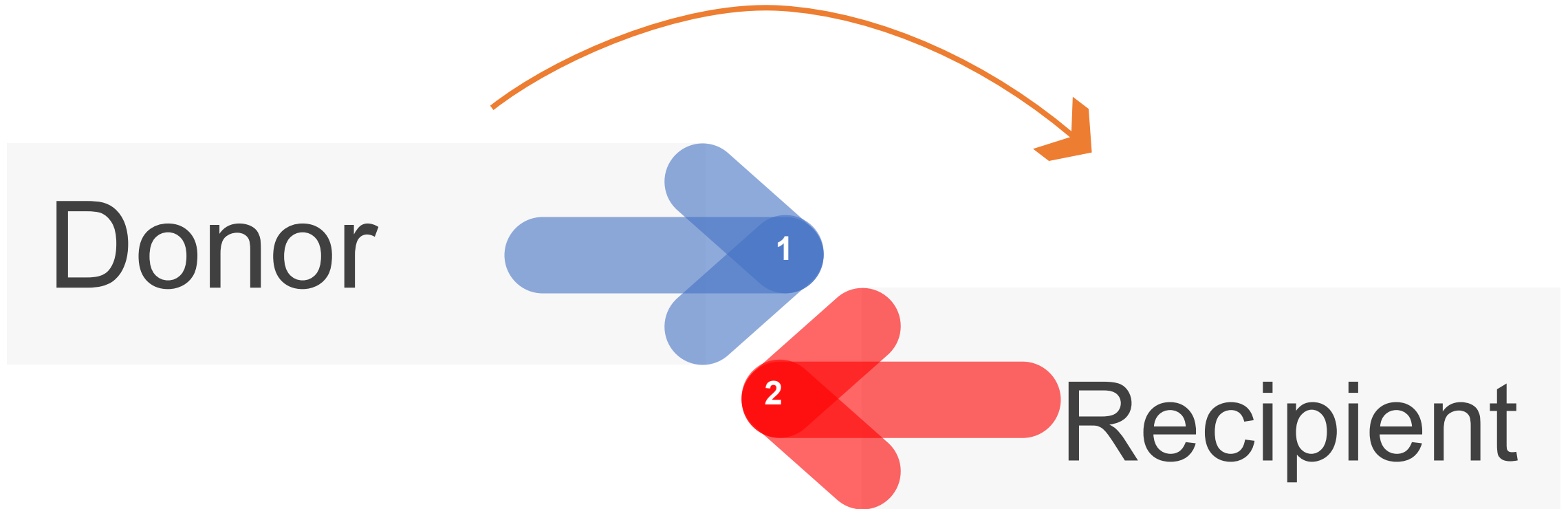


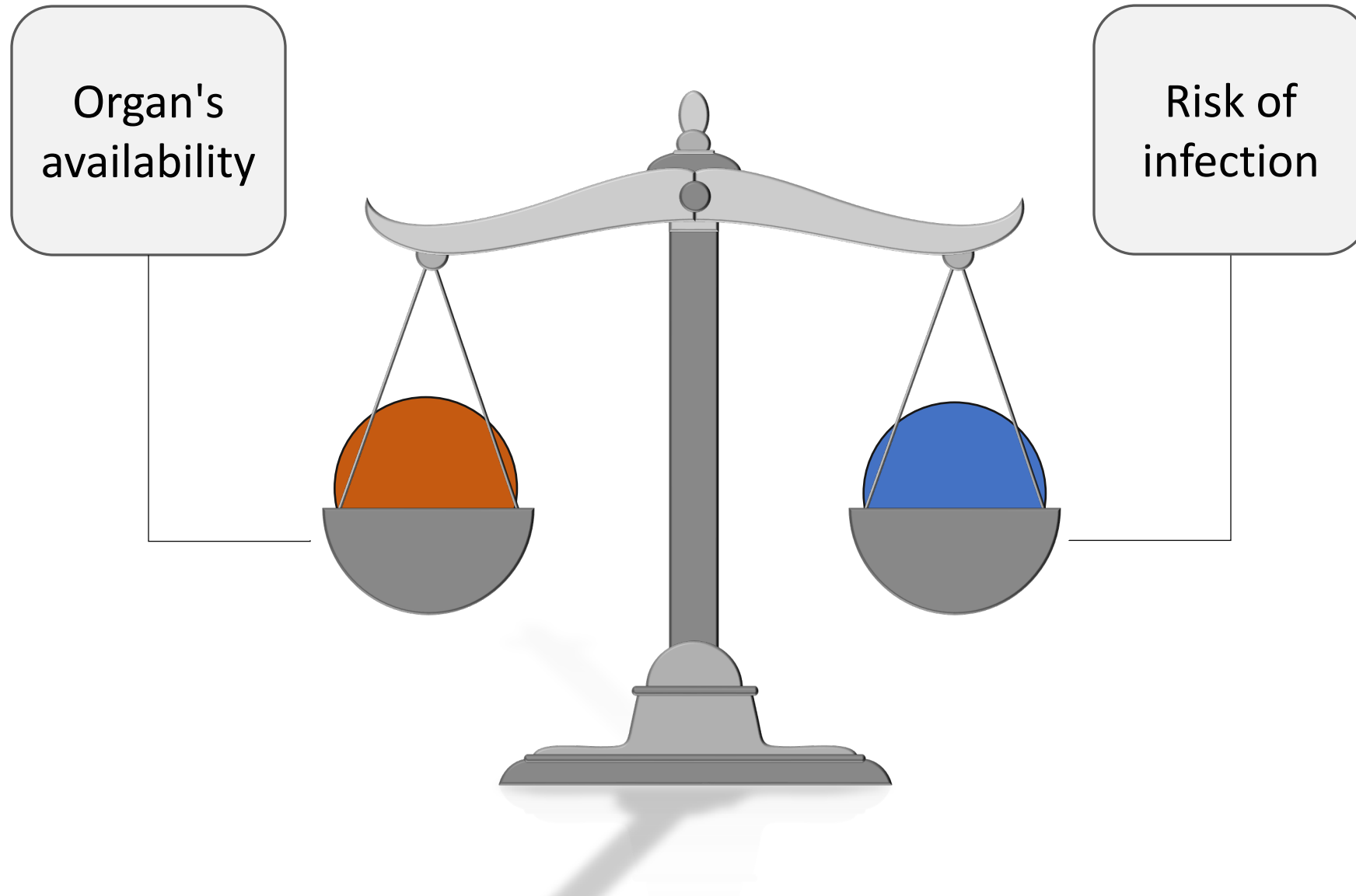
Infectious diseases risk assessment, what should we know prior to transplant?

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# Infectious Diseases risk assessment



# Remember the balance



# Risk levels for potential organ donors : Italian National Transplant Centre

**Unacceptable risk**

Includes HIV infection, metastatic cancer, untreatable systemic infection

**Increased but acceptable**

Risk- Benefit assessment

**Calculated risk**

Prophylaxis

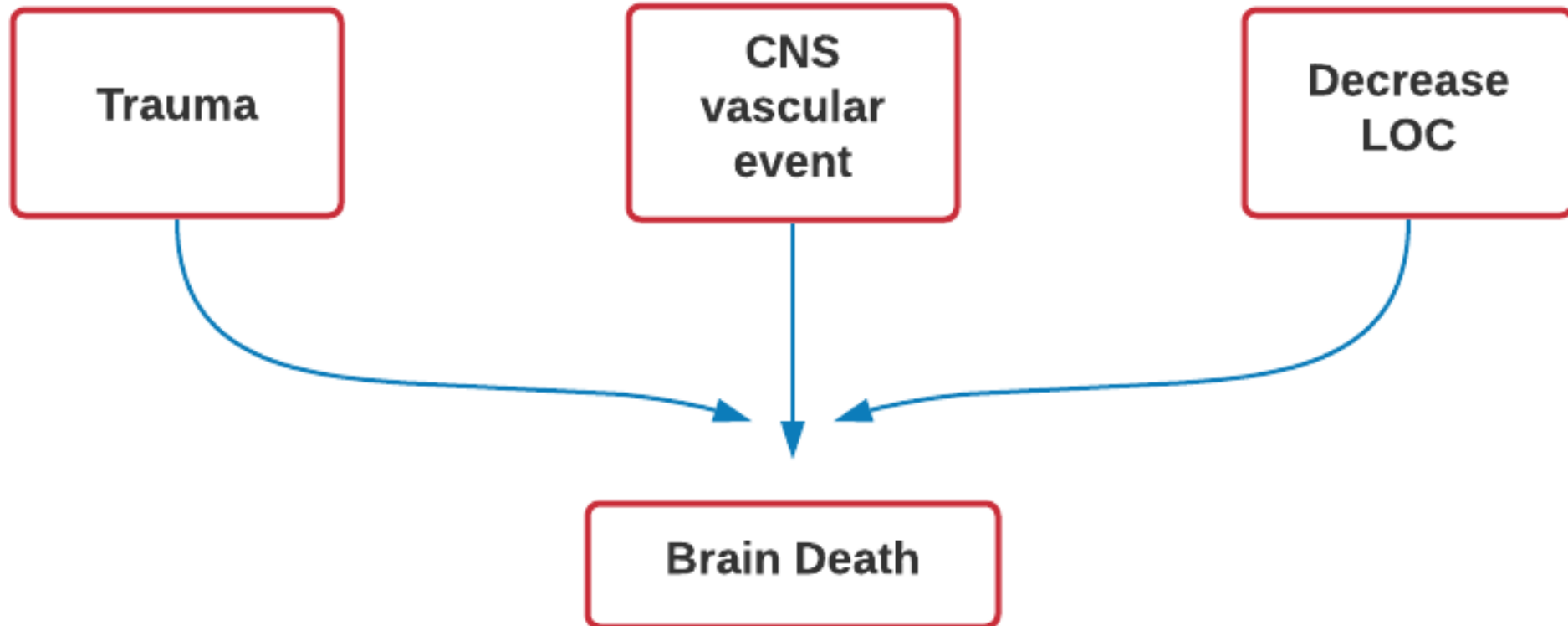
**Standard risk**

No identified infection

**Not assessable**

Can't assess risk of infection

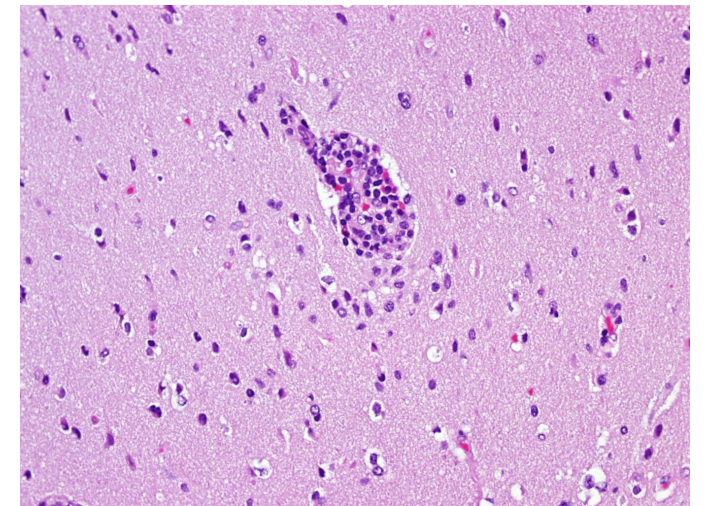
# Who is the donor ?



# Scenario !

- 19-year-old male patient
- Underwent liver transplant December 4, 2014, at KFSH&RC
- Presented to ER on March 18<sup>th</sup>, 2015, with Altered level of consciousness
- Developed dystonia
- ID team started to collect more information about other donor and other recipients

- Heart transplant recipient (done in KFSH&RC) died one month earlier
  - Admitted with behavioral changes
- 1 renal transplant in Kuwait admitted with Meningitis/encephalitis
- Donor
  - 28 M Indian HTN/DM/IHD/Obesity admitted 12<sup>th</sup> Nov 2014 with ARDS
  - Had seizure during hospitalization
- Concerns of Rabies encephalitis
- Brain Biopsy done and showed ..

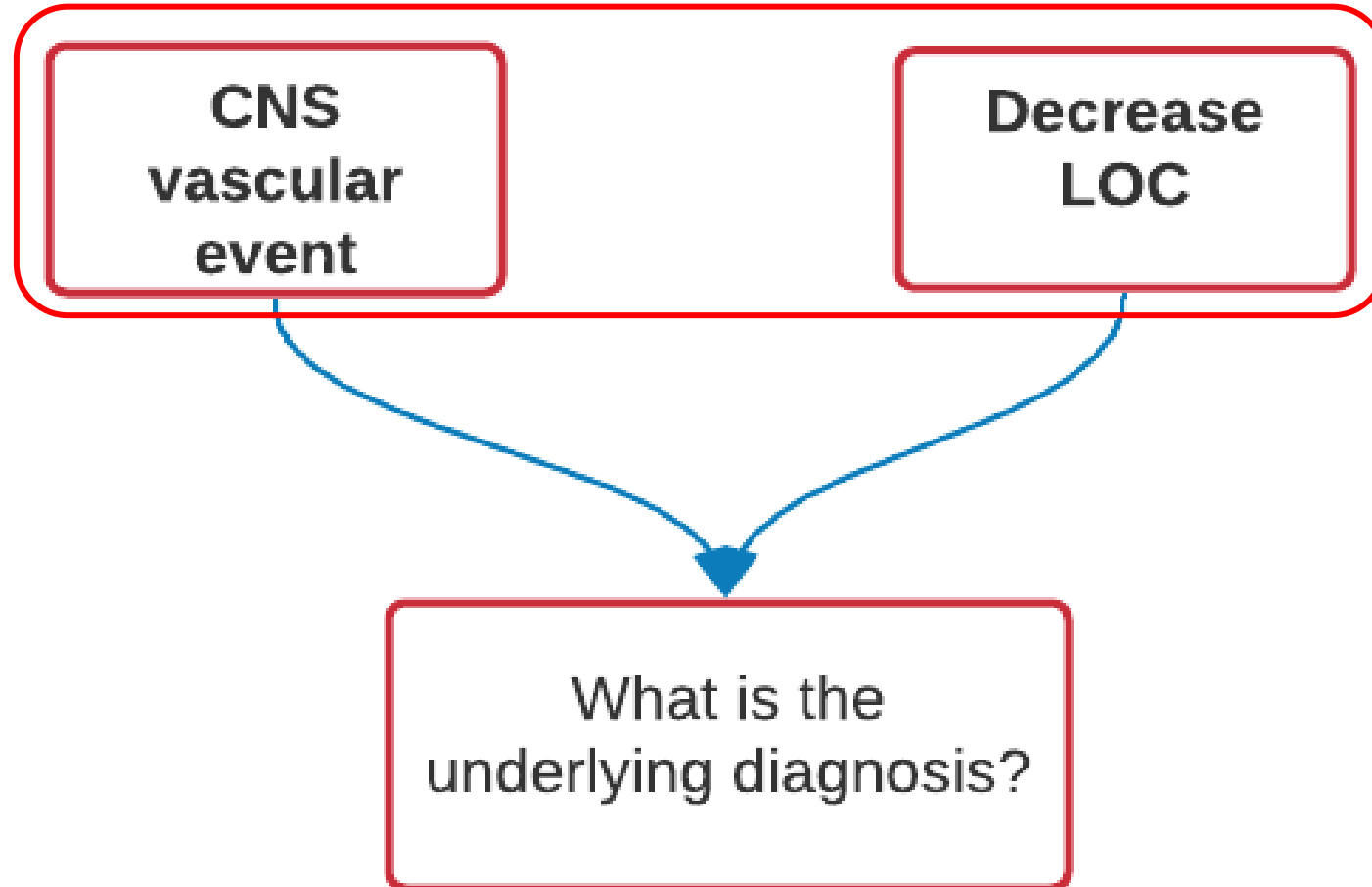


# Practical approach

What is/are the donor risk factor/s for vascular events?

Fever at presentation?

Seizure ?





**Table 3** Frequent differences between encephalopathy and encephalitis

	Encephalopathy	Encephalitis
<i>Clinical features</i>		
Fever	Uncommon	Common
Headache	Uncommon	Common
Depressed mental status	Steady deterioration	May fluctuate
Focal neurologic signs	Uncommon	Common
Types of seizures	Generalised	Generalised or focal
<i>Laboratory findings</i>		
Blood	Leucocytosis uncommon	Leucocytosis common
CSF	Pleocytosis uncommon	Pleocytosis common
EEG	Diffuse slowing	Diffuse slowing and focal abnormalities
MRI	Often normal	Focal abnormalities

Reproduced from Davis,<sup>7</sup> with permission.

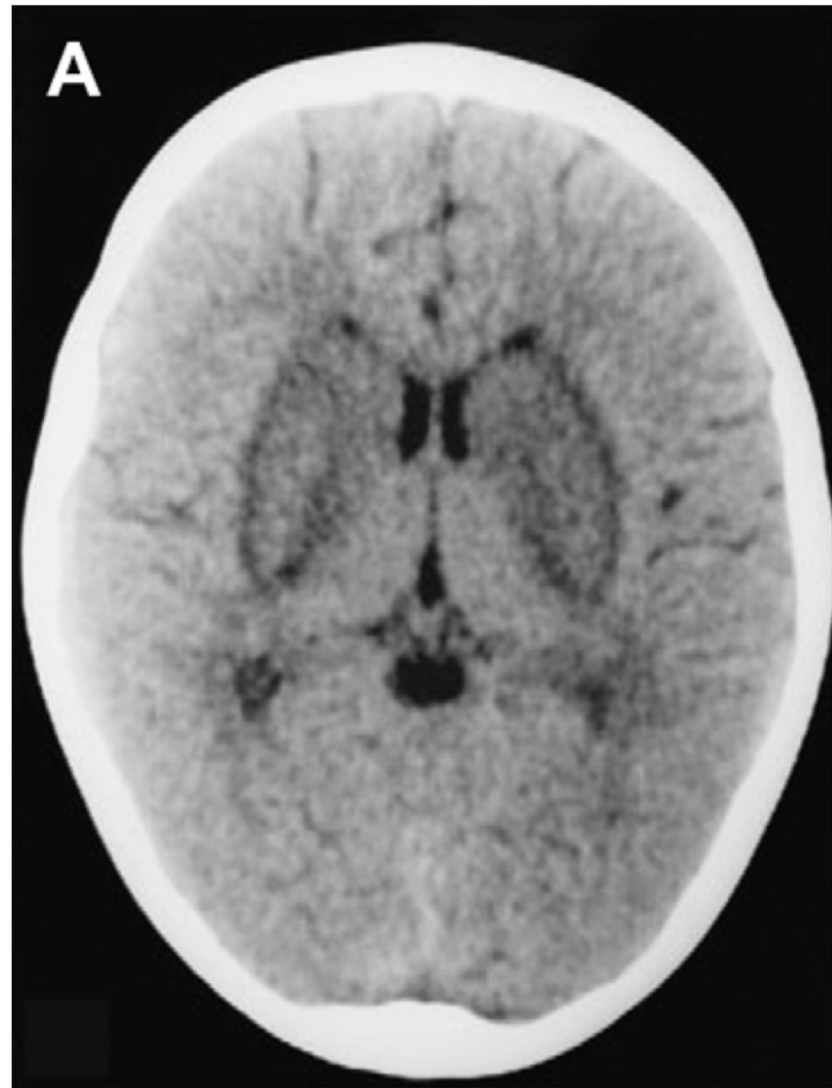
These features are only guidelines for the clinician to help in the distinction between the two conditions. An individual patient is likely to show various combinations of these features.

CSF, cerebrospinal fluid; EEG, electroencephalogram; MRI, magnetic resonance imaging.

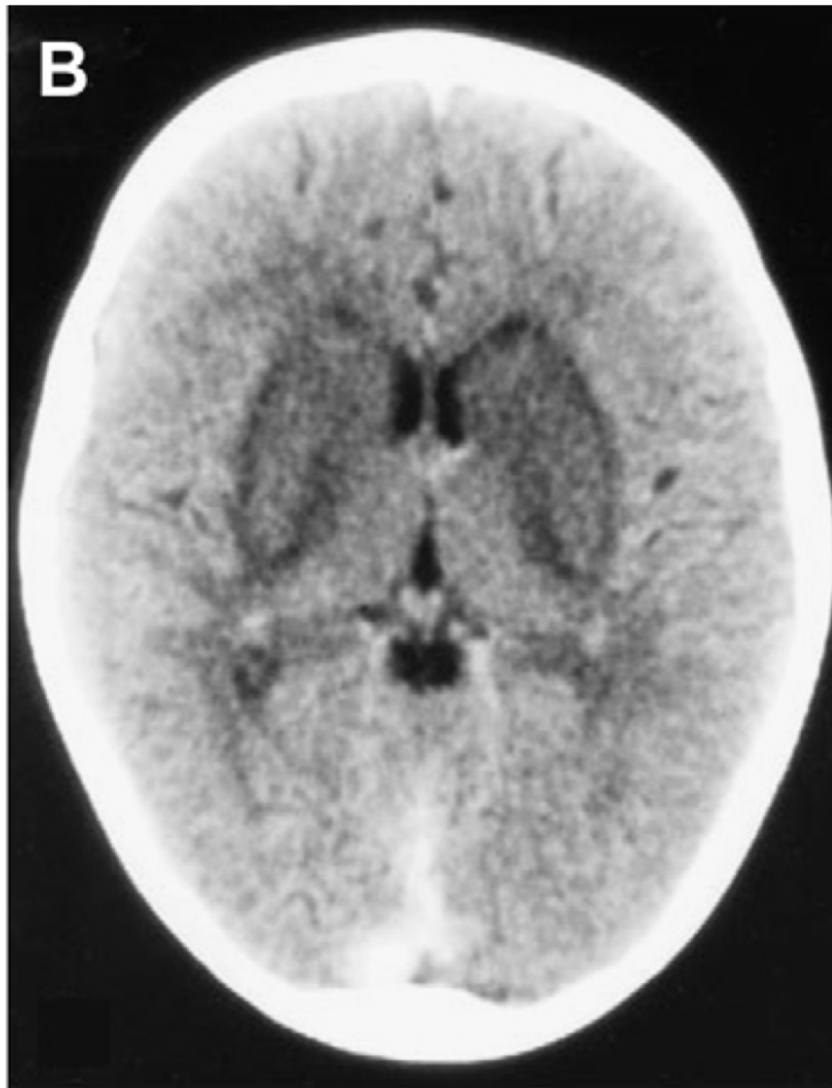
Rabies virus

Brainstem, hippocampus, hypothalamus, limbic system; predominates in gray matter; brachial plexus

**A**



**B**



**C**



## ORIGINAL ARTICLE

## Transmission of Lymphocytic Choriomeningitis Virus by Organ Transplantation

The donor was a 51-year-old man who had been found unresponsive, with apparent head trauma. Computed tomography (CT) of the brain revealed a large, right-sided subdural hematoma with a midline shift. There was no improvement in his neurologic status, and he was declared

hospitalized there. The donor was a 45-year-old woman with hypertension who had presented to the emergency department with a five-day history of right-sided headache and acute left-sided weakness. She was alert and afebrile and had left-sided hemiparesis. CT of the brain revealed an infarct in the distribution of the right middle cerebral artery, and tissue plasminogen activator

**Table 1.** Summary of Laboratory Evaluations for Lymphocytic Choriomeningitis Virus Infection in the 2003 Cluster.\*

Patient	Outcome or Status	Immunohistochemical Staining	Serologic Testing		Culture
			IgM	IgG	
Donor†	No reported disease	–	–	–	–
Lung recipient‡	Death 9 days after transplantation	+	NT	NT	NT
Liver recipient§	Death 17 days after transplantation	+	NT	NT	NT
Kidney Recipient 1¶	Death 53 days after transplantation	+	–	–	+
Kidney Recipient 2	Death 76 days after transplantation	+	+	–	+

**Table 2.** Summary of Laboratory Evaluations for Lymphocytic Choriomeningitis Virus Infection in the 2005 Cluster.\*

Patient or Source of Specimen	Outcome or Status	Immunohistochemical Staining	Quantitative Real-Time RT-PCR†	Blood and Serum Testing		Culture
				IgM	IgG	
Donor‡	No reported disease	–	–	–	–	–
Liver recipient§	Death 26 days after transplantation	+	+	–	–	+
Lung recipient¶	Death 23 days after transplantation	+	+	–	–	+
Kidney Recipient B	Death 23 days after transplantation	+	+	+	–	+
Kidney Recipient A**	Survival	+	+	+	–	+
Hamster in donor's household††	No reported disease	+	+	NT	–	+
Hamster's caregiver‡‡	No reported symptoms	NA	–	+	+	–

# One more time !

- In 2019
  - 2 SOT recipients (1 kidney and 1 liver )
  - Presented to their local hospital in Eastern province with new onset seizures, decrease LOC
  - Had neurological features consistent with RABIES
  - Donor died in 2018 !! With undiagnosed encephalitis

# Donors with bacterial meningitis

- Considered safe
- *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Escherichia coli*
- Highly virulent or intracellular organisms such as *Listeria* species
- Potential donors need to be on microbiologically active antibiotics 24-48 hrs
- Recipients typically treated with 7-14 days with antibiotics directed at cultured organism

# Multi-recipient donor-transmitted tuberculosis

**J. Edathodu, A. Alrajhi, M. Halim, S. Althawadi**

**Section of Infectious Diseases, Section of Microbiology, Department of Medicine, King Faisal Hospital & Research Centre, Riyadh, Saudi Arabia**

Donor from Indonesia

Had negative PPD skin test and CXR on arrival  
to the kingdom

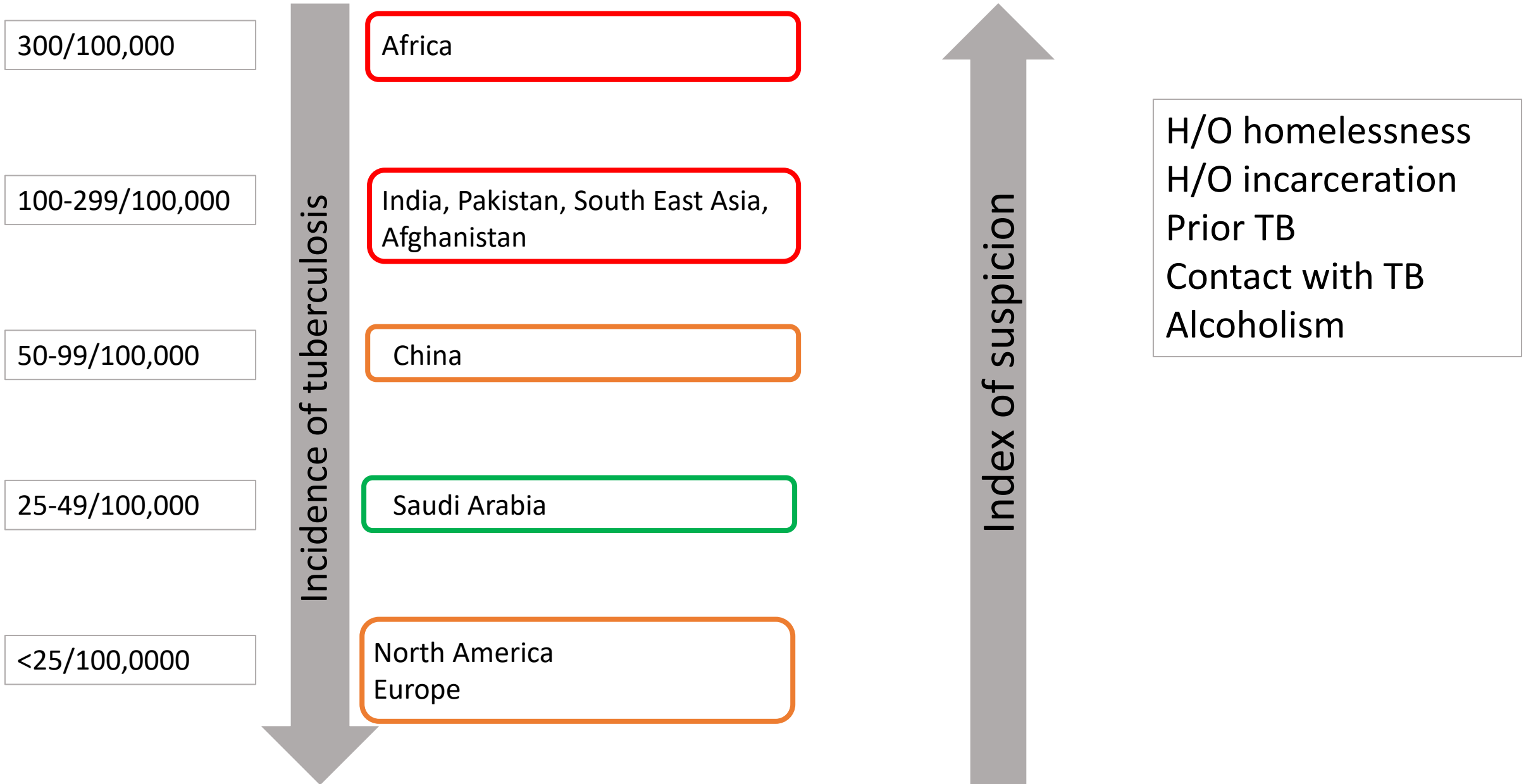
5 months later admitted with fever and altered  
mental status

Negative MRI

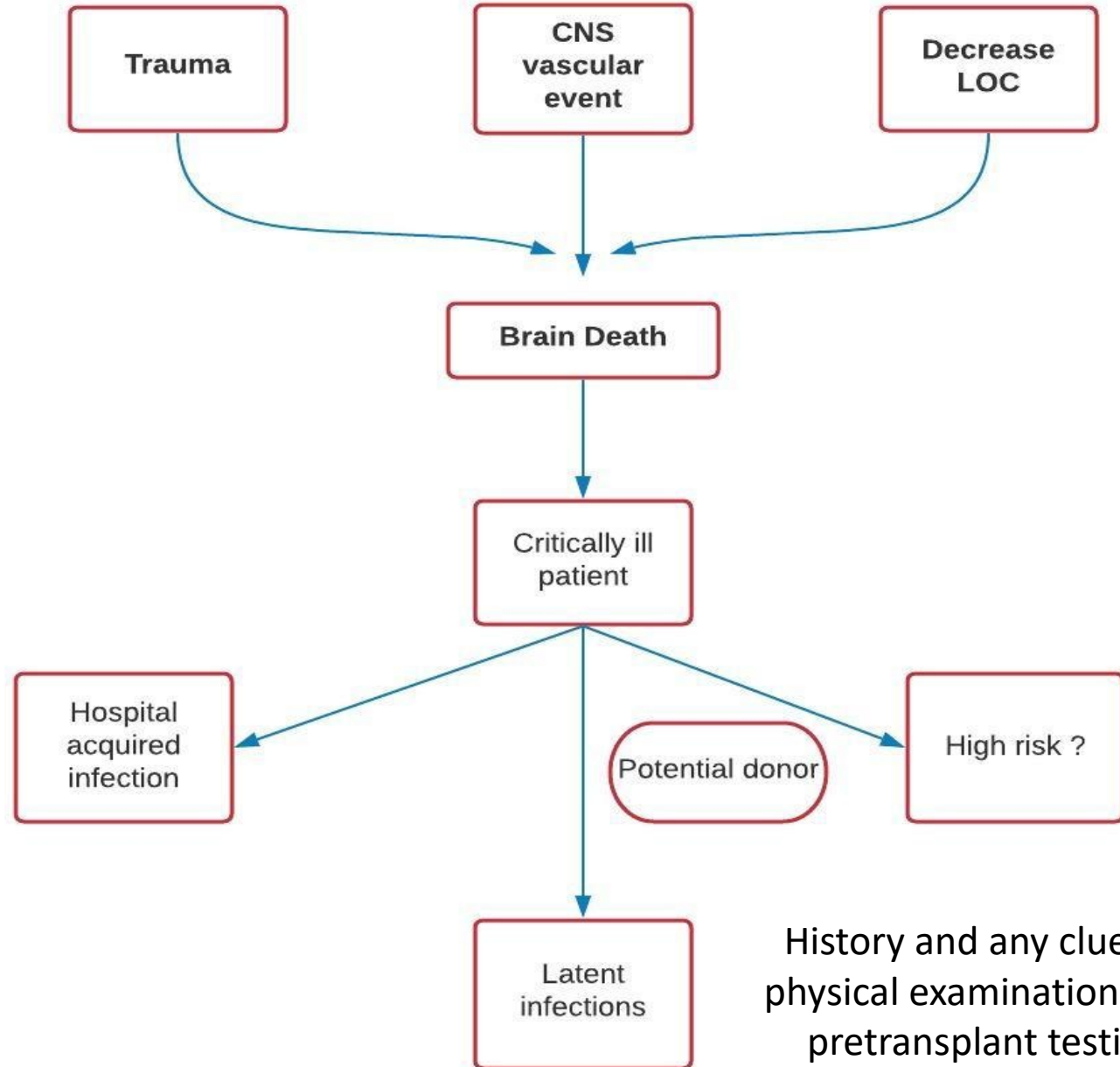
CSF exam normal apart from high protein

# Donor derived *Mycobacterium tuberculosis* infection after solid-organ transplantation: A comprehensive review

Characteristic	N (% or range)	
	Donor N = 28	Recipient N = 36
Risk factor for TB <sup>a</sup>		
Latent/active TB <sup>b</sup>	4/3 (14.3/10.7)	0/24 (0)
Residence in Endemic country	13 (46.4)	13/28 (46.4)
Socio-economic <sup>c</sup>	5 (17.9)	NR
None identified	5 (17.9)	NR
Type of TB		
Pulmonary		13 (36.1)
Extrapulmonary		10 (27.8)
Disseminated		13 (36.1)







History and any clues in physical examination

History and any clues in physical examination AND pretransplant testing

# Scenario

- During weekend on call the ID team received a call from the liver transplant coordinator
- Potential donor with bacteremia
- Verbal report MRSA
- ID recommended IV vancomycin in addition to surgical prophylaxis

- Next day
  - Total of 7 recipients
- Personal communication between ID team and referring hospital
  - Blood culture of the donor grew Vancomycin resistant Enterococcus (VRE)
- Recipients switched to targeted therapy 4 days later

Micro Reports	Susceptibilities	Specimen	Action List
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	A	B	C
1	Enterococcus faecium		
2		MDIL	MINT
3	Benzylpenicillin*	>=64	R
4	Ampicillin*	>=32	R
5	Vancomycin*	>=32	R
6	Linezolid*	2	S
7	Quinupristin/Dalfopristin*	0.5	S
8	Gentamicin synergy*	Syn-R	R
9	Streptomycin synergy*	Syn-R	R
10	Vancomycin Resistant Enterococcus*		Pos

Adult liver  
transplant-->  
Persistent  
bacteremia  
1 week  
Surgical site  
infection  
Intra-abdominal  
infection

- The pediatric liver transplant recipient
  - Persistent bacteremia for 2 weeks
  - Liver necrosis
  - Re-transplanted 3 weeks later

# Potential donors with bacterial infections

- Around 14 % of donors are colonized or infected at the time of harvesting
- 5% with unrecognized bacteremia at time of harvesting
- Transplant ID physicians willingness to accept patients with active bacterial infection varies

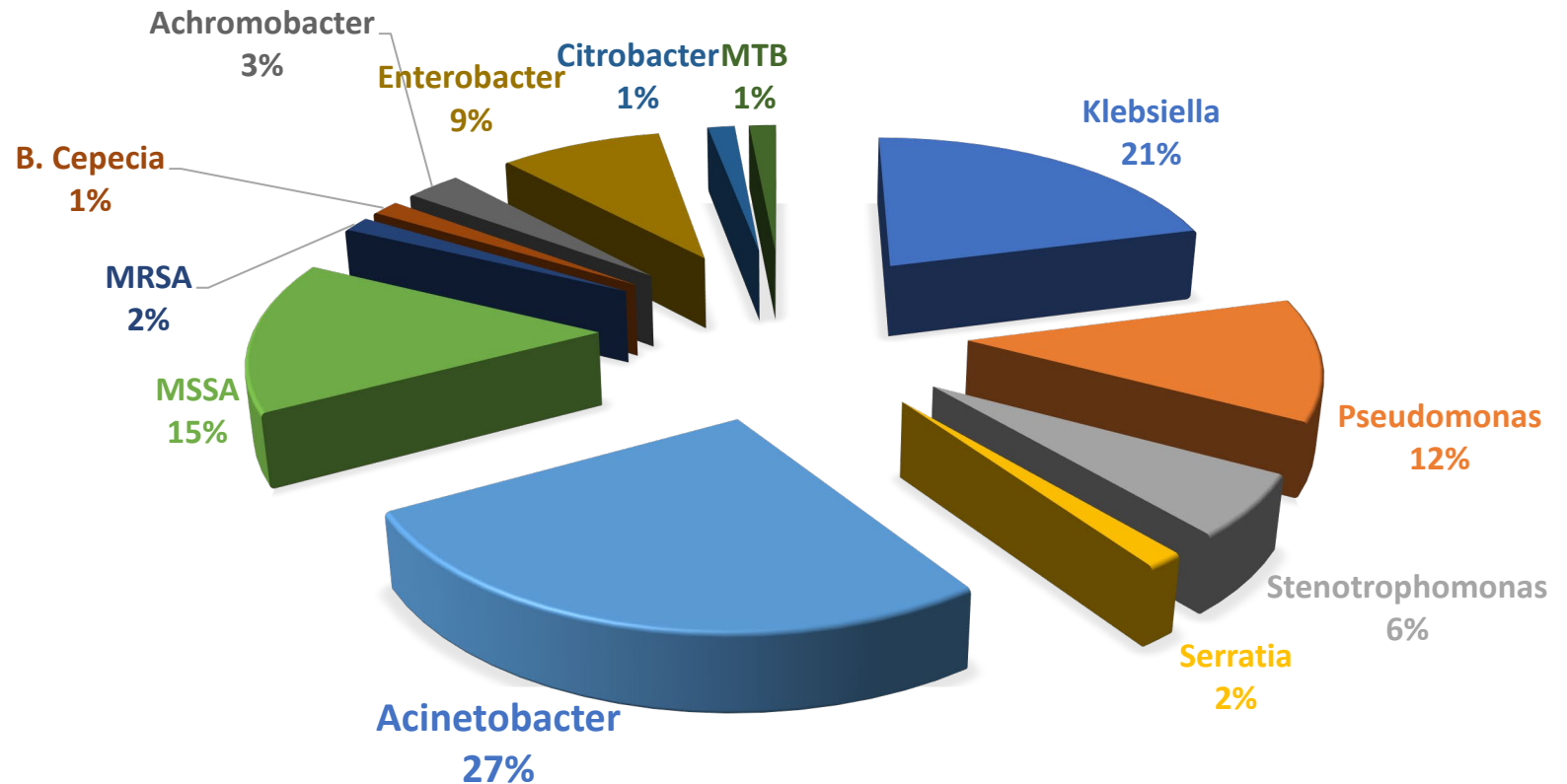
# Rate of accepting organs from donors with active infection

Pathogen	Rate of acceptance (+ Blood C/S)	Rate of acceptance (+ Resp C/S)
<b><i>Enterobacteriaceae</i></b>	<b>72%</b>	<b>42%</b>
<b>ESBL</b>	<b>54%</b>	<b>36%</b>
<b>CRE</b>	<b>10%</b>	<b>14%</b>
<b><i>Pseudomonas aeruginosa</i></b>	<b>44%</b>	<b>19.4%</b>
<b>MSSA</b>	<b>50%</b>	<b>36%</b>
<b>MRSA</b>	<b>42%</b>	<b>25%</b>
<b>Streptococci</b>	<b>72%</b>	<b>55.6%</b>
<b>VSE</b>	<b>66%</b>	<b>52.8%</b>
<b>VRE</b>	<b>50%</b>	<b>47.6%</b>

ESBL extended spectrum B-lactamase  
 CRE Carbapenem resistant *Enterobacteriaceae*  
 MSSA methicillin susceptible *staphylococcus aureus*

MRSA methicillin resistant *Staphylococcus aureus*  
 VSE Vancomycin susceptible *Enterococci*  
 VRE Vancomycin resistant *Enterococci*

# Lung transplant donors







- **Is there a defined high risk bacterial infection?**

- Meningitis ?
- Bacteremia ?
- Transplanted organ infection ?
- Colonization vs infection ?
- Pathogen related ?

**Coagulase negative  
*staphylococci***



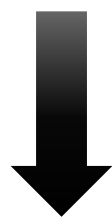
**No transmission  
Rapid clearance**

***Staphylococcus aureus*  
Enterococcus spp.**



**Bacteremia/intra abdominal infections in the recipients**

**Gram negative pathogens**



**Liver transplant associated with graft  
loss/thrombosis/mortality  
Delay in initiation of targeted therapy >24  
hrs**

Cerutti et al liver transplant 2006; 12 1253-1259  
Doucette et al Am J transplant 2013 ; 13 1080-1083  
Miceli et al Transplant Infec Dis 2017; 17: 140-146  
Wendt et al. Amer J Tranplant 2014; 11: 2633-2639

# Gram negative infections

- More than 9 published reports on clusters of MDR-GNR donor infections/colonization
- 5 proven (Phenotypic or PFGE)
  - Colonization and active infection
  - Transplanted organ/non-transplanted organ
  - 53% attack rate
  - 41% mortality
  - $\cong$  60% graft loss or mortality

Mills et al Transplant Infec Dis 2016; 18: 777-781  
Mularoni et al Amer J Transplant 2015; 15: 2674–2682  
Varotti et al Case Rep Transplant. 2016;2016:7920951  
Lewis et al Cur Opin Inf Dis. 2016;18:18

# What should be done ?

- Contact precautions
- Patient isolation and surveillance strategies
- Hand hygiene
- Antibiotic stewardship
- Environmental cleaning

# So, how should we evaluate potential donor for infection ?

- What is the cause for brain death?
  - Low threshold to suspect CNS infection in patients with no clear risk factor for vascular events
  - Get as much information about the donor as you can
    - Family, friends
    - Travel, hobbies, high risk behaviors, animal exposure, TB exposure or history

# While patient is in ICU

- Infection control and bundles to decrease risk of hospital acquired infection
- In the report to SCOT
  - Details of presentation and imaging reports
  - Details of fever, culture dates and results
  - Details of antimicrobial therapy



Any questions