Top Pediatric Medications

How to Use Them Safely
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Common Pediatric Conditions

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

Conditions of Interest

- Hyperlipidemia
- Psychosis
- Autism
- Depression

Factors Unique to Pediatric Pharmacology

- Babies
  - 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 Twenty Drugs Prescribed in Pediatric Medicine

- Amoxicillin
- Cetirizine (Zyrtec)
- Albuterol for inhalation
- Azithromycin (Zithromax)
- Children’s Motrin
- Cefdinir (Omnicef)
- Mometasone (Nasonex)
- Montelukast (Singulair)
- Hydroxyzine (Atarax)
- Ciprofloxacin/dexamethasone (Ciprodex Otic)
- Amoxicillin/clavulanate (Augmentin)
- Budesonide (Pulmicort)
- Mupirocin (Bactroban Topical)
- Prednisolone (Orapred Oral Liquid)
- TMP/sulfa (Bactrim Pediatric)
- Triamcinolone (Kenalog)

### Drugs by Classification

- **Infection**
  - Amoxicillin
  - Zithromax
  - Omnicef
  - Ciprodex
  - Augmentin
  - Bactroban
  - Bactrim
  - Nystatin

- **Asthma/Allergy**
  - Zyrtec
  - Albuterol Inhalation
  - Nasonex
  - Singulair
  - Pulmicort
  - Claritin
  - Orapred
  - Kenalog

- **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.

- 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.

- 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.
  - Observation if not severe even with a certain diagnosis. If diagnosis is uncertain, observe patient.

AOM: When to Treat

AOM Drugs of Choice

- Amoxicillin 40 to 45 mg/kg twice a 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
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.

Asthma Prevalence

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

In asthma, muscles tighten, lining swells, and mucus increases.

Triggers for Asthma

- Dust
- Dander
- Mold/Mildew
- Pollen
- Cold air
- Tobacco or other smoke
- Pollutants
- Exercise

Mold and Mildew

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)

- Serevent Diskus (salmeterol xinafoate)
- Symbicort (budesonide/formoterol)
- Ventolin HFA (albuterol sulfate)
- Xopenex (levosalbuterol HCl)
- Xopenex concentrate
- Xopenex HFA

- 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.
- 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.
- 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 Twixthaler), 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.
- Monitor for infections.
- 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.
- 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

- Newest IgE antagonist.
  - Can reduce up to 96% of IgE in blood.
  - Only approved for adults and children older than 12 years of age with a positive skin test for aeroallergen not controlled by a steroid.
  - Has a black box warning for anaphylactic responses.
  - Subcutaneous injection, typically costs $10,000/year.
  - 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 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 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**
  - Asthma is well-controlled for three months.

Treatment

- All patients should have a SABA for rescue and for symptoms.
- Step-down is preferred approach.

Treatment of Asthma

- Monitoring Drug Efficacy

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.

Flow Meter Monitoring

- Flow meter monitoring
  - Zone monitoring.
Patient Education: How to use a Flow Meter

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.
- Goal is to increase ICS and limit SABA rescue to twice a week.

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.
- Adults taking statins have a much lower rate of hospitalization due to asthma exacerbation.
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%.

The Allergy-Proof Bed

Filters to Reduce Allergens

Regular Cleaning…

Limit Exposure to Pets

Check for Comorbidities
Long-Term Effects of Asthma

Summary
• What is the best way to ensure a good outcome for your patient?
  ◦ Assess control.
  ◦ Assess compliance.
  ◦ Assess capability.
  ◦ Check for comorbidities and treat.
• Treat asthma like the chronic disease it is. Reduction of inflammation is the goal.

Other Respiratory Drugs
• Nasonex
• Zyrtec
• Claritin
• Good agents to use to limit rhinosinusitis and 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.

**Interesting Link**
- Acetaminophen use was recently linked to the development and worsening of:
  - Rhinoconjunctivitis
  - Eczema
  - Asthma
- Patients studied were 13- to 14-year-old adolescents from countries worldwide.

**Ibuprofen Dosing**
- 12-17 lbs. 50 mg 6-11 mos.
- 18-23 lbs. 75 mg 12-23 mos.
- 24-35 lbs. 100 mg 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.

**Treatment of Psychiatric Syndromes in Children**
**Depression, ADHD, Psychosis, and Autism - Updates**

**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.
Treatment of Depression in Children

- Pharmacologic Strategies
  - In 2004, the U.S. Food and Drug Administration (FDA) called for a black box warning on antidepressants due to increased suicidal thoughts and 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 a sense of hopelessness and suicidal thoughts may occur within days of treatment.

Antidepressants for Pediatric Use

- How many are approved?

Antidepressants for Pediatric Use

- Fluoxetine (Prozac) and escitalopram (Lexapro).
  - Prozac starting dose is 10 mg/day, max dose is 60 mg/day.
  - Lexapro dose is 10 mg/day.
  - Side effects include nausea, anorexia, headaches, insomnia, and anxiety.
  - Major inhibitor of certain liver enzymes.
  - Follow-up.

Antidepressants for Pediatric Use

- But other drugs are used, right?
  - Use of sertraline, citalopram, and fluvoxamine are considered off-label.
  - Paroxetine is not indicated in children due to increased suicidal thoughts.
  - May be used to treat for obsessive compulsive disorder (OCD).

Antidepressants for Pediatric Use

- Start with the 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.
- 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
  - Schizophrenia, BPAD, and autism.
- Approved for mania associated with BPAD and schizophrenia: Aripiprazole, olanzapine, quetiapine, and risperidone.
- 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.
- 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.

Percentage of Obese Children

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 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.

A Brief History

- ADHD was called Minimal Brain Dysfunction before the Diagnostic and Statistical Manual of Mental Disorders (DSM) renamed it.
  - ADD vs. ADHD
- Ritalin was a drug looking for a disorder.
- Guess which nation consumes 85% of the world’s Ritalin?

Who Takes the Most Ritalin?

- United States Taps World Consumption of Ritalin

Ritalin Use Through the Ages

- Ritalin Use on the Rise in America

Federal Classification and Penalties

- Many stimulants are Schedule II
  - Schedule II drugs must have a written prescription to be refilled.
  - One month supply only.
  - Class A felony for illicit trading in these drugs.
- Strattera (atomoxetine) is an exception; it is a non-controlled substance.

Ritalin as a Drug of Abuse

- Ritalin prescriptions have increased 1000% in the past decade.
- Ritalin is the most stolen controlled substance in the U.S.
- Permanent lung damage can result from injected Ritalin.
- Loss of nasal cartilage and nose bleeds are seen with snorted Ritalin.
Ritalin in the Schoolyard

- Sold for about $10 per pill.
- Usually crushed and snorted to give a high like cocaine.
- Sometimes called “kiddie cocaine”.
- Kids can “cheek” the medicine if given at home to snort it or sell it later.
- When coming down from the drug, agitation, depression, and mood swings may be seen.

Snorting Ritalin

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

- Dextroamphetamine 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.

Ritalin – Abuse and Risks

- 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) was recently 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.
New Approvals for Pediatric Drugs

- Escitalopram (Lexapro): Approved for major depressive disorders in adolescents 12 to 17 years of age.
- Almotriptan (Axert): For acute pediatric migraine in adolescents age 12 to 17.
- Levocetirizine (Xyzal): Antihistamine approved for children aged 2 and older for seasonal allergic rhinitis.
- Azelastine nasal spray (Astepro): For allergic rhinitis in children 12 and older.
- Bepotastine (Bepreve): For itching due to allergic conjunctivitis in children aged two to ten years of age.

Valganciclovir (Valcyte): Prevents cytomegalovirus (CMV) in pediatric transplant patients.

Guanfacine (Intuniv): Extended release alpha-adrenergic agonist for the treatment of ADHD.

Colesvelam (Welchol) and rosuvastatin (Crestor): Now approved for children 10 years and older with familial hypercholesterolemia.

New Approvals for Pediatric Drugs

- HPV vaccine (Gardasil) now indicated for males six to 26 years of age.
- Aripiprazole (Abilify) approved for irritability associated with autism.
- Olanzepine (Zyprexa) and quetiapine (Seroquel) approved to treat bipolar disorder in children 13 to 17 years of age. Quetiapine used for bipolar mania in children 10 to 17 years of age.

Antipsychotics

- Labeling revisions
- Olanzepine (Zyprexa) and ziprasidone (Geodon) are atypical antipsychotics that may cause leukopenia or neutropenia.
  - Agranulocytosis has been reported.
  - Monitor patients at risk, perform CBC, and discontinue at first sign of alterations.
  - All SGAs now carry this warning.

New Safety Warnings

- Metoclopramide (Reglan) may cause tardive dyskinesia with prolonged therapy.
  - Do not use longer than 12 weeks.
- Atomoxetine (Strattera)
  - Warning was added to monitor for severe liver disease.
- HPV vaccine (Gardasil) may cause syncope with dosing.
  - Observe patients for 15 minutes after giving the vaccine.

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.
Pediatric Drugs - Summary

- Be aware of drugs with pediatric uses and indications.
- Be aware of drugs that are NOT approved for pediatric use.