

West Coast Transplant ID Meeting

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██████ patient in █████ 60's

PMHx

- Chronic interstitial nephritis
- Prior kidney transplant (██████ and on HD)
- Coronary artery disease

PSHx

- Kidney Transplant
- AV fistula
- CABG

FHx

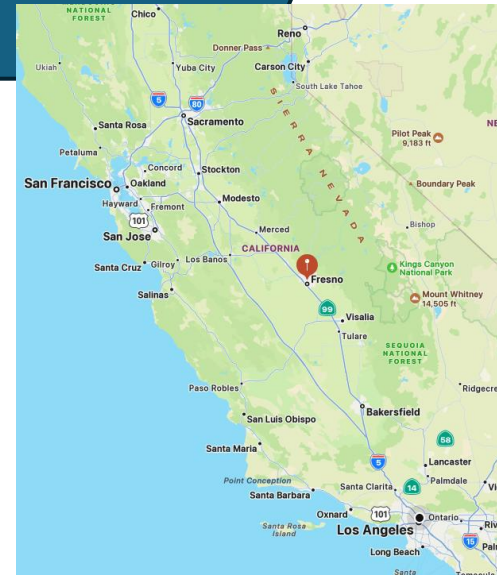
- Non-contributory

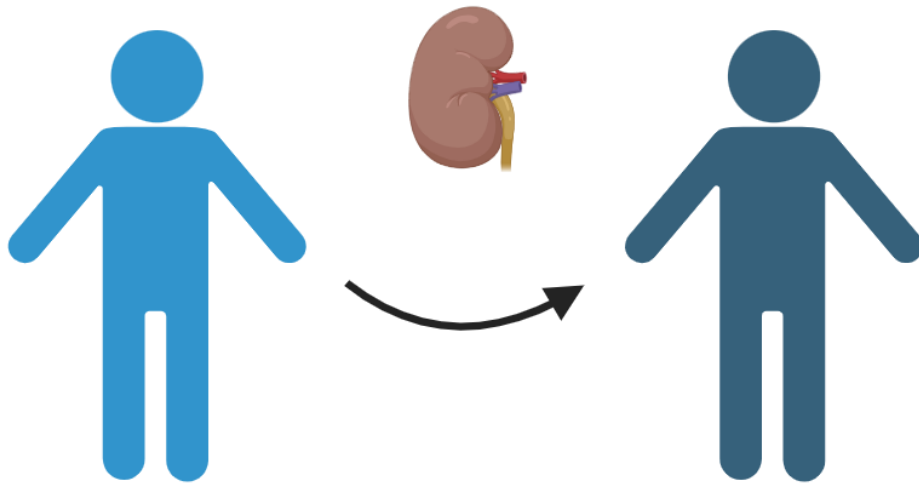
Allergies

- Hives, N/V to sulfa

Social

- Lives near █████, CA
- Not currently employed
- Tends to garden and cuts the grass
- Dog (vaccinated) and cat (limited contact)
- Chickens on property
- City water
- Marijuana use for chronic pain (ingested)





Day 0

Induction
Anti-thymocyte
globulin
Methylprednisolone

Maintenance
Mycophenolate
Tacrolimus
Prednisone

CMV D-/R+
Valganciclovir

PJP
Dapsone

Coccidioides
Isavuconazole (QTc)

Slow graft function (Cr 5.42)
Discharged Day 3

(+) Fatigue
(+) Graft pain
(+) Reduced UOP



Day 5

WBC count 7.2 (ALC 100)

Hemoglobin 8.2

Platelets 150

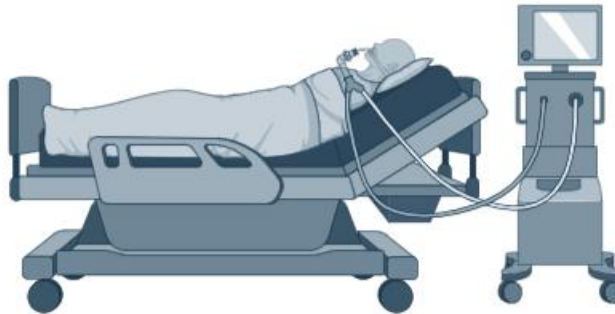
Sodium 135

Bicarbonate 22

Creatinine 5.5

LFTs normal

INR 1.59

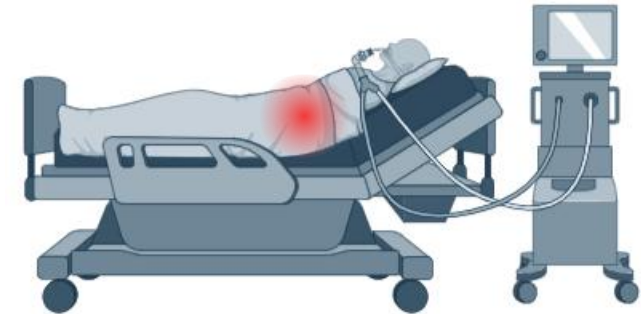


Day 5

Readmitted as Cr
remains 5.5

Kidney biopsy (ATN)

AHRF after biopsy,
required BiPAP
then intubation



Day 8

(+) Erythema and induration
of graft site
(+) ↑O₂ requirement
(+) New pressor requirement



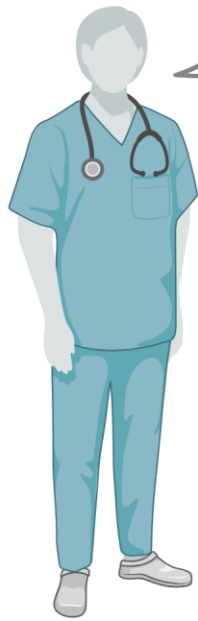
“Increased size of
transplant kidney with
regional loculated fluid
and inflammatory
changes, post-surgical
vs infectious”



Antimicrobials
Vancomycin
Cefepime

“New diffuse
consolidative
bilateral opacities”





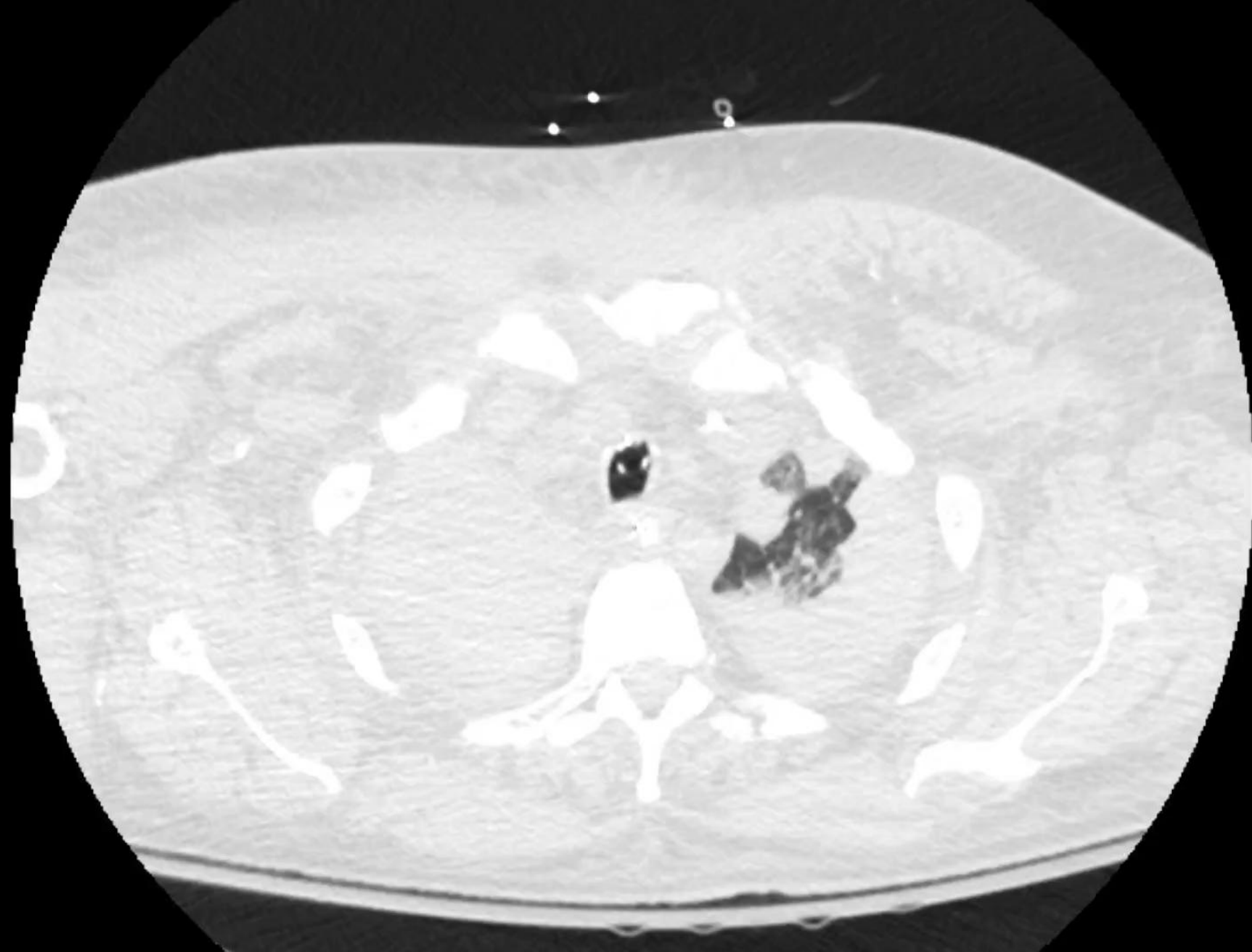
...a lot of **secretions** in the airways, it looks like they **aspirated** after their biopsy.

Support

Norepinephrine
Vasopressin
Hydrocortisone

Antimicrobials

Vancomycin
Meropenem
Amikacin x1
Micafungin
Ganciclovir

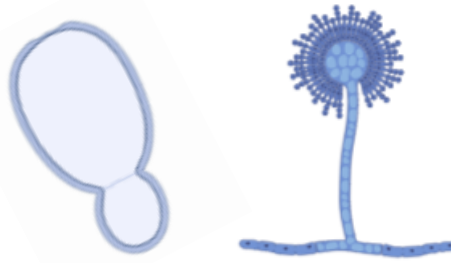


██████ renal transplant recipient in █████ 60's s/p LDKT with ATG induction, DGF, presenting 5 days post-transplant for kidney biopsy complicated by AHRF, shock and erythema of the surgical wound.

What is the most likely cause of the patient's **respiratory failure**?



Bacteria



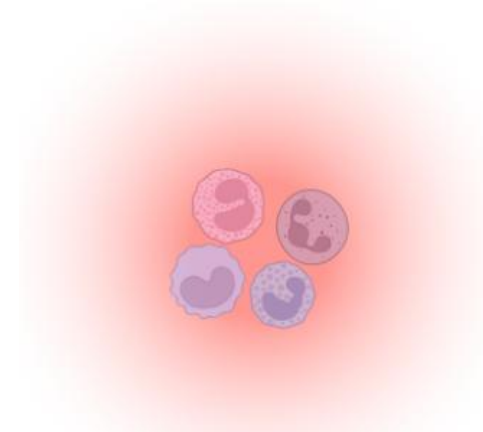
Fungus



Virus



Parasite

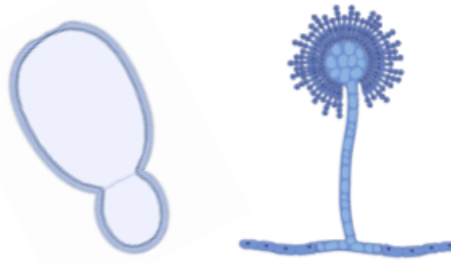


Inflammatory (non-infectious)

What is the most likely cause of the patient's **wound induration and erythema**?



Bacteria



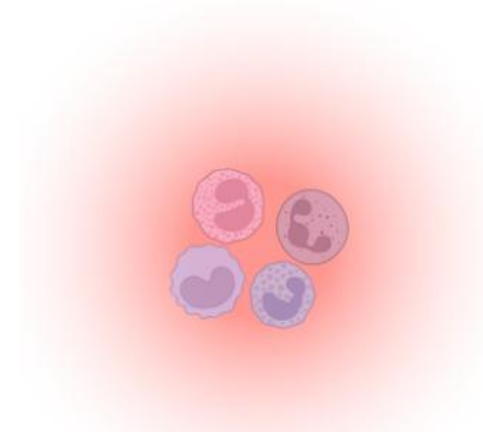
Fungus



Virus



Parasite



Inflammatory (non-infectious)



Day 10

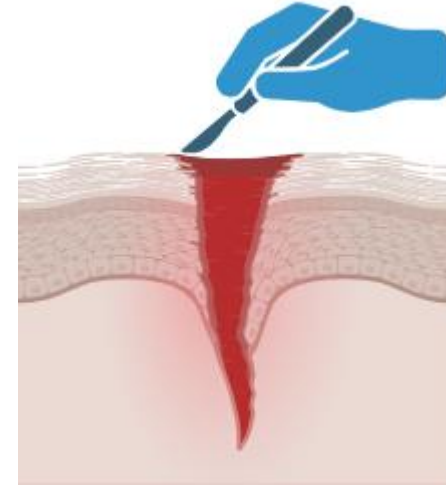
SVT and PEA arrest
30 minutes with
ROSC



Bronchoscopy

Day 11

VV ECMO started



Day 12

I&D transplant
surgical wound



Results

Urine

- Urine culture 20,000 CFU/mL *Serratia marcescens*
- Legionella urine antigen negative
- Strep pneumoniae urine antigen negative
- Histo urine Ag negative

Swabs

- RVP+ Rhino/Enterovirus

Blood

- Blood cultures negative
- BDG negative
- CrAg negative
- CMV viral load negative

Results

Bronchoscopy

- Galactomannan 1.56
- Fungal culture growing mold (septate hyphae)
- Bacterial cultures no growth to date

Antimicrobials

Vancomycin
Meropenem
Amikacin x1
Micafungin
Ganciclovir

Would you make any changes to
antimicrobial therapy?

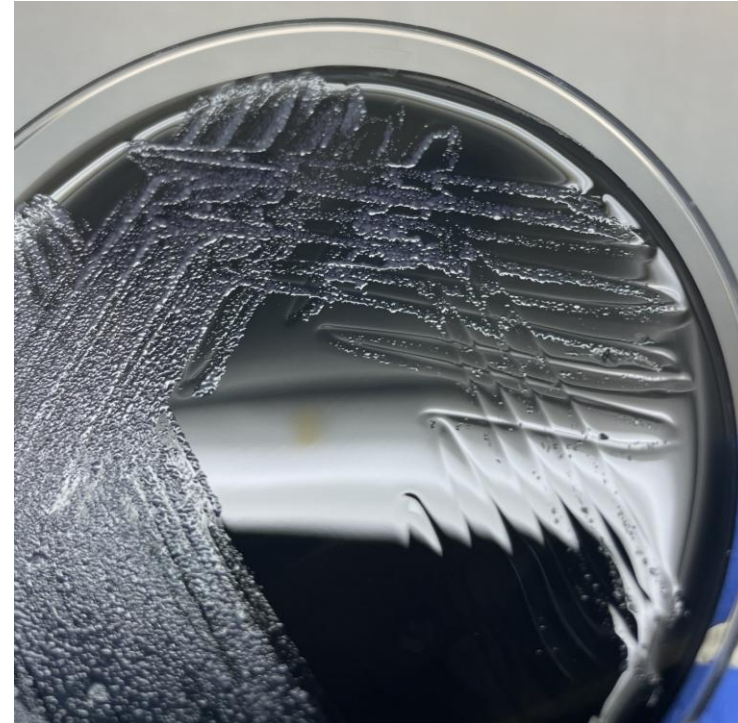
Day 13



Results

Bronchoscopy

- Galactomannan 1.56
- Fungal culture ***Aspergillus fumigatus***
- Standard bacterial cultures negative



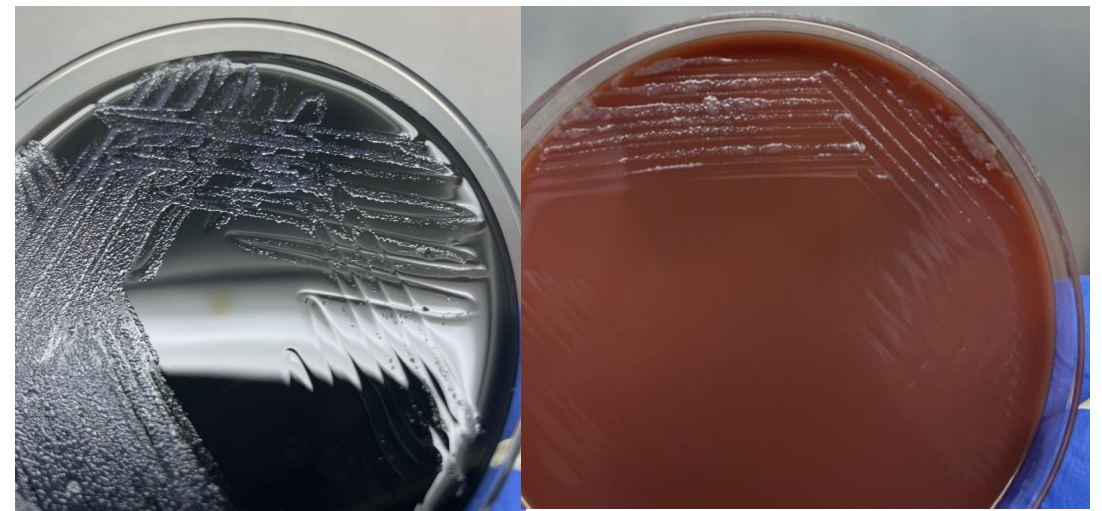
Results

Bronchoscopy

- Galactomannan 1.56
- Fungal culture ***Aspergillus fumigatus***
- Standard bacterial cultures negative
- BCYE (+) ***Legionella pneumophila***
- ***Legionella* PCR positive**

Surgical cultures

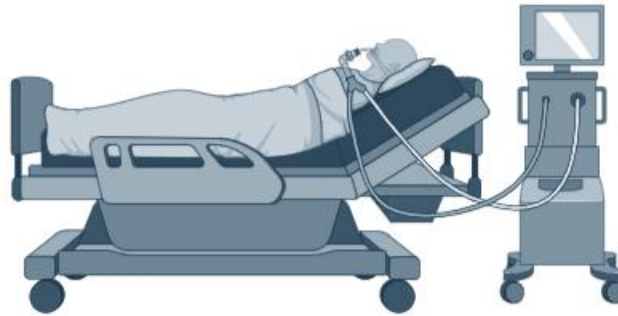
- Gram stain 4+ GNR (no growth)
- Plated on BCYE (+) *Legionella pneumophila*
- Later grew on **chocolate agar**





Day 14

Antibiotics
changed to
levofloxacin



Day 15

Remained critically
ill, family withdrew
care.

IP Investigation @ Hospital and Hotel

- Sinks
- Showers
- Ice machines
- **No source identified**
- Donor feels well

CDC Specimen

Test

Legionella Genus Screen*

Bi-plate*

Fluorescence*

Result

Positive

None

Comments and Disclaimers

* Reference Value: Not applicable

Test

Legionella pneumophila typing Real-Time PCR for isolates*

Legionella species (ssrA)*

Legionella pneumophila (mip)*

Legionella pneumophila SG1 (wzm)*

Final Identification*

Result

Detected

Detected

Not Detected

Legionella pneumophila (not Serogroup 1)

DOI: 10.1111/tid.12745

ORIGINAL ARTICLE

Legionnaires' disease in transplant recipients: A 15-year retrospective study in a tertiary referral center

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Vivian Hawkins³ | Zach Stednick¹ | Lois A. Helbert² | William A. Glover³ |
Estella Whimbey⁵ | Jeffrey Duchin^{5,6} | Guang-Shing Cheng^{5,7} | Steven A. Pergam^{1,2,5,7}

Legionella in SOT Recipients

- Single center, retrospective study at University of Washington of Legionella cases in SOT and HSCT.
- 22 transplant recipients with Legionnaires' disease identified
→ 10 SOT recipients and 12 HSCT recipients

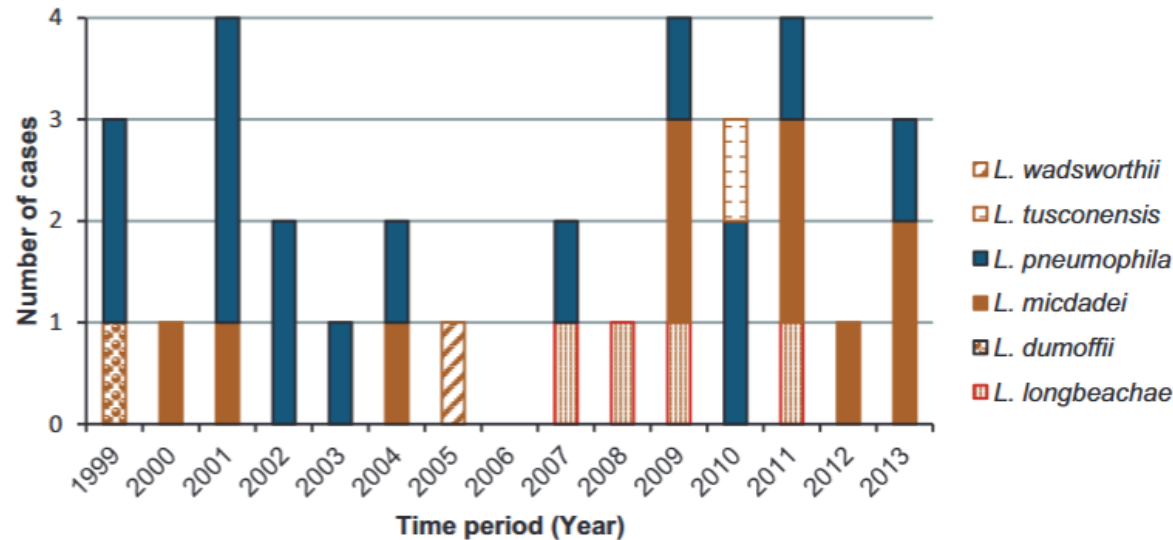


TABLE 1 *Legionella* pneumonia demographics, risk factors, and outcomes among transplant recipients (n=22)

SOT	
Total number of cases	10
<i>Legionella</i> species	<i>L. pneumophila</i> (5) <i>L. micdadei</i> (3) <i>L. longbeachae</i> (2)
Specimen type	BAL (5) Urine (3) Tissue (2)
Median age, IQR	55 (49-61) years
Gender, Male	6 (60%)
Risk factor specific characteristics	Organ transplanted: Time of infection relative to transplant: Median (range): • 845 (12, 321) months • Rejection, 6 (60%) • Heart, 4 (40%) • Kidney, 2 (20%) • Kidney-pancreas, 2 (20%) • Lung, 1 (10%) • Liver, 1 (10%) Immunosuppressive medication: • Corticosteroids, 10 • Cyclosporine, 1 • Tacrolimus, 8 • Mycophenolate, 7 • Rituximab, 1 • Azathioprine, 1 • Anti-thymocyte globulin, 1 • Alemtuzumab, 1
Intercurrent infections	0
Imaging	Nodules, 4 (40%) Consolidation, 4 (40%) Abscess/cavity, 0 Pleural effusion, 2 (20%)
Seasonal associations	Fall, 4 (40%), Spring, 4 (40%), Winter, 2 (20%), Summer, 0 (0%)
Outcome	
<i>Legionella</i> -attributed mortality	1 (10%)
Admission to intensive care unit	3 (30%)
Intubation/mechanical ventilation	1 (10%)

- Most cases identified by culture (86%) and UAT (14%).
- A third of patients were not on empiric therapy covering *Legionella* at time of diagnosis.
- Mortality rate was low in SOT (10%) but high in HSCT (50%)

Legionella in SOT Recipients

Conclusions:

- *Legionella* is an opportunistic infection after transplant with high morbidity and mortality.
- UAT had limited sensitivity for ruling out *Legionella* in immunocompromised hosts in this series.
- Imaging findings can include consolidations, nodules, cavitations, effusions.
- Numerous concurrent diagnostic possibilities (e.g. PJP, CMV) may confound diagnosis.

Legionnaires Disease in Solid Organ Transplant Recipients

A Decade-Long Nationwide Study in France

Guillaume Thizy, MD; Adrien Flahault, MD, PhD; Anne Scemla, MD; Olivier Roux, MD; Sophie Jarraud, MD; David Lebeaux, MD, PhD; Jacques Pouchot, MD, PhD; Gabriela Gautier-Vargas, MD; Paolo Malvezzi, MD; Marlene Murris, MD; Fanny Vuotto, MD; Sophie Girerd, MD; Nathalie Pansu, MD; Teresa Antonini, MD; Laure Elkrief, MD; Benoit Barrou, MD, PhD; Camille Besch, MD; Mathieu Blot, MD, PhD; Aude Boignard, MD; Henri Brenier, MD; Audrey Coilly, MD, PhD; Corentin Gouezel, MD; Kaminski Hannah, MD; Pauline Housssel-Debry, MD; Jerome Jouan, MD, PhD; Hervé Lecuyer, MD, PhD; Anne Limelette, MD; Charles Edouard Luyt, MD, PhD; Boris Melloni, MD, PhD; Christophe Pison, MD, PhD; Cédric Rafat, MD; Jean-Michel Rebibou, MD; Eric Savier, MD; Betoul Schvartz, MD; Olivier Scatton, MD, PhD; Fatouma Toure, MD; Shaida Varnous, MD, PhD; Pauline Vidal, MD; Emilie Savoye, MD, PhD; Florence Ader, MD, PhD; Olivier Lortholary, MD, PhD; Fanny Lanternier, MD, PhD; and Emmanuel Lafont, MD



Legionella in SOT Recipients

- Multi-center retrospective cohort study in France (*Legionella* is mandatorily reported) from 2009-2019.
- 101 adult patients from 51 centers identified.

TABLE 1] Comparison of Baseline Characteristics Between Severe and Nonsevere *Legionella* Infections Among 101 Solid Organ Transplant Recipients

Characteristic	Total (N = 101)	Legionellosis		OR	95% CI	P Value
		Nonsevere (n = 44)	Severe (n = 57) ^a			
Male sex	79 (78.2)	36 (82)	43 (75)	0.68	0.25-1.78	.44
Age, y ^b	62 (52-68)	61 (50-66)	62 (53-68)	1.01	0.97-1.04	.67
Comorbid conditions						
Chronic kidney disease	68 of 98 (69.4)	30 of 41 (73)	38 (67)	0.73	0.30-1.76	.49
Diabetes mellitus	39 (38.6)	17 (39)	22 (39)	1.00	0.45-2.25	> .99
Congestive heart failure	25 of 98 (25.5)	8 (18)	18 of 56 (32)	2.13	0.85-5.76	.11
Solid tumor	25 of 100 (25)	9 (20)	16 (28)	1.52	0.61-3.99	.38
Smoking	17 of 100 (17)	8 (18)	9 (16)	0.84	0.29-2.45	.75
Liver disease	13 (12.9)	4 (9.1)	9 (16)	1.87	0.56-7.34	.31
COPD	11 of 97 (11.3)	4 of 42 (9.5)	7 (12)	1.33	0.37-5.38	.66
Hematologic malignancy	3 (3)	2 (4.5)	1 (1.8)	0.38	0.02-4.04	.41
HIV infection	3 (3)	2 (4.5)	1 (1.8)	0.38	0.02-4.04	.41
Transplanted organ						
Kidney	64 (63.4)	34 (77)	30 (53)	0.33	0.13-0.77	.01
Heart	12 (11.9)	1 (2.3)	11 (19)	10.3	1.88-192	.004
Liver	16 (15.8)	6 (14)	10 (18)	1.35	0.46-4.27	.59
Other ^c	9 (8.9)	3 (6.8)	6 (11)	1.61	0.40-7.98	.51
Immunosuppressive drugs						
No. of immunosuppressive drugs	3 (2-4)	3 (2-4)	3 (2-4)	1.16	0.64-2.12	.62
Corticosteroids	80 (79.2)	32 (73)	48 (84)	2.00	0.76-5.43	.48
Corticoid dose, mg per d	10 (5-12.4)	9 (5-10)	10 (5-15)	1.02	0.99-1.07	.16
Calcineurin inhibitors	74 (73)	34 (77)	40 (70)	0.69	0.27-1.69	.42
Tacrolimus	48 (47.5)	22 (52)	25 (45)	0.71	0.32-1.57	.40
Cyclosporine	26 (25.7)	10 (24)	14 (25)	1.07	0.44-2.69	.88
Mycophenolate mofetil	76 (75.2)	36 (82)	40 (70)	0.52	0.19-1.32	.17
mTOR inhibitor	27 (26.7)	9 (20)	18 (32)	1.79	0.73-4.67	.21
Early-onset legionellosis ^d	11 of 99 (11.1)	1 of 43 (2.3)	10 (18)	9.13	1.64-171	.008
Opportunistic infection within 6 mo ^e	10 of 99 (10.1)	3 of 42 (7.1)	7 (12)	1.82	0.47-8.87	.39
CMV infection within 6 mo ^e	4 of 99 (4)	0 of 42	4 of 57 (7)	NA ^f	NA ^f	.32
Acute rejection episode in the 6 mo before diagnosis ^e	8 of 96 (8.3)	5 of 42 (12)	3 of 55 (5.5)	0.42	0.08-1.80	.24
TMP-SMX prophylaxis	4 of 100 (4)	1 (2.3)	3 of 56 (5.4)	2.43	0.30-50.2	.64

TABLE 2] Characteristics of 101 Patients With Legionellosis After Transplantation: Diagnostic, Treatment, and Outcomes

Characteristic	Total (N = 101)	Legionellosis		OR	95% CI	P Value
		Nonsevere (n = 44)	Severe (n = 57)			
Clinical						
Time to appropriate treatment, d ^a	6 (3-10)	6 (3-10)	6 (3-9)	1	0.97-1.05	.86
Fever > 38.5 °C	76 of 96 (79.2)	35 of 41 (85)	41 of 55 (75)	0.50	0.16-1.40	.19
Respiratory symptoms	77 of 95 (81.1)	28 of 40 (70)	49 of 55 (89)	3.50	1.22-11.0	.019
GI symptoms	49 of 98 (50)	21 of 43 (50)	28 of 55 (51)	1.09	0.49-2.42	.84
Neurologic symptoms	13 of 95 (13.7)	5 of 41 (12)	8 of 54 (15)	1.25	0.38-4.45	.71
Radiologic^b						
Lung consolidation	92 of 98 (94)	38 of 42 (90)	54 of 56 (96)	2.84	0.53-21.3	.51
Interstitial syndrome	55 of 85 (65)	22 of 38 (58)	33 of 47 (70)	1.71	0.70-4.26	.24
Pleural effusion	22 of 88 (25)	5 of 38 (13)	17 of 50 (34)	3.40	1.19-11.3	.022
Bilateral involvement	40 of 95 (42)	11 of 42 (26)	29 of 53 (55)	3.41	1.45-8.42	.005
Nodule	12 of 67 (18)	4 of 28 (14)	8 of 29 (21)	1.55	0.43-6.37	.51
Biological						
Liver enzymes elevation ^c	25 of 83 (30.1)	9 of 36 (24)	16 of 47 (34)	1.55	0.60-4.19	.37
Lymphocyte count < 500/mm ³	26 of 70 (37.1)	5 of 30 (17)	21 of 40 (52)	5.53	1.87-19.0	.002
Hyponatremia < 135 mM at presentation	49 of 87 (56.3)	23 of 36 (64)	26 of 51 (51)	0.59	0.24-1.40	.23
C-reactive protein, mg/L	300 (202-384)	288 (211-349)	323 (165-304)	1	1.00-1.00	.47
Microbiological						
Negative UAT results for <i>Legionella</i> at presentation	16 of 97 (16.5)	3 of 42 (6.8)	13 of 53 (23)	4.44	1.31-20.4	.015
Positive sputum culture results	7 of 34 (20.6)	2 of 12 (17)	5 of 12 (23)	1.47	0.26-11.6	.67
Positive lower respiratory specimen culture results ^d	24 of 45 (53.3)	6 of 13 (46)	18 of 32 (56)	1.50	0.41-5.65	.54
Positive PCR results for <i>Legionella</i> in respiratory specimen ^e	22 of 25 (88)	7 of 7 (100)	15 of 18 (83)	NA ^f	NA ^f	.53

Characteristic	Total (N = 101)	Legionellosis		OR	95% CI	P Value
		Nonsevere (n = 44)	Severe (n = 57)			
Treatment						
Monotherapy						
Fluoroquinolone	51 of 97 (53)	25 of 43 (58)	26 of 54 (48)	0.67	0.30-1.49	.33
Macrolide	13 of 97 (13)	6 of 43 (14)	7 of 54 (13)	0.92	0.28-3.07	.89
Combination therapy	33 of 97 (34)	12 of 43 (28)	21 of 54 (39)	1.64	0.70-3.97	.25
Rifampicin plus macrolide	1 of 97 (1)	0 of 43	1 of 54 (1.9)	NA ^f	NA ^f	> .99
Fluoroquinolone plus macrolide	30 of 97 (31)	11 of 43 (26)	19 of 54 (35)	1.54	0.66-3.91	.31
Fluoroquinolone plus rifampicin	2 of 97 (2)	1 of 43 (2.3)	1 of 54 (1.9)	0.78	0.03-20.4	.87
Duration of antimicrobial therapy, d	20 (13-21)	20 (13-21)	20 (14 -21)	0.99	0.99-1.07	.26
Outcome						
Mechanical ventilation	27 of 96 (28)	0	27 of 52 (51.9)	...	...	...
Hemodynamic compromise	21 of 97 (22)	0	21 of 53 (39.6)	...	...	...
ARDS	18 of 97 (19)	0	18 of 53 (34)	...	...	...
Dialysis	24 of 94 (26)	0	24 of 50 (48)	...	...	...
30-d mortality	8 of 101 (7.9)	0	8 (14)	...	...	...
3-mo mortality	12 of 99 (12.1)	0 of 43	12 of 56	...	...	...
Relapse	1 (1) ^e	0	1 (1.8)	...	...	...
CMV infection shortly after LD ^g	9 (8.9)	2 (4.5)	7 (12.3)	2.94	0.67-20.5	.16
Follow-up, mo	37.3 (13.6-67.3)	38 (26-71)	36 (4-66)	...	...	...

TABLE 3] Multivariate Analysis of Risk of Severe Legionellosis^a

Characteristic	Univariate			Multivariate		
	OR	95% CI	P Value	OR	95% CI	P Value
Diabetes mellitus	1.00	0.45-2.25	> .99	1.19	0.40-3.62	.8
Transplanted organ						
Kidney	0.33	0.13-0.77	.01	0.57	0.08-3.63	.5
Heart	10.3	1.88-192	.004	14.3	0.8-579	.10
Liver	1.35	0.46-4.27	.59	1.24	0.13-11.5	.8
Respiratory symptoms	3.50	1.22-11.0	.019	8.43	1.88-49.8	.010
Pleural effusion	3.40	1.19-11.3	.022	4.32	1.14-19.2	.039
Bilateral involvement	3.41	1.45-8.42	.005	2.34	0.79-7.25	.13
Lymphocyte count < 500/mm ³	5.53	1.87-19.0	.002	6.18	1.57-30.1	.014
Negative UAT results for <i>Legionella</i> at presentation	4.44	1.31-20.4	.015	5.37	1.14-34.5	.047

Boldface values are those with statistical significance ($P < .05$). UAT = urinary antigen test.

^aDefined as admission to the ICU or death within 30 d.

Legionella in SOT Recipients

- 60 patients (59%) received empiric antibiotic therapy
→ Only 28 with *Legionella* active therapy
- Time from symptom onset to treatment was much shorter with positive UAT compared to negative UAT (6 days vs 11 days, $p = 0.038$)
- Incidence rate in France in SOT recipients was about 1.5 cases per 10,000 annually

Legionella in SOT Recipients

Conclusions:

- Legionella is a rare pathogen following SOT.
- Occurs predominantly in the late post-transplant period.
- UAT was positive in >90% of cases in this series.
- Severe disease associated with respiratory symptoms, bilateral pulmonary involvement, lymphopenia, and negative UAT.



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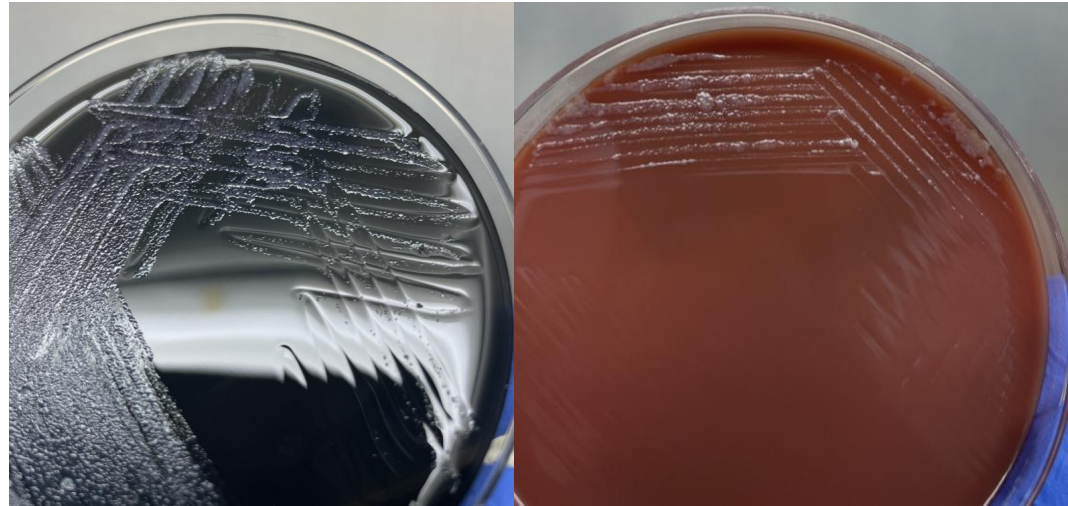
CASE REPORT

November 2015 Volume 53 Issue 11

<https://doi.org/10.1128/jcm.01116-15>

Isolation on Chocolate Agar Culture of *Legionella pneumophila* Isolates from Subcutaneous Abscesses in an Immunocompromised Patient

Mohammed Barigou^a, Laurent Cavalie^{b,c,d}, Benjamin Daviller^b, Damien Dubois^{b,c,d}, Benoît Manton^b, Pierre Delobel^{a,c,d}, Alexa Debard^a, Marie-Françoise Prere^{b,e}, Bruno Marchou^{a,d}, Guillaume Martin-Blonde^{a,c,d}



Legionella and L-Cysteine

Medium	Base / major nutrients	Enrichments / growth factors	Antibiotic components (standard formulation)	Legionella growth?
Chocolate agar	Agar + nutrient base (casein and meat peptone base)	X (hemin) and V (NAD)	None	No* (Legionella typically needs L-cysteine and may be outcompeted by flora).
BCYE agar (without L-cysteine)	Buffered charcoal yeast extract: yeast extract, activated charcoal, ACES buffer, agar	α -ketoglutarate, ferric pyrophosphate	None	No*
BCYE agar (with L-cysteine)	Buffered charcoal yeast extract: yeast extract, activated charcoal, ACES buffer, agar	α -ketoglutarate, ferric pyrophosphate, L-cysteine	None	Yes

*Rare reports of growth.

Thank You

Contact: akoff@health.ucdavis.edu