Presented by
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Transplant Infectious Diseases
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UBC / VCH

LAND ACKNOWLEDGEMENT

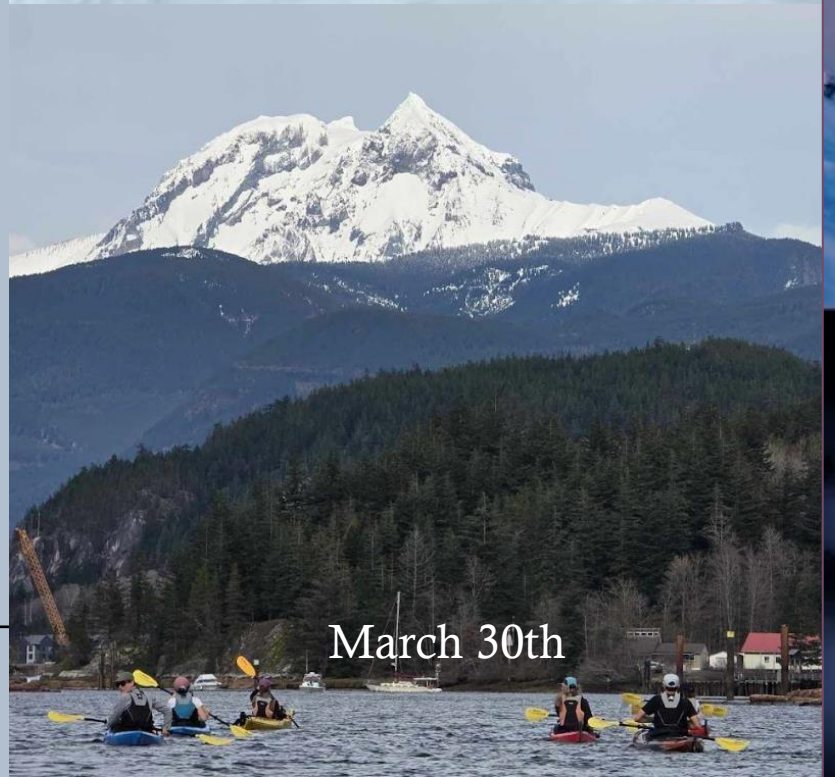
- I am gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johnmaps.net

Aboriginal Health

DISCLOSURE

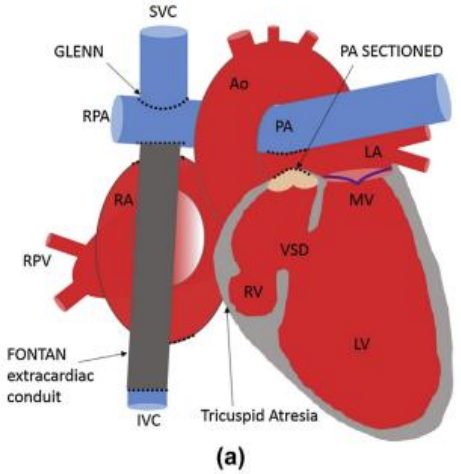
- No conflict of interest



CASE PRESENTATION - BACKGROUND

[redacted] with complex cardiac history presents with pruritus and elevated cholestatic liver enzymes (Spring 2025)

- Congenital heart disease (cyanotic heart disease with tricuspid atresia with D- transposition of the great arteries and single ventricle pathway) s/p Classic Fontan Procedure in childhood



(a)

Date	Transplant	Indication	Complications
[redacted]2023	Heart	Heart Failure from congenital heart disease	ATN requiring IHD
[redacted]2023	Liver	Fontan-associated / congestive liver disease	
[redacted]2024	Kidney (CMV D+/R-)	ATN post-cardiac transplant	Urinoma, perinephric collection with ESBL *E.coli* and *E. faecalis*

Immunosuppression:

- Tacrolimus (target 10-12), MMF 500mg PO BID (cytopenia), Prednisone 5

Navarro-Aguilar V et al. Clinical Radiology 2015

HISTORY AND BACKGROUND

Social History

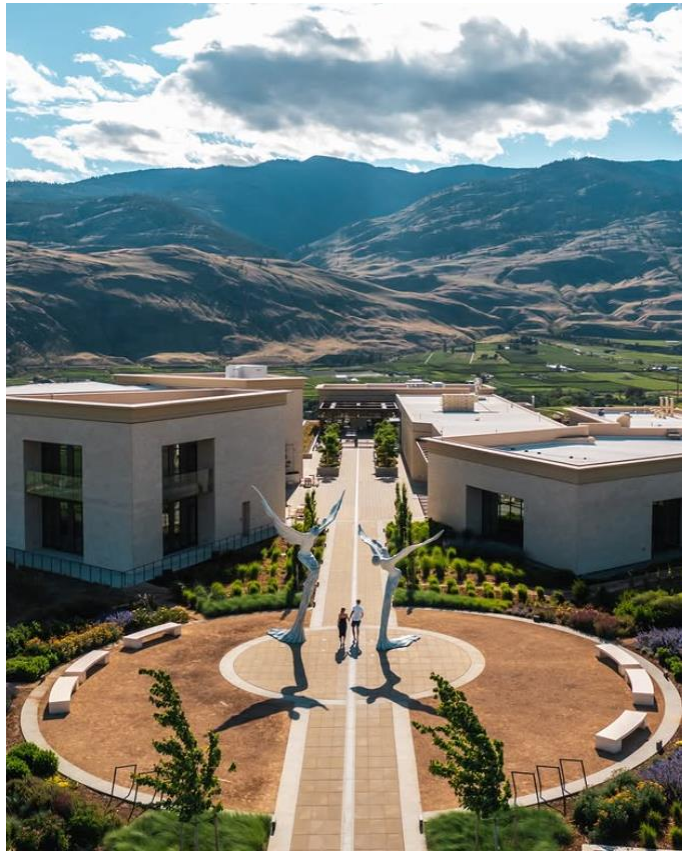
- Born in Canada, lives in rural interior BC (trailer park)
- Lives with mother and is on disability (used to work as a welder)
- No recent international travel history, no pets, had 1 adult child
- Habits:
    - Past EtOH and tobacco use prior to transplant, none since. No recreational drug use

Antimicrobial agents

- Treatment - Valganciclovir (received 6 months of CMV prophylaxis with Letermovir followed by valganciclovir)
- Prophylaxis - Dapsone (due to cytopenia with TMP-SMX)

Prior ID History

- Had primary CMV infection 3 week prior to presentation – on valganciclovir with adequate response



INITIAL PRESENTATION

Initial reason for presentation

- Presented to local hospital with elevated cholestatic liver enzymes and generalized pruritus

Prior to presentation:

- Visited ED for fever, throat pain, cough and diarrhea. Presumed to be viral illness
- Tested negative for COVID-19, Influenza, RSV and BCx were negative
- CMV DNAemia found to be 1800, initiated on valganciclovir with resolution of symptoms aside for cough

Clinical assessment

- Well appearing, afebrile, no tenderness, cough had resolved

INITIAL INVESTIGATIONS

Laboratory results, relevant for

- CBC – shows mild bicytopenia (WBC 3.8, Hb 93, PLT normal)
  - Leukopenia with neutropenia (WBC ~ 4 and ANC ~ 3.5 since Late 2024)
- Creatinine at baseline (eGFR around 25)
- Elevated cholestatic liver enzymes (ALP 431, Bilirubin T 507, GGT 452, while AST/ALT within normal limit)
- CMV 1800 –> 3130 -> 316

Imaging

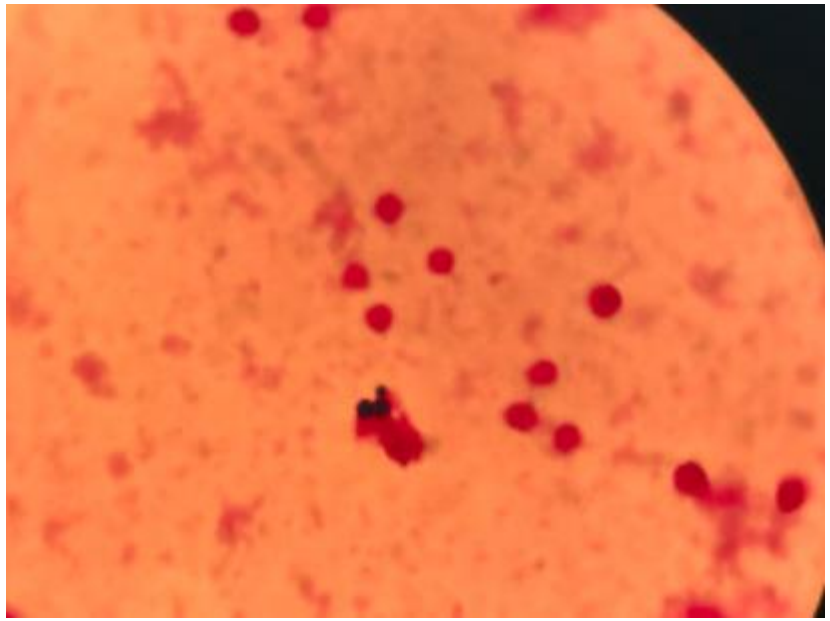
- CT A-P w/ contrast : Mod-severe intra & extra hepatic biliary duct dilatation with an abrupt transition point without obstruction lesions seen.
- MRCP – Bile duct stricture at biliary anastomosis with associated intrahepatic bile ducts

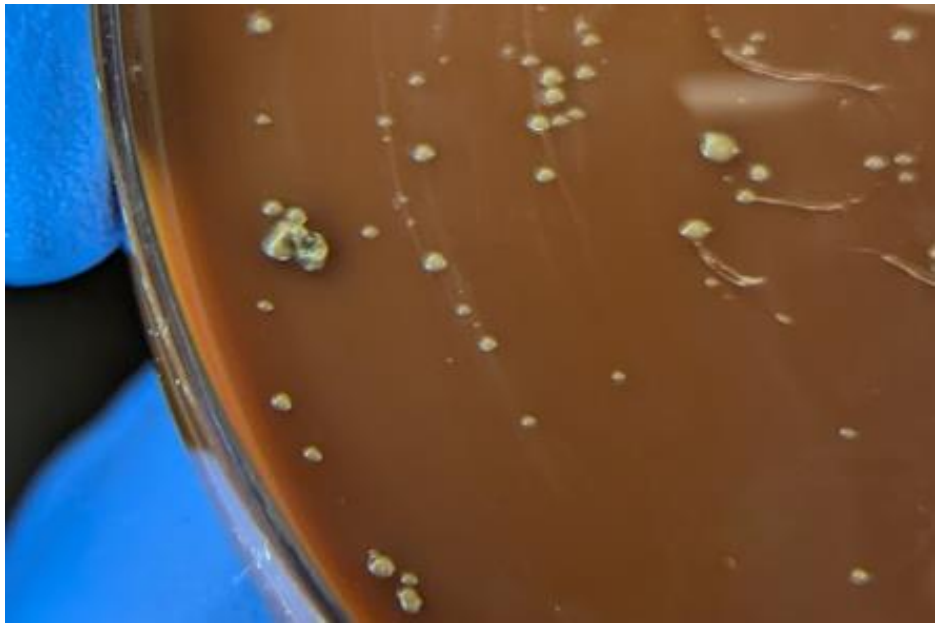
Management

- Sent to tertiary care hospital ([redacted]) for ERCP

IN THE INTERIM

- Blood culture taken routinely (no fever) yielded (2/4 bottles from aerobic, peripheral blood) positive for Gram positive after 3 days. Grew on CHOC and BA

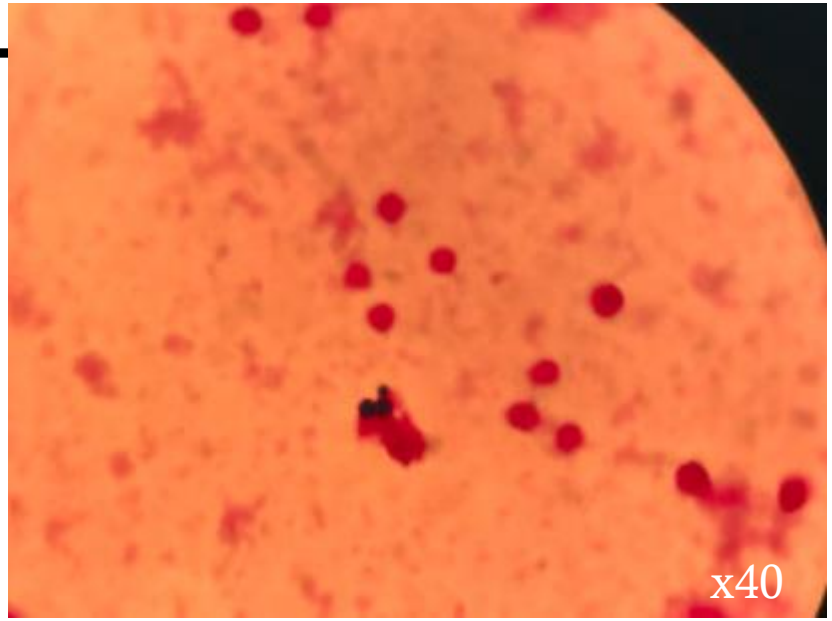


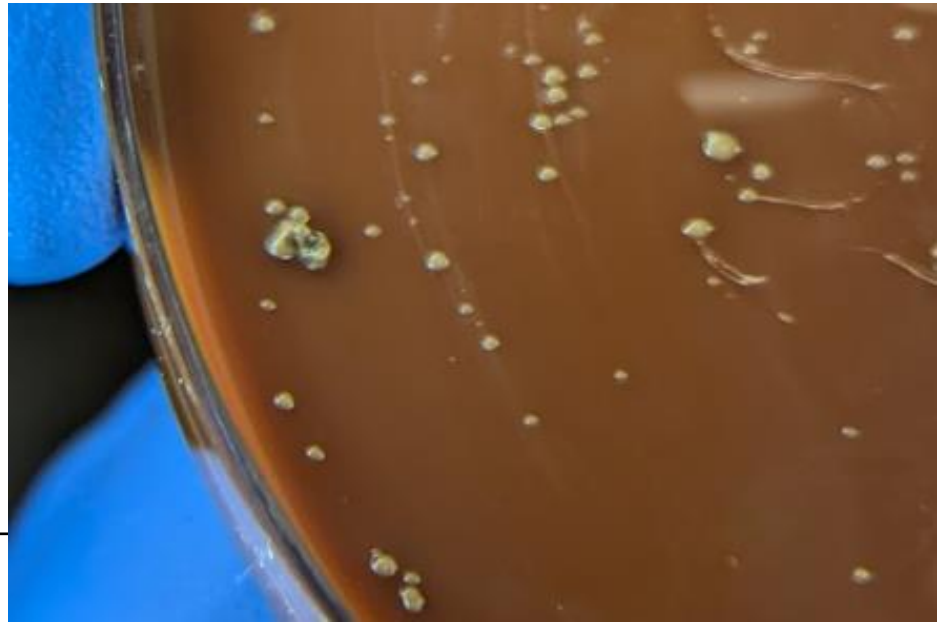


QUESTIONS

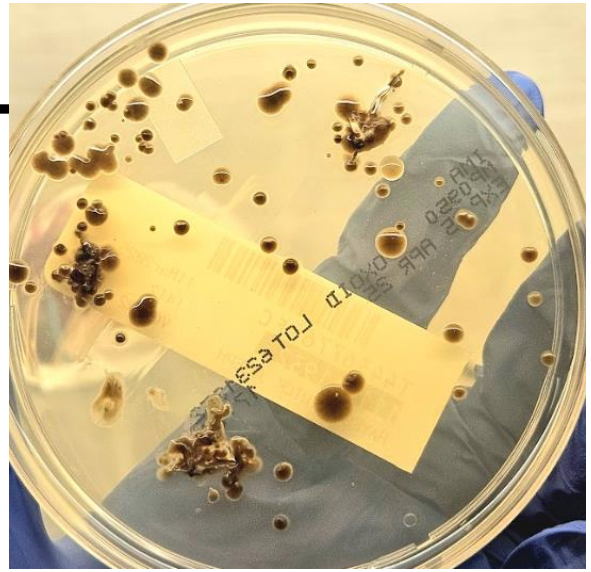
What is the organism seen?

1. Yeast – Candida
2. Yeast – Non-Candida
3. Gram positive cocci cluster
4. Gram negative cocci under-decolorized
5. Mold
6. What does Karius say?





FOLLOW-UP



- Initially started on Micafungin
- Referred to lab - MALDI-TOF confirms *Exophiala dermatitidis*, and as cultures matured
- Switched to Voriconazole on day 7th
- Repeat BCx
  - Day 4 – 2/4 positive
  - Day 8 – 1/4 positive
  - Day 10 & 12 – negative

AT [redacted]

Physical examination

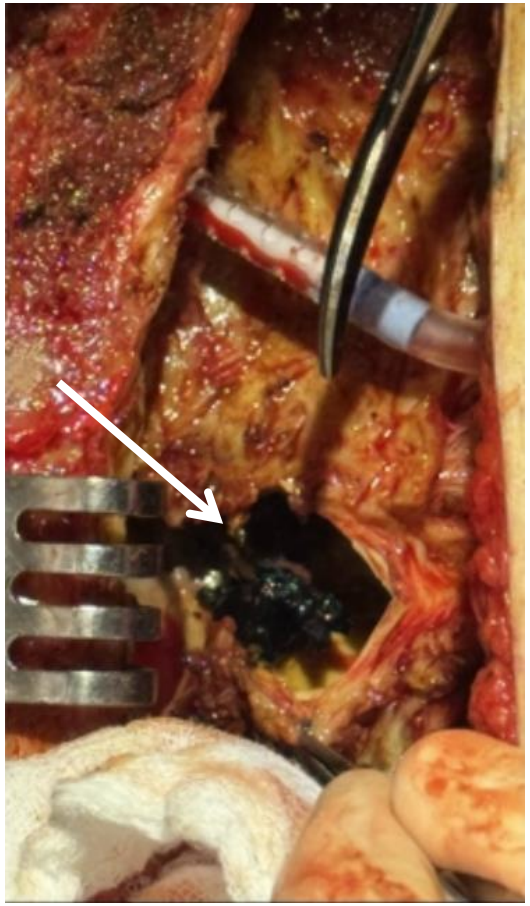
- General Appearance & Vitals : Not in apparent distress, afebrile
- CVS: Regular rhythm, Systolic murmur with large V wave
- Resp / GI / Extremities: Unremarkable
- Skin: Onycholysis of the left foot toenail

Further investigations

- Nail clipping cultures negative
- Chest CT-scan w/ contrast
  - New pseudoaneurysm arising from the native aorta at the anastomosis (40 x 40 x 33) mm
  - (16 x 11 x 14) mm thrombus adherent to the aneurysm neck

CARDIAC SURGERY CONSULTED

- Operative Room
  - Procedures
    - Redo sternotomy, repair of ascending aorta and resection of pseudoaneurysm
    - Debride and irrigation with amphotericin
  - Findings
    - TR less severe
    - Large 2 cm black fungus attached to the anastomosis
    - Area of black discolouration under the intima with infected aortic plaque
    - Full source control could not be achieved
    - Aortic replacement with hemashield
  - OR Cultures
    - Grew on fungal and bacterial cultures
      - *Exophiala dermatitidis*
      - Scant *S. epidermidis* (2 strains)



Credit: Dr. [redacted]

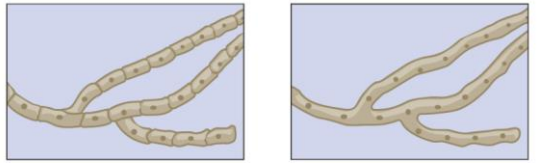
OBJECTIVES

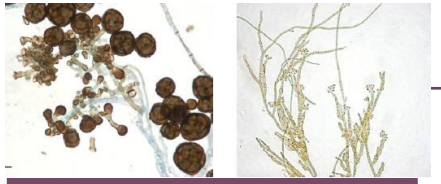
- 1. Understand the microbiological findings and terminology of dematiaceous molds infections
- 2. Review risk factors and epidemiology of *Exophiala dermatitidis*
- 3. Explore the treatment strategies for *Exophiala dermatitidis*
- 4. Discuss infection prevention strategies in transplant recipients

DISCUSSION

APPROACH TO MOLD

Mold



- Septate
  - 
    Dematiaceous – Pheohyphomycosis
    - *Cladophialophora*
      Fonsecacea
      Alterneria
      Exserohilum
      Chaetomium
      Exophiala
    - *Scedosporium*
      Lomentospora
  - Hyalin – Hyalohyphomycosis
    
    - *Aspergillus*
      Paecilomycetes
      Purpureocillium
      Penicillium
      Acremonium
      Fusarium
  - Dimorphic (7-21d)
    - *Blastomyces*
      Coccidioides (24-72h)
      Histoplasma
      Sporothrix
      Talaromyces
      Paracoccidioides
  - Dermatophytes – Digest keratin
    - *Microsporon*
      Trichophyton
      Epidermophyton
- Aseptate
  - Agent of Mucorales (48h) - Mucormycosis
    - *Rhizopus*
      Rhizomucor
      Mucor
      Lichtheimia
      Cunninghamella
      Apophysomyces
      Syncephalastrum

HISTORICALLY

Phaeohyphomycosis

Heterogenous group of mycotic infection that contains dwematiaceous yeastlike cells, pseudohyphae-like elements, hyphae, or any combination of these in tissue

Chromoblastomycosis

Chronic, localized infections of the cutaneous or SC that contain muriform cells or sclerotic bodies (medlar bodies/copper pennies) on histopathology

Eumycotic mycetoma

Also called “Madura foot” - chronic granulomatous infection of the skin and SC tissue

60% are bacterial (actinomycetoma), the rest are fungal (eumycetoma)

DEMATIACEOUS FUNGI – MELANIZED (BLACK) FUNGI

- Majority of the time = environmental, common laboratory contaminant (+/- 10% are considered significant)

- Phaeohyphomycosis – overarching term for deep seeded infection caused by molds that display dark yeast-like cells, pseudo-hyphae or hyphae.

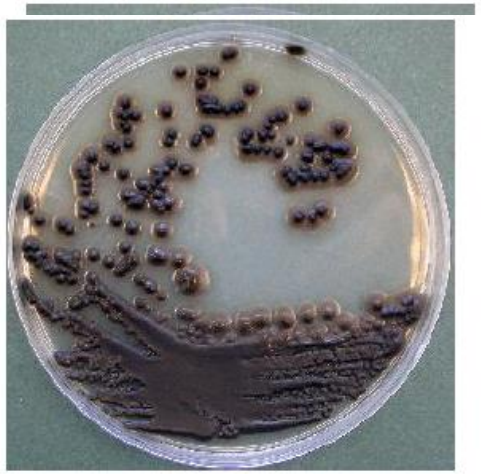
- Most infections are superficial and mild, or cause cutaneous/pulmonary colonization
  - **Superficial – secondary to trauma (cystic or popular lesions)**
    - Causes: *Alternaria* spp.*, Exophiala spp., Phialophora spp.*
    - **Histopathology** – Pheohyphomycotic cysts – single dermal lesion with minimal changes in the epidermis and granulomatous inflammation with abundant giant cell
  - **Eumycotic mycetoma – localized infections that involve cutaneous and SC tissue, facia and bone**
    - Causes: (non all dematiaceous) *Exophiala jenselmei*, *Madurella* spp., *Aspergillus nidulans*, *Acreonium* spp
    - **Histopathology and exam -** abscesses, granulomata and draining sinuses
  - **Chromoblastomycosis – chronic SC**
    - Causes: *Cladophialophora carrionii, Fonsecaea pedrosoi, Phialophora verrucosa*
    - **Histopathology** – Muriform cells or sclerotic bodies (medlar bodies/copper pennies)
  - **Invasive diseases** (CNS, endocarditis, sinusitis, disseminated diseases)

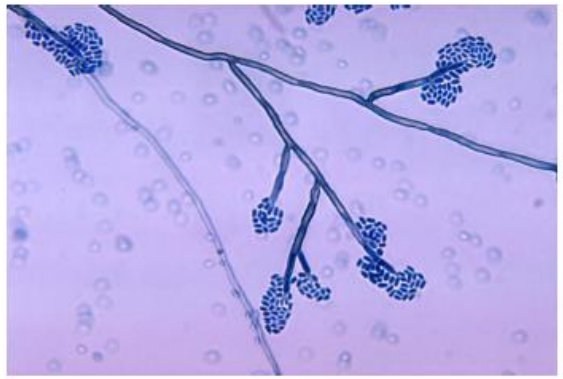
Chowdhary et al. CMI 2014
Larone 7th edition

WHERE COULD [redacted] HAVE ACQUIRED THE INFECTION?

1. Translocation of his own flora (skin or gastrointestinal)
2. Healthcare-associated source
3. Black mold from prior flooding
4. Contaminated water source
5. Soil and decaying plant material

EXOPHIALA DERMATITIDIS





- Found in organic matter (soil, wood, plant, etc.)
- Colonies are at first yeast-like (moist, black, shiny, skin like)
  - After 3-4 weeks, develops olive-gray arial hyphae

- Large spectrum of disease from skin/nails dermatophytosis, post-traumatic skin infections, Mycetoma, colonizer in CF patient to disseminated diseases (prosthetic valves, fungemia, CNS infections)
  - Most infections – cutaneous / SC
  - Dissemination – Mainly elderly, immunocompromised
- ESCMID and ECCM joint clinical guidelines for the diagnosis and management of systemic **pheohyphomycosis**: diseases caused by black fungi – CMI 2014

Chowdhary et al. CMI 2014
Larone 7th edition

EXOPHIALA DERMATITIDIS – INVASIVE DISEASES

- Limited to case series or case reports
  - High mortality (around 30-40%)

- Fungemia
  - Mainly associated with catheter

- Treatment
  - Due to propensity to cause biofilm, surgical management combined with antifungal recommended
  - High MIC to echinocandins
  - Lower MIC to triazoles
  - Clinical effectiveness remains unknown

- Per ESCMID/ECMM guidelines (expert opinion)
  - Surgery resection can be curative
  - Treatment requires itraconazole or terbinafine alone or in combination
  - Invitro MIC showed variable activities to itraconazole, voriconazole, posaconazole and amphotericin B

Chowdhary et al. CMI 2014

SOURCE? - OWN FLORA TRANSLOCATION

- Screening of 2300 feces samples from humans from samples collected from obligatory health testing for workers dealing with food. *Exophiala dermatitidis* seen in 0.52% (12), 8 individuals had diarrhea. 1-3 colonies

Table 1 Strains of *Exophiala dermatitidis* isolated from human faeces.

	Strain	Geography	M/F	Age	Date of isolation	Underlying disease	Symptoms at time of specimen collection	Occupation	ITS genotype
1.	T-6734 = DH 13600	Ljubljana, Slovenia	F	?	24 October 2003	Colicae abdominalis	Gastroenterocolitis acuta	Nurse	*Exophiala heteromorpha*
2.	T-6544 = DH 12770	Ljubljana, Slovenia	F	69	14 November 2001	Melanoma malignum	Diarrhoea	?	A
3.	T-4611 = DH 13251/ T-5262 = DH 13252	Ljubljana, Slovenia	F	3	21 July 2003/ 12 August 2003	Acute leukaemia, BMT	Diarrhoea	-	A
4.	CBS 109148 = DH 11838	Gouda, Netherlands	?	?	?	None	Diarrhoea	?	A
5.	GHP 824	Aachen, Germany	F	42	31 October 1993	Chronic diarrhoea	Diarrhoea	Medical technician	A
6.	GHP 882	Dresden, Germany	M	?	9 September 1993	Haemoblastosis	?	?	A
7.	GHP 883	Dresden, Germany	M	?	29 September 1993	Haemoblastosis	?	?	A
8.	GHP 1038	Dresden, Germany	M	?	? September 1994	?	?	?	A
9.	GHP 1166	Dresden, Germany	M	0	6 June 1996	?	?	-	B
10.	GHP 1348	Aachen, Germany	F	48	20 January 1998	Leukaemia	Diarrhoea	?	A
11.	T-139 = DH 12772	Ljubljana, Slovenia	F	37	16 December 2001	None	None	Shop assistant	A
12.	T-13831 = DH 12773	Ljubljana, Slovenia	F	43	13 November 2001	None	None	Nurse	A
13.	T-508 = DH 12771	Ljubljana, Slovenia	M	45	6 November 2001	Chronic inflammatory intestinal disease	Diarrhoea	Shop assistant	A
14.	CBS 218.88 = UAMH 8662	Angers, France	?	?	?	?	?	?	A
15.	CBS 292.49	Richmond, VA, USA	?	?	4 March 1937	Chronic diarrhoea	Diarrhoea	?[15]	A
16.	GHP 774 = IHEM 5848	Brussels, Belgium	M	?	?	None	Diarrhoea	Bank employee	A

Strains 1–10 were isolated from outpatient and inpatient with different kinds of gastrointestinal disturbance and diarrhoea. Strains 11–13 were isolated out of 1000 samples of faeces from otherwise healthy individuals working with foodstuffs. Strains 14–16 were available in reference collections. F, female; M, male; CBS, Centraalbureau voor Schimmelcultures, Utrecht, The Netherlands; DH, G.S. de Hoog working collection; GHP, G. Haase working collection; T, T. Matos working collection; IHEM, Scientific Institute of Public Health, Mycology Section, Brussels, Belgium; UAMH, University of Alberta Microfungus Collection and Herbarium, Edmonton, Canada.

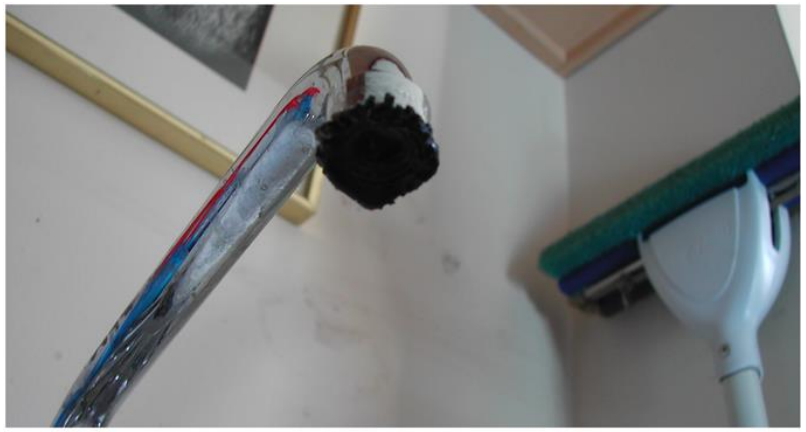
De Hoog G S et al. Mycoses 2005

SOURCE? - CONTAMINATED WATER SOURCE

RESEARCH ARTICLE | FEBRUARY 07 2025

Case report: contamination of a drinking water distribution system by *Exophiala*-dominated biofilm in the Midwestern United States

- *Exophiala* spp. biofilm contamination of customer taps in MW US after consumer complaints



J King et al. Journal of Water & Health 2025

IN OUR CASE

- Denies black molds in household
- Had no CVC or prosthetic joint material
- Reports that source of water is from a **shallow well** that sometimes get covered with a green film

PRE-TRANSPLANT COUNSELLING

Local Safe Living Strategies

Transplant recipients should avoid eating raw or poorly cooked meat and avoid contact with cooking surfaces, utensils, or other food that have been in contact with raw meat until they are cleaned thoroughly. Untreated drinking water should also be avoided. Transplant patients should avoid changing cat litter boxes or wear disposable gloves and wash hands thoroughly after contact. Litter boxes should be changed daily as it takes at least 24 hours for the parasite to become infectious after it is shed in cat feces. Contact with stray cats or kittens should be avoided. Gloves should be worn for all soil and sand contact including gardening, with hand washing after removal.[2]

How to decrease your risk of infection?

Cuts and scrapes: The skin is a major defense against infection. If you have a cut or are injured, keep the area clean and dry. Watch for symptoms of a local infection (tenderness over the area, redness, pus, and pain). Notify your doctor if signs of infection are noted. Persistent sores, blisters, lumps, or growths in armpit, groin, or elsewhere should be examined by your family physician as soon as possible.

Hand washing: Wash your hands frequently using warm water and soap. Ask your healthcare team to demonstrate proper hand washing technique. Hand washing is recommended especially before eating and handling food, before caring for wounds, before and after handling a urinary catheter, after going to the bathroom, changing diapers, playing with pets. Encourage your visitors and family members to practice good hand washing techniques. Avoid putting your fingers or hands near your mouth, eyes or nose especially if you have not washed them.

Contacts: Avoid close contact with people who have obvious illness (cold, flu) especially in the first 6 months after transplantation. Avoid crowds during cold and flu season. Wear a medical mask indoor or crowded area. Do not share utensils, cups, glasses or items for personal hygiene, like toothbrush or razors.

Pets: Ensure your pets are healthy and have all the required vaccinations. Do not handle animal waste; avoid cleaning bird cages, fish or turtle tanks or changing cat litter.

Gardening: Wear gloves when working in the garden and in soil. Wash your hands frequently.

Swimming: Six months after transplantation and after your incision and wounds have healed, you may swim in chlorinated pools, large bodies of water (ocean, sea, large lake). Avoid public hot tubs if possible and take care not to swallow water during swimming.

La Hoz R M; Morris M I Clinical Transplantation 2019

PEDIATRIC POPULATION – SAFE LIVING STRATEGIES

Table 3. Examples of Risk and Mitigation When Discussing Safe Living Strategies for Children Undergoing Transplantation

Category	Risks (example of pathogens)*	Mitigation
Food	Bacteria (*E. coli* 0157-H7, *Campylobacter*, *Salmonella*, *Yersinia*, *Staphylococcus aureus*, *Bacillus cereus*, *Listeria*, *Brucella*, *Vibrio*) Parasites (*Toxoplasma gondii*, tapeworms, *Cryptosporidium*, *Giardia*, *Trichinella*, *Cyclospora*) Viruses (norovirus, Hepatitis A virus, Hepatitis E virus)	• Thoroughly cook meats and fish, seafood, or eggs • Wash cutting boards and knives after use on raw meats and fish • Do not cross contaminate foods • Wash fresh vegetables and fruit including skins of melons and bananas; canned fruits and dried fruits are safe • Avoid raw, rare, or medium rare meat and fish • Avoid sauces or dressing made with raw egg • HCT recipients should avoid raw nuts and vegetable sprouts during periods of augmented immunosuppression • Discard any food with mold or rotting immediately
Water and drinks	Bacteria (*Campylobacter*, *E. coli*, *Shigella*, *Salmonella*) Parasites (*Giardia*, *Cryptosporidium*) Viruses (Hepatitis A Virus)	• Use treated tap water, bottled water, canned, or bottled drinks • Well water should be tested for microbial contamination at least annually - Boil well water - Use NSF-certified filters • Avoid raw or unpasteurized milk, milk products, cider, and juices • Heed water safety community advisories
Recreational water	Bacteria (*E. coli*, *Shigella*, or other enteric pathogens, *Legionella*) Parasites (*Cryptosporidium* [chlorine tolerant], *Naegleria fowleri* [warm, fresh water], avian schistosomes [ocean], *Giardia*) Viruses (norovirus, adenovirus)	• All bodies of water can harbor pathogens but in general treated swimming pools are safer than untreated recreational waters • People with diarrhea should not swim for at least 2 weeks • Water parks have risks of aerosolization of infections • Avoid discolored, smelly, foamy, or scummy water or water likely contaminated with human or animal waste • Avoid swimming when there are open sores or when increased immunosuppression • Avoid swallowing water or having water entering nose, particularly in warm freshwater • Clean wounds that occur while bathing in fresh or ocean water with a clean water source • Heed posted advisories by local monitoring agencies
Pets and animal contact	Bacteria (*Campylobacter* [kittens, puppies, chickens], *Salmonella* [reptiles, amphibians, chickens, ducks], *Bartonella henselae* [cat bite], *Chlamydophila psittaci* [birds], *Coxiella burnetii* [parturient goats, sheep], *Streptobacillus moniliformis* [rat bite fever from rodents], *Francisella tularensis* [handling infected carcasses]) Parasites (*Toxoplasma gondii*) Fungi (dermatophytes) Viruses (Rabies, lymphocytic choriomeningitis virus [LCMV])	• Older animals are generally less of a risk than young animals; traditional pets are preferred • Animals should be seen by a vet and receive all of their immunizations and flea and tick prevention • Ideally the transplant recipient should avoid contacts with animal excrement, such as with litter cleaning for cats, cage cleaning for small animals or birds, or barn muck raking; if not able to avoid, then gloves should be worn and hand washing performed afterward, consider masking if aerosolization possible • Animal bites should be attended to quickly and consideration for prophylaxis discussed with the transplant team • Avoid reptiles and amphibians due to the elevated risk of *Salmonella* • Avoid feral animals due to elevated risk of rabies and rodents due to risk of LCMV • Avoid parturient farm animals due to risk of *Coxiella burnetii* and *Brucella* • Transplant patients should not skin or be in contact with animal carcasses, if this cannot be avoided then gloves should be worn and handwashing performed afterward
Travel and environmental exposures	Variable depending on geography and epidemiology	• Individualized counseling by family's home geography • Directed counseling based on the type of travel, geography, and season, and on the specific type of activity with which they will engage (camping, spelunking) • Special considerations for being up to date on immunizations, hand hygiene, food and water safety issues, fungal, or viral exposures different from home • Optimal mosquito and tick prevention (insect repellants, netting, and cover skin) • The potential for fungal exposure should be reviewed for risks during home renovation projects or with gardening or mulching • Bring your own travel health kit, including transplant-related medications, and basic first aid supplies and sunscreen with SPF ≥15.
Family, close contacts and community contacts	Variable depending on circulating microbes and transmissible infections in household contacts Bacteria (*Staphylococcus aureus*, *Bordetella pertussis*, *Mycobacterium tuberculosis*) Viruses (community respiratory viruses, measles, mumps, varicella, hepatitis, and herpes simplex viruses)	• Promote appropriate handwashing and avoid sharing • Household members and close contacts should have their immunizations up to date • Ideally the school system should enforce school entry immunizations • Families should be queried about tuberculosis exposures • Families should be queried about methicillin-resistant *Staphylococcus aureus* infections in household contacts • Visitors should be healthy and without recent infectious exposures
Sexual activity, tattoos, piercings, recreational drugs	Bacteria (*Gonorrhea*, *Chlamydia*, syphilis, soft tissue skin infection) Viruses (Epstein Barr virus, Cytomegalovirus, Human Immunodeficiency Virus [HIV], hepatitis A virus [HAV], Hepatitis B virus [HBV], Hepatitis C virus [HCV], human papilloma virus [HPV]) Fungal (*Aspergillus* spp, other molds)	• Adolescents and teenagers need private discussions about risks of unprotected intercourse, including risks of pregnancy and infection and extragenital infections • Immunization against HPV, HBV, and HAV should be up to date • Saliva transmission of cytomegalovirus and Epstein Barr virus can be significant even from community acquisition and should be discussed during the pretransplant evaluation • Candidates should be cautioned against self-piercing and tattoos; use reputable licensed sites when immunosuppression is minimized • Inhalational marijuana can be contaminated with fungal elements

*This list provides examples of common organisms and disease states from specific exposures but is not inclusive of all microbes that could be transmitted to cause infection.

Heald-Sargent et al. Journal of Pediatric Infectious Diseases Society 2023

HOW LONG WOULD YOU CONTINUE THE ANTIFUNGAL?

1. Continue voriconazole (or other triazole) lifelong if tolerates
2. Continue voriconazole (or other triazole) until radiographic resolution with interval imaging
3. Continue voriconazole (or other triazole) for 6-12 weeks then observe
4. Once stable, recommend re-do surgery
5. Other

Susceptibility Results	
Antimicrobial Agent	Organism 1
Amphotericin B	(0.5)
Itraconazole	(0.5)
Micafungin	(>8)
Posaconazole	(0.12)
Voriconazole	(0.25)

QUESTIONS?

Photo # 3: mike lan / 604 Now Flickr Poo