

THERAPEUTIC CASE STUDIES FROM A FAMILY MEDICINE RESIDENCY

Richard Clarens, PharmD

UND School of Medicine & Health Sciences

Altru Family Medicine Residency

NDSU College of Pharmacy, Nursing, and Allied Sciences

OBJECTIVES

- Discuss pharmacotherapeutic objectives from the case-based presentation.
- Review clinically relevant therapeutic information from recent clinical trials and updated guidelines.
- Summarize up-to-date therapeutic concepts in the management of common primary care diseases.

CASE

- 80 y/o female with SOB this morning
 - ED 3 days prior with 1 mon cough – azithromycin
 - Improved until this am
 - SOB worse when flat, doesn't feel good with decreased energy
 - EMS O2sat low 80s
- COPD, HF (diastolic), HTN, T2DM, CAD, anxiety
- ASA, Escitalopram, Sitagliptan/metformin 50/1000 mg 1 tab 2xd, Lisinopril 10 mg/d, Metoprolol succinate

- 105/54; HR 78; T 36.3 C; RR 26
- WBC 14.2; Tn 0.05; CO2 22.5; AG 13.5; SCr 0.8; GFR >60; BNP 1641
- ABG 40% BiPAP
 - pH 7.29; pCO2 36; pO2 93; HCO3 17.3; BE -8.5
- Lactic acid 4.58 (2.2)
- Positive UA
- CXR – R pleural effusion
- **Acute diastolic HF, UTI, COPD, DM**
 - Furosemide, Cipro IV
 - Continue Janumet, Metoprolol, Lisinopril, ASA

- Day 2
 - 0527 Labs: CO2 22; Cr 0.8; AG 12; GFR > 60
 - Discontinue metformin, received morning dose
 - At 1733 Lactic acid 2.94
 - Echo
 - EF 35-40%; grade II diastolic dysfunction; global LV hypokinesis; RV SP 42
- Day 3
 - CO2 23.4; Cr 0.8; AG 8.6; GFR > 60
 - UC E coli
- Reason for lactic acidosis?

METFORMIN LACTIC ACIDOSIS

- Risk almost zero if recommendations followed
 - Recommendation is to assess contraindication/cautions
 - If followed would reduce metformin use by ~ 50%
- 54-73% on metformin have ≥ 1 standard contraindications (eg, renal, HF)
 - Acidosis incidence is not increasing
- Should there be a reevaluation of the contraindications esp. in stable HF or with GFR > 30?

METFORMIN LACTIC ACIDOSIS

- Overproduction & reduced clearance
 - Decrease conversion of lactate to glucose by inhibition of gluconeogenesis and glycogenolysis
 - Occurs at high metformin serum levels
 - Inhibits O₂ consumption with impaired mitochondrial function in liver & elsewhere
 - Increases intestinal lactate production
- Incidence is very rare
 - < 0-0.09 case/1000 patient y
 - **Very low if contraindications are not present**

NEJM 96;334:574-9 BMJ 07;335:508-12 NEJM 13;369:374-82 14;371:2309-19

CONTRAINDICATIONS

- **Box warning for lactic acidosis**
- Renal disease or renal dysfunction
 - **SCr \geq 1.5 (males) and \geq 1.4 (females) or decreased CrCl (eg, $<$ 60 mL/min)**
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.
- Temporarily discontinue with IV iodinated contrast – acute alteration of renal function
- Known hypersensitivity

http://packageinserts.bms.com/pi/pi_glucoophage.pdf

WARNINGS/PRECAUTIONS

- Caution with CHF requiring pharmacologic management, particularly unstable or acute HF
- Avoid in impaired liver function due to potential for lactic acidosis.
- Withhold in dehydration &/or prerenal azotemia
- Discontinue metformin and use insulin during stress (e.g., fever, trauma, infection, surgery)
- Do not use if ≥ 80 y unless measurement of CrCl demonstrates that renal function is not reduced

http://packageinserts.bms.com/pi/pi_glucoophage.pdf

LACTIC ACIDOSIS

- “perceived risk of developing lactic acidosis with metformin is high, particularly in the United States.”

BMJ 07;335:508-12

Metformin-associated lactic acidosis requiring hospitalization

- 10y data from National Pharmacovigilance Network of Italian Medicines Agency
- 59 cases of metformin-associated lactic acidosis
 - 25.4% mortality
 - 90% had ≥ 1 risk factor
 - Risk factor stronger prognostic effect than dose or renal dysfunction
- Use despite contraindications/cautions was common in all papers reviewed

Comparative Safety and Effectiveness of Metformin in DM and HF

- Systematic review 9 observational studies
 - 34,504 with DM and HF – 6624 on metformin
 - Most common comparator – sulfonyureas
 - EF < 30-40%, many NYHA III or IV
 - ~10% had moderate to severe renal dysfunction
- No increased risk of lactic acidosis with decreased EF or with HF and CKD
- Reduced mortality vs. controls ($p < 0.001$)

Comparative Safety and Effectiveness of Metformin in DM and HF

- “totality of evidence indicates that metformin is at least as safe as other ... treatments ... in DM and HF and even ... with reduced LVEF or concomitant CKD.”
- “Until trial data become available, metformin should be considered the treatment of choice for patients with DM and HF”

METFORMIN AND HF

- HF was considered an absolute contraindication by the FDA until 2006
- In 2006 FDA changed HF to a warning
 - “suggesting that the risk ... is minimal and similar to that of other DM drugs.”

Circ Heart Fail 13;6:395-402

- In stable CHF, metformin may be used if renal function is normal but should be avoided in unstable or hospitalized patients with CHF

Standards of Medical Care in Diabetes – 2014. Diab Care 14;37 (suppl I):S14-S80

CASE

- 54 y/o female with abd pain, vomiting & confusion
 - 3 d PTA increasing pain, SOB, vomiting, confusion & then unresponsive
- T2DM, HTN, CKD
- Enalapril, Metformin, Glimepiride, Imipramine, ASA, Ibuprofen
- 120/70; HR 52; 36.7C; RR 18; O2 sat 95% RA
 - Incoherent, agitated, uncomfortable, groaning
 - Skin cool

- WBC 35; Plt >483; MCV 103
- K 6.3; Cl 83; CO2 <2; BUN 94; Cr 7.9; PG 168; Lipase 595
- Lactic acid 20
- CK 656; Phosphorus 19.3 (2.6-4.5)
- EKG – AF 115
- CXR neg
- Cefepime, Vanc and Metronidazole
- Treated hyperkalemia with D50W/insulin, etc

- Increasing RR and somnolence
 - Venous BG: pH 6.62 (7.3-7.4); CO₂ 18 (38-50); pO₂ 73 (35-50); BE -35
 - Intubated
- 3 h after arrival BP 84/43
 - NE; NaHCO₃
 - CT pancreatic edema & fat stranding
- Continuous venovenous hemodiafiltration

- Differential

- Sepsis – pyelo, intraabdominal,
- Severe lactic acidosis – sepsis, cardiogenic shock, metformin
- Cancer – tumor lysis syndrome (hyperphosphatemia)
- Mesenteric ischemia
- Acute pancreatitis
- AKI on CKD – sepsis, cardiorenal syndrome, rhabdomyolysis with hyperphosphatemia, ACEI & NSAIDs

ANION GAG METABOLIC ACIDOSIS

- Type A lactic acidosis
 - Impaired tissue perfusion
- Type B lactic acidosis
 - Nonhypoxic
 - Impaired lactate metabolism with metformin, salicylates OD, INH
 - DKA
 - Lymphoma, leukemia
 - Methanol or ethylene glycol

METFORMIN LACTIC ACIDOSIS

- Risk of metformin accumulation with CKD
- **Suspect acidosis due to metformin if:**
 - h/o metformin
 - Markedly increased lactate > 15
 - Large anion gap > 20
 - Severe acidemia pH < 7.1
 - Very low $\text{HCO}_3^- < 10$
 - h/o CKD with GFR < 45 or SCr > 2

CASE DISCUSSION

- ASA, Ibuprofen and Enalapril may have precipitated AKI
 - Reduced metformin excretion
 - Increases risk of lactic acidosis
 - Toxic effects of metformin
 - Enhanced conversion of glucose to lactate in the small intestine and inhibition of gluconeogenesis by lactate, pyruvate, and alanine
- Elevated metformin level helps confirm diagnosis

Earlier Case – 80 y/o female

- h/o metformin YES
- Markedly increased lactate > 15 NO
- Large anion gap > 20 NO
- Severe acidemia pH < 7.1 NO
- Very low $\text{HCO}_3^- < 10$ NO
- h/o CKD with GFR < 45 or SCr > 2 NO

MALAdaptive: Do We Avoid Metformin Unnecessarily?

- Current contraindications do not alter incidence of lactic acidosis
- Data may support an “all metformin, all the time” approach – a cautious approach
 - Interrupt metformin whenever a significant acute illness is rational and encouraged
- If hospitalization substitute insulin
 - Restart no later than discharge

MALAdaptive: Do We Avoid Metformin Unnecessarily?

- “Any GFR cutoff seems arbitrary because the risk has not been clearly defined. However, there seems to be evidence of safety with GFRs as low as 30”
 - ADA and European Association for Diabetes “use down to a GFR of 30, with dose reduction advised at 45 . . . appear[s] very reasonable.”
- “contraindications should not be regarded as absolute, but instead . . . take the entire risk/benefit picture into account.”

METFORMIN & RENAL FUNCTION

- Despite concerns about lactic acidosis current data suggest the overall risk is low
- Estimated GFR may be better than SCr in assessing use
- Dose adjustments based on eGFR
 - 45-59 – Continue use, monitor GFR q3-6 months
 - 30-44 – Caution, lower dose (eg 50% max dose), monitor GFR q3 mon, no new starts
 - ≤ 30 – stop

J Amer Geriat Soc 13;61:2020-26

Am J Kidney Dis 14;64:510-33

ASTHMA CASE

- 29 y/o male with h/o asthma
 - 2 wks of coughing, SOB
 - Albuterol nebs & MDI for past wk
- Asthma since 12 y with multiple ER visits (last 1 y ago) & hospitalizations (last 4 y ago)
- Meds: albuterol prn, can't afford fluticasone/salmeterol & d/c'd 2 y ago
- ER – nebs without much improvement
- Admit – Methylprednisolone 125 mg IV q8h
 - Nebbs

ICS in Asthma

- Most potent and consistently effective long-term control medication
- Suppress but do not cure asthmatic inflammation
- Inflammation and airway hyperresponsiveness **back to baseline in 2 wks after stopping**

NAEPP Guidelines 2007. NEJM 09;360:1002-14

SYSTEMIC STEROIDS

Asthma Exacerbations

- DOSE
 - Outpatient “burst” 40-60 mg in 1 or 2 divided doses for 5-10 d (peds 1-2 mg/kg/d for 3-10 d)
- Severe exacerbation – no known advantage of:
 - Higher doses (e.g., 125 mg q6h)
 - IV over oral (e.g., 125 mg q6h IV) NEJM 10;363:755-64
- Steroids dosed for < 1 week no need to taper
 - Up to 10 d probably no need to taper
 - If ICSs are in the regimen

SEVERE EXACERBATION – ED

- Findings
 - FEV1 or PEF <40%
 - Patient talks in words or phrases but not sentences
 - HR >120, RR >30
 - Pulsus paradoxus (decrease SBP >25 on inspiration)
 - Loud wheezes or silent
 - SaO₂ <90% or PaO₂ <60
- Initiate treatment
 - High-dose SABS plus ipratropium bromide by MDI with chamber or neb q20min or constant for 1 h
 - Oral steroids

STEROIDS & NEUROPSYCHIATRIC

- ~ 60% mild or moderate psychiatric effect
 - Agitation, anxiety, distractibility, insomnia, irritability, lethargy, labile mood, pressured speech, restlessness, euphoria, hypomania, tearfulness
- 6% may have a “steroid psychosis”
 - Mania, depression, delirium, psychosis, suicidal
- Higher dosages greater risk
 - 1.3% with Prednisone \leq 40 mg/d
 - 5% 41-80 mg/d
 - 18% $>$ 80 mg/d daily

CASE

- 90 y/o female with a fall
 - Independent senior living center
 - No loss of consciousness or hitting head
 - Dizzy and felt weak
 - 2 d of chills, sweats, urinary frequency, dysuria
 - Had UTI several years ago
- DM, HTN, MDD, Rheumatic fever
- Promethazine/codeine HS for cough, Fluoxetine, Alendronate, Cetirizine, Losartan 25 mg/d, Diphenhydramine 50 mg HS, ASA 325 mg/d

- 157/74, 94, 37.8C, 18, O2sat 94%
- UA: nitrite pos, WBC 20-50, bacteria many
- WBC 12.6 (83.3 PMNs), Hgb 10.3
- CO2 22.6, K+ 4.2, SCr 0.8, Mg 1.8
- EKG: 92, QTc 515
- UTI
 - Rocephin 1g q24h
 - Resident purposely avoided Ciprofloxacin – WHY?

QT INTERVAL PROLONGATION

- QTc prolongation increases risk of torsades
- No established threshold below which prolongation is considered free of proarrhythmic risk
 - > 450 msec in men
 - > 460 msec in women
 - > 500 msec correlates with > risk

JAMA 03;289:2120-27 NEJM 04;350:1013-22

Antimicrobial Agents-Associated with QT Interval Prolongation

- Between 1997-2003 100 cases of FQ-TdP
- Moxifloxacin > QT prolongation vs other FQs
- Levofloxacin and ciprofloxacin do not significantly prolong the QT at recommended doses
- Ciprofloxacin appears to be FQ with lowest risk of torsades
 - Case reports with higher than recommended doses

FQs & Risk of Serious Arrhythmia: a Population-based Study

- Patients hospital discharge treated for RTI 1990-2005 in Quebec
- Moderate K⁺ channel inhibition
 - Gatifloxacin RR 7.38 arrhythmia
 - Moxifloxacin RR 3.3 arrhythmia
- Minor K⁺ channel inhibition
 - Levofloxacin no increased risk
 - Ciprofloxacin RR 2.15 arrhythmia

Azithromycin and the Risk of Cardiovascular Death

- Tennessee Medicaid cohort 1992-2006
 - No antibiotics, Azithromycin, Amoxicillin, Ciprofloxacin, Levofloxacin
- CV death risk
 - Azithro (85.2/mill) vs. no abx (29.8/mill) – HR 2.88 (p<0.001)
 - Azithro vs. amox – HR 2.49 (p=0.002)
 - Ciprofloxacin no increased risk
 - Levofloxacin – HR 1.50 (P=0.18)

FDA-APPROVED FQ PRODUCT INFORMATION

- QT prolongation has been observed in some
 - Postmarketing rare reports of v tachyarrhythmias including torsades and cardiac arrest
- Moxifloxacin, levofloxacin, and gemifloxacin
 - Avoid with known QT prolongation or other risk factors for torsades (hypokalemia, hypomagnesemia, class IA or class III antiarrhythmics)
- Ciprofloxacin should be used with caution in such patients

Up-to-date. Current through 11/14

CV Risks with Azithromycin and Other Antibacterial Drugs

- Lethal arrhythmias potential consequence of QT prolongation with azithromycin, other macrolides, and FQs
 - FQs have FDA-approved warnings
- “should give clinicians pause when they're considering prescribing antibacterial drugs, especially for patients with preexisting CV risk factors or clinical conditions in which antibacterial drug therapy has limited benefits”

CASE

- 62 y/o male with increasing DOE and edema
 - Started 2-3 mon ago
 - Occasional palpitations
 - Denies chest pain, diaphoresis, fever, chills
- PMH: obstructive sleep apnea, GERD, DVT on warfarin
- No meds

- 121/76, HR 162, RR 22, O2sat 94%, 140 kg
 - Irreg, irreg rate/rhythm
 - Lungs crackles at base
 - +JVD
 - Bilateral LE pitting edema to knees
 - BNP 806
- CXR: interstitial infiltrates lung bases
- Diltiazem IV 10 mg then 5 mg/h
 - HR dropped to 80s
- Furosemide IV
- Echo: LVEF 35%, global hypokinesis

- Card consult
 - DOE, orthopnea, PND, +JVD
 - Acute decompensated systolic HF
 - NYHA Class III HF
 - Cardiomyopathy induced AF or AF with tachy-induced cardiomyopathy
 - DC cardizem due to negative inotrope
 - Metoprolol 25 mg po 2xd
 - Use digoxin to help rate control because of HF
 - TEE then DC cardioversion if no thrombus

CLINICAL CONSEQUENCES

- Loss of effective atrial contraction (“atrial kick”)
 - 20-30% reduction of diastolic ventricular volume
 - ↓ SV → CHF
- Impaired LV systolic function
 - If already LV dysfunction → CHF
- Tachycardia induced cardiomyopathy
 - Changes in ventricular structure & function
 - Risk of decreased EF
- Intra-atrial stasis of blood
 - Thrombus formation

ATRIAL FIBRILLATION – GOALS

- Diagnosis – Etiology and reversible cause if any
- **Symptom control**
 - **Rhythm control**
 - Electrical &/or pharmacologic cardioversion
 - Maintain NSR with antiarrhythmics
 - **Rate control**
 - Rate controlled to prevent symptoms
 - Resting HR < 80, moderate exercise 90-115/min
- **Prevention of embolic stroke – risk score**
 - **No therapy, ASA (antiplatelet), Anticoagulation**

ACC/AHA – RATE CONTROL

- Ventricular response is dependent upon
 - AV node conduction
 - Vagal and sympathetic tone
 - Accessory pathways
 - Action of drugs

ACC/AHA/ ESC AF Guidelines. 2006

- Controlling HR
 - β B, nondihydropyridine CCB, digoxin, amiodarone
- Decrease AV conduction which slows RVR
(rapid ventricular response)

2014 AHA/ACC Guidelines

Heart Failure – Class I

- Absence of pre-excitation, IV β B (or non-DHP CCB in HFpEF) recommended to slow ventricular response in acute setting, caution in overt congestion, hypotension, or HF reduced EF (HFrEF) (LOE: B)
- Absence of pre-excitation, IV digoxin or amiodarone to acutely control HR (LOE: B)

DIGOXIN

- “Neither IV nor oral digoxin facilitates conversion to sinus rhythm.”
- “Digoxin is used primarily to control the ventricular response rate. However, because effective rate control with IV digoxin may take 12 h or longer, there is little role for IV digoxin in the acute setting.”

2014 AHA/ACC AF Guidelines

Heart Failure

- Class IIa
 - IV amiodarone can be useful to control HR when other measures are unsuccessful or contraindicated. (LOE: C)
- Class III
 - For rate control, IV non-DHP CCBs, IV β Bs, and dronedarone should not be used with decompensated HF. (LOE: C)

AF RATE CONTROL AGENTS

- To decide which agent(s) to use includes
 - Degree of symptoms, Hemodynamic status, Presence or absence of HF
- Route of administration
 - IV meds if rapid rate control is required
 - “Unless immediate rate control is required or an enteral route of administration is not available, oral administration is appropriate”
 - “In hemodynamically stable patients with a RVR, oral medications may be administered.”

CASE

- 85 y/o female with increasing confusion
 - Increasing weakness last few days with a fall
- PMH: DM, AF, CVA 3 mon ago, PMR
- Meds:
 - Prednisone, Dipyridamole/ASA, Metformin 500 mg/d, Furosemide 20 mg/d, KCl 20 mEq/d, Verapamil 80 mg TID, **Digoxin 0.25 mg/d**, Valsartan 160 mg/d, Metoprolol XL 50 mg/d

- 120s/50s, HR 60-75, wt. 66 kg
- UA: WBC 7-12, RBC 0-3, nitrite neg
- UTI may be cause of confusion
 - Ciprofloxacin started
- Dig level 2.7 (June was 0.6)
 - May be cause of confusion
- Why dig level increased?
 - Verapamil reduces renal excretion
 - Verapamil inhibits p-glycoprotein dig transport with increased bioavailability
 - Digoxin was increased to 0.25 mg/d 2 months previous

DIGOXIN DOSES AND SERUM LEVELS

- **No target dose**
 - **Low doses (e.g., ≤ 0.125 mg/d for most)**
 - **Sufficient to achieve beneficial outcomes**
 - High doses
 - Increase risk of toxicity for a narrow safety index drug
- **Serum levels < 0.9 ng/ml** (e.g. 0.5-0.8 ng/ml)
 - Checked to minimize risk of toxicity
 - **Decrease dose for higher levels**
 - **Do not increase dose for low levels**

BENEFIT FROM DIGOXIN?

- 2891 with recent dx of systolic HF – never on digoxin followed for 2.5 y
 - 18% started digoxin
 - **72% increase in all-cause mortality** with no effect on hospitalization

Freeman JV, et al. Effectiveness and safety of digoxin among contemporary adults with incident systolic heart failure. *Circ Cardiovasc Qual Outcomes* 2013; DOI:10.1161/CIRCOUTCOMES.111.000079

- “The data ... allow us to seriously question the advice on digoxin given by both the current and influential guidelines ...”

Opie LH. Editorial. Digitalis, yesterday and today, but not forever. *Circ Cardiovasc Qual Outcomes* 2013; DOI:10.1161/CIRCOUTCOMES.113.000544

BENEFIT FROM DIGOXIN?

- “both systolic HF & AF, providers [might] be more likely to prescribe [digoxin] ... to treat both.”
 - **“digoxin isn’t good at rate control in treating AF, is less effective than alternatives like β Bs or CCBs, and may worsen clinical outcomes in AF much as it does in HF.”**

Go AS. Medscape. 9/19/13 <http://www.medscape.com/viewarticle/811298>

To Dig or Not to Dig

- **“Contrary to what I had been taught during my training, higher therapeutic blood levels of digoxin were observed to be deleterious.”**
- “I administer ... digoxin ... usually 0.125 mg/d.”
 - With mild renal ... 0.125 mg qod
 - Dig level after 7-10 d to make sure level no > 1

Alpert JS. Editorial. AJM 14;127:461-2

Digoxin for patients with AF and HF: paradise lost or not?

- **“achieving an SDC ≥ 1 ng/ml should no longer be recommended.”**
 - “If lower SDCs can be achieved and maintained, digoxin could still be of use in HF ... as a neurohormonal modulator”

Veldhuisen DJ. Editorial. Europ H J 13;34:1468-70

Case

- 44 y/o male with nausea, abd discomfort & diarrhea for 6 days
 - Multiple, watery stools/d – no hematochezia or melena
 - Bilateral upper quadrant pain, increases with lying on side
 - h/a, dizziness and malaise
 - Outpatient lab suggests pancreatitis
- PMH
 - HTN, TH, urinary frequency

- Lisinopril, Acetaminophen 1.5 g 3xd, Chlorthalidone, L-thyroxine, Admits to Ibuprofen 800 mg 3xd
- EtOH 5-6 beers/d
- 83/47, HR 103, RR 18, 36.9C, O2 sat 100%
 - Mucous membranes dry
 - Mild tenderness in upper quadrants
- BUN 77, SCr 6.9
- K 3.5, CO2 17
- Lipase 693

Case

- Assessment
 - Pancreatitis, AKI
- Fluids
- Hold lisinopril, ibuprofen, chlorthalidone, acetaminophen
- Day 4 discharge
 - BUN 23, SCr 1.2, K 3.2, Cl 110, CO2 22.5, Ca 7.8

RENAL AUTOREGULATION

- Autoregulation
 - Maintenance of renal blood flow & GFR as MAP decreases
 - Glomerular pressure balanced by resistances in afferent and efferent renal arteries
- Afferent resistance – adjusts renal blood flow/pressure
 - **NE greater effect on afferent than efferent**
 - **Vasodilating prostaglandins**
- Efferent resistance – adjusts glomerular pressure
 - **AngII greater effect on efferent than afferent**
- Low renal perfusion – angiotensin II formation
 - **GFR maintained if efferent > afferent vasoconstriction**

HTN WITH NORMAL RENAL FUNCTION – ACEIs/ARBs

- ACEIs prevent autoregulation of efferent renal artery at low pressures

- Vasodilation → Decrease in GFR → increase SCr

Review of Medical Physiology - 22nd Ed. (2005)

- ↑ SCr < 20-30% & non-progressive ↑ SCr
 - “usually indicate that intraglomerular pressure has been successfully reduced and are not an indication to decrease or stop the antihypertensive drug”
- Stop if > 30% increase in SCr above baseline

BMJ 06;333:896-9

NSAID RENAL EFFECTS

- PGI₂ (prostacyclin) & PGE₂
 - Renal afferent vasodilators
 - Increase renal blood flow & H₂O excretion
 - Balance with renal vasoconstrictors
- NSAIDs inhibit renal vasodilating PGI₂ & PGE₂
- Renal toxicity
 - Acute reversible renal failure (most common)
 - Chronic renal failure
 - Fluid retention (edema, HTN)
 - Hyperkalemia

NSAID EFFECTS ON RENAL FUNCTION

- Use carefully
 - ACEI – hyperkalemia & increased SCr
 - K-sparing diuretics & Salt substitutes – hyperkalemia
 - Elderly, CHF, Renal dysfunction, Cirrhosis, Ascites, DM, Volume depletion, Diuretics/Na⁺ depletion – increased SCr
 - Anything that reduces effective plasma volume

ACEI CASE

- 47 y/o female with hypertension
- 2 y prior started Lisinopril/HCTZ 10/12.5 mg/d
- 2 months prior Lisinopril/HCTZ 20/25 mg/d
 - Albuterol MDI as needed for wheezing
- 6 wks prior URI symptoms – antihistamine
- 4 wks prior
 - Throat pain, ear pain and trouble swallowing
 - Denies fever, congestion, cough, nausea
 - Uvula edematous, posterior oropharyngeal erythema
 - Viral URI

- 8/19/14 ED visit for upper lip swelling
 - Had this in past but very minor
 - Has not mentioned to health care
 - Taking Lisinopril for a long time, no new meds
 - Edema upper lip with normal tongue, soft tissues, uvula, tonsils, etc
 - Easily swallows with no respiratory distress
 - Epi, methylprednisolone, diphenhydramine with no immediate improvement – admission planned
 - While waiting for room lip swelling improved
 - Adamant about going home – Prednisone Rx
 - STOP Lisinopril
 - Mandatory to f/u with primary MD tomorrow

ACEI ANGIOEDEMA

- Incidence 0.1-2.2% but widely used

Immunol Allergy Clin N Am 14;34:23-31

– ~20-57% of angioedema attacks

- Risk factors

– African ancestry, Hispanic, > 65 y, females, smokers, HF, cardiopulmonary disease, statins, ASA, any h/o drug rash, seasonal allergies, previous angioedema, hereditary angioedema, ACEI cough

Amer J Med. On-line July 21, 2014 doi:10.1016/j.amjmed.2014.07.011

Laryngoscope 14;124:2502-7

Angioedema: ACEIs, ARBs, and Aliskiren. Pharmacist's Letter/Prescriber's Letter. 7/14

- HR 3.04 vs. β Bs

Arch Intern Med. 12;172:1582-9

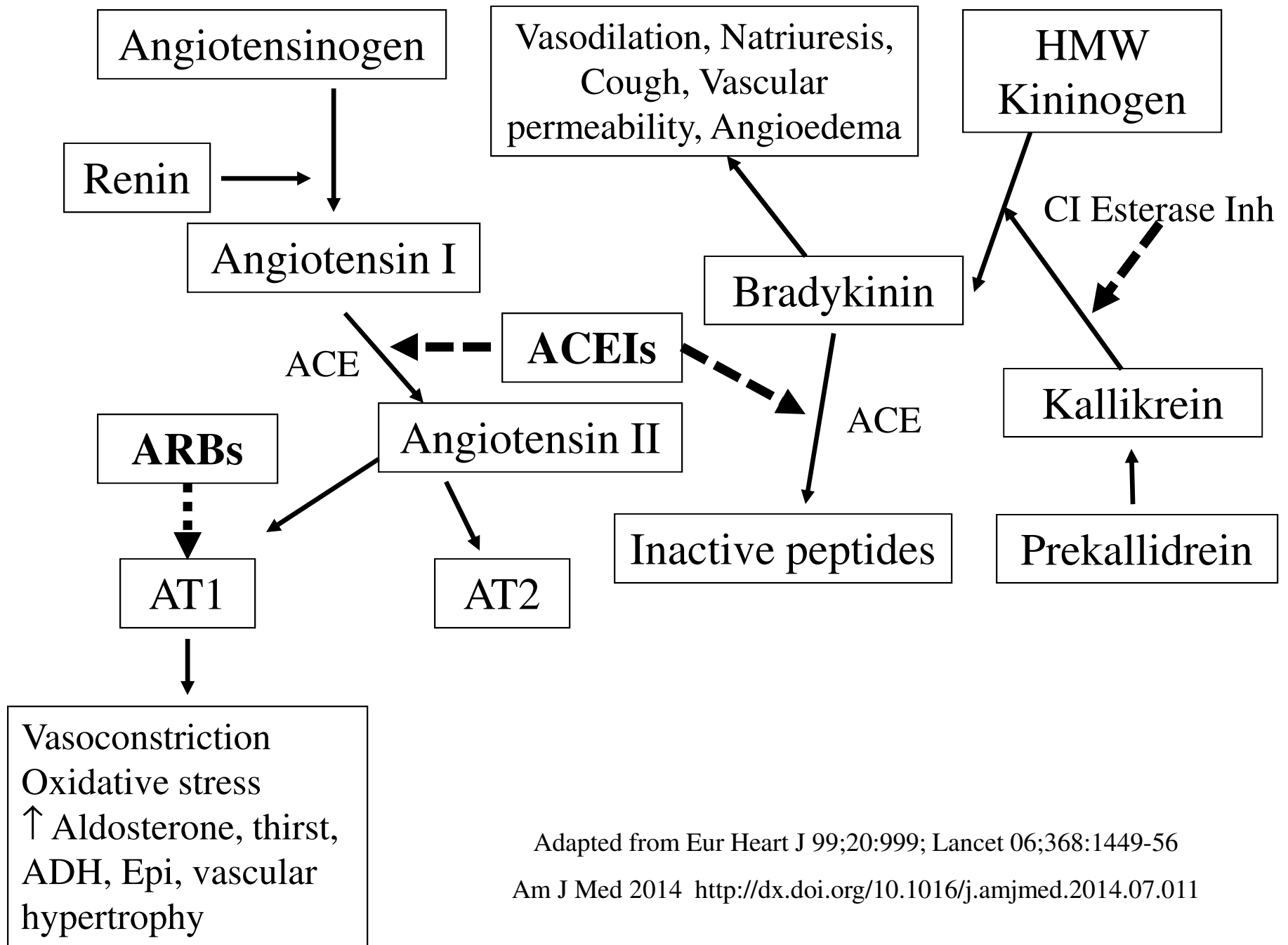
ACEI ANGIOEDEMA

- Onset anytime after 1 day or as late as 10 y
 - 50-66% within 1 week to 3 months
- **Not an IgE hypersensitivity reaction**
- **Bradykinin overproduction – vasoactive**
 - Activation of kallikrein-kinin system (eg, HAE with ↓ CI-INH inhibition of KK)
 - Inhibited bradykinin degradation by ACEIs
 - Hyperpermeability of post cap venules

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Immunol Allergy Clin N Am 14;34:23-31



Adapted from Eur Heart J 99;20:999; Lancet 06;368:1449-56
 Am J Med 2014 <http://dx.doi.org/10.1016/j.amjmed.2014.07.011>

ACEI ANGIOEDEMA

- Mild to life-threatening edema of lips, face, tongue, upper airway, eyelids, arms, or GI tract (abd pain, diarrhea, diarrhea)
 - May have respiratory difficulty if laryngeal
 - Intubation may be required in up to 10%
 - Usually no urticari
- Clinical dx based on h/o ACEI and no angioedema following d/c
 - Normal C4, Antigenic CI-INH, C3 (NEJM 08;359:1027-36)

- Progressive tongue swelling 5 h
- No hypotension, rash, bronchospasm, urticaria, or flushing
- No Hx or FH of similar episodes
- No food allergens, new meds, or insect
- ASA, simvastatin, diltiazem, enalapril
- Angioedema with ACEI
- No benefit noted after diphenhydramine, methylprednisolone, and epinephrine
- Nasotracheal intubation extubated next day

THERAPY OF ACEI ANGIOEDEMA

- Most cases improve when ACEI is stopped
 - Improvement within several hours up to 48 h
 - Monitor airway for at least 12-24 h if mouth or throat involved
 - Recurrence may occur over weeks
- If ACEI NOT stopped angioedema episodes increase in frequency and severity
- Assess airway

Amer J Med. On-line July 21, 2014 doi:10.1016/j.amjmed.2014.07.011

Laryngoscope 14;124:2502-7

THERAPY OF ACEI ANGIOEDEMA

- Antihistamines, anticholinergics, corticosteroids, epi are not effective
 - Not IgE or histamine etiology

Amer J Med. On-line July 21, 2014 doi:10.1016/j.amjmed.2014.07.011

- Antihistamines, anticholinergics, corticosteroids, epi are effective
 - ~ 90% responded quickly
 - Discharged from ED after median 6 h

Laryngoscope 14;124:2502-7

THERAPY OF ACEI ANGIOEDEMA

- FFP
- Icatibant
 - Bradykinin receptor type 2 (BR2) antagonist
 - Approved for treatment of hereditary angioedema
 - May be useful in ACEI angioedema
- Ecallantide
 - Inhibits kallikrein activity
 - Decreases conversion of kininogen to bradykinin
- Very expensive – use only if need for intubation

ACEI ANGIOEDEMA

- Class effect – avoid further use of ACEIs
 - Cross-reactivity with all ACEIs
- Avoid if h/o angioedema
 - From any cause including hereditary angioedema

Amer J Med. On-line July 21, 2014 doi:10.1016/j.amjmed.2014.07.011

ARB USE IF ACEI ANGIOEDEMA

- Should be safe since does not increase bradykinin
- Incidence 0.11%
 - HR 1.16 vs. β Bs
Arch Intern Med 12;172:1582-9
- Reports of angioedema if switched to ARB
 - Shortly after switching & most likely still from ACEI

ARB USE IF ACEI ANGIOEDEMA

- “Switching to ARBs ... quite safe, but close monitoring ... is mandatory”
 - “Previous severe life-threatening ACEI induced angioedema, we recommend avoiding both ACEI and ARB”

Amer J Med. On-line July 21, 2014 doi:10.1016/j.amjmed.2014.07.011

- “recommend avoidance of ARBs in patients with a history of ACEI-induced AE”

Laryngoscope 14;124:2502-7

ARB USE IF ACEI ANGIOEDEMA

- ACEIs and ARBs cross-reactivity?
 - “most ... able to safely use an ARB after experiencing ACE inhibitor-associated angioedema”
- Weigh benefit vs. risk
 - If other agents can be used probably safest not to use an ARB
 - Benefit may be > risk, eg, HF, CKD

Angioedema: ACEIs, ARBs, and Aliskiren. Pharmacist's Letter/Prescriber's Letter. 7/14

CASE

- 34 y/o male with L thigh pain and redness
 - Duration of 9 days
 - Seen in walk-in several days ago for redness and tenderness – Cephalexin Rx
 - Symptoms increasing and now with drainage, fever, chills, nausea
 - Denies previous skin infections
- Construction worker, Smokes 1.5 ppd
- Sertraline, Gabapentin

- 119/65, 85, 37 C
 - L upper anterior thigh >10x30 cm erythema with a central 6-7 mm eschar that had been draining
 - Intense surround erythema, warm, fluctuant
 - Tender to palpation
- WBC 14.5
- US – developing abscess
- Cellulitis with abscess
- IV Vancomycin
- I&D

CASE

- 74 y/o male with L leg wound and fever
 - Admit from transitional care s/p tib-fib fx 4 mon ago
 - Recent onset of redness & fluctuance with drainage on L lateral leg noted by staff
 - WC grew *S. aureus* and gram-neg not yet identified
 - TMP/SMX and levofloxacin was added
 - Increased L leg swelling with T103.8
- Furosemide, Gabapentin, ASA, Metoprolol

- 137/86, 89, 37.8 C, 20
 - L leg
 - 4+ pitting edema
 - Erythema ankle to knee
 - Lateral abscess that has been lanced and packed
 - Fluctuant but not indurated
- WBC 24, lactic acid 1.7
- WC – MRSA and *P. aeruginosa* (sens to FQ)
- IV Vancomycin, Aztreonam, Ciprofloxacin
- I&D

CASE

- 19 y/o male with R wrist infection
 - Pimple on R wrist several days ago, tried to pop it without success
 - Next day seen in walk-in because it was draining – TMP/SMX Rx
 - Did not improve and now has erythema and edema in wrist and hand with pain
- 142/64, 81, 36.6 C
 - R wrist 3 cm round, swollen, erythematous nodule with drainage of pus

- WBC 6.7
- Vancomycin
- I&D
- WC MSSA
 - d/c Vanc
 - Start IV cefazolin

CELLULITIS

- Skin & soft tissue infection (SSTI)
- > 600,000 hosp/y
- Cellulitis & cutaneous abscess > 9 mill office visits/y

Amer J Med 11;124:1113-22

SKIN AND SOFT-TISSUE INFECTIONS (SSTIs)

- Cellulitis: any spreading infection involving the dermis and SC tissues
 - Purulent cellulitis is associated with purulent drainage or exudate in the absence of a drainable abscess – most likely *S. aureus*
- Erysipelas: cellulitis involving superficial dermal structures
 - Raised borders and clear demarcation between involved and uninvolved skin – most likely GABHS

Amer J Med 11;124:1113-22 Curr Opin Infect Dis 08;21:122-8

Surg Clin N Am 09;89:403-20 Amer J Med 11;124:1113-22 Medicine 13;41:709-15

Med Clin N Am 14;98:445-85

SKIN AND SOFT-TISSUE INFECTIONS (SSTIs)

- Abscess: any collection of pus within the dermis or SC tissues
 - Nodules with surrounding erythema and fluctuance
 - Most likely *S. aureus*

Amer J Med 11;124:1113-22

CELLULITS – PATHOGENS

- Strep spp. and S. aureus
- GABHS – Most common in non-suppurative
- S aureus uncommon in non-suppurative ~10%
 - “little known about non-suppurative cellulitis and its relationship with MRSA”
 - Incidence and prevalence of cellulitis with/without abscess difficult to estimate

Surg Clin N Am 09;89:403-20. Epidemiol Infect 10; doi:10.1017/S0950268810001408.

Surg Infect 09;10:467-99. Guidelines

Med Clin N Am 14;98:445-85

CELLULITIS – PATHOGENS

- Staph most common identified etiology

Epidemiol Infect 10;138:313-7. Surg Infect 09;10:467-99. Guidelines

- Non-suppurative SSTIs

- Often not culturable

- “infrequently caused by *S. aureus*, despite this being the most commonly culturable pathogen”

- Non-*S. aureus* pathogens more difficult to isolate

Epidemiol Infect 10; doi:10.1017/S0950268810001408

- Suppurative SSTI CA-MRSA is most common organism

Am J Med 11;124:1113-22

ALTRU ANTIBIOGRAM 2013 DATA

1. Gram (+) Organisms

	<i>Percent Sensitive To:</i>							
	Ampicillin	Tetracycline	Ceftriax	Clinda.	Erythro.	Oxacillin	TMP/SMZ	Vanco
E. faecalis	98%	NR Gent Synergy 82%	NR	NR	NR	NR Penicillin 97%	NR	100%
E. faecium (n=43)	13%	NR Gent Synergy 83%	NR	NR	NR	NR	NR	30%
S. aureus	NR	97%	ND	79%	51%	65%	97%	100%
MRSA	NR	98%	NR	71%	NR	NR	98%	100%
S. epi / CNS	NR	88%	NR	63%	32%	46%	NR	100%
S. pneumo	ND	89%	100%	NR	61%	Penicillin 100%	85%	100%

- “There is little evidence that MRSA needs to be covered if the cellulitis is community acquired, even in the USA, unless an abscess is present”

Medicine 13;41:709-15

SSTI TREATMENT

- Erysipelas
 - Penicillin
 - Resistance does not occur for *S. pyogenes* (GABHS)

MRSA IDSA Guidelines Clin Infect Dis 11;52:e18-e55

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Outpatients with **nonpurulent** cellulitis (eg, no purulent drainage or exudate and no abscess)
 - GABHS empirical therapy is recommended (A-II)
 - CA-MRSA role is unknown
 - Empirical abx recommended if no response to β -lactams
 - Consider if systemic toxicity
 - 5-10 d of therapy is recommended (individualize based on response)

CELLULITIS TREATMENT

- Outpatient nonpurulent cellulitis
 - β -lactam (cephalexin or dicloxacillin)
 - Coverage for Strep, MSSA.
 - Clindamycin
 - β -lactam plus TMP/SMX or doxycycline
 - Coverage for Strep and CA-MRSA
 - Recommended if fail β -lactams and consider if systemic toxicity
 - Linezolid
 - Recommended if fail β -lactams and consider if systemic toxicity

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Oral empiric antibiotic therapy for nonpurulent cellulitis to cover β -hemolytic Strep \pm MRSA
- Cephalexin 500 mg QID
- Dicloxacillin 500 mg QID
- *Clindamycin 300-450 mg TID
- *Linezolid 600 mg BID
- *Also has activity against CA-MRSA

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Outpatients with **purulent** cellulitis (eg, purulent drainage or exudate in absence of a drainable abscess)
 - Empirical CA-MRSA therapy recommended
 - Empirical GABHS therapy is likely to be unnecessary (A-II)
 - 5-10 d of therapy is recommended (individualize based on response)

CELLULITIS TREATMENT

- Outpatient purulent cellulitis
 - Clindamycin
 - Coverage for Strep & S. aureas
 - Variable CA-MRSA resistance, inducible resistance
 - TMP/SMX or Doxycycline
 - Coverage for MRSA
 - Clinically poor efficacy against GABHS
 - Linezolid
 - Coverage for Strep and MRSA. Expensive, adverse effects

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Oral empiric antibiotic choices for outpatient purulent cellulitis to cover CA-MRSA
- TMP/SMX 1-2 DS tabs BID
- Doxycycline 100 mg BID
- Minocycline 200 mg initially followed by 100 mg BID
- Clindamycin 300-450 mg TID
- Linezolid 600 mg BID

Clin Infect Dis 11;52:e18-e55

NEJM 14;370:1039-47

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Hospitalized with complicated SSTI (deeper infection, surgical/traumatic, major abscesses, cellulitis, and infected ulcers and burns)
 - Surgical debridement and broad-spectrum antibiotics
 - Consider MRSA empirical therapy pending culture
 - IV vancomycin (A-I), PO or IV Linezolid (A-I), IV Daptomycin (A-I), IV Telavancin (A-I), PO or IV Clindamycin (A-III)
 - β -lactam (eg, cefazolin) may be considered with nonpurulent cellulitis – cover MRSA if no clinical response (A-II)
 - 7-14 d is recommended (individualize based on response)

CELLULITIS TREATMENT

- Hospitalized patients with cellulitis
 - Vancomycin
 - Slower killing against Staph than β -lactams for susceptible strains
 - Linezolid
 - Daptomycin
 - Expensive
 - Risk of myopathy and rhabdomyolysis. Weekly CK
 - Telavancin

MRSA IDSA Guidelines Clin Infect Dis 11;52:e18-e55

CELLULITIS TREATMENT

- Hospitalized patients with cellulitis (cont.)
 - Clindamycin
 - Nafcillin or oxacillin
 - Inactive against MRSA
 - May use if nonpurulent cellulitis
 - Cefazolin
 - Inactive against MRSA
 - May use if nonpurulent cellulitis

MRSA IDSA Guidelines Clin Infect Dis 11;52:e18-e55

SSTI Management in CA-MRSA Era

IDSA MRSA Guidelines 2011

- Oral empirical CA-MRSA abx in outpatients
 - Clindamycin (A-II), TMP-SMX (A-II), Doxycycline or Minocycline (A-II), Linezolid (A-II)
 - If both GABHS and CA-MRSA is desired
 - Clindamycin (A-II); TMP-SMX or Doxycycline (Minocycline) PLUS β -lactam (eg, Amoxicillin) (A-II); or Linezolid alone (A-II)
 - TMP-SMX, Doxy and Minocycline activity against GABHS is not well-defined
- Rifampin as a single agent or as adjunctive therapy is not recommended (A-III)

DECOLONIZATION

- Decolonization of patient and household contact may be effective in patients with recurrent infections
- Avoid sharing personal hygiene items
- Mupirocin 2% ointment to anterior nares BID for 5 d
- Chlorhexidine gluconate 4% solution to all body parts excluding the face, open wounds and mucus membranes followed by rinsing with water daily for 5 d

EAR-PIERCING INFECTION

- 18 y/o female with L ear pinna infection
 - Piercing 4 months ago
 - Started on TMP/SMX & Cephalexin 1 d ago for redness and swelling, cultures obtained
 - Today increased swelling, redness, pain and purulent drainage with fever and chills
- 124/75, 142, 39.2 C (102.6 F), 16
 - Imbedded metallic stud in L ear helix with redness, edema, pus with mild tenderness
 - L cervical anterior & posterior adenopathy

- WBC 13.2 (88.4% PMNs), CO2 20.4, AG 11.6
- Perichondritis of L ear with SIRS
 - In ED
 - LD Vancomycin then IV Ciprofloxacin 400 mg
 - While receiving FQ became generally flushed with pruritis (allergy?), probably due to vanco reaction
- Vanc plus Aztreonam
- WC neg so far (after d/c MSSA), BC neg
- ENT – I&D with stud removal
- Day 3 afebrile, ear shows marked improvement
 - Discharge TMP/SMX and Ciprofloxacin

PINNA PERICHONDritis

- 10 year review of cases at Colchester General Hospital, UK
- 10 cases with 90% chondral cartilage piercings
- 8/10 grew **P. aeruginosa**
- **All received outpatient non-pseudomonal abx** prior to admission
- Only 50% of cases ENT clinician started anti-pseudomonal abx
- 20% permanent cosmetic pinna deformity

EXTERNAL EAR INFECTIONS

- Etiology
 - Lobule – *S. aureus*
 - Helix or Tragus – *S. aureus*, *P. aeruginosa*
- Cartilaginous piercings are at greater risk than soft-tissue
 - Cartilage relatively avascular
- Usually within weeks but later onset reported
- Helix deformities (eg, cauliflower ear) may occur

PINNA PERICHONDritis

- Anti-MSSA (eg, cephalexin, cefazolin) most common abx used
 - Misses MRSA & Pseudomonas
- Empiric abx against *P. aeruginosa* & *S. aureus*
 - Oral or IV Ciprofloxacin \pm cephalosporin or IV Piperacillin/tazobactam
 - If MRSA a good possibility
 - IV Vancomycin or oral TMP/SMX or doxycycline
- Pseudomonas cultured and sensitive
 - Ciprofloxacin 750 mg 2xd for 2-4 weeks

CASE

- 18 y/o female with dysuria & frequency
 - 2 d onset of dysuria, frequency, urgency and hematuria, L back pain
 - Decreased appetite, nausea
 - Cystitis 2 months ago – resolved with TMP/SMX
- 110/68, 90, 38C
 - L CVA tenderness
- Nitrite pos; protein 300; WBC 20-50
- CBC: WBC 14
- HCG neg

- Acute pyelonephritis
- Patient want to try outpatient with oral TMP/SMX since that worked last time
- Your response to abx request?
- She received Ciprofloxacin

- UC – E. coli
 - Resistant: Ampicillin, Ampicillin/Sulbactam, TMP/SMX
 - Sensitive: Cefazolin, Ceftriaxone, Ciprofloxacin, Gentamicin, Nitrofurantoin, Tobramycin

CASE

- 74 y/o male with chills and weakness
 - Prostate bx 5 d ago
 - c/o dysuria & nausea
 - Presently on Cipro 500 mg 2xd since procedure
- PMH: BPH; DM; RLS; HTN; LDL
- 139/71; HR 99; 38.4 C
 - Nothing on exam
- WBC 6.33; BUN 24; Cr 1.1
- UA: nitrite pos; bact 1+; WBC 6-8; RBC 0-2
- UC obtained - WHAT ABX?????

- Pip/Tazo started
- UC – E. coli > 10⁵
 - Amikacin S
 - Amp R
 - Amox/clav S
 - Cefazolin S
 - Ceftriaxone S
 - Cipro R
 - Gent R
 - Nitrofur S
 - TMP/SMX R

BACTERIAL ETIOLOGY

	% Uncomplicated	% Complicated
E. coli	70-95	21-54
P. mirabilis	1-2	1-10
Klebsiella spp	1-2	2-17
Citrobacter spp	<1	5
Enterobacter spp	<1	2-10
P. aeruginosa	<1	2-19
Other gram-neg	<1	6-20
Coagulase-neg Staph	5-15*	1-4
Enterococci	1-2	1-23
Group B Strep	<1	1-4
S. aureus	<1	1-2

*S. saprophyticus

ALTRU ANTIBIOGRAM 2013 DATA

2. Gram (-) Organisms

	<i>Percent Sensitive To:</i>						
	Ampicillin	Ertapenem	Ceftriax.	Ciprofloxacin	Gentamicin	Pip/Tazo	TMP/SMZ
E. coli	63%	100%	98%	88%	95%	97%	84%
E. aerogenes	NR	98%	NR	100%	100%	87%	100%
E. cloacae	NR	91%	NR	97%	98%	84%	94%
K. oxytoca.	NR	100%	99%	98%	99%	99%	94%
K. pneumo.	NR	100%	99%	99%	99%	99%	97%
P. aeruginosa	Aztreonam 80%	Imipenem 96%	Cefepime 97%	93%	97% Tobra 99%	92%	NR
P. mirabilis	85%	97%	98%	89%	90%	100%	88%
S. marcescens	NR	100%	89%	93%	100%	ND	100%

* Less than 10 isolates tested. ND = No Data NR = Not Recommended See drugs of choice by organi

Ciprofloxacin – E. coli: 2007 96%; 2010 93%; 2011 90%

TMP/SMX – E. Coli: 2007 90%; 2010 87%; 2011 84%

USE OF TMP/SMX IN CYSTITIS

- Traditional 1st-line agent – 3-day regimen
 - Eliminates bacteria from vaginal-perineal reservoir
 - Increasing resistance – 15-40% for E. coli
- Use empirically if **local resistance < 20%** OR culture shows susceptibility

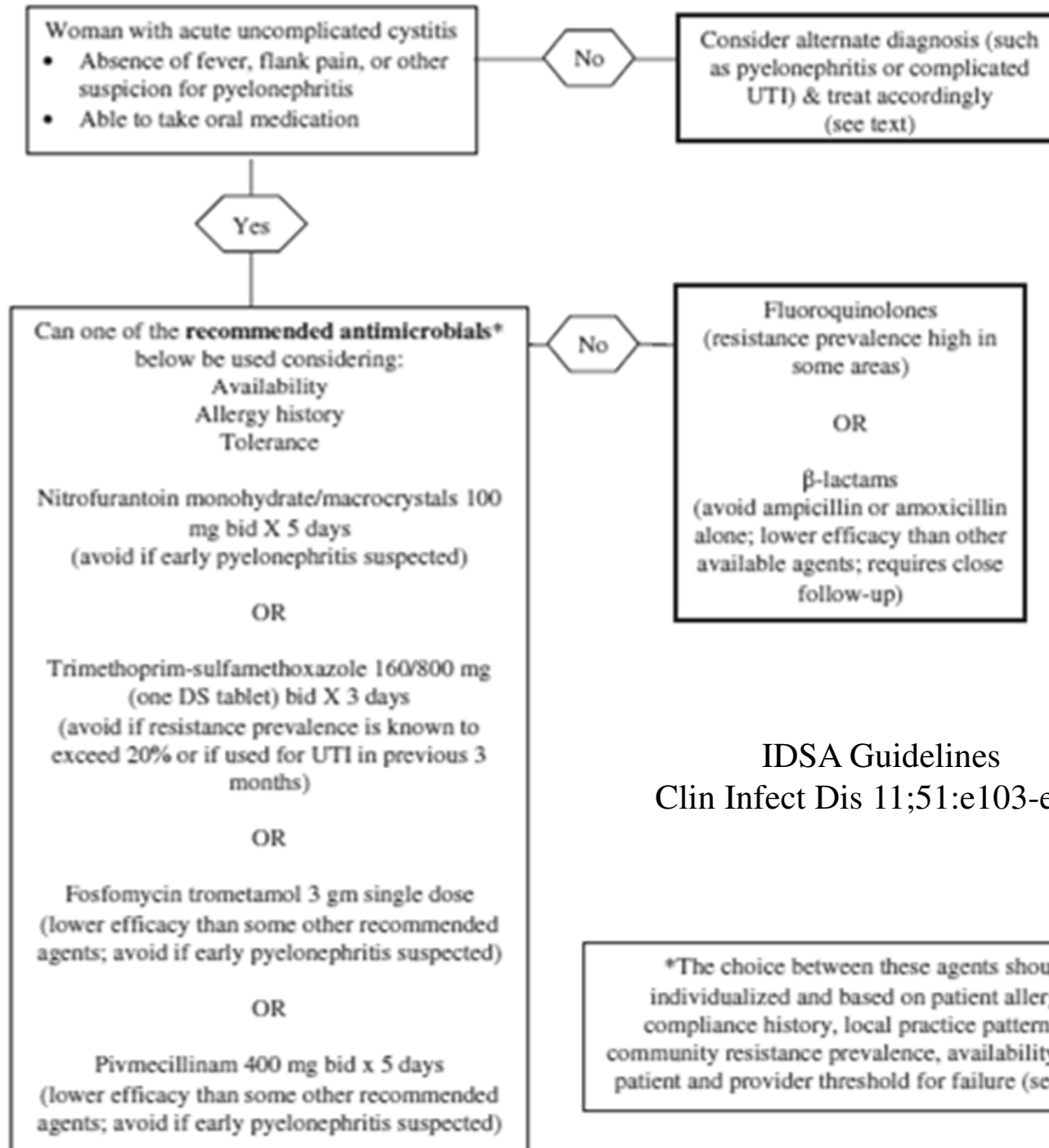
NEJM 03;349:259-66. IDSA Practice Guidelines Clin Infect Dis 11;52:e103-e120.

Pharmacist's Letter/Prescriber's Letter 2009;25(12):251206 Mayo Clin Proc 11;86:477-9

β-LACTAMS IN CYSTITIS

- Appropriate if recommended agents cannot be used
- Lower efficacy than other agents
 - > adverse effects than other UTI antimicrobials & collateral damage (e.g., intestinal flora, increasing ESBLs, *C. diff*)
 - < renal tissue levels than TMP/SMX or FQ
 - < successful in eradicating pathogens from vagina & GI
 - “use with caution for uncomplicated cystitis”
- Amoxicillin or ampicillin should not be used empirically
 - High resistance rates with poor efficacy

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120 Mayo Clin Proc 11;86:477-9 JAMA 12;307:583-9



IDSA Guidelines
Clin Infect Dis 11;51:e103-e120

EMPIRICAL TREATMENT OF ACUTE UNCOMPLICATED PYELONEPHRITIS

- **Outpatient**

- Cipro for 7 d or Levofloxacin for 5 d
 - **1st-line empiric therapy** (2nd-line for cystitis)
 - If local resistance is < 10%
- TMP/SMX for 14 d if pathogen susceptible
 - If empiric use also give initial dose of IV or IM ceftriaxone or aminoglycoside
- Oral β -lactams for 10-14d are less effective
 - If empiric use also give initial dose of IV or IM ceftriaxone or aminoglycoside

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120. NEJM 12;366:1028-37.

Ann Intern Med 12;ITC3 3/6/12

EMPIRICAL TREATMENT OF ACUTE UNCOMPLICATED/COMPLICATED PYELONEPHRITIS

- **Inpatient**
 - IV FQ; broad-spectrum cephalosporin or penicillin (e.g., piperacillin/tazobactam; carbapenem; or 3rd/4th gen ceph (+ aminoglycoside); aminoglycoside (+ ampicillin)
 - Add vanco if MRSA suspected;
 - Choice based on local susceptibility
- Ampicillin – high resistance for gram-neg
 - May use if Enterococcus is suspected (pen + β -lactamase inhibitor covers Enterococcus)

CASE

- 30 y/o male with some confusion
- Diving accident 2 y ago – quadriplegic
 - Chronic suprapubic catheter
 - Recurrent UTIs
- BP 105/67; HR 73; 36.8 C
 - Nothing on exam indicating infection
- WBC 9.05
- UA: nitrite pos; WBC 50-60
- UC ordered – started Ciprofloxacin IV

- Pseudomonas aeruginosa $> 10^5$
 - Ceftriaxone R
 - Cipro R
 - Gentamicin I
 - Imipenem R
 - Pip/Tazo S
 - Tobramycin S
- Past h/o (as recent as 2 mon ago) of Pseudomonas
- Antibiotics stopped due to probable asymptomatic catheter bacteriuria

CATHETER BACTERIURIA

- Best therapy is to remove/replace foley
- Majority are asymptomatic bacteriuria
 - Pyuria is common – not useful for identifying bacteriuria or symptomatic vs. asymptomatic
 - No antibiotics – morbidity not improved, resistance

NEJM 10;362:1804-13. Guideline for prevention of catheter UTIs 2009.

<http://www.cdc.gov/hicpac>

Infect Dis Clin N Am 12;26:13-27 Ann Intern Med 3/6/12. ITC3

CATHETER BACTERIURIA

- **Suggestive of symptomatic bacteriuria**
 - New onset or worsening fever $> 38^{\circ}\text{C}$, chills, rigors
 - Dysuria, suprapubic tenderness, CVA tenderness, pelvic discomfort, urgency, frequency
 - Acute hematuria
 - Malaise or lethargy with no other cause
 - New-onset altered mental status or delirium with no apparent cause

NEJM 10;362:1804-13. Guideline for prevention of catheter UTIs 2009. <http://www.cdc.gov/hicpac>
Infect Dis Clin N Am 12;26:13-27 Ann Intern Med 3/6/12. ITC3
Infect Dis Clin N Am 14;28:15-31

CASE

- 82 y/o male with possible UTI with confusion
 - Daughter states “he always gets like this when he has an infection”
 - Suprapubic cath 5 days ago
 - UTI dx at that time – Ciprofloxacin & NFN (chronic use)
 - 2 d after cath more confused which has progressed to today with visual hallucinations
 - In ED started on pip/tazo
- CVA 11 y ago; urinary retention; AF, HTN

- 7 mon prior – E coli
 - R – Amp, Cipro I – Amp/sulbactam
 - S – Cefazolin, Ceftriaxone, Gent, Nitrofurantoin, TMP/SMX,
- 5 mon prior – E coli
 - R – Amp, Cipro, Amp/sulbactam, TMP/SMX
 - S – Cefazolin, Ceftriaxone, Gent, Nitrofurantoin, Tobra
- 2 mon prior – E coli
 - R – Amp, Cipro, Amp/sulbactam, TMP/SMX, Nitrofurantoin
 - S – Cefazolin, Ceftriaxone, Gent, Tobra
- 1 mon prior – Citrobacter, Enterococcus, Pseudo
 - 2 wk prior – E coli, Acinetobacter

- 135/88, 117, 36.8, 18, 83.5 kg, O₂sat 92%
 - Picking at things
 - Oriented to place only, slurred speech, R hemiparesis
- UA: cath; Nitrite +; RBC TNC; WBC TNC; bacteria 2+; yeast
- WBC 10.7, SCr 1.6; CO₂ 21.7; GFR 42
- UTI
 - Hold Cipro & Nitrofurantoin
 - Start piperacillin/tazobactam

- UC – *C. albicans*
 - S – Ampho B; Caspofungin; Fluconazole; Flucytosine; Posaconazole; Voriconazole; Micafungin; Itraconazole
 - Switched to Fluconazole

ASYMPTOMATIC CANDIDURIA

- Repeat urine
 - If absent no therapy
- Previously healthy – Look for DM, renal disease, GU abnormality
 - None
 - Observation – no antifungal
- Predisposing condition outpatient
 - Treat predisposing condition
 - Observation – no antifungal

SYMPTOMATIC CANDIDURIA

- Cystitis, pyelonephritis
 - Fluconazole for 2-4 weeks
 - Flucytosine for 2-4 weeks
 - Amphotericin B
- Fungus ball
 - Fluconazole for 4 weeks
 - Flucytosine for 2-4 weeks
 - Amphotericin B
 - Surgical drainage