Obstructive Uropathy
PATHOPHYSIOLOGIC CHANGES

UOO vs BUO

Arry Rodjani
Urology Department
Ciptomangunkusumo Hospital
Jakarta
INTRODUCTION

**Obstructive uropathy** refers to the functional or anatomic obstruction of urinary flow at any level of the urinary tract.

**Obstructive nephropathy** is present when the obstruction causes functional or anatomic renal damage.

**Hydronephrosis** is the dilation of the renal pelvis or calyces. It may be associated with obstruction but may be present in the absence of obstruction.
INTRODUCTION

Urinary Tract Obstruction ➔ tubular pressure changes, renal blood flow, and glomerular filtration rate ➔ affecting the excretion function and renal homeostasis ➔ irreversible renal impaired
Obstruction of the urinary tract may occur during fetal development, childhood, or adulthood.

In Indonesia, mostly caused by stone in the urinary tract.
Posible causes of obstructive nephropathy

**Renal**

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>Polycystic kidney, renal cyst, aberrant vessel at ureteropelvic junction</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Wilms’ tumor, renal cell ca, TCC of the renal pelvis, multiple myeloma</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Calculi</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Sloughed papillae, trauma, renal artery aneurism</td>
</tr>
</tbody>
</table>
Posible causes of obstructive nephropathy

### Ureter

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>Stricture, ureteroceles, uretero-vesical reflux, ectopic kidney, retrocaval ureter, Prune-Belly syndrome</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Primary carcinoma of ureter, metastastic carcinoma</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Tuberculosis, abscess, ureteritis cystica, endometriosis</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Retroperitoneal fibrosis, pelvic lipomatosis, radiation therapy, lymphocele, trauma, urinoma, pregnancy</td>
</tr>
</tbody>
</table>
### Possible causes of obstructive nephropathy

**Bladder and Urethra**

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>Posterior urethral valve, phimosis, urethral stricture</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Bladder ca, prostate ca, ca of urethra, ca of penis</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Prostatitis, paraurethral abscess</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Benign prostatic hyperplasia, Neurogenic bladder</td>
</tr>
</tbody>
</table>
SYMPTOMS

Wide range symptoms, depend on:

1. Acute / chronic
2. Unilateral / bilateral
3. The cause of obstruction (extrinsic vs intrinsic)
4. Complete obstruction / partial obstruction
5. Presence or absence of infection
6. Compliance of collecting system
Pathophysiologic changes

Uuo vs BuO
UNILATERAL URETERAL OBSTRUCTION (UOO)

1. Acute phase (1-2 hrs)
2. Mid phase (2-5 hrs)
3. Later phase (5-24 hrs)
Triphasic relationship between ipsilateral renal blood flow and left ureteral pressure during 18 hours of left-sided occlusion

Pais V, In Walsh PC, Campbell’s Urology, WB Saunders 2007;37:1195-1126
Summary of the functional changes during and following ureteral obstruction

Pais V, Pathophysiology of Urinary Tract Obstruction In Walsh PC, Campbell's Urology, WB Saunders 2007;37:1195-1126
This difference between the two pathophysiologic conditions due to an accumulation of vasoactive substances in BUO that could contribute to preglomerular vasodilation and postglomerular vasoconstriction.

Such substances would not accumulate in UUO as they would be excreted by the contralateral kidney.

It is proved ==> diuresis and natriuresis after release of obstruction
Summary of the functional changes during and following ureteral obstruction

- **UNILATERAL**
  - **Acute phase (1-2 hrs):**
    - $\uparrow$ RBF: $\downarrow R_{\text{aff}}$ $\downarrow$ TG feedback
    - $\sim$ GFR: $\downarrow R_{\text{aff}}$ $\uparrow R_{\text{eff}}$ $\uparrow P_{\text{GC}}$ $\uparrow P_T$
    - $\uparrow$ PGE$_2$, angII, ET
  - **Mid phase (2-5 hrs):**
    - $\downarrow$ RBF: $\uparrow R_{\text{eff}}$ shift to inner cortex
    - $\downarrow$ GFR: $\uparrow P_T$ $\uparrow P_{\text{GC}}$
  - **Later phase (24 hrs):**
    - $\downarrow$ RBF: $\uparrow R_{\text{eff}}$
    - $\downarrow$ GFR: $\uparrow P_T$ $\sim P_{\text{GC}}$
    - $\uparrow$ AngII, ET
  - **Post-obstruction +24 hrs:**
    - $\downarrow$ RBF: $\uparrow R_{\text{eff}}$ ($\sim$ angII, TXA$_2$, ET)
    - $\downarrow$ GFR: $\downarrow$ P$_{\text{GC}}$ $\downarrow P_T$ [diuresis]
    - $\uparrow$ Urine flow, $FE_{\text{Na}}$; $\downarrow$ $FE_K$
    - $\downarrow$ Acidification, transporters, AQP
    - Offset by contralateral retention

- **BILATERAL OR SOLITARY**
  - **Acute phase (1-2 hrs):**
    - $\uparrow$ RBF: $\uparrow R_{\text{aff}}$
    - GFR: $\uparrow P_T$ $\sim P_{\text{GC}}$
    - $\uparrow$ Sympathetic nerve activity
  - **Later phase (24 hrs):**
    - $\uparrow$ RBF: $\uparrow R_{\text{eff}}$
    - GFR: $\uparrow P_T$ $\sim P_{\text{GC}}$
    - $\uparrow$ Systemic vasoactive factors

---

Pais V, Pathophysiology of Urinary Tract Obstruction In Walsh PC, *Campbell's Urology*, WB Saunders 2007;37:1195-1126
Summary of the functional changes during and following ureteral obstruction

Unilateral

- **RBF:** ↓ $R_{aff}$, ↓ TG feedback
- **GFR:** ↓ $R_{aff}$, ↑ $R_{eff}$, ↑ $P_{GC}$, ↑ $P_T$
- ↑ $PGE_2$, angII, ET

Bilateral or Solitary Kidney

- **RBF:** ↑ $R_{aff}$
- **GFR:** ↑ $P_T$, ~ $P_{GC}$
- ↑ Sympathetic nerve activity

Acute phase (1–2 hrs)

Pais V, In Walsh PC, *Campbell’s Urology*, WB Saunders 2007;37:1195-1126
Summary of the functional changes during and following ureteral obstruction

**Unilateral**
- RBF: ↓R\text{eff} \enspace shift to inner cortex
- GFR: ↑P_T \enspace ↑P_{GC}

**Bilateral or Solitary Kidney**
- Mid phase (2–5 hrs)
- RBF: ↑R\text{eff} \enspace less flow shift
- GFR: ↑↑P_T

Pais V, In Walsh PC, *Campbell’s Urology*, WB Saunders 2007;37:1195-1126
Summary of the functional changes during and following ureteral obstruction

Unilateral

- \( RBF: \uparrow \downarrow R_{aff} \)
- \( GFR: \downarrow P_{GC} \sim P_T \)
- \( \uparrow \text{AngII, ET} \)

Later phase (24 hrs)

Bilateral or Solitary Kidney

- \( RBF: \uparrow R_{eff} \)
- \( GFR: \uparrow \uparrow P_T \sim P_{GC} \)
- \( \uparrow \text{Systemic vasoactive factors} \)

Pais V, In Walsh PC, *Campbell’s Urology*, WB Saunders 2007;37:1195-1126
Tubular renal function changes after the release of obstruction depends on whether the obstruction is unilateral or bilateral.

After elimination of complete bilateral obstruction, natriuresis and diuresis, known as *post-obstructed diuresis*.
RENAL FUNCTIONAL CHANGES AFTER RELEASE OF OBSTRUCTION

GFR ➔ became normal after 1 week obstruction released.

Not all nephrons are functionally reversible ➔ hyperfiltration occur in normal nephrons as a compensatory mechanism ➔ GFR back to normal level
Summary of major pathways leading to tubulointerstitial fibrosis and tubular apoptosis as a consequence of ureteral obstruction

Pais V, In Walsh PC, *Campbell’s Urology*, WB Saunders 2007;37:1195-1126
Intrarenal Reflux of Bacteria

Bacterial Endotoxin → Granulocyte Aggregation

Chemotaxis (Granulocytes) → Capillary Obstruction

Bacterial Killing

Phagocytosis of Bacteria → Renal Ischemia

Superoxide Release → Reperfusion

Lysosome Release

Tubular Cell Death

Interstitial Inflammation

Microabscess

Renal Scar
The management is performed to:

(a) relief pain

(b) recover or maintain renal function

(c) avoid complication
## Indication to release obstruction

<table>
<thead>
<tr>
<th>Unilateral obstruction</th>
<th>Bilateral obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain unrelieved by analgesics</td>
<td>Same as for OUU or</td>
</tr>
<tr>
<td>Signs and symptoms of sepsis</td>
<td>Elevated BUN and creatinine</td>
</tr>
<tr>
<td>Persistent nausea and vomiting</td>
<td>Signs and symptoms of uremia</td>
</tr>
<tr>
<td>High-grade obstruction</td>
<td>Hyperkalemia</td>
</tr>
</tbody>
</table>
Haemoglobin level and parenchymal thickness are good prognostic factors for renal function recovery after percutaneous nephrostomy in obstructive uropathy patients

Fadloli A, Rodjani A, Mochtar CA

Division of Urology Department of Surgery, Faculty of Medicine, University of Indonesia - Cipto Mangunkusumo Hospital
Aim of study

Whether improvement of kidney function after drainage of the obstructed kidney are depend on parenchymal thickness and hemoglobin level
Methods

- Prospective study

- 124 patients with bilateral (or unilat in solitary kidney) obstructive uropathy underwent percutaneous nephrostomy

- BUN, serum creatinin and Hb measured
Methods

• Kidney perenchym thickness measured by Pie Medical scanner 200 ultrasound

• Patients were stratified into Hb <8 mg/dl (Hg 1) and Hb ≥8 mg/dl (Hb 2) groups; renal parenchym thickness into <0.5 cm (K1) and ≥0.5 cm (K2) groups
Results

n = 124 pts

Creatinine (mg/dl) at H 14:

Hb 1    2.8 ± 1.1
Hb 2    1.8 ± 1.1  (p < 0.01)

K 1     2.7 ± 1.0
K 2     1.7 ± 0.6  (p < 0.01)
Conclusion

Haemoglobin level and renal parenchymal thickness are good prognostic factors for renal function recovery after percutaneous nephrostomy in obstructive uropathy patients
1. Urinary tract obstruction $\Rightarrow$ tubular pressure changes, renal blood flow, and glomerular filtration rate $\Rightarrow$ affecting the excretion function and renal homeostasis $\Rightarrow$ irreversible renal impaired

1. Several substances are thought to play a role in the apoptosis $\Rightarrow$ tubulular fibrosis and atrophy $\Rightarrow$ tubulointerstitial fibrosis $\Rightarrow$ The mechanism of the development of CRF
SUMMARY

3. There are several differences between BUO and UUO ==> hemodynamic changes and some factors that might affect GFR

4. A number of vasoactive substances are thought to play a role in the changes in RBF and GFR occurring with both models of obstruction.
Thank You
URINARY TRACT INFECTIONS

CLINICAL PYELONEPHRITIS: FEVER, ABDOMINAL/FLANK PAIN; N/V

-- ACUTE PYELONEPHRITIS—RENAL PARENCHYMAL INVOLVEMENT (DMSA SCAN)

-- PYELITIS

CYSTITIS: BLADDER INVOLVEMENT ONLY; DYSURIA, FREQUENCY, URGENCY, INCONTINENCE

ASYMPTOMATIC BACTERIURIA: UNCOMMON
URINALYSIS

GREISS TEST: MEASURES NITRATE REDUCTASE

LEUKOCYTE ESTERASE: DEMONSTRATES ESTERASES IN LEUKOCYTES
UTI--INCIDENCE

GIRLS: 3% - 8.4%; RECURS IN 60% TO 80% WITHIN 5 YEARS

BOYS: 1.1% - 1.7%; DURING FIRST YEAR, RISK IN UNCIRCUMCISED BOY 10X HIGHER

FIRST YEAR: M:F 2.8-5.4 : 1; USUALLY UPPER TRACT; SX MAY BE NON-SPECIFIC

BEYOND FIRST YEAR: F:M 10 : 1
PILI

TYPE I: MANNOSE SENSITIVE
ATTACHMENT BLOCKED BY D-MANNOSE; NOT INVOLVED IN PYELO

TYPE II: MANNOSE RESISTANT
ALSO TERMED P-FIMBRIAE → GAL 1-4
GAL RECEPTOR
UTI--FIMBRIAE

TYPE I AND TYPE II CAN COEXIST ON SAME BACTERIA

76% - 94% OF E. COLI→PYELO HAVE P-FIMBRIAE

20% OF E. COLI→CYSTITIS HAVE P-FIMBRIAE
UTI: RISK FACTORS

FEMALE
UNCIRCUMCISED
VOIDING DYSFUNCTION
CONSTIPATION
URETHRAL INSTRUMENTATION
OBSTRUCTIVE UROPATHY
UTI: THERAPY

PYELONEPHRITIS: 10 - 14 DAYS LONGER IF “NEPHRONIA” NFN NOT INDICATED

CYSTITIS: 3 - 5 DAYS

ASYMPTOMATIC BACTERIURIA: IS IT TRULY ASYMPTOMATIC?
NO TX IF US AND VCUG NORMAL
ANTIMICROBIAL AGENTS

SULFONAMIDES: COMPETITIVELY BLOCK CONVERSION OF PABA TO FOLIC ACID

NITROFURANTOIN: INTERFERES WITH EARLY STAGES OF KREBS CYCLE

TMP: INTERFERES WITH DIHYDROFOLIC ACID REDUCTASE; INDUCES PHASE VARIATION
ANTIMICROBIAL AGENTS

CIPROFLOXACIN
INHIBITS BACTERIAL DNA GYRASE

AFFECTS METABOLISM OF THEOPHYLLINE

USEFUL AGAINST PSEUDOMONAS

? CARTILAGE EFFECT
RENAL SCARRING

ASSOCIATED WITH UTI AND VUR
CORRELATES WITH SEVERITY OF VUR
LESS RISK WITH PROMPT TREATMENT
IF NORMAL DMSA DURING UTI, NO SCARRING WILL RESULT
ASSOCIATED WITH HYERTENSION, RENAL INSUFFICIENCY
UTI: UPPER TRACT IMAGING

RENAL ULTRASOUND: NORMAL IN MOST WITH VUR; SHOWS 2/3 OF RENAL SCARS

IVP: SHOWS 90% OF RENAL SCARS MAY TAKE 1 TO 2 YEARS TO DEVELOP

DMSA: “GOLD STANDARD” FOR DIAGNOSING ACUTE PYELO AND RENAL SCARRING WITH GRADE III, IV, OR V VUR AND FEBRILE UTI, 80% HAVE PYELONEPHRITIS IF ACUTE PYELO, 1/2 DEVELOP SCAR
UTI: IMAGING

**US + VCUG:** ALL CHILDREN < 5 YO WITH 1 UTI
ANY CHILD WITH FEBRILE UTI
SCHOOL - AGE GIRLS WITH RECURRENT CYSTITIS
ANY AGE CHILD WITH UTI AND FH OF VUR

**US ONLY:** SCHOOL - AGE GIRLS WITH 2 EPISODES OF CYSTITIS
SCHOOL - AGE BOYS WITH 1 EPISODE OF CYSTITIS

CYSTO NOT INDICATED
VESICOURETERAL REFLUX

PRIMARY

ANTENATAL HYDRONEPHROSIS

SCREENING
MCKD; UPJ OBST.; RENAL AGENESIS
SIBLING REFLUX

SECONDARY
VOIDING DYSFUNCTION
NEUROPATHIC BLADDER
OBSTRUCTIVE UROPATHY
ASSOCIATED ANATOMIC ABNORMALITY
(UECELE, EXSTROPHY)
IATROGENIC
REFLUX NEPHROPATHY (RN): PATHOGENESIS

FETAL REFLUX CAN $\rightarrow$ RN

UTI + REFLUX CAN $\rightarrow$ RN

STERILE REFLUX USUALLY $\rightarrow$ RN

STERILE REFLUX, HIGH VOIDING PRESSURE $\rightarrow$ RN

\[ \text{Pathogenesis of Reflux Nephropathy (RN)} \]
PEDIATRIC VESICOURETERAL REFLUX

MEDICAL THERAPY - PRINCIPLES

REFLUX OFTEN RESOLVES OR BECOMES LESS SEVERE AS THE CHILD GROWS

COMPLICATIONS OF REFLUX USUALLY CAN BE AVOIDED BY PREVENTING INFECTION

AVOIDS RISKS OF SURGERY
VESICOURETERAL REFLUX:
MEDICAL MANAGEMENT

SMZ/TMP, TMP, OR NFN; 1/4 - 1/3 DOSE ONCE DAILY
REGULAR, VOLITIONAL VOIDING
IF BLADDER INSTABILITY, ANTICHOLINERGIC
UA & OR C/S IF SYMPTOMATIC
ANNUAL: HT, WT, UA; BP (IF RENAL SCARRING)
RADIONUCLIDE CYSTOGRAM OR VCUG AND UPPER TRACT STUDY Q 12-18 MONTHS
# Reflux Resolution - 5 Years

<table>
<thead>
<tr>
<th>Grade</th>
<th>% Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>92%</td>
</tr>
<tr>
<td>II</td>
<td>81%</td>
</tr>
<tr>
<td>III -</td>
<td>70%</td>
</tr>
<tr>
<td>UNI, 0-2 YR</td>
<td></td>
</tr>
<tr>
<td>UNI, 2-5 YR</td>
<td>51%</td>
</tr>
<tr>
<td>UNI, 5-10 YR</td>
<td>44%</td>
</tr>
</tbody>
</table>

-- Elder et al, 1997
# Reflux Resolution - 5 Years

<table>
<thead>
<tr>
<th>Grade</th>
<th>% Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>III-B1, 0-2 YR</td>
<td>49%</td>
</tr>
<tr>
<td>B1, 2-5 YR</td>
<td>31%</td>
</tr>
<tr>
<td>B1, 5-10 YR</td>
<td>12%</td>
</tr>
<tr>
<td>IV - UNI</td>
<td>40%</td>
</tr>
<tr>
<td>B1</td>
<td>10%</td>
</tr>
</tbody>
</table>

---

---

-- Elder et al, 1997
PEDIATRIC VESICOURETERAL REFLUX

SURGICAL THERAPY - PRINCIPLES

REFLUX HAS CAUSED OR HAS A SIGNIFICANT POTENTIAL TO CAUSE RENAL INJURY

ELIMINATION OF REFLUX REDUCES THE LIKELIHOOD OF KIDNEY INFECTION AND RENAL DAMAGE

AVoids NEED FOR LONG-TERM ANTIBIOTICS
REFLUX: SURGICAL THERAPY

INTRAVESICAL (COHEN, P=L, G-A)

EXTRAVESICAL (DETRUSORRHAPHY, LICH-GREGOIR)

TAILORING (TAPERING, PLICATION)

ENDOSCOPIC (STING)

LAPAROSCOPIC
**VUR: OPEN SURGICAL COMPLICATIONS**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent VUR</td>
<td>1% - 2.5%</td>
</tr>
<tr>
<td>Obstruction</td>
<td>1% - 2.5%</td>
</tr>
<tr>
<td>Contralateral VUR</td>
<td>5% - 10%</td>
</tr>
</tbody>
</table>
REFLUX GUIDELINES

NEW RENAL SCARRING: MEDICAL vs. SURGICAL

NO DIFFERENCE IN RANDOMIZED CONTROLLED TRIALS
REFLUX GUIDELINES

PYELONEPHRITIS: MEDICAL vs. SURGICAL

RISK 2.5 x HIGHER WITH MEDICAL THERAPY
REFLUX: INDICATIONS FOR REPAIR

GRADE V, BILATERAL GRADE IV
PERSISTENT UNILATERAL GRADE IV
FIXED ANATOMIC ABNORMALITY
? DUPLICATION

FAILURE OF MEDICAL THERAPY (BREAKTHROUGH UTI, NEW RENAL SCAR, POOR COMPLIANCE, ALLERGIC RXN, PERSISTENT REFLUX)
Urinary Tract Infections

Some Basic Sciences
## Bacterial Virulence Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pili or fimbriae</td>
<td>Adherence to uroepithelium</td>
</tr>
<tr>
<td>Capsular (K) polysaccharides</td>
<td>Protection from phagocytosis and complement-lyses system</td>
</tr>
<tr>
<td>O capsular polysaccharides</td>
<td>Protection from serum bactericidal activity (smooth &gt; rough)</td>
</tr>
<tr>
<td>Exotoxins (hemolysin)</td>
<td>Mediate inflammation and cell lysis</td>
</tr>
<tr>
<td>Siderophores (aerobactin)</td>
<td>Scavenge for iron</td>
</tr>
<tr>
<td>Urease (Proteus)</td>
<td>Increase capacity to induce pyelonephritis</td>
</tr>
</tbody>
</table>
## Host Defenses

<table>
<thead>
<tr>
<th>Level</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bladder level</strong></td>
<td>Emptying of bladder, urine - low pH, osmolality, urea, Tamm-Horsfall protein, vesicoureteric barrier, mucus (GAG) layer</td>
</tr>
<tr>
<td><strong>Ureter level</strong></td>
<td>Urine flow, peristalsis</td>
</tr>
<tr>
<td><strong>Urethral level</strong></td>
<td>Autochtonous flora</td>
</tr>
</tbody>
</table>
# Host Defenses

## Cellular/Hormonal

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular</td>
<td>Macrophages, endothelial cells, tubular cells, polys</td>
</tr>
<tr>
<td>Cytokines</td>
<td>TNF, IL-1, IL-2, IL-6, IL-10, interferon alpha</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>Vasodilation and migration of cells</td>
</tr>
<tr>
<td>Antibody response</td>
<td>IgM, IgA, IgG</td>
</tr>
</tbody>
</table>
Risk Factors
Genetic Factors

- Blood group B and AB (nonsecretors of blood group substances)
- P1 blood group phenotype
- P2 blood group phenotype in adults
- Lewis blood group nonsecretors
Urinary Tract Infections

Host Defenses vs Bacterial Virulence Factors
Antimicrobials
## Penicillins

### Aminopenicillins

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell wall</td>
<td>Hypersensitivity</td>
<td>Oral contraceptives</td>
<td>β-lactamases 35%</td>
</tr>
<tr>
<td></td>
<td>Yeast</td>
<td>(rare)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vaginitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudomembranous</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>enterocolitis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Penicillins plus β-Lactamase Inhibitors

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clavulanic acid</td>
<td>Hypersensitivity</td>
<td>Oral contraceptives (rare)</td>
<td></td>
</tr>
<tr>
<td>Sulbactam inhibit β-lactamase production</td>
<td>Yeast Vaginitis</td>
<td>Pseudomembranous enterocolitis</td>
<td>Less resistance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Augmentum (amoxicillin plus clavulanic acid)</td>
</tr>
</tbody>
</table>
# Cephalosporins

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit cell wall synthesis</td>
<td>Allergic nephrotoxicity</td>
<td>Nephrotoxic</td>
<td>Enterococci</td>
</tr>
<tr>
<td></td>
<td>hematological</td>
<td>with aminoglycosides</td>
<td>Pseudomads</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ethanol</td>
<td>Greatest Activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; gm +ve</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; anaerobes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; nosocomial</td>
</tr>
</tbody>
</table>
# Trimethoprim/Sulfamethoxazole

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit folate metabolism</td>
<td>Major AR very rare (&lt;1%)</td>
<td>Warfarin</td>
<td>E. coli and Klebsiella</td>
</tr>
<tr>
<td></td>
<td>Rash, diarrhea, vomiting</td>
<td>Sulfonylureas Phenytoin</td>
<td>(chromosome and plasmid)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5-15%</td>
</tr>
</tbody>
</table>
# Trimethoprim

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit folate metabolism</td>
<td>Rash, pruritus</td>
<td>Warfarin</td>
<td>E.coli and Klebsiella (chromosome and plasmid) 5-15%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sulfonylureas</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenytoin</td>
<td></td>
</tr>
</tbody>
</table>
## Tetracycline

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein synthesis at ribosomal level</td>
<td>GI, vaginal candidiasis, photosens. Discoloration of teeth Avoid (except doxy) in patients with renal disease (azotemia)</td>
<td>Divalent metals (Ca Mg Al Oral contraceptives diuretics</td>
<td>21% (plasmid mediated) Pseudomads Many gram neg Some gram positive</td>
</tr>
<tr>
<td>Action</td>
<td>Adverse Reactions</td>
<td>Drug interaction.</td>
<td>Resistance</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------</td>
<td>-------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Nonspecific binding to bacterial ribosomal proteins</td>
<td>GI (5-7%)</td>
<td>Mg salts</td>
<td>Unknown mechanism</td>
</tr>
<tr>
<td>Excellent for E coli S saprophyticus enterococci</td>
<td>MacroBID or Macrodictin</td>
<td></td>
<td>Low bacterial resistance</td>
</tr>
<tr>
<td>Only in urine</td>
<td>Hemolytic anemia (G-6-PD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Interstitial pneumonitis or fibrosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Aminoglycosides

<table>
<thead>
<tr>
<th>Action</th>
<th>Adverse Reactions</th>
<th>Drug Interaction.</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition of ribosomal protein synthesis</td>
<td>Ototoxicity</td>
<td>Other ototoxic and nephrotoxic drugs</td>
<td>Downregulation of drug uptake</td>
</tr>
<tr>
<td></td>
<td>Nephrotoxicity</td>
<td>Myasthenia gravis patients</td>
<td>Production of modifying enzymes</td>
</tr>
<tr>
<td></td>
<td>Neuromuscular blockade (high doses)</td>
<td>Caution in renal impairment, hepatic failure and diabetics</td>
<td></td>
</tr>
</tbody>
</table>
Urinary Tract Infections

Some Clinical Sciences
Classification

- Urinary Tract Infections
  - Uncomplicated UTI
    - Cystitis
    - Pyelonephritis
  - Complicated UTI
    - Includes Children
    - Pregnancy
  - Other Specific
    - Urethritis, Prostatitis
    - Asymptomatic Bacteriuria
Bacteriology of Uncomplicated UTI
Pyelonephritis

E. coli 85%
Proteus 4%
Klebsiella 4%
Mixed and other 7%
Bacteriology of Complicated UTI

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>32%</td>
</tr>
<tr>
<td>Enterococci</td>
<td>22%</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>22%</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>5%</td>
</tr>
<tr>
<td>Proteus</td>
<td>4%</td>
</tr>
<tr>
<td>Staph Saprophyticus</td>
<td>1%</td>
</tr>
<tr>
<td>Mixed and other</td>
<td>14%</td>
</tr>
</tbody>
</table>
Microbiological Diagnosis
Key Points

• Urine Collection
  – midstream collection
  – suprapubic aspiration
  – urethral catheterization

• Urinalysis
  – bacteriuria
  – pyuria
  – hematuria

• Rapid screen dipsticks
  – nitrite - bacteriuria
  – leukocyte esterase - pyuria

• Urine Culture
  – the relevance of $10^5$/ml colony count
Imaging in UTI

- Unnecessary in most patients with UTI
- Plain film and tomograms - gas and calculi
- IVP - traditional and still useful
- VCUG - when VUR is suspected
- Ultrasonography - noninvasive and inexpensive to rule out hydronephrosis or residual urine
- CT scan - best anatomic detail/most sensitive
- MRI - little benefits over CT scan
- Radionuclide Studies - localize abscess
KEY POINTS

Uncomplicated UTI

• healthy women
• respond to antibiotics (3 day)
• document culture (at least once)
  – relevance of bacterial count $10^5$ CFU/mL
• extensive investigation unnecessary
• prophylaxis/self treatment/post coital effective for recurrent UTIs
Antibiotics in Pregnancy

• You must know what antibiotics you can use safely in pregnancy
• You must know why you cannot use the other antibiotics in pregnancy
• Consider making up your own personal chart “Antibiotics in Pregnancy” for study review
Antibiotics to treat UTI in Pregnancy

ASB & CYSTITIS

- ACUTE
  - nitrofurantoin**
  - Sulfisoxasole*
  - Cefalexin
  - Amoxicillin
- PROPHYLAXIS
  - nitrofurantoin**

PYELONEPHRITIS

- Cefazolin
- Ceftriaxone
- Mezlocillin
- Piperacillin
- Aztronam
- Aminoglycosides

*3rd trimester jaundice
** hemolytic anemia in G6P deficiency
UTI in Pregnancy

Key Points

• UTI in pregnancy associated with pre-term birth and low birth weight.
• Asymptomatic bacteriuria should be treated and not just (symptomatic) cystitis and pyelonephritis
• UTI treatment - 3 day course
• Failure to respond in 72 hrs - further investigation
• Recurrence (40%) in non-pregnant state and subsequent pregnancy
• If recurrence, consider prophylaxis
• Treat pyelonephritis aggressively - consider hospitalization!
Complicated UTI
Key Points

• persistent infection
• unusual organisms (eg urea splitting bacteria)
• voiding dysfunction (neurogenic or obstructive)
• congenital anomalies
• stones
• catheters, stents, tubes
• immunocompromized/ diabetes
• Children
• Pregnancy

UTI in pregnancy
Complicated UTI
Key Points
Management

- culture (urine and blood) and antibiotic sensitivity
- systemic support (hydration etc)
- other investigations (U/S, CT scan etc)
- urinary drainage required (urethral or percutaneous catheter)
- long term antibiotics ± surgery
- long term follow-up required
Pyelonephritis
Diagnostic Points

- acute onset flank pain and fever
- frequency and dysuria
- flank tenderness
- pyuria and hematuria
- elevated WBC
Pyelonephritis
Patients at risk

• Children
• calculi
• congenital anomalies
• obstruction
• diabetes
• spinal cord injury
• pregnancy
• elderly