mally high degree of pressure in the cardiopulmonary arc. This increased pressure may be also brought about by remedies that produce vaso-constriction in the peripheral vessels, such as ergot, and it is most probably accentuated by the forcible action of the heart in consequence of nervous excitation occasioned by hemorrhage. It is clear that a pure cardiac sedative, e. g., aconite, by lowering the tension in the lung vessels, must meet an important indication, and it may be prescribed with much confidence in its efficacy. I have found aconite to be highly serviceable in one-drop doses every third hour; it is especially useful in cases presenting fever. Lawrason Brown⁸ suggests "that the blood pressure be frequently observed, that morphin be used when necessary to quiet the patient and so equalize the blood pressure, that sodium nitrite be exhibited to reduce when necessary the blood pressure, and that in case of a sudden hemoptysis amyl nitrite be administered at once when possible, to produce a marked fall in the blood pressure and so aid in a temporary cessation at least of the hemoptysis."

N. A. Johanson⁹ states that, in his experience, atropin in doses of gr. 1/50, repeated every twelve hours, has stopped hemorrhage when all other remedies have been of no avail. R. H. Babcock gives an immediate injection of atropin sulphate (gr. 1/50 to 1/25) when hemorrhage occurs from a cavity.

Successful treatment of the case in question must always be preceded by its reference to one of two categories previously mentioned, to-wit: (1) in which the hemoptysis is due to congestion or erosion of the smaller pulmonary vessels (most common); (2) in which there is profuse hemorrhage due to erosion of the larger pulmonary vessels or rupture of a small aneurism (comparatively rare).

The differentiation is greatly aided by remembering that the first class is composed principally of the early-appearing cases, while the second class represents the cases which, in addition to showing profuse hemorrhage, occur at an advanced stage of this disease, as a rule. As stated in other connections in this article, the point of highest importance in the treatment of hemoptysis according to the nature of the lesion producing it is that in profuse hemorrhage proceeding from one of the larger vessels or a ruptured aneurism, the cough is to be encouraged rather than stopped. Opiates are contraindicated.

SYSTEMIC BLASTOMYCOSIS AND COCCIDIOIDAL GRANULOMA.

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INTRODUCTION.

Since the description by Gilchrist in 1894 of blastomycetic dermatitis numerous instances of this infection have been recorded by American observers. The clinical course, the characteristic double-contoured, budding organisms, and the distinctive gross and microscopic anatomy—especially the marked epithelial hyperplasia, the minute epidermal abscesses, and the peculiar granulomatous infiltration of the corium—early established the entity of blastomycetic dermatitis so firmly that denial of its existence, especially by certain German writers, never has received serious notice. H. G. Wells discov-

ered the first case in Chicago, and the large number of cases observed in this city, especially by Professor Hyde and his associates, is noteworthy. Whether this apparent relative frequency of the disease here is in any way due to accidental conditions or to our being in the midst of an especially heavily infested territory remains to be seen.

The interest in blastomycetic infection enlarged when it became known that this infection may be systemic. Since 1902, when J. W. Walker and F. H. Montgomery reported the first case, nine cases of systemic blastomycosis have been reported from Chicago and its vicinity, and it is my purpose in this short communication to present in summary form the essential facts concerning these and certain other cases and to make certain comparisons with the so-called coccidioidal granuloma of California. Busse's well-known case of "saccharomycosis hominis," reported in 1894, and studied also by Buschke, clearly resembles, in many important details the cases reported from Chicago under the general name of systemic or generalized blastomycosis, and it is therefore placed first in the tabular summary. Curtis' case of human saccharomycosis also appears to belong to this group, and is therefore included in the list.

SUMMARY OF RECORDED CASES OF SYSTEMIC BLASTOMYCOSIS.

1. BUSSE-BUSCHKE (Busse, *Virchow's Archiv*, 1896, cxliv, 360; Die Hefen als Krankheitserreger, 1897; Buschke, Die Hefemykosen bei Menschen und Tieren, *Falkmann's Sammlung klin. Vorträge*, No. 218, 1898; Buschke, Die Blastomycose, 1902.); Woman, aged 31, housewife, born and lived in Germany.

Onset and Course of Disease.—Soft tumor below the knee containing glairy, reddish fluid; later disease extended to knee joint; abscess near elbow, also in left sixth rib; according to Buschke, ulcers, sometimes healing spontaneously, would appear on neck and forehead previously to development of tibial abscess. Busse describes ulcers on face as small and round with raised borders; coalescence formed larger sensitive ulcers; subcutaneous foci would form ulcers. Death.

External Lesions.—Borders of cutaneous ulcers sharp, irregular, undermined and infiltrated, surrounded by livid zone; bases composed of soft granulation tissue; numerous double-contoured parasites, often budding, in sections which on surface showed fibrin, polymorphonuclear leucocytes and red corpuscles, and a little deeper, giant cells, leucocytes, and small abscesses; epithelium either destroyed or proliferating.

Internal Lesions.—Abscesses in the right ulna, tibia, left sixth rib; abscesses and minute nodules in lungs, left kidney and spleen. No tubercle bacilli.

Microbiology.—Beginning cutaneous ulcers covered by crust, always gave pure culture of fungus. Pure cultures from abscesses in ulna and rib and from certain skin lesions, the organism proliferating chiefly by budding; Buschke, however, speaks of mycelium with cornidia; no endospores. Fungus not found in urine during life, but eight weeks before death a pure culture was obtained from the left median vein (Buschke). Organism virulent for dogs, rabbits, guinea-pigs, cats, white mice, causing inflammatory changes, the multiplication being by budding. Alcohol and carbon dioxide produced in grape sugar solution. Typical ulcers produced experimentally on skin of patient by rubbing in pure cultures (Buschke).

2. CURTIS (*Ann. de l'Inst. Pasteur*, 1896, x, 448); Male, aged 20.

Onset and Course.—Tumors in various parts of trunk, neck and extremities arising in the course of a few months. Death presumably from internal growths or meningitis after one and one-fourth years. No autopsy.

External Lesions.—Skin in places intact, in places ulcerated over tumors or abscesses, some of which were soft, others firm. Tumors composed almost wholly of organisms, intracellular and extracellular, the latter often double-contoured.

Microbiology.—Cultures obtained with which could be produced in white rats growths resembling those in the patient as well as disseminated internal nodules. No sporulating forms.

3. J. W. WALKER AND F. H. MONTGOMERY (F. H. Montgomery, *Jour. Cut. Dis.*, 1901, xix, 26; J. W. Walker and F. H. Montgomery, *THE JOURNAL A. M. A.*, 1902, xxxviii, 867); Man, 33 years old, resident of Chicago, carpenter.

Onset and Course.—Seven years before coming under observation pimple developed in skin of right shoulder following irritation and scratching; crusting and slow increase in size up to about silver dollar when stationary for years, then growth again particularly between scapulas. Recurring attacks of chills and fever lasting a few days, with signs of pulmonary involvement began 43 days before death, soon after curetting of original lesion. During this period lesions occurred under the right eye, in left temple, and in back. Lesions at first subepidermal, elevated, red, semiglobular, later epidermis fell off, leaving deep red surfaces soon assuming verrucous appearance. Emaciation, dyspnea, death. Diagnosis: Miliary tuberculosis.

External Lesions.—Original lesion raised, firm, well-defined, surfaces in places smooth, cicatricial, in others warty. Microscopically cellular infiltration in the corium with minute focal accumulations, epithelial proliferation, giant cells, and double-contoured, large organisms.

8. *Amer. Jour. Med. Sci.*, August, 1906.

9. *Denver Med. Times and Utah Med. Jour.*, June, 1906.

Internal Lesions.—Lungs, liver, spleen and kidney studded with numerous small nodules at first regarded as tubercles, but further study showed numerous typical blastomycetes.

Microbiology.—No cultures. Blastomycetes in lesions. No tubercle bacilli in sputum. Montgomery after long search found a few bacilli like tubercle bacilli in small abscess in skin near surface. Guinea-pig survived many inoculations.

4. GILCHRIST (*Brit. Med. Jour.*, 1902, ii, 1321): Man, 28 years old, negro.

Onset and Course.—In July, 1897, a small pimple appeared on abdomen which became "raw and red" and grew; a month later a second pimple appeared in right loin and followed same course. No attempt at healing. About 4 years later swellings appeared in right breast and right groin, both rupturing in a short time with discharge of mucoid pus; also fluctuating swelling at right of lower end of spine and swelling in axilla. Temperature 99-101.5 F. "Practically cured" in 6 weeks by 30 grains of potassium iodid three times a day. Gilchrist regards this case as one in which the disease just began to become generalized.

External Lesions.—Over right half of abdomen superficial ulcer, 9x16 cm.; second ulcer, 8x14 cm., extending over back from near right margin of the first; edges raised, smooth, with military abscesses, base papillary. Typical features of blastomycetic dermatitis in sections of ulcers.

Microbiology.—Pure cultures of blastomycetes (white mycelial growth with aerial hyphae) obtained from unbroken abscess in back, from swellings at right nipple and in right axilla. Smears from different lesions showed blastomycetes, but cultures were contaminated. Blood sterile. In sections organisms about 1 micron in diameter. Tubercloid nodules in lungs of dog injected intravenously with pus from unbroken abscess.

5. ORMSBY AND MILLER (*Jour. Cut. Dis.*, 1903, xxi, 121); OTIS AND EVANS (*THE JOURNAL A. M. A.*, 1903, xli, 1073): Man, 56, Swedish by birth, machinist, living in Chicago (?).

Onset and Course.—"Cold in chest" in April, 1902, followed by cough and bloody sputum. In June swelling of skin of thigh leading to discharge and ulcer. In July lesion of nose. Emaciation and weakness. October 8 nodules on arms and legs; 7 days later new crop. Lesions at onset painless nodules in which softening, often rapid, took place, with necrosis of skin and bloody purulent discharge. At one time 93 external lesions were counted. Fever. Lungs solid in places, but no tubercle bacilli in sputum. Laryngitis, purulent conjunctivitis. Death Dec. 4, 1902, body then practically covered with sores and swellings.

External Lesions.—Lesions situated mostly on posterior and internal aspects of legs; also on feet, thighs, upper extremities, scalp, face, chest, buttocks. Ulcers have irregular edges and necrotic floors with black crust. On dorsum of hand the only typical chronic blastomycetic ulcer. Microscopically, a deep nodule consists of enormous numbers of blastomycetes, often in groups, with leucocytes, red corpuscles, plasma, mast and connective tissue cells, as well as giant cells, commonly filled with organisms.

Internal Lesions.—Fibrous and fibrinous pleuritis with whitish nodules; four circular ulcers with smooth borders on epiglottis and larynx. Grayish or yellowish white nodules of varying size, liver, kidneys, pancreas, trachea, larynx—all containing characteristic organisms "in immense numbers." Center of nodules sometimes necrotic. Elastic tissue absent. Numerous and large giant cells with organisms. Parasites seen in blood vessel in kidney and in peribronchial lymph node. Lymph nodes otherwise free. Brain not examined.

Microbiology.—Remarkably large numbers of blastomycetes in lesions, especially pulmonary. Pure cultures obtained readily from various places during life and after death. Organism virulent for guinea-pigs and rabbits; in guinea-pigs local ulcers with pin head gray foci; in internal organs intact and small foci containing organism in pure growth. In this case thorough search for tuberculosis with negative result (tuberculin reaction absent, no bacilli demonstrated, no tuberculosis in inoculated animals). During necropsy an accidental inoculation of the skin of a participant took place followed by typical local blastomycetic ulcer.

6. CLEARY (*Trans. Chic. Path. Soc.*, 1904, v, 105; *Medicine*, 1904, x, 818): Man, 23 years old, Italian by birth, resident in Chicago.

Onset and Course.—Cough, mucopurulent expectoration, diarrhea, loss in weight during winter of 1903. Discharging sinus at right sterno-clavicular junction; albumin and casts in urine; no fever while under observation; edema of legs; signs suspicious of disease of apex of right lung; spleen palpable. Death June 4, 1905.

External Lesions.—None.

Internal Lesions.—Numerous gray and yellow areas, 2-4 mm. in diameter, with soft centers in both lungs, more in left; also, though smaller and less numerous, in kidneys, liver and adrenals, and microscopic foci in spleen and myocardium. Blastomycetes either free or within the giant cells, in all such nodules examined and surrounded by leucocytes and other cells. The center of the nodules commonly necrotic. Sinus in neck connected with small abscess. Amyloid in spleen, kidneys and adrenals. Chronic nephritis; bronchitis; edema of legs. Brain not examined.

Microbiology.—Typical blastomycetes, often within giant cells, but rarely seen in necrotic areas; blastomycetes in bronchioles. No cultures. Nothing said as to tubercle bacilli.

7. EISENDRATH AND ORMSBY (*Ill. Med. Jour.*, 1905, viii, 454; and *THE JOURNAL A. M. A.*, 1905, xlv, 1045); final report by LE COUNT AND MYERS (*Jour. Infect. Dis.*, 1907, iv, 187): Man, 33, Polish by birth, resident in Chicago, laborer.

Onset and Course.—Preceded by some discomfort in chest (February, 1904); external lesions began to appear in quick succession in June, 1904. When seen on Feb. 5, 1905, he was thin, pale, weak and feverish, with edema of the extremities, albumin and casts in urine, clubbed nails, dullness and bronchial breathing over right upper lobe. Blastomycetes in sputum. Under iodid of potassium internally and dressings local improvement took place, followed by relapse on abandonment of treatment. In September, 1905, symptoms of dorsal spondylitis developed, and in March, 1906, pus began to escape from the gibbus. Involuntary passages, ankylosis, eventually bloody and mucopurulent diarrhea became constant, budding organisms occurring in feces. Death in convulsions Aug. 23, 1906.

External Lesions.—Superficial, partly encrusted ulcerations with elevated edges, containing a few minute abscesses, on the legs; on the face similar lesions but more papillomatous; subcutaneous

nodules on forearms and infiltrations with pus. Lesions characterized by epidermal hyperplasia, minute abscesses and numerous giant cells enclosing blastomycetes.

Internal Lesions.—Blastomycetic bronchopneumonia; blastomycosis of the peribronchial lymph nodes, of the pleura, retropharyngeal tissue, liver, kidneys, colon (no organisms found in peculiar nodules in colon), dorsal vertebrae, external spinal dura (with compression of cord), cerebellum, left elbow, both knee and ankle joints, of the skin and subcutaneous tissue with ulcerations, fistulae and scars; fibrous induration at root of right lung. Area in cerebellum resembled large "solitary tubercle," but with more softening than usual in tuberculous brain foci and with abundant blastomycetes. Nodules in peribronchial lymph nodes and elsewhere possessed minute abscesses and necrotic areas, numerous giant cells and organisms.

Microbiology.—Blastomycetes present in pure cultures in pus; present also in sputum and in ulcers. Cultures of blood and urine sterile. No tuberculosis in guinea-pigs injected with purulent matter. Numerous blastomycetes in sections of lesions and in mass in cerebellum sporulating forms.

8. BASSOE (*Jour. Infect. Dis.*, 1906, iii, 91): Male, 17 years, born and living in Chicago.

Onset and Course.—Swelling in right scapular region since injury from fall in March, 1904. For some time previous pain in lumbar region and gnawing sensations in right upper lung with cough, night sweats and loss of weight. In July, 1904, abscess over right scapula emptied; again, in August when 500 c.c. of pus were evacuated from right lumbar region. Daily fever. Leucocytosis. Blastomycetes in sputum and in pus. Diarrhea. Albumin and casts in urine. Edema. Death June 27, 1905.

No typical cutaneous lesions.

Internal Lesions.—Chronic subcutaneous blastomycetic abscesses in right scapular region and loin; abscess and sinus walls made up of vascular granulation tissue rich in polymorphonuclear leucocytes, mast cells and blastomycetes. Blastomycetic caries of fourth and fifth lumbar vertebrae, with bilateral psoas abscesses, with blastomycetes in giant cells. Disseminated blastomycetic bronchopneumonic foci in both lungs. Areas of necrosis with Langerhans giant cells in the mediastinal glands, but no tubercle bacilli demonstrable. Amyloid degeneration of spleen, liver, adrenals retroperitoneal, mesenteric and mediastinal lymph nodes, kidneys and colon. Bilateral fibrinous pleuritis and mild serofibrinous peritonitis. Chronic parenchymatous nephritis. Atrophy of the heart. Pulmonary edema. Edema of feet and thighs. Trigolysis of ganglion cells of cerebral cortex and ventral horns of the cord (only upper cervical portions of latter examined). Only few giant cells in lungs.

Microbiology.—Pure cultures of blastomycetes from pus during life. After death cultures failed to yield blastomycetes, though organisms were present numerously in bronchial pus, pus from vertebrae and sinuses. Colon bacillus and staphylococcus obtained from various organs after death as well as other bacteria. No tubercle bacilli found in sections from lung after careful search.

9. IRONS AND GRAHAM (*Jour. Infect. Dis.*, 1906, iii, 666): Male, 47 years, German by birth, resident in Chicago, lumberman.

Onset and Course.—In March, 1905, nodule on right thigh, which "broke" and healed slowly with ulceration. Soon other similar lesions on forehead and extremities. Weakness, slight fever, swelling of ankles. When first seen (September, 1905) numerous healed and partially healed superficial lesions, resembling blastomycetic dermatitis, as well as subcutaneous abscesses. Soon cough set in with dullness and rales over lungs and appearance of blastomycetes, but no tubercle bacilli in mucopurulent, occasionally blood stained sputum. New external lesions with sloughing, extensive dissection, even denudation of bone, increasing anemia, leucocytosis, fever. Death Jan. 18, 1906.

External Lesions.—Multiple subcutaneous abscesses and sinuses involving the face, scalp and extremities; erosion of left parietal bone; deep sloughing ulcer of right thigh; numerous superficial ulcers and scars.

Internal Lesions.—Miliary blastomycosis of lungs and spleen; ulcerative blastomycetic bronchopneumonia; retroesophageal abscess with erosion of vertebrae; abscess of thyroid cartilage, fibrous pleuritis; atrophy of heart and liver; enlargement of the spleen and mesenteric lymph nodes. Microscopically nodules in lungs show necrotic centers surrounded by zone of giant cells and new tissue cells; giant cells all contain blastomycetes which also occur free; occasional bronchiole is found in center of area; blastomycetes in large blood vessel in lung near focus; blastomycetes in retroesophageal abscess; blastomycetes in cellular foci in spleen; no giant cells here. No amyloid.

Microbiology.—Cultures from the blood during life sterile; cultures from sputum and pus gave blastomycetes. Streptococci isolated after death from cerebrospinal fluid, liver, spleen, kidney and staphylococcus pyogenes aureus from liver, spleen, retropharyngeal and knee abscesses. Blastomycetes present in lesions, but after death isolated only from kidney. Virulent for guinea-pigs and rabbits causing local abscess and general miliary blastomycosis. Tubercle excluded thoroughly—no bacilli found in sputum, urine of pus, no tuberculosis in inoculated guinea-pig.

10. CHRISTENSEN AND HEKTOEN (*THE JOURNAL A. M. A.*, 1906, xlvii, 247): Male, 28 years, born in Norway, resident in Iowa, farmer and milk-peddler.

Onset and Course.—In November, 1904, acute fever lasting one week; at end of second week numerous red spots and lumps formed on face, neck, head, back and extremities; some subsided, others (especially in scalp) "broke and healed," and others grew into ulcers and abscesses. Loss of weight. In June, 1905, lesions on legs and foot extended; abscesses formed, first submaxillary, then subclavian, and on arms. In fall marked improvement, but in December all healing ulcers broke out again simultaneously; in January, 1906, 60 lesions of skin and subcutaneous tissue, most of them being ulcers and scars. Slight cough with bronchial rales. No tubercle bacilli or blastomycetes in sputum. Urine normal. Local and general treatment, including injections of blastomycetic vaccine, was followed by improvement. After leaving hospital in April, 1906, new foci appeared about right elbow. (For subsequent history I am indebted to Dr. C. Hoegh, Decorah, Iowa.) Cough subsided. Following abandonment of vaccine cutaneous lesions appeared to increase. Early in August pain between shoulder

1. The organism isolated from this case and those from cases 9, 10 and 11 have been subjected to detailed study by Hamburger, *Jour. Infect. Dis.*, 1907, iv, 201.

blades, especially on motion, with muscular tenderness, and pain in neck and upper spine on pressure on head. At noon August 15 sudden paralysis with anesthesia below neck. No cerebral symptoms. Some pain in neck, dyspnea, slowly increasing. Death August 16. No necropsy.

External Lesions.—Healed lesions often marked by brown depression. In addition to abscesses nodules with reddish blue skin discharging pus through many minute openings; when a little older red, granular, easily bleeding and tender ulcers would form; older ulcers may have elevated margins with papillomatous, crusted surface in which minute abscesses occur. Microscopically, cellular infiltration, minute abscesses, giant cells, blastomycetes and epithelial proliferation. No tubercles. No caseation.

Microbiology.—Numerous blastomycetes—no tubercle bacilli—in pus which yielded pure cultures of organisms of Ricketts' hyphomycetoid type.

11. CHRISTENSEN AND HEKTOEN (THE JOURNAL A. M. A., 1906, xvii, 247): Man, 58 years, born in Norway, farmer in Wisconsin.

Onset and Course.—Became acutely ill Jan. 23, 1905; three weeks later large abscess in left lumbo-sacral region, incision; somewhat later another similar attack with chills and weakness and development of swelling in left forearm; then on outside of right thigh, right forearm, and over left trochanter, red spots 2 cm. in diameter, increasing rapidly, forming crusts with offensive odor and assuming appearance of elevated ulcers which would heal partially and reopen. In October painful abscess of right arm, incision, sinus. Cough, fluctuating swellings of left arm. No enlarged lymph nodes. Bronchial râles, some temperature. In April tubercle bacilli, but no blastomycetes in the sputum. Died in March, 1907.

External Lesions.—Abscesses large as hen's eggs on arms. Ulcer 10x5 cm. on right thigh with undulating, elevated margins, the surface granular or papillomatous, covered with light crust. Warty area over left hip. Ulcer 13x7 cm. on right forearm, healing in center. Microscopically, no tubercles, no caseation, but typical blastomycetic infiltration with giant cells, epithelial hyperplasia and organisms.

Microbiology.—Blastomycetes, but no tubercle bacilli, in pus which yielded pure growths of organisms of hyphomycetoid type. Tubercle bacilli in sputum.

12. COLBY AND TRACY (Jour. Med. Research, 1907,): Male, 24, resident of New York City.

Onset and Course.—Several months after injury to left foot by clam shell, pain in back, and pain and swelling of back of left foot; in a few days fluctuation and a small sinus appeared, also two small swellings on outer aspect of right foot, which became encrusted, with pus underneath; about a week later like lesions appeared on the face and also numerous subcutaneous swellings in various parts, particularly thigh and arms, varying from hazelnut to small hen's egg in size, and usually breaking open spontaneously. Cough appeared and rapid emaciation. Patient still living at time of report.

External Lesions.—Lesions consisted of granulation tissue, infiltrated with leucocytes, and containing giant cells, spherical and budding blastomycetes.

Microbiology.—Blastomycetes in pus; pure cultures obtained; blood cultures sterile.

13. HERRICK, J. B. (THE JOURNAL A. M. A., 1907, xlix, 328): White, 24, resident of Chicago, wife.

Onset and Course.—April 24, 1904, illness began with "spots like bruises and pains like rheumatism;" first lesions over left gluteal region; during next two years 79 distinct lesions, from 1 to 5 cm. in width, starting as reddish or purplish spots in skin and subcutaneous tissue, and as a rule breaking open spontaneously; largest abscess over left gluteal region opened and drained; in some cases lesions destroyed bone; granulated ulcers with undermined edges would develop, leaving on healing a comparatively slight scar; lesions often highly painful. Usually some fever with exacerbations; no definite pulmonary lesions; anemia, leucocytosis, nervousness and insomnia; iodid of potassium only temporary benefit; while in California February to August, 1906, spontaneous perfect recovery.

COMMENTS ON SOME OF THE FEATURES PRESENTED BY THESE CASES.

Age, Nationality, Occupation of Patients.—The ages of the patients in these cases vary from 17 to 58 years. All save two (Cases 1 and 13) were men. The occupations given for the men all involve manual labor. While most of the Chicago cases occurred in so-called foreigners, yet the infection in every case unquestionably developed here either in Chicago itself or in its vicinity. So far there is no definite intimation in any of the published records of systemic blastomycosis that heredity or contagion have been found to play any rôle in the natural spread of the disease.

Eastman and Keene² describe an incised wound that became infected with blastomycetes and later with bacillus pyocyaneus; in this case the mother of the patient had been "troubled with boils," and when examined she was found to have in the axilla a hard mass as large as a hen's egg, and at the point of the elbow, where a swelling had existed, there was still some discharge in which were blastomycetes in large numbers. At the same time a son, 19 years old, had a swelling on the hip, which

broke spontaneously, but was still discharging. The author regards these as cases of blastomycotic family infection. Albers³ mentions the fact that the children of a man, who suffered from pain in the chest, cough and loss of strength, and whose sputum contained blastomycetes, had small pustules over the entire body, and the question is raised whether or not the disease of the children was blastomycosis.

Recovery from systemic blastomycosis has occurred in two cases, namely, in Case 4 in which Gilchrist thinks the disease was just beginning to be systemic, and in the interesting case (Case 13) reported by Herrick. In the fatal cases the duration has varied but in all months intervened between the evident systemic outbreak and death.

Onset and General Symptoms.—In some of the cases the onset seems to have been sudden (Cases 10, 11 and 13), and not unlike that of an acute febrile illness, manifestations of systemic invasion appearing shortly in the form of cutaneous, subcutaneous and deeper lesions. In these cases there is no definite indication of any early involvement of the lungs. In other cases (Cases 5, 6, 7, 8) pulmonary symptoms, such as cough, expectoration, discomfort in chest, were among the first to appear, to be followed in most cases before long by localization in various places, weakness, emaciation and fever. In Case 9 the early constitutional symptoms were slight, subcutaneous or subepidermal nodules appearing in various parts without any apparent cause. In Case 3 the systemic outbreak was marked by recurrent attacks of chills and fever, signs of pulmonary involvement and subepidermal lesions.

The lesions of systemic blastomycosis do not appear to be always painful. Some of the ulcers that form are spoken of as tender to the touch; others as highly painful.

The general course and symptoms of the established disease are in the main those of a more or less chronic, essentially pyogenic, infection, with a special tendency to superficial localizations. In the cases with subcutaneous and cutaneous lesions—nodules, abscesses, ulcers—and these cases are the more numerous, demonstration of blastomycetes in the pus or tissues is not difficult. In cases with pulmonary lesions blastomycetes may appear in the sputum, which may be blood stained. Hence there is no special difficulty in the way of a correct diagnosis in most of the cases.

Infection Atrium.—In two of the thirteen cases, namely, Case 3 (Montgomery-Walker) and Case 4 (Gilchrist), is there a history of a typical, chronic blastomycetic dermatitis existing for some time before the outbreak of the systemic infection. In Case 1 (Busse-Buschke) the facts as to this point do not seem to be quite clear. In the other cases, except Case 6, Case 8 and possibly Case 2, there occurred more or less explosive outbreaks, generally associated with well-marked febrile reactions, of subepidermal and subcutaneous lesions, some of which in time developed into typical superficial blastomycetic ulcers with raised borders, warty surface, miliary abscesses and efforts at central healing. In many of these cases the history points quite directly to the respiratory tract as the place of entrance of the infection and the bronchopneumonic character of some at least of the pulmonary lesions (Cases 7, 8, 9) may be taken to indicate their air-borne nature. In one of the cases (9) in which tuberculosis was excluded with especial care, there was some cavity formation in the

2. Annals of Surgery, 1907, 40, 613.

3. Trans. Chicago Path. Soc., 1907, vii, 21.

lungs. The occurrence of blastomycetes in the sputum in some of the cases is of interest first from the point of view of diagnosis and secondly as a means whereby the disease may be communicated to new hosts either by way of droplet or dust infection. The cutaneous lesions also would seem to afford ready avenues for escape perhaps to new hosts.

Distribution of the Lesions, etc.—In all the cases the distribution of the lesions as well as the evolution of the visible, external foci show that the dissemination of the organisms takes place in the blood. Indeed, the complete absence in the reports, except in Cases 4 and 7, of any mention of involvement of the lymph nodes, is noteworthy. The actual occurrence of the organisms in the blood has been demonstrated: Buschke obtained pure cultures from the blood in Case 1 and Otis and Evans (Case 5), as well as Irons and Graham (Case 9) found blastomycetes in the blood vessels in microscopic sections. In two cases, namely 6 and 8, were there no gross external lesions, and that in spite of localizations in the lungs, liver, kidneys, adrenals, spleen and myocardium in one, and the subcutaneous tissue, the vertebræ and lungs in the other. In nearly all the other cases the skin and subcutaneous tissue appear to have attracted the most extensive localization, which in some cases, but especially in Case 5, probably the most virulent instance in the series, continued quite steadily, or in more or less definite crops, up to the time of death.

There are several other interesting points worthy of emphasis. Thus the development of blastomycotic spondylitis in Bassoc's case (8) and also in Cases 7 and 10 (in the latter case the clinical course indicates such involvement), is noteworthy; other cases illustrate osseous involvement elsewhere. Here may be mentioned a case recently reported briefly by Brewer* of blastomycotic abscesses of the back with involvement of the vertebræ, but without any evidence as to the primary point of infection; the final outcome is not yet reported.

The facts that there has been involvement of the mucous membranes, the larynx and trachea presenting ulcers, in Case 5, and the colon peculiar nodules in Case 7, and that the central nervous system as well as the lymph nodes have been invaded (Case 7), are of great interest, but it is clear that many new cases must be studied carefully, both clinically and anatomically, before the full range of pathogenic possibilities can be defined accurately. Further observations are needed also in regard to the blood in systemic blastomycosis; especially indicated are more extended determinations of the number of leucocytes with differential counts.

In Case 11 there seems no reason to doubt the coexistence of systemic blastomycosis with pulmonary tuberculosis. In such cases it would be especially interesting to study the anatomic changes, gross as well as microscopic, in order to observe the mutual influence the two infections may have on the lesions peculiar to each.

The occurrence of amyloid in Cases 6 and 8 shows that blastomycosis must be included with those infections that may induce this change.

General Character of the Lesions.—Study of human material as well as material from inoculated animals shows that the micro-organisms in question may induce the formation of an inflammatory granulation tissue with numerous giant cells of the Langhans type associated with more or less extensive suppuration. The relative predominance of proliferative or suppurative processes appears to vary under various conditions. In

loose connective tissues, such as the subcutaneous, there seems to be a distinct tendency to abscess. And as shown in Cases 10 and 11 the pus of such abscess may contain pure cultures of blastomycetes. Microscopically, the more or less nodular lesions in which the proliferative changes are well marked, present certain general resemblances to those of tuberculosis. Real caseation and wholly typical tubercles, however, do not seem to occur. The smaller nodular lesions in the internal organs consist essentially of cellular accumulations around blastomycetes which frequently occur within giant cells commonly present in large numbers. When within giant cells and other cells the organisms may lose their adventitious capsules and evidences of disintegration of the organisms are not uncommon. In the older lesions there may be some necrosis in the center. The walls of abscesses contain phagocytic giant cells. In certain cases, e. g., Case 5, nodules or areas may form which consist largely of blastomycetes, which are rapidly proliferating by budding. The typical blastomycetic cutaneous ulcer has been described and figured so often that it is not necessary to go into details. Commonly it seems to begin as a papule or nodule, which softens, yielding a glairy, somewhat tenacious pus; a granulating surface forms which assumes a more or less verrucose appearance, and in the reddened, raised margin may be many minute abscesses. Larger subcutaneous nodules may cause pin-hole perforations of the overlying skin and even necrosis of larger areas. As the superficial lesion advances there is often cicatricial healing in the older parts. Cross-sections show in the active districts, first a papillary zone, and second a deeper, vascular, grayish-red zone, in which may be minute abscesses resting on subcutaneous fat. Microscopically, there are marked epithelial hyperplasia, sometimes spoken of as carcinomatoid, and a granulomatous infiltration of the corium with minute, often intraepithelial, abscesses and giant cells, as well as spherical, double-contoured, frequently budding organisms, generally from 10 to 30 microns in diameter. The number of blastomycetes present in such ulcers may vary, and in some cases prolonged search may be required. In sections from the ulcers in Cases 10 and 11 they were quite numerous. In the pus of larger abscesses the organisms as a rule are numerous and readily demonstrable in unstained smears of the pus diluted with 1 per cent. KOH solution or with the usual salt solution.

General Characteristics of the Micro-Organisms Concerned.—I do not wish to dwell any further on the morphologic details and staining peculiarities of the organisms in tissues. They are brought out quite distinctly by the usual stains, and according to Wolbach,⁵ Mallory's anilin-blue stain for connective tissue fibrils⁶ colors the capsule bright blue and the protoplasm red. Special stress must be laid on the fact that endogenous sporulation has not been demonstrated definitely in the organisms as they occur in the lesions of blastomycetic dermatitis and systemic blastomycosis, except that Le Count and Myers (Case 7) describe and figure endosporelation in the cerebellar lesion.

In his monograph on blastomycetic dermatitis, Ricketts⁷ points out that the organisms cultivated by various observers from the lesions of this disease up to 1902 fall into three groups: 1, Blastomycetoid; 2, oidium-like; 3, hyphomycetoid. All the organisms, however, exist in

5. Jour. Med. Research, 1906, xv, 167.

6. Ibid., 1905, xiii, 113.

7. Oidiomycosis (Blastomycosis) of the Skin and Its Fungi, Jour. Med. Research, 1902, vi, No. 3.

tissues in the blastomycetoid form and multiply there by budding principally. And such is the fact in all the cases I have tabulated as systemic blastomycosis, except in the forementioned Case 7 (Le Count and Myers), in which sporulating forms were found in the cerebellar mass only. In view of this fact the application to such cases of the term blastomycosis, which has secured a firm footing in the literature, seems not inappropriate, at least for the present. On culture media the blastomycetoid form exists chiefly as spherical or budding cells, but under suitable conditions it may produce abundant mycelium. The Busse-Buschke and the Curtis organisms appear to belong in this group. In culture the oidium-like group forms submerged mycelium which breaks up into chains of "spores," while proliferation by budding is not a prominent feature. The hyphomycetoid group produces fruit-bearing—terminal and lateral spheres—aerial hyphae, submerged hyphae, similar to those of the first two groups, and is also capable of multiplying by gemination. Hence from the first to the third group there is a gradual transit. Ricketts places all the organisms in the genus *oidium*. The organisms should be studied exhaustively by botanical methods in order to obtain better understanding of the life processes.⁸

THE "PROTOZOIC SKIN DISEASE" OF WERNICKE, RIXFORD
AND GILCHRIST—OPHÜLS' COCCIDIOIDAL GRANULOMA.

In 1891 Wernicke described an instance of a nodular and ulcerating skin disease with glandular and visceral involvement, in all the lesions of which were numerous spherical, often sporulating, double-contoured bodies, which he regarded as sporozoa. Posadas reproduced the disease in monkeys. In 1896 Rixford and Gilchrist recorded two similar cases from California which they also regarded as protozoic in nature. In 1900 two further cases were reported, also from California, one by D. W. Montgomery and one by Ophüls and Moffit. Since then several other cases have been observed (see summary). From the Ophüls-Moffit case pure cultures were secured for the first time, and Ophüls, tracing the growth in hanging drops, showed definitely that protozoan-like bodies, in every way similar to those seen in the lesions of the various human cases, give rise to a septate mycelium, which in its further growth forms spore-bearing, aerial and submerged hyphae. Further, that on inoculation of animals (dogs, rabbits, especially guinea-pigs) with this mould fungus these develop lesions that are similar to the human structure and in that the organisms they contain are spherical, double-contoured, multiplying by sporulation and not by budding. The size of the adult spherical organisms varies from 5 up to 30 microns or so. The sporulating forms which commonly show prickles or bristles on the outside membrane, may contain 100 or more minute spores; burst capsules from which the spores have escaped, or are doing so, may be seen. The protozoan-like bodies consequently belong to the life cycle of a mould which in the animal body multiplies by endogenous sporulation in media by mycelium and chlamydospores. Ophüls seconds the proposition of Ricketts to enlarge the genus *oidium* so as to include not only the organisms of blastomycosis proper, but also the sporulating variety just outlined, which Ophüls proposes to call *Oidium coccidioides*, and the disease it causes he would name coccidioidal granuloma. The principal facts concerning this disease are given in the summary.

8. Hamburger, Jour. Infect. Dis., 1907, iv, 201.

TABULATED SUMMARY OF THE RECORDED CASES OF COCCIDIOIDAL GRANULOMA ("PROTOZOIC SKIN DISEASE").

1. WERNICKE (*Jour. de Microg.*, 1891, xv, 14; *Centralbl. f. Bakt.*, 1892, xii, 861); POSADAS (*Rev. de Chir.*, 1900, xxi, 277); Man, born and living in Buenos Ayres.

Onset and Course of Disease.—Several years before death nodules began to form on face, trunk and lower extremities; nodules at first small, movable with skin, later often confluent and even ulcerating. *Diagnosis:* Mycosis fungoides. Left inguinal glands much enlarged. At time of death nearly whole body was involved.

External Lesions.—The cutaneous lesions showed a granulomatous growth in corium, often with central softening and generally with numerous giant cells, all containing coccidioidal bodies 3 to 30 microns in size.

Internal Lesions.—Numerous nodules in lymph nodes and viscera consisting of central giant cell with parasites surrounded by epithelial and embryonal cells. Numerous organisms in inguinal lymph nodes, as many as 60 being counted in one field.

Microbiology.—Cultures not obtained. Organisms observed regarded as sporulating sporozoa. No budding forms noted. Adult or vegetative form a sphere of granular protoplasm 25 microns in diameter, without nuclei, surrounded by birefractive sac, segmenting or invasive form beginning as small spherule in protoplasm. Organisms virulent for warm-blooded animals, especially monkey, causing same lesions as above, with same parasitic forms, which were constantly present in all inoculated animals.

2. RIXFORD and GILCHRIST (*Johns Hopkins Hosp. Reports*, 1896, i, 209); Man, 49, born in Azores, resident in California, laborer.

Onset and Course.—Disease first appeared on back of neck, extending slowly, remaining localized for 5 or 6 years, when like lesions appeared on eyebrows, nose, cheek, ear, back of right hand. Eventually, after eight years or so, regional lymph glands became involved, intermittent temperature, cough râles in lungs. Both eyes destroyed. Death in January, 1895.

External Lesions.—Destruction of eyes; partial of nose, left ear; extensive scars on face, neck, hand and active lesions about mouth and on scalp; sinus leading to dead bone on tibia and finger. Ulcer on neck 15 x 12 cm. (5 x 4 inches). Hyperplasia of epidermis, inflammatory infiltration with new growth of tissue and minute abscesses, giant cells and numerous "protozoa."

Internal Lesions.—Grayish nodules, 1 mm. in diameter with caseous areas, small cavities and scars in lungs; nodules on pleura, parietal peritoneum (diaphragm and pelvis), and in liver, spleen and adrenals. Purulent foci in bronchial and retroperitoneal lymph glands, in testicles, prostate and seminal vesicles. Mucous membranes normal. Nodules almost identical in microscopic structure with miliary tubercles; caseation. No tubercle bacilli found.

Microbiology.—"Protozoa" (*Coccidioides immitis*) in pus from testes, prostate, seminal vesicles, tibial sinus, sinus in hand and cutaneous lesions (during life), in lung cavities and nodules in adrenals, and infected lymph glands. "Protozoa" spherical, enveloped in double-contoured capsule, 15 to 27 microns in diameter, granular protoplasm; reproduce by sporulation, "sporozoites" escape through rupture in capsule, gradually enlarge and acquire capsule. Cultures failed. Some positive results from inoculations into animals. Infection regarded as coming from without because organisms were found embedded in stratum corneum near hair follicles.

3. RIXFORD and THORNE (*Occidental Medical Times*, 1894, viii, 704); RIXFORD and GILCHRIST (*Johns Hopkins Hospital Reports*, 1896, i, 209); Male, 33 years, Azores, laborer in California.

Onset and Course.—In June, 1894, hematemeses. In July two small pimples on forehead (left side), which became capped with vesicle and underwent purulent softening; gradual increase to patches 3 cm. in diameter. Shortly after, other spots, rather tender, appeared on face, scalp, trunk and upper extremities. In September glands of neck enlarged; rapid enlargement of epitrochlear gland after appearance of lesion on forearm; there was sore throat and cough; one inguinal node was enlarged; weakness; night sweats; fever. Death Sept. 21, 1894.

External Lesions.—Edges of ulcers red, elevated, ragged, indurated; surface papillary, bright red, covered by pus; 1 to 4 cm. in diameter; sections show numerous minute abscesses, epithelial hyperplasia, inflammatory infiltration, especially with leucocytes, and "enormous numbers of protozoa." No autopsy. Myriads of protozoa in cheesy material from bubo in left groin.

Microbiology.—"Protozoa" similar to those in Case 2, but generally larger and sporulation forms more numerous, sporozoites about 2 microns in diameter. Name of *Coccidioides pyogenes* proposed because of abundant pus production.

4. OPHÜLS and MOFFIT (*Phila. Med. Jour.*, 1900, v, 1471); OPHÜLS (*Jour. of Exp. Med.*, 1905, vi, 443); Man, 19 years, born in Azores, resident in California.

Onset and Course.—Chill followed by pleuritis, irregular fever, dulness over left apex and elsewhere; multiple acute arthritis; osteomyelitis of frontal bone; expectoration mucopurulent and blood streaked; night sweats; no tubercle bacilli in sputum. Leucocytosis 17,000. Death in three months.

External Lesions.—None.

Internal Lesions.—Irregular nodular consolidations, up to 1 cm. in diameter, with necrotic centers and abscesses in lungs in which were also distinct bronchopneumonic areas. Abscess in left lung extending through diaphragm into retroperitoneal glands. Left pleural empyema. Miliary foci in spleen, liver and both kidneys. Purulent osteomyelitis of frontal bone and both tibias with abscesses and perforation of skin; suppurative arthritis of both knee joints, right shoulder, both elbows and wrists. Lesions tuberculous in character with transitions to abscesses as well as formations of masses of fibrous tissue with occasional giant cells containing parasites.

Microbiology.—Parasites in all organs affected; adult forms in the less acute lesions and sporulating forms, especially in abscesses. First case to yield cultures of parasite (see text). No tubercle bacilli demonstrable.

5. MONTGOMERY, (D. W.) (*Brit. Jour. Dermatology*, 1900, xii, 343); Man, 21, born in Germany, telegrapher in California.

Onset and Course.—In July, 1898, first symptoms, namely, cough, night sweats, weakness, râles and dulness over lungs; no tubercle bacilli in sputum. Some 7 to 8 months later red, round, circumscribed nodules, up to one-half dollar size, with pus at top replaced eventually by an ulcer, appeared on scalp, face, neck

shoulder, forearm, wrist, upper arm, buttocks and thighs. Death June 7, 1899.

External Lesions.—Ulcers ragged, overhanging edges, granular floor, covered with scab; sections show giant cells and numerous parasites, many sporulating.

Internal Lesions.—Large fluctuating abscess over frontal eminence; abscess in mandibular fossa, supraclavicular fossa, and in subcutaneous tissue over chest, the latter connecting with one in clavicular fossa, and with pleura and lung; small abscess in lung, large in liver. Parasites in pus.

Microbiology.—Parasites spherical, with granular protoplasm, double-contoured capsule, and endogenous spores. Culture on glycerol agar gave a filamentous growth, discarded as contamination.

6. MONTGOMERY, (D. W.), RYKOGEL AND MORROW (*Jour. Cut. Dis.*, 1903, xxi, 1): Man, 54 years old, born in Switzerland, resident in California.

Onset and Course.—Gradual enlargement of left hand and forearm since 1893 and of left leg and ankle since 1894; in 1897 eruption on chest, in 1900 on left forearm and hand and soon after on neck and ears. In August, 1901, thick skin and subcutaneous tissue over left hand and forearm over both legs and left foot with separation of lower end of radius. Pigmentation of chest and abdomen. Discrete, closely placed papules and pustules over left forearm and hand. Right ear swollen and red. General health good. Some leucocytosis with eosinophilia. In December weakness, anorexia, fever; in January, 1902, superficial ulcers on chest. Death January, 1902.

External Lesions.—Diffuse infiltration of corium with groups of double-contoured, often sporulating organisms in old cicatricial tissue, each organism lying by itself.

Internal Lesions.—Left lung and upper right lobe infiltrated with bodies like milky tubercles composed of granulomatous tissue with giant cells and parasites. Suprarenals yellowish-white, friable, microscopically same as lungs.

Microbiology.—In October, 1901, cultures obtained from a macerated nodule in skin, mycelial threads arising from capsule of organisms and branching like mould fungus. Intraperitoneal inoculations of guinea-pig gave nodules on peritoneum and elsewhere, inflammation of scrotum, and caseous foci in lymph nodes. Nothing said as to tubercle bacilli in lesions of patient.

7. OPHÜLS (*Jour. Exp. Med.*, 1905, vi, 443): Male, born in Japan, resident in California.

Onset and Course.—Chronic ulcer of right foot below ankle on inner surface; inguinal lymph nodes large; later large abscess in anterior abdominal wall extending into pelvis. Large lymph nodes in neck. Patient passed out of sight. Ulcer red, elevated, 3 to 4 cm. in diameter, covered with brown scab. Inguinal lymph nodes large, dry, diffusely caseous. *Oidium coccidioides* in sections of ulcer and inguinal nodes. "Cultures in hanging-drops with usual results."

8. GARDNER AND HALTON (*California State Jour. of Med.*, 1904, ii, 386): Male, 32, born in Minnesota, of Swedish parents, living in California.

Onset and Course.—Jump from an engine sprained right foot which swelled up and became painful; abscess formed; able to return to work, but use caused swelling and pain. When seen four years later internal organs normal; no enlarged glands; right foot swollen, painful, no fluctuation; eventually small abscess opened and dead bone and granulation tissue removed; lymph nodes in right groin enlarged; no other external lesions; foot amputated and nodes removed; recovery.

Lesions.—All bones in foot except phalanges the seat of a rarifying osteitis and tibia and fibula carious. Sections showed nodules with giant cells and sporulating parasites; no tubercle bacilli present.

Microbiology.—*Oidium coccidioides* in lesions of foot and recovered in culture; no tubercle bacilli or oidia in lymph nodes; injection of cultures in abdomen of guinea-pigs caused caseous inflammation of tunica vaginalis and scrotal swelling.

9. OPHÜLS (THE JOURNAL A. M. A., 1905, xlv, 1291): Male, 62 years, born in Germany, baker in San Francisco.

Onset and Course.—Toward end of 1903 "cold abscess" developed in left side of chest and two ribs were resected; wound remained open. Large, soft, fluctuating swellings in neck. "Apparently cured." Granulation tissue from sinus in chest showed minute abscesses with giant cells containing parasites, many of which were sporulating. No skin lesions proper. Cultures obtained. (Nothing stated as to tubercle bacilli.)

10. OPHÜLS (Ibid., see Case 9): Man, Chinese, San Francisco. Resection of humerus on account of caries involving elbow joint. Patient died with symptoms of chronic pulmonary disease with purulent expectoration; no tubercle bacilli in sputum. Paraplegia. No autopsy. No external lesions. Extensive disintegration of bone with tubercle-like nodules with giant cells, areas of caseation and many organisms. Sporulating form in abscess. No cultures. (Nothing said as to search for tubercle bacilli.)

11. OPHÜLS (Ibid., see Case 9): Old man, German, living in San Francisco.

Unconscious when seen. Death. No external lesions. Scar at apex of lungs; pleural and pericardial adhesions with milky abscesses and nodules; basilar meningitis with nodules; nodules in kidneys and in spleen. Sporulating parasites in lesions; no tubercle bacilli.

12. OPHÜLS (Ibid., see Case 9): Man, 19, cannery in San Francisco.

Fever and chills for four weeks developing into symptoms of severe chronic meningitis. Death in three months. No external lesions. Old caseo-calcareous spot in peribronchial lymph node; irregular caseous process in adrenals; one nodule in kidney; basilar meningitis with nodules and extensive chronic spinal leptomeningitis with nodules and milky abscesses. Cord soft under thick pia. Terminal bronchopneumonia and urinary infection. Case regarded as one of tuberculosis until sporulating parasites were found in meninges without presence of tubercle bacilli; the latter present in adrenals.

13. WOLBACH (*Jour. Med. Research*, 1904, 13, 53).

The clinical side of this case is not discussed. The patient is still living, has traveled extensively and has been in California and New Mexico. The disease is connected with a history of chronic furunculosis for ten or more years, some of the boils having been very slow in development. Over both sides of the forehead and behind the left ear an ulcerative process had extended through the bone, stopping at the dura. All the lesions began

subcutaneously and were removed by surgical means without recurrences up to the time that the report is made. The organism was isolated in pure culture and caused in guinea-pigs tubercloid lesions containing pus in which occurred capsulated bodies 5 to 35 microns in diameter, many with spores, but without budding forms.

14. BRERROWS (unpublished case, cited by King, THE JOURNAL A. M. A., 1907, xlviii, 743).

Disease lasted 14 months; there were warty nodules at end of nose; multiple abscesses of lung, erosion of sternum, pleurisy with effusion, abscesses of sacrum, wrist, kidneys.

15. KING (Ibid., see Case 14): Man, Japanese, 25, laborer in California.

Onset and Course.—Nov. 5, 1905, fever, vomiting followed by cough and pain in joints, especially right ankle and left sterno-clavicular, later right wrist and left claviculo-scapular. Four weeks later swelling over right internal malleolus followed by similar swellings, all fluctuating successively; dorsum of right hand, right supraclavicular fossa, left supraspinous fossa; left sterno-clavicular articulation, all of which developed rapidly. Cutaneous lesions appeared. Emaciation. Jan. 23, 1906. Cutaneous lesions. Papillary lesions with tendency to progression appeared in various parts (chin, forearm, thigh, etc.).

Internal Lesions.—Abscesses with caries of the adjacent bone in the right supraclavicular region and apex of right lung, left sterno-clavicular articulation, left supraspinous fossa, dorsum of right hand, right ankle, mediastinal glands, peribronchial glands, general fibrinous peritonitis with enlarged mesenteric glands; no lesion of internal surface of digestive tract described.

Microbiology.—Pure culture from pus in supraclavicular fossa and in peritoneal exudate.

16. KING (Ibid., see Case 14): Man, 28, laborer in California.

Disease began with ulcer, punched out, red, with jagged edges, on left wrist which healed and formed again several times; ovoid tumor under left clavicle, and seventh, eighth and ninth left ribs, pus from which showed double-contoured, sporulating bodies. Three years later fatal illness diagnosed as acute milky tuberculosis.

"Autopsy showed the lungs to be studded with what appeared to be milky tubercles, and no further examination was made."

17. KING (Ibid., see Case 14): Male, 28, Japanese, railroad laborer in California.

Pain, swelling and redness in neighborhood of ankle joint and in cervical lymph nodes with suppuration, healing under surgical measures, further lesions again appearing near the old and on the face. Successful cultures from first abscess.

King also reports a case of multiple cutaneous pustules and irregular pulmonary consolidations, which he regards as probably coccidioidal granuloma, although the diagnosis is not confirmed by culture or microscopic demonstration.

FEATURES PECULIAR TO COCCIDIOIDAL GRANULOMA.

It is remarkable that all the cases so far reported have occurred in men. The occupation and nationality seem not to have any influence on the causation of the disease, all the instances of which save one (Case 1, possibly 2) appear to have originated in California. The clinical course is variable and has lasted from three months to nine years. When the disease is well established there may be intermittent fever, night sweats, increasing weakness. As in systemic blastomycosis, so also in coccidioidal granuloma we may distinguish between cases that appear to be primarily cutaneous (Cases 1, 2, 3, 16) and primarily respiratory (Cases 4, 5, 15); this leaves a larger number in which the atrium remains doubtful. Taking these cases of coccidioidal granuloma as a group we notice that while the lesions are distributed more irregularly than in systemic blastomycosis they are also distributed more widely, e. g., to the cerebrospinal membranes, to serous membranes, the joints, and, as especially noteworthy, commonly to the lymph nodes, regional as well as otherwise. In coccidioidal granuloma dissemination consequently occurs by way of the lymphatics as well as by way of the blood vessels, and it has been suggested that it is especially the minute forms—spores—that are carried by the lymphatics. As regards the cutaneous lesions in coccidioidal granuloma, suffice it to say that they vary somewhat; usually they begin as a papule or nodule and follow very much the same course as the cutaneous lesions of blastomycosis; at times, however, they may be more ulcerative. It is noteworthy that all the observers emphasize that the nodular lesions of coccidioidal granuloma may be indistinguishable from those of tuberculosis except for the fact that they contain sporulating parasites in place of the tubercle bacillus, which is absent. In fact, it has been observed that this disease presents the best mimicry of tuberculosis ever seen and the lesions

can not be distinguished from tubercles by the microscopic anatomy. Even typical caseation appears to occur. It has been noted that the adult forms of the *Oidium coccidioides* occur mostly in the less acute lesions, while the abscesses contain numerous sporulating and occasional budding forms. The spores appear to attract leucocytes which have been seen to enter the capsules (Ophüls).

On injection into the abdominal cavity of guinea-pigs the organisms from Cases 6 and 8 gave rise to caseous inflammation of the tunica vaginalis with scrotal swelling—a point worthy of consideration in working with material suspected of containing *B. mallei*.

SUMMARY.

Systemic blastomycosis and coccidioidal granuloma are caused by closely related varieties of organisms that Ricketts and Ophüls would place with the oidia. Culturally, these organisms may resemble one another very closely. In the tissues of the infected animal or human being in which both exist as spherical bodies, they present this striking difference: that the organisms of blastomycosis multiply almost wholly by budding, while those of coccidioidal granuloma multiply essentially by endogenous sporulation. Neither forms mycelium in the animal body.

Systemic blastomycosis and coccidioidal granuloma resemble each other in many respects, both clinically and anatomically, but at the same time there are certain well-marked differences of which the following appear to be constant and distinctive: 1. The nodular lesions of coccidioidal granuloma bear a closer resemblance to the typical, specific tubercle than the nodules of blastomycosis. 2. In coccidioidal granuloma there is marked tendency to involvement of the lymph nodes, in blastomycosis slight. 3. As already stated in coccidioidal granuloma the organisms multiply by endogenous sporulation in blastomycosis by budding.

Nothing is yet known concerning the conditions that lead to natural infection with either of these diseases, but human beings once infected appear susceptible and the apparent infrequency of the diseases may be explainable by assuming that as yet the occasion necessary for infection is infrequent.

MUNICIPAL REGULATION OF THE MILK SUPPLY.*

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"We can't do too much to help them. The future of this country depends on its poor children. If they are to do right, they must be saved from ill health, and ignorance and vice; and the first step is to give them good food and air so that they shall have strong little bodies."—PAUL LEICESTER FORD, in "The Honorable Peter Stirling."

If we take this statement at its worth, it means that the food of a child determines the future of the citizen and the physical strength of the potential fathers and mothers of the state. In guarding the milk supply we are not then confronted solely with the question of infantile sickness and death, with possible outbreaks of infectious disease through milk, but with a far larger problem, one of the greatest of social problems, that of the future of the race.

The first duty of man is to be a good animal. To be a good animal he must be well housed, well clothed and well nourished. In his duty to the state can he do less than to house, clothe and feed his children? Ought not the state do all in its power to aid the man in selecting shelter, clothing and food for his family, so that the wants of the many may not be exploited for the benefit of the few?

We are here to consider the ways and means by which the municipality, a political division of the state, may best protect the food of the infant. Milk is, of necessity, the sole food of the infant during the first and most important months of life, and it is to secure the municipal regulation of this food supply, by surrounding it with every possible safeguard, that we must address ourselves, both for the baby and for the state, both now and for the future.

This milk that the baby must have is the article of food that requires more care in its production and handling, and consequently more care in its supervision, than any other food. All through the many steps of production and handling this food supply of the baby must be protected. Not until the baby's milk has entered the baby's stomach must our vigilance be relaxed. For milk is unlike other foods; if once it is dirty it can not be cleansed. Most other foods may be heated without impairing their digestibility. Milk can not be so treated. Preservatives may be added to other foods without great harm to the adult. Who would permit the addition of preservatives to milk for the baby? Milk may be contaminated by the organisms of infectious diseases, diphtheria, scarlet fever, typhoid fever, tuberculosis, by any of the colon group and other allied organisms. Shall we by heat or by mechanical means chance the removal of part of the contaminating material, or shall we for the sake of the baby prevent these poisons from gaining access to milk? Other foods than milk may be kept at room temperature for long periods of time without change, cooked without change, subjected to mechanical operations without change, but it is not so with milk that is to be used as food for the baby.

We establish children's hospitals, we employ physicians to cure children affected by the diarrheal diseases of dirty milk, and at great expense we build and equip sanatoria for the treatment of men, women and children affected by the great white plague, and we permit the sale of dirty warm milk from filthy tubercular cattle, while the boards of managers of the children's hospitals and tubercular sanatoria cry out for more beds. Has not the time arrived when we may spend some more of our funds in preventing diseases, in educating the dairyman to produce clean milk, the public to demand and to pay for clean milk, and to insist that the tubercular cow be weeded out and its place taken by the clean, well-kept, disease-free cow?

If milk is so important as a food for the baby, are we not justified in protecting it from contamination? Is not the state warranted in adopting the most stringent rules and enforcing them to the extent of the law? In its extremity is there anything the state ought not to do, even to owning and thus controlling the milk supply, should such a measure be necessary to protect the food of the babies? Unless we do protect our children's food, we may some time find that, instead of strong men, we have a race of Houligans.

I think it is unnecessary to say more about the need of protecting the municipal milk supply, but before

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