A REVIEW OF THE GENUS *CANDIDA*

CHARLES E. SKINNER[1] AND DONALD W. FLETCHER[2]

Department of Bacteriology and Public Health, Washington State University, Pullman, Washington, and Department of Biology, San Francisco State College, San Francisco, California

I. Introduction

This review attempts to cover the literature on the genus *Candida* which has appeared since an earlier review (180) published 13 years ago. More literature on this genus has been published in the 13 years since 1947 than ever before. The increased interest in these yeastlike fungi has necessitated eliminating from consideration all papers dealing with the important medical aspects of *Candida* species. Over 500 papers had been examined (and the end was not in sight) when it was decided, early in the preparation of the review, that it would be better to cover the nonmedical aspects reasonably completely than to make a partial covering of the whole field.

In 1952 appeared a very important taxonomic treatise (88), "The Yeasts. A Taxonomic Study," by Lodder and Kreger-van Rij. This solid and indispensable work has, to a very considerable extent, supplemented the three earlier monographic treatises (35, 87, 182) of the Dutch School of zymologists. Actually this book is so well prepared and generally so scholarly in its detail that there is very real danger that scientists may consider it "the authority," and refuse to take issue with any of the taxonomic conclusions of the authors.

Wickerham (211) has more recently reviewed the literature concerned with yeast taxonomy, giving coverage to those reports appearing between 1948 and 1952. Included in this review, and indeed the basis for it, is the treatise by Lodder and Kreger-van Rij. Although published in the same year, the latter more effectively covers the literature to 1950. In 1958 an excellent text (33), "The Chemistry and Biology of Yeasts," edited by A. H. Cook, appeared. Here Lodder, Slooff, and Kreger-van Rij have taken the opportunity to extend somewhat but, for the most part, merely summarized their 1952 contribution.

II. Nomenclature and Taxonomy

All steps but final approval have been taken to legalize the generic name *Candida* (164) as a *nomen conservandum* and this epithet is now almost universally accepted. *Syringospora*, the name having priority, is used by few writers (118). Quite properly the always incorrect name for yeastlike fungi, *Monilia*, is now almost universally reserved for only the imperfect stage of certain ascomycetous fungi. Unfortunately, Chemical Abstracts indexes these species of *Monilia* under *Candida*, a usage not sanctioned by any other usage, or indeed by any principles of taxonomy.

Although the nomenclature for *Candida* as a genus seems to be stabilized, the taxonomy is

[1] Late Professor and Chairman, Department of Bacteriology and Public Health, Washington State University, Pullman; deceased, May 1958. This review was completed by the junior author, who takes responsibility for the accuracy of the text and citations, and for any omissions.

[2] San Francisco State College, San Francisco, California.

not. It is becoming more and more difficult to make a reasonable distinction between *Candida* on the one hand and *Cryptococcus* and *Torulopsis* (*sensibus* Lodder and Kreger-van Rij) on the other. *Candida* has a true or pseudomycelium (46), and the other two genera are supposed to lack the ability to form these structures in all media and under all conditions. Connell and Skinner (31) have shown that many cultures of anascosporogenous yeasts when first isolated were completely devoid of mycelium even in such mycelium-producing media as corn meal agar and beef peptone gelatin, but after a few years cultivation, and with frequent transfers, they became definitely mycelial. In other words, when first isolated they would have to be diagnosed as *Torulopsis* (or *Cryptococcus*), but after cultivation, as *Candida*. Also many of the cultures studied by Diddens and Lodder (35) previous to 1942 were not mycelial, and were diagnosed as *Torulopsis*, but these same cultures had to be diagnosed as *Candida* by Lodder and Kreger-van Rij (88) in 1952. This may be due partly to improved methods of study, but it may well also represent the tendency of many yeasts to become filamentous on continued cultivation (31). Moreover, it has been shown that certain isolated cultures of *Torulopsis* copulated with haploid cultures of definitely filamentous perfect yeasts and that ascospores were formed. In addition Wickerham and Burton (210, 212) have shown that isolates of *Candida chodati* and *C. guilliermondii* are heterothallic and that when certain of these strains are cultured together the perfect stage can be isolated. They further state that the cultures in various collections from all over the world are capable of producing ascospores when properly mated.

The tendency toward filamentation upon continued cultivation has resulted in transferring such well known species as *Torulopsis pulcherrima* and *T. utilis* to *Candida*. The writers do not agree with this taxonomy and, except for a few citations, will not include in this review papers which refer to these two species. It must be admitted that while we have never considered pseudomycelium a good taxonomic character for yeasts, we still have no suggestion for a better one. It would not be difficult to maintain the thesis that there is no reason other than convenience for the retention of *Candida* as a genus.

The following new species, listed with their sources, have been described since the Diddens and Lodder (35) monograph. New combinations are not included. Some of these seem to be definitely different from species already recognized but, in the opinion of the writers, little is gained and much is lost in excessive splitting of species (6). Even the mild lumping tendency by Lodder and Kreger-van Rij (88), who recognize 30 species, might, with benefit, have been carried still further. *Candida malicola:* apples, Canada (29, 30). *C. pseudotumoralis:* causative agent of canine "blastomycosis," France (119). This chlamydospore-producing species is probably *C. albicans* or *C. stellatoidea;* it has not been properly described and must be considered a *nomen nudum*. *C. silvicola:* insects, U. S. A. (177). *C. sorbosa:* insects, Hawaii (62). *C. solani:* potato starch factory, the Netherlands (88). *C. custerii:* wine, Italy (51). *C. castellanii:* yogurt, Portugal (192). *C. bovina:* bovine caecum, Portugal (194), apparently closely related to the thermophilic yeast *Tortulopsis pentolopesii*. *C. bovina* differs from the latter by its larger cells, formation of pseudomycelium, habitat, and ability to grow at room temperature. Kreger-van Rij (78) considers *C. bovina* to be the imperfect stage of *Saccharomyces tellustris* and therefore questions calling it a new species. *C. claussenii* and *C. melibiosi* are new species made by the segregating of other species (88). Wickerham and Burton (212) have challenged the formation of a new species for *C. melibiosis*, since they have subsequently shown it to be identical with *C. guilliermondii*, on the basis of assimilation and mating experiments.

Martin (109), in an excellent article, described two "strains" of *Candida reukaufii* which differ in certain rather fundamental physiological characteristics. Strain *A* characteristically produces a pseudomycelium, its growth on beer wort agar is slimy and shining, with a brown pigment, and it actively ferments glucose. Strain *B* produces little or no pseudomycelium, is cream colored, produces no slime, and shows only slight glucose fermentation.

Windisch (220) reports the formation of ascospores in *Pseudomonilia* (*Candida*) *albomargenata* (Geiger) under conditions similar to those reported by him for *Candida pulcherrima*. An excellent discussion of this original work and subsequent research can be found in the Lodder and Kreger-van Rij treatise (88) and the thesis of Van der Walt (195).

One important taxonomic change in the lump-

ing direction was made by Lodder and Kreger-van Rij. The genus *Mycoderma* has been discarded and all seven species have been relegated to one species, *Candida mycoderma*. This seems to be a good way to handle this troublesome but economically important group of organisms, all of which form a heavy pellicle on liquid media. It does involve some annoying points in nomenclature. The lumping might possibly have been extended to include the well-known pellicle-forming *C. krusei*. The differences between *C. krusei* and *C. mycoderma* seem to be the amount of fermentation of glucose and degree of filamentation. Mackinnon (98) suggested several years ago that he found it very difficult to differentiate *C. krusei* from species of *Mycoderma*, and Ansel and Gauthier (7) have put *C. krusei* in the genus *Mycoderma*. Probably neither of these suggestions to put all species in *Mycoderma* or in *Candida* as *C. mycoderma* will obtain immediate and general acceptance, but it is likely that all the film-forming imperfect yeasts will eventually be classified in the same genus, and possibly in the same species. Even the placing of all species of *Mycoderma* into the one species was not well received (202). And indeed it is evident that if Lodder and Kreger-van Rij had ignored biochemical differences in other species to the extent that they have within this group, the number of species of *Candida* would be far fewer than are now recognized.

Lodder and Kreger-van Rij have simplified the classification of the important lactose-fermenting yeasts. They have reduced *Torulopsis kefyr* to synonomy with the only lactose-fermenting species of *Candida*, *C. pseudotropicalis*, since pseudomycelium has been found in their culture after 31 years of cultivation, and have finally placed the important *Torula cremoris* in the same species. One might also regard *C. pseudotropicalis* as the filamentous form of *Torulopsis sphaerica* and both species as imperfect stages of *Saccharomyces fragilis* (63). All lactose-fermenting species could be referred to one of these three species without undue lumping, in the reviewers' opinion.

Support of the taxonomy of Lodder and Kreger-van Rij is offered by the work of Jonsen *et al.* (72), who have succeeded in the isolation of strains of *C. albicans*, *C. stellatoidea*, and *C. pseudotropicalis* which are identical with the type strains of Lodder and Kreger-van Rij, culturally, morphologically, and serologically. *C. albicans* and *C. stellatoidea* share many common antigens (agglutinogens) and unless hyperimmune sera are used they are indistinguishable. There is little sharing of antigens however between these strains and *C. pseudotropicalis*.

III. Ecology of Candida

Since the 1947 review (180) a number of new habitats have been established for several species of *Candida*. Excellent original papers on the ecology of yeasts (18, 48, 92) and several reviews (93, 123) have given a partial covering of the past literature. It should be emphasized that the common assumption of so many medical writers that the genus *Candida* is found primarily associated with the animal body is justified by scant evidence. Even less justified is the assumption that all species of *Candida* are potentially pathogenic. Di Menna (113) has made an excellent comparative study of the nonpathogenic yeasts of human skin and the alimentary tract; her results parallel those of Connell and Skinner (32). Both investigations indicate that human skin surfaces are true habitats for certain yeasts, including *Candida* spp., and there seems to be a characteristic skin flora. Yeasts seem to live and multiply on the skin and to persist there for some time, and they appear to be as normal there as, for instance, *Micrococcus* or *Staphylococcus* spp. In the carefully performed study by di Menna (113), 120 strains of yeasts isolated from human skin and 388 from air and from room surfaces were compared. Like Connell and Skinner (32), she found a quantitative and qualitative difference in the flora, but to a lesser extent. She did not find, however, the high incidence of fermenting species or the low incidence of *Rhodotorula* spp. reported by Connell and Skinner.

The following new habitats for species of *Candida* have been recorded during the past 13 years. *C. brumptii:* soil, New Zealand (112, 114). *C. guilliermondii:* fruit processing plant, U. S. A. (159); shrimp, U. S. A. (149); soil, Denmark (92); insect, U. S. A. (150, 152) and Denmark (92). *C. intermedia:* insects, Hawaii (61) and U. S. A. (117). *C. krusei:* flowers, mushrooms, dung, Denmark (92); home baked millet bread, Portugal (178); citrus fruit processing plant, U. S. A. (159); insects, U. S. A. (36); garlic bulb, Mexico (168); turbid beer, England (217). *C. lipolytica:* soil, New Zealand (114); beer, Germany (222) and England (217); air, U. S. A. (32). *C. mycoderma:* tomato, fermenting coffee,

Mexico (167, 169); dried egg yolk, Hungary (225); exudate from trees, dung, soil, Denmark (92); insects (25, 89, 152). *C. mesenterica:* mushrooms, dung, soil, Denmark (92); insects, U. S. A. (152). *C. melibiosi:* citrus fruit processing plant, U. S. A. (159). *C. monosa:* insects, Hawaii (61); olive infusion liquor, Italy (28a). *C. melinii:* citrus processing plant, U. S. A. (159). *C. parapsilosis:* soil, Denmark (92), New Zealand (114); citrus fruit processing plant, U. S. A. (159); shrimp, U. S. A. (149); flowers, fruit, root crops, dung, mushrooms, exudates from trees, Denmark (92); insects, U. S. A. (25, 89, 152). *C. macedoniensis:* soil, New Zealand (114). *C. pelliculosa:* citrus fruit processing plant, U. S. A. (159). *C. rugosa:* insects, Hawaii (62). *C. zeylanoides:* insects, Italy (166); fruit, Denmark (92); air, U. S. A. (32). *C. reukaufii:* insects, Denmark (92). *C. catenulata:* insects, U. S. A. (36, 152). *C. humicola:* breeding place of fruit flies, U. S. A. (25, 151). *C. mesenterica:* insects, U. S. A. (150). *C. bovina:* bovine caecum, Portugal (194). *C. albicans:* sapropel from fresh water lakes, U. S. S. R. (115). References to species under the name *Mycoderma* spp. are not included (56).

C. albicans is the only species of the genus which is definitely pathogenic although there is evidence that certain ubiquitous species may very rarely be involved in pathological lesions. Although *C. albicans* is very common on the mucous membranes and in the feces (104) of a considerable percentage of healthy individuals, until recently it had been found only in habitats connected with the animal body. Now it has been isolated from 3 soils (2 of them stockyards) in New Zealand (112, 114), and one in this country (3). It has also been isolated from 5 different vegetable sources in Portugal (193). In all these investigations, *C. albicans* was adequately identified; in the last, by animal inoculation and in all the others, by demonstration of chlamydospores. It seems most likely that *C. albicans* when found in nonanimal habitats is a chance invader (112). Support to this thesis is the rarity of its isolation in all the above studies and in work of Nilsby and Nordén (138), who failed to find it in 600 plates exposed to the air in the open and in homes in an area where it was common in the throats of the inhabitants, although very large numbers of many other species of the genus *Candida* were found. Further support is given to this viewpoint by the consistently negative results in similar experiments of hundreds of other workers. *C. albicans* is perhaps the easiest species of the genus to identify, and is the one that interests most workers. If it were present in nonanimal habitats in any abundance, it would have been found. Where it has been specifically sought in any habitat other than the animal body (where it is abundant) it has not been found, or found only very rarely indeed. Persons cited above who found *C. albicans* in nonanimal habitats seemed inclined to regard this organism as adventitious, which appears most likely.

Akiba and Iwata (5) have reported an interesting, almost unbelievable parasitism involving "*Bacterium candidoestruens*," a gram-negative rod similar to *Serratia marcescens*. This serratia-like organism has been reported to invade the living cells of *C. albicans* and *C. tropicalis* as well as certain species of *Saccharomyces*, causing rupture of the yeast cells after 48 hr, with release of the "Bacterium." Since the latter organism produces a brilliant red pigment, individual yeast cells and colonies thus parasitized take on a red color. This interesting observation, to the knowledge of the reviewers, is the first reported parasitism of this type and must necessarily await confirmation from other laboratories. Virtanen (198) reports a symbiosis between *Candida* spp. (*C. albicans* and *C. tropicalis*) and *Staphylococcus aureus* and *S. albus*, where associated growth of the yeast and bacterium prolongs the viability of the latter. When grown in association with some strains of *Lactobacillus bulgaricus*, *C. krusei* will stimulate the production of lactic acid by the former, presumably as a result of the concomitant production of growth factors (183).

Several reports of a similar relationship involving *C. albicans* and oral lactobacilli have recently appeared. Young *et al.* (224b), as early as 1951, observed a rise in the incidence of *C. albicans* in the mouths of healthy young adults. Further, it was shown that 86 per cent of these *Candida*-positive mouths were also carriers of oral lactobacilli (224a). Studying a possible interaction of the two organisms, Young *et al.* (224a) demonstrated an inhibitory effect of an oral lactobacillus, similar to *Lactobacillus acidophilus*, on *C. albicans* when grown in mixed culture on media capable of supporting good growth of both organisms. These investigators concluded that it was a pH effect due to the

production of lactic acid. However, in vitamin-deficient media in which single omissions of thiamine, folic acid, riboflavin, and niacin were made, growth of *L. acidophilus* occurred only in mixed cultures with *C. albicans*. Wilson and Goaz (218a) have also shown that young active cultures of *C. albicans* liberate sufficient B vitamins to meet the growth requirements of oral lactobacilli. Moreover, they show that growth of lactobacilli is proportional to the amount of thiamine, riboflavin, calcium pantothenate, and pyridoxamine liberated in such appropriately deficient media when cultured with *C. albicans*. With the exception of lysine there is no liberation of amino acids by young cultures of *C. albicans*. However, chemically defined, amino acid deficient media, preconditioned by 6 to 9 day growth of *C. albicans*, provide all amino acids required by an oral strain of *Lactobacillus casei*. Bio-assay by single omission techniques indicates liberation of the five essential amino acids, cysteine, glutamic acid, lysine, phenylalanine, and tryptophan. In addition, significant amounts of arginine, isoleucine, leucine, tyrosine, and valine were also liberated. Further, a reduction in the length of the initial stationary phase of growth of *L. casei* was induced in a mutually adequate medium when preconditioned by 3-day growth of *C. albicans*. A similar reduction could be affected by addition of an enzymatic digest of casein or saliva, suggesting the presence of a growth stimulating peptide (218b). These investigations suggest that in the normal mouth a counterbalance exists between these organisms, with *C. albicans* providing growth factors for the oral lactobacilli and the latter controlling the yeast population by lactic acid production (224b).

Browne (19a) has found that *C. albicans* may play a role in the ecology of several human pathogens, including *Corynebacterium diphtheriae* and the β-hemolytic streptococci. Testing the survival of these organisms on cotton swabs dried at room temperature, it was found that neither a strain of the β-hemolytic streptococcus nor of *C. diphtheriae* survived more than a few days. When broth cultures of these organisms were each mixed with similar cultures of *C. albicans* and tested under identical conditions, *C. diphtheriae* and the β-hemolytic streptococci were recovered from swabs left at room temperature for periods of up to 10 weeks. No *C. diphtheriae* or β-hemolytic streptococci were recovered from swabs prepared in the same manner when *C. albicans* was omitted from the mixture. Further, neither 2 per cent yeast extract nor heat-killed suspensions of *C. albicans* provided conditions for survival of *C. diphtheriae* over an extended period.

Interesting syntrophic relationships between *C. albicans* and *Mycobacterium tuberculosis* have been reported recently (101). Metabolic products of *C. albicans* appear to stimulate growth of *M. tuberculosis*. When grown in mixed culture on solid media rough (R) colonies of *M. tuberculosis* are observed around colonies of the yeast. Mankiewicz, Slackiewicz, and Liivak (102) more recently report on the nature of the growth factor produced by *C. albicans*. The growth-promoting substance has been demonstrated in the polysaccharide fraction of cell-free extracts of the yeast. In addition, this as yet unidentified substance, as well as the crude cell-free extract, have been reported to be capable of protecting *M. tuberculosis* against the inhibitory effects of streptomycin and isoniazide. The obvious importance of these observations with regard to the mechanism of antibiotic action has prompted continued research along these lines.

Mixed cultures of *C. albicans* and *M. tuberculosis* when cultured in selective dye-containing media such as that of Loewenstein, also show an interesting relationship. In such media the dye would normally be expected to inhibit growth of the yeast; however, Mankiewicz (101) observes that colonies of *M. tuberculosis* "metabolize" the dye, allowing growth of yeast colonies adjacent to those of *M. tuberculosis*. Whether the dye has been chemically altered through metabolism of *M. tuberculosis* or whether its toxicity is neutralized by a product of metabolism was not established. The latter mechanism, however, would appear more likely. Nevertheless, Mankiewicz (101a) has taken advantage of these observations by the development of a cultural method for the clinical detection of *M. tuberculosis*.

Several reports of nitrogen fixation by yeasts were cited in the 1947 review (180). None of these has been subsequently confirmed. More recently, a possible symbiotic fixation of nitrogen by larvae of bark beetles, *Ips amitanus, I. typographus*, and *I. chalcographus*, has been reported by Peklo and Satava (143). Species of *Torulopsis* and *Candida* (unnamed) were isolated from the eggs

and larvae, and speculation as to their possible relationship to the fixation of free nitrogen was presented.

IV. Methods for Study of Candida

A. Isolation

The fact that *Candida* spp. are so easily isolated on acidified (pH 4.0 to 4.5) glucose agar, even from materials heavily contaminated with bacteria, has rendered new methods or new media all but useless and practically none has been reported. If, however, the worker is attempting to isolate pathogenic fungi (including *Candida* spp.) from animal sources a strongly acid medium is not recommended, since many pathogenic fungi are unable to grow in such media. In such cases nonacid ingredients to prevent growth of bacteria are necessary. Thompson (188) in 1945 proposed the use of penicillin and streptomycin to keep down the growth of most bacteria. Numerous modifications (often published without reference to Thompson's paper) have been described. Fleury's (50) and Littman's (83) modifications and the original Thompson medium were used by one of the present authors (C. E. S.) and found to be about equally good. The use of cycloheximide (52, 54) may be helpful in isolating *Candida* spp. from sources heavily contaminated with molds.

B. Identification

In the past 10 years antagonism on the part of scientists to the use of biochemical methods for identification of species of yeasts has all but disappeared and suggested improvements in these techniques have been numerous. Perhaps Wickerham's (208, 209) method for determination of availability of various sugars and other carbon compounds as sole sources of carbon and of nitrate as sole nitrogen source has been the greatest advance. This method is undoubtedly more accurate than auxanographic methods, but since the auxanographic method is known to work it is preferable because of its simplicity. Shifrine *et al.* (176) have described an improved technique for the determination of the carbon assimilation patterns of yeasts by use of the replica plate. This method facilitates the simultaneous testing of a large number of yeasts (up to 25 per plate) for their ability to utilize a single carbon compound. Nickerson's (126) suggestion for substitution of tests for nitrate reduction to replace those for nitrate assimilation has not yet been adequately studied and it offers interesting possibilities.

In the authors' opinion, research on better routine tests for carbohydrate fermentation is in order. Lodder and Kreger-van Rij (88) often diagnose species of yeasts or even genera on fermentation of this or that sugar and put organisms showing no, or slight, fermentation in other taxa. Then too, species described by some workers as nonfermentative were found more then once by the present senior author to produce definite though weak evidence of fermentation by the formation of a few bubbles of CO_2 anaerobically. It seems reasonable that the difference between no fermentative power and some fermentative power is fundamental, but qualitative differences between degrees of fermentation are likely to be of trivial importance in a natural system and to represent only strain differences.

Most certainly the methods currently used are primitive. At best the Einhorn tube is a crude instrument for demonstration of alcohol fermentation. The Durham tube is also crude, but less so (17). The demonstration of acid production from a disaccharide by a yeast capable of fermenting either of the monosaccharides forming the disaccharide is, at the very least, an indication that the yeast might be expected to ferment the disaccharide under proper conditions. If the enzyme which hydrolyzes the disaccharide is produced so slowly that the carbon dioxide produced in alcoholic fermentation is absorbed by the culture liquid and diffused into the atmosphere, the diagnosis will be "no fermentation." Greater concentration of the disaccharide, covering the medium in the tube with paraffin wax after growth has started, or frequent transfer from one culture to another will often demonstrate that the yeast is indeed capable of anaerobic production of carbon dioxide from the disaccharide.

The statement in the previous review (180) that the author could always reproduce his fermentation results must be retracted. Frequently species of *Candida* which produced no gaseous fermentation of a disaccharide, but did produce acid, can be induced to give evidence of a slight gaseous fermentation. We are convinced that improvements in methods for demonstrating fermentation by yeasts are overdue. If Stelling-Dekker's (182) use of fermentative powers in yeast taxonomy is correct—and it seems to be—methods which will clearly differentiate fermenta-

tion from nonfermentation would appear to be absolutely necessary for separation of species. Our present methods do not always do this. Some technical improvements have been described recently; these include "the Winge fermentometer" (223), the syringe gasometer of Baird *et al.* (12), the microfermentation test described by Morris (121), and the improved fermentation tube of Morris and Kirsop (120) and Lindegren (82).

It is to be hoped that in the next 13 years greater improvements in methods of studying fermentation will be made. Perhaps the problem should be taken up by other physiologists who have an interest in yeasts. The papers of Kluyver and Custers (75a), van Niel and Cohen (137), and of Bouthilet *et al.* (17) should certainly be considered. If the alcoholic fermentation is used as a taxonomic criterion, efforts should be made to find methods that can be depended upon to demonstrate this type of metabolic activity—or the lack of it.

There is one species of *Candida*, namely *C. albicans*, whose isolation and diagnosis is routinely made in a large number of medical diagnostic laboratories. The most satisfactory method has been to streak and scratch suspected yeast isolates on and into corn (*Zea*) meal (13) or potato (*Solanum*) agar plates. The development of a few strands of mycelium with blastospores and with typical terminal chlamydospores is diagnostic for *C. albicans* or a closely related variety or species, *i.e.*, *C. stellatoidea*. Another satisfactory method is animal inoculation. Several modifications, some of them improvements, have been made. Rice (*Oryza*) infusion agar (185) was found easier to prepare than corn meal agar. Gordon *et al.* (58) found yellow corn meal better than the white or dehydrated types. Zein infusion agar (160) was easier to prepare and in the writers' experience produces more chlamydospores than corn meal agar. A soil infusion agar (14) is also an improvement. Regardless of the improvements in techniques, difficulty in the methods of detection of mycelium are reported. Zenitani (227) reports only limited success with stab cultures in rice bran extract agar, potato extract agar, and carrot extract agar. He points out, however, that the adhesion culture technique is best from a practical point of view but that it is unsuitable because of the variability of results.

The most satisfactory of all the newer media in our hands is the polysaccharide medium of Nickerson and Manokowski (132). Even old laboratory strains which had to be revived on blood agar for several transfers before producing chlamydospores in corn meal agar, produced them in large numbers upon the first inoculation in Nickerson's medium. The dehydrated commercial product seems satisfactory. More rapid and almost as productive of chlamydospores, is a buffered alkaline agar without nutrients (85) incubated for 24 hr or less under a cover slip on a slide. Kligman (75) and Wickerham (208) used, instead of scratch agar plates, the Dolmau technique, where a sterile cover slip is pressed on a surface streak on a Petri plate. All gradations between complete aerobiosis and complete anaerobiosis will be found. This method is an improvement over scratch agar plates and makes the mycelium or chlamydospores easier to find. Other methods of identifying *C. albicans*, applicable in hospital diagnosis, have been described (26, 205, 206). That these methods will be found as satisfactory as previous cultural methods is questionable. Although Lodder *et al.* (33) consider serological tests unsatisfactory as a means of differentiating species, the use of new techniques has allowed a serological differentiation of two very closely related species, *C. albicans* and *C. stellatoidea* (72). Agglutination tests would therefore appear to be reliable in the detection of *C. albicans* (27), although it is possible by cross agglutination and agglutinin absorption techniques to demonstrate a group antigen common to *C. albicans*, *Saccharomyces cerevisia* and *Hansenula anomola* (158). *C. albicans* can, however, be readily identified by species-specific agglutinins. Vogel (199) also reports a common antigen between *S. cerevisiae* and *C. albicans* and, in addition, demonstrates the presence of many common cellular polysaccharides.

C. Preservation of Cultures

For a more complete summary of this topic, the reader is referred to the discussion by Morris (122) on the preservation of yeast cultures. Yeast cultures, including *Candida* spp., can be preserved by many methods including stab and liquid cultures contained in tightly sealed tubes or bottles and stored at between 1 to 4 C. Liquid cultures are recommended (122) since fewer spores are formed and therefore the likelihood of change in the culture due to segregation of characters is reduced.

Cultures of *Candida* spp., including *C. albicans*,

C. guilliermondii, *C. parapsilosis*, *C. stellatoidea*, and *C. tropicalis*, can be preserved for many months when covered with mineral oil and left at room temperature. Viability of some cultures, which do not survive cold storage, can be maintained by this method (4). A few investigators, including Fennell *et al.* (49) and Wickerham and Andreason (207), recommend lyophilization as the method of choice for preservation of certain fungi and yeast, especially *C. albicans*. There have been few reports of physiological changes in yeast preserved by lyophilization (10, 74) and of low viability after storage. As pointed out by Morris (122), there is an unfortunate dearth of information on the use of this technique.

V. Physiology

A. Metabolic Products and Nutrition

The writer of the 1947 review (180) could find only a few references to biochemical studies on *Candida*. Today the problem is mainly which papers to cite. Diddens and Lodder (35) made rather thorough studies on the ability of various species of *Candida* to utilize a few selected carbohydrates. Wickerham (208, 209) has greatly expanded these tests and has studied a larger number of additional carbohydrates, organic acids and alcohols as to their ability to serve as sole carbon sources. Connell and Skinner (31), utilizing this method, could not find any advantage to the use of these compounds as a tool for taxonomy, as far as nonfermenting species were concerned. Indeed Thjötta and Torheim (187) indicated that acid rather than gas production might be used as a taxonomic factor. In light of van Niel and Cohen's findings (137), it may be more meaningful to determine whether the organism produces acid from a certain carbohydrate than to determine whether it produces sufficient gas to appear in a gas trap.

Most of the studies on the ability of *Candida* spp. to utilize carbon compounds have been in relation to the possible use of species, especially *C. arborea* (2, 23, 24, 57, 65, 66, 71, 79–81, 140, 142, 148, 179, 189, 191, 219, 226), as food or fodder yeasts. Particular interest has been shown in the possible utilization of naturally occurring sugars, especially pentoses, by this species. Although several species of *Candida* will utilize pentoses, Windisch (219) suggests the use of *C. tropicalis* for the production of fodder yeast from wood product fermentations. Furthermore he shows that pentose-utilizing species assimilate xylose by preference and that only xylose-assimilating species will assimilate arabinose or rhamnose. The availability of various nitrogen compounds has also been studied (23, 65, 173), as well as the effect on growth and metabolism of various growth-promoting substances (34, 37–41, 45, 65, 97, 147, 172, 197).

As to products of metabolism, most of the studies have been incidental to studies on applications. There have been many studies on vitamin production by species of *Candida*, most of them by fodder yeast, especially *C. arborea* (1, 80) and *C. guilliermondii* (86, 184), although *C. albicans* produces as much as 42.6 μg folic acid per gram of cells under certain conditions (110). An excellent review by Pridham (155) on the microbial synthesis of riboflavin appeared in 1952. His very complete report covers most of the industrial or potentially industrial processes involving *Candida* spp. up to that date. Eddy (44) has summarized vitamin production by yeast, including species of *Candida*, in his review of 1958. Pyke in the same publication (156) has reviewed much of the information regarding the industrial use of *Candida* species in his general discussion of the technology of yeast. Excellent and more complete reviews of food yeasts, including the use of *C. arborea* and *C. tropicalis*, have been published by Dunn (42, 43), Irvin (67), and Wiley (218). Since these reviews, a revision of a standard text dealing with industrial yeast fermentations has appeared (154). This most recent edition of Prescott and Dunn's *Industrial Microbiology* reviews yeast technology, but it is more valuable as a source of patent information.

It is worthy of note that species of *Candida* are now considered among the most important technological yeasts. In fact, Windisch (221) lists *Saccharomyces cerevisiae*, *Torulopsis* (*Candida*) *utilis*, and *Candida tropicalis* as the most important industrial fermenters.

The manufacture of fodder yeast from waste sulfite liquor using *C. tropicalis* has been described by Yamaguchi *et al.* (224). Windisch (219) suggests the use of *C. pseudotropicalis* in the fermentation of whey. Preliminary attempts to increase the food value of whey by yeast fermentation indicate that *C. krusei* is not as satisfactory as other yeasts, including *Torulopsis cremoris* (60). This is understandable since *C. krusei* does not utilize lactose whereas *T. cremoris*, which, according to

Lodder and Kreger-van Rij (88), is identical with *C. pseudotropicalis*, is the only lactose-fermenting species of *Candida*. With a view to the possible use of *C. lipolytica* for yeast extract production, Joslyn and Vosti (73) have studied autolysis in this species.

Information regarding the esterase activity of several species of *Candida*, especially *C. lipolytica*, has been published in recent years (124, 141, 144–147, 153, 213). Parmalee and Nelson (141) and Peters and Nelson (146) report the use of *C. lipolytica* in the manufacture of blue cheese from pasteurized milk. Their results show that cultures of *C. lipolytica* improve flavor and increase volatile acid concentration. The 11 "strains" used varied both in flavor improvement and volatile acid production. There was no flavor improvement, however, with all lipolytic bacteria tested. Peters and Nelson (144, 146, 147) have extensively studied those nutritional and environmental growth factors which influence lipase production by *Mycotorula lipolytica* (*C. lipolytica*). In general, those environmental factors which favor the development of short cells and therefore result in rapid growth reduce the lipase activity. Lipase production in a defined synthetic medium is dependent upon the presence of thiamine or pyridoxamine, either of which satisfy the requirement. Biotin, pantothenate, or thiazole will not replace either thiamine or pyridoxamine. Wilcox *et al.* (213), studying the selective release of volatile acids from butterfat by microbial lipase, found that the lipase of *C. lipolytica* was not limited to the selective release of certain volatile acids, but that several fatty acids, including butyric, caproic, and caprylic acids, were released.

Several species of *Candida* are capable of producing relatively large amounts of fat. The most productive of these are *C. pulcherrima*, *C. utilis*, and *C. reukaufii* (154). Good yields of fat have been obtained from sucrose or xylose by fermentation with *C. reukaufii* (162). An oil similar to olive oil is synthesized in abundance under cultural conditions of abundant vitamins, especially biotin, low nitrogen, intensive aeration, and at a pH above 4.5 to 5.0. Fat synthesis follows protein formation and if the amount of protein formed is low, fat synthesis is increased. An interesting change in morphology is described (162) with intensive aeration: cross walls in the mycelium fail to form and elongated structures described as "shoot" cells are formed instead. Steiner and Heinemann (181) have reported further on the formation of fat in this species.

Several of the species of *Candida* tested have been shown to produce sterols. The yield of sterol varies with the species and the medium in which it is grown. Typical yields reported by Appleton *et al.* (8) are, *C. krusei*, 0.3 per cent, and *C. parapsilosis*, 0.06 per cent, respectively. Sterols were not produced by *C. albicans* or *C. tropicalis*. *Saccharomyces* spp. appear to be the largest group of sterol-producing yeasts with yields as high as 9 per cent in some species. Eddy (44) points out that the so-called "fat" yeasts contain no more sterol than those that produce normal amounts of fat.

Salt-tolerant species of *Candida* have been reported in Japan in "Unishiokara," a Japanese fishery fermentation product (190, 227).

An excellent series of reports on the occurrence of *Candida* spp. as contaminants of English breweries and brewing yeasts have been published by Wiles and associates (214–217). Species encountered included *C. lipolytica*, *C. krusei*, *C. guilliermondii*, *C. pelliculosa*, and *C. mycoderma*. Various *Candida* and *Brettanomyces* species cause turbidity in English top fermented beer (214). *C. pelliculosa* is responsible for fruity flavors and *C. krusei* as well as *Brettanomyces* species give strong yeasty odors (216). Thirteen of sixteen film-forming yeasts isolated as contaminants of brewery yeasts were found to be *C. mycoderma* (Reess) Lodder and Kreger-van Rij (202, 215, 217). The ability of these cultures to use 35 different carbon sources was studied and of these succinic acid, mannitol, and sorbitol were found taxonomically useful in the identification of film-forming yeasts. Certain metabolic aspects of *Mycoderma* (*Candida*), specifically the relationship of thiamine concentration to the formation of alcohol, had been previously studied by Walker and Ramatchandran (201). Off flavors and odors in German beer caused by *C. krusei* and *C. mycoderma* have been reported (222). *C. rugosa* has also been reported to be among those yeasts which cause clouding of dry white wines in California (170). According to Teunisson (186) *C. krusei* and *C. tropicalis* are among those yeasts important in spoilage of rice stored in a sealed bin.

Messineva and Skadooskii (115) have described a fermentation of fresh water lake sediment by

yeasts, including *C. albicans*. Compounds isolated from salt water plants are also utilized by *Candida* species (189). Morris (122) has demonstrated that *C. krusei* and *C. solani* adaptively utilize the sea weed constituents fucoidin, fucose, laminarin, and sodium alginate.

The ability of *Candida* and other yeasts to hydrolyze pectin has been studied by Luh and Phaff (90). Of all yeasts tested only *Saccharomyces fragilis* and its imperfect form, *Candida pseudotropicalis*, produce an extracellular, nonadaptive polygalacturonase, free from pectin esterase. The polygalacturonase has optimal temperature and pH of 55 to 60 C and 3.5 to 4.0, respectively. Lukes and Phaff (91) report the best source of the enzyme, trehalase, is *C. tropicalis*, although it is produced as an adaptive enzyme. Methods of purification and the kinetics of the enzyme are discussed. Those characteristics reported are optimal temperature and pH, which are 48 C and 4.1 to 5.3, respectively.

Although extensive studies on amylase production by *Endomycopsis*, especially *E. fibuliger*, have been conducted (105–108), there has not appeared an authenticated report of amylase production by *Candida* spp. (84). Furthermore, the production of starch does not appear to be a common physiological trait of *Candida* spp.; of those tested only *C. humicola* is capable of starch synthesis according to Aschner and Curry (9).

There has been little biochemical study of *Candida* spp., except for *C. albicans*, aside from investigations concerned directly with applications to technology, taxonomy, and identification. A few such reports have recently been made but no attempt will be made to give complete coverage to those purely biochemical aspects of the genus. In this regard Bruchmann (20) has demonstrated the presence of aldolase, carboxylase, and glucose dehydrase in *C. reukaufii*. *C. albicans* contains an active cystinase (165). Bruyn (22) reportedly shows the first example of the biological oxidation of an unsaturated compound ($R—CH{=}CH_2$) giving rise to the corresponding glycol ($R—CHOHCH_2OH$), using *C. lipolytica* and with *l*(−)hexadecene-1 as the substrate.

Use of species of *Candida* for determining the extent of hydrolysis of various polysaccharides is of interest. Applications of differential fermentation tests have been described by several workers including Meyer and Gonon (116). By using *C. monosa* and *C. chodati*, which ferment only glucose and glucose and maltose, respectively, the extent of potato amylose degradation can be quantitatively determined. Auernheimer *et al.* (11) have taken advantage of the ability of *C. guilliermondii* (NRRL No. 488) to selectively ferment *d*-xylose and *l*-arabinose in their quantitative determination of hemicellulose constituents. *C. lypolytica* is also used since it ferments only *d*-xylose and not *l*-arabinose.

An interesting report (16) shows the significant uptake of the rare earth, lanthanum, by a yeast which appears to be a species of *Candida*. The physiological function, if any, is unknown.

Physical factors, especially pH, have been studied by several investigators. The range of pH over which *C. albicans* will grow has always been of interest because of this organism's pathogenic ability. In respect to pH it acts more like the saprophytic yeasts and molds. Although it was reported in the 1947 review (180) that the optimal pH was 7, recent reports indicate that best growth is obtained between 5.1 and 6.4, although varying degrees of growth do occur between pH 2.2 and 9.6 (70). Dilute solutions of boric acid have been shown to inhibit growth of *Candida* species (77). The effect varies among the species, *C. robusta* being more resistant than *C. albicans*, *C. tropicalis*, *C. krusei*, and *C. rugosa*. Christophersen and Precht (28) have studied the effect of incubation temperature on cell size of *Torulopsis kefyr* (*Candida pseudotropicalis*). Oxygen tolerance, and the effects of temperature and relative humidity on growth of *C. pseudotropicalis* have been studied by Bottomley *et al.* (15) in relation to mold growth in stored corn. These results show that growth of *C. pseudotropicalis* ceases in corn stored at a relative humidity of 80 per cent and all oxygen concentrations tested (0.1 to 21 per cent), suggesting a marked lack of tolerance to low oxygen tensions.

Gormsem (59) has reported an interesting physiological aspect of *C. albicans*; namely, production *post mortem* of ethyl alcohol. A blood alcohol content of 0.02 per cent was found *post mortem*, but ethyl alcohol of a pleural exudate was at a level 10-fold greater (0.23 per cent), due to fermentation by *C. albicans*.

Thiaminase activity has been reported in *C. albicans* and certain other fungi, but not in others including *Cryptococcus neoformans* (68). There

appears to be an equilibrium established between synthesis and inactivation of thiamine in those thiamine-producing species. The possible relationship between certain nutritional conditions and the presence of *C. albicans* in the intestinal tract of man and animals is noteworthy. This would seem to be a fruitful area of investigation in view of the numerous reports of *C. albicans* in the intestine of man and many other animals (112, 113, 180).

B. Cytology

The chemical composition of the cell wall of bacteria, fungi, and yeasts has been extensively studied in the past few years. These results show that in bacteria and certain fungi, differences in chemical composition, especially amino acids and carbohydrates, of the cell wall are important taxonomic aids. Although most of the studies on yeasts have been done with *Saccharomyces* spp. (139) there have been a few reports dealing with *Candida* spp, especially *C. albicans* (47). The cell wall of most yeasts appears to be composed of at least one or more of the following carbohydrates: mannan, chitin, and yeast glucan. All species of *Candida* studied contain all three of these compounds (64, 76, 163).

Scherr and Weaver (171) and Morris (122) and more recently Ward (203) and Falcone and Nickerson (47) have reviewed those factors influencing formation of pseudomycelia in yeasts with some emphasis on *Candida*. The most extensive investigations concerned with dimorphism have been conducted by Nickerson and associates. Of those papers by Nickerson appearing since the last review several are important in this respect (69, 127–131, 133–136). On the basis of the evidence presented in these reports, summarized by Morris (122) and Ward (203) and by Falcone and Nickerson (47), pseudomycelium production results from an impaired cell division mechanism resulting from an apparent breakdown of intracellular sulfhydryl maintenance. Nickerson has found all other physiological properties studied essentially unchanged in the filamentous form. George and Plunkett (55) also report that dissociated rough cultures are not altered in their fermentation patterns but that one out of ten lost the ability to form chlamydospores. In contrast, Ranque and Depieds (157) report that the transformation from the yeast phase to filamentation is accompanied by definite biochemical changes. Using *C. albicans*, they determined that galactose fermentaton is the most labile characteristic and that fructose and maltose may not be fermented by the rough form. Glucose fermentation however remains constant. Further they conclude that rough variants of *C. albicans* cannot be depended upon to yield reliable physiological characteristics and urge that only recent isolates be used in taxonomic studies. The results of Luterann and Langeron (95) concerned with pellicle formation in film-forming yeast are similar to those reported by Nickerson.

Speculation as to the physiological function of pseudomycelium formation continues. Magni (100) suggests that filamentation facilitates absorption of dilute essential nutrients. It appears, however, that pseudomycelium formation is a result of the nutritional environment, and that it is associated more with the presence or absence of certain nutritional factors rather than with their concentration. McClary (96) has shown that hyphal development requires the presence of certain assimilable growth factors including potassium, phosphate, and biotin and that it is not dependent upon the presence of fermentable carbohydrate. Glucose prevents filamentation and, in fact, the absence of glucose and cysteine form the nutritional basis of Nickerson's excellent polysaccharide medium for the production of pseudomycelium and chlamydospores (132). Seeliger (174) has described a semisolid medium containing Tween-80 for obtaining rapid filamentation of *C. albicans*.

Mitochondria can be readily demonstrated in the cytoplasm of mycelial cells of *C. albicans* and, in fact, they can be demonstrated by staining techniques (triphenyltetrazolium chloride) even in desiccated cells more than a month old (175).

C. Antibiosis

Even partial coverage of the antibiotic literature in relation to *Candida* spp., especially *C. albicans*, is beyond the scope and intent of this review. There are, however, a few reports of general interest which we feel should be included (19, 21, 103, 125). It is noteworthy that intestinal, oral, and vaginal moniliasis seem to be on the increase. Several antibiotics have the effect of eliminating most of the bacteria from the intestine, mouth, or the vagina. *C. albicans* is not generally affected by these antibiotics. It grows in these habitats

as a natural and harmless parasite, but not in large numbers under most conditions. Occasionally conditions, for the most part unknown, arise where numbers may become sufficient to cause a condition of moniliasis. Without competition *C. albicans* may multiply rapidly enough to cause vaginal, oral, or intestinal moniliasis. With cessation of the antibiotic treatment, the flora of these habitats becomes balanced again and the symptoms usually disappear. This represents another example of unexpected results following a disturbance of the balance of nature. Di Menna (111) in 1952 reported on the effect of antibiotics *in vivo* on dissociation of *C. albicans*. She has demonstrated repeatedly the presence of a rough variant of *C. albicans* in the yeast flora of patients treated with antibiotics. More recently Reiersol (161) has shown, by mycological examination of the stools of patients before and after treatment with Bacitracin and Neomycin, that there is an increased yeast population of the intestine during antibiotic therapy. Further, the report shows that the stools from 18 of 20 patients examined contained yeasts, whereas only 37 per cent revealed a yeast flora prior to treatment. Most of the yeasts found were *Candida* species, including *C. parapsilosis*, *C. albicans*, *C. mycoderma*, *C. krusei*, and *C. tropicalis*.

VI. References

1. Agarwal, P. N., Singh, K., King, P. S., and Peterson, W. H. 1947 Yields and vitamin content of food yeast grown in different kinds of molasses. Arch. Biochem., **14**, 105–115.
2. Agarwal, P. N. and Peterson, W. H. 1949 Utilization of non-sugar carbon of molasses by food yeasts. Arch. Biochem., **20**, 59–74.
3. Ajello, L. 1956 Soil as natural reservoir for human pathogenic fungi. Science, **123**, 876–879.
4. Ajello, L., Grant, V. Q., and Gutzke, M. A. 1951 Use of mineral oil in the maintenance of cultures of fungi pathogenic for humans. Arch. Derm. and Syphilol., **63**, 747–749.
5. Akiba, T. and Iwata, K. 1954 On the destructive invasion of a new species, "*Bacterium candidoestruens*," into *Candida* cells. Japan. J. Exptl. Med., **24**, 159–166.
6. Almeida, F. de and Lacaz, C. da S. 1946 Notas sôbre a inclusão de *Candida butantanensis* como sinônima de *Candida tropicalis*. Anais. fac. med. univ. São Paulo, **22**, 73–77.
7. Ansel, M. and Gauthier, C. 1954 Classification des levures des genres *Candida* et *Mycoderma*. Caractères morphologiques et physiologiques. Ann. parasitol. humaine et comparée, **29**, 148–162.
8. Appleton, G. S., Kieber, R. J., and Payne, W. J. 1955 The sterol content of fungi. II. Appl. Microbiol., **3**, 249–251.
9. Aschner, M. and Curry, A. 1951 Starch production in the genus *Trichosporon*. J. Bacteriol., **62**, 350–351.
10. Atkin, L., Moses, W., and Gray, P. P. 1949 The preservation of yeast cultures by lyophilization. J. Bacteriol., **57**, 575–578.
11. Auernheimer, A. H., Wickerham, L. J., and Schniepp, L. E. 1948 Quantitative determination of hemicellulose constituents by fermentation. Anal. Chem., **20**, 876–877.
12. Baird, V., Hestrin, S., and Lindegren, C. C. 1952 The syringe gasometer. Wallerstein Labs. Communs., **15**, 213–217.
13. Bakerspigel, A. 1954 A preferred method for routine identification of *Candida albicans*. J. Infectious Diseases, **94**, 141–143.
14. Bakerspigel, A. 1954 Soil-extract agar for *Candida albicans*. Arch. Dermatol. and Syphilol., **69**, 735–737.
15. Bottomley, R. A., Christensen, C. M., and Geddes, W. F. 1950 The influence of various temperatures, humidities, and oxygen concentrations on mold growth and biochemical changes in stored yellow corn. Grain storage studies. IV. Cereal Chem., **27**, 271–296.
16. Bowen, V. T. and Rubinson, A. C. 1951 Uptake of lanthanum by a yeast. Nature, **167**, 1032.
17. Bouthilet, R. J., Nielson, N. E., Mrak, E. M., and Phaff, H. J. 1949 The fermentation of trehalose by yeast and its taxonomic implications. J. Gen. Microbiol., **3**, 282–289.
18. Bouthilet, R. J. 1951 A toxonomic study of soil yeasts. Mycopathol. et Mycol. Appl., **6**, 79–85.
19. Brown, R. and Hazen, E. L. 1949 Activation of antifungal extracts of actinomycetes by ultrafiltration through gradocol membranes. Proc. Soc. Exptl. Biol. Med., **71**, 454–457.

19a. Browne, A. S. 1960 *Personal communication*. (California Department of Public Health, Berkeley, California.)

20. Bruchmann, E. E. 1953 Nachweis von

Zymohexase, Carboxylase und Glucosedehydrasen in den fettbildenen Mikroorganismen *Candida reukaufii* und *Endomyces vernalis*. Biochem. Z., **325**, 24–30.

21. Brun, R., Moser, J. J., and Judassohn, W. 1953 L'effect de quelques substances antimycotiques sur *Candida albicans*. Schweiz. med. Wochschr., **83**, 135–136.
22. Bruyn, J. 1954 An intermediate product in the oxidation of *l*-hexadecene-1 by *Candida lipolytica*. Koninkl. Ned. Akad. Wetenschap. Proc., **57C**, 41–45.
23. Bunker, H. J. 1948 The production of microbiological protein for food. Chem. & Ind., **1948**, 179–180.
24. Bunker, H. J. 1955 Yeast production. The choice of fat-producing and food yeasts. J. Appl. Bacteriol., **18**, 180–186.
25. Carson, H. L., Knapp, E. P., and Phaff, H. J. 1956 Studies on the ecology of *Drosophila* in the Yosemite region of California. III. Ecology, **37**, 538–544.
26. Chapman, G. H. 1952 The isolation and differentiation of *Monilia* and other fungi. Trans. N. Y. Acad. Sci., Ser. 2., **14**, 254.
27. Christie, R. and Morton, M. M. 1953 The detection of *Candida albicans*. Australian J. Dermatol., **2**, 87–93.
28. Christophersen, J. and Precht, H. 1954 Uber den Einfluss der Wachstumstemperatur auf die Grosse von Hefezellen. Zentr. Bakteriol. Parasitenk., Abt. II, **108**, 1–6.

28a. Ciferri, C., Verona, O., and Luparini, F. 1948 Segnalazione e descrizione de lieviti nelle "acque di vegetazione" delle olive. Mycopathologia, **4**, 249–259.

29. Clark, D. S. and Wallace, R. H. 1955 *Candida malicola* nov. sp. isolated from apples. Can. J. Microbiol., **1**, 275–276.
30. Clark, D. S., Wallace, R. H., and Davis, J. J. 1954 Yeasts occurring on apples and in apple cider. Can. J. Microbiol., **1**, 145–149.
31. Connell, G. H. and Skinner, C. E. 1951 The origin of some species of the genus *Candida* in non-pseudomycelium-producing anascosporogenous yeasts. Mycopathol. et Mycol. Appl., **6**, 65–71.
32. Connell, G. H. and Skinner, C. E. 1953 The external surface of the human body as a habitat for non-fermenting non-pigmented yeasts. J. Bacteriol., **66**, 627–633.
33. Cook, A. H. (ed.) 1958 *The chemistry and biology of yeasts*. Academic Press, Inc., New York.
34. Cutter, V. M., Jr., and Wilson, K. S. 1951 The effect of phospholipides on inhibition of growth and respiration in yeasts by sodium benzene dodecyl sulfonate. Yale J. Biol. Med., **23**, 277–281.
35. Diddens, H. A. and Lodder, J. 1942 Die anaskosporogenen Hefen, II. Halfte. North Holland Publ., Amsterdam.
36. Dobzhansky, T. H., Cooper, D. M., Phaff, H. J., Knapp, E. P., and Carson, H. J. 1956 Studies on the ecology of *Drosophila* in the Yosemite region of California. II. Ecology, **37**, 544–550.
37. Drews, B., Just, F., Olbrich, H., and Vogl, T. J. 1952 Über die Aufnahme von Kobalt und Mangan durch Microorganismen. Brauerei, Wiss. Beil., **5**, (9) 91–92.
38. Drouhet, E. and Segrétain, G. 1948 Sur l'action de la lactoflavine à l'égard de *Torulopsis histolytica* (*T. neoformans*) et d'autres champignons pathogènes. Compt. rend. soc. biol., **142**, 316–319.
39. Drouhet, E. and Mariat, F. 1950 Sur la perte de fonctions de synthèse de l'aneurine ou des constituents par quelques champigons pathogènes. Compt. rend., **230**, 319–322.
40. Drouhet, E. and Couteau, M. 1954 Facteurs vitaminiques de crossance des *Candida*. Compt. rend., **239**, 1675–1677.
41. Drouhet, E. and Canteau, M. 1954 Sur la determination des *Candida*. Étude des caractères morphologiques et physiologiques de 78 souches isolées de prélèvements pathologiques. Ann. inst. Pasteur, **86**, 602–617.
42. Dunn, C. G. 1952 Food yeast. Wallerstein Labs. Communs., **15**, 61–81.
43. Dunn, C. G. 1958 The industrial utilization of yeasts. Econ. Botany, **12**, 145–163.
44. Eddy, A. A. 1958 Aspects of the chemical composition of yeast, ch. 5. In *The chemistry and biology of yeasts*. Edited by A. H. Cook. Academic Press, Inc., New York.
45. Emery, W. B., McLeod, N., and Robinson, F. A. 1946 Comparative microbiological assays of members of the vitamin B complex in yeast and liver extracts. Biochem. J., **40**, 426–432.
46. Engstrom, H., Frisk, A., and Wersall, J. 1954 Electron microscopy study of the minute structure of yeast fungi. Acta Pathol. Microbiol. Scand., **35**, 256–258.
47. Falcone, G. and Nickerson, W. J. 1958 Enzymatic reactions involved in cellular division of microorganisms. Proc. Intern. Congr. Biochem., 4th Congr. (Vienna), **6**, 65–70.

48. FEDUCHY, E. M. 1955 Contributión al estudio de levaduras salvajes y cultividas de la microflora española. Microbiol. españ., **8,** 137–224.
49. FENNELL, D. I., RAPER, K. B., AND FLICKINGER, M. H. 1950 Further investigations on the preservation of mold cultures. Mycologia, **42,** 135–147.
50. FLEURY, C. 1952 Milieu pour l'isolement et la culture de champignons microscopiques agents de mycoses. Arch. sci. (Geneva), **5,** 319–323.
51. FLORENZANO, G. 1951 Due nuove specie di lieviti asporigeni isolati da vini. Biol. Abstr., **25,** 31558.
52. FUENTES, C. A., TRESPALACIOS, F., BANQUERO, G. F., AND ABOULAFIA, R. 1952 Effect of actidione on mold contaminants and on human pathogens. Mycologia, **44,** 170–175.
53. FUSILLO, M. H., LEARNARD, D. L., AND DOZIER, S. M. 1952 A simplified technic for the identification of *Monilia albicans* (*Candida albicans*). Am. J. Clin. Pathol., **22,** 83–85.
54. GEORG, L. K., AJELLO, L., AND PAPAGEORGE, C. 1954 The use of cycloheximide in the selective isolation of fungi pathogenic to man. J. Lab. Clin. Med., **44,** 422–428.
55. GEORGE, B. S. AND PLUNKETT, O. A. 1948 Dissociation in *Candida albicans*. J. Invest. Dermatol., **10,** 327–342.
56. GERUNDO, M. AND SCHWARTZ, G. L. 1950 Molds and yeasts present in the air during dust storms in West Texas. Texas J. Sci., **2,** 222–225.
57. GILBERT, F. A. AND ROBINSON, R. E. 1957 Food from fungi. Econ. Botany, **11,** 126–145.
58. GORDON, M. A., BRADLEY, E. G., AND GRANT, V. Q. 1952 The influence of different types of corn meal agar upon chlamydospore production by *Candida albicans*. J. Lab. Clin. Med., **40,** 316–320.
59. GORMSEM, H. 1954 Yeasts and the production of alcohol *post mortem*. J. Forensic Med., **1,** 170.
60. GRAHAM, V. E., GIBSON, D. L., KLEMMER, H. W., AND NAYLOR, J. M. 1953 Increasing food value of whey by yeast fermentation. I. Preliminary studies on the mutability of various yeasts. Can. J. Technol., **31,** 85–91.
61. HEDRICK, L. R. AND BURKE, G. C. 1950 Yeasts from Hawaiian fruit flies. Their identification and ability to produce riboflavin. J. Bacteriol., **59,** 481–484.
62. HEDRICK, L. R. AND BURKE, G. C. 1951 Two new yeasts from Hawaiian fruit flies. Mycopathol. et Mycol. Appl., **6,** 92–95.
63. HOF, T. 1943 On the identity of *Torula cremoris* Hammer et Cordes with *Candida pseudotropicalis* (A. Cast.) Basgal. Antonie van Leeuwenhoek. J. Microbiol. Serol., **9,** 77–80.
64. HOUWINK, A. L. AND KREGER, D. R. 1953 Observations on the cell wall of yeasts. An electron microscope and x-ray diffraction study. Antonie van Leeuwenhoek. J. Microbiol. Serol., **19,** 1–24.
65. HUSAIN, S. S. AND HARDIN, M. M. 1952 Influence of carbohydrate and nitrogen sources upon lipid production by certain yeasts. Food Research, **17,** 60–66.
66. IWATA, Y. 1953 Industrialization of wood saccharification. XI. J. Fermentation Technol. (Japan), **31,** 131–134.
67. IRVIN, R. 1954 Commercial yeast manufacture, ch. 9. In *Industrial fermentations*, Vol. I. Edited by L. A. Underkofler and R. J. Hickey. Chemical Publishing Co., Inc., New York.
68. JACOBSOHN, K. P. AND ROSADO, J. M. 1952 Études sur la thiaminase des champignons. Compt. rend. soc. biol., **146,** 1454–1456.
69. JILLISON, O. F. AND NICKERSON, W. J. 1948 Mutual antagonism between pathogenic fungi. Inhibition of dimorphism in *Candida albicans*. Mycologia, **40,** 369–385.
70. JOHNSON, S. A. M., GUZMON, M. G., AND AGURLERA, C. T. 1954 *Candida* (*Monilia*) *albicans*. Effect of amino acids, glucose, pH, chlortetracycline (Aureomycin), dibasic sodium and calcium phosphates, anaerobic conditions on its growth. Arch. Dermatol. and Syphilol., **70,** 49–60.
71. JOHNSON, M. C. AND HARRIS, E. S. 1948 Acclimatization of various yeasts to wood sugar. J. Am. Chem. Soc., **70,** 2961–2963.
72. JONSEN, J., THJÖTTA, T., AND RASCH, S. 1953 Quantitative agglutination studies in fungi. II. Serological relationship between *C. albicans* and *C. stellatoidea*. Acta. Pathol. Microbiol. Scand., **33,** 86–91.
73. JOSLYN, M. A. AND VOSTI, D. C. 1955 Yeast autolysis. II. Wallerstein Labs. Communs., **18,** 191–205.
74. KIRSOP, B. H. 1955 Maintenance of yeasts by freeze-drying. J. Inst. Brewing, **61,** 466–471.
75. KLIGMAN, A. M. 1950 Aids in the technic in the identification of *Candida albicans*. J. Invest. Dermatol., **19,** 173–176.
75a. KLUYVER, A. J. AND CUSTERS, M. T. J.

1940 The suitability of disaccharides as respiration and assimilation substances for yeasts which do not ferment these sugars. Antonie van Leeuwenhoek. J. Microbiol. Serol., **6,** 121–162.

76. KREGER, D. R. 1954 Observations on cell walls of yeasts and some other fungi by x-ray diffraction and solubility tests. Biochem. et Biophys. Acta, **13,** 1–9.
77. KOCKOVA-KRATOCHVILOVA, A. 1947 Action of boric acid on microorganisms of the genus *Candida*. Intern. Tijdschr. Brouw. en Mout., **1947,** 21–23. (Abst. from Chem. Abstr., **43,** 7087, 1949.
78. KREGER-VAN RIJ, N. J. W. 1958 The relationships between *Saccharomyces tellustris* and *Candida bovinia*. Antonie van Leeuwenhoek. J. Microbiol. Serol., **24,** 137–144.
79. KRYUCHKOVA, A. P. AND RODIONOVA, G. S. 1955 Greater utilization of xylose and arabinose in fermentation processes. Gidroliz. i Lesokhim. Prom., **8,** 11–13.
80. KURTH, E. F. AND CHELDELIN, V. H. 1946 Feeding yeasts from wood sugar stillage. Ind. Eng. Chem., **38,** 617–619.
81. KURTH, E. F. 1946 Yeasts from wood sugar stillage. Ind. Eng. Chem., **38,** 204–207.
82. LINDEGREN, C. C. 1956 Methods for the diagnosis of gene control. Fermentative ability in *Saccharomyces*. Wallerstein Labs. Communs., **19,** 49–69.
83. LITTMAN, M. L. 1947 A culture medium for the primary isolation of fungi. Science, **106,** 109–111.
84. LE MENSE, E. H., CORMAN, J., VAN LANEN, G. M., AND LANGLYKKE, A. F. 1947 Production of mold amylases in submerged culture. J. Bacteriol., **54,** 149–159.
85. LIU, P. AND NEWTON, A. 1954 Rapid chlamydospore formation by *Candida albicans* in a buffered alkaline medium. Tech. Bull. Registry Med. Technologists, **24,** 283–287.
86. LEVINE, H., OYAAS, J. E., WASSERMAN, L., HOOGERHEIDE, J. C., AND STERN, R. M. 1949 Riboflavin produced by *Candida* yeasts. Ind. Eng. Chem., **41,** 1665–1668.
87. LODDER, J. 1934 Die anaskosporogenen Hefen, I. Halfte. Verhandel. Koninkl. Ned. Akad. Wetenschap. Afdeal. Natuurk., Sec. II., **32,** 1.
88. LODDER, J. AND KREGER-VAN RIJ, N. J. W. 1952 *The yeasts. A taxonomic study.* North Holland Pub. Co., Amsterdam.
89. LU, K. C., ALLEN, D. G., AND BOLLEN, W. B. 1957 Association of yeasts with the Douglas-fir beetle. Forrest Sci., **3,** 336–343.
90. LUH, B. S. AND PHAFF, H. J. 1951 Studies on the polygalacturonase of certain yeasts. Arch. Biochim. Biophys., **33,** 212–227.
91. LUKES, T. M. AND PHAFF, H. J. 1952 Characteristics of trehalase in *Candida tropicalis*. Antonie van Leeuwenhoek. J. Microbiol. Serol. **18,** 323–335.
92. LUND, A. 1954 *Studies on the ecology of yeasts.* Munksgaard, Copenhagen.
93. LUND, A. 1958 *Ecology of yeasts*, ch. 2. In *The chemistry and biology of yeasts.* Edited by A. H. Cook. Academic Press, Inc., New York.
94. LUTERAAN, P. J. AND DENIS, J. 1946 Applications de la méthode auxanographique a l'étude des facteurs de crossance. Compt. rend. soc. biol., **140,** 131–133.
95. LUTERANN, P. J. AND LANGERON, M. 1949 Valeur morphologique et signification physiologique de la production de voile par les levures sur milieux synthetiques. Compt. rend., **228,** 1523–1525.
96. MCCLARY, D. O. 1952 Factors affecting the morphology of *Candida albicans*. Ann. Missouri Botan. Carden, **39,** 137–164.
97. MCVEIGH, I. AND BELL, E. 1951 The amino acid and vitamin requirements of *Candida albicans* Y-475 and *Mycoderma vini* Y-939. Bull. Torrey Botan. Club, **78,** 134–144.
98. MACKINNON, J. E. AND ARTAGAVEYTIA-ALLENDE, R. C. 1943 La identidad entre *Candida krusei* (Castellani) y *Mycoderma cerevisiae*. Desmazières Comun. Botan. Musea. Histor. Natur. Montevideo, **1,** No. 11.
99. MAGNI, G. E. Publication not dated. Analisi della ploidia in alcuni generi de lieviti asporigeni. Atti Inst. Botan. Critoogamico di Pavia. Serie 5, **10,** 89–97.
100. MAGNI, G. E. 1948 Biological significance of the pseudomycelium in asporogenous yeasts. I. Recirprocal inhibition of parallel colonies. Mycopathologia, **4,** 207–212.
101. MANKIEWICZ, E. 1954 *Mycobacterium tuberculosis and Candida albicans*. A study of growth-promoting factors. Can. J. Microbiol., **1,** 85–89.

101a. MANKIEWICZ, E. 1957 *Candida albicans*. A means of detecting *M. tuberculosis* on culture media. Am. Rev. Tuberc. Pulmonary Diseases, **75,** 836–840.

102. MANKIEWICZ, E., SLACKIEWICZ, E., AND LIIVAK, M. 1959 A polysaccharide isolated from *Candida albicans* as a growth

promoting factor for *Mycobacterium tuberculosis*. Can. J. Microbiol., **5**, 261–267.

103. MARIAT, F. 1954 Physiologie des actinomycètes anaérobies I. Ann. inst. Pasteur, **86**, 479–484.
104. MARPLES, M. J. AND DI MENNA, M. E. 1952 The incidence of *Candida albicans* in Dunedin, New Zealand. J. Pathol. Bacteriol., **64**, 497–502.
105. MARROQUÍN, A. S. AND FITCH, E. B. 1946 Estudios sobre la amilasa de *Endomycopsis fibuliger*. I. Actividad amilolitica y fermentativa en diversos substratos amiláseos. Ciencia (Mex.), **7**, 119–134.
106. MARROQUÍN, A. S. AND GAVARRON, F. F. 1947 Estudios sobre amilasa de *Endomyces fibuliger*. III. Principales caracteristicas de las preparaciones enzimaticas crudas y purificados. Anal. escuela nac. cienc. biol., **4**, 325–338.
107. MARROQUÍN, A. S. AND SOLORZANO, M. 1947 Estudio sobre amilasa de *Endomycopsis fibuliger*. II. Poder amilolítico y fermentativo en cultivos mixtos. Anales escuela nacl. cienc. biol., **4**, 311–324.
108. MARROQUÍN, A. S. AND GAVARRÓN, F. F. 1948 Estudios sobre la amilasa de *Endomycopsis fibuliger*. IV. Caracteristicas de su accion sobre amidón comercial. Anales escuela nacl. cienc. Biol., **5**, 7–12.
109. MARTIN, H. H. 1954 Beitrag zur Kenntnis der Morpholgie und Physiologie der Nektarhefe *Candida reukaufii* (Grüss) Diddens et Lodder. Arch. Mikrobiol., **20**, 141–162.
110. MATSUDA, T. 1950 Vitamin M (folic acid). II. Comparison of the synthesis by various mold fungi. Repts. Govt. Chem. Ind. Research Inst. Tokyo, **45**, 166–168.
111. DI MENNA, M. E. 1952 Natural occurrence of rough variant of a yeast, *Candida albicans*. Nature, **169**, 550–551.
112. DI MENNA, M. E. AND PARLE, J. M. 1954 Some extra-human occurrences of pathogenic yeast. Proc. Univ. Otago Med. School, **32**, 2.
113. DI MENNA, M. E. 1954 Nonpathogenic yeasts of human skin and alimentary tract. A comparative survey. J. Pathol. Bacteriol., **68**, 89–99.
114. DI MENNA, M. E. 1955 A search for pathogenic species of yeasts in New Zealand soils. J. Gen. Microbiol., **12**, 54–62.
115. MESSINEVA, M. A. AND SKADOOSKII, S. N. 1947 Growth of microorganisms on sapropel. I. Yeast fermentation of sapropel in the laboratory and *in situ*. Mikrobiologiya, **16**, 43–49.
116. MEYER, K. H. AND GONON, W. F. 1951 Dosage de produits d'hydrolyse enzymatique de l'amidon par fermentation. Recherches sur l'amidon. Helv. Chim. Acta, **34**, 290–294.
117. MILLER, W. H. AND MRAK, E. M. 1953 Yeasts associated with dried-fruit beetles in figs. Appl. Microbiol., **1**, 174–178.
118. MOORE, M. 1953 Unusual mycoses caused by uncommon or rare fungi. Trans. N. Y. Acad. Sci. Ser. 2, **15**, 219–224.
119. MORQUER, R., PUGET, E., AND BAZEK, A. 1953 Sur un nouvel agent de blastomycose chez le chien. Compt. rend., **236**, 546–548.
120. MORRIS, E. O. AND KIRSOP, B. 1953 Rapid microtechniques for the fermentation of carbohydrates by yeasts. J. Inst. Brewing, **59**, 486–491.
121. MORRIS, E. O. 1955 Microfermentation tests and colony characteristics as aids to yeast differentiation. J. Appl. Microbiol., **18**, 126–130.
122. MORRIS, E. O. 1958 Yeast growth, ch. 6. In *The chemistry and biology of yeasts*, Edited by A. H. Cook. Academic Press, Inc., New York.
123. MRAK, E. M. AND PHAFF, H. J. 1948 Yeasts. Ann. Rev. Microbiol., **2**, 1–46.
124. MUFTIC, M. K. 1954 New medium for the detection of esterase activity in microorganisms. Enzymologia, **17**, 123–126.
125. NAKAMURA, S., KENJI MAEDA, Y. O., AND Hamao, U. 1954 A new antifungal substance of streptomyces. J. Antibiotics (Tokyo), **7**, 51.
126. NICKERSON, W. J. 1944 Studies on film-forming yeasts. Acid production by *Zygopichia* and *Zygohansenula*. Mycologia, **36**, 224–230.
127. NICKERSON, W. J. AND JILLSON, O. F. 1948 Interaction between pathogenic fungi in culture. Considerations of the mechanism of cell division in the dimorphism of pathogenic fungi. Mycopathologia, **4**, 279–283.
128. NICKERSON, W. J. 1948 Enzymatic control of cell division in microorganisms. Nature, **162**, 241–245.
129. NICKERSON, W. J. AND MULLINS, L. J. 1948 Riboflavin enhancement of radioactive phosphate exchange by yeasts. Nature, **161**, 939–940.
130. NICKERSON, W. J. AND RIJ, N. J. W. VAN 1949 The effect of sulfhydryl compounds,

penicillin, and cobalt on the cell division mechanism of yeasts. Biochem. Biophys. Acta, **3**, 461–475.

131. NICKERSON, W. J. AND MANKOWSKI, Z. 1953 Role of nutrition in the maintenance of yeast shape in *Candida*. Am. J. Botany, **40**, 584–592.
132. NICKERSON, W. J. AND MANKOWSKI, Z. 1953 A polysaccharide medium of known composition favoring chlamydospore formation in *Candida albicans*. J. Infectious Diseases, **92**, 20–25.
133. NICKERSON, W. J. 1953 Reduction of inorganic substances by yeasts. I. Extracellular reduction of sulfite by species of *Candida*. J. Infectious Diseases, **93**, 43–56.
134. NICKERSON, W. J. 1954 Enzymatic locus participating in cellular division of a yeast. J. Gen. Physiol., **37**, 483–494.
135. NICKERSON, W. J. AND CHUNG, C. W. 1954 Genetic block in th cellular division mechanism of a morphological mutant of a yeast. Am. J. Botany, **41**, 114–120.
136. NICKERSON, W. J., TABER, W. A., AND FALCONE, G. 1956 Physiological bases of morphogenesis in fungi. V. Can. J. Microbiol., **2**, 575–584.
137. NIEL, C. B. VAN AND COHEN, A. L. 1942 On the metabolism of *Candida albicans*. J. Cellular Comp. Physiol., **20**, 95–112.
138. NILSBY, J. AND NORDÉN, A. 1949 Studies on the occurrence of *Candida albicans*. Acta Med. Scand., **133**, 340–345.
139. NORTHCOTE, D. H. AND HORNE, R. W. 1952 The chemical composition and structure of yeast cell wall. Biochem. J., **51**, 232–236.
140. OLBRICH, H. 1952 Pentose assimilation by *Torulopsis utilis* and *Candida tropicalis*. Branntweinwirtschaft, **74**, 265–267.
141. PARMALEE, C. E. AND NELSON, F. E. 1949 The use of *Candida lipolytica* cultures in the manufacture of blue cheese from pasteurized homogenized milk. J. Dairy Sci., **32**, 993–1000.
142. PAVECK, P. L. 1950 Technical achievements in the German feed and food yeast industry. Wallerstein Labs. Communs., **13**, 369–378.
143. PEKLO, J. AND SATAVA, J. 1949 Fixation of free nitrogen by bark beetles. Nature, **163**, 336–337.
144. PETERS, I. I. AND NELSON, F. E. 1948 Factors influencing the production of lipase by *Mycotorula lipolytica*. J. Bacteriol., **55**, 581–591.
145. PETERS, I. I. AND NELSON, F. E. 1948 The influence of *Mycotorula lipolytica* lipase on the ripening of blue cheese made from pasteurized homogenized milk. J. Dairy Sci., **31**, 611–618.
146. PETERS, I. I. AND NELSON, F. E. 1948 Preliminary characterization of the lipase of *Mycotorula lipolytica*. J. Bacteriol., **55**, 593–600.
147. PETERS, I. I. AND NELSON, F. E. 1951 Vitamin requirements for lipase production by *Candida lipolytica*. J. Bacteriol., **61**, 591–593.
148. PETERSON, W. H., SNELL, J. F., AND FRAZIER, W. C. 1945 Fodder yeast from wood sugar. Ind. Eng. Chem., **37**, 30–35.
149. PHAFF, H. J., MRAK, E. M., AND WILLIAMS, O. B. 1952 Yeasts isolated from shrimp. Mycologia, **44**, 431–451.
150. PHAFF, H. J., MILLER, M. W., RECCA, J. A., SHIFRINE, M., AND MRAK, E. M. 1956 Studies on the ecology of *Drosophila* in the Yosemite region of California. II. Ecology, **37**, 533–538.
151. PHAFF, H. J. AND KNAPP, E. P. 1956 The taxonomy of yeasts found in exudates of certain trees and other natural breeding sites of some species of *Drosophila*. Antonie van Leeuwenhoek. J. Microbiol. Serol., **22**, 117–130.
152. PHAFF, H. J., MILLER, M. W., AND SHIFRINE, M. 1956 The taxonomy of yeasts isolated from *Drosophila* in the Yosemite region of California. Antonie van Leeuwenhoek. J. Microbiol Serol., **22**, 145–161.
153. PICCI, G. 1955 Microbial mineralization of organic phosphorus. Ann. fac. agar., Univ. Pisa, **13**, 187–196.
154. PRESCOTT, S. C. AND DUNN, C. G. 1959 *Industrial microbiology*, 3rd ed., McGraw-Hill Book Co., New York.
155. PRIDHAM, T. J. 1952 Microbial synthesis of riboflavin. Econ. Botany, **6**, 186–206.
156. PYKE, M. 1958 The technology of yeast, ch. 10. In *The chemistry and biology of yeasts*. Edited by A. H. Cook. Academic Press, Inc., New York.
157. RANQUE, J. AND DEPIEDS, R. 1952 Modifications des propriétés biochimiques des souches de *Candida albicans* au cours de leur veillissement, leurs rapports avec les transformations en formes "rough." Compt. rend. soc. biol., **146**, 479–487.
158. RAWSON, A. J. AND NORRIS, R. F. 1947 Occurrence of a common group antigen among *Candida albicans*, *Saccharomyces*

cerevisiae and *Hansenula anomola*. Am. J. Clin. Pathol., **17**, 807–812.

159. RECCA, J. AND MRAK, E. M. 1952 Yeasts occurring in citrus products. Food Technol., **6**, 450–454.
160. REID, J. D., JONES, M. M., AND CARTER, E. B. 1953 A simple clear medium for demonstration of chlamydospores of *Candida albicans*. Am. J. Clin. Pathol., **23**, 938–941.
161. REIERSOL, S. 1958 Occurrence of yeasts in the intestinal tract of 20 patients during treatment with bacitracin and neomycin. Antonie van Leeuwenhoek. J. Microbiol. Serol., **24**, 23–26.
162. RIPPEL-BALDES, A., PIETSCHMANN-MAYER, K., AND KÖHLER W. 1948 *Candida* (*Nectaromyces*) *reukaufii* als Fettbildner. Arch. Mikrobiol., **14**, 113–127.
163. RODOFSEN, P. A. AND HOETTE, I. 1951 Chitin in the wall of yeasts. Antonie van Leeuwenhoek. J. Microbiol. Serol., **17**, 297–313.
164. ROGER, D. P. 1953 Generic names of fungi proposed for conservation. Intern. Bull. Bacteriol. Nomencl. Taxon., **3**, 14–16.
165. ROMANO, A. H. AND NICKERSON, W. J. 1954 Cystine reductase of pea seeds and yeasts. J. Biol. Chem., **208**, 409–416.
166. RONZONI, M. G. 1949 Funghi lievitiformi isolati dalle ovoteche de *Periplaneta orientalis* L. Mycopathologia, **4**, 333–341.
167. RUIZ ORONOZ, M. 1949 Estudio de una variedad de *Mycoderma cerevisiae* Desmasiéres, aislada del jitomate (*Lycopersiuim esculentum*). An. Inst. Biol. Univ. Méx., **20**, 43–56.
168. RUIZ ORONOZ, M. AND HERRERA SUAREZ, T. 1950 Estudio de *Candida Krusei* (A. Cast.) Rerhout aislada de la epidermis del bulbo del ajo (*Allium sativum*). An. Inst. Biol. Univ. Méx., **21**, 3–16.
169. RUIZ ORONOZ, M. AND ORTEGA, M del C. 1953 Estudio de una levadura aislada de la fermentación del café (*Coffea arabiga*) *Candida mycoderma* (Russ) Lodder y Kreger-van Rij. An. Inst. Biol. Univ. Méx., **24**, 23–40.
170. SCHEFFER, W. R. AND MRAK, E. M. 1951 Characteristics of yeasts causing clouding of dry white wines. Mycopathol. et Mycol. Appl., **5**, 236–249.
171. SCHERR, G. H. AND WEAVER, R. H. 1953 The dimorphism phenomenon in yeasts. Bacteriol. Revs., **17**, 51–85.
172. SCHOPFER, W. H. AND GILLOUD, M. 1944 Les besoins en facteurs de croissance de vingttrois especes et variétés de genre *Candida*. La production de lactoflavine. Compt. Rend. Soc. Phys. Hist. Nat., Genève, **61**, 232–237.
173. SCHULTZ, A. S. AND POMPER, S. 1948 Amino acids as nitrogen source for the growth of yeasts. Arch. Biochem., **19**, 184–192.
174. SEELIGER, H. P. R. 1955 Ein Neues Medium zur Pseudomycelbildung von *Candida albicans*. Z. Hyg. Infektionskrankh., **141**, 488–491.
175. SEYFARTH, W. 1952 Über das Studium an Chondriosomen de Soorhefe (*Monilia albicans*) und ihr Nachweis mit Triphenyltetrazoliumchloride. Naturwissenschaften, **39**, 162–163.
176. SHIFRINE, M., PHAFF, H. J., AND DEMAIN, A. L. 1954 Determination of carbon assimilation patterns of yeast by replica plating. J. Bacteriol., **68**, 28–35.
177. SHIFRINE, M. AND PHAFF, H. J. 1956 The association of yeasts with certain bark beetles. Mycologia, **48**, 41–55.
178. SILVA PEREIRA, A. DA 1943 O pão de milho aspectos cientīcos do seu fabrico caseiro., Dissert. Univ. Pôrto, 129 pp., 12 fig.
179. SINGH, K., AGARWAL, P. N., AND PETERSON, W. H. 1948 The influence of aeration and agitation on the yield, protein and vitamin content of food yeasts. Arch. Biochem., **18**, 181–193.
180. SKINNER, C. E. 1947 The yeast-like fungi: *Candida* and *Brettanomyces*. Bacteriol. Revs., **11**, 227–274.
181. STEINER, M. AND HEINEMANN, H. 1954 Grana mit positiver Nadi-Reaktion als Ort der primaren Fettbildung in Pilzzellen. Naturwissenschaften, **41**, 40–41.
182. STELLING - DEKKER, N. M. 1931 "Die sporogenen Hefen." Verhandel. Koninkl. Akad. Wetenschap. Afdel. Natuurk., Sect. II, **28**, 1.
183. SWABY, R. J. 1945 Production of lactic acid from wheat starch. J. Australian Inst. Agr. Sci., **2**, 179–187.
184. TANNER, F. W., JR., VOJNOVICH, C., AND VAN LANEN, J. M. 1945 Riboflavin production by *Candida* species. Science, **101**, 180–181.
185. TASCHDJIAN, C. L. 1953 A simply prepared identification medium for *Candida albicans*. Mycologia, **45**, 474–475.
186. TEUNISSON, D. J. 1954 Yeasts from freshly combined rough rice stored in a sealed bin. Appl. Microbiol., **2**, 215–220.
187. THJÖTTA, T. AND TORHEIM, B. J. 1955 Studies on the fermentation of sugars in the

Candida group. Acta Pathol. Microbiol. Scand., **36,** 237–249.

188. THOMPSON, L. 1945 Note on a selective medium for fungi. Proc. Staff Meetings Mayo Clinic, **20,** 248–249.
189. TOMIYASU, Y. AND ZENITANI, B. 1952 Studies on the production of yeasts from seaweeds. I. On two yeasts belonging to the genus *Candida*. J. Agr. Soc. Japan, **25,** 406–410.
190. TOMIYASU, Y. AND ZENITANI, B. 1953 On gaseous fermentation in "Uni-shiokara." Bull. Japan Soc. Sci. Fisheries, **19,** 585–588.
191. TSILENSIS, E. AND HEDRICK, L. R. 1952 Growth of food yeasts in olive residue hydrolysate. Food Technol., **6,** 107–109.
192. UDEN, N. VAN, AND ASSIS-LOPES, L. 1953 Zur Kenntnis von *Candida Castellanii* sp. nov.; Zugleich ein Beitrag zur Systematik von *Candida parakrusei* and *Candida krusoides*. Arch. Mikrobiol., **18,** 356–361.
193. UDEN, N. VAN, MATOS FAIA, M. DE, AND ASSIS - LOPES, L. 1956 Isolation of *Candida albicans* from vegetable sources. J. Gen. Microbiol., **15,** 151–153.
194. UDEN, N. VAN, AND CARMO SOUSA, DO LIDIA 1957 Yeasts from the bovine caecum. J. Gen. Microbiol., **16,** 385–395.
195. VAN DER WALT, J. P. 1952 On the yeast *Candida pulcherrima*. Doctoral Dissertation, Delft, Holland.
196. VANBREUSEGHEM, R. 1952 Les Levuroses, ch. 21 In *Précis de mycologie* 2nd ed., pp. 608–636. Langeron et Vanbreuseghem, Masson, Paris.
197. VERONA, O. 1952 Action of vitamins K_3 and K_5 on yeasts, particularly on wine yeasts. Atti Accad. Italiana, della vite e vino, Seina, **4,** 345–357.
198. VIRTANEN, I. 1951 Observations on the symbiosis of some fungi and bacteria. Ann. Med. Exptl. Biol. Fenniae, **29,** 352–358.
199. VOGEL, R. A. 1954 The polysaccharides of *Candida albicans*. Proc. Soc. Exptl Biol. Med., **86,** 373–375.
200. VOSTI, D. C. AND JOSLYN, M. A. 1954 Autolysis of several pure cultures of yeasts. Appl. Microbiol., **2,** 79–84.
201. WALKER, T. K. AND RAMATCHANDRAN, R. C. 1949 Chemical processes in *Mycoderma* species. Food (London), **18,** 295.
202. WALKER, T. K. AND WILES, A. E. 1952 Asporogenous film forming yeasts occurring as contaminants of brewery yeasts and beers. J. Inst. Brewing, **58,** 140–145.
203. WARD, J. M. 1958 Biochemical systems involved in differentiation of the fungi. Proc. Intern. Cong. Biochem. 4th Congr. (Vienna), **6,** 33–64.
204. WATANABE, D. 1952 Paper on use of *Mycotorula japonica*. J. Agr. Chem. Soc. Japan, **26,** 572–577.
205. WELD, J. T. 1952 *Candida albicans*. Rapid identification in pure culture with carbon dioxide on modified eosine-methylene blue medium. Arch. Dermatol. and Syphilol., **66,** 691–694.
206. WELD, J. T. 1953 *Candida albicans*. Rapid identification in cultures made directly from human materials. Arch. Dermatol. and Syphilol., **67,** 473–478.
207. WICKERHAM, L. J. AND ANDREASON, A. A. 1942 The lyophil process: its use in the preservation of yeasts. Wallerstein Labs. Communs., **5,** 165–169.
208. WICKERHAM, L. J. AND BURTON, K. A. 1948 Carbon assimilation tests for the classification of yeasts. J. Bacteriol., **56,** 363–371.
209. WICKERHAM, L. J. 1951 Taxonomy of yeasts, U. S. Dept. Agr., Tech. Bull. No. 1029, May.
210. WICKERHAM, L. J. AND BURTON, K. A. 1952 Occurrence of yeast mating types in nature. J. Bacteriol., **63,** 449–451.
211. WICKERHAM, L. J. 1952 Recent advances in the taxonomy of yeasts. Ann. Rev. Microbiol., **6,** 317–332.
212. WICKERHAM, L. J. AND BURTON, K. A. 1954 A clarification of the relationships of *Candida guilliermondii* to other yeasts by a study of their mating types. J. Bacteriol., **68,** 594–601.
213. WILCOX, J. C., NELSON, W. O., AND WOOD, W. A. 1955 The selective release of volatile acids from butterfat by microbial lipases. J. Dairy Sci., **38,** 775–781.
214. WILES, A. E. 1950 Wild yeasts. Brewers' Guild J., **36,** 141–159.
215. WILES, A. E. 1950 Studies of some yeasts causing spoilage of draught beers. J. Inst. Brewing, **56,** 183–193.
216. WILES, A. E. 1951 Frets and hazes. Brewers' Guild J., **37,** 114–131.
217. WILES, A. E. 1953 The identification and significance of yeasts encountered in the brewery. J. Inst. Brewing, **59,** 265–284.
218. WILEY, A. J. 1954 Food and feed yeast, ch. 10. In *Industrial fermentations*, Vol. I. Edited by L. A. Underkofler and R. J. Hickey. Chemical Publishing Co., Inc., New York.

218a. WILSON, T. E. AND GOAZ, P. W. 1959 The oral yeast-*Lactobacillus* relationship. II.

Yeast-*Lactobacillus*-saliva relationships. J. Dental Research, **38,** 1044–1051.

218b. WILSON, T. E. AND GOAZ, P. W. 1960 The oral yeast-lactobacillus relationship. III. Growth enhancement of *Lactobacillus casei* by *Candida albicans* and saliva. J. Dental Research, **39,** 365–371.

219. WINDISCH, S. 1948 Einiges über technischen Wuchshefen. Brauwelt, **3,** 203–207.

220. WINDISCH, S. 1952 Zur Biolgie und Systematik der *Pseudomonilia albomarginata* Geiger. Zentr. Bakteriol. Parasitenk. Abt. II, **107,** 84–98.

221. WINDISCH, S. 1953 Die Eigenschaften der drei für den gärungsgewerblichen Betreib wichtigsten Hefearten und ihr Erkennung bei der mikrobiologischen Betriebskontrolle. Brauerei Wiss. Beil. 6, **3,** 25–28.

222. WINDISCH, S. 1954 Uber einige Kahmhefen als Bierschädlunge. Brauerei, **8,** 139–142.

223. WINGE, Ö. AND ROBERTS, C. 1950 The polymeric genes for maltose fermentation in yeasts, and their mutability. Compt. rend. trav. lab. Carlsberg. Ser. physiol., **25,** 5–84.

224. YAMAGUCHI, T., TODA, H., AND HAMADA, C. 1953 The manufacture of fodder yeast from waste sulfite liquor. J. Japan. Tech. Assoc. Pulp Paper Ind., **7,** 12–18.

224a. YOUNG, G., KRASNER, R. I., AND YUDKOFSKY, P. L. 1956 Interactions of oral strains of *Candida albicans* and lactobacilli. J. Bacteriol., **72,** 525–529.

224b. YOUNG, G., RESCA, H. G., AND SULLIVAN, M. T. 1951 The yeasts of the normal mouth and their relation to salivary activity. J. Dental Research, **30,** 426–430.

225. ZAKARIÁS, J. 1943 The microbiology of dried egg yolk. Kisérletügyi Közlemények, **46,** 93. (Biol. Abstr., **21,** 12162, 1947)

226. ZAORSHA, H. AND ZAGRODSKI, S. 1955 The biological production of fodder yeasts from molasses which has been freed from salts. Acta Microbiol. Polon., **2,** 179–203.

227. ZENITANI, B. 1954 Yeasts occurring in fishery fermentation products. V. On the morphological characteristics of asporogenous yeasts. Sci. Bull. Fac. Agr. Kyushu Univ., **14,** 589–594.