THERAPEUTIC CASE DISCUSSIONS – I & II

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UND School of Medicine & Health Sciences
Big Sky NDAFP Conference
January, 2022

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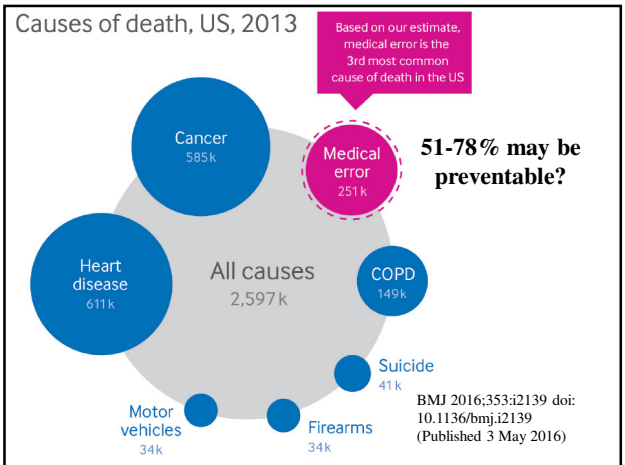
MEDICATION ERRORS

"continue to be one of the most frequent causes of preventable harms in health care."

The Joint Commission. National Patient Safety Goals. March 5, 2010.
http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/npsg8_review.htm

2



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- 79 y/o male with n & v, dizziness and diaphoresis with near syncope
  - HTN, CVA 6 y ago, h/o AF (warfarin allergy)
  - ASA, Lisinopril
  - Metoprolol XL 50 mg/d, Verapamil SR 240 mg 2xd
- 149/62, EKG in ED rate 44, PR 0.26
  - Atropine 0.5 mg IV
- Taking Verapamil SR 120 mg 2xd and was switched to 240 mg ER 240 mg/d
  - Misunderstood and took 240 mg ER 2xd

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HYPOGLYCEMIA CASE

- 59 y/o female found unresponsive
  - EMS reported PG 12
  - Per home health last insulin dose last night
  - Has had several ED visits & hospitalizations for hypoglycemia
    - Home dose administered in hospital no hypoglycemia
- DM, LDL, mild intellectual disability, MDD
  - Neuropsych testing – competent to make decisions
  - Home health daily

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- Meds include Insulin glargine 100 units/ml – 60 units 2xd
- RPh f/u with home health on home meds
  - Patient administers the insulin
  - Home health draws up insulin **60 units on U-100 syringe**
  - **Recent insulin changes to regular insulin U-500**
    - Draws up to 60 unit mark on U-100 syringe = 300 units
  - Probable cause of frequent hypoglycemia

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MEDICATION RECONCILIATION

- "a process … most accurate list of all medications … including name, dosage, frequency, and route … to provide correct medications … within the health care system."

Institute for Healthcare Improvement. Medication Reconciliation Review. Accessed 3/15/15 http://www.ihi.org/knowledge/Pages/Tools/MedicationReconciliationReview.aspx

- Collect, review, analyze meds
- Transitions of care may affect medication regimens of patients
  - Potential for reduced patient safety due to med errors and ADRs

Gooen LG. Clin Geriatr Med. Online 3/1/17 http://dx.doi.org/10.1016/j.cger.2017.01.006

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MEDICATION RECONCILIATION

- Poor communication at "hand offs" in hospital
  - Up to 50% of all med errors
  - Up to 20% of adverse drug events
- Patient should be active participant
- Should take place whenever patient changes level of care (ED, admission, transfers, discharge) as well as in the office
  - **Ensuring the med list is up to date**

Institute for Healthcare Improvement. Medication Reconciliation Review. Accessed 3/15/15 http://www.ihi.org/knowledge/Pages/Tools/MedicationReconciliationReview.aspx

Prevent Adverse Drug Events by Implementing Medication Reconciliation. Cambridge, MA: Institute for Healthcare Improvement; 2011. (www.ihi.org)

Mayo Clin Proc 14;89:1116-25

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- **NSAIDs are a safe and effective non-opioid analgesic in all patients?**

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NSAID COMMENTS

- Ibuprofen 400, 600, and 800 mg provide similar pain relief
- Ibuprofen 400 mg plus acetaminophen 1 g lowers moderate-to-severe acute extremity pain as well as many opioid and acetaminophen combinations

Analgesics for Acute Pain in Adults. Pharmacist's Letter/Prescriber's Letter. Jan 2020

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NSAID COMMENTS

- Reserve injectable (e.g., ketorolac) to unable to take an oral
- Injectable equally effective vs. oral ibuprofen for moderate to severe pain
- Topical may work as well as oral for acute musculoskeletal pain (e.g., sprain).
- Occasional/short-term use of OTC ibuprofen or naproxen should be safe for most stable patients

Analgesics for Acute Pain in Adults. Pharmacist's Letter/Prescriber's Letter. Jan 2020

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NSAID COMMENTS

- Avoid CHRONIC use in HF, DM or CKD
  - If needed & taking ACEI, ARB, or diuretic, consider checking SCr and K weekly for several weeks
- If possible, avoid with high GI risks
  - History of complicated ulcer, especially recent
  - Taking anticoagulants or corticosteroids.
  - > two risk factors: age > 65, high-dose, h/o uncomplicated ulcer, or ASA or other antiplatelet

Analgesics for Acute Pain in Adults. Pharmacist's Letter/Prescriber's Letter. Jan 2020

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NSAID EFFECTS ON RENAL FUNCTION

- Block afferent prostaglandins and may cause:
  - Na^+ retention – edema, HTN, CHF,
  - Increased SCr, Hyperkalemia
- **Use carefully**
  - ACEI – hyperkalemia & increased SCr
  - K-sparing diuretics & K^+ supplement – hyperkalemia
  - At risk for increased SCr
    - Elderly, CHF, Renal dysfunction, Cirrhosis, Ascites, DM, Volume depletion, Diuretics/Na+ depletion
    - Anything that reduces effective plasma volume

Cleveland Clin J Med 02;69[suppl I]:SI53-8

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- 38 y/o male with flu A positive
  - Poor fluid intake, febrile
- Hypertension, Alport Syndrome, Renal transplant, Gout
- Meds
  - ASA 81 mg/d
  - Allopurinol
  - Losartan 100 mg/d
  - Prilosec
  - Cinacalecet, Mycophenolate, Cyclosporine

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- T 102
- **Cr 2.8 (1.6)**
- Plan
  - NS 100/h
  - Tamiflu
  - Hold Losartan
  - Analgesia

–Ketorolac prn

WARNING
TORADOL (ketorolac) IS a NSAID

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- 47 y/o female to ED for upper lip swelling
  - Had this in past but very minor
    - Has not mentioned before 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
  - Rx – Epi, methylprednisolone, diphenhydramine with no immediate improvement – admit
    - While waiting for room lip swelling improved
    - Adamant about going home – Prednisone Rx
  - STOP Lisinopril
  - Mandatory to f/u with primary MD tomorrow

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- 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

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ACEI ANGIOEDEMA

- Onset anytime after 1 day or as late as 10 y
  - 50-66% within 1 week to 3 months
- **Not an IgE hypersensitivy reaction**
- Bradykinin overproduction – vasoactive
- **<u>Class effect – avoid further use of ACEIs</u>**
  - Cross-reactivity with all ACEIs
- **<u>Avoid if h/o angioedema</u>**
  - From any cause including hereditary angioedema

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

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CASE

- 83 y/o male with acute decompensated HF with bilateral pleural effusions
- COPD, CKD, HFpEF, HTN, DM, CAD w DES
- ASA 325 mg/d; **Furosemide 40 mg 2xd**, Clopidogrel; Isosorbide mononitrate; Metoprolol XL 100 mg/d; Simvastatin 40 mg/d
- BNP 959 pg/mL
- Cr 1.5, eGFR 35

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- Diuretic therapy
  - **Furosemide 40 mg IV without increase in UO**
  - Furosemide 80 mg IV produced diuresis
  - **d/c'd on Day 11 on Furosemide 40 mg po 2xd**
- 1 wk later admit with increased leg swelling & SOB
  - 3+ pedal edema
  - Bilateral pleural effusions
  - Cr 1.6; eGFR 31

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LOOP DIURETICS

- Must **attain a threshold concentration** at ascending loop of Henle for a response
  - Dose varies from patient to patient
  - **Individualize** dose based on response
- Bioavailability
  - **Furosemide average ~50%,** others ~90%
  - PO to IV conversion: Furosemide 2:1, others 1:1
- Relative equipotent doses
  - IV Furosemide 40 mg = Bumetanide 1 mg = Torsemide 20 mg

NEJM 17;377:1964-75 JACC 20;75:1178-95

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COMMON MISTAKES IN PRACTICE

- **HF with elevated Cr invariably show Cr increase following vigorous diuresis**
  - Often opposite occurs, and creatinine falls
  - Engorged kidney, related to cardiorenal syndrome
  - Vigorous diuresis improve renal function

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

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LOOP DIURETICS IN ACUTE HF

- Goal is UO of 3-5 L/d until euvolemic
- Initial IV furosemide > chronic oral dose
  - Increase dose if UO stays < 3 L/d
- Diuretic resistant if little response with maximum dose of furosemide 250 mg

NEJM 17;377:1964-75 JACC 20;75:1178-95

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COMMON MISTAKES IN PRACTICE

- **Receiving a statin should not eat grapefruit**
  - May interact with drugs by inhibiting CYP3A4 & p-glycoprotein transport
  - May inhibit atorvastatin, lovastatin, and simvastatin metabolism – increase blood levels
    - Only if high doses & rarely posing a problem
  - Fluvastatin and pravastatin no interaction
  - Grapefruit with statins should not pose a problem

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

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Simvastatin FDA label
Contraindicated with simvastatin: •Erythromycin •Clarithromycin •Gemfibrozil Etc.
Do not exceed 10 mg simvastatin daily with: Amiodarone, Verapamil, Diltiazem,
Do not exceed 20 mg simvastatin daily with: Amlodipine (New), Ranolazine (New)
Avoid large quantities of grapefruit juice (>1 quart daily)

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"DIGOXIN LEVEL WAS NORMAL OR THERAPEUTIC"

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DIGOXIN SERUM LEVELS

- DIG trial benefit of digoxin in men with CHF and an EF ≤ 45%
  - Optimum at digoxin level of 0.5-0.8 ng/ml
- "Unfortunately, many laboratory report forms cite the normal serum digoxin range as 0.5-2.0 or 0.8-2.0 ng/ml, whereas it appears appropriate to list the upper therapeutic range as 1.0 ng/ml"

Am J CV Drugs 18;18:427-40. review. Whayne TF

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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**

Mayo Clin Proc 10;85:180-95 HFSA Guidelines 2010 J Am Geriatr Soc 12;60:616-31
Amer J Med 15;128:1272-4

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CASE

- 82 y/o female with n, v, anorexia, weakness
  - h/o HTN, CHF (EF 20%), AF, CABG, CVA
- Meds
  - ASA 81 mg/d, Warfarin
  - Digoxin 0.125/d
  - Furosemide, Metoprolol, Enalapril, Atorvastatin
  - Azithromycin for 5 days last week – RTI
- **Dig 3.3**
- WHY?

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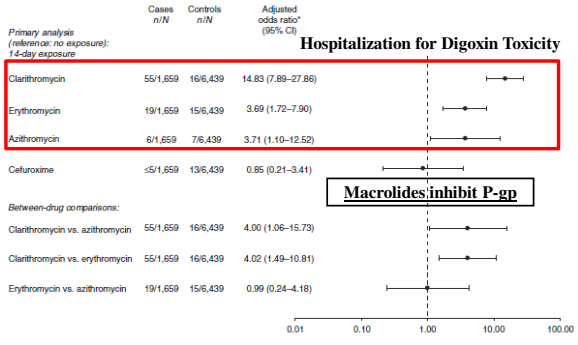
Macrolide-Induced Digoxin Toxicity



Clin Pharmacol Ther 09;86:383-6

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LIVERTOX

DRUG-INDUCED LIVER INJURY

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and National Library of Medicine. http://livertox.nih.gov

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47 y/o female

- Post-hospital and ED f/u
  - BKA 1 mon prior at Mayo from severe PAD – d/c'd with wound vac
  - ED 2 d prior – fall on surgery site, also suicidal thoughts
    - Tired of living with pain, c/o severe pain
- EtOH due to pain
- Cymbalta, Gabapentin, APAP (per husband 2 g q4h 4 d ago), Atorvastatin, Omeprazole, Amlodipine

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- Referral to wound clinic
- Referral to physical medicine
- CMP, APAP, Salicylate, coags, UDS, CBC
- Contacted patient for admission due to LFTs and positive APAP level
- IV NAC

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	5/2	2/14	2/18	2/19/19	2/20/19
Albumin	4.1	3.6	3.2	2.7	2.8
AP	89	81	211	153	144
Tbili		0.2	0.9	0.9	0.6
AST	12	19	2105	520	132
ALT	8	11	2014	1153	713
BAC		223			

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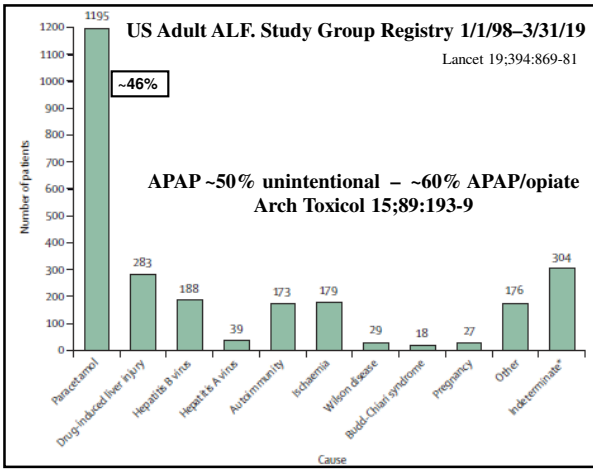

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RISK OF TOXICITY

- > 150 mg/kg or > 7.5 g in adults
  - Rumack-Matthew nomogram – **ONLY ACUTE OD**
  - Toxic range treat with N-acetylcysteine
  - Predicts if ↑ ALT, AST – Does not predict survival
- Unintentional ODs
  - 6-10 gm/d over several days
  - Often in post-op pain, pancreatitis, low back pain, opioid combinations
  - Presents after symptoms develop
  - Worse outcomes than acute ingestion

NEJM 97;337:1112-7 Hepatol. 2017 Dec; 67(6): 1324-31

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CASE

- 36 y/o female with severe n/v
- PHM aortic root repair & mechanical AVR with post-op AF 2 months ago
- Amiodarone, Metoprolol, Warfarin
- Intractable n/v - ? Amiodarone, admitted to THC use, anxiety, abdominal migraine, etc
- Na 138; K 3.2; BUN 12; Cr 0.8; Mg 1.5
- **Received antiemetics** – see MAR

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- Hospital MAR
  - ASA
  - **Dicyclomine 20 mg IV on 8/11**
  - **Haloperidol lactate 2.5 mg IV on 8/11**
  - **Metoprolol** tartrate 50 mg 2xd – slows HR
  - **Ondansetron 4 mg IV q4h 8/11-14**
  - **Pantoprazole 40 mg/d**
  - **Promethazine 25 mg IM 8/11**
  - **Promethazine 25 mg tab 8/12**
  - **Metoclopramide 10 mg IV on 8/12-14 (5 doses)**
  - Warfarin

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EKG & RHYTHM STRIPS

- 8/13 @ 1932 – NSR at 70
- 8/14 @ 0033 – PVCs – bigeminy, couplet
- 8/14 @ 0034 – PVCs then polymorphic V-tach
  - Spontaneous conversion to NSR
- 8/14 @ 0103 – EKG NSR at HR 75, QTc 570
- 8/14 @ 0446 – PVCs then polymorphic V-tach
  - Spontaneous conversion to NSR
  - IV Mg
- 8/14 @ 0527 EKG NSR 73, QTc 559

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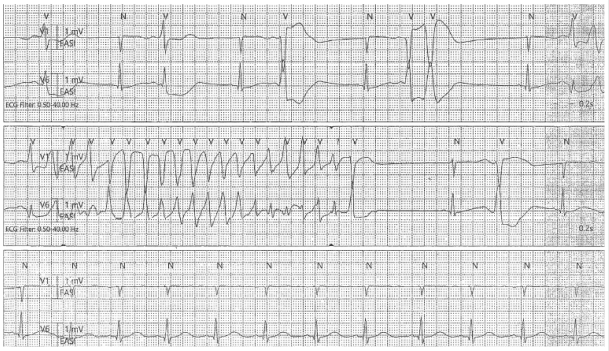
8/14 @ 0446



MgSO4 2 g IV
Serum K 3.2 – KCl 10 mEq IV x 3

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Risk of TdP

- Prolonged QT required for diagnosis of TdP
- Prolonged QT may not lead to TdP in most
- Risk increases if QT >500 msec & with:
  - Female sex – female patient
  - Congenital Long QT Syndrome (cLQTS)
  - Bradycardia – patient on metoprolol
  - Hypokalemia – patient K 3.2
  - Hypomagnesemia
  - Hypocalcemia
  - Drugs that prolong QT – patient on MANY

Crediblemeds.org

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Risk of Torsades Crediblemeds.org

- Known risk of TdP – prolong QT and clearly assoc with a known risk even when taken as recommended – Avoid in congenital long QT
  - Amiodarone
  - Haloperidol
  - Ondansetron
  - Ciprofloxacin, Levofloxacin
- Drugs to be avoided by congenital Long QT
  - TMP/SMX

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Risk of Torsades Crediblemeds.org

- Possible risk of TdP cause QT prolongation but lack evidence for risk of TdP when used as directed – Avoid in congenital long QT
  - Promethazine
- Conditional risk – assoc with TdP but only under certain conditions (eg, high dose, hypokalemia, drug interactions) – Avoid in congenital long QT
  - Metoclopramide
  - Pantoprazole (all PPIs except Rabeprazole [Aciphex] listed)

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CASE

- 90 y/o female with a fall
  - Independent senior living center
  - Dizzy and felt weak
  - 2 d of chills, sweats, urinary frequency, dysuria
  - UTI several years ago
- DM, HTN, MDD, Rheumatic fever
- Promethazine/codeine HS for cough, Fluoxetine, Alendronate, Cetirizine, Losartan, Diphenhydramine 50 mg HS, ASA 325 mg/d

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- Afebrile
- UA positive
- WBC 12.6
- EKG: 92, QTc 515
- UTI
  - Rocephin 1g q24h
  - FP Resident purposely avoided Ciprofloxacin – WHY?

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- "perfect setting for a "QT storm"...such as an elderly woman prescribed ciprofloxacin for bacterial gastroenteritis, with hypokalemia, also given ondansetron for vomiting"

https://pharmacist.therapeuticresearch.com/Content/Articles/PL/2017/Mar/Avoid-QT-Prolonging-Meds-in-High-Risk-Patients. March 2017

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OFFICE VISIT – July

- 36 y/o female with n/v
  - No urinary complaints
- 2 months ago Mayo for ECMO, aortic root repair and mechanical AVR (warfarin)
  - Post-op AF – amiodarone
- Amiodarone 200 mg/d
- Metoprolol tartrate 50 mg 2xd
- **Warfarin 0.5/1 mg**

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- **INR 2**; UA neg for WBC, bacteria, nitrite; reflex a urine culture
- **Warfarin dose (only 0.5/1 mg)**
- 2 d later **UC result – MRSA 20,000**
- Telephoned patient to start:
  - **TMP/SMX DS for 14d**

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Hospital Admission – 1 week later

- n/v for past 2-d
  - Not able to keep food/meds down
- **Meds as before including TMP/SMX**
- **INR 5.4**
- Assessment
  - Intractable n/v – d/c amiodarone
  - **Elevated INR – Hold warfarin**
    - **DDI with TMP/SMX**
  - Admitted to THC use – contributed to n/v

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DRUGS THAT INCREASE WARFARIN ANTICOAGULATION (INR)

Greatest effect

- **TMP/SMX**
- Erythromycin
- Metronidazole
- Fluconazone, Ketoconazole, Itraconazole
- **Amiodarone**

Med Clin N Am 15;99:295-310

Important effect

- Acetaminophen
- Quinolones (Ciprofloxacin)
  - Any antibiotic
- Gemfibrozil
- Omeprazole, Esomeprazole
- Cimetidine
- Azithromycin
- Lovastatin, Simvastatin
- Sertraline

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WARFARIN INTERACTIONS

- **"Awareness of these interactions is critical to safely managing patients receiving warfarin."**
- **"Collaborative care with pharmacists in anticoagulation clinics has been demonstrated to improve patient safety and outcomes."**

Am Fam Physician 19;99:558-64

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CASE

- 70 y male presents to ED with AMS and weak
  - In ED 2 d prior – L distal radial fx – splinted
    - Released from ED – Rx hydrocodone/APAP 5/325 1 q6h
    - Took 0.5h from car to front door – he says due to back pain – crawled into house
    - EMS called and moved him to living room chair
    - Stayed in chair due to weakness
- Wife states was confused when d/c from ED 2d ago – he was not when he first presented to ED
  - Has been saying odd things, asking about people not seen for 20y

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- Hydrocodone/APAP 5/325 mg 1 q6h prn up to 3 d, #12
- Plavix 75 mg/d, ASA 81 mg/d
- Montelukast 10 mg HS, Fluticasone nasal
- Tiotropium inhaler, albuterol MDI prn, ipitropium/albut neb prn
- Fluticasone/salmeterol MDI
- Metoprolol tartrate 12.5 mg 2xd
- Isosorbide mononitrate ER 60 mg/d
- KCl ER tab 10 mEq/d
- Atorvastatin 80 mg/d
- Ezetimibe 10 mg/d
- Sertraline 200 mg/d
- Cyclobenzaprine 5-10 mg 3xd prn
- Ibuprofen 200-600 mg prn
- Zolpidem 5-10 mg HS prn

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- 141/102, 104, 37.2, O2 95%
  - Alert, oriented to self and b-day, pleasantly confused
  - Decreased strength bilat upper/lower
- CK 1,727
- ED Assessment
  - Nontraumatic rhabdo, encephalopathy, leukocytosis
  - Suspect opioids
- Wife in control of meds & could not have taken more, diligent about giving opioid q6h
- Naloxone 0.4 mg IV – no change

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- Admit exam
  - **Eyes – bilateral 3-4 mm, not reactive to light**
  - **Somnolent but arousable, oriented to self/time**
  - **Bilateral inducible clonus while evaluating for Babinski**
  - Generalized weakness
- Assessment
  - Medication side effect or interaction
  - r/o infection
  - Worrisome for central pathology (attending)
- Continue home meds except hold sertraline

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- Further history from chart
- Zoloft 200 mg/d for 11 yr
- ED 2 d PTA exam reviewed
  - Fully alert, communicating with appropriate speech, interactive, not lethargic
  - Eyes equally round and reactive to light
  - Normal motor function of extremities
  - 1453 Morphine 5mg IV
  - 1642 & 1722 Morphine 4mg IV
  - 1855 Hydrocodone/APAP 10/325 mg po 1 tab

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ANY CHANGES TO THE DIFFERENTIAL?

- **Myoclonus differential**
  - **Serotonin syndrome**
  - Metabolic encephalopathy
    - Uremia, Hepatic
  - Cerebral cortical irritation
    - Encephalitis
  - Brainstem pathology
    - Encephalitis, Demyelination
  - Anoxic brain injury

Movement Disorders. Seminars in Neurology Feb 2019

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SEROTONIN SYNDROME

- **Clinical triad** – not consistently present in all
  - Altered mental status (AMS)
    - Agitation, confusion
  - Autonomic hyperactivity/instability
    - Mydriasis, fever, tachycardia
  - CNS hyperexcitability - neuromuscular
    - Movement disorders – myoclonus, tremor, akathasia, bradykinesia
    - Neuromuscular abnormalities – hyperreflexia, clonus spasticity/rigidity, seizures

NEJM 05;352:1112-20 Crit Care Clin 17;33:713-34 Aust Prescr 19;42:56-61

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Hunter Criteria – Serotonin Syndrome

- At least 1 of the following after taking a serotonergic agent:
- Spontaneous clonus
- Inducible clonus plus agitation or diaphoresis
- Ocular clonus plus agitation or diaphoresis
- Tremor plus tachycardia
- Hypertonia plus temperature more than 38 C plus ocular clonus or inducible clonus

Psychiatr Clin N Am 17;40:519-32 Internat J Tryptophan Res 19;12:1-14

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SEROTONIN SYNDROME

- **Under-recognized and underreported**
  - 85% of general physicians were not familiar with the condition in one survey
  - Mild cases are often dismissed or self-limiting
- Described after OD of a single drug, and occasionally from increasing therapeutic doses
  - Usually mild to moderate SS
- Severe S/S usually when multiple drugs are administered – DDIs

Internat J Tryptophan Res 19;12:1-14

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FDA Drug Safety 3/22/16

- Opioids with antidepressants and migraine meds may cause serotonin syndrome
- Taking an opioid with a serotonergic med
  - Seek medical attention immediately
  - Agitation; hallucinations; tachycardia; fever; diaphoresis; shivering or shaking; muscle twitching or stiffness; trouble with coordination; and/or n/v, or diarrhea
- Usually starts within several h to a few d of taking an opioid with a serotonergic med

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THERAPY

- Agitation
  - Benzodiazepines are first line
- HR & BP instability
  - Benzodiazepines help control hyperadrenergic state
- Hyperthermia
  - Benzodiazepines reduce muscle activity
- Cyproheptadine considered an antidote
  - 5HT receptor antagonist
  - 12 mg oral loading dose then 2 mg q2h or 8 mg q6h until clinical improvement

Internat J Tryptophan Res 19;12:1-14 Clev Clinic J Med 16;83:810-7

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	Neuroleptic malignant syndrome	Serotonin syndrome
Precipitant	Dopamine antagonist	Serotonergic drugs
Onset	Days to wks	Hours
Duration	Days to wks	< 24h
Temperature	Febrile, tachycardia, flushed	Febrile, tachycardia, flushed
Mental status	Depressed Consciousness	Depressed consciousness, agitated confusion
Eye signs	Normal pupils	Dilated pupils, ocular clonus
Parkinsonism	Tremor, rigidity	Tremor, rigidity
Upper motor neuron signs	Normal reflexes	Hyperreflexia, clonus, extensor plantar responses
Lead pipe rigidity	Common	Uncommon
GI symptoms	Normal	Diarrhea
Shivering	Not seen	Common

Postgrad Med J 17;93:326-32 Psychiatr Clin N Am 17;40:519-32
Lancet Neurol 19;18:880-90

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20 Common Mistakes Made in Daily Clinical Practice

All with c/c of sore throat with erythema and exudate should be treated with antibiotics to prevent rheumatic fever

- Most cases are viral including those with exudate
- Antibiotics are waste of money and may encourage growth of resistant bacteria
- **TCx appropriate with abx if cultures grow S. pyogenes**

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

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GOALS OF THERAPY

- **Prevent rheumatic fever???** (Editorial. Circ 18;138:1920-22)
  - World prevalence 39M (Pediatr Clin N Am 20;67:843-53)
  - Last epidemic in US 1985
  - **NNT about 10,000** (Hosp Pediatr 15;5:552-4)
- Prevent suppurative complications
- S/S improve within 3-10 d with/without abx
- Reduce infectivity –12(?)-24 h of antibiotic

Ped Infect Dis J 15;12:1302

- Minimize inappropriate antibiotic therapy
  - **Treat only if GABHS**

BMJ 03;327:1324. Centor RM. Editorial Arch Intern Med 12;172:852-3 Ann Intern Med. 12;157:ITC3-1
Prim Care Clin Office Pract 13;40:757-70 Prim Care Clin Office Pract 14;41:91-8

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Female Office Visit

- RTC for f/u of Implanon placed 6 mon ago
  - No menses and no breakthrough bleeding
- 8 male partners over 6 mo with occ condoms
- Pelvic exam – normal
- Assessment
  - High risk sexual behavior
- PLAN?

66

- STI screen today
  - GC; Chlamydia; HIV; HCV; RPR
- N. gonorrhoeae by PCR – neg
- C. trachomatis by NAAT – pos
- Contacted to RTC
  - Tearful, did not expect the diagnosis
  - Azithromycin 1 g po once, and Expedited Partner Therapy
  - Use condoms, notify partners

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- RTC 6 wks
- Vaginal itching, burning x 2d
- Partner may not have taken Rx
- Requests STI testing
  - Repeat screening
- Discussed responsible sexual behavior
- Retreat for chlamydia
  - Azithromycin 1 g po once

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- **N. gonorrhoeae by PCR – pos**
- **C. trachomatis by NAAT – pos**
- **Positive vaginosis screen – G. vaginalis**
- Patient called with results and told to come in for Rx
  - **Ceftriaxone 250 mg IM once**
  - **Metronidazole 500 mg po 2xd for 7 d**
  - **Already received Azithromycin 1 g**
  - RTC for test of cure in 8 wks

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Chlamydia trachomatis

- Most common **bacterial** STI in US (CDC 2018)
- **Urethritis, Cervicitis**, PID, Perihepatitis (Fitz-Hugh–Curtis syndrome), Epididymitis, Conjunctivitis, Proctitis, Prostatitis, Pharyngitis, Reiter's syndrome
- **Asymptomatic to mild** transient symptoms
  - Males 20-50%
  - **Females** up to 80%

Emerg Med Clin N Am 11;29:587-603 Emerg Med Clin N Am 19;37:725-38
Pharmacotherapy: A Pathophysiologic Approach, 11e. 2020

70

CDC 2015 Treatment of Uncomplicated Chlamydia, Cervicitis

- **Recommended regimens**
  - **Doxycycline 100 mg po 2xd for 7 d OR**
  - **Azithromycin 1 g po once (CDC 2021 Alternative)**
- Alternative regimens
  - Erythromycin base 500 mg po 4xd 7 d **OR**
  - EES 800 mg po 4xd 7 d **OR**
  - Ofloxacin 300 mg po 2xd 7 d **OR**
  - Levofloxacin 500 mg po 1xd 7 d
- Pregnant
  - Azithromycin 1 g oral single dose

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CDC 2021 Treatment of Uncomplicated Chlamydia, Cervicitis – Adults

- **Recommended regimens**
  - **Doxycycline** 100 mg po 2xd for 7 d
- Alternative regimens
  - Azithromycin 1 g po once OR
  - Levofloxacin 500 mg/d po for 7 d
- **Pregnant**
  - **Azithromycin** 1 g oral single dose
- **Cervicitis also test/treat for gc if at risk**

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GC CASES 2019

Rank	State	Cases	Per 100K
1	MS	12,068	404
9	**SD**	**2,170**	**246**
21	**ND**	**1,447**	**190**
	US total	616,392	188
35	**MT**	**1,595**	**150**
38	**MN**	**8,013**	**143**
50	VT	175	28

https://www.cdc.gov/std/statistics/2019/tables/13.htm

73

GONORRHEA

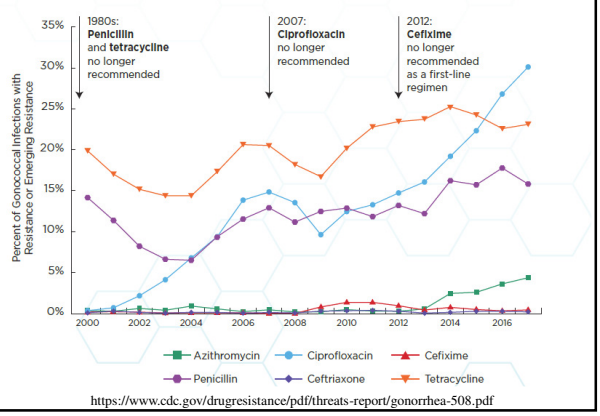
- Neisseria gonorrhoeae
  - Gram-negative diplococcus
- **High rate of concomitant chlamydia**
- **Increasing resistance to antibiotics**

NEJM 18;379:1795-7 Infect Dis Clin N Am 13;27:705-22

2015 STD Surveillance. https://www.cdc.gov/std/stats15/tables/1.htm Dis Mon 16;62:260-8

74

Gonorrhea rapidly develops resistance to antibiotics—ceftriaxone is the last recommended treatment.



https://www.cdc.gov/drugresistance/pdf/threats-report/gonorrhea-508.pdf

75

The Emerging Threat of Untreatable Gonococcal Infection

- "It is time to sound the alarm. During the past 3 y, the wily **gc has become < susceptible** to our last line of antimicrobial defense …"
- Slight increasing MIC to Ceftriaxone
  - Still most effective agent

NEJM 12;366:485-7. Perspective

- "We expect gonorrhea will eventually **wear down our last highly effective antibiotic**"

CDC Press Release. 8/28/18 https://www.cdc.gov/nchhstp/newsroom/2018/press-release-2018-std-prevention-conference.html

76

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

- Recommended: **Ceftriaxone 250 mg IM single dose PLUS Azithromycin 1 g single dose**
  - **Increases effectiveness of urogenital & pharyngeal gc**
  - **Different mechanisms of action - may ↓ emergence & spread of resistance to ceftriaxone**
  - **Treats possible concurrent Chlamydia**
- Alternative: Cefixime 400 mg oral single dose PLUS azithromycin 1 g once
  - < effective for pharyngeal

CDC STD Guidelines 2015

Lancet Infect Dis 17;17:e235-79 NEJM 18;379:1795-7

77

Updated CDC's Treatment Guidelines for GC Infection, 2020

- Azithromycin
  - Isolates with resistance have increased
    - 0.6% (2013) to 5.1% (2019)
  - > in MSM vs MSW
  - May be due to azithro exposure in dual treatment gc regimens
  - Also increasing resistance M. genitalium, Shigella, Campylobacter

Morbidity and Mortality Weekly Report 20;69:1911-6. Dec 18, 2020

CDC STI 2021

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CDC Regimens for Uncomplicated Gonococcal Infections, 2021

- **Cervix, urethra, or rectum and pharynx**
  - **Ceftriaxone 500 mg IM single dose** <150 kg
  - ≥150 kg 1 g of IM ceftriaxone
- **If Chlamydial has not been excluded**
  - **Doxycycline 100 mg orally 2xd for 7 d**
  - If pregnant azithromycin 1 g single dose
- Alternative regimens (none available for pharynx)
  - Gentamicin 240 mg IM single dose PLUS azithromycin 2 g orally single dose **OR**
  - Cefixime 800 mg orally single dose. If chlamydial infection has not been excluded treat as above

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CASE

- 65 y/o with syncopal episode with BRBPR
  - Hypotensive, tachycardic,
- PMH: HTN (HCTZ)
- Pantoprozole IV
- EGD – duodenal bulb ulcer
- Path report gastric biopsy
  - Benign gastric antral mucosa with moderate to severe chronic inflammation
  - No ulcer/erosion, neoplasm or metaplasia
  - H pylori present

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H. Pylori and GI

- Asymptomatic to acute/chronic gastritis ~85%
- PUD in 10% – 50-80% of GU; >95% of DU
- Atrophic gastritis 1-2%
- Gastric adenocarcinoma in 1-2%
- Mucosa-assoc lymphoid-tissue (MALT) lymphoma
- Functional dyspepsia
- Gastric polyps
- Immune thrombocytopenia, B12 or Fe deficiency

NEJM 10;362:1597-604; 19;380:1158-65 Mayo Clin Proc 17;92:599-604
J Clin Med. online 11/30/20 Dig Dis Sci 20;65:1917-31
Gastroenterol Clin N Am 21;50:261-82

81

TRIPLE THERAPY
NO LONGER 1ST-LINE

- Due to increasing resistance combination with clarithromycin or levofloxacin should not be used empirically

Houston Consensus Conference on testing for H. pylori infection in US. Clin Gastroenterol Hepatol 18;16:992-1002

- Standard treatment for years was triple therapy
- "growing resistance to clarithromycin … such that it is no longer recommended, unless clarithromycin resistance rates are known to be low."

Gastroenterol Clin N Am 21;50:261-82

82

TRIPLE THERAPY
NO LONGER 1ST-LINE

- PPI 2xd Amox 1 g 2xd; Clari 500 mg 2xd
  - Or Metronidazole 500 mg 3xd; Clari 500 mg 2xd
- Only if local clarithromycin resistance <15%
  - US >20%???? Gastroenterology 18;155:1372–82
  - May assume >15% unless local data otherwise
- Consider triple if:
  - No history of recent macrolides use
  - Local eradication rate >85%

ACG. Am J Gastroenterol 17;112:212-39 Dig Dis Sci 20;65:1917-31
H. pylori. Pharmacist's Letter/Prescriber's Letter. May 2020
The Medical Letter 20;62:83-5 Gastroenterol Clin N Am 21;50:261-82

83

FIRST-LINE RECOMMENDATIONS

- **Bismuth quadruple therapy** for 14d
  - PPI 2xd; Bismuth (subcitrate 120-300 mg 4xd [in Pylera] OR subsalicylate 300 mg); Metronidazole 250-500 mg; Tetracycline 500 mg (not doxy, lower eradication) all given 4xd
  - **May be best initial choice**
    - "the majority … should be treated initially with 14 d of bismuth-based quadruple therapy" Letter. NEJM 19;381:587-9

NEJM 19;380:1158-65 Gastroenterology 2019;157:44-53
Dig Dis Sci 20;65:1917-31 The Medical Letter 20;62:83-5

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PROTON PUMP INHIBITORS (PPIs)

- Standard use in acid-related disease
  - GERD, dyspepsia, PUD, H. pylori treatment, GI bleed, GI prophylaxis (NSAIDs, corticosteroids and stress ulcer), Zollinger-Ellison (Z-E) syndrome
  - Very effective
- >$25B/y worldwide – OTC and Rx
  - GERD most common reason
  - **Much use may be inappropriate especially long-term use**

Aliment Pharmacol Ther 21;54:129-43

85

PPIs: Review of Emerging Concerns

- Recent studies on long-term use of PPIs have noted potential adverse effects
  - Fractures, pneumonia, C. diff, hypomagnesemia, vit B12 deficiency, renal, and dementia
- "most of the published evidence is inadequate to establish a definite association"
- "when clinically indicated … at the lowest effective dose for symptom control"

Mayo Clin Proc 18;93:240-6
Pharmacist's Letter/Prescriber's Letter. February 2019
Aliment Pharmacol Ther 21;54:129-43
Cureus. 13(1): e12759. DOI 10.7759/cureus.12759 JAMA 20;324:2536-47

86

DEPRESCRIBING PPIs

- PPIs are linked to possible adverse effects
- Consider benefits vs. risks and alternative treatments (eg, H2RAs, lifestyle changes)
- Patients may be taking PPIs for no clear reason after GERD symptoms have resolved
- Periodically stop to determine if continued use is needed

JAMA IM Published online January 11, 2016, editorial
JAMA IM 20;180:571-3 commentary

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CASE

- 22 y/o seen in walk-in clinic with URI symptoms
  - Started with cold symptoms 12 d ago
    - Runny nose and congestion, cough, no fever
    - Symptoms improved (but still present) and 2 days ago had some chills, headache and worsening nasal congestion with thick discharge
- Afebrile, moderate maxillary sinus tenderness
- Acute bacterial sinusitis
  - Azithromycin for 5 days

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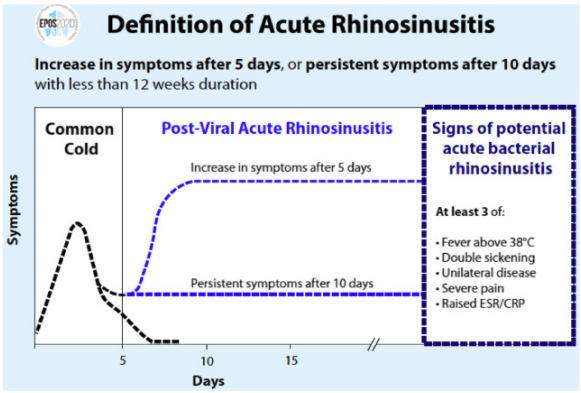
Updated European Position Paper on Rhinosinusitis 2020



Curr Allergy Asthma Rep. online 6/3/20 https://doi.org/10.1007/s11882-020-00917-5

90

Altru & Sanford Fargo – 2020 Antibiograms

Gram-pos % suscep	**Penicillin (non-meningitis)**	**Ampicillin**	**Ampicillin/sulbactam**	Ceftriaxone	**Erythromycin**	**TMP/SMX**	Clindamycin	Tetracycline	Vancomycin	Levofloxacin
S. Pneumo	**95-100**			95-100	**52-76**	**81-91**	84-96	100	100	97-100
ß-hemolytic Strep	100			100	**40-59**		47		100	
H. influen		**64-94**	**94**	100	97 Azi	**64-74**				100

91

ANTIBIOTIC CHOICE FOR ACUTE BACTERIAL RHINOSINUSITIS

- If observation failure by 7 d or worsens
  - Reassess patient, exclude other causes
  - Begin antibiotic
- **1st-line: Amoxicillin (1.5-4 g/d or 90 mg/kg/d) ± clavulanate** for 5-10 d
- 2nd-line: Doxycycline, Clinda + 3rd gen ceph, FQ
- Abx failure by 7 d or worsens
  - Change antibiotic

Guideline. Otolaryngol Head Neck Surg 15;152(no. 2 suppl):S1-S39
Emerg Med Clin N Am 19;37:41-54

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ACUTE BACTERIAL SINUSITIS THERAPY

- If PCN allergy – Doxycycline or FQ
  - **FQ not recommended** as 1st-line empiric therapy
  - Clindamycin plus 3rd-gen oral Ceph if non-IgE
- **Macrolides are not recommended** empirically
  - S. pneumoniae resistance (>40%)
- **TMP/SMX is not recommended** empirically
  - S. pneumoniae (~30% resistance)
  - H. flu resistance (~50%)

Guideline. Otolaryngol Head Neck Surg 15;152(no. 2 suppl):S1-S39
Emerg Med Clin N Am 19;37:41-54

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ANTIBIOTICS INDICATED IN COPD EXACERBATION

- **s/s suggesting bacterial infection**
  - **↑dyspnea**
  - **↑ cough with sputum production/volume**
  - **↑ sputum purulence (e.g., green-yellow color)**
    - 94% sensitivity, 52% specificity for high bacterial load
- Give antibiotics for 5-7d
  - If all 3
  - 2 of above if includes purulence
  - No abx if sputum white or clear in color

Med Clin N Am 12;96:789-809 Anaesthesia Intensive Care Med 14;10:460 GOLD 2021

94

ANTIBIOTICS IN AECB

- Choice for outpatient for 3-10d
  - Mild to moderate COPD
    - Amox ± clav, azithromycin, doxycycline, TMP/SMX
  - Severe COPD
    - Amox/clav; azithromycin; 2nd or 3rd gen ceph; FQ
- h/o frequent exacerbations, severe COPD and/or mechanical ventilation
  - Gram-neg (e.g, Pseudomonas) or resistant bacteria
  - ß-lactam with Pseudomonas activity; FQ; 3rd gen ceph; carbapenem

Mandell ID, 7th ed. 2009 Med Clin N Am 12;96:789-809.
Am J Respir Crit Care Med. 07;176:532-55. G OLD Guidelines 2020

95

CASE

- 50s y/o male with bladder spasm presents to office
  - Thinks he has a UTI
  - Quadriplegia, indwelling foley cath x 20y, frequent UTIs,
  - Cath changed 2 d ago
  - Denies fever, chills, abd pain, hematuria
- Probiotics, Nitrofurantoin 100 mg/d X 12 y, Methenamine 1 g 2xd, Cranberry plus vit C
- Nothing on exam, UA: nitrite +, WBC 300, bacteria many

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- Antibiotics – possible yes since states he has UTI symptoms
- TMP/SMX DS 2xd x 10d started empirically
- UC: P. aeruginosa
  - S: Amikacin, Aztreonam, Cefepime, Gent, Meropenem, Pip/tazo, Tobra
  - R: Ciprofloxacin, Nitrofurantoin
- What now?????

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- **BEFORE INITIATING EMPIRIC ANTIBIOTIC**
- **LOOK FOR PAST UC AND BC TO GUIDE THE SELECTION OF ABX!!!!!!**

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- **1 mon PTA P. aeruginosa x 2**
  - S: Amikacin; Cefepime; Cipro; Gent; Meropenem; Pip/Tazo; I: Aztreonam
- **4 mon S. marcescens**
  - S: Ceftriaxone; Gent; Tobra
  - R: Cipro; Nitrofurantoin, TMP/SMX
- **7 mon P. aeruginosa**
  - S: Cipro; Gent; Pip/Tazo; Tobra
  - I: Aztreonam
- **11 mon S. marcescens**
  - S: Ceftriaxone; Gent; Tobra, TMP/SMX
  - R: Cipro; Nitrofurantoin

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SANFORD – FARGO
E. coli Resistance – Urine – 2016, 2018, 2020

	Outpatient %	Inpatient %
• Ciprofloxacin	15, 11, 9	17, 17, 13
• TMP/SMX	17, 16, 15	22, 19, 16
• Ceftriaxone	4, 3, 3	6, 5, 5
• Pip/Tazo	3, 3, 2	4, 4, 4
• Cefazolin	12, 11, 9	14, 15, 12
• Ertapenem	0, 0, 0	0, 1, 0
• Nitrofurantoin	3, 2, 2	4, 2, 2

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EMPIRIC THERAPY OF
UNCOMPLICATED CYSITIS

- Preferred
  - TMP/SMX DS 2xd or TMP 100 mg 2xd for **3 d**
    - **Don't use if local resistance > 20%** or used within 3 mon
  - Nitrofurantoin 100 mg 2xd for **5 d**
  - Fosfomycin 3 gm **single dose**
- Alternative
  - ß-lactams for **5-7d** (eg, amox/clav, cephalexin)
  - Cipro 250 mg 2xd or Levo 250 mg/d for **3 d**
    - **Risk may outweigh benefit** FDA 7/10/18
    - Increasing resistance

IDSA Guidelines. Clin Infect Dis 11;51:e103-120 Prim Care Clin Office Pract 19;46:191-202
Emerg Med Clin N Am 19;37:707-23 Postgrad Med 20;132:234-50

101

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

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- Acute pyelonephritis
- Patient wants to try outpatient with oral TMP/SMX since that worked last time
- Your response to abx request?
- She received Ceftriaxone IM 1g and Ciprofloxacin 500 mg 2xd po for 7 d
- UC – E. coli
  - Resistant: Ampicillin, Ampicillin/Sulbactam, **TMP/SMX**
  - Sensitive: Cefazolin, Ceftriaxone, **Ciprofloxacin**, Gentamicin, Nitrofurantoin, Tobramycin

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EMPIRICAL TREATMENT OF ACUTE **PYELONEPHRITIS**

- **Outpatient**
  - Cipro for 7 d or Levofloxacin for 5-7 d
    - **1st-line empiric therapy** (2nd-line for cystitis)
    - **If local resistance is < 10%**
    - **If >10% resistance** or patient risk factors increase likelihood of resistance **initial dose of ceftriaxone**, ertapenem or aminoglycoside is often warranted
  - TMP/SMX for 10-14 d if pathogen susceptible
    - Due to resistance initial dose (above) often warranted
  - Oral 3rd gen Ceph for 10-14d may be effective

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120. NEJM 12;366:1028-37. JAMA 14;311:844-54 Dis-a-Mon 15;61:45-59 In the Clinic: UTI. Ann Intern Med 10/3/17 NEJM 18;378:48-59 Postgrad Med 20;132:234-50

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EMPIRICAL TREATMENT OF ACUTE PYELONEPHRITIS

- **Inpatient - IV agents**
  - Choice based on local susceptibility & risk factors for resistance
  - **FQ alone not** recommended NEJM 18;378:48-59 review
  - **Ceftriaxone** or Cefepime monotherapy 7-10d
  - Piperacillin/tazobactam monotherapy 10-14d
  - Ertapenem or Meropenem monotherapy 7-10d
  - Aminoglycoside monotherapy 7-10d
  - Add vanco if MRSA or enterococcus (or ampicillin)

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120 NEJM 12;366:1028-37 Disease-a-Month 15;61:45-59 NEJM 18;378:48-59 Postgrad Med 20;132:234-50

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- 84 y/o female with generalized weakness
  - **Nausea, subjective fever, chills**
  - **Episodes of dysuria**
- **38.2C**
- No flank or CVA tenderness
- WBC 8.8; Na 126;
- UA: **nitrite neg; WBC 26; RBC 18; bacteria high**
  - UC pending

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- Assessment/Plan
  - **Complicated UTI**
  - **Ceftriaxone in ED**
- Next day
  - UC pending
  - **Start TMP/SMX oral**
  - **D/C on TMP/SMX oral for 10d**
- **UC results after d/c – E coli**
  - **R: amp/sulb, Cipro, TMP/SMX**
  - S: Ceftriaxone, nitrofurantoin

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COMMON MISTAKES IN PRACTICE

- **"All patients with asymptomatic bacteriuria require antibiotic treatment."**
  - There is an overuse of antibiotics that is leading to the emergence of resistance
  - IDSA discourages this practice – except special circumstances

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice Frishman WH & Alpert JS. AJM 20;133:1-2

108

CASE

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

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- 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 resistant to FQ
- **Antibiotics stopped by ID due to probable asymptomatic catheter bacteriuria**

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CATHETER BACTERIURIA

- **Suggestive of symptomatic bacteriuria**
  - New onset or worsening fever > 38°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 Dis-a-Mon 15;61:45-59 Infect Dis Clin N Am 18;32:885-97

111

Older with Functional &/or Cognitive Impairment

- **Evidence does not show a causal relationship between bacteriuria and asymptomatic patients with changes in mental status or falls**
- Antibiotics in those with **delirium** (low or very low certainty)
  - **No benefit in severity or duration of delirium**
  - **No benefit for decreasing sepsis, death, or hospitalizations**
  - **Increases risk of adverse effects**

IDSA 2019 Guideline. Clinical Infectious Diseases 2019;XX(XX):1-28

112

COMMON MISTAKES IN PRACTICE

- **Erythema & swelling of distal lower extremity is cellulitis and should receive abx**
  - Chronic venous insufficiency is common imitator of cellulitis and does not respond to abx

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

113

CELLULITIS

- **"nearly always unilateral"** JAMA 16;316:325-37
  - **"Bilateral … uncommon and should prompt consideration of alternative diagnoses"** Infect Dis Clin N Am 21;35:49-60
- **Misdiagnosed in ~30%**
  - Mimics – stasis dermatitis, irritant dermatitis, erythema nodosum, acute gout, DVT
- "accurate diagnosis of cellulitis … is crucial to prevent harm … of overtreatment … and the undertreatment" Infect Dis Clin N Am 21;35:61-79

IDSA Guideline 2014 Prim Care Clin Office Pract 15;42:485-99 JAMA 16;316:325-37

114

COMMON MISTAKES IN PRACTICE

- **Hospitalized on IV abx should remain in hospital for 1 d following transition to oral**
  - Safe to discharge on oral as long as demonstrated clinical and lab evidence that infection is resolving

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

115

CASE

- 65 y/o female presents with 3 d of watery diarrhea with flecks of blood
  - At least 11 episodes so far today with diffuse abdominal pain and cramping
  - Also c/o mild nausea, weakness and chills
- 10 d prior received Clindamycin from dentist for a dental infection
- 115/72; HR 105; 38.2
- WBC 15,750; Cr 1.5 (1.1)
- C. diff – positive

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Clostridioides difficile Infection(CDI)

- New name for Clostridium difficile infection
- ~500,000/y in US
  - Most common nosocomial pathogen
  - ~25% community-acquired
- Infections
  - Fulminant colitis in 3-8% – Mortality 30-90%
  - Pseudomembranous colitis (PMC)
  - Toxic megacolon, Colon perforation, Sepsis
  - Death
    - Linked to ~30,000 deaths/y vs 32,000 in traffic accidents

http://www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_HCP.html. Curr Opin Crit Care 07;13:450-5
NEJM 15;372:1539-48.

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RISK OF C. diff DIARRHEA

High Risk	Moderate Risk	Low Risk
Clindamycin	Other penicillins	Aminoglycosides
		Bacitracin
Cephalosporins	Macrolides	Carbapenems
		Daptomycin
FQ	TMP/SMX, Sulfonamides	Metronidazole
		Nitrofurantoin
Broad-spectrum PCN (e.g., amoxicillin)		Rifampin
		Rifaximin
		Tetracyclines
		Tigecycline
		Vancomycin

J Clin Gastroenterol 07;41:S24–9 J Intensive Care Medicine 14;29:190-9 NEJM 15;372:1539-48

118

CLINDAMYCIN Diarrhea

- Use of Clindamycin and occurrence of diarrhea
- Antibiotic-associated diarrhea occurs in ~20% of patients
- C. diff colitis occurs in ~10% of patients

J Hand Surg 14;39:989-91
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition, 29,.e6

119

C. DIFFICILE TREATMENT

- ORAL Vancomycin, Metronidazole or Fidaxomicin
- ORAL Vancomycin **was** considered preferred therapy
  - Metronidazole no longer preferred in mild CDI

2017 IDSA/SHEA Guidelines

- Fidaxomicin is **NOW** considered preferred therapy

2021 IDSA/SHEA Guidelines
Gastroenterol Clin N Am 21;50:323-40
Mayo Clin Proc 21;96:2192-2204 Med Lett Drugs Ther 2021 Sep 6;63(1632):137-41

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CHOICE OF AGENTS

Infection Severity	Clinical Status	Therapy
Initial episode		**Fidaxomicin 200 mg 2xd X10 d** **Alternate: Vancomycin 125 mg po 4xd X10d**
Non-severe	**WBC ≤ 15,000 AND Scr < 1.5**	**Alternate: if above not available Metronidazole 500 mg po 3xd 10-14d**
Initial episode Fulminant	**Hypotension or shock, ileus, megacolon**	**Vancomycin 500 mg PO/NG qid (If ileus, consider adding rectal vanco) PLUS Metronidazole 500 mg IV q8h (if ileus)**

2021 C. diff Update by the IDSA & SHEA 2021 ACG Guide. Am J Gastroenterol 21;116:1124–47
Med Lett Drugs Ther 2021 Sep 6;63(1632):137-41

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COMPARISON OF AGENTS

	Vancomycin	Metronidazole	Fidaxomicin
FDA-approved	Yes	No	Yes
Mild Disease Severe	++++ Superior	++ **Inferior**	++++ Superior
Relapse rate	10-25%	10-25%	**~40% < Vanco**
Cost for 10 d	4xd Capsules 125 mg: ~$200 Oral Soln (Firvanq): ~$140 IV taken po: ~$60, bitter taste	Tablets 500mg: ~$15	2xd Tablets (Dificid) 200 mg: **~$4,300** **May be cost-effective with < recurrence & improved quality of life**

Adapted from Bartlett JG. Presented at 45th Annual Meeting of IDSA, 10/07. San Diego, CA
Mayo Clin Proc 21;96:2192-2204 Med Lett Drugs Ther 2021 Sep 6;63(1632):137-41

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IDSA/SHEA C. Diff GUIDELINE UPDATE SEPT. 2021

- Initial C. diff episode we **suggest using fidaxomicin rather than a standard course of vancomycin** (conditional recommendation, moderate certainty of evidence). Comment: This recommendation places a high value in the **beneficial effects and safety of fidaxomicin**, but its implementation depends upon available resources. **Vancomycin remains an acceptable alternative.**

Clin Infect Dis 21;73:e1029-44

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