THE SIMILARITY OF THE FUNGI CAUSING SOUTH AMERICAN BLASTOMYCOSIS (PARACOCCIDIOIDAL GRANULOMA) AND NORTH AMERICAN BLASTOMYCOSIS (GILCHRIST'S DISEASE)[1]

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Two serious granulomatous fungous infections, simulating each other and tuberculosis, have been known to occur in North America. The first, coccidioidal granuloma, was described by Rixford (1) and Rixford and Gilchrist (2) as a protozoan infection of the skin and other organs. *Coccidioides immitis* the large thick-walled, *endospore* filled organism seen in lesions of this disease was shown by Montgomery (3), however, to be a fungus and to develop a filamentous growth with *arthrospore* formation on suitable media. The second disease, blastomycosis, was described by Gilchrist (4) and Gilchrist and Stokes (5, 6) and *Blastomyces dermatitidis*, the large thick-walled *budding* organism, seen in lesions of this disease was shown to develop a filamentous growth with *lateral conidia* on suitable media. Since both the tissue and cultural forms of these organisms were quite distinct, there has been little difficulty, in this country at least, in diagnosing these two fungus infections in spite of the similarity of their lesions.

A granulomatous fungous infection confined to the mouth and regional lymphatics, was described from South America by Lutz (7) as pseudococcidioidal granuloma and by Carini (8) as blastomycosis. Splendore (9) described the first case of a generalized infection and later (10) named the fungus *Zymonema brasiliense*. Because of various interpretations of the method of reproduction of the fungus in tissue, Haberfeld (11) named the fungus *Zymonema histosporocellularis* while Arantes (12), Fonseca and Leao (13), Fonseca (14, 15), and Almeida (16) placed the fungus in the genus *Coccidioides*. Later, Almeida (17) compared vultures of *C. immitis* and the brasilian fungus and considered them sufficiently different to separate them and named the South American organism *Paracoccidioides brasiliensis*. Jordan and Weidman (18) also compared cultures of *C. immitis* and the South American fungus and found them to be different.

Moore (19, 20) further showed that the South American fungus should not be

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placed in the genus *Coccidioides* by demonstrating clearly that *Paracoccidioides* reproduced in tissue by single and multiple budding and not by endospore formation. The single budding forms, however, were said to be similar to and difficult to differentiate from those seen in lesions of North American blastomycosis (Gilchrist's disease). He separated the fungi, however, on the multiple budding characteristic of some forms of *Paracoccidioides* in tissue and on the presence of 8 spored asci in cultures of *Blastomyces*.

Although the South American fungus has been shown by these comparative studies not to belong to the genus *Coccidioides*, no detailed comparative study of several strains of *Blastomyces dermatitidis* and *Paracoccidioides brasiliensis* has been undertaken to show the relationship, if any, between the fungi causing South American blastomycosis and North American blastomycosis. It is the purpose of this paper, therefore, to make a comparative study of cultures obtained from these two diseases.

MATERIALS AND METHODS

The following cultures from cases of South American blastomycosis (paracoccidioidal granuloma) were obtained from Dr. Juan E. Mackinnon of the Facultad de Medicine, Instituto de Higiene, Montevideo, Uruguay and from the Centraalbureau voor Schimmelcultures, Baarn, Holland:

\#980 Instituto O. Cruz—Dr. Area Leão—*P. brasiliensis*
983 Instituto O. Cruz—Dr. Area Leão—*Systemic blastomycosis*
685 Instituto de Higiene, Montevideo—\#264 of F. de Almeida
717 Instituto de Higiene, Montevideo—\#96 of F. L. Niño, *P. cerebriformis*
718 Instituto de Higiene, Montevideo—125 of F. L. Niño, *P. brasiliensis*
724 Instituto de Higiene, Montevideo—G. Schouten, Asuncion, Paraguay.
673 *P. brasiliensis* C. B. S.
675 P. *cerebriformis* C. B. S.

The following cultures from cases of North American blastomycosis (Gilchrist's disease) were obtained from patients studied at Duke Hospital:

\#2 *Blastomyces dermatitidis*—systemic blastomycosis
65 *Blastomyces dermatitidis*—systemic blastomycosis
133 *Blastomyces dermatitidis*—systemic blastomycosis
4 *Blastomyces dermatitidis*—systemic blastomycosis
132 *Blastomyces dermatitidis*—cutaneous blastomycosis
657 *Blastomyces dermatitidis*—cutaneous blastomycosis
677 *Blastomyces dermatitidis*—cutaneous blastomycosis

All strains were compared as to their macroscopic and microscopic morphologic characteristics when grown on Sabouraud's dextrose agar, beef infusion agar, beef extract agar, blood agar and glycerine agar both at room and at incubator temperature (37°C.). The conversion of the filamentous form of these fungi to the yeast-like form seen in diseased tissue was followed by repeated examination of Van Tieghem cell preparations maintained at 37°C. All strains were studied for pathogenicity by injecting white mice intraperitoneally with 1 cc. of a 1:200

suspension (by volume) of the yeast-like form obtained from one week old cultures on blood agar at 37°C. Dr. Roger D. Baker of the Department of Pathology, Duke Hospital, kindly examined the sections prepared from these mice.

STUDY OF CULTURES

Blastomyces dermatitidis

Room temperature. When first isolated, most of the strains developed membranous, wrinkled or mealy colonies. The change from the membranous or mealy to the aerial type of growth usually took place first by projections of hyphae to give the coremial or so-called prickly stage of growth, but this was not constant. After several transfers all strains developed fast growing colonies, 35–40 mm. in diameter, at first with a well developed white cottony aerial mycelium which later became buff to brown (Plate I, fig. 1). All strains, therefore, at one time or another, displayed the three cultural types described for *Blastomyces*; namely, the mealy, the prickly and the filamentous stages.

Microscopically the mealy type of colony showed many single or budding, large round, thick-walled forms, 7–18 μ in diameter, identical with those seen in infected tissue or pus. Mixed with these forms was an initial mycelial development with the hyphae broken up into short, thick-walled, square ended elements (arthrospores), 2–2.5 μ x 4–6 μ in size (Plate II, fig. 2). At this time the culture was pasty, easily picked up with a loop and the scattered elements in the microscopic preparation were *Oidium*-like in appearance. As the mycelium developed further, however, the growing ends narrowed, 1.5 to 2 μ in diameter, septa, 10–15 μ apart appeared and the *Oidium*-like character of the fungus was lost. In the submatrical mycelium were seen many raquette cells, intercalary chlamydospores and many non-characteristic hypha swellings. With the development of aerial mycelium all strains produced sessile, round to oval condia, 3–4 μ in diameter, which were attached to the hyphae near septations. Borne on lateral sterigmata of varying lengths were seen round to pyriform condia, 4–5 μ in diameter (Plate I, fig. 3; Plate II, fig. 1). In old filamentous cultures many large, round to pyriform, thick-walled chlamydospores, 7.5 to 18 μ in diameter, were produced (Plate II, fig. 4). The outer walls of many of these chlamydospores were sometimes wavy in appearance and greatly thickened to give unusual sculpturing resembling closely the chlamydospores described in cultures of *Monosporium* (*Scedosporium*).

In none of the strains studied was there any evidence of ascospore formation. Although many hyphae fusions were seen in Van Tieghem cell preparations and slide cultures, repeated examinations over a long period of time (six months) failed to demonstrate any evidence of ascus formation resulting from the fusions. Lateral conidia, both sessile and on sterigmata, had numerous intracellular bodies which might be mistaken for ascospores. These bodies, however, were deeply stained with Scarlet Red, Sudan III, and Osmic acid and were considered to be fat droplets.

Incubator temperature. When the cottony, aerial growth of the room temperature cultures was transferred to blood, beef infusion, beef extract, glycerine

or Sabouraud's dextrose agar and incubated at 37°C., the resulting growth was smooth and waxy or cerebriform and wrinkled (Plate I, fig. 2). Microscopically these cultures were found to contain the yeast-like, budding forms of *Blastomyces* (Plate I, fig. 4). There were also several short, thick-walled, square-ended cells, (of the *Oidium*-type) either single or in chains of 3–4 cells.

The conversion from the filamentous to the yeast-like type of growth was followed microscopically by a study of Van Tieghem cell cultures which were inoculated with the mycelial form and incubated at 37°C. Small fragments of hyphae were seen to concentrate their protoplasmic content in one or two cells from which round or pyriform structures were formed. These bodies continued to grow by budding until they developed a mass of large, thick-walled, round cells (Plate II, fig. 9 a, b, and c). After breaking away from the mass, individual cells enlarged, continued reproducing by single buds and attained the character of the tissue form of *Blastomyces dermatitidis*.

Pathogenicity studies. All strains were grown on blood agar at 37° C. for one week and homogenous saline suspensions of the resulting yeast-like growth made.

TABLE I

Results of intraperitoneal injection of mice with 1 cc. of a 1:200 suspension of Blastomyces dermatitidis

NUMBER OF STRAIN	NUMBER OF MICE	SPONTANEOUS DEATH
		days
2	1	32
4	3	24, 25, 36
65	2	24, 37
132	1	18
133	4	(2) 24, (2) 33

№ 657 and № 677; mice were killed at 40 days.

White mice were injected intraperitoneally with 1 cc. of a 1:200 suspension (by volume) of this material. Some of the mice died spontaneously as a result of the infection; others were killed for gross and microscopic examination (Table I).

Macroscopically the mice which died as a result of the infection, showed a large yellow mass of caseous material lying at the lower curve of the stomach next to the spleen. Nodules of varying size were scattered through the omentum, mesentery and on the peritoneal surface and numerous nodules could be seen also on the surface of the liver, spleen, diaphragm and lungs (Plate III, Fig. 1). Cut surfaces of the liver and spleen showed an extension of the blastomycetic nodules deep into the parenchyma. The lungs showed an even distribution of nodules which was the result obviously of a blood stream invasion. The mice injected with № 657 and 677 showed minimal lesions with a few nodules in the mesentery and single nodules on the liver (№ 657) and spleen (№ 677).

Fresh preparations of the infected organs, made by crushing bits of tissue or caseous nodules in a drop of saline on a slide, showed the large, thick-walled, single budding forms of the fungus. In mice infected with strains № 2, 133, and 657, however, some of the yeast-like forms reproduced by two or more buds and

appeared not unlike those seen in the tissue form of the South American fungus (Plate II, Figs. 5, 8).

Microscopically the lesions consisted of masses of budding organisms with polymorphonuclear cells, lymphocytes, and large mononuclear cells (Plate III, Figs. 2, 3, 4, 5). Old lesions showed central necrosis with many poorly stained organisms, occasional polymorphonuclear cells, macrophages and surrounding fibroblastic cells.

Blastomyces brasiliensis

Room temperature. When first received, all of the strains were filamentous and could not be separated by colony characteristics into the three described species *brasiliensis, cerebriformis* or *tenuis.* Cultures started from material obtained from infected mice or from yeast-like cultures developed at 37°C. would irregularly become heaped, folded and glabrous and, for a time, would remain cerebriform in appearance. This cerebriform colony characteristic was most prominent on beef extract agar (pH 7.4). With continued growth, however,

TABLE II

Results of intraperitoneal injection of mice with 1 cc. of a 1:200 suspension of Blastomyces brasiliensis

NUMBER OF STRAIN	NUMBER OF MICE	SPONTANEOUS DEATH
		days
675	1	15
718	1	51
983	1	51
980	1	51
724	3	(1) 16, (2) 17

685 and #717. Mice were killed at 62; and 21, 41 and 62 days, respectively.

projections of aerial hyphae would occasionally give these cultures a prickly appearance. On all of the media used, the various strains studied eventually became covered with a short aerial filamentous growth and were white to light brown in color (Plate I, Fig. 5). All cultures were slow to develop, 1.5–2 cm. in diameter in three weeks, and the agar frequently split as a result of the compact manner of growth.

Microscopically the young glabrous, yeast-like colonies showed many round to pyriform, thick-walled, single and multiple budding forms, 3–25μ in diameter, identical to those seen in infected tissue or pus. The mycelium was composed of short, thick-walled cells, 2–3 x 4–7μ in size, which readily dissociated into arthrospores. These cultures were easily picked up with a loop.

As the cultures became older the submatrical mycelium varied greatly in size, produced numerous intercalary and terminal chlamydospores and many non-characteristic hyphal swellings. On the short aerial mycelium were developed round to pyriform, sessile conidia, 3–25μ in diameter (Plate I, Fig. 7; Plate II, Fig. 10). These older cultures were more compact, adhered to the agar and were not easily broken up.

PLATE I

FIGS. 1 TO 4. *Blastomyces dermatitidis*.

1. Mycelial culture 21 days at room temperature on beef infusion glucose agar.
2. Yeast-like culture 21 days at 37°C. on beef infusion glucose agar.
3. Photomicrograph of mycelial culture 700 x.
4. Photomicrograph of yeast-like culture 700 x.

FIGS. 5 TO 8. *Blastomyces brasiliensis*.

5. Mycelial culture 21 days at room temperature on beef infusion glucose agar.
6. Yeast-like culture 12 days at 37°C. on beef infusion glucose agar.
7. Photomicrograph of mycelial culture 700 x.
8. Photomicrograph of yeast-like culture 700 x.

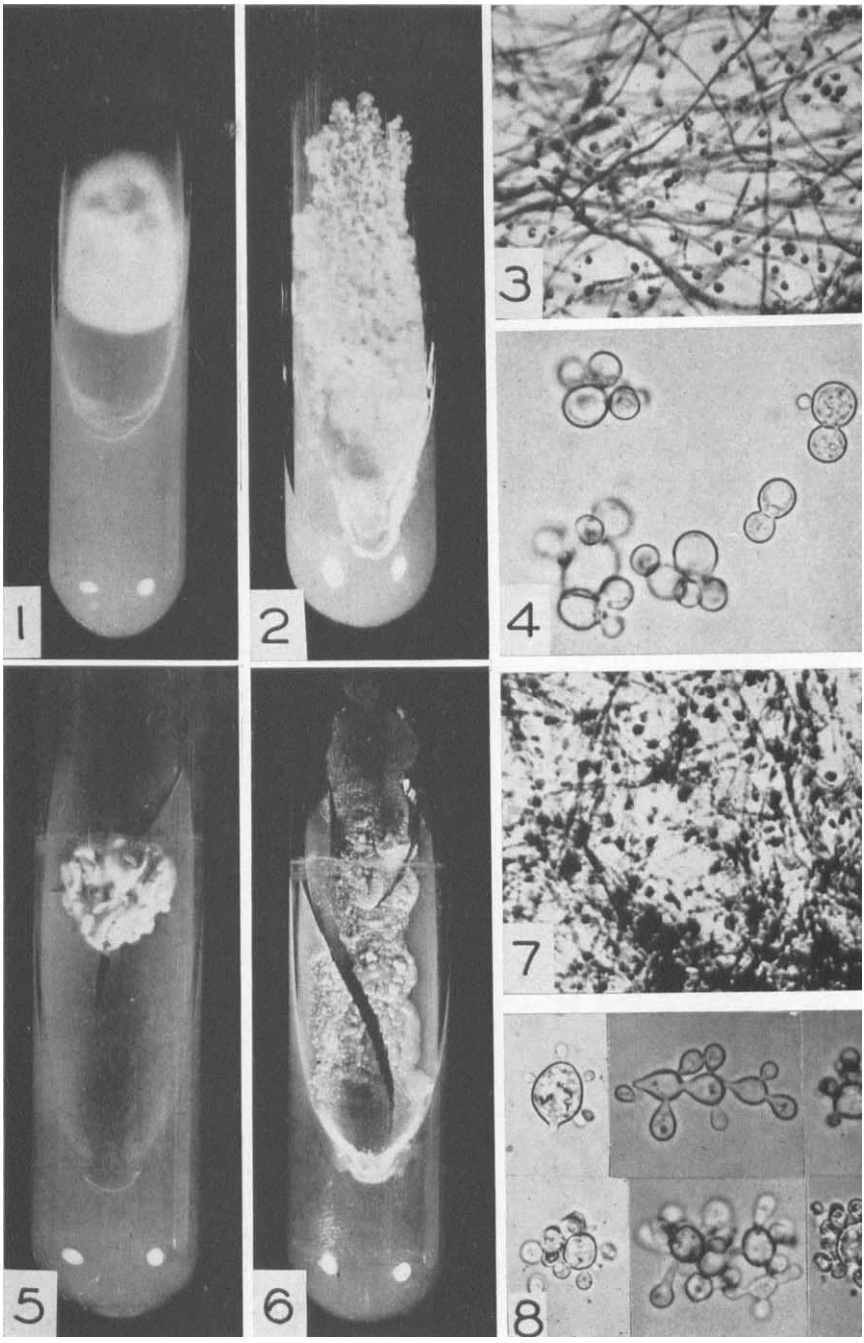

PLATE I
FIGS. 1–8

PLATE II

All drawings were made with the aid of a camera lucida at a magnification of 2000x.

FIGS. 1 TO 9. *Blastomyces dermatitidis.*

1. Conidia borne laterally either sessile or on short sterigmata; from Van Tieghem cell preparation on Sabouraud's glucose agar.

2. Short, thick-celled formation of "Oidium" type. Drawn from slide culture.

3. a, b, and c. Formation of lateral conidia by concentration of protoplasm from adjacent cells from Sabouraud's glucose agar.

4. Large, thick-walled chlamydospore from Sabouraud's glucose agar.

5 and 8. Single cells showing formation of two buds drawn from fresh mounts (saline preparations) of material from nodes in peritoneal cavity of mouse injected with culture #657 and #2.

6. Budding thick-walled cell drawn from fresh preparation (saline mount) of material from peritoneal cavity of mouse.

7. a and b. Formation of germ tubes from typical large, thick-walled cells of the tissue form.

9. a, b, and c. Conversion of mycelium to yeast-like stage. Drawn from Van Tieghem cell preparation at 37°C.

FIGS. 10 to 22. *Blastomyces brasiliensis.*

10. Conidia borne laterally from mycelium in two months culture on Sabouraud's glucose agar at room temperature.

11 to 15. Multiple budding forms from blood agar and beef infusion glucose agar at 37°C.

16 and 17. Bacilliform structures from blood agar and beef infusion glucose agar at 37°C.

18 and 22. Conversion of mycelium to multiple budding forms from beef infusion agar 3½ days at 37°C.

19. a, b, and c. Formation of lateral conidia by concentration of protoplasm from adjacent cells.

20. Germination of bud from a large multiple budding yeast-like form.

21. Single budding cell from beef infusion agar at 37°C.

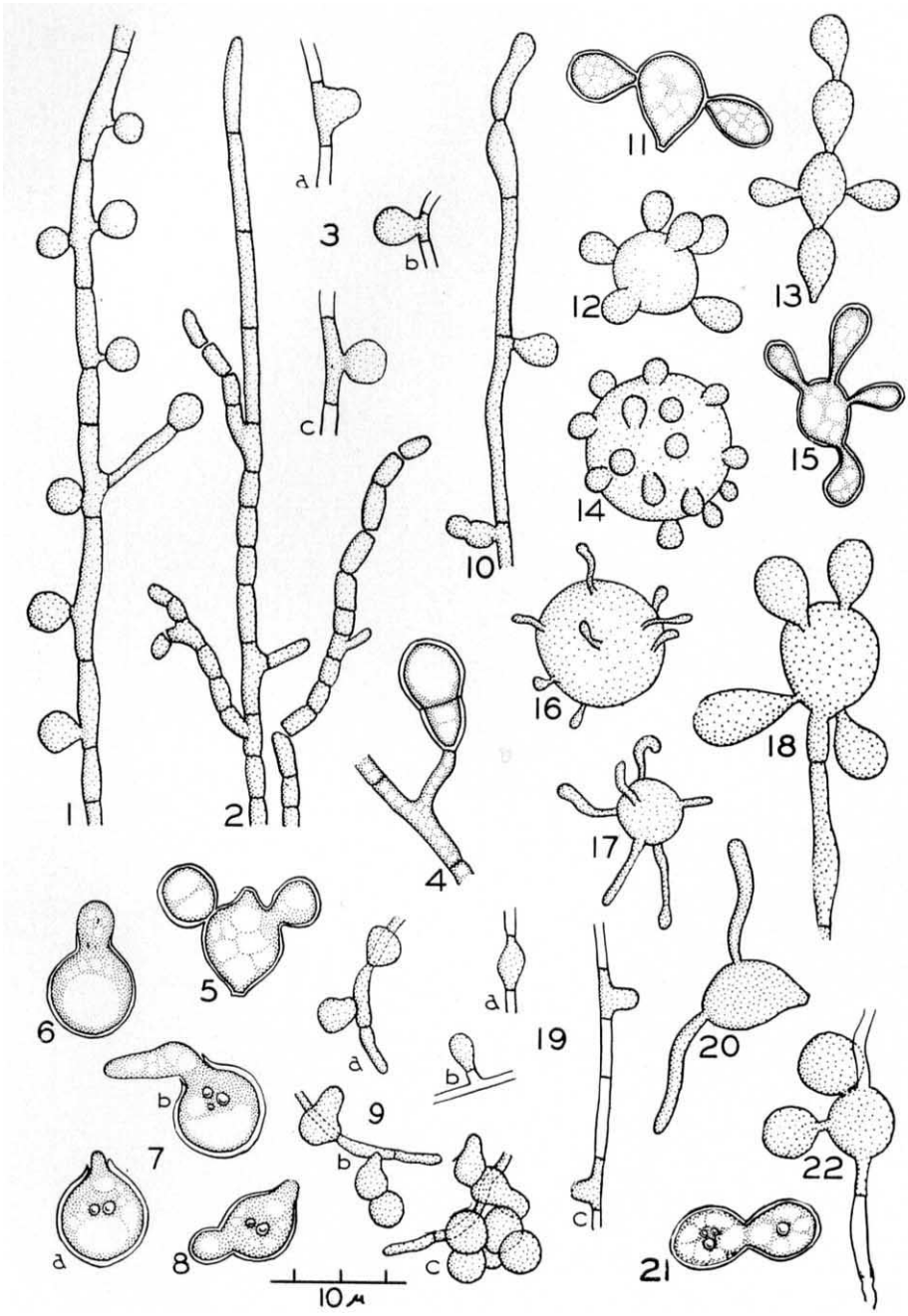

PLATE II

Figs. 1–21

PLATE III

FIG. 1. Mouse injected with 1 cc. of a 1:200 suspension of *Blastomyces dermatitidis* from blood agar culture at 37°C. Lungs, diaphragm, liver, spleen and masses of nodules in peritoneal cavity show extent of invasion.

2. Abscess in liver showing many invading organisms (287 x).
3. Abscess in spleen (287 x).
4. Abscess in kidney (287 x).
5. Extensive lesion in lung (287 x).

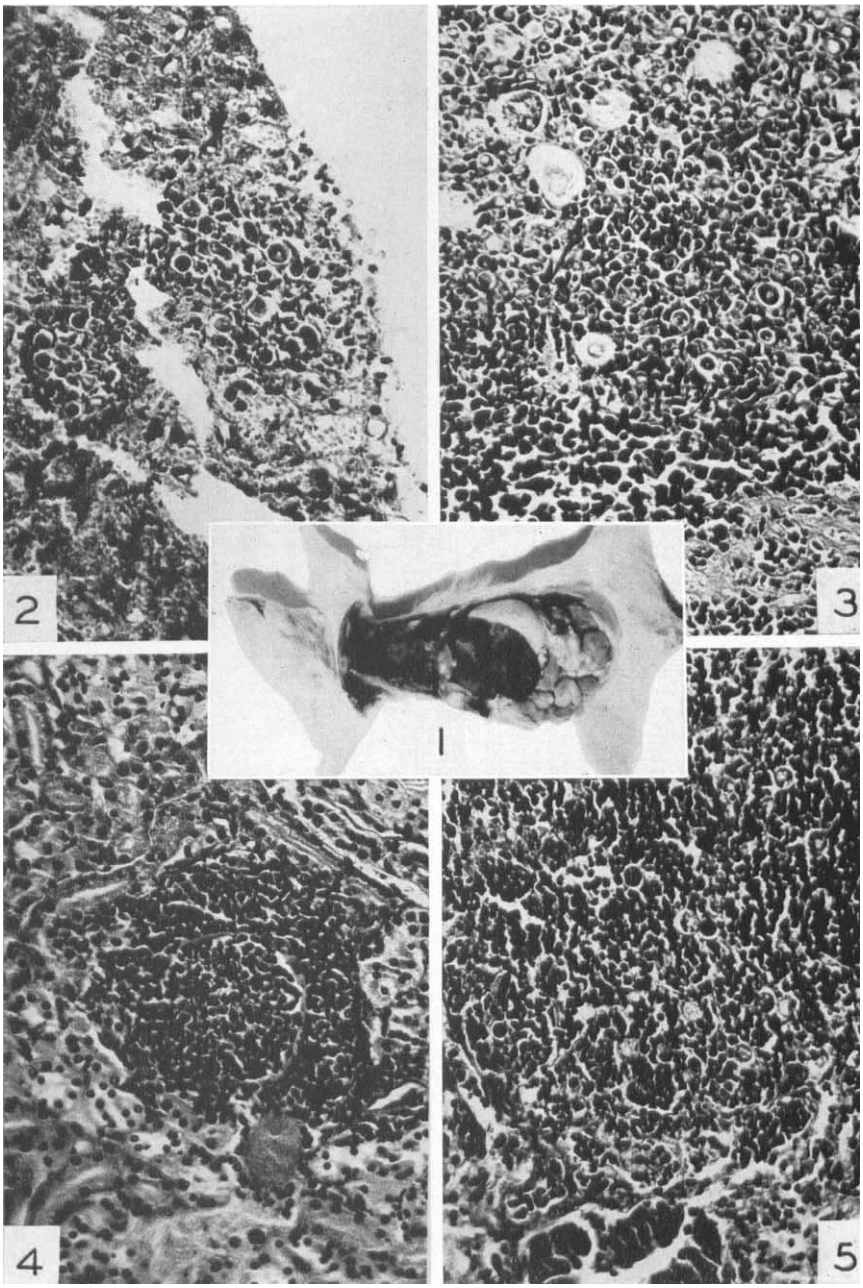

PLATE III

FIGS. 1–5

Plate IV

Fig. 1. Old fibrotic lesion in liver of mouse injected with 1 cc. of a 1:200 suspension of *Blastomyces brasiliensis* from blood agar culture at 37°C. (143 x).

2. Same showing organisms at edge of caseous central mass (287 x).

3. Section of lesion on diaphragm (287 x).

4. Section of lesion in spleen (287 x).

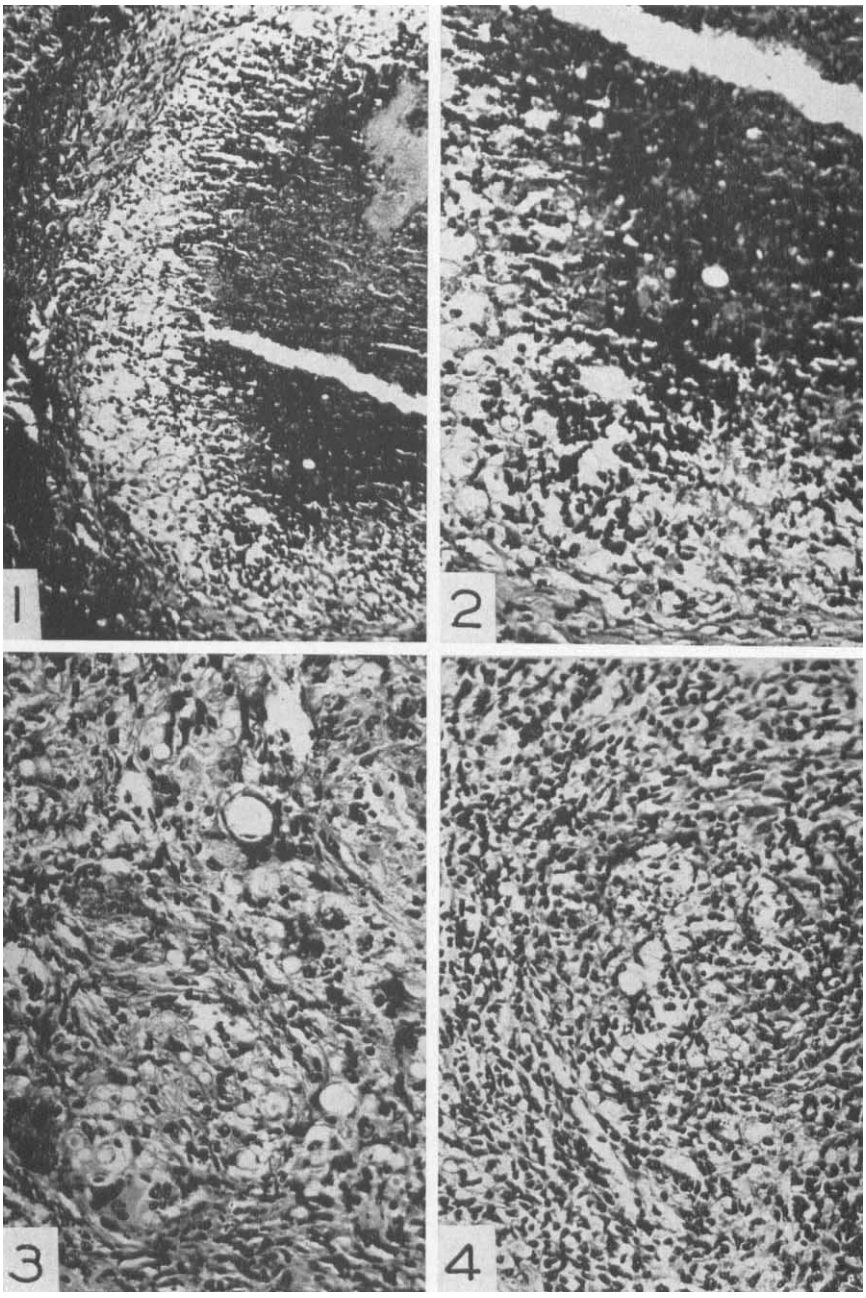

PLATE IV

FIGS. 1–4

Incubator temperature. When the filamentous growth of the room temperature cultures was transferred to blood, beef infusion, beef extract, glycerine, or Sabouraud's dextrose agar and incubated at 37°C., the resulting growth was smooth and waxy or heaped and cerebriform (Plate I, Fig. 6). Microscopically these cultures contained round to pyriform, single and multiple budding tissue forms of the fungus (Plate I, Fig. 8; Plate II, Figs. 11, 12, 14, 15, 21). While strains #673, 724, 718, 983 and 980 were composed entirely of the round, multiple budding forms, there also appeared a few short moniliform chains of 2–5 cells (Plate I, Fig. 8; Plate II, Fig. 13). Strains #675 and 717 were predominantly composed of the moniliform chains of cells but also had several of the round, multiple budding forms. The buds appearing on the surface of these large, thick-walled cells were round to oval, 1–15μ in diameter, or bacilliform (Plate II, Figs. 16, 17).

Conversion from the filamentous to the yeast-like type of growth was followed in Van Tieghem cell culture preparations inoculated with the mycelial form and incubated at 37°C. Here, as in *Blastomyces dermatitidis,* the hyphal fragments were seen to concentrate their protoplasmic content in one cell which became greatly enlarged, produced buds and finally assumed the appearance of the tissue forms (Plate II, Figs. 18, 22).

Pathogenicity studies. All strains were grown on blood agar at 37°C. for one week and homogenous saline suspensions of the resulting yeast-like growth made. White mice were injected intraperitoneally with 1 cc. of a 1:200 suspension (by volume) of this material. Mice injected with five of the strains (675, 718, 983, 980 and 724) died spontaneously as a result of the infection. Those injected with strains 673, 685 and 717, did not die spontaneously and were killed at various time intervals for gross and microscopic examinations (Table II).

With an equal quantity of material (1 cc. of a 1:200 suspension) *Blastomyces brasiliensis* took much longer to kill mice than did *Blastomyces dermatitidis.* On the whole, the lesions produced were milder, less extensive and had a tendency to resolve rather than progress. In none of the mice were lung lesions noted although one, infected with #717 and killed in 41 days, showed enlarged and caseous lymph nodes in the neck from which cultures were obtained.

Grossly the mice showed yellowish blastomycetic nodules on the liver, spleen and diaphragm with scattered nodules in the mesentery. One mouse, injected with #983, died in 51 days with fibrous adhesions of the liver and spleen to the peritoneal wall. There was also a mass of caseous material between the stomach and spleen which formed adhesions to the peritoneal wall.

Microscopically the lungs showed no infection. Lesions in the spleen, were composed of masses of fungus cells with lymphocytes and a peripheral accumulation of fibroblasts. Lesions in the spleen had caseous centers, poorly staining organisms at the periphery and, beyond this was seen cellular debris with polymorphonuclear cells and macrophages. The whole lesion was encircled with fibroblastic tissue. The nodules in the diaphragm showed mostly a fibroblastic reaction with numerous dead organisms, occasional polymorphonuclear cells through the mass and macrophages at the edge of the lesion. A few giant cells with intracellular organisms were seen in these lesions (Plate IV, Figs. 1, 2, 3, 4).

DISCUSSION

There are several parallelisms to be drawn between the fungi causing North American blastomycosis and South American blastomycosis. Both fungi produced yeast-like cultures at incubator temperature which contained the parasitic or tissue form of the fungus. Moore (19) separated these fungi generically because the South American form reproduced in tissue not only by simple, single budding cells as does *Blastomyces dermatitidis* but reproduced also by distinctive multiple budding cells not seen in the North American fungus. De Monbreun (21), however, first drew attention to multiple budding in *Blastomyces dermatitidis* when he described a few multiple budding forms from blood agar cultures at 37°C. The multiple budding forms reported in this paper, seen in fresh preparations of material obtained from mice infected with cultures of *B. dermatitidis*, were indistinguishable from some of the forms observed in the South American cultures and infected tissue. Therefore, while single budding forms predominated in the North American, and multiple budding forms predominated in the South American fungus, both fungi displayed morphologic types characteristic of each other.

Both fungi displayed a glabrous cerebriform and a filamentous type of growth at room temperature. An additional secondary prickly type of growth, long associated with the cultural characteristics of *B. dermatitidis*, was described and pictured by Almeida (22) for the South American fungus. In the cerebriform cultures of both the North and South American fungi were seen a few of the tissue forms and many *Oidium*-like arthrospores. The filamentous cultures of *B. dermatitidis* produced numerous sessile or pediculate conidia. Although these conidia were not frequent in the South American fungus, they did occur and were identical to those seen in *B. dermatitidis*.

These fungi could be separated generically only on the presence of 8-spored asci said to occur in *B. dermatitidis*. Most investigators have failed to confirm this and these structures could not be found in the strains studied in this paper or in a previous compartive study (23).

The fungi have been separated also on the clinical aspects of the diseases which they produced. The South American disease begins usually with oral lesions which may remain localized on the buccal mucosa with extension to the gums, tongue, and skin of the face especially around the nose. This so-called "lymphatic tegumentary" type may, after a period of chronicity, spread through the lymphatics to produce a generalized infection. The "lymphatic-visceral" type may also begin in the mouth but invasion of the tonsils quickly leads to a lymphangitis with cervical, axillary and inguinal nodes becoming enlarged. The liver, spleen, abdominal nodes and intestines are involved in this generalized form of the disease. The North American disease, on the other hand, begins in the lungs or on the skin and two types of infection, the cutaneous and generalized are recognized. The prominent mouth lesions and the intestinal lesions of the South American disease are lacking. Both diseases are essentially granulomatous, however, and the cellular reactions to the parasites are indistinguishable.

It is doubtful that different clinical manifestations in fungus infections should

always indicate great differences in the etiologic agents. It is now recognized that clinically different dermatomycoses may be caused by generically related fungi, e.g., classical favus caused by *Trichophyton Schoenleini* and Tokelau caused by *Trichophyton concentricum*.

It is our opinion, therefore, that the South American and North American fungi should be placed in the same genus. The differences noted in their cultural aspects and clinical behavior should be considered of specific rather than of generic importance. It is agreed that *Blastomyces* is not a satisfactory generic name for these fungi but should be retained until some generally accepted name is agreed upon. As only one species causes North American blastomycosis (23, 24) and the various species reported (19, 20) from South American blastomycosis differ only slightly in cultural aspects and morphologic characteristics and have, therefore, been reduced to synonymy (25, 26, 27), only two species need be considered, namely, *Blastomyces dermatitidis* and *Blastomyces brasiliensis*.

CONCLUSIONS

A comparative study of eight cultures from South American blastomycosis and seven cultures from North American blastomycosis shows these fungi to be sufficiently similar to be placed in the same genus; namely, *Blastomyces*. Two species are recognized; *Blastomyces brasiliensis* the etiologic agent of South American blastomycosis (paracoccidiodal granuloma) and *Blastomyces dermatitidis* the etiologic agent of North American blastomycosis (Gilchrist's disease).

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DISCUSSION

Dr. Morris Moore, *St. Louis:* I was very much interested in this report, principally because I went to South America in 1935 especially to study this disease and its organisms. While there I examined close to 300 cultures in the laboratories of Rio de Janeiro and São Paulo, Brazil, plus additional cultures in Uruguay and Argentina. Unfortunately, I cannot agree in regard to the classification of the organisms as presented. I am sure that you would agree that the clinical features are dissimilar. The South American organism may at times present forms in tissue which are similar to our North American organism, except that you find this curiosity. In the former there is a multiple-budding type of cell which produces many, many more types of buds than you find in the fungus of Gilchrist's disease.

There is a distinctly different type of organism found in South America, but when you go by the extreme variation in culture and morphology you will find that there are two specific types or species, each producing a different type of lesion. One produces the cutaneous lesion which may become systemic, and the other the localized buccal mucosa type of lesion which becomes systemic only in the terminal stages of the disease. The organism of the second type is much larger in appearance, is yeasty and cerebriform in growth while the former is not yeasty, but filamentous with aerial growth. Between these two there are variations.

I brought with me some cultures, clinical pictures and microscopic pictures which show these differences.

DR. FRED WEIDMAN, *Philadelphia:* I want to go a little further than Dr. Moore and say that I must disagree entirely with the presentor. A number of cultures of Paracoccidioides and also tissue have been sent to my laboratory from South America, and from studies of these I feel that for the purpose of diagnosis at least, there should not be any difficulty in distinguishing between the two parasites. It is true that their size is approximately the same, but the manner of budding is entirely different. Contrasting with the large buds of the North American form, there may be an absence of demonstrable ones in Paracoccidioides, or they may be so small that they can be mistaken for cocci,—at least in ordinary routine stains. Incidentally, it may be regarded as axiomatic that if there are any features which are likely to be of differential diagnostic value with respect to deep fungous infection, those seen in tissue are more effective than those seen in culture. The morphology of the microorganisms of several deep mycoses is far less distinctive in culture than it is in tissue. Of course, that stands in good stead for us; it is the "tissue form" that is the particular phase of mycology which should receive emphasis as we attempt to differentiate between the species.

When Dr. Conant first started to show his lantern slides, I thought that he was trying to prove that the two parasites were entirely different, which was contrary to the title of his paper. It seemed to me that even apart from the matter of tissue reactions, he showed that the morphology both in tissue and culture were sufficient to separate these two forms of fungus. Accordingly, all that is left in the way of similarity will have to reside in a common phylogenetic ancestor (in the perfect stage of the fungi in question), and at present that is far, far away. For practical medical purposes, I do not believe that the two forms are similar enough to bring them even into the same species.

DR. J. GARDNER HOPKINS, *New York, N. Y.:* Many of us recognize the desirability of simplifying the classification of these fungi and eliminating species that have been separated for no sufficient reason. In this discussion I suspect there has been some misunderstanding on account of a slip of the tongue. I understood Dr. Conant to say one species could include both the fungi under discussion, and yet he gave them two specific names and one generic name. Certainly anyone looking at the South American form as seen in section would feel sure he could differentiate it from the North American Coccidiodes, and I doubt whether Dr. Conant meant to include both in one species.

DR. N. F. CONANT, *Durham, N. C.:* It was my intention to demonstrate that one genus is probably sufficient to cover the two organisms; the one from South America could be called *Blastomyces brasiliensis*, the one from North America could be called *Blastomyces dermatitidis*.

We feel that the similarity of these two fungi outweigh the noted differences and that the latter should be considered of specific rather than of generic importance. As Dr. Weidman says, the South American fungus in tissue appears as a large body with multiple, small, 1μ buds which is quite unlike the large single budding appearance of the North American fungus in tissue. There have been numerous reports, however, describing the South American disease in which the infecting fungus was seen as a large single budding form.

While the North and South American forms of blastomycosis are similar histologically, they are quite different clinically. The clinical differences noted among fungus infections do not always mean, however, that different fungi are involved. We are all familiar with classical Favus and a tropical fungus infection known as Takelau. These two fungus infections are notably different clinically; but when we get cultures from both of these diseases the fungi are found to be identical macroscopically and microscopically. Very probably, they both belong not only to the same genus but to the same species. There are also many other widely separated clinical conditions which are known and are recognized as being caused by the same fungus.