FRIEDLÄNDER'S BACILLUS OF PNEUMONIA (*Pneumobacillus*).—This organism was discovered by Friedländer (1883) and declared to be the cause of fibrinous pneumonia. Subsequently it was shown that it is seldom found in pneumonia patients, being often present in the mucous membranes of the mouth and air passages of healthy persons and in the air.

Microscopical Appearances.—Short rods (0.6 to 3 μ long by 0.5 to 0.8 μ broad) with rounded ends, often resembling micrococci, especially in recent cultures; commonly in pairs or chains of four. A capsule is present in specimens from sputum and inoculated animals; rarely seen in cultures.

Motility.—Absent.

Spore Formation.—Does not form spores.

Staining Reactions.—Stains readily with the ordinary aniline dyes, but not by Gram's method.

Biological Characters.—Grows luxuriantly both in the presence and absence of oxygen (facultative anaërobic) and on all the usual culture media, at the room temperature and in the incubator.

In *gelatin plates* small, round, elevated white colonies develop, slightly granular in structure and of a brownish color. In *gelatin stab cultures* a typical nail-shaped growth occurs; the gelatin is not liquefied. On *agar and blood serum* large grayish-white, moist colonies develop. The growth on *potato* is abundant,—a thick, yellowish-white, glistening coating containing gas bubbles. *Bouillon* is clouded. *Milk* is not coagulated. Media containing glucose are decomposed, undergoing *fermentation* with the production of acid. Indol and H_2S are sparingly produced.

Pathogenesis.—This bacillus is pathogenic for mice and guinea-pigs, less so for dogs, and rabbits are apparently immune (thus distinguished from Fraenkel's *diplococcus pneumoniæ*). Susceptible animals are inoculated directly into the pleural and abdominal cavities. They can also be affected by inhalation of dried pulverized cultures. In some cases pneumonic lesions are produced.

Active *immunity* against Friedländer's bacillus is readily produced, and although the organism is non-motile the agglutinating serum reaction is said to be present.

This bacillus has been found outside the body in the dust of floors, in the air, etc. It has been met also in the saliva of healthy persons. It is the cause of only a small proportion of the cases of lobar pneumonia; in one hundred and twenty-nine cases examined by Weichselbaum the pneumobacillus was found in nine. According to Netter and Weichselbaum the cases due primarily to this organism are distinguished by their peculiarly malignant type and by the viscidity of the exudate produced. It is also probably concerned, primarily or secondarily, under certain circumstances, in the production of pleurisy, abscess of the lungs, pericarditis, endocarditis, otitis media, and meningitis, in all of which diseases it has been found at times. It has been met with in all the organs of the body and also in the blood.

THE PUS-PRODUCING ORGANISMS.

Many bacteria are capable of producing, under certain conditions, inflammatory and suppurative processes, abscess, cellulitis, septicæmia, etc. The micro-organisms most commonly found associated with suppuration are staphylococci, streptococci, pneumococci, and tetracocci. The following species are also occasionally met with: the colon bacillus and allied members of that group, the typhoid bacillus, the influenza bacillus, and the bacillus pyocyaneus. In so-called "cold abscesses" the tubercle bacillus is usually the only organism present. Besides these bacteria, other species may sometimes cause circumscribed suppurative processes.

STAPHYLOCOCCUS PYOGENES AUREUS.—This is one of the commonest pathogenic bacteria, being present almost everywhere. It is the most frequent cause of acute circumscribed suppurative inflammations. Though first observed by Ogston (1881) in the pus of acute abscesses, it was not obtained by him in pure culture but was isolated and accurately described by Rosenbach in 1884.

Microscopical Appearances.—Small, spherical cells, having a diameter of about 0.8 μ, occurring singly or in pairs, but usually arranged in irregular masses simulating clusters of grapes; hence the name, from σταφυλή, "grape." (See Plate XI., Fig. 3.)

Motility.—Non-motile.

Staining Reactions.—Stains easily in aqueous solutions of the basic aniline dyes; is not decolorized by Gram.

Biological Characters.—Aërobic and facultative anaërobic, but produces pigment only in the presence of oxygen. It grows readily at a temperature of from 18° to 20° C., but best at 39° C., on all the ordinary culture media.

Growth on Gelatin.—Grown on *gelatin plates* at room temperature, it develops within forty-eight hours punctiform colonies, which, when examined under a low-power lens, appear as circular discs of a pale or yellowish brown color, somewhat darker at the centre and surrounded by a transparent zone with well-defined border. Immediately around the colonies, which grow rapidly and are slightly granular in structure, there is a deepening of the surface of the gelatin, due to its liquefaction. Later, the liquefaction becomes general, the colonies running together. In *gelatin stab cultures* a white confluent deposit first develops along the line of puncture, followed by liquefying of the medium in the form of a stocking. At the end of two days the yellow pigment begins to form, and this increases in intensity until finally (after a week) complete liquefaction takes place and the "golden staphylococci" fall as an orange-colored deposit to the bottom of the tube. Under unfavorable conditions the staphylococcus aureus gradually loses its property of liquefying gelatin and producing pigment.

Growth in Agar.—In *streak* and *stab cultures* on nutrient agar a whitish growth is at first produced, and this after a few days also becomes golden yellow on the surface. Colonies found at the bottom of a stab culture or under a layer of oil remain white; showing the inability of this organism to produce pigment in the absence of oxygen.

Bouillon is densely clouded by the luxuriant growth.

Milk is coagulated in from one to eight days with the production of acid.

Chemical Effects.—The production of an orange-yellow pigment, but only in the presence of oxygen; agar cultures smell like glue or spoiled paste; gas and acid production from carbohydrates; the production of H_2S abundantly and a little indol; the decomposition of urea by certain species,—these are the chemical effects of the staphylococcus.

Vitality.—Several cases of osteomyelitis have been reported in which staphylococci have been found alive in the body in the centres of infection after many years, during this time having been encapsulated apparently. In cultures they retain their vitality for a year or more. The staphylococcus is distinguished from most other pathogenic bacteria by its greater power of resistance to all outside influences, desiccation, heat, chemical agents, etc. It does not, however, form spores, as far as we know. In dried pus, according to Hägler, it stands desiccation for from fifty-six to one hundred days. But it is rapidly killed by moist heat at 70° C. It retains its vitality in ice sixty-six days (Prudden). Disinfectants act on it slowly. Meade Bolton found that a one-per-cent. carbolic acid solution destroyed it in two hours; mercuric chloride 1 to 1,000 killed it in five to ten minutes. But there is a considerable difference in the resisting power of the micrococci.

Pathogenesis.—The pathogenic effect of the staphylococcus pyogenes aureus on test animals varies much according to the mode of application and the virulence of the culture employed. Experiments have shown that this organism as found in suppurative processes in the human subject is not as infectious for animals as it is for man. The order of susceptibility seems to be as follows: man, horses, dogs, cattle, goats, sheep, rabbits, guinea-pigs,

mice. In man a simple rubbing of the unbroken skin with pus from an acute abscess is usually sufficient to produce purulent inflammation. Cutaneous inoculation of animals is negative, but subcutaneous injection causes a local abscess in rabbits, guinea-pigs, and mice, and intravenous injection in rabbits sometimes produces pyæmia and after injury to the cardiac valves ulcerative endocarditis.

The filtrates from bouillon cultures contain highly virulent toxic substances. Injection of these into the peritoneal cavity of dogs causes sero-sanguineous peritonitis, and ecchymoses in the serous and mucous membranes of the intestines, finally resulting in death with bloody diarrhœa. *Immunity* against staphylococcus infection may be produced by the injection of gradually increasing doses of the pure culture either living or previously sterilized by boiling. The blood serum of animals which have been thus immunized possesses slight protective and curative effects in other animals, but no practical use of this serum has been attempted in man.

The staphylococcus aureus occurs outside the body in milk, water, soil, air, etc. Ten per cent. of the micro-organisms present in the air of surgical clinics consist of staphylococci (Ullmann). It is found on the healthy skin, in the mouth, vagina, cervix uteri, and milk of nursing mothers. It is the chief cause of all acute inflammatory suppuration, in many cases the sole cause. It is commonly found, however, in association with streptococci, pneumococci, colon bacilli, typhoid bacilli, etc. The following affections particularly are frequently caused by the staphylococcus aureus and other species: acne, sycosis, impetigo, pemphigus, conjunctivitis, furuncle, abscess, periostitis, osteomyelitis, parotitis, tonsillitis, mammitis, ulcerative endocarditis, pyelonephritis, etc. It is the principal etiological factor in the production of pyæmia in the various pathological forms of that condition.

Not all persons, however, are equally susceptible to infection by the staphylococcus; those who are in a cachectic condition or suffering from constitutional diseases, like diabetes, are especially liable to infection. In healthy individuals certain parts of the body, as the back of the neck, and seat, seems to be more subject than others to attack by furuncles, carbuncles, and the like. In persons in whom sores are readily produced in consequence of disturbances of nutrition, the micrococci find a suitable resting place at the points of least resistance, as in the bones of weakly children, in fractures, and injuries in general.

STAPHYLOCOCCUS PYOGENES ALBUS is morphologically identical with staphylococcus pyogenes aureus, and is probably a variety of the same organism which has lost its power of producing pigment. On the average it seems to be somewhat less pathogenic.

STAPHYLOCOCCUS PYOGENES CITREUS is also probably identical with the above-mentioned species, except that it forms by its growth a lemon-yellow pigment. It is found in about ten per cent. of cases in the pus of acute abscesses, usually in association with other pyogenic cocci.

STAPHYLOCOCCUS EPIDERMIDIS ALBUS is another variety no doubt of staphylococcus pyogenes albus, but found on the surface of the body and often in parts of the epidermis deeper than can be reached by any known means of cutaneous disinfection except by heat. According to Welch it is far less virulent than the staphylococcus pyogenes aureus. It is frequently present in aseptic wounds, but does not seem to interfere with their healing, although sometimes it may cause suppuration along the drainage tube, and is the common source of "stitch abscess."

MICROCOCCUS TETRAGENUS (*Tetracoccus*).—This micrococcus was discovered by Koch in 1884 in a phthisical lung cavity. Gaffky made a further study of it and described its pathological properties for various test animals. Biondi found it in human saliva; here, however, it is sometimes simply an evidence of mouth contamination, not of lung infection. In pulmonary tuberculosis it is commonly associated with other pathogenic bacteria, which, though playing no part in the etiology of the primary affection, contribute no doubt to the progressive destruction of the lung tissue. Its pyogenic character is shown by its not infrequent presence in the pus of acute abscesses, empyema, etc.

Microscopical Appearances.—When obtained from the animal body it occurs mostly in groups of four surrounded by a capsule. In cultures the cocci are seen in various stages of division as large round, undivided cells, in pairs of oval elements, and in groups of three or four. When the division is complete they remind one of sarcina in appearance, except that they divide in four instead of in three directions and are not built up like cotton bales. (See Plate XI., Fig. 4.)

Motility.—Non-motile.

Staining Reactions.—Stains readily with the ordinary aniline dyes; is not decolorized by Gram.

Biological Characters.—Grows both in the presence and absence of oxygen, but best with oxygen, in the usual culture media. It may be cultivated at room temperature (20° C.); the optimum being between 35° and 38° C. The growth is slow under all conditions.

Growth in Gelatin.—On *gelatin plates* small, white to grayish-yellow, shiny, prominent, round, or lemon-shaped colonies develop. In *gelatin stab cultures* it grows equally as well on the surface as along the track of the needle; forming on the surface a thick, white, shiny mass, and filling out the fissures along the line of puncture. The gelatin is not liquefied.

On *agar and blood serum* the growth on the surface is moist and glistening. The colonies appear as small, transparent, round points of a grayish-yellow color and slightly elevated.

Pathogenesis.—Subcutaneous injections of a culture of this micrococcus in minute quantity are usually fatal to white mice in from three to six days. The organisms are found chiefly in the spleen, lungs, liver, and kidneys, few in the blood. Gray mice are generally immune. Rabbits and dogs are also little susceptible. In guinea-pigs only a local reaction or abscess sometimes follows inoculation, and again they die from septicæmia; intraperitoneal injections produce purulent peritonitis, groups of micrococci being found in the exudate.

STREPTOCOCCUS PYOGENES (*Streptococcus Erysipelatis*).—This micro-organism was first observed by Koch in stained sections of tissues attacked by septic processes, and by Ogston in the pus of acute abscesses (1882). It was obtained in pure cultures by Fehleisen (1883) from a case of erysipelas, and its pathological properties proved. Rosenbach (1884) and Krause and Passet (1885) isolated it from pus and gave it the name of *streptococcus pyogenes*. It has since been shown to be the chief cause of many suppurative inflammations. Formerly the streptococci of erysipelas, acute abscess, septicæmia, puerperal fever, etc., were thought to belong to different species, because they possessed certain differences in their pathological effects and morphological peculiarities, according to the source from which they were derived. But now it is recognized that these slight differences are not sufficient to constitute separate species, but only varieties of the same species. At the same time, however, there would appear to be some streptococci, which, in so far as their specific reaction in the presence of a protective serum is concerned, are as distinct from the streptococcus pyogenes as is the pneumococcus. This question is of practical importance, for upon its solution depends our ability to select a suitable protective serum in different cases of streptococcus infection.

Microscopical Appearances.—Spherical micrococci from 0.4 to 1 μ in diameter, usually larger than the staphylococci, characteristically arranged in chains of eight, ten, twenty, or more elements, but also associated in pairs and sometimes in irregular masses. (See Plate XI., Fig. 2.)

Motility.—Non-motile.

Staining Reactions.—Stains easily with all the basic aniline dyes and by Gram's method.

Biological Characters.—Facultative anaërobic, growing

both in absence and presence of oxygen, and on the various liquid and solid culture media. The growth is slow, developing best at from 30° to 37° C., but also at room temperature (18° to 20° C.). There is no growth over 47° C.

Growth on Gelatin.—In *gelatin plates* small, white to yellowish or brownish granular round colonies develop, which do not liquefy the gelatin; though occasionally, with unusual varieties, a certain amount of liquefaction has been observed. Under a high power, chains of streptococci may be seen projecting from the sides of the discs. In *gelatin stab* cultures the growth is not confluent, but individual colonies are arranged beside one another along the line of puncture.

Growth on Agar.—On *agar plates* the colonies are visible after twelve to thirty hours' growth, and when magnified sufficiently show beautiful chain cocci often in the form of twisted loops. The colonies are circular in shape when thinly scattered over the plates, but irregular when crowded together.

Growth in Bouillon.—The growth in this medium is variable in different varieties; in slightly alkaline bouillon at 37° C. reaching their full development within thirty-six to forty-eight hours. Streptococci which grow in long chains usually give an abundant flocculent deposit and leave the liquid clear; the deposit may, however, be granular, in larger flakes or in tough masses; sometimes the broth is clouded. Those growing in short chains, as a rule, cause diffuse clouding of the bouillon, with a granular deposit at the bottom of the tube. The development in a mixture of ascitic fluid and bouillon, which is the best medium for the growth of the streptococcus, is more abundant than in plain bouillon.

Growth in Solidified Blood Serum.—This is also an excellent medium for the cultivation of the streptococcus. Tiny grayish colonies appear after twelve to eighteen hours. *Milk* is usually coagulated with the production of acid, but not always.

The growth on *potato* is scanty.

Vitality.—Cultures of the streptococcus die much sooner than those of the staphylococcus, very few living over a month and the majority dying within a few days; they live longest in serum bouillon or a mixture of ascitic fluid and bouillon, and may be kept thus for a considerable time in small sealed glass tubes in the ice chest. When dried in blood or pus, the streptococci retain their vitality for several months at room temperature, and still longer in the refrigerator. The thermal death point, according to Sternberg, is between 52° and 54° C., the time of exposure being ten minutes.

Chemical Effects.—As products of their growth the streptococci form but little pigment, no indol, a little H_2S, and as a rule no acids or gases from carbohydrates. From albuminous culture media they produce toxins which are precipitated by alcohol but are soluble in water. To obtain these toxins the cultures are killed by chloroform or filtered through porcelain. Introduced into animals in considerable quantities they cause suppuration and fever and even death; they seem to belong to the class of so-called toxalbumins.

Pathogenesis.—The majority of test animals are not very susceptible to infection by the streptococcus, and hence it is difficult to obtain any definite pathological changes in their tissues by inoculations of cultures. White mice and rabbits are the most susceptible, and these animals are, therefore, usually employed for experimentation. The virulence of streptococci, however, varies greatly for animals and is different from their virulence for the human subject. The most virulent cultures, when injected in small quantity into the circulation or the subcutaneous tissues of a mouse or rabbit, produce death by septicæmia. Less virulent varieties require the injection of large quantities to produce a similar result, while some produce only abscess or erysipleas when injected subcutaneously, and others have no effect at all when introduced directly into the circulation. Many of the streptococci obtained from cases of cellulitis, abscess, empyema, and even septicæmia belong to this group.

A number of varieties of streptococci have thus been discovered, differing in virulence and in their growth in culture media; but all attempts to separate them into classes until recently, through the use of specific serum, have failed, because the differences observed, though often marked, are not constant. Knorr has enunciated the following important facts with regard to the virulence of streptococci: All varieties when cultivated for any length of time on artificial media gradually lose their virulence. By continuous passage through certain susceptible animals, as mice, a streptococcus is obtained which is very pathogenic for those animals, but at the same time has lost its virulence for others, as rabbits. The more virulent is any variety of streptococcus for an animal, the more certainly it kills without suppuration, which is produced only by less virulent forms. There seems also to be a strong tendency for a streptococcus to produce the same kind of inflammation, when inoculated, as the one from which it was derived; for example, streptococci from erysipelas tend to produce erysipelas, from septicæmia to produce septicæmia, etc. Streptococci, however, obtained from different sources (abscesses, puerperal fever, sepsis, erysipelas, etc.) are sometimes capable of producing erysipelas when inoculated into the ear of a rabbit, provided they possess sufficient virulence. By continued passage of fatal doses through susceptible animals Marmorek has obtained cultures of streptococci of such virulence that 0.0001 c.c. subcutaneously injected into mice almost invariably killed them, while 0.000001 c.c. sometimes produced death—*i.e.*, in amounts which contained but a very few organisms. According to this investigator, the virulence may be retained by cultivation in mixtures consisting of two parts of serum and one part of bouillon, or one part of ascitic or pleuritic fluid and two parts of bouillon, such cultures being kept for two months or more without transplantation to fresh media.

Streptococci have been found outside the body in the soil, in water, and in the air of surgical clinics, etc. In healthy persons they have been observed in the mouth, nasal cavities, vagina, and infrequently in the cervix uteri, sometimes in virulent forms. The streptococcus pyogenes may give rise in man to a number of inflammatory and suppurative processes. It is frequently the primary cause of infection in erysipelas, acute abscesses, cellulitis, lymphangitis, tonsillitis, bronchitis, pneumonia, sepsis, puerperal fever, impetigo contagiosa; less commonly in pleuritis, pericarditis, meningitis, periostitis, osteomyelitis, otitis media, mastoiditis, empyema, etc. Associated with other bacteria in diseases of which they are the specific cause, the streptococcus has also been found contributing to secondary or mixed infection in pulmonary tuberculosis, broncho-pneumonia, scarlet fever and septic diphtheria, playing an important part in these affections in the production of septicæmia and fever. So uniformly present are streptococci in the pseudo-membranous inflammations of scarlatina that some authorities have claimed that a certain variety of streptococci (*streptococcus conglomeratus* of Kurth and Klein) is the specific cause of this disease. The streptococcus pyogenes is further the probable cause of a number of cases of nephritis, arthritis, and myelitis, being frequently found in the blood and urine, with or without symptoms of general intoxication.

In animals such as horses, asses, cows, sheep, goats, and dogs, the streptococcus also produces diseases similar to those observed in man. These organisms have not infrequently been found in the vaccine lymph of stations where this is prepared, though generally the non-virulent varieties.

Almost all of the diseases above mentioned have been produced experimentally in animals, the result depending upon the susceptibility of the animals employed, the virulence of the streptococci, and the amount of infective material injected. The causal relation of this organism to disease has also been demonstrated in man. Fehleisen has inoculated cultures obtained from the skin of patients suffering from erysipelas into persons with inoperable

malignant growths—lupus, carcinoma, and sarcoma—and has produced a typical erysipelatous inflammation in from fifteen to sixty hours. Persons who had recently recovered from an attack of erysipelas proved to be immune. In such persons also it was observed that malignant tumors apparently improved or entirely disappeared after inoculation. During the last few years this fact has been made use of in the treatment of cancers by the artificial production of erysipelas through inoculation of pure cultures or of their toxic products, and in some cases of spindle-celled sarcoma, according to Coley, with considerable success. In carcinomata the results have been very slight.

Susceptibility and Immunity.—As with the staphylococcus, the streptococcus is more liable to invade the tissues and produce inflammation and suppuration when the standard of health is reduced from any cause, and especially when by absorption or retention toxic products are present in excess in the body. Thus local streptococcus infections are more likely to occur as complications or sequelæ in various specific diseases, in chronic alcoholism, in constitutional affections in those exposed to septic emanations from sewers, etc., and in cases in which there is absorption of toxic products formed in the alimentary canal as the result of the ingestion of improper food, of constipation, etc.

Just as in persons who have recovered from an attack of erysipelas there has been observed a slight immunity to further infection, so it has been found that animals, after recovering from artificial inoculation of the toxic products of the streptococcus, acquire a moderate immunity, which may be increased by the administration of gradually increasing doses of the culture. In this way Knorr has immunized rabbits against an intensely virulent streptococcus by injections of slight virulent cultures; Pasquale has partially immunized these animals against septicæmia; and Marmorek has protected sheep, asses, and horses against very large doses of a streptococcus which though but slightly virulent for them was intensely so for rabbits.

In none of the streptococcus infections in man, however, is there apparently produced lasting immunizing substances in the blood after a single attack. In cases of erysipelas, cellulitis, and abscess, recovery after periods varying from a few days to several months would seem to indicate the presence of slight or transitory protective substances; but the severe forms of infection, such as septicæmia following operations and puerperal fever, show little tendency to recovery when once well established.

Marmorek was the first to attempt to produce a curative anti-streptococcus serum obtained from immunized animals (asses and horses) for the treatment of streptococcus infections. The results reported from the use of this serum since his first communication in 1895 have been very variable, and on the whole unsatisfactory. The protective power of anti-streptococcus serum is undoubtedly specific, but it soon loses this power and often is practically useless six weeks after its preparation. It has, moreover, been shown that the same serum does not confer immunity apparently to any other variety of streptococcus than the one which was originally employed in the immunizing inoculations, each variety of streptococcus producing a serum which is protective only against its own variety. In order to produce a serum, therefore, which should have a successful therapeutic effect, the animals must be immunized against every variety of pathogenic streptococci. This being the case it will be readily understood that the anti-streptococcus serum which has been heretofore employed in the majority of cases was probably valueless. The poor results so far obtained from the clinical use of this remedy may have been due either to the preparations having already lost their protective power, or to this power not being sufficient in the doses given to have any effect, or to the cases having been those of severe general septicæmia upon which the serum could have no action, or to the infection having been due to some variety of streptococcus different from that for which the animals were immunized, or to the cases not being those of streptococcus infection at all, but due to other organisms, as the staphylococcus, colon bacillus, pneumococcus, etc. It is evident, therefore, that the therapeutic use of anti-streptococcus serum is at present very problematical; at the same time, however, it does not follow that a preparation may not be obtianed which shall have practical value.

The following varieties of streptococci have been described by some authors:

Streptococcus Brevis.—Develops in bouillon slightly curved, short chains; the bouillon is clouded. Gelatin is liquefied immediately around the colonies. There is a distinctly visible growth on potato. Grows at 10° to 12° C. Is usually non-virulent.

Streptococcus Longus.—Develops in bouillon long twisted chains, with a granular or flocculent sediment, the supernatant liquid remaining clear. Gelatin is not liquefied. There is no visible growth on potato. No growth under 14° to 16° C. Is usually highly virulent.

The following subdivisions of the streptococcus longus have also been described: (1) *Streptococcus turbidus* with clouded bouillon culture; (2) *Streptococcus viscosus* with clear bouillon culture and slimy sediment; (3) *Streptococcus conglomeratus* with clear bouillon culture and granular sediment.

The Pneumococcus (*Micrococcus Lanceolatus; Diplococcus Pneumonia*).—This micrococcus was first observed by Sternberg, and almost simultaneously by Pasteur (1880), in the blood of rabbits inoculated from human saliva. It was subsequently described by Talamon (1883) and demonstrated by him to be capable of producing fibrinous pneumonia in rabbits when introduced directly into the lung of these animals. In 1885–1886 this microorganism was subjected to an extended series of investigations by Fraenkel, Weichselbaum, Sternberg, and others, and proved to be the chief cause of lobar or croupous pneumonia in man.

Microscopical Appearances.—Very irregular; occurs as spherical or oval and lancet-shaped cocci usually united in pairs (diplococci), but sometimes as short chains consisting of four to six elements and resembling streptococci. In stained specimens from sputum, the fibrinous exudates of croupous pneumonia, the blood of inoculated animals and cultures on blood serum, the lancet-shaped cells are commonly surrounded by a gelatinous capsule. Variation in form and arrangement is characteristic of the pneumococcus, there being great differences according to the source from which it is obtained. (See Plate XI., Figs. 5 and 6.)

Motility.—Non-motile.

Staining Reactions.—Stains readily with ordinary aniline dyes; is not decolorized by Gram's solution. The capsule may be demonstrated in cover-glass preparations either by Gram's or Welch's (glacial acetic acid) method.

Biological Characters.—Aërobic and facultative anaërobic, grows equally well in the presence and absence of oxygen. It develops on almost all culture media having a slightly alkaline reaction; but the growth is slow and scanty, and the virulence and power of reproduction are soon lost. Grows very slowly, often not at all at room temperature; optimum 37° C., maximum 42° C.

Growth on Gelatin.—The growth on this medium is slow, often none at all, owing to the low temperature (22° to 25° C.) at which gelatin has to be kept. The gelatin is not liquefied.

Growth on Agar and Blood Serum.—At the end of forty-eight hours in the incubator, there appears on agar a thin colorless layer of non-confluent colonies. If blood serum or ascitic fluid be added to the agar the colonies are larger and closer together, the growth being more luxuriant. The growth of Loeffler's blood-serum mixture is very similar to that on agar, but is somewhat more vigorous, appearing on the surface as small, fairly granular dew-drop-like colonies.

Growth in Bouillon.—At the end of twelve to twenty-four hours in the incubator a slight clouding is produced, due to the development of the organisms, which on micro-

scopical examination are seen to consist of pairs or longer and shorter chains. After two or three days the medium again becomes transparent, the cocci sinking to the bottom of the tube. The best fluid medium for the cultivation of the pneumococcus is a mixture composed of bouillon two parts and ascitic or pleuritic fluid one part. In this medium the organisms grow well, and cultures kept in a cool place and prevented from drying retain their vitality for a number of months.

Milk is a favorable medium, and in some cases coagulation takes place.

Vitality.—In cultures the pneumococcus soon loses its vitality; it lives longest in media containing blood or serum. Pneumonic sputum attached to cloths, air-dried and exposed to diffuse daylight, retained its virulence for rabbits for periods of nineteen and fifty-five days in different experiments. Exposed to direct sunlight the same material retained its virulence after twelve hours' exposure (Bordoni-Uffreduzzi). This resistance of the organism for so long a time under these conditions is attributed in part to the protective influence afforded by the albuminous envelope surrounding the micrococci in the sputum.

Chemical Effects.—Three varieties of pneumococci have been isolated which produce a brick-red pigment. Filtered and dead unfiltered cultures contain toxins as products of growth. For other chemical effects, see Streptococcus.

Pathogenesis.—The pneumococcus is quite pathogenic for some animals, especially mice and rabbits; rats are less susceptible, and guinea-pigs, sheep, dogs, and birds are almost immune. In mice and rabbits the subcutaneous injection of small quantities of pneumonic sputum in the early stages of the disease, or of a pure, virulent culture of the micrococcus, usually results in the death of these animals in from twenty-four to forty-eight hours. The course of the disease produced and the post-mortem appearances indicate that it is a typical form of septicæmia—so-called sputum septicæmia. The most marked pathological lesion is the enlargement of the spleen. The blood after death often contains large numbers of pneumococci. True localized pneumonia does not usually result from subcutaneous injections into susceptible animals, but injections made through the thoracic walls into the substance of the lung may induce a typical fibrous pneumonia. Attenuated cultures produce, according to the point of inoculation, pneumonia and pleurisy, peritonitis, etc. Attenuation of the virulence of cultures of the pneumococcus may be produced artificially by the action of heat or several days' growth in the incubator, by continued passage through unsusceptible animals (guinea-pigs), by cultivation in unsuitable media, etc. Virulence is restored and increased by passage through highly susceptible animals of the same species from which the organism was originally obtained.

The pneumococcus has not been found outside the body, except in sputum. It is frequently present in the saliva of healthy individuals. In diseased persons it is one of the most important pathogenic bacteria. It is associated with various inflammatory processes, especially of the mucous and serous membranes; and is the chief etiological factor in the production of lobar and catarrhal peneumonia, pleurisy, pericarditis, endocarditis, empyema, peritonitis, otitis, meningitis, conjunctivitis, and keratitis; less frequently of nephritis, parotitis, metritis, pyosalpinx, strumitis, amygdalitis, arthritis, osteomyelitis, periostitis, abscesses, and general septicæmia. Erysipelas can also be caused by it. In many of these affections the organism is found not only locally, but also in the blood. Very often the pneumococcus is associated with and acts as a synergist of other pus-producers, as the staphylococcus, streptococcus, etc.

It is carried from its original seat in the lungs to distant organs of the body by means of the circulation, being often found in the lymphatics and the blood both during life and after death. Knowing that the saliva and nasal secretions under normal conditions so frequently afford a resting place for the pneumococci, we have only to assume the production of a suitable medium for these parasites in the body, brought about by an abnormal condition of the mucous membranes from exposure to cold, or a reduction of the vital resistance of the tissue cells in an interior organ, by disease, traumatism, excesses of various kinds, alcoholism, etc., readily to comprehend how an individual may become infected primarily or secondarily with pneumonia.

Immunity.—Fraenkel has shown that subcutaneous injections of rabbits with virulent cultures of the pneumococcus produced infection in only a small proportion of them; those which recovered were found to be somewhat immune to a second infection. Artificially attenuated cultures or material containing naturally weakened micrococci have also been used for inoculation. Another series of experiments were based on the assumption that the protective substances are contained in the natural or artificial products of the growth of the organisms. Thus cultures freed from bacteria by filtration and emulsions of pneumonic sputum, portions of pneumonic lung, pleuritic exudates, etc., were employed for inoculation by different experimenters. But the quantity of material required for inoculation by these methods having been found inconveniently large, attempts have been made to obtain the immunizing products in a more concentrated form. Foá and Scabia, and the Klemperer brothers prepared glycerin extracts, after the manner of Koch's tuberculin, calling their product "pneumotoxin." At present, however, a protective serum is obtained from horses by the repeated injections of fully virulent pneumococci in exactly the same way as in the production of antistreptococcus or diphtheritic antitoxic serum.

Curative experiments in man have been recently made with this antipneumococcus serum obtained from immunized animals. The most successful of these were conducted by the Klemperers. They hold that in man during the pneumonic process there is a constant absorption into the circulation of the toxic substances produced by the bacteria. This continues until eventually the same antitoxic substance is produced naturally in the body as is seen to occur experimentally. It is then, they think, that the crisis takes place. The bacteria are neither destroyed nor is their power to produce pneumotoxin lessened; but the third factor, the antitoxin, now exists and neutralizes the toxin. These authors state that they have been able to show that the blood serum of patients after the crisis contains antitoxic substances, and is capable, in a fair number of cases, of curing the disease when injected into infected animals. They have also made observations upon patients with a view of inducing the crisis by the injection of the blood serum of immunized animals and of persons convalescent from pneumonia. Somewhat favorable results have been reported in a certain number of cases thus treated by the Klemperers, Jansen, De Rienzi, Weisbäcker, Washburn, Passé, Ugheti, Mennes, Lambert, and others, but nothing definite so far has been accomplished. It may, therefore, be concluded that the curative treatment by antipneumococcus serum, like that of antistreptococcus serum, is still in the experimental stage. All that can be said about the results obtained is that the cases treated have, as a rule, done better than was expected, though no striking curative effects have been produced. In many instances there was no development of pneumococcus blood infection; and even if the serum does not hasten the crisis and bring about a positive cure, yet it may be able to prevent a general infection. It is known that there are several varieties of the pneumococcus, as of the streptococcus, possessing different biological and pathological properties and varying virulence. Possibly it may be found that pneumococcus serum obtained from animals immunized against a certain variety of pneumococcus protects only fully against that variety, as with the streptococcus serum. But whether that be so or not, the injections, at any rate, of the serum have been shown to be practically harmless, and the benefits to be derived from the discovery of a curative remedy for pneumonia

EXPLANATION OF
PLATE XI.