

Rhodotorula infection. A systematic review of 128 cases from literature

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Summary Rhodotorula is an emerging opportunistic pathogen, particularly in immunocompromised patients. Many cases of fungemia associated with catheters, endocarditis, peritonitis, meningitis, and endophthalmitis are infections incited by this yeast. The main purpose of this study was to review all cases of *Rhodotorula* infection reported in the literature and to describe risk factors, underlying conditions and outcome. From 128 cases, 79% were fungemia (103 cases), 7% eye infections (nine cases) and 5% (six cases) peritonitis associated with continuous ambulatory peritoneal dialysis. Eighty seven percent of Rhodotorula infections are associated with underlying immunosuppression or cancer. The most common isolated risk factor associated with Rhodotorula infection was the use of a central venous catheter, which was found in 83.4% of Rhodotorula fungemia (86 cases). Rhodotorula mucilaginosa was the most common species of fungemia (74% of cases), followed by *Rhodotorula glutinis* with 7.7%. The species was not identified in 17% of the cases of fungemias. Amphotericin was the drug of choice in the treatment of fungemia and most of the eye infections were treated with topical amphotericin, although all patients lost their vision. All peritonitis cases associated with continous ambulatory peritoneal dialysis needed to have the Tenckoff catheter changed. The overall mortality of Rhodotorula infection was 12.6%.

Key words Rhodotorula, Fungemia, Central venous catheter, Immunosuppressed

Infección por Rhodotorula. Revisión de 128 casos

Rhodotorula es un patógeno emergente oportunista, especialmente presente Resumen en pacientes inmunodeficientes. Este microorganismo está involucrado en numerosos casos de fungemia asociada a catéteres, endocarditis, peritonitis, meningitis y endoftalmitis. El propósito del presente estudio fue revisar todos los casos de infecciones por *Rhodotorula* publicados en la literatura, describiendo los factores de riesgo. De 128 casos, el 79% (103 casos) correspondían a fungemias, el $7\tilde{\%}$ (nueve casos) a infecciones oculares y el 5% (seis casos) a peritonitis asociada con diálisis peritoneal ambulatoria continua. El 87% de las infecciones se asociaban con inmunosupresión o cáncer. El factor de riesgo más importante asociado a infección por Rhodotorula fue el uso de catéter venoso central, encontrado en el 83,4% de los casos de fungemia (86 casos). Rhodotorula mucilaginosa fue la especie encontrada en la mayor parte de los casos de fungemia (74%), seguida de Rhodotorula glutinis (7,7%). La identificación de la especie no fue posible en un 17% de los casos de fungemia. El tratamiento de elección en las fungemias fue la anfotericina B, y la mayor parte de las infecciones oculares fueron tratadas tópicamente con anfotericina B, si bien todos los pacientes sufrieron pérdida de la visión. Todos los casos de peritonitis asociados a diálisis peritoneal continua ambulatoria requirieron el cambio del catéter Tenckoff. La mortalidad debida a la infección por Rhodotorula fue del 12,6%.

Palabras clave Rhodotorula, Fungemia, Catéter venoso central, Inmunosuprimido

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©2008 Revista Iberoamericana de Micología Apdo. 699, E-48080 Bilbao (Spain) 1130-1406/01/10.00 € *Rhodotorula* is a basidiomycetous yeast in the fungal family Sporidiobolaceae (Phylum Basidiomycota) [17]. Widespread in nature and isolated from environmental sources and products [1,48], it was previously considered non-pathogenic. During the last two decades, however, it has emerged as an opportunistic etiologic agent, particularly in immunocompromised patients [27]. Fungemia associated with catheters, endocarditis, peritonitis, meningitis, and endophthalmitis is one of the most common infections reported in the literature [63]. This yeast fulfills the criteria of an emerging pathogen [27].

Although several publications have described this yeast as a cause of human mycoses, there is no review in the literature regarding the epidemiology, risk factors and outcome related to *Rhodotorula* infection. A previous systematic review was published, but only central venous catheter-associated fungemias were evaluated [69]. The main purpose of this study was to review all cases of human *Rhodotorula* infection reported in the literature, and to describe the risk factors, underlying conditions and outcomes for the different forms of *Rhodotorula* infection.

Methods

A careful search of all articles about *Rhodotorula* infections published in the MEDLINE, EMBASE and LILACS was performed (until January, 2006). The search terms (key word) were "*Rhodotorula*", "fungal infections", "fungal endophthalmitis", "fungal eye infection", "fungal peritonitis", "yeast infection", "fungal abscess", "fungal central nervous system infection" and "fungal endocarditis". The reviews of "fungal infections" or "emergent fungal infections" were included in this search. No limitations were placed on language or types of studies published. A detailed examination of the references from all articles chosen in the first selection was performed for ascertainment of additional case reports. The studies were initially selected by two physicians independently. Disagreements were resolved by consensus.

The classification of *Rhodotorula* infection was based on epidemiologic data and anatomical location. Epidemiologic data included: 1) isolation of the yeast from a previous sterile site; 2) information regarding age and gender; 3) underlying conditions; 4) current and previous therapies and; 5) outcome. No contact was made with the original authors. We checked the clinical findings, age and gender of all cases to avoid overlapping cases.

Rhodotorula infection was stratified by anatomical location (blood, peritoneum, meningitis and eye) according to the following criteria: 1) a blood stream infection required at least one criteria published by Garner et al. [21], which was defined as one positive culture for *Rhodotorula* either from the central venous catheter (CVC) tip or the peripheral blood; 2) fungal peritonitis in patients on CAPD (Continuous Ambulatory Peritoneal Dialysis) was determined by a positive peritoneal fluid culture and at least two of the three following criteria which included abdominal pain, a cloudy peritonealfluid, and/or a cell count from the peritoneal fluid with more than 100 neutrophils per mm³ [60]; 3) fungal meningitis was defined by positive culture with pleocytosis and clinical signs of meningitis [46]; 4) diagnostic criteria of eye *Rhodotorula* infection were described previously by Thomas [68].

Epi Info 2000 was used to develop a database of all clinical information and underlying conditions, previous medications, any kind of immunosuppression, invasive procedures, antifungal therapy, year of publication, and outcome. Previous antibiotic use was accepted if a broad spectrum antibiotic was used for at least one week prior to yeast identification. We considered overall mortality in this systematic review. No statistical test was performed.

Results

A total of 1233 articles were found. However, 1092 articles were excluded because no *Rhodotorula* infection was identified. From 141 articles, only 128 cases were included in our database because they fulfilled the inclusion criteria. The other cases were excluded because inclusion criteria for *Rhodotorula* infection were not adequate.

The mean age was 34.5 years (range 1-74 years) and sixty five percent of all cases of *Rhodotorula* infection occurred in males. Fungemia was documented in 103 cases (79% of the *Rhodotorula* infections). Among fungemia patients, 86 cases were associated with CVC (66% of *Rhodotorula* infection) [2,3,5,8,9,16,24,28,29,39, 40,42,44,54,55,57,58,65,66,71,72]. Other cases of fungemia were endocarditis (seven cases) [19,36,41,43,51,55,64] and in ten patients the source of the fungemia was not evident [30,31,36,37,40,63,66] (Table 1). The mortality of *Rhodotorula* fungemia was 14.4%. Fungemia not associated with CVC had a higher mortality than endocarditis and CVC fungemia (20% vs. 14.2% vs. 13.5%).

After fungemia, eye infection, with a total of nine cases, was the second most common *Rhodotorula* infection (endophthalmitis, keratitis and corneal infections) [4,7,26,38,45,47,53,59,61] followed by six cases (5% of *Rhodotorula* infection) of peritonitis associated with CAPD [12,14,56,67].

The most common eye *Rhodotorula* infection was keratitis, which had a good prognosis with topical antifungal treatment. Endophthalmitis caused by *Rhodotorula* had a worse prognosis as all patients lost vision and required either a vitrectomy or enucleation (Table 2).

A total of five cases of meningitis and one case of ventriculitis were described. The underlying conditions were AIDS (two cases), meningioma (one case) and acute lymphoblastic leukemia (one case); only one patient had no

Table 1. Epidemiological data of fungemia caused by Rhodotorula spp.

| CVC ¹ related | Fungemia isolated | Endocarditis | |
|-----------------------------|---|---|--|
| 86 | 10 | 7 | |
| 63.8% | 60% | 71.4% | |
| 32 years | 31 years | 47 years | |
| n | | | |
| 69 | 6 | 2 | |
| 4 | 1 | 1 | |
| _ | - | - | |
| 11 | 3 | 4 | |
| | | | |
| 39 | 1 | 1 | |
| 18 | _ | _ | |
| 7 | _ | _ | |
| 18 | _ | _ | |
| 13 | _ | _ | |
| 24 | 3 | 7 | |
| 17 | 1 | 1 | |
| 11 | 1 | _ | |
| | | | |
| 5/** | 2/1 | 0/0 | |
| 39/34 | 2/1 | 4/3 | |
| 1/1 | 0/0 | 1/1 | |
| 15/11 | 6/6 | 2/2 | |
| 26/25 | 0/0 | 0/0 | |
| 10 | 2 | 1 | |
| | related 86 63.8% 32 years n 69 4 2 11 39 18 7 18 13 24 17 11 5/** 39/34 1/1 15/11 | related isolated 86 10 63.8% 60% 32 years 31 years n 69 69 6 4 1 2 - 11 3 39 1 18 - 7 - 18 - 13 - 24 3 17 1 11 1 5/** 2/1 39/34 2/1 1/1 0/0 15/11 6/6 26/25 0/0 | |

¹CVC: fungemia associated with central venous catheter; ²5-FC: 5-fluorocytosine ^{**} From five cases with fluconazole use, four cases without outcome described and one with cure. predisposing factor. In the patient with ventriculitis, the underlying condition was the use of an intraventricular catheter. The outcome for meningitis was good, with only two deaths. One of these cases was not attributed to *Rhodotorula* infection and the outcome was progressive coma due to leukemic infiltration of central nervous system (Table 3). Although neither considered nosocomial nor related to an invasive procedure, four cases of meningitis appear to have been healthcare-related.

All *Rhodotorula* peritonitis cases were associated with chronic renal failure and patients on CAPD in the presence of a Tenckhoff catheter. In the six cases published, only one patient had not received antibiotics prior to developing fungal peritonitis. The prognosis of *Rhodotorula* peritonitis was death in one case due to hospital associated pneumonia (not attributed to *Rhodotorula* infection). All patients required removal of their Tenckoff catheter and hemodialysis (Table 4).

Other unusual sites of *Rhodotorula* infection described in the literature were hydrosalpingitis [23], an orthopedic prosthesis infection [11], and two cases of disseminated *Rhodotorula* infection with bone marrow isolation of the agent [50,62].

Immunosuppression was found in 40% of patients with *Rhodotorula* infection. The causes of immunosuppression were corticosteroid use (13 cases - 10%), neutropenia (20 cases - 15%), AIDS (nine cases - 7%) and malnutrition (12 cases - 9%). Solid neoplasm was found in 13.2% of patients with *Rhodotorula* infection (17 cases) and hematological neoplasm in 32.8% (42 cases). Twelve

transplanted patients developed Rhodotorula infection (11 cases of bone marrow, one case of lung and one case of kidney transplantation) [19,50]. The interval of Rhodotorula infection after organ transplant was 1.6 years. All cases were attributed to immunosuppressive drugs. Although 87% of patients with Rhodotorula infection had an underlying immunosuppression or cancer, the most common isolated underlying condition associated with Rhodotorula infection was the use of a CVC found in 83.4% of Rhodotorula fungemia (86 cases). Only five patients with *Rhodotorula* fungemia had no underlying disease, although all these patients had previous use of broad spectrum antibiotics. Thirty-eight percent of patients with Rhodotorula infection used broad spectrum antibiotics and 15.1% were receiving parental nutrition. The underlying conditions associated with each form of Rhodotorula infection are described in tables 1-4.

Rhodotorula mucilaginosa was the most common species of fungemia (74% of cases) followed by *Rhodoto-rula glutinis* in 7.7%. The species was not identified in 17% of the cases of fungemia.

Seventy-one percent of patients with *Rhodotorula* fungemia associated with CVC received specific therapy. The most common antifungal used was amphotericin B and the treatment duration ranged from 14 to 41 days with a mean total dose of 1,318 mg. Seven patients received fluconazole; 5-fluorocytosine was used in two patients. Four patients used the combination of amphotericin with 5-fluorocytosine. The overall mortality of *Rhodotorula* infection was 12.6%.

Table 2. Ocular infections caused by Rhodotorula spp.

| Year | Author | Agent | Sex/Age | Disease | Systemic Disease | Treatment | Outcome |
|------|----------|------------------|---------|-------------------|---------------------|------------------|-------------|
| 1973 | Romano | R. mucilaginosa | F/29 | Keratitis | None | TA + nystatin | Cure |
| 1975 | Segal | R. mucilaginosa | M/29 | Keratitis | None | TA + nystatin | Cure |
| 1992 | Casolari | R. glutinis | M/40 | Keratitis | None | TA + SA + 5-FC | Cure |
| 1992 | Gregory | R. minuta | F/71 | Endophtalmitis | None | Ketoconazol | Vitrectomy |
| 1999 | Panda | Rhodotorula spp. | M/55 | Corneal infection | None | ТА | Cure |
| 2001 | Pinna | R. minuta | M/27 | Endophtalmitis | HCV | TA + Ketoconazol | Vitrectomy |
| 2002 | Merkur | R. mucilaginosa | M/26 | Endophtalmitis | AIDS | SA + TA | Enucleation |
| 2003 | Bawazeer | Rhodotorula spp. | F/63 | Keratitis | None | ТА | Cure |
| 2005 | Lifshitz | R. mucilaginosa | M/78 | Keratitis | None | SA + TA | Cure |

SA: Systemic amphotericin; TA: Topical amphotericin; HCV: Hepatitis C infection; 5-FC: 5-fluorocytosin

Table 3. Central nervous system infections caused by Rhodotorula spp.

| Year | Author | Agent | Sex/Age | Diagnosis | Previous Disease | Treatment | Outcome |
|------|------------|-----------------|---------|---------------|---------------------|------------|---------|
| 1976 | Pore | R. mucilaginosa | M/14 | Meningitis | ALL | AmphoB | Death |
| 1987 | Donald | R. mucilaginosa | F/32 | Ventriculitis | Meningioma | 5-FC | Cure |
| 1996 | Gyaurgieva | R. mucilaginosa | M/39 | Meningitis | AIDS | 5-FC | Cure |
| 1998 | Huttova | R. mucilaginosa | M/13 | Meningitis | Neuroblastoma | Miconazole | Cure |
| 1998 | Ahmed | R. mucilaginosa | F/65 | Meningitis | AIDS | Miconazole | Death |
| 2001 | Lanzafame | R. glutinis | M/69 | Meningitis | None | AmphoB | Cure |

5 FC: 5-Fluorocytosine; AmphoB: Amphotericin B; ALL: Acute lymphocytic leukemia

| Table 4 | . Peritonitis | associated | with | CAPD | caused | by | Rhodotorula | spp. |
|---------|---------------|------------|------|------|--------|----|-------------|------|
|---------|---------------|------------|------|------|--------|----|-------------|------|

| Year | Author | Agent | Sex/Age | Disease | Previous Antibiotic | Treatment | Outcome |
|------|------------|------------------|---------|----------|------------------------|-----------|---------------------|
| 1983 | Eisenberg | R. mucilaginosa | M/16 | CRF | Yes | C+IPA | Cure + Hemodialysis |
| 1983 | Eisenberg | R. mucilaginosa | M/50 | Diabetes | Yes | C+IPA | Cure + Hemodialysis |
| 1983 | Eisenberg | R. mucilaginosa | M/59 | No | Yes | C+IPA | Death |
| 1995 | Pennington | R. mucilaginosa | F/37 | CRF | Yes | C+SA | Cure + Hemodialysis |
| 2004 | Soylu | Rhodotorula spp. | F/4 | No | No | C+IPA | Cure + Hemodialysis |

C: Removal the Tenckoff catheter; IPA: Intraperitoneal amphotericin; SA: Systemic amphotericin; CRF: Chronic renal failure

Discussion

The first case of *Rhodotorula* infection, a patient with endocarditis, was reported in 1960 by Louria [41]. After this first case, several articles have been published and an increase in the number of *Rhodotorula* infections has been reported, mainly in the last two decades. However, this increase could be a publication bias after the recognition of *Rhodotorula* as a pathogen. Another explanation is the dramatic expansion in new modalities of treatment related to critical care medicine and transplantation, short and long term CVC with or without parental nutrition, broad spectrum antibiotics, and chemotherapy. *Rhodotorula* is the etiological agent in 0.5 to 2.3% of all cases of fungemia described in some epidemiologic studies [3,22,32,33,52].

Rhodotorula is a yeast which produces mucoid colonies with a characteristic carotenoid pigment and is widely distributed in the environment [17]. Previously considered a low virulence organism in comparison to Candida or Trichosporon, Rhodotorula must be considered a potential pathogen in patients with immunosuppression and CVC [25,62]. Patients with hematological neoplasms who are both neutropenic and have long term CVC use are at risk for Rhodotorula infections. Solid neoplasms, AIDS, corticosteroid therapy and organ/bone marrow transplant are other immunosuppressive conditions associated with Rhodotorula infection. Previous antibiotic use and parenteral nutrition for malnutrition secondary to chronic diseases are other underlying conditions found in patients with *Rhodotorula* infection. These facts were well described in this study, where neoplasm was present in 46% of cases, followed by bone marrow transplant and AIDS.

Less common conditions cited in this study that were associated with fungemia included abdominal surgery, cirrhosis (two patients), autoimmune disorders, and burns [10].

The mortality of *Rhodotorula* fungemia was 14.4%. Fungemia without CVC had a higher mortality than endocarditis and CVC fungemia, however, no risk specific factor was related to increased mortality. A case control study could explain this difference, if it exists.

Obviously, non-systemic *Rhodotorula* infection such an eye infection and peritonitis on CAPD patients had no association with immunosuppression. Nevertheless, previous conditions allowing colonization of *Rhodotorula* were found in most patients.

The major risk factor for *Rhodotorula* fungemia was the insertion of CVC, which was present in 83.4% of the fungemia. Two important series on *Rhodotorula* fungemia were published [29,72] and they also demonstrated the importance of CVC in the fungemia, mainly when long-term catheters were inserted.

There are few publications reporting the in vitro susceptibility testing of Rhodotorula strains with a standardized method. Although there is no specific protocol for this yeast, it is reasonable to assume that it might be reliably tested by the CLSI (Clinical and Laboratory Standard Institute's) protocol. Amphotericin B yield the lowest MICs (MIC₉₀, 0.5 µg/ml) followed by itraconazole and voriconazole [15,18,25,72]. The MICs for fluconazole has been described as very high (MIC₉₀ > 64 μ g/ml) [13,18,20]. The resistance mechanism of Rhodotorula for fluconazole is not known but the repeated pattern of high MICs suggests the presence of intrinsic resistance. Previous reports have suggested good in vitro activity of 5-fluorocytosine. Results determined for voriconazole by Gomez-Lopez et al. using the E-test and Sensititre YeastOne appeared controversial [25]. Diekema et al and Zaas et al. found poor in vitro activity of caspofungin and micafungin, highlighting the lack of effectiveness of the echinocandins for heterobasidiomycetous yeasts [13,72]. Despite the low MICs to ravuconazole and posaconazole, there is no clinical experience with these drugs, however they may have potential efficacy.

Currently amphotericin B appears to be the drug of choice for *Rhodotorula* infection, although seven patients treated with fluconazole and one treated with miconazole responded. There are no prospective studies that have evaluated antifungal treatment for *Rhodotorula* infections.

Patients on CAPD have an incidence of peritonitis of about one episode per patient-year [49]. Fungal peritonitis is a relatively uncommon complication of peritoneal dialysis and although it accounts for less than 5% of all peritonitis episodes in patients on CAPD, it contributes significantly to morbidity, drop out from the CAPD program, and mortality [6]. Contamination of the dialysis catheter with these ubiquitous organisms from the environment serves as a portal of entry [49]. Patients receiving CAPD are at risk for Rhodotorula peritonitis and, as are those who have previously received antibiotics for bacterial peritonitis. Rhodotorula is easily recovered from the peritoneal fluid, thereby providing early identification and antifungal therapy. Eighty percent of patients who survived their *Rhodotorula* peritonitis dropped out of the CAPD program and were started on hemodialysis, which increased the risk of other infections.

Endogenous fungal endophthalmitis has increased owing to widespread use of immunosuppressive therapy, parental nutrition, injectable drug use, and AIDS [59]. *Candida* and *Aspergillus* are the most common organisms [34]. *Rhodotorula* seldom causes ocular infections and most common cases described include keratitis and endophthalmitis. Dacryocystitis and corneal lamellar graft infection were also reported [47,53]. Although the therapy of *Rhodotorula* eye infections is not well-defined, some reports recommend that endophthalmitis should be treated with systemic antifungals, and some keratitis cases clear with topical treatment [4,7]. The worst outcomes requiring enucleation occurred in two patients, both with underlying conditions and drug abuse histories [45,59].

It appears *Rhodotorula* meningitis should be considered a hospital infection, as five cases of central nervous system infections were nosocomial, including a case of ventriculitis. One case of community-acquired infection was reported in 2001 [35], although it is difficult to explain how *Rhodotorula* gets access to cerebral spinal fluid without a barrier leak, such as a catheter or neoplasm, in a non-hospitalized patient.

Rhodotorula spp. appear to be emerging yeasts, although some infections not documented histopathologically appear doubtful [50]. Immunosuppression and CVC appear to be risk factors. Correct identification is necessary for appropriate managements, as *Rhodotorula* spp. are resistant to some antifungal agents such as fluconazole and the echinocandins. Reports of *Rhodotorula* infections resolving without the use of specific antifungal treatment may suggest their low virulence in immunocompetent individuals. Additional studies including an immunosuppressed model, and prospective randomized trials in humans are need to better understand this intriguing infection and to determine optimal management.

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References

- Alekhova TA, Aleksandrova AA, Novozhilova TI, Lysak LV, Zagustina NA, Bezborodov AM. [Monitoring of microbial degraders in manned space stations]. Prikl Biokhim Mikrobiol 2005; 41: 435-443.
- Alliot C, Desablens B, Garidi R, Tabuteau S. Opportunistic infection with *Rhodotorula* in cancer patients treated by chemotherapy: two case reports. Clin Oncol (R Coll Radiol) 2000; 12: 115-117.
- Anaissie E, Bodey GP, Kantarjian H, Ro J, Vartivarian SE, Hopfer R, Hoy J, Rolston K. New spectrum of fungal infections in patients with cancer. Rev Infect Dis 1989; 11: 369-378.
- Bawazeer AM, Hodge WG. *Rhodotorula* infection in a corneal graft following penetrating keratoplasty. Can J Ophthalmol 2003; 38: 225-227.
- Braun DK, Kauffman CA. *Rhodotorula* fungaemia: a life-threatening complication of indwelling central venous catheters. Mycoses 1992; 35: 305-308.
- Bren A. Fungal peritonitis in patients on continuous ambulatory peritoneal dialysis. Eur J Clin Microbiol Infect Dis 1998; 17: 839-843.
- Casolari C, Nanetti A, Cavallini GM, Rivasi F, Fabio U, Mazzoni A. Keratomycosis with an unusual etiology (*Rhodotorula glutinis*): a case report. Microbiologica 1992; 15: 83-87.
- Chung JW, Kim BN, Kim YS. Central venous catheter-related *Rhodotorula rubra* fungemia. J Infect Chemother 2002; 8: 109-110.
- Colombo AL, Dantas LS, Abramczyk ML, Cypriano M, Fischman O, lazzetti AV, Petrilli AS, Selijan MP. *Rhodotorula glutinis* fungemia: a case report and literature review. Braz J Infect Dis 1997; 1: 204-207.
- Costa SF, Marinho I, Araujo EA, Manrique AE, Medeiros EA, Levin AS. Nosocomial fungaemia: a 2-year prospective study. J Hosp Infect 2000; 45: 69-72.
- Cutrona AF, Shah M, Himes MS, Miladore MA. *Rhodotorula minuta:* an unusual fungal infection in hip-joint prosthesis. Am J Orthop 2002; 31: 137-140.
- Zoyoa JR, Searle M, Lynn KL, Robson RA. Successful treatment of CAPD peritonitis caused by *Rhodotorula mucilaginosa*. Perit Dial Int 2001; 21: 627-628.
- Diekema DJ, Petroelje B, Messer SA, Hollis RJ, Pfaller MA. Activities of available and investigational antifungal agents against *Rhodotorula* species. J Clin Microbiol 2005; 43: 476-478.
- Eisenberg ES, Alpert BE, Weiss RA, Mittman N, Soeiro R. *Rhodotorula rubra* peritonitis in patients undergoing continuous ambulatory peritoneal dialysis. Am J Med 1983; 75: 349-352.
- Espinel-Ingroff A. In vitro activity of the new triazole voriconazole (UK-109,496) against opportunistic filamentous and dimorphic fungi and common and emerging yeast pathogens. J Clin Microbiol 1998; 36: 198-202.
- Fanci R, Pecile P, Martinez RL, Fabbri A, Nicoletti P. Amphotericin B treatment of fungemia due to unusual pathogens in neutropenic patients: report of two cases J Chemother 1997; 9: 427-430.
- Fell JW, Boekhout T, Fonseca A, Scorzetti G, Statzell-Tallman A. Biodiversity and systematics of basidiomycetous yeasts as determined by large-subunit rDNA D1/D2 domain sequence analysis. Int J Syst Evol Microbiol 2000; 50: 1351-1371.

- Galan-Sanchez F, Garcia-Martos P, Rodriguez-Ramos C, Marin-Casanova P, Mira-Gutierrez J. Microbiological characteristics and susceptibility patterns of strains of *Rhodotorula* isolated from clinical samples. Mycopathologia 1999; 145: 109-112.
- Gamma R, Carrel T, Schmidli J, Zimmerli S, Tanner H, Hullin R, Mohacsi PJ. Transplantation of yeast-infected cardiac allografts: a report of 2 cases. J Heart Lung Transplant 2005; 24: 1159-1162.
- Garcia-Martos P, Dominguez I, Marin P, Garcia-Agudo R, Aoufi S, Mira J. [Antifungal susceptibility of emerging yeast pathogens]. Enferm Infecc Microbiol Clin 2001; 19: 249-256.
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988; 16: 128-140.
- Gaytan-Martinez J, Mateos-Garcia E, Sanchez-Cortes E, Gonzalez-Llaven J, Casanova-Cardiel LJ, Fuentes-Allen JL. Microbiological findings in febrile neutropenia. Arch Med Res 2000; 31: 388-392.
- Gogate A, Deodhar L, Gogate S. Hydrosalpinx due to *Rodotorula glutinis* (a case report). J Postgrad Med 1987; 33: 34.
- Goldani LZ, Craven DE, Sugar AM. Central venous catheter infection with *Rhodotorula minuta* in a patient with AIDS taking suppressive doses of fluconazole. J Med Vet Mycol 1995; 33: 267-270.
- Gomez-Lopez A, Mellado E, Rodriguez-Tudela JL, Cuenca-Estrella M. Susceptibility profile of 29 clinical isolates of *Rhodotorula* spp. and literature review. J Antimicrob Chemother 2005; 55: 312-316.
- Gregory JK, Haller JA. Chronic postoperative *Rhodotorula* endophthalmitis. Arch Ophthalmol 1992; 110: 1686-1687.
- Hazen KC. New and emerging yeast pathogens. Clin Microbiol Rev 1995; 8: 462-478.
- Hsueh PR, Teng LJ, Ho SW, Luh KT. Catheter-related sepsis due to *Rhodotorula glutinis*. J Clin Microbiol 2003; 41: 857-859.
- Kiehn TE, Gorey E, Brown AE, Edwards FF, Armstrong D. Sepsis due to *Rhodotorula* related to use of indwelling central venous catheters. Clin Infect Dis 1992; 14: 841-846.
- Kiraz N, Gulbas Z, Akgun Y. Case report. Rhodotorula rubra fungaemia due to use of indwelling venous catheters. Mycoses 2000; 43: 209-210.
- Kofteridis D, Mantadakis E, Christidou A, Samonis G. *Rhodotorula glutinis* fungemia successfully treated with fluconazole: report of two cases. Int J Infect Dis 2007; 11: 179-180.
- Krcmery V, Krupova I, Denning DW. Invasive yeast infections other than Candida spp. in acute leukaemia. J Hosp Infect 1999; 41: 181-194.
- 33. Krcmery V, Laho L, Huttova M, Ondrusova A, Kralinsky K, Pevalova L, Dluholucky S, Pisarcikova M, Hanzen J, Filka J, Sejnova D, Liskova A, Purgelova A, Szovenyova Z, Koren P. Aetiology, antifungal susceptibility, risk factors and outcome in 201 fungaemic children: data from a 12-year prospective national study from Slovakia. J Med Microbiol 2002; 51: 110-116.

- Kresloff MS, Castellarin AA, Zarbin MA. Endophthalmitis. Surv Ophthalmol 1998; 43: 193-224.
- Lanzafame M, De Chechi G, Parinello A, Trevenzoli M, Cattelan AM. *Rhodotorula glutinis*-related meningitis. J Clin Microbiol 2001; 39: 410.
- Leeber DA, Scher I. *Rhodotorula* fungemia presenting as "endotoxic" shock. Arch Intern Med 1969; 123: 78-81.
- Leibovitz E, Rigaud M, Chandwani S, Kaul A, Greco MA, Pollack H, Lawrence R, Di JD, Hanna B, Krasinski K, Disseminated fungal infections in children infected with human immunodeficiency virus. Pediatr Infect Dis J 1991; 10: 888-894.
- Lifshitz T, Levy J. *Rhodotorula rubra* keratitis and melting after repeated penetrating keratoplasty. Eur J Ophthalmol 2005; 15: 135-137.
- Lo R, V, Fishman NO, Nachamkin I. Recurrent catheter-related *Rhodotorula rubra* infection. Clin Microbiol Infect 2003; 9: 897-900.
- Louria DB, Blevins A, Armstrong D, Burdick R, Lieberman P. Fungemia caused by "nonpathogenic" yeasts. Arch Intern Med 1967; 119: 247-252.
- Louria DB, Greenberg SM, Molander DW. Fungemia caused by certain nonpathogenic strains of the family Cryptococcaceae. Report of two cases due to *Rhodotorula* and *Torulopsis* glabrata. N Engl J Med 1960; 263: 1281-1284.
- Lui AY, Turett GS, Karter DL, Bellman PC, Kislak JW. Amphotericin B lipid complex therapy in an AIDS patient with *Rhodotorula rubra* fungemia. Clin Infect Dis 1998; 27: 892-893.
- Maeder M, Vogt PR, Schaer G, von GA, Gunthard HF. Aortic homograft endocarditis caused by *Rhodotorula mucilaginosa*. Infection 2003; 31: 181-183.
- 44. Marinova I, Szabadosova V, Brandeburova O, Krcmery V Jr. *Rhodotorula* spp. fungemia in an immunocompromised boy after neurosurgery successfully treated with miconazole and 5-flucytosine: case report and review of the literature. Chemotherapy 1994; 40: 287-289.
- 45. Merkur AB, Hodge WG. *Rhodotorula rubra* endophthalmitis in an HIV positive patient. Br J Ophthalmol 2002; 86: 1444-1445.
- Michael W, Richard J, Christina M. Infections of the Central Nervous System. New York, 2004.
- Muralidhar S, Sulthana CM. *Rhodotorula* causing chronic dacryocystitis: a case report. Indian J Ophthalmol 1995; 43: 196-198.
- Nagahama T, Hamamoto M, Nakase T, Horikoshi K. *Rhodotorula lamellibrachii* sp. nov., a new yeast species from a tubeworm collected at the deep-sea floor in Sagami bay and its phylogenetic analysis. Antonie Van Leeuwenhoek 2001; 80: 317-323.
- Nannini EC, Paphitou NI, Ostrosky-Zeichner L. Peritonitis due to Aspergillus and zygomycetes in patients undergoing peritoneal dialysis: report of 2 cases and review of the literature. Diagn Microbiol Infect Dis 2003; 46: 49-54.
- Navarro JT, Lauzurica R, Gimenez M. *Rhodotorula rubra* infection in a kidney transplant patient with pancytopenia. Haematologica 2001; 86: 111.

- Naveh Y, Friedman A, Merzbach D, Hashman N. Endocarditis caused by *Rhodotorula* successfully treated with 5-fluorocytosine. Br Heart J 1975; 37: 101-104.
- Nucci M, Pulcheri W, Spector N, Bueno AP, Bacha PC, Caiuby MJ, Derossi A, Costa R, Morais JC, de Oliveira HP. Fungal infections in neutropenic patients. A 8-year prospective study. Rev Inst Med Trop Sao Paulo 1995; 37: 397-406.
- Panda A, Pushker N, Nainiwal S, Satpathy G, Nayak N. *Rhodotorula* sp. infection in corneal interface following lamellar keratoplasty--a case report. Acta Ophthalmol Scand 1999; 77: 227-228.
- Papadogeorgakis H, Frangoulis E, Papaefstathiou C, Katsambas A. *Rhodotorula rubra* fungaemia in an immunosuppressed patient. J Eur Acad Dermatol Venereol 1999; 12: 169-170.
- Pasqualotto GC, Copetti FA, Meneses CF, Machado AR, Brunetto AL. Infection by *Rhodotorula* sp. in children receiving treatment for malignant diseases. J Pediatr Hematol Oncol 2005; 27: 232-233.
- Pennington JC, III, Hauer K, Miller W. *Rhodotorula rubra* peritonitis in an HIV+ patient on CAPD. Del Med J 1995; 67: 184.
- Petrocheilou-Paschou V, Prifti H, Kostis E, Papadimitriou C, Dimopoulos MA, Stamatelopoulos S. *Rhodotorula* septicemia: case report and minireview. Clin Microbiol Infect 2001; 7: 100-102.

- Pien FD, Thompson RL, Deye D, Roberts GD. *Rhodotorula* septicemia: two cases and a review of the literature. Mayo Clin Proc 1980; 55: 258-260.
- 59. Pinna A, Carta F, Zanetti S, Sanna S, Sechi LA. Endogenous *Rhodotorula minuta* and *Candida albicans* endophthalmitis in an injecting drug user. Br J Ophthalmol 2001; 85: 759.
- Riella MC. Princípios de Nefrologia e Distúrbios Hidroeletrolíticos. Río de Janeiro, Guanabara Koogan, 2003.
- Romano A, Segal E, Ben-Tovim T. Epithelial keratitis due to *Rhodotorula*. Ophthalmologica 1973; 166: 353-359.
- Rusthoven JJ, Feld R, Tuffnell PG. Systemic infection by *Rhodotorula* spp. in the immunocompromised host. J Infect 1984; 8: 241-246.
- Samonis G, Anatoliotaki M, Apostolakou H, Maraki S, Mavroudis D, Georgoulias V. Transient fungemia due to *Rhodotorula rubra* in a cancer patient: case report and review of the literature. Infection 2001; 29: 173-176.
- 64. Shelburne PE, Carey RG. *Rhodotorula* fungemia complicating staphylococcal endocarditis. JAMA 1962; 180: 38-42.
- Sheu MJ, Wang CC, Wang CC, Shi WJ, Chu ML. *Rhodotorula* septicemia: report of a case. J Formos Med Assoc 1994; 93: 645-647.
- 66. Silva J, Runco de Laborda R, Almendro G, Salim R. *Rhodotorula glutinis* and *R. rubra*: agents of opportunistic mycoses in man. Bol Micol 1989; 4: 171-174.

- Soylu A, Demircioglu F, Turkmen M, Yucesoy M, Kavukcu S. Unusual cause of peritonitis during peritoneal dialysis. *Rhodotorula rubra* and amphotericin B. Pediatr Nephrol 2004; 19: 1426-1428.
- Thomas PA. Current perspectives on ophthalmic mycoses. Clin Microbiol Rev 2003; 16: 730-797.
- Tuon FF, de Almeida GM, Costa SF. Central venous catheter-associated fungemia due to *Rhodotorula* spp. --a systematic review. Med Mycol 2007; 45: 441-447.
- Vas SI. Microbiologic aspects of chronic ambulatory peritoneal dialysis. Kidney Int 1983; 23: 83-92.
- 71. Walsh TJ, Gonzalez C, Roilides E, Mueller BU, Ali N, Lewis LL, Whitcomb TO, Marshall DJ, Pizzo PA. Fungemia in children infected with the human immunodeficiency virus: new epidemiologic patterns, emerging pathogens, and improved outcome with antifungal therapy. Clin Infect Dis 1995; 20: 900-906.
- Zaas AK, Boyce M, Schell W, Lodge BA, Miller JL, Perfect JR. Risk of fungemia due to Rhodotorula and antifungal susceptibility testing of *Rhodotorula* isolates. J Clin Microbiol 2003; 41: 5233-5235.