ID Pearls in Solid Organ Transplantation

Vanderbilt Transplant Advanced Practice Provider Symposium
August 28,2026

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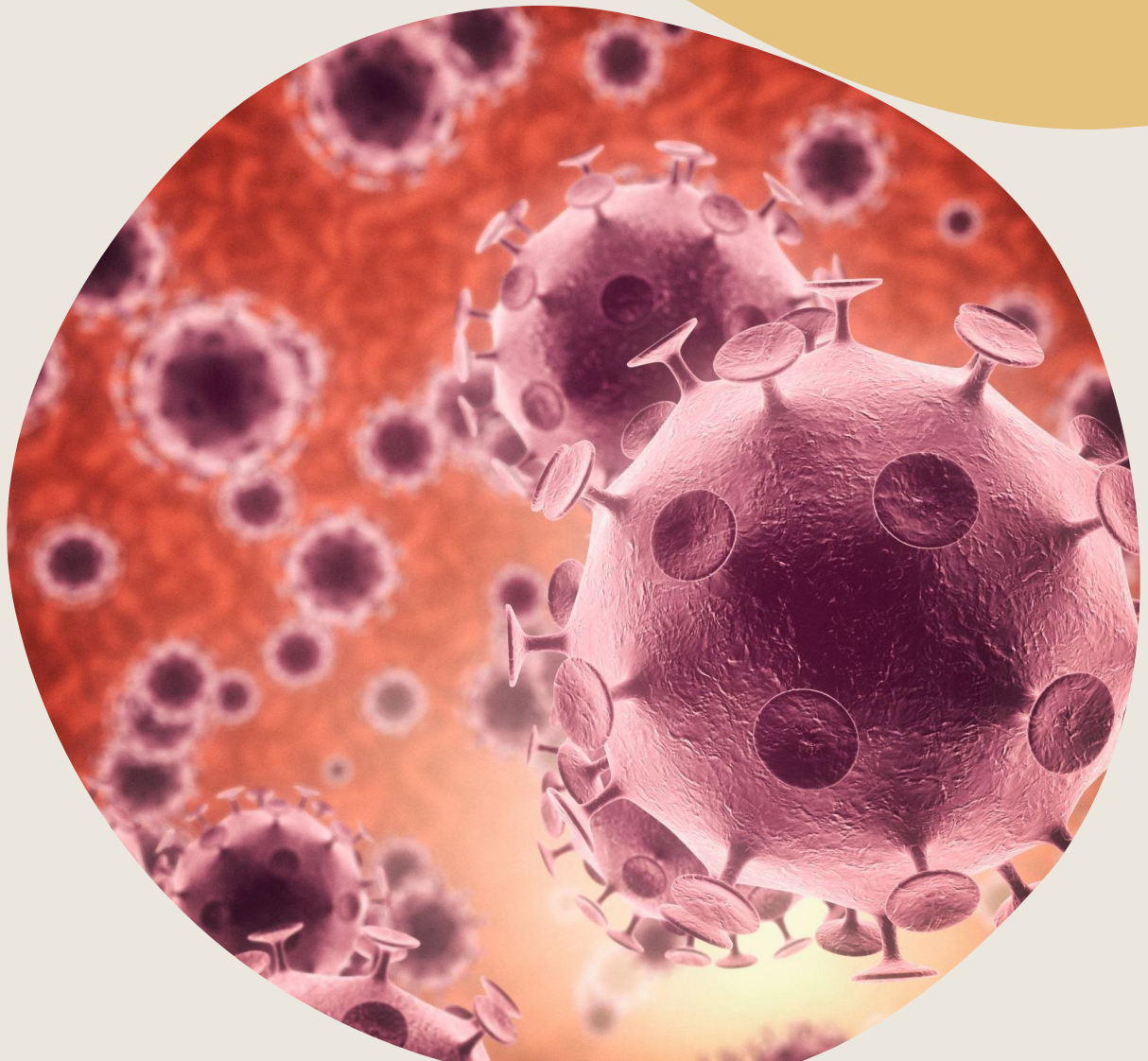
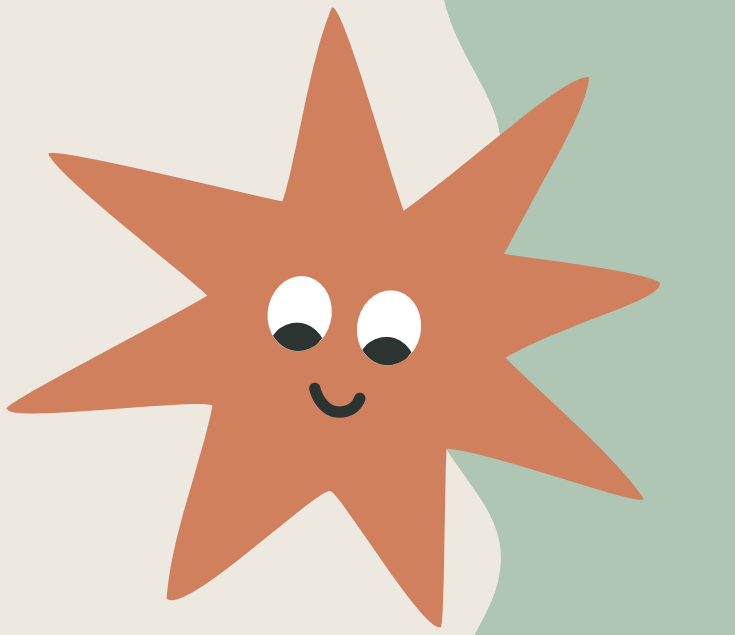
Cytomegalovirus

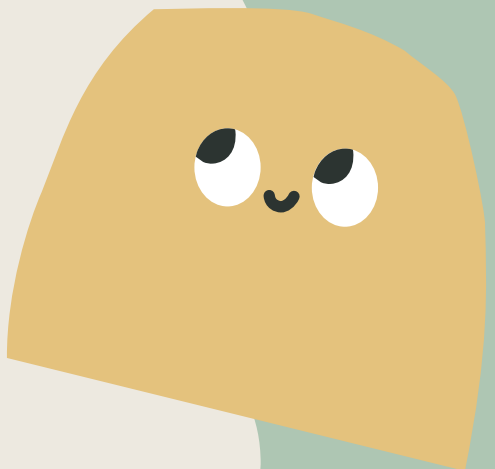


CMV Breakdown

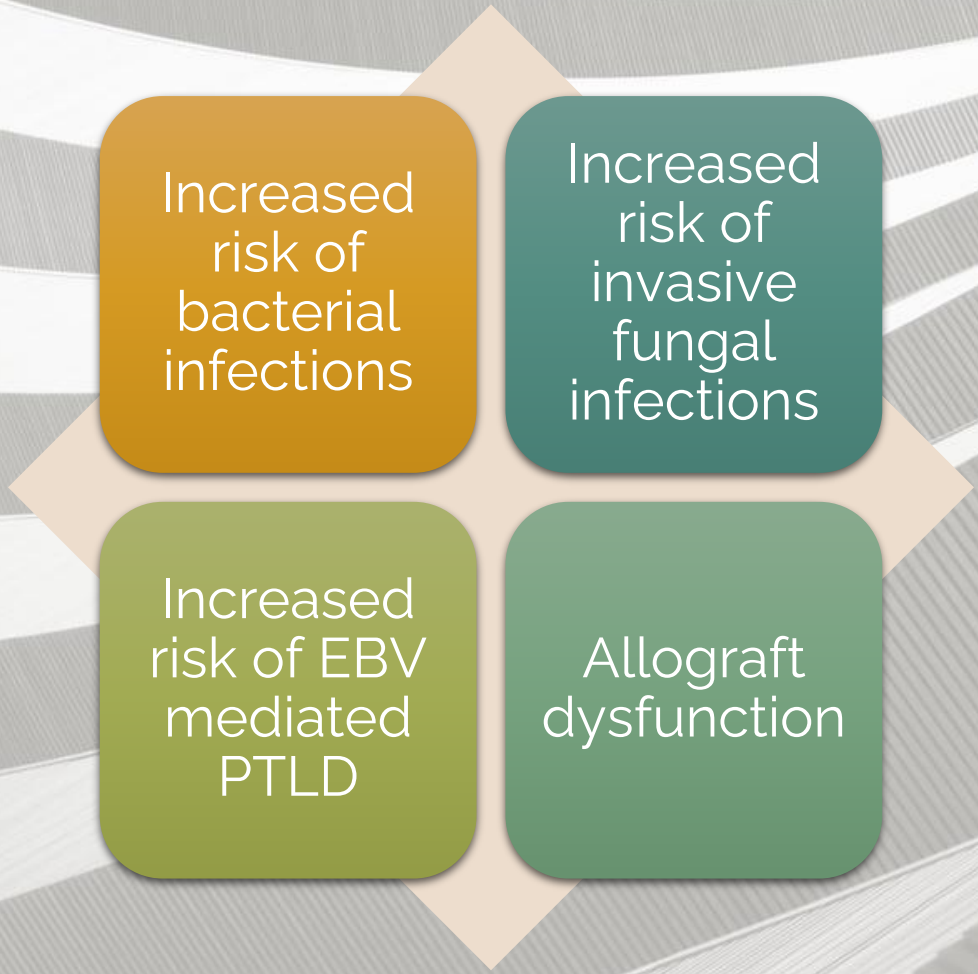
CMV infection: CMV replication in asymptomatic patient (PCR +)
CMV disease: CMV replication with symptoms

- CMV syndrome: malaise, fever, leukopenia
- CMV end organ involvement: CMV presence in GI tract, liver, heart, lungs, eyes, or brain





Indirect Immunomodulatory effects of CMV



When do I start antiviral treatment for CMV reactivation?

High risk patient (+/-)

- Treat any level for primary CMV infection regardless of symptoms.
  - Why?
    - Higher incidence of CMV disease
    - Faster doubling time

Moderate risk patient (+/+)

- Treat any level *if symptomatic*.
- Generally, will opt to treat if PCR >1000 IU/ml, institution dependent
- Depends on overall net state of IS

1 Couzi A, Am J Transplant. 12.1 (2012): 202-209
2 Atabani S. Am J Transplant. 12.9 (2012): 2457-2464
3 Kotton C. Transplantation 109 (2025): 1066-1110

CMV Case 1

45M with history of ESRD from hypertension who underwent DDKT in 01/2025 with alemtuzumab induction, CMV D+/R-, on tacrolimus, MMF, and prednisone 5mg daily. He was found to have CMV PCR 800 IU/ml. He is asymptomatic. No fatigue, diarrhea, abdominal pain, or other symptoms.

Start treatment dose valganciclovir for primary CMV infection.

CMV Case 2

- 56F with alcohol induced cirrhosis who underwent deceased donor liver transplant in 2020 with methylprednisolone induction, CMV D+/R+, on tacrolimus. Routine testing showed low level CMV DNAemia at 900 IU/ml. She is asymptomatic.
- Close monitoring off antivirals with weekly CMV PCR.

CMV Case 3

35M with nonischemic cardiomyopathy who underwent heart transplant in 2022 with basiliximab induction, CMV D+/R+, on tacrolimus, MMF, prednisone 5mg daily. CMV DNAemia at 15,000 IU/ml, log 4.2. He reports fatigue, fever, and poor appetite. No diarrhea. You start valganciclovir 900mg BID.

After 2 weeks of treatment, his viral load increased to 98,000 IU/ml, log 5. He now has watery diarrhea and nausea.

What is your next step?

CMV Case 3 Cont'd. . .

Patient is started on IV Ganciclovir. Despite this, his viral load continues to increase from 98,000 IU/ml, log 4.2 now to 250,000 IU/ml, log 5. He reports persistent have watery diarrhea and fatigue.

What is your next step?

CMV Case 3 Cont'd. . .

Patient was admitted and started on Foscarnet with subsequent improvement. His MMF was stopped. After 2 weeks, his CMV improved to 40,000 IU/ml, log 4.7. He asks you if he can be discharged home and switch to an oral medication.

What do you advise?

CMV Case 3 Cont'd. . .

Can transition from IV foscarnet to maribavir.

His CMV viral load ultimately became undetectable on maribavir. He asks you if he needs to take a medication to prevent another CMV infection.

What do you advise?

Overall Net State of Immunosuppression

IS regimen

Rejection

Neutropenia, lymphopenia

Hypogammaglobulinemia

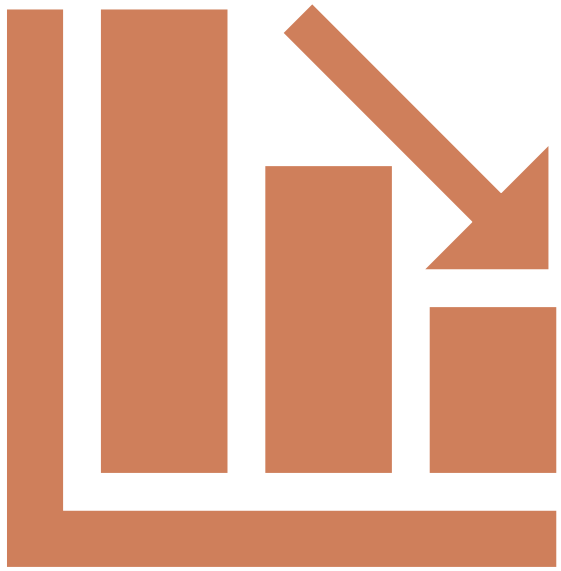
Technical complications

Underlying immune defects

Chronic co-morbidities

Acute illness

Co-infections



Who benefits form secondary prophylaxis?

- Limited data. Can consider if:
  - Recurrent CMV infection
  - Recent IS augmentation especially lymphodepleting agents
  - Low absolute lymphocyte count (ALC)
  - High viral load at presentation, especially if CMV D+/R-

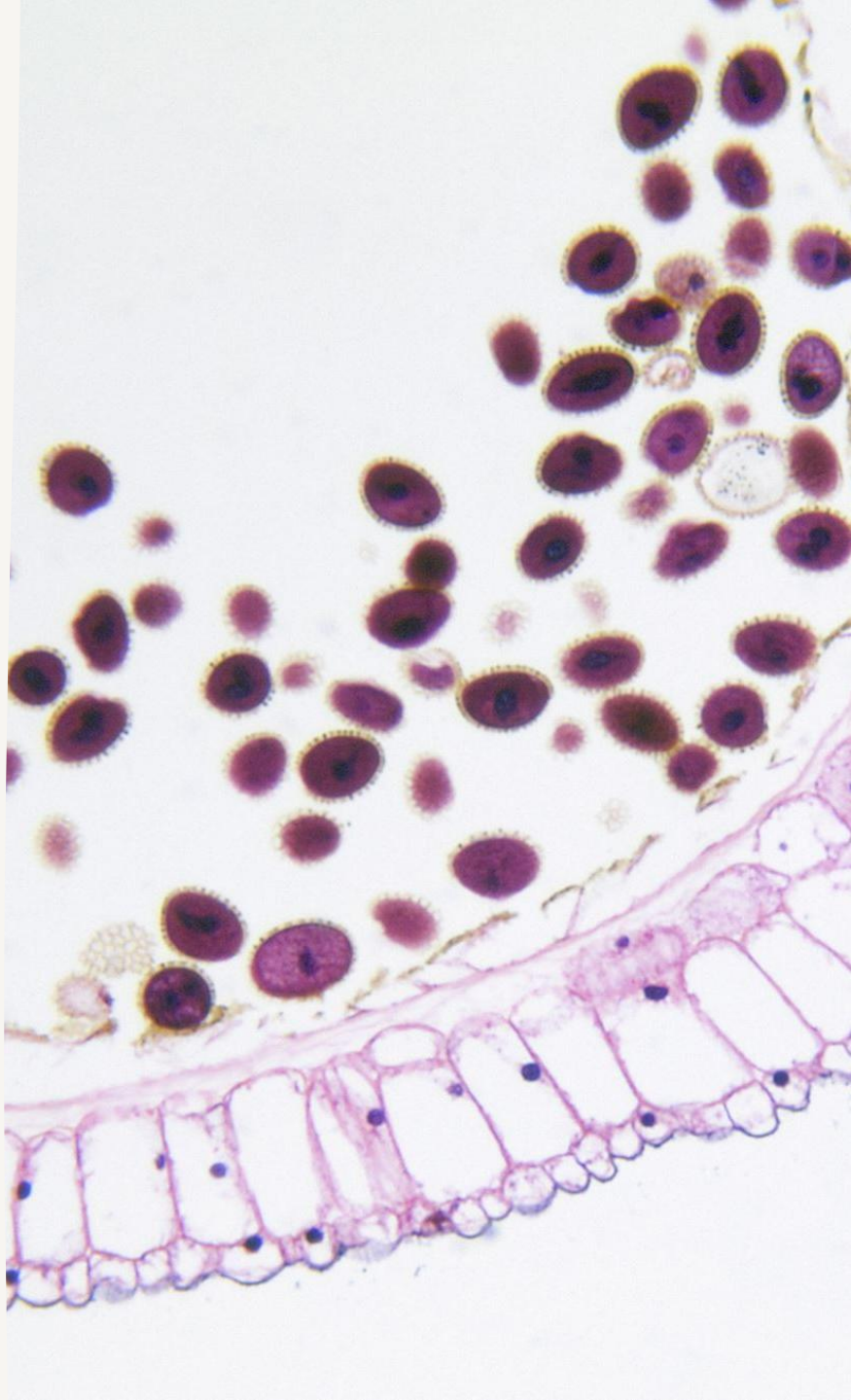
- Secondary prophylaxis prevents CMV infection but does not reduce the overall rate of recurrences after prophylaxis discontinuation. There has been no RCTs studying this. Optimal duration is unknown.

CMV Treatment Options

Medication	Indication	Adverse Effects
Valganciclovir (PO)	• Preferred due to PO formulation • Limited PK data to confirm adequate bioavailability in GI disease	• Myelosuppression
Ganciclovir (IV)	• First-line for life-threatening or sight-threatening disease • May be preferred in very high levels of DNAemia	• Myelosuppression
Foscarnet (IV)	• Second-line • Intolerance with first-line agents • Refractory or resistant CMV • May be preferred in very high levels of DNAemia	• Nephrotoxicity • Electrolyte derangements • Headache • Fever • GI intolerance
Maribavir (PO)	• Second-line • Refractory or resistant CMV • Intolerance with first-line agents • AVOID in severe infection • High cost	• Dysgeusia • GI intolerance

Maribavir

- Maribavir does not cross the blood brain barrier. Patients with CMV retinitis and meningitis were excluded from the trial.
- What about maribavir resistance?
    - RCT done on HCT showed after at least 21 days of maribavir exposure 10% developed maribavir resistance with median of 56 days after starting treatment.
        - Higher incidence of resistance if baseline CMV >9100 IU/ml than with loads <9100 IU/ml.
    - Viral rebound during maribavir therapy high suspicion of drug resistance
    - Very high viral load alternative therapy preferred.



Avery R. *Clin Infect Dis.* 75(4) 2021: 690-701
Chou S. *J Infect Dis*. 231(3). 2025:e470-477

When to send resistance testing?

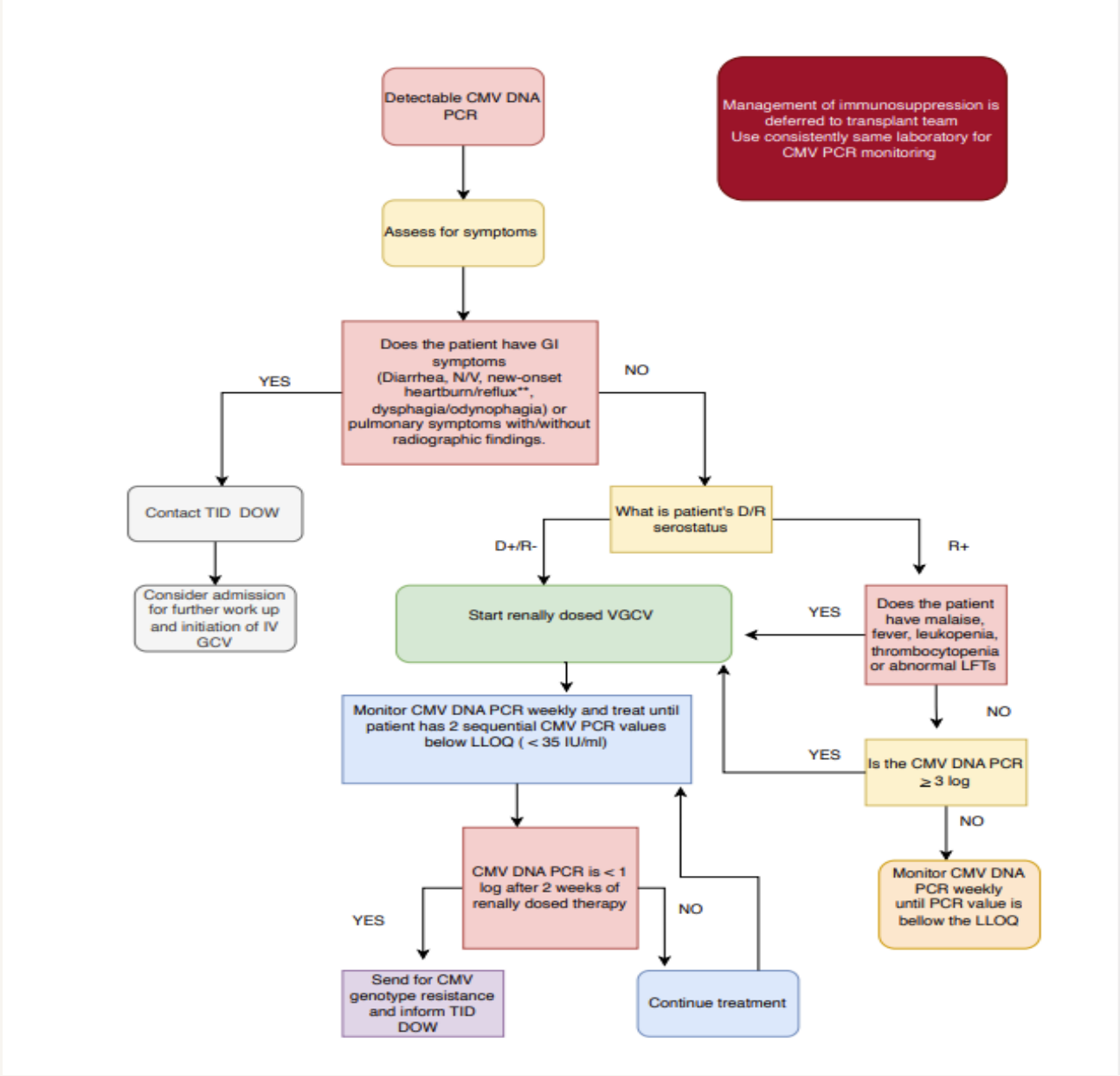
- Refractory disease despite appropriately dosed antiviral therapy for at least 2 weeks
- Cumulative antiviral exposure of ≥4 weeks
- Viral load rebound while on therapy

Chou S. Journal of Inf Dis.231.3 (2025):e470-e477
Fisher CE. Clin Inf Dis. 65.1 (2017):57-63
Kotton C. Transplantation 109 (2025): 1066-1110

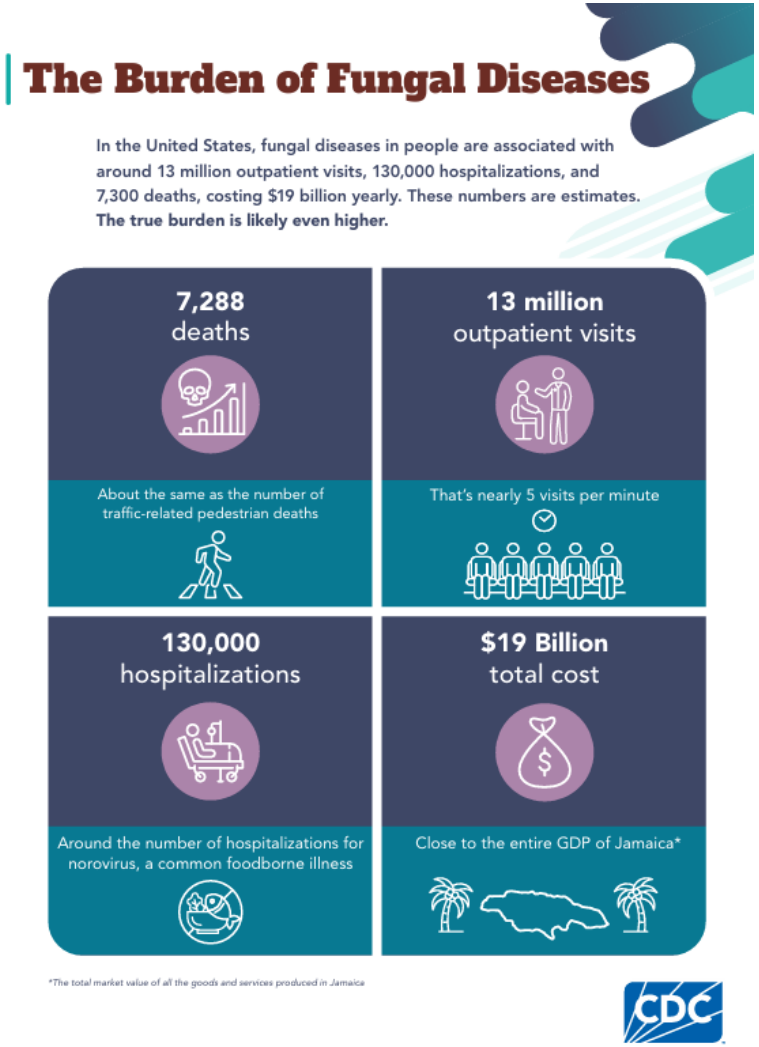
CMV Prophylaxis Options

Medication	Indication	Adverse Effects
Valganciclovir (PO)	• First-line prophylaxis	• Myelosuppression
Letermovir (PO)	• Second-line prophylaxis if resistant or intolerance to VGCV • Low barrier to resistance • May be cost-prohibitive • More data in BMT and kidney transplant	• GI intolerance

CMV Algorithm Considerations

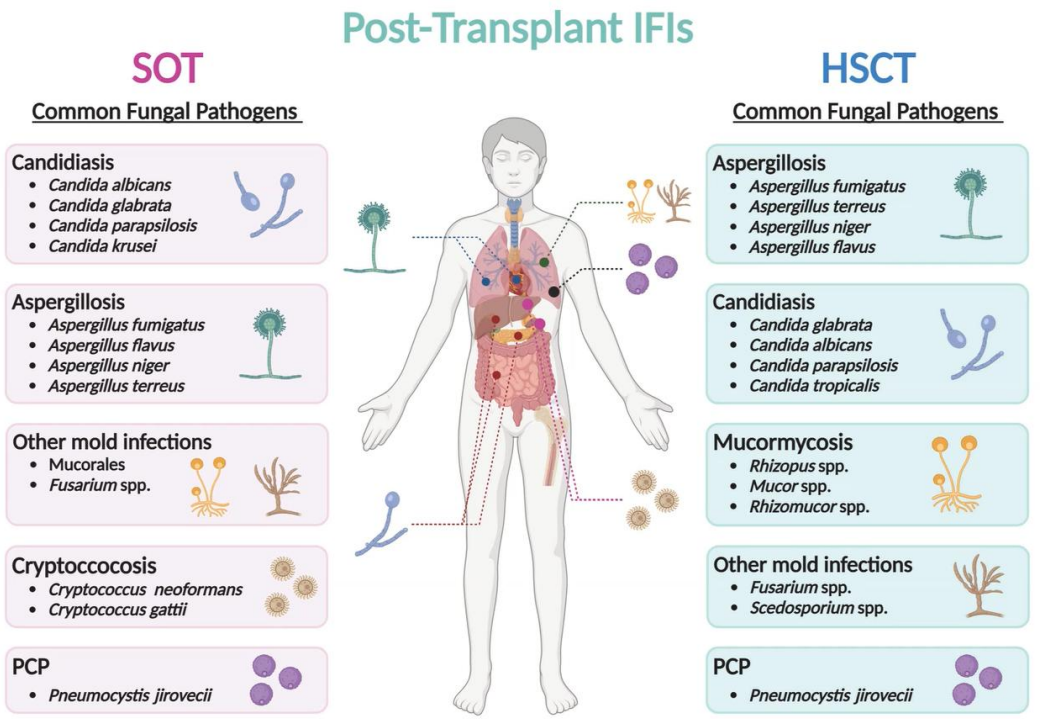



I'M A
FUN
GUY

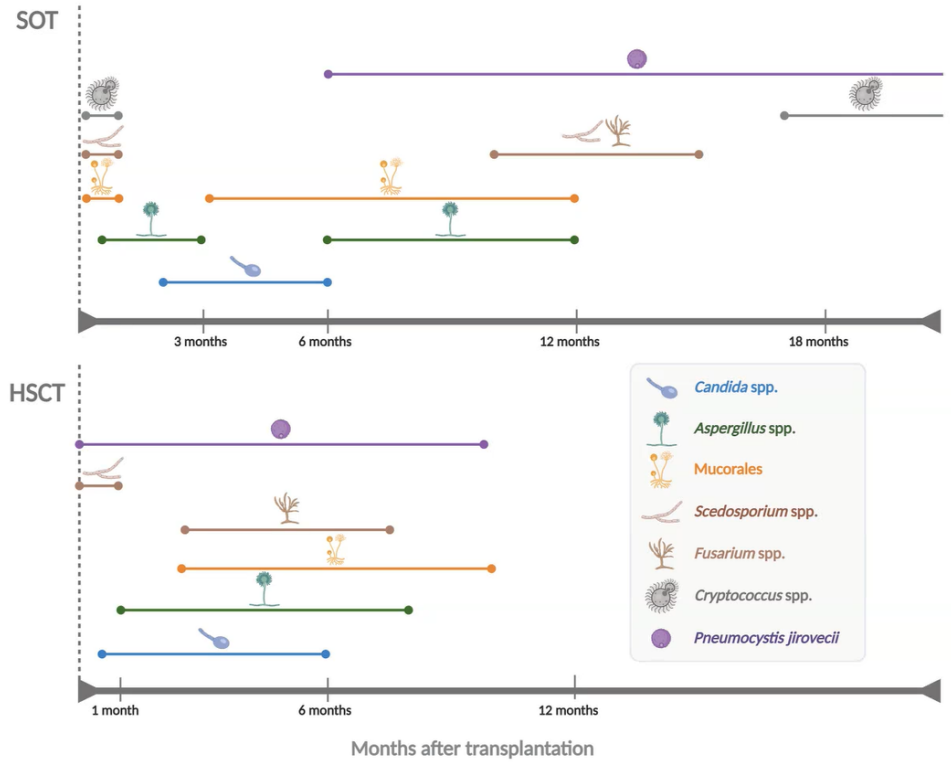


CLOSER LOOK AT THE UNITED STATES

IN TRANSPLANT RECIPIENTS



Biomed J. 2024 Jun;47(3):1(



Biomed J. 2024 Jun;47(3):100719.

FUNGI UNFILTERED

- The world of antifungals
  - Understand the spectrum of activity of different antifungals and their side effects
- Cocci – How to prevent an unwanted guest
  - Recognize criteria to screen recipients in the pre and posttransplant setting
- To screen or not to screen ?
  - Discuss guidelines for fungal (crypto and histo) pre transplant screening

THE WORLD OF ANTIFUNGALS

Where do antifungals hit the fungus?

A cellular map of the major drug classes and their principal molecular targets

ECHINOCANDINS

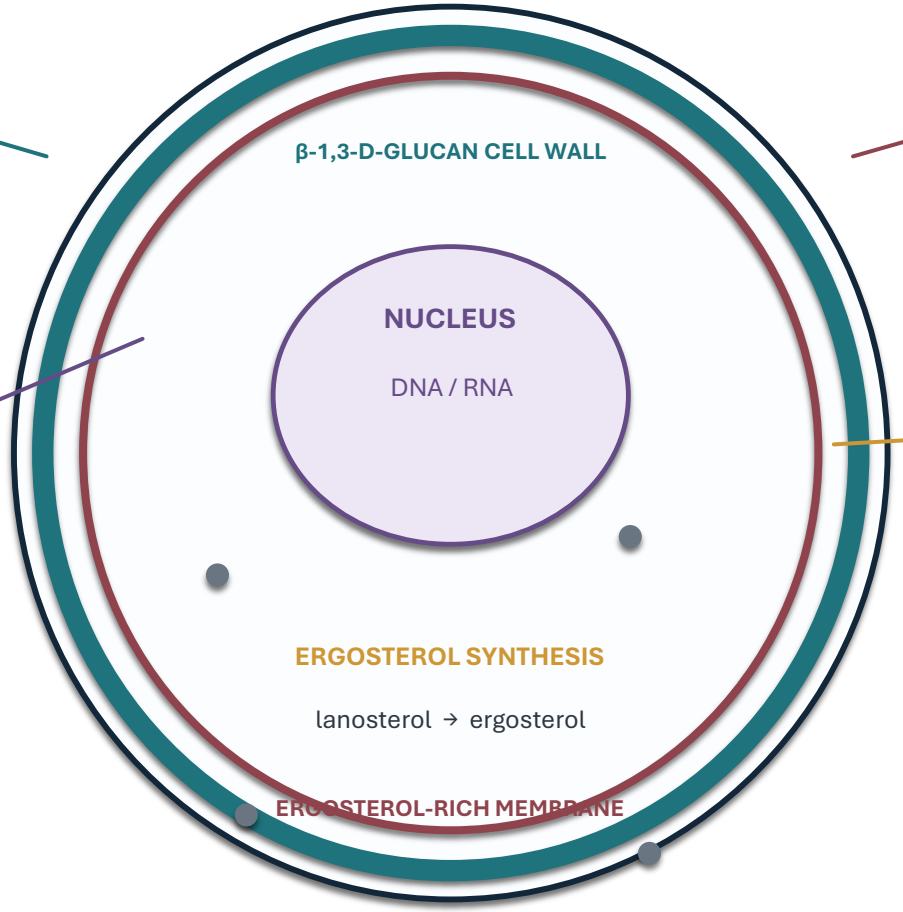
Caspofungin • Micafungin • Anidulafungin

β-1,3-D-glucan synthase → cell wall

FLUCYTOSINE

5-Flucytosine

→ 5-FU metabolites → DNA/RNA synthesis



POLYENES

Amphotericin B • Nystatin

Bind ergosterol → membrane disruption

AZOLES

Fluconazole • Itraconazole • Voriconazole
Posaconazole • Isavuconazole
Inhibit CYP51/lanosterol 14α-demethylase

Spectrum of activity

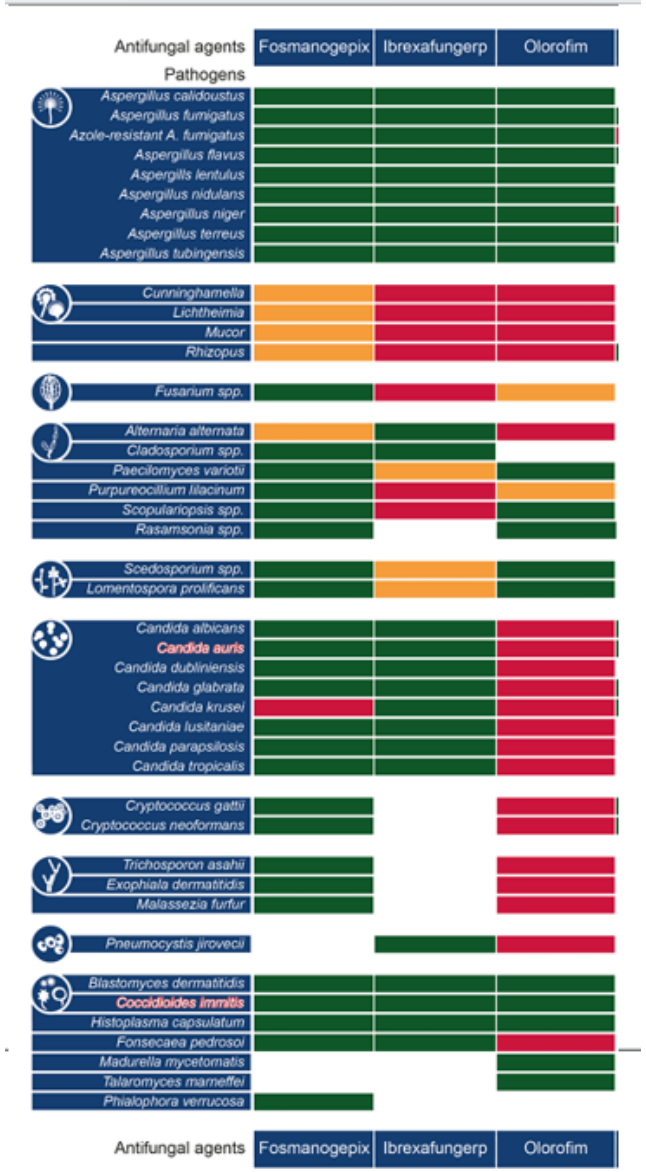
Antifungal	Candida albicans	Candida non-albicans*	Aspergillus	Mucorales	Cryptococcus	Dimorphic fungi**
Fluconazole	✓	±	✗	✗	✓	±
Itraconazole	✓	±	✓	✗	✓	✓
Voriconazole	✓	✓	✓	✗	✓	✓
Posaconazole	✓	✓	✓	✓	✓	✓
Isavuconazole	✓	✓	✓	✓	✓	✓
Micafungin	✓	✓	±	✗	✗	✗
Amphotericin B (liposomal)	✓	✓	✓	✓	✓	✓

Main side effects and monitoring

Antifungal	Main side effects	Recommended monitoring
Fluconazole	Hepatotoxicity, QT prolongation, GI upset	Liver function tests; ECG if risk factors
Itraconazole	Hepatotoxicity, negative inotropic effect (heart failure), GI upset	Liver function tests; avoid in decompensated heart failure; trough level
Voriconazole	Hepatotoxicity, transient visual disturbances, photosensitivity (long-term skin cancer risk), hallucinations, QT prolongation	Liver function tests; trough level; skin exam with prolonged use; ECG
Posaconazole	Hepatotoxicity, QT prolongation, GI upset	Liver function tests; trough level; ECG
Isavuconazole	Hepatotoxicity, QT shortening (opposite of other azoles)	Liver function tests
Micafungin	Generally well tolerated; rare hepatotoxicity; infusion-related reactions	Liver function tests
Amphotericin B (liposomal)	Nephrotoxicity, infusion-related reactions (fever, chills), hypokalemia, hypomagnesemia	Renal function; electrolytes (K^+, Mg^{2+}); CBC

Drug interactions

Antifungal	Main interactions
Fluconazole	Moderate CYP2C9/3A4 inhibitor — warfarin, phenytoin, sulfonylureas
Itraconazole	Strong CYP3A4 inhibitor — statins, immunosuppressants (tacrolimus, cyclosporine); absorption reduced by PPIs/H2 blockers; avoid ergot derivatives
Voriconazole	Strong CYP2C19/2C9/3A4 inhibitor — contraindicated with rifampin, rifabutin, carbamazepine, sirolimus, ergot derivatives; adjust tacrolimus/cyclosporine
Posaconazole	Strong CYP3A4 inhibitor — reduce tacrolimus/cyclosporine/sirolimus dose, vincristine; avoid rifabutin and phenytoin
Isavuconazole	Moderate CYP3A4 inhibitor — fewer interactions than other azoles; monitor immunosuppressants; contraindicated with strong CYP3A4 inducers/inhibitors
Micafungin	Few clinically significant interactions — mild increase in sirolimus and nifedipine concentrations
Amphotericin B (liposomal)	Synergistic nephrotoxicity (aminoglycosides, cyclosporine, cisplatin); loop diuretics → hypokalemia → risk of digoxin toxicity


Antifungal agents
Fosmanogepix
Ibrexafungerp
Olorofim
Pathogens
Aspergillus calidoustus
Aspergillus fumigatus
Azole-resistant A. fumigatus
Aspergillus flavus
Aspergillus lentulus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Mucor
Rhizopus
Fusarium spp.
Alternaria alternata
Cladosporium spp.
Paecilomyces variotii
Purpureocillium lilacinum
Scopulariopsis spp.
Rasamsonia spp.
Scedosporium spp.
Lomentospora prolificans
Candida albicans
Candida auris
Candida dubliniensis
Candida glabrata
Candida krusei
Candida lusitaniae
Candida parapsilosis
Candida tropicalis
Cryptococcus gattii
Cryptococcus neoformans
Trichosporon asahii
Exophiala dermatitidis
Malassezia furfur
Pneumocystis jirovecii
Blastomyces dermatitidis
Coccidioides immitis
Histoplasma capsulatum
Fonsecaea pedrosoi
Madurella mycetomatis
Talaromyces marneffei
Phialophora verrucosa
Antifungal agents
Fosmanogepix
Ibrexafungerp
Olorofim

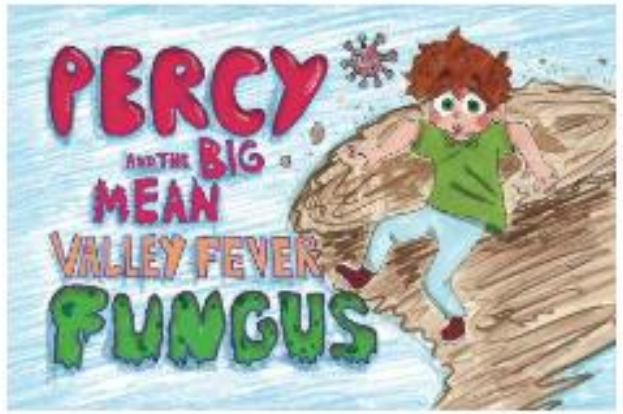
COCCI – HOW TO PREVENT AN UNWANTED GUEST

Percy and The Big Mean Valley Fever Fungus

by Raegina Rico (Author), Mia Beedon (Illustrator), Taylor Rico-Pekerol (Editor) | Format: Kindle Edition

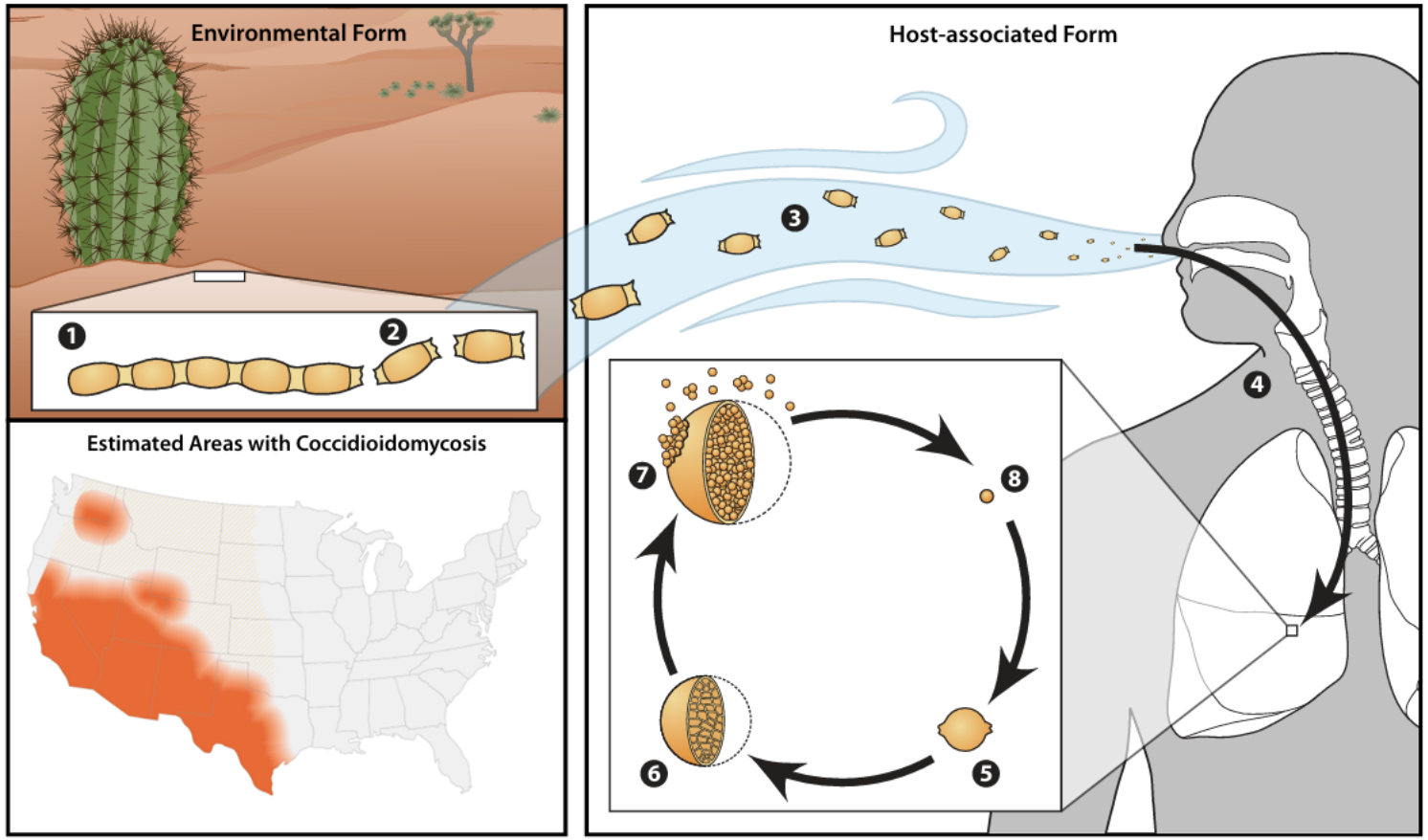
5.0 ★★★★★ (1)

"Percy and The Big Mean Valley Fever Fungus" is a story of a young boy named Percy and his curiosity about a disease called Valley Fever. With help from his mother, Percy learns what it is, how to prevent himself from getting sick, and ways to play outside safely.



Read sample

Let’s talk more about coccidioidomycosis



Coccidioides immitis / C. posadasii

A thermally dimorphic, soil-dwelling fungus — mold in the environment, spherule form in tissue.

Endemic regions

Arid Southwestern U.S. (California's San Joaquin Valley, Arizona, New Mexico, west Texas), plus Mexico and parts of Central and South America.

Why do we worry about it in transplant patients?

Immunosuppression converts a usually self-limited respiratory illness into a disease with high rates of dissemination and death.

INFECTION IN THE TRANSPLANT RECIPIENT

Environmental (de novo)

Inhalation of airborne conidia from disturbed soil — construction, dust storms, gardening, farming — while immunosuppressed.

Reactivation

The recipient's own remote, often clinically silent, prior infection reactivates once T-cell immunity is suppressed — the most common mechanism, even decades after exposure.

Donor-derived

Rare but often fulminant: transmitted via the allograft from a donor with unrecognized active or latent infection. Lung allografts carry the highest reported risk.

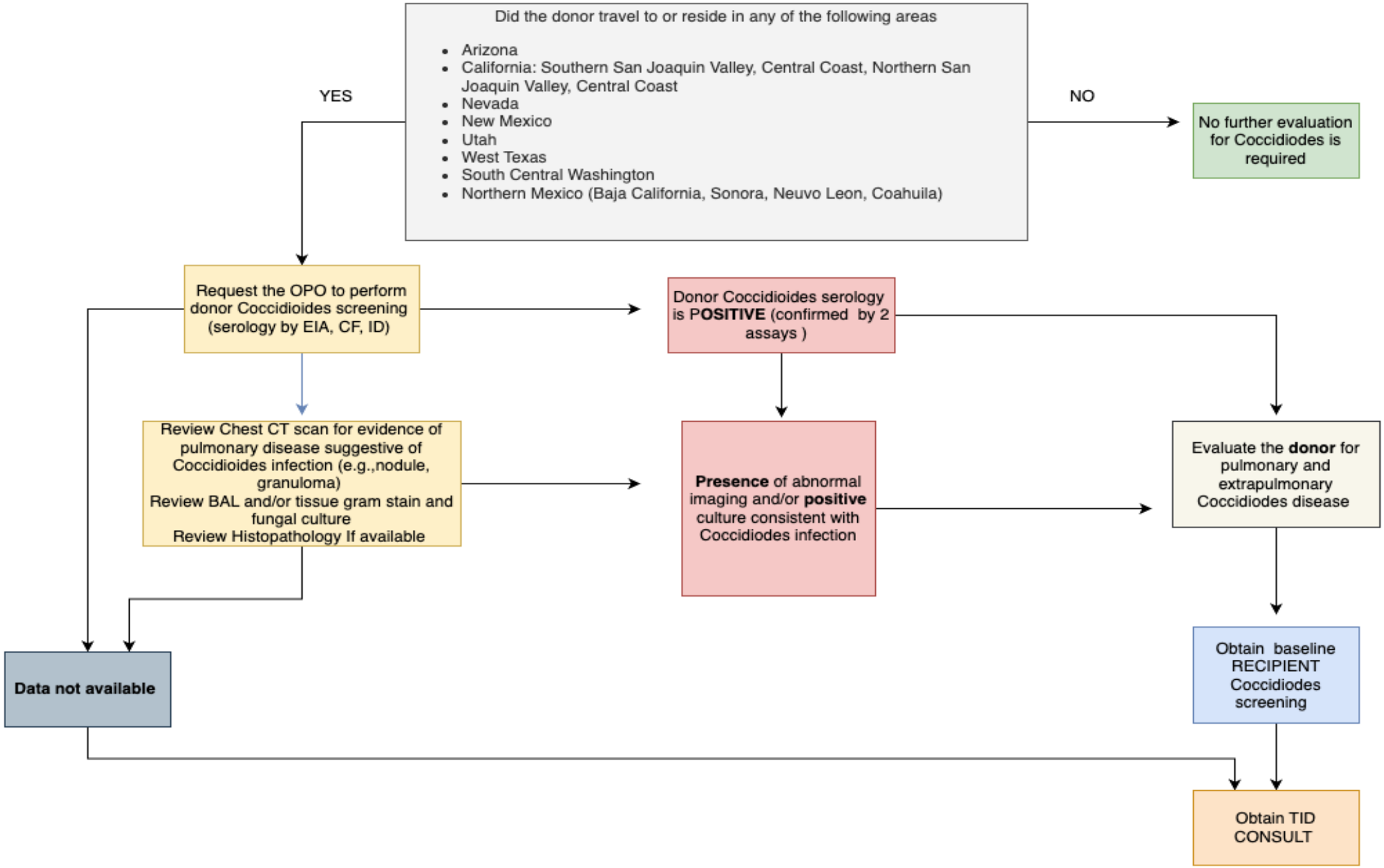
AST IDCOP GUIDANCE

Transplant candidate – Screening before transplant

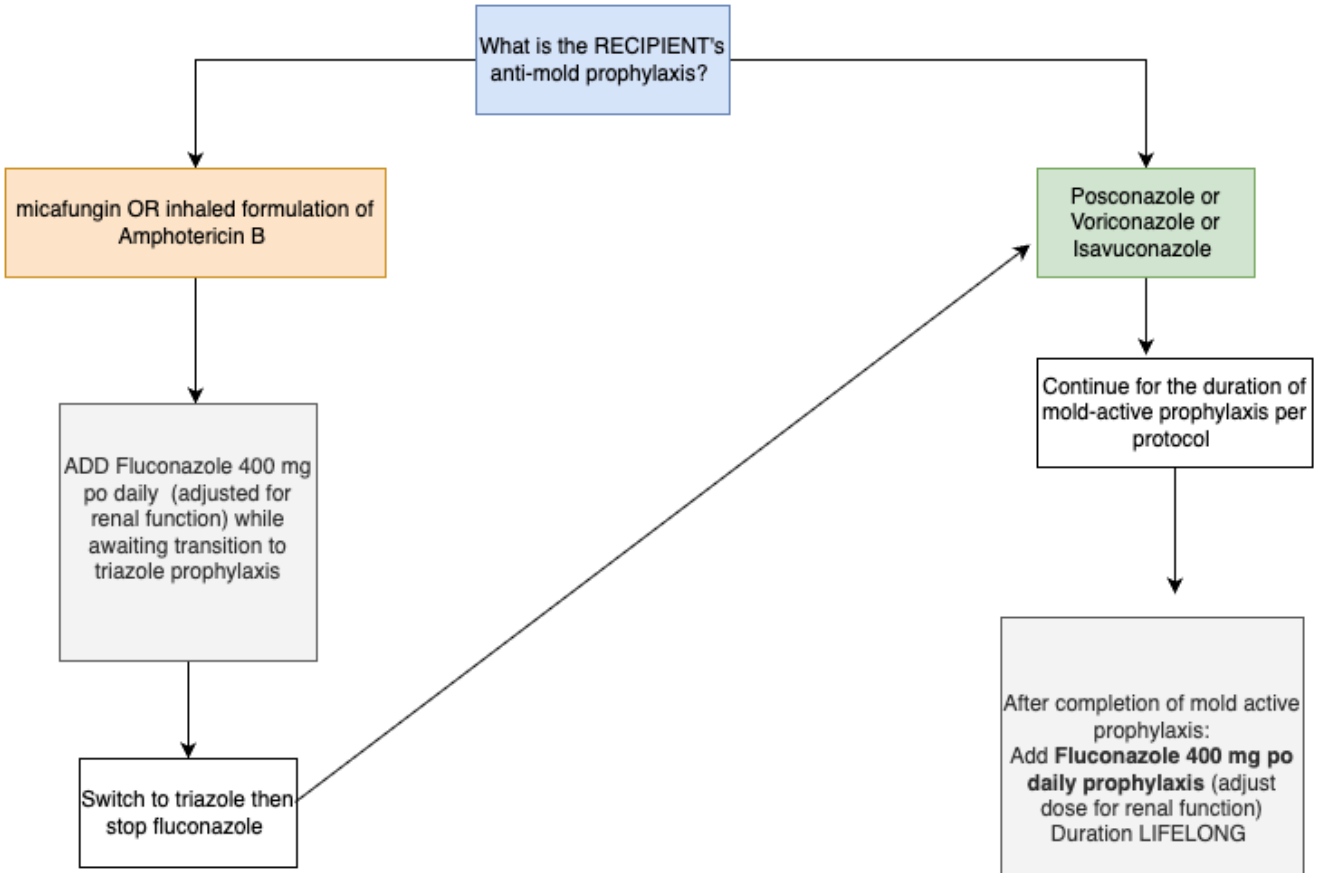
- Assess every candidate for residence in or travel to an endemic region.
- If exposure history is positive: symptom review, chest X-ray, and serology (EIA, immunodiffusion, complement fixation).
- Active infection is a contraindication to transplant until clinical, radiographic, and microbiologic resolution.
- Prior disease and/or seropositivity may prompt lifelong azole prophylaxis after transplant.

Organ donor – Preventing DDI

- Review donor residence, travel, and exposure history to an endemic area.
- Targeted serologic screening for donors from, or who have lived in, endemic regions.
- Active coccidioidomycosis in the donor is a contraindication to donation of the affected organ(s).
- Any donor risk factors identified should be communicated to the recipient team to guide preemptive therapy.


Did the donor travel to or reside in any of the following areas
Arizona
California: Southern San Joaquin Valley, Central Coast, Northern San Joaquin Valley, Central Coast
Nevada
New Mexico
Utah
West Texas
South Central Washington
Northern Mexico (Baja California, Sonora, Neuvo Leon, Coahuila)
YES
NO
No further evaluation for Coccidiodes is required
Request the OPO to perform donor Coccidioides screening (serology by EIA, CF, ID)
Donor Coccidioides serology is POSITIVE (confirmed by 2 assays)
Review Chest CT scan for evidence of pulmonary disease suggestive of Coccidioides infection (e.g.,nodule, granuloma)
Review BAL and/or tissue gram stain and fungal culture
Review Histopathology If available
Presence of abnormal imaging and/or positive culture consistent with Coccidiodes infection
Evaluate the donor for pulmonary and extrapulmonary Coccidiodes disease
Data not available
Obtain baseline RECIPIENT Coccidiodes screening
Obtain TID CONSULT

Prophylaxis choice for Prevention of Donor Transmission of Coccidiodes to The Recipient



In instances where antifungal prophylaxis is withdrawn, serological monitoring should be performed every 2–3 months in the first 6–12 months, and every 6–12 months thereafter.

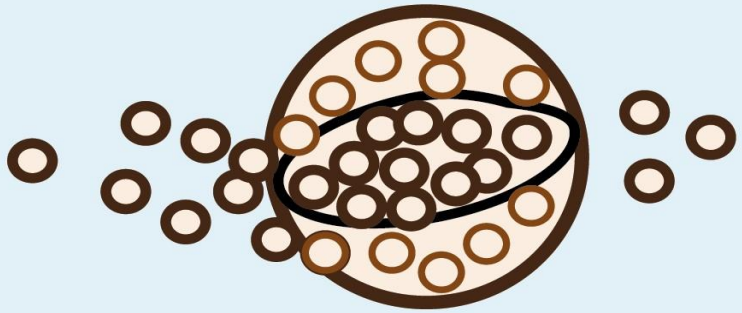
Universal lifelong fungal prophylaxis and risk of coccidioidomycosis in lung transplant recipients living in an endemic area

Retrospective cohort study, lung transplant recipients in the Southwestern U.S. followed over a 6-year period

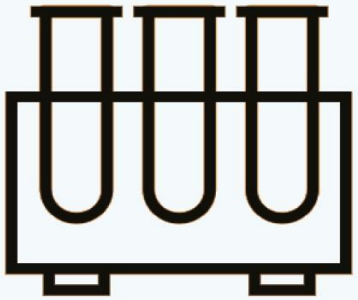
493

Lung transplant recipients receiving universal lifelong azole antifungal prophylaxis

Proven/Probable *Coccidioides* Infection



New Asymptomatic Seropositivity



	Proven/Probable *Coccidioides* Infection	New Asymptomatic Seropositivity
Incidence (median follow-up = 31 mo)	**0.2%** (1/493)	**0.2%** (1/493)

Lifelong azole antifungal prophylaxis was effective for the prevention of coccidioidomycosis

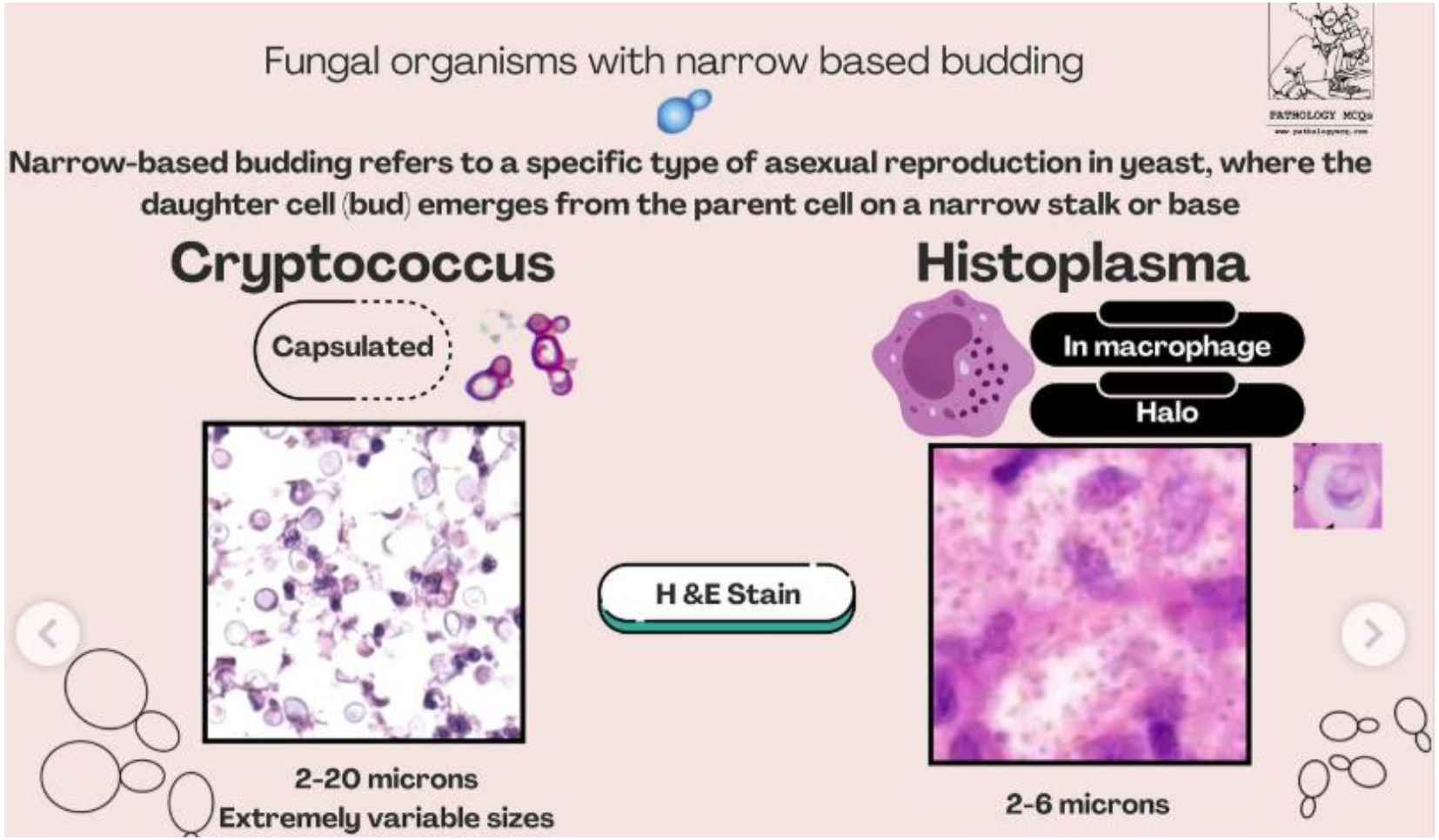
Truong CN, Nailor MD, Walia R, Cherrier L, Nasar A, Goodlet KJ. Universal lifelong fungal prophylaxis and risk of coccidioidomycosis in lung transplant recipients living in an endemic area. *Clinical Infectious Diseases* 2021.

Clin Infect Dis, Volume 74, Issue 11, 1 June 2022, Pages 1966–1971, https://doi.org/10.1093/cid/ciab752

TO SCREEN OR NOT TO SCREEN ?

HOW CAN WE TRULY ANSWER THE QUESTION?

TWO FUNGAL ENTITIES



THE VALUE OF CRYPTOCOCCAL ANTIGEN SCREENING PRIOR TO LIVER TRANSPLANT: EXPERIENCE FROM A TERTIARY ACADEMIC CENTER

Justin Hofmann MD, Maricar Malinis MD, Anthony Dreher MPA and Sara Haddad MD

Vanderbilt University Medical Center

Division of Infectious Diseases

1 in **270**

Solid Organ Transplant Recipients

**liver uniquely at risk*

(2) Marinelli T et al. Transpl Inf Dis. PMID 31785187
(3) Sun HY et al. CID. PMID 20879857
(4) Singh N & Sun HY. Liver Transpl. PMID 18756456

(1) Malinis M & Boucher HW. Clin Transplant. PMID 30900327

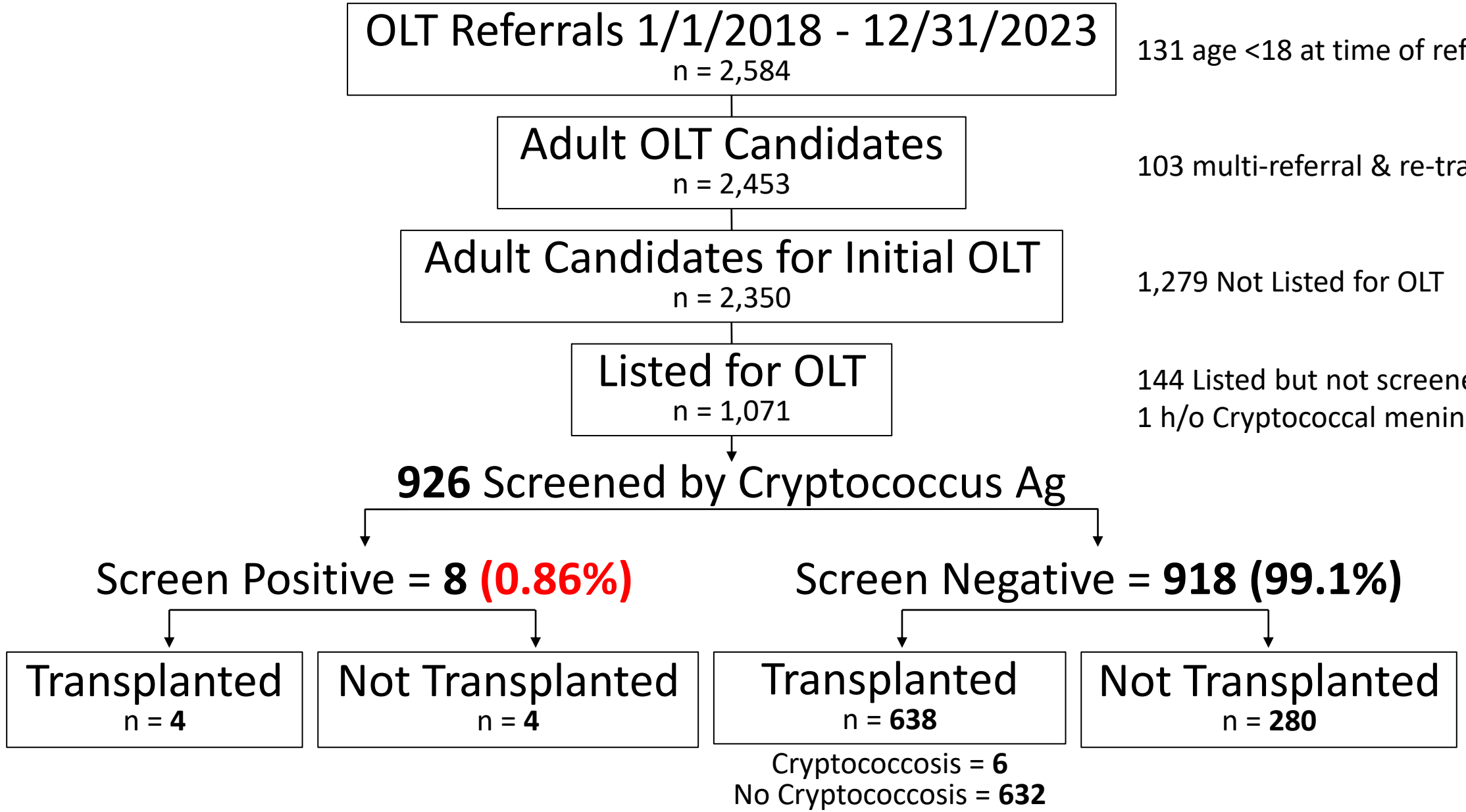
Methods

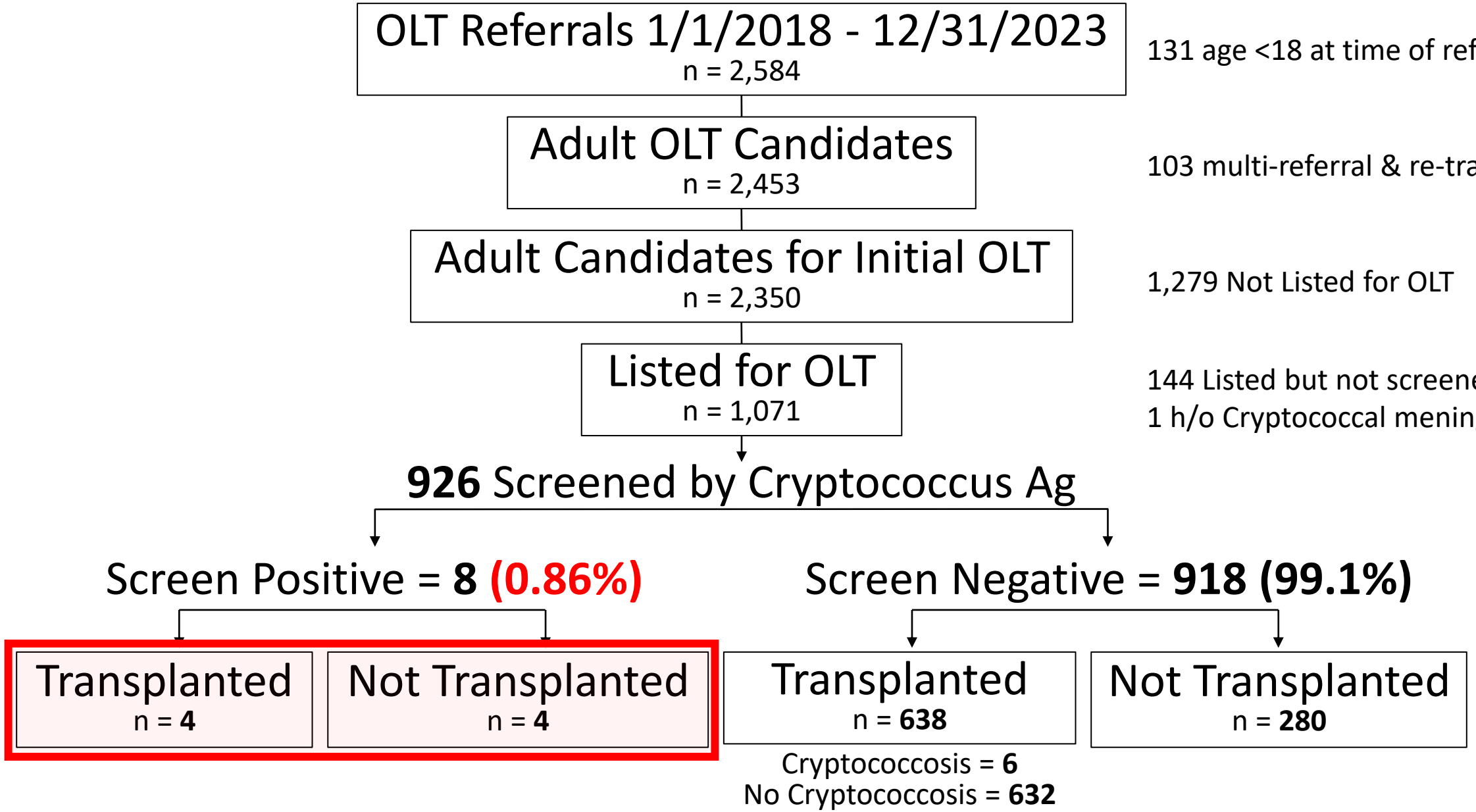
- Retrospective, non-interventional chart review study

Inclusion:
- All Liver Transplant Referrals 1/1/2018 – 12/31/2023

Exclusion:
- Age <18
- Known cryptococcosis
- Re-transplant
- Duplicate referrals → index listing

- *Cryptococcus* testing results
- If screen-positive: patient characteristics, transplant details, labs & imaging results reviewed in-depth


OLT Referrals 1/1/2018 - 12/31/2023
n = 2,584
131 age <18 at time of referral
Adult OLT Candidates
n = 2,453
103 multi-referral & re-transplant
Adult Candidates for Initial OLT
n = 2,350
1,279 Not Listed for OLT
Listed for OLT
n = 1,071
144 Listed but not screened
1 h/o Cryptococcal meningitis
926 Screened by Cryptococcus Ag
Screen Positive = 8 (0.86%)
Screen Negative = 918 (99.1%)
Transplanted
n = 4
Not Transplanted
n = 4
Transplanted
n = 638
Cryptococcosis = 6
No Cryptococcosis = 632
Not Transplanted
n = 280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Not Transplanted
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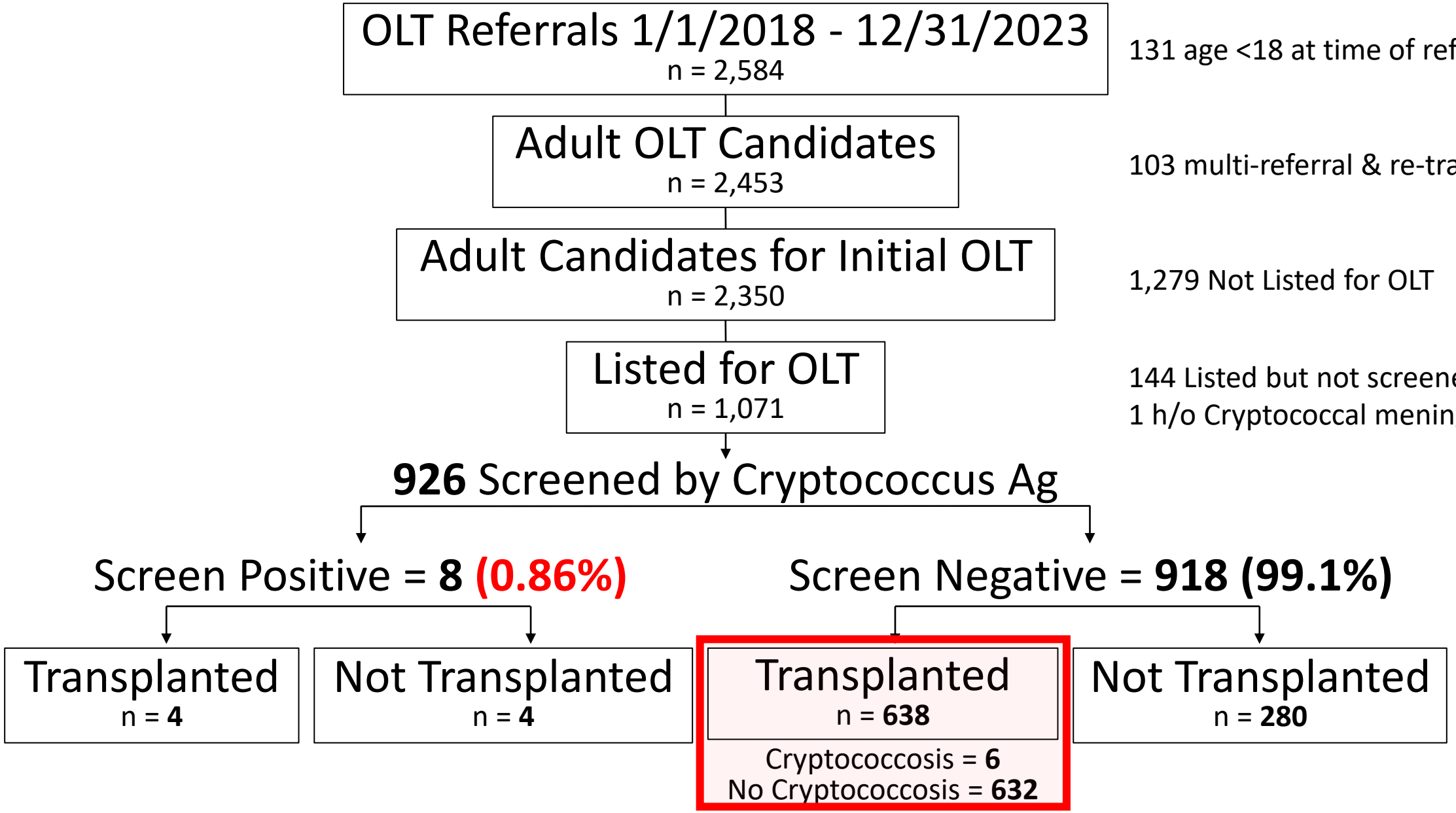
Cryptococcosis = 6
No Cryptococcosis = 632

CrAg-Screen **POSITIVE** patients

Patient	68 y/o F	64 y/o F	70 y/o M	67 y/o M	59 y/o F	68 y/o M	61 y/o F	71 y/o F
Dx, MELD	MASH, 15	EtOH, 21	EtOH, 22	Idiopathic, 21	MASH, 25	EtOH, 43	Idiopathic, 18	MASH, 16
CrAg	<1:5	<1:5	<1:5	1:5	1:10 (1:5 repeat)	1:20	1:40	1:640
Exposures	Bird feeders	-	Kept ducks	-	-	Lives on farm, kept ducks	Kept chickens	Kept chickens
CT	Chest CT: No focal abnormality	Chest CT: R effusion w/atelectasis & groundglass. Unchanged LNs, some calcified	Cardiac CT: Large R effusion w/atelectasis, No nodules	Chest CT: RLL atelectasis w/small effusion. No consolidation. No nodules. Multiple calcified LNs	Cardiac CT: patchy nonspecific GGO in LLL, suspect edema	Chest CT: **multiple** 5-8mm LUL **nodules** new since '15	Chest CT: **LLL nodular consolidation** w/possible cavitation c/w infection	Cardiac CT: **Extensive solid** and ground glass **opacities** in the LUL & LLL w/moderate L effusion
Symptoms	Cough	-	-	-	-	-	DOE, HA	-
Treatment	399d Fluc	1,000d Fluc	524d Fluc	332d Fluc	189d Fluc	104d Fluc	350d Fluc	on Fluc 1,216d
Outcome	OLT Alive & well	OLT, **Died** +1331d of MI	OLT Alive & well	**Died** +388d of CLD	**Died** +522d of CLD	**Died** +169d of CLD	Recovered, de-listed	OLT Alive & well


OLT Referrals 1/1/2018 - 12/31/2023
n = 2,584
131 age <18 at time of referral
Adult OLT Candidates
n = 2,453
103 multi-referral & re-transplant
Adult Candidates for Initial OLT
n = 2,350
1,279 Not Listed for OLT
Listed for OLT
n = 1,071
144 Listed but not screened
1 h/o Cryptococcal meningitis
926 Screened by Cryptococcus Ag
Screen Positive = 8 (0.86%)
Screen Negative = 918 (99.1%)
Transplanted
n = 4
Not Transplanted
n = 4
Transplanted
n = 638
Cryptococcosis = 6
No Cryptococcosis = 632
Not Transplanted
n = 280

CrAg-Screen **Negative** patients who were **transplanted** and later developed **infection**

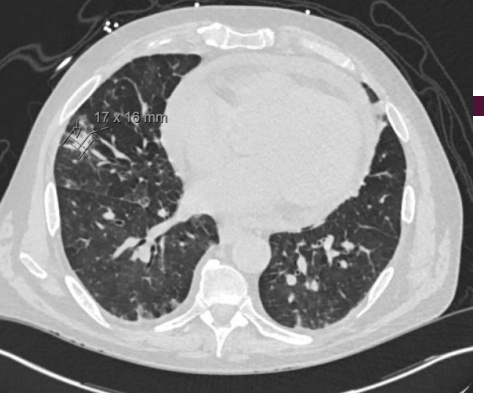
Patient	67 y/o M	70 y/o F	47 y/o M	54 y/o F	70 y/o F	69 y/o M
Dx, MELD	MASH, 35	MASH, 18	PSC, 21	PSC, 30	PSC, 27	HCV/HCC, 12
CrAg, (OLT→illness)	1:640 (+78)	1:20 (+199)	1:20 (+641)	1:80 (+826)	1:5 (+908)	1:640 (+1071)
Exposures	Lives on **farm**	-	-	"birds where she lives"	Lives on **farm**	-
IS @ dx	TAC/MMF/P10	TAC	TAC	TAC/MMF	TAC	TAC/AZA
Symptoms @ dx	Fever, AMS	Dyspnea, CP, Resp failure	Fever, cough, night sweats	Dyspnea	None, nodule on CT	Dyspnea, cough
CT @ screen	no PE, no inflammatory changes	multiple nodules, unchanged from '21	-	-	-	UIP, mediastinal LAD. No nodules.
Treatment	14d AmB+5FC, on fluc 2,900d	154d Fluc	on Fluc 620d	30d Fluc/Isavu up to death	180d Fluc	AmB+5FC up to death
Outcome	Meningitis Alive & Well	Alive & Well	Alive & Well	**Died** malignancy OLT +856	Alive & Well	BAL w/Crypto. **Died** OLT +1120

<1 year from OLT

>1 year from OLT

Conclusions

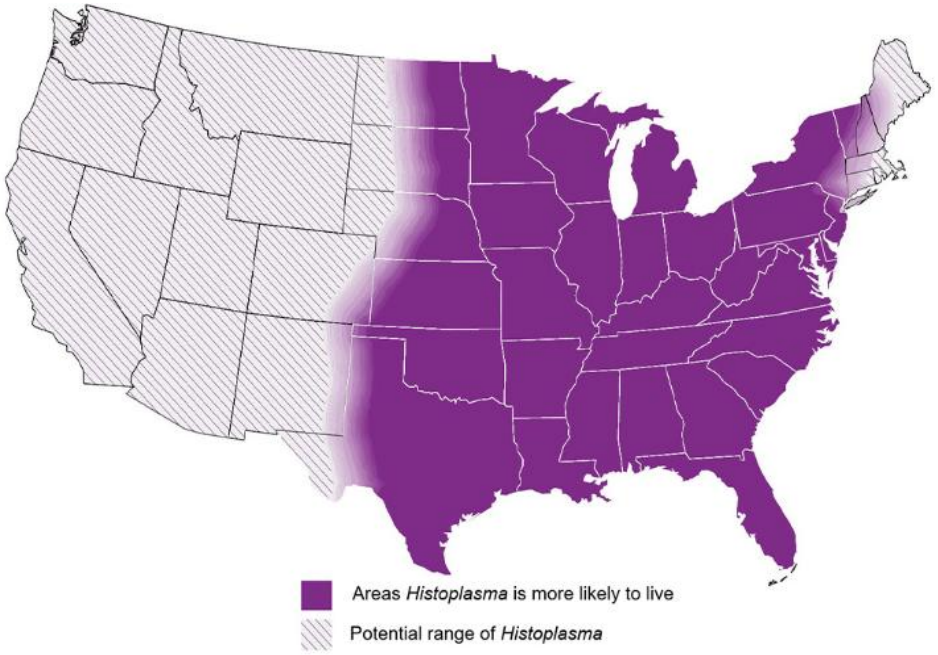
- Incidence of asymptomatic *Cryptococcus* antigenemia is low **(0.86%)**
- Patients with titers >1:5 had **abnormal chest imaging**
- Weakly positive screening (≤1:5) with normal chest imaging given an avg 548 days fluconazole
- Negative screening was **not predictive** of cryptococcosis-free course (+83 and +199d from OLT w/negative pre-OLT screen)



HISTOPLASMOSIS

Manifestations

- Pulmonary
- GI disease
- CNS infection
- Cutaneous
- Infiltrative disease



Endemic to the Ohio and Mississippi River Valleys

Exposure : disrupted soil, farming, caving with bats, chicken coops

AST IDCOP GUIDANCE

Unlike coccidioidomycosis, pretransplant screening for histoplasmosis in endemic areas is not recommended as a routine part of candidate evaluation.

What the candidate work-up should focus on instead

Detailed exposure history

Residence in or extended travel to an endemic area; occupational or recreational exposure to bird or bat droppings (caves, chicken coops, demolition, excavation).

Incidental imaging findings

Calcified pulmonary, hilar, or splenic granulomas are common residua of old infection in endemic areas and are not, by themselves, a contraindication to transplant.

Active disease before transplant

Any candidate with symptomatic or radiographically active histoplasmosis should be treated and show clinical/microbiologic improvement before proceeding to transplant.

Heightened posttransplant awareness

Because pretransplant screening is unreliable, the real safeguard is a high index of suspicion for histoplasmosis in any unexplained fever, pneumonia, or cytopenia after transplant in a patient from an endemic area.

Approach to Diarrhea in SOT

Fionna Feller, MD

VANDERBILT HEALTH

Diarrhea in SOT: Clinical Relevance

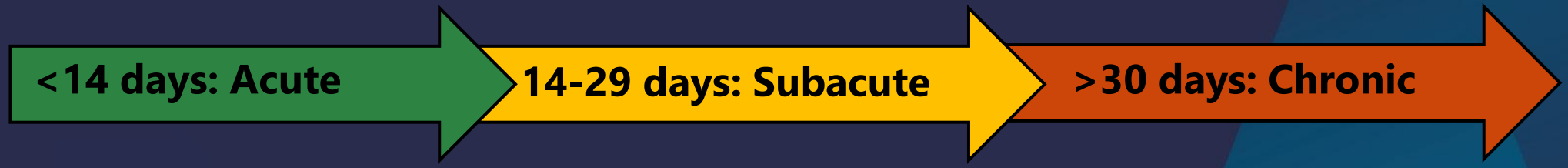
- Diarrhea is common in SOT, with prevalence from 20-50%
- Diarrhea in SOT may result in significant morbidity in SOT, including dehydration, organ dysfunction, medication toxicity, and allograft rejection
- Can lead to poor quality of life, weight loss, and recurrent hospital admissions
- Higher incidence of opportunistic pathogens and risk of developing chronic diarrhea
- Diagnosis is needed for targeted therapy

Learning Objectives

- Identify common causes of infectious and noninfectious causes of diarrhea in transplant recipients.
- Understand the pathogenesis, diagnosis, and management of the most common etiologies of infectious diarrhea including: C. difficile, Norovirus, Cyclospora, and Giardia.
- Develop algorithmic, stepwise approach in diarrhea evaluation.

CLINICAL PRESENTATION OF INFECTIOUS DIARRHEA

- Diarrhea is defined as: Increased frequency of bowel movement (≥3 BM/day) with change in stool consistency (IDSA)
- Possible associated symptoms that could serve as "clues":
  - Fever
  - Abdominal pain
  - Hematochezia: concern for invasive bacterial infection
  - Vomiting: only certain pathogens can cause upper GI symptoms



Causes of Diarrhea in Transplant Patients

Bacterial	Viral	Parasitic
C. difficile *E. coli* *Salmonella* spp. *Campylobacter* spp.	CMV Norovirus Adenovirus Sapovirus Enterovirus	Cyclospora Giardia Cryptosporidium Entamoeba

Medications	Other
IS: Mycophenolate, tacrolimus, cyclosporine, sirolimus Non-IS: Antibiotic, anti-diabetic, anti-arrhythmic. PPI, laxatives	IBD Malabsorption Colon cancer PTLD

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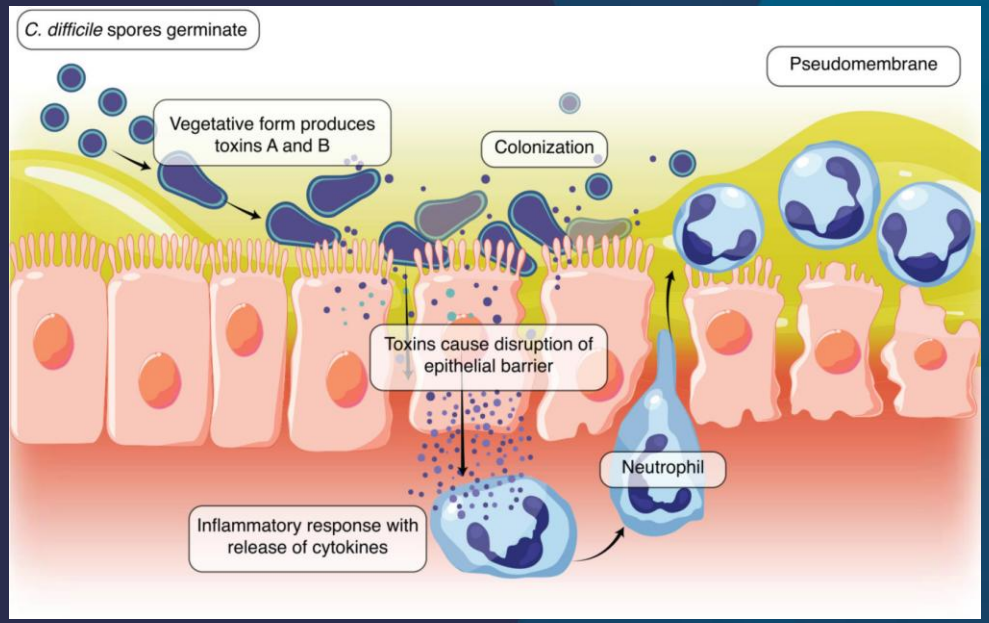
C. DIFFICILE INFECTION (CDI)

- Spore-forming anaerobic bacteria that produces 2 toxins: toxin A and B
- Prevalence in SOT vary between 1-23%, with lowest incidence in kidney transplant, and highest incidence in liver and lung transplants
- Risk factors:
  - Antibiotic exposure
  - Prior CDI
  - Older age >55 years
  - Use of ATG
  - Re-transplantation



Nagesh VK. World J Gastrointest Pharmacol Ther. 2024

CDI TREATMENT

IDSA-SHEA Treatment Recommendations for CDI in Adults

Type of Infection	Preferred Regimen[a]	Alternative Regimen[a]	Additional Recommen-dations	Selected ADRs/ Considerations for Use
Initial episode[b]	Fidaxomicin (standard dosing): 200 mg po bid for 10 days	Vancomycin (standard dosing): 125 mg po qid for 10 days	For nonsevere CDI, metro-nidazole 500 mg po tid for 10-14 days is an alternative if other agents are not available	**Fidaxomicin:** minimal systemic absorption; hypersensitivity potential in patients with macrolide allergy. **Oral vancomycin:** minimal systemic absorption; consider monitoring trough levels owing to potential for systemic absorption and drug accumulation in patients with renal failure, prolonged duration of use (≥10 days), and/or altered integrity of intestinal mucosa. **Metronidazole:** avoid repeated or prolonged courses owing to risk of neurotoxicity; avoid alcohol during treatment and for 3 days after therapy completion

Table 2

Criteria for Determining CDI Severity

Definition	Supportive Data
Nonsevere infection	WBC count ≤15,000 cells/ mL and SCr <1.5 mg/dL
Severe infection	WBC count ≥15,000 cells/ mL or SCr >1.5 mg/dL
Fulminant infection	Hypotension or shock, ileus, or megacolon

CDI: Clostridioides difficile infection; SCr: serum creatinine. Source: References 5, 13.

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RECURRENT CDI TREATMENT

First recurrence	Fidaxomicin (standard dosing): 200 mg po bid for 10 days or Fidaxomicin (extended-pulsed dosing): 200 mg po bid for 5 days, then once every other day for 20 days	Vancomycin (standard dosing): 125 mg po qid for 10 days or Vancomycin (example of tapered and pulsed regimen): 125 mg po qid for 10-14 days, then bid for 7 days, then once daily for 7 days, then q2-3d for 2-8 wk	Adjunctive bezlo-toxumab 10 mg/kg IV given once during antibiotic therapy (in selected patients)[b]	**Bezlotoxumab:** use only in patients with history of CHF when benefit outweighs risk; limited data on its use with fidaxomicin
Second or subsequent recurrence	Fidaxomicin (standard dosing): 200 mg po bid for 10 days or Fidaxomicin (extended-pulsed dosing): 200 mg po bid for 5 days, then once every other day for 20 days or Vancomycin 125 mg po qid for 10 days followed by rifaximin 400 mg po tid for 20 days or Vancomycin (example of tapered and pulsed regimen): 125 mg po qid for 10-14 days, then bid for 7 days, then once daily for 7 days, then q2-3d for 2-8 wk or FMT		Reserve FMT for patients who have received appropriate antibiotic treatment for ≥2 episodes of recurrence (or 3 CDI episodes). Adjunctive bezlo-toxumab 10 mg/kg IV given once during antibiotic therapy (in selected patients)[b]	**Rifaximin:** minimal systemic absorption; concerns about rates of *Clostridioides difficile* resistance. **FMT:** risk for infection

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FULMINANT CDI TREATMENT

Fulminant	Vancomycin 500 mg po or via nasogastric tube qid and metronidazole 500 mg IV q8h. If patient has ileus, consider adding vancomycin rectal enema (created by combining 500 mg of vancomycin with 100 mL of normal saline) given q6h as retention enema	Surgical intervention may be necessary	**Rectal vancomycin:** may be systemically absorbed in the case of inflamed intestinal mucosa

- Bezlotoxumab (monoclonal antibody) discontinued in January 2025
- The benefit of probiotics is unknown. No RCT data

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CDI SECONDARY PROPHYLAXIS

- **No sufficient RCT to evaluate this.**
- Most recent data on secondary prophylaxis was RCT in 2025 with 81 patients who needed antibiotics for non-CDI indication. Recurrent CDI occurred in 43% of participants in vancomycin group vs 57% in placebo group at 8 weeks. However, study was underpowered and did not reach clinical significance.

- Prophylaxis can be considered in those with recent history of CDI who require antibiotic treatment and are at high risk for recurrent infection. Dose is PO vancomycin 125mg once daily.
- Risk factors for recurrent CDI:
- >65 years
- Immunocompromised
- <3 months of severe CDI

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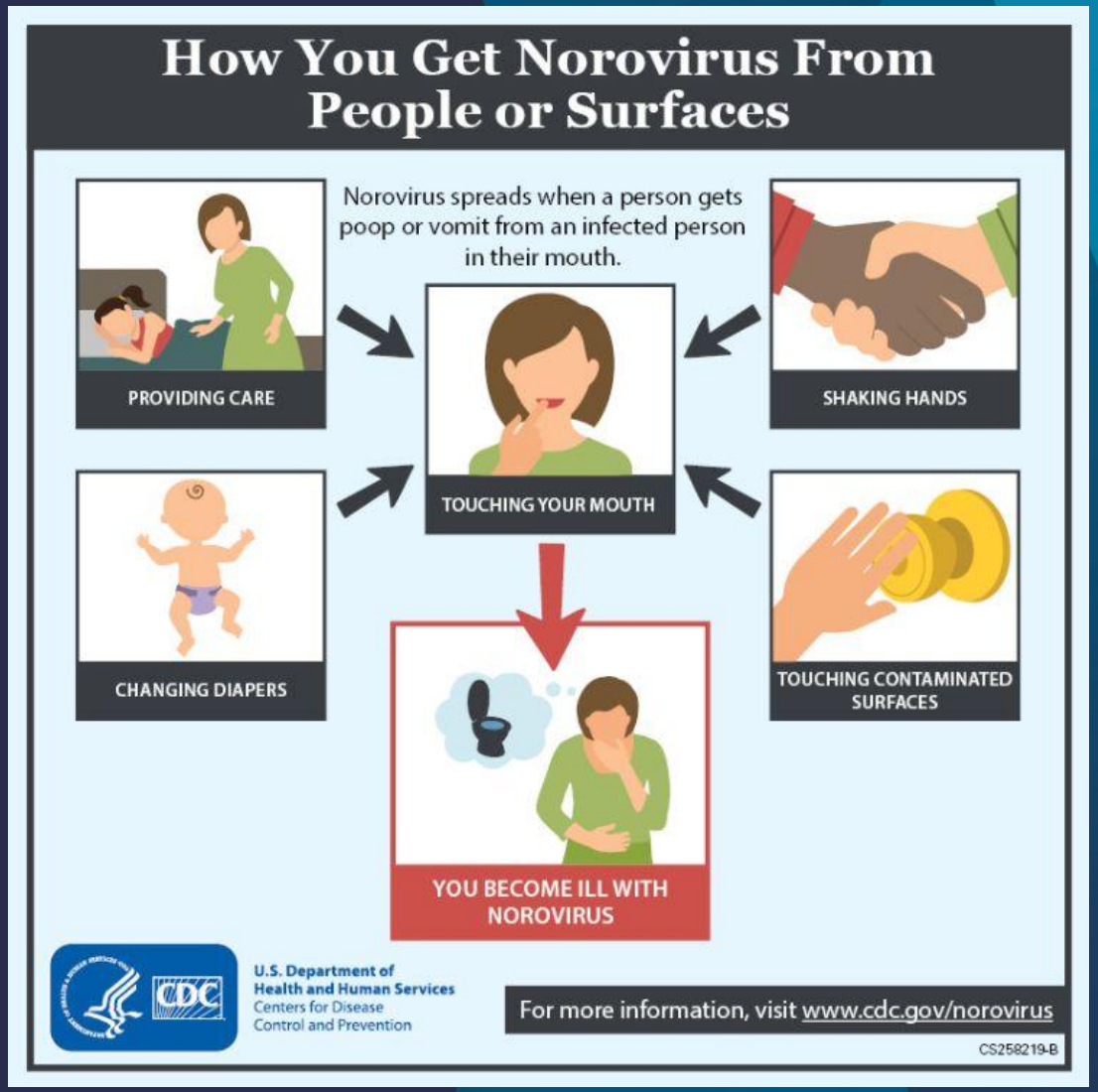
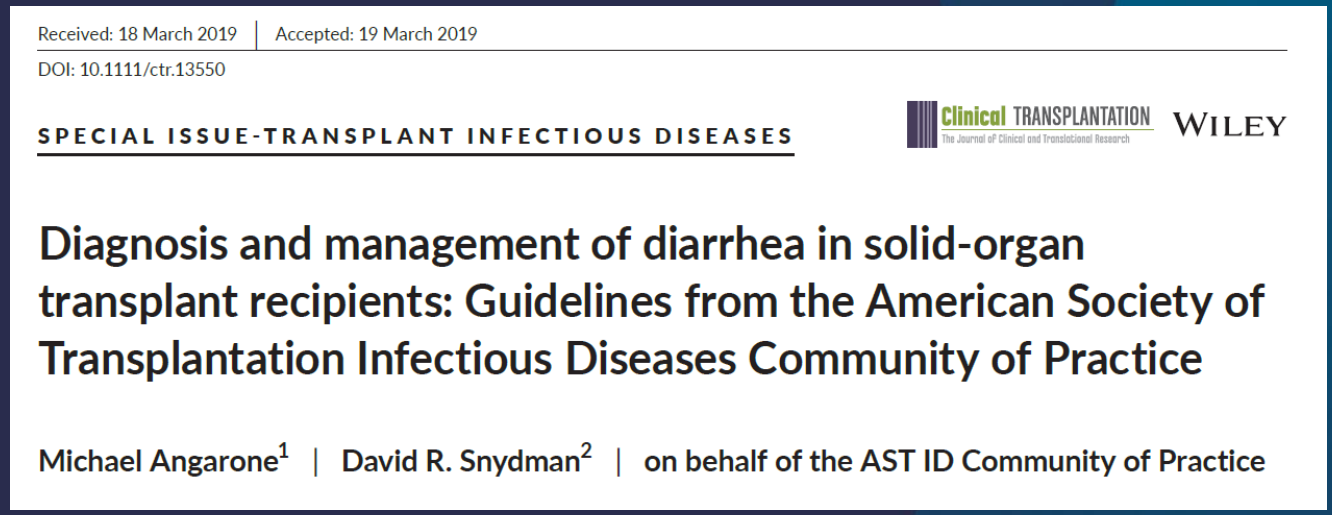
Norovirus

- Five major genogroups: GI-GV, with serogroups GI, GII, GIV associated with human disease
- One of the leading causes of diarrhea, accounting for **>90% of nonbacterial infections** and **estimated 19-22 million cases in U.S. annually**
- Transmission is fecal-oral route, via inhalation of aerosols from vomitus, or contact with contaminated environmental surfaces
- Chronic shedding can lead to chronic, debilitating diarrhea.
- Viral shedding median is 289 days



Norovirus Treatment

- Rehydration
- Antimotility agent
- IS reduction
- Nitazoxanide



Received: 18 March 2019 | Accepted: 19 March 2019
DOI: 10.1111/ctr.13550

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research
WILEY

Diagnosis and management of diarrhea in solid-organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Michael Angarone[1] | David R. Snydman[2] | on behalf of the AST ID Community of Practice

NITAZOXANIDE (NTZ)

- **Multicenter, double-blind RCT** on NTZ for treatment of norovirus-infected adult patients between 2018-2021.
- 31 subjects with symptoms and PCR+ were randomly assigned 1:1 to NTZ or placebo group.
  - **30/31 patients were SOT**
  - **77% had chronic symptoms >14 days**
- Primary endpoint was time to symptom resolution.
  - 19 days in NTZ vs 11 days in placebo group (p=0.459).
  - Time to 1st negative stool PCR not statistically significant.

American Journal of Transplantation
Available online 22 May 2026
In Press, Corrected Proof What's this?

Original Article

A phase 2 multicenter, prospective, randomized, double-blind study to assess the clinical and antiviral efficacy and safety of nitazoxanide for the treatment of norovirus in hematopoietic stem cell and solid organ transplant recipients

Catherine-Audrey Boutin [1], Michelle Callegari [2], Diana Florescu [3], Minh-Hong Nguyen [4], Daniel Kaul [5], Robin Avery [6], Pearlie Chong [7], Cynthia Fisher [8], Ajit P. Limaye [8], Lisa Clough [9], Steven A. Pergam [10], Michael Green [11], Marian G. Michaels [11], Lara A. Danziger-Isakov [12], Michael Angarone [2], Laurie Keefer [13], Amna Daud [2], Ramon Lorenzo-Redondo [2], Ming Tan [12], Michael G. Ison [14]

NTZ did not shorten the time to symptom resolution or viral shedding. Although safe, NTZ likely contributes little to the management of chronic NoV.

Oral Human Immunoglobulin (OHIG)

- Limited data supporting its use based on case reports and retrospective case series. No RCT
- Rationale is to maximize intestinal epithelial concentrations by enteral delivery where viral particles may be prevented from adhering to enterocytes
- Product is susceptible to gastric acid degradation

Cornerstone management of NoV infection is reduction of immunosuppression

CYCLOSPORA

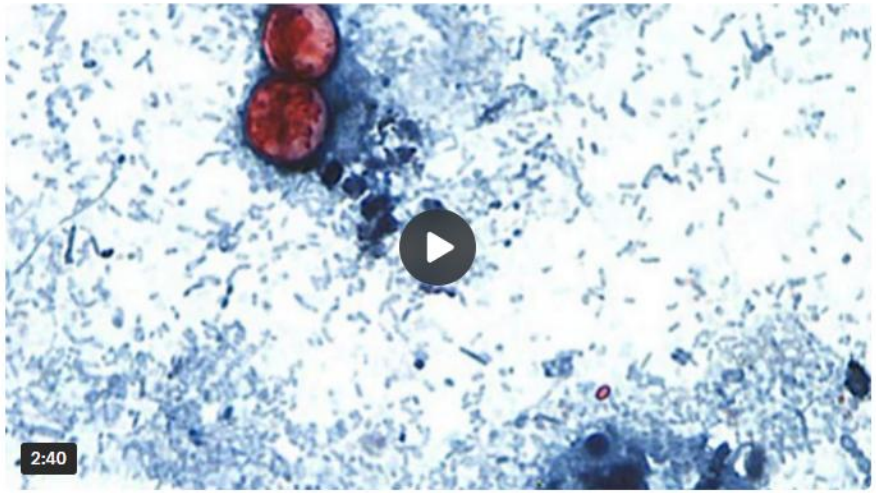
Investigation of Multistate Outbreak of Cyclospora Illnesses: Iceberg Lettuce (July 2026)

FDA's investigation is ongoing.

More than 24,000 cyclosporiasis infections reported as new cases appear to slow: CDC

Cyclosporiasis is behind an outbreak linked to shredded iceberg lettuce.

By Mary Kekatos
August 12, 2026, 10:04 AM



2 dead from cyclosporiasis in Michigan Over 18,000 people have been diagnosed with the parasitic illness cyclosporiasis across 45 states.

Health

Michigan cyclosporiasis outbreak tops 13,900 cases; 35 additional hospitalizations in past week

By Paula Wethington, Joseph Buczek

Updated on: August 13, 2026 / 4:22 PM EDT / CBS Detroit

HEALTH

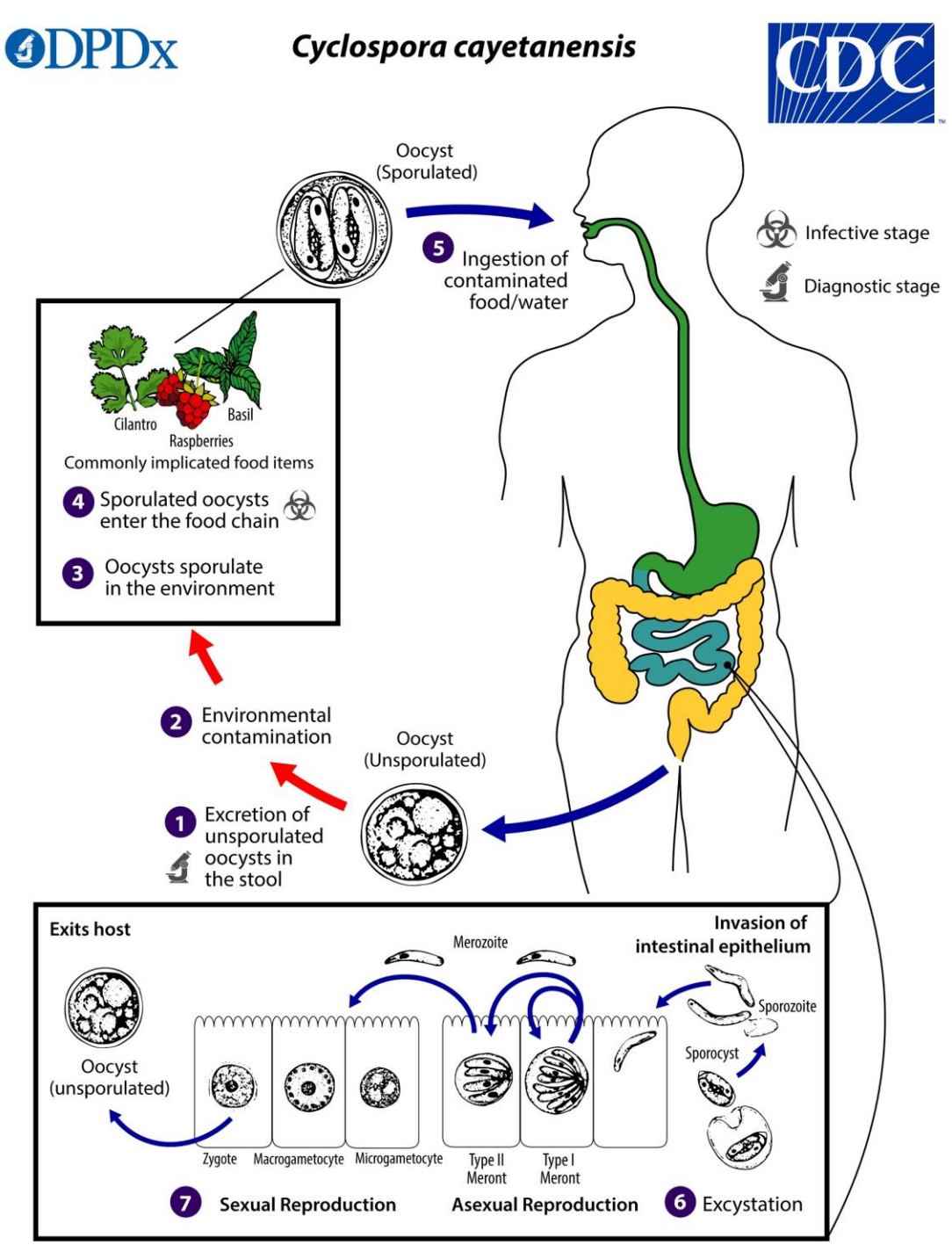
Cyclospora infections are rising in Tennessee. What a Nashville food safety expert says

Beth Warren
Nashville Tennessean

July 31, 2026, 5:02 a.m. CT

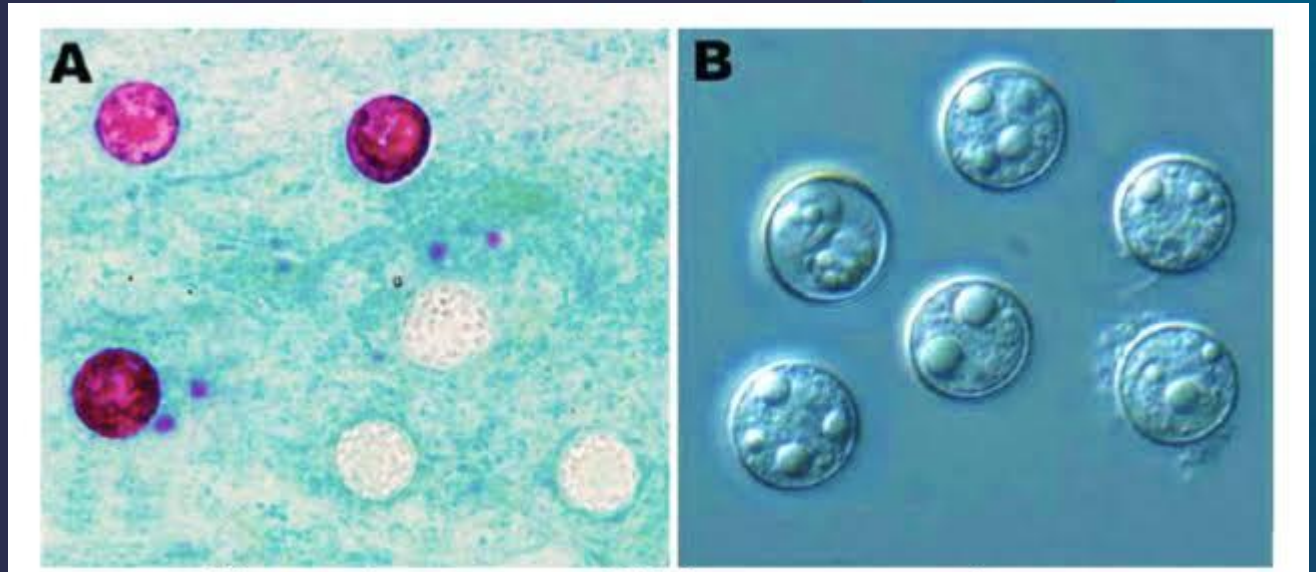
CYCLOSPORA

- Obligate intracellular parasite
- Incubation period: 2-14 days
- Can manifest with acute diarrhea or prolonged waxing/waning course
- Often asymptomatic, but illness is characterized by:
  - Watery diarrhea
  - Abdominal cramping
  - Flatulence
  - Nausea
  - Anorexia
  - Weight loss



CYCLOSPORA DIAGNOSIS

- NAAT/PCR – highest sensitivity and specificity
- Stool microscopy for identification of oocysts



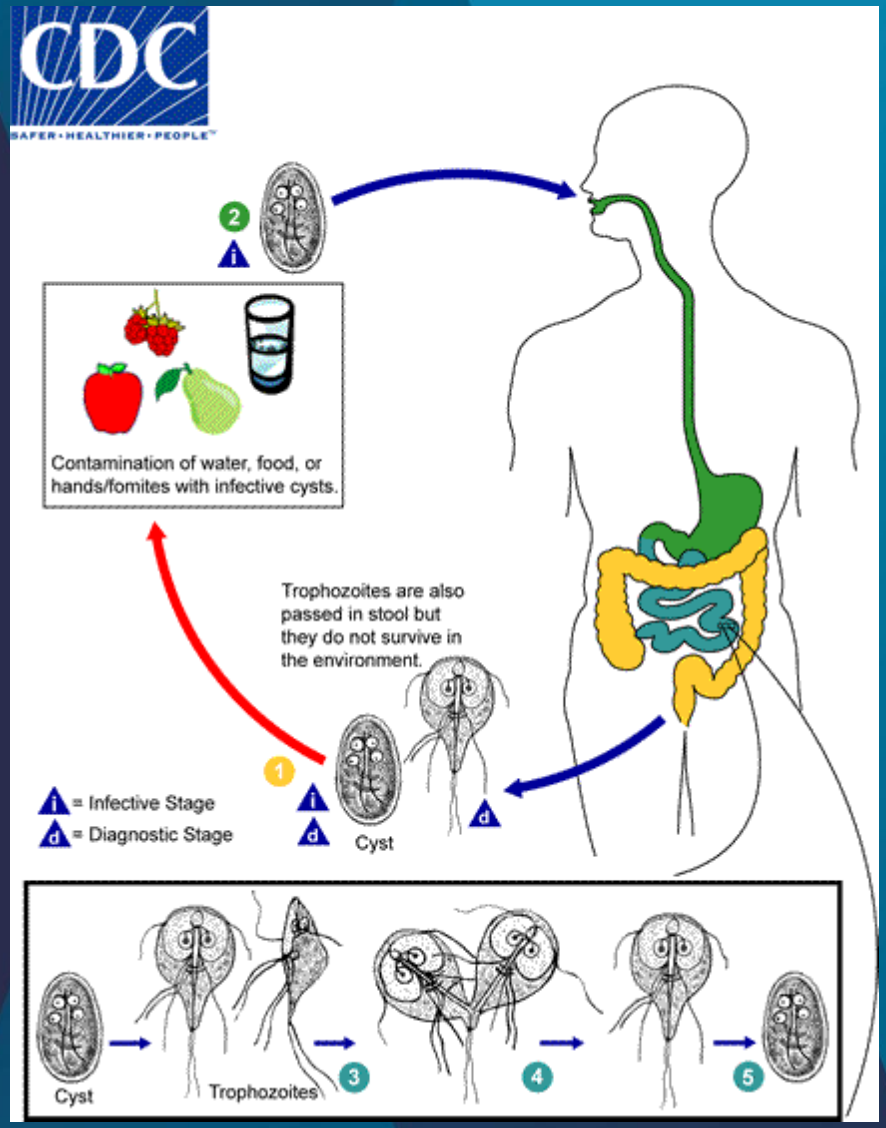
Microscopic appearance of *Cyclospora cayetanensis* oocysts
Source: Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 10, October 2011

TREATMENT

- **PO TMP-SMX 160/800 mg every 6 hours x10 days**, then secondary prophylaxis 3x/week. Relapse is common in immunocompromised patients.
- **If sulfa allergic: Ciprofloxacin 500mg PO BID x7 days,** then 3x/week for secondary prophylaxis.
- Duration for secondary prophylaxis is **unknown.**
- Reduction of immunosuppression
- Supportive care

GIARDIA

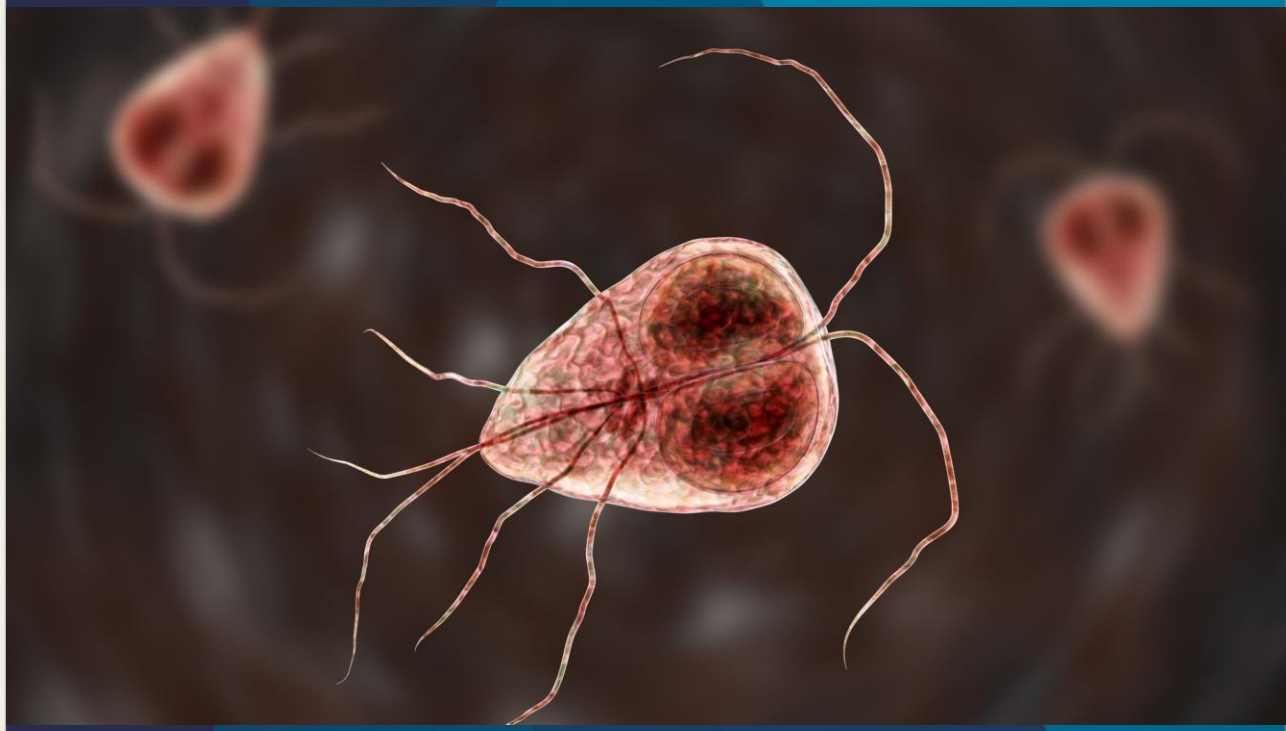
- Most common cause of intestinal parasite infection in the U.S.
- Main modes of transmission: water exposure, person-to-person, contaminated food
- Private residences and childcare facilities most common setting for outbreaks
- **Diagnosis:**
  - Stool antigen detection
  - GI multiplex molecular assay



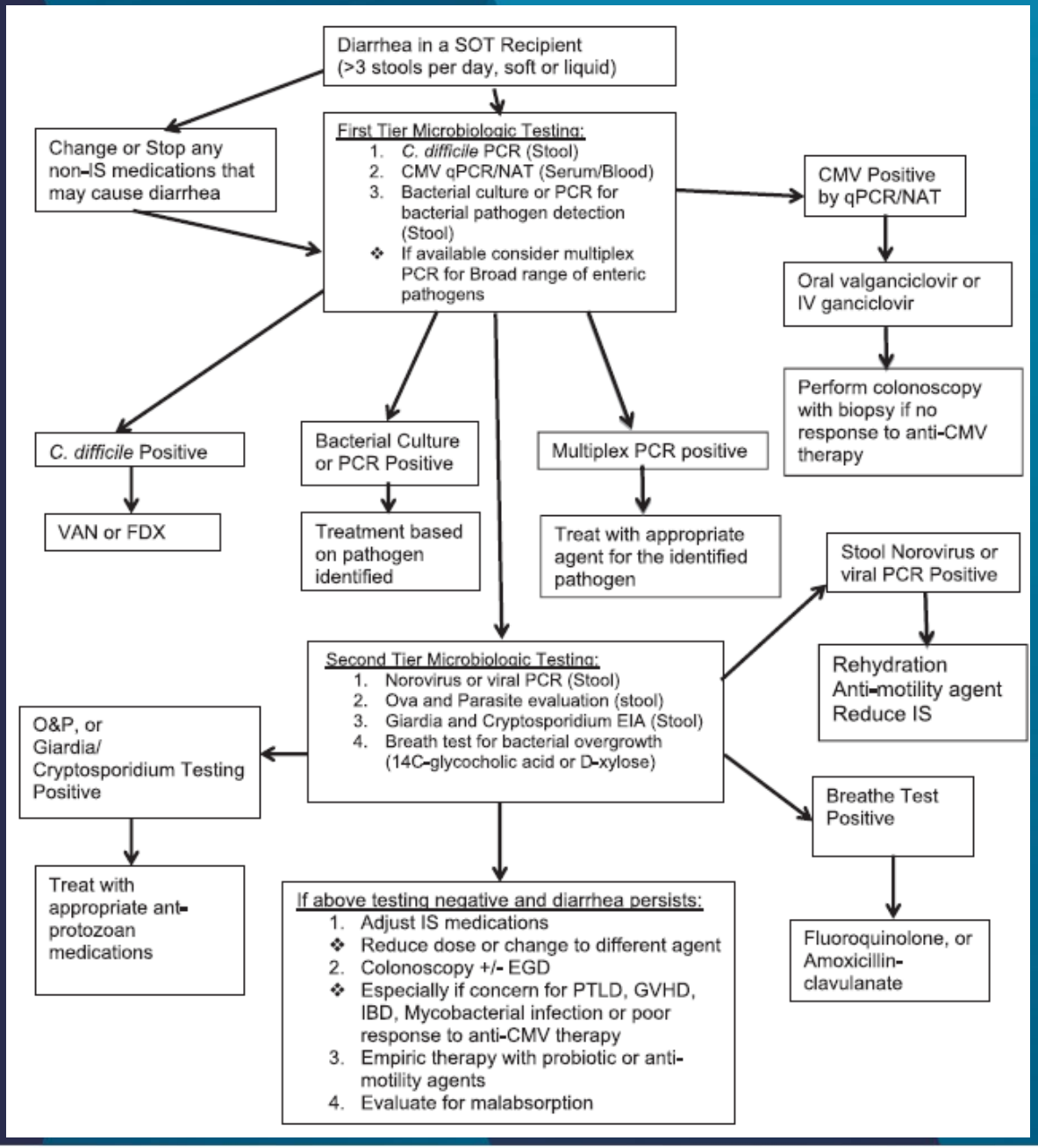
TREATMENT

- **Tinidazole 2g PO once is treatment of choice**
- Alternatives:
  - Nitazoxanide 500mg PO BID x3d
  - PO Metronidazole 500-750 mg PO TID x5 days
  - Paromomycin 500mg PO QID x7d

- **Prevention:** avoid untreated water or lake water



Algorithm for Diarrhea Workup



Angarone M. Clin Tranpslant. 2019

Thank you!

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