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Analysis of *Candida albicans* Phenotypes from Different Geographical and Anatomical Sources

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Strain phenotypes of 330 *Candida albicans* isolates from five areas in the United States were determined on the basis of nine biochemical tests. Statistical analysis of the distribution of phenotypes revealed no significant differences among types from different anatomical sources. However, there were some differences among the phenotypes of strains from the different geographical areas, and there were substantial differences in biochemical phenotypes associated with strains susceptible and resistant to 5-fluorocytosine and between strains of serotypes A and B. Geographical differences in phenotypes of *C. albicans* were also noted between the 330 U.S. isolates and 247 isolates from Britain. Cluster analysis of the U.S. strains alone and of all of the U.S. and U.K. strains showed that *C. albicans* phenotypes can be grouped into fewer than 20 clusters with common biochemical properties.

Methods for the differentiation of phenotypes of *Candida albicans* (5, 10) offer the potential for determination of strain characteristics associated with virulence, anatomical distribution, geographical distribution, and other characteristics of the species. A survey of *C. albicans* phenotypes from patients attending a genitourinary clinic has shown that the majority of individuals who harbor *C. albicans* in the mouth, anus, or genital tract harbor a single phenotype in all sites, and the same phenotype is usually recovered from a given individual over a period of several weeks (4, 6). However, exceptions to these generalizations were seen in the survey, and in 2 of 13 women who harbored *C. albicans* in the vagina and the urethra, the urethral phenotype differed from the vaginal phenotype (4); these were extreme examples of differences in microbial flora in adjacent anatomical sites.

It is not known whether particular *C. albicans* phenotypes are associated with particular forms of *Candida* infection, for example, whether certain phenotypes are more likely than others to cause systemic infections. Such information could be obtained by determination of phenotype for large numbers of *C. albicans* isolates. In this paper, we present the results of a survey of strain characteristics of 330 *C. albicans* isolates obtained from a variety of sources in the United States. The characteristics of these strains are also compared with those of 247 isolates from Great Britain.

MATERIALS AND METHODS

Sources of *C. albicans*. A total of 330 *C. albicans* isolates were received from the United States. These were subcultures from an original 402 isolates from five medical centers in different areas of the United States (8). The centers were Baylor University, Boston University, the Mayo Clinic, the National Institutes of Health (NIH), and the University of California at Los Angeles (UCLA). For each of the 330 isolates, the *C. albicans* serotype (A or B) had been determined by slide agglutination (8), and resistance to 5-fluorocytosine (5-FC) concentrations > 12.5 μg/ml had been assessed after 1, 2, and 7 days of growth at 37°C in tube dilution tests (8). The anatomical or pathological source of each isolate was documented (see Table 1), and none of the isolates came from patients with a history of treatment with 5-FC.

A further 247 isolates came from subjects in Leicester, England. The majority of these were genital isolates from patients attending a venereal disease clinic (6); the remainder were isolates from the mouths of hospital staff in the Leicester area.

The identification of all 577 isolates as *C. albicans* was based on a positive germ tube test (9) or chlamydospore formation on corn meal-Tween 80 agar or both. Only a single isolate from any one subject was included in the study.

Differentiation of strain types and analysis of data. The method of Odds and Abbott (5) was used to determine the strain characteristics of all 577 *C. albicans* isolates in nine agar plate biochemical tests. The tests were: growth at pH 1.40, production of proteinase, resistance to 5-FC at 25 μg/ml, urea assimilation, sorbose assimilation, salt tolerance, citrate assimilation, glycine assimilation, and resistance to safranine.

To examine differences in strain characteristics between pairs of subgroups of isolates, a computerized chi-square test was performed to determine the extent of variations in the proportions of positive test results for all nine tests taken singly, all possible pairs of tests, and all possible triple combinations of test data. Differences were considered to be potentially significant only when the null hypothesis was rejected at $P < 0.001$.

To examine similarity between strains, a cluster analysis was performed with statistical methods originally designed for numerical taxonomy of bacteria (7). Gower's coefficient (2) was calculated for all strain pairs, a similarity matrix was compiled and sorted, and a dendrogram was drawn on the basis of unweighted average linkage between strains. This procedure reveals the degrees of similarity between each of the strains tested, and the dendrogram representation facilitates assignation of isolates to clusters of broadly similar strain types. For this purpose, groups of strains with a similarity > 70% were arbitrarily regarded as homogeneous clusters.

To facilitate reference to the biochemical test reaction patterns of individual strain types, the results of the tests were encoded in a three-digit number (5). The nine test results were divided into three sets of three tests. Within each set, negative results were scored zero, and positive results were scored 1, 2, or 4. Thus, for sets with the results +−+, −++, and ++−, the scores would be 1, 0, 4; 0, 2, 4; and 1, 2, 0, respectively, giving total scores of 5, 6, and 3, written as biotype 563. Similarly, a strain coded 307 would be positive in the first two and the last three of the nine tests (1+2+0; 0+0+0; 1+2+4).

RESULTS

Differences among *C. albicans* isolates from different anatomical sites. There was variation in the distribution of positive test results among the isolates from the United States, which were grouped according to their anatomical origin (Table 1). However, only five differences in the test results significant at the $P < 0.001$ level were revealed by statistical comparison of data for each of the groups in Table 1 against each other. Since this analysis involved 8,514 chi-square calculations, 8.5 such differences would be expected to arise by chance alone. When the isolates were grouped under the broader headings of "superficial," "intermediate," and "systemic," (see Table 1), no significant differences between the results were found.

Differences among *C. albicans* isolates of different serotype and different susceptibility to 5-FC. Considerable variations in distributions of positive test results were apparent when isolates were grouped according to their serotype or their susceptibility to 5-FC in tube dilution tests (Table 2). Serotype A isolates were significantly less often resistant to 5-FC than were serotype B isolates, and they were significantly less salt tolerant. Statistical analysis revealed 70 further significant differences in biochemical test results considered two at a time and three at a time; none would be expected by chance alone.

When isolates were grouped according to their susceptibility to 5-FC after 1, 2, and 7 days in tube dilution tests, the biochemical tests showed many phenotypic differences between resistant and susceptible isolates. Since resistance to 5-FC was one of the standard biochemical strain tests, the data afforded the opportunity to compare results of tube and plate tests done under different conditions in different laboratories. Overall, the agreement between the quantitative tube test data and the qualitative plate test data was good. None of the isolates susceptible to 5-FC after 7 days in tube tests was found to be resistant in the agar plate tests, and 83% of the strains that were resistant in tube dilution tests were also found to be resistant in the plate tests (Table 2). The overall agreement between the two test methods was 93%.

Although isolates exhibited resistance to 5-FC after 1, 2, or 7 days in tube tests, there were no statistically significant differences among the biochemical data for groups of strains that showed 5-FC resistance at these different times (Table 2). However, among all isolates that had shown 5-FC resistance by 7 days and those susceptible to 5-FC by 7 days, there were many differences in the biochemical profiles: susceptible isolates were significantly more often proteinase positive and significantly less often salt tolerant, safranine resistant, and able to assimilate citrate. Among the biochemical patterns of the four groups of 5-FC susceptibility (Table 2), there were 168 significant differences overall. Chance expectation of significant differences was 0.8.

Differences among *C. albicans* isolates from different geographical origins. When isolates were grouped according to their geographical origin, several significant biochemical differences were noted in plate tests (Table 3). Among the isolates from the United States, there were significantly more strains that grew at pH 1.40 and significantly fewer 5-FC-resistant strains from Boston University than from NIH, significantly fewer sorbose-positive strains from NIH than from the Mayo Clinic or Baylor, and significantly more salt-tolerant strains from NIH than from UCLA. In addition to these 5 significant differences in proportions of positive results in individual tests, there were a further 20 differences in tests analysed in pairs and threes. The expectation of significant differences by chance alone was 1.3. Comparison of all the U.S. isolates with all of the United Kingdom (U.K.) isolates revealed large numbers of statistically significant differences (Table 3); differences were still evident even when the analysis was restricted to genital isolates only (since most of

TABLE 1. Percentages of U.S. *C. albicans* strains giving positive results in each of nine biochemical tests[a]

Source of isolation	No. of strains	% of strains positive for the following biochemical test:								
		pH 1.4 growth	Proteinase secretion	5-FC resistance	Urea assimilation	Sorbose assimilation	Salt tolerance	Citrate assimilation	Glycine assimilation	Safranine resistance
Superficial										
Mouth/upper respiratory tract	50	50.0	28.0	32.0	90.0	36.0	64.0	80.0	94.0	80.0
Rectum/anus/feces	19	47.4	10.5	42.1	89.5	15.8	52.6	94.7	100.0	94.7
Female genital tract	31	35.5	32.3	51.6	87.1	22.6	74.2	93.5	100.0	87.1
Skin/male genitalia	34	50.0	26.5	23.5	82.4	26.5	64.7	79.4	97.1	88.2
Wounds	18	55.6	27.8	38.9	94.4	44.4	66.7	88.9	100.0	100.0
Nails	8	37.5	12.5	50.0	100.0	25.0	100.0	87.5	100.0	100.0
Intermediate										
Gastrointestinal tract	7	85.7	57.1	14.3	85.7	42.9	42.9	71.4	100.0	71.4
Sputum	39	48.7	20.5	25.6	97.4	41.0	76.9	97.9	100.0	92.3
Urine	51	51.0	31.4	29.4	84.3	31.4	74.5	84.3	96.1	92.2
Deep										
Respiratory tract	23	69.6	34.8	34.8	69.6	21.7	69.6	65.2	91.3	78.3
Blood/intravenous catheter	25	60.0	32.0	32.0	92.0	56.0	60.0	80.0	100.0	96.0
Other deep tissues	22	45.5	40.9	27.3	86.4	40.9	98.2	77.3	95.5	86.4
All superficial isolates		46.9	25.6	36.9	88.8	29.4	66.9	85.6	97.5	88.1
All intermediate isolates		52.6	28.9	26.8	89.7	36.1	73.2	87.6	97.9	90.7
All deep isolates		58.6	35.7	31.4	82.9	40.0	65.7	74.3	95.7	87.1

[a] Strains were grouped according to their anatomical source of isolation. The designations "superficial," "intermediate," and "deep" are nominal only; for example, many of the samples of urine and sputum may have contained *C. albicans* picked up as a contaminant from the perineum or the mouth. For three isolates, the available information on sources was insufficient to allow their assignment to anatomical site.

TABLE 2. Percentages of *C. albicans* strains giving positive results in each of nine biochemical tests[a]

Source of isolation[a] (strain type)	No. of strains	% of strains positive for the following biochemical test:								
		pH 1.4 growth	Proteinase secretion	5-FC resistance	Urea assimilation	Sorbose assimilation	Salt tolerance	Citrate assimilation	Glycine assimilation	Safranine resistance
Resistant to 5-FC after 24 h	13	46.2	23.1	92.3	69.2	46.2	76.9	92.3	100.0	84.6
Resistant to 5-FC after 48 h	51	51.0	15.7	82.4	92.2	37.3	82.4	92.2	100.0	96.1
Resistant to 5-FC after 7 days	65	36.9	10.8	81.5	87.7	29.2	87.7	93.8	98.5	95.4
Susceptible to 5-FC	201	56.2	38.3	0.0	88.1	34.3	58.2	78.1	96.0	85.1
Serotype A isolates	170	54.8	34.5	5.4	89.9	38.1	51.8	80.4	97.0	86.3
Serotype B isolates	157	49.0	21.7	61.8	86.0	28.0	87.3	88.5	98.1	91.1

[a] Strains were grouped according to their susceptibility to 5-FC and their serotype. Serotype was indeterminate for three isolates.

the British strains came from this source). There were 79 significant differences between all U.S. and all U.K. isolates: in single tests, the significant differences were for growth at pH 1.40, 5-FC resistance, urea assimilation, sorbose assimilation, glycine assimilation, and safranine resistance, but the urea assimilation test was the only single test to show a statistically significant difference in positivity when the analysis was restricted to U.S. genital strains versus U.K. genital strains.

Cluster analysis of U.S. isolates. For the 330 *C. albicans* isolates from the United States, a dendrogram derived from a sorted similarity matrix was drawn up on the basis of 10 strain characteristics. Serotypes A and B were scored 1 and 2, respectively. 5-FC susceptibility data from tube dilution tests were scored as follows: 1 = susceptible; 2 = resistance apparent after 7 days; 3 = resistance apparent after 2 days; 4 = resistance apparent within 24 h. Because the 5-FC susceptibility data from the tube tests offered this greater opportunity for quantitation, the 5-FC data from plate tests were not used. The data from the other eight biochemical tests were scored as follows: 1 = negative; 2 = variable; 3 = positive. The results of the analysis, shown in simplified form in Fig. 1, indicated that the strains fell into 11 clusters with an intragroup similarity of 70% or greater, and that the majority of strains fell into clusters A, B, and C, which showed internal structure and could be divided into subclusters (Fig. 1). The major characteristics of the strains in each cluster are summarized in Table 4.

Strains in cluster A were all serotype B, proteinase negative, citrate and glycine positive, and predominantly resistant to 5-FC by 7 days. In subcluster A2, there were more strains from NIH and fewer from Boston University than expected. Strains in cluster B were predominantly serotype B and mostly susceptible to 5-

TABLE 3. Percentages of *C. albicans* strains, grouped by geographical origin, giving positive results in each of nine biochemical tests

Source of isolation	No. of strains	% of strains positive for the following biochemical test:								
		pH 1.4 growth	Proteinase secretion	5-FC resistance	Urea assimilation	Sorbose assimilation	Salt tolerance	Citrate assimilation	Glycine assimilation	Safranine resistance
U.S. isolates										
Baylor	73	53.4	35.6	37.0	89.0	46.6	69.9	87.7	94.5	91.8
Boston University	68	63.2	33.8	22.1	92.6	32.4	67.6	91.2	97.1	94.1
Mayo Clinic	66	47.0	31.8	28.8	84.8	42.4	68.2	75.8	100.0	81.8
NIH	63	38.1	19.0	46.0	88.9	17.5	84.1	87.3	98.4	84.1
UCLA	60	53.3	21.7	28.3	81.7	28.3	51.7	78.3	96.7	91.7
All U.S. isolates	330	52.0	28.3	32.6	88.0	33.2	68.9	84.3	97.5	88.6
All U.K. isolates	247	38.3	27.6	21.8	66.7	23.0	70.0	78.2	90.9	78.6
U.S. genital isolates	39	48.7	20.5	25.6	97.4	41.0	76.9	94.9	100.0	92.3
U.K. genital isolates	215	38.1	24.7	21.4	63.3	21.9	69.8	77.2	90.2	78.6

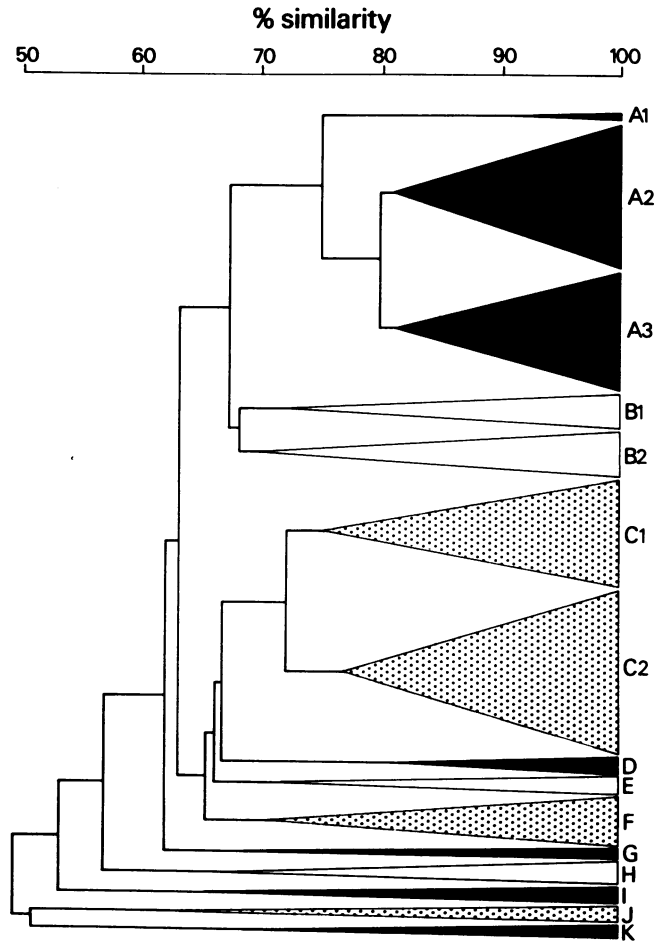

FIG. 1. Simplified average-linkage dendrogram of 330 *C. albicans* isolates from the United States. The length of the base of each isosceles triangle is proportional to the number of strains in the cluster indicated by that triangle. The apex of each isosceles triangle indicates the lowest percentage similarity of strains within the cluster. Intergroup similarities are indicated by the perpendicular linkages.

FC. They were all proteinase positive, and subclusters B1 and B2 were distinguished principally by the ability to grow at pH 1.40. Cluster C contained the greatest number of strains of all of the clusters and probably represented the commonest phenotypes of *C. albicans*. All but 1 of the 114 strains were serotype A; all but 13 were susceptible to 5-FC in tube dilution tests (the highest noncorrelation between tube and plate 5-FC data was for strains in this cluster). The strains in cluster C were all citrate and glycine positive, and most were safranine positive; few were positive in the plate 5-FC resistance test. Subcluster C2 contained almost all pH 1.40-tolerant types, whereas group C1 contained very few. There were more strains from Boston University than statistically expected in cluster C2.

Clusters D to K represented the numerically less common *C. albicans* phenotypes. In cluster D, the strains were all 5-FC susceptible and negative in the pH 1.40, proteinase, urea, and sorbose tests. Cluster E contained safranine-susceptible, 5-FC-susceptible, proteinase-negative strains, all of serotype A. All eight strains in this cluster were isolated from superficial sites, in contrast to statistical expectations. Strains in group F were citrate negative and mostly serotype A. Those in group G were resistant to 5-FC and were proteinase negative. In group H, the strains were all salt tolerant, but otherwise they had a mixture of phenotypic characteristics. There were more strains from the Mayo Clinic in cluster H than expected. Strains in group I were all safranine sensitive and mostly 5-FC sensitive. Those in group J were all 5-FC sensitive (in

TABLE 4. Characteristics of *C. albicans* strains in the clusters shown in Fig. 1

Cluster no.	No. of strains	No. resistant to 5-FC	No. of serotype A	No. of strains from[a]:					No. of strains from anatomical sites that were[b]:			Biochemical strain types within cluster
				Ba	Bo	Ma	NIH	UCLA	Sup	Int	Deep	
A1	3	3	0	0	0	1	1	1	2	0	1	467
A2	61	51	0	13	10	6	23	9	36	16	8	017, 057, 077, 417, 453, 457, 477, 553, 557
A3	50	40	0	7	15	14	9	5	22	16	10	147, 157, 177, 547, 557, 567, 577
B1	14	3	0	1	6	2	1	4	5	6	3	317, 337, 357, 377, 717
B2	18	5	9	7	5	1	4	1	10	3	5	247, 253, 256, 257, 273, 647, 657
C1	45	10	44	9	12	11	6	7	18	20	7	017, 037, 057, 077, 177, 217, 237, 277, 637
C2	69	3	69	10	12	21	9	17	34	19	16	113, 117, 137, 147, 153, 157, 217, 317, 357, 377
D	6	0	5	1	1	1	1	2	3	2	1	006, 007, 047
E	8	0	8	4	1	2	0	1	8	0	0	011, 013, 033, 132, 133
F	21	5	19	5	5	3	3	5	8	6	7	016, 036, 076, 116, 156, 166, 176, 216, 236, 376
G	4	4	3	1	1	2	0	0	2	1	1	127, 175, 537, 577
H	11	2	2	5	1	2	1	2	4	3	4	146, 156, 344, 346, 352, 356, 446
I	6	1	3	4	1	0	1	0	2	2	2	332, 352, 353, 372, 373
J	9	0	3	0	2	1	2	4	4	2	3	024, 030, 064, 200, 202, 204, 206, 212, 213
K	5	2	5	0	1	1	1	2	3	0	2	100, 512, 543

[a] Ba, Baylor; Bo, Boston University; Ma, Mayo Clinic.
[b] Sup, Superficial; Int, intermediate.

tube and plate tests), sorbose negative, salt sensitive, and safranine sensitive. The strains in group K were all serotype B, proteinase negative, sorbose negative, and safranine sensitive.

Cluster analysis of strains from the United States and the United Kingdom. To compare strain similarities among *C. albicans* isolates from the United States and the United Kingdom, a dendrogram was again drawn by computer on the basis of a sorted similarity matrix. This time, only the nine characters from the plate strain differentiation tests were used to determine similarities. Use of the plate test data for 5-FC resistance in place of the tube test data was essential to allow sensible comparison of the U.K. isolates, for which tube test data were not available. Although the substitution of this test undoubtedly affected the reclustering of the U.S. isolates, the 93% agreement between plate and tube susceptibility data means that such changes should be minimal. For this cluster analysis, negative test results were scored 1, variable results were scored 2, and positive results were scored 3. The dendrogram, shown in simplified form in Fig. 2, showed that the strains tended to group in 14 clusters on the basis of 70% similarity or greater. Three of these clusters divided naturally into subclusters. The clusters in Fig. 2 were numbered rather than lettered to avoid confusion in comparison with the clusters in Fig. 1.

Strains in cluster 1 were all pH 1.40, proteinase, and urea negative and were susceptible to 5-FC. All of the U.S. group D strains and one group G strain fell within this cluster. There were more U.K. strains in group 1 than statistically expected (Table 5). Group 2 strains were pH 1.40 and proteinase negative, 5-FC susceptible, and urea positive. Most of the U.S. strains in this group were from cluster C1 in Fig. 1, with a few from groups A2 and E. Group 3 contained only two strains, one from each country; they were types O11 and O15. Group 4a strains were pH 1.40 tolerant, proteinase negative, 5-FC susceptible, and citrate positive. All but one of the U.S. strains in this cluster were from group C2 in Fig. 1. Strains in group 4b differed from those in 4a in that they were all sorbose positive.

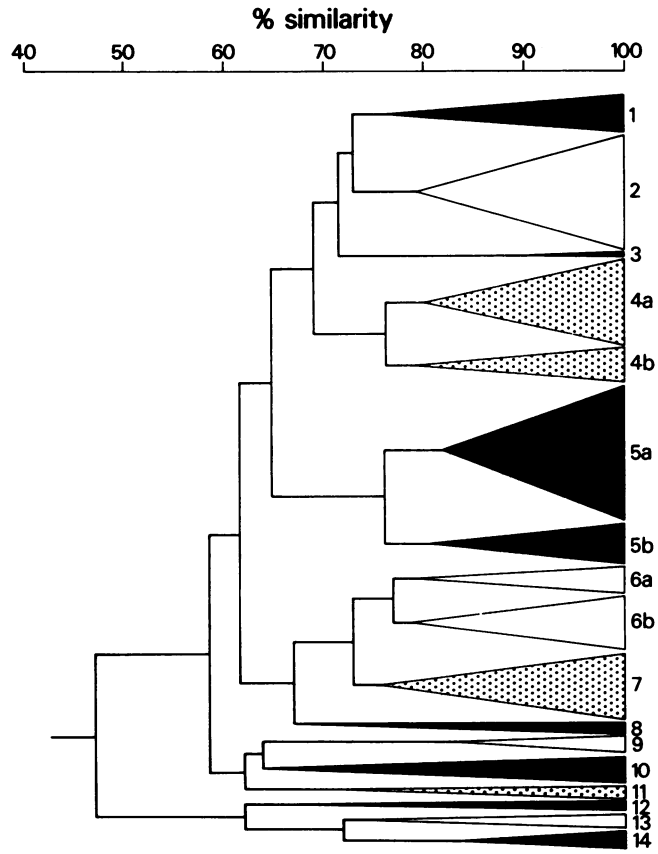

FIG. 2. Simplified average-linkage dendrogram of 577 *C. albicans* isolates from the United States and the United Kingdom. For explanation, see the legend to Fig. 1.

TABLE 5. Distribution of U.S and U.K. *C. albicans* strains in the clusters shown in Fig. 2

Cluster no.	No. of strains from the U.S.		No. of strains from the U.K.	
	Observed	Expected	Observed	Expected
1	7	17	23	13
2	49	53	44	40
3	1	1	1	1
4a	41	39	28	30
4b	19	15	8	12
5a	80	61	27	46
5b	12	18	20	14
6a	13	11	7	9
6b	19	26	26	19
7	42	33	15	24
8	2	4	5	3
9	8	9	7	6
10	18	13	4	9
11	11	10	6	7
12	1	4	6	3
13	3	8	11	6
14	4	7	9	6

Again, most U.S. strains in this group were from group C2 in Fig. 1, though there were also some strains from groups A3, E, F, and G. Strains in group 5 were all 5-FC resistant, citrate and glycine positive, and salt tolerant. Those in subcluster 5a were urea positive, and those in 5b were urea negative. U.S. strains in group 5a were mainly from group A2 in Fig. 1, and there were more U.S. strains in this group than expected. Strains in group 5b were mainly from group A3 in Fig. 1.

The strains in cluster 6 were all proteinase positive, and most were pH 1.40 negative, and urea and salt positive. Subclusters 6a and 6b differed in their ability to assimilate sorbose. Group 6a, containing the sorbose-positive strains, had U.S. strains from cluster C1 in Fig. 1, with only one exception. U.S. strains in group 6b were mostly from group B2 in Fig. 1. Group 6b contained slightly more U.K. strains than statistically expected (Table 5). Cluster 7 in Fig. 2 contained U.S. strains, mainly from clusters B1 and C2; all were pH 1.40, proteinase, urea, citrate, and glycine positive. There were more U.S. strains in this cluster than statistically expected.

Clusters 8 to 14 represented only a minority of all strains tested. Those in group 8 were all pH 1.40 negative, urea negative, and citrate and glycine positive, and the U.S. strains came mainly from group B2 in Fig. 1. U.S. strains from group F in Fig. 1 were split between clusters 9 and 10 in Fig. 2. Those in group 9 were all 5-FC-sensitive and salt and citrate negative, and those in group 10 were citrate negative and urea positive. Group 11 in Fig. 2 contained strains that were 5-FC susceptible, mostly salt positive, sorbose negative, and citrate negative; the U.S. strains in this group were mainly from group H in Fig. 1. Six of the seven strains in cluster 12 were from the United Kingdom. They were all pH 1.40, citrate, and glycine negative, and 5-FC sensitive. Group 13 strains, all proteinase, urea, sorbose, and citrate negative, contained U.S. strains only from group K in Fig. 1, and group 14 strains, all proteinase positive, urea, sorbose, salt, and citrate negative, contained U.S. strains only from group J in Fig. 1. Groups 12 to 14 contained a higher number of U.K. strains than statistically expected (Table 5).

DISCUSSION

The nine biochemical tests used to differentiate *C. albicans* phenotypes in this study allow for a theoretical maximum of 512 strain types. In practice, we have seen only about 160 different types among more than 700 old and new isolates tested in this and another study (6). This suggests that, as for most organisms, there are more likely to be discrete groups of strains, each with a set of common phenotypic characters, than a continuous spectrum of phenotypes representing all possible properties. The data presented in this paper support and amplify this contention. We have identified and described the predominant groups of *C. albicans* phenotypes. Strains from a wide variety of sources fall naturally into fewer than 20 clusters of statistically similar types, and the great majority of phenotypes belong to only 10 of these clusters (Fig. 2). Some of the biochemical properties of *C. albicans* phenotypes showed correlation with the serotype of the strain and with its susceptibility or resistance to 5-FC, but such correlations were not absolute, so that it would not easily be possible to determine serotype or 5-FC susceptibility on the basis of biochemical profiles.

Although there may be limitations on the number of strain types that may be encountered in the whole, natural population of *C. albicans* phenotypes, there are clear variations in their geographical distribution between the United States and the United Kingdom and even between different areas of the United States. There is a higher preponderance in the United States of strains that are tolerant of low pH, resistant to 5-FC or safranine, and able to assimilate urea, sorbose, or glycine.

It cannot be concluded for certain whether any of these biochemical properties correlate with virulence of *C. albicans* strains, since no direct markers of virulence were used in this study. However, it is likely that isolates from deep tissues, representing the most severe forms

of *C. albicans* infection, would contain a smaller proportion of the least virulent types than isolates from superficial sites. There were no statistically significant differences among the biochemical profiles of *C. albicans* strains isolated from superficial, intermediate, or deep sites (Table 1), which indicates either that the biochemical profiles bear no relation to virulence at all, or that the inherent virulence levels of naturally occurring *C. albicans* strains differ very little. This observation matches that of a study with genital isolates in the United Kingdom, in which there were no significant differences between strain types associated with clinical symptoms of genital candidosis and those from patients without such symptoms (6). This similarity in distribution of strain types (within a given geographical area), regardless of their pathological source, is entirely compatible with the long-held view of *C. albicans* as an opportunistic pathogen that is so low in virulence it can cause infection only when there are changes in host defenses (3).

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