Staff Meeting Bulletin Hospitals of the » » » University of Minnesota

Actinomycosis

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STAFF MEETING BULLETIN
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INDEX

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William A. O'Brien, M.D.

I.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS
May 7 - 12, 1945

No. 70

Monday, May 7

9:00 - 10:00 Roentgenology-Medicine Conference; L. G. Rigler; C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 11:30 Allergy in Dermatology; Stephen Epstein; W-312

9:00 - 11:00 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; Interns Quarters, U. H.

12:30 - 1:30 Pathology Seminar; The Incidence of Auricular Fibrillation in Bacterial Endocarditis; Roger McDonald; 104 I.A.

4:00 - Public Health Seminar; Mental Hygiene; Dr. McKinley; 6th Floor Health Service, Women's Lounge

Tuesday, May 8

9:00 - 10:00 Roentgenology-Pediatrics Conference; L. G. Rigler, I. McQuarrie and Staff; Eustis Amphitheater, U. H.

11:00 - 12:00 Urology Conference; C. D. Creevy and Staff; Main 515 U. H.

12:30 - 1:30 Pathology Conference; Autopsies; Pathology Staff; 104 I. A.

12:30 - 1:30 Physiology-Pharmacology Seminar; Intermediate Fat Metabolism; George Burr; 214 M. H.

4:00 - 5:00 Physiological Pathology of Surgical Diseases; Physiology and Surgery Staffs; Todd Amphitheater, U. H.

4:00 - 5:30 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; Station 54, U. H.

4:00 - 5:30 Pediatrics Grand Rounds; I. McQuarrie and Staff; W-205 U. H.

4:30 - 5:30 Ophthalmology Ward Rounds; Erling Hansen and Staff; E-534, U. H.

5:00 - 6:00 Roentgen Diagnosis Conference; M. B. Hanson, 515 U. H.

Wednesday, May 9

9:00 - 11:00 Neuropsychiatry Seminar; J. C. McKinley and Staff; Station 60; Lounge, U. H.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Rheumatic Heart Disease with Mitral Stenosis; E. T. Bell, C. J. Watson, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

12:30 - 1:30 Pediatrics Seminar; Pathological Conference (Pediatric Cases); Dr. Schmidt; W-205 U. H.

12:30 - 1:30 Physiological Chemistry Literature Review; Staff; 116 M. H.

4:30 - 5:30 Neurophysiology Seminar; The Physiology of the Parietal Lobe; Helen Safford; 214 M. H.

Thursday, May 10

9:00 - 10:00 Medicine Case Presentation; C. J. Watson and Staff; Todd Amphitheater, U. H.

12:30 - 1:30 Physiological Chemistry; Intermediary Metabolism of Carbohydrates; M. F. Utter; 116 M. H.

4:00 - 5:00 Pediatric Journal Club; Review of Current Literature; Staff; W-205 U. H.

4:30 - 5:30 Ophthalmology Ward Rounds; Erling Hansen and Staff; E-534, U. H.

4:30 - 5:30 Roentgenology Seminar; Hernia of the Diaphragm; Solveigh Bergh; M-515 U. H.

Friday, May 11

9:00 - 10:00 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff; E-214 U. H.

10:30 - 12:30 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Otolaryngology Department, U. H.

11:45 - 1:15 University of Minnesota Hospitals General Staff Meeting; The Need for Physical Therapy in Pediatrics; Alice K. Brill; Powell Hall, Recreation Room.

1:00 - 2:30 Dermatology and Syphilology; Presentation of Selected Cases of the Week; Henry Michelson and Staff; W-206 U. H.

1:30 - 3:00 Roentgenology-Neurosurgery Conference; H. O. Peterson, W. T. Peyton and Staff; Todd Amphitheater, U. H.

8:15 - J. B. Johnston Lecture on Neurology; Comparative Neurology and our Present Knowledge of the Cerebellum; O. Larsell; Museum of Natural History Auditorium.

Saturday, May 12

8:00 - 9:00 Surgery Journal Club; O. H. Wangensteen and Staff; M-515 U. H.

9:00 - 10:00 Pediatrics Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U.H.

9:15 - 10:30 Surgery Roentgenology Conference; O. H. Wangensteen, L. G. Rigler and Staff; Todd Amphitheater, U. H.

9:00 - 10:00 Medicine Case Presentation; C. J. Watson and Staff; M-515 U. H.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff; E-221 U. H.

11:30 - 12:30 Anatomy Seminar; The Relations of the Ventral External Arcuate Fibers to the Nucleus Cuneatus and Nucleus Gracilis; A.T.Rasmussen;226 I.A.

II. ACTINOMYCOSIS

Fred T. Kolouch, Jr.,
Leonard Peltier

Introduction

Recently a case of extensive abdominal actinomycosis was treated over a period here during which time the progress of the disease was arrested, the patient rehabilitated to a normal life, and possibly cured. Since the last review of our experience with the treatment of actinomycosis at this hospital 11 years ago[13] reported that we had had no cures of abdominal actinomycosis, we felt that it was time to re-evaluate the entire problem of actinomycosis in the light of the more recent experience with the sulfonamide drugs and penicillin as adjuvants in therapy. We will correlate the extensive literature of the etiology, pathogenesis and treatment of this disease and present an analysis of the results of the treatment of actinomycosis here at the University of Minnesota Hospitals.

Clinically, actinomycosis is a chronic disease affecting man and animals characterized by the formation of granulomatous tumors usually associated with multiple fistulae to the overlying skin. Typical yellow sulfur-like granules may be obtained from these lesions which have been reported to occur in all parts of the body, but which in man are commonly situated in the cervico-facial, abdominal or thoracic regions.

The clinical picture of actinomycosis is produced by 3 entirely different microorganisms: Actinomyces (actinomycosis); a Staphylococcus (botryomycosis)[11] and Actinobacillus lignieresi (actinobacillosis)[9]. Botryomycosis and actinobacillosis occur infrequently in man, but are common in animals[4]. Actinomycosis occurs frequently in both man and animals. The differential diagnosis of the conditions affecting animals is important as it affects the theory of etiology and the rationals of treatment of actinomycosis in man. The studies of Magnusson[10], Griffith[5] and Shohan and Davis[16] indicate that only a fraction of all of the animals with a clinical diagnosis of actinomycosis suffer from the disease. It follows from this that a history of contact with so-called actinomycotic cattle is of little significance etiologically in human actinomycosis, unless the nature of the disease in the animal is conclusively determined. The value of therapeutic agents successfully used in the treatment of so-called actinomycotic animals is questionable when applied in the treatment of true actinomycosis in man.

History

In 1877, Bollinger[1] reported that while examining material from a diseased jaw bone of a cow, he had found branching mycelia which he considered to be the causative agent of the condition. Harz[6] named the organism Actinomyces or "ray fungus". At the same time Israel[7] described this organism from pathological specimens. Ponfick[12] first recognized the condition clinically in 1879. Israel[8] in 1885 reviewed 38 cases of actinomycosis and clearly defined the disease as a clinical entity. Investigation of the etiological agent was first carried out by Bostroem[2] and by Wolff and Israel[17].

Incidence and Distribution

The exact incidence of actinomycosis is not available. In the years 1930 to 1936, the annual number of reported deaths due to the disease in the United States was just over 60[3]. The number of reported deaths has been slowly rising during the last 25 years, due to more accurate diagnosis. The incidence in Minnesota is shown in Table I.

Actinomycosis has a world wide distribution. Cope[3] believed that the number of reported cases depended upon the clinical acumen of the diagnostician. Sanford[14] believed that the apparent increased incidence of actinomycosis in the north central states was due to more accurate diagnoses. In an analysis of 670 cases of actinomycosis, Sanford and Voelker[15] found that the median age incidence fell between 20 and 30 years; 80 per cent of the patients were males; environment or occupation appeared to be of no significance.

In 1936, Wangensteen[69] wrote that the

Table I

Actinomycosis Cases and Deaths
reported to
Minnesota Department of Health
(1922-1944, inclusive)

Year	Total Cases	Out-of-State Cases*	Deaths
1922	4		4
1923	5		4
1924	4		4
1925	2		2
1926	7		4
1927	5		3
1928	6		4
1929	8		6
1930	8		8
1931	3		3
1932	2		2
1933	9		10(a)
1934	1		2(b)
1935	11	3	8
1936	11	1	8
1937	7	1	3
1938	7	0	4
1939	4	2	4
1940	10	7	2
1941	25	14	6
1942	22	17	2
1943	30	20	3
1944	28	19	5

(a) 5 cases with first symptoms prior to 1933
(b) 1 case with first symptoms prior to 1934

*Included under "Total Cases" also.

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most significant problem relating to actinomycosis was the problem of its etiology. This problem has slowly begun to resolve itself through the ensuing years.

The actinomycetes are Gram positive micro-organisms characterized by the formation of a mycelium or network of branched filaments. Waksman[43] considered them to be an independent group of organisms closely related to the bacteria which had adopted a fungus-like form of growth. The actinomycetes are[21,42,31,38] closely related to the tubercle bacillus, the diphtheroid bacilli and the leprosy bacillus. The members of this group live in the soil, on grains and grasses and in water. Several species are pathogenic for plants (potato scab). Only a very small minority of these organisms are pathogenic for man and animals.

On the basis of their oxygen requirements, the pathogenic actinomycetes may be divided into an aerobic group and an anaerobic or micro-aerophilic group. Using this scheme, Waksman and Henrici[44] have classified them in the genus Actinomyces which contains the anaerobic or micro-aerophilic organisms and the genus nocardia which contains the aerobic organisms. Prior to this, the classification of these organisms has been chaotic.

Organisms of both genera will produce actinomycosis in man. The theory of Bostroem, that actinomycosis was produced by an aerobic organism and that of Wolff and Israel, that it was produced by an anaerobic organism have both been substantiated. Naeslund[36], Erikson[29] and Biggart[23] have reported pathogenic strains of aerobic actinomyces. Benbow Smith and Grimson[20], in reporting two cases of pulmonary actinomycosis due to aerobic organisms, estimate that 10% of thoracic actinomycosis is due to aerobic organisms. By far the largest share of actinomycosis is produced, however, by anaerobic or micro-aerophilic actinomyces.

It was Naeslund's impression that the anaerobic actinomyces were associated with actinomycosis related to the gastro-intestinal tract, while aerobic infections were most common in the chest or in cases with metastatic foci of infection. Erikson[30] has shown that human strains of anaerobic actinomyces form rough colonies, show greater polymorphism, and possess greater powers of fermentation than the bovine strains which are smooth colony forms.

The normal habitat of the anaerobic actinomyces is in the oral cavity. Aerobic actinomyces, widespread in nature, have rarely been isolated from the mouth[22,27]. Lord[32], Emmons[26,27,28] and, Slack[40], have isolated pathogenic actinomyces from the tonsils. Davis[25], however, has called attention to the fact that all tonsillar granules are not

actinomycotic. Actinomyces have been isolated from pyorrhea pus, dental scum, salivary calculi, and the contents of carious teeth by Slack[40], Lord[33], and Trevett[34], Rosebury et al[39], and Sullivan and Goldsworth[41]. Using these organisms, the pathologic picture of actinomycosis has been produced in laboratory animals by Slack[40], Rosebury et al[39], Lord[32,33] and Naeslund[36]. These organisms found in the normal mouth and representing the anaerobic group almost exclusively are considered an endogenous source of infection. The aerobic forms from the exogenous source of infection. The vast majority of actinomycotic infections are anaerobic and are considered endogenous.

Pathogenesis

The relationship of dental caries to actinomycosis was first noted by Lord[33], who stated that under certain conditions persons with carious teeth are liable to develop actinomycosis. Axhausen[18] and Sullivan and Goldsworth[41] have noted that the acute form of facial actinomycosis not infrequently follows exodontia. Israel reports a case (cited by Naeslund[36]), in which pulmonary actinomycosis followed aspiration of a tooth. Colebrook[24] and Robinson[37] have reported cases of actinomycosis of the extremity following trauma from the teeth of an adversary.

The close relationship between dental sepsis and cervicofacial actinomycosis is clearly seen in Table II which is an analysis of 38 cases of actinomycosis from the University of Minnesota Hospitals.

Table II

Type	Number	Dental Sepsis	Appendicitis	Right Lower Quad. Abscess	Diverticulitis
Cervicofacial	15	14			
Lingual	2	2			
Abdominal	14	6	8	3	2
Thoracic	7	2			

Minor trauma, inflammation associated with root abscesses or exodontia may afford the opportunity for the actinomyces to become active. Access to the gastro-intestinal tract is made easy by the constant swallowing of saliva. Here there is a close correlation between appendicitis and diverticulitis and the onset of actinomycosis. Actinomyces may reach the bronchial tree by aspiration of oral contents or from the air through the respiratory tract. That aspiration is the most common route of infection is shown by the high percentage of anaerobic organisms in pulmonary actinomycosis. Aerobic infections, when they occur, are most common in the lung so that infection via the respiratory tract cannot be ignored. The precipitating factor in producing any of these infections is as yet unknown.

Successful reproduction of the disease in animals is difficult. Simultaneous implantation of foreign bodies or the addition of other micro-organisms to produce mixed infections have failed to increase the positive results. The role of Actinobacillus actinomycetum-comitans is unknown[19]. Axhausen[18] stresses the role of pyogenic cocci in initiating the disease. Wright[45] observed that only a minority of cases he studied seemed to be pure infections. The disease, however, has been produced in animals with pure cultures. Naeslund[36] believed that mixed infections were of significance only in producing a more rapid spread of the infection and a greater inflammatory response. Henrici[35] and his group considered allergic sensitization to play a role in the development of progressive actinomycosis.

Pathology

The pathology of actinomycosis has been well described[3,46,47]. Histologically the lesions represent a chronic suppurative process. The organisms may appear as a radially arranged mass of branching mycelia surrounded by a collection of polymorphonuclear leucocytes, small round cells, and mononuclears on the periphery of which is a marked fibro-

blastic reaction. In stained section the actinomycotic granules show a central gram positive portion consisting of mycelial threads and a peripheral zone of thickened Gram negative mycelial clubs. This picture differentiates actinomycotic granules from those of botryomycosis and actinobacillosis. When granules are not demonstrable the infected tissue presents the appearance of a non-specific chronic inflammation.

The incubation period of actinomycosis is unknown but is usually assumed to be a matter of weeks. The infection begins in the subcutaneous, submucous, or subperitoneal connective tissue as a small area of brawny or "wooden" induration. Following the stage of induration there is a progressive erosion of the connective tissue. As the process progresses the overlying skin becomes tight and red. When fluctuation occurs, the skin breaks down with the formation of multiple sinuses which drain a seropurulent discharge usually containing sulfur granules. Extension occurs through the activity of the macrophages which carry some of the filaments out into the surrounding tissue. Spread through the blood stream is uncommon, but a lesion may rupture into a vessel and give rise to metastatic foci in distant organs. Actinomyces have been obtained in pure culture from the blood stream[50]. Extension through the lymphatics occurs only rarely and the entire lymphatic system enjoys a surprising degree of immunity. The infection tends to spread beneath, but not across epithelial or endothelial barriers. The peritoneum is quite resistant to attack; large masses of actinomycotic tissue may form behind the peritoneum without perforating into the abdominal cavity. The pleura does not have the same powers of resistance and is commonly involved in thoracic actinomycosis.

At the time of surgical operation the actinomycotic tissue may be readily identified by its characteristic yellow color, its fibrous consistency, the presence of multiple small sinuses, and by its vascularity.

Clinical Manifestations

The clinical manifestations of actinomycosis in man are commonly divided into 4 types: cervico-facial, abdominal, thoracic, and miscellaneous.

Table III

Author	No. of Cases	Cervico-facial	Abdominal	Thoracic	Miscellaneous
Sanford & Voelker[15]	670	60%	18%	14%	8%
Cope[3]	1330	57%	22%	15%	5%
University Hospitals	38	38%	36%	18%	8%

The classic picture of cervico-facial actinomycosis is that associated with a slow onset of swelling and induration with sinus formation although Axhausen[18] has pointed out the importance of recognizing the acute forms. The mortality of cervico-facial actinomycosis is due to the involvement of vital tissue by extension from the original site of infection. The prognosis depends upon the degree of localization at the time treatment is begun. We have classified our cases of cervico-facial actinomycosis into 3 types: 1) a circumscribed abscess or area of induration without sinuses; 2) lesions with sinuses but not invading vital structures; 3) lesions extending into the orbit, sinuses, spine or mediastinum. The prognosis with the first 2 types is good. Lesions of the third type usually terminate with an antinomycotic meningitis or thoracic involvement.

Thoracic actinomycosis may be primary or secondary. Secondary involvement may be due to extension from the cervical

region or from the abdomen. In these cases the primary lesions usually indicate the diagnosis. Primary thoracic actinomycosis presents much more of a diagnostic problem, being similar in many ways to other forms of chronic pulmonary suppuration. Naussac[49] has classified pulmonary actinomycosis into 3 anatomical divisions: 1) broncho-actinomycosis; 2) pneumo-actinomycosis; and 3) pleuro-pneume-actinomycosis. Fever, Cough and expectoration are common to all types. Hemoptysis is rare. Depending upon the type of infection the symptoms may be predominately those associated with a bronchitis, a pulmonary effusion or empyema, or a pulmonary consolidation. The diagnosis can be made by demonstrating sulfur granules in the sputum or pleural fluid. Periostitis of the ribs associated with non-specific changes in the lung may lead to the roentgenologic diagnosis[48]. Empyema necessitatis is frequently the presenting symptom in thoracic actinomycosis.

Abdominal actinomycosis shows a predilection for the right lower quadrant and frequently follows operations for acute appendicitis or drainage of abscesses in this region. Occasionally it is associated with diverticulitis of the colon (See Table II). Any draining sinus on the abdominal wall should be carefully examined to exclude actinomycosis. In order to make a more accurate estimate of the prognosis of abdominal cases, Morton[153] has divided them into 3 groups: 1) those resembling acute appendicitis with a residual sinus tract; 2) those presenting a mass in the right lower quadrant without signs of obstruction; 3) those associated with psoas spasm or a flexed thigh. He reports on 20 cases of abdominal actinomycosis classified according to this scheme: type 1, 5 cases, all recovered; type 2, 2 fatalities, 3 recoveries; type 3, 10 fatalities.

The ideal way of confirming a diagnosis of actinomycosis is by obtaining the organism in pure culture from the lesions. This, however, is difficult. The characteristic microscopic appearance of the stained granules may be considered to be specific. Material for examination may be obtained from sputum, pus, or from biopsy. All of the cases from the University Hospitals reported here were diagnosed by demonstration of typical sulfur granules.

Treatment of Actinomycosis

Introduction

The history of the treatment of actinomycosis simulates that of all infectious diseases. Groping through the available therapeutic armamentaria, following current fads, physicians have employed surgery, chemotherapy, vaccines, radiation therapy and latterly the current chemotherapeutic panaceas, the sulfonamides and antibiotics, in an effort to cure the disease. Success with the methods has been variable. Their number attests to the lack of uniform results with any one of them. A review of the literature reveals many ambitious claims for all of the remedies devised. In general the fact evolves that cervico-facial and other circumscribed actinomycotic lesions have been amenable to treatment with the majority of the methods offered. This is in contrast to the relative incurability of the abdominal disease and with the exception of isolated cases the almost inevitable mortality in the thoracic cases of actinomycosis.

Surgery

Incision into and drainage of collections of pus is one of the most ancient surgical remedies. No doubt, long before actinomycosis was described as an entity, surgeons were draining the abscesses associated with the disease. The exact history of the establishment of the surgical treatment of actinomycosis is difficult to trace. The search for other methods of treatment in the disease early in its history suggests that the results of the incision and drainage of actinomycotic lesions were not attended by favorable results. The proper effective surgical treatment of actinomycosis gradually evolved from the experience gathered in the treatment of the disease. As far as we can determine, the principles were first clearly stated in 1905 by Waring[70], a British surgeon. This man cured 4 of 7 cases of abdominal

actinomycosis originating in the right lower quadrant by means of surgery and adjuvant potassium iodide therapy. He wrote, "The limits of surgery appear to be incision, evacuation, scraping, draining of abscesses immediately they can be diagnosed, and afterwards repeated irrigation with an antiseptic solution, with iodine, or better, with a solution of peroxide of hydrogen. The latter chemical agent appears to be the most effective agent in arresting the local growth of the parasite." This paper established the proper surgical technic for the care of patients with actinomycosis. The factor of meticulous local wound hygiene was emphasized by Smith[67] and we feel it is exceedingly important. Colebrook[124] in 1921 amplified Waring's principles in his paper on vaccine therapy and he prophesied the possibility of success in extensive thoracic and abdominal actinomycosis with radial surgical management. Brickner[53] of New York reported in 1925 that he cured 5 patients suffering with severe low abdominal and pelvic actinomycosis by means of radical incision, excision and currettage followed by oral potassium iodide, and the local application of Lugol's solution. One of Brickner's patients, case #4, bears a striking resemblance to our surviving abdominal case. In 1925, this patient treated similarly to ours, was cured without recourse to adjuvant sulfadiazine and penicillin. It illuminates the fact pointed out by Wangensteen[68] in 1932 and reemphasized by him in 1936 that radical surgery per se is the sine qua none of the treatment of extensive actinomycosis. Wangensteen[69] rationalizing the surgical treatment of actinomycosis, concluded: "The most direct agency in the treatment of actinomycosis is surgery. The rationale of surgical treatment lies in the fact that the infection is essentially an anaerobic one. Removal of the dead tissue, which is poorly oxygenated and in consequence an excellent culture median, will usually terminate the disease". He relied mainly on the removal of dead tissue by repeated currettment rather than by radical excision.

A list of the larger series of cases of actinomycosis gleaned from the literature which were treated surgically is tabulated (see Table IV). Adjuvant potassium iodide treatment was used by most of the surgeons reporting their results in actinomycosis. A list of the authors with a summary of the types of cases, types of treatment, and their results is made. This series and the subsequent reviews of the other therapeutic measures include the majority of papers dealing with the treatment of actinomycosis.

Potassium Iodide

Potassium iodide was introduced empirically by Thomasson[77] in 1885 for the treatment of lingual actinomycosis of cattle. Nocard[76] championed the drug and stimulated its introduction in the treatment of human actinomycosis by Iterson and Netter[75] in the same year. In spite of the optimistic recommendations and the success attending the use of potassium iodide in other granulomatous disease, (i.e., luetic gummata), its therapeutic ineffectualness in both bovine and human actinomycosis was soon obvious. In an attempt to rationalize the use of the drug in actinomycosis, Harbitz and B-Grondahl[73] and later Henrici[74] found in '*in vitro*' studies luxuriant growth of actinomycetes in media containing 2% potassium iodide. Clinical experience fortified by these studies established the inutility of potassium iodide therapy in actinomycosis. An interesting sidelight on the history of potassium iodide therapy in actinomycosis related to Thomasson's success with what he thought was lingual actinomycosis. As first described by Ligniers and Spitz[9] and shown by Griffith[5] and others[16], granulomatous lesions of the bovine tongue are usually due to Actinobacillosis which is specifically amenable to potassium iodide therapy. The universal application of potassium iodide to human actinomycosis is an example of a world wide medical hebetude resulting from Thomasson's ignorance of the bacteriology of the disease he treated. At the present time, enlightened clinicians share the opinions of Colebrook[124], Jungling[100], and Wangensteen[69] that reliance upon potassium iodide for the treatment of actinomycosis is not warranted and at the present time no indications for its use exist.

Table IV

Results of Surgical Treatment of Actinomycosis

Author	Date	Therapy	Cervico-facial					Thoracic					Abdominal				
			#	C	I	D	N	#	C	I	D	N	#	C	I	D	N
Gangolphe, M. & Duplant, Fr.[58]	1897	S, 1											1		1		
Bell, J.[51]	1905	S,I,AgN	3	3				1			1		4	1		3	
Choyce, C.C.[55]	1910	S,I											1		1		
McKenty, F.E.[60]	1913	S,I	19	15		0	4	2			2		11	2		9	
Cope, V.Z.[56]	1915	S,I	6	4	2			3			3		2		1	1	
Ramsted, N.O.[64]	1916	S,I	4	3		0	1	1				1	1			1	
Ochsner, A.J.	1917	S,I											1		1		
McCallem, A.I.[62]	1919	S,I	4	1	1	2?							2	1			1
Matz, F.[61]	1922	S											7	4		3	
Brockman, R.[54]	1922	S,I,V.											4			4	
Brickner, W.[53]	1925	-----											5	5			
Smith, F.L.[67]	1930	S											7		5	2	
Wangensteen, Owen	1932	S,I						1	1								
Pope, E.L.[63]	1935	S,X*	10	10				1			1		2			2	
Ellis, R.[57]	1935	S						2		1	1		3			3	
Bisgard, D.[52]	1938	S,I,X						2	2								
Schmitt, G.R. & Olson, A.M.[66]	1941	?						2			1	1					
Randall, O.S.[65]	1942	S	16	12		1	3										
Ziskin, et al[71]	----	S,I,X	17	11	4	2		4		1	3		5	1		4	
U. of Minn., Surgical Dept.	1945	S,I,X,Sn	17	10	3	4		7			7		14	1		13	
Totals			96	69	10	9	8	26	3	2	19	2	70	15	9	45	1

*X-ray Therapy was added to surgical treatment in 3 cases of Pope's series.

S - Surgery
I - Potassium Iodide
X - X-ray
Sn - Sulfonamide
- Number of Cases
C - Number of Cases Cured
I - Number of Cases Improved
D - Number of Deaths
N - No Follow-up

Copper Sulfate

Copper sulfate was introduced by Bevan[72] in 1905 for the treatment of actinomycosis as an adjuvant to surgical drainage. He was influenced by the experience of agriculturists who had found this chemical an effective fungicide for grains contaminated with molds. The drug was administered orally and the sinus tracts were irrigated with a 1 per cent solution. Several authors used copper sulfate in their shot gund approach to the treatment of actinomycosis. Von Baracz[78] treated successfully 30 out of 36 cases of actinomycosis by the parenchymatous injection of copper sulfate solution. His cured patients had cervico-facial disease while 2 cases with abdominal disease died and 4 cases were still under treatment at the time of his report.

Table IV

Results of Surgical Treatment of Actinomycosis

Types of Cases and Results

Author	Date	Therapy	Cervico-facial #	C	I	D	N	Thoracic #	C	I	D	N	Abdominal #	C	I	D	N
Gangolphe, M. & Duplant, Fr.[58]	1897	S, 1											1		1		
Bell, J.[51]	1905	S,I,AgN	3	3				1			1		4	1		3	
Choyce, C.C.[55]	1910	S,I											1		1		
McKenty, F.E.[60]	1913	S,I	19	15		0	4	2			2		11	2		9	
Cope, V.Z.[56]	1915	S,I	6	4	2			3			3		2		1	1	
Ramsted, N.O.[64]	1916	S,I	4	3		0	1	1				1	1			1	
Ochsner, A.J.	1917	S,I											1		1		
McCallem, A.I.[62]	1919	S,I	4	1	1	2?							2	1			1
Matz, F.[61]	1922	S											7	4		3	
Brockman, R.[54]	1922	S,I,V.											4			4	
Brickner, W.[53]	1925	-----											5	5			
Smith, F.L.[67]	1930	S											7		5	2	
Wangensteen, Owen	1932	S,I						1	1								
Pope, E.L.[63]	1935	S,X*	10	10				1			1		2			2	
Ellis, R.[57]	1935	S						2		1	1		3			3	
Bisgard, D.[52]	1938	S,I,X						2	2								
Schmitt, G.R. & Olson, A.M.[66]	1941	?						2			1	1					
Randall, O.S.[65]	1942	S	16	12		1	3										
Ziskin, et al[71]	----	S,I,X	17	11	4	2		4		1	3		5	1		4	
U. of Minn., Surgical Dept.	1945	S,I,X,Sn	17	10	3	4		7			7		14	1		13	
Totals			96	69	10	9	8	26	3	2	19	2	70	15	9	45	1

*X-ray Therapy was added to surgical treatment in 3 cases of Pope's series.

S - Surgery
I - Potassium Iodide
X - X-ray
Sn - Sulfonamide
- Number of Cases
C - Number of Cases Cured
I - Number of Cases Improved
D - Number of Deaths
N - No Follow-up

Copper Sulfate

Copper sulfate was introduced by Bevan[72] in 1905 for the treatment of actinomycosis as an adjuvant to surgical drainage. He was influenced by the experience of agriculturists who had found this chemical an effective fungicide for grains contaminated with molds. The drug was administered orally and the sinus tracts were irrigated with a 1 per cent solution. Several authors used copper sulfate in their shot gund approach to the treatment of actinomycosis. Von Baracz[78] treated successfully 30 out of 36 cases of actinomycosis by the parenchymatous injection of copper sulfate solution. His cured patients had cervico-facial disease while 2 cases with abdominal disease died and 4 cases were still under treatment at the time of his report.

Other chemotherapeutic methods employing the arsenicals, methylene blue and iodine-iontophresis are scattered through the literature but are not of sufficient importance to warrant detailed discussion.

X-ray - Radium

The radiation therapy of actinomycosis was introduced by Harsha[93] in 1904. He reported a case of cervico-facial actinomycosis at the Chicago Surgical Society which was a surgical failure but responded favorably and was cured by means of combined potassium iodide and x-ray therapy. By 1905 Bevan[80] had treated 6 patients with radiation. In 1914 Heyerdahl[96] of Oslo reported a cervico-facial case cured by radium emanations and by 1919 had reported success in 6 cases[97]. An incomplete review of the literature on radiation therapy of actinomycosis is summarized in a table similar to that listing the surgical results. The number of authors reporting attests to the popularity of this method of treatment.

Investigators have attempted to rationalize the effectiveness of radiation therapy in the eradication of actinomycosis. Employed initially with potassium iodide, it was thought that the X-rays caused the release of nascent iodine which killed the actinomyces in the lesions. Jungling[100] and others have shown that radiation is effective in actinomycosis in the absence of adjuvant potassium iodide. Kleesattel[103] subjected pure cultures of pathogenic actinomyces to irradiation. He found that they tolerated up to 10 erythema skin doses, a quantity infinitely greater than the amount employed in clinical therapy. He concluded that the effects of radiation therapy in actinomycosis were non-specific. Smith[117] theorized that either the actinomycete in vivo was more susceptible to radiation than in vitro or the effectiveness of radiation therapy resulted from the destruction of synergistic organisms in the actinomycotic lesions which enabled the natural defenses of the body to cope with the actinomyces present. At the present time, clinical results prove the effectiveness of radiation therapy in actinomycosis but the mode of action is unknown.

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Table V

Results with Radiation Therapy of Actinomycosis

Author	Date	Therapy	Cervico-facial					Thoracic					Abdominal				
			#	C	I	D	N	#	C	I	D	N	#	C	I	D	N
Harsha, W.[93]	1904	X,I	1	1													
Bevan, A.O.[80]	1905	X,S,I	1	1				1		1			4	0	3	1	
Levy, B.R.[105]	1913	X	3	3													
Sardemann,E.[114]	1914	X,S	4	4													
Nordentoft,J.[111]	1914	X	2	1		1											
Schmidt[116]	1915	X,1	1	1													
Heyerdahl[96, 97, 98]	1916																
	1919																
	1927	R	21	21													
Melchior,E.[109]	1916	X,1	3	3													
Dittrich,R.[85]	1920	X,S,I	21	19	2	0											
Steinkamm,J.[119]	1921	X	3	3													
Jungling,O.[100]	1920	X,S,I	12	11		1											
Prikul,A.[112]	1921	X,S	1	1													
Brofelt,S.[81]	1922	X,S	87	67			20	15		15			49	22		27	
Brogden,J.C.[82]	1922	X,S,I,C											14	2	3	6	3
Beck,[79]	1922	X,Ne,FP											2	2			
Sattler,E.[115]	1923	X,S,M											3	2		1	
Wakeley,C.P.[122]	1923	X,S,I	4	3		1		3		3			2	2			

Table V (Cont.)

Author	Date	Therapy	Cervico-facial #	C	I	D	N	Thoracic #	C	I	D	N	Abdominal #	C	I	D	N
New, G.B. & Figi, F.A.[110]	1923	R,S,I	85	60	18	7											
Kaplan, I.I.[101]	1924	R,S											1	1			
Brunzel[83]	1925	X	1	1													
Eiken, T.[86]	1926	X,S,I	3	2	1								1	1			
Grunthal, J.[91]	1927	X											1	1			
Tempsky, V.[121]	1927	X,I	36	32			4	4	1		3		3		1	2	
Desjardins, A[84]	1928	X,S,I						7			6	1	23	1	5	17	
Heeren, J.[94]	1929	X	12	8	2	2		3			2	1	1			1	
Good, L.P.[89]	1930	X,S,I						13		1	6	6					
Good, L.P.[90]	1931	X,I											55	8	6	29	12
Stocker, Hans[120]	1931	X,I	15	9	0	3	3	5		1	2	2	2	1			1
Engelstadt, RB[87]	1932	R	28	25	1	1	1										
[88]	1933	R											1	1			
Harrison, R.[92]	1934	X	22	22				4			4		4			4	
Smith, E.[117]	1934	X,S	7	5	2												
Masson, D.[108]	1936	X,I											2	2			
Martin-Crespo[107]	1936	X	3	3													
Keijser, S.[102]	1936	X,I	69	64	3	2		3			3		27	9		18	
Weysser, C.[123]	1937	X											1			1	
Kuhlman, B.[104]	1937	X,I						4			4		1			1	
Renander, A.[113]	1937	X	31	26		5		3			3		13	5		8	
McWhirter, R.[106]	1938	X	8	7	1			2	1	1			4	3	1		
Starlinger, F.[118]	1938	X,I,L											1	1			
Holdre, J. & Koskvee, L.[99]	1941	X,I	120	87		10	23	4	1	1	2		17	9	2	6	
Henkel, K.[95]	1941	X,I											2	2			
Totals			604	490	30	33	51	72	3	5	54	10	235	75	21	123	16

X - X-ray
R - Radium
I - Potassium Iodide
S - Surgery
C - Copper SO_4
Ne - Neoarspheramine
FP - Foreign Protein
L - Lymph Extract
- Number of Cases
I - Number of Cases Improved
C - Number of Cases Cured
D - Number of Deaths
N - No follow-up

Extreme variations in therapeutic radiation technic have been described with similar results attending most of them. The majority of radiologists used deep, filtered x-rays in doses varying between 3 and 4 thousand roentgens divided in different manners. Harrison[92] felt that the best results were obtained by using protracted fractional daily doses of 100 roentgens until 4 thousand roentgens were administered. At the other extreme, Heeren[94] gave 90 to 120 per cent erythema skin doses at monthly intervals. Usually potassium iodide and auxiliary surgical measures were employed. The superfluity of potassium iodide is known by some but

definitely not accepted by all of the roentgen therapists reviewed. Some authors insisted upon adequate drainage and currettage of the lesions but the majority shared Smith's[117] attitude toward surgery who wrote: "Radical surgery including curretting is probably inadvisable. A study of the cases reported by the authors quoted herein shows that, all other things being equal, those cases which had a minimum of surgical interference recovered more rapidly than did the remainder. Surgical procedures should probably not be resorted to except to provide drainage and to assist in definitely establishing a diagnosis. They should then be limited to a small incision preferably a stab wound."

The efficacy of radiation therapy in circumscribed superficial actinomycosis is established without a doubt. On the other hand the results indicate its ineffectiveness in widespread disease.

Vaccines

Specific vaccine therapy of actinomycosis was introduced by Wynn[128] in 1908. The method gained a few adherents in Europe but has never gained popularity in the UnitadStates. Colebrook[124] of England and the Hungarian dermatologist Neuber[126] are the most energetic proponents of vaccine therapy. The former emphasized the value of concomitant surgery while the latter relies solely upon immunologic methods. A summary of the results with vaccine therapy by several authors is tabulated below.

Table VI

Results with Vaccine Therapy of Actinomycosis

Author	Date	Therapy	Cervico-facial					Thoracic					Abdominal				
			#	C	I	D	N	#	C	I	D	N	#	C	I	D	N
Wynn, Wm.[128]	1908	V,S						1	1								
Colebrook,L.[124]	1911	V,S	10	9		1		8			7	;	6	;		5	
Dean, C.W.[125]	1917	V,S	1	1													
Schuchardt,K.[127]	1939	V,S.	14	12		2											
Neuber,E.[126]	1940	V.	2	2				1	1								
Totals			27	24		3		10	2		7	1	6	1		5	

V - Vaccine
S - Surgery
- Number of cases
C - Number of cases cured
I - Number of cases improved
D - Number of deaths
N - No follow-ups

The influence of surgical drainage and currettage upon the results reported and attributed to the vaccines is evident and emphasized by Colebrook[124] who wrote: "The treatment of actinomycosis by vaccines facilitates recovery when efficient surgical drainage of the affected tissues is secured and maintained: when, however, drainage is unsatisfactory the use of appropriate vaccines will not usually suffice to stay the progress of the infection." Colebrook's contribution to the treatment of actinomycosis was really surgical since throughout his report he insisted that in the absence of complete surgical drainage and currettage of the actinomycotic lesions the disease could not be cured. On the other hand Neuber[126] who claims almost 100% success with the vaccine treatment of actinomycosis writes that surgical measures, X-ray therapy and iodides, are superfluous and unnecessary in curing the disease. He insists that if the immunologic status of the patient suffering with actinomycosis is carefully evaluated regarding the presence of allergy or anergy and if fresh polyvalent or autovaccines are properly administered in only the allergic patient, cure of the disease is

inevitable. The only failures he admits are in anergic patients and in these success may follow the administration of convalescent serum or blood transfusions. Although no statistical data is presented in his recent general review of the subject, the cases illustrated are quite impressive.

Thymol

Thymol was found to be effective in the treatment of a local occupational fungus dermatitis among fruit orchard workers by Myers and Theines[134] in 1925. They cured a patient with cervico-facial actinomycosis by giving him 1½ grams of thymol twice weekly for 2 months. Myers[135] observed that actinomyces were killed in vitro by 1 minute's exposure to a 1 to 1000 concentration of thymol in the culture mediu. Employing adequate surgical drainage with the oral administration and local application of thymol in 6 cases of cervico-facial actinomycosis Myers[136] reported cures in 5 of them. A summary of the literature on the results of thymol therapy in the treatment of actinomycosis is presented in table 7.

Table VII

Results with Thymol Therapy of Actinomycosis

Author	Date	Therapy	Cervico-Facial				Thoracic				Abdominal			
			#	C	I	D N	#	C	I	D N	#	C	I	D N
Myers, H.B.[134] & Thienes, C.H.	1925	T	1	1										
Myers, H.B.[136]	1937	T,S	6	5		1								
Bancroft, F.W., & Brown, M.S.[139]	1938	T,S									1		1	
Fang, H.C.[132]	1938	T,C	1	1										
Joyce, T.M.[133]	1938	T	5	3		2								
Etter, L.E. & Schumacher, F.L.[131]	1939	T					1	1						
Clemmons, H.H.[130]	1940	T	1	1										
Totals			14	11		3	1	1			1		1	

T - Thymol
S - Surgery
- Number of cases
C - Number of cases cured
I - Number of cases improved
D - Number of deaths
N - No follow-up

Fang[132] emphasized the importance of surgical curettage of the actinomycotic lesions when thymol was to be used. Adequate exposure of the depths of the lesions to the thymol applied locally was important.

In the cases summarized it is difficult to evaluate the relative importance of the thymol and the surgery employed. The beneficial effects of the surgery cannot be denied. It is interesting, however, that the patient reported by Clemmons[130] failed to respond to sulfanilamide and X-ray therapy and then healed favorably under the influence of thymol administration.

Etter and Schumacher's[131] cured thoracic case is quite amazing. The patient had evidence of right upper lobe lung abscesses and coughed up considerable sputum containing sulfur granules. The process healed and X-ray evidence of the disease disappeared after the administration of two grams of thymol daily for 17 days.

Sulfonamides

Sulfonamide therapy was applied to a patient suffering with abdominal actinomycosis which responded badly to radia-

tion and potassium iodide by Poulton[156] in 1937. His report was part of a general discussion on sulfonamide therapy by the Royal Society of Medicine. He stated that his patient gained weight and left the hospital afebrile but he did not mention whether she was cured. The apparent cure of an abdominal case of actinomycosis by means of sulfanilamide in a 23 year old man who developed the disease following the removal of a gangrenous appendix was reported in the Lancet in 1938 by Walker[158]. This paper stimulated interest in the sulfonamides in the treatment of actinomycosis. The results obtained with sulfanilamide, sulfapyridine, and sulfadiazene in the treatment of cervico-facial, thoracic, and abdominal actinomycosis have been gratifying as is revealed in the summary of all of the cases reported in the available literature listed in Table 8.

Table VIII

Results with Sulfonamide Therapy of Actinomycosis

Author	Date	Therapy	Cervico-Facial				Thoracic				Abdominal			
			#	C	I	D	#	C	I	D	#	C	I	D
Poulton,E.P.[156]	1937	Sn									1		1	
Walker, O.[158]	1938	Sn									1	1		
Miller,E.M.& Fell,E.H.[150]	1939	Sn									1	1		
Sudler, M.T. & Johnson,C.B.[157]	1939	Sn	2	2										
Hall, W.[143]	1939													
McCharles, M.& Kipper,JW[148]	1939	Sn,S	3	3										
Moene, I.[152]	1940	Sp.S	1	1										
Ogilvie,W.H.[154]	1940	Sp,S									1	1		
Morton,HS[153]	1940	Sn	1			1	1			1				
Christopher,F.& Karabin,J.E.[138]	1940	Sn,S									1		1	
Dorling,G.C.& Eckhoff,NL[140]	1940	Sn,S,X									5	4		1
Eckhoff,N.L.[142]	1941	Sn,S									2	2		
Woodman,J.[160]	1941	St,S.I									1			1
Dobson,L,Holman, E.& Cutting,W[145]	1941	Sn,S	1	1			1	1			1	1		
Wilkinson,E.[159]	1941	Sn,S					1	1						
Mitchell,H.S.[151]	1942	Sp.					1	1						
Lyons,C.,Owen,CR Ayers,W.B.[147]	1943													
Atwood,H.S.[137]	1942	Sn					1	1						
Ladd,W.E.,& Bill,A.H.[146]	1943	Sd					1	1						
Hollenbeck,W.F.& Turnoff,D.[144]	1943	Sd	1	1										
McCloy,A.[149]	1943	Sp.	1	1 (tongue)										
Pillsbury,N.R.& Wassersug,J.[155]	1944	Sd.I					1	1						
Benbow,E.P., Smith,D.T. & Grunson,K.S.[20]	1944						2	1	1					
Totals			10	9		1	9	7	1	0 1	14	10	2	2 0

Sn - Sulfanilamide
St - Sulfathiazole
Sd - Sulfadiazene
S - Surgery

I - Potassium Iodide
- Number of cases
C - Number of cases cured

I - Number cases Improved
D - Number of deaths
N - No follow-up

Although the sulfonamides were employed empirically in the treatment of actinomycosis by the pioneers of 1938, their rationale has been experimentally established in the laboratory by Cutting and Gebhardt[139] who found the growth of two strains of Actinomyces hominis was inhibited to some extent by the addition to the culture media of 10 mgm.% of sulfanilamide and almost completely by the addition of 50 mgm.%. Sulfathiazole and sulfadiazene were much more effective than sulfanilamide in similar concentrations. Experimental actinomycosis could be prevented or cured in rats by the oral administration of sulfanilamide.[141]

Ogilvie[154], and Holman, Dobson, and Cutting[145] opined that the sulfonamides are beneficial in actinomycosis because of their effect on the concomitant secondary invaders which are inhibited by the drug and allow the natural defenses of the body an opportunity to dispose of the fungus. In all probability the effectiveness of the drugs is due to inhibition of both the specific and the secondary infectious organisms.

Although there have been no definite opinions expressed regarding the simultaneous use of surgical drainage and curettage with the sulfonamides, it is interesting to note that in the majority of cases reported cured a combination of surgical and drug therapy have been utilized. Although the number of cases reported is small and probably the poor results obtained with the drugs have not reached the literature, no doubt can exist that the sulfonamides are effective adjuvants to the treatment of extensive actinomycosis.

Penicillin

Penicillin was employed in the treatment of 2 cases of actinomycosis by Florey and Florey[161] in 1943. They refused to draw any conclusions as to the efficacy of the drug because of the limited amount which was used. Herrell[162] early in 1944 reported 3 cases of cervico-facial actinomycosis treated with penicillin with 2 cures and 1 failure. A case of abdominal actinomycosis complicated by carcinoma of the colon treated at this time failed to respond to penicillin. Later in the year Herrell[163] and his associates reported that they had treated 12 cases of actinomycosis with penicillin but did not report their success because of the short follow-up period. Lyons[164] reported 4 cases of actinomycosis treated with penicillin but did not draw any conclusions for the same reason. In 1945, Walker and Hamilton[165] reported 6 cases of actinomycosis treated successfully with penicillin and surgical drainage. Five cases of cervico-facial actinomycosis, all associated with either dental sepsis or extraction, were given penicillin over long periods, the average total dosage being 5,892,000 units. This, combined with excision of scar and underlying granulation tissue in two instances, resulted in cure in all patients. A long standing case of thoracic actinomycosis with a metastatic focus below the right knee was reported arrested with no signs of recurrence during seven months of follow-up. The small amount of experience reported with penicillin in the treatment of actinomycosis suggests its efficacy. The rationale of the success with the drug has been established by Waksman and Woodruff[166] who found actinomyces susceptible to penicillin in vitro.

Discussion of Treatment

The results obtained in the treatment of cervico-facial, thoracic, and abdominal actinomycosis by means of surgery, radiation, vaccines, sulfonamides, and penicillin are summarized in Table IX. This, however, is an obscure evaluation of the methods of treatment since as mentioned before surgical drainage and curettage has been employed concurrently with most of the methods described. Minimal surgical measures were employed by the radiologists although in most cases abscesses

Table IX

Summary of Therapeutic Results in Actinomycosis*

Type of Treatment	# Authors	# Cases	# Cured	# Dead	# Imp.	# NFu
Cervico-facial Actinomycosis						
Surgery	9	96	69-72%	9- 9%	10-11%	8- 8%
Radiation	28	604	490-81%	33- 5%	30- 5%	51- 9%
Vaccine	4	27	24-89%	3-11%	------	------
Thymol	7	14	11-78%	------	------	3-22%
Sulfonamides			9-90%	1-10%	------	------
Radiation	7	10				
Penicillin	2	8	7-87½%	1-12%	------	------
Thoracic Actinomycosis						
Surgery	11	26	3-11%	19-71%	2- 9%	2- 9%
Radiation	14	72	3- 4%	54-78%	5- 6%	10-12%
Vaccine	3	10	2-20%	7-70%	------	1-10%
Thymol	1	1	1-100%	------	------	------
Sulfonamides	8	9	7-78%	1-11%	1-11%	------
Penicillin	1	1	1-100%	0%	0%	0%
Abdominal Actinomycosis						
Surgery	16	70	15-21%	45-66%	9-12%	1- 1%
Radiation	26	235	75-31%	123-52%	21- 9%	16- 8%
Vaccine	1	6	1-16 2/3%	5-83 1/3%	------	------
Thymol	1	1	------	------	1-100%	------
Sulfonamide	9	14	10-71%	2-14.5%	2-14½%	------
Penicillin	--	---	------	------	------	------

*The types of treatment are listed as emphasized by authors using them. However, potassium iodide was used in connection with surgery and radiation in many cases. Surgical drainage was used to some extent with radiation therapy and extensively in the patients treated with vaccines, thymol, sulfonamide, and penicillin.

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were drained. Potassium iodide was used by the majority of authors. In spite of the difficulties, however, certain general conclusions can be drawn from this summary.

The influence of sulfonamide administration on the surgical treatment of actinomycosis is evident in the elevation of the cure rate in cervico-facial actinomycosis from 70 to 90 per cent, thoracic actinomycosis from 11 to 78 per cent, and abdominal actinomycosis from 21 to 71 per cent. The influence of the sulfonamides on results with radiation therapy has not been studied to any extent.

The results reported with the employment of penicillin as an adjunct to surgical treatment of actinomycosis suggest it is as valuable as the sulfonamides. More experience with this drug is needed.

Sulfonamides and penicillin are both valuable adjuncts to the surgical treatment of actinomycosis. Their benefit is most pronounced in the treatment of extensive actinomycosis. However, reliance upon these drugs in the absence of adequate surgical drainage and curettage would be dangerous and not justified. They have not replaced but have enhanced the effectiveness of surgery in the treatment of actinomycosis.

Hospital Experience

An analysis of the experience here at the University of Minnesota Hospitals with actinomycosis has been made. We were able to find 38 cases of actinomycosis in which actinomyces were demonstrated either in smears of pus or biopsies of the lesions. There were 4 clinical types of cases; Cervico-facial, 15; Lingual, 2; Thoracic, 7; and Abdominal, 14. The treatment in these patients was predominately surgical, reliance being placed chiefly on reported currettage. Adjuvant measures, i.e., potassium iodide, copper sulfate packs, deep x-ray therapy, and recently the sulfonamides and penicillin, have been used with surgery in some of the patients. A summary of the therapeutic results in these cases is presented in Table X.

Table X

Results of Treatment of Actinomycosis at University of Minnesota Hospitals

Type	# Cases	# Cured	# Improved	# Dead
Cervico-facial	15	9-60%	2-13%	4-27%
Lingual	2	2-100%	------	------
Abdominal	14	1*- 7%	1- 7%	12-80%
Thoracic	7	0	1-14%	6-86%

*Patient has disease arrested--to be reported in detail.

The patients in this series who died of actinomycosis all had very extensive infections. Three patients, Nos. 7, (1933), 13 (1941), and 8 (1935), with extensive cervico-facial actinomycosis died from actinomycotic meningitis. Patient No. 7 died a few days after admission to the hospitals. The other two died during the course of their surgical treatment. Patient #1 (1925) died as the result of mediastinal extension of actinomycosis. He was treated with surgical drainage, potassium iodide and copper sulphate packs. The patients who died of thoracic and abdominal actinomycosis all had extensive infection on admission which progressed in spite of surgical and supportive therapy. Investigation of the cases treated here since the advent of the sulfonamides and penicillin reveals 2 patients with thoracic actinomycosis, No. 23 (1944) and No. 24 (1944), and 4 patients with abdominal actinomycosis Nos. 35 (1943), 36 (1944), 38 (1944, and 37 (1944), in which the drugs were used in addition to surgical treatment. Patient No. 23 had a clinical arrest with cessation of drainage from a thoracic sinus with sulfadiazine and sulfamerazene treatment only for 5 weeks. No recent follow-up has been made. Patient No. 24 had extensive thoracic actinomycosis treated by means of radical surgery coupled with sulfadiazine, penicillin, and a high caloric diet, and died of a cerebro-vascular accident while under treatment. At time of death the actinomycosis was under fair control. Patients Nos. 35 and 36 developed right lower quadrant actinomycosis following appendectomies. In spite of multiple surgical procedures and sulfathiazole and supportive care both expired. Patient No. 37 with extensive pelvic actinomycosis and fecal fistulae was improved by means of a colostomy, energetic supportive transfusions, forced feeding, and administration of sulfadiazine and penicillin. One patient, No. 38, with abdominal actinomycosis treated by means of radical surgery, energetic supportive care, adjuvant sulfadiazine and penicillin is at present free of the disease.

Case Report

Patient No. 38 who is at present free of the disease is a 17 year old girl who on admission to this hospital on 8-14-44 presented a Morton type 3 right lower quadrant actinomycotic infection with numerous draining sinuses along the iliac crest, severe right psoas spasm, marked anemia, hypoprotienemic edema and cachexia. In January 1944 she had an attack of right lower quadrant pain,

nausea and vomiting which subsided in 2 days. She gradually developed a flexion deformity of the right leg and severe back aches. On March 17,1944 she first consulted her local doctor who made a diagnosis of ruptured appendix, hospitalized her, and on March 27, 1944 removed her appendix. She had a febrile, stormy immediate postoperative reaction and on the tenth postoperative day was discharged from the hospital with a temperature of 102°. No microscopic examination of the appendix was made. Following surgery her general health deteriorated and although the operative wound healed primarily she developed multiple sinus tracts along the right iliac crest. In July, 1944, she was hospitalized by her local doctor and received 800,000 units of penicillin with no beneficial effect. The disease progressed until her admission to this hospital on 8-14-44. The past history was noncontributory. Her essential physical findings were: emaciation (wt. 33.2 K), pallor, cachexia, weakness, moderate dental caries, healed low right rectus scar, numerous draining sinuses above the right iliac crest extending posteriorly over right join to the vertebral column, a pitting edema of her legs and vulva, and severe right psoas spasm. The pus draining from the right lower quadrant sinsues contained typical sulfur granules. Her admission hemoglobin was 6 Gms., total plasma proteins 6.9 Gm.% with a reversal of the albumin/globulin ratio. An intravenous pyelogram revealed the right kidney and ureter free of involvement and a barium enema revealed an extrinsic mass pressing against the cecum. The lumbar vertebra were free of disease. A diagnosis of right lower quadrant abdominal actinomycosis with secondary cachexia and anemia was made.

The patient's treatment was directed at the restoration of her general physical health and surgical ablation of the diseased actinomycotic tissue. She received a high caloric (average of 3500 calories daily) diet. Her anemia was treated by liberal blood transfusions and ferrous sulfate; 3500 cc. of blood being used the first two weeks of her hospital stay. A total of 10,750 cc. of blood was administered during the course of her treatment. Adjuvant penicillin, 10,000 units every three hours daily was given for 12 weeks, and during the remainder of her hospital stay and for 2 months after discharge she was given sulfadiazine in the dose of 1 Gm. four times a day. The diseased tissues of the right lower quadrant were removed in 3 stages (8-25-44, 9-7-44, 9-28-44) by means of radical excision and currettage. It was necessary to free the abdominal muscles from the right iliac crest and remove tissue over the iliacus and psoas muscles posteriorly to the vertebral column and superiorly to lower pole of the kidney and inferiorly into scarpas triangle.

The care of the wound consisted of daily irrigations with hydrogen peroxide followed by Dakin's solution and application of gauze packs impregnated with Dichloramine-T in oil. Granulation of the wound progressed favorably so that we were able to cover the raw surface with dermatone skin grafts (1/12,000 inch thick). The posterior aspect of the wound was grafted on 10-19-44 and the anterior on 1-2-45. Since the application of the final skin grafts no evidence of recurrence of the actinomycosis has manifested itself. The patient appears healthy, has a good appetite and has steadily gained weight. A mild scoliosis of her spine has resulted from the detachment of the abdominal muscles from the iliac crest.

We believe the apparent cure of this severe abdominal actinomycosis in this patient was the result of the concurrent use of energetic supportive treatment with radical surgery coupled with careful daily wound care plus the administration of penicillin and sulfonamides. The application of dermatone grafts shortened the convalescent period. The favorable course of events with this therapeutic regimen in such a severe case of actinomycosis coupled with the reports in the literature on the use of sulfonamides suggests that the prognosis in most cases of extensive actinomycosis should be quite good. Likewise the administration of penicillin and sulfonamides is established as an adjuvant to the surgical treatment of actinomycosis.

Summary and Conclusions

1. A case of successful radical surgical treatment of a patient with an extensive abdominal actinomycosis has been presented.

2. Energetic supportive measures; a high caloric, high protein, high carbohydrate, low fat diet with supplementary vitamins, numerous blood transfusions, and adjuvant sulfonamides and penicillin contributed greatly to the therapeutic success in this patient.

3. The observation of dental spesis in 14 of 15 patients with cervico-facial actinomycosis treated here at the University of Minnesota Hospitals bares out the supposition of an endogenous source of the anaerobic infection.

4. A review of the literature indicates circumscribed actinomycotic lesions may be successfully treated by either surgery or radiation. Extensive actinomycosis should be treated by radical surgical currettage plus energetic supportive measures and concomitant sulfonamide or penicillin administration.

5. In the surgical treatment of actinomycosis, reliance should be placed on repeated currettage of lesions with eventual ablation of all of the actinomycotic tissue rather than excision. Meticulous daily wound care consisting of irrigation with hydrogen peroxide, Dakins solution, and packing with gauze impregnated with Dichloramine-T in oil facilitates healing of the curretted wounds.

6. The sulfonamides and penicillin are valuable adjuncts to surgical treatment of extensive actinomycosis.

7. Thirty-eight patients with proven actinomycosis were treated surgically at the University of Minnesota Hospitals since 1917. Of 17 cases with cervico-facial disease, 10 were cured, 3 improved, and 4 died. Of the 7 thoracic cases, 1 was improved by means of sulfonamides, 1 died of an intercurrent cerebro-vascular accident during treatment, and the remainder died of the disease. Only 1 patient of 14 abdominal cases survives.

Cervico-facial actinomycosis (University of Minnesota)

No.	Sex	Age	Condition of teeth or related conditions	Type	Treatment	Results	Duration	Year
1	M	43	Carious	3	KI, $CuSO_4$, incision of abscesses	Died of mediastinal invasion	10 mos.	1925
2	M	65	Carious	2	X-ray, KI currettage	Cured	11 mos.	1927
3	M	34	Septic roots	2	KI, X-ray incision	Cured	4 mos.	1927
4	M	40	Abscessed teeth exodontia	1	Excision & currettage	Cured	3 mos.	1930
5	F	29	Abscessed teeth exodontia	1	Excision	Cured	6 mos.	1931
6	F	13	Carious	1	Excision & currettage	Cured	8 mos.	1932
7	F	31	Exodontia (Comatose on admission)	3	Supportive	Died of meningitis	8 yrs.	1933
8	M	65	Abscessed teeth exodontia	2	KI-X-ray currettage	Died of meningitis	5 yrs.	1930
9	M	7	Mastoiditis	2	Currettage	Cured	8 mos.	1934
10	M	24	Carious	1	Numerous currettments	Improved	9 mos.	1937
11	F	5	Carious, abscessed	1	Currettage	Cured	3 mos.	1937
12	M	55	Ulcer from poorly fitting dentures	2	Excision & currettage	Improved	8 mos.	1937
13	F	26	Apical abscesses	3	X-ray currettage	Died of meningitis	1 yr.	1941
14	M	18	Exodontia	1	Currettage sulfonamides X-ray, Lugol's	Cured	8 mos.	1942
15	M	53	Carious	1	Excision & currettage	Healing	4 mos.	1945
Lingual Actinomycosis								
16	M	43	Edentulous		Incision & currettage	Cured	3 mos.	1930
17	M	39	Severe dental sepsis		Incision & currettage	Cured	1 mo.	1932
Thoracic Actinomycosis								
18	M	21	Teeth in good condition		Excision, KI X-ray, Currettage	Died	32 mos.	1927
19	M	13	Carious		Supportive	Died	7 mos.	1930
20	F	29	Carious		Currettage, KI, incision, X-ray	Died of metastatic cerebral abscess?	4 yrs.- 6 mos.	1930
						disease arrested for a time		
21	F	14	Condition of teeth not noted		Incision, currettage, transfusions	Died	11 mos.	1935
22	M	45	Appendicitis; postoperative pneumonia and empyema		Drainage of abscesses	Died of meningitis	14 mos.	1935
23	M	44	Not noted		Sulfamerazine sulfadiazine, total Rx 5wks.	No follow-up		1944

No.	Sex	Age	Condition of teeth or related conditions	Treatment	Results	Duration	Year
Thoracic Actinomycosis (Cont.)							
24	M	57	Diverticulitis of colon	Excision & currettage, sulfadiazine penicillin	Died of cerebro-vascular accident while under Rx, actinomycosis had improved.		1944
Abdominal Actinomycosis							
25	M	37	Pyorrhea, appendectomy with drainage	Incision, cauterization, currettage	Died	2 yrs.	1917
26	M	27	Appendectomy with drainage	X-ray, KI drainage	Died	1yr. 8mos.	1928
27	F	40	Carious	Drainage of subdiaphragmatic abscess, supportive	Died	3 mos.	1928
28	F	51	Appendectomy with drainage	KI, X-ray drainage	Died	3 yr.	1931
29	M	22	Appendectomy with drainage	KI, X-ray drainage	Died	13 mos.	1936
30	M	15	Abdominal abscess	Drainage transfusions	Died	7 mos.	1932
31	M	59	Appendectomy	Excision currettage	Died of pulmonary extension	6yr. 4mos.	1938
32	M	28	Appendectomy with drainage	Excision currettage	Died	1 yr.	1935
33	M	57	Right lower quadrant abscess	Supportive	Died with pulmonary extension	8 mos.	1935
34	M	22	Caries	Transfusion Currettage	Died	10 mos.	1937
35	M	38	Oral sepsis appendectomy	Drainage, X-ray sulfathiazole	Died	10 mos.	1943
36	M	11	Appendectomy	Incision & drainage, sulfadiazine	Died	2 yrs.	1944
37	M	52	Pyorrhea, diverticulitis of colon	Transverse colostomy, X-ray, penicillin, supportive	Improved	4 yr.	1944
38	F	16	Pyorrhea appendectomy	Penicillin, sulfadiazine, excision skin grafting	Living and well		1945

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III. GOSSIP

The late Dean J. B. Johnston, taught neuroanatomy in the medical school before taking over the deanship of the Arts College. For 15 years he was recognized as one of the 4 leading comparative neurologists of the world, during which time he published more than 40 technical papers on the subject. These contributions are models of accuracy and clarity, and are full of stimulating originality. He produced the first book on the Morphology of the Nervous Systems of Vertebrates on a thorough going, functional basis, setting a pattern that has been extensively followed by subsequent leaders. From 1914 until his retirement in 1937, he headed the Arts college. His contributions to the field of general education were outstanding. One of his unique conclusions dealt with the type of student he would most like to see enter the University. He felt that the children of the poor were the best. He admitted there was a certain amount of natural selection, but when this was coupled with a thirst for knowledge the result was outstanding. His widow now living in Los Altos, California, has given a sum of money to the University to provide a lectureship in honor of her husband. She, too, shared her husband's interest in neurology, and worked on the nervous system of the embryos of the white fish at the University of Michigan. During Dr. Johnston's study abroad, she taught his classes at the University of West Virginia. Olof Larsell who will present the first of these lectures was born in Sweden, but received most of his education in this country. He has been investigating the nervous system for over 30 years. After obtaining his Ph.D. in 1918 from the Northwestern Universith, he was associate professor of anatomy at the University of Wisconsin for 2 years, and for 1 year at Northwestern University. Since 1921 he has been professor of anatomy at the University of Oregon Medical School and for several years has also acted as Dean of the Graduate Division of Oregon State System of Higher Education. In addition to his work on the cerebellum, Doctor Larsell has carried on other outstanding investigations, particularly on the innervation of the lungs and on the ear. He is the author of the section on the nervous system in the current edition of Morris' Human Anatomy and of an independent general textbook on the anatomy of the nervous system and sense organs. His broad approach to the fundamental morphology and significance of the different parts of the cerebellum will interest many biologists as well as the medical profession generally. The J. B. Johnston Lecture in Neurology will be on the "Comparative Neurology and Our Present Knowledge of the Cerebellum", Friday, May 11, 8:15 P.M., at the Museum of Natural History Auditorium. On Thursday, May 10, at 5:00 P.M. Dr. Larsell will speak to students and faculty at the Institute of Anatomy Amphitheater on the "Development of Medicine in the Northwest", a subject on which he has worked for many years and on which he is now preparing a book. ...Dr. Ovid O. Meyer, Associate Professor of Medicine, University of Wisconsin, will speak at the Hennepin County Medical Society, Monday, May 7, at 8:00 P.M. on "Anticoagulants and Thrombosis"....To New Prague, Minnesota on Sunday, April 29 to speak about Dr. E. E. Novak at a community celebration in honor of an important event. Fifty years ago on his 22nd birthday, he had come to New Prague to practice after graduating from the University of Iowa Medical School. He has been there since, and has become a power for god in the community. In addition to taking care of their sick problems, he has created for them a fine structure in business and education. He is president of the bank, and has headed the Commercial Association. He has served on the School Board, and has helped to develop agriculture. He is a breeder of fine cattle, and owns many farms. He was instrumental in establishing the community hospital, and has sent more promising young men to medical school than any other Doctor in Minnesota. His example to promising young men is reflected in the large number of successful physicians from this small town. His interest in education carried him to the state association where he became President of the Association of School Boards, and a Regent of the University of Minnesota. At a large dinner which was limited in size because of rationing, 350 patients and friends came to do him honor. Nearly a thousand wished to attend. Speakers vied with one another to tell of his contributions.....