Bugs and Narcs:
Appropriate Prescribing of Antibiotics and Pain Medications

Kentucky Coalition of Nurse Practitioners and Nurse Midwives

Disclosure

- Melinda C. Joyce, Pharm.D., FAPhA, FACHE has nothing to disclose for this presentation

Objectives

- Review the microorganisms most likely implicated in common types of infections
- Discuss antimicrobial resistance and prudent prescribing
- Review the core elements for both inpatient and outpatient antimicrobial stewardship programs
- Outline the most common types of chronic pain
- Review current treatment options for chronic pain
- Discuss the CDC guidelines for appropriate use of opioids

Antimicrobial Therapy

- Improving antibiotic prescribing in all healthcare settings is critical to combating antibiotic-resistant bacteria
- Antibiotic resistance is considered to be among the greatest public health threats
- More than 2 million infections and over 23,000 deaths are attributed to infection caused by resistant organisms
- Drug choices for many bacterial infections are becoming more limited, expensive, and in some cases, non-existent
- New antibiotics to treat these resistant organisms are slow to be developed
A "Superbug" is an organism that shows significant antibiotic resistance, usually to two or more classes of antibiotics.

A clear area around the disc represents "zone of inhibition" or sensitive to that antibiotic.

Superbugs Include:
- Resistant strains of Staphylococcus aureus
  - Methicillin-Resistant Staphylococcus aureus (MRSA)
  - Vancomycin-Resistant Staphylococcus aureus (VRSA)
  - Linezolid-Resistant Staphylococcus aureus (LRSA)
  - Daptomycin-Resistant Staphylococcus aureus (DRSA)
- Vancomycin-Resistant Enterococci (VRE)
- Penicillin-Resistant Pneumococci (PRP)
- Extended-Spectrum β-lactamases (ESBLs)
- Multi-Drug Resistant (MDR)
  - Salmonella
  - Clostridium difficile
  - Mycobacterium tuberculosis
  - Neisseria gonorrhoeae
  - Carbapenem-Resistant Enterobacteriaceae (CRE)

Critical Threats
- Can cause severe infections and have high mortality rates, especially for patients in the hospital or in a long-term care facility
- Can see high mortality in patients on ventilators, central lines, are undergoing chemotherapy or are transplant recipients
- Acinetobacter baumannii
- Pseudomonas aeruginosa
- Enterobacteriaceae, including E. coli and Salmonella

The World Health Organization (WHO) Critical Threats

CDC Hot List for Resistant Organisms

Urgent Threats
- Clostridium difficile
- Carbapenem-Resistant Enterobacteriaceae (CRE)
- Neisseria gonorrhoeae

Poor Antibiotic Prescribing
- Poor antibiotic prescribing puts patients at risk
- About half of hospitalized patients receive an antibiotic for at least one day during the course of an average hospital stay
- The most common types of infections for which hospital clinicians wrote antibiotic prescriptions were lung infections (26%), urinary tract infections (14%), and suspected infections by MRSA (17%)
- About 3 out of 5 times, prescribing practices to treat urinary tract infections do not have proper testing or evaluation and the antibiotics are given for too long
- Over half of antibiotic prescribing in outpatient settings is unnecessary and most of the inappropriate use is for acute respiratory infections, such as pharyngitis, sinusitis or bronchitis
Antimicrobial Resistance

1. Use and overuse of antibiotics
2. More complex, higher acuity patients
3. Use of antibiotics in agriculture
4. Improper use of antibiotics
   - Treatment of viral infections
   - Sharing antibiotics
   - Not completing full regimens
   - Inadequate dosing
5. Passing infections from person to person, via contact or fomites

Antibiotic Use Leads to Antibiotic Resistance

- Resistant bacteria or their genetic determinates are selected when colonizing or infecting bacteria are exposed to antibiotics
- Resistant bacteria can then be transmitted between patients
- Highest risk patients:
  - Immunocompromised
  - Hospitalized
  - Invasive devices (central venous catheters)

The single most significant factor in the development of resistant organisms is antibiotic usage!

Mechanisms of Antibiotic Resistance

- Can be related back to how the antibiotic works
- Bacteria are capable of becoming resistant through several mechanisms
- One or many mechanisms may exist in an organism
- Multidrug-resistant bacteria often have multiple mechanisms
- Genes encoding resistance may exist on plasmid or chromosome

Measures of Resistance

- Resistant bacteria or their genetic determinates are selected when colonizing or infecting bacteria are exposed to antibiotics
- Resistant bacteria can then be transmitted between patients
- Highest risk patients:
  - Immunocompromised
  - Hospitalized
  - Invasive devices (central venous catheters)

Antibiotics by Mechanism of Action

<table>
<thead>
<tr>
<th>Cell Wall Synthesis</th>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Vancomycin</th>
<th>Carbapenems</th>
<th>Monobactams</th>
<th>Polymyxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein Synthesis Inhibitors</td>
<td><em>16S</em> Subunit</td>
<td><em>23S</em> Subunit</td>
<td>Aminoglycosides</td>
<td>Tetracyclines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA Synthesis Inhibitors</td>
<td>Fluoroquinolones</td>
<td>Metronidazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RNA Synthesis Inhibitors</td>
<td>Rifampin</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
| Folic Acid Synthesis Inhibitors | Sulfonamides | Trimethoprim | 9/4/2017
Drug Inactivation orModification
- Sulfonation, phosphorylation, or esterification
- Especially a problem for aminoglycosides
- β-lactamases
  - Multiple types:
    - Simple, extended spectrum β-lactamases (ESBL)
    - Cephalosporinases
    - Carbapenemases
- Chromosome-mediated – intrinsic resistance
- Plasmid-mediated – acquired resistance
- Confer resistance to some, many, or all β-lactam antibiotics
- More potent in gram-negative bacteria
- Examples: S. aureus, H. influenzae, N. gonorrhoeae, E. coli, Klebsiella sp., Enterobacter sp., Serratia sp., other enteric bacteria, anaerobes

Multidrug Resistant Gram-Negative Organisms
- Development of resistance to multiple antimicrobial classes severely limits treatment options and the incidence of resistance is rising
- Proportion of isolates resistant to three antibiotic classes ranged from 10 to 60% for different gram-negative bacteria, while some are resistant to four antibiotic classes

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>Resistant to 3 antibiotic classes (%)</th>
<th>Resistant to 4 antibiotic classes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginoasa</td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>60%</td>
<td>34%</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>15%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Extended Spectrum β-lactamases (ESBLs)
- β-lactamases capable of hydrolyzing extended spectrum cephalosporins, penicillins, and aztreonam
- Most often associated with E. coli and Klebsiella pneumoniae but spreading to other bacteria
- Usually plasmid mediated
- Aminoglycoside, ciprofloxacin and trimethoprim-sulfamethoxazole resistance often encoded on same plasmid
- Has become a significant resistance determinant in acute and long-term care facility enteric pathogens

Carbapenem-Resistant Enterobacteriaceae (CRE)
- Most common in Klebsiella pneumoniae (KPC)
- Also seen in E. coli, Enterobacter, Citrobacter, Salmonella, Serratia, Pseudomonas, and Proteus spp.
- CRE are bacteria that are resistant to most antibiotics
- These bacteria can cause pneumonia, urinary tract infections, and bloodstream infections
- Most often seen in hospitalized, critically ill patients
- Almost half of the hospitalized patients with CRE bloodstream infections die
- There are very few antibiotics that are available to treat infections caused by CRE
  - meropenem (Merrem); tigecycline (Tygacil) as adjunct therapy; colistin

Multidrug Resistant Gram-Negative Organisms
- Widespread use of cephalosporins and beta-lactam combination antibiotics has led to extended-spectrum beta-lactamases (ESBLs), which are resistant to both classes
- Carbapenems have been the only effective agents for ESBLs
- Emergence of carbapenemases, such as Klebsiella pneumoniae carbapenemase (KPCs) are threatening carbapenems as the antibiotics of last resort
- Significant issue for many military personnel due to the high amount of Acinetobacter in the desert
- Responsible for causing urinary tract infections and pneumonia
- New antibiotics are in the developmental stage, but will be a while before on the market

Changing the Target Site
- DNA gyrase
- Fluoroquinolones
- Many gram-negatives, S. pneumoniae
- Penicillin-binding protein
- Methicillin-resistant S. aureus (MRSA)
- Penicillin-resistant S. pneumonia
- Gram positive cell wall
- Vancomycin
- Enterococcus spp.
Change the Metabolic Pathway

- Ribosome
- Tetracyclines
- Macrolides
  - S. pneumoniae, Staphylococcus sp., N. gonorrhoeae, enteric gram-negative rods

Decreasing Drug Concentrations

- Decreased Permeability
  - Pseudomonas spp.
  - Affects many antibiotics including carbapenems
- Efflux Pumps
  - Pseudomonas spp. (multiple antibiotics)
  - Tetracyclines
  - Macrolides

How to Fight Antimicrobial Resistance

1. Prevent infections and prevent the spread of resistance
2. Track resistant bacteria
3. Improve the use of today’s antibiotics
4. Promote the development of new antibiotics and develop new diagnostic tests for resistant bacteria

CDC, Antibiotic resistance threats in the US, 2013

Prudent Prescribing

Misconception: Antibiotics are no longer effective because people who have taken the medication have developed a tolerance to the drug

Truth: People do NOT develop a tolerance to drugs; the reason drugs no longer work is because the bacteria is no longer killed by the drug because they have become resistant to the effects

Misconception: My patient is getting better, so I will just continue the antibiotics although I am not sure if there really is a bacterial infection

Truth: Many other treatment options may be causing that patient to feel better—fluids; respiratory treatments; better nutrition. The continued use of the antibiotic must be questioned in the absence of a documented infection

Misconception: Isolation precautions are not a big deal—they are mainly to make sure that I don’t get sick

Truth: Isolation precautions must be followed 100% of the time by all caregivers in order to protect the patient, other patients, and the healthcare provider

Misconception: Stop dates for antibiotics are not really necessary. Patients will just stop taking antibiotics when they start to feel better.

Truth: Stop dates (hard stops) are very important and patients must understand the importance of taking all of their antibiotic as prescribed.
Misuse of Antibiotics

• Incorrect Diagnosis
  • Antibiotics given when the infection is viral and are not needed
  • Antibiotics given without symptoms, such as asymptomatic bacteriuria
  • Treating colonization or contamination – not an actual infection

• Incorrect Prescription
  • The wrong antibiotic is given to treat an infection
  • Given at the wrong dose (sub-therapeutic dosing)
  • Broad spectrum agents used to treat bacteria that are susceptible to many other narrow-spectrum agents

• No De-escalation
  • Continuing antibiotics when they are no longer necessary
  • Continuing IV antibiotics when the patient can tolerate an equivalent oral antibiotic

• Incorrect Prescription
  • The wrong antibiotic is given to treat an infection
  • Given at the wrong dose (sub-therapeutic dosing)
  • Broad spectrum agents used to treat bacteria that are susceptible to many other narrow-spectrum agents

Patient Issues

• Not completing the full course of the antibiotic
• Keeping antibiotics at home “just in case someone in the family needs them”
• “Doctor shopping” to find a provider that will prescribe antibiotics
• Not staying home or away from others when ill

Agricultural Issues

• Use of antibiotics in livestock to prevent disease
• Low-dose antibiotics have also been associated with a method for animal weight gain
• It is thought that resistant strains of salmonella, campylobacter, enterococcus, and E. coli have been transmitted from animals to humans

Three Questions to Ask During Each Assessment

1. Does the patient have an infection?

2. What is the patient most likely infected with?
   • Organism, site of infection

3. What is the preferred treatment?
   • Patient-specific considerations
   • Length of treatment with specific stop date identified

Common Infections

Skin and Soft Tissue

Skin and Soft Tissue Infections

• Caused by overuse of antibiotics as well as inadequate infection control measures
• Mechanism of resistance seems to be target modification
• Over time, the number of infections caused by S. aureus has not changed, but proportion of infections due to MRSA has increased substantially
• Most common in hospitals, critical care and long-term care settings
• Can also be acquired in the community
• S. aureus infections result when patients who are carriers infect themselves (autoinoculation)
• Same strain found at the infection site and in the patient’s nares
• Carriers (such as healthcare workers or other patients) can infect immunocompromised patients

Methicillin-Resistant Staph aureus (MRSA)

• Caused by overuse of antibiotics as well as inadequate infection control measures
• Mechanism of resistance seems to be target modification
• Over time, the number of infections caused by S. aureus has not changed, but proportion of infections due to MRSA has increased substantially
• Most common in hospitals, critical care and long-term care settings
• Can also be acquired in the community
• S aureus infections result when patients who are carriers infect themselves (autoinoculation)
• Same strain found at the infection site and in the patient's nares
• Carriers (such as healthcare workers or other patients) can infect immunocompromised patients
An increasing proportion of hospital-acquired Staph aureus strains are methicillin-resistant. Initially reported in the 1970's and the prevalence has increased, especially in institutions. Usually involves various types of infection: Bacteremia, Intravenous lines, Pneumonia, Skin and soft tissue infections. Transmission is person to person. Growth rate is slow. Resistant to multiple antibiotics.

Risk Factors for HA-MRSA

- Older patient
- Prolonged hospitalization
- Critical care stay
- Long-term care resident
- Prolonged antimicrobial therapy
- Surgical procedures
- Dialysis
- In-dwelling percutaneous medical devices and catheters
- Close proximity to a hospitalized patient who is infected or colonized with MRSA

Antibiotic Therapy for HA-MRSA

- Usually resistant to multiple antibiotics
- Resistant to penicillins and cephalosporins
- May be resistant to clindamycin and trimethoprim-sulfamethoxazole
- Drugs of choice include vancomycin, linezolid, daptomycin, or quinupristin-dalfopristin

Community-Acquired Methicillin-Resistant Staph aureus (CA-MRSA)

- Initially reported in the late 1980's, it was thought to be linked to a HA-MRSA infection
- More reported infections lacked this correlation, suggesting that a new and different reservoir of MRSA had developed in the community
- There does seem to be a correlation between sharing of close quarters
- Transmission is person to person
- Growth rate is fast
- The prevalence factor is PVL (panton-valentine leukocidin) and two major clones have been identified - makes this strain more virulent
- Resistant to beta-lactams, but sensitive to other agents

CA-MRSA Risk Factors

- Not clearly identified
- Younger patients (median age of 23 years as compared to 63 years for HA-MRSA)
- Chronic non-infectious dermatological conditions, such as eczema, were the most common underlying issue for those < 18 yrs
  - Cosmetic body shaving/tattoo
  - Injectable drug use
- Among older patients > 18 yrs, other underlying medical conditions included smoking, diabetes, and dermatological conditions

Antibiotic Therapy for CA-MRSA

- When the infection is skin/soft tissue, incision and drainage of area may be needed
- Most boils only require drainage
- Usually resistant to the beta-lactams (penicillin and cephalosporins)
- Usually sensitive to clindamycin, trimethoprim-sulfamethoxazole, minocycline, doxycycline
- May be beneficial to add rifampin for synergistic effect
- Also sensitive to vancomycin, daptomycin, and linezolid, although these agents are not first-line
Antibiotics for Skin and Skin Structure Infections

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Adult Dose</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalbavancin</td>
<td>1000 mg IV on day 1 then 500 mg IV on day 8</td>
<td>$4500 course of therapy</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>IV 6 mg/kg/dose IV q24h</td>
<td>$200/day – 5 to 14 days</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg IV or PO q12h</td>
<td>$275/day – either IV or PO for 10 days</td>
</tr>
<tr>
<td>Minocycline</td>
<td>100 mg PO q12h</td>
<td>$2/day (generic) – 5 to 10 days</td>
</tr>
<tr>
<td>Orivancin</td>
<td>1200 mg IV single dose</td>
<td>$2900 for single dose</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>200 mg IV or PO q24h</td>
<td>$295/day (PO) for 6 days</td>
</tr>
<tr>
<td>Teixobacins</td>
<td>10 mg/kg IV q24h</td>
<td>$300/day - 7 to 14 days</td>
</tr>
<tr>
<td>TMP/SMX</td>
<td>2 to 3 double strength tablets PO q12h</td>
<td>$1/day (generic) – 7 to 14 days</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1000 mg (5 mg/kg) IV q12h</td>
<td>$20/day (generic) – 7 to 14 days</td>
</tr>
</tbody>
</table>

Wounds/ Skin Infections
- Necrotizing infections/fasciitis require aggressive and immediate surgical intervention
- Need to cover for gram-positive, gram-negative, and anaerobes
- Empiric therapy should include
  - A beta-lactam plus clindamycin plus an agent with MRSA activity
- Most important to treat topically with dressing changes
- Underlying nutritional status is vital

Upper Respiratory Tract Infections
- Symptoms are those of the common cold
  - Cough, sneezing, congestion, lethargy
  - A variety of illnesses comprise URIs
  - Most are viral in nature
    - Rhinovirus
    - Enterovirus
  - Antibiotics should be avoided unless there are compelling reasons for their use
  - A common reason for antibiotics in the outpatient setting, many of which are not indicated

Acute Pharyngitis
- One of the four most common episodic clinic visits
  - May be viral or bacterial
  - Group A beta-hemolytic streptococcal (GABHS) infection is the only common indication for antibiotic therapy for sore throat
    - Only 5-10% of adult cases of acute pharyngitis are caused by group A beta-hemolytic streptococcal (GABHS)
    - Streptococcal pharyngitis is most commonly seen in children aged 5 to 15 years and is rare in pre-school children
  - Explore other causes of sore throat include:
    - Viral causes
    - Allergies
    - Cigarette smoking or second-hand smoke
    - Environmental causes – pollution
    - Dry air
    - Gastric reflux

Pharyngitis
- Lab tests will determine if the pharyngitis is bacterial
  - Rapid Streptococcal Antigen Detection Test (RADT)
  - Need two or more criteria for testing
    - History of fever
    - Lack of cough
    - Tender anterior cervical adenopathy
  - Patients with none or only one of these symptoms should not be tested or treated for GABHS
  - Testing is generally not done on adults or children under the age of 3
  - In children or adolescents with a negative RADT, should be backed up with a throat culture
Pharyngitis

- Treatment
  - No antibiotics when viral!
  - Recommended treatment with antibiotics is 10 days if bacterial
  - Penicillin VK or Amoxicillin is recommended for initial treatment of GABHS
  - If the patient is penicillin allergic:
    - First generation oral cephalosporin, such as cephalexin or cefadroxil
    - Macrolide, such as clarithromycin or azithromycin
    - Clindamycin
    - Fluoroquinolones are NOT appropriate

Rhinosinusitis

- Most cases are viral
  - In both adults and pediatrics, 90 to 98% of cases are viral
  - Resolves in about 7 days
- Bacterial - often caused by atypical microorganisms
  - Double-sickening – symptoms last longer than 10 days
  - Nasal congestion
  - Cough - often worse at night due to drainage
  - Facial pain - above or below the eyes when patient leans forward
  - Toothache - if maxillary sinuses are involved
  - Headache
  - Purulent drainage, although nasal discharge alone is not a good predictor of a bacterial infection
- Clear to yellow to green
- High fever – 102 or higher

Watchful waiting is encouraged!!

Pharmacologic Treatments

- Regardless of whether the etiology is infectious, allergic, or irritant, treatment should focus on relieving obstruction and establishing drainage
- Analgesics
- Decongestants
- Antihistamines
- Corticosteroids
- Mucolytics

Antibiotics for Sinusitis

- Treatment should be continued for 10 to 14 days
- For milder infections
  - Penicillins, such as amoxicillin/clavulanate is recommended as first-line therapy
  - If penicillin allergic, doxycycline or a second or third generation cephalosporin is used
  - If the patient cannot tolerate oral medication, a single dose of ceftriaxone may be used
- Macrolides, such as azithromycin are not recommended due to high levels of Streptococcus pneumoniae resistance (> 40%)
- For more serious infections
  - Amoxicillin/clavulanate (high dose)
  - Quinolone with antipneumococcal activity, such as levofloxacin

Most common childhood infection for which antibiotics are prescribed

Definitive diagnosis requires either

- Moderate or severe bulging of tympanic membrane or new onset otorrhea not due to otitis externa
- Mild bulging of the tympanic membrane AND recent (<48 hours) onset of otalgia or intense erythema of the tympanic membrane
- Watchful waiting in most cases is sufficient as most cases are viral
- Studies have shown that the symptoms of OM spontaneously resolved in 80% of children at 2 to 7 days. (Otalgia – endpoint)

Ibuprofen or acetaminophen are the best options for pain control

Analgesic ear drops can also provide symptomatic relief

Some controversy over the use of decongestants in children, although fluid accumulating behind the ear drum is often a contributing factor

Most children typically will not need a decongestant

Use care in recommending over-the-counter cough/cold preparations considering that many products are combinations

Most contain acetaminophen – watch the total dose of acetaminophen

Watchful waiting is encouraged!!
Antibiotics for Acute Otitis Media

- Amoxicillin 80 to 90 mg/kg/day remains first-line therapy for children who have not received amoxicillin within the last 30 days
- If no response in 72 hours, consider alternative agents
- Amoxicillin/clavulanate is recommended if the child has had amoxicillin within the last 30 days or if there is concurrent purulent conjunctivitis
- For penicillin allergic, second or third generation cephalosporins may be appropriate

Pneumonia

- Common lower respiratory tract infection that causes inflammation of the lung parenchyma
- Pneumonia is still the leading cause of death worldwide in children under the age of 5
- The defense mechanisms of the lung usually help to prevent passage of foreign materials
- Disease states, such as COPD
- Age
- Smoking
- Immunization!
- Pneumococcal vaccination will help to decrease incidence and severity of susceptible strains of pneumonia
- Annual influenza vaccination is very important as pneumonia can be a secondary infection behind the flu

Antibiotic Resistance for Pneumonia

- Over the past decade, antimicrobial resistance has increased dramatically for pneumonia
- More than 15% of S. pneumoniae are highly resistant to penicillin and increasingly resistant to macrolides and cephalosporins
- Most pneumococcal isolates in the United States remain susceptible to the respiratory fluoroquinolones, such as levofloxacin
  - Ciprofloxacin has limited activity against pneumococcal infections
  - Some specific populations, such as elderly patients in long term care facilities have shown increased levels of pneumococcal resistance

Community-Acquired Pneumonia (CAP)

- Most common pathogens
  - Streptococcus pneumoniae
  - Chlamydia pneumoniae
  - Mycoplasma pneumoniae
  - Legionella spp
  - Haemophilus influenzae

Empiric Treatment for CAP

<table>
<thead>
<tr>
<th>Extensive</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-ICU</td>
<td>ICU</td>
</tr>
<tr>
<td>Previously healthy and no antimicrobial therapy in the previous 3 months</td>
<td>Co-Morbidities (chronic illnesses, such as COPD, heart disease, or diabetes) or antimicrobial therapy in the previous 3 months</td>
</tr>
<tr>
<td>Macrolide OR Doxycycline</td>
<td>Respiratory Fluoroquinolone OR Beta-lactam plus Macrolide</td>
</tr>
<tr>
<td></td>
<td>Beta-Lactam plus Azithromycin OR Respiratory Fluoroquinolone plus Beta-lactam Penicillin Allergy, Respiratory Fluoroquinolone plus Aztreonam</td>
</tr>
</tbody>
</table>

Treatment for CAP

- Treatment duration for CAP is a minimum of 5 days
- If the patient remains febrile for 2 to 3 days or fails to meet more than one sign of clinical stability, a longer treatment duration may be indicated
- Criteria for clinical stability
  - Temperature < 37.8°C
  - Heart rate < 100 beats/min
  - Systolic blood pressure >90 mmHg
  - Arterial oxygen saturation > 90% or P02 > 60 mmHg on room air
  - Ability to tolerate oral medication
  - Baseline mental status for patient
Hospital-Acquired Pneumonia/ Ventilator-Associated Pneumonia (HAP/VAP)

- HAP – defined as pneumonia that presents at least 48 hours following hospitalization
- Risk factors for multi-drug resistant organisms for HAP
  - Previous IV antibiotic use within 90 days
- VAP – defined as pneumonia that presents at least 48 hours after intubation
- Risk factors for multi-drug resistant organisms for HAP
  - Previous IV antibiotic use within 90 days
  - Septic shock
  - Acute respiratory distress syndrome prior to VAP onset
  - > 5 days of hospitalization prior to VAP onset

**Empiric Treatment for HAP/VAP**

<table>
<thead>
<tr>
<th>Antibiotics with MRSA Coverage</th>
<th>Beta-Lactam based Antibiotics with Pseudomonas Coverage</th>
<th>Non-Beta-Lactam Antibiotics with Pseudomonas Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin 15 mg/kg IV q8-12h OR</td>
<td>Piperacillin/Tazobactam 4.5 g IV q6h OR</td>
<td>Levofloxacin 750 mg IV q24h OR</td>
</tr>
<tr>
<td>Linezolid 600 mg IV q12h OR</td>
<td>Ceftazidime 2 g IV q8h OR</td>
<td>Amikacin 15-20 mg/kg IV q24h OR</td>
</tr>
<tr>
<td></td>
<td>Cefepime 2 g IV q8h OR</td>
<td>Gentamicin 5-7 mg/kg IV q24h OR</td>
</tr>
<tr>
<td></td>
<td>Meropenem 1 g IV q8h OR</td>
<td>Tobramycin 5-7 mg/kg IV q24h OR</td>
</tr>
<tr>
<td></td>
<td>Aztreonam 2 g IV q8h OR</td>
<td>Colistin 5 mg/kg IV loading dose followed by 2.5 mg IV q12h OR</td>
</tr>
</tbody>
</table>

Duration of Therapy for HAP/VAP

- The recommended duration of therapy is 7 days regardless of microbial etiology
- The shorter course of therapy did not show any significant differences in:
  - Length of stay
  - Mortality
  - Treatment failure
  - Duration of mechanical ventilation

Acute Bronchitis

- Infection of the tracheobronchial tree that causes reversible bronchial inflammation
- Most patients will present with cough and symptoms can last from 7 days to longer than 14 days
- Bronchitis is often thought of as a diagnosis of exclusion (rule out more serious causes of cough)
- Greater than 95% of cases of acute cough are non-bacterial
- Colored sputum does NOT automatically indicate a bacterial infection

Differentiation from Pneumonia

- Pneumonia is unlikely if all of the following are absent:
  - Fever > 38°C
  - Tachypnea > 24 breaths/ min
  - Tachycardia > 100 beats/ min
  - Evidence of consolidation (rales) on chest exam
  - Should consider a chest X-ray for cough lasting longer than 3 weeks

Treatment Options for Bronchitis

- No antibiotics!
- Increase hydration
- Expectorants/Antitussives, such as codeine or dextromethorphan
- Antipyretics
- Antihistamines, such as diphenhydramine or a non-sedating antihistamine
- Decongestants, such as phenylephrine (for 3 days or less)
  - Use caution in patients with other co-morbid conditions, such as heart disease or thyroid disease
- Beta-agonists, such as albuterol
**Clostridium difficile Infections (CDI)**

- *C. difficile* is a spore-forming, gram-positive anaerobic bacillus that produces two exotoxins: toxin A and toxin B
- It is a common cause of antibiotic-associated diarrhea (15-25%)
- 14,000 deaths attributed to CDI per year
- 90% of the deaths are in patients > 65 years of age
- Disruption of the bowel microflora, generally by antibiotics, creates an environment that allows *C diff* to proliferate
- The organism produces the toxins that cause intense inflammation of the colonic mucosa
- Antibiotic exposure is the single most important risk factor for the development of *C diff* infections
- Up to 85% if patients with *C diff* have had antibiotic exposure in the last 28 days
- Has been associated with all classes of antibiotics
- Clindamycin was the first antibiotic implicated
- In recent years, this infection has been highly related to third-generation cephalosporins and fluoroquinolone use
- In general, broad spectrum antimicrobial therapy is more likely than narrow spectrum treatment to lead to *C diff* infections

**Risk Factors**
- Antibiotic exposure – type and duration – most important risk factor
- GI surgery/ manipulation
- NG tubes
- Enemas
- Use of proton pump inhibitors
- Long length of stay in institutions
- Serious underlying illnesses
- Immunocompromised
- Advanced age
### Treatment of *C. difficile*

- In less than half of patients, *C. difficile*-associated disease will resolve within 2 to 3 days of antibiotic discontinuation
- Avoid anti-motility agents
- If patient is hospitalized, patient should be placed in isolation until symptoms have resolved
- Cleaning of surfaces with bleach
- Initial mild to moderate episodes (WBC <15,000)
  - Oral metronidazole 500 mg three times per day for 10 to 14 days
- Initial severe episodes (WBC >150,000)
  - Oral vancomycin 125 mg four times a day for 10 to 14 days
- Likely to take 2 to 4 days of antibiotic therapy before the diarrhea stops
- Oral agents preferred but may use IV metronidazole if patient cannot tolerate oral therapy or if the patient has a more complicated presentation with hypotension, shock, or severe colitis on CT scan
- Vancomycin enemas should only be used when all other treatment modalities have failed or if patient has developed toxic megacolon
- Fecal bacteriotherapy (stool transplant) should be considered for second or more recurrence
- Infection is considered resolved once the antibiotic regimen has been completed and the patient is diarrhea-free for 48 hours AFTER treatment has been completed

### Fecal Bacteriotherapy (Stool Transplant)

- Gaining more acceptance
- No standard administration approach
- Administration options include:
  - Enema/colonoscopy through NG tube
  - Stool slurry that needs to be used immediately from donor
  - Fecal microbiota transplantation (FMT) capsules
  - Approximately a 70% efficacy with a single administered dose of 30 capsules
  - Cumulative clinical cure rate of 94% if retreated with an extended dose of 30 capsules daily for two consecutive days
- Success is measured through resolution of symptoms and absence of relapse within 8 weeks

### What About Probiotics?

- Theory – replace beneficial GI flora that is killed off by the antibiotics
- Dietary supplements containing live microorganisms
- Colonize the intestine to help restore microbial balance
- Helps to decrease GI side effects
- Probiotics should not be taken within 2 hours of the antimicrobial agent
- Should be taken for the entire course of the antimicrobial treatment and for an additional week after
- Probiotics have been studied for the prevention of *C. difficile* infections, but not currently recommended due to limited studies showing efficacy
- *Lactobacillus*
- *Bifidobacterium* species
- *Saccharomyces boulardii*

### Urinary Tract Infections (UTIs)

- Broad term used to describe bacterial infections of the urethra, bladder, and kidneys
- UTIs lead to nearly ten million provider visits each year
- Usually classified as either complicated or uncomplicated
- Lower UTIs include urethritis and cystitis
- Upper tract infections include pyelonephritis and renal abscesses

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**Note:**

- www.openbiome.org
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**UTI**

- Diagnosis can be made by the presence of bacteria in the urine from a clean, mid-stream collection and symptoms, such as dysuria or urgency
  - 10^5 colony-forming units (CFU)/ml of pathogens for a diagnosis of acute pyelonephritis and asymptomatic bacteriuria
  - 10^3 for cystitis
- Dipstick urinalysis is frequently used due to its cost and fast results
- Should be a compelling reason to obtain a urine culture
  - Foul-smelling or cloudy urine without other signs and symptoms is not a reason to order a urine culture

**Pathogens**

- *E. coli* causes 80-90% of all community-acquired UTIs and about half of UTIs in the hospital
  - Other pathogens include gram-negative rods, such as *Proteus*, *Klebsiella*, and *Enterobacter*
- *E. coli* has become increasingly resistant to TMP-SMX to where it is no longer a first line agent for complicated UTI or pyelonephritis
  - Although the quinolones are used for complicated UTIs, more resistance is being seen with *Enterococci*
  - Beta-lactams are associated with about a 40% resistance rate for *E. coli*
  - Nitrofurantoin has low resistance, but has little use beyond the urinary tract because of poor tissue perfusion

**Treatment**

- Prevention
  - Avoid products that may irritate the urethra
  - Cleanse genital area before and after sexual intercourse
  - Change soiled diapers for infants and toddlers frequently
  - Drink plenty of water
  - Do not delay the urge to urinate
  - Women should wipe front to back
  - Remove catheters
  - Herbal remedies???
    - Cranberry juice

**Uncomplicated Cystitis**

- Local symptoms only (frequency, urgency, painful urination)
  - No fever or flank pain
  - TMP/SMX twice daily for 3 days
    - Avoid if resistance in area is greater than 20% or antibiotics taken in the previous 3 months
  - Nitrofurantoin twice daily for 5 days
  - Older patients or pregnant patients require 7 days of therapy

**UTIs During Pregnancy**

- In 20 to 40% of cases, UTIs during pregnancy are a progression of asymptomatic bacteriuria
  - More likely to be a complicated UTI and may progress to pyelonephritis
  - Safest antibiotics to use during pregnancy are: amoxicillin; amoxicillin-clavulanate; nitrofurantoin; and cephalaxin
  - Resistance to the penicillins may be as high as 33%, so should not be used as first-line
  - Duration of treatment may be 3 days if caught early but 7 to 10 days may be more appropriate
Complicated UTI

- Pre-disposing factors
  - Urinary obstruction
  - Incomplete bladder emptying due to anatomic or neurogenic causes
  - Foreign bodies
  - Systemic conditions
  - Male

- Treatment options
  - Fluoroquinolones for 7 to 14 days
  - IV cephalosporin, such as ceftriaxone
  - Aminoglycosides

- Streamline once culture results are available
- Convert to oral therapy once patient can tolerate oral therapy

UTIs in the Elderly

- Symptoms may be atypical
  - Mental status changes
  - Lethargy
  - Weakness

- Important to assess renal function before prescribing antibiotics

- Patients that are otherwise healthy at home
  - Treat as uncomplicated cystitis
  - Duration of 7 days

- Long-term care patients with no catheter
  - Treat as uncomplicated cystitis
  - Duration of 7 days

- Long-term care patients with catheter
  - Treat as catheter-associated UTI

Catheter-Associated UTIs (CAUTIs)

- Definition of CAUTI
  - Indwelling urethral or suprapubic catheter or intermittent catheterization
  - Presence of signs or symptoms of UTI with no other identified source of infection
  - >100 CFU/ml of one bacterial species
  - Catheter urine specimen or midstream voided specimen if catheter was removed within 48 hours

- Treatment options
  - Ampicillin plus gentamicin
  - Piperacillin/Tazobactam
  - Fluoroquinolone
  - Carbapenem, if suspect an extended-spectrum beta-lactamase producing organism

  - Treat for 7 days for most patients, but if a delayed response, 10 to 14 days may be required

Pyelonephritis

- A more severe infection, involving the upper urinary tract, including the kidneys
- Systemic symptoms that requires prompt treatment to avoid progressing to urosepsis

- Treatment options
  - Patients not requiring hospitalization
    - Ceftriaxone (single dose) followed by either
      - Fluoroquinolone for 5 days OR
      - TMP/SMX for 14 days
  - Beta-lactams should be avoided

Pyelonephritis

- Patients requiring hospitalization
  - Fluoroquinolone for 5 days OR
  - Aminoglycoside plus Beta-Lactam OR
  - Extended-spectrum Beta-lactam plus Aminoglycoside OR
  - Carbapenem (if resistant organism suspected)

- Other than fluoroquinolone, duration of therapy should be 10 to 14 days
- Streamline once culture and sensitivity results available
- Switch to oral therapy when indicated

Hospital-Acquired UTI

- UTIs are responsible for about 40% of hospital-acquired infections
- Most are associated with catheter use

- Remove the catheter if possible

- Treatment options
  - Extended-spectrum beta-lactam plus aminoglycoside
  - Carbapenem, if resistant organism is suspected

- Duration of therapy if usually 10 to 14 days
- Streamline therapy based on culture and sensitivity results
• 105 colony forming units is often used as a diagnostic criteria for a positive urine culture
• It does NOT prove infection; it is just a number to state that the culture is unlikely due to contamination
• Pyuria also is not predictive on its own
• It is the presence of symptoms AND pyuria AND bacteriuria that denotes infection
• No adverse outcomes associated with asymptomatic bacteriuria in older adults and there are no benefits associated with antibiotic treatment
• Asymptomatic bacteriuria should not be treated with antibiotics unless the patient is pregnant, undergoing urological surgery, or has received a kidney or kidney/pancreas transplant

**Pearls for Antibiotic Treatment**

- Carbapenem Indications:
  - Multi-drug resistant gram-negative infections
  - Documented infection, not colonized wounds
  - HAP/VAP empiric therapy in critically ill patients where alternatives are not reasonable
  - Preferred regimen: Vancomycin + Cefepime or Piperacillin/Tazobactam
  - Polymicrobial coverage needing strong anaerobic spectrum where alternatives are contraindicated
  - Preferred regimen: Piperacillin/Tazobactam; Aztreonam + Metronidazole; Ampicillin/Sulbactam + Quinolone

**Key Points for Antibiotics**

- Carbapenem Indications:
  - Empiric therapy in critically ill febrile patients at risk for multi-drug resistant gram-negative organisms that have two or more indicators without a clear source of known infection
  - Multiple antibiotic exposure
  - Recent hospitalization (within past 3 months)
  - Multiple surgeries
  - Percutaneous lines
  - Ventilator-dependent
  - Preferred regimen: Cefepime; Piperacillin/Tazobactam; Ceftazidime + Tobramycin

- Necrotizing pancreatitis or hospital-acquired cholecystitis/ peritonitis after prolonged hospitalization

---

**Acute Pyelonephritis**

- Most patients are hospitalized
- Fluoroquinolones plus an aminoglycoside are good first-line agents
- Other options include aminoglycosides plus an extended-spectrum cephalosporin or ampicillin
- For acute, uncomplicated pyelonephritis, therapy usually ranges from 7 to 14 days
- Complicated pyelonephritis will often require 24 to 21 days, usually of parenteral therapy
- Need to de-escalate and use the most sensitive antibiotic

**Key Points for Antibiotics**

- Carbapenems
  - Not all agents are the same
  - Ertapenem – notable omissions in the spectrum of activity of this agent; No coverage against Pseudomonas aeruginosa; Acinetobacter; methicillin-resistant staphylococci; Enterococcus species
  - Doripenem – concern about use in pneumonia as studies have shown a 23% higher mortality
  - All carbapenems should be used very carefully due to the development of carbapenamases
  - Should be used very sparingly for specific indications

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- Necrotizing pancreatitis or hospital-acquired cholecystitis/ peritonitis after prolonged hospitalization
New Agent!

- Meropenem and Vaborbactam (Vabomere)
- Combination agent of a carbapenem and a non-suicidal beta-lactamase inhibitor
- Indicated for the treatment of adults with complicated urinary tract infections, including pyelonephritis caused by susceptible strains of Enterobacteriaceae
  - E. coli, Klebsiella, and Enterobacter
- Not found to be effective for carbapenem-resistant Enterobacteriaceae (CRE)
- Headache, infusion site reactions, and diarrhea were the most common adverse events

Key Points for Antibiotics

- Clindamycin
  - Good choice for CA-MRSA
  - Pseudomembranous colitis
- Daptomycin
  - Should not be used for pneumonia
  - May be useful for significant wound infections
  - Watch for myositis
- Linezolid
  - Same effect either PO or IV
  - Should be reserved for when resistance to vancomycin is present
  - Thrombocytopenia – more common after 10 days of therapy
  - Potential serotonin syndrome?

New Agent

- Delafolexacin (Baxdela)
- Fluoroquinolone indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible strains of Staph aureus (including MRSA and MSSA), Streptococcus pyogenes, Enterococcus faecalis; E coli; Enterobacter cloacae; Klebsiella pneumonia; and Pseudomonas aeruginosa
- Available in both an IV formulation for infusion and an oral form
- Adverse effects, potential drug-drug interactions, and precautions similar to other available fluoroquinolones

Key Points for Antibiotics

- Fluoroquinolones
  - Same effect either PO or IV
  - Starting to see more issues with resistance
  - May be more problematic with ciprofloxacin
  - Watch for tendon issues as well as other adverse effects, such as glucose changes
  - Not indicated for children under the age of 16
  - Can be responsible for resistance patterns with other organisms due to overuse
- Metronidazole
  - Same effect either PO or IV
  - Potential for several adverse reactions
    - GI
  - Watch for disulfiram-like reaction with alcohol

Key Points for Antibiotics

- Penicillins
  - Use may be limited because of resistance
    - Addition of other agents, such as clavulanic acid are beneficial in treating resistant organisms
    - Addition of other agents to help combat resistance
- Rifampin
  - Should not be used as monotherapy because quick development of resistance
  - Used in combination with other antibiotics in the treatment of CA-MRSA for synergistic effect
  - Change in secretions to red-orange

Key Points for Antibiotics

- Sulfonamides
  - Several potential drug-drug interactions
  - Many potential adverse reactions
  - Watch for hypersensitivity reactions
- Tetracyclines
  - Drug-drug and drug-food interactions
  - Contraindicated in pregnancy and in children under age 16
- Vancomycin
  - IV for MRSA only
  - PO for C diff only
  - Watch renal function and monitor trough levels
Prudent Prescribing

**Principles of Prudent Prescribing**

- For all patients, re-evaluate, de-escalate or stop therapy at 48-72 hours based on diagnosis and microbiologic results
- For inpatients, re-evaluate, de-escalate or stop therapy with transitions of care (e.g. ICU to step-down or ward)
- De-escalation
  - If cultures are negative, then must consider stopping the antibiotics
  - If cultures are positive, must tailor the antibiotic therapy to what the cultures are telling us
  - Switch to the more narrow spectrum antibiotic rather than the broad-spectrum
  - Make sure that all prescriptions/orders for antibiotics have the appropriate dose, duration, and indication
  - Limit duration of surgical prophylaxis to <24 hours perioperatively

- Do not give antibiotic with overlapping activity
- Do not "double-cover" gram-negative rods (i.e. Pseudomonas sp.) with two drugs with overlapping activity
- Use rapid diagnostics if available (e.g. respiratory viral PCR)
- Prevent infection
  - Use good hand hygiene and infection control practices
  - Consider whether or not a central-line is really needed
  - Should be reserved for total parenteral nutrition (TPN) or long-term IV antibiotics
- Remove catheters
- Consult infectious disease

- **Antimicrobial Stewardship (AS)**
  - The thought is that by 2020, implementation of Antimicrobial Stewardship through the National Plan will lead to major reductions in the incidence of urgent and serious threats, including:
    - Carbapenem-resistant Enterobacteriaceae (CRE)
      - 60% reduction of CRE infections acquired during hospitalizations compared to 2011 estimates
    - Methicillin-resistant Staphylococcus aureus (MRSA)
      - 50% overall reduction in MRSA bloodstream infections as compared to 2011
    - Clostridium difficile (C. diff)
      - 50% reduction compared to 2011 estimates
    - Ceftriaxone-resistant Neisseria gonorrhoeae
      - Maintain the prevalence of this resistant organism below 2% compared to 2013 estimates

- **IV to PO**
  - If the gut works, USE IT!
  - Potential benefits of IV to PO include...
    - Increase patient comfort
    - Reduce length of stay / discharge facilitation
    - Removal of IV catheters and risks they bring
    - Reduced healthcare (and drug) costs
  - **Common IV to PO Targets**

<table>
<thead>
<tr>
<th>Common IV to PO Targets</th>
<th>Azithromycin</th>
<th>Ciprofloxacin</th>
<th>Moxifloxacin</th>
<th>Doxycycline</th>
<th>Fluconazole</th>
<th>Levofloxacin</th>
<th>Linezolid</th>
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- Consult infectious disease

- **National Action Plan**
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**Effective Antimicrobial Active Strategies**

**Supplemental Strategies**

**Comprehensive Multidisciplinary Approach**

**Core Elements of Antimicrobial Stewardship**

- Similar for hospitals and nursing homes
- Leadership
  - Dedicate necessary human, financial, and information technology (IT) resources (hospital)
  - Demonstrate support and commitment to safe and appropriate use in the facility (LTC)
- Accountability
  - A single leader needs to be appointed to be responsible for program outcomes. This is often a physician, although it is not a requirement.
- Drug Expertise
  - A single pharmacist leader needs to be appointed to support improved prescribing.
  - For long-term care facilities, establishing access to consultant pharmacists with experience and training.

**What Is Antimicrobial Stewardship?**

- Antimicrobial stewardship is a multidisciplinary approach for rational antibiotic therapy
  - Must be based on evidence-based guidelines
  - Must be based on data
  - Must apply to all practitioners
- There are five main principles of antimicrobial stewardship
  1. Preventing infections
  2. Prevent the spread of resistance
  3. Tracking and surveillance
  4. Improve antibiotic prescribing through stewardship
  5. Development of new antibiotics and new diagnostic tests for resistance bacteria

**Core Elements of Antimicrobial Stewardship**

- Action
  - Implement at least one recommended action, policy, or practice to improve antibiotic use
    - Antibiotic time-out after 48 hours
    - Antibiotic use guidelines that are specific to the facility
    - IV to PO switch programs
- Tracking
  - Monitoring antibiotic prescribing and resistance patterns
  - Drug-Bug "Mismatches"
- Reporting
  - Providing regular feedback to clinicians, nurses, and other staff
- Education
  - Education to clinicians, staff, patients, and families about antibiotic resistance and opportunities for improvement
The Joint Commission (TJC)

- Medication Management Standards for ambulatory centers, critical access hospitals, hospital, nursing care centers (long-term care), and behavioral health facilities
- Although housed within the Medication Management standards, there are ties back to the Leadership and the Infection Prevention chapters
- MM.09.01.01: The organization has an antimicrobial stewardship program based on evidence-based national guidelines
  - Several elements of performance for this standard

www.jointcommission.org

Readmission Penalties

- **All cause** 30 day readmissions for patients with heart failure, pneumonia, acute myocardial infarction (AMI), chronic obstructive pulmonary disease (COPD), elective total hip and total knee replacements, and coronary artery bypass graft (CABG) surgery
  - The reason for readmission may often be related back to an infection
  - The maximum penalty can be as high as 3.0% of base operating DRG payments for our Medicare patients
    - The penalty is assessed on all Medicare admissions
  - FY 2018
    - 30.6% of acute care hospitals no penalty
    - 77.9% of acute care hospitals had some penalty
    - 0.5% of acute care hospital had the maximum 3% penalty

Core Elements of Antimicrobial Stewardship

- For Outpatient Antimicrobial Stewardship
  - Commitment
    - Demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety
  - Action for Policy and Practice
    - Implement at least one policy or practice to improve antibiotic prescribing, assess whether it is working, and modify as needed
    - Examples: Policy or practice to reduce or eliminate antibiotic prescriptions for acute respiratory conditions
  - Tracking and Reporting
  - Education and Expertise
    - Education to clinicians, staff, patients, and families about appropriate antibiotic prescribing and resistance

Common Antimicrobial Stewardship Interventions for Outpatient Practices

- Identify one or more high-priority conditions for intervention
  - Conditions for which antibiotics are over-prescribed
    - Strep throat without testing
    - Conditions for which antibiotics might be indicated but where the wrong drug, dose, or duration is selected
  - Conditions for which “watchful waiting” is underused
- Establish standards for antibiotic prescribing, following national guidelines

Ambulatory Measures

- If involved in an Accountable Care Organization (ACO), there are quality metrics regarding appropriate immunization for influenza and treatment of pneumococcal pneumonia
- Other third-party payors may also require submission of immunization data along with appropriateness measures (HEDIS measures) for:
  - Appropriate treatment for children with upper respiratory infection
  - Appropriate testing for children with pharyngitis
  - Avoidance of antibiotic treatment in adults with acute bronchitis

Quality Measures by CMS

- Various quality programs that impact infections and antibiotic usage
  - Possible to have multiple penalties for one infection
- Hospital Value-Based Purchasing (VBP) Score
  - Impacts the reimbursement for Medicare patients
- Harm Domain of VBP: Healthcare Associated Infections
  - **CLABSI**: Central line-associated blood stream infections among adult, pediatric, and neonatal patients
  - **CAUTI**: Catheter-associated urinary tract infections among adult and pediatric patients
  - **SSI**: Surgical site infections specific to abdominal hysterectomy and colon surgeries
  - **Clostridium difficile** infections: Laboratory identified
  - **MRSA** bacteremias: Laboratory identified

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Common Antimicrobial Stewardship Interventions for Outpatient Practices

- Partner with others for antibiotic stewardship activities
  - Hospitals
  - Long-term care facilities
  - State and local health departments
  - Health plans and payors
  - Community pharmacists
  - Local microbiologic laboratories
  - Educational campaign for patients and families

Resources

- Many!!!
- Antimicrobial resistance and prudent prescribing
  - www.cdc.gov/drugresistance
  - www.cdc.gov/getsmart
  - www.cdc.gov/vitalsigns
  - www.cdc.gov/antimicrobial-therapy
- Core Elements of Antibiotic Stewardship Programs
  - Hospital
  - Nursing Homes
  - Outpatient
    - https://www.cdc.gov/getsmart/community/pdfs/16_268900-a_coreelementsoutpatient.pdf

Barriers to Antimicrobial Stewardship

- Lack of staff resources to identify or implement stewardship interventions
  - Pharmacists
  - Physician resources
  - Administrative support
- Resistance from front-line providers
- Difficulty in obtaining data to determine opportunities or impact
  - Real-time data
- No good mechanisms for feedback and communication
- Disconnect between the inpatient and the ambulatory settings
- Lack of communication with patients/families

Resources

- Antimicrobial stewardship
  - www.idsociety.org
- Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America
- CMS Quality Measures

Conclusions

- Antibiotics clearly save lives but resistance is costing lives
- Poor prescribing of antibiotics are putting patients at unnecessary risk
  - Adverse reactions
  - Development of resistant organisms
- Every time an antibiotic is prescribed
  - If at all possible, order recommended cultures before antibiotics are given
  - Make sure an indication, dose, and expected duration are part of the prescription order
  - Reassess within 48 hours and adjust antibiotic or discontinue if warranted
  - Pay for performance indicators
  - Issue affects ALL healthcare providers and patients

Pain Management
Institute of Medicine

Greater than 100 million people in the US suffer from chronic pain
25 million people experience acute pain from injury or surgery

Multi-factorial
Psychological

90% of all diseases have some pain component
Up to 50% of patients with pain also suffer from depression
Newer research is pointing to the fact that underlying depression and anxiety may increase the chance of addiction with opioids

Psychosocial
Spiritual

Determine etiology to better treat the pain
Type of pain will determine the best treatment approach
Determine if correctable, intractable or potentially dangerous causes
Determine impact on patient’s life and that of their family
Decrease the potential for misuse or addiction

What is the Opioid Problem?

More than one out of three average Americans used a prescription opioid in 2015
Reported opiate overdose deaths nationwide are currently between 40,000 – 50,000
Annual opiate overdose deaths exceed traffic fatalities since 2008 and continue to rise
Drug overdoses are now the leading cause of death among Americans under the age 50
President Donald Trump declared the opioid epidemic a national emergency on August 11, 2017
Federal funding can be increased and directed toward programs to combat the problem
Treatment centers are likely to benefit from the increased funding
Philosophy regarding the treatment of chronic pain is undergoing a complete revision

CDC Vital Signs July, 2014

PAINKILLER Prescription Rate by State

Some states have more penicillin prescriptions per person than others.

Source: CDC, NAMCS 2013. Doses per 1,000 population

Kentucky Controlled Substance Usage: 2016

Top Prescription Controlled Substances Abused by Americans

Number of Americans Abusing:
700,000

1,700,000

4,300,000

7,200,000

Hydrocodone
Oxycodone
Tramadol
Morphine

Data from the Substance Abuse and Mental Health Services Administration: Report to Congress June 15, 2017
Kentucky overdose fatalities increased in 2016 (1404 deaths) as compared to 2015 (1248 deaths)

People aged 35 to 44 were the largest demographic in overdose deaths

Autopsied and toxicology reports from coroners show that approximately 34% of overdose deaths involved the use of heroin in 2016, up from 28% in 2015

Fentanyl, either combined with heroin or alone was involved 47% of all deaths, up from 34% on 2015

What is Addiction?

A primary, chronic disease of brain reward, motivation, memory and related circuits

Dysfunction in these circuits leads to characteristics biological, psychological, social and spiritual manifestations

Like other chronic diseases, addiction often involves cycles of relapse and remission

Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death

Opioid Use Disorder (OUD) – a problematic pattern of opioid use leading to clinically significant impairment or distress

Top 10 State Drug Overdose Death Rates - 2014

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
<th>Number of Drug Overdose Deaths</th>
<th>Age-Adjusted Overdose Death Rate per 100,000 of Population</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>West Virginia</td>
<td>627</td>
<td>58.5</td>
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<tr>
<td>2</td>
<td>New Mexico</td>
<td>547</td>
<td>27.3</td>
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<td>3</td>
<td>New Hampshire</td>
<td>314</td>
<td>16.7</td>
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<tr>
<td>4</td>
<td>Kentucky</td>
<td>1,077</td>
<td>24.7</td>
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<tr>
<td>5</td>
<td>Ohio</td>
<td>1,744</td>
<td>24.8</td>
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<tr>
<td>6</td>
<td>Rhode Island</td>
<td>247</td>
<td>23.4</td>
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<tr>
<td>7</td>
<td>Utah</td>
<td>603</td>
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<tr>
<td>8</td>
<td>Pennsylvania</td>
<td>2,722</td>
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<td>9</td>
<td>Delaware</td>
<td>189</td>
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<td>10</td>
<td>Oklahoma</td>
<td>197</td>
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<tr>
<td></td>
<td>United States</td>
<td>47,055</td>
<td>14.7</td>
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</tbody>
</table>
**Misuse, Abuse, Diversion**

- **Misuse**
  - Incorrect use of a controlled substance medication by a patient
  - Wrong time, wrong dose, wrong reason
- **Abuse**
  - Maladapted pattern of controlled substance use leading to significant impairment or distress
- **Diversion**
  - Controlled substance medication outside of the legal distribution channels
  - Manufacture, Transport, Pharmacy, Patient

**Misuse of Opioids**

- The National Survey on Drug Use and Health
- Survey that allows participants to log answers directly into a computer, providing anonymity
- 32.8% of the population took a legitimately prescribing opioid
- 4.7% of the population misused prescription opioids obtained by illicit means
  - Of those, 40.8% obtained the medications from family and/or friends
- 0.8% of the population (about 1.9 million people) reported full-fledged opioid addiction
  - 2/3 stated opioids were abused to combat physical pain while the remainder misused opioids to relax or get high

---

**How to Identify Patients with Opioid Use Disorder**

- Problematic opioid use pattern resulting in significant impairment or distress, manifested by at least two of the following within 12 months
  - Opioid is taken in larger quantity or longer duration than originally planned
  - Continuing desire to cut back or failed efforts to cut back
  - Significant time is spent obtaining or using the opioid, or recovering from its effects
  - Craving or strong desire or urge to use
  - Use interferes with obligations
  - In patients over 45 years of age, women have higher rates of OUD while men have higher rates in those younger than 45 years of age
  - Patients receiving high-dose, long-duration prescriptions are more than 40 times as likely to develop OUD than patients on low-dose, short-duration therapy

---

**Opioid Prescribing**

- As newer, sustained-release opioids became available in the late 1990s, more healthcare providers began using these opioids to treat chronic pain (not related to cancer), such as arthritis and back pain
- This started a cycle:
  - More opioid prescriptions written
  - More prescriptions for longer durations of therapy
  - More prescriptions at higher doses
  - Taking opioids for longer periods of time or in higher doses increases the risk of addiction, overdose, and death
- In 2015, the Morphine Milligram Equivalent (MME) prescribed per person was more than 3 times as high as in 1999

---

**How to Identify Patients with Opioid Use Disorder (CONTINUED)**

- Use continues despite persistent or recurrent social or interpersonal problems caused or worsened by the opioid use
- Use continues despite knowledge of having a persistent or recurrent physical or psychological problem likely caused or worsened by the opioid
- Important social, work, or recreational activities are abandoned or reduced due to opioid use
- Opioids are used in situations where use is physically hazardous
- Tolerance
  - Need for markedly increased amounts to achieve intoxication or desired effect, or markedly diminished effect with continued use of the same amount

- Withdrawal

---

**National Survey on Drug Use and Health – 2015 data:**

- Problematic opioid use pattern resulting in significant impairment or distress, manifested by at least two of the following within 12 months
  - Opioid is taken in larger quantity or longer duration than originally planned
  - Continuing desire to cut back or failed efforts to cut back
  - Significant time is spent obtaining or using the opioid, or recovering from its effects
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  - Use interferes with obligations
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  - Patients receiving high-dose, long-duration prescriptions are more than 40 times as likely to develop OUD than patients on low-dose, short-duration therapy

---

**The amount of opioids prescribed per person varied widely among counties in 2015:**

- The table shows the amount of opioids prescribed per person in different counties, with color-coded levels indicating low, moderate, and high prescription rates.

---

**References:**

- National Survey on Drug Use and Health - 2015 data
- The amount of opioids prescribed per person varied widely among counties in 2015
- Opioid Prescribing
- How to Identify Patients with Opioid Use Disorder
- Misuse, Abuse, Diversion

---

**Notes:**

- The information provided is based on the National Survey on Drug Use and Health (NSDUH) data from 2015.
- The survey allows participants to log answers directly into a computer, providing anonymity.
- Key statistics include:
  - 32.8% of the population took a legitimately prescribing opioid.
  - 4.7% of the population misused prescription opioids obtained by illicit means.
  - Of those, 40.8% obtained the medications from family and/or friends.
  - 0.8% of the population (about 1.9 million people) reported full-fledged opioid addiction.

- The opioid prescribing trend indicates a significant increase, with the Morphine Milligram Equivalent (MME) prescribed per person being more than 3 times as high as in 1999.

- The table showing the amount of opioids prescribed per person varied widely among counties in 2015 highlights regional differences in prescription rates.
Characteristics of Counties with Higher Opioid Prescribing

- Small cities or large towns
- Higher percent of Caucasian residents
- More dentists and primary care physicians
- More people who are uninsured or unemployed
- More people with other chronic illnesses, such as diabetes, arthritis, or disability

How Can an Impact Be Made?

- Awareness of opioid use disorder
- Education of patients regarding appropriate pain control
- Follow the CDC Guideline for Prescribing Opioids for Chronic Pain
- Careful attention to the dose and the duration of the opioid
- Use of state-based prescription drug monitoring programs, which can help identify patients at risk of addiction or overdose

Multimodality Approach

- Rarely does just one approach help with chronic pain
- Multimodal interventions should be part of a treatment strategy or plan for patients with chronic pain
- Periodic and regular follow-up evaluations should be developed and implemented as part of the overall treatment strategy
- Patients must understand that they are not likely to be pain-free but a realistic pain goal should be established for the patient to be able to have as much quality of life as possible

Treatment Options for Pain

- Rarely does just one approach help with chronic pain
- Multimodal interventions should be part of a treatment strategy or plan for patients with chronic pain
- Periodic and regular follow-up evaluations should be developed and implemented as part of the overall treatment strategy
- Patients must understand that they are not likely to be pain-free but a realistic pain goal should be established for the patient to be able to have as much quality of life as possible

Therapeutic Strategies in Pain management

- Lifestyle changes
- Rehabilitative
- Psychological
- Complementary and integrative medicine
- Educational
- Pharmacotherapy
- Injection, surgical, neuromodulation
- Ablative techniques
- Minimally invasive procedures
- Pharmacotherapy

Pharmacologic Treatments
Medications for Pain
- Non-Opioid Analgesics are typically first line for chronic pain as well as many types of acute pain
  - NSAIDs
  - Acetaminophen
  - Antidepressants
  - Anticonvulsants
- Opioids are used for severe pain and when moderate pain does not respond well to the non-opioid treatments
- Other Options
  - Muscle relaxants
  - Local anesthetics
  - Corticosteroids

Non-Steroidal Anti-Inflammatory Agents (NSAIDs)
- Mainstay for treatment of inflammatory disorders
- Also useful for pain and for fever
- May also be useful for the treatment of low back pain
- Inhibits cyclooxygenase
- Some agents are more specific to COX-1 while others are more specific to COX-2
  - The more COX-1 specificity, the more likely to see bleeding and serious GI effects
  - The more COX-2 specificity, the more likely to see cardiovascular effects
- Ketorolac – very specific to COX-1 – much more likely to see bleeding
- Rofecoxib – very specific to COX-2 – much more likely to see cardiovascular effects

NSAIDs
- Proprionic Acid Derivatives
  - Ibuprofen, Naproxen, Ketoprofen
- Acetic Acid Derivatives
  - Diclofenac, Ketorolac
- Oxicam Derivatives
  - Meloxicam
- Coxibs (selective COX-2 inhibitors)
  - Celecoxib
- Salicylates
  - Diflunisal

NSAIDs
- Recommended as initial therapy for:
  - Mild to moderate pain
  - Pain associated with inflammation
  - Patient unresponsive to acetaminophen
  - Combination approach with opioids for more severe pain
  - Often used for osteoarthritis, migraine headache and low back pain
  - Will have a ceiling effect
  - Higher doses do not cause greater analgesia but do cause greater side effects
  - Should use at the lowest effective dose for the shortest time
  - If one type of NSAID is not effective, try a different class
  - Need to make sure that patients are not taking more than one type of NSAID

NSAIDs
- NSAIDs have boxed warnings about cardiovascular risk
  - Use cautiously in patients with pre-existing cardiovascular disease
  - May be related to increase in fluid retention
  - May potentially lessen the beneficial antiplatelet effects of aspirin
- GI upset
  - Take with food
  - Increasing evidence that NSAID-related GI complications frequently occur lower in the small intestine (below the duodenum) and possibly in the large intestine and not just the stomach
  - Taking the NSAID with a proton pump inhibitor (PPI) may increase the likelihood of lower intestinal ulceration and bleeding because of suppressing gastric acid secretion
- Increase in bleeding
  - Potential drug-drug interactions with anticoagulants, aspirin

Cardiovascular Concerns
- In July, 2015, the FDA strengthened warnings that NSAIDs increase the chance of heart attack or stroke
  - Observational studies, a large combined analysis of clinical trials, and other scientific publications were used as evidence for the strengthened warnings
  - Labeling requirements
    - The risk of heart attack or stroke can occur as early as the first few weeks of using an NSAID
    - The risk may increase with longer use
    - The risk appears greater at higher doses
    - May increase the risk in patients with or without underlying cardiac conditions or risk factors for the development of cardiac disorders
**Cardiovascular Concerns**

- If a NSAID is necessary in a patient with cardiovascular risk factors, use the lowest dose possible for the shortest time period.
- Consider adding aspirin 81 mg/day (studies have not fully shown that the addition of aspirin will mitigate NSAID-associated CV risk).
- Monitor renal function and blood pressure.
- Watch for the development of edema and GI toxicity.
- If a NSAID is used in a high-risk patient, including those taking an ACE-I, ARB, or diuretic, consider checking serum creatinine and potassium levels weekly for the first few weeks of therapy and then periodically after that.
- Try to avoid the agents with the greater COX-2 specificity.

**Potential Drug Interaction with Aspirin?**

- Some NSAIDs may interfere with aspirin’s anti-platelet effect.
- Aspirin exerts its anti-platelet effect through irreversible effects on COX-1, which prevents the formation of thromboxane A2 for the life of the platelet.
- Although NSAIDs have anti-platelet effects, the effect is reversible and variable.
- If a NSAID has a greater affinity for COX-2, it may block aspirin’s access to its site of action.
- Aspirin’s onset of action is quick, so taking the NSAID at least one hour after the aspirin will minimize or avoid the interaction.

**NSAID Renal Risks**

- NSAIDs can damage the kidneys by decreasing renal blood flow.
- Risk factors for an increased chance of acute kidney damage include:
  - Older age
  - Diabetes
  - Pre-existing kidney disease
  - Heart failure
- Must watch for potential drug-drug interactions:
  - Diuretics
  - ACE-inhibitors or ARBs
- Check serum creatinine and potassium levels weekly for the first few weeks and then periodically after that.

**Renal Risks**

- Watch for patients with dehydration – may increase the chance of acute renal failure.
- Consider the use of those agents with a greater affinity for COX-2, as those agents may be safer from a renal perspective.
- Consider lower doses and less frequent dosing.

**Anticonvulsants**

- Gabapentin (Neurontin) – first line
- Pregabalin (Lyrica) – first line
- Carbamazepine
- Phenytoin
- Divalproex
- Most often used as an adjunct in neuropathic types of pain
- Mechanism of action is thought to be either through prevention of repetitive discharges by blocking voltage-sensitive calcium channels or by targeting the GABA inhibitory neurotransmitter system to augment this inhibitory effect.
- Must remember that gabapentin is now a Schedule V in Kentucky!

**Anticonvulsants**

- Can see many adverse effects, such as dizziness, drowsiness, or sedation.
- Recommended to start with a low dose and slowly titrate upwards until the desired effect is seen.
- Also want to taper the dose downward when discontinuing the medication.
- Depending on the agent, routine laboratory monitoring may be needed, such as CBC, renal function tests, or liver function tests.
- Need to be aware of the potential for an increase in suicidal ideation.
Antidepressants

- Tri-Cyclic Antidepressants (TCAs)
  - Amitriptyline; Nortriptyline; Doxepin
- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Citalopram, Fluoxetine, Sertraline
- Selective Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
  - Milnacipran (Savella); Duloxetine (Cymbalta)

Good evidence of small to moderate benefit from tricyclic antidepressants or SNRIs, although any antidepressant may be useful because of underlying depression often seen with chronic pain.

Opioids

Theses agents stimulate the mu and kappa receptors in the brain.
- Most often used for nociceptive types of pain
- Neuropathic pain is less responsive to the opioid
- No ceiling effect if drug is appropriately titrated

By stimulating these receptors, the major effects that are seen include:
- Analgesia
- Euphoria
- Sedation
- Respiratory depression

Opioid Analgesics

- Chronic opioid use can change/decrease many neurotransmitters
- Antidepressants can augment the opioid
- Doses are usually lower than what is used for the treatment of depression
- Many side effects and the side effects vary based on the class of antidepressant
- Some side effects may be beneficial – help with sleep
- All antidepressants do carry a boxed warning about the potential for suicidal thinking and ideation
- Still in place – whether used as an adjunct for pain or as an antidepressant

Opioid Side Effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Manifestation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased gastrointestinal motility</td>
<td>Constipation</td>
<td>Increase fluid intake, increase fiber, use stool softeners and non-stimulant laxatives, specific agents for OIC</td>
</tr>
<tr>
<td>Stimulation of chemoreceptor trigger zone</td>
<td>Nausea and vomiting</td>
<td>Use anti-emetics, take with food, switch to another opioid</td>
</tr>
<tr>
<td>Somnolence (inability to concentrate)</td>
<td>Sedation</td>
<td>Slowly taper dose, lower dose, change time of day that medication is taken, potentially add a CNS stimulant (only if all other options are considered)</td>
</tr>
<tr>
<td>Histamine release</td>
<td>Itching</td>
<td>Use of non-sedating antihistamine, switch to another opioid</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Decreased respiratory rate</td>
<td>Use of a non-opioid, slowly titrate dose</td>
</tr>
<tr>
<td>Increase in sphincter tone</td>
<td>Urinary retention</td>
<td>Use of a non-opioid, slowly titrate dose</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Fatigue, depression, sexual dysfunction</td>
<td>Use of a non-opioid, slowly titrate dose, add an antidepressant</td>
</tr>
</tbody>
</table>

Opioid-Induced Constipation (OIC)

- 40-80% of patients receiving opioids for chronic non-cancer pain will develop OIC
- Can lead to serious effects other than patient discomfort and may be a reason that patients stop taking their medication
- Important to start lifestyle/behavioral modifications when the opioid is initiated
  - Increase in fiber
  - Increase in fluids
  - Physical activity
  - Regular routine for bowel movement
- Next step is generally OTC laxatives, such as lactulose or a stool softener
- Want to try to avoid the stimulant laxatives, such as bisacodyl for occasional use only
- Prescription laxatives should be reserved for more significant cases when the stool softener or lactulose is not effective
• Designed to antagonize peripheral mu opioid receptors in the gut without reversing analgesia
• Does not cross the blood-brain barrier
• Will not produce withdrawal effects
• Two agents available that are indicated for OIC
  • Methylnaltrexone (Relistor)
  • Naloxegol (Movantik)
  • Alvimopam (Entery)
  • Rarely used due to the potential of significant cardiovascular effects
  • Limited distribution
  • Naldemedine (Symproic) – approved in March, 2017

Methylnaltrexone (Relistor)
• Methyl group added to naltrexone allows blocking of opioid receptors in the gut without crossing the blood-brain barrier
• Analgesia is not affected
• Approved for opioid-induced constipation for both cancer and non-cancer pain patients
• Studies outside of the palliative care area are limited
• Subcutaneous injection
  • 8-12 mg SQ every other day for advanced illness (cancer patients)
  • 12 mg SQ daily for non-cancer pain patients
• GI side effects are the most common and generally well-tolerated
• Expensive - $55 for a 22 mg dose

Naloxegol (Movantik)
• Naloxegol is a pegylated derivative of naloxone that is a peripherally-acting mu-opioid receptor antagonist that is effective following oral administration
• Treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain
• Dosage:
  • 25 mg once a day in the morning at least 1 hour prior to the first meal of the day or 2 hours after the meal
  • Dose should be reduced to 12.5 mg once daily in patients with moderate, severe, or end-stage renal disease or in patients that cannot tolerate the higher 25 mg dose
  • Should be used cautiously in the pregnant patient as the naloxegol could precipitate withdrawal in the neonate
• Potential for drug-drug interactions, especially with strong CYP3A4 inhibitors
  • Use should be avoided
• Adverse Effects:
  • Abdominal pain (21%)
  • Diarrhea (9%)
  • Nausea (8%)
  • Flatulence (6%)
  • Vomiting (5%)
• Patients taking methadone may see a greater incidence of the GI side effects
• Expensive - $10/dose

Opioid-Induced Hyperalgesia (OIH)
• Controversial condition in which patients treated with high doses of opioids experience worsening pain that cannot be overcome by increasing the dose
• Can cause new or paradoxically worsening pain
• Different than tolerance, which can be alleviated by increasing the dose of the opioid
• Different than addiction but may be the reason that misuse begins because the pain is so uncontrolled
• Common characteristics of OIH
  • Worsening pain over time despite increases in opioid doses
  • Nociceptive sensitization
  • Response to painful stimuli is much more painful than expected
  • Area of pain more diffuse
  • Pain persists despite removal of the original source of pain or healing of the damaged tissue
• Mechanism of OIH is not understood
  • Believed that certain opioids and/or metabolites antagonize the N-methyl-D-aspartate (NDMA) receptors
  • Enhances the excitability of the neurons and transmit painful impulses through the release of substance P
• Treatment is to completely discontinue the opioid, significantly reduce the dose, or change to an alternative agent, such as a non-opioid
• COX-2 inhibitors are often considered
  • If an opioid is required, switching to an opioid that is structurally unique, such as fentanyl, buprenorphine, or methadone may offer some benefit
**Allergies**

- Although true opioid allergies are rare, most reactions, such as itching or rash are due to the associated histamine release and not a true allergic or immunoglobulin-E (IgE) or T-cell response.
- Although caution is always advised, a decrease in potential cross-sensitivity is thought to exist when moving from one opioid structural class to another.
  - Phenathrenes (morphine-like agonists)
  - Phenylpiperidines (meperidine-like agonists)
  - Diphenylheptanes (methadone-like agonists)

**Time for a Break!!!**

**New Medications and Concerns/Warnings for Specific Medications**

**August, 2016**

- FDA requires strong warnings for opioid analgesics, prescription opioid cough products, and benzodiazepine labeling related to serious risks and deaths from combined use.
- Part of the Opioids Action Plan.
- Boxed warning for nearly 400 different products to alert that combined use may lead to:
  - Extreme sleepiness
  - Respiratory depression
  - Coma
  - Death

**Extended-Release Morphine (Embeda)**

- Formulation as capsules of extended-release morphine pellets that contain a sequestered core of naltrexone.
  - If the pellets are swallowed whole, then the morphine is gradually released and absorbed and the naltrexone core passes through the GI tract.
  - If the pellets are crushed, chewed, or dissolved, the naltrexone is released and blocks morphine-induced euphoria.

**Extended Release Morphine (MorphaBond)**

- Abuse-deterrent, extended-release form of morphine.
  - Has increased resistance to cutting, crushing, or breaking.
  - When subjected to a liquid environment, forms a viscous material that resists passage through a needle.
  - 100 mg tablets administered every 12 hours and is best suited for patients that are opioid-tolerant.
  - Should still monitor for respiratory depression when first initiating the medication.
**Extended Release Morphine (Arymo ER)**

- Indicated for the treatment of severe pain requiring around-the-clock, long-term opioid treatment when other alternatives are not available
- Opioid naïve patients:
  - 15 mg every 8 to 12 hours
  - Dosage adjustment may be made every 1-2 days
- Life-threatening respiratory depression may occur within the first 24-72 hours when first initiating the medication and following dose increases
- Should be used cautiously, if at all, in patients with pre-existing respiratory conditions
- Accidental exposure may cause fatal overdose in children
- Even after a single dose
- Available in 15 mg, 30 mg, and 60 mg tablets
- Expensive!
  - $560.00 for 60 tablets of the 30 mg strength

**Fentanyl Issues**

- Fatal overdoses have been reported with the use of fentanyl patches
- Improper patient selection – should be used for chronic pain patients only
- Improper initial dose – starting doses are often too high
- Improper dose titration – must give at least 12 hours for the initial doses to be absorbed into the system. Other medications can be used for breakthrough pain while the dose is being titrated. Must also remember that it will take 12 hours for the drug to be out of the body if an adverse event occurs
- Use of heat – direct heat will ↑ the absorption of the fentanyl leading to adverse reactions

**Fentanyl Issues (cont.)**

- Reports of fatal adverse events with the buccal form of fentanyl (Fentora)
- Should ONLY be used in patients that are opioid-tolerant for breakthrough pain in chronic pain patients
- Fentora and Actiq (transmucosal lozenge) are not interchangeable products
- Reports of fatal adverse events with the nasal spray
- Should ONLY be used in patients that are opioid tolerant for breakthrough pain
- Must be kept away from children

**Hydrocodone**

- Two single ingredient extended-release hydrocodone products are now available
  - Zohydro ER – twice daily
  - Hysingla ER – once daily
- Both medications are available in abuse-deterrent formulations
- Indicated for severe forms of pain that would require around-the-clock dosing
- Similar to when either sustained release morphine or oxycodone would be required
- Both can cause serious respiratory depression and should not be used in an opioid naïve patient
  - Should be used cautiously in patients with respiratory illnesses
  - Should be kept away from children
- Expensive!

**Hydrocodone (Vantrela ER)**

- Fixed dose, extended-release formulation of hydrocodone for the oral treatment of acute pain severe enough to require an opioid
- Is an abuse deterrent formulation
- Crushing, chewing, or dissolving of the tablets may result in uncontrolled administration of the hydrocodone, possibly leading to overdose
- Available in 15, 30, 45, 60 mg, and 90 mg tablets
- Recommended dose:
  - For opioid naïve patients: 15 mg every 12 hours
  - Patients already receiving oral hydrocodone may be switched to this product by administering one-half of the patient's total daily as the extended release product

**Methadone**

- Complicated pharmacokinetics and pharmacodynamics, with a variable half-life of up to 5 days that can lead to accumulation
- Warnings about potential respiratory depression and death from unintentional overdose and drug interactions
  - Analgesic activity similar to morphine but respiratory depression lasts much longer
  - Patients do not “feel a buzz” – may not think the drug is working and take more
  - May also prolong QT interval leading to potential arrhythmias (especially at higher doses)
  - May need to ↓ frequency of dosing due to accumulation
  - Initiate at every 6 hours and then decrease to every 8 to 12 hours
Oxycodone

- Classified as a CII
- PRN use
  - Immediate-release single formulation (Roxicodon, Oxecta; RoxyBond)
  - Oxycodon aspirin (Percodan)
  - Oxycodon acetaminophen (Percocet or Tylox)
- Scheduled use
  - Fixed dose, extended-release formulation of oxycodone and acetaminophen for the oral treatment of chronic pain severe enough to require an opioid (Xartemis XR)
- Immediate-release oxycodone (OxyContin; Xtampza ER; Troxyca ER)
- Sustained release oxycodone (OxyContin; Xtampza ER; Troxyca ER)
- Tamper-resistant formulation (Aversion technology)
  - The tablet breaks into chunks instead of a powder if crushed
  - The tablet turns into a gel when mixed with water
  - Also contains sodium laurel sulfate, which irritates the nose if snorted
  - Should not be used in feeding tubes – clog

Oxycodon/Acetaminophen (Xartemis XR)

- Fixed dose, extended-release formulation of oxycodone and acetaminophen for the oral treatment of acute pain severe enough to require an opioid
- Is an abuse deterrent formulation
  - 7.5 mg/325 mg
- Contain immediate-release and extended-release layers designed to release the active ingredients at a steady state over an extended period
  - Steady state is achieved within 24 hours after the first dose
- Recommended dose:
  - Two tablets every 12 hours without regards to meals
  - The second dose of 2 tablets may be administered as early as 8 hours after the initial dose if patients require additional analgesia at that time
  - Subsequent doses should then be 2 tablets every 12 hours

Extended-Release Oxycodone (Xtampza ER)

- Abuse-deterrent, extended-release form of oxycodone
- Uses the DETERx technology, which provides extended-release drug delivery while safeguarding against common methods of abuse and tampering including crushing, chewing, heating, and injecting
  - Each bead of the drug in the capsule is in an abuse-deterrent form
- Contents can be opened and sprinkled on food or administered via G-tube
- Indicated for severe pain, requiring around-the-clock pain management
- Can be used in opioid-naïve patients
- Initial dose is 10 mg every 12 hours with food and may be slowly increased to a maximum total dose of 320 mg/day
- Dosage should be adjusted in patients with renal and/or hepatic impairment

Oxycodone Immediate Release (RoxyBond)

- Immediate-release oxycodone (RoxyBond) was approved for oral use for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are ineffective
- The product is an abuse deterrent formulation that uses physical and chemical barriers to deter abuse
- Laboratory test data have shown that compared to another approved immediate-release product, RoxyBond has increased resistance to cutting, crushing, grinding, or breaking and is also resistant to extraction by selected household solvents
- The product will be available in three strengths: 5 mg, 15 mg, and 30 mg

Oxycodone

- Immediate release form – (Oxy IR; Roxicodon)
  - Indicated for breakthrough pain in combination with a longer-acting agent
- New formulation – immediate release form – (Oxecta)
  - Tamper-resistant formulation (Aversion technology)
    - The tablet breaks into chunks instead of a powder if crushed
    - The tablet turns into a gel when mixed with water
    - Also contains sodium laurel sulfate, which irritates the nose if snorted
    - Should not be used in feeding tubes – clog
- The immediate-release products that are not formulated as an abuse deterrent or combined with other agents are highly sought after because they require no manipulation before injecting or inhaling (snorting)
  - “Perc 30s”
Oxycodone/Naltrexone (Troxyca ER)

- A combination opioid agonist/opioid antagonist indicated for the management of severe pain requiring daily, around-the-clock, long-term opioid treatment where alternative treatment options are inadequate
- Is an abuse-deterrent formulation
- Best for opioid-tolerant patients, but can be used in opioid-naive patients at the lowest possible dose
- Capsules should be swallowed whole or the capsule contents may be sprinkled on applesauce provided there is no chewing
- Opioid-naive:
  - 10 mg/1.2 mg capsule every 12 hours
  - Increase no more often than once per week
- Strengths available (oxycodone/naltrexone capsules): 10 mg/1.2 mg, 20 mg/2.4 mg, 30 mg/3.6 mg, 40 mg/4.8 mg, 60 mg/7.2 mg and 80 mg/9.6 mg
- Must be used cautiously with any pre-existing respiratory issues

Oxymorphone (Opana ER)

- In March, 2017, the FDA voted to remove a previously approved opioid medication because "the benefits of the drug may no longer outweigh its risks"
- Although the product had been reformulated in 2012 in an abuse deterrent formulation, data showed a significant shift in the route of abuse from nasal to injection
  - The injection abuse has been associated with outbreaks of HIV and hepatitis C due to the sharing of needles
  - The manufacturer voluntarily complied with the FDA request

Buprenorphine (BuTrans)

- Agonist-antagonist agent
- Transdermal patch for chronic pain, such as chronic back pain but may not be that effective of chronic cancer pain
- Unlike most agonist-antagonist agents, it is compatible with pure agonists, so patients can be switched to the patch without withdrawal symptoms
- Can be used in opioid-naive patients at the lowest dose (5 mcg/hr)
- Patch should be changed every 7 days
- The patched area should not be exposed to heat

Buprenorphine Buccal Film (Belbuca)

- Does have an FDA indication for the treatment of chronic pain, including for opioid-naive patients
  - Should not be used in pregnant patients as it may precipitate withdrawal in the neonate
  - Should not be used for "PRN" use
  - For patients with poor pain control with other opioids, there is limited data that suggests switching to the sublingual form of buprenorphine may improve control
  - The risk of respiratory depression is not common when usual doses for pain are used and the doses are slowly titrated upwards
  - Wide range of doses available to help tailor pain treatment
  - For opioid-naive patients, initiate the drug at 75 mcg once daily for 4 days and then increase to every 12 hours
  - Dose may be increased to 150 mcg every 12 hours as needed
  - Higher doses of the drug are indicated for those patients being switched from other opioids

Buprenorphine Buccal Film

- The film should be applied to the inside of the mouth – cheek - at around the same time each day
- The inside of the cheek should be moist before applying
- The patient should be cautioned to not eat or drink until the film is fully absorbed
- The patient should also be cautioned to not chew the film
- The film should not be placed in the mouth with any lesions or open sores

Are Abuse Deterrent Formulations (ADFs) Effective?

- Opioid formulations that contain abuse-deterrent properties have great potential as part of multi-pronged efforts to contain opioid abuse
- Still unknown is the true extent to which reduction in abuse from ADFs may have been countered by increase use of heroin and other illicit opioids
### ADFs

**Agonist-Antagonist Combinations**
- Addition of naloxone or naltrexone to prevent desirable effects of the opioid secondary misuse
- The antagonist is active only with inappropriate manipulation and use of the product (such as crushing, dissolving, or injecting)
- The naloxone component has no therapeutic effect with oral administration
- Pentazocine/Naloxone (Talwin NX)
- Buprenorphine/Naloxone (Suboxone) (Zubsolv)
- Morphine/Naloxone (Embeda)
- Oxycodone/Naltrexone (Tramycra ER)

### Abuse Deterrent Formulations

**Physical Barriers**
- Make chewing, crushing, cutting, or dissolving a formulation more difficult
- May be difficult to crush or may form a gel if dissolved
- May be more difficult for injection
- Hydromorphone, extended release (Exalgan)
- Morphine, extended release (Opana ER)
- Oxycodone, immediate release (Oxecta; RoxyBond)
- Oxycodone, controlled release (OxyContin; Xtampza ER)

### Market Shares of different ADFs

#### Nationaly Estimated Number of Prescriptions Dispensed for Opioid Analgesic Products with abuse-deterrent properties from U.S. Outpatient Retail Pharmacies

<table>
<thead>
<tr>
<th>Year</th>
<th>OxyContin ER</th>
<th>Embeda</th>
<th>OxyTangalora ER</th>
<th>OxyContin IR</th>
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</tr>
</tbody>
</table>

### Abuse of ADFs

- Although, it may be more difficult, ADFs can still be abused
- Swallowed
- Crushed and swallowed
- Crushed and snorted
- Crushed and smoked
- Dissolved and injected
- The most common form of abuse is through swallowing

### Postmarket studies: Abuse and Misuse

Direct interview with 153 participants entering substance abuse program. Did ADF OxyContin influence the drugs that participants used for abuse?

- Yes, replaced OxyContin with other drugs: 28%
- No, continued to use OxyContin: 34%
- No, did not use OxyContin: 38%
- Stopped abusing drugs: 3%


### Prescriber Best Practices
There are opposing pressures from:

1) Patients and pain management experts who advocate providing opioids for individuals with pain and
2) Families, caregivers, and regulatory officials, who want to prevent prescription drug diversion, abuse and overdose

Finding the right balance to provide safe and effective pain management is a duty of healthcare professionals.

- Benefits Include:
  - Analgesia
  - Improved function
  - Improved quality of life

- Risks Include:
  - Overdose
  - Life-threatening respiratory depression
  - Abuse by patient or household contacts
  - Misuse and addiction
  - Physical dependence and tolerance
  - Interactions with other medications
  - Inadvertent exposure/ingestion by children

PROBLEM: Too many prescriptions
In 2015, the amount of opioids prescribed was enough for every American to medicated around the clock for 3 weeks!

SOLUTION: Fewer prescriptions
Use opioids only when benefits are likely to outweigh risks.
Options other than opioids include:
- Pain medicines, such as acetaminophen, ibuprofen, and naproxen
- Physical therapy and exercise
- Cognitive behavioral therapy
- Therapies that don’t involve opioids may work better and have fewer risks and side effects

PROBLEM: Too many days
Even at low doses, taking an opioid for more than 3 months increases the risk for addiction by 15 times!
In 2006, the average days supply per prescription was 12
In 2015, the average days supply per prescription was 17
Three days or less is often enough and more than seven days is rarely needed
If continuing opioids, ask whether benefits continue to outweigh risk. If not, use other treatment options and taper opioids gradually

PROBLEM: Too high of a dose
A dose of 50 MME or more per day doubles the risk of opioid overdose or death, compared to 20 MME or less per day.
At 90 MME or more, the risk increases 10 times!

SOLUTION: Lower doses
Use the lowest effective dose of immediate-release opioids when starting and reassess benefits and risks when considering dose increases
Avoid a daily dose of 90 MME or more.
If already taking high doses, offer the opportunity to gradually taper to a safer dose
Consider a supplemental prescription for naloxone for potential overdose

SOLUTION: Fewer days
For acute pain, prescriptions should only be for the expected duration of pain severe enough to need opioids.
Three days or less is often enough and more than seven days is rarely needed
If continuing opioids, ask whether benefits continue to outweigh risk. If not, use other treatment options and taper opioids gradually

SOLUTION: Lower doses
Use the lowest effective dose of immediate-release opioids when starting and reassess benefits and risks when considering dose increases
Avoid a daily dose of 90 MME or more.
If already taking high doses, offer the opportunity to gradually taper to a safer dose
Consider a supplemental prescription for naloxone for potential overdose
1. Assess Pain and Function
   • Use validated pain scale
   • PEG Scale
     • Three individual questions
     • 30% improvement from baseline is clinically meaningful
     • Q1: What number from 0-10 best describes your PAIN in the last week?
       0= “no pain” to 10= “worst pain that you can imagine”
     • Q2: What number from 0-10 describes how, during the past week, pain has interfered with your ENJOYMENT OF LIFE?
       0= “not at all” to 10= “complete interference”
     • Q3: What number from 0-10 describes how, during the past week, pain has interfered with your GENERAL ACTIVITY?
       0= “not at all” to 10= “complete interference”
     • May also want to use diagnostic tests

2. Consider if non-opioid and non-pharmacologic therapies are appropriate

3. Talk to patients about treatment plan
   • Set realistic goals for pain and function based on diagnosis
   • Discuss treatment options used in the past
   • Discuss and document benefits, side effects, and risks, especially addiction and overdose if opioids are being considered
   • Set criteria for stopping or continuing opioid
   • Set criteria for regular progress assessments
   • Use teach-back methods to check patient understanding about treatment plan

4. Evaluate Risk of Harm or Misuse
   • Known risk factors
     • Regular drug use
     • Prescription drug use for non-medical reasons
     • History of substance use disorder or overdose
     • Family history of substance use disorder
     • Mental health conditions
     • Sleep-disordered breathing
     • Prescription drug monitoring program data
     • Reverse KASPER can also be beneficial
     • Urine drug screen to confirm presence of any prescribed substances, for undisclosed prescription drugs, or any illicit substances
     • Current medications
     • Evaluate for any other CNS-active medications

5. Pain History
   • O = Other associated symptoms (nausea, swelling, depression, anxiety)
   • P = Palliative/provocative factors (mobility, touching, “what makes the pain better or worse?”)
   • Q = Quality of life
   • R = Region/radiation
   • S = Severity (pain scale)
   • T = Timing (when does the pain start? Continuous? Intermittent? Vary by time of day?)
   • U = Untoward effects on effect or quality of life, including psychosocial, spiritual effects

6. Establish Diagnosis
   • X-rays, MRI, CT, Neurophysiological studies
   • Psychological evaluation
   • Physical examination
   • Precision diagnostic interventions
     • Guarding of the painful area
     • Relief of pain following injection of local anesthetic into trigger points helps to support a diagnosis
     • A neuropathic component may be indicated by weakness, sensory impairment, or loss of deep tendon reflexes
     • Ask about the ability to open jars or increased tripping episodes
     • Sympathetic nervous system involvement includes the presence of swelling, changes in skin color and temperature or joint tenderness

7. Before Prescribing
   • An adequate trial of opioid therapy may require 3 to 6 months
   • Before starting the opioid, consider alternatives to opioids including non-pharmacological approaches
   • Start at a low dose and titrate slowly, with close monitoring
   • Start with immediate-release (IR) opioids at the lowest dose for the shortest therapeutic duration
   • IR opioids are recommended over extended-release or long-acting (ER/LA) opioids when starting an opioid
   • Choice of drug, dose, formulation, and titration schedule will be based on many factors
   • Generally, a long-acting agent given around-the-clock with an additional agent for breakthrough pain may be the preferred approach
   • “PRN” or as needed should be avoided in chronic pain
### Initiation of Opioids

- Avoid > 90 MME/day
- If prescribing > 50 MME/day, increase follow-up frequency and consider prescribing naloxone for overdose risk
- For acute pain, prescribe < 3 day supply
  - A refill could be requested for some patients, but generally more than 7 days will rarely be required

### Morphine Milligram Equivalents (MME)

- Calculating the total daily dose of opioids helps identify patients who may:
  - Benefit from closer monitoring
  - Reduction or tapering of opioids
  - Prescribing naloxone
  - Institution of other strategies to reduce the risk of overdose
- 50 MME/day
  - 50 mg of hydrocodone (10 tablets of hydrocodone/acetaminophen 5/300)
  - 33 mg of oxycodone (approximately 2 tablets of oxycodone sustained release 15 mg)
  - 12 mg of methadone (< 3 tablets of methadone 5 mg)

### Total Daily Dose Calculation

1. Determine the total daily amount of each opioid the patient takes
2. Convert each to MMEs — multiply the dose for each opioid by the conversion factor
3. Add them together
   - Caution: Do not use the calculated dose in MMEs to determine dosage for converting one opioid to another.
   - Continue to use equi-analgesic dose tables

### Dosing

- Initial stages of acute pain
  - Short-acting agents are generally sufficient
  - Analgesics should be given around the clock
  - Titrations of dose should be based on response and side effects, such as sedation
  - As the painful state subsides, the need for medication should decrease and “as needed” dosing schedules should be appropriate for pain that is intermittent or sporadic
- For chronic pain
  - Immediate-release analgesics should be given around the clock and then converted to extended-release forms
  - Immediate-release forms should be available on an "as needed" basis for breakthrough pain
- Little evidence to favor one opioid over another, however, some products are not indicated for opiate-naïve patients

### How To Treat Acute Pain in Chronic Opioid Patients

- Document the daily home opioid dose to avoid under- or overdosing during acute treatment
- Determine what the patient is actually taking – not what is prescribed
- Use tools such as the prescription drug monitoring program, the pharmacy, and ask the patient
- If there is a question about what the patient is actually taking, consider splitting the reported daily dose into two or four divided doses with monitoring for side effects and withdrawal until the dose can be verified
- Assess baseline pain control and functional status
- Consider previous experience with pain treatments
- Medication allergies

### How To Treat Acute Pain in Chronic Opioid Patients

- Set realistic and practical goals for pain and function based on the baseline pain and functional status
- Continue the patient’s chronic opioid therapy and add short-acting analgesics to treat the acute event
  - Avoid escalating the patient’s long-acting opioid regimen
  - Do not use long-acting opioids for acute pain
  - Try non-opioids first
  - Add a short-acting opioid only if needed and at the smallest dose necessary
  - Oral route is preferred
  - Parenteral route is not more effective unless the patient cannot tolerate oral therapy
  - Assess relief, distinguishing between acute and chronic pain
  - Ensure that any short-acting opioid that was added for acute pain is discontinued in a timely fashion
**Titration of Opioid Therapy**

- Reassess benefits/risks within 1-4 weeks after initial assessment
- Assess pain and function using the same methods as done prior to initiating opioids
  - Compare to baseline
- Schedule reassessments at regular intervals (<3 months)
- Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm
  - If over-sedation or overdose risk, then taper dose
- Tailor taper rates individually to patients and monitor for withdrawal symptoms

**Monitoring of Opioids**

- State laws may dictate specific documentation
  - Thorough documentation!
- Low-risk patients on stable doses should be monitored at least every 3 to 6 months
- Higher risk patients may require monthly or even weekly monitoring
  - At each visit – 5As
    - Analgesia: Assess effectiveness for pain control
    - Activity: Assess effectiveness with regards to the activities of daily living
    - Adverse effects
    - Affect: Psychological issues
    - Aberrant: Behaviors or adherence problems

**Monitoring of Opioids**

- Assess for potential side effects
- Prescription drug monitoring programs
- Consider routine urine drug screens if patient may be at high-risk for developing dependence
  - if not high-risk, then periodic urine drug screens
- Any aberrant behaviors
  - Requesting refills early
  - Missing appointments but still requesting the medication prescription
  - The need for rapid increases in either the quantity or dose of the opioid

**Discontinuation of Opioids**

- Indications for tapering off opioids include lack of progress toward goals after an adequate trial
- Unmanageable side effects
- Serious, unsafe, or persistent aberrant behaviors
- Rapidity of tapering depends on the reason for discontinuation, the presence of co-existing conditions, and the development of withdrawal symptoms

**Tapering**

- Should be individualized and should minimize symptoms of opioid withdrawal while maximizing pain treatment with non-pharmacologic therapies and non-opioid medications
- Go Slow:
  - A decrease of 10% of the original dose per week is a reasonable starting point
  - If the patient has taken opioids for a long time might find slow tapers, such as 25% per month easier to tolerate
  - Adjust the rate and duration of the taper according to the patient's response
  - Don't reverse the taper, however the rate may be slowed or paused while monitoring and managing withdrawal symptoms
  - It is important to discuss the increased risk for overdose if patients quickly return to a previously prescribed higher dose
  - Once the smallest available dose is reached, the interval between doses can be extended and opioids may be stopped when taken less than once per day

**Tapering**

- Consult
  - Coordinate with specialists and treatment experts as needed, especially for patients at high risk for harm, such as pregnant patients or patients with an opioid use disorder
  - Use extra caution during pregnancy due to possible risk to both the pregnant patient and the fetus if the patient goes into withdrawal
- Support
  - Make sure patients receive appropriate psychosocial support
  - If needed, work with mental health providers, arrange for treatment of opioid use disorder or offer naloxone for overdose prevention
  - Watch for signs of anxiety, depression, and opioid use disorder during the taper
- Encourage
  - Let patients know that most people have improved function without worse pain after tapering opioids although the pain may briefly get worse at first
Special Considerations: Elderly

- Reduce the dose to 1/3 to 1/2 that of the usual adult dosage IF used at all
- Remember, that the opiates are on the Beer’s Criteria for Potentially Inappropriate Medications
- Watch for adverse effects
- Respiratory depression more likely in elderly, cachectic or debilitated patients
  - Monitor closely when initiating and titrating extended release products
  - Watch other medications that can depress the CNS
- Older adults are more likely to develop constipation
  - Initiate a bowel regimen at the beginning of the pain medications

Special Considerations: Pregnant Women

- Potential risks of opioid therapy to the newborn include:
  - Low birth weight
  - Premature birth
  - Hypoxic-ischemic brain injury
  - Neonatal death
  - Neonatal opioid withdrawal syndrome
- Encourage minimal/no opioid use during pregnancy, unless potential benefits outweigh risks
  - If chronic opioid therapy is used during pregnancy, anticipate and manage risks to the patient and the newborn

Special Considerations: Children < 18 Years

- Safety and efficacy of most long-acting opioids are not fully known
- Most opioid studies focus on inpatient use
- Opioids are common sources of drug errors in pediatric patients
- Opioid indications are primarily for life-threatening conditions
- New studies have questioned the use of codeine in pediatric patients due to little evidence of efficacy and a greater chance of respiratory depression
- However, pediatric patients do have pain and pediatric pain specialists should be consulted

APRN Kentucky Specifics

- As of July 1, 2017
- Prescriptions for Schedule II opioids for acute pain are limited to a 72 hour supply
  - Exceptions
    - The practitioner believes that more than a 3 days’ supply of medication is necessary to treat the condition and documents the acute condition and lack of treatment alternatives to justify more than a three day supply
    - Treatment of chronic pain
    - Treatment of a patient with a valid cancer diagnosis
    - Treatment of pain for a patient receiving treatment in hospice or end of life
    - Treatment in an approved narcotic treatment program
    - Treatment of pain following major surgery or significant trauma
    - Treatment of pain in an in-patient setting

Resources

- American Chronic Pain Association (ACPA)
  - http://www.theacpa.org
- American Pain Society
  - www.ampainsoc.org
- Arthritis Foundation
  - http://www.arthritis.org
- National Institute on Drug Abuse
  - www.nida.nih.gov
- Substance Abuse and Mental Health Services Administration
  - www.samhsa.gov

Conclusions

- Chronic pain is prevalent in today’s society
- Careful attention must be paid to signs and symptoms in order to appropriately classify a patient’s pain
- Multi-modality approaches generally have the better response rates including both non-pharmacologic and pharmacologic approaches
- Treatment must be individualized
- Consider referrals to pain specialists if patient are not adequately responding to treatment
- No matter the medication, close monitoring is necessary to help identify and treat side effects early
Conclusions

- Non-opioid agents should be utilized as first-line agents
- Opioids should be reserved for patients with more severe pain or patients with an inadequate response to the non-opioids
- The potential for misuse, abuse, and addiction with the opioids is possible
- Patient education is necessary for patients to have realistic goals
  - Not to be "pain free" but to have a tolerable pain level