Essential Clinical Microbiology: An Introductory Text

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A Wiley Medical Publication

JOHN WILEY & SONS

Chichester · New York · Brisbane · Toronto · Singapore

Library of Congress Cataloging in Publication Data:

Cooke, Edith Mary.
Essential clinical microbiology.
(A Wiley medical publication)
Includes index.
1. Medical microbiology. I. Gibson, G. L. (George Lees) II. Title. III. Series. [DNLM: 1. Microbiological technics. 2. Microbiology. QW 4 C772c]
QR46.C78 1983 616'.01 82-11164
ISBN 0 471 90017 6

British Library Cataloguing in Publication Data:

Cooke, E. M.
Essential clinical microbiology.
1. Medical microbiology.
I. Title. II. Gibson, G. L.
616'.01 QR46
ISBN 0 471 90017 6

Phototypeset by Dobbie Typesetting Service, Plymouth, Devon
Printed and bound in Great Britain at The Pitman Press, Bath

Preface

This book has arisen out of our experience of teaching medical students in Leeds during the past eight years. Microbiology is studied both in the pre-clinical period and then as part of the 'systems teaching' in the clinical course. We have felt the need for a text book which would give an adequate grounding in microbiology and have at the same time a clinical orientation. This book represents an attempt to meet this need.

Recognizing that many systems are affected by a wide variety of micro-organisms, we have included viruses, fungi, and protozoa as well as bacteria. The emphasis is on those diseases which are regularly seen in the United Kingdom, although exotic infections, rarer to us, are briefly included. We have attempted to meet the difficulties which students have expressed, and in order to promote familiarity with the large and daunting nomenclature of micro-organisms we have given the names of organisms in full on each occasion except when this would be too repetitious.

The principles of laboratory methods are stressed, but technical information is given only in sufficient detail to assist in the understanding of these principles. We hope that a reasonable knowledge of laboratory work may be gained so that useful clinical and laboratory liaison will be possible in later years.

We are indebted to our respective secretaries, Mrs E. Ellis and Mrs J. Brennan, who have been most patient and meticulous, and to Miss Renee Bailey for the great help she has given us by drawing the illustrations.

E. Mary Cooke
George L. Gibson

Acknowledgements

Several of the figures in this book are adaptations of illustrations originally published elsewhere. The authors of this book wish to acknowledge that the following publications were used as reference sources for the creation of the figures listed below:

Figures 1.6, 1.7(a + b)–1.11: Chatterjee, K. D., 1962. *Parasitology, Protozoology and Helminthology in Relation to Clinical Medicine.* 4th Edition. Calcutta.

Figures 1.4, 1.5(a + c), 11.13b: Cruickshank, R., Duguid, J. P., and Swain, R. H. A., 1965. *Medical Microbiology.* 11th Edition. E. & S. Livingstone Ltd. Edinburgh and London.

Figure 1.12: Timbury, M C., 1975. *Notes on Medical Virology.* 5th Edition. Churchill Livingstone. Edinburgh, London and New York.

Figure 1.13: Duguid, J. P., Marmion, B. P., and Swain, R. H. A., 1978. *Medical Microbiology.* 13th Edition. Churchill Livingstone. Edinburgh, London and New York.

Figures 11.5 and 11.9: Gillies, R. R., and Dodds, T. C., 1976. *Bacteriology Illustrated.* 4th Edition. Churchill Livingstone. Edinburgh, London and New York.

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Contents

CHAPTER I

Introduction

GENERAL CHARACTERISTICS OF MICRO-ORGANISMS

Micro-organisms are almost ubiquitous and show great variety in structure and activity. They ensure the fertility of the soil and the degradation of sewage. They are useful in the food, brewing, and pharmaceutical industries and more recently, as a consequence of genetic engineering, they have been used to synthesize complex therapeutic substances such as insulin.

The micro-organisms which cause disease and in which clinical microbiologists are interested form only a very small part of the total microbial population of the world. The fall into the Kingdom Protista, a large group of simple organisms. The protists can be further divided into:

a) the higher protists which are eucaryocytic and which comprise the algae, protozoa, fungi, and slime moulds;
b) the lower protists which are procaryocytic and which comprise the bacteria and the blue and green algae.

The procaryocytes are distinguished from the more complex eucaryocytes by:

a) the possession of a simple nucleus with no nuclear membrane;
b) the absence of internal membranes isolating separate enzyme systems;
c) the possession of a rigid cell wall containing a specific mucopeptide.

Viruses are quite distinct from the organisms mentioned so far in that they reproduce only within living cells and contain DNA or RNA but not both. They must be considered as a separate group.

Bacteria

These are small procaryocytic structures which may have a variety of shapes. The cell consists of the genetic material and the cytoplasm, which is bounded by the cytoplasmic membrane and usually by a rigid cell wall. Other structures such as capsule, spore, flagella, and fimbriae may also be present (Fig. I,1).

Cytoplasm

This is a soft gel which contains the ribosomes. These are smaller than those of eucaryocytic organisms and are strung on strands of messenger RNA. The cytoplasm of some bacteria may also contain inclusion granules. These may consist of a variety of substances. They are usually energy stores and may be helpful in identification of the bacteria.

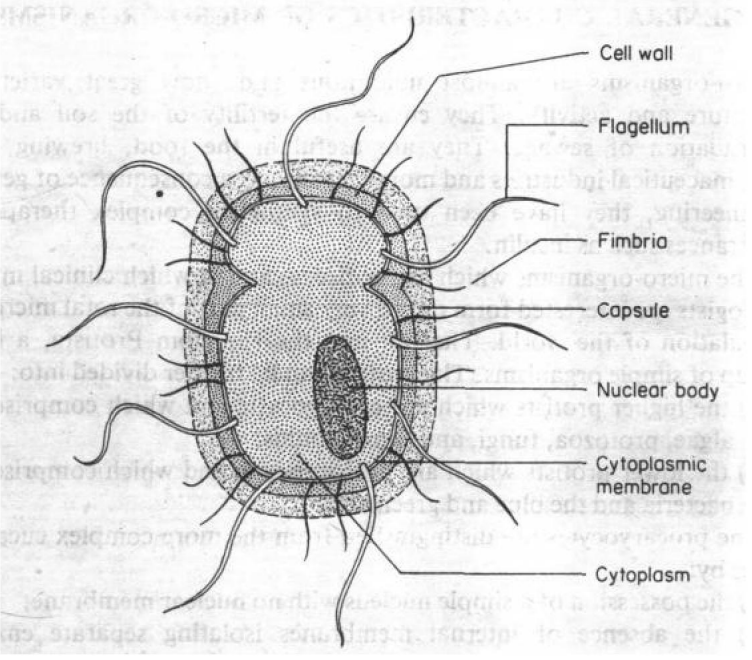

Figure I.1 The structure of the bacterial cell

Genetic material

The nucleus is a closed circle of double-stranded DNA. Bacteria replicate by binary fission, and because nuclear and cell division are not always synchronous, usually one but occasionally more nuclear bodies may be present. Additional genetic material may also be in the form of plasmids. These are small, usually circular, pieces of double-stranded DNA and they can replicate autonomously. They are smaller than the chromosome and are not essential to cell function. Plasmids are important in clinical microbiology because they may mediate for antibiotic resistance and also for properties associated with pathogenicity.

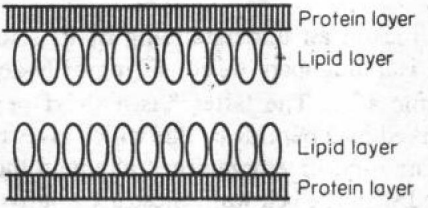

Figure I.2 The structure of the cell membrane

Cytoplasmic membrane

This limits the bacterial cytoplasm. Its structure is shown diagrammatically in Fig. I,2. Water diffuses passively through it, but inward transport of nutrients and outward transport of waste products is active. In Gram-positive organisms and less commonly in Gram-negative, invaginations of the cytoplasmic membrane called mesosomes occur. They may have a number of functions including the separation of the DNA between the daughter cells at cell division.

Cell wall

This is a rigid structure. It is complex, and because there is no counterpart in the eucaryocytic cells which make up human tissues it is the site of attack of some of the most effective and non-toxic antibiotics that are

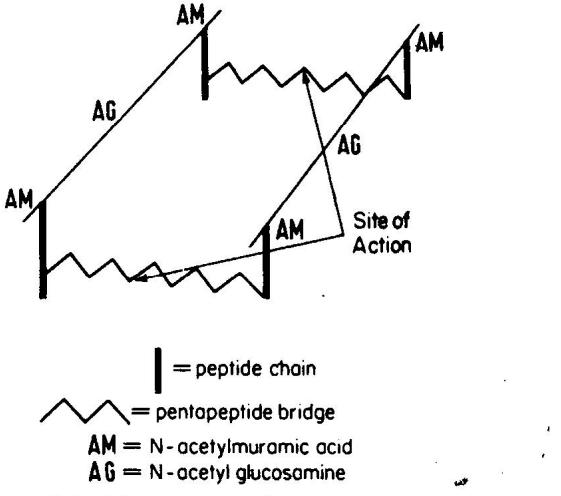

Figure I.3 The structure of the bacterial cell wall

available. For this reason an understanding of its structure is needed. The main structure is a mucopeptide consisting of N-acetyl glucosamine and N-acetylmuramic acid. The latter has a short peptide side chain. Chains are cross-linked by a peptide bridge which gives rigidity to the cell wall (Fig. 1,3). In Gram-positive organisms, although there are additional structures associated with the cell wall, these are relatively simple, but in Gram-negative organisms they may include lipopolysaccharide which is the endotoxin of the organism and may constitute a large proportion of the cell wall.

Spheroplasts are bacteria with an intact but weakened cell wall and protoplasts contain no cell wall. These rupture unless kept in solutions of high osmolarity.

L. forms and mycoplasmas are also bacteria with no cell wall.

Capsules

These surround some bacteria outside the cell wall and are usually composed of polysaccharide. Some capsulate organisms are surrounded by loose slime.

In some bacteria the capsule is small, can only be demonstrated serologically, and is known as a microcapsule. The capsule may protect against phagocytosis. Important capsulate organisms include pneumococci and klebsiellas.

Flagella

These are filamentous appendages and are the mechanism of locomotion in bacteria. Their number and distribution round the bacteria varies between species. Many medically important bacteria have flagella and are motile. These include pseudomonas, proteus, and salmonellas.

Fimbriae or pili

Fimbriae are fine hair-like structures surrounding some bacteria. They were first described in Gram-negative bacilli. They are shorter, finer, and more numerous than flagella and are organs of attachment. They may be of importance in pathogenicity.

Certain specialized fimbriae, 'sex fimbriae' or 'sex pili', take part in the transfer of DNA between bacteria in conjugation. They are longer than the common pili and are the site of attachment of specific phages, which are viruses which attack bacteria.

Spores

Sporulation is a complex activity resulting in the formation of structures which are able to remain dormant for long periods and to resist adverse conditions, particularly heat and absence of nutrients. Germination occurs when conditions are favourable and may be triggered by short periods of heat. Spores are of importance because they may allow organisms to survive for long periods and to be transferred for long distances, as for example with anthrax. Modern autoclaving, sterilizing, and canning procedures are all designed to destroy spores. In autoclaving, tetanus spores are particularly important and in canning, botulinus spores are the most important organisms which must be destroyed.

L forms and mycoplasmas

Both of these possess no cell wall and both may be cultured on cell-free media. L forms are often produced in the laboratory by exposure to penicillin. They are non-pathogenic but their persistence during penicillin administration may account for relapse following apparently successful therapy.

Mycoplasmas do not revert to the original bacterial form and they are pathogenic; the most important human pathogen is *Mycoplasma pneumoniae.*

Rickettsia, coxiella, and chlamydia

These are all bacteria but differ from most others by being obligate intracellular parasites. They must be distinguished from viruses from which they are quite separate. Typhus is an important rickettsial disease.

Fungi

These are non-photosynthetic eucaryocytic organisms with a rigid chitinous cell wall. They are divided into the moulds, which are filamentous mycelial fungi, and the unicellular yeasts. Yeast-like fungi grow partly as yeasts and partly as moulds and dimorphic fungi may exist as either according to the conditions. The systematic classification of fungi is based on their morphology, including the sporangium or spore-case borne on aerial hyphae and the macro- and micro-conidia which are also asexual spores. The structures of some of these of medical interest are shown in Fig. 1,4. From the clinical point of view fungi are most

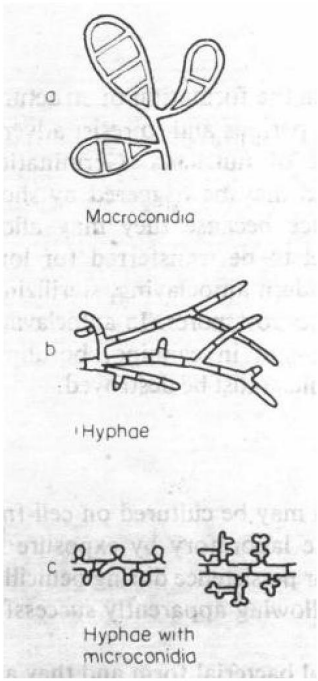

Figure 1.4 Some common fungal structures (Adapted from Cruikshank: *Medical Microbiology*, 12th Edition, by permission of Churchill Livingstone)

easily considered as candida spp., those causing systemic infections, and those dermatophytes which cause infections of the skin, hair and nails. They are discussed under these headings in Chapters 2, 9, and 11.

Viruses

These are quite different from the micro-organisms previously described, in that the genome consists of either DNA or RNA and this is reproduced within living host cells, where it directs the infected cell to produce the virion, the infective virus particle. This consists of the genome within a shell of protein, the capsid, which is composed of morphologically distinct units, the capsomeres. Some viruses also have an outer covering or envelope which is a lipo-protein and the whole virion has a defined symmetrical structure.

After a virion enters the host cell the capsid is removed and as a consequence of the presence of the viral nucleic acid, the host cell synthesises new viral nucleic acid, either DNA or RNA, and also the protein capsid. These are then assembled into new infectious particles which are released from the cell. Viruses are classified according to a number of properties particularly as to whether they contain RNA or

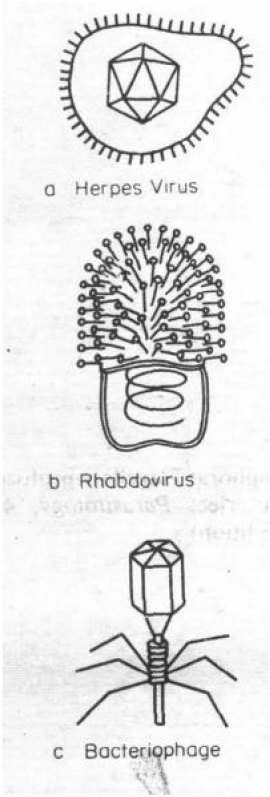

Figure I.5 Some common viral structures (a and c adapted from Cruikshank: *Medical Microbiology*, 12th Edition, by permission of Churchill Livingstone)

DNA, their morphology, mode of transmission and the disease they cause (Fig. I,5).

Protozoa

These are unicellular non-photosynthetic eucaryocytic organisms. They are divided into four main groups and the mechanism of locomotion is important in the classification.

Mastigophora are flagellate, and trichomonads, giardia and trypanosomes are medically important flagellate protozoa (Fig. I,6). Amoeboid protozoa are the Rhizopoda and of these *Entamoeba histolytica*, a causative agent of dysentery, is the most important human pathogen of this group (Fig. I,7). Ciliated protozoa, the Ciliata, are of much less importance to man but the Sporozoa which have no organs of locomotion and have a complex life cycle include the plasmodium species, the causative agents of malaria (Fig. I,8).

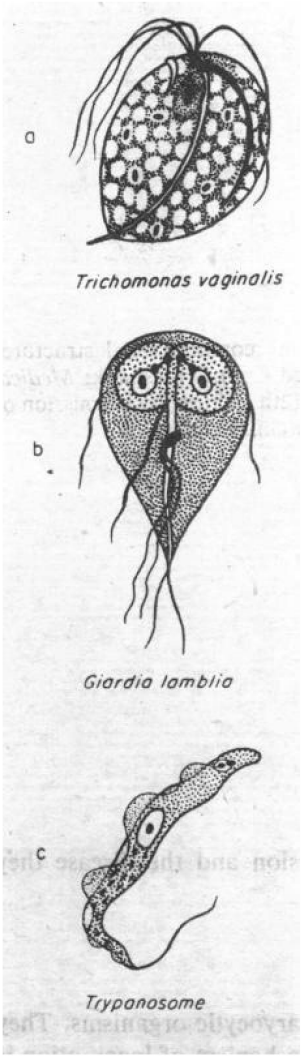

Figure I.6 Mastiogophora: Flagellate protozoa (adapted from Chatterjee: *Parasitology*, 4th Edition)

Helminths

These are not Protists but belong to the Animal Kingdom. They are mentioned briefly here because they are important parasites of man and give rise to clinical syndromes which often resemble those caused by micro-organisms.

They are divided into the platyhelminths and the nemathelminths. (flat worms and round worms).

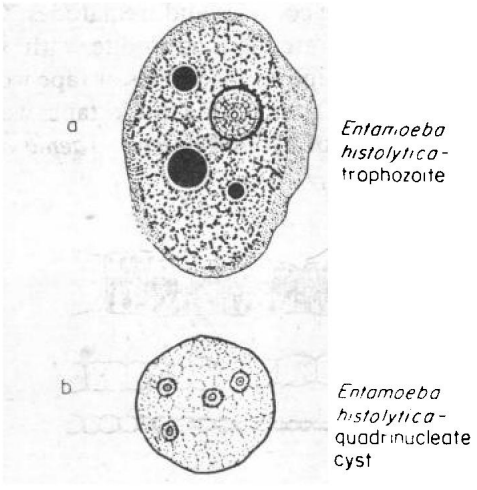

Figure 1.7 Rhizopoda: Amoeboid protozoa (adapted from Chatterjee: *Parasitology*, 4th Edition)

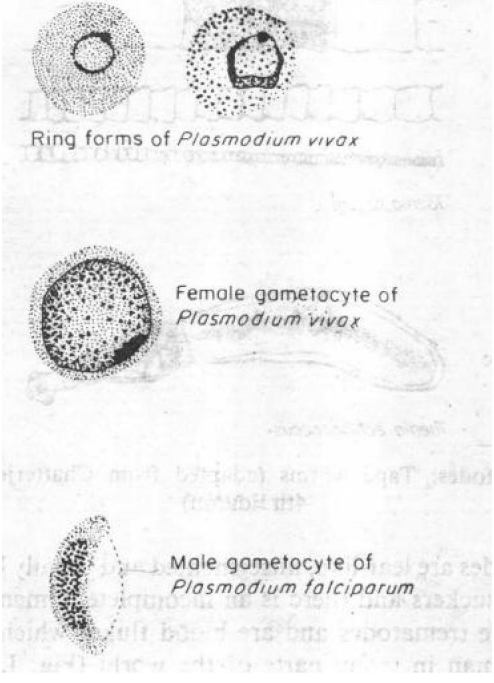

Figure 1.8 Sporozoa: Protozoa with a complex life cycle (adapted from Chatterjee: *Parasitology*, 4th Edition)

The platyhelminths include the cestodes and trematodes. Cestodes are tape-like and segmented; they are hermaphrodite with suckers and sometimes hooks on the head. Important cestodes or tape worms include the beef tape worm, *Taenia saginata*, the pork tape worm, *Taenia solium*, and the causative agent of hydatid disease, *Taenia echinococcus* (*Echinococcus granulosus*, Fig. i,9).

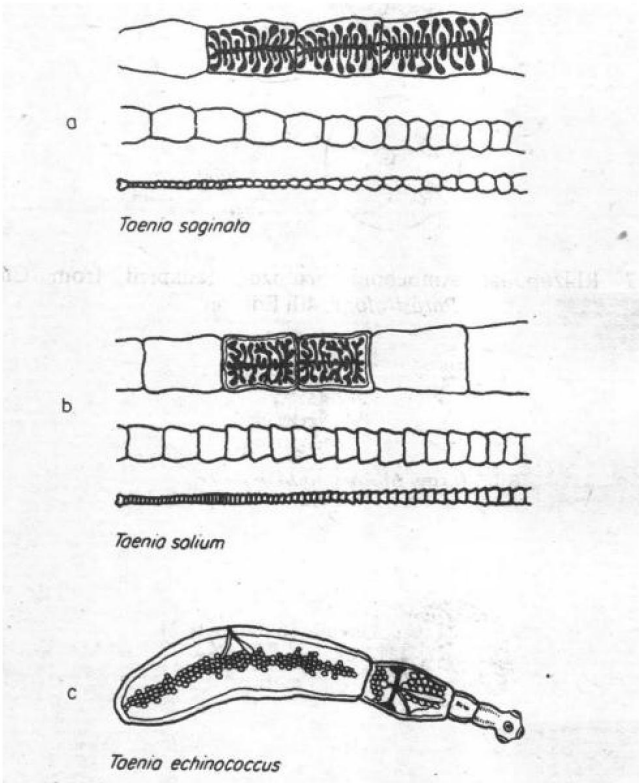

Figure I.9 Cestodes: Tape worms (adapted from Chatterjee: *Parasitology*, 4th Edition)

The trematodes are leaf-like, unsegmented and usually hermaphrodite. The head has suckers and there is an incomplete alimentary tract. The schistosoma are trematodes and are blood flukes which are important pathogens of man in many parts of the world (Fig. I,10). Liver and intestinal flukes are also trematodes.

Nematodes are elongated, cylindrical, and unsegmented. There are distinct sexes. There are no hooks or suckers and the alimentary canal