INFECTION AND IMMUNITY, Feb. 1981, p. 783-791
0019-9567/81/020783-09$02.00/0

Vol. 31, No. 2

Persistence and Spread of *Candida albicans* After Intragastric Inoculation of Infant Mice

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Infant mice have been shown previously to be a useful model for the study of gastrointestinal (GI) and systemic candidosis. In this study, the virulence of four strains of *Candida albicans* was compared in intragastrically inoculated infants and in adult mice inoculated intravenously. The four strains differed in their ability to kill both infant and adult mice. A smaller inoculum was required to kill adult mice inoculated intravenously. Neonates could not be inoculated intravenously. The ability of the strains to spread systemically from and to persist for long periods of time in the digestive tract was also examined in intragastrically inoculated infants. The yeast cells spread to liver, lungs, kidneys, and spleen within 30 min postinoculation. Yeast were not detectable in the lungs or in blood from the pleural cavity up to 15 min post-inoculation, thus making it unlikely that systemic spread resulted from faulty inoculation or from aspiration. The region where *C. albicans* crossed the GI tract of infant mice was visualized histologically in the upper third of the small intestine. The four strains varied in their ability to persist for long periods in the GI tract, in the rate at which they appeared systemically, and in ability to kill infant mice. Three of the four strains colonized the gut for up to 10 weeks postinoculation without use of any compromising agents.

Candida albicans is an opportunistic pathogen which normally resides unnoticed in the digestive tract of humans, but which can take advantage of host debilities and disorders to cause infections in a variety of tissues. Physiological, mechanical, and iatrogenic factors have been shown to predispose the host to infection by *Candida* (12).

The lack of a suitable animal model for the study of systemic spread of *C. albicans* from the gastrointestinal (GI) tract has limited understanding of the mechanisms of onset and development of candidosis. Efforts to produce persistent colonization of *C. albicans* in the digestive tract of mice have relied on the use of various compromising agents, including sublethal X irradiation, immunosuppressive treatment, and antibiotic therapy (3-5, 9, 18, 19, 22). The recent publication by Pope et al. (13) demonstrated, however, that neonatal mice can be killed after an oral inoculation with *C. albicans* and that systemic spread occurs after an interval of 3 h.

There is abundant evidence in the literature establishing the ability of inert particles such as polyvinyl chloride spheres, potato and corn starch granules, and yeast cells to transmigrate the wall of the digestive tract by a process known as persorption (20, 21). This results in the invasion of the bloodstream via the thoracic duct drainage. Persorption has been demonstrated in dogs (7, 17), rhesus monkeys (15, 17), and humans (10) after oral or intraintestinal inoculation with *C. albicans*.

One of the uncertainties in using an intragastric (i.g.) inoculation of infant mice is the possible aspiration of yeasts into the upper respiratory tract. Because of this, studies were designed to ascertain whether the invasion of tissues resulted from aspiration or from persorption. Lungs of infant mice were sampled early after i.g. inoculation to determine if yeast could be recovered from the respiratory tree.

In these studies, four strains of *C. albicans* were compared for mouse virulence, ability to spread systemically from the GI tract, and capacity to persist for long periods of time in the digestive tract after i.g. inoculation. In addition, histological preparations of the upper segment of the small intestine were examined in an attempt to visualize the penetration of the gut mucosa by *C. albicans*.

MATERIALS AND METHODS

Animals. CFW mice obtained from Charles River Farms, Wilmington, Mass., were used to establish a breeding colony, and the offspring of these animals were used in all experiments.

Organisms. *C. albicans* strains NS33 and CA30 were provided by G. D. Ahearn, Department of Biology, Georgia State University, Atlanta. Strain B311A was supplied by Edward Balish, Department of Microbiology, University of Wisconsin School of Medicine, Madison. Strain UT1015 was obtained from the departmental stock culture collection and was designated as an ASM workshop strain. Before use, all strains except UT1015 were inoculated i.g. into infant mice and reisolated from liver homogenates. Frozen stock cultures were prepared from the animal-passaged strains, and these were used in all of the experiments.

Intravenous (i.v.) inoculation of adult mice. Dilutions of *C. albicans* were prepared in nonpyrogenic saline, and mice were inoculated with 0.1-ml suspensions in the lateral tail vein. Deaths were recorded daily for 9 days, and the 50% lethal dose (LD_{50}) for each strain tested was determined according to Reed and Muench (14).

Intragastric inoculation of infant mice. Infant mice 5 to 6 days old (2.5 to 3.0 g) were isolated from mothers 3 to 4 h before inoculation and held at 35°C. Inocula were delivered i.g. in a volume of 0.05 ml, using a 1-ml tuberculin syringe equipped with a blunted 21-gauge needle tipped with polyethylene tubing. After inoculation, infants were held at 35°C for 1 h before being returned to their mothers.

Test for aspiration after i.g. inoculation. To insure that early systemic spread was not occurring as a result of aspiration of *C. albicans* into the lungs after inoculation, infants were killed immediately after i.g. inoculation with an overdose of Nembutal (approximately 1 mg/mouse) administered subcutaneously in the nuchal region. This method of sacrifice was used to avoid disturbing the esophageal contents. The lungs were quickly dissected, placed in saline, homogenized, and plated immediately thereafter along with samples of pleural cavity blood on Sabouraud dextrose agar (SDA) (Difco Laboratories, Detroit, Mich.) plus chloramphenicol (50 μg/ml). The mice usually died within 5 min of Nembutal administration, and the dissection required an additional 3 to 5 min. The total time between inoculation and completion of the sampling was approximately 10 min. Viable *C. albicans* were never recovered under these conditions from the lungs or the pleural cavity blood, thus making it unlikely that systemic spread was resulting from a faulty inoculation technique or aspiration. Nembutal was used, therefore, to kill mice in subsequent experiments when samples were taken 30 min or less after i.g. inoculation. Mice sacrificed at later periods were killed by decapitation.

Enumeration of organisms in tissues. Homogenization of tissues and fecal pellets was carried out in 1- to 5-ml volumes of saline, and dilutions were plated on SDA plus chloramphenicol. After 48 h of incubation at 37°C, the number of colony-forming units (CFU) per tissue or per fecal pellet was determined. The number of fecal pellets counted was sufficient to compensate for size variation. Moreover, fresh pellets dry rapidly, making weighing inaccurate.

Torulopsis was differentiated from *Candida* after 48 h of incubation by colony size difference. The former has pinpoint-sized colonies (no more than 0.2 mm), whereas the colonies of *Candida* are 2 to 3 mm in diameter.

Histology. Tissues for histological examination were quickly removed, placed in 10% buffered neutral Formalin, and processed in a Fischer Tissuematon. Tissue preparation consisted of three changes in Formalin, dehydration in 70, 80, and 100% ethanol (two times), clearing in xylene (two times), and infiltration in paraffin. Serial sections 5 μm thick were cut with a rotary microtome and placed on slides which were heated to 85°C for 10 min before staining with periodic acid-Schiff reagent and counterstaining with hematoxylin.

RESULTS

Virulence of *C. albicans* for infant mice after i.g. inoculation. The virulence for infant mice of three strains (CA30, B311A, and NS33) used in this study was reported previously (13). The lethality of these same strains as well as of UT1015 was reevaluated over a longer period of time with a newly established breeding colony of CFW mice (Table 1).

The strains differed in their ability to kill infant mice, although in most cases inoculation with any of the four strains resulted in some deaths within 1 to 3 weeks. Strain CA30 was clearly the most virulent, killing 61% of the mice. Infant mice inoculated with CA30 consistently appeared runted and failed to gain weight normally. As the survivors matured, they often had ruffled fur and appeared sickly. After 4 to 6 weeks, mice surviving inoculation with strain CA30 seemed improved. Mice inoculated with strains B311A, UT1015, and NS33 had fewer deaths and only rarely showed outward symptoms of disease. In the previous publication (13), strain NS33 was more lethal than shown in the data of Table 1. The reason for this discrepancy is unknown.

The same four strains were tested for virulence in adult mice inoculated i.v. (Table 2). Deaths were distributed throughout the 9-day

TABLE 1. *Virulence of C. albicans strains for infant mice after i.g. inoculation*

Time post-inoculation	No. surviving/total no. inoculated with the following strains of *C. albicans*[a]:			
	CA30, 6.2×10^7–1.2×10^{8}[b]	B311A, 8.7×10^7–1.1×10^{8}	UT1015, 7.9×10^7–1.2×10^{8}	NS33, 2.5×10^{8}
1 day	74/74 (100)	32/32 (100)	35/35 (100)	11/11 (100)
2 days	74/74 (100)	32/32 (100)	35/35 (100)	11/11 (100)
3 days	73/74 (99)	32/32 (100)	35/35 (100)	11/11 (100)
5 days	63/74 (85)	32/32 (100)	35/35 (100)	11/11 (100)
1 wk	55/74 (74)	32/32 (100)	35/35 (100)	11/11 (100)
2 wk	35/74 (47)	32/32 (100)	31/35 (89)	11/11 (100)
3 wk	30/74 (41)	29/32 (91)	25/35 (71)	11/11 (100)
4 wk	29/74 (39)	29/32 (91)	23/35 (66)	10/11 (91)
5 wk	29/74 (39)	28/32 (88)	23/35 (66)	10/11 (91)
6 wk	29/74 (39)	28/32 (88)	23/35 (66)	10/11 (91)

[a] Percentage survival is shown in parentheses.

[b] Range of the inoculum doses expressed as CFU administered per mouse.

period of observation. The greatest difference in LD_{50} (about sevenfold) was seen between strains B311A and NS33, but the range for all strains, with the sample size used, was not great. Comparing these results with those obtained after i.g. inoculation (Table 1) makes it evident that a smaller inoculum was lethal for adult mice after i.v. inoculation than after i.g. inoculation of infant mice. There did not appear to be any correlation between virulence measured after i.v. inoculation and the ability of the same strain to colonize or cross the digestive tract, as will be shown by the data in Tables 3 through 7.

TABLE 2. *Virulence of C. albicans strains for adult mice (eight per group) after i.v. inoculation*

Strain	Challenge dose	No. surviving/total no. inoculated after day:						LD_{50}
		1	2	4	6	8	9	
CA30	7.7×10^4	7					7	9.7×10^5
	7.7×10^5	8		6	5		5	
	7.7×10^6	1					1	
	7.7×10^7	1	0				0	
B311A	1.2×10^5	8				7	7	4.7×10^5
	1.2×10^6	7		4		2	2	
	1.2×10^7	0					0	
	1.2×10^8	0					0	
NS33	1.6×10^5	8					8	3.2×10^6
	1.6×10^6	7					7	
	1.6×10^7	3	2			1	0	
	1.6×10^8	0					0	
UT1015	1.1×10^5	8					8	1.1×10^6
	1.1×10^6	8					8	
	1.1×10^7	5	4	3	1	0	0	
	1.1×10^8	1			0		0	

Systemic spread of *C. albicans* from the GI tract. We have reported (13) that strain NS33 spreads systemically from the GI tract to liver, kidneys, and spleen within 3 h after i.g. inoculation. Experiments were designed to determine whether NS33 and other strains emerged from the GI tract of infant mice in a shorter time, since Fisher (7) reported recovery of yeasts in livers of dogs 30 min after oral administration of *C. albicans*.

Mice that had been inoculated i.g. with an average of 9×10^7 CFU of each of the four strains of *C. albicans* were used to measure the systemic spread to kidneys, liver, lungs, and spleen between 15 min and 3 h postinoculation (Tables 3–6). *Candida* was recovered only occasionally after 15 min, but after 30 min the frequency of isolation increased. If persorption from the intestine occurs via the thoracic lymph duct, one would expect the lungs to be the first organ where capillary filtration occurs, followed soon thereafter by appearance in the liver. This route of transmission is suggested by our data, since lungs and livers were infected more or less simultaneously and with approximately equal numbers of yeast. Kidneys and spleens were less often positive for *Candida* at all time periods.

Strain NS33 was the most invasive of those tested, both in the number of positive organs

TABLE 3. *Systemic spread of C. albicans CA30 from the digestive tract of infant mice*

Time post-inoculation[a] (min)	Kidney		Liver		Lungs		Spleen	
	No. pos[b]/total	CFU[c]/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ
15	1/4	3.3	1/4	3.3	2/4	7.2×10^1	0/4	0
30	4/15	$2.8 \times 10^1 \pm 7.5$	7/14	$1.8 \times 10^2 \pm 3.6 \times 10^1$	11/15	$8.1 \times 10^1 \pm 1.7 \times 10^1$	2/15	3.3
60	1/5	6.6	4/5	$1.3 \times 10^2 \pm 2.6 \times 10^1$	4/5	$6.2 \times 10^1 \pm 1.7 \times 10^1$	0/5	0
90	0/5	0	0/5	0	1/5	2.3×10^1	0/5	0
180	1/5	3.3	1/5	8.7×10^1	1/5	1.1×10^2	0/5	0

[a] Mean inoculum in four separate experiments was 8.2×10^7 CFU. The range was 6.0×10^7 to 9.8×10^7 CFU.
[b] Number of organs containing culturable *C. albicans* over total number examined. Pos, Positive.
[c] Mean number of CFU of *C. albicans* found in positive organs ± the standard error of the mean.

TABLE 4. *Systemic spread of C. albicans B311A from the digestive tract of infant mice*

Time post-inoculation[a] (min)	Kidney		Liver		Lungs		Spleen	
	No. pos[b]/total	CFU[c]/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ
15	0/5	0	0/5	0	0/5	0	0/5	0
30	1/15	3.3	7/15	$6.6 \times 10^1 \pm 2.1 \times 10^1$	8/14	$4.1 \times 10^1 \pm 6.2$	1/15	3.3
60	1/5	6.6	1/5	3.0×10^1	2/5	5.1×10^2	0/5	0
90	3/10	5.5 ± 1.3	7/10	$4.9 \times 10^1 \pm 8.1$	8/10	$8.5 \times 10^1 \pm 1.5 \times 10^1$	1/10	3.3
180	2/10	2.8×10^1	4/9	$5.9 \times 10^1 \pm 1.6 \times 10^1$	6/9	$3.0 \times 10^1 \pm 6.6$	2/9	3.3

[a] Mean inoculum in four separate experiments was 9.4×10^7 CFU. The range was 7.2×10^7 to 1.2×10^8 CFU.
[b,c] See Table 3.

TABLE 5. *Systemic spread of C. albicans UT1015 from the digestive tract of infant mice*

Time post-inoculation[a] (min)	Kidneys		Liver		Lungs		Spleen	
	No. pos[b]/total	CFU[c]/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ
15	0/4	0	1/4	3.3	1/4	6.7	0/4	0
30	2/10	3.3	3/10	$2.8 \times 10^1 \pm 1.4 \times 10^1$	4/10	$7.4 \times 10^1 \pm 3.1 \times 10^1$	0/10	0
90	1/10	6.0×10^1	4/10	$1.9 \times 10^1 \pm 5.0$	3/10	$3.2 \times 10^2 \pm 1.7 \times 10^2$	1/10	1.0×10^1
180	2/10	9.1	4/10	$2.1 \times 10^2 \pm 1.0 \times 10^2$	5/10	$3.5 \times 10^2 \pm 1.4 \times 10^2$	2/10	6.6

[a] Mean inoculum in three separate experiments was 1.0×10^8 CFU. The range was 8.2×10^7 to 1.1×10^8 CFU.
[b,c] See Table 3.

TABLE 6. *Systemic spread of C. albicans NS33 from the digestive tract of infant mice*

Time post-inoculation[a] (min)	Kidneys		Liver		Lungs		Spleen	
	No. pos[b]/total	CFU[c]/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ	No. pos/total	CFU/organ
15	0/5	0	0/5	0	0/5	0	0/5	0
30	8/25	9.1 ± 1.1	20/25	$4.7 \times 10^2 \pm 4.0 \times 10^1$	16/20	$1.5 \times 10^2 \pm 2.1 \times 10^1$	6/25	6.6 ± 0.7
90	5/10	$3.0 \times 10^1 \pm 5.8$	6/10	$1.5 \times 10^2 \pm 3.0 \times 10^1$	5/10	$7.5 \times 10^2 \pm 2.6 \times 10^2$	5/10	$3.1 \times 10^1 \pm 7.4$
180	3/10	3.3 ± 0.0	7/10	$6.0 \times 10^1 \pm 6.0$	7/9	$8.9 \times 10^1 \pm 1.4 \times 10^1$	4/10	9.1 ± 2.0

[a] Mean inoculum in five separate experiments was 8.5×10^7 CFU. The range was 4.8×10^7 to 1.3×10^8 CFU.
[b,c] See Table 3.

and in the higher counts per organ. At time periods beyond 30 min, the percentage of animals showing *Candida* in organs tended to decrease with the exception of strain NS33, in which case all organs remained essentially constant up to 3 h.

Histological examination of tissues. The number and distribution of yeast cells in the GI tract of infant mice inoculated i.g. with 50×10^7 CFU of strain NS33 was evaluated in tissues processed for light microscopy. Histological examination of the upper third of the small intestine of several mice at 30 min postinfection (Fig. 1 to 3) revealed the presence of yeast cells in the lumen and deep between the villi. Some were intimately associated with the microvilli and appeared to have penetrated the mucosa. Yeast cells at the same time postchallenge were found also in the sinuses of liver (Fig. 4).

Persistence of *Candida* in the GI tract. The duration of colonization of the GI tract was determined in infant mice inoculated with 9×10^6 CFU of strain NS33. The mice were sacrificed at various time intervals. The digestive tracts were removed, cut into segments, weighed, homogenized, and plated on SDA plus chloramphenicol (Fig. 5–7). An initial drop in counts was noted in all areas of the GI tract (except the large intestine) between 30 min and 24 h. Between 3 and 7 days, counts remained constant in all areas. With the exceptions of the cecum and large intestines, an increase in the number of *C. albicans* in all other segments of the GI tract was found between 2 and 3 weeks. The counts then dropped to zero by 4 weeks.

The ability of the three remaining strains to persist in the GI tract of infant mice after i.g. inoculation was assessed by monitoring the numbers of CFU of *Candida* shed in fecal pellets over a 10-week period. Strain NS33 was also administered at a higher inoculum dose (2.5×10^8 CFU/mouse) than that used for the results given in Fig. 5 through 7. The presence of indigenous *Torulopsis* spp. was scored also in these experiments at each time period (Table 7).

Even with an inoculum of 2.5×10^8, strain NS33 was cleared between 5 and 6 weeks, whereas the other three strains appeared to be more successful at long-term colonization. Most mice inoculated with strains CA30, B311A, and UT1015 remained colonized for periods of 7 weeks, and a significant number were still colonized after 10 weeks. The number of mice shedding *Torulopsis* spp. in their feces increased from 3 weeks to the end of the 10-week observation period when most animals were positive for *Torulopsis* spp. As the number of mice colonized with *Torulopsis* spp. increased, especially between 4 and 8 weeks, the number of mice positive for *Candida* declined.

DISCUSSION

Our results validate the usefulness of the infant mouse model for the study of experimental candidosis. Systemic spread after i.g. inoculation and long-term colonization of the intestine was observed with several strains of *C. albicans*.

The dissemination of *C. albicans* from the digestive tract via the bloodstream to multiple organs in the body has become an important

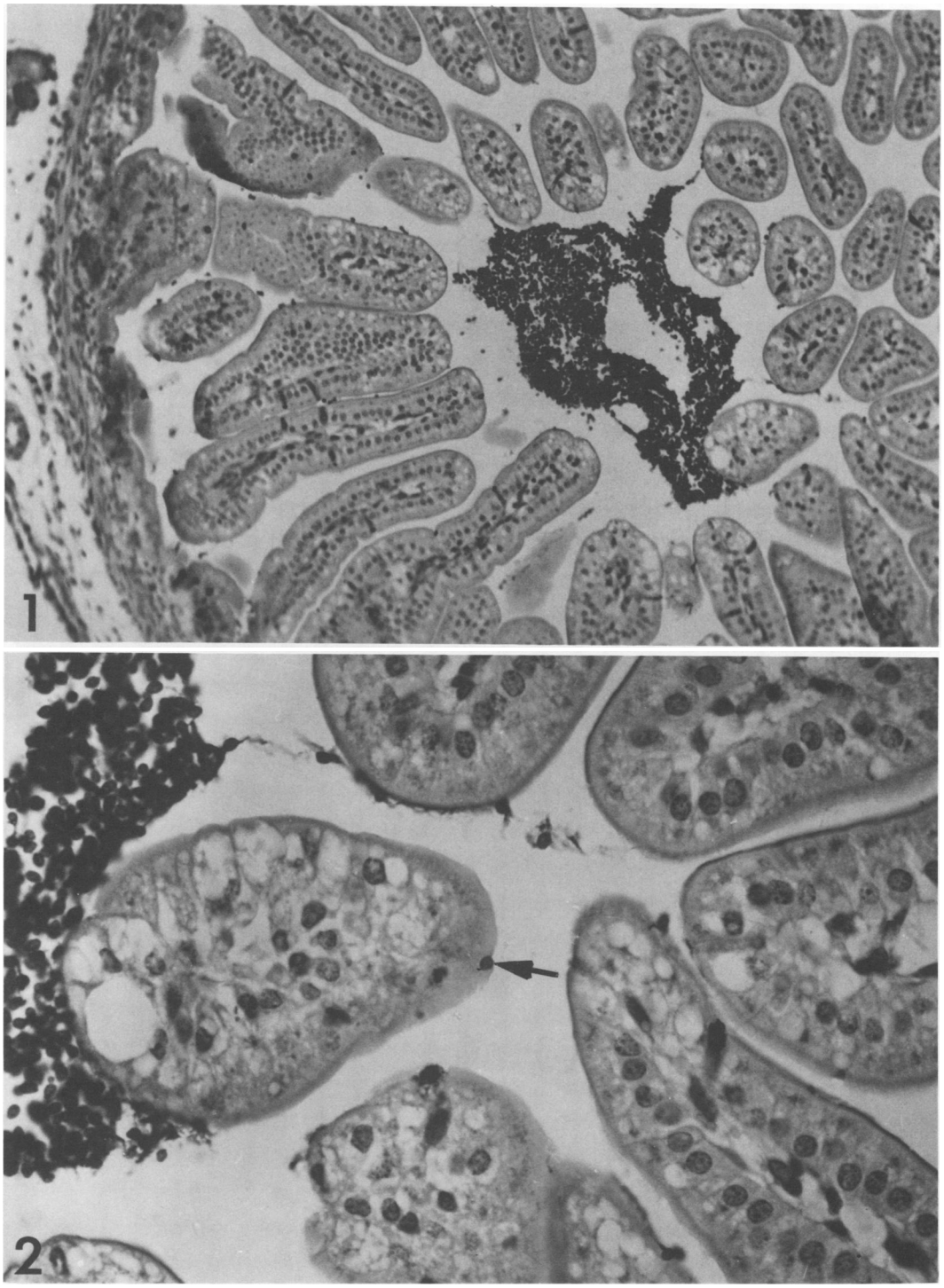
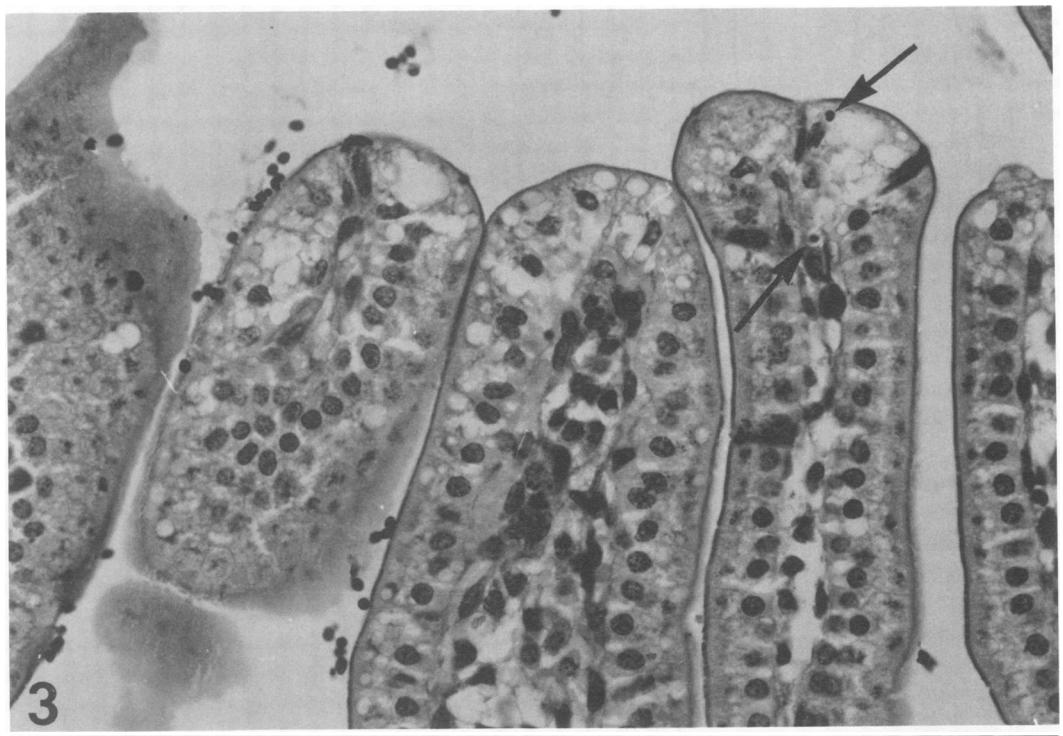


FIG. 1. *Cross section of the upper third of the small intestine of the infant mouse 30 min after i.g. inoculation with C. albicans NS33. Note that most of the yeast are in the lumen. Magnification ×350.*

FIG. 2. *Higher magnification of an area in the lower right quadrant of Fig. 1. A yeast cell appears to be penetrating a villus (arrow). Magnification ×1,300.*



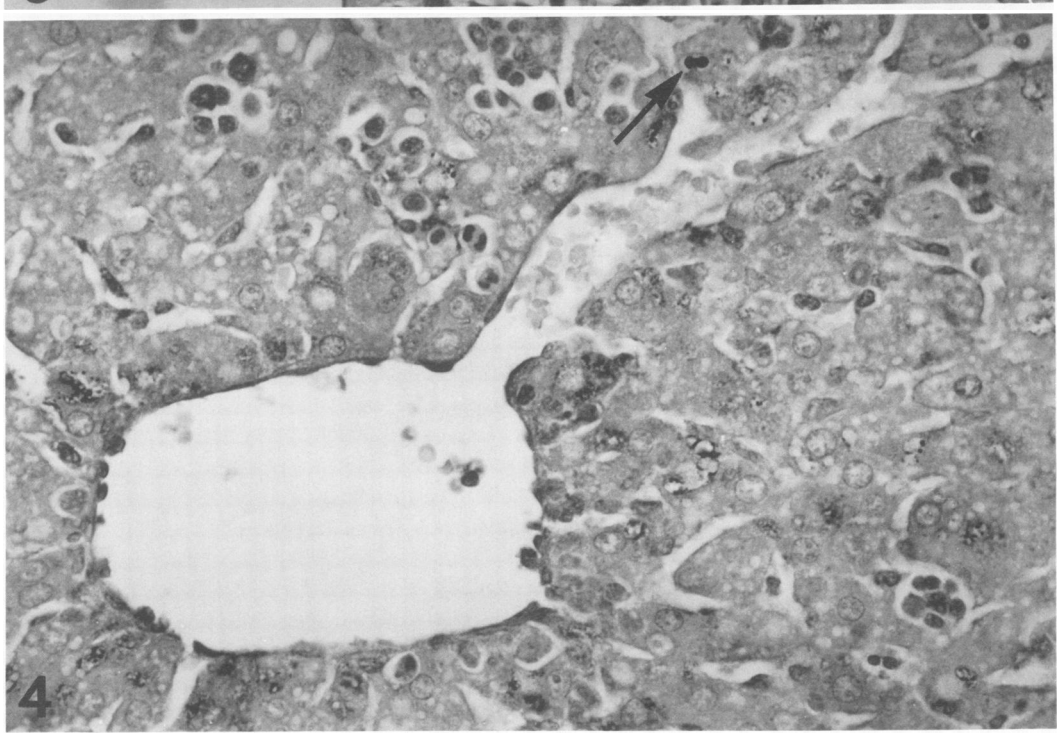


FIG. 3. *Section of the upper third of the small intestine 30 min after i.g. inoculation with C. albicans NS33. A number of single yeast cells have penetrated the intervillous spaces and have become embedded in the villous surface. Arrows indicate yeast which appear to have penetrated into villi. Magnification ×1,100.*

FIG. 4. *Liver section 30 min after inoculation with C. albicans NS33. Yeast cells trapped in a sinus near a blood vessel are indicated by an arrow. Magnification ×880.*

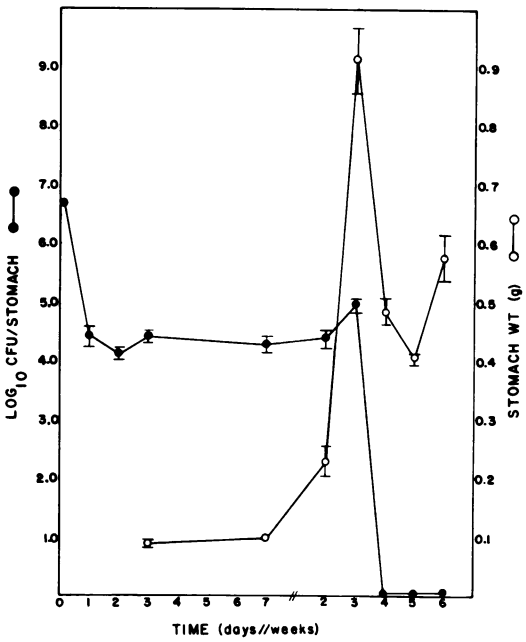


FIG. 5. *Persistence of C. albicans NS33 in the stomach of infant mice. Infant mice were inoculated i.g. with 8.8 × 10⁶ CFU of C. albicans NS33. Mice were sacrificed at different times postinoculation, and the GI tract was removed, cut into segments, weighed, homogenized, and plated on SDA plus chloramphenicol (50 μg/ml). Each point represents the mean value for five mice ± the standard error of the mean. The first time point sampled was 30 min postinoculation*

medical complication in seriously debilitated patients (6, 12, 15–17). Although yeast may be introduced into the bloodstream from a variety of exogenous sources (including contaminated i.v. catheters and infected wounds), numerous authors consider direct persorption from the gut into the thoracic duct to be the most important portal of entry leading to *Candida* septicemia (6, 10, 12, 15–17). Factors which result in an overgrowth of yeast in the intestine, such as the prolonged use of antibiotic therapy, render the host more susceptible to *Candida* invasion.

Evidence derived from organ counts and careful examination of histological sections have demonstrated that *C. albicans* readily pass across the intestines of the infant mouse and spreads to liver, lungs, kidneys, and spleen. Yeast were persorbed within 30 min of i.g. inoculation of approximately 10^7 CFU/mouse. This rapid dissemination from the intestines agrees with reports in the literature. Yeast have been recovered within 30 min from the liver of dogs orally challenged with *C. albicans* (7) and within 3 h from the blood of an adult human volunteer who drank 10^{12} cells of *C. albicans* (10). Penetration of the gut mucosa by production of germ tubes and hyphae from which buds subsequently arise (12) could not have occurred in such a short time period. In fact, neither germ tubes nor hyphae were observed in histological sections of intestines prepared 2 h postinfection with strain NS33, the yeast isolate persorbed most rapidly.

The region where *C. albicans* crossed the GI tract of infant mice was found histologically to be the upper third of the small intestine. Although *Candida* has been shown to enter the portal vein of dogs from all levels of the intestines (17), it selectively transmigrates the jejunum of rhesus monkeys and not the stomach or colon (15). No penetration of the stomach or other areas of the intestines of the infant mouse was observed histologically between 15 min and 2 h postinoculation.

The mechanism of persorption has not been defined and whether it is dose related needs to be determined. The infant mouse is a suitable model for such studies with *Candida*. Reports in the literature indicate that high numbers of

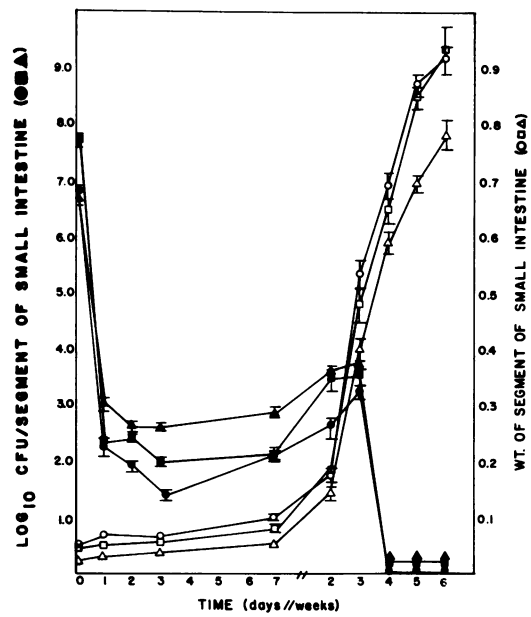


FIG. 6. *Persistence of C. albicans NS33 in the small intestine of infant mice. Infant mice were inoculated i.g. with 8.8 × 10⁶ CFU of C. albicans NS33. Mice were sacrificed at different times postinoculation, and the GI tract was removed, cut into segments, weighed, homogenized, and plated on SDA plus chloramphenicol (50 μg/ml). Each point represents the mean value for five mice ± the standard error of the mean. The first time point sampled was 30 min postinoculation.* (△, ▲) *upper third of the small intestines;* (□, ■) *middle third of the small intestines;* (○, ●) *lower third of the small intestines.*

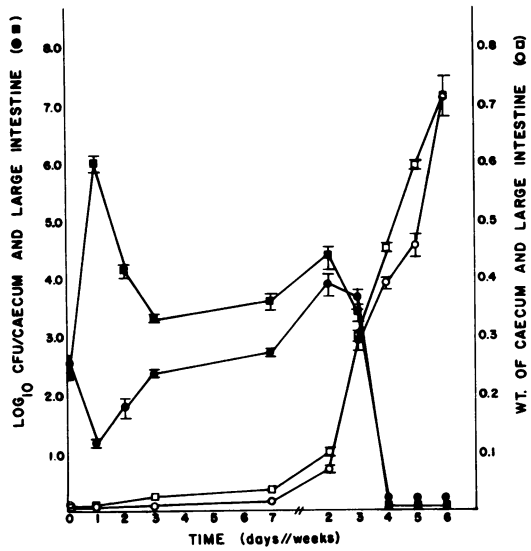


FIG. 7. *Persistence of C. albicans NS33 in the cecum and large intestine of the infant mice. Infant mice were inoculated i.g. with 8.8 × 10⁶ CFU of C. albicans NS33. Mice were sacrificed at different times postinoculation, and the GI tract was removed, cut into segments, weighed, homogenized, and plated on SDA plus chloramphenicol (50 μg/ml). Each time point represents the mean value for five mice ± the standard error of the mean. The first time point sampled was 30 min postinoculation. Symbols:* (○, ●) *cecum;* (□, ■) *large intestine.*

organisms are required for the persorption process (12). This is not unexpected since septicemia occurs in humans under conditions where large numbers of *Candida* are present in the gut (10, 12).

It is important to recognize that infant mice can be successfully colonized with *C. albicans* for periods of up to 10 weeks. Successful colonization of conventional or germ-free adult mice requires that the animals be subjected to various compromising agents (3–5, 9, 18, 19, 22). When colonized as infants, the use of compromising agents is not required and the adults thus obtained can be used in a variety of studies. We are now testing the ability of anticandidal agents to eliminate the organisms from the GI tract and the effect of compromising agents on enhancement of the infection. Stone (17) has stated that clearance of *Candida* from the GI tract of compromised patients is the most effective means of preventing *Candida* septicemia.

Differences among the four strains of *Candida* used in these studies were readily apparent in infant mice but not in i.v.-challenged adult mice. Nevertheless, there are conflicting reports in the literature regarding differences in individual strains of *C. albicans* (1, 2, 8, 11). The virulence

TABLE 7. *Persistence of C. albicans in feces of i.g. inoculated mice*[a]

Time post-inoculation (wk)	CA30, 5.7×10^7–1.2×10^8[b]			B311A, 8.8×10^7–1.1×10^8			UT1015 7.8×10^7–1.2×10^8			NS33, 2.5×10^8		
	No. pos[c]/total *Candida*	CFU[d]/pellet *Candida*	No. pos[e]/total *Torulopsis*	No. pos/total *Candida*	CFU/pellet *Candida*	No. pos/total *Torulopsis*	No. pos/total *Candida*	CFU/pellet *Candida*	No. pos/total *Torulopsis*	No. pos/total *Candida*	CFU/pellet *Candida*	No. pos/total *Torulopsis*
3	14/14	2.1×10^3	6/14	26/26	7.1×10^3	8/26	15/15	6.7×10^3	8/15	8/10	9.0×10^2	8/10
4	17/18	2.6×10^3	14/18	27/27	4.5×10^3	12/26	14/14	2.4×10^3	11/14	5/9	2.4×10^2	8/9
5	19/19	8.6×10^2	17/19	26/28	3.0×10^3	14/28	21/23	1.2×10^3	20/23	2/10	6.4×10^1	9/10
6	14/18	5.7×10^2	5/18	22/27	1.9×10^3	15/27	20/23	1.7×10^3	21/23	0/10	0	10/10
7	10/19	3.4×10^2	18/19	17/27	2.3×10^3	15/27	12/23	9.9×10^2	23/23	0/10	0	10/10
8	10/24	9.2×10^1	20/24	14/27	1.5×10^3	16/27	11/14	9.9×10^2	14/14	ND[f]	ND	ND
10	4/15	1.4×10^2	15/15	11/25	1.9×10^3	16/25	10/23	4.5×10^2	22/23	ND	ND	ND

[a] Infant mice were inoculated i.g. with the indicated strains of *C. albicans*. Beginning at 3 weeks postinoculation, fecal pellets were collected, homogenized in saline, and plated on SDA plus chloramphenicol (50 μg/ml). CFU of *C. albicans* were determined, and the presence or absence of the indigenous yeast *Torulopsis* spp. was noted.

[b] Range of inocula (as CFU/animal) administered.

[c] Total number of mice containing *C. albicans* in the feces over the total number inoculated. Pos, Positive.

[d] Mean CFU of *C. albicans* recoverable per fecal pellet.

[e] Total number of mice containing *Torulopsis* in the feces over the total number inoculated.

[f] ND, Not done.

of species and strains of *Candida* has been reviewed by Odds (12). In these investigations, strain CA30 was clearly the most lethal for infant mice. It was not, however, the most efficiently persorbed even though it colonized the intestine in about half the mice for a period of 8 weeks. These results suggest that factors responsible for lethality, persorption, and colonization are not identical. Elucidation of virulence factors of specific strains of *C. albicans* should lead to a more complete understanding of candidosis.

The infant mouse lends itself to a variety of host-pathogen studies with *C. albicans*. This model will be used to explore a number of these interactions, including the role of competitive microflora, such as the indigenous yeast, *Torulopsis* spp., observed in the present study and of bacterial competitors yet to be examined. The evaluation of both passive and active immunity in these animals is also feasible.

ACKNOWLEDGMENTS

This work was supported in part by Public Health Service grant AI-15583 from the National Institute of Allergy and Infectious Diseases.

We thank Larry Foote for his valuable technical assistance.

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