ever spread by cockroaches but these well-constructed, efficient insects can certainly be experimentally infected with the organisms: and they may be contaminated in nature with such unpleasant pathogens as *Yersinia pestis, Vibrio chol-*

erae and *Entamoeba histolytica. Salmonella typhi* is not, as I previously thought, exclusively a pathogen of man; it has been isolated, apparently quite often, from fruit-eating bats in Madagascar though whether this has any relevance to the disease in man I am not so sure. These items get little more than a mention in the text, but they illustrate a few of the innumerable incidents which occur constantly in nature and which are relevant to the wider study of infectious disease.

Viral hepatitis is one of the great infections throughout the world, developed and developing, and articles appear constantly in the medical press on new aspects of its epidemiology, immunology, virology and so on. I have completely re-written the chapter on this disease and have attempted to cope, often to the limits of my understanding, with these various aspects. I have listed some 750 references on hepatitis but these are but a small fraction of the uncountable total. I hope, however, that these make a representative and fair selection, but I can scarcely hope that my interpretation of their findings is always adequate. Legionnaires' disease is one of the new, or newly discovered diseases and I have tried to give an up-to-date account of the findings: but 'up-to-date' must always be a relative term, and it is impossible to include reference to articles that appear after the manuscript has gone to the publishers, a point not always appreciated by otherwise kindly reviewers. Acute haemorrhagic conjunctivitis seems to be a truly new disease, at least in its epidemic form, and I have included a short account of it in the chapter on enteroviruses where it apparently belongs. Rabies continues to be a threat and I have greatly enlarged the chapter to take more account of fox ecology, of colonial and non-colonial bats, and of the many possible reservoirs of the virus in nature: I have also enlarged the section on control, and on the use of vaccines, both in man and possibly in the fox. I have tried to wrestle more closely with that slippery virus, influenza A, but my attempt to come to grips with it was interrupted by a personal encounter with its relative, influenza virus B, for which, in convalescence, I now have profound respect.

The study of infectious disease is really the study of man and his environment, and any changes in one or the other lead to changes in the pattern of infections. We live in a transplant world, some of us; in a permissive world, most of us; in an antibiotic world, probably all of us. Microorganisms as well inhabit all three. So we get cytomegalovirus and other infections after transplant surgery, hepatitis in clinics for sexually transmitted diseases and antibiotic-resistant *Salmonella typhi* and other organisms almost everywhere. But the breakthrough is not always with the microorganism. As I write in 1980, eradication of smallpox has not yet been proclaimed, but the proclamation is almost certainly only a few months ahead. And 'proclamation' is the right type of word, for surely this is one of man's greatest achievements in preventive medicine and also, in a divided world, in international cooperation. The WHO expanded programme of immunization seeks to carry on this work in the developing world against diseases that have almost disappeared from the other world: I have been privileged to have a small part in this work, and I have tried in the chapter on immunization and elsewhere in this edition to illustrate some of the difficulties, human, virological and mechanical, that have to be overcome.

Throughout the revision for this third edition I have tried to keep abreast of the literature on my subject but I know that, even as I write, my material may be going out of date. So I make no claims, except that I have done my best. No place, said Dr Johnson, affords a more striking conviction of the vanity of human hopes than a public library, and this has been borne in on me in the hours and days I have spent turning over other men's pages. I have spent most time in the library of the Liverpool Medical Institute, both upstairs and down in the dusty vaults, and I am greatly indebted to the librarian, Mr Crook and his assistants for their constant expert help. I have also used the library of the Liverpool School of Tropical Medicine and of the Royal Society of Medicine in London. In Libya I used the library at the Ministry of Health in Tripoli and the magnificent library at the University of Garyounis, Benghazi. In Alexandria I spent much time in the library at WHO headquarters. I have even spent some hours in the libraries in Medillin, Colombia and in Jakarta, Indonesia. So although I have been wandering around I have always taken my book, and the need to revise it, with me. It has become part of my life. Unfortunately it has become part of my wife's life too and she has felt the strain more than I have: but without her support, both morally and as a self-

taught typist, I might not have made it. During my work on hepatitis in Libya I have had as a colleague from time to time Dr David Dane of the Middlesex Hospital, London, and I am in his debt both for friendship and for expert advice. Dr Mufta Usta Omer, Secretary of Health, Libya Arab People's Socialist Jamahereyah, has given me every encouragement in the work which it has been a great pleasure to share with Dr Aschiur Gebreel. I had a typical down-to-earth discussion with Professor Ralph Hendrickse of the Liverpool School of Tropical Paediatrics on getting fluid into babies at village level, and Dr Carl Taylor Robinson of Liverpool University helped me when I was having difficulty with the microbiology of cholera. My colleague of many years Dr Hugh Parry has again helped me with the index, a formidable task. I am most grateful to my publishers for their forbearance when for various reasons I have failed to meet their deadline. For the rest, the book, as I offer it, is my own, written at times with some effort, but mostly with pleasure, for I have found, again with Dr Johnson, that a man may write any time if he will set himself doggedly to it.

Liverpool, 1980 A.B. Christie

1. Charles Lamb. The Superannuated Man.

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 of 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 problems are discussed in chapter 21. 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 in 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.

Liverpool, 1973 A. B. Christie

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 controlled 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'.

Liverpool, 1969 A. B. Christie

Contents

1

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, microorganisms 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.

2

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. *Sal-*

monella 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 hoplessly 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 poisoning' may be, the general concept of poisoning by foodstuffs is intelligible enough, and there is no difference of opinion, lay or medical, about the undesirability of eating food that is in any way unsound or contaminated. If such unsoundness or contamination were properties that could be detected by sight, smell or taste, the control of food poisoning would be no great problem, but food that is dangerous may appear sound and attractive so that the senses are deceived; palatability is not the same as wholesomeness. Part of the definition of the term may depend on a time element; if symptoms develop quickly after eating food, as, for example, apples stewed in a galvanized pan, the condition is food poisoning, but if there is an interval of a fortnight between the meal and the symptoms, the condition may be typhoid fever but it will not be food poisoning. On the other hand, salmonellae and shigellae may both cause diarrhoea and vomiting after a short incubation period, yet in only the former case will the condition be labelled food poisoning. It is clear therefore, that though both the temporal and the bacteriological elements are involved in the definition, neither factor provides the essential criterion. And indeed, though food poisoning is a condition notifiable by law, it is impossible to lay down an exact or legal definition of the condition that must be notified. Yet everyone knows what food poisoning is—the family doctor, the Medical Officer of Health, the Public Health Inspector, the public, and not least, the Press—and it is as much on the level of such general acceptance of the term, as on any strict legal or scientific basis, that food poisoning must be described.

Bearing all this inexactitude and lack of definition in mind, one may state that the condition, or conditions, known as food poisoning may occur as a result of eating any of the following:

Substances containing specific poisons

These may be of two types:

1. Substances that are intrinsically poisonous and are eaten in mistake for some wholesome food. Mushroom poisoning[5] is one of the best known, and is not due to eating edible mushrooms (which are always wholesome) but some other fungi such as *Amanita phalloides,* which are invariably poisonous. Many berries that are attractive to the eye are deadly to the stomach.[12] The use of ortho-tricresyl phosphate in mistake for cooking oil also comes into this class.[1, 13]

2. Substances that are normally wholesome but which, from some abnormal circumstance, become poisonous. Potatoes normally contain about 8 mg per cent of the alkaloid solanine, a concentration which is harmless, but sometimes, if the potatoes have sprouted or if, during their growth, the tubers have

been exposed to light, the concentration in parts of the potato may rise to 20 or 25 mg per cent or higher, and this concentration is likely to cause food poisoning (p. 5).[2] Mussels are normally an acceptable form of sea-food but if they have fed on certain dinoflagellates which flourish in warm marine waters, they may contain a curare-like substance, and their consumption may give rise to paralysis.[14, 174-5, 303-4] Dark-meated fish such as mackerel and tuna, scombroid fish, usually contain less than 50 mg/l of histamine in the meat. On rare occasions, possibly as a result of bacterial action on the histidine in the meat, the concentration of histamine may rise to over 100 mg/l or even over 1000 mg/l. Eating such fish may result in histamine-like reactions called scombrotoxic fish poisoning.[334, 391] Both these examples are rare forms of food poisoning, but they are mentioned because they illustrate how, in the complex aetiology of food poisoning, the normal may not always be readily distinguishable from the abnormal.

Food contaminated by poisons

These may be considered under two heads:

1. Substances in which the contamination has occurred as a result of some process unrelated to the preparation of food though important in the production of foodstuffs. These are generally agricultural or industrial hazards, and result from the use of poisons to kill pests on growing crops,[1, 159] or the accidental introduction of injurious substances during some stage of the preparation or curing of perishable foods.[15]

2. Substances in which the contamination occurs as a result of mistakes in the preparation of food for the table. This usually takes the form of metallic poisoning, and results from the storing or cooking of acid fruit or vegetables in cheap enamel dishes or in galvanized pans or pails.[3, 4] Zinc, antinomy and other metals may be absorbed by the part of the food in contact with the container and be unevenly present through the rest, while in the case of liquids such as fruit drinks, the metal is distributed throughout the contents. But this form of food poisoning is becoming rare, for the risks are now well known to caterers, whereas, in the former group, contamination occurs before the food reaches the kitchen and is beyond the control of the person preparing the meal.

Foods infected with organisms

This is bacterial food poisoning and is, of course, by far the commonest form. While the others already mentioned must not be lost sight of in any study of the subject or in any investigation of outbreaks, they are nevertheless to a large extent clinical or epidemiological curiosities. But bacterial food poisoning is of daily occurrence, and in some part or other of the country there will always be someone attempting to trace the origin of an outbreak. The organisms concerned may be of many types, for it is probably true to say that almost any organism, if present in sufficient numbers in the food, may cause an intestinal upset in some of those who consume it.[16] But in most outbreaks of food poisoning, the search can be narrowed down to three bacterial groups — salmonella, clostridium and staphylococcus—and it is with these three groups of organisms and with the complex epidemiological web they weave that most of this chapter is concerned.

Before passing on to the subject of bacterial food poisoning, it may be profitable to glance briefly at some of the non-bacterial forms of food poisoning mentioned above.

NON-BACTERIAL FOOD POISONING

Some examples of non-bacterial food poisoning will be considered.

Mushroom poisoning

The edible mushroom is the most innocent of foods: a flavour, the slightest of textures and nothing more. By contrast, some closely related fungi may produce dramatic symptoms of poisoning. *Amanita pantherina,* the false blusher, and *Amanita muscaria,* the fly agaric, are two of the commoner poisonous fungi eaten in mistake for edible mushrooms and they owe their poisonous effect to the presence of muscarine.[5, 55] Symptoms come on rapidly within a few minutes up to six hours. Abdominal pain, vomiting and severe diarrhoea may be prominent, but sometimes these are absent and there may then be sweating, twitching, miosis, muscular incoordination, double vision and convulsions. The patient with such symptoms may pass into coma within three

hours of eating the fungi,[5] and may remain comatose for 24 hours or more before recovery. In cases where muscarine is the poison concerned the outlook is not hopeless, for atropine is an effective antidote, and may be given intravenously in a dose of 0.02 mg per kg body weight.

Amanita phalloides, 'the death cap', *Amanita verna,* 'the fool's mushroom', and *Amanita virosa,* 'the destroying angel', derive their poisonous properties mainly from amanitine which is intensely cytotoxic; phallin has haemolytic properties and phalloidin is a gastric irritant, but both these substances are destroyed by cooking and so produce symptoms only if the fungi are eaten raw.[60] The incubation period of amanitine poisoning may be from 6 to 24 hours: vomiting, diarrhoea and abdominal pain are usually prominent symptoms, and jaundice and acute renal failure may follow, with coma as a terminal state. Mortality is from 50 to 90 per cent and, at autopsy, fatty infiltration is found in the kidney, the liver and the myocardium. No antidote is known for this form of poisoning. Exchange transfusion, peritoneal dialysis and haemoperfusion over charcoal have been used with some success.[37,9]

Solanine poisoning

The concentration of solanine in the potato, *Solanum tuberosum,* is related to the metabolic activity of the plant. It is therefore higher in the sprouts on the skin of the potato and in the shoots above the ground; if the skin has been exposed to light during growth, or even after the tubers have been dug, solanine may reach high concentrations in and just under the skin. The alkaloid is very soluble in water so that, if the potatoes are peeled and boiled, it is dissolved out into the water and the potatoes when eaten may contain little solanine.[2] The alkaloid remains in the potatoes if they are baked in their skins, however, and if the initial concentration was high, symptoms of solanine poisoning may develop within a few hours. These consist usually of headache and fever, abdominal pain, often with vomiting and severe diarrhoea, weakness and depression. The patients usually recover within a few days, but there have been one or two fatal cases.[56,57]

An outbreak described by Wilson vividly illustrates how minor changes in presentation may render the same potatoes safe for one consumer and poisonous for another. A hotel proprietor had for weeks served boiled potatoes to his guests without incident, but on each of three successive Sundays he served potatoes baked in their jackets to his own family. Four members of his family ate the potatoes and their skins, but he himself ate only the flesh. He remained well, but all the others developed symptoms of solanine poisoning after seven or eight hours, and the severity of their symptoms varied according to whether they ate one, two or three potatoes.[2] The boiled and the baked potatoes were all from the same batch, and analysis showed a concentration of solanine of 50 mg per 100 g, well above the safe level of 20 mg per 100 g.[58] The potatoes themselves were normal in appearance and flavour and showed no signs of sprouting; they had been imported from Israel and there is apparently some evidence that certain varieties of potato form more solanine when grown in hot than in temperate climates.[2] Clearly in this case there was nothing to indicate that the potatoes might be harmful and the only advice that can be given is not to eat potatoes which are green or sprouting or, if one must, it is safer to boil than to bake them. With such a universal food as the potato, it is fortunate that the incidence of solanine poisoning is exceedingly low.

Zinc poisoning

In a review of food poisoning due to zinc in Great Britain between 1942 and 1956 only eight outbreaks were recorded,[3] a low incidence due to the fact that the risks of storing foods, especially acid foods, in cheap enamel or galvanized iron containers are now well known. Of the eight outbreaks, four were caused by stewed apples, the concentration of zinc in the apples being as high as 1200 to 5000 parts per million so that a 4-oz helping might contain as much as 0.5 to 1 g of zinc sulphate. Rhubarb tart, bottled bilberries and stewed bilberries each caused one outbreak as, rather surprisingly, did mashed potatoes, the concentration of zinc in the potatoes being 31 parts per million. Only a small number of those at risk developed symptoms, due to the fact that the metal was unevenly distributed through the food. The incubation period varied from a minute or two to an hour or two, the main symptom being vomiting with fairly quick recovery; there was no diarrhoea.