Veterinary Microbiology and Microbial Disease

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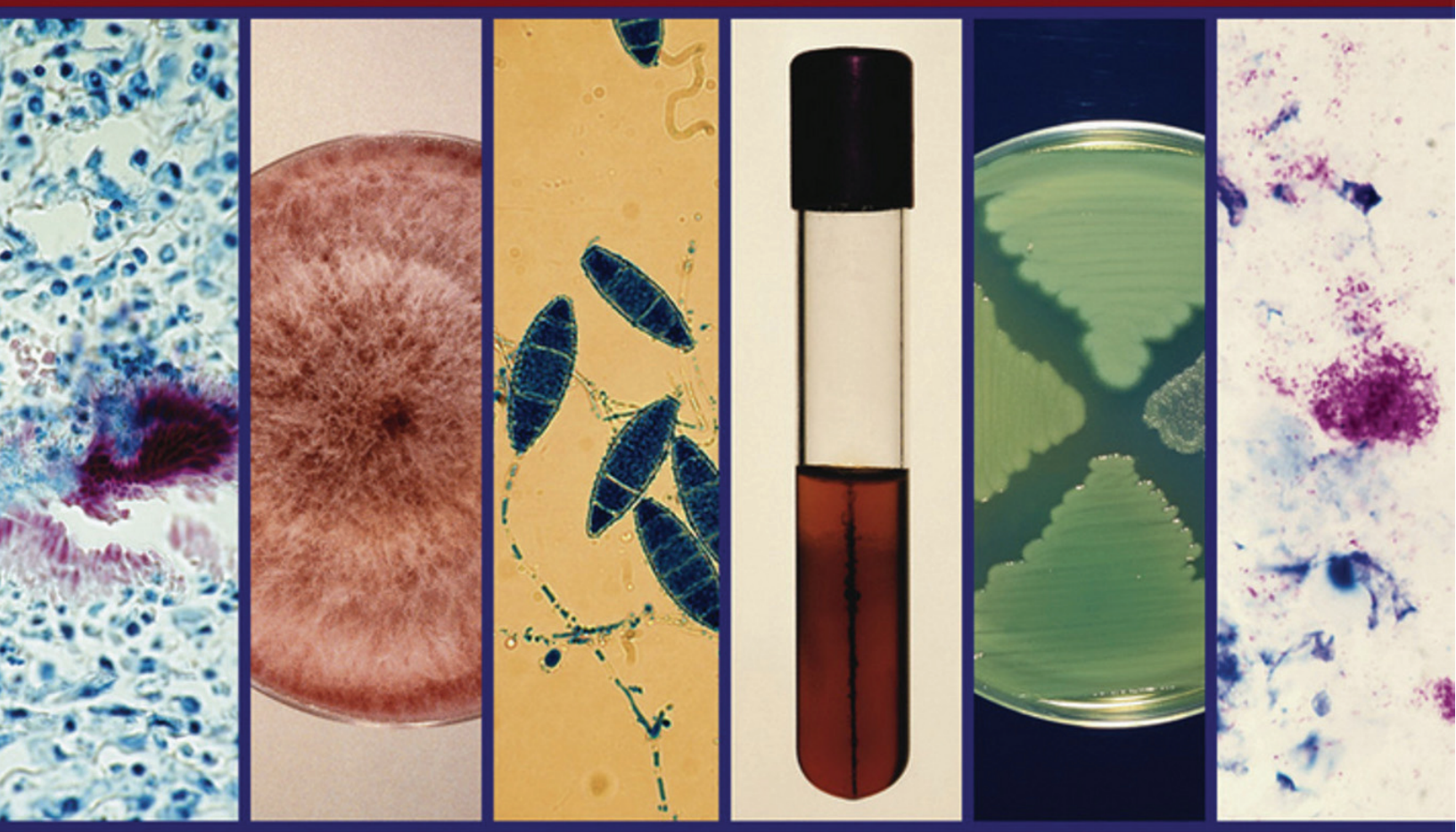
Second Edition



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Contents

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This book is dedicated to the memory of
Margery E. Carter
and
W.J.C. (Bill) Donnelly, co-authors of the first edition

Preface

The pace of change in microbiology has accelerated in recent years as molecular techniques, applied to microbial pathogens, elucidate the pathogenesis of many infectious diseases and improve the reliability of diagnostic test procedures. Today, microbiology occupies a central position in the veterinary curriculum and has developed into a subject of vast complexity. Since the publication of *Veterinary Microbiology and Microbial Disease* in 2002, many changes have occurred in veterinary microbiology, some on the recommendations of international committees and others as a consequence of relevant research.

The second edition of our book incorporates changes in individual chapters which have been updated and expanded. In addition, new chapters on immunodeficiency diseases, vaccines and vaccination, molecular diagnostic methods, antibacterial resistance, antifungal chemotherapy, antiviral chemotherapy and microbial diseases of the urinary tract, cardiovascular system, musculoskeletal system and the integumentary system have been added.

This edition is divided into seven sections. The first section provides an introduction to microbiology, infection, immunity and molecular diagnostic methods. Section II contains chapters on introductory bacteriology. Pathogenic bacteria are dealt with in Section III. The twelve chapters in Section IV are concerned with mycology. Introductory virology is presented in Section V. Viruses and prions are covered in Section VI. The final section, Section VII, includes chapters on the interactions of microbial pathogens with body systems. A separate chapter in this section deals with bovine mastitis and the final chapter provides a comprehensive review of disinfection, biosecurity and other aspects of disease control.

To facilitate readers requiring additional information on topics included in the book, a list of websites is provided at the end of Section VII.

The use of colour in this edition enhances the quality of the illustrations and facilitates the interpretation of complex diagrams.

The authors would be pleased to receive notification of errors or inaccuracies in this edition of our book.

Acknowledgements

We wish to acknowledge the constructive comments of the following colleagues who offered scientific, technical and editorial advice on individual chapters or who assisted in other ways: Hester McAllister, Marijka Beltman, Aidan Kelly, Paul Stanley, Carolyn Cummins, Eva Maischberger, Jane Irwin, Robert Shiel, Clodagh Kearney, Gráinne McCarthy, Hanne Jahns, Joe Cassidy, Yvonne Abbott, Dores Maguire, Frances LeMatti, Ruth Henry, Pauline Coyle, Sean Hogan, Jarlath Nally, Steve Gordon, Brian Sheahan, Mark Rogers, Shane Cooney, Orla Condell, Marta Martins, Matthew McCusker, Stephen O'Brien, Katie Solomon, Karen Power, Paul Whyte, Patrick Wall and Theo De Waal, School of Veterinary Medicine, University College Dublin; Cliona O'Farrelly, Tim Foster and Patrick Prendergast, Trinity College Dublin; Pat Lenihan, Maire McElroy, Kevin Kenny, Peter O'Neill and Pat Raleigh, Central Veterinary Research Laboratory, Backweston; Patrick Rogan, Department of Agriculture, Fisheries and Food; Hywel Ball, Agri-Food and Biosciences Institute, Stormont; Patrick McDonough, College of Veterinary Medicine, Cornell University; Helen O'Shea, Department of Biological Sciences, Cork Institute of Technology; Alan Reilly and Wayne Anderson, Food Safety Authority of Ireland; Brendan Crowley, Department of Medical Microbiology, St. James's Hospital, Dublin; Donal Walsh, School of Veterinary Medicine, University of California, Davis; Ross Fitzgerald, Universitry of Edinburgh; Davida Smyth, NewYork University; Clive Lee, Royal College of Surgeons in Ireland; James Buckley, Veterinary Department, Cork County Council.

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Justinia Wood, Nick Morgan, Lucy Nash and their colleagues at Wiley-Blackwell provided advice and assistance throughout this long project. The careful editing of the manuscript by Mary Sayers, copy editor, improved the accuracy of the text, illustrations and references. As Project Manager, Ruth Swan coordinated corrections and advised the authors on technical aspects of changes to the manuscript.

Dublin, July 2011

Author biographies

P.J. Quinn, MVB, PhD, MRCVS, was Professor of Veterinary Microbiology and Parasitology and Head of the Department in the Faculty of Veterinary Medicine, University College Dublin, from 1985 to 2002. After graduating from University College Dublin in 1965, he spent some time in veterinary practice before enrolling as a postgraduate student in Ontario Veterinary College, University of Guelph, Canada. In 1970, he was awarded a PhD for research in veterinary immunology and he remained on the staff of Ontario Veterinary College until his return to the Faculty of Veterinary Medicine, University College Dublin, in 1973.

His research interests have included allergic skin reactions in the horse to biting insects, the epidemiology of toxoplasmosis in sheep, immune mechanisms in the respiratory tract of calves, leptospirosis in dairy cattle, immunomodulation, mechanisms of immunity in the respiratory tract of specific pathogen-free and conventional cats, botulism in gulls around the Irish coastline, factors influencing the tuberculin test in cattle, airborne dispersal of bacteria during slurry spreading, and evaluation of the efficacy of chemical disinfectants against *Brucella abortus* and *Mycobacterium bovis.*

In addition to many refereed publications in journals and chapters in books, he edited *Cell-mediated Immunity* (1984), is senior co-author of *Animal Diseases Exotic to Ireland* (1992), *Clinical Veterinary Microbiology* (1994), *Microbial and Parasitic Diseases of the Dog and Cat* (1997), *Veterinary Microbiology and Microbial Disease* (2002) and *Concise Review of Veterinary Microbiology* (2003) and is co-author of *Veterinary Embryology* (2006).

He was awarded the title Professor Emeritus by University College Dublin in 2002. In 2006, he was recipient of the Association of Veterinary Teachers and Research Workers outstanding teaching award. For his contribution to teaching and faculty development in the Faculty of Veterinary Medicine in Tirana, he was awarded an honorary doctorate by the Agricultural University of Tirana, Albania, in May 2010.

Bryan K. Markey, MVB, PhD, MRCVS, Dip Stat, graduated from the Faculty of Veterinary Medicine, University College Dublin, in 1985. Following a short period in general practice he was appointed house surgeon in the Faculty of Veterinary Medicine, University College Dublin. In 1986, he joined the academic staff as an assistant lecturer in the Department of Veterinary Microbiology and Parasitology. He spent one year on study leave at the Veterinary Sciences Division, Belfast, and enrolled for a PhD degree at Queen's University. He was awarded a PhD from Queen's University, Belfast in 1991 and was promoted to senior lecturer in veterinary microbiology in 1997. From 2002 to 2004 he served as Head of Department. In 2005 he was visiting professor at the College of Life Sciences, Queensland University of Technology, Brisbane.

His research interests include chlamydial infections of domestic animals and methicillin-resistant *Staphylococcus aureus* infection in veterinary species. He has contributed chapters to books on veterinary disinfection and is co-author of *Animal Diseases Exotic to Ireland* (1992), *Clinical Veterinary Microbiology* (1994), *Microbial and Parasitic Diseases of the Dog and Cat* (1997), *Veterinary Microbiology and Microbial Disease* (2002) and *Concise Review of Veterinary Microbiology* (2003).

Finola C. Leonard, MVB, PhD, MRCVS, graduated from the Faculty of Veterinary Medicine, University College Dublin, in 1983. She was house surgeon in the Department of Large Animal Medicine, Royal (Dick) School of Veterinary Studies, Edinburgh, for one year and engaged in veterinary practice for three years. She commenced postgraduate studies in the Faculty of Veterinary Medicine, University College Dublin, on leptospirosis in dairy cattle while based at Teagasc, Moorepark, Co. Cork, and was awarded a PhD for research on this topic in 1991. She remained in Moorepark as a postdoctoral research worker until 1997. Her research was concerned with foot lameness in dairy cattle and the influence of housing on the behaviour and welfare of cattle and pigs.

She was appointed college lecturer in the Department of Veterinary Microbiology and Parasitology in the Faculty of Veterinary Medicine, University College Dublin in 1997 and was promoted to senior lecturer in veterinary microbiology in 2002. Her research interests include *Salmonella* infection in pigs, other zoonotic infections, and antimicrobial resistance, including methicillin-resistant *Staphylococcus aureus* infection in farm and companion animals.

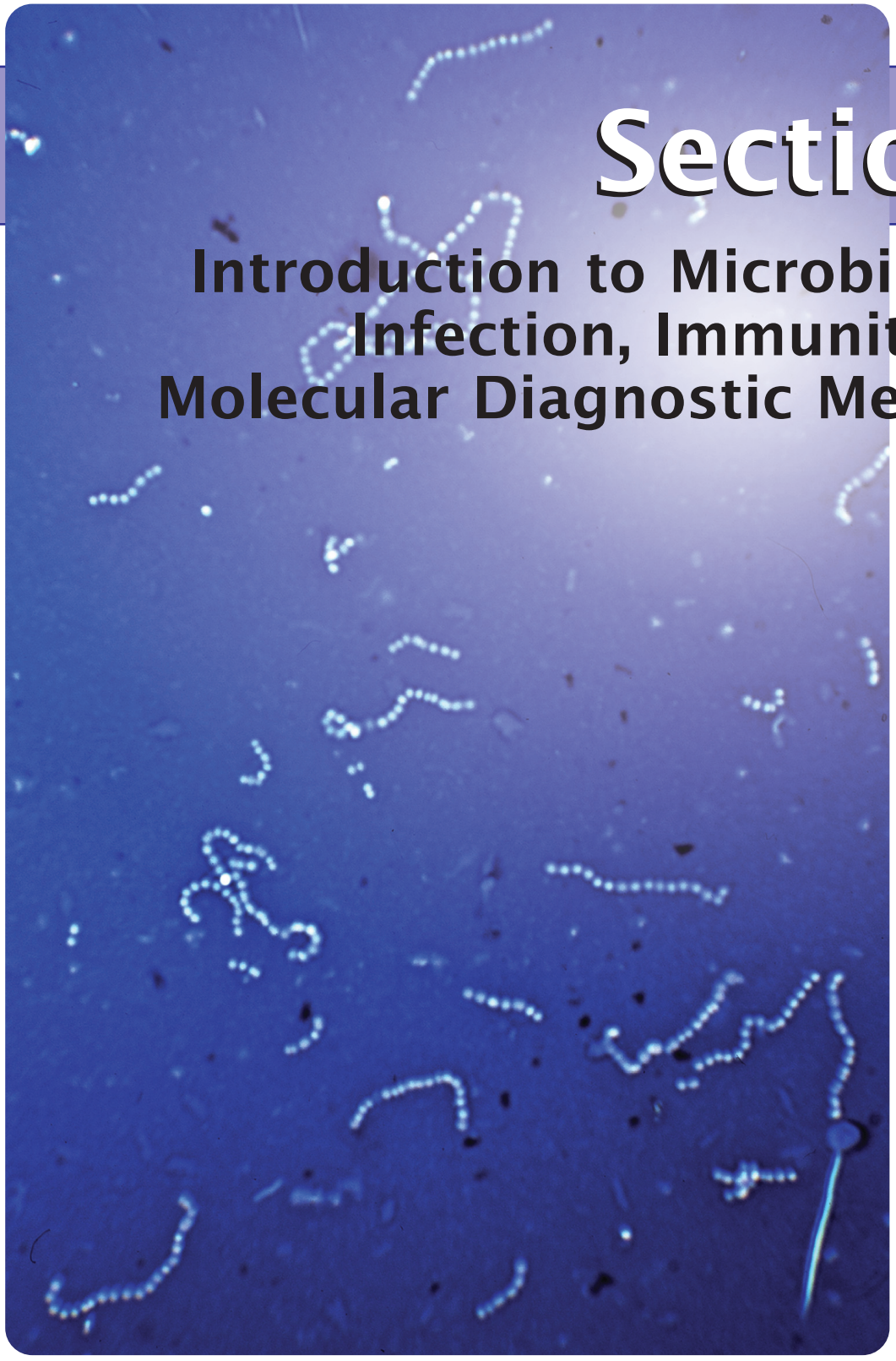
Eamonn S. FitzPatrick, FIBMS, was awarded Fellowship of the Institute of Biomedical Science in 1978 and was appointed to the post of Principal Technician in the Department of Veterinary Anatomy, University College

Dublin. He was appointed to the Histopathology Advisory Committee of the Irish Academy of Medical Laboratory Sciences in 1979. From 1987 to 1989 he was External Examiner for the Diploma in Medical Laboratory Science—Histopathology Option, at the Dublin Institute of Technology, where he also lectured for many years on electron microscopy in the Medical Laboratory Sciences Degree course. He was appointed Chief Technical Officer in the Veterinary Science Unit of the School of Veterinary Medicine, University College Dublin, in 2006. He has been teaching veterinary anatomy and histology for over 25 years.

Recent published work includes papers on hormone receptors in the bovine reproductive tract and the effect of diet supplements on the alimentary tracts of weanling pigs. His current research interests are centred mainly on mucins, mucus gels and the interaction of microbial pathogens with epithelial surfaces, especially of the bovine and equine reproductive tracts. He is co-author of *Veterinary Embryology* (2006).

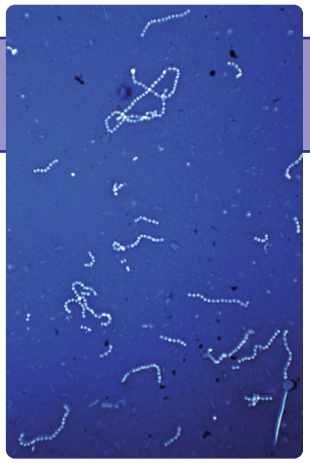
Séamus Fanning, BSc, PhD, graduated in Biochemistry and Microbiology from University College Cork. He was awarded a Fulbright Fellowship in 1995 and worked at Baylor College of Medicine, Houston. In 2002 he was appointed as the Professor of Food Safety and Zoonoses at University College Dublin and set up the UCD Centre for Food Safety. Currently, his research interests include the application of molecular methods to food safety to aid in the control of zoonotic bacteria. A significant part of his research is related to the characterization of the genetic mechanisms contributing to the emergence of multiple drug resistance in food-borne pathogens. In particular, this work is related to strain virulence and its influence on survival in the food chain. His research group is involved in characterizing the emerging pathogen, *Cronobacter* species (formerly known as *Enterobacter sakazakii*), linked to powdered infant milk formula. The UCD Centre for Food Safety was designated as the World Health Organization (WHO) Collaborating Centre for Research, Reference and Training on *Cronobacter*.

Patrick J. Hartigan, BSc, MVM, MA, PhD, MRCVS, graduated from the Veterinary College of Ireland in 1955. After a decade in large animal practice in Co. Kerry, he registered as a graduate student at the School of Veterinary Medicine, Trinity College, Dublin. His studies on uterine pathology in repeat breeder cows were rewarded with a PhD in 1970. After 10 years as a pathologist in the School of Veterinary Medicine, he moved to a post as Senior Lecturer in Reproductive Physiology at the Department of Physiology in the Faculty of Health Sciences at Trinity College, where he remained until retirement. At present, he is a Research Associate in the Department of Physiology.



Section I

Introduction to Microbiology, Infection, Immunity and Molecular Diagnostic Methods



Chapter 1

Microbiology, microbial pathogens and infectious disease

The earliest forms of life on this planet are presumed to have had characteristics resembling those of bacteria, most likely anaerobic bacteria. It is postulated that prokaryotes evolved from primitive forms of life and that the subsequent availability of oxygen resulting from photosynthesis contributed to microbial diversity. The chronological sequence of evolutionary events relating to the emergence of microbial life and, subsequently, eukaryotic cells is outlined in Fig. 1.1. This proposed scheme is based on limited factual information, some deriving from information gleaned from fossilized remains of prokaryotic cells approximately 3.5 billion years old and also from studies of ribosomal RNA among microorganisms.

Before the causes of infectious diseases could be discussed and evaluated in a rational manner, events associated with the emergence of life forms required explanation. Traditional views on the origin of life were strongly influenced by the writings of classical Greek and Roman scholars, many of whom espoused the view of spontaneous generation of small living entities. Disease was often attributed to evil forces associated with disturbances in the upper atmosphere, poisonous vapours called miasmas, supernatural events and other influences unrelated to biology. Awareness of the possible existence of forms of life not visible to the naked eye emerged slowly. As early as 1546, in his treatise *De Contagione*, Girolamo Fracastoro suggested that animate agents were responsible for disease. Concepts of infectious diseases were closely related to the demonstration of organisms too small to be observed without magnification and to the isolation and characterization of these small organisms, termed microorganisms. Major developments in microbiology, the study of these microorganisms, began with theories relating to the causes of infectious diseases and continued with the development of microscopy, which confirmed the existence of microorganisms visible only by substantial magnification. Towards the middle of the nineteenth century, the pioneering work of Louis Pasteur and Robert Koch confirmed the microbial aetiology of infectious diseases. Progressive developments contributed to the rapid expansion of knowledge and the establishment of microbiology as a subject of major importance not only in human and animal health but also in food processing and preservation.

Spontaneous generation as an explanation for the emergence of life from decaying organic matter was a commonly held view for many centuries. It was postulated that life began as a consequence of putrefaction or some other associated change in organic matter. A number of practical experiments aimed at testing this concept were carried out, often with equivocal results. Improved scientific methodology and the availability of suitable instrumentation gradually challenged the acceptance of spontaneous generation. The development of the microscope around 1600 offered a means of exploring minute living entities, and the amateur Dutch scientist, Antonie van Leeuwenhoek, took a keen interest in the examination of water, fluids and organic material. In fluids he observed large numbers of motile structures, not visible to the naked eye, which he called 'animalcules'. In 1675, van Leeuwenhoek recorded the structures he observed, which were probably bacteria, yeasts and protozoa. However, van Leeuwenhoek's discovery of microorganisms did not resolve the issue of spontaneous generation.

The occurrence of maggots on putrefying meat was taken as evidence of spontaneous generation. The Italian physician and naturalist Francesco Reddi (1626–1697) carried out relevant experiments on this

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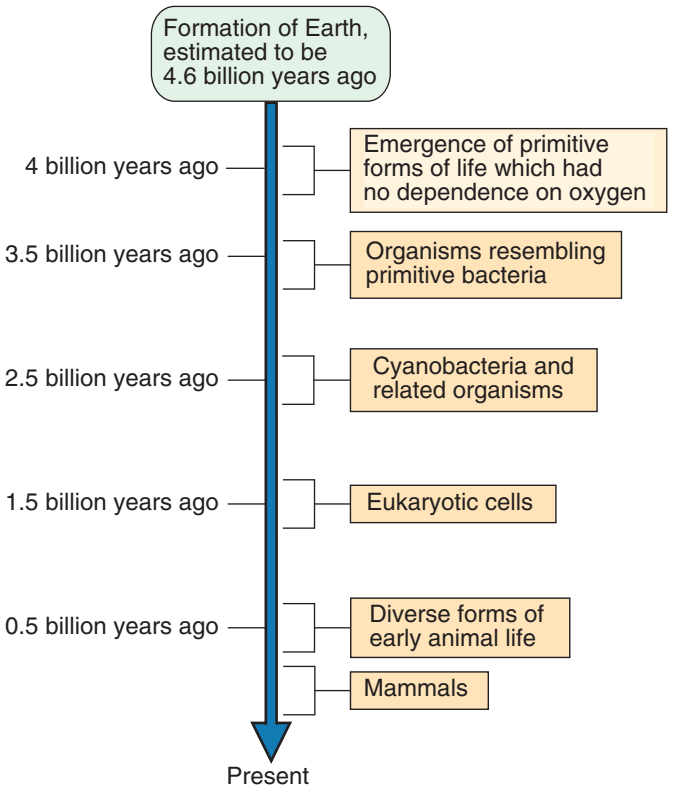

Figure 1.1 Chronological sequence of biological events from the formation of Earth, relating to the evolution of different forms of microbial life and, later, eukaryotic cells. Although supporting scientific evidence documenting the earliest forms of microbial life is not currently available, data from microfossils confirm the existence of organisms resembling cyanobacteria approximately 3.5 billion years ago.

topic and demonstrated that maggots developed in meat only when flies laid their eggs on it. In the mid-eighteenth century, the English naturalist John Needham investigated the effect of boiling broth on the survival of microorganisms. He claimed to have detected microorganisms in boiled broth several days later. Needham's experimental procedures were shown subsequently to have been unreliable. In 1769, Lazzaro Spallanzani repeated Needham's experiments and demonstrated that no organisms survived in broth boiled for 1 hour. Needham argued that air was essential for all life and that Spallanzani had excluded air from the flasks containing broth. As a defined branch of science, microbiology could not advance until the concept of spontaneous generation was disproved. When the French chemist Louis Pasteur (1822–1895) became involved in investigations relating to microbiology, his careful planning and intuitive understanding of biology brought a new energy and appropriate methodology which conclusively refuted the prevailing theories of spontaneous generation. Pasteur's interest in spontaneous generation was prompted by experiments which he had conducted on spoilage during the fermentation of beet alcohol. He showed that a contaminating yeast that produced lactic acid during fermentation and which differed morphologically from brewers' yeast was responsible for the spoilage. He deduced that both alcoholic and lactic fermentation resulted from the metabolism and replication of the living yeast cells. The solution to the spoilage problem during fermentation of wine and beer products lay in heating the raw materials to about 120°F (49°C) in order to kill contaminating microorganisms prior to the addition of the appropriate yeast cells. This process, now known as pasteurization, is widely used to reduce microbial contamination in order to prolong the shelf-life of milk and some other foods.

Pasteur effectively ended the controversy about spontaneous generation through definitive confirmation of Spallanzani's experiments. Furthermore, he demonstrated that contamination of nutrient broth when exposed to air resulted from microorganisms in dust particles settling on the fluid.

An important technical advance, which stemmed from Pasteur's fermentation studies, was the development of a fluid medium suitable for culturing yeast cells. He then developed other liquid media containing specific ingredients that favoured the growth of particular pathogenic bacteria. It was this development which eventually allowed him to formulate the germ theory of disease. The germ theory formed the

basis for Pasteur's experiments on vaccination against fowl cholera, anthrax and rabies. An additional practical application of the theory was the introduction of phenol as a disinfectant for surgical procedures by the British surgeon Joseph Lister.

Together with Pasteur, the German physician Robert Koch is considered to be a co-founder of modern microbiology. Having observed bacilli in the blood of animals that had died from anthrax, Koch demonstrated their pathogenicity by injecting mice with the blood. The injected mice died and the bacilli were present in preparations from their swollen spleens. He was also able to transfer the infection from mouse to mouse and to demonstrate the bacilli in each newly infected mouse. Initially, Koch used blood serum for growing the anthrax bacillus *in vitro*. Later, he developed solid media which allowed isolation of individual bacterial colonies. Using a solid medium, he was eventually able to isolate the tubercle bacillus from the tissues of an experimental animal in which he had demonstrated microscopically the presence of the organism. As a result of these observations, Koch formulated certain principles for proving that a specific microorganism caused a particular disease (Box 1.1). Pasteur's germ theory of disease and Koch's postulates are the two cornerstones on which microbiology is based and without which this branch of biology could not have advanced.

By the end of the nineteenth century a number of important infectious diseases had been confirmed as bacterial in origin. Both Pasteur and Koch contributed to the identification and confirmation of the causal agent of anthrax. Pasteur demonstrated that fowl cholera, malignant oedema and suppurative lesions were each associated with a specific bacterial infection. The causative organisms of tuberculosis and typhoid fever were recognized by Koch and his associates. Other bacterial agents responsible for serious infectious diseases including glanders, gas gangrene, diphtheria and dysentery were isolated by laboratory scientists in Europe, North America and Japan.

The basic technical approaches, pioneered by Pasteur and Koch, failed to shed light on the causes of such serious infectious diseases as rabies, smallpox, foot-and-mouth disease and rinderpest. Despite the absence of specific knowledge about the aetiology of these diseases, successful vaccines were introduced both for smallpox, by Edward Jenner in the late eighteenth century, and for rabies, by Pasteur and his associates in the latter half of the nineteenth century. The development by Pasteur's co-worker, Charles Chamberland, of the porcelain filter to produce bacteriologically-sterile water for use in culture media, eventually facilitated isolation of the filterable agents which caused viral diseases. Remarkably, the technique was first used to elucidate the cause of a plant viral disease, tobacco mosaic disease.

Dmitri Ivanovsky, a Russian scientist, reported in 1892 that it was possible to transmit tobacco mosaic disease from diseased to healthy plants using filtered leaf extract as inoculum. The filters used by Ivanovsky were Chamberland porcelain filters designed to remove bacteria from drinking water. In 1898, Martinus Beijerinck, unaware of the work of Ivanovsky, also demonstrated the filterability of the agent of tobacco mosaic disease. Moreover, he realized that the disease could not be due to a toxin as the filtered sap from infected plants could be used for serial transmission of the disease without loss of potency. In the same year, Loeffler and Frosch identified the first filterable agent from animals, the virus of foot-and-mouth disease. Yellow fever virus, a filterable agent pathogenic for humans, was described by Walter Reed and his team in 1901. Ellerman and Bang, in 1908, demonstrated the oncogenic potential of a filterable agent, the cause of avian leukosis. In 1915, Frederick Twort observed that bacteria were susceptible to a filterable agent, and two years later Felix d'Herelle made a similar observation. D'Herelle named these viruses 'bacteriophages' and developed a technique for establishing their concentration in active preparations. Bacteriophages have proved to be particularly useful in studies on viral replication and bacterial genetics.

Initially, the only method available for recovering large quantities of virus was through infecting susceptible animals. In 1913 Steinhardt and his colleagues succeeded in growing vaccinia virus in explants of guinea-pig cornea embedded in clotted plasma. Some 20 years later, Furth and Sturmia used mice as a host species for propagating viruses, while Woodruff and Goodpasture were successful in propagating fowlpox virus on the chorioallantoic membrane of embryonated eggs. A major advance was made in the early 1950s with the development of single cell cultures. Factors critical in this development included the availability of antibiotics to control bacterial contamination, and the use of trypsin to obtain cell suspensions

Box 1.1 Koch's postulates

- The pathogenic microorganism must be present in every case of the disease but absent from healthy animals
- The suspected microorganism must be isolated and grown in pure culture
- The same disease must occur when the isolated microorganism is injected into healthy susceptible animals
- The same microorganisms must be isolated again from the injected animals which developed disease

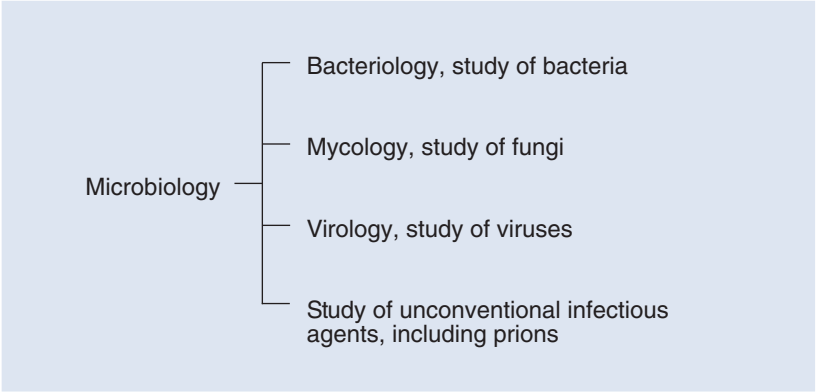

Figure 1.2 Subdivisions of microbiology, a subject which has areas of common interest with pathology, immunology, pharmacology, medicine and therapeutics.

from embryonic or adult tissue. The separated cells could then be grown as monolayers on glass surfaces. Continuous cell lines, capable of multiplying indefinitely, provided a reliable source of cells for virus cultivation.

In 1887 Buist observed vaccinia virus using a light microscope. However, because of the limited resolving power of this type of microscopy, the structure of the virus was not discernible. In 1939 Kausche and his co-workers employed the newly-developed electron microscope and a metal shadowing technique to identify tobacco mosaic virus in purified preparations. Ultrastructural studies of viruses were greatly expanded and enhanced in the 1950s by the development of negative staining and methods for cutting ultrathin sections. X-ray diffraction methods have been applied to viruses since the 1930s, when it was discovered that simple viruses could be crystallized. The first complete high-resolution structure of a crystalline virus, tomato bushy stunt virus, was obtained by Harrison and his co-workers in 1978. Computer analysis of the diffraction patterns obtained by such studies has contributed to knowledge of the molecular structure of viruses.

The crystallization of tobacco mosaic virus (TMV) by Stanley in 1935 provided a boost to the analysis of the chemical composition of viruses. In 1937 Bawden and Pirie showed that TMV contained nucleic acid as well as proteins, and helped to promote the idea that viruses consisted of nucleic acid contained within a protein coat. Having elucidated the structure of DNA and observed the limited coding capacity of viral nucleic acid, Watson and Crick in 1956 suggested that viral nucleic acid was surrounded by a shell of identical protein subunits. In 1962 Lwoff and his colleagues proposed a universal system on which the modern classification of viruses is based. The method of classification proposed was based on the following criteria: (1) the type of nucleic acid; (2) the symmetry of the virus; (3) the presence or absence of an envelope; (4) the diameter of the nucleocapsid (helical viruses) or the number of capsomers (icosahedral viruses). The discovery of the enzyme reverse transcriptase in 1970 by Temin and Baltimore helped to elucidate retrovirus replication and provided an essential tool for producing complementary DNA (cDNA). This ushered in the recombinant DNA revolution. The study of retroviruses has made a substantial contribution to the advancement of basic research in neoplasia and the role of oncogenes in the emergence of malignant tumours.

During the past century, major developments have taken place in microbiological concepts, techniques and applications. Modern microbiology encompasses the study of bacteria, fungi, viruses and other microscopic and submicroscopic organisms (Fig. 1.2). In veterinary microbiology, emphasis is placed on those microorganisms associated with infectious diseases of animals. Immunology, the study of host responses to infectious agents, is a discipline closely related to microbiology and is sometimes considered a distinct but cognate subject.

Further reading

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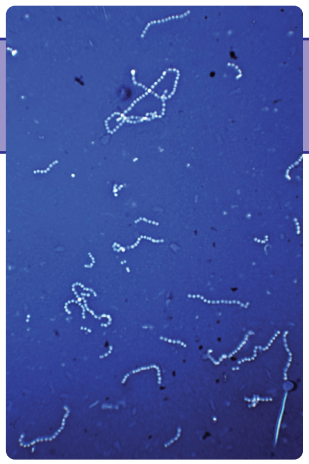

Chapter 2

Subdivisions, classification and morphological characterization of infectious agents

Living cells, the smallest units capable of independent existence, can be divided into two sharply differentiated groups, eukaryotes and prokaryotes. The main differentiating features of eukaryotic and prokaryotic cells are presented in Table 2.1. Eukaryotes possess true nuclei which contain chromosomes, and individual cells replicate by mitosis. In addition, a typical eukaryotic cell contains organelles such as mitochondria, a Golgi apparatus, lysosomes and relatively large ribosomes. Organisms in the domains *Archaea* and *Bacteria*, which are less complex than eukaryotic organisms, are prokaryotes which lack true membrane-bound nuclei. Their genetic information is contained in a single circular chromosome. In some prokaryotic cells such as bacteria, extrachromosomal DNA in the form of plasmids encodes for certain characteristics of the organism. Although the origin of life is a much debated subject, it is probable that primitive microorganisms originated from ancestral life forms several billion years ago. The degree of relatedness among microorganisms can be assessed by comparison of their ribosomal ribonucleic acid (rRNA). There is some evidence that all organisms developed from a group of primitive cells rather than from a single organism (Doolittle, 1999). Prokaryotes are considered as one branch of the phylogenetic tree and eukaryotes as the second branch (Fig. 2.1). Lateral as well as horizontal transfer of genetic material probably occurred in the course of evolutionary development, with some bacterial genes incorporated into members of the *Archaea* and perhaps with some prokaryotic genes incorporated into eukaryotes. This lateral gene transfer may explain how complex eukaryotic cells acquired some of their genes and organelles. The endosymbiosis hypothesis proposes that at some stage in their early development, eukaryotic cells became primitive phagocytes and acquired particular bacterial cell types which enhanced their respiratory activity (de Duve, 1996). It is proposed that the engulfed bacteria provided extra energy through this enhanced respiration to the host cell and eventually evolved into mitochondria. A similar phenomenon may account for the development of chloroplasts in plant cells. The cytoplasmic membrane is the site of respiratory or photosynthetic energy generation in prokaryotes, unlike eukaryotes in which these activities occur in the membranes of mitochondria and chloroplasts.

Microscopical techniques

A number of different microscopical methods are employed for examining microorganisms. These include bright-field, dark-field, phase-contrast and electron microscopy. Table 2.2 summarizes common techniques employed for the examination of microorganisms and the particular types of microorganisms for which the techniques are appropriate. Units of measurement employed in microscopy are indicated in Table 2.3.

The maximum magnification obtainable by bright-field microscopy, using oil-immersion objectives, is approximately 1,000×. With bright-field microscopy, suitably stained bacteria as small as 0.2 μm in size can

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Table 2.1 Comparative features of prokaryotic and eukaryotic cells.

Feature	Prokaryotic cell	Eukaryotic cell
Size of individual cells	Usually less than 5 µm in greatest dimension	Typically greater than 5 µm
Genetic material	Not separated from cytoplasm	Nucleus separated from cytoplasm by a nuclear membrane
Characteristics of chromosomes	Usually single and circular	Multiple and linear
Mitochondria	Absent	Present
Golgi apparatus	Absent	Present
Endoplasmic reticulum	Absent	Present
Location of ribosomes	Dispersed throughout cytoplasm	Dispersed throughout cytoplasm and also attached to endoplasmic reticulum
Cell division	Binary fission	Mitosis

Table 2.2 Microscopical techniques used in microbiology.

Technique	Comments
Bright-field microscopy	Used for demonstrating the morphology and size of stained bacteria and fungi; staining affinity may allow preliminary classification of bacteria and the morphology of fungal structures permits identification of the genus
Phase-contrast microscopy	Used for examining unstained cells in suspension
Dark-field microscopy	Used for examining unstained bacteria such as spirochaetes in suspension
Fluorescence microscopy	Used for identifying microorganisms with specific antibodies conjugated with fluorochromes
Transmission electron microscopy	Used for demonstrating viruses in biological material and for identifying ultrastructural details of bacterial, fungal and mammalian cells
Scanning electron microscopy	Used for demonstrating the three-dimensional structure of microorganisms

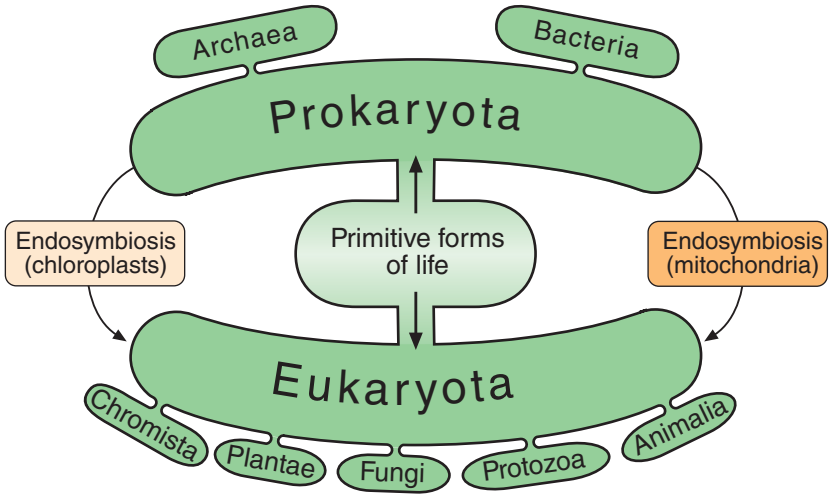


Figure 2.1 The evolutionary relationships of living organisms. Endosymbiosis is one of the postulated mechanisms whereby eukaryotic cells acquired mitochondria or chloroplasts by incorporation of prokaryotic cells.

be visualized. With dark-field microscopy, the scattering of light by fine microorganisms such as spirochaetes suspended in liquid allows them to be observed against a dark background. In common with dark-field techniques, phase-contrast microscopy can be used to examine unstained specimens. This procedure is more appropriate for research purposes than for routine diagnostic microbiology.

In transmission electron microscopy, beams of electrons are used in place of visible light to visualize small structures such as viruses. Specimens, placed on grids, are negatively stained with electron-dense compounds such as potassium phosphotungstate and viewed as magnified images on a fluorescent screen. Magnifications greater than 100,000× are possible with modern instruments. Scanning electron microscopy is used to obtain three-dimensional views of microorganisms when coated with a thin film of heavy metal. With this technique a wide range of magnifications up to 100,000× is feasible.

Table 2.3 Units of measurement used in microbiology.

Unit	Abbreviation	Comments
Millimetre	mm	One thousandth of a metre (10^{-3} m). Bacterial and fungal colony sizes are usually measured in mm. When growing on a suitable medium, bacterial colonies range in size from 0.5 mm to 5 mm
Micrometre (micron)	µm	One thousandth of a millimetre (10^{-6} m). Used for measuring the size of bacterial and fungal cells. Most bacteria range in size from 0.5 µm to 5 µm. A small number of bacteria may exceed 20 µm in length
Nanometre	nm	One thousandth of a micrometre (10^{-9} m). Used for expressing the size of viruses. Most viruses of veterinary importance range in size from 20 nm to 300 nm

Table 2.4 A comparison of the morphology and size of bacterial cells relative to a mammalian red blood cell.

Cell	Morphology / size	Comments
Red blood cell		Readily seen using conventional light microscopy
Bacillus		Rod-shaped cells, usually stained by the Gram method. Using bright-field microscopy, a magnification of 1,000× is required to observe most bacterial cells
Coccus		Spherical cells, often occurring in chains or in grape-like clusters
Spirochaete		Thin, helical bacteria. Dark-field microscopy (without staining) or special staining methods are required to demonstrate these unusual microorganisms

Pathogenic microorganisms

Most microorganisms found in nature are not harmful to humans, animals or plants. Indeed, many bacteria and fungi make an important contribution to biological activities which take place in soil, in water and in the alimentary tract of animals and humans. Those microorganisms that can cause disease in animals or humans are referred to as pathogenic microorganisms.

Bacteria

Microorganisms belonging to the domain *Archaea* (formerly *Archaebacteria*) are not associated with diseases of domestic animals. Organisms (bacteria) belonging to the domain *Bacteria* (formerly *Eubacteria*) include many pathogens of veterinary importance.

Bacteria are unicellular and are smaller and less complex than eukaryotic cells such as mammalian red blood cells (Table 2.4). They usually have rigid cell walls containing a peptidoglycan layer, multiply by binary fission and exhibit considerable morphological diversity. They occur as rods, cocci and helical forms and occasionally as branching filaments. Despite their morphological diversity, most bacteria are between 0.5 μm and 5 μm in length. Motile bacteria possess flagella by which they can move through liquid media. The majority of bacteria can grow on suitable inert media; some require special growth supplements and particular atmospheric conditions for growth. Two groups of small bacteria, rickettsiae and chlamydiae, which are unable to multiply on inert media, require living cells for *in vitro* growth. Cyanobacteria, formerly referred to as blue-green algae, utilize chlorophyll for some metabolic pathways. Unlike algae, which store chlorophyll in organelles referred to as chloroplasts, cyanobacteria have chlorophyll distributed inside their cell membranes.

Fungi

Yeasts, moulds and mushrooms belong to a large group of non-photosynthetic eukaryotes termed fungi. Fungi may be either unicellular or multicellular. Multicellular fungi produce filamentous microscopic structures called moulds; yeasts, which are unicellular, have a spherical or ovoid shape and multiply by budding. In moulds, the cells are cylindrical and attached end to end, forming branched hyphae (Table 2.5). A notable feature of fungi is their ability to secrete potent enzymes that can digest organic matter. When moisture is present and other environmental conditions are favourable, fungi can degrade a wide variety of organic substrates. A small number of yeasts and moulds are pathogenic for humans and animals. Some fungi invade tissues whereas others produce toxic

Table 2.5 A comparison of the morphology and size of a bacterial cell and two fungal forms.

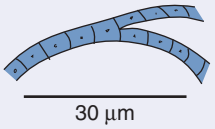
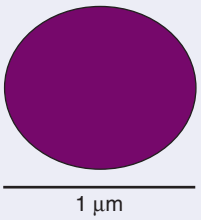
Structure	Morphology / size	Comments
Bacterial cell		
Coccus		Often occur in chains or grape-like clusters
Fungal forms		
Yeast		Reproduce by budding
Mould		Branched structures (hyphae) composed of many cells

Table 2.6 A comparison of a bacterial cell and a large and a small virus.[a]

Structure	Morphology / size	Comments
Bacterial cell		
Coccus		Readily seen at magnification of 1,000×
Viruses		
Poxvirus		Viruses cannot be seen using conventional bright-field microscopy
Parvovirus		Electron microscopy at a magnification of up to 100,000× is used to demonstrate viruses in clinical specimens or in laboratory preparations

a, not drawn to scale.

substances called mycotoxins which, if present on crops or in stored food such as grain or nuts, can cause disease in animals and humans.

Algae

A morphologically and physiologically diverse group of organisms, algae are usually considered plant-like because they contain chlorophyll. Many algae are free-living in water; others grow on the surfaces of rocks and on other structures in the environment. Some algae produce pigments which impart distinct coloration to water surfaces containing algal blooms. When water temperatures are high, algal growth may be marked, leading to the production of toxins that can accumulate in shellfish or in water containing algal blooms.

Viruses

Unlike bacteria and fungi, viruses are not cells. A virus particle or virion consists of nucleic acid, either DNA or RNA, enclosed in a protein coat called a capsid. In addition, some viruses are surrounded by envelopes. Viruses are much smaller than bacteria, and typically range in size from 20 nm to 300 nm in diameter (Table 2.6). Despite their simple structure, viruses occur in many shapes. Some are spherical, others are brick-shaped or bullet-shaped and a few have an elongated appearance. Because they lack the structures and enzymes necessary for metabolism and independent reproduction, viruses can multiply only within living cells. Both prokaryotic and eukaryotic cells are susceptible to infection by viruses. Those viruses that invade bacterial cells are called bacteriophages. Pathogenic viruses which infect humans and animals can cause serious disease by invading and destroying host cells. A small number of viruses are aetiologically implicated in the development of malignant tumours in humans and animals.

Prions

Infectious particles that are smaller than viruses have been implicated in the neurological diseases of animals and humans that are termed transmissible spongiform encephalopathies. These particles, called prions, are distinct from viruses and appear to be devoid of nucleic acid. Prions seem to be composed of an abnormally-folded protein capable of inducing conformational changes in homologous normal host cell protein. Following the induced changes, structurally-altered abnormal protein accumulates in and damages long-lived cells such as neurons. Genetic factors seem to influence the susceptibility of humans and animals to prion diseases. Prions exhibit remarkable resistance to physical and chemical inactivation procedures.

Biological classification and nomenclature

Microscopic living organisms were formerly classified on the basis of phenotypic expression including mor-

phology and distinct attributes reflecting unique metabolic properties. Increasingly, classification methods for microorganisms have come to rely heavily on genotypic analysis. In recent years this has led to changes in the classification and nomenclature of microorganisms.

The practice and science of orderly classification of organisms into hierarchical units termed taxa (singular taxon) is known as taxonomy. There are three interrelated parts to taxonomy: identification, nomenclature and classification. Taxonomy is important in microbiology because (1) it permits accurate identification of organisms; (2) it provides precise names that permit efficient communication; (3) it groups similar organisms in a way that allows predictions to be made and hypotheses to be framed with reasonable confidence regarding members of the same group. Most organisms are grouped according to their genotypic and phenotypic characteristics. Traditionally, great emphasis was placed on anatomical or morphological similarities but this has increasingly been replaced by a polyphasic approach facilitated by the availability of highly sophisticated methods of identification and the inclusion of additional criteria for the description of new species. Examples of phenotypic characteristics used in taxonomy include morphology, metabolism, physiology, cell chemistry (particularly fatty acid composition in the case of bacteria) and motility. DNA profiling, DNA–DNA hybridization, multilocus sequence typing (MLST) and percentage of guanine plus cytosine in an organism's DNA (GC ratio) are examples of the genetic methods used. Complementing these two types of analyses is phylogenetic analysis, which attempts to create a framework of evolutionary relationships. The exponential growth in the availability of genetic sequencing data has permitted taxonomy to increasingly reflect phylogenetic relationships among microorganisms.

The basic taxonomic unit or group is the species. Similar species are grouped into genera, which in turn are placed in families. Several levels or ranks are used in this classification, with higher ranks including individual groups based on the shared properties of these groups. The levels in ascending order are species, genus, family, order, class, phylum and kingdom or domain (Fig. 2.2). Traditionally, biologists have grouped organisms into five kingdoms: animals, plants, fungi, protists and bacteria. However, analysis of small subunit ribosomal RNA gene sequences has suggested that cellular life has evolved along three primary lineages. The three resulting groups are called domains and are usually placed above the kingdom level. Two of the domains, *Bacteria* and *Archaea*, are exclusively microbial and prokaryotic, while the third domain, *Eukarya,* contains the eukaryotes.

In terms of sexually reproducing higher organisms, a species is defined as a group or population composed of similar individuals that are capable of interbreeding naturally and are reproductively isolated from other groups. However, the definition of what constitutes a species poses particular problems in microbiology. Members of the *Bacteria* and *Archaea* do not undergo true reproduction. As a result, bacteria tend to be defined operationally or in subjective terms as a collection of strains that share many similar properties but differ significantly from other strains. It is possible to be more precise by using a definition based on genetic data with a species expected to share 70% or greater binding in standardized DNA–DNA hybridization studies and/or over 97% gene-sequence identity for 16S ribosomal RNA (rRNA). Recently a threshold range of 98.7 to 99% sequence similarity has been recommended as the point at which DNA–DNA reassociation experiments should be required for testing the genomic uniqueness of a novel isolate (Stackebrandt and Ebers, 2006). Further debate and refinement regarding the definition of a bacterial species is on-going.

Microorganisms are generally named according to the binomial system devised by the Swedish botanist Carolus Linnaeus in the eighteenth century. The names are Latin or Latinized Greek derivations and are printed in italics. There are two parts, a capitalized generic name and a specific epithet. For example, the bacterium that causes anthrax in humans and animals is termed *Bacillus anthracis, Bacillus* being the generic name and *anthracis* the specific name. The naming of species and higher groups of bacteria is regulated by the Bacteriological Code – *The International Code of Nomenclature of Bacteria*. *The International Journal of Systematic and Evolutionary Microbiology* is the official publication for recording taxonomical changes of *Bacteria* and *Archaea*. Websites providing listings of approved names include List of Prokaryotic Names with Standing in Nomenclature (http://www.bacterio.cict.fr) and Bacterial Nomenclature Up-to-Date (http://www.dsmz.de/bactnom/bactname.htm).

Viruses pose particular taxonomic problems in that they are regarded as subcellular, non-living, infectious entities and are often ignored or considered alongside their host species by scientists dealing with the global taxonomy of organisms. However, virologists are agreed that viruses should be considered as a separate group of organisms regardless of their host species, and have established a free-standing virus taxonomy derived from classical Linnean systematics but with rules unique to the discipline of virology. The system is operated by the International Committee on Taxonomy of Viruses (ICTV) with the latest information on viral taxonomy published periodically in

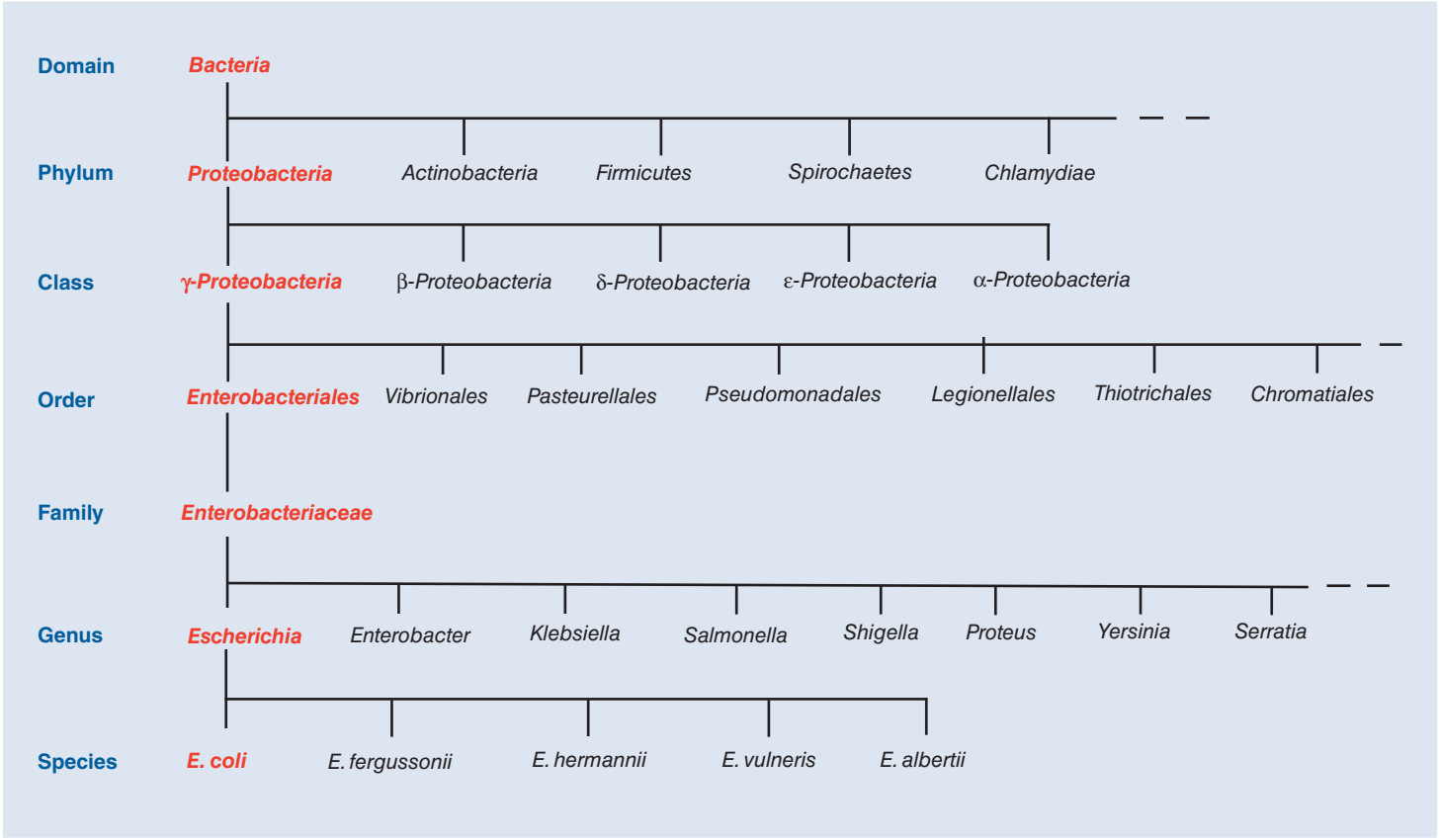


Figure 2.2 Example of hierarchical levels of taxonomy using the bacterium *Escherichia coli*. Note that many of the levels are deliberately incomplete to simplify the diagram.

report form (Fauquet *et al*., 2005) or available electronically at http://ictvonline.org/virusTaxonomy.asp. A number of points must be borne in mind when considering the taxonomy of viruses: (1) it is considered unlikely that viruses evolved from a single original protovirus and, as a result, the highest level recognized is that of order; (2) some viruses frequently undergo genetic recombination and reassortment resulting in chimeric organisms with polyphyletic genomes; (3) some viruses infect both vertebrate and invertebrate hosts, evolving differently in the different host species; (4) some viruses integrate into the genome of their host but can switch between horizontal and vertical transmission by moving in and out of the host cell genome, which may result in the incorporation of host genes into the viral genome. As a result, it is inevitable that the classification system will at times appear artificial and give rise to misfits. A non-systematic, polythetic, hierarchical system of classification is used for viruses. In essence a virus species is defined by a consensus group of properties without any one of these properties being essential. Viruses are generally grouped in families based on virion morphology and nucleic acid type. Further subdivision of pathogenic animal viruses frequently relates to the species of host affected and to the clinical disease which is produced. Each viral genus contains a type species, which is defined as the virus species responsible for the original creation of the genus and whose name is linked to the use of the genus name. Virus species names are commonly abbreviated, for example BPIV-3 for bovine parainfluenza virus 3. In presenting taxonomic descriptions of viruses, several informal categories, collectively known as the order of presentation, are used based on the composition and structure of the viral genome, including genome polarity and reverse transcription: double-stranded DNA viruses, single-stranded DNA viruses, DNA and RNA reverse transcribing viruses, double-stranded RNA viruses, negative-stranded single-stranded RNA viruses and positive-stranded single-stranded RNA viruses. In addition there is a category of unassigned viruses and one for subviral agents including viroids, satellites and prions.

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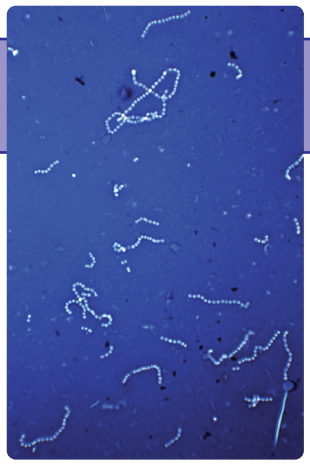

Chapter 3

Infection and immunity

Infectious disease is a major cause of morbidity and mortality in avian and mammalian species. Individual body systems supply the host's respiratory, nutritional and sensory needs, and the immune system is uniquely equipped to provide defence against microbial or parasitic infection irrespective of the source or the route of transmission. Some microorganisms cause opportunistic infections in domestic animals; other infectious agents, termed pathogenic microorganisms, are capable of causing serious infection if they gain entry into the body. The immune system is composed of an array of structures, cells and secretions which offer defence not only against opportunistic infections but also against pathogenic microorganisms which can cause life-threatening infections in susceptible animals.

The first barriers to infection that offer rapid, protective responses are components of innate immunity. These components include anatomical structures such as the skin and mucous membranes, inhibitory secretions, antimicrobial factors and phagocytic cells (Fig. 3.1). If an infectious agent enters the tissues, material from this invading pathogen can be presented to lymphocytes by phagocytic cells such as macrophages. These lymphocytes then undergo functional changes, proliferate and secrete soluble factors which promote the involvement of other cells of the immune system in an attempt to contain the infection. This response on the part of lymphocytes is referred to as an adaptive immune response. Moreover, following an encounter with a microbial pathogen, the body's immune system learns from the experience by responding in a specific manner to the pathogen and by 'remembering' the interaction. Immunological memory resides in some lymphocytes that are produced in the course of a response to an infectious agent, and these memory cells react quickly to subsequent invasion by the same agent. The immune system, therefore, has components that function as innate, non-specific barriers to infectious agents, and components that exhibit specificity combined with immunological memory. It provides protection against a vast array of actual or potential pathogens present in the immediate environment of animals. Immune responses, however, are not confined to infectious agents and responses to innocuous substances such as pollens, foreign proteins and some therapeutic drugs, can cause potentially destructive hypersensitivity reactions. Although the primary activity of the immune system is usually considered to be associated with protection against infectious agents, it has a defined role in immune surveillance for the detection of neoplastic tissue changes and, in some instances, elimination of such undesirable mutated cells or neoplastic cells by immune mechanisms.

Soon after birth the external surfaces of the body, extensive portions of the alimentary tract and regions of the respiratory and urinary tracts become colonized by bacteria. The host and colonizing bacteria live in a relatively peaceful state of coexistence, with microorganisms restricted to parts of the body where they can be tolerated and microbial invasion of tissues can be prevented by natural antibacterial defence mechanisms. Bacteria that colonize tissues of the body without producing disease constitute part of the normal flora. This harmonious relationship between animals and their environment can be reinforced by good management systems, optimal nutrition, adequate floor space and effective disease control

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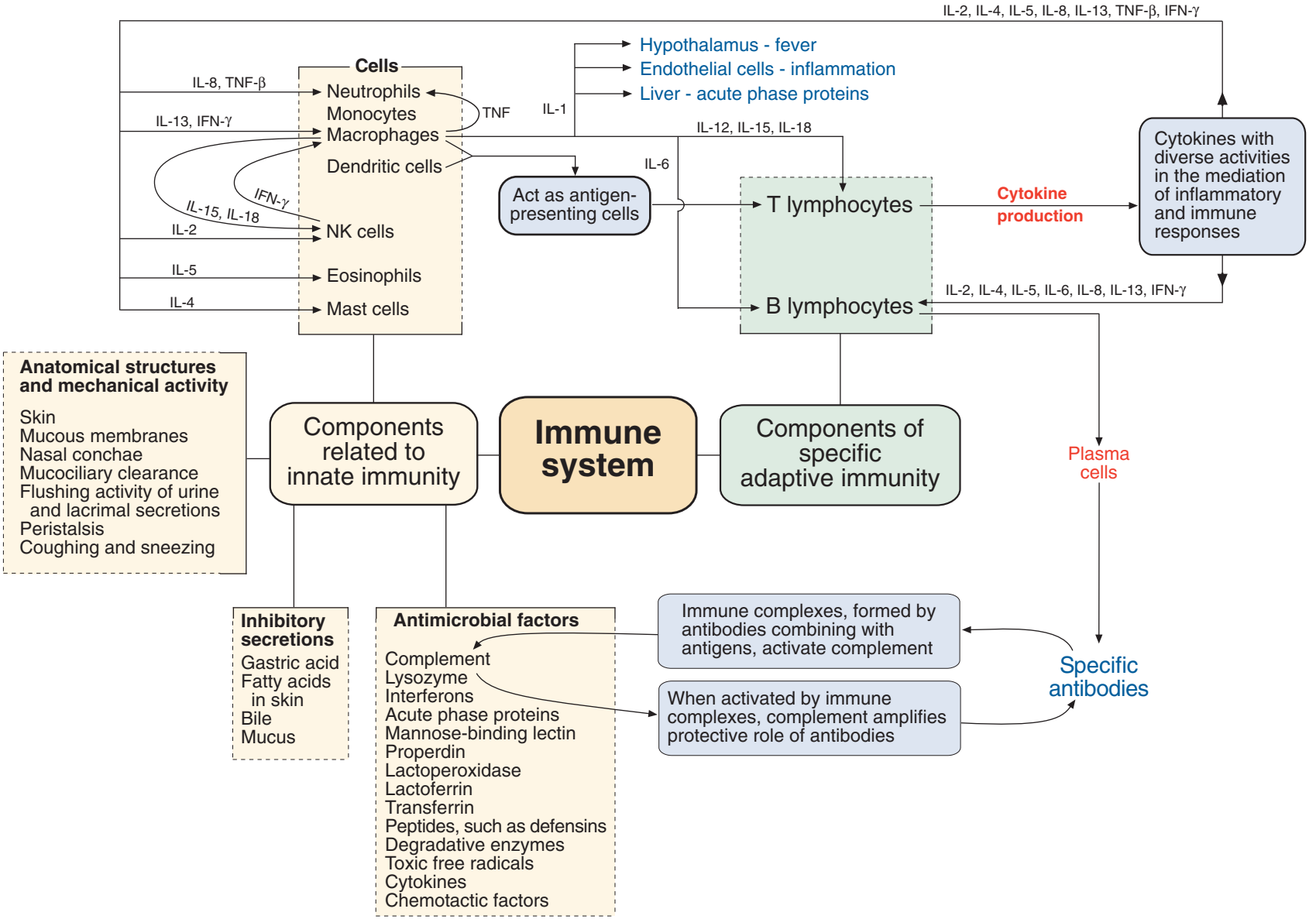

Figure 3.1 Cells, secretions and other elements of innate and adaptive immunity which contribute to protection against infectious agents. IL: Interleukin; IFN-γ: interferon-γ; TNF: tumour necrosis factor.

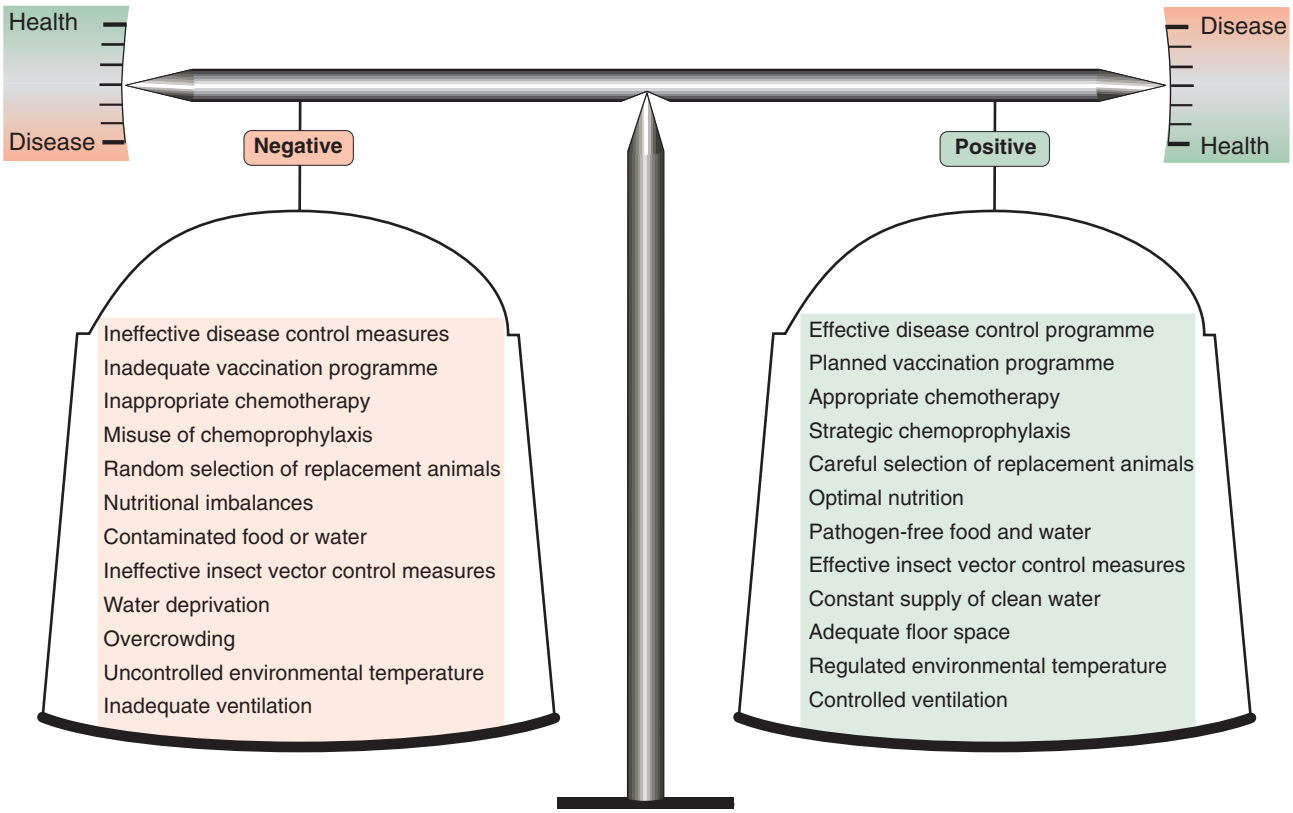

Figure 3.2 The influence of disease control programmes, environmental conditions and other factors on the health status of animal populations. The balance between positive factors that promote health, and negative factors that predispose to disease can determine the health and welfare status of animal populations.

programmes (Fig. 3.2). Negative factors that can tilt the balance in favour of potential or actual pathogens include overcrowding, uncontrolled environmental temperature, nutritional imbalances and absence of a well designed and implemented disease control programme. Even if bacteria, fungi or viruses succeed in entering the tissues and causing infection, disease is not an inevitable outcome. Characteristics of the infectious agent, environmental influences and the susceptibility of the infected animal usually determine the outcome of infection. If infection is not quickly eliminated, clinical disease or subclinical infection is the likely result (Fig. 3.3). Characteristics of individual species of pathogenic bacteria can strongly influence their ability to overcome host defences and produce disease. Structural, metabolic and other features of bacteria that promote disease development are presented in Table 3.1.

Normal flora

Soon after birth, neonatal animals are exposed through contact, ingestion or inhalation to microorganisms present on the dam. Bacteria, yeasts and eventually other microorganisms from the animal's immediate environment may colonize particular sites on the skin and regions of the alimentary, respiratory or urogenital tracts. Microorganisms that compete successfully for particular sites gradually form a stable normal flora. Different regions of the body may have a distinctive resident flora suggesting that regional colonization may reflect a selective advantage on the part of successful microorganisms. The ability to survive acidic conditions in the alimentary tract or tolerance for some naturally occurring antimicrobial factors confers particular survival capabilities on some resident flora. Adherence to host cells or synthesis of metabolic substances antagonistic to competitors may enhance colonization of the skin, mucous membranes or parts of the alimentary tract by some bacteria and yeasts. There is evidence that the normal flora can compete with and sometimes prevent establishment of pathogenic microorganisms. This may be achieved by competition for nutrients, by formation of inhibitory substances, or by attachment to receptors on cell surfaces, thereby preventing colonization by invading pathogens. Although the normal flora is not directly associated with non-specific immunity, their competitive role can be considered beneficial for the host. In