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Actinomycosis

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Morphology of Actinomyces

Actinomyces are mold-like fungi characterized by very delicate gram positive mycelium possessing no visible septae or nuclei. They reproduce by the budding off of small spherical bodies (conidia) from the tips of certain of the mycelial threads (conidiophores) and also by fragmentation of the mycelium.

ium into bacilli-like bodies (oidia).

The various members of the family are variable in the manner of growth. Most genera grow well on all media under aerobic conditions. Nearly all have the same pH requirements as bacteria for growth. The acid media used for cultivation of most fungi is unsatisfactory. Some genera, notably the one associated with the disease actinomycosis proper, require enriched anaerobic media. In liquid media, the growth is at the bottom without cloudiness. Some genera produce a pedicle. Smears of the growth from liquids resemble very little that from other fungi. The conidia and oidia look like a mixture of coccus and bacillary forms of bacteria.

Clubs: These structures are peculiar acidophilic and gram negative "caps" or dilatations over the ends of mycelia. The nature of this cap of material is unknown. The evidence points to the belief that the substance is a product from the mycelium probably of a protective nature. The clubs are produced only by the pathogenic genera in tissues.

The sulphur-granules are peculiar formations also found only in tissues. The granule consists of a core of tangled mycelium and a lobulated periphery made up of the projecting ends of the mycelia which have been transformed into clubs. Since the mycelium is gram positive and the "cap" of the club is gram negative after gram staining, the body of the granule is blue and the lobulated edge pink.

Acid-fast reaction: Some forms, both saprophytic and pathogenic, are acid-fast.

Systemic relationships: The formation of mycelium and conidia definitely relates the organisms to the higher fungi. On the other hand, the fragmentation into bacillary bodies, the acid-fast reaction, the delicate size and the manner of growth appears to place the group close to the tubercle bacillus and also the diphtheroid organisms. Immunological reactions and allergic phenomena are being studied and increase the evidence of this phylogenetic relation-

ship to bacteria.

Synonyms: Certainly one of the most formidable problems in the literature on actinomycosis is the enormous number of terms. Anyone but a specialized mycologist soon becomes lost because he does not know just which organism is being described. The terms are not always used synonymously. The paper by Kerlan tabulates an apparently complete list of the terms with his interpretation of their meaning. Henrici lists the commonly used terms and with a good understanding of these, the literature can be followed fairly well: Streptothrix, Cladothrix, Cospora, Nocardia and Discomyces. A concise discussion of the terms with references to the literature for more detail are given. The term "Streptothrix" is very commonly used in the literature, particularly that on pulmonary diseases. Its usual meaning is to designate the pathogenic actinomyces which do not produce "clubs" or granules in the tissues. Its value in this respect appears quite definite. (Some higher molds unfortunately have also been called "Streptothrix.")

The pathological-clinical terminology is also involved. Frequently, particularly in the past, all diseases with chronic suppuration showing sulphur-granules were referred to as actinomycosis. More recently, as specific etiological factors have been uncovered, new terms have had to be devised. The reaction is like that toward tuberculoma. The proliferative and necrotic lesions of syphilis, tuberculosis or other conditions are being referred to as "tuberculoid reactions." Similarly, the chronic suppurative states showing granules in the pus are best designated as mycetomae. When due to actinomycosis, these are then called actinomycosis. When due to higher fungi, they are known as maduremycosis, e.g., certain forms of Madura foot. Finally, some genera of actinomyces do not form the sulphur-granules in the exudate and these diseases are most frequently referred to as streptothrichosis (see above).

Actinobacillosis, a term suggesting a relation to actinomyces, is used to designate a pathological condition of

an entirely different etiology. The organism is a bacillus and not a fungus. As will be stated in detail later, the prefix "actino" is used because the disease has a form like actinomycosis proper and sulphur-granules are also formed.

The family of actinomyces: It seems that no one group of bacteria or fungi has as many genera and such a wide distribution as the actinomyces. Most of the genera are purely saprophytic and these are of enormous economic value, for instance in soil transformation and fertilization. Many are plant pathogens, the most important of which are those producing potato scab. A relative few affect animals and only a very few of the total affect man. The animals affected range from muscol through reptiles, birds and mammals. A disease like actinomycosis proper has been described in the fossils of prehistoric elephants. The "lumpy-jaw" of cattle is of the greatest economic importance. It has been described in epidemic form among wild animals.

In man actinomycotic infection is in three general forms: actinomycosis proper, Madura foot and the tuberculoid forms without granules designated as "Streptothricosis." In the last group, the organisms are usually acid-fast.

Mycetomae: suppurations with sulphur-granules: Chronic proliferative inflammation with sulphur-granules in the exudate is characteristic of actinomycosis. However, it is not specific of this disease either in animals or man. It was the lack of appreciation of this point that lead to so many errors regarding etiology of true human actinomycosis.

In Madura foot the sulphur-granules may be due to actinomyces (*A. Maduræ*) but at least seven genera of other families of the higher fungi also producing granules have been isolated in this disease. In certain diseases of the udders of cows and a chronic suppuration of the subcutaneous tissue of horses, sulphur-granules due to masses of staphylococci are present. In some of the forms of so-called actinomycosis of cattle, the woody-tongue or soft tissue variety, granules are formed but the disease is due to a gram negative bacillus. The

bacillus may be pathogenic for man and cases of human infection have been reported (Thompson). Typical sulphur-granules can be found in the mouth and particularly in the crypts of the tonsils and about carious teeth in humans. Some of these masses are due to fusion of bacterial bodies. In human tissues, particularly in lung, lymph nodes and abscess walls, similar amorphous clumps of bacteria may be found and the tissue may be confused with that from true actinomycosis (Randall).

The presence of lobulated granules in pus or tissue therefore is not diagnostic of actinomycosis. These bodies must show acidophilic and gram negative "clubs" in the periphery in order to establish the diagnosis. The most certain method (Randall and Wangensteen) of identifying these structures is to treat the pus like other transudates or exudates: sediment the material, imbed the sediment in paraffin, cut sections and stain these with routine tissue stains and also by the method of Gram.

The Organism of Actinomycosis Proper: The organism has the general characteristics of the other actinomyces already described. It is, however, much more difficult to cultivate. It requires anaerobic conditions for the first growth in all cases and usually for many transplants before it becomes accustomed to aerobic states. Nearly always media enriched with blood is necessary. Other organisms overgrow the fungus and therefore in contaminated abscesses it is useless to attempt its cultivation as a clinical procedure. In old abscesses and frequently in sinuses which have been draining for some time, the organisms are crowded out by the secondary invaders. Important practical applications hinge on these points. The organisms are most numerous in unopened abscesses and shortly after incision careful search may fail to show their presence. Material obtained from the first puncture must be used for making the diagnosis (Randall). The absence of the typical granules in old abscesses does not rule out the diagnosis of actinomycosis.

The arguments as to the sensitive

agent in actinomycosis proper in many are only of historical interest at this time. The Wolff-Israel type is conceded by all as the truly causative genus.

Animal actinomycosis is of two types: the lumpy-jaw type and the soft tissue or wooden-tongue type. The former is due to the same organism which produces the human disease. The second type is produced by the actino-bacillus, a number of an entire different group of organisms.

Serological diagnostic tests and skin tests have been attempted. Reference to these is made now and then but no definite data seems to be available.

Dissociation has been observed in the actinomyces family (Henrici). The author had the experience of observing the Berkfeld filtrate of a culture of a saprophytic genus transform into a common-appearing yellow "staphylococcus" and then reverting back to its mycelial state. By modification and adjustment of the media, the changes could be stimulated at will. Other cultures of the same genus or other genera would not transform.

The distribution of the organism other than in diseases tissue is unknown. It has been suggested for a long time that it is a "normal" inhabitant of mouths about carious teeth and diseased tonsils. Many such "organisms" have been disproven as actinomyces. Lord in numerous writings has maintained that he has found the true A. Wolff-Israel in these areas. Furthermore, he quotes Noeslund to the effect that this author has cultivated the organism and shown it to be "morphologically, culturally, and serologically similar to the actinomyces of the Wolff-Israel type." (References to this phase of the problem: J. Thoracic Surg. Vol. 1, (Aug.) '33, p. 632).

The studies of geographical distribution show the maximum localization of the disease to the upper Mississippi Valley region and to certain areas on the Atlantic seacoast notably New York and New Jersey. This suggests strongly the peculiar geographic localizations which have been observed for Rocky Mountain spotted fever, blastomycosis and coccidial granuloma. Some unknown factor

governs these odd locations and it brings to mind some of the highly specialized factors necessary for dissociation of bacteria. For instance, media from potatoes of certain years in certain stages of storage in one author's experience were most potent in stimulating dissociation of streptococci.

Cyclic increases of incidence of the disease have also been noted (Ostfeld).

Pathology: The area involved most frequently is the head and neck. Appendiceal or cecal and thoracic involvement follow next in order. The following (Kerlan) gives the collected statistics:

<u>Author</u>	<u>Cases</u>	<u>Head and neck</u> <u>%</u>	<u>Abdominal</u> <u>%</u>	<u>Thoracic</u> <u>%</u>
Foulertan	78	51	27	18
Acland	101	38	32	18
Ruhrah	632	57	21	15
Sanford & Vollker	670	60	13	14
Total:	1481	59	21	15

Apparently any part of the body may be involved: skin, central nervous system, pelvis, spine, stomach or duodenum, etc. In these areas, the primary portal of entry may have healed and the secondary deposits may persist.

Pelvic: Blasek, Rumpf, Ahltrop have reviewed the literature. "Closed" and "open", i.e. with or without sinuses, are described. About 70 cases have been reported. Most of these represent extensions or metastatic infections wherein the primary focus was healed.

Spine: Tabb and Tucker collected 35 cases of the disease involving the spine. The roentgenographic features are reviewed: two or more vertebrae involved with a perivertebral abscess but with intact intervertebral disks without collapse of the bodies; involvement of the transverse processes and laminae; sharply defined paravertebral areas with normal bone in between and

no sequestration.

Intracranial actinomycosis: MacKee reviewed the literature. He reported one case with neurological signs pointing to intracranial extension and quotes Moersch who found 10% of such cases in a group of 74 and Snokes who in four autopsies found two with involvement. The most frequent lesion is a basal meningitis. Extension or metastatic?

Upper gastro-intestinal tract is apparently immune to the infection. Blain reports one case of involvement which was unquestionably a primary infection. Extension into the duodenum from retroperitoneal abscesses has been described.

Metastatic infection from any of the various foci is common. The liver is most frequently affected but any organ may be involved. The infection travels through the blood stream.

The spread of the infection is chiefly by direct extension. The process is one of necrosis and liquefaction about the organisms and a peripheral fibrosis. There is a marked tendency for burrowing with progression of the liquefaction on one end and healing on the other. In this manner, there is extension of the lesion with multiple sinuses and healing of the older lesions. New sinuses redevelop in the old scars. No fascial planes are followed and unrelated structures including bone are invaded by extension. There is no particular lymph drainage type of extension. The sinuses are narrow and as they approach the surface the fluctuant area on incision or aspiration does not yield as much pus as is expected. In spite of the intense and stony-hard fibrosis, the tissue is remarkably vascular. Invasion of a vein allows systemic dissemination.

Healing is a prominent part of the process. In most instances, the focus of entry heals and cannot be identified and it is the secondary spread that produces the recognizable changes.

The microscopic appearance is not characteristic. There is marked fibrosis, numerous blood vessels and many collections of leucocytes often forming military

abscesses. Near the advancing end of the sinus, there is a lipoid degeneration of the tissue with many vacuolated macrophages. The granules, when properly identified, are specific. The most frequent source of confusion is with clumps of staphylococci.

Clinical features: From 65 to 80% of the cases in the collected series of over 1,000 cases occur in males (Kerlan).

	<u>Cases</u>	<u>% Male</u>	<u>% Female</u>
Foulertan	78	65	35
Leith	405	73	27
Acland	101	65	35
Sanford & Voelky	670	80	20
Kerlan	9	66	33

About 60% occur in the ages between 15 and 35 but cases occur at any age.

The symptomatology and findings are extremely variable because of the wide range of areas that may be involved. The process is one of tumorous formation with suppuration of a chronic nature involving any tissue or area of the body and the clinical features vary accordingly.

Treatment: Throughout the literature, there is a very pessimistic attitude toward the outcome. Spontaneous healing of parts of the infected area is characteristic of the disease. It is intimated that the improvement after some of the forms of treatment may be a spontaneous occurrence. The duration of cases averages less than one year but is extremely variable. Cases have been reported living 15 to 30 years after onset. Three methods of treatment are in practice: iodide administration, irradiation and surgical procedures.

Iodides: The basis for the administration of this drug is the results obtained with some cases of so-called actinomycosis in cattle. Recent work has shown that the cases so called are the cases of woody-tongue or soft tickle "actinomycosis." These are due to the actinobacillus and this organism is entirely unrelated to the actinomyces. True actinomycosis seems to respond very

poorly or not at all to iodides and the same applies of the mycotic or true form of cattle actinomycosis. Henrici has shown that the organisms can grow in a solution of the drug.

Irradiation: In spite of the fact that this form of treatment was first advocated by an American (Bevan). The American literature is not very optimistic over the results obtained. On the other hand, European reports cite excellent results. These authors give unusual statistics on end results. Engelstad's articles summarize and collect this data.

Cervico-fascial type:

<u>Author</u>	<u>No. Cases</u>	<u>% "Cured"</u>	<u>Treatment</u>
Jungling	30	100	Radiation
Rahm	36	100	"
Heyerdahl	21	100	Radium
Engelstad	28	89	"

In the thoracic and abdominal forms, the results of radiation are not decisive. The following cases are quoted as "cured": Rahm - 1 case, Eiken - 1 case; Sattler - 2 cases; Beck - 2 cases; Engelstad reports another case.

Heyerdahl's and also Engelstad's cases were treated in the same hospital (not same cases in these series), the Reichshospital in Oslo. In the entire group, therefore, in 49 cases, 46 were "cured" by radium. The dosage is 35 to 55 mg. radium element with a 2 mm. filter given over 48 hours. Incision is said to delay healing.

A summary of period of follow-up in the group listed by Engelstad is as follows:

Less than 2 mo.	- 6
2 - 6 mo.	- 4
6 mo. - 1 yr.	- 3
1 - 2 yr.	- 10
2 - 3 yr.	- 1
over 3 yr.	- 3

Note over 50% were followed over 1 year. Many cases were treated over a long period so that the time under treatment may be 3 to 5 years in addition to the period of freedom from symptoms.

Surgery: The incisions and cauterization of newly-forming abscesses has not proven to be of much value. The reports are all quite uniform in their statements in regard to the poor outcome.

Wangensteen and Randall strongly recommend more radical procedures. In the cervico-fascial type, block dissections with removal of as much of the diseased tissue as it possible is advocated. Complete removal as in malignancy may not be necessary since the procedure allows the remaining areas to heal. The same principle has been applied to thoracic types and Wangensteen reports one such case as cured.

Randall's group may be summarized as follows:

#	Age	Sex	Type	Duration	Treatment	Length of Follow-up	Outcome
1	13	M	Generalized	18 mo.	---	---	Died
2	15	M	" "	7 "	Incision	---	"
3	13	F	C.F.	4 "	Radical excision	?	No recurrence
4	44	M	"	1 "	" "	?	" "
5	29	F	"	1 " 4 "	Incision "	?	Recurrence, 3mo. No recurrence
6	65	M	"	6 "	Incision, K.I. Radiation	6 yr.	" "
7	39	M	" (tongue)	4 da.	Incision	4 mo.?	" "
8	21	M	Thr.	2 yr.	Incision 125% S.E.D.	---	Died in "few mo."
9	31	M	"	13 mo.	---	---	" , 7 mo.
10	27	M	Abd.	1 yr.	---	---	" , 6 mo.
11	51	M	"	3 yr.	200% S.E.D. (in 2 courses) Incisions	---	" in few mo.
12	28	M	Thr.	6 mo.	---	---	Died of hemorrhage after biopsy
13	27	F	Abd.	5 mo.	Drainage of liver abscess	---	Died post-operatively
14	27	M	Abd.	16 mo.	Drainage		
15	40	M	C.F. C.F. (cheek)	6 wks.	140% S.E.D. Radical excision	---	Died 1 mo. later No recurrence
16	43	M	C.F. (tongue)	1 mo. 3 "	Incision Incision, K.I. 140% S.E.D.	---	Recurred 1 mo. No recurrence
17	43	F	C.F.	3 mo.	Wide incision Radium 81 mc. (2 doses)	---	Died, 7 mo.
18	46	M	C.F.	2 yr.	Radium excision	1 yr.	No recurrence
19	34	M	C.F.	2 mo.	Incision, K.I. 130% S.E.D.	?	" "
20	29	F	Thr.	7 mo.	Rad. incisions, K.I. 225% S.E.D.	2 yr.	Had lesions on last exam.
21	57	M	Abd.	1 yr.	Incisions	---	Sinus closed

The period of follow-up is not clearly stated in several cases. Of those free of recurrences with a stated period of 1 or more years, there are:

<u>Case #</u>	<u>Treatment</u>	<u>Period</u>
6	Incision, K.I., Radiation	6 yr.
15	Radical excision	2½ "
16	Incision, K.I., Radiation	2½ "
18	Radical excision	1 "

In addition to the above, those said to be free of recurrence at an indefinite time include 2 others treated by radical excision, 2 more treated by incision alone and 1 treated by incision, K.I. and radiation.

The cases treated by radical procedures appeared to do much better than the others.

From Randall's study of end results, the surgical treatment apparently should consist of more radical procedures. The author does not put much faith in any beneficial results from radiation. In only one instance was interstitial radiation used.

Wangensteen collected 26 cases of thoracic actinomycosis reported as cured or improved. The treatment used was extremely variable and ranged from simple aspiration to extensive surgical procedures.

Graham cited one case apparently cured by caustery lobectomy. (J. Thoracic Surg. 1: 632-634, (Aug.) '33.

Impressions

1. Actinomyces are fungi of very delicate nature reproducing both by conidia and by fragmentation of the mycelium into bacilli-like bodies. The growth of the organism is very similar to that of bacteria. Smears from cultures look like a mixture of cocci and bacillary forms of bacteria. The "clubs" are acidophilic and grow negative "caps" over ends of mycelium. Apparently the clubs are protective in nature. The sulphur-granules consist of a coil of tangled mycelium and a lobulated periphery

made up of the projecting ends of the mycelia which have been transformed into clubs. After gram staining, the center of the granule is blue and the periphery is pink. Some actinomyces are acid fast.

2. Apparently the actinomyces are the stepping-stones between bacteria, such as the tubercle bacillus, diphtheroid organisms, and the higher form of fungi. Immunological reactions of allergic phenomena are being studied and the evidence so far points still further toward this relationship.

3. Synonyms used in the literature on actinomycosis are obstacles in the study of the problem. Most commonly used synonyms are as follows: Streptothrix, Cladothrix, Cospora, Nocardia and Discomyces. The term "Streptothrix" illustrates that these terms are not always synonymous. This particular term is used to designate the disease produced by pathogenic actinomyces which do not form clubs or granules in the tissue.

4. Pathological-clinical terminology is also difficult to follow. The most recent tendencies are to call the various chronic suppurative conditions which show granules in pus as mycetomae. When these conditions are due to actinomyces, the disease is called actinomycosis and there are several varieties. When due to higher fungi, the disease is designated as a Maduro mycosis. Finally, when the condition is due to actinomyces which do not form sulphur-granules, the condition is referred to as streptothrichosis. Actinobacillosis is used to designate a disease resembling very much the actinomycosis in cattle but which is due to a bacillus and not a fungus.

5. The family of actinomyces is extremely widespread. Most of the genera are saprophytic and are valuable in soil transformation and fertilization. Some are plant pathogens, for instance those producing potato scab. A few affect animals and of the total only a small number affect man. The animals which may be involved include practically all the various species. It has been

described in pre-historic animals.

6. In man, actinomycotic infection is of 3 general types: actinomycosis proper, Madura foot and the tuberculoid form without granules designated as "Streptothricosis."

7. In the various chronic suppurations which show sulphur-granules (Mycotomae), the nature of the infection may be extremely variable. In Madura foot, the sulphur-granules sometimes are clumps of actinomyces but at least 7 genera of other families of the higher fungi have also been isolated. In a disease of the udders of cows and also in a suppurating disease of horses, sulphur-granules due to masses of staphylococci are present. Same is true in some of the chronic inflammations of man. The woody-tongue or soft tissue variety of cattle actinomycosis is not due to a fungus but is due to a gram negative bacillus. Finally in the mouth of humans, sulphur-granules can be found and many of these are apparently due to fusion of bacterial bodies. The conclusion, therefore, can be made that the presence of lobulated granules in pus or tissue is not diagnostic of actinomycosis. It is necessary to show that there are acidophilic and gram negative "clubs" present.

8. One of the most valuable methods of identifying these granules is to sediment the exudate in methods of paraffin and cut sections and stain these with tissue stains and with the gram stain.

9. The organism causing actinomycosis proper is of the type described by Wolff and Israel. It is an anaerobe and requires enriched media for its first cultivation. It is not a sturdy organism and secondary invaders crowd the fungus out so that old abscesses and draining sinuses usually fail to show the organism. Even old unopened abscesses may not contain the typical granule. The material obtained from the first puncture is most suitable for making the diagnosis.

10. Animal actinomycosis is of 2 types: the lumpy-jaw type which is due to the same organism as produces the disease in man; and the soft tissue or wooden-tongue type, which is due to a gram negative

bacillus.

11. Dissociation in some of the genera of actinomyces has been observed. The organisms have been seen to dissociate into diphtheroid organisms and into a common appearing yellow staphylococcus and back to its original mycelial state.

12. The distribution of the organism other than in diseased tissue is unknown. Many authors have suggested that it is normal inhabitant of mouths about carious teeth and diseased tonsils. Some authors claim to have cultivated this organism and say that it is morphologically identical with the actinomyces of the Wolff-Israel type. These statements are not accepted by all.

13. The greatest incidence of the disease is in the upper Mississippi Valley, New York and New Jersey. This suggests a peculiar geographic localization which has been observed for other diseases such as Rocky Mountain spotted fever and coccidial granuloma. Cyclic increases of incidence also have been known.

14. Area most frequently involved is the head and neck; next in order, follow abdominal and then involvement. Percentage in 1,481 cases follows: head and neck 60%, abdominal 20%, thoracic 15%, other 5%.

15. Any part of the body may be involved. Usually the primary focus of entry heals entirely. The metastatic infection (or extension) gives rise to the clinical forms of the disease so that odd localization, such as isolated involvement of spine, stomach or meninges or uterus may be found.

16. About 70 cases of pelvic involvement said to be primary have been reported. The portal of entry is difficult to determine because in most cases it is healed.

17. 35 cases of the disease involving the spine have been reported. Roentgenographic features described are as follows: two or more vertebrae involved with a perivertebral abscess but with intact intervertebral disks without

collapse of the bodies; involvement of the transverse processes and laminae; sharply defined rarefied areas with normal bone in between and no sequestration.

18. In one group of 74 cases, 10% showed intracranial involvement. The most frequent lesion is a basal meningitis which may be either extension (or metastatic?) in origin.

19. Involvement of the upper gastrointestinal tract is extremely rare. Only 1 case of primary infection of the stomach seems to have been reported.

20. The spread of the infection is chiefly by direct extension. There is marked tendency to burrowing with progression at one end of sinus and healing at the other. Multiple sinuses are formed with healing of the older ones. The extension does not follow any line of cleavage and there is no particular spread by lymph drainage. At any time the invasion of a vein may allow systemic dissemination.

21. Microscopic appearance is not characteristic. Marked fibrosis, numerous blood vessels, many collections of leucocytes often forming miliary abscesses give the usual picture. Lipoid degeneration with macrophages and some giant cells usually are seen in the active portions.

22. In 5 groups of cases, totalling about 1,000, the percentage of males in the group range from 65 to 80%. About 60% occur between the ages of 15 and 35. Symptomatology and findings are extremely variable because of the wide draining areas that may be involved by the process. It is essentially one of tumor formation with suppuration.

23. The general literature is very pessimistic in regard to the outcome. Apparently spontaneous may occur. The usual duration of the disease is only a few months but cases up to 15 or 20 years have been reported.

24. Three methods of treatment are in common practice: iodide administration, irradiation, and surgical procedure.

25. The basis for the administration of iodide is the result obtained in some cases of actinomycosis in cattle. Recent work, however, has shown that these cases are due to a gram negative bacillus and are entirely unrelated to the disease actinomycosis proper.

26. American literature is not very optimistic in regard to treatment by irradiation. European reports, however, cite very excellent results. Of one group of 49 cases, 46 were "cured" by radium. The dose given was 35 to 55 mgs. of radium element over a period of 48 hours. Incision said to delay healing. Same results were obtained in 66 cases of the disease treated by deep x-ray. 100% "cures" reported. In the thoracic and abdominal forms, the results of radiation are not decisive. 7 cases of "cures" are cited.

27. 50% of these cases were followed longer than 1 year.

28. Incision and cauterization of newly-forming abscesses has not proven to be of much value. However, recent writers strongly recommend more radical procedures. (Wangensteen, Randall). In the cervico-facial type, particularly block dissections with removal of as much of the diseased tissue as is possible is advocated. Complete removal is not necessary since the procedure allows the remaining areas to heal. One series of 21 cases, is tabulated. The cases treated by radical procedure appear to do much better than the others. The length of follow-up is not clearly stated in some of the cases.

29. Nine cases said to be free of recurrence were treated as follows: 4 by radical excision, 5 by incision, K.I. and radiation and 2 by incision alone.

30. Twenty-six of thoracic actinomycosis reported as "cured" or improved have been collected from the literature. Treatment used was extremely variable and ranged from simple aspiration to extensive surgical procedure.

31. Impression obtained in regard to treatment was that those who have been encouraged by radiation have developed a technique employing very heavy dosages and feel that their results are extremely good. These people feel that surgical procedures hinder or delay the healing. On the other hand, those who have been encouraged by surgical results take the directly opposite view and feel that more radical surgery should be employed and that radiation is of secondary importance.

II. CASE REPORT

ABDOMINAL ACTINOMYCOSIS

Case is that of a white male, 15 years of age, admitted to the Minnesota General Hospital 12-10-32 and expired 2-4-33 (56 days).

Primary Lesion in Cheek (?) Healed

8- -31 - Had large sore on left cheek. Like a large boil. Drained and "cut out" by physician. Lesion healed.

Abdominal Symptoms, 1 year later

7- -32 - Complained of tenderness over stomach. Pain localized below umbilicus. Aggravated by over-eating and during periods of hunger. Vegetables and fruits without greasy foods relieved pain to some extent. During next few months, lost about eighteen pounds in weight and became weak.

Sinus Formation

9- -32 - Small swellings developed over left costal margin. Soon opened spontaneously. Following this, another swelling appeared about 2 inches from first and again opened spontaneously.

Tuberculosis Considered

12- -32 - Admitted to tuberculosis sanatorium. Mantoux negative. No signs of tuberculosis found. Began to regain some weight.

Past history

Usual childhood diseases.

Findings Entirely in Abdomen

12-10-32 - Admitted. Physical examination: Head - negative except for slightly enlarged tonsils and slight cervical adenopathy. Lungs - clear to percussion

and auscultation, no rales heard, dullness on left side below level of 4rd interspace. Heart - normal in size and shape, no murmurs heard, no thrills felt, pulse 104. Abdomen - some rigidity around umbilicus, liver enlarged 3 fingerbreadths below costal margin (extremely tender), whole abdomen and area of liver tender to percussion; over left lower costal margin, there are two sinuses--one in the anterior axillary line and the other posterior in the mid-axillary line, both are dry and surrounded by an erythematous area (not indurated) but apparently are not attached to the ribs. It is a question whether these sinuses lead into the abdominal or thoracic cavity. Caseous material obtained. Rectal - negative. Extremities - negative.

Laboratory: Urine - 150 cc., 1+ albumen, 6 wbc's per high power field (centrifuged), few hyaline and granular casts. Blood - Hb. 54%, wbc's 25,700, rbc's 2,930,000, Pmn's 82%, L 14%, M 4%. Blood Wassermann - negative. Crust removed from reddened sinus tracts over left lower costal margin; dry cheesy, purulent material obtained. Cultures of material taken. Smears - show no actinomyces. Temperature 101. Pulse 100. Respirations 20.

X-rays

12-12-32 - Gastro-intestinal study - enlarged liver and spleen, bilateral diaphragmatic pleurisy, possible slight amount of fluid at both bases, primary tuberculous focus.

Biopsy

12-13-32 - Diagnosis of actinomycosis verified by sections.

12-14-32 - Temperature 105.

Operation

12-15-32 - 7th rib resected. There appears to be an induration of the pleura in the lower portion of the wound. Peritoneum not entered. Exact lesion origin still somewhat obscure.

12-16-32 - Wbc's - 44,000.

12-18-32 - Epistaxis of 150 cc.

Liver Abscesses

12-21-32 - Thorotrast shows multiple abscesses of liver and left pleural effusion. Temperature 98.5. Ectasia in

right chest.

12-27-32 - Pleural effusion has increased. 350 cc. bloody fluid aspirated. Cultures reveal no actinomyces.

12-28-32 - 450 cc. bloody fluid removed.

12-31-32 - X-rays show hydropneumothorax with adhesions and pocketing left; pleural effusion, slight, right.

1-3-33 - Growing gradually weaker and more listless.

1-7-33 - X-ray of chest shows less fluid in chest. 300 cc. citrated blood given by vein

Operation

1-8-33 - Small, high, right rectus incision disclosed abscess beneath peritoneum which discharged sulphur granules and pus copiously. Packed and Penrose drains left communicating with costal sinus already open. Small piece taken from liver margin for biopsy. Microscopic diagnosis - actinomycosis.

1-12-33 - Lemon-yellow color of skin without tinting of sclera. Icteric index - 10 units. Appears somewhat stronger. Has good appetite. Septic type of temperature going up to 103 in the last few days.

1-14-33 - Abdomen distended. Probably some fluid present. Dulness in flanks. Slight cough.

1-15-33 - Gradually becoming weaker.

1-23-33 - Appears weaker but is still optimistic. Old blood in nose, bloody crusts over lips. Not so dyspneic. Chest - normal percussion note anterior except that the liver can be percussed above at the 5th interspace. In right axilla, fine crepitant rales heard at end of inspiration. Breath sounds (anterior) are normal.

1-31-33 - Probed fistula for some distance and inserted a drain.

2-4-33 - 5 P.M. - Nurses moved patient to make him more comfortable and left room. Came back 10 minutes later and found patient unconscious and breathing very slowly and deeply. Pulse rapid, very weak and thready. No cyanosis. 0.2 cc. of 1:1000 adrenalin given intravenously. Breathing became better and pulse more strong. 500 cc. 10% glucose in saline with 1 cc. adrenalin (1:1000) given intravenously. Did not respond. 4:05 P.M. - Expired.

Autopsy

Emaciation, Sinuses, Operative Incisions

The body is that of an extremely emaciated, poorly developed, white male, 15 years of age, measuring about 150 cm. in length and weighing approximately 100 lbs. Rigor is present. No hypostasis. 1+ edema of ankles and lower legs. No cyanosis. Skin is suggestively yellow tinted but the sclerae show no jaundice. The right pupil measures 5 cm. in diameter as does the left; they are regular and round. There is an incision over the left 7th rib with a rib resection. There are two draining sinuses in the left epigastrium, one just below the costal margin in the mid-mammary line and the other about 2 inches lateral to this. There are numerous ecchymoses in both antecubital fossae. The skin around these sinuses is not particularly indurated although it is somewhat reddened. A good deal of caseous material can be expressed from both sinuses. The medial sinus was opened.

Abscess, Multiple Sinuses. Appendix not involved.

Abdominal cavity. The sinuses are carefully dissected out. They are both subdiaphragmatic and extend into a cavity in the Peritoneal cavity, well walled-off above and below the stomach, and from these one sinus tract leads to the intra-hepatic region and another leads to a small pocket just above the spleen. There are a great deal of adhesions throughout this area. There is a localized peritoneal reaction in the epigastrium, well walled-off above and behind the stomach. No generalized peritonitis. There is about 1000 cc. of clear fluid in the abdominal cavity. The appendix is small and adherent to the right lower quadrant. There is no evidence of any old or new inflammatory process present.

Pleural spread?

Pleural cavities: There are a few adhesions in both spaces posteriorly. No fluid. The visceral pleura at both bases is densely adherent to the diaphragm. The level of both diaphragms is difficult to make out because of the

dense adhesions on the right and left side. There is the normal amount of fluid in the pericardial sac. No evidence of any inflammatory process.

The heart weighs 250 grams. The heart muscle is rather soft and flabby. No evidence of acute dilation, or valvular lesions, or insufficiency of any of the valves. The root of the aorta is smooth and shows no atheromatous changes. The coronaries are normal.

Direct Extension to Lungs

Both lungs weigh (together) 1175 grams. There is rather marked congestion throughout both lungs and slight atelectasis of both lower lobes. The only evidence of any actinomycosis is in the lower lobe on both sides and it appears that there is a small direct extension of the actinomycosis up to the diaphragm particularly on the right side. The extension of the actinomycosis in the right lower lobe is only several millimeters into the lung parenchyma, being present mostly in the pleura of the right base. There is some extension of the actinomycotic process through the left diaphragm but it does not involve the lung parenchyma although there is some caseous material of the pleura at the left base. There is no evidence of any bronchopneumonic process in either lung. The bronchi and trachea are patent.

Extension to Spleen

The spleen weighs 255 grams. There are many adhesions around the spleen. The capsule is extremely thick. There are small, caseous areas scattered throughout which are actinomycoses. The spleen is adherent to the stomach and pancreas. It is extremely difficult to remove. There is a rather large pocket just above the spleen containing a good deal of caseous material.

Liver Abscesses

The liver weighs 1950 grams. It is adherent to the diaphragm and on section throughout there are large abscess formations filled with caseous material measuring anywhere from 2 to 3 mm. to 3 or 4 cm. in diameter. There is a good deal of normal liver parenchyma left.

The gall-bladder is thickened and filled with bile. No stones. It is extremely adherent to its surrounding tissue.

Primary in bowel not seen

Gastro-intestinal tract: There is no evidence of any obstruction or tumors present. There is a slight kinking of some of the coils of the intestines but no evidence of any exudate. The gastro-intestinal tract was opened in its entire length and there was absolutely no evidence of any thickening of the mucosa or submucosa or any evidence of any actinomycotic lesions.

The pancreas is hard but normal in size and shape. No evidence of fat necrosis shown.

The adrenals are normal in size, shape and show no evidence of tumors, degeneration or hemorrhage.

Pyelitis

The right kidney weighs 200 grams and the left 175. No stones. The capsules strip with ease. There is some injection of the pelvis and a small amount of what appears to be pus in the left pelvis.

The bladder is normal in thickness. No cystitis.

Genital organs - negative.

The aorta is smooth and shows no atheromatous plaques.

Neck negative

There is adenopathy of the cervical lymph nodes, otherwise no general glandular enlargement.

The thyroid is normal in size and shape, and shows no adenomatous changes.

Head - not examined.

Microscopic

Heart - the muscle appears to be of good texture. No fragmentation or evidence of any

inflammatory process.

Lungs - Extension of the actinomycotic process in the pleura, there being several sulphur granules found with lymphocytic infiltration around them and a marked thickening of the pleura. Remainder of lung shows areas in which there are large endothelial cells in the alveoli. There is no marked congestion. Several of the smaller bronchioles are plugged with polymorphonuclear leucocytes but there is no infiltration outside of the bronchi. There are no areas of atelectasis in the sections cut.

Liver - shows large areas of necrosis with some lymphocytic infiltration scattered throughout. There are sulphur granules scattered throughout. In the sections taken, there are very few functioning liver cells although grossly the greater part of the liver was fairly normal in appearance.

Spleen- shows marked fibrotic reaction throughout. The malpighian corpuscles are small and contain very few cells. The pulp is extremely thinned out.

Kidneys - mild cloudy swelling. The glomeruli appear normal. The cells in the tubules are somewhat edematous. No marked congestion or degenerated process present.

Adrenals - appear normal. No tumor formation, degeneration or hemorrhage.

Gastro-intestinal tract - the sections of the mucosa appear normal. No evidence of any actinomycotic lesion in the sections taken.

Diagnosis

1. Actinomycosis with abscesses in spleen and liver and extension through diaphragm into both

- pleural cavities.
2. Congestion of lungs.
3. Adhesions, both bases of pleura.
4. Slight hemorrhagic effusion, right.
5. Multiple actinomycotic abscesses of liver.
6. Actinomycotic abscesses of spleen with fibrosis.
7. Cloudy swelling of kidneys.
8. Sinuses of abdomen.

III. MEETING

Date: February 15, 1934

Place: Recreation Room,
Nurses' Hall

Time: 12:15 - 1:17

Attendance: 120

Program: Mixed Tumor

Discussion: R. W. Koucky
L. G. Rigler
C. W. Waldron
W. T. Peyton
K. W. Stenstrom
C. W. Waldron

Theme: R.W.K.: Slides are shown illustrating the various phases of the mixed tumor problem from the pathological standpoint. (1) Knobby tumor showing difficulty in removing entire growth because of possibility of leaving behind projections. (2) Typical microscopic structure of mixed tumor with invasion of mandible. Condition not reported in literature. (3) Uncommon structure resembling thyroid tissue. (4) Pseudo-cartilaginous structure. (5) Section resembling carcinoma (squamous). This is the tumor which rolled out from the side of the cheek when attempts were made to implant radium. (6) Tumor which grew rapidly from parotid into neck structure and still retained alveolar arrangement and pseudo-cartilaginous make-up.

- (7) Metastasis of tumor to lymph nodes.
 (8) Fairly benign appearing tumor which has recurred six times. Structure remains same throughout all.

Impression: Apparently impossible to predict clinical course from microscopic structure, although more resembling carcinoma behave like carcinoma.

L.G.R.: Changes in mandible of patient reported resemble osteogenic sarcoma. Note new bone spicules and possible pathological fracture. Very unusual change, differing from extension of tumors into bone. Believe that primary lesion is in bone. It is possibly low grade soft tissue invasion or has origin in subperiosteal tissue. Slow growing tumors tend to produce new bone.

C.W.W.: I believe that this tumor arose either extraperiosteally or periosteally rather than from an ulcer. Dr. Rigler brought up the question of pathological fracture. I wonder if one is present. We frequently see changes like this in osteomyelitis without being able to demonstrate a fracture.

W.T.P.: (Slides) (1) Patient first seen here in 1920 for recurrent tumor. Tumor and 7th nerve excised. No recurrence in 14 years. (2) Female seen in 1926 for recurrent tumor. Tumor and lower branches of 7th nerve excised. Developed paralysis and vasomotor disturbance on side of face. No recurrence in 6 years. (3) Male (1927), tumor for 2 years, grew more rapidly in last 6 months; treated by excision and deep therapy. Branches of 7th nerve excised. Last seen about 6 months after operation; no recurrence. (4) Female (1931). Previous incision into tumor; thought to be superficial to 7th nerve, and on removing it did not find nerve. Complete paralysis developed; no recurrence in 2 years. Tumor looked so superficial; we tried to remove it.

Demonstration of patients: (1) Male with history of tumor in submental region of several months duration. Protruded into oral cavity. Biopsy shows mixed tumor. Was implanted with radium and given deep x-ray therapy. Not very much effect.

Mass now attached to mandible. Lesion began in glands of tongue or sublingual. Now involves both sides. Cannot be removed and does not respond to radiation. It is to be noted in some cases that most, not all, of the tumor shrinks following radiation. Dr. Stenstrom suggests that we may destroy the more active element and leave behind more mature tissue. (2) Man seen here in 1927. Tumor involved hard palate. Too extensive for surgery at that time. Did not change very much. One and one-half years ago, had complete nasal obstruction with sinuses filled with tumor. Palate broken down. Unroofed major portion of tumor and cleaned out antra and ethmoids, followed by radiation. Tumor now growing in from edges of defect. Patient more comfortable. (3) Woman seen in clinic this morning. Tumor grew from lower part of parotid. Simple to treat if it was not for 7th nerve. Malignant possibility worries patient. If nerve is not involved, tumor can usually be enucleated. This tumor had been aspirated. Completely removed with injury of inframandibular nerve. No facial involvement except when tired or nervous. Operation done one year ago.

The nerves sometimes run through the tumor. You have to cut across it or leave tumor behind. Often difficult to manipulate away from nerve without injury. Nerve involvement great drawback in treating these growths. Our preference is to remove them surgically without injury to nerve if possible. Do not agree with McFarland who says that large tumors are more favorable than small. If the tumor is allowed to grow, the nerve is caught in the growth. If you cannot remove masses without destruction of nerve, we incise capsule and remove mass. This is followed by radium around remaining capsule and immediately after healing x-ray therapy is given. Our results seem good but we never know when they may recur it is impossible to give end-results.

We have treated several tumors by irradiation. We have had some very complications following radiation. In one case, irritation developed when a

patient ate anything sweet or ran down-stairs. This would cause his eye to close and the mouth pull over.

K.W.S.: We have treated 20 cases by radiation. Most of our patients have been excision plus radiation. Because we fear recurrences, we radiate all after operation. The small remnants which are left may be very sensitive, although, as a general rule, the tumors are radio-resistant. It might be advisable in some cases to radiate first.

C.W.W.: These tumors represent an oral problem. We have a group that occur in the hard palate. On microscopic diagnosis it is difficult to separate benign from malignant. In some, the resemblance to chronic inflammation is marked. It may not be possible to demonstrate capsule but gross excision seems to be helpful. I saw a man about 8 or 9 years ago with low grade carcinoma of palate. Tumor removed and radium applied. Recurred. Removed again with same microscopic picture. At this time, the diagnosis changed to mixed tumor. I saw him about one month ago and he was apparently well.

Gertrude Gunn,
Record Librarian.

IV. ANNOUNCEMENT

JOHN R. MEADE, M.D.

announces the opening of his offices at
741 Lowry Medical Arts Building
Saint Paul, Minnesota

Practice limited to Diagnosis and General Medicine	Office Hours 10 to 1 and 2 to 5 and by appointment
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Residence Telephone Dale 0141	Office Telephone Garfield 1084
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V. CALENDAR

Friday, March 2

11 A.M. "Renal Insufficiency Due to Chronic Glomerulonephritis or Hypertension."
Hospital Clinico-Pathological Conference, Todd Lecture Hall.

12:30 P.M.

Dr. R. W. Bieter:
"Spinal Anesthesia"
116 Millard Hall.

4 P.M. "Subject to be announced."
Pediatric Seminar,
Departmental Office.

5 P.M. Radiological Seminar -
"Review of Literature"
Room 515, Hospital

Saturday, March 3

11:30 A.M. F. Jarvis,
"Oliver Wendell Holmes and
the Medical Profession."
O. P. Jones,
"Consideration of the American
Views regarding the Megaloblast-
Normoblast Problem."
Anatomy Seminar, Room 226,
Institute of Anatomy.

Monday, March 5

9 A.M. "Grand Rounds"- Obstetrics and
Gynecology.
Departmental Office.

9:30 A.M.
"Medical Grand Rounds"
Main Office, Hospital.

12:30 P.M.
M. H. Nathanson,
"Sudden Death in Heart Disease."
Pathology Seminar, Room 102,
Institute of Anatomy.

Monday, March 5 (Cont)

- 3 P.M. Arthur Steindler, Professor of Orthopedic Surgery, University of Iowa.
"Title to be announced."
Eustis Lecture Hall.
- 8 P.M. Special meeting of Hennepin County Medical Society for Medical Students and Internes.
20th Floor, Medical Arts Building. Music.- Lecture by Dr. Steindler.

Tuesday, March 6

- 9:15 A.M.
"Grand Rounds" - Surgery
M-4, Hospital
- 9 A.M. "Grand Rounds" - Pediatrics
Station 53, Hospital
- 12:30 P.M.
Autopsy Conference
Room 104, Institute of Anatomy
- 3 P.M. Mayo Foundation Lectures, 1934.
William C. MacCarty,
"Early Diagnosis of Cancer."
Todd Lecture Hall.
- 5 P.M. Radiological Conference
Minneapolis General Hospital

Thursday, March 8

- 11:45 A.M.
General Staff Meeting
Recreation Room, Nurses' Hall
- 4:30 P.M.
Carl W. Waldron,
"Tumors of the Jaw."
Surgical Seminar, Todd Lecture Hall.

Friday, March 9

- 9 A.M. "Grand Rounds" - Pediatrics
Station 53, Hospital

- Incomplete - Please hand in notices by Wednesday!