

jected intraperitoneally with pure cultures die in about two days of acute septicæmia, few bacteria being found in the tissues. At the point of inoculation there will be seen a hemorrhagic infiltration and œdema, with enlargements of the mesenteric glands and parenchymatous congestion of the organs. The spleen sometimes shows minute nodules resembling miliary tubercles, which contain zoöglœa-like masses of the bacilli. Guinea-pigs are also easily infected through the digestive tract. Flies, bedbugs, fleas, and other insects take up the organisms with the blood of plague-infected animals, but apparently they rarely transmit the disease. Infection, however, is rapidly communicated from one animal to another.

Hankin and Yersin have repeatedly found non-virulent plague bacilli in the dust of infected houses and in the soil. They have never been found in healthy individuals. Among animals the bubonic plague is known to occur spontaneously in rats, which often are affected previously to human epidemics. It is thought that these animals communicate the disease to man. In patients suffering from plague the bacilli are found chiefly in the pus of the characteristic buboes and also in the sputum from the pneumonic forms of the disease; more rarely in the internal organs and the blood.

This organism is the specific cause of true Oriental bubonic plague, the mortality from which is from fifty to eighty per cent. of cases. It gains access to the body (1) through the skin. Here the bacilli may remain localized and multiply at first in the neighboring lymph glands; frequently at the point of inoculation a pustule is formed which takes on the nature of a furuncle or carbuncle containing many bacilli. Death may occur without further diffusion of the organisms, but ordinarily they are distributed throughout the entire body, producing death by septicæmia. (2) Through the lungs. This constitutes the so-called pneumonic form, or plague pneumonia. The bacilli are present in the sputum and sometimes in the blood; other pus cocci are found in association. (3) Through the digestive tract. This mode of infection has been demonstrated in animals, but is uncertain in man.

*Immunity.*—Yersin, Calmette, and Borrel have succeeded in producing passive immunity against the plague bacillus in animals, and also to a certain extent in man, by subcutaneous inoculations with the serum of horses which were previously immunized by intravenous inoculation of dead cultures. Such serum possesses also some curative effect in men and animals suffering from the plague, if inoculated with large quantities and within twelve hours after infection. Roux maintains that this serum contains only antitoxic, not bactericidal, substances. Active immunity may also be produced, and apparently without danger, by Haffkine's method of preventive inoculation in the same manner as with cholera. This method consists in the subcutaneous injection of 2.5-3 c.c. of a fully grown bouillon culture heated for one hour at 70° C. to kill the organisms. The reaction caused (fever and pain) is usually slight, and the injection is best repeated after ten days. This treatment is essentially protective rather than curative, and although the immunity afforded is not absolute and lasts only for a month or two, the majority of those inoculated are protected or have the disease only in a mild form and recover.

The German Plague Commission considers puncture of the unopened bubo for diagnostic purposes somewhat dangerous, on account of possible infection of the blood; but the English physicians in India make a long incision in the affected gland, which is afterward dressed with antiseptics. In this way material is obtained for cover-glass specimens, plate and other cultural methods. The pus of the buboes, and especially the sputum in the pneumonic forms, contain numbers of bacilli. In these cases microscopical examination alone suffices often to make a probable diagnosis of the plague from the peculiar bipolar staining of the organisms. Microscopical examination of the blood is attended with success only in cases of general infection, and here cultures yield better results. It is recommended to make streak cultures on

gelatin plates at 22° C., at which temperature the plague bacillus grows fairly well, while the streptococcus and other associated bacteria usually exhibit only scanty growth. According to Hankin, when the bacilli are grown on agar containing 2.5 to 3.5 per cent. of salt at 31° C., in twenty-four to forty-eight hours inoculation forms, consisting of pear-shaped bodies and spheres, are developed, which he considers characteristic enough to form a means of diagnosis. Finally, the serum of men and animals affected with the plague possesses the power of agglutinating the bacillus pestis. This reaction is said to be present in the second week, and is most pronounced in the second and third weeks of the disease.

#### THE STREPTOTHRICES.

The varieties of the streptothrix group of micro-organisms have not as yet been clearly described. Some of them at least are pathogenic. These organisms, while having many points of resemblance to bacteria, yet differ from them in other important respects which connect them with the fungi. Like the mould fungi they develop from spore-like bodies into cylindrical dichotomously branching threads which grow into colonies, finally becoming visible to the naked eye as irregular radiating thread masses or mycelia. Under favorable conditions single threads or fruit hyphæ grow upward out of the substance, free in the air, and break up into chains of round, spore-like bodies or conidia, which being detached from the plant are carried by the air, and thus the preservation of the species is assured. The bacilli of tuberculosis, leprosy, diphtheria, and glanders are believed by some properly to belong to the streptothrices on account of the true branching forms developed by them under certain conditions. The best known of this group is the actinomyces or ray fungus.

*STREPTOTHRIX ACTINOMYCES.*—This micro-organism was first described by Bollinger (1871) in cattle, in which it forms the affection known as "big jaw." In man actinomycosis was first recognized by Israel (1885), and subsequently Ponfick insisted upon the identity of the affection in man and cattle. So-called "madura-foot," an ulcerative disease of the feet, rarely of the hands, is by some also thought to be another form of infection caused by this organism.

*Microscopical Appearances.*—In both man and animals the organism can be observed in the pus from the affected regions as small, yellowish granules from 0.5 to 2  $\mu$  in diameter. Microscopically these bodies are seen to be made up of threads which radiate from a centre and present bulbous, club-like terminations. These are generally arranged in pairs, closely crowded together, and exhibit a glistening appearance. The threads which compose the central masses are from 0.3 to 0.5  $\mu$  in diameter; the clubs are from 6 to 8  $\mu$  in diameter, and are either single or branching.

*Staining Reactions.*—The thread fungi, not the clubs, stain best by Gram's method. Double staining can be obtained with the Gram method and then with picrocarmine or saffronin, the thread being stained a blue-black color by Gram's solution, while the clubs are stained red.

*Biological Characters.*—Aerobic and facultative anaerobic, growing on all artificial culture media at room temperature, but best with access of air and at the temperature of the body.

On *blood serum* and *agar* isolated colonies at first develop on the surface of these media, but on keeping the cultures for a week or two the colonies run together and form a thick, wrinkled mass which sinks into the medium. The individual colonies are yellowish to red in color, and are covered by a whitish fluffy down, consisting of fine cobweb-like hairs; occasionally the culture is colored brown. In *stab cultures* the growth usually presents a tree-like appearance, but this varies considerably. *Bouillon* is not clouded, but round masses are formed in the bottom of the tube, which are separated with difficulty by shaking. On *potato* the growth is somewhat

slower, resulting in a thick, viscid, membranous deposit on the surface, upon which the same yellowish-red color and cobweb-like thread are developed. On eggs, either raw or cooked, Wolff and Israel have cultivated especially well-developed branching forms.

**Vitality.**—The cultures are quite resistant to outside influences, old cultures retaining their vitality for months. Dried they may be kept for a year or more. They are killed by a temperature of 75° C. in five minutes.

**Pathogenesis.**—The actinomyces have never been found outside the animal body, but they probably occur in the husks and straw of grains and grasses, as the usual mode of acquiring the disease is apparently through the introduction of these materials, which have been met with in the centres of actinomycotic infection. They have never been found in healthy animals. The chief modes of infection in man are through the mouth and mucous membranes of the throat, through the air passages, through the intestinal canal, and through the skin. From the primary centres of infection the fungus is conveyed by wandering cells and emboli to all parts of the body, giving rise to soft granulation tissue which has a tendency to break down, and contains, in addition to small round cells, epithelial elements and giant cells, not unlike those found in tubercles. The formation of fistulae which undermine the skin favors the passage of the organism through muscular tissues and furthers the spread of the disease. More rarely, circumscribed tumors, as seen in cattle, also occur in man. The fungi are found in the pus of the affected parts, there being scarcely an organ or tissue of the body free from actinomyces.

Among animals cattle are especially subject to the disease; more rarely, pigs, dogs, and horses. The most common seat of infection is in the interior of the bone of the jaw, with the formation of granulation tissue and of new bone from the periosteum. In other cases the soft parts of the face are primarily attacked and the bone affected from the outside. The walls of the throat and stomach are sometimes first infected. The affection of the jaw gives to the disease its name of "big jaw"; it was formerly mistaken for osteosarcoma and other similar affections.

The experimental production of actinomycosis in animals has not been satisfactory. When artificially introduced into the tissues the organism becomes absorbed or encapsulated. If injected in large quantities multiple nodules are formed in some cases, and these suggest the production of a general infection, but no growth of the organisms really takes place. Pontick, John, Rotter, and others claim to have obtained positive results in animals, but Boström does not consider these conclusive. The animals used for experimentation have been calves, pigs, dogs, rabbits, and guinea-pigs; the points of inoculation, the anterior chamber of the eye, the subcutaneous tissue, the peritoneal cavity, and the blood-vessels; and the material injected, pus from the affected parts, very rarely cultures.

A number of other streptothrices have been described in connection with various pathogenic processes, but most of them are not well defined. They have been found in abscess of the brain, cerebro-spinal meningitis, inflamed pneumonic areas, and other pathological conditions. Eppinger injected cultures of a streptothrix found by him in brain abscess into rabbits and guinea-pigs, and from this a pseudo-tuberculosis developed. Consolidation of portions of both lungs, thickening of the peritoneum, and scattered nodules closely resembling tubercles were also noted by Flexner in a case of human infection from a variety of streptothrix, the pathological conditions so nearly resembling tuberculosis that the two diseases could be distinguished only by the morphological and other characteristics of the causative micro-organisms in each case.

#### THE HYPHOMYCETES OR MOULD FUNGI.

Most of the mould fungi are not pathogenic and are of interest to us only as organisms which are apt to contaminate our bacteriological media. Some of them, however,

are true parasites, among which the best known are the *achorion Schönleinii*, *trichophyton, oïdium albicans*, and *microsporon furfur*. These can be only briefly touched upon in this article, as they are not bacteria, and yet some reference to them would seem to be called for here.

**ACHORION SCHÖNLEINII (Favus Fungus).**—This fungus, which is the cause of favus in man and animals (horses, cattle, dogs, cats, rabbits, mice), was discovered by Schönlein in 1839. The disease is communicated to man by contact with animals. Want of cleanliness is a contributing factor. The fungus seems to find a more favorable soil for its development on the skin of persons in a debilitated condition, especially from phthisis, than in healthy individuals.

Pathologically the disease represents the reaction of the tissues to the irritation caused by the growth of the fungus, the spores finding their way into the hair follicles, where they develop around the hair seat. The achorion grows in the epidermis, the density of the growth causing pressure on the parts below, thus crushing out the vitality of the hair and giving rise to atrophic scarring. This disease shows a marked preference for the scalp possessing hair but it is also found on skin devoid of hair, and even the mucous membranes or the nails may be attacked. Kaposi describes a case of favus universalis. On the scalp it first appears as a tiny sulphur-yellow disc or *scutum*, depressed in the centre like a cup and pierced by a hair. This is the characteristic lesion. The cup shape is attributed by Unna to growth at the sides proceeding more vigorously than at the centre.

According to Unna, Quincke, and others there are several varieties of favus fungi, but later investigations would seem to indicate that the achorion Schönleinii is the only species of fungus producing favus.

As seen under the microscope the mycelium consists of branched radiating hyphae. Some of the hyphae swell at their free ends, becoming club-shaped, while others give off lateral buds containing Kral's so-called "yellow bodies," which rupture, allowing their contents to escape as free bodies. When this takes place, moss-like offshoots develop in the form of dense, twisted threads. Later, the individual threads break up into cell-like, oval structures.

The favus fungus is readily cultivated at both room and body temperatures on the ordinary nutrient media. The growth develops slowly and shows a preference to grow beneath the surface of the medium. The characteristic form of growth is that of moss-like projections from a central body, the color being at first grayish white and then becoming yellow. To obtain the fungus in pure cultures the "favus crusts" are mixed with sterile silicic acid, reduced in a sterile mortar, and plate cultures on gelatin or agar are made from this mixture. Blood serum is the only medium on which the spores are developed, the most favorable temperature being 30° C. Artificial infection can be produced only with material containing spores.

**TRICHOPHYTON (Ringworm Fungus).**—Ringworm of the body or hairless parts (*tinea circinata*), and ringworm of the hairy parts (*tinea tonsurans* and *tinea barbae* or *sycois*) are due to the fungus *trichophyton*, discovered by Gruby in the human hair, and between the epidermal cells by Hebra.

According Sabouraud (whose conclusions are based on an exhaustive series of microscopical examinations of cases of *tinea* in man and animals, of cultivation of artificial media, and of inoculation experiments), there are two distinct types of the fungus *trichophyton*, causing ringworm in man; they are distinguished by the size of their spores—one with small spores 2 to 3  $\mu$  in diameter, which he calls *Trichophyton microsporon*, and another with large spores, 7 to 8  $\mu$  in diameter, which he calls *Trichophyton megalosporon*. These differ both in their mode of growth on artificial media and in their pathological effects on the human skin and its appendages.

*Trichophyton microsporon* is the common fungus of *tinea tonsurans* in children, more particularly the severe affection known as the "Maladie de Gruby," which is re-

bellious under treatment, and its special seat of growth is the substance of the hair. *Trichophyton megalosporon* is essentially the fungus of ringworm of the beard and of the smooth parts of the skin in adults.

Under the microscope the single mycelial threads are distinctly separate and from them conidia are given off. The spores of *T. microsporon* are contained in a mycelium; but this is not visible, the spores appearing irregularly piled up like zoöglæa masses; and growing outside, they form a dense sheath around the hair. The spores of *T. megalosporon* are always contained in distinct mycelium filaments, which may be either resistant when the hair is broken up, or fragile and easily separating into spores.

The *trichophyton* grows at room temperature, but best at 30° C. on the usual media. It liquefies gelatin, agar, and blood serum. The two types when grown on artificial cultures also show a downy surface and white color; those of *T. megalosporon* a powdery surface, with arborescent peripheral rays, and often a yellowish color.

Although the morphological appearances, mode of growth, and pathological effects of each type of *trichophyton* show certain characters in common, yet there are some constant minor differences which point to the fact that there are several varieties or species of fungi included under each type. The species included under *T. microsporon* are few in number, and with one exception (that which causes the contagious herpes of the horse) almost entirely human. The species of *T. megalosporon* are numerous, and many animals as well as man are subject to affections caused by the various species.

In contradistinction to other fungi, the cultures of *trichophyton* retain their vitality for a long time. The disease has been produced artificially in animals by inoculation with material containing spores.

**OÏDIUM ALBICANS (Thrush Fungus).**—This fungus, which was discovered by Bery and fully described by Gruby, is the cause of thrush, and occurs in all mucous membranes with squamous epithelium, especially in the mouths of infants, where it is manifested by white points or patches on the inflamed surface. The usual seat of thrush is the buccal membrane of children, but occasionally it occurs in the faucial and oesophageal surfaces; rarely in the middle ear, trachea, and subdiaphragmatic portion of the digestive tract.

Under the microscope this parasite is seen to consist of mycelial threads; numerous spherical or ovoid spaces or conidia are also present surrounding the mycelium and covering the epithelial cells.

The *oidium albicans* is strongly aerobic, growing on all the usual culture media in the presence of oxygen, best at 37° C. It does not liquefy gelatin, upon this medium forming white colonies. On agar a yellowish-white growth is developed.

It is pathogenic for rabbits when inoculated intravenously, the fungus becoming localized in the internal organs.

Haller considers that this organism is identical with, or very closely allied to, the *oidium lactis*, which occurs in milk undergoing acid fermentation.

**MICROSPORON FURFUR (Pityriasis Fungus).**—This fungus is the cause of *tinea* or *pityriasis versicolor*, and is found in the scales cast off by the skin in this affection. When these scales are treated with a five-per-cent. solution of caustic potash and examined microscopically, short, slightly branched mycelial threads are seen with very large conidia lying together in clusters. The fungus has not been cultivated artificially, but *tinea versicolor* has been produced by experimental inoculation, both in men and animals.

#### THE BLASTOMYCETES OR YEAST FUNGI.

The yeast fungi are divided into two groups: (1) *Saccharomyces* or true yeasts, in which true spore formation occurs; (2) *torula*, in which no spore formation has been observed.

The blastomycetes reproduce themselves by germi-

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nation or budding, which distinguishes them from the schizomycetes or bacteria which reproduce themselves by fission or division. From the hyphomycetes or mould fungi they are distinguished by being unicellular and by a sexual reproduction. They are round or oval cells, usually many times larger than bacteria.

These organisms are of the greatest practical importance in various commercial industries, such as brewing, baking, etc., but as yet very little is known of their pathogenic properties in man. Certain varieties, when injected into animals, have proved to be pathogenic and capable of producing tumors, and recently they have apparently been demonstrated (by Sanfelice, Plimmer, and others) in the epithelial cells in cases of cancer in the human subject; but what relation they bear, if any, to this affection is yet to be determined. They are not infrequently present in the air and in cultures made from the healthy throat.

Memmo has also stated that in some cases of hydrophobia he found a blastomycete possessing pathogenic properties which he considers to be the cause of the infection. The fungus was found in the cerebro-spinal fluid, the substance of the brain, aqueous humor, stroma of the parotid gland, and in the saliva, but never in the heart's blood or in other organs. Dogs injected with cultures of this micro-organism began, in from thirty to sixty days, to emaciate, became rabid, vomited, and finally died. Paralysis of the extremities immediately preceded death. The fungus was also found in sections of the spinal cord of a dog dead of rabies.

Judging from these experiments, which, however, require confirmation, the yeast fungi may eventually prove to be of considerable pathogenic importance.

#### THE PROTOZOA OR ANIMAL PARASITES.

The protozoa are the lowest forms of animal life, embracing organisms consisting of a single cell or groups of cells not separable into different tissues. They reproduce usually by fission, germination, or spore formation. The protozoa are divided into: (1) *Gymnomyxa* (including proteromorphs, mycetozoa, lobosa, labarinthulida, heliozoa, radiolaria, and foraminifera); (2) *corticata* (including infusoria and sporozoa).

To this family of animal parasites belong the amoeba coli, the plasmodium malariae, and the pyrosoma bigemium,—the specific cause, respectively, of tropic dysentery, malarial fever, and Texas cattle fever. These organisms will be described elsewhere, so that we only refer to them here in order to complete the list of interesting pathogenic micro-organisms.

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**BACTERIAL TECHNIQUE.** See *Micro-Organisms: Technology*.

**BAEL FRUIT.**—The fruit of *Aegle Marmelos* Correo (fam. *Rutaceae*). The bael is a sacred tree among the Hindus, and its use in medicine pertains largely to religion and mythology. It is a near relative of the orange, to which it bears a general resemblance in tree, flower, and fruit. The fruit, of the size, shape, and structure of an orange and with a somewhat similar pulp, differs in having a hard smooth shell, the pulp mucilaginous, and the seeds enclosed in a woolly covering. For medicinal purposes it is collected and dried in slices, usually in quarters, with the shell retained. In the dried condition the pulp is dry, hard, and gummy, and of a mucilaginous, slightly acid, and somewhat bitter taste. Although it contains no tannin, or any other constituent which might be expected to be medicinal, it has been recommended in diarrhoea and dysentery. Possibly the large amount of mucilage which it yields may act as a demulcent. There is no fixed dose. H. H. Rusby.