

Treating Common Infections in Patients with Diabetes

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Case Presentation (1)

A 35-year-old woman with a history of diabetes on insulin has had a cough for 3 days. On physical exam she has a fever of 102.3, pulse 124, respiration 26, and BP 90/46.

She appears toxic and has labored breathing. The lung exam is notable for left-base bronchial breath sounds and egophony. Lab exam is notable for BUN 22, Creatinine 0.8, WBC 15K. CXR confirms LLL pneumonia with a small non-layering effusion.



Questions

- What is the impact of diabetes on this patient?
- Where should the patient go?
 - Home
 - Medical Ward
 - ICU
- What antibiotics should be started?
- What should be avoided?
- What can be done to prevent pneumonia?

Impact of Diabetes on Pneumonia

- Kornum et al Diabetes Care 30: 2251–2257, 2007
 - Population-based cohort control study
 - 29,9000 patients with pneumonia in Northern Denmark
 - 9.8% of the patients had diabetes mellitus type 2
 - Mortality was 19.9% vs. 15.1% for diabetics vs. other patients at 30 days and 27% vs 21% at 90 days
 - Diabetes was not a predictor of pulmonary complications of bacteremia
 - High blood glucose was a predictor of death

Triage of the Pneumonia Patient

- CURB-65 (one point each)
 - Confusion
 - BUN > 20
 - RR > 30
 - SBP < 90 or DBP < 60
 - Age > 65
- Interpretation:
 - 0–1 Outpatient
 - 2–3 Inpatient
 - 4–5 ICU

Outpatient Pneumonia

- No recent antibiotics within three months and **no diabetes**
 - Azithromycin 500 mg po x 1 then 250 mg po daily x 4 days
- Recent Antibiotics or Comorbidities including **diabetes mellitus:**
 - Azithromycin 500 mg po x 1 then 250 mg po daily x 4 days plus Amoxicillin 1 gm po tid x 7–10 days
- Alternate agents
 - Levofloxacin 750 mg po daily x 5 days or 500 mg po daily x 7 days
 - Use this drug only if allergic to the regimens above
 - **Use with extreme caution** in pneumonia Rx:
 - **C difficile collateral damage**
 - **This drug masks tuberculosis**
 - **This drug causes dysglycemia**

Empiric Treatment Community-Acquired Pneumonia with Fluroquinolones, and Delays in the Treatment of Tuberculosis

MAJOR ARTICLE

Empiric Treatment of Community-Acquired Pneumonia with Fluoroquinolones, and Delays in the Treatment of Tuberculosis

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- Dooley et al (CID 2002): retrospective analysis of 33 pts with TB
 - 48% received prior quinolone therapy for pneumonia
 - Patients who received quinolones started first TB meds at day 21
 - Patients who did not started first TB meds at day 5
- Chen et al (Int J of ID 2011): meta-analysis of 9 eligible studies
 - Quinolone Rx delayed TB Rx by **19 days**
 - The **RR** of quinolone resistant TB developing was **2.7**

Inpatient Ward Admission for Pneumonia

- Patients with no drug allergies:
 - Ceftriaxone 1 gm IV daily plus Azithromycin 500 mg IV daily
 - Consider substituting doxycycline for azithromycin if allergic or prolonged QTc
- Cephalosporin/macrolide allergic patients
 - Clindamycin 600 mg IV q 8h plus Levofloxacin 500 mg po daily
- Cautions
 - Use caution in using macrolides in patients with heart disease
 - Use caution in using macrolides and quinolones in patients with QTc prolongation
 - Doxycycline 100 mg IV q 12h can be substituted for Azithro or Levo

Inpatient ICU Admission for Pneumonia

- Community Acquired
 - Ceftriaxone 1 gm IV daily plus Azithromycin 500 mg IV daily
 - (Ceftriaxone 1 gm IV daily plus Levofloxacin 750 mg IV daily)
- Pseudomonas suspected (underlying lung disease)
 - Piperacillin 4.5 gm IV q 6h plus Levofloxacin 750 mg IV daily
- Allergic to penicillins:
 - Clindamycin 600 mg IV q8h plus Levofloxacin 750 mg IV daily

Hospital-Acquired Pneumonia

- Two drug therapy for average risk patients:
 - Piperacillin-Tazobactam 4.5 gm IV q 6 h
 - Vanco 15 mg /kg q 12h (trough goal 15-20) or Linezolid 600 gm IV q 12h
- Add Levofloxacin 750 mg IV daily for high risk patients if:
 - Prior IV antibiotics within 90 days
 - Shock
 - Intubation
- Special Considerations:
 - Consider prolonged infusion Pip-Tazo (allows for q 8h dosing)
 - Be careful with Levofloxacin in patients with prolonged QT or possible TB
 - Avoid Vancomycin in patients with renal failure
 - Avoid Linezolid in patients on SSRIs and related agents

Other Special Situations...

- Aspiration Pneumonia options:
 - Ampicillin Sulbactam 3 gm IV q 6h
 - Piperacillin Tazobactam 3.75 gm IV q 6h
 - Clindamycin 600 gm IV q 6h
- Influenza
 - Oseltamivir 75 mg po bid for 5 days
- Hantavirus
 - Transfer patient to tertiary care center for ECMO
- Tuberculosis
 - Avoid quinolones
 - Airborne Isolate if upper lobe, miliary, immunocompromised, unexplained effusion
 - Consult ID early

How Long to Treat

- Community-Acquired Pneumonia
 - 5–7 days
- Hospital-Acquired Pneumonia
 - 7–8 days
 - Chastre et al, JAMA, 2003: 8 vs 15 days of therapy
 - Mortality 18.8% vs 17.2%
 - Recurrence 29.9% vs 26%

Duration of therapy not modified for diabetes

Vaccination

- Influenza:
 - All patients > 6 months of age
- Pneumovax (PPSV23):
 - All Patients > 65 years of age
 - Patients with selected age 19–64
 - CHF, Chronic lung disease (COPD, asthma), alcoholism, DM
 - Cigarette smoking
 - Residents of nursing homes/LTC facilities

Vaccination (cont.)

- Prevnar (PCV13):
 - **All patients 65 and older**
 - CSF leak/Cochlear implants or asplenia
 - Patients age 19–64 with highly immunocompromising conditions:
 - HIV
 - Congenital or acquired immunodeficiency
 - CKD/Nephrotic syndrome
 - Leukemia/Lymphoma/Myeloma
 - Generalized malignancy
 - Solid Organ Transplant
 - Iatrogenic immunosuppression (steroids, XRT, etc.)
 - Give **PCV13** first followed by **PPSV23** one year later if age > 65, 2 months later if immunocompromised
 - Give **PCV13** one year after **PPSV23** if that was given first

Tuberculosis and DM

- DM increases the risk of reactivation of latent TB infection three-fold
- The prevalence of TB infection is as high as 30% in some IHS Areas
- TB death rates for American Indian patients in the US are **15-fold higher** than for white patients
 - (Reilley et al, Am J Public Health. 2014 Jun; 104 Suppl 3:S453-9)
- Latent TB infection can now be treated with just 12 weekly doses of Isoniazid and Rifapentine. (3HP)

Case Presentation (2)

A 34-year-old man with DM type 2 is seen in the urgent care clinic with a red, hot, swollen left leg. He abraded his ankle 5 days ago and has a 1 cm purulent ulcer over the anterior surface with purulent drainage. He was seen elsewhere yesterday and was placed on Cephalexin 500 mg po qid but today says his leg is worse.



Cellulitis

- How does diabetes impact this patient?
- Is inpatient treatment needed?
- What is the best antibiotic for this patient?
- Are there special considerations?

Diabetes and Soft Tissue Infections

- Pathogenesis:
 - C4 Complement levels are lower in DM
 - Mononuclear cells secrete less IL-1 in diabetics
 - Hyperglycemia causes decreased polymorphonuclear leukocyte mobilization, chemotaxis, phagocytosis, and transmigration across the endothelium
 - CD4 lymphocyte proliferation is not impaired if the HbA1c is $< 8\%$
 - Glycation of immunoglobulin increases with increasing HbA1c
 - Casqueiro et al, Indian J Endocrinol Metab. 2012 Mar; 16 (supp 1): S27-36

Outpatient vs Inpatient Rx for Cellulitis

- Consider admission:
 - Failure to respond to oral antibiotics
 - Infection involving the hand and face
 - Systemic Inflammatory Response symptoms: high fever, hypotension
 - Findings consistent with a severe soft tissue infection:
 - SIRS
 - Blister formation
 - Necrosis
 - Pain out of proportion to appearance of skin

Outpatient Cellulitis

- **No draining wound**

- Keflex 500 mg po qid for most cases
- Use Clindamycin 300 mg po TID if PCN/cephalosporin allergic

- **Draining Wound = MRSA!**

- Trimethoprim Sulfa DS 1–2 po bid or Clindamycin 300 mg po TID

- **Draining Wound but Strep suspected**

- Trimethoprim Sulfa DS 1–2 po bid plus Keflex 500 mg po qid
- Trimethoprim Sulfa DS 1–2 po bid plus Clindamycin 300 mg po TID

Inpatient Cellulitis

- Moderate infection with **no drainage**:
 - Cefazolin, Ceftriaxone, Clindamycin, or PCN
- Severe Infection with **no drainage**:
 - ***Consult surgery immediately***
 - Vancomycin plus Piperacillin-Tazobactam empiric therapy
 - Specific Therapy
 - Gp A Streptococcus: High-dose PCN plus high-dose Clindamycin
 - Clostridium species: High-dose PCN plus high-dose Clindamycin
 - Vibrio vulnificus: Doxycycline plus Ceftazidime
 - Aeromonas: Doxycycline plus Cipro
 - Polymicrobial: Vancomycin plus Piperacillin-Tazobactam

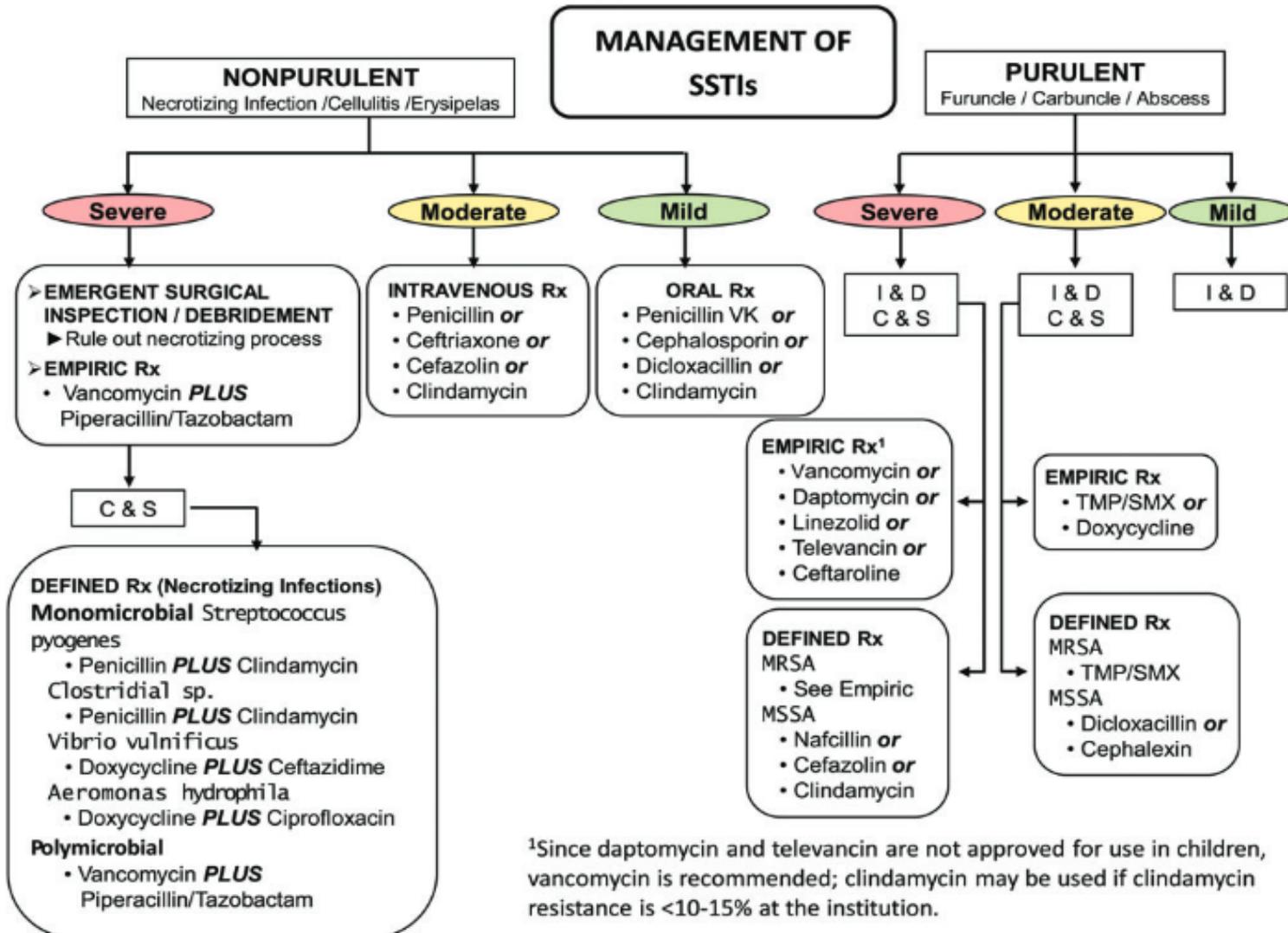
Inpatient Cellulitis — Draining Wound

- Inpatient cellulitis with draining wound:
 - Vancomycin 15, mg/kg IV q 8-12h
 - Linzeolid 600 mg IV q 12h (better in CKD)
 - Daptomycin 4 mg/kg IV daily (beware CPK incr, eosinophilic pneumonia)
- If MRSA, continue one of the above.
- If MSSA, switch to Cefazolin, Nafcillin or Clindamycin.

Inpatient Cellulitis — Draining Wound (cont.)

- Consider adding Clindamycin if there is an abscess
- Wargo et al, Clin Infect Dis, October 1, 2015
 - Retrospective review of 269 bacterial skin infection in 941 bed in northern Alabama
 - Vancomycin **vs.** vancomycin plus clindamycin
 - Addition of clindamycin led to improved outcomes
 - **Length of stay was 18.2 % shorter** with addition of clindamycin [**OR 0.81**]
 - **Readmission rate** at 90 days was 5.3% with clindamycin, 15.3% without [**OR 3.2**]

Management of SSTIs



Diabetic Foot Infection Diagnosis

- Diabetic foot ulcers
 - Do not culture if not infected!
 - Culture wound before starting antibiotics
 - Swabs are inferior
 - Preferred culture is deep tissue biopsy after wound cleansing and debridement
- Osteomyelitis
 - Probe to bone test if there is an open wound
 - Plain films are low sensitivity and specificity but recommended
 - **MRI is the best test** to rule out osteomyelitis
 - Debrided bone biopsy is most definitive
 - Consider needle biopsy if there is uncertainty

IDSA DFI Severity Rating

- **Mild**

- Local infection of skin **0.5–2cm** around ulcer
- Rule out noninfectious causes (gout, Charcot joint, DVT, etc.)

- **Moderate**

- Local Infection: Inflammation extends **> 2cm** around the ulcer
- No SIRS

- **Severe**

- Local Infection plus SIRS
 - $T > 38$ or < 36
 - $HR > 90$
 - $RR > 20$ or $PaCO_2 < 32$
 - $WBC > 12K$ or $< 4K$ or bands $> 10\%$

Who to Admit...

- Admit all Severe
- Admit Moderate if there is a complicating feature:
 - Peripheral arterial disease
 - Poor home support
 - Non-adherent patient

Diabetic Foot Infection Treatment

- **Mild Outpatient Case** (Focus on aerobic Gm Positive Cocci)
 - Amox-Clavulanate 850 mg po bid (add TMP/SMZ if MRSA is likely)
 - Clindamycin 300 mg po tid plus Cipro 500 mg po bid if PCN allergic
 - Consider Keflex for mild cases with no prior antibiotic exposure

Diabetic Foot Infection Treatment (cont.)

- Inpatient case or OPAT
 - Piperacillin-Tazobactam 3.375 gm IV q 6h if severe or pseudomonas suspected
 - Ertapenem 1 gm IV daily (convenient for OPAT)
- Consider adding empiric vancomycin or linezolid if **severe** or already **MRSA (+)**

Avoid automatic “*VANCO-SIN*” unless it is a necrotizing infection

Diabetic Foot Infections

- **Mild infection**
 - Treat **1–2 weeks**
- **Moderate to Severe**
 - Treat **2–3 weeks**
- **Osteomyelitis**
 - If all infected bone has been resected
 - Treat for **14–21 days** (IV plus PO)
 - Treat **2–5** days after radical resection (BKA)
 - If residual osteomyelitis is present treat for **6 weeks with IV therapy**

Diabetic Foot Guidelines from IDSA

- Lipsky et al, 2012 IDSA Clinical Practice Guideline for the diagnosis and treatment of diabetic foot infection, *Clin Infect Dis* 2012; 54 (12): 132-173

http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/2012%20Diabetic%20Foot%20Infections%20Guideline.pdf

Hand Infections

- Extremely mild, very early onset, outpatient case (**very, very rare**)
 - Amoxicillin-Clavulanate 875 mg po bid
- Inpatient case (**the majority of hand infections**)
 - Ampicillin-Sulbactam 3 gm IV q 6h
- Special considerations
 - **Most hand infections should be admitted to the hospital**
 - Surgical consultation for urgent debridement is the key to success

Necrotizing Fasciitis

- **Diagnosis**

- Severe pain
- SIRS
- Blue-black discoloration, bullae

- **Empiric Therapy**

- Vancomycin or Linezolid plus Piperacillin-Tazobacam or Meropenem
- Urgent Surgical debridement
- Use high-dose PCN plus Clindamycin if Group A Strep isolated
- **Consult ID, please!**

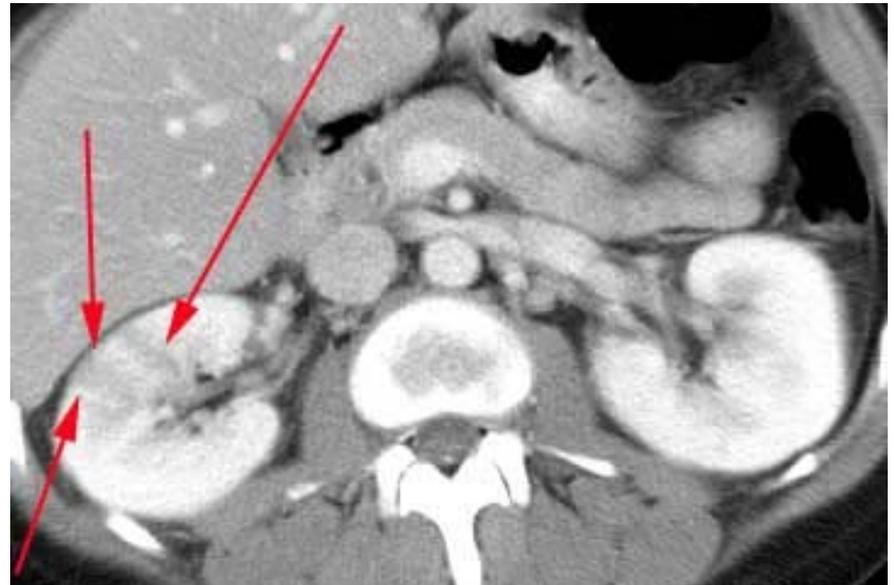
Group A Streptococcal Infection in American Indians

- Recent outbreak of Community Acquired invasive Gp A Strep
 - Three-fold increase 2012–2013 in one Arizona hospital
 - 11 cases diagnosed
 - All were AI
 - Nine (82%) had open wounds/abrasions
 - Nine (82%) had underlying obesity, DM, CKD, heart disease, or alcoholism
 - 2 had bacteremia
 - 4 had Necrotizing fasciitis
 - Prophylaxis was given to contacts

Harris A, Yazzie D et al. Community Acquired Invasive GAS Disease among Native Americans. *Emerging Infect Dis* 2015

Case Presentation (3)

A 65-year-old female with diabetes mellitus type 2 and CKD II presents to the clinic with dysuria and urinary frequency. She is treated with cephalexin and is discharged home. Three days later she presents with a fever, left flank pain, and vomiting. She has a moderately ill appearance and her blood pressure is 80 systolic. She is admitted to the ICU and her blood cultures subsequently grow *E coli* sensitive to cipro, TMP-Sulfa, and gentamicin.



Questions

- How does Diabetes impact UTIs?
- How is simple cystitis managed?
- How do you treat pyelonephritis?
- How do you manage emphysematous UTIs?

Impact of DM on Urinary Tract Infection

- Diabetics have a higher incidence of bacteriuria (two- to four-fold)
- The upper urinary tract is involved in 80% of diabetics with UTI
- Complications of UTI in diabetics include:
 - Perinephric abscess
 - Renal abscess
 - Papillary necrosis (manifest as flank and abdominal pain)
 - Emphysematous cystitis/pyelonephritis

Cystitis

- Women, not pregnant, uncomplicated UTI
 - Nitrofurantoin Macrocrystals 100 mg po bid x 5 days
 - Now OK to use in the elderly if eGFR > 30
 - Trimethoprim/Sulfa: E coli now greater than 20% resistant to this drug in some Areas
 - Keflex 500 mg po bid for 7 days. (inferior to nitrofurantoin and TMP/Sulfa)
 - Avoid using
 - Quinolones: creates resistance and selects for C difficile — Collateral Damage
- Men
 - Ciprofloxacin 500 mg po bid for 10 days
 - TMP-sulfa DS 1 po bid for 10 days

Pyelonephritis

- **Outpatient, not pregnant**
 - Ciprofloxacin 500 mg po bid
 - Consider giving a single dose of Gentamicin 5 mg/kg or Ceftriaxone 1gm IV
- **Inpatient, ward patient**
 - Ceftriaxone 1–2 gms IV daily
 - Ciprofloxacin 400 mg IV q 12h
- **Inpatient, ICU case or Healthcare-Acquired**
 - Pip-Tazo 4.5 gm IV q 6h
 - Add Gentamicin 5 mg/kg IV q 24h if in shock

Pyelonephritis (cont.)

- Special Consideration
 - Treat non-diabetics for 7 days and diabetics for 7–14 days
 - Treat 14–28 days if there is abnormal anatomy:
 - Abscess or lobar nephronia
 - Stone
 - Transplanted kidney
 - Rule out prostatitis with rectal exam for men with UTI
 - The average time to defecation is 4 days

Pyelonephritis (more)

- Consider renal imaging with US or CT if:
 - Fever persists over 4 days
 - Bacteremic or hypotensive
 - Renal failure present with possible obstructive uropathy
 - History of nephrolithiasis
- Patients who are doing well can be converted early on to oral quinolone therapy even if bacteremic as long as the organism is sensitive.

Emphysematous UTI

- **Epidemiology**

- Diabetes is the risk factor for most cases
 - Most are women over age 60

- **Pathophysiology**

- Elevated glucose levels in blood lead to production CO₂, H₂, N₂, and O₂

- **Two syndromes:**

- **Emphysematous cystitis:**

- Air in the bladder wall: Treat 10 days

- **Emphysematous pyelonephritis**

- IV antibiotics are a must
- Percutaneous drainage if moderately severe and nephrectomy for severe disease