

# The Actinomycetes, and their Occurrence in Soil and in the Organisms of Warm-blooded Animals.

By

OLAF GRYPHE,

Oslo.

616. 31002. 892

The actinomycetes or ray fungi have always offered and still offer certain difficulties on classifying them in a bacteriological system.

This holds good both when we apply a phylogenetic systematism, that is, when we place them in the botanical system according to the view-point of descendance theory, and when we make use of a morphological system, which, as far as clearness is concerned, may offer greater advantages, as many of the phylogenetic facts are not so easily expressed in a system. For this reason we resort to biological qualities to support systematism where morphology fails. In the botanical nomenclature (WETTSTEIN) the organisms described as Actinomycetes are classed with the *Schizomycetes* among the lowest vegetable strains (the Schizophytae), and among the Schizomycetes they are ranked as the second order or group, which here bears the name of Mycobacteriales.

In the medical nomenclature the classification of the text-books concerning the bacteria is somewhat different and also more detailed, even though it follows the botanical lines, and I will, therefore deal with it more closely.

In BERGEY's last classification (1934) the second order or group of the class of the bacteria is called Actinomycetales and is again divided in two families, viz. the first family being the Actinomycetaceae and the second the Mycobacteriaceae including among

others the Corynebacteria and the Mycobacteria as genera. As the first genus of the family of the Actinomycetaceae we have the Leptothrix and as the second genus of this family the Actinomycetes with their different species.

Also LEHMAN-NEUMANN in their systematism let the Actinomycetales follow the true bacteria as a second group or order (the so-called group B), although not as a clearly circumscribed group. The group of the Actinomycetales is then subdivided in two families. The first family is here called Proactinomycetaceae (with the Corynebacteria and Mycobacteria), and supposed to connect the true bacteria with the Actinomycetaceae. As a second family rank the Actinomycetaceae proper which the authors define as true ramified Hyphomycetes, and further more as the only genus the Actinomyces Harz.

LEHMAN-NEUMANN are of the opinion that the Actinomycetales do not fit quite into the frame of the bacteria, but chose to reckon them among the bacteria as a transition to the higher fungi, the Hyphomycetes. They say: One has either to do this or to place them in class with the lower Hyphomycetes. For comparison LEHMAN-NEUMANN classify, for instance, the Leptothrix in the first group (A), the Schizomycetes, and these again in the third family, the Desmobacteria.

Later LACHNER-SANDOVAL gave the name of Actinomycetes to this group. (It would have been more correct to use the name of Actinomycetales for these Hyphomycetes, which in the opinion of the said authors are very closely related to the bacteria.)

Against the term Actinomyces for the first time employed by the botanist HARZ in 1878 several investigators have raised objections, COHN calling the first known organism in this group Streptothrix. This name was however disapproved of, as CORDA in 1839 had used the term for mould. According to international rules the oldest correct name becomes prescriptive.

The main cultural characteristics of the Actinomycetes are the following: They are chlorophyll-free organisms, forming thin, 0.5 to 0.8  $\mu$  thick threads, resembling bacteria with true ramifications. Younger and older cultures have the same thickness. Especiallly when grown in broth they have a richly branched mycelium. Many of the strains easily fall into small pieces, particularly at the points of ramification, and one often sees young cultures similar to bacteriform, nonramified rods, that in no way can be distinguished from common bacteria.

All Actinomycetes are grampositive. Only some old cultures may be gramnegative, besides some thermophil strains living at temperatures above 50° C. Actinomyces has no spores and no dissepiments in the threads. The formation of spores takes place in the following way: There comes about an endogenous division of the protoplasm of the threads into smaller or larger particles, called fragmentation spores, that is to say one has to do with a simple break-up of the vegetative thread. This may also be expressed thus: the mycelium is divided into segments that function as conidia. By partitioning off the conidia resistant airspore-like structures are formed. They are not pronouncedly acid resistant, and on culture in broth the latter does not become turbid. Frequently growth in cultures is very slow.

In connection with the characteristics of Actinomyces it is of importance at once to mention a few things concerning their distinction from the Hyphomycetes. This can in no way be drawn very clearly. The threads of the latter are considerably thicker and the content of the threads more differentiated; they have, for instance, dissepiments. Furthermore, they are plasmolysable. This, according to LIESKE, is not the case with Actinomyces.

LIESKE also draws a very sharp boundary line against the Mycobacteria to which every transition is found, and states among other things, for comparison, that the Actinomyces always multiplies by forming a mycelium. This cannot be observed with Mycobacteria in the hanging drop, the formation of a mycelium being completely missing. One sees only that the threads undergo transversal division and that the small rods partitioned off lay tightly together.

Like other bacteria Actinomyces lives on organic carbon compounds. Biochemically it thus belongs to the heterotrophic organisms with a very rapid metabolism. Of these there exist, as you know, two subdivisions viz. the parasites, taking their food from the living organism, and the saprophytes, that live on dead material or products of excretion.

In the living organism Actinomycetes are the cause of disease, and are called pathogenic Actinomycetes. Outside of the organism they represent an important factor in the chemical metabolism of Nature, and are named zymogenic Actinomycetes.

All in all the action of the Actinomycetes, as that of other bacteria, is highly dependent of the appearance of products of

metabolism. These are called enzymes in the zymogenic and toxins in the pathogenic Actinomycetes.

Among the Actinomycetes not only distinctly parasitic respectively saprophytic forms are known, but also facultative ones.

Moreover, one may, as with other bacteria, distinguish aerobic and anaerobic forms by their oxygen demand. This classification based on their respiration is not for all the forms an absolute one either. Also here facultative Actinomycetes are found. The latter have thus the faculty to make use of both respiratory systems.

To divide the genus Actinomyces into species is, especially after the thorough investigations of LIESKE, connected with considerable difficulties. LIESKE thinks it unfeasible to form the notion of species in the case of Actinomyces. Actinomyces in its morphological and physiological properties shows a much greater variability than any other group of organisms, with the possible exception of the Leptothrix forms of the oral cavity. One observes that both the form and colours of the colonies, the length of the threads and the formation of spores may be changed by external influences, and even without any such, sudden changes may be seen. COHN was able to show, after having studied 75 different types, that in particular the formation of the mycelium and of dye-stuffs are changeable, and that the changeability on the whole was too great as to allow to classify them into species, and LIESKE goes even so far as to call anaerobic Actinomycetes grown from the organisms of warm-blooded animals and thermophil forms growing at 60° C. variants of the same strain of Actinomyces. By this does not follow that all the forms of Actinomyces should be taken as developmental forms of one and the same organism. But there do exist great difficulties and the whole matter is by no means settled. (Investigations of the variability were especially carried out by COHN, ERB and WIGAND).

With Actinomyces the biological methods of classification show no lawfulness, the serological methods fail completely and the morphological properties are highly variable.

Despite that one had to classify forms or groups of forms as species, what was done with the definite assumption that sharp bordering lines could not be drawn.

A mode of classification much discussed, particularly by the investigators of actinomycosis or the ray fungus disease, is the distinction of aerobic and anaerobic forms. LIESKE, as mentioned, kept aloof from this view. I will, however, mention that the

view, that only anaerobic types cause actinomycosis in man and animals, works its way in the newer literature (COPE). I will come back to this below.

One of the large groups of Actinomycetes is always present in soil, water and air. These are not pathogenic or at least very seldom so.

The other great group of forms lives in the organisms of warm-blooded animals, such as man and other animals. They are greatly pathogenic, but saprophytic too, and to this group belong the forms that to-day are regarded as the cause of actinomycosis.

Actinomyces has a very wide-spread occurrence in Nature. Everywhere there is any basis for bacteria or fungi, Actinomycetes are found in large quantities. They are as frequent as moulds and certain soil bacteria.

These organisms have become known to us relatively late, what is due to the fact that they first do not occur in so thick layers that they become visible to the unaided eye, and second that many of the forms grow so slowly on artificial and natural substrates that they easily get overgrown by other microorganisms.

That Actinomyces plays a considerable part in the household of Nature is rather certain, considering its wide-spread occurrence. In soil Actinomyces is present in extremely large amounts. It may be discovered in all sorts of soil: garden soil, farm soil, sandy soil etc.

FOUSEK in his paper gives the following values: In spring from 6.45 to 23 per cent. of all the micro-organisms in the soil are Actinomycetes. In autumn the percentage varies from 8.6 to 64. In the soil of woods Actinomycetes formed from 24 to 27 per cent. of all the microorganisms present.

In all natural waters Actinomyces can be demonstrated, most frequently it is found in large quantities in water contaminated with organic matter. This was particularly pointed out by A. REISS in his investigations of the water in Mayence. In pure water their number is smaller. Even in hot springs with temperatures above 65° C. Actinomyces has been found in great number, and RIGLER found it in 27 per cent. of all mineral waters.

Actinomyces is found on all green herbs, such as grass and plants, and on all sorts of fruit, vegetables and berries. Upon the whole Actinomyces can be detected in all parts of plants either they

grow over or under the ground. BEIJERINCK demonstrated Actinomyces on the root of a series of different plants, and LEMMERMANN found it on various algae.

As a natural consequence of its wide-spread occurrence in the localisations mentioned, it is also found in large quantities in the air. The sojourn in the air naturally is subject to the same conditions as with other micro-organisms. Propagation does not take place in the air. The Actinomycetes are only whirled into it from the soil and water.

I mentioned before that Actinomyces always was present as a saprophyte both in the human and in the animal organisms, its number being particularly large in the intestinal tract, in a highest degree in herbivores, while somewhat less in carnivores. Many authors have also suggested that multiplication of the Actinomyces occurred in the intestinal tract of warm-blood animals. This is not the case according to LIESKE's investigations.

I have mentioned above that the Actinomycetes play an important rôle in the household of Nature. Actinomycetes with its enzymes is (according to WAKSMANN) supposed to take an active part in the decomposition of the organic matters of the soil, either these are nitrogenous or non nitrogenous in nature. Many species for instance decompose cellulose very rapidly under conditions favourable for their development. The ray fungi play an important part in this process. MACE (1905) showed that Actinomyces disintegrates proteins into amino acids and ammonia. Active decomposition of proteins was observed by several authors (FOUSEK (1913), MÜNTER (1914) and WAKSMANN (1919)),

It is further assumed by LIESKE that Actinomyces also takes part in the splitting of lipoids (lipases). One thinks that there exists a difference compared with true mould, as the Actinomycetes neutralize the fat by producing alcali, while with moulds no production of alcali takes place. LIESKE is, besides, of the opinion that the cleavage of fat by ray fungi is not only due to the action of alcali.

Generally speaking one thinks (WAKSMANN) that Actinomyces is one of the very few organisms which are able to attack the most resistant materials in soil and to decompose them, and in this way, for instance, the nitrogen of the soil is liberated, from a number of substances not attacked by other micro-organisms, and this disintegration is of importance for the fertility of the

soil. With respect to the importance of the zymogenic Actinomyces otherwise in the chemical exchange I will mention that Actinomyces acts as an antagonist to other micro-organisms, so that the growth of the latter is inhibited or they get killed, and this takes place in spite of the slow growth of the ray fungus. One does not know whether this phenomenon is due to a specific enzyme or not.

The same holds good for the hemolytic action of the Actinomyces. One has here not to deal with enzymes in the proper sense, as they, for instance, are not affected by heating. The action is not either dependent of whether the strain is pathogenic or not. The hemolytic power of the ray fungi is very considerable compared with that of other organisms, but on the other hand it is no unchangeable quality. Besides, it is known from a series of investigations that the micro-organisms of the soil exert a considerable influence on the growth of higher plants.

As mentioned before, FOUSEK (1912) made investigations into the importance of the Actinomyces of the soil for the higher plants, and claimed to have observed a richer growth in garden soil after inoculation with Actinomyces. This view was supported by WAKSMANN. LIESKE found however in his experiments with corn and tomatoes that the difference in the growth rate of plants grown on inoculated soil or not inoculated soil was insignificant if present at all. Later exact experiments of MÜNTER (1913) again showed, as mentioned, that Actinomyces is able to form ammonia from nitrogenous organic substances, and this ammonia serves as a nitrogen supply to the higher plants. It has thus been established that Actinomyces takes part in the promotion of growth of higher plants.

An assimilation of the free nitrogen of the air by Actinomyces has not been clearly demonstrated. It has been stated that Actinomyces as well as other micro-organisms is of importance for the disintegration of organic matter. Some disease in higher plants have also been referred to the ray fungi of the soil. LUTMAN and CUNNINGHAM thus claim that the so-called scurf disease of the potato and turnip be caused by Actinomyces. This is supported by STIFT and FULMEK. The same holds good for a disease on the root of the alder in the form of tubers and coral-like formations. This question was settled especially through the work of PEKLOS from 1910. Generally speaking one must however say that Actinomyces does relatively little harm to plants. The

fungus penetrates only rather shallowly into the tissue and does not cause the death of the plant.

Physiologically Actinomyces is different both from fungi and from the bacteria proper. Fungi for instance are characterized by their greater resistancy to acids compared with bacteria. WAKSMANN thinks that, with very few exceptions, the Actinomycetes are less resistant to acid than bacteria; they can endure only relatively small deviations from the neutral point. A series of bacteria is characterized by their formation of different gases (hydrocarbons). This is not the case with Actinomyces, except for CO<sub>2</sub> (carbon dioxyd), a product of energy exchange. Of physiological characteristics I will further mention the faculty of the ray fungi to form the strong oxidizing agent *quinone*, and that, particularly the aerobic types, spread a more or less characteristic smell. The intensity of the smelling substances is dependent of the nutritive substrate. In particular the carbonhydrates promote the production of smells. Several species have a pronounced fruit-like smell. Putrid smells, on the other hand, have not been observed with Actinomycetes. Should this be the case, the smell is due to impurity of material.

The faculty of forming dye-stuffs is very marked in Actinomycetes. Particularly frequent are purple and vermilion, likewise an intensive orange, and yellow and green colours. Also deep black colonies are seen, reminding of ebony. Compared with other bacteria external factors, such as substrate, light, temperature and other factors have relatively little influence on the production of the colours.

It has, as I have mentioned, been established that ray fungi are to be found as saprophytes in the organisms of warm-blooded animals. A distinct locus of predilection in this respect is the *oral cavity*. Certain forms or groups of forms also cause a disease in man and animals, the so-called *ray fungus disease or actinomycosis*, and it is the study of the etiology and pathogenesis of this disease that before others is the reason why both botany and medicine have succeeded in making our knowledge of the Actinomycetes as comprehensive as it is to-day. For the sake of clearness I shall in the following treat separately the saprophytic and the pathogenic forms of the Actinomycetes occurring in warm-blooded organisms.

Saprophytic forms of the ray fungus are always present in the

oral and nasal cavities, in the throat and tonsils of healthy individuals. Especially the tonsils often contain Actinomycetes. In the sputum of healthy individuals Actinomycetes can be demonstrated. Consistent with what has been said about the occurrence of the Actinomycetes, it is obvious that the digestive and respiratory tracts are the main ways of entrance. In the oral cavity special circumstances prevail, which I shall deal with more closely. The Actinomyces usually present in the oral cavity belongs to both the anaerobic and the aerobic groups. Of these the first is supposed to have its permanent residence in the mouth. SACHARY COPE in his book on "Actinomycoses", published in 1938, claims that the strictly anaerobic type of Actinomyces is to be regarded as belonging to the flora of the oral cavity, while the other easily growing type is an organism of more accidental occurrence, migrated into the mouth from the outside. This view was held before by the Swedish surgeon, Professor G. SÖDERLUND, in his paper on salivary concretions, and also by Professor CARL NAESLUND in Stockholm Sweden in his publications treating with the bacteriological etiology in the formation of tartar and salivary calculi. The Russian investigators GRINW and BARANOW maintain that Actinomycetes have an extremely important physiological task to fulfill in the oral cavity. Under normal conditions the Actinomycetes further the decomposition of food residues and thus support the normal cleansing of the mouth. They inhibit processes of putrefaction and turn them into oxidative processes. As mentioned above they are able to form the strong oxidant quinone. Relatively little the literature tells us about the occurrence of saprophytic forms elsewhere in warm-blooded organisms. On the other hand the lack of systematic investigations is emphasized.

If one keeps in mind the tremendous occurrence of Actinomyces in Nature, one must say, that the disease developing in warm-blooded organisms, viz. actinomycosis, is relatively seldom. By this I do not want to say that the number of cases of actinomycosis in man and animals be small, it is indeed very large. Our knowledge of this disease is relatively new, as it was first in the second half of the last century that the disease became better known. The first who described a case of Actinomyces in man was LANGENBECK about 1850.

BOLLINGER, however, was the first who in 1877—78, in collaboration with the botanist HARZ, gave a, from the stand-point

of science, correct description of *the disease in cattle*. HARZ described and classified it and gave both to the microbe and to the disease the names we use to-day. The first to show that actinomycosis in man and in animals were identical diseases was PONFICK in 1880. Then JAMES ISRAEL has to be mentioned, who settled the problem of actinomycosis in man about 1880. Subsequent to this the demand of pure cultures of the microbe causing the disease was put forth, and now the strange thing happened, that one arrived at highly different results on starting from undoubted cases of true actinomycosis.

BOSTRÖM, who was the first who prepared pure cultures of pathogenic Actinomyces, always obtained an *aerobic* organism, which in broth grew as long threads, while WOLFF and ISRAEL received an anaerobic organism growing as short, richly ramified rods. This led to a violent discussion in which the last word as yet has not been said. BOSTRÖM thus claimed that this Actinomyces was aerobic and grew at room temperature, and the fact that he often found parts of plants in the pathological tissue made it seem likely that the Actinomyces was derived from the vegetable kingdom. WOLFF-ISRAEL on the other hand stated that their *anaerobic* form did not grow except at body temperature (37° C.), and did not exist without the organisms of warm blooded animals. In 1905 an important paper by WRIGHT appeared supporting WOLFF-ISRAEL'S view. So did also later publications by SHIOTA, Japan, HARBITZ and BACKER-GRÖNDAHL, Norway, KLINGER, Germany, and COLEBROOK, England. They all maintained that the microbe was anaerobic and conform to WOLFF-ISRAEL'S description.

The first experimental work on actinomycosis carried out here in Norway, by the way, was that of Professor HARBITZ in 1898, who later, in 1910, together with BACKER-GRÖNDAHL published an important paper on the occurrence of actinomycosis in Norway, including the pathological anatomy and bacteriology of the disease.

That the Norwegian authors already at that time had adopted a quite modern view may be seen from the following quotation:

»Infection through the mucous membranes of the mouth and throat seems at present to be the mode of infection for which the best reasons may be given.»

Of the above mentioned investigators especially WRIGHT in his excellent paper had a very decided standing-point, claiming

that there was just one single species of micro-organisms that formed the characteristic agent in typical actinomycosis. The other authors cited, however, thought that also the aerobic organism might play an insignificant rôle in the production of actinomycosis. LIESKE thus maintained that the two forms were variants of one and the same type, as he was of the opinion that anaerobic forms of *Actinomyces* after repeated subcultures became aerobic. LIESKE from this inferred that one type was able to turn into the other. Against this view the fact was emphasized by COPE that one has never seen any anaerobic variant change into an aerobic. The view held by LIESKE, according to COPE, has not either been corroborated clinically.

In 1931 appeared the monograph of Professor CARL NAESLUND, which of all workers on this field is said to be the most careful and extensive investigation on actinomycosis published so far, and is based on 10 years' research and experiments. In this paper it was established by NAESLUND through cultural investigations and experimental inoculations in animals that the paramount number of cases of actinomycosis are caused by an anaerobic organism of the type of WOLFF-ISRAEL, which is encountered in the oral cavity of healthy individuals. He found, however, that in some few cases, particularly of pulmonary and cutaneous actinomycosis, aerobic organisms were the cause, or at least aerobic organisms with pathological action were implicated. These aerobic *Actinomycetes*, says NAESLUND, in cultural and other respects were analogous with the forms of *Actinomyces* he had found to be pathogenic among 500 strains from soil dust, straw and hay tested by him. NAESLUND, therefore, thinks that infection with *Actinomyces* by inhalation of dust containing dried fungous elements only occurs quite occasionally. The view of NAESLUND is supported by BIGGART in his paper from 1934, and by COPE in 1938. The same occasional importance must also be attributed to vegetable material and other foreign bodies. Their significance is a more casual one and in no way necessary for the appearance of actinomycosis.

Our present knowledge seems therefore to point in the direction that all actinomycosis is to be connected with the anaerobic organism, and that this form ought to retain the name originally given to it by HARZ and BOLLINGER.

One should be aware of the fact that a tremendous amount of work would be necessary to determine throughout the two

single types that might be pathological among the huge number of aerobic types.

As to the relative distribution of the cases of actinomycosis within the organisms of warm-blooded animals, as far as man is concerned the disease occurs to a large extent in so to speak every organ. There exists practically no part of the body that is not affected. The majority of the infections belongs to the oral cavity. One thought that carious teeth might play a certain rôle. This is, in NAESLUND's opinion, of lesser importance. Even if *Actinomyces* frequently is found in carious teeth, NAESLUND claims on the basis of his experiments, that he just as often was able to demonstrate the pathogenic anaerobic type in the dental film of healthy teeth than in that of carious.

Actinomycosis thus cannot be brought into direct relation to dental caries. Furthermore, in the oral cavity actinomycosis essentially affects the soft parts, while the bone not so frequently is affected. The reserve is true e. g. in cattle, where the bone, particularly the lower jaw, is predominantly affected. One part of the skeleton, however, is relatively easily affected in man, namely the spine, particularly through abscesses arising from the oral cavity.

In the mouth the salivary ducts and salivary glands before all are exposed to actinomycosis to a marked degree. The parotid and the sublingual glands are equally subject to infection. Here *Actinomyces* also substantially participates in the formation of salivary calculi (NAESLUND, SÖDERLUND).

Moreover primary infection in the tonsils and in the pharyngeal cavity are frequent. Actinomycosis may occur both primarily and secondarily in the lungs and in the various other organs, such as the stomach, guts, liver, kidney etc. Finally I will mention that actinomycosis of the skin is not quite infrequent, and that the nervous system often is affected.

One has thought of the possibility that the occurrence of pathogenic *Actinomyces* in actinomycosis should be dependent of the simultaneous presence of definite other micro-organisms. KLINGER in particular claimed that bacterium *actinomycetum comitans* was of importance, a bacterium of somewhat varying shape. Furthermore a certain rôle was attributed to *Bacterium fusiforme*. NAESLUND however declares that a mixed infection with different micro-organisms did not have any noticeable influence on the development of actinomycosis. Concomitant

bacteria, according to NÆESLUND, are of no etiological importance so ever. Thus, secondary infection with pyogenic bacteria did neither lead to spread the disease wider nor to increase suppuration.

The pathogenic Actinomycetes for the rest do not affect the tissues of the warm-blooded animals in a way parallel to that of other pathogenic microbes.

The tissue, for instance, does not show any tendency to ulcerations as in tuberculosis, nor is it, on the other hand, as circumscribed as a gumma, and, besides, actinomycosis differs from septic or tuberculous infections particularly with respect to one thing, namely it exhibits none or little tendency to affection of the lymphatic system. From infection with the anaerobic form of Actinomycetes the lymphatic system is almost immune (COPE). Moreover, it is a peculiarity of the Actinomycetes not to cause an inflammation *immediately* after having penetrated through the submucous or subcutaneous tissues. They may do so, but otherwise a shorter or longer period of latency is the usual. This latency is a phenomenon characteristic of this disease.

As for metastases within the organism these may form via the circulatory system. A spreading of the disease in this manner is however most frequent when the lungs form the site of the primary infection. Very often one sees the statement that traumas be of final importance for the development of actinomycosis. Any larger significance as etiological factors could not be attributed to traumas, but the latter act to a lesser extent both on the appearance and the spreading of actinomycosis.

The occurrence of the disease in warm-blooded animals, one has every reason to believe, corresponds grossly to the conditions met with in man with the variation due to whether the animal in question belongs to the herbivores or to the carnivores. To judge from the occurrence on the basis of the number of cases of actinomycosis, the latter is much more common in cattle than in man. As to the distribution between the different animal species, the hog is affected particularly often. In the horse, sheep and dog it is very rare. Otherwise every animal species may be affected, both mammals and birds. Actinomycosis plays on the whole an important part as animal disease. It is especially wellknown in domestic animals, but whether this is due to that the latter are more susceptible or that the disease is better known in these than in other animals species, one does not know.

Purely geographically one thinks to have observed that actinomycosis in cattle occurs more frequently in the dusty low plains than in the highland. BROFELDT published an interesting investigation about how the geographical occurrence of actinomycosis in man and animals follow each other. He showed by means of a map the prevalency of actinomycosis in different parts of Finland. By comparing the maps showing the occurrence in man with that for animals one gets the impression that there exists a certain relation between the occurrences of both forms. There seem to be climatic and other circumstances in some parts of the country which increase the frequency of this disease both in man and in animals. It is, therefore, of interest to compare this purely geographical investigation with the possible entrance of vegetable matter into the organisms, mentioned above.

Without being able to say that there really exists a large material, it is claimed by SANFORD in 1921 that in the U. S. A. 57 out of 96 cases of actinomycosis are found in farmers and further that in the typical agricultural districts in the Middle and North West of the U. S. A. the occurrence of actinomycosis was much higher than in other parts of the country.

Regarding our knowledge of the Actinomycetes, what we know of their classification in a bacteriological system, of their general occurrence in Nature and their physiological and pathogenic properties — I will, to conclude, say that even though our present knowledge of this field has reached far, indefinitely much is left to be done before our understanding of this manifold group of organisms becomes exhaustive. This holds good for all the facts concerning the behaviour of the microbe in every respect, and its great variability favours the belief that our knowledge of this matter never will be able to form an entirety.

#### Literature.

- BIGGART, J. H. Actinomycosis graminis. John Hopkins Bull. 1934. 54.  
BROFELDT. Über Actinomycose in Finland. Act. Med. Duod. Helsinki 1926. 7. H. 61.  
BOSTRÖM. Untersuchungen über die Aktinomycose der Menschen. Beitr. zur Path. Anat. 1890. 9.

- COLEBROOK, L. Brit. Jour. of exp. Med. 1920.  
 —, The Anaerob. Actinomycosis. Med. Res. Counc. Syst. of Bact. vol. 8 p. 78.
- BOLLINGER, O. Centr. f. Med. Wissenschaft 1877. 481.
- FELLINGER. Centr. f. Bact. 1931. 122.
- ISRAEL, J. Neue Beiträge z. mykot. Erkrankungen d. Menschen. Arch. f. Path. Anat. 1897. 78.  
 —, und WOLFF.) Über Reinkulturen der Act. und ihre Übertragbarkeit auf Tiere. Vierch. Arch. 1891. Bd. 126.
- GRIENEW und BARANOW. Odontologia H. 1. 1928.
- HARBITZ, F. Bidrag til Læren om Actinomycosis hominis. N. Mag. f. Lægevidenskab. 1898.
- HARBITZ, F., BACKER GRØNDAHL, N. Aktinomykosen, strålesoppsygdommen i Norge. Kristiania 1910.
- COPE, ZACHARY. Actinomycosis, Oxford Med. Public. Oxford University Press. 1938.
- GRYTHE, OLAF. Leptotrix. Experimentelle Studien an Leptotrix die aus klinisch gesunden Zahnfleisch gezüchtet wurden. Fabritius, Oslo 1938.  
 —, The role of Actinomyces and Leptotrix as an etiological factor in the formation of Tartar and salivary calculi. Den norske tannlægeforenings tidende, H. 7, 1938.
- KLINGER, R. Untersuchungen über der menschlichen Actinomycose. Centr. f. Bact. 1912. 62. 191.  
 —, Zur Äthiologie der Actinomycose. Centr. f. Bact. 1921. 85.
- LIESKE, RUDOLF. Morphologie und Biologie der Strahlenpilze. Leipzig 1921.
- NAESLUND, CARL. Experimentelle Studien über die Äthiologie und Pathogenese der Actinomycose, Levin u. Munksgaard, Kjøbenhavn 1931.  
 —, Über Kalkausfällungen durch Mikroorganismen. Biol. Zeitschr. Bd. 184. 1927.  
 —, Untersuchungen über die Ursachen und das Entstehen des Zahnsteines, Odont. Tidskr. 3. 1926.
- LEHMAN-NEUMANN. Bakteriologie 2 Bd. 6 Aufl. 1927.
- PONFICK. Die Act. der Menschen. 1882. Berlin.
- SMITH, DAVID T., A. B., M. D. "Oral Spirochetes" and Related Organisms in Fusio-Spirochetal Disease. The Williams & Wilkins Company, Baltimore, U. S. A.
- SÖDERLUND, G. Die Speichelsteinkrankheit und ihre Verhalten zu der primären und dukto-genen Speicheldrüseaktinomycose. Act. Chir. Scand. 1928. 63. suppl. 9.
- WASSMUND, M. Eine neue aussichtreiche Behandlung der Actinomycose Iontophorese. Zentr. bl. f. Chir. 1935. 62. 111 2791.
- Waksman. Principles of Soil Mikrobiologi. 2 opl. 1931.
- WETTSTEIN, RICH. Handbuch der Systematischen Botanik. 4. opl. 1935.
- LANGENBECK cit. efter ISRAEL.