ACTINOMYCOSIS IN PUERTO RICO *

A. L. CARRIÓN
From the Department of Mycology, School of Tropical Medicine, San Juan, Puerto Rico.

The climatologic features of Puerto Rico are highly favorable for the development of fungi in general. As a matter of fact, the richness of our mycological flora has been observed by many well-known workers in this field of science. On the basis of this knowledge and, in view of the unfavorable living conditions which prevail among our poorer classes, the pathogenic group of fungi should be expected to play an important rôle in the production of human disease in this country. In contrast with this expectation, however, comparatively little is found in our medical literature on the actual existence of mycotic infections in the Island.

During recent years we have earnestly endeavored to determine the fungous diseases that are prevalent here, to observe their clinical behavior, and to learn something about the various etiologic species involved. In previous publications we have already presented the clinical and mycological aspects of a dermatophytosis due to *Trichophyton rubrum* (1, 2, 4) and of chromoblastomycosis (6–11), as well as cultural studies of the fungi related to ringworm infections of the hands and feet (3, 5). In this communication we are reporting two cases of actinomycosis with a description of the Actinomyces obtained in culture.

CASE REPORT

Case 1.—R. E., a male, white, Puerto Rican child (see plate I), residing in Santurce, aged 8 years was admitted to the University Hospital on June 5, 1934 (U. H. No. 1840).

C. C. (1) Pain below the right scapular region. (2) Fever.

P. I. Patient apparently well until about 3 months ago when he began complaining of pain on the lower portion of the right scapula. This symptom became progressively worse making the child cry frequently. The pain, though continuous, was aggravated at night and would interfere with sleep. About four weeks after the onset of pain a hard, round, sub-cutaneous nodule, about the size of a large split-pea, was noted a short distance below the scapular

* Received for publication July 15, 1937.

region, no change being observed on the overlying skin. This lesion, which was particularly tender, gradually increased in size and, in a month's period covered an area of approximately a half dollar.

On May 12, 1934 (one month prior to admission at the University Hospital; 2 months after onset of disease) the child developed chills and fever and was admitted to the Presbyterian Hospital at San Juan where he was carefully examined. The lesion on the chest wall, which was now the size of a half orange and showed fluctuation, was opened and drained twice (May 15 and May 25). Laboratory studies of the pus revealed the presence of small granules and Gram-positive filaments. These findings, as well as a biopsy done at the School of Tropical Medicine, established a diagnosis of actinomycosis.*

Since the onset of disease, the general health condition of the boy had been progressively impaired, with loss of weight and increased pallor of the skin. However, his activity, good disposition and appetite were fairly well preserved and his bowel movements were regular. It should be noted that the patient, wearing pants with suspenders—upper trunk exposed—used to play in a grazing pasture near his home. However, there is no history of any abrasion of the skin or lesion of any sort at the site where the abscess was developed or anywhere else.

P. H. Mother and father not known; facts related to his birth also unknown. Guardians took charge of the baby at the age of 6 weeks. During infancy child was fed on cow's milk; was also given Klim and condensed milks, with few unimportant gastrointestinal upsets. Development apparently normal, though the child was always sickly in appearance and predisposed to frequent colds. Suffered from measles several years ago. Last year had intermittent tertian episodes of chills, fever and sweats, lasting 14 days, which disappeared with quinine treatment. No whooping cough, chickenpox or diphtheria; no accidents and no operations except for incision of small abscesses. Occasional diarrhea without blood. Cardiorenal functions, negative. The urine was often dark in color. Frequency, retarded flow and incontinence were also reported.

PHYSICAL EXAMINATION—A well-developed, thin, pale, undernourished child, looking chronically ill and crying frequently during examination.

Head: Essentially negative. Eyes, also negative. Pupils, react normally. Ear, nose, mouth and pharynx, clear. Tonsils, small. Tongue, clean and moist. No atrophy of papillae. Teeth, many missing; remainder, dirty and showing advanced caries.

Neck: Negative. No thyroid enlargement.

Lymph nodes: Enlarged, non-tender submaxillary nodes; axillary nodes, large and tender; inguinal nodes, palpable, shotty, not painful.

* We are very much indebted to the staff of the Presbyterian Hospital, at San Juan, and particularly to Dr. W. R. Galbreath, its former Director, for permitting the transfer of the patient from that institution to the University Hospital for further study and treatment.

Thorax: Anteriorly—On right side of chest over the eighth rib in the anterior axillary line, there was a small, firm, non-fluctuant, exquisitely tender swelling measuring 2 cm. in diameter. It was, apparently, not fixed to the underlying bony structure and the skin covering it showed nothing abnormal.

Posteriorly—On the right thorax, beneath the angle of the scapula, there were two oval areas of heaped up, dirty, granulation tissue measuring about 2.5 cm. in their major diameters. These corresponded to the two incisions made at the Presbyterian Hospital. A small amount of yellowish exudate covered the granulating surfaces.

In addition, a certain amount of scoliosis was noted, the maximum lateral deviation being at the level of the ninth dorsal spine with the convexity to the left. This was opposite the level of the two previously described lesions. There was also a moderate compensatory cervical and lumbar scoliosis.

Lungs: The resonance, breath and voice sounds were normal, anteriorly. Posteriorly, at right base, there was dullness to percussion, while the stethoscope revealed fine rales, and diminished voice and breath sounds.

Heart: Not enlarged. Sounds forceful. No arhythmias. There was a loud systolic murmur heard all over the precordium and maximal over pulmonic area and left border of sternum; not transmitted to shoulder or neck vessels. Blood pressure: 90 over 60.

Abdomen: Protuberant. Dilated superficial veins over the ensiform and lower sternum. Lower pole of spleen felt three fingerbreadths below the costal margin. It is tender to palpation. Liver not felt. No other masses or tender areas made out.

Genitalia: Normal. Rectal: Not done. Extremities: Essentially negative. Reflexes: Patella, equal and active. Temperature: At the time of examination, 100.4°F. Pulse: 136. Respiration: 30.

LABORATORY FINDINGS:

Blood:

June 8, 1934—R.B.C., 4,600,000; hemoglobin, 62 per cent (9.0 gm.) color index, 0.67; W.B.C., 15,000; lymphocytes, 26 per cent; mononuclears, 8 per cent; polymorphonuclear neutrophiles, 60 per cent; eosinophiles, 6 per cent.

June 28, 1934—W.B.C., 18,600; lymphocytes, 23 per cent; mononuclears, 1 per cent; polymorphonuclear neutrophiles, 71 per cent; eosinophiles, 5 per cent.

June 4, 1934—Kahn test, 0.0.0. June 22, 1934—Blood culture —negative.

Urine:

June 6, 1934—Color, pale yellow; appearance, turbid; reaction, slightly alkaline; specific gravity, 1012; albumin, negative; sugar, negative; amorphous phosphates, moderate amount; few epithelial cells; W.B.C., 1 or 2 per microscopic field (H.P.).

Feces:

June 6, June 13, June 14 and June 15, 1934 (4 specimens)—*Ascaris lumbricoides* and whipworm ova. Cysts of *E. coli.*

Exudate:

June 22, 1934—Positive for *Actinomyces bovis* (See below: Mycology).

X-RAY REPORTS:

June 11, 1934—The ribs and thoracic spine are negative. A slight scoliosis with convexity towards the left is noted in the lower thoracic region. With reference to the lung fields, the descending branches of the right side present an exaggerated density. There is also a slight peribronchial thickening.

July 13, 1934—The lung fields are clear, except for the peribronchial thickening mentioned in previous report. The right base suggests fluid.

August 8, 1934—There is a marked periosteal reaction towards the inferior third of right femur, especially on its medial aspect.

COURSE: The disease followed a slow but progressively downward course. Treatment did not affect the infection in any way. The fever was continuous and spiking in character, ranging between 99 and 103°F. The pulse and respiration rates followed fairly well the temperature curve. Subcutaneous metastatic abscesses appeared in succession at varying intervals. In addition to the original focus, opened and drained prior to admission in our Hospital, not less than 19 abscesses were noted over a period of less than four months. They occurred almost anywhere throughout the skin: on the neck, chest wall, lumbar region, the buttocks, upper and lower extremities. Their size varied from that of an almond to that of a small orange. The overlying skin, at first normal in appearance, would become red or violaceous in color as the lesions aged. Pain was most intense. The development of new lesions did not affect the course of the fever; neither was this affected by the incision and drainage of the septic foci. After surgical treatment some of the lesions would heal, while others continued to drain indefinitely.

As the infection progressed the general condition of the child became worse and worse. There was increased pallor, marasmus and loss of appetite. The appearance of intense and continuous cephalalgia on September 1st marked the invasion of the central nervous system. Three days later nausea and vomiting set in. From then on, the clinical picture was that of a severe toxemia. The patient finally became drowsy and entered into a semi-comatous condition. Death occurred on September 29.

Treatment was directed to: (1) Eliminate intestinal parasites. (2) Build up general health. (3) Combat specific infection. (4) Relieve the symptoms.

The patient was put to bed and offered a plain nourishing diet. Cod liver oil and ferric-ammonium citrate were prescribed as tonics, and early in July, oil of chenopodium in castor oil was administered for the intestinal parasites.

On July 10, iodide treatment was initiated with a daily dose of 0.50 gm. of potassium iodide given by mouth; while two days later a series of intravenous injections of the sodium salt was started.

The oral doses were gradually increased to 3.25 gm. a day until July 24 when the child refused to take it any more. The intravenous injections, however, were continued, the dose being raised slowly to a maximum of 1.25 gm. a day. This latter dose was maintained over a period of 40 days, that is, until 2 days before death occurred.

Nine of the skin abscesses already mentioned were incised and drained. The rest broke open spontaneously and were treated on ordinary principles.

Aspirin and, less often, codeine sulphate were given for pain and insomnia.

AUTOPSY REPORT (Abstract)*:

Gross Findings: The examination was performed 7½ hours post-mortem. The inguinal and axillary lymph glands were barely palpable. Small ulcers were found in the following situations: (1) over the center of the left scapula, (2) opposite the left acromion process, (3) below the angle of the right scapula, (4) in the right hypochondriac region, (5) in the lateral aspect of each hip, (6) in the right buttock opposite the spine of the ischium, and (7) over the flexor surface of the middle and distal thirds of the right thigh. These ulcers measured 1 to 2 cm. in diameter and had pinkish granulating bases. The skin about most of them was reddish or violaceous and somewhat swollen; pressure on the area of swelling yielded thick greenish pus which flowed from the edge of the ulcers. The amount of pus thus obtained from the thigh was very large, and dissection of this region showed diffuse infiltration of pus throughout the muscles down to the periosteum. The latter was slightly thickened, but no involvement of the bone itself could be demonstrated. The right leg could not be extended at the knee beyond an angle of approximately 150°.

Peritoneal cavity—The serosal surfaces were normal. A large pocket of pus was found retroperitoneally below the lower pole of the left kidney and measured some 5 by 3 cm. Abundant pus was also found infiltrating the right iliacus muscle. The inferior edge of the liver extended to about the level of the umbilicus. The spleen was fixed to the diaphragm by dense fibrous adhesions. Between the spleen, diaphragm and left hepatic lobe there was a sharply delimited abscess.

Thoracic cavity—The left pleural cavity contained approximately 600 cc. of amber-colored fluid. Half this amount of similar fluid was found in the right pleural cavity. The lower pulmonary lobe on this side was diffusely adherent to the parietal wall in its lowermost portions, and also to the diaphragm. A small amount of thick pus had collected in a pocket lying between this lobe and the diaphragm.

Heart—Weighed 115 gm. Several abscesses were found at various places in the myocardium: posteriorly, beneath the groove of the posterior descending coronary branches, in the lateral surface of the wall of the left ventricle and near the apex, and in the upper portion

* The autopsy was performed by Dr. A. Rivero, and this abstract was prepared by Dr. E. Koppisch, both of the Department of Pathology.

of the interventricular septum anteriorly. These abscesses varied in principal diameter from 0.8 to 3 cm., were nearer the endocardial surface in some regions and closer to the epicardium in others, and contained thick greenish pus. Most of them presented a distinct fibrous wall and some were multiloculated. A dense fibrous tag extended between the visceral and parietal pericardium from a point on the anterior wall of the left ventricle, 2 cm. above the apex. The valves were unaltered, and there were no evidences of acute endocarditis or pericarditis over the abscesses. The main coronary branches were normal.

Right lung (see plate II, fig. 1)—Weighed 190 gm. The lower half of the lower lobe was dense, particularly medially and posteriorly. On section this area was grayish-white and fibrosed. Numerous abscesses measuring 3 to 5 cm. in diameter were present close to the diaphragmatic and mediastinal surfaces. Many of these had broken into the pleural cavity posteriorly, while inferiorly they had led to formation of a honey-combed subdiaphragmatic abscess 5 cm. in diameter. The remainder of the right lung, and the left, were normal. The hilus lymph glands were not enlarged.

Spleen (see plate III, fig. 1)—Weighed 100 gm. and was adherent to the diaphragm, tail of the pancreas and left hepatic lobe. Confluent abscesses averaging 0.5 cm. in diameter were found on section in various portions of this organ. The intervening pulp was somewhat bulging and dark reddish-brown.

Kidneys (see plate II, figs. 2 and 3)—The right one weighed 120 and the left, 100 gm. Abscesses were found in both organs, both in the cortex and in the medulla. In places they had coalesced, forming honey-combed spaces filled with pus. One such group situated in the lower pole of the right kidney had led to formation of a large abscess, 4 by 2 cm., beneath the capsule. These abscesses averaged 1 cm. across when single, but a confluent area in the right kidney involved most of the lower pole. The parenchyma between these lesions showed fairly regular striations, and the renal pelvis was not involved.

Tonsils—Only the right one was extracted. It was not enlarged but presented on section a single greenish abscess measuring 0.3 by 0.1 cm. and situated in the depths of the gland.

Thyroid—The gland was of average size. A sharply encapsulated abscess 0.6 cm. in greatest diameter was present in the capsule of the isthmus anteriorly, and a few minute abscesses were found on section in the subjacent glandular tissues.

Brain (see plate III, fig. 2)—The leptomeninges were congested and the gyri slightly enlarged and flattened over areas of cystic consistence that were proved, after hardening and sectioning, to be abscesses. These were situated near the dorsal surface of the vermis of the cerebellum; in the right and left occipital poles; opposite the middle of the right inferior temporal convolution; opposite the middle of the medial orbital gyrus of the left frontal lobe; opposite the center of the right middle frontal gyrus, and in the extreme

posterior portion of the left inferior parietal convolution. The abscesses measured from 0.4 to 2 cm. across, on section, and were surrounded by a thin grayish capsule of fibrous tissue. They were situated in the cortex and beneath it; none had ruptured into a ventricle.

The organs not mentioned were found free of pathologic alterations. The gastrointestinal tract was not at all involved.

Microscopic Description: The changes were most advanced in the lower lobe of the right lung, where there were numerous abscesses containing polymorphonuclear leukocytes and Actinomyces granules. About the abscesses were most extensive areas of well-advanced fibrosis, with more or less intense round-celled infiltration (see plate IV). Areas of granulation tissue occurred here and there. The bronchioles in the areas of fibrosis often showed infiltration of their walls with round cells, while polymorphonuclear leukocytes and Actinomyces granules were present in their lumens (see plate V). Leukocytes and Actinomyces granules were also found within one or two medium-sized veins with necrotic walls (see plates VI and VII).

The actinomycotic abscesses in the other organs consisted of polymorphonuclear leukocytes and Actinomyces granules in the center, a layer of granulation tissue about the periphery, more or less densely infiltrated by round cells and fat-laden macrophages, and a fibrous capsule enveloping the whole area of necrosis (see plate VIII).

A splenic tumor was not in evidence. The liver was the seat of early fatty changes.

Anatomical Diagnoses: Actinomycosis of lung (right lower lobe), with direct extension to pleura, diaphragm and skin; metastases to heart, kidneys, liver, spleen, thyroid gland, tonsil (right), brain, iliacus and femoral muscles; fatty liver and secondary anemia.

COMMENT

The pathologic condition described in the above history represents a good example of generalized actinomycosis. It is the first unquestionable case of human infection with *Actinomyces bovis* recognized in Puerto Rico.* From the clinical point of view, it was remarkable for its severe and spectacular course. The striking limitation and apparent unimportance of the pulmonary symptoms misled us to the wrong impression that the infecting fungus had entered the body through an unnoticed abrasion or trauma of the skin below the right scapular region. However, after the postmortem examination, it became evident that the pulmonary focus, with its dense fibrotic reaction, was the true starting

* The history of this case was presented and discussed at a Clinic held at the School of Tropical Medicine on the evening of November 15, 1934.

point of the infection. The histopathology in general was remarkable for the extraordinary dissemination of metastatic foci throughout the organs and tissues.

*Case 2.**—J. S., a white boy, 13 years old, from the town of Canóvanas was admitted to the University Hospital on August 10, 1934 (U. H. No. 1939).

C. C. (1) Pain and swelling of right arm and right leg lasting 28 days. (2) Fever.

P. I. Onset took place 28 days prior to admission with general malaise, fever and pain, which was first located on right arm and right leg, but which later extended to left arm, chest and other regions. The pains were followed by inflammatory swellings. Before the patient was first seen by us, abscesses had formed on left elbow, right arm, occipital and renal regions and either were incised or opened spontaneously.

P. H. Child has been always pale and faint. At the age of 2, he suffered from epileptiform convulsions.

F. H. Father suffers from bronchial asthma.

PHYSICAL EXAMINATION.—On admission, the child appeared acutely ill, pale, emaciated, with loss of turgor of the skin, irritable and restless. His temperature was 102°F.; pulse, 120; respiration, 30.

Head: There was a small abscess on superior occipital region. Teeth: Negative. Throat: Hypertrophic tonsils. Neck: Few small palpable submaxillary lymph nodes. Chest: Thin and symmetrical. Lungs: Widely distributed over both lung fields, there were fine moist rales which were accentuated with cough. Heart: Normal. Abdomen: Scaphoid. No palpable masses or tenderness. Liver of normal size. Spleen not palpable. Back: On lower sacral region there was a punched-out ulcer with undermined edges. Extremities: There was marked limitation in the movements of the left shoulder, right elbow, right ankle and knee, and left knee, with extreme tenderness of the affected joints. Draining wounds were noted on the left arm and right elbow.

LABORATORY FINDINGS:

Blood:

A blood examination made on August 10, 1934, showed: R.B.C., 2,250,000; hemoglobin, 52 per cent; W.B.C., 13,900; lymphocytes, 16 per cent; mononuclears, 2 per cent; polymorphonuclear neutrophiles, 80 per cent; eosinophiles, 2 per cent.

The Kahn was negative. Agglutination tests against *B. melitensis*, *B. typhosus*, Para A and Para B were negative. A blood grouping test classed patient in type II, Moss. Among seven blood cultures done in the Department of Bacteriology, three were reported sterile; two showed, respectively, a slightly hemo-

* We wish to thank Dr. José Noya Benítez, of the Department of Surgery, University Hospital, for permitting us to include this case in the present report. The patient was hospitalized under his service.

lytic *Staphylococcus albus* and a Gram-positive non-hemolytic coccus with tendency to form short chains, most probably contaminants; finally, in the two remaining cultures, a branching, filamentous and rodshaped, aerobic, Gram-positive organism * was obtained.

Urine:

Numerous urine examinations done at different dates usually showed white blood cells and occasionally albumin and red blood cells.

Feces:

In repeated specimens, whipworm ova and larvae of *Strongyloides stercoralis* were reported present.

Sputum:

Negative for Koch's bacillus several times.

Exudate:

Of three samples of exudate examined at the Department of Bacteriology, one coming from an abscess of the abdominal wall was reported sterile; another, coming from a bone, showed hemolytic *Staphylococcus aureus;* while a third, from a suppurating inguinal gland produced a growth which was reported negative in culture, direct smears from the exudate showing "thin Gram-positive rods with a suggestion of branching". In this specimen we found typical Actinomyces granules, and an anaerobic Actinomyces (*A. bovis*) was obtained in culture.

HISTOPATHOLOGY.—Biopsies performed on November 14 and December 8, 1935 were reported as "chronic osteomyelitis with formation of sequestrum".

X-RAY REPORTS.—An X-Ray picture of the chest taken on August 20, 1934 revealed "exaggerated density of the ascending broncho-vascular branches on the right side". A second one taken on January 31, 1935, showed "tracheo-bronchial adenopathy with exaggerated density of the ascending broncho-vascular branches on both sides, the diaphragm appearing higher than normal".

On December 22, 1934, a fistula on the left lower quadrant of the abdominal wall was roentgenographed after injection with bismuth paste. The picture demonstrated a superficial sac without connection to iliac bone.

An X-Ray picture of the left humerus (September 30, 1934) revealed osteomyelitis in almost the entire length of the bone, with destruction and fracture of the neck. The head proper was not involved. Several other check-up X-Ray pictures of the same region were taken following sequestrectomies. The last one (January 19, 1935) showed disappearance of the sequestrum with apparently no union between the head and the shaft of the humerus.

* A. Pomales, of the Department of Bacteriology, who isolated and studied these organisms, will probably publish his observations in the near future.

COURSE.—Although there were periods when the temperature remained above 100°F. for several days, the patient ran mostly a septic type of fever during his stay in the Hospital. He had four operations, all for incision and drainage or purulent accumulations, after which the temperature usually came down to normal for a day or two. In addition, eight transfusions of citrated blood were done—the smallest, of 35 cc.; the largest, of 225 cc. During the period of hospitalization, there was a gradual, though at times imperceptible, improvement, the condition on discharge being decidedly better than when the patient was admitted 6 months before. The child was released on February 11, 1935 at the persistent request of the family.

On June 25, 1935 the patient was readmitted. The mother declared that, after a short period of improvement, the child started losing ground again, the fever becoming higher than usual. A few days prior to her visit, an abscess, which had formed over the left hip-bone, broke out giving way to a large amount of pus and was still draining profusely.

During the physical examination done on the day of readmission the following observations were thought to be of significance: Old lesion of left arm was healed. There were: edema of face; extreme paleness of conjunctivae; very poor hygiene of mouth; ulceration of lower right gum; hard nodule in right cheek with ulceration of the bucal mucosa overlying it; right tonsil was enlarged and apparently discharging. Examination was made difficult because patient could not open his mouth well. Lungs were clear anteriorly; posteriorly, there were coarse, dry râles at the bases. The abdomen was distended; palpation impossible because of tenderness. There was a large opening in abdominal wall with exposure of practically entire left iliac crest. Fecal matter would come out through this wound at times. Another abscess opened in right lower quadrant with profuse discharge of pus and necrotic tissue. Lower extremities showed marked edema of ankles and feet.

The general condition of the boy was extremely poor. He stayed in the Hospital for five days, at the end of which the mother decided to take him back home, which she did on June 29, and after this we were unable to follow up the case.

COMMENT

In this case it was impossible to follow up the condition as thoroughly as in the previous one. The determination of the etiologic factor was a difficult matter and for some time after the patient was hospitalized, the true nature of the infection remained in obscurity. Biopsies done on two different occasions did not reveal actinomycotic granules in

the tissues and this naturally tended to withdraw the mind from the possibility of a mycotic infection. After considering a number of bacterial diseases, a diagnosis of actinomycosis was finally established. This was based on the insidious, pyemic character of the illness, the presence of the so-called sulphur granules in the exudate and the recovery, in laboratory cultures of the infected material, of an organism which was indistinguishable from *Actinomyces bovis*.

In its clinical course, case No. 2 was quite similar to case No. 1. In the former, however, it was impossible to determine the portal of entry of the infection. We have often wondered if this was not a case of actinomycosis superimposed upon a preexisting bacterial process which made conditions favorable for the invasion by the fungus.

MYCOLOGY

Material and Methods Used.—The material used consisted of pus coming from draining sinuses or from closed abscesses. When obtained from the latter source, it was aspirated with a syringe under sterile conditions and poured into a test tube from which the material was used as necessary.

Fresh preparations were made by crushing a few drops of the fluid with granules between a slide and cover slip, and smears were stained by various methods for microscopical examination.

Some of the material was inoculated into chopped meat broth and veal infusion agar melted at 45°C. for cultural studies. The cultures were first incubated at 37°C. for 48 hours and then kept at room temperature (25°C.), observations being made every 2 to 3 days. Photographs and photomicrographs were taken whenever thought convenient.

The rest of the material was diluted 1:1 with sterile saline solution for experimental inoculations. Several animals—three dogs, two rabbits, two guinea pigs, and two white rats—were inoculated subcutaneously on the back and on the angle of the jaw. The injections in the latter region were given by way of the mucosa of the mouth, except in the two rats where the puncture was made through the

overlying skin. In each case the point of the needle was thrust deep into the tissues until the surface of the bone could be felt and scratched. Doses of 0.5 to 1 cc. of the 1:1 dilution of the exudate were used. The animals were examined daily and records were made of the changes noted.

Characters of the Exudate and Granules.—The contents of the abscesses consisted of a thick, reddish-yellow, malodorous fluid with an abundance of tiny granules, a small fraction of a millimeter in diameter. These granules could be readily seen by shaking the fluid within the test tube, upon which a thin film of the exudate with granules would adhere to the glass walls of the container. Examined with the magnifying glass they appeared as opaque, grayish white, spherical bodies which could be easily crushed. Microscopical examination of the crushed granules revealed a thick felt of very fine mycelium surrounded by numerous, refringent, club-shaped bodies (see plate IX, figs. 1, 2 and 3). Fragments of the felted mycelium, as well as rod-like structures, were easily detected in stained preparations (see plate IX, fig. 4). These structures were non-acid-fast and, when stained by Gram's method, they retained the basic dye, though not uniformly.

Cultures.—The shake cultures in beef infusion agar failed to show any growth in case No. 1. In case No. 2, an abundance of colonies, many of them bacterial, were observed in the depth of the agar one week after the inoculation. The Actinomyces, which was easily isolated and subcultured from the primary tubes, formed numerous, white, rounded or lobulated colonies of variable size, not quite reaching one millimeter in diameter, at the end of the first week. These colonies were more abundant and better developed at a depth of about one centimeter from the surface of the agar.

In chopped meat broth, colonies were detected within five to six days in all the tubes as minute, whitish, spherical granules. These granules increased gradually in size, reaching from 1.3 to 2 millimeters in diameter at the end of the eighteenth day. At this time they had become definitely lobulated, their color was white with an almost imperceptible touch of blue, they were very soft in consistency and could

be easily broken or crushed with the needle (see plate X, figs. 1 and 2). With ageing, the granules would gradually change their color to gray and finally to black. Under the microscope, the pigmented colonies showed an abundance of finely granular, black, pigment deposits. We were not able to definitely determine the cause of this darkening. There is a possibility that a contaminant may have produced the change by some chemicobiological action, but we could never recover, from these colonies, anything but Actinomyces.

Fresh preparations made from healthy cultures revealed an intricate mat of fine mycelial elements (see plate X, figs. 3 and 4), many of which appeared fragmented into rod-shaped forms. Branching was easier to observe in young colonies obtained from shake cultures in veal infusion agar. The branches would often overgrow the mother hypha and, when this phenomenon was repeated in succession, the structures would present a characteristic zigzag arrangement. Careful observations revealed the presence of transverse septa in some of the colonies. Although some of the rod-shaped forms appeared somewhat swollen on one extremity, true club formation, of the type noted in granules from the exudate, was not observed in cultures.

Experimental inoculations.—The rabbits, white rats and guinea pigs inoculated with the exudate did not develop any reaction worthy of note, either locally or systemically.

Three days after inoculation, dog No. 1 showed small swellings at the site of the injections, namely, the angle of the jaw and the back. These swellings increased progressively in size, there was intense local pain, and, in a few days, fluctuation was noted. In the meantime the animal lost its appetite, becoming feverish and shaky, and looking extremely ill. These symptoms, however, quickly disappeared upon the spontaneous rupture and drainage of the abscesses. The exudate consisted of a moderately thick, grayish yellow fluid, stained with blood. The characteristic Actinomyces granules were not observed, either macroscopically or microscopically, cultures of the pus being likewise negative. Complete healing of the lesions occurred as in any ordinary abscess, without sinus formation.

Dog No. 2 developed a small swelling at the angle of the jaw, but this never grew to any considerable extent, it produced apparently no discomfort and eventually disappeared within two weeks.

Dog No. 3 showed no reaction to the jaw injection. On the back, however, a walnut-sized swelling was developed, there was loss of appetite and the animal looked moderately ill, but these symptoms gradually subsided, the swelling was reabsorbed spontaneously and in three weeks there was complete recovery.

SUMMARY

In this communication we are presenting two cases of generalized actinomycotic infection. Case No. 1 showed the usual histopathologic picture with typical granules in the tissues, as well as in the exudate from the lesions. Biopsies (two) in case No. 2 failed to show the granules in the tissues, but these were present in the exudate. Careful cultural studies of the abscess fluids carried out in the laboratory revealed the presence of *Actinomyces bovis* in the two instances. The characteristics of the fungus were carefully noted. In case No. 2, the portal of entry of the infection was not clear. Post-mortem examination of case No. 1 disclosed an original pulmonary lesion. The extreme dissemination of mycotic foci throughout the viscera in the latter case was quite a remarkable feature.

Inoculation of the infective exudate to various species of laboratory animals failed to reproduce specific lesions, although in a few of the animals abscess formation took place and a certain amount of systemic reaction was observed. It was impossible, however, to recover actinomycotic granules or positive cultures from any of them.

COMMENT

Although there is every reason to believe that actinomycosis has existed in Puerto Rico from time immemorial, its occurrence here, up to the present time, had never been established upon a scientific basis. Undoubtedly, infections of this type must have been often overlooked by clinicians who were not well acquainted with the symptomatology of

the disease and did not bear this possibility in mind. It is probable that the incidence of actinomycosis among us is not nearly as low as is usually thought. If *Actinomyces bovis* may exist as a common saprophyte in the human mouth and throat, as would appear to be the case according to the observations of Lord [12, 13], Lord and Trevett [14], Naeslund [15] and Emmons [16], it would be reasonable to expect a larger number of actinomycotic infections in our human pathology. These considerations call for the greatest care on the part of clinicians, who should focus more of their attention on this important mycosis when making a differential diagnosis in cases like those here reported, where the clinical picture is that of a severe general infection, the course more or less insiduous, and the etiology not readily apparent.

BIBLIOGRAPHY

1. Carrión, A. L.: Observations on dermatomycosis in Porto Rico. Arch. Dermat. & Syph. **7**: 773–777. 1923. Illus.

2. Carrión, A. L.: Preliminary report on the fungus causing epidermophytosis of the general surface of the skin in Porto Rico. P. R. Jour. Pub Health & Trop. Med. **5**: 40–44. 1929. 2 plates.

3. Carrión, A. L.: Observations on dermatomycosis in Porto Rico: Report on the fungus commonly associated with foot dyshidrosis. P. R. Jour. Pub. Health & Trop. Med. **5**: 278–282. 1930. 5 plates.

4. Carrión, A. L.: Observations on dermatomycosis in Puerto Rico: Report on epidermophytosis of the general surface of the skin. P. R. Jour. Pub. Health & Trop. Med. **6**: 217–220. 1930. 12 plates.

5. Carrión, A. L.: Observations on dermatomycosis in Puerto Rico: Further report on the etiology of epidermophytosis. P. R. Jour. Pub. Health & Trop. Med. **10**: 255–261. 1935. 7 plates.

6. Carrión, A. L. and Koppisch, E.: Observations on dermatomycosis in Puerto Rico. Report on a case of chromoblastomycosis. P. R. Jour. Pub. Health & Trop. Med. **9**: 169–190. 1933. 18 plates.

7. Carrión, A. L.: Chromoblastomycosis. Preliminary report on a new clinical type of the disease caused by *Hormodendrum compactum*, Nov. Sp. P. R. Jour. Pub. Health & Trop. Med. **10**: 543–548. 1935. 2 plates.

8. Carrión, A. L. and Emmons, C. W.: A spore form common to three etiologic agents of chromoblastomycosis. P. R. Jour. Pub. Health & Trop. Med. **11**: 114–115. 1935.

9. Emmons, C. W. and Carrión, A. L.: *Hormodendrum pedrosoi*, an etiologic agent in chromoblastomycosis. P. R. Jour. Pub. Health & Trop. Med. **11**: 639–650. 1936.

10. CARRIÓN, A. L.: Chromoblastomycosis. A new clinical type caused by *Hormodendrum compactum*. P. R. Jour. Pub. Health & Trop. Med. **11**: 663–682. 1936. 8 plates.

11. EMMONS, C. W. and CARRIÓN, A. L.: The Phialophora type of sporulation in *Hormodendrum pedrosoi* and *Hormodendrum compactum*. P. R. Jour. Pub. Health & Trop. Med. **11**: 703–710. 1936. 5 plates.

12. LORD, F. T.: A contribution to the etiology of actinomycosis. The experimental production of actinomycosis in guinea pigs inoculated with the contents of carious teeth. Boston Med. & Sur. Journ. **163**: 82–85. 1910.

13. LORD, F. T.: The etiology of actinomycosis. The presence of Actinomyces in the contents of carious teeth and the tonsillar crypts of patients without actinomycosis. Jour. A. M. A. **55**: 1261–3. 1910.

14. LORD, F. T. and TREVETT, L. D.: The pathogenesis of actinomycosis. Recovery of actinomyces-like granules from the normal mouth. Journ. Infect. Dis. **58**: 115–120. 1936.

15. NAESLUND, CARL: Experimentelle studien über die atiologie und pathogenese der Aktinomycose. Acta Path. et Microbiol. Scand. Suppl. VI. **8**: 1–156. 1931.

16. EMMONS, C. W.: Strains of *Actinomyces bovis* isolated from tonsils. P. R. Jour. Pub. Health & Trop. Med. **11**: 720–727. 1936. 2 plates.

PLATE I:

Patient with abscess on left scapular region (Case No. 1).

LÁMINA I:

Enfermo con un absceso en la región escapular izquierda (Caso Núm. 1).

CARRIÓN ACTINOMYCOSIS

PLATE I

PLATE II:

Figure 1.—Sagittal section of lung showing diffuse fibrosis of basal portions of right lower lobe and actinomycotic abscesses that have ruptured through diaphragmatic pleura.

Figure 2.—Decapsulated surface of kidney with abscesses.

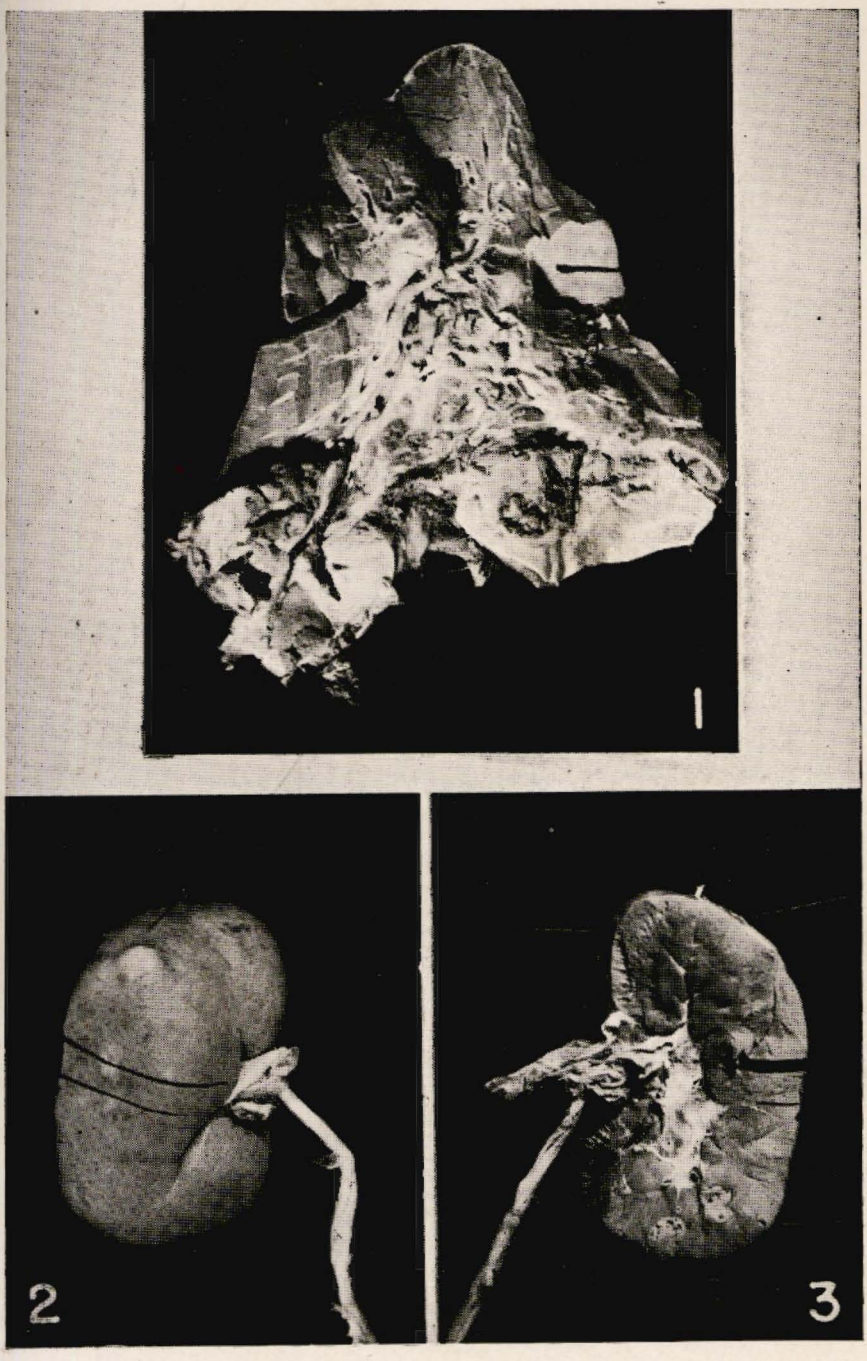
Figure 3.—Cut surface of kidney showing isolated and conglomerated abscesses.

LÁMINA II:

Grabado 1.—Corte sagital del pulmón, donde se puede observar una fibrosis difusa en ciertos sitios de la base del lóbulo inferior derecho y abscesos actinomicósicos que se han abierto a través de la pleura diafragmática.

Grabado 2.—Superficie descapsulada del riñón con varios abscesos.

Grabado 3.—Corte superficial del riñón mostrando abscesos aislados o conglomerados, en varios puntos.



CARRIÓN ACTINOMYCOSIS

PLATE II

PLATE III:

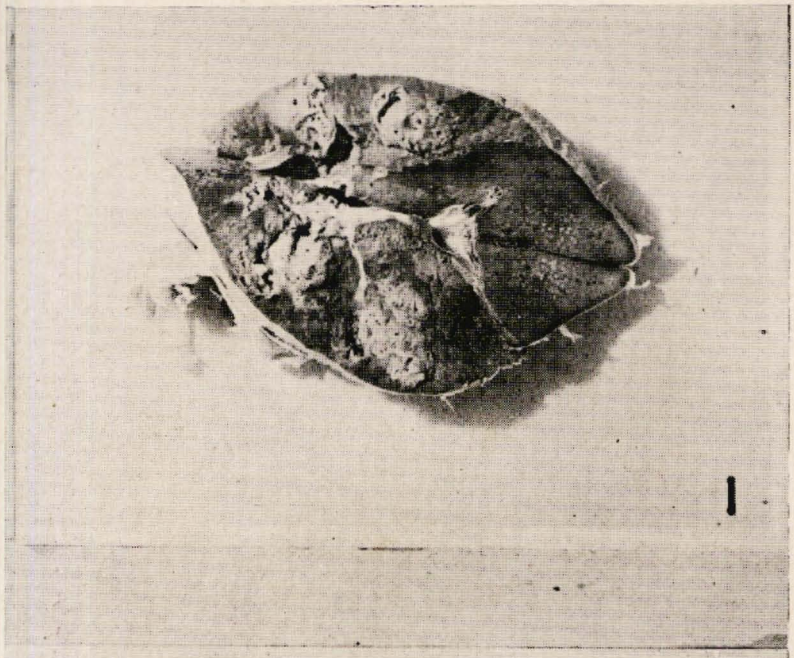
Figure 1.—Multiple metastatic abscesses in spleen.

Figure 2.—Large actinomycotic abscess of brain. Note the thick fibrous capsule.

LÁMINA III:

Grabado 1.—Abscesos metastásicos múltiples en el bazo.

Grabado 2.—Gran absceso actinomicósico en el cerebro. Nótese el espesor fibroso de la cápsula.



CARRIÓN ACTINOMYCOSIS

PLATE III

PLATE IV:

Lung: intense fibrosis of lower portions of right lobe, with round-celled infiltration and trapped alveoli lined by cuboidal epithelium. (x 80.)

LÁMINA IV:

Pulmón: fibrosis intensa de la porción inferior del lóbulo derecho, con infiltración de células redondas englobando los alveolos, que aparecen tapizados por epitelio cuboide. (x 80.)

PLATE V:

Lung: Actinomyces granule and polymorphonuclears in lumen of bronchiole. (x 344.)

LÁMINA V:

Pulmón: gránulo actinomicético con polinucleados, en la luz de un bronquiolo. (x 344.)

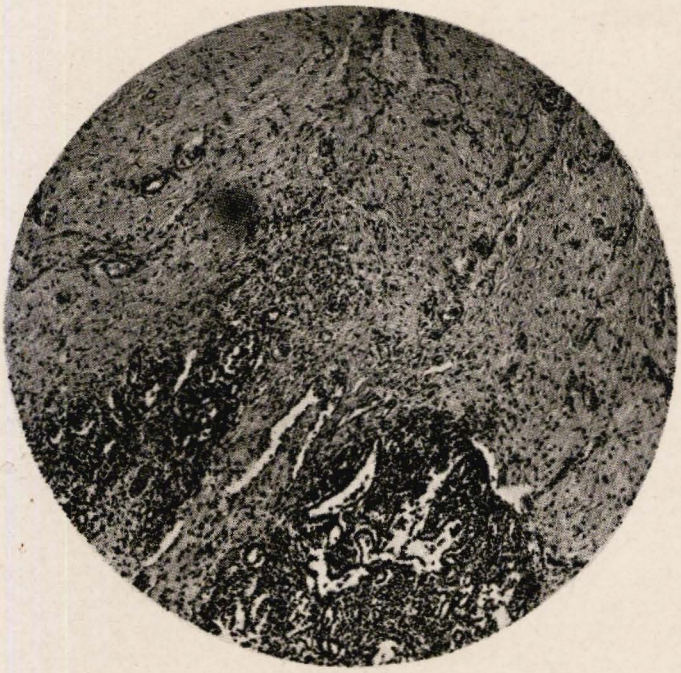
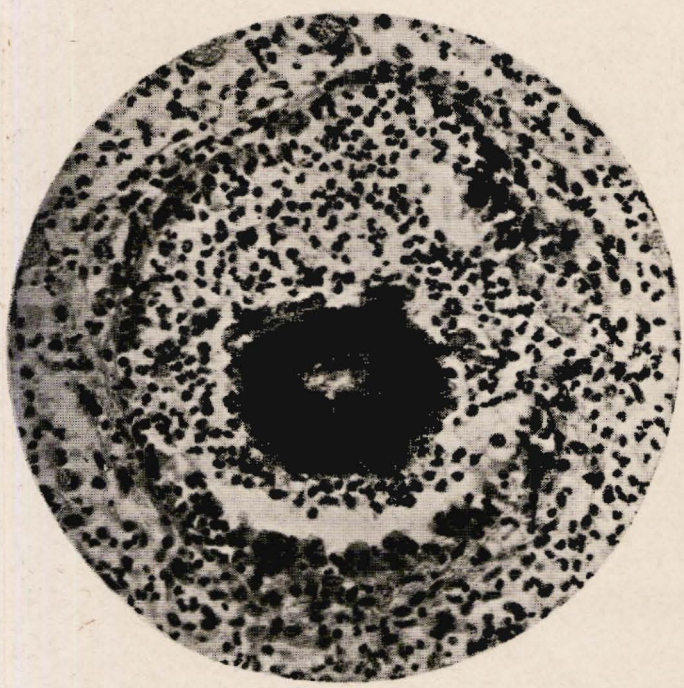


PLATE IV



CARRIÓN ACTINOMYCOSIS

PLATE V

PLATE VIII:

Heart: metastatic abscesses in myo- and epicardium containing Actinomyces granules and showing early peripheral fibrosis. (x 80.)

LÁMINA VIII:

Corazón: abscesos metastásicos en el miocardio y epicardio conteniendo gránulos actinomicéticos; puede verse además la degeneración fibrosa precoz en la periferia. (x 80.)

PLATE VIII

PLATE IX:

Figure 1.—Crushed, unstained granules from the exudate under low-power magnification (Case No. 1).

Figure 2.—Portion of marginal zone of one of the granules shown in Fig. 1.

Figure 3.—Oil-immersion view of the border of a granule showing clubs.

Figure 4.—A smear of the exudate stained by Gram's method (Case No. 1).

Figure 5.—Biopsy of lesion in Case No. 1, with typical actinomycotic granule. Note marginal clubs (high-dry magnification).

LÁMINA IX:

Grabado 1.—Gránulos desmenuzados (preparación fresca) procedentes del exudado, vistos a bajo aumento (Caso Núm. 1).

Grabado 2.—Porción de la zona marginal de los gránulos que aparecen en el grabado anterior.

Grabado 3.—Borde de un gránulo con mazas visto bajo el objetivo de inmersión.

Grabado 4.—Frotis del exudado teñido con Gram (Caso Núm. 1).

Grabado 5.—Biopsia de una lesión del Caso Núm. 1, con gránulos actinomicéticos típicos. Nótense las mazas marginales (objetivo de gran aumento, a seco).

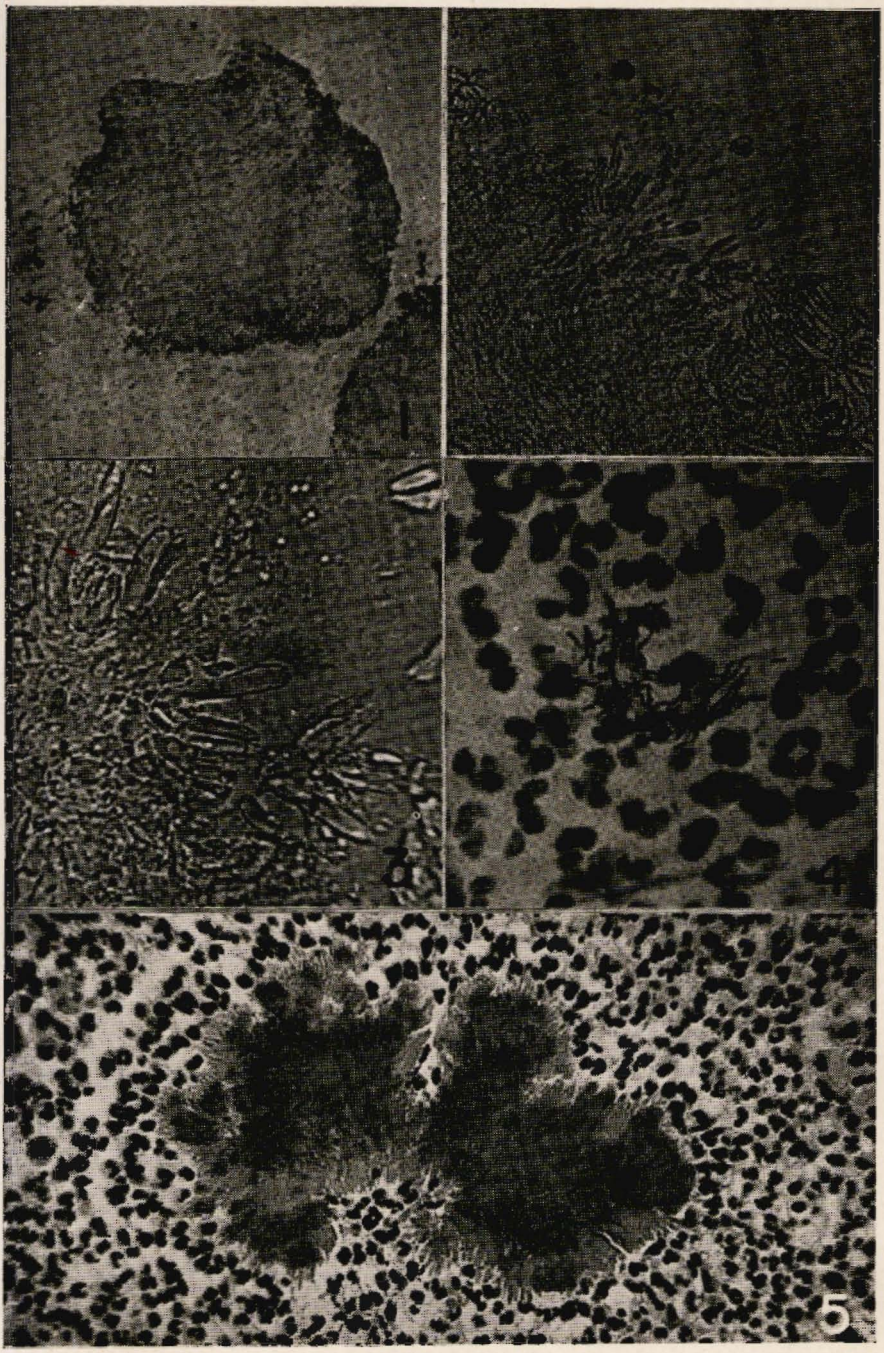


PLATE IX

PLATE X:

Figures 1 and 2.—Chopped meat broth cultures of the exudate (Case No. 1) showing typical colonies of *Actinomyces bovis*.

Figure 3.—Fresh preparation from a young culture of the fungus (*A. bovis*) in Case No. 2 (high-dry magnification).

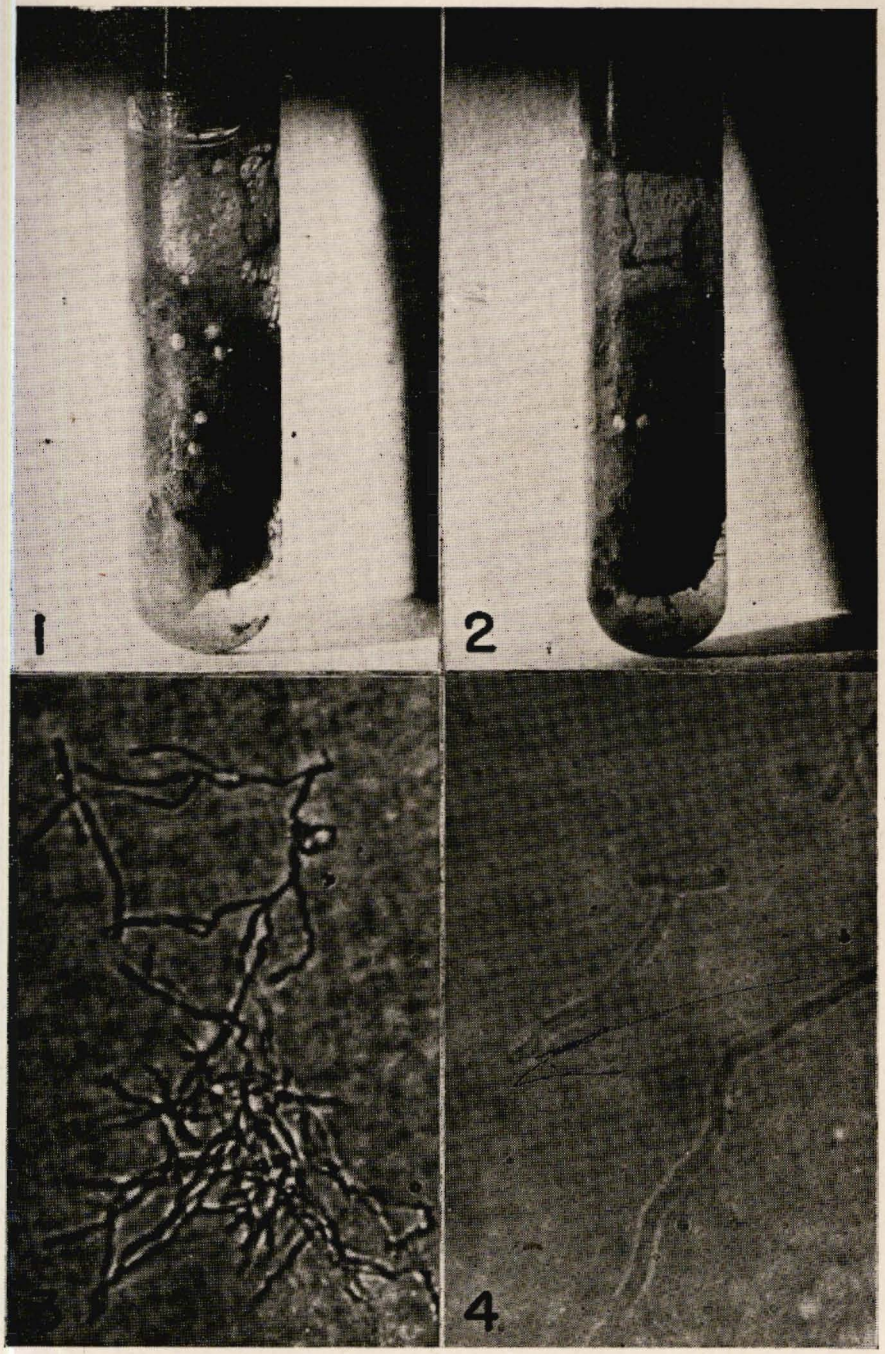
Figure 4.—Same as in Fig. 3 under higher magnification (oil immersion—x 2250).

LÁMINA X:

Grabados 1 y 2.—Cultivos del exudado en caldo con picadillo de carne (Caso Núm. 1), con colonias actinomicéticas típicas de A. bovis.

Grabado 3.—Preparación fresca de un cultivo reciente de A. bovis del Caso Núm. 2 (gran aumento, a seco).

Grabado 4.—La misma preparación anterior a gran aumento (objetivo de inmersion: (x 2250).



CARRIÓN ACTINOMYCOSIS

PLATE X