Isolation Precautions and Environmental Concerns for Transplant Recipients

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Host

- Intrinsic host factors
- Immunosuppression
- Type of transplant
- Time from transplant
- Coinfections

Exposures

- Donor
- Hospital
- Community
- Reactivation

Preventive Measures

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- **Hospital**
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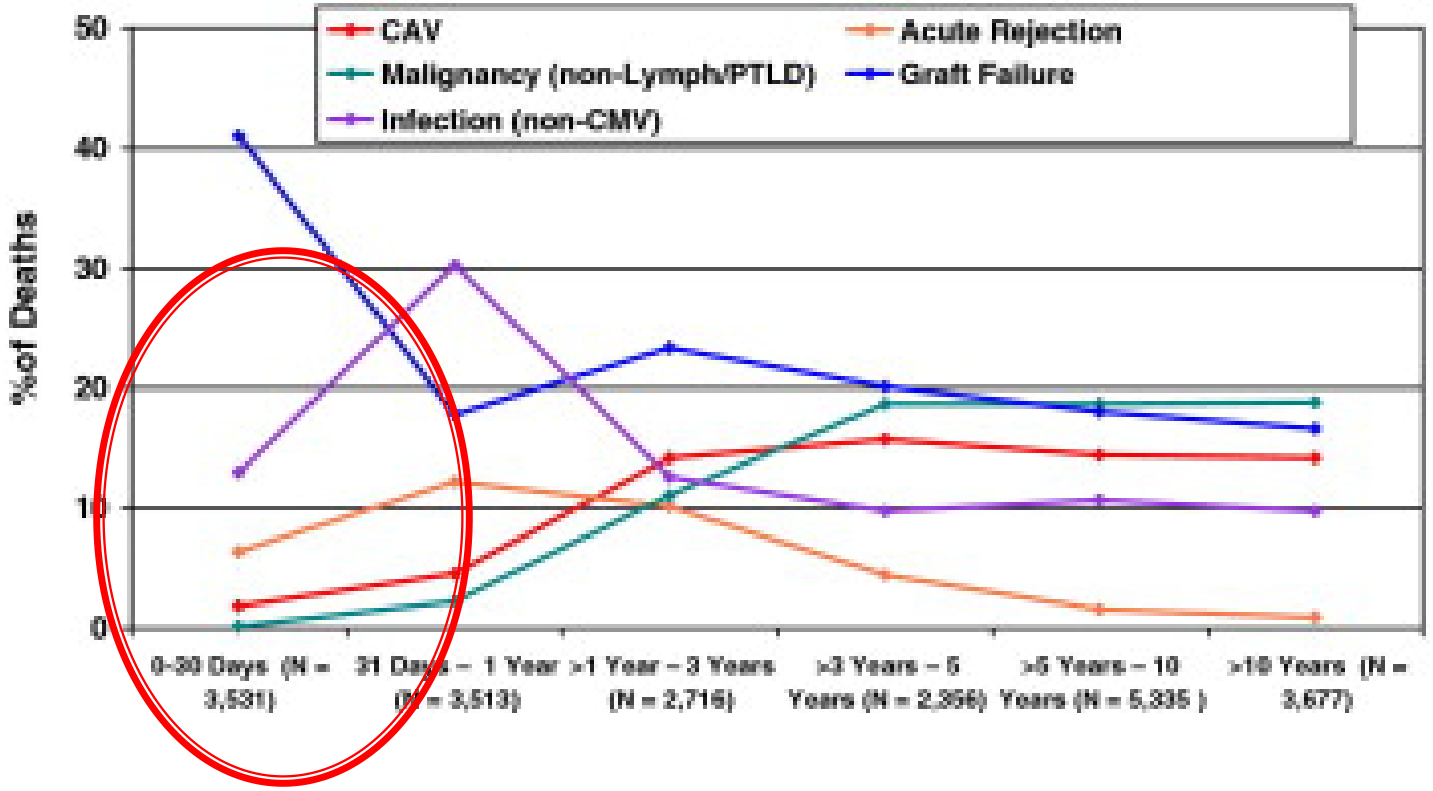
Preventive Measures

Mortality in Heart Transplant Recipients



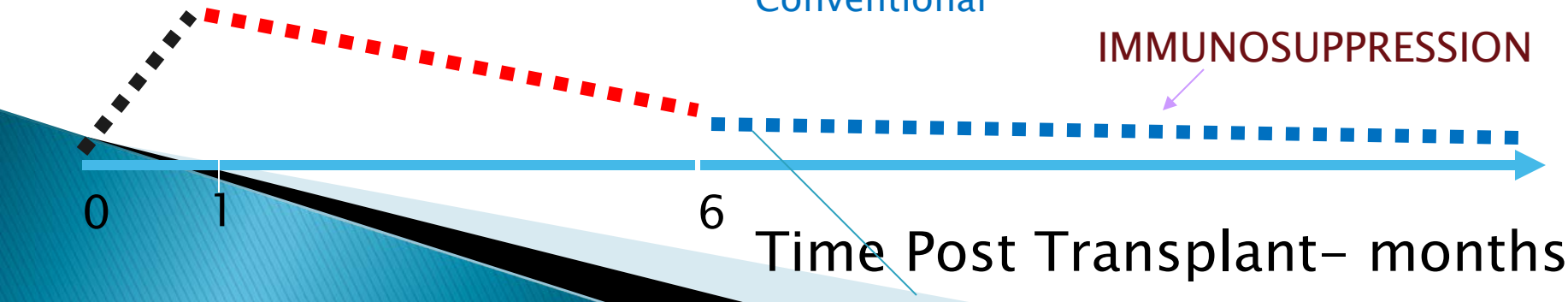
Taylor, et al. J Heart and Lung Transplantation 10:1007, 2009

Timeline of Infections: Solid Organ Transplantation

EARLY/CONVENTIONAL
Donor
Technical
Nosocomial

OPPORTUNISTIC
Donor
Recipient
Exposure

COMMUNITY EXPOSURES
Opportunists
Conventional



Timeline of Infections: Stem Cell Transplantation

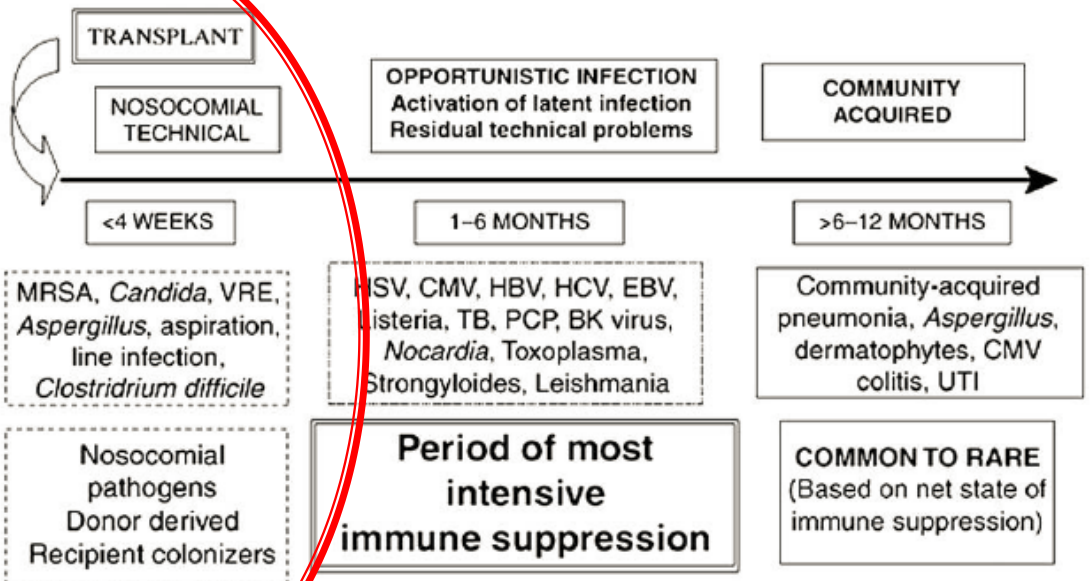


Fig. 4. Timeline of posttransplant infections following solid organ transplantation. (*From* Gabrielli A, Layon AJ, Mihae Y. Civetta, Taylor and Kirby's Critical Care. 4th edition. Philadelphia: Lippincott Williams & Wilkins; 2009; with permission.)

Nosocomial Infections Following Heart & Lung Transplant

	Lung Tx (*n* = 137)	Heart Tx (*n* = 51)	Combined Tx (*n* = 20)	Total (*n* = 208)
Pneumonia	**42 (30.7%)**	**5 (9.8%)**	**8 (40%)**	**55 (26.4%)**
Primary sepsis	**18 (13.1%)**	**6 (11.8%)**	**4 (20%)**	**28 (13.5%)**
Wound infection	**15 (11.0%)**	**5 (9.8%)**	**7 (35%)**	**27 (13.0%)**
Urinary tract infection	**20 (14.6%)**	**6 (11.8%)**	**5 (25%)**	**31 (14.9%)**
Any nosocomial infection (%)	**65 (47.5%)**	**13 (25.5%)**	**13 (65%)**	**91 (43.8%)**
Acute graft rejection	**17 (12.4%)**	**4 (7.8%)**	**5 (25%)**	**26 (12.5%)**
Death	**20 (14.5%)**	**7 (13.7%)**	**4 (20%)**	**31 (14.9%)**

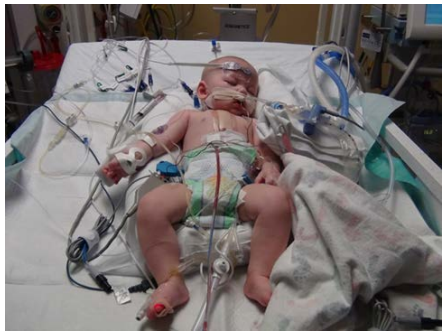
Mattner, et al. J Heart Lung Transplant 2007

Surgical Site Infections: RESITRA

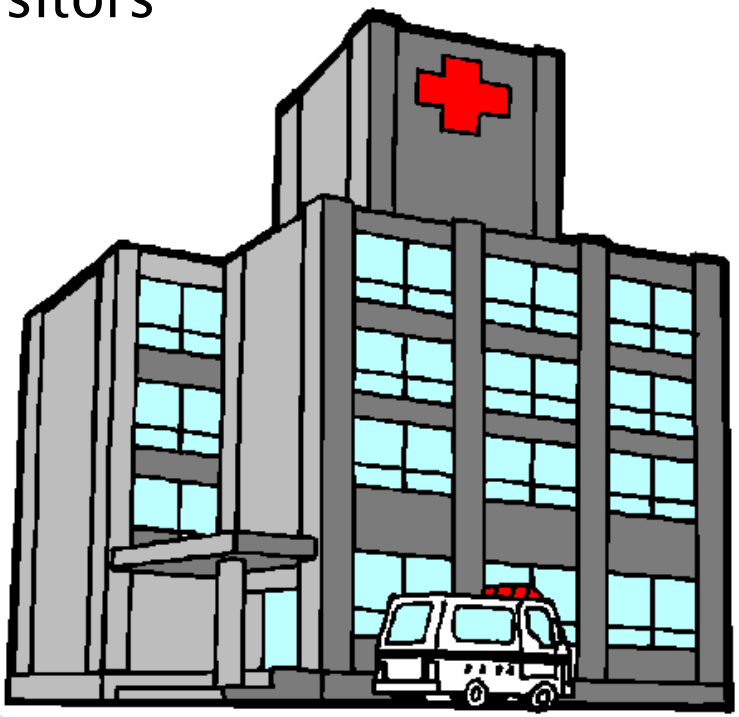
- Common following transplantation
  - Risk after liver transplantation – 8.8 per 100 patients[1]
  - 42% incisional, 39% peritonitis, 16% intra-abdominal abscess, 10% hepatic abscess
  - Risk after kidney transplantation – 4.3 per 100 patients with incisional surgical wound infection[2]
  - Risk after heart transplantation – 5.8 episodes per 100 patients with incisional surgical wound infection[3]
- Decreased graft survival (long term)[4]

[1]Asensio, et al, Liver Transplantation 2008, [2]Ramos, et al, Urology 2008, [3]Ramos et al, Transplant Infectious Diseases 2008; [4]Humar, et al. Transplantation 2001

Nosocomial Threat



- Bypass of 'normal' host defenses
  - Invasive devices (urinary and intravenous catheters, ventilator)
    - Bacteria (including multidrug resistant)
    - Fungi
- Potential for person to person spread
  - Health care workers, patients, visitors
    - Respiratory viruses
    - Clostridium difficile
    - Pneumocystis jirovecii
    - Tuberculosis
- Role of environment
  - Fomites
  - Air handling



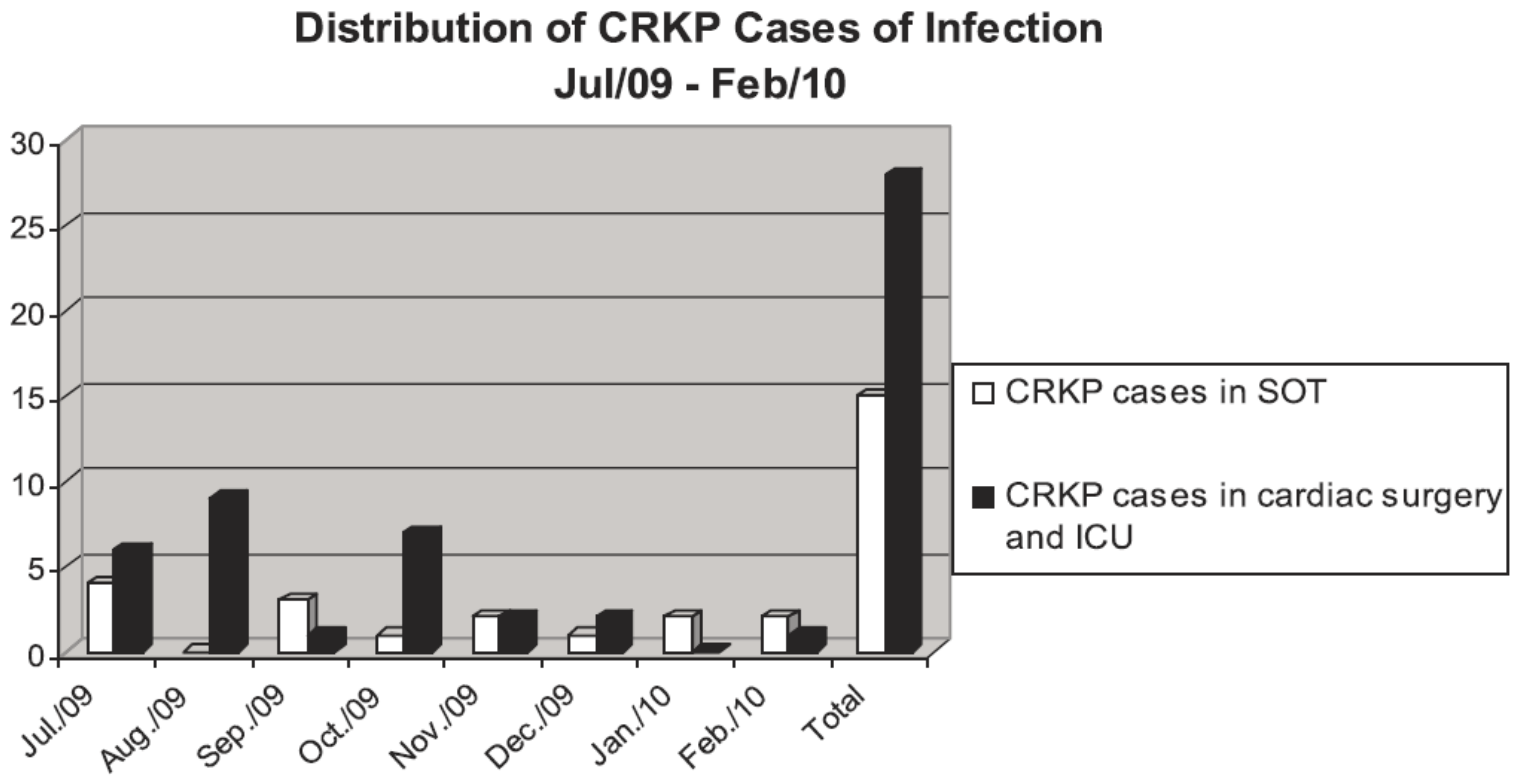
Diverse sources of infection control recommendations with shared recommendations

- General guidelines
  - ESCMID
  - CDC
  - National Disease Surveillance Centre
  - Asian Pacific Society of Infection Control
- Stem cell transplant specific
  - Global guidelines from
    - Center for International Blood and Marrow Transplant Research (CIBMTR®),
    - National Marrow Donor Program (NMDP)
    - European Blood and Marrow Transplant Group (EBMT)
    - American Society of Blood and Marrow Transplantation (ASBMT)
    - Canadian Blood and Marrow Transplant Group (CBMTG)
    - Infectious Disease Society of America (IDSA)
    - Society for Healthcare Epidemiology of America (SHEA)
    - Association of Medical Microbiology and Infectious Diseases Canada (AMMI)
    - Centers for Disease Control and Prevention (CDC)

Outbreaks and Transplant Recipients

KPC producing Klebsiella pneumoniae outbreak in SOT

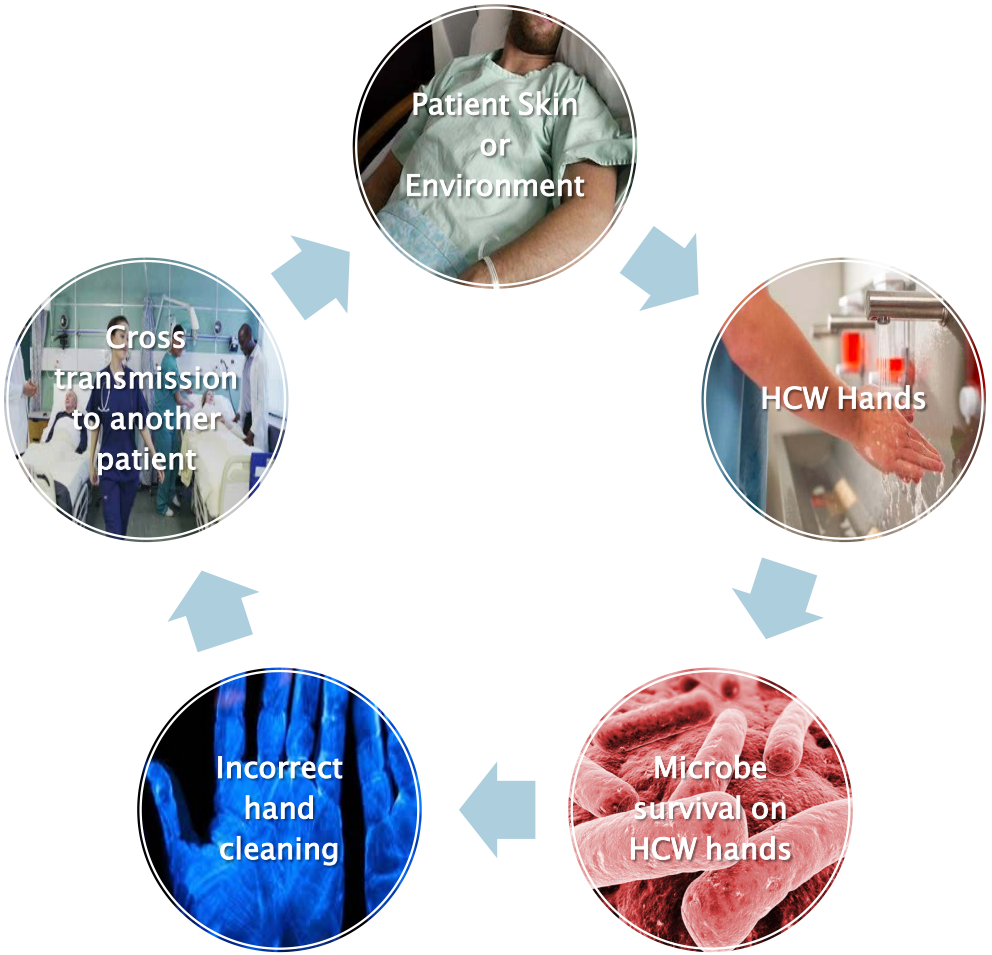
Bergamasco, et al Transplant ID 2012; 14:198–205



Nosocomial outbreaks may disproportionately affect transplant recipients

- Susceptible patient population
  - Immunosuppression
  - Increased use of invasive devices
  - Cohorting on hospital units
- Role of colonization pressure
- Resistant pathogens especially important due to widespread antibiotic use

Cascade of Contamination



Control measures: ESCMID Guidelines Tacconelli, et al. Clin Micro Infect 2014; 20 (suppl 1):1-55

- Standard precautions (Minimum)
  - Hand hygiene
  - Personal protective equipment guided by risk assessment and extent of blood/body fluid exposure
- Contact precautions for specific bacteria (e.g., multidrug resistant bacteria, C difficile)
  - Gown/gloves upon entering room
  - Dedicated patient vs single use equipment (stethoscopes, BP cuffs) to minimize transmission by fomites
  - Consider patient cohorting
  - *No consensus regarding criteria for suspending contact precautions*

ESCMID Control measures: Epidemics vs Endemic Settings

Tacconelli, et al. Clin Micro Infect 2014; 20 (suppl 1):1-55

	Epidemic	Endemic
Contact precautions	ESBL Enterobacteriaceae MDR K pneumoniae MDR A baumanii, MDR P aeruginosa	ESBL Enterobacteriaceae (except E coli) MDR K pneumoniae MDR A baumanii, MDR P aeruginosa
Alert codes	ESBL Enterobacteriaceae MDR K pneumoniae	MDR A baumanii
Patient isolation (single room)	ESBL Enterobacteriaceae MDR K pneumoniae MDR A baumanii, MDR P aeruginosa	
Cohort staff	MDR K pneumoniae	

MDR: Multidrug resistant; ESBL: Extended spectrum beta lactamase

Surveillance cultures

- Surveillance cultures allow for early identification of patients colonized with MDR pathogens
  - Pathogen detection varies with organism and site cultured
    - Culturing multiple sites increases likelihood of detecting organism
  - Some linkage with colonization and infection (varies with organism)
    - Colonization may predate clinical infection
- ESCMID recommends active surveillance in epidemic settings at hospital admission with contact precautions
  - ESBL Enterobacteriaceae, MDR K pneumoniae, MDR A baumanii, MDR Ps aeruginosa

Microbiologic Factors Facilitating Surface-Mediated Transmission (courtesy of Dr. David Pegues)

Microbiologic Factor	Acinetobacter	C difficile	MRSA	VRE
Survive for prolonged periods on environmental surfaces	+	+	+	+
Virulent after environmental exposure	+	+	+	+
Frequent contamination of hospital environment	+	+	+	+
Ability to colonize patients	+	+	+	+
Ability to contaminate hands of HCWs	+	+	+	+
Transmission via HCW hands	+	+	+	+
Small inoculating dose		+		
Relative resistance to disinfectants		+		

Weber D, et al. Am J Infect Control 2010;38:S25-33.

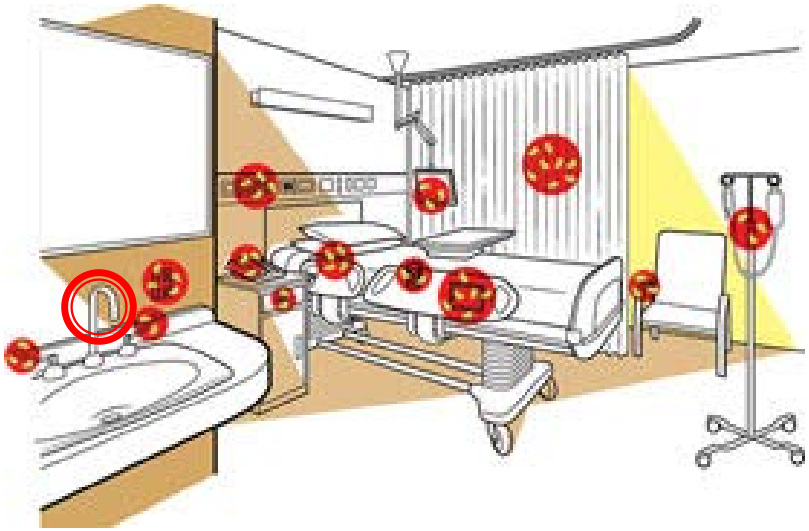
Effect of Colonization/Infection Status of Prior Room Occupant on Pathogen Acquisition (courtesy of Dr. David Pegues)

Author (year)	Organism	Setting	Adjusted ratio (95% CI)
Dress et al (2008)	VRE	ICU	HR 3.8 (2.0–7.3)
Nseir et al (2010)	A. baumannii P. aueruginosa	ICU	OR 4.2 (2.0–8.8) OR 2.3 (1.2–4.3)
Huang et al (2006)	MRSA VRE	ICU	1.4 (1.1–1.8) 1.4 (1.10–1.9)
Shaughnessy et al (2008)	C. difficile	ICU	HR 2.3(1.2–4.5)

Otter JA, et al. Infect Control Hosp Epidemiol 2011;32:687–99.

Environmental Cleaning

- Recovery of organisms related to
  - Specific surface (high touch areas)
  - Setting (ICU vs standard room)



- *Can hand hygiene contaminate surfaces???*

Environmental cleaning

- Optimal approach probably requires multiple interventions
  - Detergents
  - Disinfectants
    - Including more novel methods
      - Automated systems using steam, hydrogen peroxide, ozone, UV light
      - Antimicrobial surfaces
  - ESCMID guidelines focus on epidemic situations
    - Monitor cleaning performance to ensure consistent environmental cleaning (EC).
    - Vacate units for intensive cleaning.
    - Implement regular EC procedures and, when available, dedicate non-critical medical items for use on individual patients colonized or infected with ESBL Enterobacteriaceae and MDR A baumannii

Rapid diagnostics

Weinstein, et al; 2013;56:1614–20

Goal: To rapidly identify MDROs from clinical specimens
Example: mecA for MRSA most widely used

Table 3. Summary of Studies Assessing Impact of Rapid Versus Culture-Based Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Carriage, Limited to Those Using Concurrent Control Groups and Reporting MRSA Infection or Colonization Outcomes

Study	Design	TAT Difference	MRSA Outcome	Major Limitations
Aldeyab et al [46]	Nonrandomized cluster crossover trial	PCR: 19 h Culture: 52 h	No difference in event rates (acquisition + infection)	• Long TATs • Not randomized
Hardy et al [47]	Nonrandomized cluster crossover trial	PCR: 22 h Culture: 79 h	Reduced acquisition rate in PCR group (0.29 vs 0.41 per 100 bed-days)	• Long TATs • Not randomized • More unscreened in culture arm • 71% decolonized in PCR arm vs 41% in culture arm • Only 17% of MRSA carriers placed in isolation rooms
Jeyaratnam et al [48]	Cluster-randomized crossover trial	PCR: 22 h Culture: 46 h	No difference in acquisition or infection	• Long PCR TAT

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction; TAT, turnaround time.

Rapid Diagnostics: Challenges

Weinstein, et al; 2013;56:1614–20

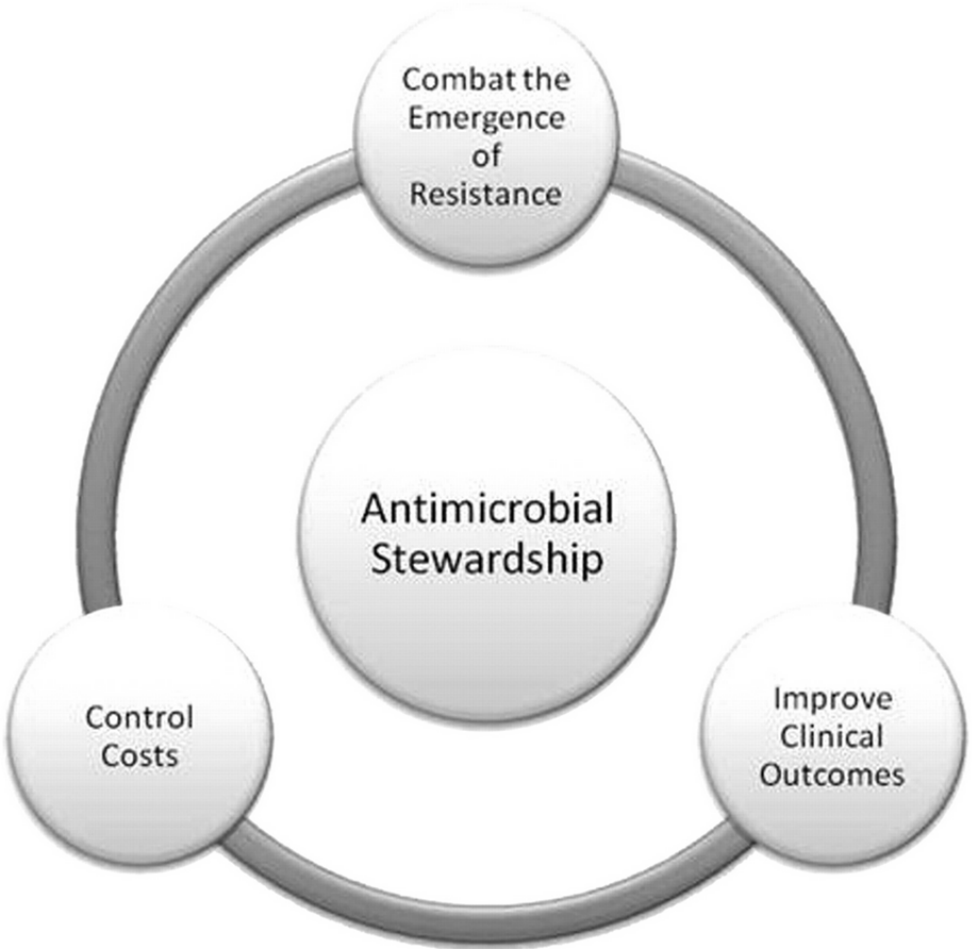
Table 1. Selected Challenges to Rapid Multidrug-Resistant Organism Detection Directly From Patient Samples

Challenge	Example(s)
Resistance gene shared by commensals	• *mec*A in CoNS • *van*B in intestinal anaerobes
Resistance gene not expressed or epidemiologically important	• Chromosomal AmpC cephalosporinase in *Escherichia coli*
Resistance phenotype multifactorial	• Carbapenem resistance associated with porin protein mutation + AmpC overexpression
Natural evolution and mutation of resistance genes	• Empty cassette variants of MSSA • Novel *mec*A homologues • Emergence of new β-lactamases
No organism available for molecular typing, additional susceptibility testing, or prospective validation of assay	• Broadly applicable to molecular tests, requires running culture in parallel
Approved/validated only for 1 sample type	• MRSA nares-only testing misses carriers at other body sites (eg, throat, skin)

Abbreviations: CoNS,coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

Impact of antimicrobial stewardship

Lawrence, et al, Am J Resp Care Crit Care Med 2009; 179:434

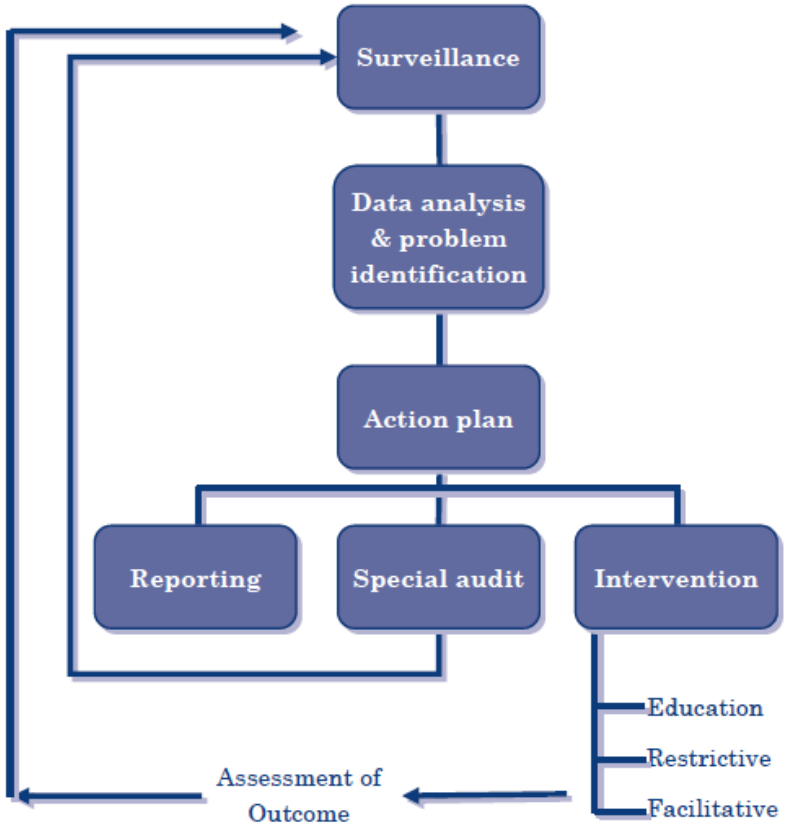


Impact of antimicrobial stewardship

- Antimicrobial exposure is risk for multidrug resistance
- Controlled prescribing has become common practice with goal to decrease resistance
  - RECOMMENDED by professional societies worldwide
  - Potential approaches
    - Approval programs
    - Automatic stops
    - Justification forms
    - Scheduled changes in antimicrobials
    - Antibiotic cycling
  - Despite absence of transplant specific data, ESCMID recommends ASP for both epidemic and endemic settings

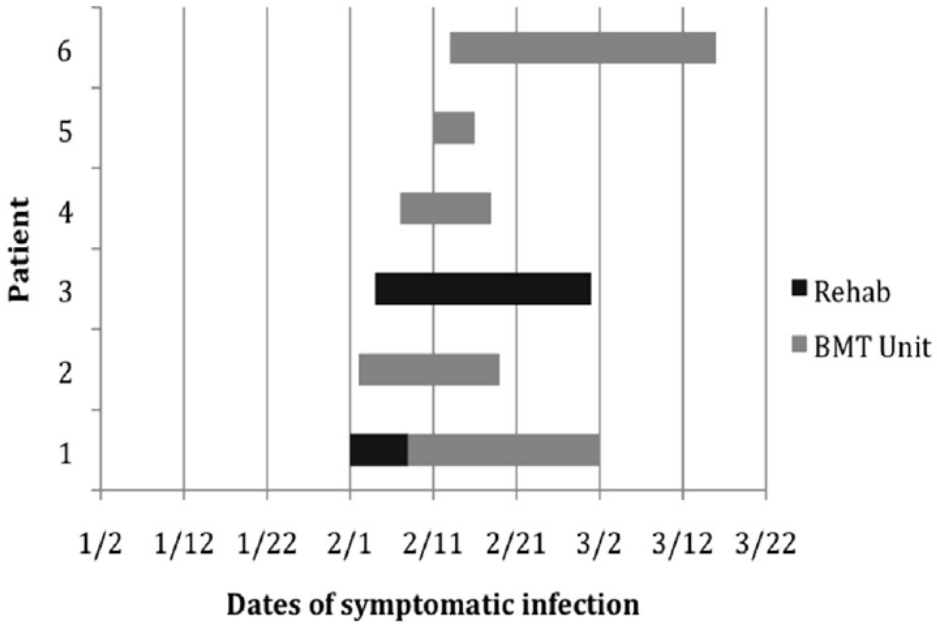
Infrastructure of an antimicrobial stewardship program

Handbook of Infection Control for the Asian Healthcare Work 3rd Edition, 2011



Special Situations

Norovirus in Stem Cell Transplant Unit Doshi, et al. Am J Infect Control 2013;41:820



- SCT patients on same unit; 3 in adjacent rooms
- Multiple sick HCW worked during illness

Nosocomial acquisition of norovirus

- Factors facilitating transmission
  - Small inoculating dose
  - Prolonged survival on environmental surfaces
    - Relative resistance to disinfectants
  - Virulence after environmental exposure
  - Frequent contamination of hospital environment
  - Delayed recognition due to prevalence of diarrhea
  - Prolonged shedding in immunocompromised
    - Proximity of immunocompromised patients
  - Ability to contaminate hands of HCWs
  - Other sources of transmission food/water and ?aerosol

Control of norovirus: HICPAC guidelines (2007)

- Contact Precautions for diapered or incontinent persons for the duration of illness or to control institutional outbreaks
  - Masks for persons who clean areas heavily contaminated with feces or vomitus
- Disinfection with focus on restrooms even when apparently unsoiled
  - Hypochlorite solutions if continued transmission
  - Alcohol less active, but possibly acceptable for hand
  - decontamination
- Cohorting of affected patients to separate air spaces and toilet facilities

Respiratory viruses

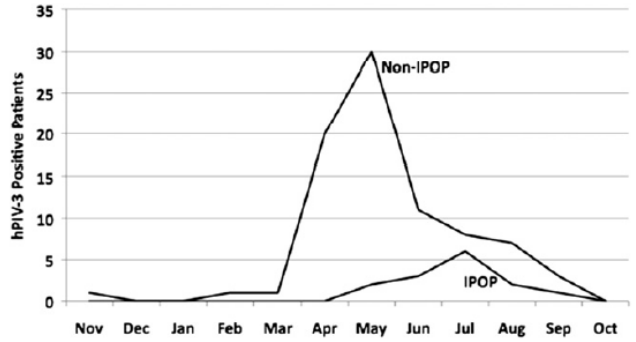
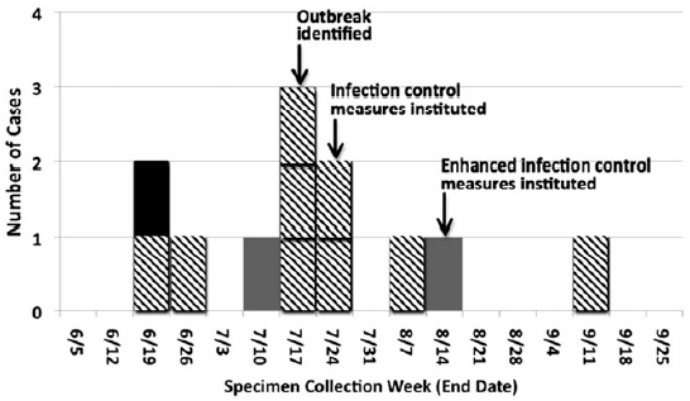


Fig 2. Number of hPIV-3–positive patients detected at JHSKCCC by month, November 2009 to October 2010.

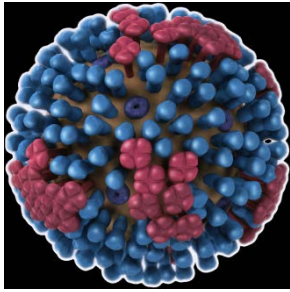


- Major cause of morbidity and mortality, especially in hematopoetic stem cell transplantation
  - Multiple outbreaks reported involving inpatient and outpatient settings

Sydnor, et al. Am J Infect Control 2012;40:601-5

Factors complicating control of respiratory viruses in transplant recipients

Control of Respiratory Viruses

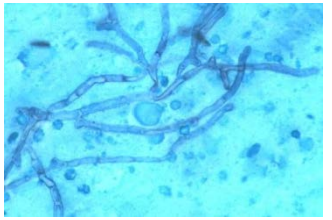


- Contact and droplet precautions for patients with URI or LRTI symptoms and possible respiratory virus pending diagnosis
- If confirmed diagnosis
  - Contact isolation – RSV, Parainfluenza
  - Droplet precautions – Influenza
  - Droplet + Contact – Adenovirus
- Hand hygiene
- Face shields, gowns, gloves if procedures with aerosolization of secretions
- Daily screening* if symptoms during outbreaks
  - Screening to determine termination of shedding
  - ??? Screening of asymptomatic patients
- Restriction of visitors and HCWs with symptoms
  - ??? Restriction of pediatric visitors
- Cohorting of HCW working with affected patients
- Influenza vaccine

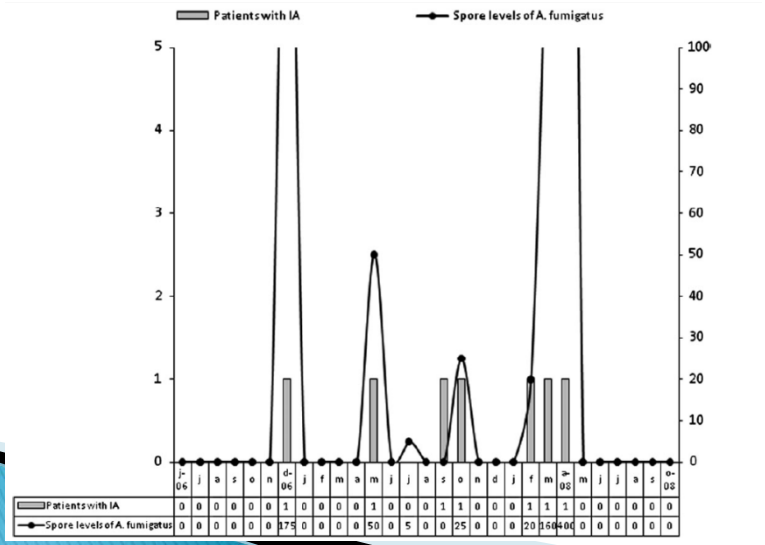
*PCR or antigen detection

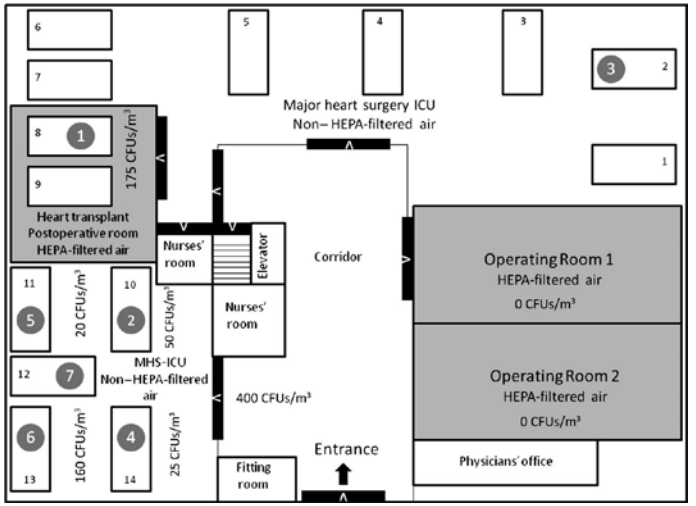
Yokoe, et al. Bone Marrow Transplant 2009;44:495-507

Aspergillus



- Significant cause of morbidity and mortality in SCT and SOT
  - Pulmonary, wound, disseminated infections
- Association with construction
  - Minimum concentration of spores necessary to cause infection remains unknown – range 0 to >100 cfu/m3





Pelaez, et al. Clin Infect Dis 2012;54:e24-31

Construction and Renovation

(Courtesy of Dr. David Pegues)

- Perform infection control risk assessment (ICRA) before construction or renovation
  - 4 project types (A–D)
  - 4 patient risk groups (HCT and SOT—highest)

Patient Risk Group	Project Type A	Project Type B	Project Type C	Project Type D
LOW Risk	Class I	Class II	Class II	Class III/IV
MEDIUM Risk	Class I	Class II	Class III	Class IV
HIGH Risk	Class I	Class II	Class III/IV	Class IV
HIGHEST Risk	Class II	Class III/IV	Class III/IV	Class IV

  - Rigid, dust-proof barriers (BIII); negative air pressure (AII); tacky floor mats
  - Monitor air quality during construction (particle counts, air sampling, ventilation pressure differentials (CIII)

Biol Blood Marrow Transplant 2009;15:1143–1238.

Legionella

- Legionella is commonly found in potable water, including in 25% hospitals, 70% water supplies 1 survey*
- Outbreaks in transplant units
  - Considered nosocomial if onset ≥10 days after admission (possible if 2-9 days)
- Nosocomial cases should be investigated
- Water source sampling (AI)
  - showers, tap water, faucets, cooling towers and hot water tanks
- Decontamination of water sources (AIII)
- Sterile water sources for respiratory treatments (BII)
- Avoid decorative fountains (BIII)
- Environmental surveillance of potable water in transplant centers (CIII)
  - Maintain Legionella free water supply and avoid transplant patient contact with contaminated water (drinking/bathing, etc)

*Stout JE, et al. Infect Control Hosp Epidemiol 2007;28:818-24
Yokoe, et al. Bone Marrow Transplant 2009;44:495-507

Should transplant patients be isolated (in the absence of communicable illness)?

- Initial goal of protective environment rooms not practical
  - Reserve for highest risk (GVHD, prolonged neutropenia)
  - Protective environment room characterized by
    - Air exchanges (12/per hour)
    - Central or point-of-use high-efficiency particulate air (HEPA) filters (AIII)
    - Directed air flow so that air intake occurs at one side of the room and air exhaust occurs at the opposite side (BIII)
    - Consistent positive air pressure differential between patient room and hallway (BIII)
    - Well-sealed rooms (BIII)
    - Continuous pressure monitoring, especially while rooms are occupied (BIII)
    - Self-closing doors to maintain constant pressure differentials (BIII)

Yokoe, et al. Bone Marrow Transplant 2009;44:495-507

In the absence of protective environment

- Portable HEPA filters for higher risk
- No clear benefit from laminar air flow

- SOT rooming guidelines and protective environment not standardized

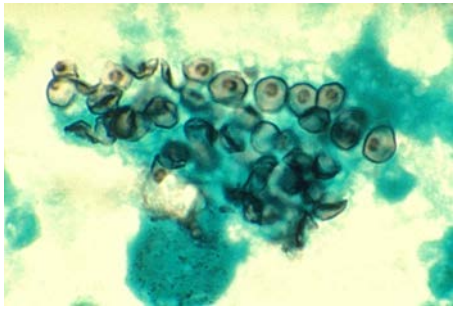
What about plants?

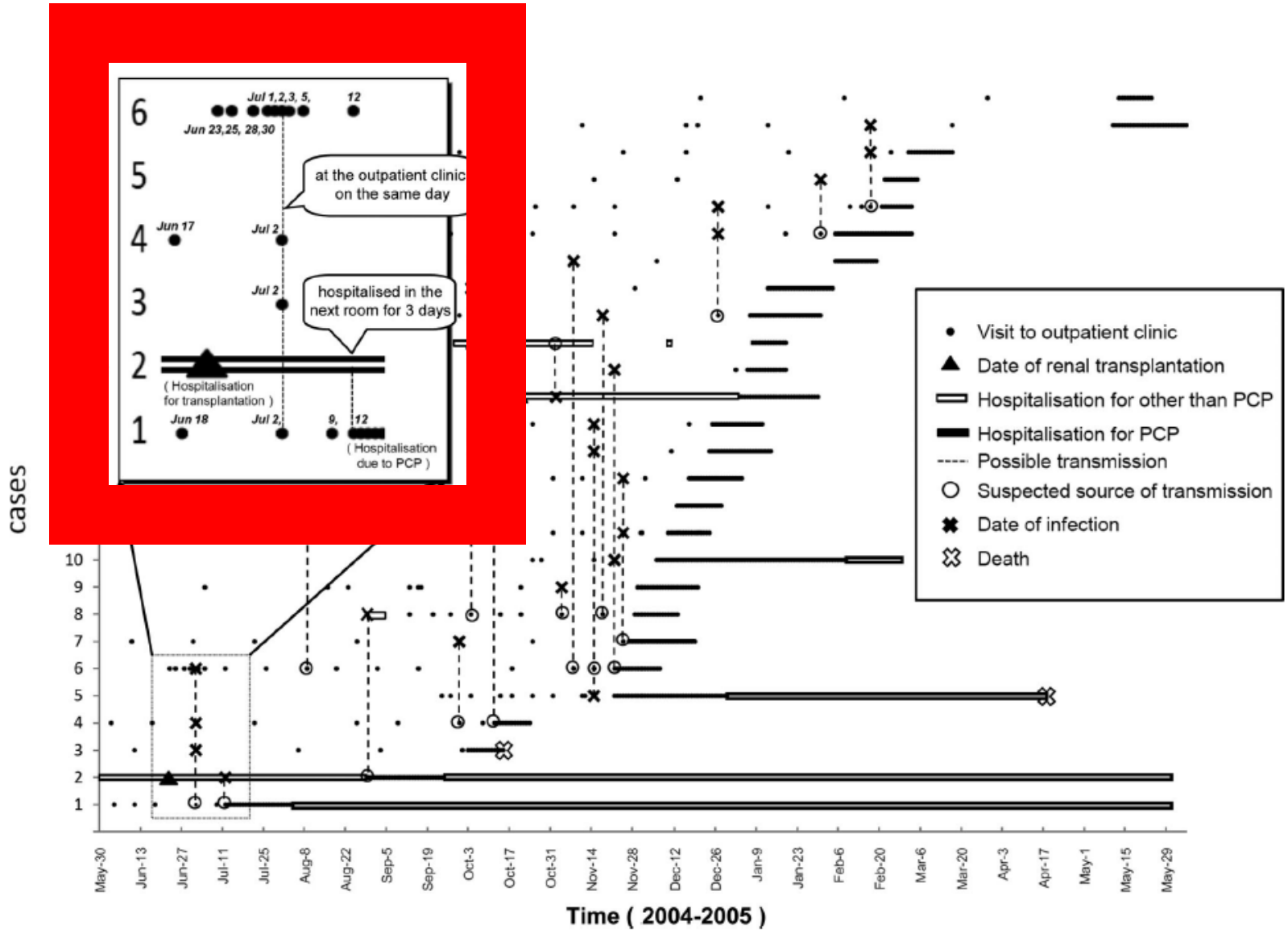
- Data linking plants to infection is limited
  - Aspergillus isolated from surfaces of dried flowers, soil of potted plants, fresh flowers
  - Gram negatives (especially Pseudomonas) isolated from water in vases
    - After 72 hours ~10^7 to 10^{10} bacteria/mL*
- Avoid contact with plants, soil (DIII)
  - Recommendations specific for SCT, but consider for SOT

*Rosenzweig AL. Lancet 1973;2:598.
Yokoe, et al. Bone Marrow Transplant 2009;44:495-507

Are infection control interventions necessary for Pneumocystis prevention?

- Transplant recipients at high risk for PCP
  - Immunosuppression targeting T cell function
    - Mycophenolate mofetil
  - Corticosteroids
  - Co-infection with immunomodulatory viruses (CMV)
- Pneumocystis not usually considered hospital acquired, but….
  - Infection clusters on transplant units
    - Stem cell/cancer
    - Renal transplant
    - Liver transplant

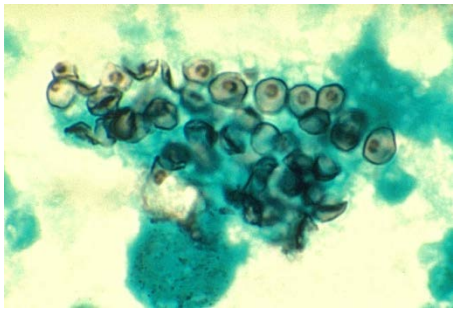




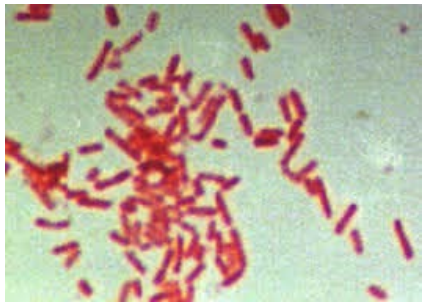
Yazaki, et al Transplantation 2009;88:380-5

Pneumocystis transmission

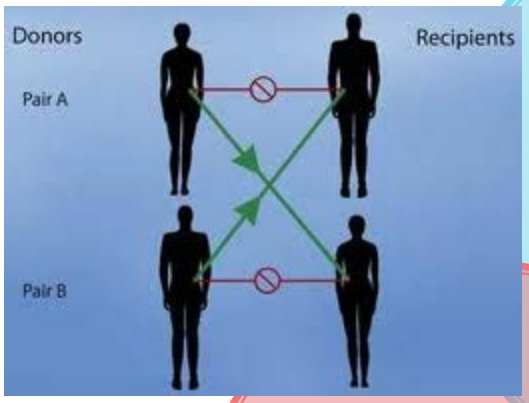
- Evidence for nosocomial transmission
  - Clustered cases
  - Molecular typing confirms strain homology suggesting common source
    - Person to person spread, possibly asymptomatic individuals
    - Air sampling
- However, insufficient evidence for transmission to warrant infection control intervention
- Preferred prevention: antimicrobial administration to susceptible hosts



Future challenges



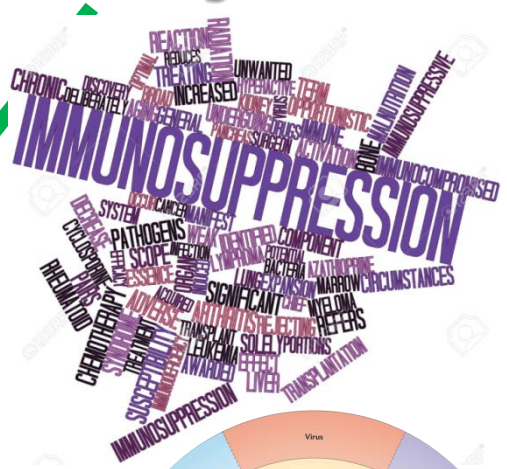
Multidrug Resistance

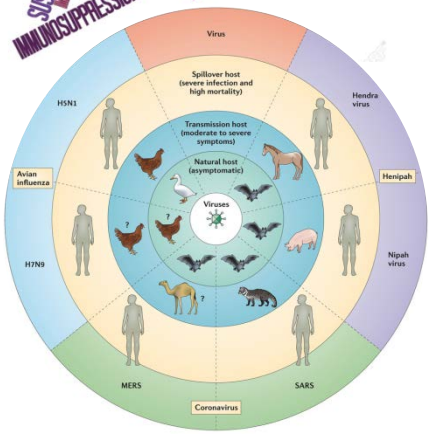


Hospital

Community

Long term care





Emerging Pathogens