"You asked, We answered..."

Hot Topics with Transplant ID

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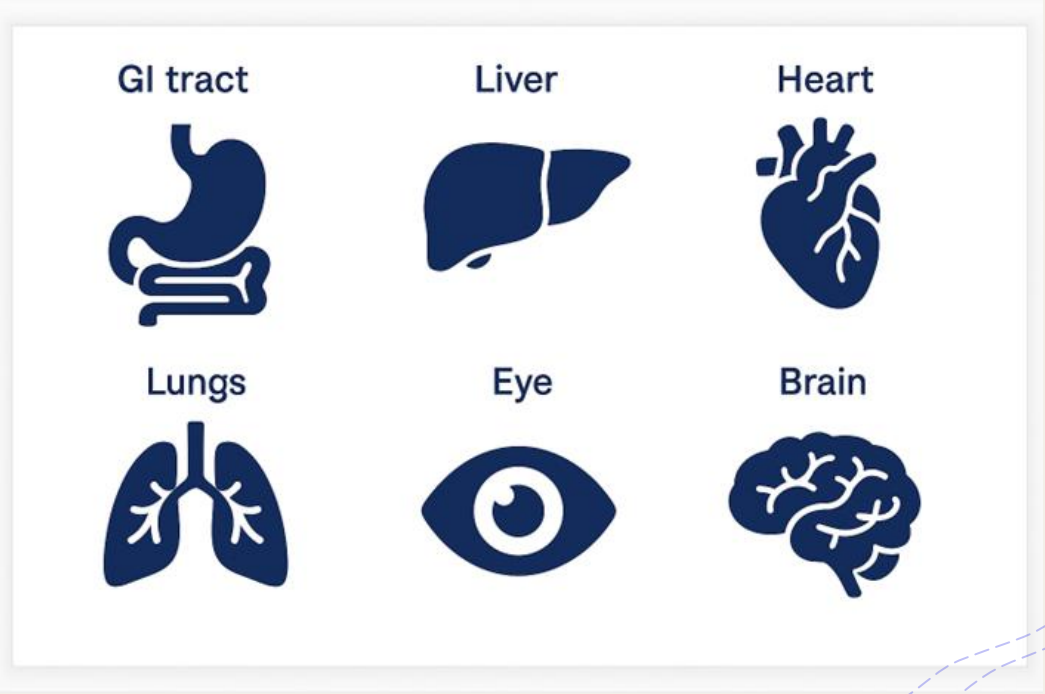
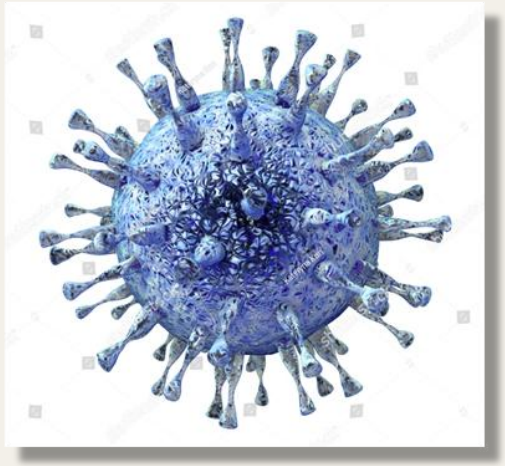
Cytomegalovirus

- **CMV infection**: CMV replication in asymptomatic patient (PCR+)
- **CMV disease**: CMV replication with symptoms
- **CMV syndrome**: malaise, fever, leukopenia
- **CMV end organ involvement**



Indirect Immunomodulatory Effects of CMV

↑ risk of bacterial infections



↑ risk of EBV-mediated PTLD

↑ risk of invasive fungal infections

Allograft dysfunction

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.

What is your next step?

CMV Risk Stratification

▶Transplant risk stratification for CMV infection is based on CMV IgG serostatus of donor (D) and recipient (R)

▶CMV IgM is not useful. Do not send

D+/R-	High risk
R+	Moderate risk
D-/R-	Low risk

When do I start antiviral treatment for CMV reactivation?

If High Risk (+/-)

General consensus is to **treat at any level** for primary CMV infection regardless of symptoms

Higher incidence of CMV disease[1]

Faster CMV doubling time [2]

[1] Couzi A, *Am J Transplant.* 12.1 (2012): 202-209
[2] Atabani S. *Am J Transplant.* 12.9 (2012): 2457-2464

If Moderate Risk (R+)

Treat at **any level if symptomatic**

Varying viral threshold for asymptomatic [3]

Institution-dependent, generally >1000 IU/ml

Depends on overall net state of IS

[3] Kotton C. *Transplantation* 109 (2025): 1066-1110

CMV Case 1

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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**.

What is your next step?

If Moderate Risk (R+)

Treat at **any level if symptomatic**

Varying viral threshold for asymptomatic

Institution-dependent, generally >1000 IU/ml

Depends on overall net state of IS

Thresholds used for preemptive therapy in research publications in the last 7 years

Study design	Participants	CMV monitoring	Threshold for treatment
D^+/R^-			
RCT	Adult LTX (n = 205), D^+/R^-	Plasma RT-PCR	Any level of DNAemia (detection level >20 IU/mL)
Retrospective real-world effectiveness	LTX (N = 50), D^+/R^-	Plasma RT-PCR	Any level of DNAemia (detection level >20 IU/mL)
R^+			
Long-term outcomes of RCT	Adult KTX (n = 299), any R^+	Plasma RT-PCR	>400 copies/mL
Retrospective	Adult and pediatric KTX (n = 132), any R^+	Whole blood RT-PCR	>4000 copies/mL
Retrospective	Adult LTX (n = 124), R^+	Whole blood RT-PCR	≥4000 IU/mL
Retrospective	Adult KTX (n = 540), any R^+	Initially pp65, then plasma RT-PCR	≥10 pp65 positive cells or symptoms attributable to CMV with any positivity. RT-PCR ≥5000 IU/mL or symptoms attributable to CMV with any DNAemia
Retrospective	Adult KTX (n = 251), any R^+	Plasma RT-PCR	Significant CMV DNAemia defined as $\geq 10^4$ IU/mL. Threshold treatment not specified
Retrospective	Adult HTX (n = 563), any R^+	Plasma or whole blood RT-PCR	Treatment thresholds individual to each site
Mixed: R^+ with or without D^+/R^- and D^-/R^-			
RCT	Adult KTX (N = 140), any R^+, D^+/R^-	Whole blood RT-PCR	≥1000 IU/mL
Retrospective	Adult LTX, KTX, LKTX, D^+/R^- and any R^+	Whole blood RT-PCR	Any R^+: >3000 genomes/mL. D^+/R^-: >3000 genomes/mL (old protocol); >200 genomes/mL (168 IU/mL; new protocol)
Retrospective	Adult KTX (n = 556), any D^+, R^+ as well as D^-/R^-	pp65 or RT-PCR (biosample not specified for PCR)	Any positive value for high-risk patients. Treatment individualized for low risk patients
Retrospective	Adult and pediatric KTX (n = 87), any R^+ or D^+ or D unknown	pp65 CMV antigenemia	>10 pp65 positive cells in 200 000 neutrophils in peripheral blood (for D^+/R^-, any pp65 positive cell)
Retrospective	Adult and pediatric lung TX (n = 129)	Whole blood RT-PCR or pp65 and BAL RT-PCR	≥100 pp65 positive cells/2 × 10^5 leukocytes, Blood CMV PCR >300 000 DNA copies/mL, BAL CMV >100 000 DNA copies/mL
Retrospective	Adult KTX (n = 2198), D^+/R^- or R^+	Plasma CMV PCR	>600 IU/mL plasma (1000 IU/mL plasma from March 2021).
Retrospective	Pediatric KTX (N = 126), R^+ or D^+/R^-	Plasma CMV PCR	Low viral load threshold (>400 but <2000 IU/mL) compared with high viral load threshold (≥2000 IU/mL)

Kotton C. *Transplantation* 109 (2025): 1066-1110

Overall Net State of Immunosuppression

- IS regimen
- Rejection
- Neutropenia, lymphopenia
- Hypogammaglobulinemia
- Technical complications
- Underlying immune defects
- Chronic co-morbidities
- Acute illness
- Co-infections

Risk of 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 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

CMV Case 3 Continued

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?


THIS IS FINE.

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
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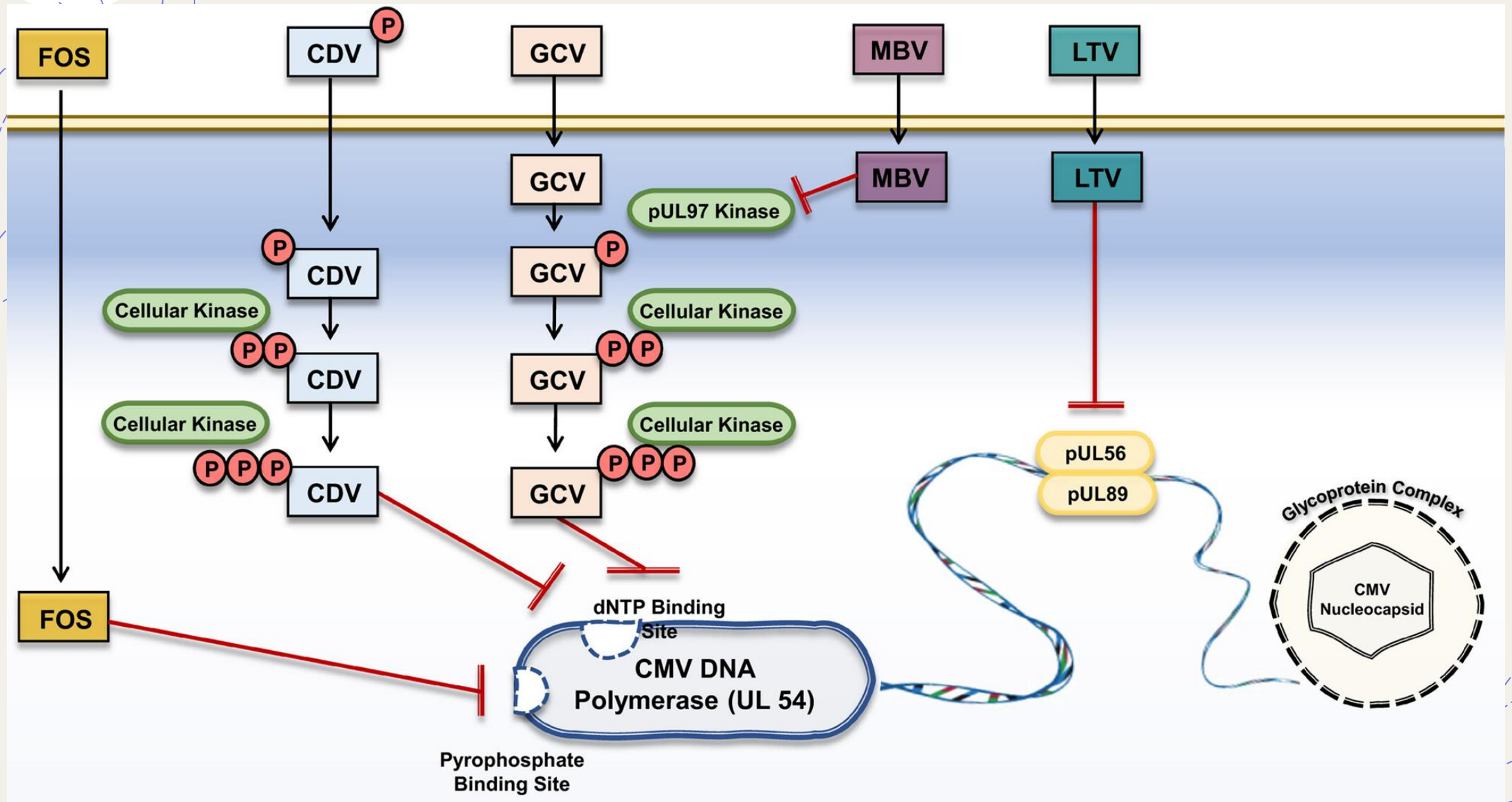
When to send resistance testing?

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

- GCV resistance takes >6 weeks of drug exposure to develop, whereas maribavir resistance developed after median of 8 weeks

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



Dickter JK. *J Clin Pharm Ther.* 2022 May;47(5):699-702

CMV Case 3

Patient was admitted and started on Foscarnet with subsequent improvement. His MMF was stopped. After 2 weeks, his CMV improved to 40,000 000 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 Treatment Options

Medication	Indication	Adverse Effects
Valganciclovir (PO)	• Preferred due to PO formulation • Limited PK data to confirm adequate bioavailability in GI disease	• Myelosuppression
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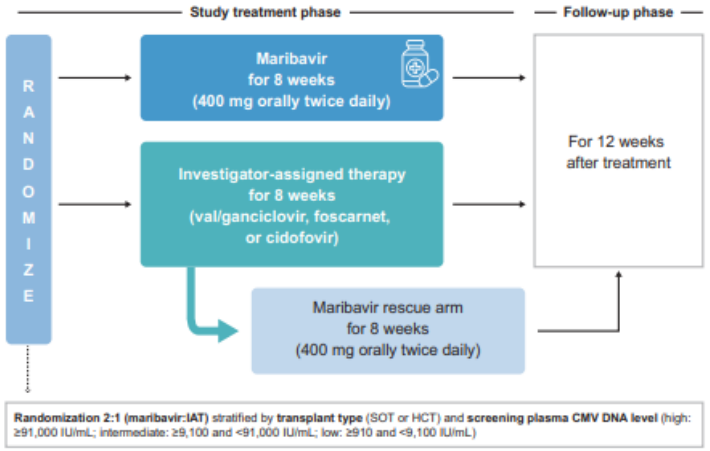
Results from a Phase 3 Randomized Clinical Trial

Robin K. Avery, Sophie Alain, Barbara D. Alexander, Emily A. Blumberg, Roy F. Chemaly, Catherine Cordonnier, Rafael F. Duarte, Diana F. Florescu, Nassim Kamar, Deepali Kumar, Johan Maertens, Francisco M. Marty, Genovefa A. Papanicolaou, Fernanda P. Silveira, Oliver Witzke, Jingyang Wu, Aimee K. Sundberg, and Martha Fournier, for the SOLSTICE Trial Investigators

INTRODUCTION

This was a phase 3, multicenter, randomized, open-label, active-controlled study to assess the efficacy and safety of maribavir compared with IAT in HCT and SOT recipients with CMV infections refractory to most recent treatment, with or without resistance to ganciclovir/valganciclovir, foscarnet, and/or cidofovir.

STUDY DESIGN



STUDY ENDPOINTS

The primary endpoint was confirmed CMV viremia clearance at the end of Week 8 (regardless of premature treatment discontinuation).

The key secondary endpoint was a composite of confirmed CMV viremia clearance and symptom control at the end of Week 8, maintained through Week 16 after receiving exclusively study-assigned treatment.

RESULTS

352 patients were randomized (maribavir, n=235; IAT, n=117)

PRIMARY ENDPOINT (WEEK 8)

Adjusted difference (95% CI): 32.8 (22.80–42.74)

A significantly higher proportion of patients treated with maribavir achieved the primary endpoint of confirmed CMV viremia clearance at Week 8 compared with IAT.

KEY SECONDARY ENDPOINT (WEEK 16)

Adjusted difference (95% CI): 9.5 (2.02–16.88)

A greater proportion of patients treated with maribavir achieved the composite key secondary endpoint of CMV viremia clearance and symptom control at Week 8, with maintenance through Week 16 compared with IAT.

SAFETY

Median (range) duration of exposure was 57 (2–64) days with maribavir and 34 (4–64) days with IAT.

Fewer patients discontinued maribavir than IAT due to TEAEs (13.2% vs 31.9%).

Dysgeusia was the most frequently reported TEAE in the maribavir group (maribavir: 37.2%; IAT: 3.4%).

Maribavir was associated with less acute kidney injury versus foscarnet (8.5% vs 21.3%) and neutropenia versus valganciclovir/ganciclovir (9.4% vs 33.9%).

One patient per treatment group had fatal treatment-related TEAEs.

CONCLUSIONS

Maribavir was superior to IAT for cytomegalovirus viremia clearance, and viremia clearance plus symptom control, with maintenance of these effects post-therapy in transplant recipients with refractory cytomegalovirus infections with or without resistance.

Maribavir demonstrated an improved safety profile versus valganciclovir/ganciclovir for myelotoxicity and versus foscarnet for nephrotoxicity, with fewer patients discontinuing maribavir than IAT.

The availability of an orally bioavailable therapy without the tolerability issues associated with current therapies may confer patient management benefits.

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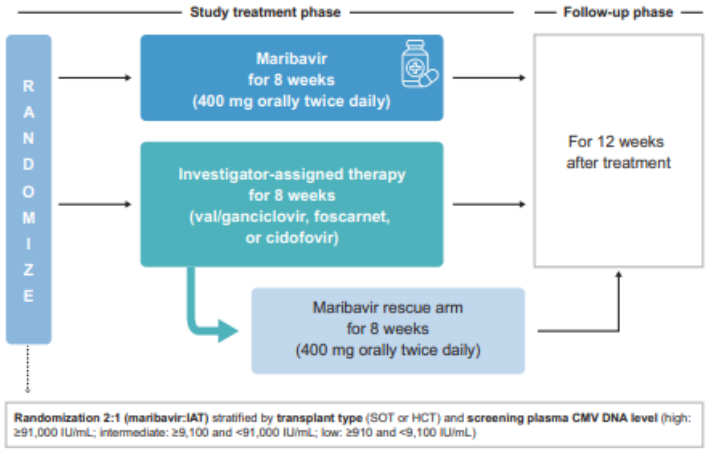

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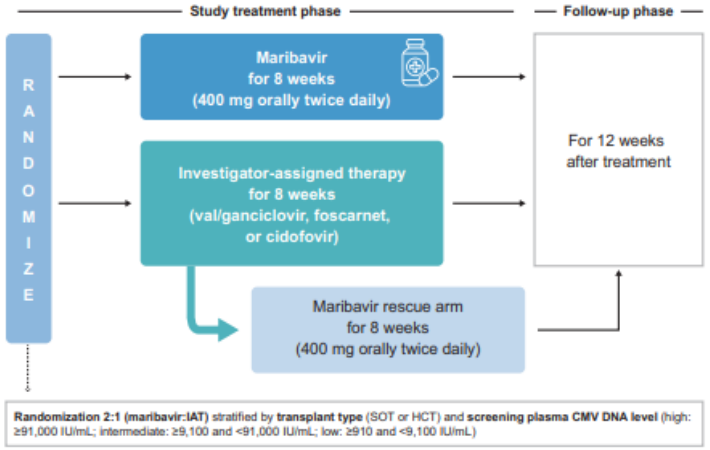

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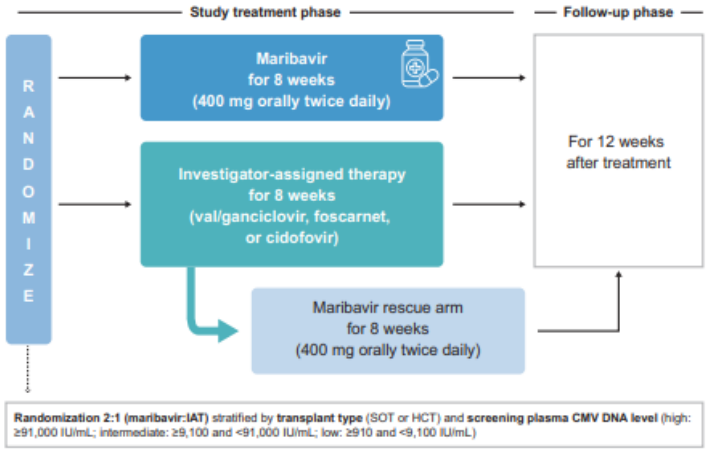

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Maribavir

- **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 that **after at least 21 days** of maribavir exposure, 24/241 **(10%) developed maribavir resistance** with median of 56 days after starting treatment
    - Higher incidence of resistance if baseline CMV >9100 IU/ml (29%) than dose with <9100 IU/ml (6%)
  - **Compared to 2.5% developing GCV resistance** after receiving same duration VGCV
  - SOLSTICE trial with majority of participants with starting VL <100K
    - 65% with starting VL <9100, 29% with ≥9100 to <91,000, and only 6% with >91,000

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

CMV Case 3

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?

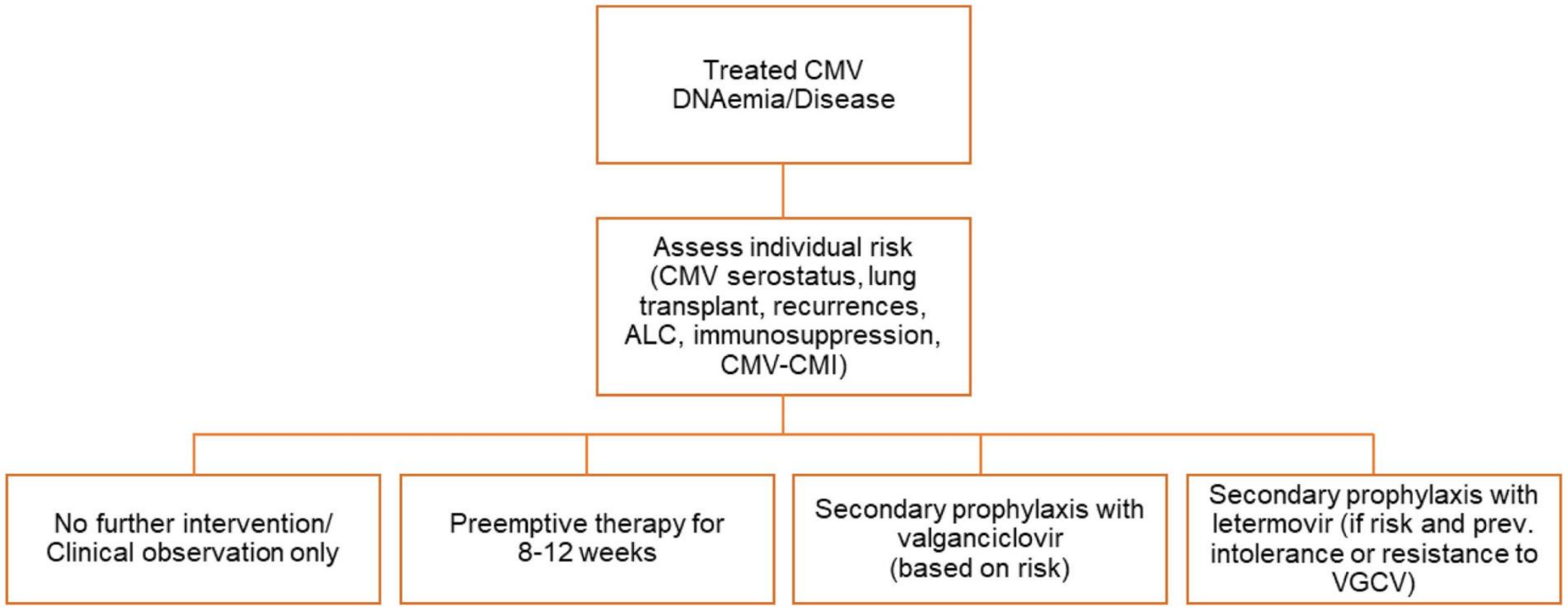
CMV Prophylaxis Options

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

Who benefits from 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.



Suggested options for secondary prevention after an episode of treated CMV DNAemia/disease. In R^+ kidney recipients, consider switching from mycophenolate to mTOR and reduce CNI. ALC, absolute lymphocyte count; CMI, cell-mediated immunity; CMV, cytomegalovirus; CNI, calcineurin inhibitor; mTOR, mammalian target of rapamycin; VGCV, valganciclovir.

Cell Mediated Immunity (CMI) Testing

- 3 tests commercially available: T-SPOT, Quantiferon, and inSIGHT
- **InSIGHT: Intracellular Cytokine Staining**
  - The only test currently available in USA
  - Post-exposure to proprietary CMV antigen mix evaluating the % of CD4 and/or CD8+ T cells expressing IFN-γ
    - **Positive: CD8+ >0.2%**
    - Most useful if positive. PPV 85% for protection from CMV reactivation
    - **Very low positivity in D+/R- (<5%)**
  - Currently being piloted in lung transplant with CMV +/+ at VUMC
    - Obtained after 6 months of CMV prophylaxis and if ALC >750, CMV InSIGHT is obtained
      - If positive, end prophylaxis at 6 months
      - If negative, extend prophylaxis to 9 months

Slide courtesy of Dr. Augusto Dulanto

Almaghlouth N. *Diagn Microbiol Infect Dis.* 2024: 108(2)
Descourouez JL. *Ann Pharmacother.* 2024: 58(8):796-802

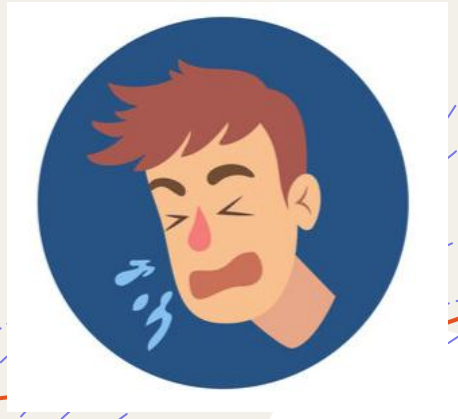
One Presentation, Different Scenarios

PRESENTATION

+ 59 year old man with a past medical history of ESRD 2/2 HTN s/p DDKT (2022), maintained on tacro, MMF and prednisone.
+ Presents to the ED with shortness of breath and cough, progressively worsening for the last two weeks. Felt warm but never took his temperature.

IN THE ED

+ VS : sat 90% on RA, BP 132-87, HR 87, afebrile
+ On exam : NAD, oriented, lungs with faint rhonchi, heart RRR, abdomen is soft, no rash



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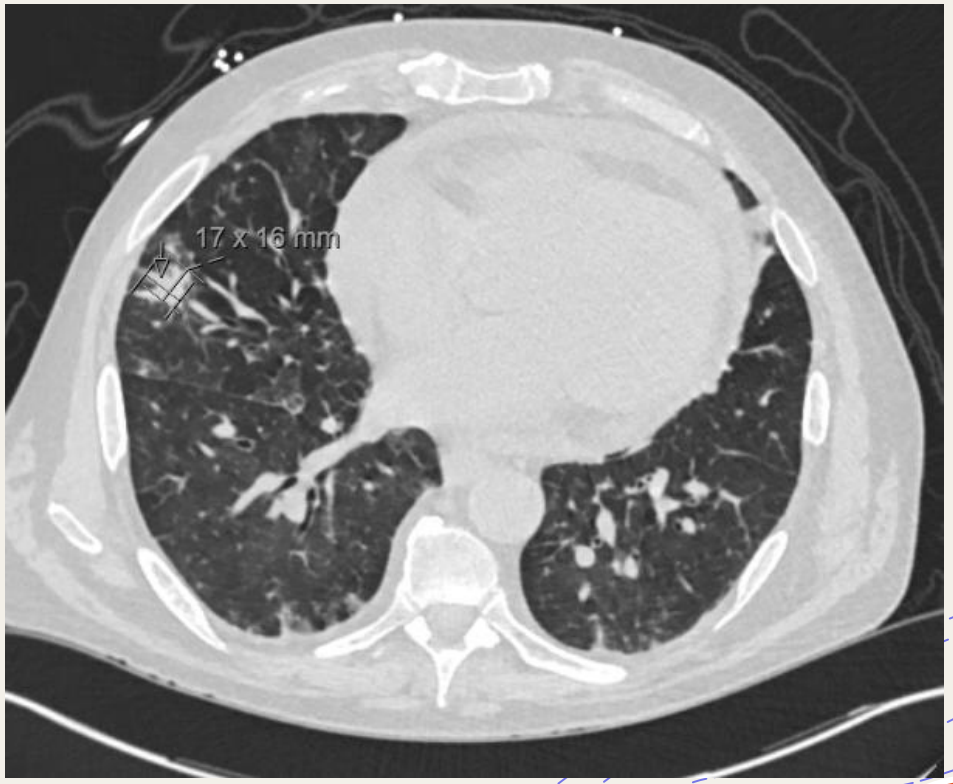
IN THE ED

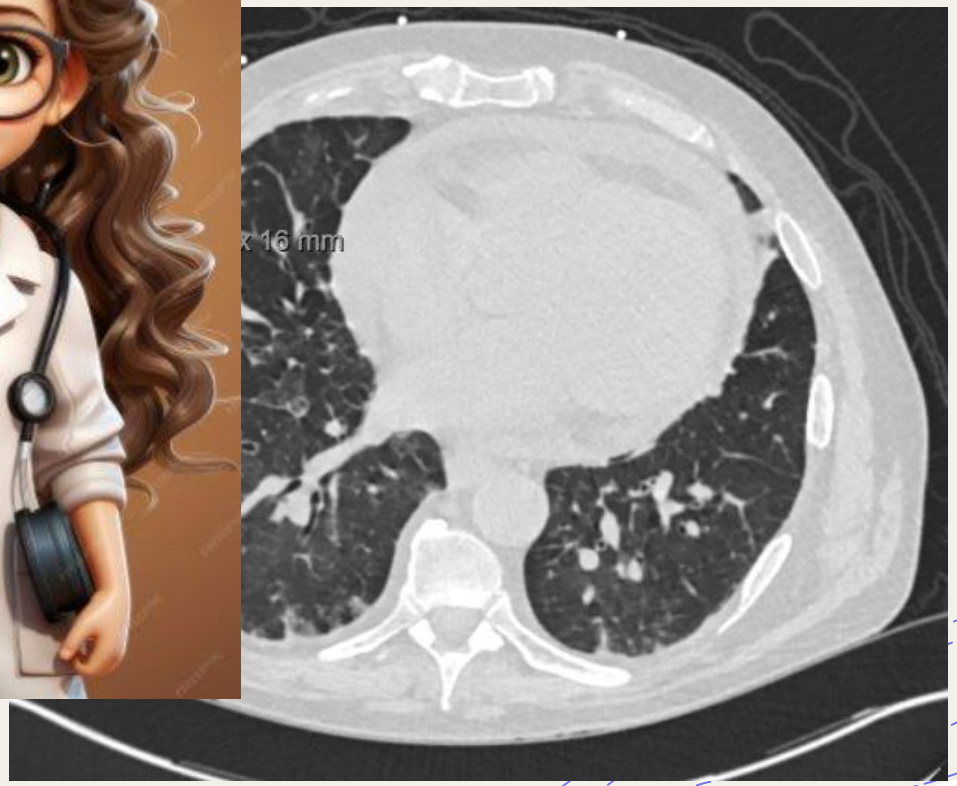


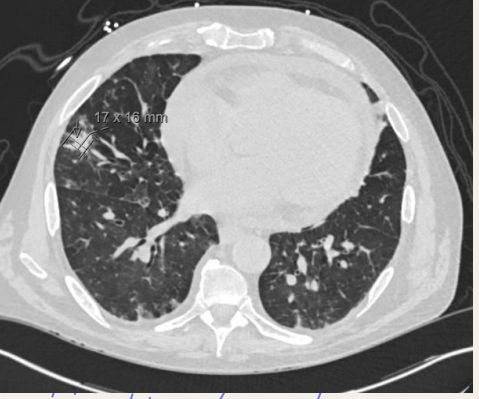
One Presentation, Different Scenarios

PRESENTATION

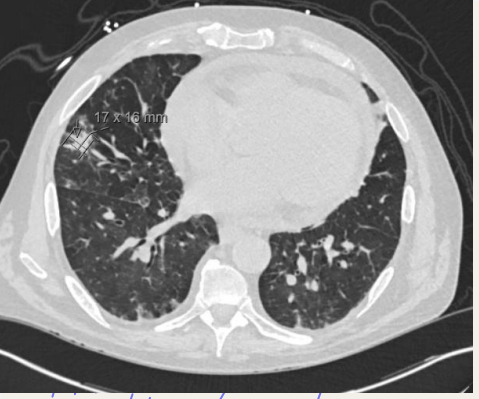
- 59 year old man with a past medical h
  2/2 HTN s/p DDKT (2022), maintained
  MMF and prednisone.
- Presents to the ED with shortness of b
  cough, progressively worsening for the
  weeks. Felt warm but never took his t

D



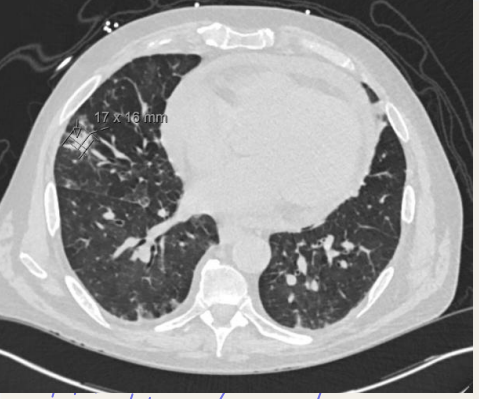


Exposures



ID workup

Recommended workup	Results
Blood cultures	Negative
Sputum culture	Negative
Aspergillus galactomannan	5.71
Urine and serum histoplasma ag	Negative
Urine blasto antigen	Negative
Cryptococcal antigen	Negative



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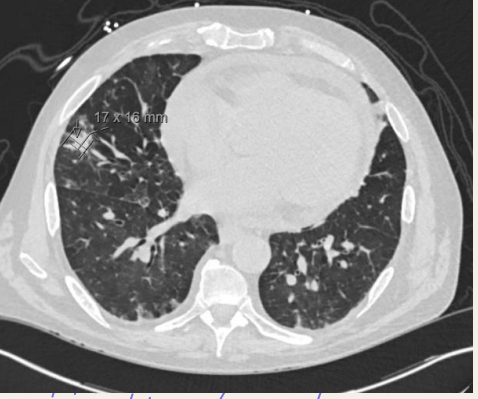


Aspergillosis

Manifestations

- Pulmonary
- Rhinosinusitis
- CNS infection
- Cutanneous

Diagnosis

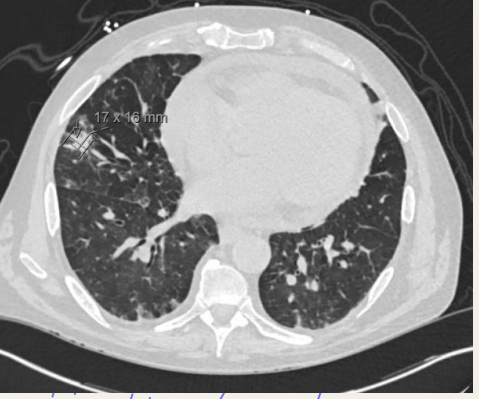
- Culture
- Histopath
- Galactomannan

KEEP IN MIND , GM is not a perfect test ：
Sensitivity of GM decreased with concomitant use of mold active agents

False positivity 2/2 cross reactivity

Sensitivity of GM testing		
	Serum	BAL
Kidney	58%	Reported from 70-100%
Liver	55.6%	
Lung	30%	

Husain, Shahid,--- Camargo. "Invasive aspergillosis in solid-organ transplant recipients: guidelines from the AS TID COP." *Clinical transplantation* 33.9 (2019): e13544.



Aspergillosis

Pulmonary aspergillosis Rx

Voriconazole as 1st line therapy

Alternatively : posaconazole, isavuconazole

- Measurement of serum trough concentration within 7-10 d.
- Monitoring of hepatic function and CNI/mTOR inhibitor agent levels is recommended
- Treatment is usually continued for 12 weeks; however, the precise duration of therapy should be guided by clinical response rather than an arbitrary total dose or duration.
- A reasonable course would be to continue therapy until all clinical and radiographic abnormalities have resolved

Husain, Shahid,--- Camargo. "Invasive aspergillosis in solid-organ transplant recipients: guidelines from the AS TID COP." *Clinical transplantation* 33.9 (2019): e13544.

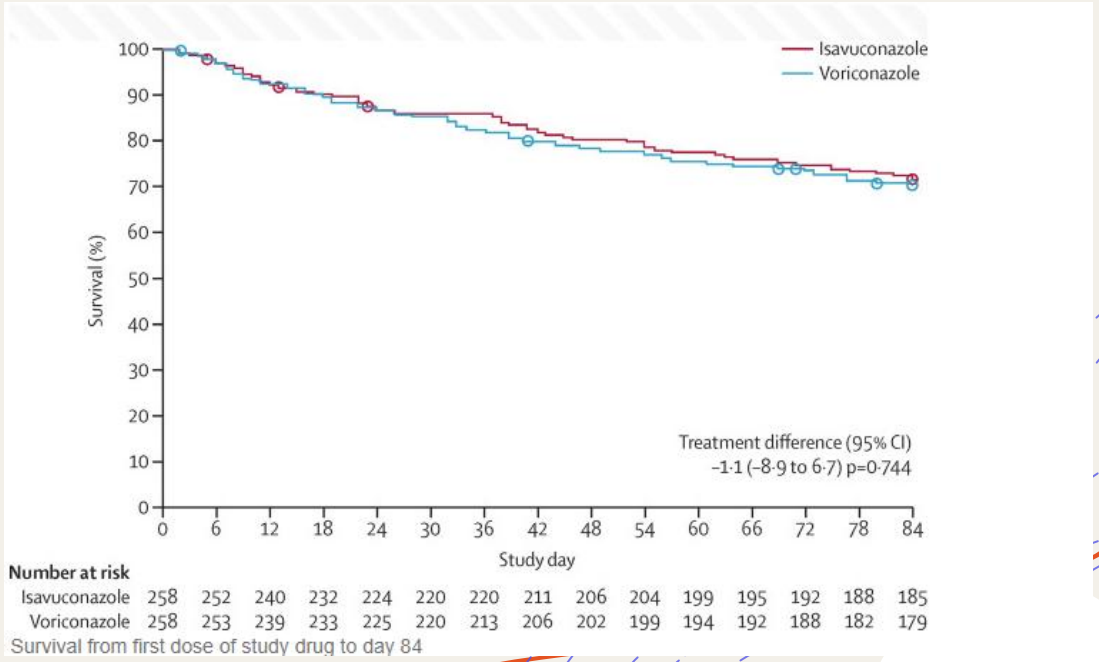
The SECURE TRIAL

Patients treated with Cresemba demonstrated non-inferiority to voriconazole on the primary endpoint of **all-cause mortality** at day 42.

The all-cause mortality reported in the Cresemba treatment group was 18.6%, while it was 20.2% in the voriconazole treatment group.

Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial

Johan A Maertens [1], Issam I Raad [2], Kieren A Marr [3], Thomas F Patterson [4], Dimitrios P Kontoyiannis [5], Oliver A Cornely [6], Eric J Bow [7], Galia Rahav [8], Dionysios Neofytos [9], Mickael Aoun [10], John W Baddley [11], Michael Giladi [12], Werner J Heinz [13], Raoul Herbrecht [14], William Hope [15], Meinolf Karthaus [16], Dong-Gun Lee [17], Olivier Lortholary [18], Vicki A Morrison [19], Ilana Oren [20], Dominik Selleslag [21], Shmuel Shoham [22], George R Thompson 3rd [23], Misun Lee [24], Rochelle M Maher [24], Anne-Hortense Schmitt-Hoffmann [25], Bernhardt Zeiher [24], Andrew J Ullmann [26]



The SECURE TRIAL

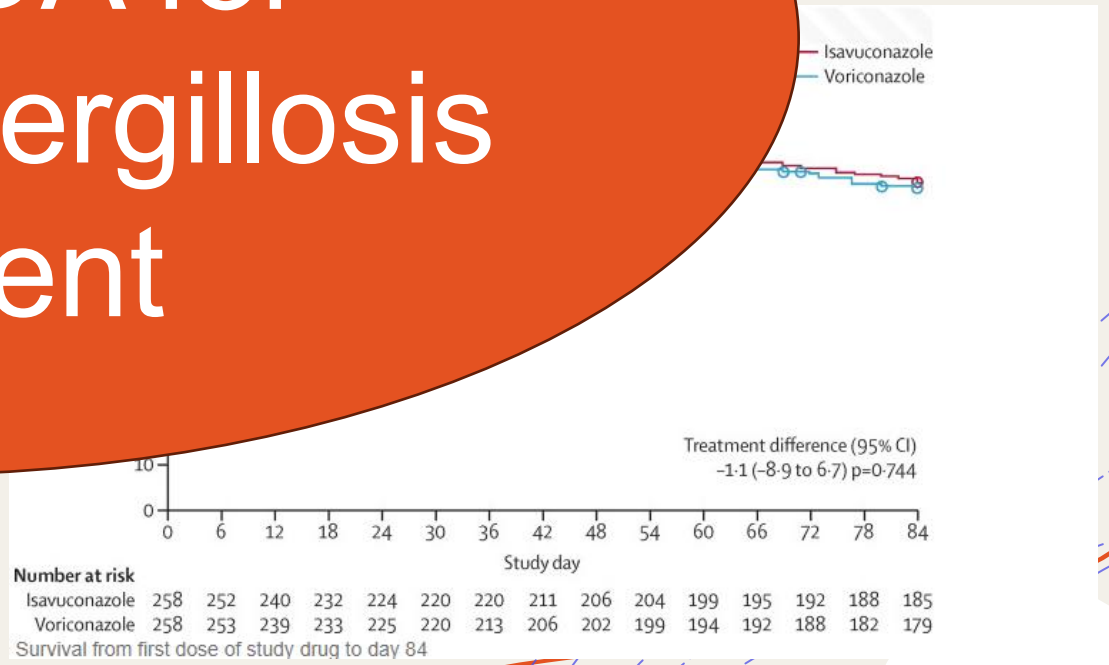
Patients treated
demonstrated
voriconazol
all-cause

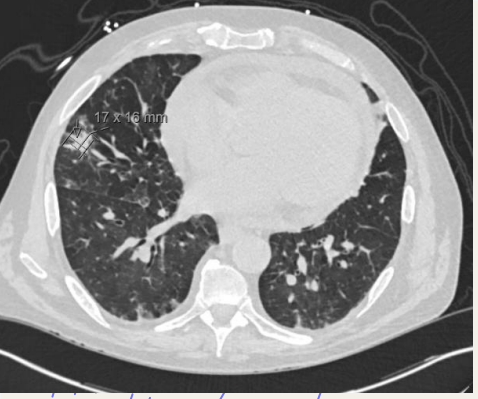
The all-
Cresemb
while it w
treatment g

Cresemba Approved by the FDA for invasive aspergillosis treatment

Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial

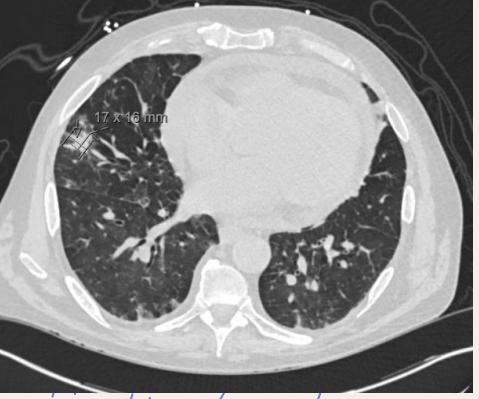
Kieren A Marr [3], Thomas F Patterson [4], Eric J Bow [7], Galia Rahav [8], Dionysios Neofytos [9], Werner J Heinz [13], Raoul Herbrecht [14], Olivier Lortholary [18], Vicki A Morrison [19], George R Thompson 3rd [23], Misun Lee [24],





ID workup

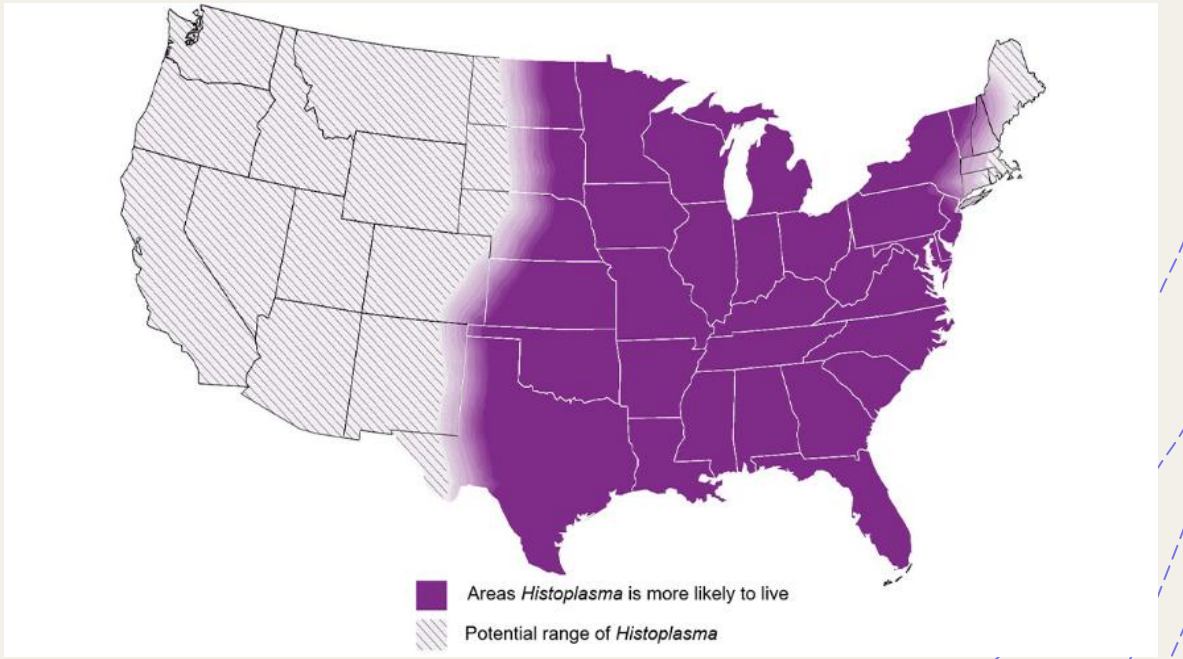
Recommended workup	Results
Blood cultures	Negative
Sputum culture	Negative
Aspergillus galactomannan	Negative
Urine and serum histoplasma ag	Urine Histo = 4.5 Serum Histo = 3.2
Urine blasto antigen	Urine blasto = 2.1
Cryptococcal antigen	Negative



Histoplasmosis

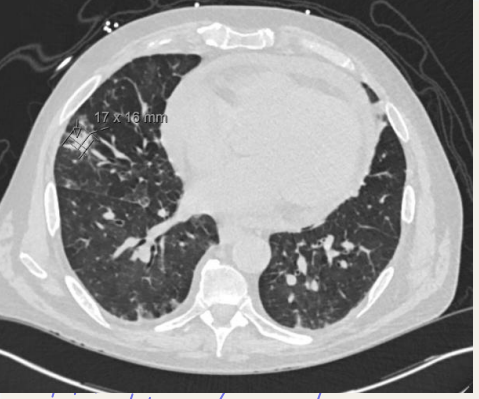
Manifestations

- 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



Histoplasmosis

Diagnosis

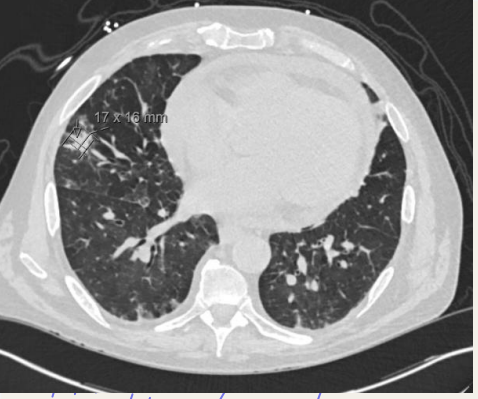
- Culture
- Histopath
- Antigen detection

Sensitivity of Ag testing		
	Pulmonary	Disseminated
Urine	73%	97%
Serum	59%	89%
BAL	93%	

KEEP IN MIND :

- Cross reactivity specially with blastomycosis
- Combining both urine and serum testing increases the likelihood of antigen detection
- The higher the fungal burden of disease the higher the antigen value --> used to track response to therapy

Miller, Rachel... ASTIDCOP. "Endemic fungal infections in solid organ transplant recipients—Guidelines from the AST ID COP." *Clinical Transplantation* 33.9 (2019): e13553.



Histoplasmosis

Pulmonary histoplasmosis Rx

itraconazole

Alternatively : posaconazole, voriconazole

- Duration depends on serial Ag testing and radiographic findings.
- Antigen levels should be measured at the time treatment is initiated, at 2 weeks, 1 month, then every 3 months during therapy
- Net reduction in immunosuppression, especially the calcineurin inhibitors, is an important treatment adjunct.
- Therapeutic monitoring of serum drug levels is strongly recommended to optimize therapy once steady state has been reached

Miller, Rachel... ASTIDCOP. "Endemic fungal infections in solid organ transplant recipients—Guidelines from the AST ID COP." *Clinical Transplantation* 33.9 (2019): e13553.

Clinical Infectious Diseases

IDSA GUIDELINES

2025 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Histoplasmosis: Treatment of Mild or Moderate Acute Pulmonary Histoplasmosis in Adults, Children, and Pregnant People

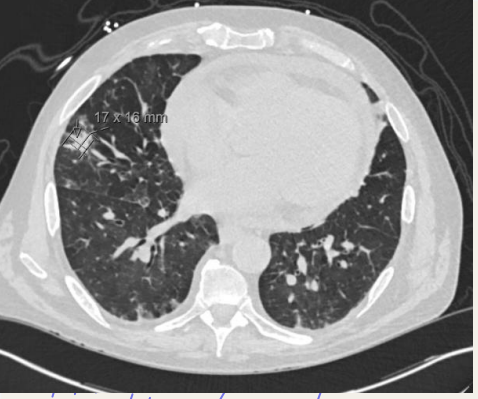
Peter Pappas,[1,a] Robert J. Lentz,[2,a,©] Kayla R. Stover,[3,©] Nathan P. Wiederhold,[4,©] Monica I. Ardura,[5,6,©] John W. Baddley,[7] Nevert Badreldin,[8] Nathan C. Bahr,[9,10,©] Karen Bloch,[11] Carol A. Kauffman,[12] Rachel A. Miller,[13] Satish Mocherla,[14] Michael Saccente,[15] Ilan Schwartz,[13,©] Joshua Wolf,[16,©] Jennifer Loveless,[17,b] Andrej Spec,[18,b,©] and Sandra R. Arnold[19,20,b]

In immunocompromised adults and children presenting with mild or moderate acute pulmonary histoplasmosis who are at moderate to high risk of progression to disseminated disease, the panel suggests antifungal treatment

Table 1. Categories of Immunocompromise and Risk for Disseminated/Severe Histoplasmosis

Categories of immunocompromise represent a continuum rather than distinct categories. Conditions are categorized here as a guide; given limited evidence, this table is not exhaustive or exact.

High	Moderate	Low[a]
Receiving corticosteroids: [15] ≥2 mg/kg/d of prednisone (or equivalent) for persons ≤10 kg or ≥20 mg/d of prednisone (or equivalent) for persons >10 kg for at least 2 wks	Receiving corticosteroids: [15] 0.5–2 mg/kg/d of prednisone (or equivalent) for persons <10 kg or 5–20 mg/d of prednisone (or equivalent) for persons >10 kg for at least 4 wks	Receiving corticosteroids: [15] <0.5 mg/kg/d of prednisone (or equivalent) for persons <10 kg or ≤5 mg/d of prednisone (or equivalent) for persons >10 kg for at least 4 wks
Primary cellular immunodeficiency (eg, SCID, autosomal dominant hyperIgE syndrome [AD HIES], interferon-gamma receptor/IL-12 pathway defects)	Primary immunodeficiency (eg, common variable immunodeficiency, NF-kappaB pathway defects [NEMO], chronic mucocutaneous candidiasis, X-linked hyper IgM syndrome, autosomal recessive HIES)	
Advanced or untreated HIV/AIDS (CD4 <200 cells/mm^3)[b] [16]	HIV (CD4 200–300 cells/mm^3) [16–26]	HIV (CD4 ≥300 cells/mm^3); VL undetectable [16]
Hematopoietic stem cell transplant within 100 d or receiving immunosuppressive therapy for graft versus host disease	Hematopoietic stem cell transplant >100 d prior and no evidence of graft versus host disease	
	Hematologic malignancy	
CAR T-cell therapy within 90 d [27]	CAR T-cell therapy >90 d and resolved cytopenias [27]	
Solid organ transplant and treatment of rejection[c]	Solid organ transplant recipient on maintenance immunosuppressive regimen[c]	
Autoimmune and rheumatic diseases requiring treatment with biologic agents[d], especially those that interfere with T-cell function and granuloma		Autoimmune and rheumatic diseases not requiring treatment



ID workup

Recommended workup	Results
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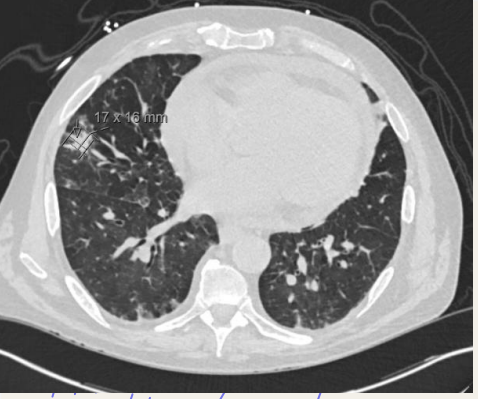
Aspergillus galactomannan	Negative
Urine and serum histoplasma ag	Negative
Urine blasto antigen	Negative
Cryptococcal antigen	1:64

Let's talk about Cryptococcosis



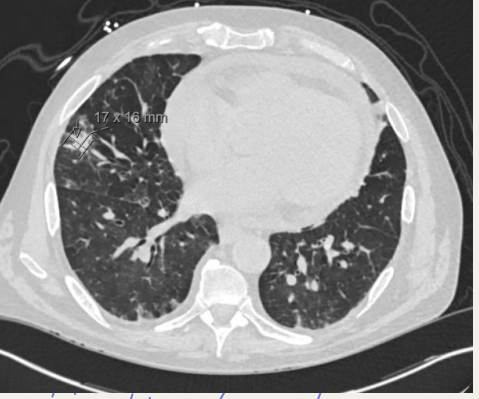
Cryptococcosis

Manifestations

- Pulmonary
- GI disease
- CNS infection
- Cutaneous

- Typically, a late occurring infection, with the median time to onset ranging from 16 to 21 months post-transplantation.
- Reactivation of quiescent infection vs acquisition of primary infection
- Receiving a lung transplant, when compared toother organ type, was independently associated with an increased risk of cryptococcosis
- Receiving a liver transplant when compared to other types was associated with higher risk of developing disseminated disease

Baddley, John W... AST Infectious Diseases Community of Practice. "Cryptococcosis in solid organ transplantation—guidelines from the American Society of Transplantation Infectious Diseases Community of Practice." *Clinical transplantation* 33.9 (2019): e13543.



Cryptococcosis

Diagnosis

- Culture
- Histopath
- Antigen detection

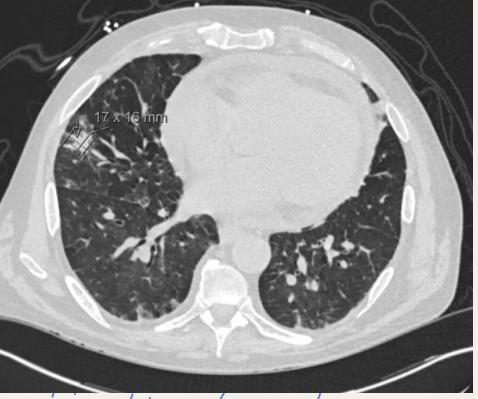
Pulmonary cypto Rx

- fluconazole
- Alternatively : posaconazole, voriconazole

KEEP IN MIND :

- Important to determine extent of disease (in SOT patients, usually recommend an LP)
- Ag testing for CSF and serum is the preferred diagnostic method
- Fungitell will be negative (no glucan in cell wall)
- No need to follow Ag testing but rather symptoms and radiographic evolution

Baddley, John W... AST Infectious Diseases Community of Practice. "Cryptococcosis in solid organ transplantation—guidelines from the American Society of Transplantation Infectious Diseases Community of Practice." *Clinical transplantation* 33.9 (2019): e13543.



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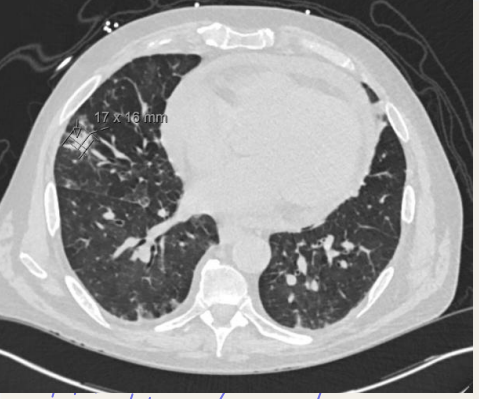
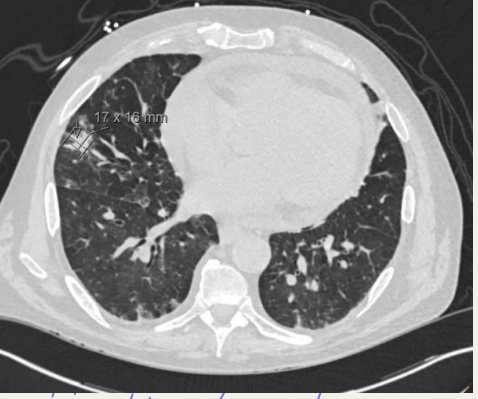
Cryptococcal antigen	Negative

Let's call our friends in pulmonology 



Disseminated fungal infections

	Aspergillosis	Histoplasmosis	Cryptococcosis
Induction	If severe : vori + echinocandin	Amphotericin x 1-2 weeks	Amphotericin + flucytosine for at least 2 week *
Maintenance	voriconazole	Itraconazole for 12 months	Fluconazole 800 mg daily for 8 weeks
Secondary Prophylaxis		None	Fluconazole 200 mg daily
Keep in mind	Serial imaging	Serial antigens + imaging Therapeutic drug levels	*with negative CSF cx



Pearls about azoles

Azole	Histo, blasto,cocci	Aspergillus	Mucor, Rhizopus	QTc prolongation	Toxicities	Keep in mind
Itraconazole	**+**	+	-	Yes	• Hepatotoxicity • Negative inotropy • Pedal edema	All azoles **interact with CNIs** to a different extent --> need to adjust dosing accordingly
Voriconazole	+	**+**	-	Yes	• Hepatotoxicity • Photosensitivity • Visual hallucinations • Alopecia	
Posaconazole	+	+	Salvage	Yes	• Hepatotoxicity	
Isavuconazole	+/-	**+**	**+**	No	• Hepatotoxicity	

Pre transplant screening for fungal infections

Pre-transplant screening for endemic mycoses is most useful in areas endemic for **coccidioidomycosis**, where a pre-transplant history of active disease and/or seropositivity may prompt lifelong azole prophylaxis.

Pre-transplant screening for **histoplasmosis/blastomycosis** is of limited value since latent infection may be present with negative serology. Studies recommend against routine screening.

Pre-transplant screening for **cryptococcosis** is not recommend except if there is radiographic finding suggestive of possible infection.

SPECIAL ISSUE: TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION WILEY

Screening of donor and candidate prior to solid organ transplantation—Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Maricar Malinis[1] | Helen W. Boucher[2] | on behalf of the AST Infectious Diseases Community of Practice

ABSTRACT ONLY · Volume 25, Issue 8, Supplement 1, S782-S783, August 2025

Histoplasmosis Screening Prior to Heart Transplant: A Quality Improvement Analysis from a High-Prevalence Institution

L. Withrow · M. Newlun · A. Sooter · E. Stohs · S. Lundgren · E. Lyden

Journal of Microbiology, Immunology and Infection

Volume 58, Issue 1, February 2025, Pages 103-111

Original Article

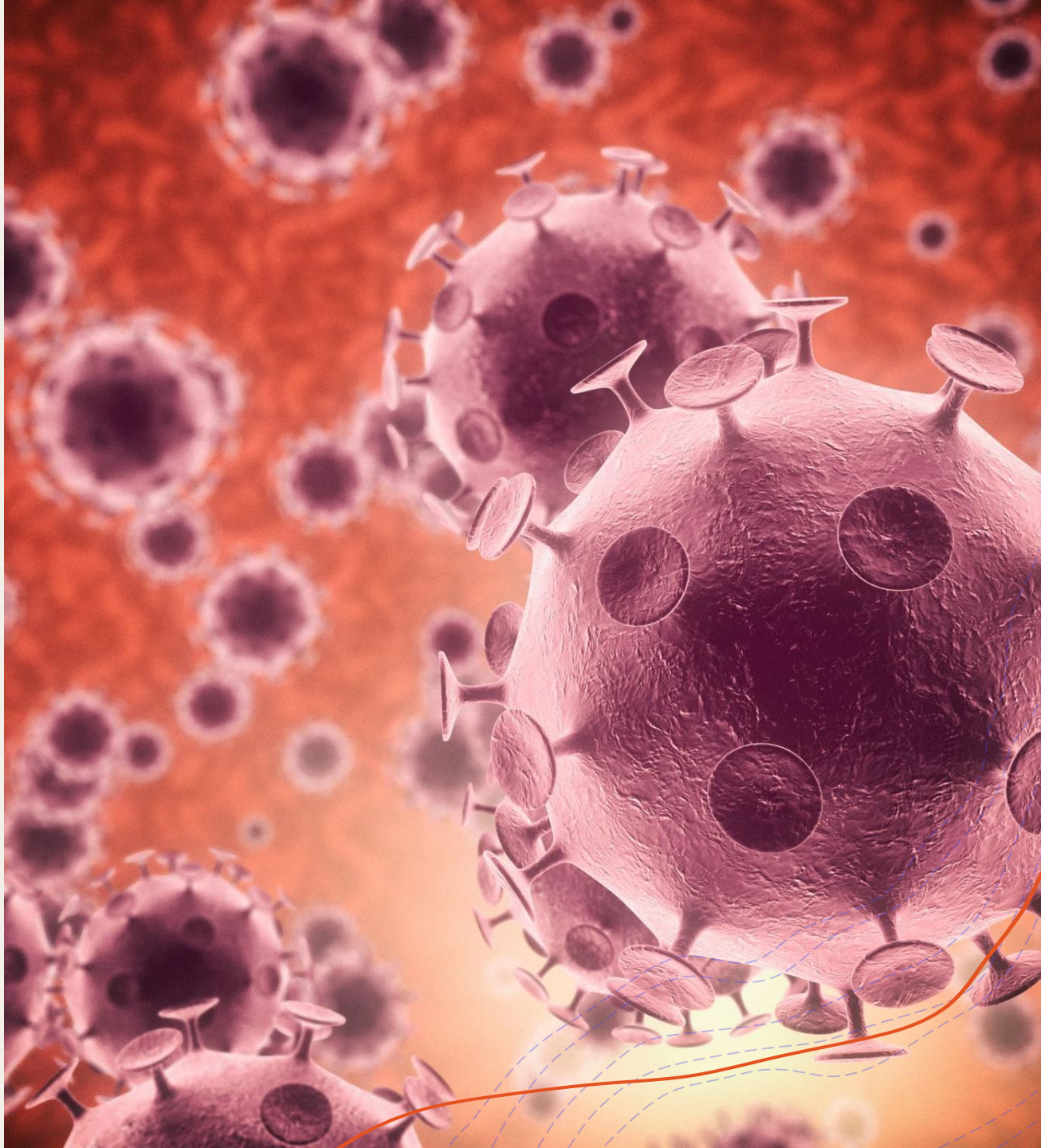
Cryptococcosis in wait-listed liver transplant candidates: Prevalence, manifestations, and risk factors

Wan-Ting Tsai [a b], Aristine Cheng [a], Yu-Chung Chuang [a], Cheng-Maw Ho [c], Yao-Ming Wu [c], Ming-Chih Ho [c], Hsin-Yun Sun [a] ✉, Ray-Hung Hu [c], Yee-Chun Chen [a]

'Tis the Season! Respiratory Virus Review

+ RSV
+ Adenovirus
+ Influenza
+ Human Metapneumovirus

*And Mycoplasma and Parvovirus Infections



Respiratory syncytial virus (RSV)

Year-round prevalence, peak incidence from September through April.

Overall mortality for RSV infections ranges form 10-20% among immunocompromised patients.

In one study 72% of lung txp recipients developed graft dysfunction.

May be associated with bronchiolitis obliterans syndrome.

RSV Prevention and Treatment

+ Prevention:
  - AREXVY
    - Must be 50+ years old
    - Single dose

+ Treatment Considerations:
  + Inhaled ribavirin (logistically difficult, teratogenic potential)
  + PO/IV Ribavirin
  + Consider combination of steroids, ribavirin or IVIG

Adenovirus

Symptoms: Sore throat, fever, acute bronchitis, PNA, conjunctivitis, acute gastroenteritis, urinary tract infections

Prevalent all year (no specific peak)

Highest incidence among intestinal, GI, and kidney transplant recipeints

Adenovirus Prevention and Treatment

Prevention:

- No vaccines.

Treatment:

- Supportive care and reduction in IS
- No FDA approved medications, but could consider cidofovir.

Al-Heeti OM, Cathro HP, Ison MG. Adenovirus Infection and Transplantation. Transplantation. 2022 May 1;106(5):920-927. doi: 10.1097/TP.0000000000003988. Epub 2021 Nov 24. PMID: 34856601; PMCID: PMC9050944.

Influenza

Drug	Adults	Adjustment for renal failure in adults		Children (≥1 y old)	
		Renal function	Dose	Weight	Dose
Oseltamivir	75 mg BID	CrCl ≥ 30 mL/min	75 mg BID	≤15 kg	30 mg BID
		CrCl < 30 mL/min	75 mg OD	16-23 kg	45 mg BID
		Hemodialysis/CAPD	30-75 mg after	24-40 kg	60 mg BID
		CRRT	dialysis	>40 kg	75 mg BID
			75 mg BID	Infants (<1 y old)	
				3 mg/kg/dose BID	

- Prevention
  - Inactivated Flu vaccines yearly!
- Treatment
  - Antivirals: oseltamivir (Tamiflu)
  - Early administration of antivirals is associated with better outcomes. All symptomatic patients should receive antiviral therapy, irrespective of duration of symptoms onset.
  - Duration of antivirals: minimum of 5 days, may be prolonged in cases of persistent clinical symptoms.

Human Metapneumovirus

- Most prevalent in early January through mid-spring.
- Frequent co-infections w/ RSV, influenza, rhinovirus, and COVID (10-30% cases).
- Prevention: No vaccines available.
- Treatment:
  - Supportive care is mainstay of treatment
  - For severe cases: Consider ribavirin with/without IVIG.
  - If lung transplant + lower tract disease, can consider ribavirin with/without IVIG and CS can be considered.

Mohammadi K, Faramarzi S, Yaribash S, Valizadeh Z, Rajabi E, Ghavam M, Samiee R, Karim B, Salehi M, Seifi A, Shafaati M. Human metapneumovirus (hMPV) in 2025: emerging trends and insights from community and hospital-based respiratory panel analyses-a comprehensive review. Virol J. 2025 May 20;22(1):150. doi: 10.1186/s12985-025-02782-y. PMID: 40394641;

Quick Respiratory Viral Review

Viral Infections	Potential Treatments
RSV	Steroids, ribavirin, or IVIG
Adenovirus	No FDA approved meds- supportive care! - If severe case, can consider cidofovir
Influenza	Tamiflu
Human Metapneumovirus	Supportive care is mainstay. - If severe case, can consider Ribavirin, CS, or IVIG

What are mycoplasma infections?

- Types of Mycoplasma/Ureaplasma infections:
  - Mycoplasma pneumoniae, commonly known as "walking PNA".
  - Mycoplasma hominis and ureaplasma spp are frequently commensal urogenital organisms leading to UTI and PID as well as extragenital infections such as PNA and septic arthritis.

Common scenarios to start thinking about mycoplasma/ureaplasma infections

- Lung transplant recipients post-operatively with abrupt onset of encephalopathy.
- Kidney transplant or other immunocompromised patients with UTI sx, but negative cultures.

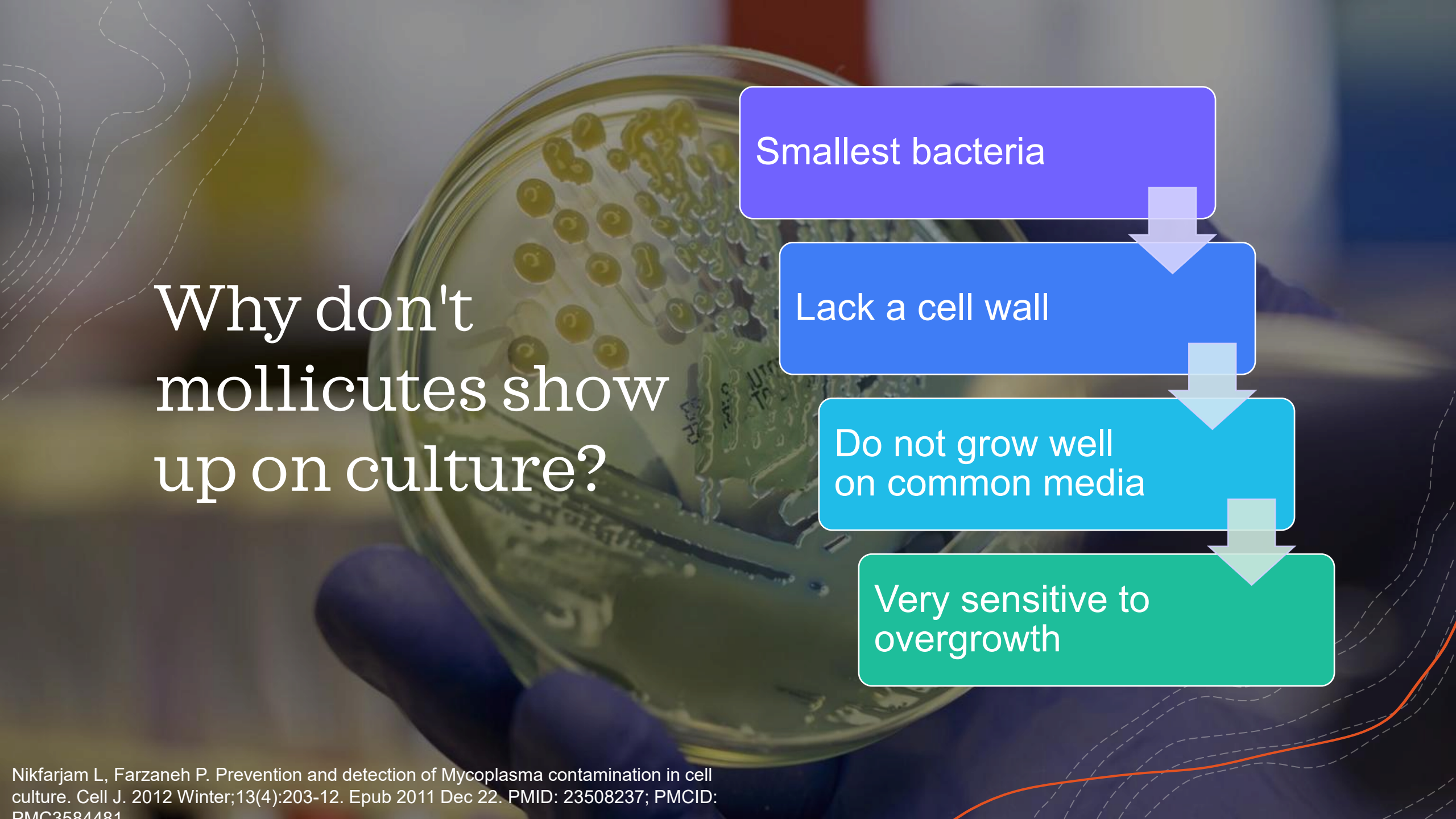
Concern s/p Lung Transplant?

Determine why encephalopathic:

- Anesthesia
- Liver disease
- Poor renal function
- Mollicute infection?

Check serum ammonia level, is it high?

- Why do we check this?



Why don't mollicutes show up on culture?

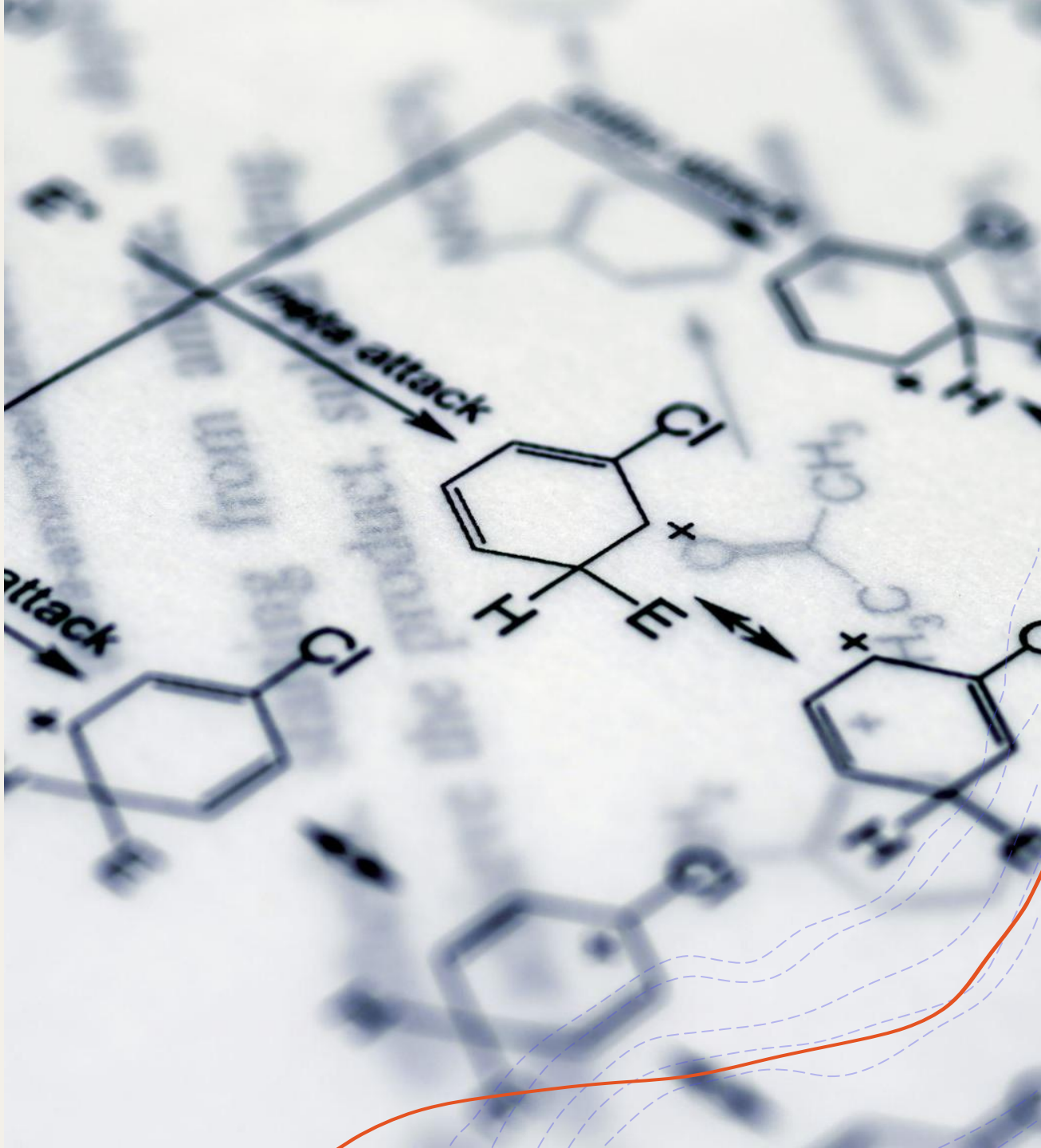
- Smallest bacteria
- Lack a cell wall
- Do not grow well on common media
- Very sensitive to overgrowth

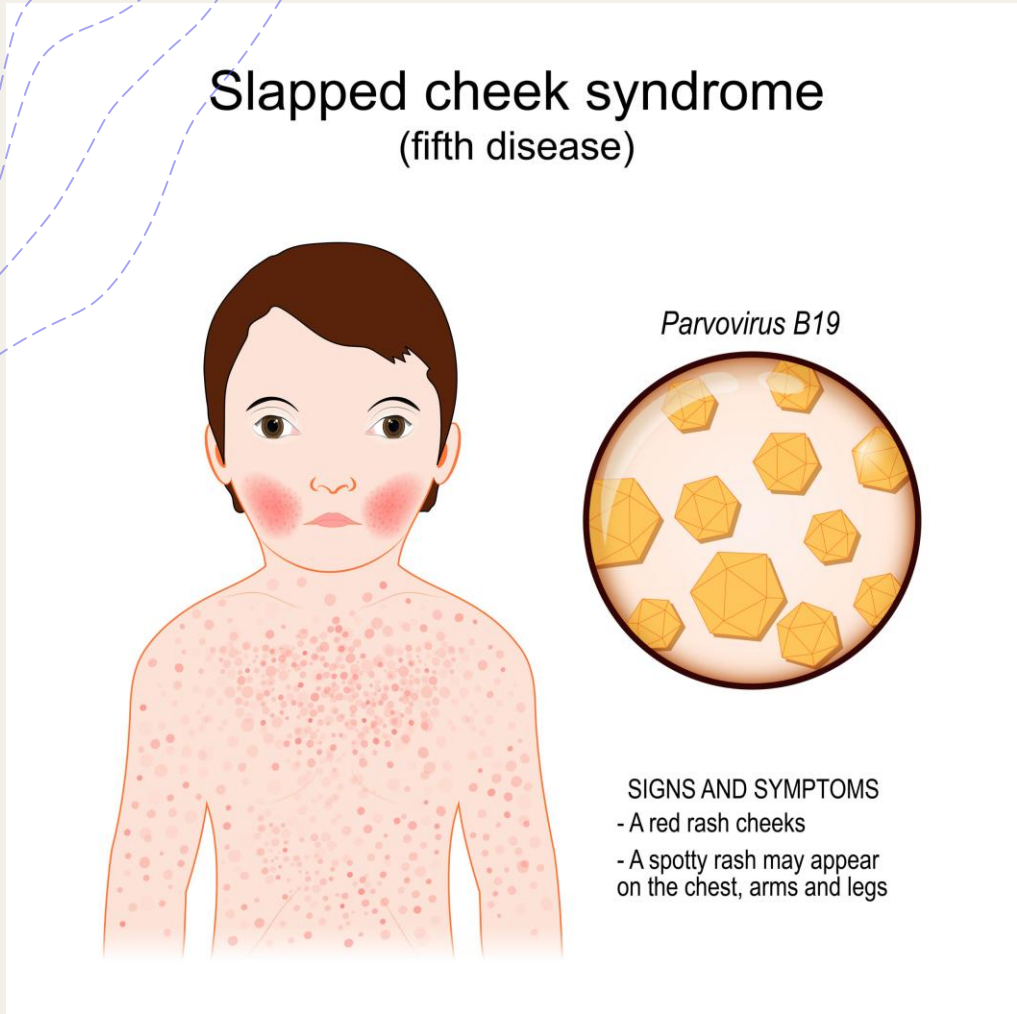
Nikfarjam L, Farzaneh P. Prevention and detection of Mycoplasma contamination in cell culture. Cell J. 2012 Winter;13(4):203-12. Epub 2011 Dec 22. PMID: 23508237; PMCID: PMC3584481

Mycoplasma Diagnosis & Treatment

- Diagnosis: PCR testing!

- Treatment:
  - First line: Doxycyline
  - Second line: Can consider levofloxacin





Parvovirus

- Clinical signs: Usually atypical
  - Otherwise unexplained anemia
  - Pancytopenia
  - Clinical syndromes including:
    - Fever, arthralgia or rash
    - Painful, swollen or stiff joints (adults)

Parvovirus Work-Up

- Initial work up:
  - Parvovirus B19 serology (IgG and IgM) and serum parvovirus PCR.

- Treatment:
  - No antiviral drugs.
  - May consider use of IVIG.

Eid AJ, Ardura MI; AST Infectious Diseases Community of Practice. Human parvovirus B19 in solid organ transplantation: Guidelines from the American society of transplantation infectious diseases community of practice. Clin Transplant. 2019 Sep;33(9):e13535. doi: 10.1111/ctr.13535. Epub 2019 Apr 11. PMID: 30973192.

Questions?