Infection Control in Immunocompromised Patients

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คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี
Outline

- Type of immunocompromised state
- Infection complications in kidney transplant recipient
- Infection in other types of host
Immunocompromised state

- Impaired phagocyte function and number
  - Neutropenia
  - Steroid users
- Impaired cellular immune response
  - Kidney and other organ transplant recipients
  - Steroid users
  - AIDS
- Anatomical barrier: solid organ transplant
Usual Sequence of Infections after Organ Transplantation

Viral
- HSV
- Onset of CMV
- EBV, VZV (shingles), influenza, RSV, adenovirus
- Onset of hepatitis B or hepatitis C

Bacterial
- Wound infections, catheter-related infections, pneumonia
- Nocardia
- Listeria, tuberculosis

Fungal
- Pneumocystis
- Aspergillus
- Cryptococcus
- Candida
- Geographically restricted, endemic fungi

Parasitic
- Strongyloides
- Toxoplasma
- Leishmania
- Trypanosoma cruzi

Conventional Nosocomial Infections

Unconventional or Opportunistic Infections

Community-Acquired or Persistent Infections

Fishman JA NEJM 1998; 38:1741-51
Infectious complications after kidney transplantation

Protocol and findings

- Observational study in 127 adult recipients transplanted from 2001 to 2004
- Induction: thymoglobulin (50%) or basiliximab (50%), maintained on mycophenolate mofetil, either tacrolimus (73%) or sirolimus (27%), and prednisone (79%)
- Antimicrobial prophylaxis: perioperative cefazolin

Protocol and findings

- 127 infections in 65 patients
  - 60 episodes of UTI 47% among 31 pts.
    - 16 recurrent UTI
    - 8 bacteremia
    - 6 caused by gram-negative bacilli
  - Viral infections 17%
  - Pneumonia 8%
  - Surgical wound infections (7%)

Time course and frequency of infections after transplantation

- UTI
- Viral inf
- SWI
- Pneumonia
- SSTI
- Bacteremia
- Other

## Risk factors for infections

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk factor</th>
<th>OR</th>
<th>p-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial</td>
<td>LD</td>
<td>4.4</td>
<td>0.004</td>
<td>1.6–11.9</td>
</tr>
<tr>
<td></td>
<td>DM</td>
<td>2.65</td>
<td>0.03</td>
<td>1.1–6.6</td>
</tr>
<tr>
<td></td>
<td>ATG</td>
<td>3.3</td>
<td>0.009</td>
<td>1.3–7.9</td>
</tr>
<tr>
<td></td>
<td>SRL</td>
<td>2.5</td>
<td>0.047</td>
<td>1.1–6.4</td>
</tr>
<tr>
<td>Viral</td>
<td>DGF</td>
<td>3</td>
<td>0.034</td>
<td>1.1–8.3</td>
</tr>
<tr>
<td>Fungal</td>
<td>DM</td>
<td>13.5</td>
<td>0.035</td>
<td>1.2–151.0</td>
</tr>
<tr>
<td>UTI</td>
<td>Retransplant</td>
<td>4.5</td>
<td>0.059</td>
<td>0.95–21.2</td>
</tr>
<tr>
<td></td>
<td>Stent</td>
<td>2.9</td>
<td>0.029</td>
<td>1.1–7.4</td>
</tr>
<tr>
<td>Recurrent UTI</td>
<td>DM</td>
<td>12.6</td>
<td>0.025</td>
<td>1.4–114.7</td>
</tr>
<tr>
<td></td>
<td>ESRD yr</td>
<td>0.7</td>
<td>0.033</td>
<td>0.54–0.97</td>
</tr>
<tr>
<td></td>
<td>Retransplant</td>
<td>140.4</td>
<td>0.001</td>
<td>6.9–2873.2</td>
</tr>
</tbody>
</table>

Urinary tract infections (UTIs) occurring in patients receiving kidney transplants have continued to be a perplexing problem.¹⁻⁶ Urinary tract infections are the most common infection in this group of immunosuppressed patients,⁷ are reportedly associated with severe morbidity in terms of sepsis,⁵,⁸ and have been implicated as a possible cause in transplant rejection.⁹

Don E. Ramsey, MD; W. Tyree Finch, MD; Alan G. Birtch, MD

*Arch Surg* 114:1022-1025, 1979
Pathogenesis of CAUTI in general patients

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>GPC</th>
<th>Yeast</th>
<th>GNB</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extraluminal</td>
<td>79%</td>
<td>69%</td>
<td>54%</td>
<td>66%</td>
</tr>
<tr>
<td>Intraluminal</td>
<td>21%</td>
<td>31%</td>
<td>46%</td>
<td>34%</td>
</tr>
</tbody>
</table>

**Extraluminal**
- *Early*, at insertion
- *Late*, by capillary action

**Intraluminal**
- Break in closed drainage
- Contamination of collection bag urine

Maki DG and Tambyah PA. EID 2001; 7:342-7
Pathogenesis of CAUTI in general patients

### Risk factors for CA-UTI in general patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged catheterization &gt;6 days</td>
<td>5.1-6.8</td>
</tr>
<tr>
<td>Female gender</td>
<td>2.5-3.7</td>
</tr>
<tr>
<td>Catheter insertion outside operating room</td>
<td>2.0-5.3</td>
</tr>
<tr>
<td>Urology service</td>
<td>2.0-4.0</td>
</tr>
<tr>
<td>Other active sites of infection</td>
<td>2.3-2.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.2-2.3</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>2.4</td>
</tr>
<tr>
<td>Azotemia (creatinine &gt;2.0 mg/dL)</td>
<td>2.1-2.6</td>
</tr>
<tr>
<td>Ureteral stent</td>
<td>2.5</td>
</tr>
<tr>
<td>Monitoring of urine output</td>
<td>2</td>
</tr>
<tr>
<td>Drainage tube below level of bladder and above</td>
<td>1.9</td>
</tr>
<tr>
<td>collection bag</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial-drug therapy</td>
<td>0.1-0.4</td>
</tr>
</tbody>
</table>

Maki DG., Tambyah PA. Emerg Infect Dis 2001; 7:1-6
UTI in kidney transplanted-recipients

### Major risk factors for bacterial UTI in renal transplant recipients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>5.8 (3.79–8.89)</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.02 (1.01–1.04)</td>
</tr>
<tr>
<td>Reflux kidney disease prior to transplantation</td>
<td>3.0 (1.05–8.31)</td>
</tr>
<tr>
<td>Deceased donor</td>
<td>3.64 (1.0–12.7)</td>
</tr>
<tr>
<td>Duration of bladder catheterization</td>
<td>1.50 (1.1–1.9)</td>
</tr>
<tr>
<td>Length of hospitalization prior to UTI</td>
<td>0.92 (0.88–0.96)</td>
</tr>
<tr>
<td>Increase in immunosuppression</td>
<td>17.04 (4.0–71.5)</td>
</tr>
</tbody>
</table>

### TABLE 3. Risk factors for early UTI (Growth of $10^5$ or more colony-forming units/mL urine)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n  ( % )</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per decade increase)</td>
<td>1166 (100.0)</td>
<td>1.11 (1.01–1.23)</td>
</tr>
<tr>
<td>Female</td>
<td>452 (38.8)</td>
<td>2.87 (2.21–3.73)</td>
</tr>
<tr>
<td>African American</td>
<td>320 (27.4)</td>
<td>1.01 (0.75–1.35)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>364 (31.2)</td>
<td></td>
</tr>
<tr>
<td>Prior kidney transplant</td>
<td>125 (10.7)</td>
<td></td>
</tr>
<tr>
<td>Deceased-donor transplant</td>
<td>607 (52.1)</td>
<td>0.97 (0.72–1.32)</td>
</tr>
<tr>
<td>Ureteral stent</td>
<td>532 (45.6)</td>
<td>1.40 (1.07–1.82)</td>
</tr>
<tr>
<td>Vancomycin prophylaxis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>136 (11.7)</td>
<td>1.19 (0.84–1.69)</td>
</tr>
<tr>
<td>Antithymocyte globulin induction</td>
<td>1008 (86.4)</td>
<td></td>
</tr>
<tr>
<td>Corticosteroid maintenance&lt;sup&gt;b&lt;/sup&gt;</td>
<td>217 (18.6)</td>
<td></td>
</tr>
<tr>
<td>DGF&lt;sup&gt;c&lt;/sup&gt;</td>
<td>249 (21.4)</td>
<td>1.38 (0.99–1.92)</td>
</tr>
<tr>
<td>Prolonged use of Foley catheter&lt;sup&gt;d&lt;/sup&gt;</td>
<td>89 (7.6)</td>
<td>3.92 (2.83–5.43)</td>
</tr>
<tr>
<td>TMP/SMX prophylaxis&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1112 (95.4)</td>
<td>0.55 (0.34–0.89)</td>
</tr>
</tbody>
</table>

<sup>d</sup>Continued use of Foley catheter or intermittent self-catheterization beyond 7 days after kidney transplantation

Lee JR et al. Transplantation 2013;96: 732Y738
Effect of ureteric stent

- 201 patients were studied, stent (112) and a no-stent (89)
- At 3 months there were significantly more cases of urinary leakage (8.9% vs 0.9%, p <0.008) and ureteral obstruction (7.7 % vs 0%, p <0.004) in the no-stent
- A significant increase in UTI when stent was left >30 days after transplantation compared to the rate in the no-stent group (p <0.02)

Major risk factors for candiduria in renal transplant recipients

<table>
<thead>
<tr>
<th>Risk factor (references)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>12.5 (6.70–23.0)</td>
</tr>
<tr>
<td>ICU care</td>
<td>8.8 (2.3–35.0)</td>
</tr>
<tr>
<td>Prior antibiotic use</td>
<td>3.8 (1.7–8.3)</td>
</tr>
<tr>
<td>Indwelling urethral catheter*</td>
<td>4.4 (2.1–9.4)</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td>7.6 (2.1–27)</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>2.4 (1.3–4.4)</td>
</tr>
</tbody>
</table>

*days of bladder catheterization for each day (OR, 1.44; 95% CI, 1.05–1.96; P = .023)
Major risk factors for acute pyelonephritis in renal transplant recipients

<table>
<thead>
<tr>
<th>Risk factor (references)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>5.14 (1.86–14.20)</td>
</tr>
<tr>
<td>Acute rejection episodes</td>
<td>3.84 (1.37–10.79)</td>
</tr>
<tr>
<td>Number of UTIs</td>
<td>1.17 (1.06–1.30)</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>1.9 (1.2–2.3)</td>
</tr>
</tbody>
</table>

Factors affecting the net state of immunosuppression in transplant recipients

- Immunosuppressive therapy: dose, duration, and temporal sequence
- Underlying immune deficiency: autoimmune disease, functional immune deficits
- Integrity of the mucocutaneous barrier: catheters, epithelial surfaces
- Devitalized tissue, fluid collections
- Neutropenia, lymphopenia
- Metabolic conditions: Uremia, malnutrition, DM, alcoholism with cirrhosis
- Infection with immunomodulating viruses: CMV, Epstein–Barr virus, hepatitis B and C viruses, HIV

Fishman JA NEJM 1998; 38:1741-51
Clinical features of UTI in kidney transplant

- No Pyuria: 27
- Pyuria: 38
- Dysuria: 2
- Fever: 2
- Fever and Dysuria: 2
- No Symptoms: 59
The majority of renal transplant recipients with bacteriuria do not have symptoms with their UTI, hence have “asymptomatic bacteriuria” (ASB).
Cytokine response in ASB

Median IL-6 and IL-8 urine concentration (pg/mg creatinine), logarithmic scale

Ciszek M et al Transplantation 2006;81: 1653–1657
Implications

- Definition of “UTI”: symptoms included?
- Prolonged urinary catheterization >7 days definitely increased risk of both symptomatic UTI and ASB
- Ureteric stent plays role, but to what extent? – plus weight against risk of leakage
Urinary tract infection

Key factors:
- Long-standing kidney disease
- Kidney stone
- Urinary catheterization
Summary of recommendations:

- Appropriate Urinary Catheter Use
- Proper Techniques for Urinary Catheter Insertion
- Proper Techniques for Urinary Catheter Maintenance
- Quality Improvement Programs
- Administrative Infrastructure
- Surveillance

Guideline for prevention of catheter-associated urinary tract infections, CDC; 2009
Appropriate Urinary Catheter Use:

- Acute urinary retention or bladder outlet obstruction
- Accurate measurements of urinary output
- Perioperative use: only as necessary
Appropriate Urinary Catheter Use:

- Assist in healing of open sacral or perineal wounds in incontinent patients
- Prolonged immobilization
- Improve comfort for end-of-life care

Properly secure indwelling catheters
Proper Techniques for Urinary Catheter Care

- Hand hygiene immediately before and after insertion or any manipulation of the catheter device or site.
Proper Techniques for Urinary Catheter Maintenance

- If breaks in aseptic technique, or disconnection, or leakage occur, replace the catheter and collecting system using aseptic technique and sterile equipment.
Proper Techniques for Urinary Catheter Maintenance

- Use urinary catheter systems with preconnected, sealed catheter-tubing junctions
Proper Techniques for Urinary Catheter Maintenance

- Maintain unobstructed urine flow; free from kinking, below the bladder all the times, do not rest the bag on the floor.
Proper Techniques for Urinary Catheter Maintenance

- Do not clean the periurethral area with antiseptics to prevent CAUTI while the catheter is in place.
- Routine hygiene (eg, cleansing of the meatal surface during daily bathing or showering) is appropriate.
Surgical site infections
Other infections
Food-borne illness

- Salmonella enterica
- Aeromonas hydrophila
- Vibrio vulnificus
- Streptococcus suis
Airborne diseases

- Droplet transmissions
  - Respiratory virus
- Airborne transmissions
  - Herpes zoster (disseminated)/ varicella zoster
  - Tuberculosis
ไข้หวัดใหญ่แพร่ได้อย่างไร

- ไอ จา الموجودة
- การสัมผัสสารคัดหลั่งโดยตรงหรือสัมผัสพื้นผิวที่เปื้อนสารคัดหลั่ง
- การใช้สิ่งของรับประทานอาหารร่วมกัน
การป้องกัน

- ผู้ป่วยที่มีสุขภาพไม่ดี อาจเสียชีวิตจาก การติดเชื้อไวรัสระบบทางเดินหายใจ ได้
- การป้องกัน
  - วัคซีน
  - Respiratory Hygiene/Cough Etiquette
Respiratory Hygiene/Cough Etiquette

- Source control measures
Respiratory Hygiene/Cough Etiquette

- Source control measures

![Image showing source control measures: Covering mouth with elbow or arm, and using tissue or sleeve.](image)
Respiratory Hygiene/Cough Etiquette

- Hand hygiene after contact with respiratory secretions

- Spatial separation, ideally >3 feet, of persons with respiratory infections
ข้อปฏิบัติสำหรับบุคลากร

- หลีกเลี่ยงการอยู่ใกล้ชิดกับผู้ป่วยเมื่อทำาเป็นหัวด
- สวม surgical mask เมื่อป่วย
- ฉีดวัคซีนทุกปี
Airborne disease
Herpes zoster

- 1 dermatome: standard precautions
- Disseminated: airborne precautions
Herpes zoster

- Exposed HCW or patients: HZV immunoglobulin and HZV vaccine
- All HCWs without protective antibody against HZV should receive 2 doses of varicella zoster vaccine
- Exposed HCW should be monitored starting D8 after exposure for possible HZV disease
Tuberculosis
Key Points for TB Prevention in Hospitals

- Early diagnosis
  - Check CXR, esp. those who will enter closed area – OR, wards with air-conditioning systems
- Early treatment
- Early isolation or discharge
  - Negative pressure ventilation or open air
  - Surgical mask for patients, N-95 mask for HCWs