Top Pediatric Medications

Updates on Safe Use
Elizabeth VandeWaa, PhD
Lecturer/Consultant
Barkley and Associates
Professor
University of South Alabama

Common Pediatric Conditions
- Asthma
- Attention-deficit hyperactivity disorder (ADHD)
- Infections
- Pain/fever
- Allergies/rashes
- Gastrointestinal (GI) complaints

Conditions of Interest
- Hyperlipidemia
- Psychosis
- Autism
- Depression

Factors Unique to Pediatric Pharmacology
- Infants
- Underdeveloped metabolic and excretory processes:
  - Conjugation reactions are not developed until one year of age. Hence, many drugs cannot be used in neonates, newborns, and infants up to one year of age.
  - Excretory processes are not at adult levels until 1 year of age.

Factors Unique to Pediatric Pharmacology
- Children one to 12 years of age.
- Metabolism:
  - Is generally faster than normal adult levels until age 2, then slowly declines until puberty, and finally drops to normal adult levels.
  - This may mean increased dosage or dosing frequency for drugs eliminated by hepatic metabolism.

Drug Dosing in Children
- Doses are often extrapolated from adult doses:
  - Based on body surface area.
  - Approximation.
- Future dosing should be done based on clinical outcome to maximize therapeutic benefit and minimize adverse effects.
### Top Drugs Prescribed in Pediatric Medicine

- Amoxicillin
- Amox/Clavulanate (Augmentin)
- TMP/Sulfa (Bactrim Pediatric)
- Cephalexin (Keflex)
- Cefdinir (Omnicef)
- Mupirocin (Bactroban Topical)
- Nystatin Topical
- Cipro/Dexamethasone (Ciprodex Otic)

### Top Drugs Prescribed in Pediatric Medicine

- Loratidine (Claritin)
- Albuterol
- Budesonide (Pulmicort)
- Fluticasone
- Prednisone
- Hydrocortisone
- Prednisolone (Orapred Oral Liquid)
- Mometasone (Nasonex)
- Triamcinolone (Kenalog, Nasocort)
- Dextromethorphan/Phenylephrine/Chlorpheniramine

### Top Drugs Prescribed in Pediatric Medicine

- Infants Tylenol
- Children's Motrin
- Morphine
- Lisdexamfetamine
- Methylphenidate
- Amphetamine/Dextroamphetamine

### Acute Otitis Media (AOM)

- AOM is one of the most common childhood infections.
- 30 to 35 million cases per year.
- Initial peak age of incidence occurs between six to 12 months of age.
- Second peak age of incidence occurs between four and five years of age.
- Accounts for 3% of all visits.
- Is the #1 reason for a prescription.
AOM with Effusion

AOM: To Treat, or Not to Treat?

- Three signs and symptoms must be present:
  - Acute onset of signs and symptoms.
  - Fever, pain.
  - Middle-ear effusion
    - Often difficult to confirm.
  - Middle-ear inflammation
    - Erythema and/or otalgia.

AOM: To Treat, or Not to Treat?

- Pain medications are always indicated, as are relief measures.
- More than 80% of AOM cases resolve spontaneously within a week.
  - Treating with antibiotics means unnecessary costs, risk of SE, and increases the chance for emergence of resistance.
- Observation for 48 to 72 hours is most often warranted.
  - Delaying treatment does not increase risk of mastoiditis.

AOM: When to Treat

- Less than 6 months old:
  - Treat with antibiotics.
- Six months to two years of age:
  - Antibiotics if diagnosis is certain or disease is severe; otherwise, observe patient.
- Two years and older:
  - Antibiotics if illness is severe; observation if not severe even with a certain diagnosis. If diagnosis is uncertain, observe patient.

AOM Drugs of Choice

- Amoxicillin 80 to 90 mg/kg/day.
  - Cefdinir (Omnicef): For non-type 1 allergy, 14 mg/kg/day in one or two doses.
  - Azithromycin: For type 1 allergy, 10 mg/kg day one and 5 mg/kg on days two through five.
- For persistent symptoms after 48 to 72 hours:
  - Augmentin ES-600 twice a day.
  - Ceftriaxone: Non-type 1 allergy, 50 mg/kg.
  - Clindamycin: Type 1 allergy, 30 to 40 mg/kg/day in three divided doses.

Bugs That Cause AOM and Resistance

- *Haemophilus influenzae* and *Moraxella catarrhalis* are most likely to be resistant to beta-lactam antibiotics.
- *Streptococcus pneumoniae* is resistant to erythromycin, beta-lactams, and TMP-Sulfa.
- Vaccination against influenza and treatment with oseltamivir are associated with a decreased incidence of AOM during flu season.
- Vaccination against *S. pneumoniae* is associated with a decreased incidence of AOM.
Resistance and Recurrence

- Resistance is best treated with high-dose amoxicillin/clavulanic acid (Augmentin ES-600).
  - Alternatively, parenteral ceftriaxone.
- Recurrence is defined as three or more episodes in six months, or four or more in 12 months.
  - Prophylaxis has not been shown to be effective.
  - Use only during cold and flu season.
  - Select amoxicillin.

Otitis Externa - Swimmer's Ear

- Treated easily, and inexpensively, with either a 2% solution of acetic acid, or a solution of alcohol plus acetic acid.
- If either of the above do not work, Ciprodex may be used.
  - Consider cost.
  - Consider promotion of resistance.

TREATMENT OF ASTHMA

Epidemiology of asthma:
- Process and triggers

Drugs for asthma:
- Delivery methods
- Recommendations
- Monitoring drug efficacy

Other strategies for the patient with asthma:
- Summary

Treatment of Asthma
Who Has Asthma?
- 20 million Americans
- 9 million children
- 11 million adults
- There is a known trigger in about 50% of children.
  - Asthma is the main reason for missed school days and ER visits for children in the U.S.

The Nature of Wheezing
- More than 50% of children wheeze due to:
  - Small airways
  - Male gender
  - Low birth weight
  - Smoker in the home
  - Allergy
- Immunoglobulin E (IgE)-mediated, allergic wheezing is the most common cause in children.

How Severe Is It?
- Mild asthma
  - Symptoms occur at least two times per week, and one to two nighttime attacks per month.
- Moderate asthma
  - Daily symptoms, nighttime attacks three to four times per month.
- Severe asthma
  - Daily symptoms that significantly affect quality of life and severe nighttime attacks every night.

During an Asthma Attack
- Two-Step process
  - Step 1: Allergenic molecules bind to IgE antibodies on mast cells. Histamine, leukotrienes, interleukins, and prostaglandins are released, causing bronchoconstriction.
  - Step 2: Inflammatory cells infiltrate the airway where the bronchoconstriction occurred and release mediators that cause edema, mucus plugging, and airway obstruction.

Process of Asthma
Triggers for Asthma
- Dust
- Dander
- Mold/Mildew
- Pollen
- Cold air
- Tobacco or other smoke
- Pollutants
- Exercise

Treatment of Asthma
- Drugs for Asthma
  - Delivery Methods
  - Recommendations

Drugs for Asthma
- Two main classes: Anti-inflammatories and bronchodilators.
- Anti-inflammatory drugs: Glucocorticoids, cromolyns, leukotriene modifiers, IgE antagonist.
- Bronchodilators: Beta-2 agonists, methylxanthines, anticholinergics.

Delivery of Drugs
- Metered-Dose Inhalers (MDIs)
- Dry-Powder Inhalers
- Nebulizers
- Per Os (PO)
- IV

Metered-Dose Inhalers
- May require good hand-lung coordination.
- Only about 10% of the dose gets to the lung, 80% gets deposited in the oropharynx, and the remaining 10% is left in the device or exhaled.
  - A spacer helps increase drug delivery to the lungs and reduce waste. It also reduces the need for hand-lung coordination, to a degree.
Dry Powder Inhalers
- Breath-activated.
- No hand-lung coordination required.
- Contain no propellants to harm environment.
- Deliver about 20% of the drug dose to the lungs.

Nebulizers
- Converts a drug solution into a mist.
- Inhalation of the mist can be done through a facemask or through a mouthpiece held between the teeth.
- Takes several minutes to deliver the drug to the lungs.

Inhalation Drugs for Asthma
- Advair Diskus (fluticasone/salmeterol)
- Advair HFA
- Aerobid (flunisolide)
- Aerobid-M
- Albuterol
- Alvesco (ciclesonide)
- Asmanex Twisthaler (mometasone furoate)

- Atrovent HFA (ipratropium bromide)
- Atrovent
- Azmacort (triamcinolone acetonide)
- Cromolyn
- Flovent (fluticasone propionate)
- Foradil Aerolizer (formoterol fumarate)
Inhalation Drugs for Asthma
- Serevent Diskus (salmeterol xinafoate)
- Symbicort (budesonide/formoterol)
- Ventolin HFA (albuterol sulfate)
- Xopenex (levalbuterol HCl)
- Xopenex concentrate
- Xopenex HFA

Inhalation Drugs for Asthma
- Maxair Autohaler (pirbuterol)
- Metaproterenol
- Proair HFA (albuterol sulfate)
- Proventil HFA (albuterol sulfate)
- Pulmicort Flexhaler (budesonide)
- Pulmicort Respules
- Qvar (beclomethasone dipropionate HFA)

Recommendations
- Mild asthma
  - Occasional beta2-agonist.
- Moderate asthma
  - Daily beta2-agonist.
- Severe asthma
  - Beta2-agonist plus steroids; systemic steroids for exacerbations.

Well-Controlled Asthma
- What is the goal?
  - Albuterol rescue less than two times a week.
  - All patients should have a SABA
- Why are patients poorly controlled?
  - Compliance issues.
  - Variable response.
  - Not measuring the right thing (e.g., only measuring the FEV1).

Drugs Used for Asthma
- Short- and Long-acting beta-agonists
- Inhaled corticosteroids (ICS)
- Cromones
- Leukotriene modifiers
- Omalizumab

Short-Acting Beta-Agonists (SABA)
- Overused
  - Watch for abuse and overuse.
  - Use of more than one canister per month indicates a poorly controlled patient.
  - Examples: Albuterol (Ventolin, Proventil), levalbuterol (Xopenex), bitolterol (Tornalate), pirbuterol (Maxair), and terbutaline.
Considerations of SABA Use

- Avoid excessive use.
- Watch for cardiovascular effects, seizures, diabetes, hyperthyroidism, and hypertension.
- Most are pregnancy category C, not recommended for nursing mothers.
- Notable drug interactions: Monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), and sympathomimetics.
- Monitor digoxin and other drugs that may cause hypokalemia.

Long-Acting Beta-Agonists (LABA)

- Prescribed to patients not controlled on other medications or requiring two or more maintenance medications.
- Usually given with ICS to children older than 12 years of age if ICS alone is unable to control condition.
- Black box warning due to increased risk of asthma-related deaths and exacerbations.
- BBW removed for LABA/ICS combinations
- Examples: Formoterol (Foradil), salmeterol (Serevent), albuterol, and Terbutaline PO.

Considerations of LABA Use

- Not for acute attacks. Do not exceed recommended dose.
- Watch in diabetes, thyroid disorders, cardiovascular disease, and seizures.
- Do not use with spacers. Prescribe a SABA for acute symptoms.
- Pregnancy category C, not recommended for nursing mothers.
- Hypertension, sinus congestion, rhinitis, bronchospasm, transient hypokalemia, and muscle cramps.
- Watch with MAOIs, TCAs, and drugs that decrease potassium.

Corticosteroids

- Inhaled or PO
- ICS
  - Good news: Decreased symptoms, increased quality of life and lung function. Decreased exacerbations and decreased hyperresponsiveness of airways.
  - Bad news: Bruising, adrenal suppression, thrush, dysphonia, bone demineralization, and possible growth suppression. Does not help patient grow out of asthma.

Examples of Corticosteroids

- ICS: Beclomethasone (QVAR), budesonide (Pumicort Turbohaler), flunisolide (Aerobid), fluticasone (Flovent), mometasone (Asmanex Twisthaler), triamcinolone (Azmacort).
- PO GCs: Prednisone, prednisolone.
- Combination Agent: Fluticasone plus salmeterol (Advair Diskus).

Considerations for CS Use

- Monitor for infections.
  - Chicken pox, measles, URI.
- Monitor for adrenal insufficiency and suppression of the HPA axis.
- Monitor for osteoporosis, growth suppression, and hypercorticism.
- Monitor intraocular pressure.
- Pregnancy category C: Use caution while nursing.
- Headache, respiratory infections, oral candidiasis, sinusitis, gastrointestinal upset, depression, and dysmenorrhea.
- Discontinue if bronchospasm occurs.
Cromones
- Only for prophylactic use.
- Better at treating symptoms of allergic rhinitis than asthma.
- Moving away from these as asthma treatment, or may be used in combination with a bronchodilator for long-term control in children.
- Examples: Cromolyn (Intal), nedocromil (Tilade).

Leukotriene Modifiers
- Safe and effective for pediatric and adult use.
- Alternative or add-on to ICS.
- Not as effective as ICS when added to a LABA.
- Examples: Montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo).
- Available as tablets, chewables, and granules.

Considerations of Leukotriene Receptor Antagonists (LTRA)
- Pregnancy category B.
- Adults may complain of headache, fatigue, fever, and GI upset.
- Children may complain of urticaria, flu and cold symptoms, ear or leg pain, and thirst.

Omalizumab
- IgE antagonist.
  - Can reduce up to 96% of IgE in blood.
  - Only approved for adults and children 6 years or older with a positive skin test for aeroallergen not controlled by a steroid.
  - Has a black box warning for anaphylactic responses.
  - Subcutaneous injection, expensive.
  - Trade name: Xolair

Considerations for Omalizumab Use
- Base dosage and frequency based on total IgE and body weight.
- Subcutaneous injection over five to 10 seconds, max 150 mg at injection site.
- Max dosage is 375 mg every two or four weeks.
- Monitor for 2 hours after injection.
- Risks include anaphylaxis, malignancy, injection site reactions, URIs, and headache.
- Pregnancy category B

Other Biologics to Consider
- Mepolizumab (Nucala): Approved for children ≥ 12 years of age. Anti-IL-5 biologic.
- Reslizumab (Cinqair): Approved for adults and children ≥ 18 years of age. Anti-IL-5 biologic.
- Benralizumab (Fasenra): Anti-eosinophilic antibody approved for children ≥ 12 years of age.
- Dupilumab (Dupixent): Antibody to the alpha subunit of the IL 4 receptor. Reduces asthma exacerbations and improves lung function. Approved for children ≥ 12 years of age.
Other Drugs for Asthma

- Methylxanthines: Theophylline (Theo-Dur), aminophylline (Truphylline), oxtriphylline, and dyphylline.
  - All are related to caffeine.
- Anticholinergics: Ipratropium (Atrovent, Combivent), tiotropium (Spiriva).
  - Approved for COPD, but used for asthma, especially in patients who do not respond to other medications.

Asthma Exacerbations

- Severe, unremitting attacks
  - Relieve airway obstruction and decrease hypoxemia.
  - Managed with repetitive SABAs, PO steroids, and oxygen.
  - Epinephrine may be given to an unconscious patient.
- Most common in severe asthma.

Step-Wise Approach to Asthma Treatment

- Step 1: SABA pro re nata
- Step 2: Low-dose ICS or cromolyn, LTRA, or theophylline.
- Step 3: Low-dose ICS with either LABA or medium dose CS.
  - Alternatively, medium-dose ICS with LTRA, theophylline, or zileuton.

Step-Wise Approach to Asthma Treatment

- Step 4: Medium-dose ICS plus LABA or medium dose CS.
  - Also, medium-dose ICS plus LTRA, theophylline, or zileuton.
- Step 5: High-dose ICS with LABA and consider omalizumab for patients with allergies.
- Step 6: High-dose ICS plus LABA and PO steroid.
  - Consider omalizumab for patients with allergies.

Do the Steps Work?

- It is estimated that less than 15% of patients received add-on care beyond step 4 or were treated properly for asthma exacerbations.
  - Cost issue?
  - Education issue?

How To Use the Steps

- Step Up
  - Check adherence, environmental control, and comorbid conditions.
  - With each step (two to four), consider subcutaneous allergen immunotherapy for patients with allergic asthma.
  - Use of SABA more than two days a week for symptom relief usually indicates a step up.
- Step Down—the preferred approach
  - Asthma is well-controlled for three months.
Monitoring for Control
- Flow meter monitoring
- Monitor every day
  - Check peak expiratory flow rate (PEFR).
  - If PEFR is less than 80%, more frequent monitoring is warranted.
  - Dosage adjustment or regimen change might be needed.
  - Zone monitoring.

PEFR Monitoring
- Green zone: PEFR is 80% or higher.
- Yellow zone: If 50 to 80% of PEFR and symptoms are present, use a SABA.
  - If this fails to return patient to green zone, PO steroids for four days may be used.
- Red zone: If PEFR is less than 50% and symptoms present at rest, use a SABA.
  - If PEFR remains below 50%, seek medical help.

New Guidelines
- Look at number of ER visits each year.
- Look at number of rescue inhalers needed per year.
- Look at how asthma is impacting quality of life.
- Regular visits with accurate patient history and spirometry are the best indicators, along with biomarkers and bronchial thermoplasty.
- Goal is to assess ICS use and limit SABA rescue to twice a week.
  - Consider biologics and long-acting muscarinic antagonists

Treatment of Asthma
- Other Strategies for the Patient with Asthma

What Else Do We See in the Asthma Patient?
- 60 to 80% of patients with allergic asthma have rhinosinusitis (10 to 20% of the general population).
- In pediatric patients with severe atopic dermatitis, 100% developed inhalant allergen sensitivity and 75% developed allergic respiratory disease.

What Else Do We See in the Asthma Patient?
- Four to eight percent of asthma patients also have food allergies (one to two percent of the general population).
- 60 to 80% of pediatric asthma patients also have gastroesophageal reflux disease (GERD). Nocturnal wheezing may be related to GERD.
- Exercise-induced bronchospasm occurs in 90% of people with asthma.
  - May be an indicator of poor asthma control.
What Else Do We See in the Asthma Patient?

- Childhood obesity is linked to asthma and increased IgE levels.
- If a child had pneumonia in infancy and received antibiotics, the risk of developing childhood asthma is increased 2.5-fold.

Control Household Triggers

- Encase patient's pillow, mattress and box spring in an allergen impermeable cover.
- Wash all bedding and stuffed animals weekly in hot water wash cycle.
- Remove carpet or rugs from bedroom.
- No pets in the bedroom.
- Avoid sleeping or lying on upholstered furniture.
- Keep indoor humidity below 50%.

Long-Term Effects of Asthma

Asthma Summary

- What is the best way to assure a good outcome for your patient?
  - Assess control
  - Assess compliance
  - Assess capability
  - Check for comorbidities and treat
  - Follow spirometry over time
  - Use biomarkers to select and monitor therapy
  - Consider immunotherapy
- Treat asthma like the chronic disease it is. Reduction of inflammation is the key!

Influenza Vaccine Paradigms

- Very important in the patient with asthma (and all pediatric patients!)
- If the child did not receive 2 doses before July of the current year, dose with the current trivalent or quadrivalent vaccine
- If one dose was received prior to July 1, dose with one dose of the trivalent or quadrivalent vaccine.
  - Doses should be administered at least 4 weeks apart

Influenza Vaccine Comparisons

- For adults and older children, the recommended site of IM administration is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.
- Persons with a history of egg allergy may receive any licensed, recommended influenza vaccine appropriate for recipient's age and health status. Those who report having had reactions to egg involving symptoms other than urticaria, or who required epinephrine or another emergency medical intervention, should be vaccinated in an inpatient or outpatient medical setting, under the supervision of a healthcare provider who is able to recognize and manage severe allergic reactions.
Influenza Vaccine Comparisons

<table>
<thead>
<tr>
<th>Brand</th>
<th>Age</th>
<th>Allergies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afluria</td>
<td>≥ 5 years</td>
<td>Eggs, neomycin, polymyxin</td>
</tr>
<tr>
<td>Alurix Quadrivalent</td>
<td>≥ 5 years</td>
<td>Eggs, neomycin, polymyxin</td>
</tr>
<tr>
<td>FluMist Quadrivalent</td>
<td>2-49 years</td>
<td>Eggs, gelatin, arginine, gentamicin</td>
</tr>
<tr>
<td>FluLaval Quadrivalent</td>
<td>≥ 6 months</td>
<td>Eggs</td>
</tr>
<tr>
<td>Flucellvax Quadrivalent</td>
<td>≥ 4 years</td>
<td>Eggs</td>
</tr>
<tr>
<td>FluLaval Quadrivalent</td>
<td>6 mos-15 months, &gt; 3 yrs</td>
<td>Eggs</td>
</tr>
<tr>
<td>FluZone Quadrivalent</td>
<td>6 mos-35 months; &gt; 3 yrs</td>
<td>Eggs</td>
</tr>
</tbody>
</table>

Influenza Vaccine Comparisons—Egg Allergy

- If the patient has had a severe allergic reaction to the influenza vaccine (anaphylaxis), future receipt of the vaccine is contraindicated.
- If the patient experiences ONLY urticaria after eating eggs, administer the inactivated influenza vaccine (trivalent or quadrivalent) appropriate for age or the live, attenuated vaccine quadrivalent.
- In severe egg allergy, the above vaccines may be used, but only in the inpatient or outpatient setting with monitoring.

Other Respiratory Drugs

- Mometasone (Nasonex)
- Cetirizine (Zyrtec)
- Loratidine (Claritin)
- Good agents to use to limit rhinosinusitis. This will decrease asthma attacks.
- May be used prophylactically.

Drugs for Infection and Inflammation

- Topical nystatin
  - Antifungal for skin infections.
- Triamcinolone (Kenalog)
  - Used for skin lesions or atopic dermatitis.
- Bactroban topical ointment
  - Used for impetigo.

Ibuprofen vs. Acetaminophen

- Ibuprofen does 4 things: Antipyretic, anti-inflammatory, analgesic, and antiplatelet.
- Inhibits cyclooxygenase (COX) reversibly in the periphery (PNS) and central nervous systems (CNS).
- Watch renal function.
**Ibuprofen vs. Acetaminophen**

- Acetaminophen: Analgesic, antipyretic.
- Inhibits COX in the CNS only.
- Watch levels and monitor hepatic function.
- Age-based dosing.
- Watch for fever of unknown origin (FUO).

**Acetaminophen Dosing**

- 0-3 mos. 40 mg
- 4-11 mos. 80 mg
- 1-2 years 120 mg
- 2-3 years 160 mg
- 4-5 years 240 mg
- 6-8 years 320 mg
- 9-10 years 400 mg
- 11 years 480 mg
- Do not exceed five doses within 24 hours.

**Acetaminophen Dosing**

- Prescription acetaminophen preparations will contain no more than 325 mg of the drug per dose.
  - Over-the-counter (OTC) prescriptions may have higher dosage.
- Caution patients against using acetaminophen along with prescriptions that already have acetaminophen in them.
- Look for the paracetamol (APAP) label on cough syrups, elixirs, etc.

**Ibuprofen Dosing**

- 12-17 lbs. 50mg 6-11 mos.
- 18-23 lbs. 75mg 12-23 mos.
- 24-35 lbs. 100mg 2-3 years
- 36-47 lbs. 150 mg 4-5 years
- 48-59 lbs. 200 mg 6-8 years
- 60-71 lbs. 250 mg 9-10 years
- 72-95 lbs. 300 mg 11 years
- Do not use for more than 10 days.
- Dosage is based on weight is preferred to age.

**Hydrocodone/Codeine**

- Do not use hydrocodone or codeine-based cough syrups in children under 18 years of age.
- Codeine, Tramadol and Hydrocodone may cause excessive respiratory suppression and sedation in children.
  - No codeine or tramadol in children younger than 12 years of age.
  - In children 12-18 years of age, no codeine or tramadol in children who are obese, who have obstructive sleep apnea or lung disease.
Depression

- Affects about 5% of the pediatric population.
- Tends to run in families.
- Several signs and symptoms.
  - Low self-esteem, isolation, sadness, hopelessness, boredom, low energy, talk of suicide, physical complaints such as headaches and stomachaches, etc.
- Cognitive behavioral therapy, counseling, and drug therapy may all be considered.

Diagnosis of Depression

- A major depressive episode in children and adolescents typically includes at least 5 of the following symptoms (including at least 1 of the first 2) during the same 2-week period:
  - Depressed (or irritable) mood
  - Diminished interest or loss of pleasure in almost all activities
  - Sleep disturbance
  - Weight change, appetite disturbance, or failure to achieve expected weight gain
  - Decreased concentration or indecisiveness
  - Suicidal ideation or thoughts of death
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or inappropriate guilt

Treatment of Depression in Children

- Pharmacologic Strategies
  - In 2004, FDA called for Black Box warning on antidepressants for increased suicidal thoughts/tendencies especially in adolescent populations
  - Many of the drugs used in this age group were not approved for use
  - Mood improvement may take a month, but sense of hopelessness/suicidal thoughts may occur within days of treatment
  - Cognitive Behavioral Therapy should be offered as a strategy to children and adolescents with Major Depressive Disorder (MDD)

Antidepressants for Pediatric Use

- Three SSRIs are considered main use:
  - Fluoxetine, Sertraline and Escitalopram
  - Follow pediatric dosing ranges based on age and dose. Start low and escalate only based on approved ranges based on age. Not all SSRIs are approved for all age ranges.
  - SE include nausea, anorexia, headaches, insomnia, anxiety; is a major inhibitor of certain liver enzymes
  - Follow-up!

Antidepressants for Pediatric Use

- Use of other SSRIs and other drugs such as citalopram, and fluvoxamine is considered off-label. Paroxetine is not indicated in children due to increased suicidal thoughts; may be used for OCD
  - Start with lowest dose possible!
  - GI side effects, insomnia and anxiety are especially worrisome.
  - TCAs and MAOIs: use with caution, use is considered unlabeled

How Long Should Therapy Last?

- Within the first year of therapy, consider withdrawing the patient
- In mild cases, psychosocial interventions should occur; in more severe cases, psychosocial interventions should be an adjunct to medication
- Risk assessment and continued monitoring are key to successful therapy
- If relapse is imminent….restart!
Psychosis - Schizophrenia
- Usually seen in children older than 12 years of age.
- Signs and symptoms include delusions, hallucinations, disorganized speech, disorganized behavior, and negative symptoms.
- Rule out bipolar disorder, substance abuse, and other medical causes.
- Genetics play a role.

Antipsychotics
- First generation: Effective against symptoms of schizophrenia.
- Sometimes used to treat nausea and vomiting.
- Also used to treat mania in bipolar affective disorder (BPAD), Tourette syndrome, dementia, and Huntington's disease.

Antipsychotics
- Causes various side effects, most notably extrapyramidal symptoms (EPS).
  - Acute dystonia (within hours, up to five days)
  - Parkinsonism (five to 30 days)
  - Akathisia (five to 60 days)
  - Tardive dyskinesia (months to years)

First-Generation Antipsychotics (FGAs)
- Chlorpromazine (Thorazine)
- Thioridazine (Mellaril)
- Loxapine (Loxitane)
- Molindone (Moban)
- Perphenazine
- Trifluoperazine
- Thiothixene (Navane)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)
- Pimozide (Orap)

Antipsychotics
- FGAs range in potency.
  - Low-potency: Chlorpromazine (Thorazine)
  - Medium-potency: Molindone (Moban)
  - High-potency: Haloperidol (Haldol)
- High-potency agents actually cause fewer side effects overall, and are preferred for initial therapy.
- Some even approved for young children.

Drugs for Psychosis
- What's new: Expanding antipsychotic drug use in young people
  - For schizophrenia, bipolar, autism
- Approved are aripiprazole, olanzepine, quetiapine, risperidone for bipolar mania and schizophrenia
- Aripiprazole and risperidone are approved for aggression associated with autism
Second Generation Antipsychotics (SGAs)
- Clozapine (Clozaril, FazaClo)
- Olanzepine (Zyprexa)
- Risperidone (Risperdal)
- Paliperidone (Invega)
- Quetiapine (Seroquel)
- Ziprasidone (Geodon)
- Aripiprazole (Abilify)

Antipsychotics
- Clozapine is the most effective drug for schizophrenia, but it can cause agranulocytosis and myocarditis (BBW).
- All SGAs cause side effects.
  - Metabolic effects include weight gain, dyslipidemia, and diabetes.
  - Some can cause seizures and anticholinergic effects.
- EPS are far less.

Side Effects of Antipsychotics in Children
- Greater incidence than seen in adults.
- Sedation
- EPS (except for akathisia)
- Withdrawal dyskinesia.
- Prolactin elevation.
- Weight gain and metabolic abnormalities.
  - dyslipidemia

How Much Weight Do Kids Gain?
- Normally after 10.8 weeks.
- Olanzepine - 18.7 lbs.
- Quetiapine - 13.4 lbs.
- Risperidone - 11.7 lbs.
- Aripiprazole - 9.7 lbs.
- Lipids, glucose, and insulin were variously affected, depending on agent.
- Must weigh benefit vs. cardiometabolic risks.

What are Prescription Stimulants?
- A class of drugs that enhances brain activity.
- Prescription stimulants were used historically to treat asthma, obesity, neurological disorders, and a variety of other ailments before their potential for abuse and addiction became apparent.
ADHD and Stimulants

- Most common neuropsychiatric syndrome in children.
  - More than two million children are affected in the U.S.
  - Incidence in boys is two to three times than in girls.
  - Symptoms usually appear between three to seven years of age.
  - Symptoms may persist into adolescence and adulthood.
- Ritalin is the most prescribed drug.

What are the Effects of Stimulants?

- Stimulants increase the amount of norepinephrine and dopamine in the brain, which increases blood glucose, breathing, blood pressure and heart rate, and constricts blood vessels.
- Effects can feel like increased alertness, attention, and energy, along with a sense of euphoria.

Usually Prescribed For:

- Narcolepsy
- ADHD - hyperactivity, impulsivity, and inability to concentrate.
- Depression that does not respond to other treatment.

Effects in the Body

- Stimulants enhance brain activity, causing an increase in alertness, attention, and energy.
- As a result, they are prescribed for use first thing in the morning.
- In abuse, they may be used to offset sleepiness late in the day.

In Normal Use

- Normal users of stimulants should take them once a day.
- Drug holidays are encouraged.
  - Weekends
  - School holidays
  - Spring break, Christmas, Summer vacation
- Regular assessment should be done to determine if continued use is necessary.

Effects of Short-Term Use

- Elevated blood pressure
- Increased heart rate
- Increased respiration
- Suppressed appetite
- Sleep deprivation
- A “wearing off” effect as short-term drugs stop working. This can be lessened with caffeine (soda, coffee, energy drinks, etc.)
Effects of Long-Term Use

- Potential for physical dependence and addiction.
- Stimulants have many “desirable” gains, such as increased alertness, attention, and weight loss.
- Euphoric feelings are most intense when the user snorts or injects the drug.
- Increased risk for cardiovascular effects, seizures, paranoia, hostility, and agitation.

Stimulants

- Dextroamphetamine (Dexedrine, Dextrostat)
- Methylphenidate (Ritalin, Metadate, Methylin, Concerta, and Daytrana)
- Dexmethylphenidate (Focalin)
- Amphetamine mixture (Adderall)
- Lisdexamfetamine (Vyvanse)
- Note: Atomoxetine (Strattera) is a non-stimulant.
  - Potential for abuse is lower because results take about a week to be seen.

Drugs and Duration

- Ritalin, Methylin: 3 to 5 hours
- Ritalin SR, Metadate ER, Methylin ER: 6 to 8 hours
- Concerta, Metadate CD, Ritalin LA: Up to 14 hours.
- Focalin: 4 to 5 hours
- Focalin XR: Up to 12 hours
- Dexedrine, DextroStat: 4 to 6 hours

Drugs and Duration

- Dexedrine Spansule: 6 to 10 hours
- Adderall: 4 to 6 hours
- Adderall XR: 10 to 12 hours
- Vyvanse: 10 to 12 hours
- Strattera: 24 hours

Potential Side Effects

- Dangerously high body temperature or an irregular heartbeat after taking high doses.
- Cardiovascular failure or lethal seizures.
- With some stimulants, hostility or feelings of paranoia after taking high doses repeatedly over a short period of time may occur.

Drug Interactions With Stimulants

- OTC decongestant medications (Sudafed, Phenylephrine): High BP, irregular HR.
- Antidepressants, unless supervised by a physician (Nardil, Prozac, Paxil): Psychosis, high HR.
- Some asthma medications (Proventil): High HR.
- Any drug that raises blood pressure is a dangerous combination (energy drinks?)
- Any drug that affects mood, including alcohol, should be assessed.
Methylphenidate – Abuse and Risks
- Diversion and abuse of Methylphenidate
  - Street names include Jif, R-ball, Skippy, the smart drug, vitamin R, and kiddie cocaine.
  - Injected, swallowed, or snorted.
  - May cause an increase or decrease in blood pressure, psychotic episodes, digestive problems, weight loss, and loss of appetite.

Judicious Prescribing of Stimulants
- Goals are to increase attention span and decrease impulsivity, hyperactivity, and distractibility.
  - Most children do well for two to three years on stimulants, then the drugs have little benefit.
    - This may be enough time for child to learn strategies for dealing with impulse and hyperactivity issues.
    - Cognitive therapy plus stimulants appears to be the most helpful.
    - Assess.

Guanfacine for ADHD
- Guanfacine (Intuniv) is approved to treat ADHD.
  - Extended release alpha-adrenergic agonist that works in the CNS on the alpha-2 receptor.
    - Approved for children age six and up.
    - Start with 1 mg daily.
    - Do not use with other antihypertensives.
    - Monitor heart rate and BP.
    - May cause sedation, dizziness, somnolence, and bradycardia.

Clonidine (Kapvay) for ADHD
- Approved for children age six and up.
  - 0.1 and 0.2 mg extended release tablets.
  - May be used alone, or with methylphenidate or amphetamine.
  - Somnolence, fatigue, URIs, and throat pain are common side effects.
    - Watch for respiratory depression.
  - Caution with other sedatives or antihypertensives.
  - Do not abruptly discontinue use.

Drugs With Pediatric Indications
- Best Pharmaceuticals for Children Act
  - Encourages companies to do pediatric research on drugs with pediatric indications.
  - Enhances safety of these agents.
  - Directs therapy to pediatric populations.

Pediatric Drugs - Summary
- Drugs for infection, asthma, pain, and fever are the top drugs for children.
- For older children, psychotropic drugs are commonly prescribed.
- Because of metabolic and excretory differences, dosing adjustments have to be considered for children.
- Not all adult drugs can be used in children, but increasingly “adult conditions” are being diagnosed in children.
Pediatric Drugs - Summary

- Be aware of drugs with pediatric uses and indications.
  - Ever changing indications and safety updates, including BBW
- Be aware of drugs that are NOT approved for pediatric use.