医学微生物学

（英文版）

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MEDICAL MICROBIOLOGY

CONTENTS

CONTENTS

SECTION I

Basic bacteriology

Chapter 1 Introduction

It used to be considered that the living world consists of two Kingdoms, the animated and non-animated. This conception has recently been changed to include a third Kingdom, that of the minute elements behaving neither as the plants nor the animals. With this understanding, in order to avoid the arbitrary assignment of transitional groups to one or the other long known kingdoms, it has been suggested as long as 1866, to place microorganisms, visible usally only with light microscope, and sometimes only with electon microscope, as a group in itself, i.e. the protista. The characteristics of this group are: simple organization, they are either unicellular, or if multicellular, their cells show little differentiation one from the other. Besides, the Protista can be further divided into 2 large classes, according to the nature of their nuclei: the higher protista have regular nuclei, so called eukaryotic group, and the lower protista, the primitive nuclei, so-called prokaryotic. Among these two large classes these usually known as microbes bacteria, viruses, spirochetes, actinomyces, etc.: are included

Microbes are distributed all over the world both outside in the enviroment and inside or on the animals and human bodies. They are vitally important in the cycle of natural materials such as nitrogen. and carbon which largely through the action of the microbes are released from protein, fats and carbohydrates. Their fermentation activity have also been found most useful in industry which can perform

the work that the chemicals will take much longer and much harsher conditions of temperature and pressure to carry out. At the same time, there are a large group of microbes which cause disease and are poisonous to man and animals, and these are really that concern us in the study of medical microbiology.

During the process of evolution, it is estimated over 1,000,000,000 years ago, these have already been formed. And with the development of plants, animals and human beings some of these microbes have become parasitic, that is they are able to live in the bodies of these hosts, most of them as mere commensals, whereas a number of species have become actual pathogens for the hosts which frequently resultsin injury and death to the individuals involved. But the most successful of these parasitic species are those which are able to live and grow and produce diseases, and at the same time they can be passaged by contact, droplets, feces, urine, or by the bites of insects or even animals. In this way, their life is preserved in their hosts from person to person, and they may even cause epidemics when the number of persons involved is very great.

Because microbes are not visible by the naked eyes, some means will have to be found for their detection, and study. It was in 1676 that a Dutch glass worker by hobby, by the name of Leeuwenhoek, who was most ingenious in preparing lenses, with which he could see some of the larger bacteria and spirochetes both in water and in the materials obtained from the crypts between the teeth.

He made numerous studies of the morphology of different kinds of microbes that he could find, and reported them all to the Royal Society of Great Britain which made him a corresponding fellow. Thus, the science of bacteriology was begun, and eventually, microbiology which covers besides microbes, also the other protista, became the great field it is.

The development of microbiology starts with morphological description which was facilitated greatly by the discovery of staining methods to make the orgainsms much clearer and it is then possible to visualize some of the special structures of these tiny organisms. Their staining appearance, as well as their reaction, have been used for differentiation into the various genera and even species. But it was not until Pasteur and Koch in the middle of 19th century, when the bacteria were first cultured in artificial media that bacteriology really began as one of the natural sciences comparable to botany and zoology. It is then possible to study the growth and death of these organisms, as well as to obtain and study the metabolic products of these. So the second stage of development may be said to be one of bacterial physiology.

The next stage started with the discovery that agents which produce diseases can pass through the filters which retain most of the ordinary bacteria. The first one so studied was tobacco mosaic organism, which was given the name virus to differentiate it from the ordinary bacteria. It was a Russian botaniat, Ivanoff who made this important contribution which

was followed by the methods of tissue cultures, that is the cultivation of living cells in which these filterable viruses can grow and multiply and produce their damage to the cells in which they grow. Then, the discovery of electron microscope again made a revolution in the study of microbes. By this means, the morphology of not only those previously invisible by the light microscope can be made much more refined and their substructures clearly visible, their surface and various attachments defined, but most of the viruses as well as those microbes smaller than ordinary bacteria can now be seen after a modification of more than 10,000 times.

Discovery of infection and immunity.

It was before the understanding of the nature of infectious diseases that men had already, based upon their keen observation, attempted to use means to prevent the occurrence of disease.

One of the first attempts was against the very serious disease which was especially damaging to the facial features of girls.

That was the small pox, known to have occurred over two thousand years ago, and in about 1000 years ago, the Chinese have already made use of the materials obtained from the pox, vesicular, or pustular fluids or the scabs of the lesion, and after due storage for some times, probably to lower the number of viable virus, it was reinsufflated into the nose of the children. The result was very satisfactory. whereas those children not receiving such insufflation usually came down with the disease on contact

with the patients, those with such treatment were protected, not only shortly after treatment, but it seemed to last for a long time. Another step in the right direction was the observation of Jenner's who considered that those milk-maids suffered from cow pox transmitted from the infected cow, were also protected from naturally exposed small pox.
That was a great constribution by Jenner in the latter part of 18th century.

Further step in the development of immunology, which was then purely anti-infectious in nature, was carried on by the experiements made by the school originated by Louis Pasteur on animals on the prevention of previous inoculations with chicken cholera, anthrax, and finally rabies which made such a big hit with the patients having been dog bitten, that Pasteur was famous over night.

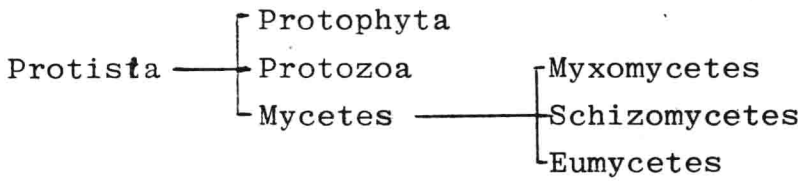
On the other hand, Metchnikoff championed the cellular aspects of immunity by his phagocytosis theory, which even now plays an important part in the mcahanism of immune reaction, whereas the German school of immunologists concentrated on works on toxin and antitoxin as well as antibacterial humoral immunity. Over the years, controversy over humoral and cellular theories was finally resolved by the double effectors in most immune reactions. It finally resulted in the evolvement of a complete set of immune system, consisting of organs, tissues, cells and mediators. All these through their interaction maintain regulation and mutual interaction among these various elements to complete the immune functions of the body

It must be mentioned, nowadays, immunology as a science has long transcended the barrier of infections, and its non-infectous aspects are even now much more extensively studied in such widely different feilds as hematology,oncology,transplantation, parasitology, endocrinology etc.

Classification of microbes.

Since the beginning of the history of microbiology, many students have concentrated their efforts in nomenclature of the various elements of these microbes. For a long time, before the onslaught of molecular biology and computer sciences, most classification was based upon morphology, physiology, antigenic structure, pathogenicity, genetics and mutation. The microbes were then divided into classes, genera, and species, but the most important may be presented in the table 1-1.

Table I-1. Classification of microbes



It is in the classes of Schizomycetes and Eumycetes that the microbes of medical interest are located. They are:bacteria, actinomycetes, rickettsia; chlamydia, Mycoplasma, Spirochete, and Virus. But nowadays, microbial classication methods have been much changed. They are: In the first place, descriptive properties are arranged in such a way that an organisms to be classified is readily identified by looking up at a "key". Second, phylogenetic classification which groups together types that are related, and those

which share common ancestor. A key may be found on page 31, of Jawetz, Review of Microbiology. Another method of classification is by means of computer which has been developed for groups of bacteria in which a large number of strains exists which can be described in terms of 100 or more clear cut characteristics. These are: presence of absence of certain enzymes, presence or absence of certain pigments, presence or absence of certain morphological characteristics, etc. Punch cards are prepared for each strain; the computer then compares the cards and prints out a list of the strains in such an order that each strain is followed in the list by the strain with which it shares the most characteristics. By this way, broad groups can often be revealed, and the medium strain within each group can then be arbitrarily considered as a type species. Contents of microbiology.

Microbiology is a science for the study of the evolution, classification, morphology under certain definite conditions, their law of life activities, and its interaction with human, animal or plants as well as with natural enviroment. The number of known microbes is extremely large. Take an example of fungi which has been estimated to be more than several hundred thousand species. On the other hand, the pathogenic fungi number only a handful.

Owing to practical considerations, microbiology has been divided usually according to its application as general microbiology, agricultural microbiology, industrial microbiology, veterinary microbiology and

medical microbiology

The study of medical microbiology.

The study of different groups of pathogenic micro-organisms or their biological characteristics, and its relationship with their human hosts under certain conditions are the fields occupied by medical microbiology. It is one of the essential basic medical sciences, and the objective in studying are: To learn the basic core of the fundamental knowledge of medical microbiology and fundamental immunology as well as to understand the necessary methodology and most commonly employed technics of examination with the objective of control and elimination of various infectious diseases research into the mechanism of the development of these diseases, provision of microbiological and immunological methods for the diagnosis, prevention and therapy with the final aim to raise the health standard of the general population.

Recent advances in medical microbiology and immunology.

Since the turn of the century, in company with the advance in physics, chemistry, biology including genetics, histology, and biochemistry, as well as pathology and clinical sciences both in their theoretical knowledge and their numerous methods and technics, microbiology and immunology, both in our country and abroad, have made tremendous advances. Just take the following examples. The submicroscopic structures of bacteria, fungi, spirochetes etc. have now been much studied, and the morphology and structure of viruses are much better known, as well as

their reduplication and multiplication, rapid cultures of bacteria together with the use of radioimmunoassay and enzyme labelled antibody technics have all been now extensively employed, the knowledge of toxiciology of bacteria and fungi and the increase in the quality of biological products studied It is especially due to the new knowledge obtained from molecular biology and genetics that the genetic materials DNA has been now transferred into bacteria for engineering purpose to produce various hormones, such as insulin, and other mediators, such as interferon have already made a very good beginning, indicating a new era for medical microbiology. On the immunological front, the development of immunobiology, immunochemistry, immunogenetics, immunopathology, immunopharmacology, immunohematology, and tumor immunology, transplantation immunology and clinical immunology have much enriched the fast growing immunological sciences. In our country, since liberation, inspite of interference and difficulties, much progress has also been made in some of the above fields mentioned. With stability and unity, it can be envisaged that a rapid progress in medical microbiology will, as with other sciences, make its proper contribution to the four modernizations.

"Along the long, long trail,
We shall look for the truth everywhere."

The poet correctly points out that the trail for truth is long and tortuous, as well as never ending, but we will try our best to find out the truth no matter how difficult it will be. We beli-

even in the investigation in the field of microbiology, in all its theoretical, practical, and methodological aspects, thousand blooms will soon come to bear fruits for the benefit of the whole mankind.

Section I. Basic Bacteriology

Chapter 2 Bacterial morphology

I. What are bacteria?

Bacteria are members of microbes, belong to prokaryotic microorganisms. Their characteristics are:

1. Single cell organisms, colorless and transparent.
2. Only nuclear material, without nuclear membrane neither is there any nucleoli.
3. No autonomous plastids such as mitochondria or chloroplasts. But bacteria often store material in the form of cytoplasmic granules.
4. Most bacteria have a definite cell wall, similar to those of the plant cells.
5. Some bacteria are motile, possessing flagella.
6. Bacteria possess definite cell membrane, sommon to all cells.

The basic forms of bacteria are as follows: coccal, rodshpaed, spiral shaped.Under definite nutrition and temperature enviroments they are relatively constant which may be visualized by special staining under light microscope. The finer details may be best examined by electron microscope.

Most bacteria do not require very stringent requirements of nutrition, and most of these may be grown on artificial culture media. They have their metabolic activities similar to all living cells and may

be divided according to their requirement for oxygen, as aerobic and anaerobic. However, many bacteria can live under either conditions and are known as facultative anaerobes. Some bacteria can secrete toxic substances which are related to their ability to produce disease. Except for those bacteria possessing spores, their resistance to external enviromental influence is not great. Moreover, quite a large number of them are sensitive to the action of many antibiotics. Through genetic changes and enviromental influences, bacteria can vary through different processes of mutation.

II. Morphology of bacteria.

1. The size of bacteria.

The bacteria are so minute that they must be visualized at least with the light microscope, while their superstructures only seen by the electron microscope, either by the penetrating or the scanning type. The unit for the measurement of bacteria is micron or micrometer which corresponds to 10^{-6} millimeter. The size varies with the types of bactera, which is of all sorts of sizes and which may be related to age, and external enviroment. The round bacteria, cocci, are usually measured by their diameters, with an average of 1.0 μm. The rod shaped bacteria or bacilli may vary from 2-3 μm to 6 or 7. Their thickness is 0.5 to 1 μm. The smallest rods measure 0.2 x 0.2 x0.7, and the largest pathogenic bacteria, 1x3x10.

2. The shape of the bacteria.

According to their shape, bacteria may be divided

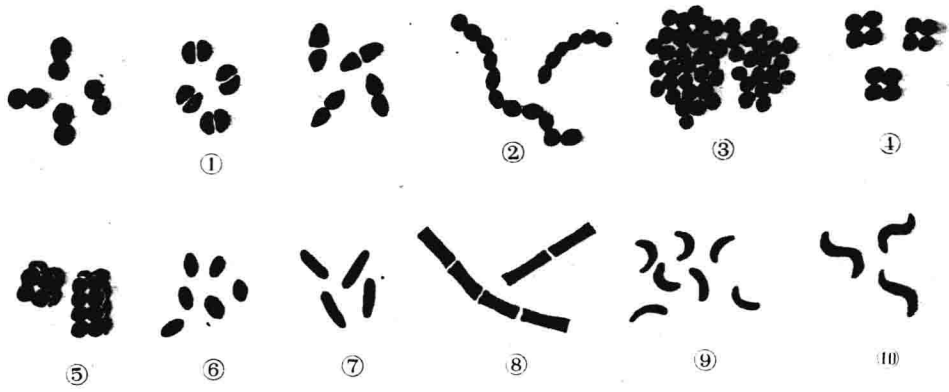


Figure I - 1 Shapes of bacteria

1. Diplococci 2. Streptococci 3. Staphylococci
4. Tetracocci 5. Sarcina 6. Coccobacilli
7. Bacilli 8. Streptobacilli 9. Vibrio
0. Spirilla