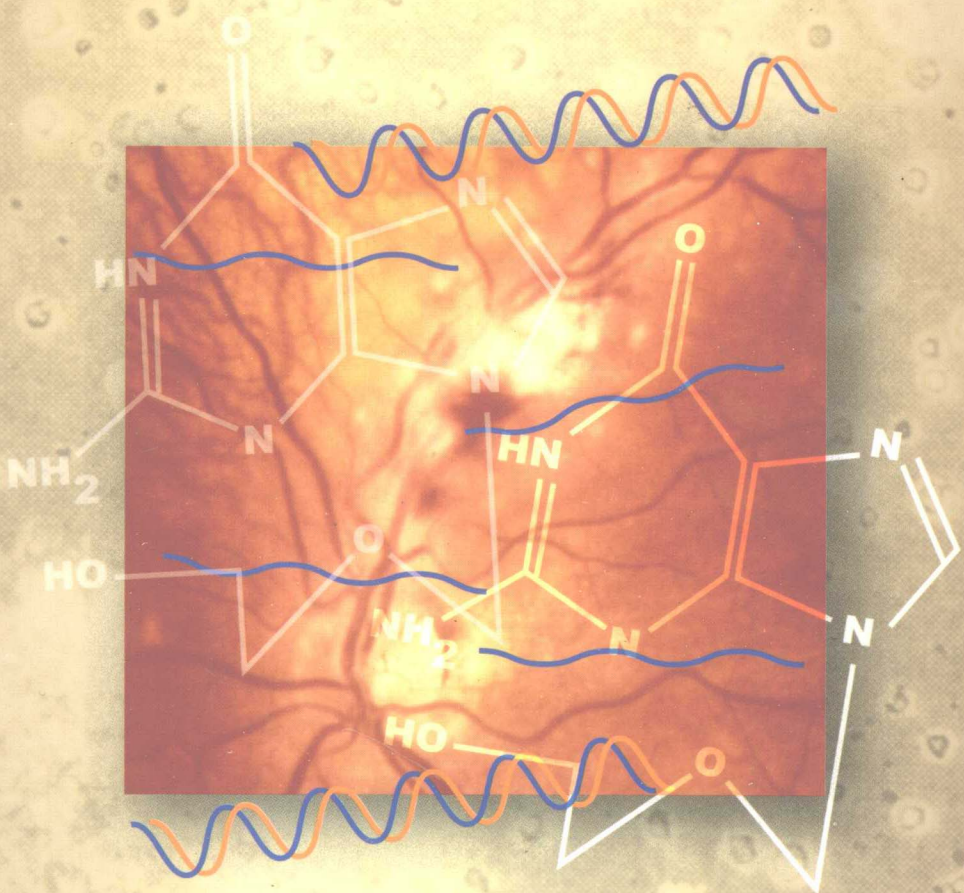
BIOS Instant Notes

Medical Microbiology



William Irving, Tim Boswell
& Dlawer Ala'Aldeen

BIOS Instant Notes

Medical Microbiology

Professor Will Irving

Department of Microbiology, University Hospital, Queens Medical Centre, Nottingham, UK

Professor Dlawer Ala'Aldeen

Department of Microbiology, University Hospital, Queens Medical Centre, Nottingham, UK

Dr Tim Boswell

Nottingham City Hospital NHS Trust, Nottingham, UK

Taylor & Francis

Taylor & Francis Group

Published by:
Taylor & Francis Group
In US: 270 Madison Avenue
New York, NY 10016
In UK: 4 Park Square, Milton Park
Abingdon, OX14 4RN

First published 2005

ISBN: 1-8599-6254-8

A catalog record for this book is available from the British Library.

Library of Congress Cataloging-in-Publication Data

Irving, William L.
Medical microbiology / Will Irving, Dlawer Ala'Aldeen, Tim Boswell.
p. ; cm. -- (BIOS instant notes)
Includes index.
ISBN 1-85996-254-8 (alk. paper)
1. Medical microbiology -- Outlines, syllabal, etc.
[DLM: 1. Communicable Diseases -- microbiology -- Outlines. 2. Infection -- microbiology -- Outlines. 3. Bacterial Infections -- microbiology -- Outlines. 4. Mycoses -- microbiology -- Outlines. 5. Parasitic Diseases -- microbiology -- Outlines. 6. Virus Diseases -- microbiology -- Outlines. QW 18.2 I72m 2005] I. Ala'Aldeen, Dlawer A. A. II. Boswell, Tim. III. Title. IV. Series.
QP46.I78 2005
616.9'041 -- dc22 2005022853

Editor: Elizabeth Owen
Editorial Assistant: Chris Dixon
Production Editor: Georgina Lucas/Simon Hill
Typeset by: Phoenix Photosetting, Chatham, Kent, UK
Printed by: TJ International, Padstow, Cornwall

Printed on acid-free paper

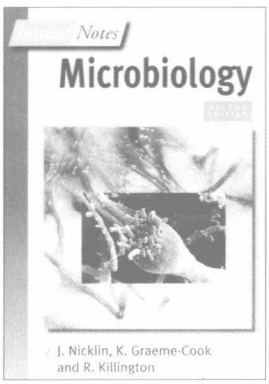
10 9 8 7 6 5 4 3 2 1

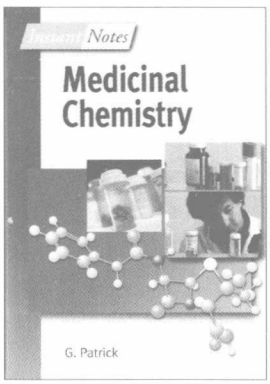
T&F informa

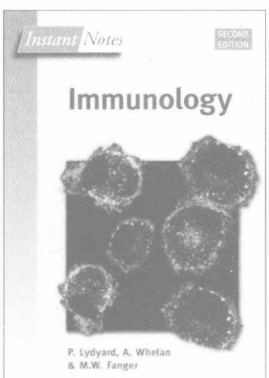
Taylor & Francis Group
is the Academic Division of T&F Informa plc.

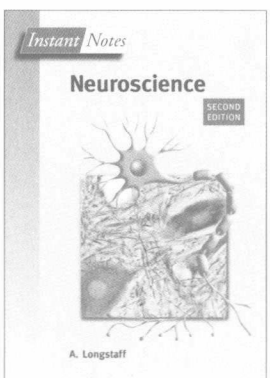
Visit our web site at http://www.garlandscience.com

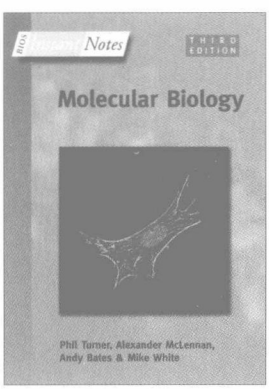
Related titles in the BIOS Instant Notes series

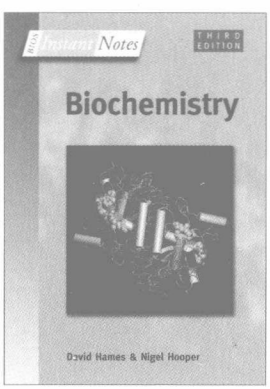












For up-to-date title information, current prices and a complete series listing, please consult

www.garlandscience.com

BIOS Instant Notes

Medical Microbiology

BIOS INSTANT NOTES

Series Editor: B.D. Hames, School of Biochemistry and Molecular Biology, University of Leeds, Leeds, UK

Biology
Animal Biology, Second Edition
Biochemistry, Third Edition
Bioinformatics
Chemistry for Biologists, Second Edition
Developmental Biology
Ecology, Second Edition
Genetics, Second Edition
Immunology, Second Edition
Mathematics & Statistics for Life Scientists
Medical Microbiology
Microbiology, Second Edition
Molecular Biology, Third Edition
Neuroscience, Second Edition
Plant Biology, Second Edition
Sport & Exercise Biomechanics
Sport & Exercise Physiology

Chemistry
Consulting Editor: Howard Stanbury
Analytical Chemistry
Inorganic Chemistry, Second Edition
Medicinal Chemistry
Organic Chemistry, Second Edition
Physical Chemistry

Psychology
Sub-series Editor: Hugh Wagner, Dept of Psychology, University of Central Lancashire, Preston, UK
Cognitive Psychology
Physiological Psychology
Psychology
Sport & Exercise Psychology

ABBREVIATIONS

AAFB	acid–alcohol-fast bacilli
Ad	adenovirus
AIDS	acquired immunodeficiency syndrome
AME	aminoglycoside-modifying enzymes
APC	antigen-presenting cells
ART	automated reagin test
BCG	Bacille Calmette–Guérin vaccine
BCYE	buffered charcoal yeast extract agar
BSE	bovine spongiform encephalopathy
CAP	community-acquired pneumonia
CAPD	continuous ambulatory peritoneal dialysis
CF	cystic fibrosis
CFT	complement fixation test
CGD	chronic granulomatous disease
CJD	Creutzfeldt–Jakob disease
CMV	cytomegalovirus
CNS	central nervous system
CoNS	coagulase-negative staphylococci
COPD	chronic obstructive pulmonary disease
CPE	cytopathic effect
CRS	congenital rubella syndrome
CSU	catheter specimen of urine
CT	computed tomography
DEAFF	detection of early antigen fluorescent foci test
DHF	dengue hemorrhagic fever
ds	double-stranded (DNA/RNA)
EBV	Epstein–Barr virus
EIA	enzyme immunoassay
EIEC	enteroinvasive *E. coli*
ELISA	enzyme-linked immunosorbent assay
ENT	ear, nose and throat
EPEC	enteropathogenic *E. coli*
ESBL	extended spectrum β-lactamases
ETEC	enterotoxigenic *E. coli*
FI	fusion inhibitors
FTA-ABS	fluorescent treponemal antibody-adsorption test
GE	gastroenteritis
GNAB	Gram-negative anaerobic bacteria
GRE	glycopeptide-resistant enterococci
GVHD	graft-versus-host disease
HACEK	*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella* group of organisms
HAI	hospital-acquired infection
HAP	hospital-acquired pneumonia
HAV	hepatitis A virus
HBIg	hepatitis B immunoglobulin
HBV	hepatitis B virus
HCV	hepatitis C virus
HDV	hepatitis D virus
HEPA	high-efficiency particulate air
HEV	hepatitis E virus
HHV	Human herpesviruses
Hib	*Haemophilus influenzae* type b
HIV	human immunodeficiency virus
HLA	human leukocyte antigens
hMPV	human metapneumovirus
HPV	human papillomavirus
HSE	Herpes simplex encephalitis
HSV	herpes simplex virus
HTLV	human T-cell lymphotropic virus
HUS	hemolytic–uremic syndrome
IE	infective endocarditis
IFN	interferon
IL	interleukin
IUCD	intrauterine contraceptive device
KDO	ketodeoxyoctonate
KSHV	Kaposi's-sarcoma associated human herpesvirus
LCMV	lymphochoriomeningitis virus
LJ	Löwenstein–Jensen medium
LOS	lipo-oligosaccharide
LP	lumbar puncture
LPS	lipopolysaccharides
LRTI	lower respiratory tract infection
MAI	*Mycobacterium avium–intracellulare* complex
MBC	minimum bactericidal concentration
MHC	major histocompatibility complex
MIC	minimum inhibitory concentration
MMR	measles-mumps-rubella vaccine
MRI	magnetic resonance imaging
MRSA	methicillin-resistant *Staph. aureus*
MSU	mid-stream urine

NA	neuraminidase
NNRTI	non-nucleoside analogue reverse transcriptase inhibitors
NRTI	nucleoside analogue reverse transcriptase inhibitors
OMP	outer membrane proteins
PAE	post-antibiotic effect
PBP	penicillin binding protein
PCP	*Pneumocystis* pneumonia
PFGE	pulsed field gel electrophoresis
PI	protease inhibitors
PID	Pelvic inflammatory disease
PMLE	progressive multifocal leukoencephalopathy
PMN	polymorphonuclear leukocytes
PTLD	post-transplant lymphoproliferative disorder
PUO	pyrexia of unknown origin
PVE	prosthetic valve endocarditis
RAPD	random amplified polymorphic determinants
RPR	rapid plasma reagin
RSV	respiratory syncytial virus
RT–PCR	reverse transcriptase–polymerase chain reaction
SARS CoV	severe acute respiratory syndrome coronavirus
SBE	subacute endocarditis
SPA	suprapubic aspirate
ss	single-stranded (DNA/RNA)
SSPE	subacute sclerosing panencephalitis
TB	tuberculosis
Tc	cytotoxic T cells
TCBS	thiosulfate–citrate bile sucrose
TCR	T-cell receptor
Th	helper T cells
TPHA	*T. pallidum* hemagglutination test
TPN	total parenteral nutrition
TPPA	*Treponema pallidum* particle agglutination
TSE	transmissible spongiform encephalopathies
TTP	thrombotic thrombocytopenic purpura
URTI	upper respiratory tract infection
UTI	urinary tract infection
VAP	ventilator-associated pneumonia
VDRL	venereal disease reference laboratory test
VRE	vancomycin-resistant enterococci
VRSA	vancomycin-resistant *Staph. aureus*
VZV	varicella-zoster virus
WHO	World Health Organization
ZN	Ziehl–Neelson stain

PREFACE

Medical microbiology is potentially an intimidating subject for new students. Not only does it appear to have a language all of its own, including plenty of obscure Latin terminology, but it covers a bewilderingly wide range of material, from the molecular biology of the infectious agents themselves (of which there is an alarmingly large – and ever-increasing – number) right through to the clinical management of the infected patient, passing disease pathogenesis, diagnosis, and the use of antimicrobial therapy on the way. This book seeks to identify, explain and expound upon the essentials of each of these aspects of the subject, in suitable 'bite-sized' chunks (a philosophy inherent in all of the books in the Instant Notes series).

We do not expect students to start this book at page 1 and work their way meticulously through to the last page (although to do so would undoubtedly assist them in gaining excellent examination marks!). Many courses concerned with medical microbiology will have their own particular emphasis, and will provide scant, if any, cover of the other aspects of the subject. Also, certainly at undergraduate level, it is unlikely that any one course would intend to cover each and every microbe, at least not in the same depth of detail. It would be appropriate therefore for students undertaking those courses to concentrate on the subject areas and microorganisms relevant to their own course. Nevertheless, as practising medical microbiologists, we felt it entirely appropriate to aim to cover the many facets of our subject in a single text, and also to be comprehensive in dealing with all of the infectious agents with which our patients present on a routine basis.

The book is divided into a number of sections. In section A we provide introductory background information on the nature of the infectious agents, the host response to infection, and how micro-organisms give rise to disease. Sections B, C, and D deal with the organisms themselves in more detail, the sections being ordered from the least (viruses) to the most (eukaryotes) structurally complicated. Within these sections, each group of related organisms is dealt with in a separate topic, which are ordered, very roughly, according to their clinical importance, and, for the bacteria, their Gram stain characteristics. Section E is concerned with general principles of the laboratory diagnosis and management of infection, including the mechanisms of action of antimicrobial agents, and possible strategies for prevention of infection. The final section, F, deals with infection from the point of view of the patient, i.e. clinical microbiology.

We hope that students find this approach to be logical and useful. We have benefited enormously from our own experiences of teaching students, both medical and non-medical, and would welcome any constructive feedback which students might wish to raise. Most of all we hope that at least some students will be as fascinated by this subject as we are, and will see this text as their first step on the road to a medical microbiologically related career.

William Irving, Tim Boswell and Del Ala'Aldeen

CONTENTS

A1 INTRODUCTION

Key Notes

Microbiology

Microbiology is the 'biology of microscopic organisms'.

Medical microbiology

Medical microbiology is the study of microbes that cause disease in humans.
Microbes are everywhere, both within and outside our body. Most are harmless.

Types of microbes

Microbes vary in shape, size and structure and are categorized into eukaryotic (fungi, worms and protozoa), prokaryotic (bacteria, rickettsia and chlamydia) or noncellular (viruses and prions). Eukaryotic organisms are uni- or multicellular; prokaryotes are unicellular. Viruses and prions are incapable of independent life.

Epidemiology of infection

Epidemiology is the study of spread of infection, including the source, transmission, distribution and prevalence of infection in the community.

Sources of infection are either endogenous or exogenous. Acquisition of pathogens may occur via many routes, including direct contact, inhalation, ingestion, injection or vertical transmission.

Epidemiologists assess infection in a community by using various measurements, including incubation period of disease, incidence, prevalence, attack rate and mortality rate.

Definitions and terms

Infection is a generic term used to indicate invasion of the host by a microorganism.

Infection may be subclinical or asymptomatic when the patient is unaware of the infection. Clinical infection is associated with the presence of overt signs and symptoms of disease.

The term 'colonization' should be restricted to the presence of a microbe at an expected site.

A pathogen is a microbe that potentially can cause harm, i.e. tissue damage. An opportunistic pathogen is a microbe that causes infection in patients with impaired immunity, e.g. fungal infections in cancer patients.

Introduction

Microbiology is the study of the 'biology of microscopic organisms' whereas medical microbiology is the study of microbes (infectious agents) that cause disease in humans. Microorganisms vary tremendously in terms of shape, size, structure and importance.

Medical microbiology is of increasing importance in health and disease. For example:

- approximately half of all patient visits to general practitioners are for infections;

- there are increasing numbers of patients with impaired immune systems in hospital, who are susceptible to a wide range of life-threatening infections;
- infectious diseases are associated with major public health implications, e.g. in the control of infection with human immunodeficiency virus (which leads to the acquired immunodeficiency syndrome – AIDS), tuberculosis and food-poisoning;
- costs of antimicrobial agents are increasing, as is the problem of microbial resistance to these agents;
- infection is by far the most common cause of morbidity and mortality in developing countries.

Microbes are ubiquitous. We are surrounded by microorganisms, the vast majority of which are harmless. Microorganisms live inside and outside the human body. They colonize the skin and mucous membranes of the mouth, nose, eyes, ears, sinuses, throat, gastrointestinal tract and vagina. They also live in the surrounding environment, including water, food, vegetables, animals and birds.

There are 10^{12} bacteria in each gram of feces. The vast majority of these are harmless, and some possibly useful.

Types of microbes

Microbes can be divided into three main categories (*Fig. 1*).

Eukaryotic organisms

These include fungi (e.g. molds and yeasts) and parasites (helminths and protozoans). They have a complex cellular structure, similar to those of humans and animals. Their cells have nuclei and mitochondria and they are largely self-sufficient and capable of independent life.

Prokaryotic organisms

These are simple and largely self-sufficient unicellular organisms which have no nuclei or internal dividing membranes but are usually capable of independent life (*Table 1*). Cell walls contain mucopeptides (peptidoglycans). They are collectively named bacteria. Some genera, e.g. rickettsiae and chlamydiae, are not capable of independent life and are therefore named 'atypical bacteria'. The latter group of organisms are obligate intracellular pathogens which require the presence of viable eukaryotic host cells for growth and reproduction.

Noncellular organisms

Viruses consist simply of DNA or RNA plus a few other components such as proteins. They are not capable of independent life, and therefore must infect cells of higher organisms (eukaryotic or prokaryotic) for their growth and reproduction. Some viruses infect bacterial cells – these are called bacteriophage or simply phage. Also included among the noncellular infectious agents are the recently characterized 'prions' which cause bovine spongiform encephalopathy (BSE) in animals and Creutzfeldt–Jakob disease (CJD) in humans.

Fig. 1(a). Cell structure of a typical eukaryotic organism.

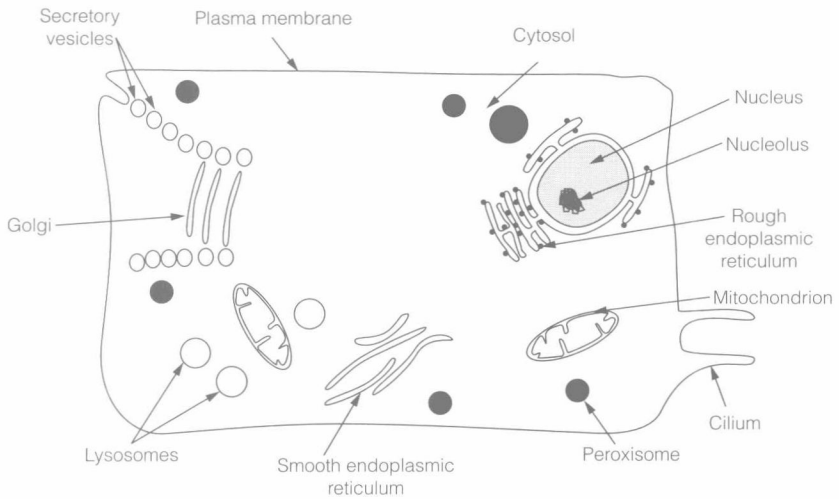


Fig. 1(b). Cell structure of a typical (Gram negative) prokaryotic organism (bacterium).

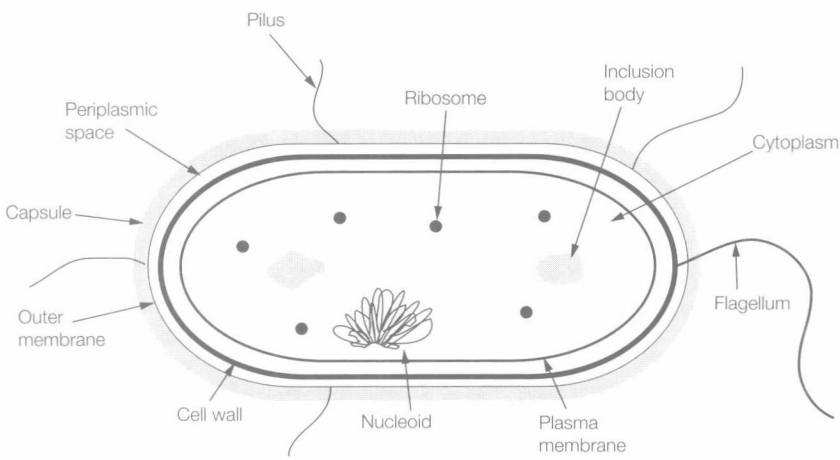


Fig. 1(c). A non-cellular organism (virus)

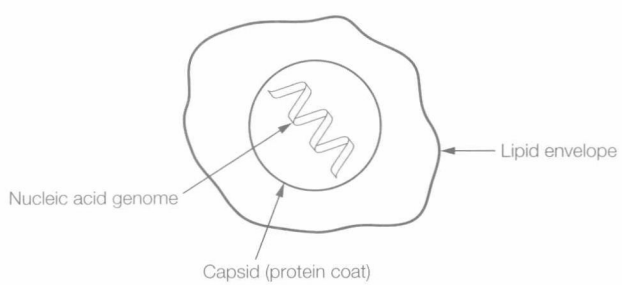


Fig. 1. Types of microbes.

Table 1: Some basic differences between eukaryotic and prokaryotic cells

	Eukaroytic cell	Bacterial cell
Size	>5 μm	1–3 μm
DNA and RNA	+	+
Paired chromosomes	+	–
Mitotic division	$+_m$	–
Binary fission	$-_m$	+
Structured nucleus	+	–
Golgi apparatus	+	–
Endoplasmic reticulum	+	–
Mitochondria	+	–
Ribosomes	+	+
Cell membrane	+	+

m = majority

Size and characteristics of microbes

Most microbial cells cannot be seen except by microscopy (light or electron).

Fungi are larger organisms with thick walls containing chitin. They exist either in the form of **molds** which grow by tubular branching filaments, or **yeasts** which are oval or spherical and grow by budding (*Fig. 2a*).

Protozoa are larger than bacteria. **Helminths** vary in size, ranging from a few millimetres to meters long (*Fig. 2b*).

Bacteria can be **seen under light microscopes**. They are 0.5–1 μm broad, 0.5–8 μm long and vary in shape and size. They are mostly either spherical (**cocci**) or cylindrical (**bacilli**) (*Fig. 2c*). Some bacteria assume different cellular morphologies, e.g. rickettsiae are pleomorphic (different shapes) and spirochaetes are spiral. Different bacteria have different growth characteristics. **Strictly aerobic** bacteria cannot grow in the absence of oxygen, **strictly anaerobic** bacteria cannot grow in the presence of oxygen and **facultatively anaerobic** bacteria can grow in the presence or absence of oxygen. Some bacteria are **fastidious** and have specific nutritional or other environmental requirements for growth.

Viruses are too small (fractions of a micrometer) to be seen by an ordinary light microscope, but can be seen under an **electron microscope** (EM). They vary in shape and structure (*Fig. 2d*). Many species have distinctive morphological characteristics that can be spot-diagnosed under EM.

Epidemiology of infection

Epidemiology is the study of spread of infection. This includes the source, transmission, distribution and prevalence of infection in the community.

Infecting organisms commonly originate from **endogenous sources** (the patient's own normal human flora, *Fig. 3*) or **exogenous** sources (e.g. other infected patients, animals, plants or contaminated objects, food or water *Fig. 4*). Endogenous sources are by far the most common. The source and **reservoirs** of infection are often (but not always) the same.

Fig. 2(a). Fungal Eukaryotic cells similar to those of higher plants and animals.

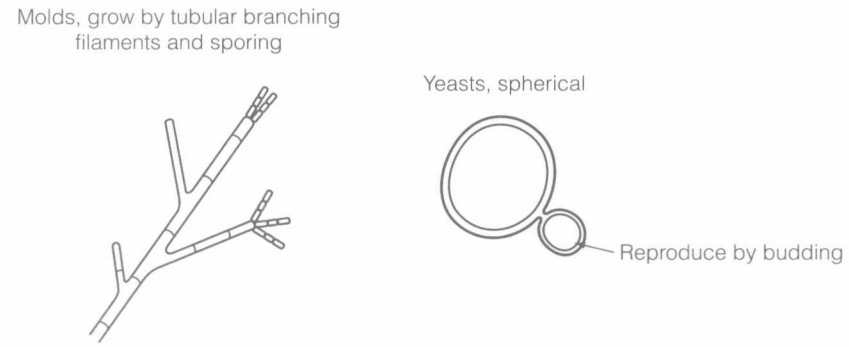


Fig. 2(b). Parasitic eukarytoic cells-helminths and protozoa.

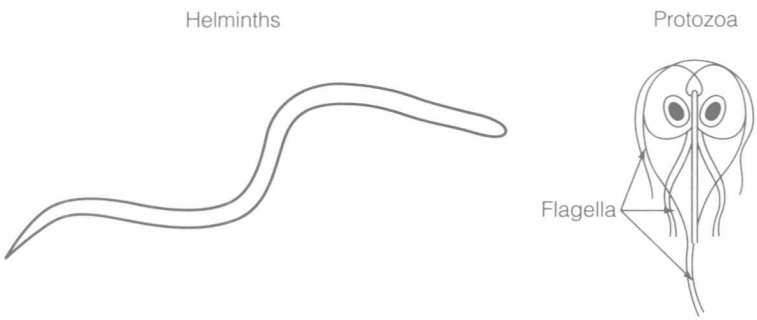


Fig. 2(c). Bacteria.

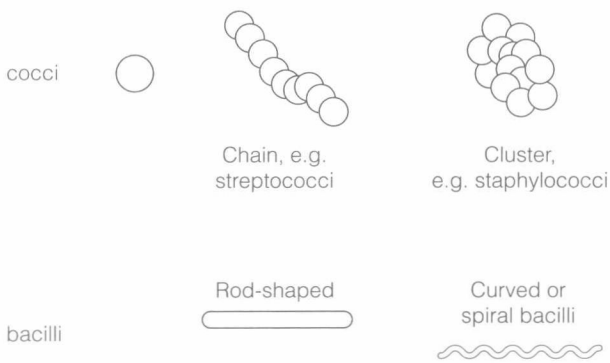


Fig. 2(d). Viruses.

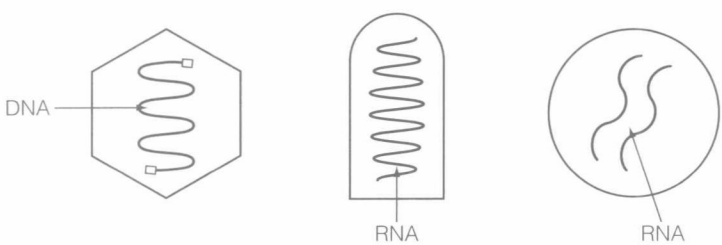


Fig. 2. Differing shapes of microbs (not drawn to scale).

Routes of infection

Acquisition of pathogens may occur via many routes, including:

- **direct skin or mucosal contact** with contaminated hands, body fluids, animals or objects; this includes sexual transmission of infection;
- **inhalation** of contaminated aerosols or droplets generated by sneezing, coughing, talking;
- **ingestion** of contaminated food or drink;
- **inoculation, penetration or injection** of contaminated fluids (e.g. during surgery or drug administration);
- **vertical transmission** from mother to baby (e.g. transplacental);
- **vector-borne** transmission.

The control and prevention of **outbreaks** of infections depend mainly (not entirely) on understanding the epidemiology of the disease and identification of the reservoirs, sources and routes of transmission. Important factors in control and prevention of infectious diseases include the number of **susceptible** humans, pathogenicity (virulence capability) of the organism, route of spread, identification of carriers, **incubation period** of disease and other environmental contributors. **Surveillance** (i.e. constant monitoring) of important infectious diseases is very important for implementing measures for the control of outbreaks.

Epidemiologists assess infection in a community by using various measurements. These include:

- incubation period of disease;
- **incidence and incidence rate**: number of cases of disease in the community per given population (e.g. 100 000);
- **prevalence**: incidence of disease within a given time;
- **attack rate**: incidence within a defined population group;
- **secondary attack rate**: number of cases of disease among contacts of the primary (index) case;
- **mortality rate**: number of deaths from a particular infection within a given population (e.g. 100 000).

Definitions and terms

Infection is a generic term used to indicate invasion of the host by a microorganism. This invasion is usually associated with a host response (e.g. inflammation) with or without clinical manifestations. Thus, infection may be **subclinical (asymptomatic, nonapparent)** when there is no apparent disease, and the patient is unaware of the infection. Alternatively, a **clinical** infection is one associated with the presence of overt signs and symptoms of disease.

It is important to remember that the presence of microorganisms in the host does not always mean disease. Healthy individuals may be 'colonized' without disease. The term **colonization** should be restricted to the presence of a microbe at an expected site, e.g. *Escherichia coli* in the large bowel, or *Staphylococcus epidermidis* on the skin, but occasionally it is also used to describe the presence of a potential pathogen in an unexpected site without causing symptomatic infection, e.g. *Staph. aureus* in the upper respiratory tract. Colonized patients are often also described as **carriers**.