Neonatal rectal colonization with *Malassezia furfur*

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GJ GROSS, NE MACDONALD, AMR MACKENZIE. Neonatal rectal colonization with *Malassezia furfur*. Can J Infect Dis 1991;3(1):9-13. *Malassezia furfur* and *Candida albicans* are fungal pathogens which have been recognized with increasing frequency as agents of mortality and serious morbidity in neonatal intensive care unit patients. A longitudinal study of oral, rectal and umbilical colonization by these organisms of newborns admitted to a neonatal intensive care unit within 24 h of birth was undertaken. Of 71 infants followed for a minimum of 10 days, 24 were colonized with *M furfur* and 12 with *C albicans* during the first 10 days of life. The lower gastrointestinal tract was found to be the most common colonization site for both organisms. Statistically significant ($P<0.05$) inverse associations were demonstrated between gestational age and risk of colonization with either organism at any site, and between birthweight or gestational age and risk of rectal colonization with either organism. Antibiotics were associated with a relative risk colonization of 4.06 ($P=0.06$) with either organism at any site. It is concluded that *M furfur* and *C albicans* are common colonizing organisms in a neonatal intensive care unit setting and are most frequently harboured in the lower gastrointestinal tract. *M furfur*, recently implicated as a systemic pathogen in this population, has not been previously recognized as a gastrointestinal commensal organism. The relationship between colonization and invasive fungal disease, and potential roles for preventive strategies, remain to be elucidated.

Key Words: Malassezia furfur, *Neonates*

Colonisation rectale néonatale par *Malassezia furfur*

RESUME: *Malassezia furfur* et *Candida albicans* sont des agents pathogènes fongiques de plus en plus souvent incriminés dans la mortalité et la morbidité sérieuse qui sévissent dans les unités de soins intensifs néonatals. On a entrepris une étude longitudinale de la colonisation orale, rectale et ombilicale par ces organismes chez les nouveaux-nés admis à l'unité de soins intensifs néonatals dans les 24 heures qui suivent la naissance. De ces 71 nourrissons suivis sur un minimum de 10 jours, 24 étaient colonisés par *M furfur* et 12 par *C albicans* durant les dix premiers jours de vie. Les voies gastro-intestinales basses étaient le site le plus commun pour ces deux organismes. Des associations inverses statistiquement significatives ont été démontrées entre l'âge gestationnel et les risques de colonisation par l'un ou l'autre de ces organismes quel que soit le site, et entre le poids de naissance ou l'âge gestationnel et les risques de colonisation rectale par l'un ou l'autre des deux organismes. L'antibiothérapie était associée à un risque relatif de colonisation de 4,06 ($P=0,06$) par l'un ou l'autre organisme quel que soit le site. On conclut que *M furfur* et *C albicans* sont des organismes colonisateurs courants dans les unités de soins intensifs néonatals et qu'ils sont le plus souvent présents dans les voies digestives basses. *M furfur*, récemment impliqué en tant que pathogène systémique dans cette population, ne comptait pas, jusqu'ici, parmi les organismes commensaux gastro-intestinaux. Il faut encore élucider la relation existant entre la colonisation et l'affection fongique invasive, et les rôles potentiels des stratégies préventives.

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MALASSEZIA FURFUR AND *CANDIDA ALBICANS* ARE FUNGAL pathogens which have been recognized with increasing frequency during the past decade as important causes of neonatal morbidity, particularly in low birthweight infants (1-6). *M furfur*, a dimorphic lipophilic yeast, was previously recognized as the causative agent for tinea versicolor, a chronic infection of the skin. Since 1981, a number of cases of *M furfur* sepsis occurring in the presence of parenteral lipid infusions via central venous catheters have been reported in both neonates and adults (1-3,7,8). Although the mortality from *M furfur* appears to be low, this is not the case for *C albicans* infection in very low birthweight infants. Very low birthweight infants have been shown to have a 2 to 4% risk of acquiring disseminated candidiasis (4-6), with reported mortality rates ranging from 26 to 70% (4,5).

The purposes of this study were: to compare the rates, sites and timing of *M furfur* colonization in neonatal intensive care unit infants to those of *C albicans* colonization; and to define subgroups of patients at increased risk of colonization with either organism or both.

PATIENTS AND METHODS

All neonates admitted within 24 h of birth to the neonatal intensive care unit at the Children's Hospital of Eastern Ontario between October 1, 1985 and June 1, 1986 were eligible for the study. The hospital has no obstetrical unit, and receives newborns via transfer from a large number of referring institutions in the Ottawa region. Of 150 eligible patients, 100 neonates were studied. The 50 who were not recruited did not differ significantly from the study group in terms of sex ratio, gestational age or birthweight; however, the non-study group did have a much higher mortality (36% versus 1%) and a shorter mean duration of stay in the unit (15.4±21.0 days versus 29.9±20.7 days, $P<0.01$). Exclusion of eligible patients in the study usually resulted from an expectation that their stay in the neonatal intensive care unit would be brief, due to either an excellent or a very poor prognosis; occasionally, exclusion was due to oversight.

Criteria for discontinuation of a neonate from the study included death, discharge or transfer from the neonatal intensive care unit, initiation of antifungal therapy, and age greater than 70 days.

Cultures were taken from the mouth, rectum and umbilical areas on days 1, 3, 5, 7, 10 and 14, and weekly thereafter. Oral and rectal cultures were obtained by careful insertion of sterile cotton swabs into each cavity. Swabs were plated on Sabouraud agar (Oxoid Canada Inc) with and without a thin layer of sterile olive oil on the surface. Plates were examined daily for four days. Criteria for identification of *M furfur* colonies were growth on olive oil-supplemented Sabouraud agar but not on unsupplemented agar, appropriate colonial characteristics and microscopic appearance (9). Colonies were identified as *C albicans* if there was growth on unsupplemented Sabouraud agar, colonial characteristics and microscopy were appropriate, and growth on ox gall agar yielded chlamydospores (10). A selective enrichment medium was made up as follows: Sabouraud broth (Oxoid Canada Inc), cefoperazone 50 mg/L, vancomycin 25 mg/L and gentamicin 20 mg/L. This medium was distributed in tubes in 2 mL volumes, and 0.1 mL olive oil was added to each tube. Swabs were added to the medium and vortexed. *M furfur* grew on the underside of the olive oil layer, and *C albicans* grew uniformly in the aqueous layer.

χ^2 tests were used to examine the association between colonization at any time during the first 10 days of life and various suspected risk factors. The Cramer's V (phi) coefficient was used to measure strength of association (11). This coefficient can be interpreted as a Pearson correlation coefficient for nominal and ordinal variables. Statistical analyses were performed using the SPSS-X Information Analysis System (12) and BMDP Statistical Software (13).

RESULTS

Of 100 neonates enrolled in the study, 37 yielded cultures positive for *M furfur*, and 16 grew *C albicans*. There were no documented cases of invasive disease caused by either organism in the neonatal intensive care unit throughout the period covered by the study.

Seventy-one infants were followed for a minimum of 10 days; statistical analysis was restricted to the first 10 days of life in this group. Of these 71, 24 were colonized with *M furfur* and 12 with *C albicans* during the first 10 days of life. Figure 1 presents the cumulative patient colonization data by site for *M furfur*, demonstrating that the rectal site was the most common. Colonization with either *M furfur* or *C albicans* at any site did not disappear during the course of follow-up – but other sites often subsequently became colonized.

Gestational age, birthweight, gender and antecedent antibiotic use were assessed as possible risk factors for fungal colonization. Gestational age proved to be the strongest single predictor of colonization. Statistically significant inverse correlations were observed between gestational age category and risk of colonization with either organism at any site and between gestational age category and risk of rectal colonization with either organism (Table 1). Furthermore, gestational age showed an inverse correlation with rectal colonization with *M furfur* (phi=0.236); 55.6% of babies of 29 weeks or less of gestation were colonized, compared with 19.0% of those of at least 36 weeks' gestation, with the intermediate group yielding 31.7% positive cultures.

Although birthweight could be expected to confound gestational age as a predictor for colonization, the only statistically significant relationship established was the

TABLE 1
Relationship between gestational age and neonatal colonization of the mouth, umbilicus or rectum with *Malassezia furfur* or *Candida albicans* during the first 10 days of life

Category	Gestational age 24-29 weeks n=9	30-36 weeks n=41	>36 weeks n=21	P
Any site, either or both organisms	7	20	6	<0.05
Rectal site, either or both organisms	7	18	6	<0.05
Rectal site, *M furfur*	5	13	4	0.139
Rectal site, *C albicans*	4	5	2	0.054

inverse correlation between birthweight category and rectal colonization with either organism (phi=0.299, P<0.05) (Table 2). This would suggest that lack of maturity, rather than low birthweight per se, is of greater importance in establishing colonization.

Antecedent use of antibiotics (ampicillin and gentamicin in standard neonatal dosages) increased the risk of subsequent colonization with either organism to an extent approaching statistical significance (P=0.06). The relative risk of colonization for babies who received antibiotics was 4.06 compared to those who did not. Failure to reach statistical significance was most likely, due to the fact that only eight of 71 babies did not receive antibiotics at any time during the first 10 days, a very small group for comparison.

Gender was not shown to be a significant predictor of colonization.

DISCUSSION

Previous studies of *M furfur* have focused on the skin as a major source of lipid substrate for the growth of this organism. Accordingly, Faergemann and Fredriksson (14) showed increasing frequency of skin colonization in children aged five to 15 years, but were unable to culture *M furfur* from those aged one year and less, including newborns. Powell and colleagues (1) did culture *M furfur* from the skin of eight of 25 hospitalized premature infants. In a more recent study involving 361 infants, the same group found *M furfur* skin colonization in 36.8% of neonatal intensive care unit patients, and identified statistically significant associations with prematurity, low birthweight, length of hospital stay and a number of environmental factors (15). The present data indicate a lower prevalence of surface colonization (8.5% at 10 days), with no significant relationship to gestational age; this difference can be explained on the basis of the longitudinal nature of the authors' study compared with Powell et al's cross-sectional approach, in which colonized infants had spent a mean of 51.3 days in the neonatal intensive care unit (1). Bell and colleagues (16) have also reported an

TABLE 2
Relationship between birthweight and neonatal rectal colonization with either *Malassezia furfur* or *Candida albicans* during the first 10 days of life

	Birthweight <1500 g (n=20)	1500-2500 g (n=29)	>2500 g (n=22)	P
Colonization with either organism	12	14	5	<0.05

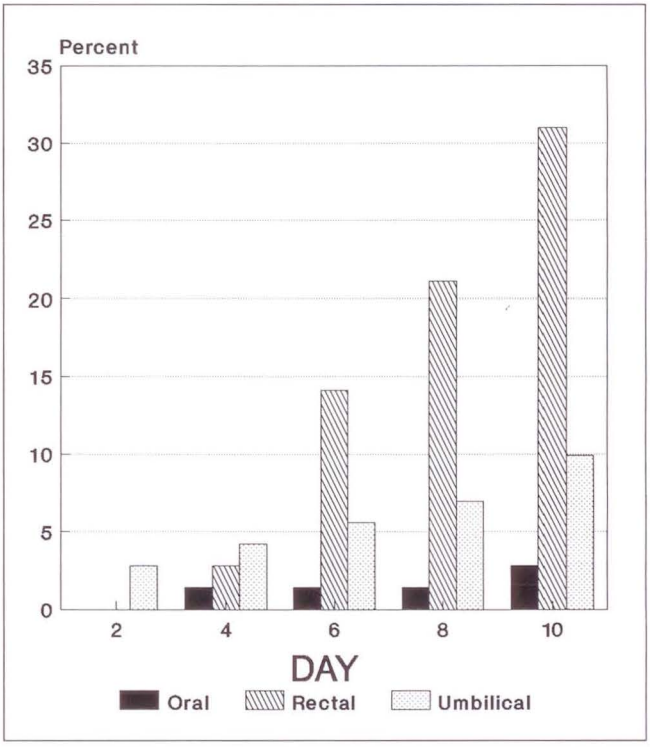

Figure 1) *Cumulative colonization with* Malassezia furfur

increase in skin colonization with length of neonatal intensive care unit stay. In contrast, they detected only rare colonization in healthy infants of comparable age seen in well baby clinics. Aschner et al (17) also reported high skin colonization rates in their neonatal intensive care unit patients, as well as the detection of *M furfur* in eight of 25 consecutively examined central venous catheters from these patients.

To the authors' knowledge, the lower gastrointestinal tract has not been previously reported as a potential reservoir for *M furfur* in neonates. Data from the present study indicate that this site is rapidly colonized by *M furfur* during the first 10 days of hospitalization, and that by the 10th day the prevalence of colonization exceeds 30% (Figure 2).

Terasaka and co-workers (18) analyzed the fatty acid content of meconium from healthy, full term newborns. They found the samples to contain an average of 137 μg fatty acids/g meconium; palmitic (C16), stearic (C18)

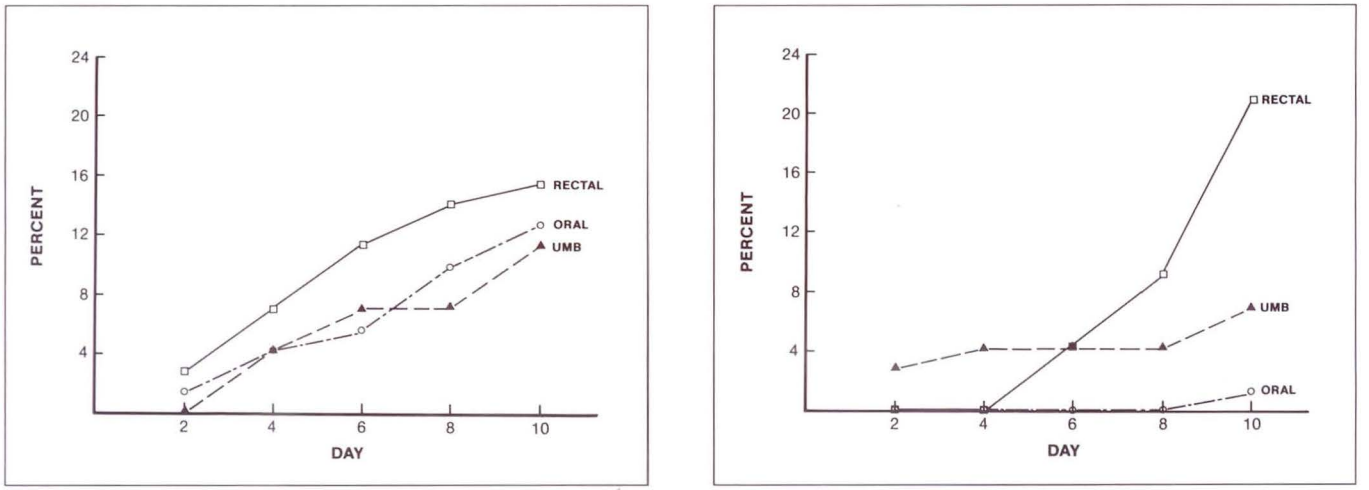

Figure 2) *Cumulative percentage of* Candida albicans **(left)** *and* Malassezia furfur **(right)** *colonization by site. UMB Umbilical*

and oleic (C18) acids were the predominant constituents identified, accounting for 75% of the total in most samples. This would suit the requirement of *M furfur* for C12 to C24 fatty acids (19), even in the absence of enteral feeding. Furthermore, although the meconium of premature infants has apparently not been analyzed in similar fashion, it is evident that lipid absorption is less efficient in preterm than in full term infants due to a number of mechanisms, including reduced pancreatic lipase levels and bile acid pool (20). This could explain the present finding of increasing colonization with decreasing gestational age, though the actual fatty acid content of meconium and stool from premature infants remains to be elucidated.

The use of broad spectrum antibiotics has long been associated with an increase in candida colonization (6,21,22) and systemic infection (4-6). The present data suggest that this association involves *M furfur* as well as *C albicans*.

The use of prophylactic oral nystatin in infants at risk of developing systemic candida infections has been advocated (23). In at least two studies a significant reduction in rates of *C albicans* colonization resulted from this practice (24,25). Nevertheless, well documented cases of systemic yeast infection in infants on prophylactic nystatin have been reported (5). To the authors' knowledge, the role of oral nystatin in preventing *M furfur* colonization and infection in infants has not been evaluated. Since the gastrointestinal tract appears to be an important reservoir for this organism in premature infants, dietary or pharmacological manipulation of the fatty acid content of stools might provide alternative modes of prevention of infection.

The authors conclude that *M furfur* is a common colonizing organism in their neonatal intensive care unit patients. In contrast with previous reports, they found *M furfur* colonization to be more prevalent than *C albicans*. Both organisms are most frequently harboured in the lower gastrointestinal tract, a previously unrecognized site for *M furfur*. Investigations aimed at devising preventive strategies for systemic *M furfur* infection in neonatal intensive care unit patients will have to take into account the important role of the lower gastrointestinal tract as a reservoir for this organism.

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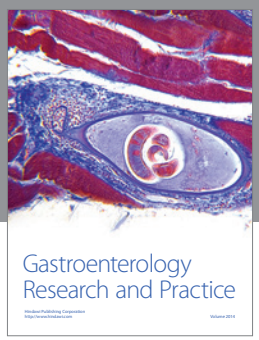

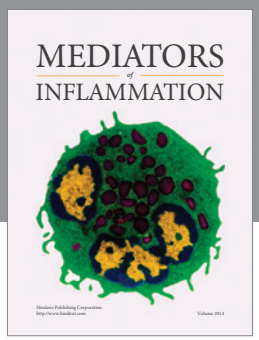

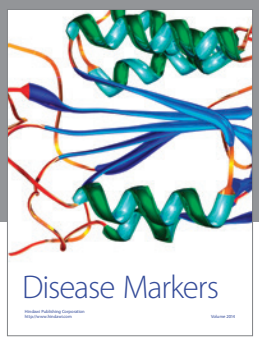

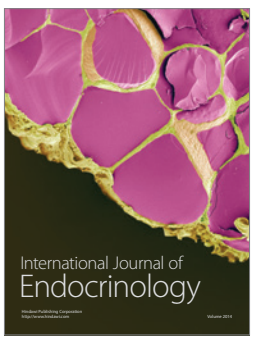

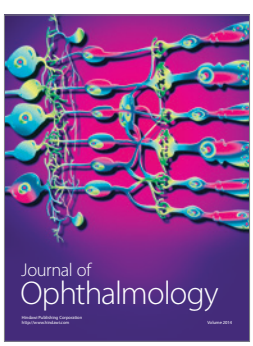

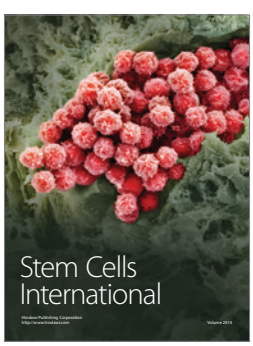

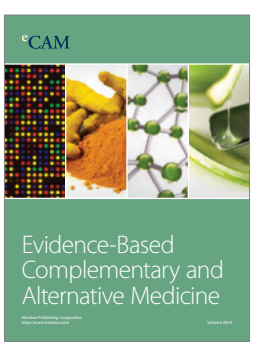

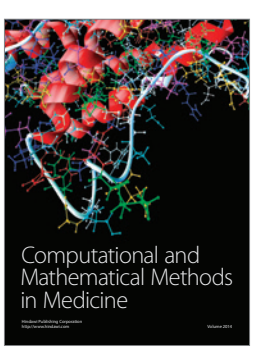

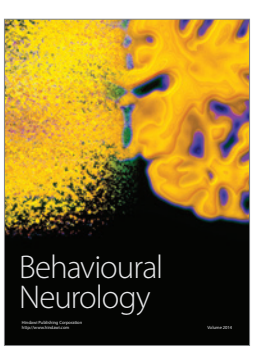

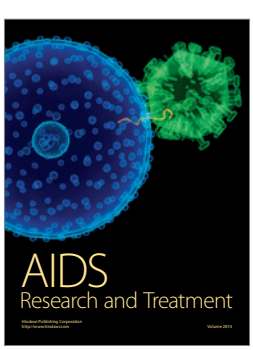

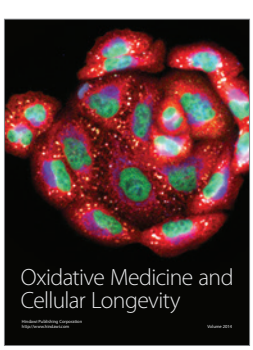

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