Top Things to Know About Five Commonly Encountered Diseases

Top Things to Know about Hepatitis C Virus Now

Michelle T. Martin, PharmD, BCPS, BCACP

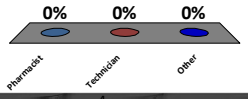
Appointments and Disclosures

- Clinical Pharmacist
  - Bobby and Marvin Fink Family Liver Clinic
  - University of Illinois Hospital and Health Sciences System
- Clinical Assistant Professor
  - University of Illinois at Chicago College of Pharmacy

- I hold shares of Gilead stock. I have no other financial conflicts of interest related to the content of this presentation. Conflicts were resolved through peer review
- I will discuss off-label use of medications, and medications that are not yet FDA-approved.

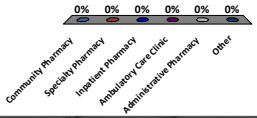
What is your role?

A. Pharmacist
B. Technician
C. Other



What is your primary practice site?

A. Community Pharmacy
B. Specialty Pharmacy
C. Hospital Pharmacy
D. Ambulatory Care Clinic
E. Administrative Pharmacy
F. Other



Learning Objectives

1) Describe critical therapeutic concepts for commonly encountered disease states
2) Identify clinical information that can be applied to your work setting
3) List potential future developments for commonly encountered disease states

Do you work with hepatitis C virus treatment?

A. Yes
B. No

Learning Objective 1

- Describe critical therapeutic concepts for hepatitis C virus (HCV)
  - Guidelines for HCV management
  - Recent medication approvals

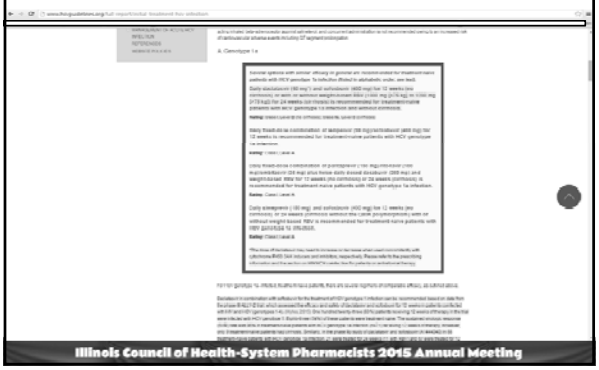
Starting HCV Treatment

- To ensure correct HCV agent and length of treatment, you need to know (at minimum):
  - Genotype
  - Previous treatment history
  - Presence/absence of cirrhosis
- Concomitant comorbidities (renal impairment)
- Check concomitant medications to avoid DDIs
- Use guidelines to select proper agent

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

- First published online 1/29/2014, updated several times since: http://www.hcvguidelines.org/

Sample from Guidelines



HCV Medication Class Suffixes

- -previr = NS3/4A protease inhibitors (PI)
  - simeprevir, paritaprevir
- -asvir = NS5A replication complex inhibitors
  - ledipasvir, ombitasvir, daclatasvir
- -buvir = NS5B inhibitors
  - sofosbuvir, dasabuvir

PrOD (PTV/r/OBV+DSV) (Viekira Pak™) Pearls

- FDA approved for treatment of HCV GT 1
  - Treatment naïve, treatment experienced, cirrhotic, and non-cirrhotic patients
- ADRs: asthenia, fatigue, nausea, insomnia, anemia
- Dosing: x 12 or 24 weeks
  - 2 tablets once daily (OBV 12.5mg, PTR 75mg, ritonavir 50mg) with food
  - 1 tablet twice daily (DSV 250mg) with food
  - +/- ribavirin (RBV)
  - Up to 10 pills daily
  - Ensure patient can verbalize understanding of administration / importance of adherence

http://www.hepmag.com/articles/abbvie_viekira_pak_2501_26610.shtml

PTV/r/OBV (Technivie™) + RBV Pearls

- FDA approved for treatment of HCV GT 4
  - Treatment naïve, treatment experienced, and non-cirrhotic patients
- ADRs: asthenia, fatigue, nausea, insomnia, anemia with RBV
- Dosing: x 12 weeks
  - 2 tablets once daily (OBV 12.5mg, PTR 75mg, ritonavir 50mg) with food
  - + ribavirin (RBV)
  - Ensure patient can verbalize understanding of administration / importance of adherence
  - Up to 8 pills daily

http://www.medscape.com/viewarticle/848090

PTV/r/OBV +/- DSV Pearls

- Drug-drug interaction considerations
  - Paritaprevir: inhibitor of OATP1B1,OATP1B3, BCRP, and P-gp; substrate of CYP3A4
  - Ritonavir: inhibitor of CYP3A4, BCRP, and P-gp, substrate of CYP3A4
  - Strong CYP3A4 and CYP2C8 inducers may decrease efficacy of PrO+/-D)
  - CYP2C8 inhibitors (may increase DSV levels and risk of QT prolongation)
- Examples of contraindicated concurrent medications
  - Combined oral contraceptives
  - Carbamazepine, phenytoin, phenobarbital
  - Efavirenz, simvastatin, sildenafil for PAH
- Cyclosporine and tacrolimus doses must be adjusted

http://www.hepatitisc.uw.edu/page/treatment/drugs/3d

Ledipasvir (LDV)/Sofosbuvir (SOF) (Harvoni™) Pearls

- FDA-approved for treatment of HCV GT 1
  - Treatment naïve, treatment experienced, cirrhotic, and non-cirrhotic patients
- Dosing: x 8, 12, or 24 weeks
  - 1 combination tablet (LDV 90mg / SOF 400mg) once daily
- ADRs: fatigue, headache, nausea, diarrhea
- Drug-drug interactions
  - Substrate of P-gp
    - Contraindications with phenytoin, carbamazepine, etc
  - Requires acidic environment for absorption
    - Timing with PPIs, H2RAs, antacids

http://www.empr.com/harvoni/drug/34390/

SOF + Daclatasvir (DCV) (Daklinza™) Pearls

- FDA approved for treatment of HCV GT 3
  - Treatment naïve, treatment experienced patients
    - ALLY-3: 90% in TN, 86% in TE, 63% SVR in cirrhotics, 96% in non-cirrhotics
- ADRs: fatigue, headache, nausea, diarrhea
- Dosing: x 12 weeks
  - 2 tablets once daily (DCV 60mg + SOF 400mg) x 12 weeks → 2 copays
- Drug-drug interactions
  - DCV is a substrate of CYP-3A4
    - Decrease dose to 30mg daily with strong inhibitors, increase dose to 90mg daily with moderate inducers
  - Substrate and inhibitor of P-gp
    - Contraindications with phenytoin, carbamazepine

http://www.egyreg.com/2015/04/sovaldi-plus-daklinza-effective-for.html

SOF + RBV Pearls

- FDA approved for treatment of HCV GT 2
  - Treatment naïve, treatment experienced; cirrhotic and non-cirrhotic patients
- ADRs: fatigue, headache, nausea, diarrhea
- Dosing
  - 1 tablet once daily (SOF 400mg) x 12-16 weeks
  - + RBV
  - Up to 7 tablets daily
- Monitor hgb and CrCl during treatment

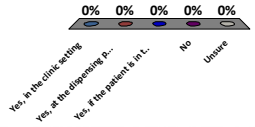
http://www.forbes.com/sites/theapothecary/2014/08/18/uk-says-sovaldi-is-worth-it-we-should-listen/

Learning Objective 2

- Identify clinical information that can be applied to your work setting
  - Role of pharmacists in different settings
  - Insurance restrictions
  - Patient assistance programs

Does a pharmacist interact with HCV patients on treatment at your institution? (even if it is not you)

A. Yes, in the clinic setting
B. Yes, at the dispensing pharmacy
C. Yes, if the patient is in the hospital
D. No
E. Unsure



Ambulatory Care HCV Management Pearls

- Aid in medication selection
  - Use guidelines to confirm/select regimen
- DDI screening and management
- Pt management
  - Clinic visits
  - Provide education – ADRs, dosing, adherence
  - Monitor labs
- Liaison for medication assistance programs
- Recommend screening, team involvement

Community / Specialty HCV Management Pearls

- Verify medication selection and length of treatment / refills
- Work with payors and patient assistance programs to ensure coverage
- Patient education - counsel on:
  - Adherence
  - Coadministration with food (PrO +/- D)
  - DDIs and coadministration with other medications
- Refill management

Inpatient HCV Management Pearls

- Prevent interruption in HCV treatment (unless team stops treatment)
  - Family or friend to bring pt's HCV medication to hospital
- Counsel on adherence
- DDI screening
- Ensure appropriate labs are drawn
- HCV screening

Payors

- Want to prevent treatment failure and encourage successful treatment
- Prioritization of patients for treatment
- Some insurance plans cover only one course of HCV treatment

Examples of Payor Requirements

Select Insurance Plan Requirements for HCV Medication Coverage (as of 8/10/15)

Insurance Plan	Documentation of sobriety (EtOH and illicits)	Documentation of treatment adherence and counseling	Metavir Fibrosis Score Covered	HCV RNA required in the last:	Additional Lab Testing
Aetna Better Health	12 months – in MD note + Tox Screen	letter signed by pt	F4 only	3 months	Not required
Cigna Health Spring Medicaid	12 months - EtOH/Tox screen in last 15 days	letter signed by pt - commitment to treatment plan	F4 only	3 months	Negative pregnacy test
County Care	6 months – in MD note	must be documented by MD in clinic note	F3/F4	6 months	HIV Ab test in last 6 months and Hep B serologies
IHFS (Illinois Medicaid)	12 months – in MD note + Tox Screen in last 15 days	letter signed by pt	F4 only	3 months	Not required

Patient Assistance Programs

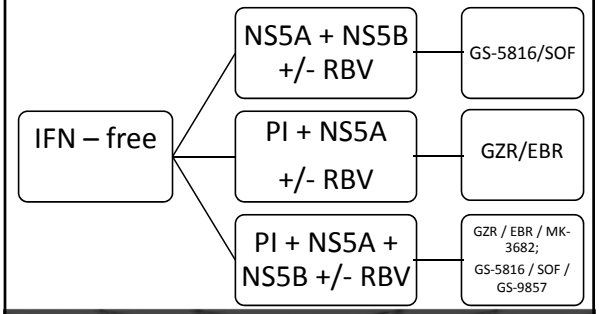
	My Support Path (Gilead)	ProCeed (AbbVie)	(Bristol-Myers Squibb)
Medications Covered	sofosbuvir, ledipasvir / sofosbuvir	paritaprevir/ ritonavir/ombitasvir, +/- dasabuvir; ribavirin	daclatasvir
Website	http://www.mysupportpath.com/	https://www.viekira.com/proceed-support	http://www.bms.com/products/Pages/programs.aspx
Phone	1-855-7-MYPATH (855-769-7284)	1-844-2PROCEED (844-277-6233)	1-844-44-CONNECT (844-442-6663)

Learning Objective 3

- List potential future developments for HCV
  - Guidelines – continual updates
  - Medications in the pipeline

http://www.hcvadvocate.org/hepatitis/hepC/HCVDrugs.html

Select HCV Pipeline Combinations



Grazoprevir/Elbasvir FDC

- NDA filed on 5/28/2015 for GT 1, 4, 6
  - Breakthrough status
    - for renal impairment and GT 4
  - PDUFA date in 12/2015
- Future plans for triple DAA (GZR/EBR with MK-3682 in a FDC)

Grazoprevir/Elbasvir Phase III

Trial Name	Patient Population	Regimen	SVR
C-EDGE TN	N=316 Treatment Naïve, GT 1,4,6, 22% cirrhotics	12 weeks GZR/EBR	95%
C-EDGE TE	N=420 Treatment Experienced, GT 1,4,6, 35% cirrhotics	12 wks GZR/EBR 12 wks GZR/EBR + RBV 16 wks GZR/EBR 16 wks GZR/EBR + RBV	92% 94% 92% 97%
C-EDGE CO-INFXN	N= 218 HIV/HCV pts, GT 1,4	12 weeks GZR/EBR	95%
C-SURFER	N=224 GT 1,4,6; CrCl <30mL/min, 75% on dialysis	12 wks GZR/EBR	94%

GS-5816 100mg / SOF 400mg FDC

- Pangenotypic
- ADRs: fatigue, headache, nausea, insomnia (anemia with RBV)
- Phase III data forthcoming in 11/2015 (ASTRAL-1, -2, -3 trials)
- Future plans for triple DAA (GS-5816 / SOF / GS-9857 in a FDC); shorter duration?

Summary

- HCV is a major public health concern
- Online guidelines are updated regularly
- HCV treatment is advancing rapidly; approval of more pipeline agents is anticipated in late 2015 and 2016
- Pharmacists have an important role in educating patients and providers about HCV medications
- DDIs and insurance coverage will continue to complicate HCV treatment

Top Things to Know about Hepatitis C Virus Now

Michelle Martin

1. Which of the following direct acting antiviral combinations was recently FDA-approved for HCV Genotype 4?

    A. Paritaprevir / Ritonavir / Ombitasvir + Ribavirin

    B. Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir

    C. Sofosbuvir + Daclatasvir

    D. Sofosbuvir + Simeprevir

Heart Failure

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE
Associate Professor, Pharmacy Practice
Midwestern University Chicago College of Pharmacy
Clinical Pharmacist, Advocate Medical Group

The speaker has no conflicts of interest to disclose in relation to this presentation

What Is Heart Failure?

- Structural or functional impairment of ventricular filling or ejection of blood

Classification	EF (%)	Description
Heart failure with reduced ejection fraction (HFrEF)	≤ 40	Also referred to as systolic heart failure Randomized control trials have demonstrated efficacious therapy options
Heart failure with preserved ejection fraction (HFpEF)	≥ 50	Also referred to as diastolic heart failure Lack of evidence supporting benefit of medication therapy

J Am Coll Cardiol. 2013;62:e147–239.

ACC/AHA Classification Table			NYHA Functional Class	
Stage	Description	Examples	Class	Description
A	High risk of developing HF. No identified structural or functional abnormalities. No signs or symptoms	HTN, CAD, DM, h/o alcohol abuse, h/o rheumatic fever, FH of CMP	No comparable functional class	
B	Developed structural heart disease, but have never shown s/sx of HF	LV hypertrophy or fibrosis; asymptomatic vavlular heart disease; previous MI	I	No limitation of physical activity
C	Current or prior symptoms of HF associated with underlying structural heart disease	Dyspnea or fatigue due to left ventricular systolic dysfunction; asymptomatic patients who are undergoing treatment for prior symptoms of HF	I	No limitation of physical activity
			II	Comfortable at rest, but ordinary physical activity results in symptoms of heart failure
			III	Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes symptoms of HF
			IV	Unable to complete any physical activity without discomfort and symptoms at rest
D	Advanced structural heart disease and marked symptoms of HF at rest despite max med therapy	Frequently hospitalized for HF; at home receiving continuous IV support for symptom relief or supported with a mechanical circulatory assist device	IV	Unable to complete any physical activity without discomfort and symptoms at rest

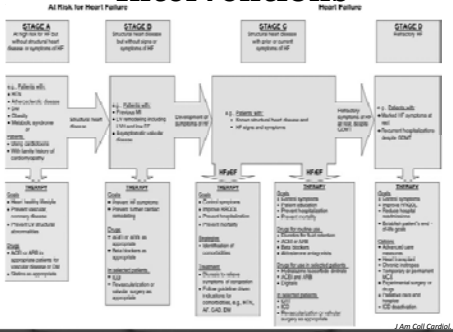
J Am Coll Cardiol. 2013;62:e147–239.

Nonpharmacological Interventions

- Self-care is an important component
  - Daily weights
  - Sodium restriction
  - Fluid restriction
  - CPAP use
  - Physical activity/cardiac rehab

J Am Coll Cardiol. 2013;62:e147–239.

HFrEF Pharmacological Interventions



J Am Coll Cardiol. 2013;62:e147–239.

Clinical Question

A 52 yo Caucasian male with idiopathic dilated cardiomyopathy presents to clinic today for medication management. A recent ECHO shows an EF of 25-30%. His medication regimen includes furosemide 40 mg twice daily, lisinopril 20 mg daily, and metoprolol succinate 150 mg daily. Vital signs include BP 138/86 mmHg and HR 56 bpm. Laboratory values include Scr 1.3 mg/dL and K+ 4.3 mEq/L. Which of the following recommendations is the most appropriate at this time?

a) Increase metoprolol succinate to 200 mg daily
b) Initiate hydralazine 25 mg three times daily and isosorbide dinitrate 10 mg three times daily
c) Initiate spironolactone 25 mg daily
d) Increase lisinopril to 40 mg daily

Recently Approved Medications for HFrEF

- Sacubitril/valsartan (Entresto™)
  - LCZ696 (PARADIGM-HF)
- Ivabradine (Corlanor®)

Sacubitril/Valsartan

- Sacubitril – neprilysin inhibitor
  - Neprilysin is an endopeptidase that degrades natriuretic peptides, bradykinin and adrenomedullin
  - Counteract neurohormonal activation
    - → vasoconstriction, sodium retention and remodeling
- Combination of ACEI and neprilysin inhibitors has been associated with severe angioedema

Entresto(TM) [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015.

Sacubitril/Valsartan

- Dosing:
  - Sacubitril 49 mg and valsartan 51 mg twice daily
  - Double dose every 2 – 4 weeks
  - Target dose: sacubitril 97 mg and valsartan 103 mg twice daily
  - Concomitant use of ACEI is CI
    - Allow 36 hour washout period when switching
  - Initiate sacubitril 24 mg and valsartan 26 mg twice daily in patients previously taking ACEI or ARB or in patients with eGFR < 30 mL/min/1.73m^2

Entresto(TM) [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015.

PARADIGM-HF

- 8442 patients
  - Class II, III, IV HF with EF ≤ 40% (≤ 35%)
- Received sacubitril/valsartan (LCZ696) 200 mg twice daily or enalapril 10 mg twice daily
- Primary outcome:
  - Composite death from cardiovascular causes or hospitalizations for heart failure
- All patients on ACEI/ARB prior to trial
- At randomization:
  - Diuretics (80%), BB (93%), AA (54,57%), Digitalis (29,31%)

N Engl J Med. 2014;371:993-1004.

PARADIGM-HF

- Trial stopped early at median follow-up of 27 months

Primary outcome	LCZ696 (N = 4187)	Enalapril (N = 4212)	Hazard Ratio (95% CI)	P-value	NNT
Death from cardiovascular causes or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73 – 0.87)	< 0.001	21
Death from cardiac causes	558 (13.3)	693 (16.5)	0.80 (0.71 – 0.89)	< 0.001	31
First hospitalization for worsening heart failure	537 (12.8)	658 (15.6)	0.79 (0.71 – 0.89)	< 0.001	36

N Engl J Med. 2014;371:993-1004.

PARADIGM- HF

- Secondary outcomes:
  - LCZ696 decreased death from any cause ($p < 0.001$)
  - Decreased symptoms and physical limitations of heart failure ($p = 0.001$)
- Adverse events with LCZ696:
  - Higher risk of hypotension and angioedema
  - Lower risk of renal impairment, hyperkalemia and cough

N Engl J Med. 2014;371:993-1004.

Ivabradine

- ↓ HR via direct sinus node inhibition
  - No direct effects on myocardial contractility and intracardiac conduction
- Shown to reduce hospitalizations but not death in patients receiving HF standards of care

Lancet. 2010;376(9744):875-885.

Ivabradine

- Indicated in patients with LVEF ≤ 35% in sinus rhythm with resting HR ≥ 70 bpm
- Use in patients who are taking max dose beta-blocker or have CI to beta-blocker

Lancet. 2010;376(9744):875-885.

Heart Failure Preserved Ejection Fraction (HFpEF)

- 50% of all HF diagnosis
- Morbidity and mortality rate similar to HFrEF
- Diagnosis of exclusion
  - Presence of clinical HF with preserved LVEF
  - Rule out other causes
    - Valvular disease, COPD, pulmonary HTN, etc.
- Lack of evidence supporting benefits of medication therapy

Pharmacotherapy. 2015;35(4):351-360.

Heart Failure Preserved Ejection Fraction (HFpEF)

- Acute therapy similar for both HFrEF and HFpEF
  - Diuretics to reduce volume overload and improve dyspnea
- Chronic management
  - Treat precipitating conditions
    - E.g. Atrial fibrillation, HTN
  - Control symptoms with diuretics
  - Counsel patients on nonpharm measures
- Risk factors for exacerbation similar
  - Nonadherence
  - Excessive sodium or fluid intake
  - Atrial fibrillation, HTN, MI
  - NSAIDs and other medications which cause Na+/H2O retention

Pharmacotherapy. 2015;35(4):351-360.

Heart Failure Preserved Ejection Fraction (HFpEF)

- Pharmacotherapy Literature Review
  - ARBs
    - CHARM-Preserved and I-PRESERVE
      - No significant difference in CV death or HF hospitalization
  - ACEIs
    - PEP-CHF
      - No significant difference in all-cause mortality or HF hospitalization at the end of follow-up
  - Beta-blockers
  - Aldosterone Antagonists
    - TOPCAT
      - Primary outcome – composite of CV death, HF hospitalization, or aborted cardiac arrest not significant
      - Spironolactone reduced HF hospitalizations in secondary outcomes HR 0.89 (95% CI 0.69 – 0.99)

Lancet. 2003;362:777–81.
N Engl J Med. 2008;359:2456–67.
Eur Heart J. 2006;27:2338–45.
N Engl J Med. 2014;370:1383–92.

Clinical Question

A 55yo male patient presents to clinic with worsening edema and dyspnea on exertion. His PMH is significant for HTN and Type 2 DM. A recent ECHO shows an EF of 60-65% and grade III diastolic dysfunction with moderate tricuspid valve regurgitation. Pertinent vitals and labs include: BP 160/85 mmHg, HR 68 bpm, Scr 0.9 mg/dL, and K^+ 4.3 mEq/L. His current weight is 10 lbs above baseline and he is currently taking aspirin 81 mg daily and atorvastatin 10mg daily. Which of the following recommendations is the most appropriate at this time?

a. Initiate candesartan and furosemide
b. Initiate candesartan and carvedilol
c. Initiate carvedilol and furosemide
d. Initiate furosemide

Transitions of Care

Recommended for all heart failure patients	Exacerbating factors addressed
	Near optimal volume status observed
	Transition from IV to oral diuretics completed
	Patient and family education completed, including clear discharge instructions
	LVEF documented
	Smoking cessation counseling initiated
	Near optimal pharmacologic therapy achieved (e.g. ACEI, BB)
	Follow-up clinic visit scheduled within 7-10 days
Should be considered for patients with advanced HF or recurrent admissions for HF	Oral medication regimen stable for 24 hours
	No IV vasodilator or ionotropic agent for 24 hours
	Ambulation before discharge to assess functional capacity after therapy
	Plans for post-discharge management (scale, visiting nurse, scheduled telephone call 3 days after discharge)
	Referral for other disease state management

J Card Fail. 2010;16:e1-194.

References

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;62:e147–239.
2. Entresto[TM] [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015.
3. McMurray JV, Parker M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med.* 2014;371:993-1004.
4. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomized placebo-controlled study. *Lancet.* 2010;376(9744):875-885.
5. Basaraba JE, Barry AR. Pharmacotherapy of heart failure with preserved ejection fraction. *Pharmacotherapy.* 2015;35(4):351-360.
6. Yusuf S, Pfeffer MA, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM Preserved Trial. *Lancet.* 2003;362:777–81.
7. Massie BM, Carson PE, McMurray JJ, et al. Irbesartan in patients with heart failure and preserved ejection fraction. *N Engl J Med.* 2008;359:2456–67.
8. Cleland JGF, Tendera M, Adamus J, et al. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. *Eur Heart J.* 2006;27:2338–45.
9. Pitt B, Pfeffer MA, Assmann SF, et al. Spironolactone for heart failure with preserved ejection fraction. *N Engl J Med.* 2014;370:1383-92.
10. Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. *J Card Fail.* 2010;16:e1-194.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Top 5 things to know about heart failure

Christie Schumacher2

Self-assessment questions:

1. The cardiologist in your clinic would like to switch a patient from enalapril 10 mg twice daily to sacubitril-valsartan 24-26 mg twice daily. He would like for you to counsel the patient on the new medication and when to start. How long should you counsel the patient to wait before he/she starts the sacubitril-valsartan prescription after discontinuing enalapril?
    a. 12 hours
    b. 24 hours
    c. 36 hours
    d. 48 hours

2. Which of the following patients would be a candidate for ivabradine?
    a. A 55 year old patient in sinus rhythm with a LVEF of 25% and a pulse of 74 bpm on a max dose beta-blocker, ACEI, spironolactone and furosemide
    b. A 55 year old patient in atrial fibrillation with a LVEF of 25% and a pulse of 74 bpm on a low dose beta-blocker, ACEI, spironolactone and furosemide
    c. A 55 year old patient in sinus rhythm with a LVEF of 55% and a pulse of 64 bpm on a max dose beta-blocker, ACEI, spironolactone and furosemide
    d. A 55 year old patient in sinus rhythm with a LVEF of 25% and a pulse of 64 bpm on a low dose beta-blocker, ACEI, spironolactone and furosemide

The Top 5 Things Pharmacists Can **Do** for Patients with COPD

Lori Wilken, PharmD

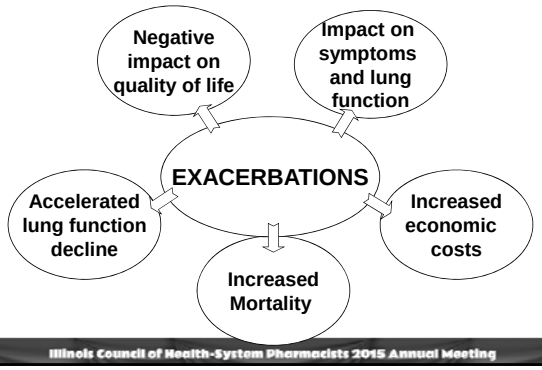
Disclosure

- Grant money was received in the past year from Pfizer. All conflicts were resolved through peer review.
- I will be discussing "off label" uses of the following medications:
  - Nicotine replacement patch, gum, inhaler, nasal spray and lozenge
  - Bupropion SR and Varenicline

Top 5: Number 5

USE CORTICOSTEROIDS CAUTIOUSLY

Consequences Of COPD Exacerbations



GOLD Category	COPD SEVERITY		Exacerbations in the past 12 months
4 3	C	D	≥2 or any COPD related hospitalizations
2 1	A	B	1 or less and not leading to hospitalization
	CAT <10 Few symptoms	**CAT ≥10** Many symptoms	

COPD Severity Grade

goldcopd.org 5

GOLD Category	COPD SEVERITY		Exacerbations in the past 12 months
4 3	LAMA or ICS/LABA	LAMA and/or ICS/LABA	≥2 or any COPD related hospitalizations
2 1	SAMA or SABA	LAMA or LABA	1 or less and not leading to hospitalization
	CAT <10 Few symptoms	**CAT ≥10** Many symptoms	

COPD Severity Grade

goldcopd.org 6

Pneumonia and Inhaled Corticosteroids

	Mortality	Exacerbation	Pneumonia
Placebo	15.2%	1.13	12.3%
Salmeterol	13.5%	0.97 (P<0.001)	13.3%
Fluticasone	**16%**	0.93 (P<0.001)	18.3% (P<0.001)
Combo	12.6% (P=0.052)	0.85 (P<0.001)	19.6% (P<0.001)

N Engl J Med 2007 356;775-789

7

Combination ICS and Long-Acting Bronchodilator

- Clinical Use
  - Severe COPD
  - Repeated exacerbations
    - *2 or more exacerbations in the past year or*
    - *1 COPD hospitalization*
  - **Patient has asthma and COPD**

http://www.goldcopd.org/

8

Acute COPD Exacerbation

- Prednisone 40mg for **5 days**
  - Improves spirometry, ABGs, and symptoms
  - Reduced relapse rates at 30 days and prolonged time to relapse

goldcopd.org

9

Withdrawal of ICS?

- 12 month, double blind, parallel-group
- Randomized to withdrawal fluticasone over 12 weeks
- 2485 patients with history of COPD exacerbations
- Triple therapy (tiotropium + salmeterol +fluticasone)

Magnussen H. N Engl J Med 2014; 371:1285-1294.

Withdrawal of ICS?

- Time to first exacerbation
  - 110 days in withdrawal group
  - 107 days in the continuation group
- Loss of lung function **worse in withdrawal group**
- QOL and safety similar at 52 weeks

Top 5: Number 4

CHECK ADHERENCE TO LONG-ACTING INHALERS

↓ Exacerbations and/or Hospitalizations

Medication Class	Generic
LAMA	Tiotropium Aclidinium
LABA	Formoterol Indacaterol Salmeterol
ICS/LABA	Budesonide/formoterol Fluticasone/salmeterol Fluticasone/vilanterol
Phosphodiesterase 4 Inhibitor	Roflumilast

New Inhalers

Generic	Brand	MOA	Indication	Picture
Fluticasone furoate and Vilanterol 100/25 mcg 200/25 mcg	Breo Ellipta	ICS LAMA	COPD and Asthma ≥ 18	
Umeclidinium and Vilanterol 62.5/25 mcg	Anoro Ellipta	LAMA LABA	COPD	
Umeclidinium 62.5 mcg	Incruse Ellipta	LAMA	COPD	
Tiotropium 2.5 mcg	Spiriva Respimat	LAMA	COPD	
Olodaterol 2.5 mcg	Striverdi Respimat	LABA	COPD	
Tiotropium and Olodaterol 2.5 mcg	Stiolto Respimat	LAMA LABA	COPD	
Albuterol 90 mcg	ProAir Respiclick	SABA	Asthma ≥ 12	

Top 5: Number 3

WATCH INHALER TECHNIQUE

Every Visit
Every Inhaler

http://use-inhalers.com/

70% of people use inhalers incorrectly!

Top 5: Number 2

SCREEN AND PROVIDE IMMUNIZATIONS

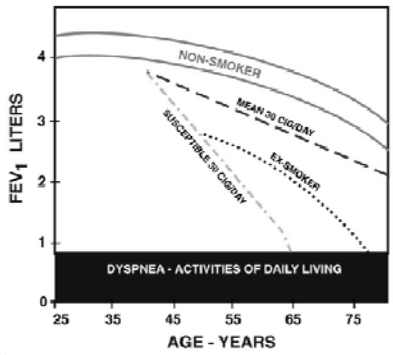
Immunizations

- Influenza vaccine
  - Reduces serious illness and death by **50% in COPD patients**
  - Intramuscularly
  - Annually (October-March)

Top 5: Number 1

ASSIST WITH TOBACCO DEPENDENCE

Relationship of FEV_1, age and smoking



BMJ 1977;1:1645

20

Treatment of Tobacco Dependence

- Nicotine Replacement Therapy (NRT)
  - Transdermal patches
  - Gum
  - Nasal Spray
  - Inhaler
  - Lozenges
- Bupropion SR
- Varenicline
- Combination therapy

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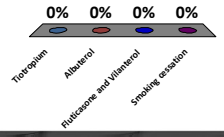
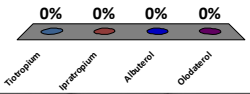
Which of the following treatments has been shown to slow the decline in lung function for patients with COPD?

A. Tiotropium
B. Albuterol
C. Fluticasone and Vilanterol
D. Smoking cessation



Which of the following medications has demonstrated decreased COPD exacerbations and hospitalizations?

A. Tiotropium
B. Ipratropium
C. Albuterol
D. Olodaterol



FUTURE DEVELOPMENTS

Pipeline for COPD

Drug Entity	MOA	Study Phase	Company
Indacaterol Glycopyronnium	LABA/LAMA	Expected launch 2016	Novartis
Glycopyrronium	LAMA	Expected launch 2016	Novartis
Fluticasone Umeclidinium Vilanterol	ICS/LAMA/LABA	Expected launch 2019	GSK
Aclidinium formoterol	LAMA/LABA	Phase 3	Astra Zeneca
Benralizumab	Biologic IL-5 antibody	Phase 3	Astra Zeneca
Mepolizumab	Biologic IL-5 antibody	Phase 3	GSK
TD-4208	LAMA nebulized soln daily	Phase 3	Theravance Biopharma/Mylan
Losmapimod	p38-kinase inhibitor	Phase 2	Pfizer

Pipeline Drug for Tobacco Dependence

"

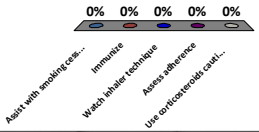
- "A New Strategy for Smoking Cessation: Characterization of a Bacterial Enzyme for the Degradation of Nicotine"
  - Xue S, Schlosburg JE, Janda KD. *Journal of the American Chemical Society*, 2015

Summary

1. Assist with **stopping smoking**!
2. Screen and provide (or recommend) **influenza vaccine**
3. ***Watch*** inhaler technique
4. Check **adherence** to long-acting inhalers
5. Use corticosteroids cautiously

What do you plan to do when you return to work to help patients with COPD?

A. Assist with smoking cessation
B. Immunize
C. Watch inhaler technique
D. Assess adherence
E. Use corticosteroids cautiously



Illinois Council of Health-System Pharmacists 2015 Annual Meeting

References

- Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. http://www.goldcopd.org
- Calverley PMA, Anderson JA, Bartolome C, Ferguson GT, Jenkins C, Jones PW, et al. Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease. N Engl J Med 2007 356;775-789.
- Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA 2013;309 (21): 2223-31
- Magnussen H, Disse B, Rodriguez-Roisin R, Kirsten A, Watz H, Tetzlaff K, et al. Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD. N Engl J Med 2014; 371:1285-1294.
- Fiore MC, Bailey WC, Cohen SJ, et al. *Treating Tobacco Use and Dependence; 2008 Update.* Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Top Things to Know About Community-acquired Pneumonia

John Esterly, PharmD, BCPS AQ-ID
Chicago State University COP
Northwestern Memorial Hospital

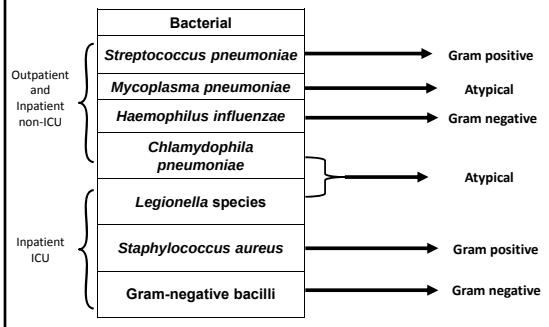
Disclosures

- The speaker has served on an Advisory Board for BioCryst Pharmaceuticals, Inc. (10/2014)
- All conflicts resolved through peer review

What is CAP?

- Pneumonia (lower respiratory track infection) in a patient who otherwise does not have risk factors for exposure to "nosocomial" pathogens
  - Diagnosis plus rule out of HCAP, HAP, VAP qualifying criteria
  - Essentially limits scope of pathogens and expected resistance profiles requiring empiric coverage

Etiology of CAP - Review



How to Decide Who Gets What Therapy?

- **Pneumonia severity scoring guides treatment location and pathogen risk**
  - CURB-65, PORT index
- **Risk factors requiring *Pseudomonas* coverage for CAP**
  - Advanced COPD w/ steroids, structural lung disease (brochiectasis), +++ antibiotic exposures
- **HCAP (so CAP rule-out) qualifiers**
  - Hospitalization w/in 90 days, nursing home/long-term care, recent antibiotics or IV chemo or wound care, visited hemodialysis clinic past 30 days

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

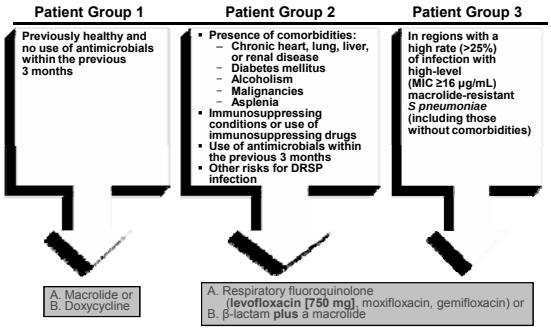
CAP Severity Assessment: CURB-65

- British Thoracic Society Scoring Tool
- Score: 0–5, with 1 point for each of the following
  - **C**onfusion
  - B**U**N >19.6 mg/dL
  - **R**R ≥30 breaths/min
  - S**B**P <90 mm Hg or D**B**P ≤60 mm Hg
  - Age ≥**65** yr
- 2 points - consider hospital admission
- ≥3 points - consider ICU admission

CURB-65 Score	Mortality Risk	Disposition
0	Low (0.6%)	Outpatient
1	Low (2.7%)	Outpatient
2	Moderate (6.8%)	Out/Inpatient
3	Significant (14.0%)	Inpatient
4	High (27.8%)	Inpatient/ICU
5	High (27.8%)	Inpatient/ICU

Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Outpatient Treatment Recommendations for CAP



Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Inpatient Treatment Recommendations for CAP

Non-ICU
β-lactam + Macrolide
Antipneumococcal Quinolone
β-lactam + Doxycycline
Tigecycline

Non-ICU with Pseudomonal Risk
Antipseudomonal β-lactam + Antipseudomonal Quinolone
Antipseudomonal β-lactam + Aminoglycoside + Quinolone
Antipseudomonal β-lactam + Aminoglycoside + Macrolide

ICU
β-lactam + Macrolide
β-lactam + Quinolone
β-lactam + Aminoglycoside + Macrolide
β-lactam + Aminoglycoside + Quinolone

Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Other New/Emerging CAP Treatment Options?

With Current FDA Approval

- Linezolid (2000)
  - Option with anti-MRSA activity
  - MRSA causes <1% of CAP in studies
  - Level III recommendation in current guidelines
- Ceftaroline (2010)
  - Approved for CABP
  - Too recent to make last guideline iteration (2007)

Investigational Drugs currently in Phase 3 Trials

- Ceftobiprole
  - Broad IV cephalosporin
- Cethromycin, Solithromycin
  - Oral/IV ketolide antibiotics
- Faropenem
  - Oral carbapenem
- Nemonoxacin
  - Oral quinoline (non-FQ)

Data from www.clinicaltrials.gov using search terms "Community-acquired neumonia, bacterial" and limited to "Phase 3".

Ceftaroline CABP Data

- FOCUS 1 & 2
  - Identical Phase 3, randomized, multinational studies
- Compared 5-7 days of ceftaroline 600 mg i.v. every 12 hrs vs. ceftriaxone 1 g i.v. every day
- Hospitalized patients with PORT risk class III & IV
- Primary outcome was non-inferiority in clinical cure rates for clinical efficacy and modified intent-to-treat efficacy

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405.

Pooled Results from FOCUS 1 & 2

Clinical Cure Rates by Study Population at the Test-of-Cure Visit.

Variable	CE	MITTE	ME	mMITTE
FOCUS 1				
Ceftaroline	194/224 (86.6)	244/291 (83.8)	62/69 (89.9)	66/75 (88.0)
Ceftriaxone	163/234 (78.2)	233/300 (77.7)	54/71 (76.1)	60/80 (75.0)
Difference, % (95% CI)	8.4 (1.4–15.4)	6.2 (−0.2 to 12.6)	13.8 (1.3–26.4)	13.0 (0.7–25.2)
FOCUS 2				
Ceftaroline	199/235 (84.7)	235/289 (81.3)	68/85 (81.2)	72/90 (80.0)
Ceftriaxone	166/215 (77.2)	209/273 (75.5)	57/76 (75.0)	66/88 (75.0)
Difference, % (95% CI)	4.9 (−2.5 to 12.5)	5.9 (−1.0 to 12.7)	6.2 (−6.7 to 19.2)	5.0 (−7.4 to 17.4)
Integrated FOCUS				
Ceftaroline	387/459 (84.3)	479/580 (82.6)	131/154 (85.1)	138/165 (83.6)
Ceftriaxone	349/449 (77.7)	439/573 (76.6)	111/147 (75.5)	126/168 (75.0)
Weighted treatment difference, % (95% CI)	6.7 (1.6–11.8)	6.0 (1.4–10.7)	9.7 (0.7–18.8)	8.7 (−0.6 to 17.4)

NOTE. Data are proportion (%) of patients, unless otherwise indicated. CE, clinically evaluable population; CI, confidence interval; FOCUS, Ceftaroline Community Acquired Pneumonia Trial versus Ceftriaxone in Hospitalized Patients; ME, microbiologically evaluable population; MITTE, modified intent-to-treat efficacy population; mMITTE, microbiological modified intent-to-treat efficacy population.

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405; by permission of Oxford University Press.

Pooled Results from FOCUS 1 & 2

Clinical Cure Rates by the Most Common Baseline Pathogens at Test-of-Cure Visit, Integrated Microbiological Modified Intent-to-Treat Efficacy Population.

	Proportion (%) of patients					
	FOCUS 1		FOCUS 2		Integrated FOCUS	
Variable	Ceftaroline (group)	Ceftriaxone (group)	Ceftaroline (group)	Ceftriaxone (group)	Ceftaroline (group)	Ceftriaxone (group)
Gram positive						
Streptococcus pneumoniae	24/27 (88.9)	20/30 (66.7)	35/42 (83.3)	28/40 (70.0)	59/69 (85.5)	48/70 (68.6)
MDRSP[a]	2/2 (100)	0/1 (0)	2/2 (100)	2/8 (25.0)	4/4 (100)	2/9 (22.2)
Staphylococcus aureus	9/10 (90.0)	9/14 (64.3)	10/15 (66.7)	9/16 (56.3)	19/25 (72.0)	18/30 (60.0)
MRSA[b]	NA	0/1 (0)	NA	1/1 (100)	NA	1/2 (50.0)
Gram negative						
Haemophilus influenzae	4/5 (80.0)	7/10 (70.0)	13/15 (86.7)	13/14 (92.9)	17/20 (85.0)	20/24 (83.3)
Haemophilus parainfluenzae	7/8 (87.5)	9/10 (90.0)	9/9 (100)	6/8 (75.0)	16/17 (94.1)	15/18 (83.3)
Klebsiella pneumoniae	7/8 (87.5)	3/5 (60.0)	7/7 (100)	7/8 (87.5)	14/15 (93.3)	10/13 (76.9)
Escherichia coli	8/8 (100)	5/7 (71.4)	2/4 (50.0)	4/6 (66.7)	10/12 (83.3)	9/13 (69.2)

NOTE. FOCUS, Ceftaroline Community Acquired Pneumonia Trial versus Ceftriaxone in Hospitalized Patients; MDRSP, multidrug-resistant *S. pneumoniae*; MRSA, methicillin-resistant *S. aureus*; NA, not applicable.

[a] MDRSP was defined in these studies as strains resistant to ≥2 antimicrobial classes of drugs, including penicillin, macrolides, tetracycline, fluoroquinolones, chloramphenicol, trimethoprim-sulfamethoxazole, and cephalosporins.

[b] Patients with confirmed or suspected community-acquired pneumonia caused by MRSA at baseline were excluded from the study.

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405; by permission of Oxford University Press.

Treatment Considerations - Ceftaroline?

- "Non-inferior" for CABP in 2 RCTs
  - Compared ceftaroline 600 mg IV q 12 hours with regimen of ceftriaxone 1 g IV daily x 5-7 days
- Higher response rates for *S. pneumoniae*?!?
  - 85.5% vs. 68.6% (n=~70 each arm)
  - Sub-group analysis was *post hoc* so results are underpowered
  - Too few multi-drug resistant strains to make an evaluation
- Too early to be guideline endorsed for either of FDA-approved indications!

CMS Measures for CAP

- Which of the following statements is correct regarding CMS reimbursement tied to pneumonia?
- A. Antibiotics must start with 4 hours
- B. Antibiotics must start with 8 hours
- C. Antibiotics must start with 24 hours
- D. There is no mandate to start therapy on a specific timeline

What Does CMS Care About?

Set Measure ID#	Measure Short Name
~~PN-3a~~	~~Blood Cultures Performed Within 24 Hours Prior to or 24 Hours After Hospital Arrival for Patients Who Were Transferred or Admitted to the ICU Within 24 Hours of Hospital Arrival~~
PN-3b	Blood Cultures Performed in the Emergency Department Prior to Initial Antibiotic Received in Hospital
~~PN-5c~~	~~Initial Antibiotic Within 6 hours of Arrival~~
PN-6	Initial Antibiotic Selection for Community-acquired pneumonia (CAP) in Immunocompetent Patient
PN-6a	Initial Antibiotic Selection for CAP in Immunocompetent – ICU Patient
PN-6b	Initial Antibiotic Selection for CAP Immunocompetent – Non ICU Patient

Centers for Medicare & Medicaid Services. The Joint Commission. Specifications manual for national hospital inpatient quality measures. (URL in ref list)

How Does CMS Evaluate You?

- Guideline concordant antibiotic therapy
  - Mandate to start antibiotics within a specific timeframe pushed out to 24 hours
  - Therapy choice must be consistent with current guidelines and inpatient location
- 30-day risk-standardized measures
  - Mortality
  - 30-day readmission
    - "Higher than expected" readmissions can lead to reduced reimbursement rates

Centers for Medicare & Medicaid Services. The Joint Commission. Specifications manual for national hospital inpatient quality measures. (URL in ref list).

How Can Stewardship Efforts Be Complimentary with CMS?

- Ensure appropriate use per guidelines
  - Implementation of CAP order sets!
- Avoid overuse of antibiotics
  - CMS allows "outs" for unsure diagnosis, antibiotics with previous 24 hours, transfer from other acute care facilities, pathogen-directed therapy, study enrollment, comfort care patients
- Clearly define the need for anti-pseudomonal therapy
  - Distinguish CAP vs. HCAP

Pneumonia ED Order Set Example

LAB		
If cultures are obtained, they should be collected prior to initiating antibiotics		
Choose Both BC orders for 2 sets		
Blood Culture	Stat, Add On = No	
Blood Culture	Stat, Add On = No	
Respiratory Culture s/Gram Stain	Stat, Once, Specimen type: Sputum	
A viral PCR test should ALWAYS be ordered with a rapid influenza test due to limited sensitivity of the rapid influenza test.		
Influenza Antigen Test, Direct	Stat, Specimen type: Nasopharyngeal	
Influenza A/B & RSV A/B Detection by PCR	Routine, Once, Specimen type: Nasopharyngeal	
The Streptococcal Pneumoniae Antigen test should be ordered in patients with suspected CAP.		
Strept Pneumoniae Antigen Test	Stat, Urine, Once	
Legionella Urine Antigen	Stat, Urine, Once	
CAP - ORAL TREATMENT		
Continue "ZPak" for 4 additional days		
azithromycin (Zithromax)	500 mg, DF: Tab, PO, Once	
or moxifloxacin 400 mg daily x 5 days		
moxifloxacin (Avelox)	400 mg, DF: Tab, PO, Once	
CAP - INPATIENT FLOOR ADMISSION		
Choose Both		
ceftriaxone (Rocephin)	1 g, IVPB, Once	Rate: 300 mL/Hr, Infuse Over: 20 Minutes
azithromycin (Zithromax)	500 mg, IVPB, Once	
or		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes

Pneumonia ED Order Set Example

CAP - ICU ADMISSION		
Choose Both		
ceftriaxone (Rocephin)	2 g, IVPB, Once	Rate: 300 mL/Hr, Infuse Over: 20 Minutes
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
Alternative to ceftriaxone if Beta-lactam allergy		
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
HEALTH-CARE ASSOCIATED PNEUMONIA (HCAP)		
Choose ALL 4 antibiotics		
cefepime	2g, IVPB, Once	
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
amikacin	15 mg/Kg, IVPB, Once	
azithromycin (Zithromax)	500 mg, IVPB, Once	
Alternative to cefepime if Beta-lactam allergy		
aztreonam (Azactam)	2 g, IVPB, Once	
LUNG ABSCESS		
Choose both amp-sulbactam and vancomycin		
ampicillin-sulbactam (Unasyn)	3 g, IVPB, Once	
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
Choose moxifloxacin for alternative to amp-sulbactam for Beta-lactam allergy		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
SEVERE ACUTE EXACERBATION OF COPD		
azithromycin (Zithromax)	500 mg, IVPB, Once	
or		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
INFLUENZA		
For outpatients, efficacy of treatment is only proven if started within 48 hours of symptom onset (Continue BID for 5 days)		
oseltamivir (Tamiflu)	75 mg, DF: Cap, PO, Once	

Antibiotic De-escalation Strategies

- Definitively confirm diagnosis of pneumonia
  - Radiology, oxygnation, cultures, other supporting labs (e.g. procalcitonin, CRP)
- Target antibiotics with single-drug therapy when possible
  - Cultures/susceptibilities, PCR, antigen testing results
- Convert to PO therapy when clinically stable
  - Can discharge as soon as able to take PO if no other medical problems and a safe transition environment

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

Optimizing Treatment Duration

- 5 days minimum recommended
  - Afebrile for 48-72 hours before discontinuation of therapy
  - ≤1 CAP-associated sign of clinical instability
  - No sign of extrapulmonary infection
- Shorter courses of therapy → reduced resistance, adverse events, and cost
  - Education!!!

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

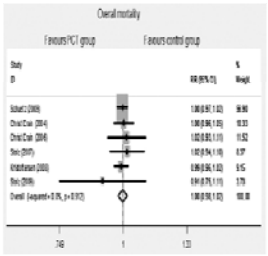
Procalcitonin (PCT)

- PCT is a pro-hormone of calcitonin
  - No known biological role
- Produced by cells in a wide range of organs and tissues in response to inflammation
- Conversion to calcitonin is inhibited by cytokines and bacterial endotoxins
- PCT levels are selectively elevated in patients with bacterial infections and a strong correlation exists

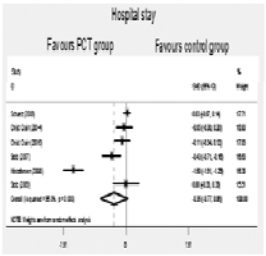
Scheutz, et al. Arch Intern Med. 2011 Aug 8;171(15):1322-31.

Meta-analysis of PCT in Respiratory Infections

Comparison of all-cause mortality between the PCT-guided antibiotic group and the control group



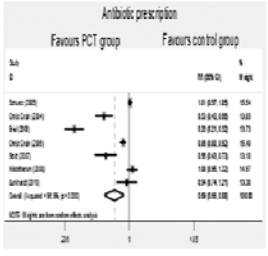
Forest plot for the weighted mean difference in length of hospital stay



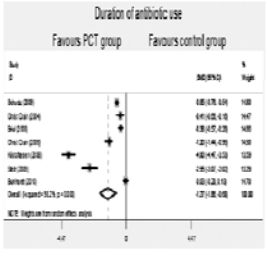
Li, et al. Antimicrob Agents Chemother. 2011 Dec;55(12):5900-6.

Meta-analysis of PCT in Respiratory Infections

Forest plot for odds ratio of antibiotic prescriptions in PCT-guided antibiotic treatment groups and control groups.



Forest plot for the weighted mean difference of duration of antibiotic use.



Li, et al. Antimicrob Agents Chemother. 2011 Dec;55(12):5900-6.

Clinical Role for PCT?

- PCT shows promise as another clinical tool to contribute to clinician evaluation of initiation and duration of antibiotic therapy
- Predominance of data comes from trials evaluating respiratory infections
- The most useful role for PCT may be to help guide discontinuation of antibiotic unnecessary antibiotic therapy

ACIP Updates for Pneumococcal Vaccination Recommendations

Prevnar-13® (PCV-13)

- 13-valent conjugate vaccine
- Improved response when given with PPSV-23
- Recommended for:
  - Routine use in adults ≥65 years
  - Use in adults >18 years with immunocompromising conditions, asplenia, CSF leak, cochlear implant
- ACIP Category A recommendation

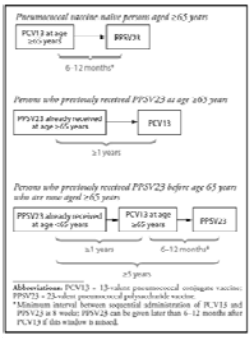
Pneumovax-23® (PPSV-23)

- 23-valent polysaccharide vaccine
- Recommendations for administration have not changed except to accommodate for inclusion of PCV-13

CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2014; 63:822-25.

PCV-13 and PPSV-23 Recommendations

- Both vaccines should be routinely given to patients ≥65
  - PCV-13 first, followed by PPSV-23 in 6-12 months
  - If PPSV-23 given, PCV-13 follows in 1 year
  - If PPSV-23 given prior to age 65, PCV-13 first, followed by PPSV-23 in 6-12 months after 5 year period



CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Ye
Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2014; 63:822-25.

Thank You for Your Attention!

Bibliography with Expanded References

- Mandell LA, Wunderink RG, Anzeuto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clin Infect Dis.* 2007;44:S27-S72. (http://cid.oxfordjournals.org/content/44/Supplement_2/S27.full.pdf+html)
- File TM Jr, Wilcox MH, Stein GE. Summary of ceftaroline fosamil clinical trial studies and clinical safety. *Clin Infect Dis.* 2012 Sep;55 Suppl 3:S173-80.
- The Joint Commission Specifications Manual for National Hospital Inpatient Quality Measures. (http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx)

Bibliography with Expanded References

- Schuetz P, Chiappa V, Briel M, Greenwald JL. Procalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. *Arch Intern Med.* 2011 Aug 8;171(15):1322-31.
- Li H, Luo YF, Blackwell TS, Xie CM. Meta-analysis and systematic review of procalcitonin-guided therapy in respiratory tract infections. *Antimicrob Agents Chemother.* 2011 Dec;55(12):5900-6.
- CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2014; 63:822-25. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a4.htm)

Top Things to Know about Community-acquired Pneumonia

John Esterly

1. Which of the following statements is correct regarding CMS reimbursement tied to Community-acquired Pneumonia?
    A. Antibiotics must start with 4 hours
    B. Antibiotics must start with 8 hours
    C. Antibiotics must start with 24 hours
    D. There is no mandate to start therapy on a specific timeline

2. Which of the following newer antimicrobials was most recently approved for the treatment of Community-acquired Bacterial Pneumonia?
    A. Ceftaroline
    B. Cethromycin
    C. Tedizolid
    D. Nemonoxacin

Top Things to Know About Five Commonly Encountered Diseases: Chronic Kidney Disease

Ayesha Khan, PharmD, BCPS
Assistant Clinical Professor, Internal Medicine
Chicago State University College of Pharmacy
September 11, 2015

Conflicts of Interests

- No conflicts to disclose

CKD Discussion Points

Methods available to estimate renal function

⇩

Strengths/limitations of each estimation tool

⇩

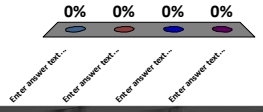
Patient care considerations for the pharmacist

⇩

Chronic hyperkalemia treatment options
• Current options & Pipeline drugs

Which of the following do you utilize most often to estimating renal function for drug dosing?

A. Modification of Diet in Renal Disease (MDRD)
B. Cockroft-Gault
C. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)
D. Any of the above
E. None of the above



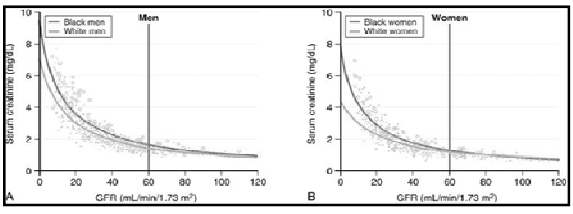
Glomerular Filtration Rate

- Indicator of overall kidney function
- Serum markers used to estimate GFR
  - Achieves stable plasma concentration
  - Inert, freely filtered by glomeruli
  - Not reabsorbed, secreted or metabolized
  - Gold standard: inulin, iothalamate, iohexol
  - Endogenous markers: serum creatinine, serum urea, serum cystatin C

Stevens LA, Corest J, Greene T, et al. *N Engl J Med.* 2006;354:2473-2483.

Serum Creatinine (SCr)

- Secreted by proximal tubule & filtered by glomerulus → clearance exceeds GFR
- Isolated use to assess renal function is not advised
- Inverse relation between GFR and SCr is nonlinear



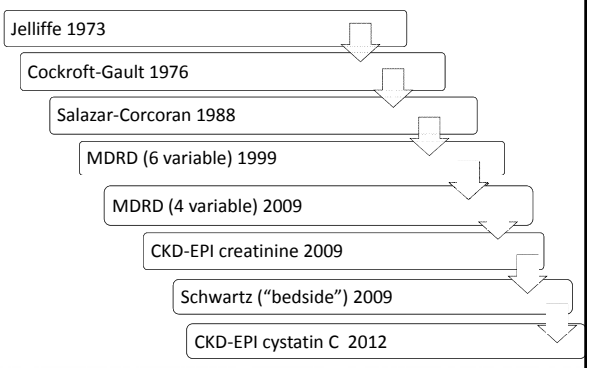
Levey AS, et al. *Ann Intern Med.*1999;130:461-470

Factors Affecting SCr

- Demographics
  - Aging ↓
  - Female gender ↓
  - Ethnicity
    - AA ↑, Hispanic ↓, Asian ↓
- Body Habitus
  - Muscular ↑
  - Malnourished/amputation ↓
- Medications
  - Cimetidine, trimethoprim, probenecid, K-sparing diuretics ↑

Levey AS. *Am J Kidney Dis.* 1993;22(1):207-214.

GFR Estimation Equations



Estimation of renal function

Cockroft-Gault (CG)

$$CrCl = \frac{(140 - age) \times (weight)}{72 \times SCr} \quad (X\ 0.85\ if\ female)$$

- Gold-standard
- 249 males with stable renal function
- Utilized ABW, suggest correction with ascites or obesity
- Adjustments in obesity (40%)

Cockroft DW, Gault MH. *Nephron.* 1976;16(1):3141.
Verhave JC, Fesler P, Ribstein J, et al. *Am J Kidney Dis.* 2005;46:233-241.

Estimation of renal function

Modification of Diet in Renal Disease (MDRD)

IDMS calibrated assays:
GFR= 175 x $SCr^{-1.154}$ x $age^{-0.203}$ x (0.742 if female) x (1.21 if AA)

Non-IDMS assays:
GFR= 186 x $SCr^{-1.154}$ x $age^{-0.203}$ x (0.742 if female) x (1.21 if AA)

- 6-variable equation simplified in 2 variations
- 1628 participants with CKD and mean GFR 40 ml/min/1.73 m^2
- More accurate than CG when using TBW
- Validated in GFR <60 ml/min/1.73 m^2 only

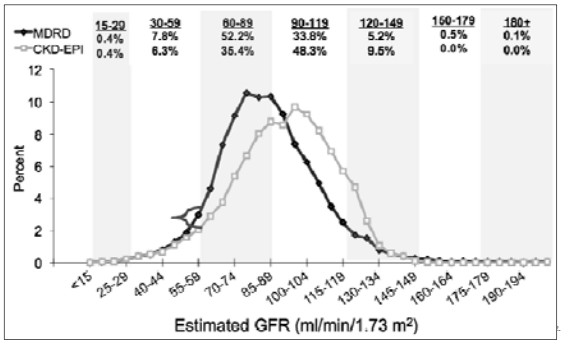
Level AS, Bosch JP, Lewis JB, et al. *Ann Intern Med.* 1999;130:461-470.
Froissart M, Rossert J, Jacquot C, et al. *J Am Soc Nephrol.* 2005;16:763-773

CG and MDRD Limitations

- Require stable SCr concentrations
  - Use cautiously in the critically ill, AKI
- SCr rounding in elderly patients
  - Rounding to 1.0 mg/dL may underestimate renal function
  - Percentage based correction
- Obesity
  - May lead to increased renal plasma flow and GFR
  - 2009 MDRD study
    - 999 overweight patients & 1039 obese patients
    - Tended to underestimate measured GFR
  - Use of adj. BW has been validated in aminoglycoside dosing
  - Use of lean body weight recommended by some experts

Pai MP, Paloucek FP. *Ann Pharmacother.* 2000;34(9):1066-9.
Lamb EJ, Webb MC, O'Riordan SE. *Age Ageing.* 2007; 36:689-692..

MDRD vs CKD-EPI



Levey AS, et al. *Ann Int Med.* 2009;150:604-612.

Estimation of renal function

Chronic Kidney Disease Epidemiology Collaboration (CKD- EPI)

GFR = 141 x min (Scr/k, 1)$^{\alpha}$ x max (Scr/k, 1)$^{-1.209}$ x 0.993^{Age} x 1.018[female] x 1.159 [if Black]

- F/u to MDRD equation to improve accuracy with GFR >60
- Validated retrospectively in 8,254 patients from 10 studies
- Renal failure patients excluded
- 45% women, 87% non-black patients

Levey AS, et al. *Ann Int Med.* 2009;150:604-612.

CKD-EPI Serum Cystatin C

- Freely filtered at the glomerulus, metabolized in the proximal tubule
- Generation is uniform across populations
- Produced by nucleated cells
  - Levels may differ in rapid cell turnover, uncontrolled thryoid, or corticosteroid use
- Cystatin C use may improve classification of GFR
- Screening beneficial in persons with:
  - Borderline estimated GFR (Cr based equation)
  - High risk of CKD
  - Conditions impacting creatinine sensitivity

Stevens LA, Coresh J, Schmid CH, et al. *Am J Kidney Dis.* 2008;51:395-406.
Shlipak MG, et al. *Am J Kidney Dis.* 2013;62(3):595-603.

Drug Dosing

- CG used in PK studies→ standard for drug dosing
- Insignificant translation into drug dosing (MDRD and CG)
  - CG more practical for bedside applicability
- MDRD or CG can be used to estimate kidney function for drug dosing
- Review package insert to determine body weight
  - Ex. rivaroxaban utilizes actual body weight

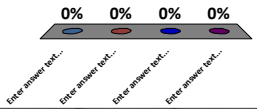
National Kidney Disease Education Program. Chronic Kidney Disease and Drug Dosing: Information for Providers. Available at http://www.nkdep.nih.gov/.../CKD_DrugDosing_508.pdf. Updated April 18, 2015. Accessed July 13, 2015.

Take Home Points

- All current eGFR methods have limitations
- Scr must be stable if used to for eGFR
- Estimate GFR from serum creatinine
  - MDRD and Cockroft-Gault
- Suggest use of CKD-EPI for general population
- Suggest use of cystatin C for confirmatory testing
- Renal function is a mosaic representation
  - Consider labs, clinical signs, symptoms in addition to renal function estimation equations

Patiromer is a new medication currently under FDA review for the treatment of:

A. Hypophosphatemia
B. Hypocalcemia
C. Hyperparathyroidism
D. Hyperkalemia



Hyperkalemia in CKD

- Hyperkalemia (>5 mmol/L) reported in up to 50% of CKD patients
  - Reported in 2-3% of general population
- Contributing risk factors in CKD
  - Dietary modifications
  - Blood transfusions
  - Kidney transplant
  - Diabetes (insulin deficiency and hypertonicity)
  - Cardiovascular disease (medications)
  - RAAS inhibitors (RAASi)

Weir MR, Rolfe M. *Clin J Am Soc Nephrol.* 2010;5:531-548.
Kovesdy CP. *Nat Rev Nephrol.* 2014;10(11):653-62.

Hyperkalemia Treatment

- Avoid NSAIDs, low-dose ACEi/ARB
- Thiazide or loop diuretics
- Sodium polystyrene sulfonate (SPS)
  - Na^+ cation exchange polymer
  - Approved in 1958 → *Prior to Kefauver-Harris Drug Amendments*
  - Limited efficacy data
    - 0.4 mEq/L drop in 23/30 patients in 24 hours
    - About 5mmol of K^+ delivered to colon per day
  - Colonic necrosis and mucosal injury of upper GI tract with long-term use

Scherr L, et al. *N Engl J Med.* 1961;264:115-119.
Parham WA, et al. *Tex Heart Inst J.* 2006;33(1):40-47.

Hyperkalemia: Pipeline Drugs

ZS-9

- Submitted for FDA approval in 2015
- Insoluble, non-absorbed zirconium silicate
- Inorganic cation exchanger with high selectivity for K^+
- Tasteless powder dissolvable in water
- HARMONIZE trial:
  - 2/3 of patients on RAASi therapy, 60% had CKD, 41% had heart failure, 58% had diabetes
  - 84% of patients normokalemic by 48 hours, maintained over the 28 day study period ($p<0.001$)
  - Safety: adverse events, including GI symptoms, similar to placebo group, edema (15mg group)

Packham DK, et al. N Engl J Med. 2015; 372:222-231.
Kosiborod M, et al. JAMA. 2014;312(21):2223-33.
Ingelfinger JR. N Engl J Med. 2015;372:275-277.

ZS-9

- Compound does not swell in the GI tract
  - Results in limited GI symptoms
- Very well tolerated
- Long-term safety and efficacy studies needed
- Potential for continuation of RAASi therapy
- Cost of therapy?

Patiromer

- Phase III study
- Non-absorbed polymer binds K^+ in exchange for Ca^+
- Predominantly binds in distal colon → K^+ level highest
- Oral suspension
- AMETHYST-DN trial:
  - 304 patients with stage 3-4 CKD
  - 76% (95% CI, 70-81) of patients normokalemic by at week 4
  - Safety: mild-moderate constipation (11%), hypokalemia (3%)

Bakris GL, et al. *JAMA.* 2015;314(2):151-161.
Weir WR, et al. *N Engl J Med.* 2015;372:211-221.

Patiromer

- Long-term safety and efficacy studies needed (>12 weeks)
- Decrease in K^+ appears to be gradual
  - Use in acute situation is unclear
- Potential for continuation of RAASi therapy
- Cost of therapy?