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Usefulness of Serial Antibody Determinations in Diagnosis of Candidiasis as Measured by Discontinuous Counterimmunoelectrophoresis Using HS Antigen

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We have followed the candida antibody response in 115 patients with different types of candidiasis by discontinuous counterimmunoelectrophoresis using HS antigen to learn whether any early antibody response occurs in systemic candidiasis and whether there are differences in the antibody response in candidiasis involving different organ systems. We found that 23 of 32 (72%) patients with systemic candidiasis had a rise in antibody titer within the first 2 weeks of infection and that high titers were relatively insensitive indicators of infection. No differences were seen in the antibody response in different types of candidiasis. Patients with aspergillosis and torulopsosis had titer rises as well which were attributed to either inapparent candida infection or cross-reacting antibody. A rise in titer was not seen in any patient with candida colonization, bacterial or viral infection, or no infection in contrast to titers ≥1/1 or ≥1/8 which were seen in these conditions.

The importance of *Candida albicans* and related species as a cause of systemic infection in compromised hosts and the great difficulty encountered in diagnosing this type of infection are well recognized (34). Differences in the sensitivity and specificity of serological tests for systemic candidiasis have been noted (9, 11, 15, 29, 30). Relatively little is known about the time course and magnitude of the antibody response in different types of candidiasis. Yet the usefulness of a serological test in the diagnosis of systemic candidiasis not only depends on the identification of an early antibody response but also on the existence of a difference in the magnitude of the antibody response in different types of candidiasis.

We have followed the candida antibody response in 115 patients with different types of candidiasis by discontinuous counterimmunoelectrophoresis (DCIE) to learn whether an early antibody response occurs and whether there are differences in the amount of antibody produced in different types of candidiasis. We have compared these results with antibody determinations in patients with other conditions to determine the specificity of this serological test for candidiasis. The sensitivity and specificity of single and serial determinations of antibody titer were compared.

(A preliminary report of this work has been presented previously [R. Marier and V. T. Andriole, Clin. Res. 24:349A, 1976]).

MATERIALS AND METHODS

Patient population and diagnostic criteria. A total of 262 patients hospitalized at the Yale-New Haven Hospital or at an affiliated hospital between January, 1975, and January, 1977, were the subjects of this report. Diagnostic criteria were adopted as follows.

For systemic candidiasis (45 patients): direct (i.e., histological) identification of *Candida* in tissue (i.e., hearts, lungs, kidneys, livers, spleens, or central nervous systems) or repeated isolation from blood, peritoneal, pleural, or cerebrospinal fluids.

For gastrointestinal candidiasis (12 patients): direct (i.e., histological) identification of *Candida* in gastrointestinal tissue only, excluding the oropharynx, or signs and symptoms of esophageal candida infection, i.e., severe dysphagia or retrosternal pain and an unequivocal response to antifungal therapy.

For urinary tract candidiasis (35 patients): repeatedly positive (two or more) urine cultures in patients without evidence of candidiasis elsewhere.

For superficial candidiasis (23 patients): signs and symptoms of oropharyngeal, skin, or wound infections plus repeatedly positive smears and cultures for *Candida*.

For other fungal infections (24 patients): direct (i.e., histological) identification of the fungus in tissues and exclusion of candidiasis. Aspergillosis (18 patients), torulopsosis (2 patients), mucormycosis (2 patients), cryptococcosis (1 patient), and *Trichosporon cutaneum* endocarditis (1 patient).

For candida colonization (18 patients): repeated isolation of *Candida* from the gastrointestinal tract or airway with no evidence of local or systemic candida infection.

For bacterial or viral infection (60 patients): isolation of the microorganism from clinical material or serological evidence of infection, with exclusion of current candida colonization and infection as defined above. Bacterial endocarditis (10 patients), active tuberculosis (7 patients), salmonellosis (3 patients), and other bacterial or viral infections (40 patients).

For no infection or colonization (44 patients): no infection or colonization as defined above. Antibody-positive patients in this group had negative urine and sputum cultures.

Onset of infection was defined as the appearance of signs or symptoms or radiographic abnormalities subsequently proven to be due to candidiasis or some other infection. Onset of urinary tract candidiasis or colonization was defined as the time of the first positive culture.

Candida were identified by standard methods (32).

Antibody assay. The method used in this study has been described in detail elsewhere (19). Briefly, electrophoresis plates were prepared by precoating glass plates (7.8 by 10.2 cm) with 4 ml of 1% ion agar in distilled water. After drying, these plates were coated with 14 ml of 1% agarose in 0.015 I barbital buffer. Pairs of wells, 2 mm in diameter and separated by 4 mm horizontally and 2 mm vertically, were cut in the gel through a plastic template. Antibody was placed in the left-hand (anodal) row, and antigen was placed in the right-hand (cathodal) row. The antigen used in this study was purchased from the Hollister Stier Laboratories and has been termed HS antigen (see below). Each dilution of serum was reacted with five dilutions of antigen (1/4 to 1/64). Plates were subjected to electrophoresis for 20 min at 30 mA (18 V/cm) and examined under indirect light for precipitin bands. The appearance of a precipitin band at any dilution of antigen was defined as a positive result at that dilution of serum. No multiple bands were seen in positive sera. A rise in antibody titer was defined as a fourfold increase in titer or conversion from negative to positive.

Statistical tests. The significance of differences observed between groups was measured by the chi-square test.

RESULTS

The effect of the time course of the antibody response on the sensitivity of antibody determinations in the diagnosis of systemic candidiasis is summarized in Table 1. Details for each patient are tabulated in Appendix A. Patients were studied at weekly intervals after the onset of infection. The number of patients with titers ≥1/1 increased from 8 of 34 (24%) at the onset of infection to 20 of 28 (71%) and 17 of 23 (74%) by 7 and 14 days after the onset of infection. In addition, a titer rise was seen in 13 of 23 (57%) and 23 of 32 (72%) patients studied serially 7 and 14 days after the onset of infection. In contrast, high titers (≥1/8) were seen less often than titers ≥1/1 or titer rises.

A significant fall in antibody titer (≥4-fold fall or conversion from positive to negative) was observed in four cases. Two patients had candidemia and candiduria associated with infected intravenous sites. The intravenous lines were removed, and the cultures reverted to negative without specific antifungal therapy. (There were no other patients in this study with "transient" candidemia.) The third patient with a fall in antibody titer had a perforation of the large bowel after surgery. Blood and abdominal abscess cultures were positive for *C. albicans*. She was started on amphotericin B. Two days later she died. Candidiasis involving the heart and kidneys was identified at autopsy. The fourth patient had acute nonlymphocytic leukemia in relapse. He was admitted with fever, a large perirectal abscess, and pseudomonas bacteremia. The fever persisted, and he died 14 days after admission. Cultures of sputum, urine, blood, and abscess drainage were negative for candida. At autopsy he had candidiasis involving the lung, kidney, heart, and spleen (Appendix A).

TABLE 1. *Effect of the time course of the antibody response on the sensitivity of DCIE for systemic candidiasis*

Days after onset	Antibody determination [no. of patients positive/total (%)]		
	Titer ≥1/1	Titer ≥1/8	Titer rise[a]
0	8/34 (24)	0/34 (0)[b]	
7	20/28 (71)[c]	3/28 (11)[b]	13/23 (57)
14	17/23 (74)[c]	9/23 (39)[c,d]	23/32 (72)
21	9/11 (82)[c]	2/11 (18)[b]	26/33 (79)
28	9/11 (82)[c]	3/11 (27)[b,e]	28/34 (82)

[a] ≥Fourfold rise in titer or conversion from negative to positive.

[b] Significant difference versus titer ≥1 or titer rise at this time ($P < 0.01$).

[c] Significant difference versus day 0 for this type of antibody determination ($P < 0.01$).

[d] Significant difference versus titer ≥1 or titer rise at this time ($P > 0.05$).

[e] Significant difference versus day 0 for this type of antibody determination ($P < 0.05$).

The effect of underlying disease on the antibody response in systemic candidiasis was determined by comparing the antibody response of patients with different underlying diseases. A rise in titer was seen in acute leukemia (6 of 8), renal failure (5 or 7), and other conditions (17 of 19). Peak titers ≥1/8 were seen in only 1 of 9 (11%) patients with acute leukemia in contrast to 14 of 36 (37%) patients with other conditions ($P > 0.05$).

The specificity of this serological test for different types of candidiasis was determined by comparing the antibody response in 115 patients with candida infection involving different organ systems (Table 2). Details for each patient are

tabulated in Appendixes A and B. No significant differences were seen in the percentage of patients with different types of candidiasis who had peak titers ≥1/1, ≥1/8, or titer rises except for patients with urinary tract candidiasis, fewer of whom had titer rises than did patients with systemic candidiasis.

The specificity of this serological test for candidiasis in general was determined by comparing the antibody titers of the 115 candidiasis cases with 147 other patients (Table 3). Titers ≥1/1 were seen in many patients with other fungal infections, candida colonization, and other conditions. Titers ≥1/8 were seen in most patient categories as well but less often. In contrast, a titer rise was seen only in patients with candidiasis or some other fungal infection (aspergillosis or torulopsosis). In patients without candidiasis or some other fungal infection, titers ≥1/1 were seen more often than a rise in titer (12 of 123 versus 0 of 57, $P < 0.02$).

TABLE 2. *Specificity of DCIE for different types of candidiasis*

Type of candidiasis	Antibody determination[a] [no. of patients positive/total (%)]		
	Titer ≥1/1	Titer ≥1/8	Titer rise[b]
Systemic	39/45 (87)[c]	15/45 (33)	28/34 (82)[c]
Gastrointestinal	7/12 (58)[d]	1/12 (8)	5/8 (67)[d]
Urinary tract	24/35 (69)[c]	5/35 (14)	7/21 (33)[d,e]
Superficial	18/23 (78)[c]	7/23 (30)	6/12 (50)
Total	88/115 (76)[c]	28/114 (25)	49/75 (65)[c]

[a] Within 1 month after the onset of infection.

[b] ≥Fourfold rise in titer of conversion from negative to positive.

[c] Significant difference versus titer ≥1/8 for this type of candidiasis ($P < 0.01$).

[d] Significant difference versus titer ≥1/8 for this type of candidiasis ($P < 0.05$).

[e] Significant differences versus systemic candidiasis ($P < 0.01$).

TABLE 3. *Specificity of DCIE for candidiasis*

Patient category	Antibody determination(s)[a] [no. of patients positive/total (%)]		
	Titer ≥1/1	Titer ≥1/8	Titer rise[b]
Candidiasis	88/115 (76)	28/114 (25)	49/75 (65)
Other fungal infection	12[c]/24 (50)[d]	3/24 (13)	7/11 (64)
Candida colonization	8/19 (42)[d]	2/19 (11)	0/12 (0)[d]
Bacterial or viral infection	0/60 (0)[d]	0/60 (0)[d]	0/25 (0)[d]
No infection or colonization	4/44 (9)[d]	2/44 (4)[d]	0/20 (0)[d]

[a] Within 1 month after the onset of infection.

[b] ≥Fourfold rise in titer or conversion from negative to positive.

[c] Aspergillosis (10/18); torulopsosis (2/2).

[d] Significant difference versus candidiasis for this type of antibody determination ($P < 0.01$).

DISCUSSION

We have shown that most patients with systemic candidiasis have a rise in candida antibody using DCIE and HS antigen within the first 2 weeks of infection and that high titers are relatively insensitive indicators of infection (Table 1). We have also shown that patients with different types of candidiasis have similar antibody responses (Table 2) and that a titer rise is more specific for candida infection than titers greater than or equal to 1/1 and more sensitive than titers greater than or equal to 1/8 (Table 3).

We also found that some patients with torulopsosis and aspergillosis had rises in candida antibody. This was attributed to either inapparent candida infection or cross-reacting antibody. Cross-reacting antibody has been identified in torulopsosis (27) and in one (22) but not other (4, 10, 25, 27) reports of aspergillosis. More study is needed of the antigenic relationships between *Aspergillus* and *Candida* species.

An increase in antibody titer was not seen in any of 10 patients with bacterial endocarditis studied by us in contrast to the findings of Bacon et al. (2). Because there is some evidence that tuberculosis and salmonellosis may be associated with cross-reacting agglutinating antibody (30), we studied 10 such patients; none of these patients was positive.

Studies of patients after open heart surgery suggest that they may have a rise in candida antibody titer as well (2, 20, 30). At present, no explanation for this phenomenon exists. We have confirmed this observation in preliminary studies of our own. In any case a long follow-up period is required, however, before excluding candida endovascular infection. Until further studies are completed, the significance of a rise in candida antibody in the open heart surgery postoperative period remains unknown.

A variety of antigens has been used to measure the antibody response in candidiasis. The major antigens present in the cell wall of *C. albicans* are polysaccharides called mannans (12). Antibody reacting with cell wall antigens has been measured by agglutination or immunofluorescence of yeast cells or by immunodiffusion (ID) or hemagglutination. According to most reports, candida cell wall antibody may be identified in many normal subjects (7–9, 14, 16, 22, 26, 33) and may not be as useful in the diagnosis of candidiasis as is antibody reacting with "cytoplasmic" antigens. A variety of protein, polysaccharide, and glycoprotein antigens is present in the cytoplasm of *C. albicans*. These antigens may be isolated by mechanical (25) or ultrasonic disruption (28) of yeast cells or protoplasts (31) and have been termed C, S, or HS antigen. C, S,

or HS antigens may contain some cell wall or mannan antigen as well (3). We used the HS antigen to detect antibody by DCIE in this study because it is commercially available, standardized if not defined, and has been used by others (5, 6, 10, 23, 28). Antibody reacting with these antigens has been measured by ID, latex agglutination, and CCIE (Table 4). Differences observed in the specificity of serological tests for candidiasis using this type of "antigen" are in part due to differences in the composition of the control groups. Most studies have found that 80% or more of patients with systemic candidiasis are positive by one of these tests (Table 4).

Counterimmunoelectrophoresis using a continuous buffer system (CCIE) and HS antigen was first used for the measurement of candida antibody by Remington et al. who found that 19 of 19 patients with systemic candidiasis were positive (titer ≥ 1/1) whereas 0 of 67 healthy preoperative patients were positive (23). Dee and Rytel reported that 21 of 24 (88%) patients with systemic candidiasis and 62 of 140 (44%) patients with other conditions, including candida colonization and other types of fungal infections, were positive as well (6). In these studies the timing of the antibody determination was not stated. In general our results are in agreement with these studies. Our methodology differed only in that we used a discontinuous buffer system which we have shown to be more sensitive and faster than CCIE (19).

The usefulness of measuring antibody titer by CCIE was emphasized by Dee and Rytel (5, 6)

TABLE 4. *Sensitivity and specificity of tests for antibody reacting with S, C, or HS antigens in the diagnosis of candidiasis*

Study	Yr	No. of patients positive (titer ≥1/1)/total			Method[a]
		Systemic infection	Superficial infection	Controls	
Taschdjian et al. (30)	1964–1973	42/52	9/66	0/75	ID
Stallybrass (25)	1964	1/1	0/15	0/228	ID
Coudert et al. (4)	1967	1/1	0/17	0/200	ID
Louria et al. (17)	1967		10/10		ID
Preisler et al. (21, 22)	1969–1971	10/37	3/3	3[b]/150	ID
Remington et al. (23)	1972	19/19		0/67	ID
Stanley et al. (26)	1972		11/91[c]	4[d]/99	ID
Stickle et al. (27)	1972	38/43	3/9	1[e]/102	ID
Gaines and Remington (10)	1973	24/26	1/1	1[f]/106	ID
Jones et al. (14)	1973	8/8	4/35	1/60	ID
Andersen and Stenderup (1)	1974	5/11	6/43	3[g]/301	ID
Dee and Rytel (5)	1975	9/10		0/60	ID
Everett et al. (8)	1975	7/12		0/59	ID
Weiner and Yount (33)	1976	9/14		2[h]/18	ID
Ellsworth et al. (7)	1977	3/20	3/11	2/8	ID
Filice et al. (9)	1977	10/12	7/8	12[i]/47	ID
Dee and Rytel (6)	1977	21/24		2/140[j]	ID
Stickle et al. (27)	1972	41/43		5[k]/102	LA
Remington et al. (23)	1972	19/19		0/67	CCIE
Hellwege et al. (13)	1972	4/5	3/3	7[l]/98	CCIE
Dee and Rytel (5)	1975	9/10		26[m]/60	CCIE
Dee and Rytel (6)	1977	22/24		62/140[j]	CCIE
Marier and Andriole (present study)	1978	39/45	18/23	24[n]/147	DCIE

[a] LA, Latex agglutination.
[b] Aspergillosis, 1; ? aspergillosis, 1; histoplasmosis, 1.
[c] Multiple specimens per patient included.
[d] Healthy subjects, 4.
[e] Torulopsosis, 1.
[f] Chronic lung disease, 1.
[g] Candida colonization, 2, healthy subject, 1.
[h] Candida colonization, 2.
[i] Candida colonization, 6.
[j] Candida colonization, superficial candidiasis, and transient candidemia, 97; other fungal infections, 9.
[k] Cryptococcosis, 3; torulopsosis, 1; tuberculosis, 1.
[l] Healthy subjects, 2; asthma, 4; newborn-maternal candidiasis, 1.
[m] Candidemia colonization, 15; bacteremia, 9; healthy subjects, 2.
[n] Aspergillosis, 10; torulopsosis, 2; candida colonization, 8; chronic lung disease, 1; lung cancer, 1; Hodgkin's disease, 1; midline granuloma, 1.

who found that 17 of 24 (71%) patients with systemic candidiasis had high titers (≥1/8), whereas only 3 of 140 "controls" had titers in this range. We found fewer patients with systemic candidiasis with high titers (15 of 45) (33%), but otherwise our results are comparable.

The value of serial determinations of antibody titer in the diagnosis of systemic candidiasis was first reported by Preisler et al (21, 22). A significant rise in candida antibody was seen in 21 of 37 (57%) patients as measured by agglutination and in 10 of 37 (27%) patients as measured by ID using S and M antigen; 3 of 150 (2%) control patients had a similar rise in antibody titer. These three patients had other types of fungal infection. A significant rise in antibody titer as measured by ID using S antigen and by agglutination was seen in 4 of 8 (50%) patients studied by Rosner et al. (24) and 5 of 5 (100%) patients as measured by CIE using HS antigen studied by Dee and Rytel (6), whereas an equal number of controls was negative. Patients with other types of fungal infection, however, were not included in the control groups studied by Rosner et al. and Dee and Rytel. We found a significant rise in antibody titer in a higher percentage of systemic candidiasis cases (85%) than did Priesler et al. or Rosner et al., but otherwise our results are comparable.

Ultimately, the standardization of serological tests for candidiasis may depend on the isolation and characterization of cell wall or cytoplasmic antigens and on the identification of a more specific antibody response. A great variety of antigens are present in the cell wall and cytoplasm of *Candida* species, and the use of isolated antigens might permit increased serological specificity for candidiasis.

We have shown that most patients with candidiasis have a titer rise in candida antibody over the first 2 weeks of infection and that a titer rise is more specific for candidiasis than a single titer ≥1/1 and more sensitive than a single titer ≥1/8. Other methods are needed to distinguish systemic from local forms of candidiasis. A more sensitive assay for candida antibody is needed to identify an early antibody response in patients who are negative by DCIE.

APPENDIX A

Antibody response in systemic candidiasis (45 patients)

Patient no.	Age	Sex	Associated conditions[a]	Positive cultures[b] (premortem)	Antibody titer (reciprocal) on day after onset:				
					0	7	14	21	≥28
1	72	M	CRF, PD	Per fluid	0	0	1		
2	6	M	Surg, TT	Bile	2	4	8		
3	65	M	IV	Bl[c]		2			8
4	44	M	CRF, PD	Per fluid	0	0	0	2	2
5	69	F	IV	Bl, ur	0	0	0	0	1
6	68	M	IV	Bl, ur			8		
7	60	M	Surg, VPS	CSF	0		0		
8	40	F	Surg, TT	Bile					4
9	1 week	M	Prem	Bl, CSF	0				
10	73	F	Apl anem	Bl	1	8			
11	49	F	Surg	Bl, ur, w	0	2	16	8	16
12	28	F	IVHA	Bl	0	0	1		
13	57	M	Im lymph	Bl, ur	0	1			
14	20	M	IV	Bl, IV site, ur	0	8			2
15	36	M	NHL	Bl, ur, sp	0				
16	70	F	DM	Bl, ur[d]	0	4			
17	19	F	ANLL	None	0[e]	4			
18	66	F	Surg, IC, S	Bl, ur, w, sp					16
19	86	F	Surg, ARF	Abscess				8	
20	82	M	ARF, PD	Per fluid, ur, sp	0	4	4	4	
21	94	M	Surg	Bl, ur				4	
22	38	F	NHL, S	Bl, ur, sp	0	1			
23	29	F	ARF	Bl, IV site, ur	2	4	8	4	2
24	41	F	Surg, ARF	Per fluid, ur, w, sp[d]		0	0	1	
25	36	M	Burn, ARF, PD	Bl, ur, per fluid	1		1		
26	41	F	ANLL	None	0	4			
27	63	M	Surg, ARF	Bl, ur		2	16		
28	41	F	Surg, ARF	Bl, abscess		8	4	2	0
29	7	M	Apl anem	Bl, sp			8		

APPENDIX A—*Continued*

Antibody response in systemic candidiasis (45 patients)

Patient no.	Age	Sex	Associated conditions[a]	Positive cultures[b] (premortem)	Antibody titer (reciprocal) on day after onset:				
					0	7	14	21	≥28
30	72	F	Surg, IVHA	Bl, ur, IV tip	0			0	
31	73	F	ANLL	Pl fluid, ur	0		2		
32	75	M	DM, Surg	None	0[c]				
33	29	M	ALL	Sp	2[c]				
34	46	M	Surg	Ur, w	0	0	0	2	
35	60	M	DM	Bl, ur, sp		4	16		
36	75	M	CLL	Bl, CSF	1				
37	70	M	Surg, DM, ARF	Ur, sp	0	4	1		
38	71	F	ANLL	Bl, ur, skin	0	2			
39	38	F	RA, Surg, S	Per fluid, w, sp	0		4		4
40	47	F	ANLL	Bl, ur[f]	0	0	8		
41	68	M	ANLL, ARF	None	0	0			
42	38	F	ANLL	Bl, ur	1	4			
43	11	M	Burn	Bl, ur, sp	0	4			0
44	79	M	ANLL	None	1	1	0		
45	85	M	Surg	Pl fluid	0		16		

[a] ALL, Acute lymphocytic leukemia; ANLL, acute nonlymphocytic leukemia; Apl anem, aplastic anemia; ARF, acute renal failure; CRF, chronic renal failure; DM, diabetes mellitus; IC, ileal conduit; Im lymph, immunoblastic lymphadenopathy; IV, intravenous catheter; IVHA, intravenous hyperalimentation; NHL, non-Hodgkin's lymphoma; prem, prematurity; RA, rheumatoid arthritis; S, steroids; Surg, surgery; TT, "T" tube drainage of bile duct; VPS, ventriculo peritoneal shunt; CLL, chronic lymphocytic leukemia; PD, peritoneal dialysis.

[b] Bl, blood; CSF, cerebrospinal fluid; pl fluid, pleural fluid; per fluid, peritoneal fluid; sp, sputum; ur, urine; w, wound. All isolates were *C. albicans* unless otherwise indicated.

[c] *Candida* species.

[d] *C. tropicalis.*

[e] Onset uncertain.

[f] *C. parapsolosis.*

APPENDIX B

Antibody response in gastrointestinal, urinary tract, and superficial, (oropharangeal, skin, and wound) candidiasis[a]

Patient no.	Age	Sex	Associated conditions	Site	Antibody titer (reciprocal) on day after onset:				
					0	7	14	21	≥28
46	57	M	ANLL	GI	2	0	0	0	
47	43	F	ANLL	GI	0	2		2	
48	65	M	ANLL	GI			0		
49	30	F	ANLL	GI	0	2			
50	63	M	ANLL	GI		2		8	8
51	40	M	CRF	GI	0	0	1		
52	59	M	Stomach cancer	GI	0[b]				
53	50	F	Bowel ischemia	GI	2	2			
54	53	M	NHL	GI	0				
55	80	F	ALL	GI		0			
56	36	F	CML	GI	0		4		
57	28	F	ANLL	GI	0		0		
58	56	M	Surg	UT	2			8	2
59	44	M	ARF, DM	UT		0	0		
60	59	M	ARF, CBD	UT	0	8	4		2
61	69	F	DM, CBD	UT	0	0		2	
62	73	F	DM	UT			1	0	
63	60	F	Surg, CBD	UT	0		0		0
64	61	M	S, CBD	UT		8	2		
65	69	F	DM	UT	0		0	0	
66	79	F	CBD	UT	0		1		
67	77	M	Surg, CBD, IVHA	UT			0	0	

APPENDIX B—*Continued*

Antibody response in gastrointestinal, urinary tract, and superficial, (oropharangeal, skin, and wound) candidiasis[a]

Patient no.	Age	Sex	Associated conditions	Site	Antibody titer (reciprocal) on day after onset:				
					0	7	14	21	≥28
68	66	M	CBD	UT		0	0		
69	57	M	CBD	UT	0		2		
70	72	M	CBD	UT	0	0		0	
71	65	M	DM	UT		0		0	
72	60	M	Surg, DM, CBD	UT			1	1	0
73	44	F	CBD	UT	0	0		0	
74	64	M	ARF, Surg, CBD	UT	2				1
75	19	F	S, ARF, SLE	UT	0	0			
76	68	M	CBD	UT	4		2		
77	82	M	ARF, CBD	UT	1	4	8		
78	72	F	ARF, Surg, CBD	UT	0	4	4		
79	76	F	ARF, CBD	UT	2				
80	73	F	DM, CBD	UT				0	
81	30	F	Surg, DM, CBD	UT	4				
82	72	M	Surg, CBD	UT		4			
83	66	M	Cystotomy, CBD	UT					4
84	60	M	Surg, DM	UT	2				
85	75	F	DM	UT		4			
86	56	M	CBD	UT	8				
87	50	M	AML	UT	1				
88	72	F	CRF, DM	UT	0				
89	75	F	CBD, DM	UT	4				
90	51	M	CBD	UT			1		
91	49	M	DM	UT	2				
92	37	M	CBD	UT	2				
93	27	F	AML	OP	0				2
94	39	M	NHL	OP	0		2		
95	15	M	Burn	OP	0	0	2		0
96	65	F	AML	OP	0		2		2
97	57	F	NP-Ca	OP	0	0			
98	28	M	CRF, renal tx	OP	0	0	0		
99	60	M	S	OP			2		2
100	50	M	S	OP			1		
101	17	M	AML	OP	0	0			
102	29	F	CMC	Skin					8
103	6	M	CMC	Skin					16
104	3	M	CMC	Skin					0
105	4	M	CMC	Skin					0
106	24	F	CMC	Skin					8
107	28	F	CMC	Skin					4
108	30	F	CMC	Skin					2
109	22	F	CMC	Skin					32
110	70	M	DM	Wound				16	8
111	31	F	Surg	Wound	0			1	
112	60	M	Coma	Wound					8
113	35	M	Paraplegia	Wound					4
114	60	M	Surg	Wound	4		16		
115	56	M	Surg	Wound	4	4			

[a] CBD, Chronic bladder drainage; CMC, chronic mucocutaneous candidiasis; CLL, chronic lymphocytic leukemia; NP-Ca, nasopharangeal cancer; renal tx, renal transplant; SLE, systemic lupus erythematosis; GI, gastrointestinal; OP, oropharynx; UT, urinary tract. Other abbreviations are the same as in Appendix A.

[b] Onset uncertain.

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