CLINICAL AND ORAL MICROBIOLOGY

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Clinical and Oral Microbiology

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To Terry and Diana

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Preface

Most dental disease is infectious in nature, and dental caries and periodontal disease together form the most common diseases affecting the human race. The majority of dentists, therefore, spend the greater part of their working life trying to prevent or repair the ravages of these diseases.

Many other infections can affect the oral cavity, and occasionally these oral microorganisms can cause severe disease, particularly infective endocarditis, or death.

Microbiology is clearly, therefore, one of the most important scientific disciplines in the dental curriculum and of direct practical relevance to the management or prevention of dental disease.

Another clinically important aspect of microbiology has been the development of increasing numbers of antibiotics. Antibiotics, which were developed as a result of microbiologic discoveries, are outstandingly important scientific advances that have had a major effect on the world in overcoming many infections that were at one time lethal. In spite of the benefits that antibiotics can confer, they can also be double-edged weapons, so that wise and safe use of these remarkable drugs depends on an understanding of general microbiology.

Another by-product of microbiology has been the development of immunology and the appreciation that immunologic reactions may not necessarily be protective phenomena alone but may contribute in varying degree to diseases that are not apparently infectious in nature. The advances in immunology, in turn, have made possible kidney, heart, and other organ transplants.

All of these aspects of microbiology are important in the care of the dental patient, and there is hardly any branch of this discipline that does not impinge on dentistry in some degree. A contributory reason for this is the remarkably wide range of bacteria present in the mouth and the potential of many of them for causing disease. In addition, dental caries, a process in which bacteria produce disease in a unique and complex fashion, has been studied in unusual detail. The findings in some of these studies have, in turn, produced major contributions to general microbiology and the understanding of how bacteria may initiate disease or interact with their environment.

There can be little doubt that the science of microbiology is both intellectually stimulating and of direct practical relevance in dentistry.

The aims of this book are, therefore, in essence, to bring together the general and systematic aspects of microbiology and to relate them to clinical oral infectious disease as a scientific basis for the diagnosis and management of the many aspects of infectious disease affecting the mouth and systemic infections related to the practice of dentistry.

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Section One

General Aspects of Pathogenic Microorganisms and Immunity

Chapter 1

Pathogenic Microorganisms

CHAPTER OUTLINE

Bacteria
Fungi
Viruses
Protozoa
Helminths
Commensals
Colonization and infection
Koch's postulates and proof of etiology in microbial disease
Apparent exceptions to Koch's postulates

The microorganisms that can cause human infections are (1) bacteria, (2) fungi, (3) viruses, and (4) protozoa. The parasitic worms (helminths) also can cause human disease but are mostly too large and complex to be called microorganisms.

The helminths and protozoa are commonly considered together in the science of parasitology, while bacteria, fungi, and viruses are the subjects of microbiology.

BACTERIA

Bacteria are procaryotes, a characteristic of which is the lack of an organized nucleus within a nuclear membrane (Table 1.1). Bacteria, along with fungi, algae, slime molds, and protozoa, were formerly included in the kingdom Protista. More recently they have been placed in a separate kingdom, the Procaryotae. The photobacteria that comprise division I of the Procaryotae have no role in human disease and will not be considered in this text. Pathogenic bacteria are, however, to be found in all three classes of division II, the scotobacteria (nonphotosynthetic bacteria):

Table 1.1 Comparative Properties of Procaryotes and Eucaryotes

Property	Procaryotes	Eucaryotes
Organized nucleus with nuclear membrane	−	+
Double-strand DNA	+	+
Sites of DNA		
Nucleus	−	+
Mitochondria	−	+
Cytoplasm	+	−
Sites of RNA		
Ribosomes	+	+
Mitochondria	−	+
Sterols in cytoplasmic membrane	−	+
Cell wall murein	+	−
Energy transfer involves adenosine triphosphate	+	+
Cell division by mitosis	−	+

1 Class I (bacteria) includes the majority of bacteria that are human pathogens.

2 Class II (rickettsiae) are scotobacteria that are obligatory intracellular parasites of living eucaryotic cells. This class also includes the chlamydiae.

3 Class III (Mollicutes) are those scotobacteria that do not possess cell walls. The genus *Mycoplasma* is included in this class.

Rickettsiae, chlamydiae and mycoplasmas all include important pathogenic bacteria.

FUNGI

Fungi are eucaryotes that have an organized nucleus and nuclear membrane. The other properties of eucaryotes are summarized in Table 1.1. Fungi have now been assigned to a separate kingdom, the Mycetidae. One characteristic that distinguishes fungi and bacteria is their method of reproduction. Fungi can reproduce both by asexual and sexual processes and are classified on the basis of the types of spores produced following sexual reproduction. Fungi whose sexual stages have not yet been determined are called "imperfect fungi." Most fungi that cause human disease belong either to the imperfect fungi (Deuteromycotinae) or to one other subdivision (the Ascomycotinae) (see Chap. 17).

VIRUSES

Viruses are a distinctive group of microorganisms. They are essentially infective nucleoprotein, basically consisting of a core of nucleic acid (RNA or DNA) surrounded by a protein layer and, in some instances, an envelope derived from host cell nuclear or cytoplasmic membranes. Viruses are obligatory intracellular parasites that can infect the cells of animals, insects, plants, and bacteria. The classification of viruses is still evolving but is generally based on the type and properties of the nucleic acid, the morphology of the nucleoprotein, and the presence and properties of the envelope (Chap. 19).

PROTOZOA

Protozoa are unicellular animals, of which a few species are parasitic for humans. Each protozoal cell can carry out numerous physiologic functions. They are eucaryotes that may reproduce both sexually or asexually by a variety of different processes. Many can be cultured by methods similar to those used for bacteria. The protozoa that cause human disease are, with rare exception, either parasites of the alimentary tract or the hemolymphatic system. Protozoa are beyond the scope of this text, but the pathogenic protozoa are summarized in the Appendix.

HELMINTHS

Helminths are multicelled organisms whose cells may show considerable differentiation into specialized forms. Helminths belong to the phylum Metazoa and are of three main groups: roundworms (nematodes), tapeworms (cestodes), or flukes (trematodes) (see Appendix). Like protozoa, helminths are, generally speaking, parasites of the human alimentary or hemolymphatic system.

COMMENSALS

Among the countless varieties of microorganisms with which humans may come into contact, relatively few are pathogenic (able to cause disease).

Those microbes that normally inhabit the skin and mucous membranes but cause no adverse effects to the host are called commensals. Most organisms that comprise the normal microbial flora of the body are commensals. However, under certain circumstances, almost any commensal can become pathogenic, particularly in patients whose immunity is impaired by disease or treatment or both. In these cases, organisms that are usually harmless can invade and cause disease. Such organisms are called *opportunists* and cause opportunistic infection. With the advances in treatment of cancer, diseases of the immune system, and transplantation of tissues, opportunistic infections are now common and frequently very serious.

Commensalism, strictly defined, differs from *parasitism*, in which the relationship is harmful to the host and beneficial to the organism.

An important example of bacterial commensalism is the normal bacterial flora of the oral cavity, which teems with microorganisms. The vast majority of the latter appear to be not merely harmless but may even have a protective role. Thus, the deep wounds involving the bone of the jaw, which are the inevitable result of extraction of teeth, heal very quickly and far more rapidly than similar-sized wounds through the skin and into bone. Similarly, bacterial infections of the oral mucous membrane are rare in comparison to those of the skin.

Saprophytes (saprobes) are microorganisms that live on dead and decaying organic matter. They are incapable of causing disease in the human host whose defenses are intact but can infect immunosuppressed individuals. Certain fungi, *Mucor* species for example, are common, generally harmless saprophytes that can cause fatal infection in diabetic or leukemic patients.

COLONIZATION AND INFECTION

When organisms multiply on a body surface but their presence causes no reaction in the neighboring tissues, they are said to *colonize* that surface. It is extremely common, for example, to find that the umbilical stumps of newborn infants in hospital nurseries are colonized by *Staphylococcus aureus* shortly after birth. Most of these infants, however, do not develop staphylococcal disease.

Multiplication of microbes within organs or on a body surface with an associated cellular or tissue reaction to their presence causing disease is characteristic of infection. In the example given above, colonization of *S. aureus* in newborn infants may be followed by skin sepsis; that is to say, colonization can be followed by infection. The latter, however, is by no means an inevitable event.

KOCH'S POSTULATES AND PROOF OF ETIOLOGY IN MICROBIAL DISEASE

In the early years of bacteriology when many bacteria were being isolated for the first time, numerous claims were made that bacteria cultured from patients were the cause of the patient's illness. For example, *Branhamella (Neisseria) catarrhalis* was once thought to cause the common cold, although it is now known as a commensal of the upper respiratory tract. *Haemophilus influenzae* was and is frequently found in sputum cultures from patients with influenza. Although this bacterium can cause a variety of human infections, it does not, as was once thought, cause influenza, which is a viral disease.

Robert Koch (1843-1910) proposed a set of postulates that must be fulfilled in order to establish the etiologic role of an organism. Koch's postulates are as follows:

1 The organism is always present in diseased animals but not in healthy animals.

2 The organism can always be isolated in pure cultures from diseased animals.

3 The organism, in pure culture, when inoculated into susceptible animals must reproduce the disease.

4 The organism must again be isolated from the inoculated animals.

APPARENT EXCEPTIONS TO KOCH'S POSTULATES

The postulates were of great importance in establishing the true microbial causes of diseases such as anthrax, diphtheria, and tetanus and are still applied today when an organism is proposed as an etiologic agent of a disease. However, they have some limitations. The bacterium that causes leprosy and possibly the organism that causes syphilis have not yet fulfilled the postulates completely since they have not been successfully cultured.* Nevertheless, epidemiologic and serologic data overwhelmingly support their etiologic role. A similar situation exists today with the viruses that appear to cause gastroenteritis. They have not yet been cultured, but the epidemiologic evidence for their etiologic role is very strong.

The fact that organisms that can be readily isolated from healthy persons can also cause disease is now clearly established despite their apparent exclusion by the first postulate. *Staphylococcus aureus, Candida albicans*, and adenoviruses are examples of bacteria, fungi, and viruses that fall into this category. Finally, as mentioned before, virtually any microorganism can cause disease in the immunosuppressed individual.

*It has recently been reported that *Mycobacterium leprae* can be grown on media containing hyaluronic acid. If this observation is confirmed, Koch's postulates may then be fulfilled.

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Chapter 2

The Immune System

CHAPTER OUTLINE

Immunology is a rapidly changing area of medical science in which skeptics tend to suggest that much of what is considered orthodox today may be unacceptable tomorrow. A knowledge of the basic concepts of the complex activities of the immune system and its role in disease is, however, essential. In brief terms, the main clinical importance of understanding the nature and effects of immunologic reactions is in the following respects:

1 The protective role of the immune response in resistance to infectious disease
2 Induction of resistance to infections by immunization
3 Defects of the immune system (immunodeficiency diseases) and their complications
4 Disorders of immune function leading to immunologically mediated disease
5 Immunologically mediated tissue injury complicating infectious disease
6 Deliberate suppression of immune responses to improve tolerance of organ grafts or to treat immunologically mediated disease
7 Use of immunologic reactions in the laboratory in the diagnosis of infectious and other disease and for other purposes

OVERVIEW OF THE IMMUNE RESPONSE

The components that interact to produce immune responses are:

1 Immunocompetent cells. The immune response depends on immunocompetent lymphocytes.
2 Antigens. Antigens are any materials, including cells or cell components, that are capable of activating an immune response.

Immune responses are of two main types:

1 Humoral immunity depends on the production of antibodies.
2 Cell-mediated immunity depends on the activities of lymphocytes and other effector cells, particularly macrophages.

Antibodies are globulins produced by plasma cells that are derived from activated lymphocytes. The term "immunoglobulin" is synonymous with antibody.

In simple terms, circulating antibodies bind to specific antigens. In a few diseases, such as diphtheria and tetanus, antibodies (antitoxins) can combine with and inactivate the antigen (bacterial exotoxin) in the circulation. In most other infections, however, protection depends on more complex reactions.

In cell-mediated immunity, the antigen, such as a bacterial cell, may be attacked by activated lymphocytes or, more often, ingested by macrophages whose activities are modulated by lymphocytes.

Three characteristic features of immune responses are that they are (1) specific, (2) have a memory, and (3) show an increased response to further exposure to the antigen.

It is convenient to consider humoral and cell-mediated immunity as separate entities, but in life the two responses overlap to a considerable degree since all immune responses are due to lymphocytes and their activities. Both humoral