Conflict of Interest Disclosures

- I have nothing to disclose

Learning Objectives

1. Review the etiology and epidemiology for heart, liver, lung, kidney, pancreas, and intestinal transplantation.
2. Discuss the advantages and disadvantages of induction and maintenance and immunosuppressant strategies.
3. Describe appropriate surgical prophylaxis as well as bacterial, fungal and viral prophylaxis post solid organ transplantation.
4. Formulate prophylaxis and immunosuppressant treatment regimens for solid organ transplant recipients.
5. Compare and contrast drug interactions and adverse event profiles of typical transplant medications.
6. Review and understand treatment options for patients who are refractory to standard therapies and determine the best option based on patient’s medication profile.
7. Demonstrate the need to understand and appreciate the potential drug-drug interactions among transplant medications and other medications in a recipient’s profile used to treat concomitant illnesses.
8. Educate patients, caregivers, and prescribers regarding appropriate use and toxicities of immunosuppressant pharmacologic agents.

Chapter Outline

- Solid organ transplant overview
- Etiology and epidemiology of end-stage disease leading to transplant
- Immunosuppressive therapies
- Infectious prophylaxis
- Immunosuppressive pharmacotherapy management key issues

Transplant Immunology 101
Cells of the Immune System

Antigen Presenting Cell (APC)

T cell

B cell

Transplanted Organ

- The transplanted organ is made up of antigens (Ag)
- Antigen: protein; causes the production of an antibody

Transplant Immunology 101

1. The antigen presenting cell (APC) envelops circulating antigen
2. The antigen is processed within the APC into small protein fragments called peptides

Transplant Immunology 101

3. The peptides bind to human leukocyte antigen (HLA)
4. The HLA/peptide complex migrate to the cell membrane of the APC

Transplant Immunology 101

5. The APC presents the HLA/peptide complex to T cells
6. T cell receptors (TCR) on T cells recognize a specific HLA/peptide
7. T cell activates and initiates proliferation via a complex pathway

T cell Activation

- Cytokines
- Calcineurin
- DNA synthesis
- IL-2
- IL-2 gene
- NF-AT
- T cell
B cell activation

8. Cytokines activate and induce proliferation of B cells
9. B cells produce antibodies specific to the antigen

Immunosuppressive Therapies (ISP)

- Goals of therapy
  - To use a multidrug approach to target various stages of the immune cascade to prevent and/or decrease the incidence of acute and chronic rejection while minimizing toxicities

ISP Therapies: Categories of Regimens

- “Ideal” immunosuppressant
  - Selectively inhibit immune system
  - Prevent allograft rejection
  - Free of adverse events
  - Few drug interactions

ISP Therapies: Induction

- Administration of selective, potent agents during the initial period of allograft placement
  - To decrease risk of acute rejection especially in high risk patient populations (e.g. high immunologic risk, history of prior transplant, extended cold ischemic times, donation from extended donor types)
  - To minimize and/or delay the use of maintenance therapy

ISP Therapies: Induction

- Use not considered mandatory
- May lead to increased risk of infection and certain types of cancer
- Decision to use
  - Specific (organ-specific, patient-specific and center-specific)
  - Risk versus benefit

Points to consider:
1) FDA indications are included in chapter; however many ISP therapies are used off label.
2) Dosing recommendations AND dose adjustment for toxicities included in chapter are per prescribing guidelines and may vary within the clinical setting
### ISP Therapies: Induction

<table>
<thead>
<tr>
<th>Agent</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basiliximab</td>
<td>T cells</td>
</tr>
<tr>
<td>Muromonab-CD3</td>
<td>T cells</td>
</tr>
<tr>
<td>Antithymocyte globulin equine</td>
<td>T cells, CD4, CD6, CD8, CD10, CD20, CD25, CD44, HLA class I and DR subsets</td>
</tr>
<tr>
<td>Antithymocyte globulin rabbit</td>
<td>T cells, CD2, CD3, CD4, CD8, CD25, CD28, CD48, HLA class I and DR subsets</td>
</tr>
</tbody>
</table>

### ISP Therapies: Induction

<table>
<thead>
<tr>
<th>Agent</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab</td>
<td>T &amp; B cells, monocytes, macrophages, natural killer cells, granulocytes</td>
</tr>
<tr>
<td>Rituximab</td>
<td>B cells</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Proteosomes</td>
</tr>
<tr>
<td>Eculizumab</td>
<td>Complement protein C5 Membrane attack complex</td>
</tr>
<tr>
<td>Intravenous immunoglobulin</td>
<td>Antibodies</td>
</tr>
</tbody>
</table>

### ISP Therapies: Induction

- Summary of trends over the past decade (OPTN/SRTR)

### Solid Organ Transplant

- Data in chapter is adapted from OPTN/SRTR 2010 annual report
- OPTN: Organ Procurement and Transplant Network
- SRTR: Scientific Registry of Transplant Recipients
- National database of statistics related to solid organ transplant
- Publication of U.S. Department of Health and Human Services
- Includes comprehensive data during the previous 10 years (2000-2009)
**Induction ISP: Trend summary**
- Induction is not used in all transplants performed
- 2009: antithymocyte globulin rabbit (Thymoglobulin®) was most commonly used agent, across all organ types
- Muromonab-CD3 (Orthoclone OKT3) is seldom used in clinical practice today
- Simultaneous pancreas kidney (SPK) transplant has the highest incidence of induction use (87.4% in 2009)
- Liver transplant has the highest incidence on NO induction use (74.1% in 2009)

**ISP Therapies: Categories of Regimens**
- Induction
- Maintenance
- Rejection

**ISP Therapies: Maintenance**
- Long-term regimen (“lifelong”) initiated within the early post-operative period
- Typically
  - Combines two or more medications from different drug classes with different mechanisms of action
  - Includes: calcineurin inhibitor (CNI), antimetabolite & corticosteroids
  - Selected for individual patient to minimize toxicities, prevent adverse events and decrease risk of exacerbating comorbidities

**Calcineurin Inhibitors (CNI)**
- Cyclosporine (Sandimmune, Neoral, Gengraf etc.)
- Tacrolimus (Prograf)

**Corticosteroids**
- Prednisone (Deltasone)
- Methylprednisolone (Solu-medrol, Medrol)
- Dexamethasone (Decadron)

**Antimetabolites**
- Azathioprine (Imuran)
- Mycophenolate mofetil (Cellcept)
- Mycophenolic sodium (Myfortic)

**mTOR inhibitors**
- Sirolimus (Rapamune)
- Everolimus (Zortress)

**Tcell fusion protein**
- Belatacept (Nulojix)

**Maintenance: Tacrolimus**
- **Mechanism of action**
  - Forms complex with FK-binding protein 12, which binds to and inhibits calcineurin phosphatase

- **Dosing**
  - 0.01 to 0.03 mg/kg/day in two divided doses (dose adjust for toxicities)
  - Varies based on organ type, length of time post transplant, concomitant ISP and comorbidities

- **Formulations**
  - IV and oral (0.5, 1.0 and 5.0 mg capsules)
  - NOT bioequivalent
  - Generics available
**Maintenance: Tacrolimus**

- Therapeutic drug monitoring (efficacy and toxicity)
  - Tacrolimus whole blood trough concentrations
    - Obtain 12 hours after last administered dose
    - Target typically ranges from 5 - 20 ng/mL
      - Depends on type of organ transplanted, elapsed time since transplant and should be individualized
    - When to perform?

**Tacrolimus trough monitoring**

- Dose taken at 8:00pm, what time should trough be drawn?

**Maintenance: Cyclosporine**

- Agents
  - CyA (Sandimmune); first approved 1983, variable absorption
  - CyA modified (Neoral, Gengraf); approved in 1994, improved PK profile
    - NOTE: Gengraf is brand-name generic drug
  - Products are NOT bioequivalent and should NOT be used interchangeably

**Maintenance: Cyclosporine**

- Mechanism of action
  - Forms complex with cyclophilin protein, which binds to and inhibits calcineurin phosphatase

**Updates in Therapeutics® 2012:**

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Maintenance: Cyclosporine

- Dosing
  - 4–18 mg/kg/day in two divided doses (dose adjust for toxicities)
  - Varies based on organ type, length of time post-transplant, concomitant ISP and comorbidities

- Formulations
  - CyA: IV and oral (capsules and solution)
  - CyA modified: oral (capsules and solution)
  - Generics available

Maintenance: Selection of CNI

- Cyclosporine or tacrolimus?
  - Efficacy – conflicting study reports
  - Adverse event profiles

Maintenance: Cyclosporine

- Therapeutic drug monitoring (efficacy and toxicity)
  - CyA whole blood trough concentrations
    - Obtain 12 hours after last administered dose
    - Target typically ranges from 50 – 400 ng/mL
    - Depends on type of organ transplanted, elapsed time since transplant and should be individualized
    - When to perform?

Maintenance: Selection of CNI

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Tacrolimus</th>
<th>Cyclosporine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrotoxicity</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Hypertension</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Malignancy</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Mucositis</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>GI adverse effects</td>
<td>±</td>
<td>±</td>
</tr>
</tbody>
</table>

Note: ± = posttransplant.
5 = low incidence; 1 = moderate incidence; 10 = high incidence.

Maintenance: CNI’s and nephrotoxicity

- CNIs remain cornerstone of ISP regimens despite recognition of renal impairment caused by their nephrotoxic effects
- Protocols developed to alter CNI exposure
  - CNI avoidance: eliminate CNI
  - CNI minimization: reduce CNI
  - Efficacy and utility of these strategies remains to be elucidated, thus to date there are no clear recommendations

Maintenance: CNI’s and metabolism

- Substrates of cytochrome P4503A4 isozyme system and p-glycoprotein.
- Significant drug interactions have been reported when additional medications metabolized by the same pathway are administered concurrently
  - Inhibition ↑ whole blood concentrations
  - Induction ↓ whole blood concentrations
Maintenance: Corticosteroids

**Agents**
- Prednisone (Deltasone)
- Methylprednisolone (Solu-Medrol, Medrol)
- Dexamethasone (Decadron)

**Mechanism of action**
- Inhibits cytokine transcription, decreases T-cell activation and anti-inflammatory effects

**Dosing**
- Variable
  - Usually high-pulse doses during surgery and perioperatively; then tapered
- Not performed

**Adverse events**
- Hyperglycemia
- Weight gain
- Psychosis
- Fluid retention
- Peptic ulcer
- Osteoporosis
- Cataracts
- Acne
- Glaucoma
- Growth retardation
- Mood swings
- Hypernatremia
- Hypokalemia
- GI upset

**Maintenance Therapy**

**Calcineurin Inhibitors**
- Cyclosporine (Sandimmune, Neoral, Gengraf etc.)
- Tacrolimus (Prograf)

**Corticosteroids**
- Prednisone (Deltasone)
- Methylprednisolone (Solu-Medrol, Medrol)
- Dexamethasone (Decadron)

**Antimetabolites**
- Azathioprine (Imuran®)
- Mycophenolate mofetil (Cellcept®)
- Mycophenolic acid (Myfortic®)

**mTOR inhibitors**
- Sirolimus (Rapamune®)
- Everolimus (Zortress®)

**T-cell fusion protein**
- LEA29Y (Belatacept®)

**Considered adjuvant to CNIs**

**Agents**
- Azathioprine (Imuran®)
- Mycophenolate mofetil (Cellcept®)
- Mycophenolic acid (Myfortic®)

**Adverse events**
- GI (diarrhea, nausea and vomiting)
- Myelosuppression
**Maintenance: Mycophenolate mofetil**

- **Mechanism of action**
  - Prodrug of mycophenolic acid (MPA)
  - MPA inhibits inosine monophosphate dehydrogenase and subsequent de novo purine synthesis; T cells are inhibited

- **Dosing**
  - 2000 - 3000 mg/day in two to four divided doses (dose adjust for toxicities)

- **Formulations**
  - IV and oral (250 and 500mg capsules/tablets)
  - Generics available

- **Therapeutic drug monitoring**
  - Can be done; however is not routinely performed
  - Monitor for signs of myelosuppression and GI adverse effects

---

**Maintenance: Mycophenolic sodium**

- **Dosing**
  - 1440 mg/day in two divided doses (dose adjust for toxicities)

- **Formulations**
  - Oral (180 and 360 mg tablets)

- **Therapeutic drug monitoring**
  - Not performed
  - Monitor for signs of myelosuppression and GI adverse effects

---

**Patient Case #1**

- **HPI:** M.D. is a 57 year old male liver transplant recipient presents to transplant clinic 14 months posttransplant with a fine tremor that he notices when trying to write or read the newspaper. In addition he mentions he has had diarrhea (more than four stools a day) for the past week or so.
Patient Case #1

During the visit you review his labs from last week and notice everything is normal except his tacrolimus level is 17 ng/mL.

ISP medications:
- Tacrolimus 4 mg twice daily
- Mycophenolate mofetil 500 mg twice daily

Which one of the following is the most appropriate course of action to resolve M.D.’s hand tremor?

A. Discontinue tacrolimus
B. ↓ dose of mycophenolate mofetil
C. Change tacrolimus to cyclosporine
D. ↓ dose of tacrolimus

Maintenance Therapy

Calcineurin Inhibitors
- Cyclosporine (Sandimmune, Neoral, Gengraf etc.)
- Tacrolimus (Prograf)

Corticosteroids
- Prednisone (Deltasone)
- Methylprednisolone (Solu-medrol, Medrol)
- Dexamethasone (Decadron)

Antimetabolites
- Azathioprine (Imuran)
- Mycophenolate mofetil (Cellcept)
- Mycophenolic sodium (Myfortic)

mTOR inhibitors
- Sirolimus (Rapamune®)
- Everolimus (Zortress®)

T-cell fusion protein
- Belatacept (Nulojix)

Maintenance: mTOR inhibitors

Mechanism of action
- Binds to and inhibits the activation of mTOR, which impairs IL-2 induced T-cell proliferation and activation

Adverse events
- Most common: Leukopenia, thrombocytopenia, hyperlipidemia and peripheral edema
- Delayed wound healing, rash, mouth ulcers
- FDA box warning
Maintenance: Sirolimus

- **Dosing**
  - Loading dose of 6mg, followed by 2 mg/day maintenance dose (dose adjust for toxicities)
  - Use of loading dose is varies; many centers do not load
- **Formulations**
  - Oral (0.5, 1 and 2 mg tablets), oral solution [1mg/ml])

Maintenance: Sirolimus

- **Therapeutic drug monitoring (efficacy and toxicity)**
  - Whole blood concentrations
  - Target typically ranges from 3–12 ng/mL
    - Depends on organ transplanted and elapsed time since transplant and should be individualized
  - When to perform?
    - Half-life is approx 62 hours (range 46–78 hours)

Maintenance: Sirolimus

- **When to use?**
  - Less nephrotoxic regimen
    - CNI minimization (in combination with CNI)
    - CNI avoidance (as an alternative to CNI)
    - Currently, clinical research trials are evaluating conversion from CNI to sirolimus to prevent CNI nephrotoxicity
  - Alternate adverse event profile
    - In place of CNI (switch to sirolimus due to CNI toxicity)

Maintenance: Everolimus

- **Structural analog of sirolimus**
- **Dosing**
  - 0.75 mg orally twice daily
- **Formulations**
  - Oral (0.25, 0.2 and 0.75 mg tablets)
- **Therapeutic drug monitoring (efficacy and toxicity)**
  - Whole blood drug concentrations
  - Recommended target range is 3–8 ng/mL
  - When to perform?

Maintenance: Comparison of mTORs

- **Sirolimus versus Everolimus?**
  - Comparative trials have not been performed
  - **Everolimus**
    - Requires twice daily dosing
    - Has a shorter half-life (approximately 30 hours)
    - Data suggestive of potential antiviral properties

Maintenance: mTOR’s and metabolism

- **Substrates of cytochrome P450 isozyme system and p-glycoprotein.**
- **Significant drug interactions have been reported when additional medications metabolized by the same pathway are administered concurrently**
  - Inhibition → whole blood concentrations
  - Induction ↓ whole blood concentrations
  - (Refer to Table 19)
**Maintenance Therapy**

**Calcineurin Inhibitors**
- Cyclosporine (Sandimmune, Neoral, Gengraf etc.)
- Tacrolimus (Prograf)

**Corticosteroids**
- Prednisone (Deltasone)
- Methylprednisolone (Solu-medrol, Medrol)
- Dexamethasone (Decadron)

**Antimetabolites**
- Azathioprine (Imuran)
- Mycophenolate mofetil (Cellcept)
- Mycophenolic sodium (Myfortic)

**mTOR inhibitors**
- Sirolimus (Rapamune)
- Everolimus (Zortress)

**T-cell fusion protein**
- Belatacept (Nulojix)

---

**Maintenance: Belatacept**

**Mechanism of action**
- Selective T-cell costimulation blocker
- Binds to CD80 and CD86 on APC; blocking CD28 mediated costimulation of T-cell activation

**Dosing**
- Based on actual body weight
  - Do NOT modify dose unless > 10% change in ABW

**Formulations**
- Available as IV infusion ONLY
  - Administer over 30 minutes

**Adverse Events**
- PTLD (EBV negative > EBV positive)
- Most common (≥20%)
  - Anemia, diarrhea, urinary tract infection, peripheral edema, constipation, hypertension, pyrexia, graft dysfunction, cough, nausea, vomiting, headache, hypokalemia, hyperkalemia, and leukopenia

---

**Maintenance: T-cell fusion proteins**

**Agents**
- Belatacept (Nulojix®)
  - Approved June 2011

**FDA indication**
- Prophylaxis of organ rejection in adult kidney transplant recipients in combination with basiliximab induction, mycophenolate mofetil and corticosteroids

**Limitations of use**
- Use ONLY in EBV+ positive patients

---

**Maintenance: Belatacept**

- **Mechanism of action**
- Selective T-cell costimulation blocker
- Binds to CD80 and CD86 on APC; blocking CD28 mediated costimulation of T-cell activation

- **Dosing**
  - Based on actual body weight
  - Do NOT modify dose unless > 10% change in ABW

<table>
<thead>
<tr>
<th>Table 11: Belatacept Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase</strong></td>
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<tr>
<td>Initial Phase</td>
</tr>
<tr>
<td>Initial Phase</td>
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<tr>
<td>Initial Phase</td>
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<td>Initial Phase</td>
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<td>Initial Phase</td>
</tr>
<tr>
<td>Initial Phase</td>
</tr>
</tbody>
</table>

---

**Maintenance: Belatacept**

**Therapeutic drug monitoring**
- NOT REQUIRED

**Adverse Events**
- PTLD (EBV negative > EBV positive)
- Most common (≥20%)
  - Anemia, diarrhea, urinary tract infection, peripheral edema, constipation, hypertension, pyrexia, graft dysfunction, cough, nausea, vomiting, headache, hypokalemia, hyperkalemia, and leukopenia
ISP Therapies: Maintenance

Summary of trends at hospital discharge (OPTN/SRTR)

- At 1 year, at least 60% of all recipients remain on corticosteroids.
- Sirolimus use increases from discharge to 1 year post transplant (0.4 – 14.3% versus 6 – 16.3%).
- Mycophenolic sodium use is variable, with kidney and SPK using the most by 1 year post.
- Azathioprine use is minimal; still often used in lung transplant (30%).

Patient Case #2

HPI: J.P. is a 47 year old female 10 months post SPK transplant, returns to posttransplant clinic with severe, persistent diarrhea (more than 6 stools per day). Previous diarrhea workups and a stool sample obtained last week was negative.

Laboratory: Scr 1.2 ng/mL (baseline 1.0 ng/mL); all others within normal limits.

Medications: cyclosporine 100 mg twice daily, mycophenolate mofetil 1000 mg twice daily, prednisone 7.5 mg daily, cilatrapam 10 mg daily, loratadine 10 mg once daily and zolpidem 10 mg once daily as needed for insomnia.

The medical team is convinced the diarrhea is caused by mycophenolate mofetil; what is the best option to modify J.P.’s current mycophenolate mofetil dose to address this issue?
**Patient Case #2**

Current dose: 1000 mg twice daily

- A. Increase dose to 1500 mg twice daily
- B. Discontinue therapy
- C. Increase the frequency of administration from twice daily to four times daily
- D. Continue the same dose and decrease the frequency to once daily

---

**Patient Case #3**

HPI: 62 year-old man received a liver transplant 3½ years ago secondary to HCV and hepatocellular carcinoma. He comes to clinic today because of an elevated SCr over the past few months; the hepatologist wants to bring him in to discuss options for changing him to a less nephrotoxic immunosuppressant regimen.

The decision is made at today’s appointment to initiate sirolimus in an attempt to decrease CNI exposure.

---

**ISP Therapies: Categories of Regimens**

- Induction
- Maintenance: No Guidelines!
- Rejection

---

**Immunology 101 - Rejection**

- T-cell mediated
  - T cells directly attack the transplanted organ
- Antibody mediated
  - Antibodies produced by B cells directly attack the transplanted organ

---

**ISP Therapies: Rejection**

- Rejection episodes classified according to:
  - Immune process
  - Time of occurrence post transplant:
    - Hyperacute – minutes to hours
    - Acute – days to weeks
    - Chronic – months to years
ISP Therapies: Rejection

- Treatment regimen options
  - T and/or B cell depleting (“induction”) agents often with corticosteroids
  - Corticosteroid boluses followed by a taper
  - Increase dose of maintenance medications (i.e. CNIs)

ISP Therapies: Rejection

- Treatment regimens vary according to
  - Immune system involved (T and/or B lymphocytes)
  - Rejection type (acute versus chronic)
  - Rejection severity (mild, moderate, or severe)
  - Type of organ transplanted
  - Risk/benefits to treatment
  - Transplant center

ISP Therapies: Rejection

- Additional points
  - “Recycle” prophylaxis
  - Adjust maintenance regimen?

Chapter Outline

- Solid organ transplant overview
- Etiology and epidemiology of end-stage disease leading to transplant
- Immunosuppressive therapies
  - Induction, maintenance and rejection
- Infectious prophylaxis
- Immunosuppressive pharmacotherapy management key issues

Infectious Prophylaxis

- Transplant recipients are highly susceptible to many infections due to compromised immunity.
- Infectious complications generally occur in a predictable pattern and can significantly increase morbidity and mortality, thus prevention is the fundamental management strategy.

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15
Infectious Prophylaxis

- **Antimicrobial**
  - Routine surgical prophylaxis
  - *Pneumocystis jiroveci*
  - Vaccination

- **Antifungal**

- **Antiviral**

Lack universal approach for prescribing practices

Chapter intended to highlight commonly used agents and likely regimens.

---

### Pneumocystis jiroveci

- Sulfamethoxazole/trimethoprim is recommended as first-line therapy
- 6 month duration has been shown to be safe and effective for most recipients, except lung where lifelong prophylaxis is typically recommended

---

### Vaccination

- Recommended to complete series PRE transplant
- LIVE vaccines are contraindicated POST transplant

---

**Table 15: Therapy Options for *Pneumocystis jiroveci* Prophylaxis in Adult Transplant Recipients**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Usual Dosing</th>
<th>Common Adverse Events</th>
</tr>
</thead>
</table>
| **First line**
  - Sulfamethoxazole/trimethoprim (Bactrim, Septra, SMX/trimethoprim)
  - One-week regimen (1000 mg SMX/600 mg TMP single/day twice daily) or
  - One-month regimen (1000 mg SMX/600 mg TMP single/day twice daily) |
| **Second line**
  - Pentamidine (NeuPrep) 500 mg intravenous every 3-4 weeks |
  - Trimethoprim (100 mg orally per day) |
  - Azithromycin (Mycoplasm) 500 mg intravenously weekly or daily |

---

**Table 16: Recommended Vaccines for Adult Transplant Recipients**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Advocate</th>
<th>Recomended in Transplant</th>
<th>Recommended in Transplant Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>influenza</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>hepatitis B</td>
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<td>Yes</td>
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</tr>
<tr>
<td>meningococcal, A</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Haemophilus influenzae, type b</td>
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<td>Yes</td>
</tr>
<tr>
<td>pneumococcus pneumonia</td>
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<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>rubeola</td>
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<tr>
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<td>Yes</td>
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</tr>
<tr>
<td>zoster</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
<tr>
<td>IPV*</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*IPV = Inactivated Poliovirus Vaccine

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16
Infectious Prophylaxis

- Anti-fungal
  - Typical: non-
    Albicans candida and Aspergillus
  - Management is highly variable across centers
  - Candida prophylaxis
    - Triazoles antifungals (i.e. fluconazole, itraconazole) or echinocandins (i.e. caspofungin, micafungin)
    - Triazoles inhibit CYP3A4 system, thus use results in potential DDIs with immunosuppressive agents

- Anti-viral
  - Cytomegalovirus continues to be problematic infection post transplant
  - Risk
    - Highest in CMV negative recipients that receive an organ from a CMV positive donor (D+/R-)
    - Highest during first 3-6 months post transplant
  - Optimal regimen remains undefined

<table>
<thead>
<tr>
<th>Infectious Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-fungal</strong></td>
</tr>
<tr>
<td>Typical: non-Albicans candida and Aspergillus</td>
</tr>
<tr>
<td>Management is highly variable across centers</td>
</tr>
<tr>
<td><strong>Candida prophylaxis</strong></td>
</tr>
<tr>
<td>Triazoles antifungals (i.e. fluconazole, itraconazole) or echinocandins (i.e. caspofungin, micafungin)</td>
</tr>
<tr>
<td>Triazoles inhibit CYP3A4 system, thus use results in potential DDIs with immunosuppressive agents</td>
</tr>
</tbody>
</table>

- **Candida albicans** (thrush) prophylaxis
  - Clotrimazole troches or nystatin suspension

- **Aspergillus** prophylaxis
  - Echinocandins or polyenes (i.e. amphotericin B, lipid based amphotericin B products)
ISP Pharmacotherapy: Key Issues

- ISP pharmacotherapy management is an important aspect of post-transplant patient care
  - ISP medications are for a lifetime
  - Optimal management is critical to positive long-term outcomes

ISP Key Issues: Drug–drug interactions

- Drug–drug interactions
- Accompanying morbidities
- Nonprescription/Complementary & alternative medications
- Patient/Caregiver education
- Use of generic immunosuppressants

ISP Key Issues: DDI

- Potential
  - ISP regimens typically contain 10-20 medications
  - CNI’s and mTOR’s metabolized via CYP3A4
- Significant consequences
  - Adverse events
  - Graft rejection
  - Decreased quality of life
- Management

ISP Key Issues: Comorbidities

- Despite advances in patient and graft survival, long-term morbidities continue to be problematic for transplant recipients
- Post-transplant pharmacotherapy has shifted its focus to include strategies aimed at minimizing toxicities and preventing/controlling comorbid disease progression

ISP Key Issues: Comorbidities

- Points to consider
  - First-line therapies for a particular disease may not be the optimal choice for a transplant recipient
  - Data from large general population trials may be used as a guide but must be done cautiously in this subpopulation

ISP Key Issues: OTCs and CAMs

- Points to consider
  - Medication reconciliation should include questions regarding the use of these agents
  - Educate transplant recipients and caregivers about the use and potential hazards
  - Stay up to date with published literature and develop standard recommendations regarding use
**ISP Key Points: Patient/Caregiver education**

- Points to consider
  - Education regarding ISP pharmacotherapy should be delivered frequently via multiple mechanisms and repeated often
  - Key topics
    - Adherence: definition, importance, and tools to improve
    - Notification: new medications and any medication changes

**ISP Key Points: Generics**

- Points to consider
  - Use with caution, on an individual basis, and especially consider when financial consequences are present
  - Assist the transplant team to ensure laboratory and clinical monitoring is adjusted when necessary
  - Include generic discussions when performing medication reconciliation

**Chapter Outline**

- Solid organ transplant overview
- Etiology and epidemiology of end-stage disease leading to transplant
- Immunosuppressive therapies
- Infectious prophylaxis
- Immunosuppressive pharmacotherapy management key issues

---

**Thank you!**

*Solid Organ Transplantation*

Tiffany E. Kaiser, Pharm.D., BCPS
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Immunizations
Ann M. Philbrick, Pharm.D., BCPS
University of Minnesota College of Pharmacy

Learning Objectives
- Differentiate between passive and active immunity.
- Compare and contrast live attenuated and inactivated vaccines and their subtypes.
- Describe the circumstances in which vaccines can be given concurrently and when they need to be separated.
- Describe vaccines that are routinely administered, including their route of administration, number of doses, indication, contraindications, and common adverse effects.
- Assess a patient’s vaccine history and recommend necessary vaccines.

Types of Immunity
- Passive
  - Mother to child
- Active
  - Survive infection
  - Vaccination
  - Usually permanent

Types of Vaccines
- Live Attenuated
  - Modified and weakened live virus
  - Adverse effects = similar to the vaccinated disease
  - Contraindicated: immunosuppressed, pregnant, < 1 year old
- Inactivated
  - Virus has been inactivated by heat or chemicals
  - Usually requires several doses
- Polysaccharide
  - Inactivated vaccine containing long chains of sugar molecules
  - Subtypes
    - Pure
    - Conjugate
- Recombinant
  - Uses a host to grow antigen
Patient Case #1

R.M. is a 22-year-old woman in pharmacy school. She has received the first two doses of the HPV, but unfortunately, between school and her job, it has been 8 months since her second dose. Which one of the following is the best plan for today?

A. Restart the series.
B. Give the final dose today.
C. Give a dose today and a booster in 4 weeks.
D. Do not give a dose because she is already immune.

Workbook Page 1-524; Answer: Page 1-552

Spacing

- No limit to the number of vaccines that can be given in one visit
- Live attenuated vaccines must be separated by 4 weeks
  - Does not apply to oral polio, rotavirus
- Inactivated vaccines can be given without regard to spacing
- Increasing the interval between doses will never diminish the effect

1-523 to 1-524

Patient Case #2

J.M. is a 12-month-old boy whose older brother is undergoing chemotherapy for leukemia. Which one of the following vaccine combinations is most likely to be given to J.M. at his 12-month visit?

A. LAIV and MCV4
B. MMR and LAIV
C. Hib and MMR
D. MCV4 and Hib

Workbook Page 1-526; Answer: Page 5-552

Adverse Reactions

- Local injection site reactions
- Systemic
- Allergic

1-524 to 1-525

Contraindications & Precautions

- Temporary – Live Vaccines
  - Pregnancy
  - Immune Suppression
- Permanent
  - Severe allergic reaction following previous dose
  - Encephalopathy not attributable to another cause within 7 days following pertussis vaccination

1-525 to 1-526
Invalid Contraindications

- Mild illness
- Antimicrobial therapy
- Disease exposure
- Household contact with pregnant or immunosuppressed person
- Breastfeeding
- Preterm birth
- Family history of adverse events
- Multiple simultaneous vaccines
- Current administration of tuberculin skin test

Patient Case #2

J.M. is a 12-month-old boy whose older brother is undergoing chemotherapy for leukemia. Which one of the following vaccine combinations is most likely to be given to J.M. at his 12-month visit?

- A. LAIV and MCV4
- B. MMR and LAIV
- C. Hib and MMR
- D. MCV4 and Hib

Workbook Page 1-525; Answer: Page 5-552

Patient Case #3

Which one of the following patients would be most appropriate to receive the live attenuated influenza vaccine?

- A. 16-year-old girl with asthma.
- B. 36-year-old man working in the oncology department.
- C. 52-year-old healthy man.
- D. 28-year-old pregnant woman.

Workbook Page 1-528; Answer: Page 1-552

Influenza

- Types of virus
  - Type A
    - Moderate to severe disease
    - All ages
  - Type B
    - Mild illness
    - Children
  - Type C
    - Rare

Workbook Page 1-526

Influenza

- Clinical features
  - Fever, chills
  - Cough
  - Sore throat
  - Runny/stuffy nose
  - Muscle and body aches
  - Headache
  - Fatigue
  - Vomiting/diarrhea

Workbook Page 1-526
Influenza

- Complications
  - Pneumonia
  - Reyes syndrome
  - Myocarditis
  - Worsening of bronchitis
  - Death

Influenza Vaccine

- Vaccine composition
  - Always contains 2 Type A, 1 Type B
- Naming
  - Type/origin/strain/year isolated (subtype)
- 2011 – 2012 Influenza Vaccine Composition
  - A/California/7/2009 (H1N1)
  - A/Perth/16/2009 (H3N2)
  - B/Brisbane/60/2008

Influenza Vaccine

- Inactivated Influenza Vaccine (TIV)
  - IM injection
  - Approved for all persons 6 months and older
  - Grown in chicken embryos
- Live attenuated influenza vaccine (LAIV)
  - Intranasal
  - Approved only for healthy patients, age 2-49
  - Contraindications

Influenza Vaccine

- Vaccination should begin October/November
- Who should be vaccinated?
  - All patients over 6 months who do not have a valid contraindication to vaccination
  - High risk:
    - Pregnancy
    - Seniors (50+)
    - Young children (< 5, but especially < 2)
    - Asthma / DM / other chronic conditions
    - Residents of nursing home/LTC facilities
    - People who live with or care for those at high risk

Patient Case #3

Which one of the following patients would be most appropriate to receive the live attenuated influenza vaccine?

A. 16-year-old girl with asthma.
B. 36-year-old man working in the oncology department.
C. 52-year-old healthy man.
D. 28-year-old pregnant woman.

Workbook Page 1-528; Answer: Page 1-552
Patient Case #4

D.S. is a 14-year-old boy recently given a diagnosis of asthma. Which one of the following pneumococcal vaccines would be the best to give to him at this time?

A. PCV13.
B. PPSV23.
C. Either vaccine is appropriate.
D. Neither vaccine is appropriate.

Workbook Page 1-530; Answer: Page 1-553

Pneumococcal Vaccine

- Used to prevent infection by *S. pneumoniae*
- IM injection
- Pneumococcal conjugate vaccine (PCV13)
  - 13 serotypes of pneumococcal bacteria
  - Recommended for all children < 2 years old
  - 4 dose series
    - 2, 4, 6 and 12-15 months
    - Also approved for use in ages 50 & over

Pneumococcal Vaccine

- Revaccination with PPSV23
  - Received < 65 years
    - Revaccinate at 65 years or in 5 years (whichever is longer)
    - Except patients with:
      - Chronic renal failure
      - Nephrotic syndrome
      - Functional/anatomic asplenia
      - Immunocompromised
  - Received > 65 years
    - Revaccinate in 5 years

- No one needs to be revaccinated more than once

Workbook Page 1-530; Answer: Page 1-553

Meningococcal Vaccine

- *Neisseria meningitidis*
  - Meningitis, sepsis, pneumonia, arthritis, otitis media
- IM administration
- Meningococcal polysaccharide vaccine (MPSV4)
  - Less effective than MCV4
  - Reserved for patients > 55 years old

Workbook Page 1-530; Answer: Page 1-553
Meningococcal Vaccine

- Meningococcal conjugate vaccine (MCV4, MenACWY-CRM)
  - Recommendations
    - All children at 11-12 year physical
    - As catch up for all children age 13 – 18
    - College age freshmen living in a dormitory
    - Patients age 2-54 at risk for meningococcal disease
      - Microbiologists
      - Military recruits
      - Travelers to endemic areas
      - Asplenia

Variella

- Variella zoster virus (VZV)
  - Primary: Chickenpox
  - Secondary: Shingles (Herpes zoster)

Herpes Zoster Vaccine

- Live attenuated
- SQ injection
- Same antigen as varicella vaccine – much higher dose
- Approved for ages 50 and older
- ACIP Recommendation
  - 1 dose after age 60
  - Regardless of history of shingles

Patient Case #5

J.S. is a 62-year-old woman who is worried about getting shingles because some friends from bridge club have gotten it. She tells you she has never had chickenpox. Which one of the following would be the best vaccine option to give to J.S. today?

- A. The varicella vaccine today.
- B. The HZV today.
- C. Varicella today and HZV in 4 weeks
- D. Neither vaccine because she does not meet the age requirements.

Workbook Page 1-534; Answer: Page 1-552
**Patient Case #6**

D.R. is a 29-year-old man who stepped on a nail while walking his dog yesterday. The last time he received a tetanus booster was right before he started college. Which one of the following forms of vaccine would be best to give D.R. today?

A. DTaP.
B. DT.
C. Td.
D. Tdap.

Workbook Page 1-537; Answer: Page 1-553

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**Patient Case #7**

M.C. is a 24-year-old woman with a medical history of genital warts. Which one of the following would be the best recommendation you could give her regarding the HPV?

A. Do not give; she already has HPV.
B. Do not give; she is too old for the vaccine.
C. Give; it would help future outbreaks.
D. Give; it could protect her from other HPV types.

Workbook Page 1-538; Answer: Page 1-552

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**Tetanus, Diptheria & Pertussis**

- Tetanus
  - Clostridium tetani
- Diptheria
  - Corynebacterium diphtheriae
- Pertussis
  - Bordetella pertussis

**Tetanus-Diphtheria-Pertussis Vaccines**

- Inactivated
- IM injection
- Capital letters indicate full-strength dose
- DTaP & DT
  - Larger doses of all 3 components
  - Approved for ages birth – 7 years
- Tdap & Td
  - Smaller doses of diphtheria & pertussis
  - Approved for ages 7 & older

1-534

1-536

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26
Human Papillomavirus (HPV) Vaccine

- HPV
  - Types 6 & 11 – cervical cell abnormalities, genital warts and laryngeal papillomas
  - Types 16 & 18 – cervical cancer
- Recombinant
- IM injection
- Types
  - Quadrivalent – HPV types 6, 11, 16 & 18
    - Approved for males & females age 9 – 26
  - Bivalent – HPV types 16 & 18
    - Approved for females age 9 - 26

Series of 3 doses
- Baseline, 1 & 6 months
- Give regardless of infection history
- Recommendations
  - Females
    - 11 – 12 year physical
    - 13 – 26 if not previously vaccinated
  - Quadrivalent/Bivalent decision is left to parent/patient
  - Males
    - 11-12 year physical
    - 13-26 if not previously vaccinated, or series was incomplete
    - 22-26 years

Patient Case #7
M.C. is a 24-year-old woman with a medical history of genital warts. Which one of the following would be the best recommendation you could give her regarding the HPV?

- A. Do not give; she already has HPV.
- B. Do not give; she is too old for the vaccine.
- C. Give; it would help future outbreaks.
- D. Give; it could protect her from other HPV types.

Workbook Page 1-538; Answer: Page 1-552

Measles, Mumps and Rubella

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cause</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Paramyxovirus</td>
<td>Rash</td>
</tr>
<tr>
<td>Mumps</td>
<td>Paramyxovirus</td>
<td>Parotitis</td>
</tr>
<tr>
<td>Rubella</td>
<td>Togavirus</td>
<td>Rash</td>
</tr>
</tbody>
</table>

MMR Vaccine

- Live attenuated
- Subcutaneous injection
- Series of 2 doses
- Recommendations
  - All children
    - First dose at 12 months
    - Second dose at 4 – 6 years (or earlier)
  - Adults
    - One dose if not vaccinated in childhood
    - Persons born before 1957 are considered immune

Hepatitis A Vaccine

- Prevents Hepatitis A infection
- Inactivated whole cell virus vaccine
- IM injection
- Two available vaccines
  - pediatric & adult versions
- Two doses, at least 6 months apart
- 100% seroconversion

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Hepatitis A Vaccine

**Recommendations**
- All children 12-23 months
- Catch up vaccination for persons at high risk:
  - Travelers to countries with a high rate of the disease
  - Men who have sex with men
  - Use of illicit drugs
  - Patients with chronic liver disease
  - Patients who are treated with clotting factor concentrates
  - Patients who work with hepatitis A–infected animals or in a hepatitis A research laboratory

Patient Case #8
Which one of the following people is most likely to get a hepatitis B vaccine?

- A. A 1-year-old female at her next check-up.
- B. A 38-year-old female with COPD.
- C. A 19-year-old male entering college.
- D. A 56-year-old male being considered for dialysis.

Workbook Page 1-543; Answer: Page 1-552

Hepatitis B Vaccine

- Recombinant
- IM injection
- Two formulations
  - Recombivax HB
    - Pediatric & adult formulations can be used at any age
  - Engerix-B
    - Pediatric formulation for patients <20 years
    - Adult formulation for patient >11 years
- 3 dose series
  - 2 dose alternative in 11 – 15 years

Patient Case #9
A.D. is a 13-month-old girl who is brought to your clinic for vaccines. You note that she has never received the Hib vaccine. You ask her parents, and they agree to this series. You carry the PRP-OMP vaccine in your clinic. Which one of the following is the best recommendation regarding A.D.’s Hib series?

- A. Give a total of three doses, at least 2 months apart, with a booster at 12–15 months.
- B. Give a total of two doses at least 2 months apart, with a booster at 12–15 months.
- C. Give one dose today and a booster in 2 months.
- D. Give one dose today and no booster is recommended.

Workbook Page 1-545; Answer: Page 1-552
Hib Vaccine

- *Haemophilus influenzae type B*
  - Encapsulated bacteria
  - Polysaccharide vaccine – unavailable
  - Polysaccharide-protein conjugate
    - IM injection
    - Types
      - PRP-T – polyribosylribitol phosphate conjugated to tetanus toxoid
      - PRP-OMP – Hib conjugated to meningococcal group B outer membrane protein
- Recommendations
  - All children starting at 2 months

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age at First Dose (months)</th>
<th>Primary Series</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRP-T</td>
<td>2-6</td>
<td>Three doses, 2 months apart</td>
<td>12-15 months</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>Two doses, 2 months apart</td>
<td>12-15 months</td>
</tr>
<tr>
<td></td>
<td>12-14</td>
<td>One dose</td>
<td>2 months later</td>
</tr>
<tr>
<td></td>
<td>15-59</td>
<td>One dose</td>
<td>Unnecessary</td>
</tr>
<tr>
<td>PRP-OMP</td>
<td>2-6</td>
<td>Two doses, 2 months apart</td>
<td>12-15 months</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>Two doses, 2 months apart</td>
<td>12-15 months</td>
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<tr>
<td></td>
<td>12-14</td>
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<td>2 months later</td>
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<tr>
<td></td>
<td>15-59</td>
<td>One dose</td>
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</tr>
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Patient Case #9

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B. Give a total of two doses, at least 2 months apart, with a booster at 12–15 months.
C. Give one dose today and a booster in 2 months.
D. Give one dose today and no booster is recommended.

Workbook Page 1-545; Answer: Page 1-552

Polio Vaccine

- Poliomyelitis (viral infection)
- Oral Polio
  - Activated
  - No longer used in the United States
- Inactivated poliovirus vaccine (IPV)
  - SQ injection
  - Series of 3 – 4 doses
  - Recommendation
    - All children at 2, 4 and 6 – 18 months
    - 4th dose prior to school entry if 3rd dose given <4 years

Rotavirus Vaccine

- Rotavirus gastroenteritis
- Live attenuated
- Oral
- Types
  - RV5 – 5 strains
    - Three doses at 2, 4 and 6 months
  - RV1 – 1 strain
    - Two doses at 2 and 4 months
- Duration of protection unknown

Rotavirus Vaccine

- Recommendations
  - All children
  - No preference to either vaccine
- Adverse reactions
  - Intussusception – rare
Patient Case #10
R.G. is a 12-month-old infant in your clinic today and his parents are requesting his 12 month vaccines. You note in the chart that one week ago he was in clinic to receive the varicella vaccine because of a chickenpox outbreak at his day care. Which one of the following is the best combination to be given today?

A. MCV4 and MMR
B. MMR and Hib
C. Hib and PCV
D. PCV and MCV4

Workbook Page 1-549; Answer: Page 1-553

Vaccine Storage
- Most are kept refrigerated (2-8 °C)
  - Frozen:
    - Varicella
    - Zoster
    - MMR
- Multi-dose vials
  - Use until expiration date unless visible contaminant present

1-549 to 1-550

Travel Vaccines

Safety
- CLIA Waiver
  - All places that perform diagnostic tests are considered a laboratory
  - CLIA waiver allows places that perform test of insignificant risk and not need to be registered as a laboratory
- Blood borne Pathogens
  - All persons exposed to bodily fluids should be supplied with adequate personal protective equipment (PPE)
  - Sharps/needles should not be bent, clipped or recovered
  - Sharps disposal
  - Food and drink must be separate from hazardous materials

1-550

Safety
- Human Subject Safety
  - Persons involved in a research study must be given informed consent
    - Confidentiality
    - Consent
    - Answers to questions
    - Voluntary nature of participating
  - Adequate time to review
  - In a language understood by the patient

1-522
Corrections to Immunization Chapter

1. 1-533. Under IX. C. Delete “with a history of chickenpox”
2. 1-534. In patient case 5, change option C to “Varicella today and HZV in 4 weeks”
3. 1-543. Under C. Add: subsection 5. All patients with diabetes mellitus types 1 & 2, age 19-59 and those 60 and over at the discretion of their provider.
4. 1-543. In patient Case #8, change option B to A 38-year old female with chronic obstructive pulmonary disease.
5. 1-552. Under answer for patient case 8, change “diabetes” in third sentence to read “COPD”
Pulmonary Disorders and Smoking Cessation
Ila M. Harris, Pharm.D., FCCP, BCPS
University of Minnesota

Conflict of Interest Disclosures
Ila M. Harris, Pharm.D.
– I have no conflicts of interest to disclose

Learning Objectives
- Select and monitor appropriate acute and preventive treatment for adult patients with asthma and chronic obstructive pulmonary disease (COPD).
- Classify a patient according to his/her asthma severity class and assess his/her control, according to the NHLBI.
- Educate a patient about their therapy for asthma and COPD, including use of inhalers and holding chambers.
- Provide behavioral counseling and select appropriate pharmacotherapy in assisting a patient to quit smoking.
- Discuss public health, practice management, and patient advocacy issues as they pertain to asthma, COPD, and smoking cessation.

Topics Covered
- Asthma
- COPD
- Smoking Cessation

Patient Case 1
JH is a 23-year-old woman who started running on a treadmill twice weekly. She has been coughing and having trouble breathing while running but it does not limit her activity.
- What asthma severity class is JH in?
  A. Intermittent
  B. Mild persistent
  C. Moderate persistent
  D. Severe persistent

ASTHMA
In adults and children
### Classifying Asthma Severity ≥ age 12

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Mild Persistent</th>
<th>Moderate Persistent</th>
<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>≤ 2 days / week</td>
<td>&gt; 2 days / wk but not daily</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Night Awakenings</td>
<td>≤ 2 x / month</td>
<td>3-4 x / month</td>
<td>&gt; once / weak but not nightly</td>
<td>Often 7 x / week</td>
</tr>
<tr>
<td>β-agonist Use</td>
<td>≤ 2 days / wk</td>
<td>&gt; 2 days / wk</td>
<td>Daily</td>
<td>Several times per day</td>
</tr>
<tr>
<td>Interference with activity</td>
<td>None</td>
<td>Minor</td>
<td>Some</td>
<td>Extreme</td>
</tr>
<tr>
<td>Lung Function</td>
<td>Normal</td>
<td>Normal</td>
<td>FEV1, 60-80%</td>
<td>FEV1/FVC ↓ 5%</td>
</tr>
<tr>
<td>Risk Systemic Steroids</td>
<td>≤ 2 / yr</td>
<td>≤ 2 / yr</td>
<td>≤ 2 / yr</td>
<td>≤ 2 / yr</td>
</tr>
</tbody>
</table>

### Treatment Step to Initiate
- Step 1
- Step 2
- Step 3
- Step 4 or 5

### Patient Case 1
- A. Intermittent
- B. Mild persistent
- C. Moderate persistent
- D. Severe persistent

Need to consider exercise-induced asthma

### Patient Case 2

- Which of the following medications is best to recommend for J.H. (intermittent asthma), in addition to albuterol MDI 1-2 puffs prior to exercise and as needed?
  - A. No additional therapy needed
  - B. Montelukast 10 mg daily
  - C. Omalizumab 150 mg SC Q4 weeks
  - D. Mometasone MDI 220 mcg 1 puff daily

### Stepwise Therapy for Asthma for ≥ 12 years of age

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Step 1 SABA prn</th>
<th>Step 2 Low Dose ICS</th>
<th>Step 3 Low Dose ICS + LABA OR medium dose ICS</th>
<th>Step 4 Medium Dose ICS + LABA AND Consider omalizumab for patients with allergic asthma</th>
<th>Step 5 High Dose ICS + LABA AND Consider omalizumab for patients with allergic asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose</td>
<td>ICS + LABA OR medium dose ICS</td>
<td>Low dose ICS + LABA</td>
<td>Medium Dose ICS + LABA AND Consider omalizumab for patients with allergic asthma</td>
<td>High Dose ICS + LABA AND Consider omalizumab for patients with allergic asthma</td>
<td>High Dose ICS + LABA AND Consider omalizumab for patients with allergic asthma</td>
</tr>
</tbody>
</table>

Cromolyn & nedocromil MDI were alternatives for Step 2 but have been D/C'ed by manufacturers

### Patient Case 2

- Which of the following medications is best to recommend for J.H. (intermittent asthma), in addition to albuterol MDI 1 or 2 puffs prior to exercise?
  - A. No additional therapy needed
  - B. Montelukast 10 mg daily
  - C. Omalizumab 150 mg SC Q4 weeks
  - D. Mometasone MDI 220 mcg 1 puff daily
Patient Case 3

Your recommendation has somewhat improved J.H.’s symptoms. However, now she started coughing at night once weekly. What is the preferred medication to add?

- A. Budesonide-formoterol MDI 80/4.5 2 puffs BID
- B. Montelukast 10 mg daily
- C. Salmeterol MDI 2 puff BID
- D. Fluticasone 110 mcg/puff 1 puff BID

Assessing Control: Adults

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 days/week</td>
<td>≥ 2 days/week</td>
<td>Throughout the day</td>
<td></td>
</tr>
<tr>
<td>≤ 2 x/month</td>
<td>&gt; 2 x/month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Some Limitation</td>
<td>Extremely Limited</td>
<td></td>
</tr>
<tr>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week</td>
<td>Several times/day</td>
<td></td>
</tr>
<tr>
<td>Lung Function FEV1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;80%</td>
<td>60% - 80%</td>
<td>&gt;60%</td>
<td></td>
</tr>
<tr>
<td>Risk Exacerbations requiring OCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2/year</td>
<td>2 – 4/year</td>
<td>≥ 4/year</td>
<td></td>
</tr>
</tbody>
</table>

Action

- Same regimen; F/U 1-6 mo.
- Step up 1 step; F/U 2-6 weeks
- Consider short course OCS; Step up 1-2 steps F/U 2 weeks

Stepwise Therapy for Asthma

for ≥ 12 years of age

Therapy

- Intermittent Asthma
  - Step 1: SABA
  - Step 2: Low Dose ICS + LABA OR LTRA
  - Step 3: Medium Dose ICS + LABA OR LTRA
  - Step 4: High Dose ICS + LABA AND LABA TO LABA
  - Step 5: High Dose ICS + LABA AND LABA TO LABA

Alternative

- LTAM, theophylline, or cromolyn nebs
- Low-dose ICS + LTAM or theophylline
- Medium-dose ICS + LTAM or theophylline
- High-dose ICS + LABA OR LTRA

ICS Comparative Daily Doses ≥12 y/o

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide DPI (Pulmicort 90, 180)</td>
<td>180 – 600 mcg</td>
<td>&gt;600 – 1,200 mcg</td>
<td>&gt; 1,200 mcg</td>
</tr>
<tr>
<td>Fluticasone (Flovent) (MDI 44, 110, 220)</td>
<td>88 – 264 mcg</td>
<td>&gt;264 – 440 mcg</td>
<td>&gt; 440 mcg</td>
</tr>
<tr>
<td>Beclomethasone MDI (QVAR 40, 80)</td>
<td>80 – 240 mcg</td>
<td>&gt;240 – 480 mcg</td>
<td>&gt; 480 mcg</td>
</tr>
<tr>
<td>Mometasone DPI (Asmanex 110, 220)</td>
<td>220 mcg (QD)</td>
<td>440 mcg (QD)</td>
<td>&gt; 440 mcg (QD or divided BID)</td>
</tr>
<tr>
<td>Ciclesonide MDI (Aerosol 80, 160)</td>
<td>160 mcg</td>
<td>320 mcg</td>
<td>640 mcg*</td>
</tr>
</tbody>
</table>

* Newer agent; doses not provided in guidelines; doses estimated

Patient Case 4

J.H. returns one month later. No longer awakening at night. Uses albuterol MDI 2 puffs once per week to treat symptoms. She also uses albuterol MDI 2 puffs 6 days per week prior to working out at the gym; she does not have symptoms while working out. Which of the following is correct?

- A. Continue current controller
- B. Increase fluticasone to 110 mcg 2 puffs BID
- C. Change to fluticasone/salmeterol DPI 100/50 BID
- D. Add montelukast 10 mg/d
Assessing Control in Adults

### Impairment

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2 days/week</td>
<td>1-3x/week</td>
<td>Throughout the day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nighttime Awakenings</th>
<th>None</th>
<th>Some Limitation</th>
<th>Extremely Limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2 x/month</td>
<td>≥3 x/month</td>
<td>Several times/day</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SABA use for symptoms</th>
<th>None</th>
<th>Minor</th>
<th>Some</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2 days/week</td>
<td>≥3 days/week</td>
<td>Several times/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lung Function FEV</th>
<th>≥80%</th>
<th>60%-80%</th>
<th>&lt;60%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily</td>
<td>≥4 days/week</td>
<td>Extremely Limited</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Exacerbations requiring OCS</th>
<th>Same regimen; FU 1-6 mo. Can step down if stable for ≥3 mo.</th>
<th>Step up 1 step; FU 2-6 weeks</th>
<th>Consider short course OCS; Step up 1-2 steps; FU 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2/year</td>
<td>≥2/year</td>
<td>≥2/year</td>
<td>≥2/year</td>
</tr>
</tbody>
</table>

### Patient Case 4

- J.H. returns one month later. No longer awakening at night. Uses albuterol MDI 2 puffs once per week to treat symptoms. She also uses albuterol MDI 2 puffs 6 days per week prior to working out at the gym; she does not have symptoms while working out. Which of the following is correct?
  - A. Continue current controller.
  - B. Increase fluticasone to 110mcg 2 puffs BID
  - C. Change to fluticasone/salmeterol DPI 100/50 BID
  - D. Add montelukast 10 mg/d

### Patient Case 5

- R.J. is an 8 year old boy that has daytime asthma symptoms once or twice a week. He is awakened twice a week at night with coughing. What is his asthma severity classification?
  - A. Intermittent
  - B. Mild persistent
  - C. Moderate persistent
  - D. Severe persistent

### Patient Case 6

- In addition to albuterol MDI 1-2 puffs every 4-6 hours as needed, which is the best initial controller therapy for R.J.?
  - A. Beclomethasone 80 mcg/puff 1 puff BID
  - B. Montelukast 10 mg daily
  - C. Fluticasone-salmeterol 100/50mcg 1 puff BID
  - D. Fluticasone 110 mcg/puff 1 puff BID
**Classifying Asthma Severity: Age 5-11**

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Mild Persistent</th>
<th>Moderate Persistent</th>
<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night Awakenings</td>
<td>&lt;2 days/week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B-agonist Use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference with Activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lung Function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic Steroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatment Step to Initiate**

- Step 1
- Step 2
- Step 3
- Step 3 or 4

**ICS Comparative Daily Doses: Age 5-11**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Dose Step 2 – 3</th>
<th>Medium Dose Step 3 – 4</th>
<th>High Dose Step 5 – 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide DPI (Pulmicort 90, 180)</td>
<td>180 – 400 mcg</td>
<td>&gt;400 – 800 mcg</td>
<td>&gt; 800 mcg</td>
</tr>
<tr>
<td>Fluticasone MDI (Flonase 44, 110, 220)</td>
<td>88 – 176 mcg</td>
<td>&lt;176 – 352 mcg</td>
<td>&gt;352 mcg</td>
</tr>
<tr>
<td>Budesonide DPI (QVAR 40, 80)</td>
<td>80 – 160 mcg</td>
<td>&gt;160 – 320 mcg</td>
<td>&gt; 320 mcg</td>
</tr>
<tr>
<td>Mometasone DPI (Asmanex 110, 220)</td>
<td>110 mcg (QD)</td>
<td>110 mcg (QD)</td>
<td>110 mcg (QD)*</td>
</tr>
<tr>
<td>Ciclesonide MDI (Alvesco 80, 160)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Budesonide for nebulizer use</td>
<td>0.5 mg</td>
<td>1 mg</td>
<td>2 mg</td>
</tr>
</tbody>
</table>

*Recently approved for use < age 12; doses from package insert

**Assessing Control: Children**

<table>
<thead>
<tr>
<th>AGE RANGE (yrs)</th>
<th>0-4</th>
<th>5-11</th>
<th>0-4</th>
<th>5-11</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/wk but not ≥1x on each day</td>
<td>≥2 days/wk or ≥1x on any day</td>
<td>≤2 days/wk</td>
<td>≥1x on any day</td>
</tr>
<tr>
<td>Nighttime Awakenings</td>
<td>≤1x/month</td>
<td>&gt;1x/night</td>
<td>≥2x/night</td>
<td>≥2x/night</td>
</tr>
<tr>
<td>Interference with Activity</td>
<td>None</td>
<td>Some Limitation</td>
<td>Extremely Limited</td>
<td>Extremely Limited</td>
</tr>
<tr>
<td>SABA use for Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times/day</td>
<td>Several times/day</td>
</tr>
<tr>
<td>Lung Function FEV1</td>
<td>≤80%</td>
<td>80-90%</td>
<td>≤80%</td>
<td>80-90%</td>
</tr>
<tr>
<td><strong>Action</strong></td>
<td>FIU 1-6 mo.</td>
<td>Step up 1 step</td>
<td>Consider OCS burst if severe control needed</td>
<td>FIU 2 weeks</td>
</tr>
</tbody>
</table>

**Classifying Asthma Severity: Age 0-4**

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Mild Persistent</th>
<th>Moderate Persistent</th>
<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night Awakenings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B-agonist Use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference with Activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lung Function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic Steroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatment Step to Initiate**

- Step 1
- Step 2
- Step 3
- Step 3 or 4

**Stepwise Therapy for Asthma for 5-11 years of age**

- **Therapy**
  - Interim asthma
  - Persistent asthma

- **Preferred**
  - Step 1
    - Low Dose ICS
  - Step 2
    - Medium Dose ICS + LABA
  - Step 3
    - Medium Dose ICS + LTM or LABA
  - Step 4
    - Medium Dose ICS + LTM or LABA
  - Step 5
    - High Dose ICS + LABA
  - Step 6
    - High Dose ICS + LABA or OCS

- **Alternative**
  - Low Dose ICS
  - Medium Dose ICS + LABA
  - Medium Dose ICS + LTM or LABA
  - High Dose ICS + LABA
  - High Dose ICS + LTM or LABA

- *Medium dose ICS is preferred initial therapy (either option for step-up)
  - Cromolyn and nedocromil were alternatives for Step 2 but are no longer available

- **Patient Case 6**
  - In addition to albuterol MDI 1-2 puffs every 4-6 hours as needed, which is the best initial controller therapy for R.J.?
  - A. Beclomethasone 80 mcg/puff 1 puff BID
  - B. Montelukast 10 mg daily
  - C. Fluticasone-salmeterol 100/50mcg 1 puff BID
  - D. Fluticasone 110 mcg/puff 1 puff BID
Stepwise Therapy for Asthma

for 0-4 years of age

Therapy

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA pm</td>
<td>Montelukast or cromolyn nebs</td>
</tr>
<tr>
<td>Low Dose ICS</td>
<td>Medium dose ICS</td>
</tr>
<tr>
<td>Medium dose ICS</td>
<td>Medium dose ICS + LABA or montelukast</td>
</tr>
<tr>
<td>High Dose ICS + LABA or montelukast</td>
<td>High Dose ICS + LABA + OCS</td>
</tr>
</tbody>
</table>

*Cromolyn is no longer available in MDI formulation

ICS Comparative Daily Doses: Age 0-4

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Dose Step 2 – 3</th>
<th>Medium Dose Step 3 – 4</th>
<th>High Dose Step 5 – 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide DPI</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Fluticasone MDI</td>
<td>176 mcg</td>
<td>&gt;176 – 352 mcg</td>
<td>&gt; 352 mcg</td>
</tr>
<tr>
<td>Beclomethasone MDI</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Monelukast MDI</td>
<td>110 mcg (OD) (age 4 only)</td>
<td>110 mcg (OD) (age 4 only)</td>
<td>110 mcg (OD)* (age 4 only)</td>
</tr>
<tr>
<td>Ciclesonide MDI</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Budesonide for nebulizer use</td>
<td>0.25 - 0.5 mg</td>
<td>&gt; 0.5 - 1 mg</td>
<td>&gt; 1 mg</td>
</tr>
</tbody>
</table>

Long-Acting Beta<sub>2</sub> Agonists

- February 18, 2010
- FDA issued a safety announcement due to safety concerns with LABA
  - LABA contraindicated without concomitant controller
  - Long-term LABA should only be used in patients who are inadequately controlled on controllers
  - Use LABA short-term when possible and attempt to discontinue after control is achieved
  - Pediatric/adolescent patients who require LABA should use a combination product

Asthma Action Plan

- Asthma Action Plan (AAP)
  - Previously used peak-flow/zone based; now moving towards symptom based

Patient Case 7

- You are developing an asthma action plan for S.K., a 25 year old man using Advair (fluticasone/ salmeterol) 250/50 1 puff BID and albuterol HFA (ProAir) 1-2 puffs q 4-6 hr PRN. Personal best PFM: 500. You are developing an asthma action plan for him. What are his instructions when he is doing well; PFM 400-500:
  - Hold Advair when asthma is under good control
  - Use Advair regularly; may use albuterol HFA 1-2 puffs q 4-6 hr if needed
  - Albuterol HFA 2 puffs, repeat in 20 min if needed, then reassess
  - Albuterol HFA 6 puffs, repeat in 20 min; start prednisone 50mg QD x 5 days, then reassess

Asthma Action Plan (Adults): Green Zone

- Doing well, no symptoms
- PFM ≥ 80% personal best
- Take controller drug only
- Use 2 puffs of SABA 5-15 min before exercise if exercise-induced asthma
- May use SABA as needed for periodic mild symptoms
Patient Case 8

Which of the following (in addition to using Advair regularly) are best asthma action plan instructions for when he has some worsening of wheezing and dyspnea (mild exacerbation), with peak flow 250-399?

- A. May use albuterol HFA 1-2 puffs every 4-6 hr if needed
- B. Albuterol HFA 2 puffs; repeat in 20 min if needed; then reassess; consider OCS burst
- C. Albuterol HFA 8 puffs; repeat in 20 min; start prednisone 50mg QD x 5 days, then reassess
- D. Albuterol HFA 10 puffs; repeat every 20 min for 4 hr; start prednisone 50mg QD x 5 d, then reassess

Patient Case 9

Which of the following (in addition to using Advair regularly) are best asthma action plan instructions for when he has a more severe exacerbation, with marked wheezing and dyspnea some worsening of wheezing and dyspnea, with peak flow < 250?

- A. May use albuterol HFA 1-2 puffs every 4-6 hr if needed
- B. Albuterol HFA 2 puffs; repeat in 20 min if needed; then reassess
- C. Albuterol HFA 6 puffs; repeat in 20 min; start prednisone 50mg QD x 5 days, then reassess
- D. Albuterol HFA 10 puffs; repeat every 20 min for 4 hr; start prednisone 50mg QD x 5 d, then reassess
Asthma Action Plan (Adults): Red Zone

- Medical alert; marked wheezing and dyspnea, inability to speak more than short phrases, use of accessory muscles, drowsiness
- PFM < 50% of personal best
- Use SABA: 2-6 puffs by MDI or 1 neb tx; repeat in 20 minutes; if incomplete or poor response, repeat SABA again in 20 minutes
- Higher dose of 4-6 puffs SABA MDI usually recommended
- Add OCS burst (prednisone 40-60mg/d x 5-10 d)

- Proceed to ED or call 911 if distress is severe and unresponsive to treatment
- Call 911 or go to ED immediately if lips or fingernails are blue or gray, or if trouble walking or talking due to SOB
- Contact clinician immediately
- Continue SABA every 3-4 hr regularly for 1-2 days

Choice C is correct

Patient Education: MDIs

- Prime before use
- How to wash
- How to tell when they are empty
- Holding chambers

Dry Powder Inhalers- Pt Ed

- Do not contain aerosol; contain a small amount of powder
- Will feel different; no “spray” or “puff”
- Do not shake
- Once dose is “prepped”, breathe out fully, away from the mouthpiece
- Close lips around mouthpiece and inhale quickly, forcefully and deeply (different from MDI)
- Hold breath for 10 seconds, then exhale
COPD

Diagnosis

- Consider COPD and perform spirometry if > 40 years old with any of the following:
  - Dyspnea
  - Chronic cough
  - Chronic sputum production
  - History of exposure to risk factors
    - Most common: tobacco smoke

ACP/ACCP/ATS/ERS Guidelines:

- Single best predictor of airflow obstruction is the presence of all three of the following:
  - Smoking history of > 55 pack-years
  - Wheezing on auscultation
  - Patient self-reported wheezing

Criteria for diagnosis of COPD:

- Symptoms and risk factors plus
- FEV₁/FVC < 70%

Validated Symptom Scales

- Modified British Medical Research Council breathlessness scale (mMRC)
  - Only measures severity of breathlessness
  - Score of 0: 1: less symptoms
  - Score of ≥ 2: more symptoms
- COPD Assessment Test (CAT)
  - Measures health status impairment in COPD
  - www.catestonline.org
  - Score of < 10: less symptoms
  - Score of ≥ 10: more symptoms

Patient Case 10

- P.D. is a 62 year old male smoker with COPD.
  - Spirometry showed: FEV₁/FVC: 60%;
  - Pre-bronchodilator FEV₁: 70% predicted;
  - Post-bronchodilator FEV₁: 72% predicted
  - Symptoms very bothersome; mMRC grade 2
  - 1 exacerbation in past year

- Which is most appropriate GOLD patient group?
  - A. Patient Group A
  - B. Patient Group B
  - C. Patient Group C
  - D. Patient Group D
**Patient Case 10**

- **P.D.** is a 62 year old male smoker with COPD.
  - Spirometry showed: FEV1/FVC: 60%.
  - Pre-bronchodilator FEV1: 70% predicted;
  - Post-bronchodilator FEV1: 72% predicted
  - Symptoms very bothersome; mMRC grade 2
  - 1 exacerbation in past year

Which is most appropriate GOLD patient group?

A. Patient Group A  
B. Patient Group B  
C. Patient Group C  
D. Patient Group D

---

**Patient Case 11**

- In addition to albuterol HFA 2 puffs every 4-6 hours as needed, which of the following is the most appropriate to initiate?
  - A. No additional therapy needed
  - B. Formoterol inhal 1 cap BID
  - C. Salmeterol/fluticasone 50/500 1 puff BID
  - D. Salmeterol/fluticasone 50/500 1 puff BID plus Daliresp 500 mcg PO once daily

---

**Pharmacotherapy for Stable COPD (GOLD)**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>First Choice</th>
<th>Second Choice</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SA anticholinergic/PBO or SABA/PBO</td>
<td>LA anticholinergic or LABA or ICS + SA anticholinergic or LA anticholinergic + LABA</td>
<td>Theophylline*</td>
</tr>
<tr>
<td>B</td>
<td>ICS + LABA or LA anticholinergic</td>
<td>LA anticholinergic + LABA or ICS + LA anticholinergic or LABA and LA anticholinergic or ICS + LABA and PDE 4 inhibitor or LA anticholinergic + LABA or LA anticholinergic + PDE 4 inhibitor</td>
<td>N/A or/SA anticholinergic Theophylline*</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LA anticholinergic</td>
<td>LA anticholinergic + LABA or ICS + LA anticholinergic or LABA and LA anticholinergic or ICS + LABA and PDE 4 inhibitor or LA anticholinergic + LABA or LA anticholinergic + PDE 4 inhibitor</td>
<td>N/A or/SA anticholinergic Theophylline*</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA or LA anticholinergic</td>
<td>LA anticholinergic + LABA or ICS + LA anticholinergic or LABA and LA anticholinergic or ICS + LABA and PDE 4 inhibitor or LA anticholinergic + LABA or LA anticholinergic + PDE 4 inhibitor</td>
<td>N/A or/SA anticholinergic Theophylline*</td>
</tr>
</tbody>
</table>

*Alternative medications can be used alone or in combination with first and second choice therapies.

Theophylline is not recommended unless other long-term bronchodilators are unavailable or unfeasible.

---

**Treatment Guidelines (ACP/ACCP/ATS/ERS)**

- For patients with respiratory symptoms and FEV1 < 50% of predicted, escalation with long-acting inhaled bronchodilators is suggested. (Grade C, Evidence D)
- For patients with respiratory symptoms and FEV1 < 50% of predicted, treatment with long-acting inhaled bronchodilators is recommended. (Grade A, Evidence M)
- Monotherapy using either long-acting inhaled anticholinergics or LABAs is recommended for symptomatic patients with FEV1 < 60% of predicted. The choice of specific monotherapy should be based on patient preference, cost, and adherence profile. (Grade C, Evidence M)
- Combination inhaled therapies (long-acting inhaled anticholinergics, LABAs, or ICS) may be used for symptomatic patients with FEV1 < 60% of predicted. (Grade W, Evidence M)

---

**Patient Case 11**

- In addition to albuterol HFA 2 puffs every 4-6 hours as needed, which of the following is the most appropriate to initiate?
  - A. No additional therapy needed
  - B. Formoterol inhal 1 cap BID
  - C. Salmeterol/fluticasone 50/500 1 puff BID
  - D. Salmeterol/fluticasone 50/500 1 puff BID plus Daliresp 500 mcg PO once daily

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**Patient Case 12**

- T.L. is a 52 year old woman with COPD. Gradual worsening of SOB past few years. Spirometry: FEV₁/FVC: 55%; FEV₁: 63%. CAT score: 10. Never had a COPD exacerbation; no OCS in past 2 yrs. Meds: tiotropium (Spiriva®) once daily and albuterol HFA prn. Which of the following is most appropriate according to GOLD?

A. Add salmeterol 1 puff BID
B. Add long-term azithromycin 250 mg QD
C. Add fluticasone 110 mcg 2 puffs BID
D. D/C tiotropium & start Advair 250/50

**Gold Guidelines: Assessment of Severity and Risk**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Characteristics</th>
<th>Spirometric GOLD Classification</th>
<th>Exacerbations per Year</th>
<th>Symptom Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low risk Less symptoms</td>
<td>1 Mild (FEV₁ &lt; 80% pred) or 2 Moderate (50% ≤ FEV₁ &lt; 80% of pred)</td>
<td>≤ 1</td>
<td>mMRC 0-1 CAT &lt; 10</td>
</tr>
<tr>
<td>B</td>
<td>Low risk More symptoms</td>
<td>1 Mild (FEV₁ &lt; 80% pred) or 2 Moderate (50% ≤ FEV₁ &lt; 80% of pred)</td>
<td>≤ 1</td>
<td>mMRC 0-1 CAT &lt; 10</td>
</tr>
<tr>
<td>C</td>
<td>High risk Less symptoms</td>
<td>3 Severe (FEV₁ ≤ 50% pred) or 4 Very severe (FEV₁ &lt; 30% of pred)</td>
<td>≥ 2</td>
<td>mMRC ≥ 2 CAT ≥ 10</td>
</tr>
<tr>
<td>D</td>
<td>High risk More symptoms</td>
<td>3 Severe (FEV₁ ≤ 50% pred) or 4 Very severe (FEV₁ &lt; 30% of pred)</td>
<td>≥ 2</td>
<td>mMRC ≥ 2 CAT ≥ 10</td>
</tr>
</tbody>
</table>

**Pharmacotherapy for Stable COPD (GOLD)**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>First Choice</th>
<th>Second Choice</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SA anticholinergic PEN or LABA PEN</td>
<td>LA anticholinergic or LABA or SA anticholinergic</td>
<td>Theophylline³</td>
</tr>
<tr>
<td>B</td>
<td>LA anticholinergic or LABA</td>
<td>LA anticholinergic or LABA</td>
<td>SA anticholinergic or LABA or SA anticholinergic Theophylline³</td>
</tr>
<tr>
<td>C</td>
<td>ICS / LABA or LA anticholinergic</td>
<td>LA anticholinergic or LABA</td>
<td>PDE-4 inhibitor SA anticholinergic Theophylline³</td>
</tr>
<tr>
<td>D</td>
<td>ICS / LABA or LA anticholinergic</td>
<td>ICS / LABA and LA anticholinergic or PDE-4 inhibitor or LA anticholinergic or LABA or SA anticholinergic + PDE-4 inhibitor</td>
<td>SAH and/or SA anticholinergic Theophylline³</td>
</tr>
</tbody>
</table>

Patient Case 12

- T.L. is a 52 year old woman with COPD. Gradual worsening of SOB past few years. Spirometry: FEV₁/FVC: 55%; FEV₁: 63%. CAT score: 10. Never had a COPD exacerbation; no OCS in past 2 yrs. Meds: tiotropium (Spiriva®) once daily and albuterol HFA prn. Which of the following is most appropriate according to GOLD?

A. Add salmeterol 1 puff BID
B. Add long-term azithromycin 250 mg QD
C. Add fluticasone 110 mcg 2 puffs BID
D. D/C tiotropium & start Advair 250/50

**Roflumilast (Daliresp)**

- Oral phosphodiesterase-4 inhibitor
  - Anti-inflammatory; no direct bronchodilator activity
  - Indicated as a chronic treatment to reduce the risk of COPD exacerbations in patients with severe COPD (FEV₁ < 50% pred) associated with chronic bronchitis and a history of exacerbations
  - Studies show a reduction in exacerbations, and a reduction in the composite end-point of moderate exacerbations treated with oral or systemic corticosteroids or severe exacerbations requiring hospitalization or causing death. (Evidence: B)
  - Also shown when roflumilast is added to long-acting bronchodilators (Evidence: B). No comparison has been done with ICS.

**Chronic Azithromycin for Prevention of Exacerbations**

- Recent study in patients with COPD at risk of exacerbations
- Azithromycin 250mg daily vs. placebo x 1 year

**Results:**

- Longer time to exacerbation (266 vs. 174 days; 90 days difference; p < 0.001)
- Decreased rate of exacerbations (1.48 vs. 1.83; p = 0.01)
- NNT to prevent one exacerbation of COPD: 2.86
- QOL improved more with azithro vs. placebo (p=0.03)

Chronic Azithromycin for Prevention of Exacerbations

**Adverse effects**
- Hearing decrements were more common with azithromycin vs. placebo (25% vs. 20%, p=0.04) (NNH=20)
- Increased incidence of colonization with macrolide-resistant organisms (81% vs. 41%, p<0.001)

**However**
- The most recent GOLD guidelines still do not recommend treatment with antibiotics, except for when indicated during acute exacerbations.

**Patient Case 13**

J.J. is a 64 y/o woman with COPD (GOLD patient group A) who, in past few days, has had worsening SOB, worsening coughing & production of “cloudy” sputum (much more sputum than usual). Pulse ox 95%. In addition to nebulized albuterol/ipratropium q 1-4 hours, what else should be added?

- A. No additional therapy needed
- B. Add oral prednisone 40 mg once daily for 10 days
- C. Add TMP/SMX DS 1 tablet BID for 7 days
- D. Add oral prednisone 40 mg once daily for 10 days and TMP/SMX DS 1 tablet BID for 7 days.

Managing Exacerbations

- Short-acting albuterol is preferred (Evidence C)
  - 2.5mg via nebulizer every 1-4 hours or
  - 4-8 puffs via MDI/holding chamber every 1-4 hr
  - Generally, short acting ipratropium is also given
- Systemic corticosteroids are effective (Evidence A)
  - Use in most exacerbations
  - GOLD guidelines no longer provide criteria
  - Dose in outpatients: 30-40 mg QD prednisolone or equivalent QD x 10-14 days (Evidence D)

Antibiotics should be given if:
- COPD exacerbation with all **THREE** cardinal symptoms (Evidence B)
- COPD exacerbation with **TWO** cardinal symptoms, if one is increased sputum purulence (Evidence C)
- Severe COPD exacerbation requiring mechanical ventilation (Evidence B)

Empiric antibiotics are used to cover the most common pathogens: *Streptococcus pneumonia*, *Hemophilus influenzae* and *Moraxella catarrhalis*.
- In Gold 3 and 4 patients, *Pseudomonas aeruginosa* is more prevalent
- Recommended antibiotic duration is 5 – 10 days (Evidence D)
Antibiotics for COPD Exacerbations

<table>
<thead>
<tr>
<th>Uncomplicated COPD</th>
<th>Azithromycin, clarithromycin, doxycycline, TMP/SMX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated COPD with risk factors</td>
<td>Amoxicillin/clavulanate, levofloxacin, moxifloxacin</td>
</tr>
<tr>
<td>Risk of Pseudomonas infection</td>
<td>High dose levofloxacin (750mg) or ciprofloxacin</td>
</tr>
</tbody>
</table>

Risk factors: comorbid diseases, severe COPD, > 3 exacerbations/year, antibiotic use in past 3 months.

Patient Case 13

- J.J. is a 64 y/o woman with COPD (GOLD patient group A) who, in past few days, has had worsening SOB, worsening coughing & production of “cloudy” sputum (much more sputum than usual). Pulse ox 95%. In addition to nebulized albuterol/ipratropium q 1-4 hours, what else should be added?
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SMOKING CESSATION

The health warnings will appear on the upper portion of the front and rear panels of each cigarette package and comprise at least the top 50 percent of these panels.

Deadline: September 2012:
All cigarettes and advertisements must carry one of these warnings.
### Patient Education

- **Health consequences of smoking**
- **Health and other benefits of quitting**
- **Develop quit plan (STAR)**
  - Set a quit date
  - Tell family, friends, coworkers
  - Anticipate challenges (including withdrawal)
  - Remove tobacco products/ paraphernalia from environment
    - Clean home, car

### Patient Assessment & Education

- **The 5 “A”s:**
  - **ASK, ADVISE, ASSESS, ASSIST, ARRANGE**
  - **ASK**
    - AT EVERY VISIT, ask about smoking and document in chart
    - Consider making “tobacco use” a vital sign

### Patient Education

- **ADVISE**
  - Even a few strong statements show that you care and may help a patient decide that they want to quit
  - Advice should be clear, strong and personalized
  - Brief behavioral counseling (< 10 minutes) has been shown to significantly increase cessation rates
    - Shorter interventions (< 3 minutes) is less effective, but still increases quit rates
  - *Quitting smoking is the single most important thing you can do for your health*
    - "I think it is important for you to quit smoking now, and I will help you"

### Patient Education

- **ASSESS** (Assess smoking; identify smokers willing to quit)
  - Smoking level
  - Patient’s willingness to quit / stage of smoking cessation
    - "How badly do you want to quit now (1-10)?"
  - Self-efficacy (Motivation + confidence + effort + believing he/she can quit)
    - "Do you think you can successfully quit smoking, with my help?"

### Patient Case 14

- DG is a 39 y/o smoker with obesity, type 2 diabetes and HTN. Smokes 2 ppd. She is not interested in quitting. Which of the following is best?
  - A. Do nothing; she is uninterested in quitting at this time
  - B. Provide individualized messages on how quitting smoking will improve her personal health for a minimum of 10 minutes
  - C. Use motivational interviewing strategies to discuss her concerns and benefits to tobacco cessation
  - D. Explore various medication options and set a quit date

### Patient Education

- If the patient does not want to quit:
  - Discuss reasons why they should quit
  - Discuss BARRIERS to quitting
    - "Why do you smoke?" / "What scares you about quitting?"
  - Use motivational interviewing strategies
  - Discuss the five “Rs” (shown to improve future quit attempts):
    - Relevance, Risks, Rewards, Roadblocks, Repetition

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Motivational Interviewing

- “How important do you think it is for you to quit smoking?”
- “So you think smoking helps you to maintain your weight.”
- “Many people worry about managing without cigarettes.”
- “I hear you saying you are not ready to quit smoking right now. I’m here to help you when you are ready.”
- “Sounds like you are feeling pressured about your smoking.”
- “It sounds like you are very devoted to your family. How do you think your smoking is affecting your children?”
- “It’s great that you are going to quit when you get through this busy time at work.”

Patient Education

- ASSIST
  - Once the patient has decided to quit, help them!
    - **When patient is ready to quit:**
      - Combination of medication and counseling is more effective than either medication or counseling alone (Evidence: A) - USPSTF

General Approach to Pharmacotherapy

- Assess patient’s smoking (chain smoking, smokes when nervous, etc.)
- Assess past attempts; what worked & didn’t work; involve patient in decision of what therapy to use
  - Prior success with a medication may be helpful in a subsequent quit attempt
  - With prior failure with a medication, it is not clear if the medication should be retried for future quit attempts; data is conflicting on this issue; discuss with the patient
- No accepted algorithm to guide selection of therapy
- All smokers attempting to quit should be offered medication

Patient Case 15

- KG is a 50 y/o man presents for smoking cessation. He smokes 1 ½ ppd x 24 years. He has COPD, seizures, depression/anxiety (well-controlled; no suicidal ideation). Has tried patches, inhalers and lozenges (none helped). He wants to try something different. Which would be most appropriate?
  - A. Buproprion
  - B. Varenicline
  - C. Nicotine gum 2mg
  - D. Varenicline plus nicotine gum 2 mg

Buproprion SR

- Blocks dopamine and/or NE reuptake
- Six month abstinence rate: 24.2%
- Dose: 150 mg twice daily for 3 months
  - Start at once daily for 1st 3 days
  - Start 1-2 weeks before quit date
  - Duration: generally 3 months
  - Consider maintenance therapy for up to 6 mo.
- Side effects: dry mouth, insomnia
  - Contraindicated if h/o seizures or bulimia
Varenicline

- Binds to neuronal nicotinic acetylcholine receptors (α4β2 subtype)
  - Agonist and antagonist activity at these receptors
- Six month abstinence rate: 33.2%
- Delays weight gain
- Dose:
  - 0.5mg QD x 3 days then 0.5 mg BID x 4 days then 1 mg BID (start at final dose on quit date)
  - Recent study showed that “preloading” with varenicline for 4 wk before quit date significantly increased abstinence rates, especially when reducing nicotine use before quit date
- Duration: 3 months; maintenance up to 6 mo.

Side effects: nausea, insomnia, vivid dreams
- If smoking or using NRT, causes more nausea
- Take with food to reduce nausea
- Adjunctive use with NRT not recommended

Caution: OK to use if controlled depression/psych illness
- Monitor for changes in mood, behavior, psychiatric/depression symptoms and suicidal ideation
- Report any depression symptoms
- Patients may experience impaired ability to drive or operate machinery

FDA Drug Safety Communication: Varenicline & Bupropion

  - Depressed mood, behavior changes, hostility, agitation, suicidal thoughts/behavior, and attempted suicide have been reported, some without psych history, and have worsened in patients with psychiatric illness. Possible confounding by withdrawal symptoms.
  - Monitor for changes in mood and/or behavior.
  - D/C if symptoms of depressed mood, agitation, or behavior changes not from nicotine withdrawal, or if suicidal thoughts.

FDA Safety Communication: Varenicline & Bupropion

- The FDA makes it clear that varenicline and bupropion are effective smoking cessation aids and that these risks should be discussed in the context of the benefits of quitting smoking.
- 2011: FDA reported data showing no difference in psych risk resulting in hospitalization between varenicline and NRT
- Newer data (2012) shows reports of increase suicide-related events that may not have resulted in hospitalization. No changes to FDA recommendations made.

New FDA Drug Safety Communication: Varenicline 2011

- Varenicline may be associated with a small increased risk of cardiovascular events in patients with CVD
  - Numerically increased risk of nonfatal MI, revascularization, angina pectoris, and PVD vs. placebo (not designed to measure stat. sig.)
- After FDA warning released, meta analysis published:
  - 14 trials; 8216 subjects; all except 1 trial excluded subjects with a history of heart disease
  - Significantly increased risk of serious cardiovascular events
    - Ischemia, arrhythmia, heart failure, sudden death, cardiovascular-related death
  - 1.06% vs. 0.82%; Peto OR 1.72 (95% CI 1.09-2.71)

Nicotine Gum (OTC)

- 6 month abstinence rate:
  - 19 - 26.1%
- Directions:
  - Chew until “peppery” taste, then “park” the gum between gum and cheek
  - Rechew every few minutes and park again on other side
  - Chew each piece for 30 minutes; 1 every 1-2 hrs
  - 1st 6 weeks: fixed schedule, then use ad libitum
- Dose:
  - Use 2mg if smoke 1-24 cig/day
  - Use 4mg if smoke > 24 cig/day
  - Max 24 pieces/day
  - Taper dose slowly; use for 3 months; consider maintenance for 6 months
  - Don’t eat or drink anything but water while chewing
  - Side effects: mouth and jaw soreness, dyspepsia
  - 4 mg strength delays weight gain

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Efficacy

- Medications shown to be more effective than the nicotine patch alone (should consider these first if possible and/or not contraindicated): (DHHS; PHS)
  - Varenicline
  - Combination of nicotine patch plus ad libitum short-acting NRT

Patient Case 15

- KG is a 50 y/o man who presents for smoking cessation. He smokes 1 ½ ppd x 24 years. He has COPD, seizures, depression/anxiety (well-controlled; no suicidal ideation). Has tried patches, inhalers and lozenges (none helped). He wants to try something different. Which would be most appropriate?
  - A. Bupropion
  - B. Varenicline
  - C. Nicotine gum 2mg
  - D. Varenicline plus nicotine gum 2 mg

Patient Case 16

- GG is a 27 y/o woman who wants to quit smoking. She is only interested in NRT (not “pills”). Has only tried quitting cold turkey in the past; was unsuccessful. Smokes 1 ppd; 1st cigarette is 1 hr after waking. Which NRT choice is best?
  - A. Patch 21/14/7mg (4 wk/2 wk/2 wk)
  - B. Inhaler 6 cartridges/day (regularly x 6wk then ad libitum)
  - C. Gum 4mg (max 10/day) (regularly x 6wk then ad libitum)
  - D. Patch 21/14/7 (4 wk/2 wk/2 wk) plus nicotine gum 2mg

Nicotine Patch

- Nicoderm CQ, generics (24 hr) –OTC
  - 21 mg (4 wk), 14 mg (2 wk), 7 mg (2 wk)
    - (If smoking 1 ppd)
  - Apply once daily; remove at night if sleep SE
  - Start with 14mg patch if smoking ½ ppd
  - Start with 2x 21mg patches if smoking 2 ppd (off-label)
- Six month abstinence rate: 23.4 – 26.5%
- Side effects:
  - Local skin irritation, insomnia, vivid dreams

Nicotine Gum (OTC)

- 6 month abstinence rate:
  - 19 - 26.1%
- Directions:
  - Chew until “peppery” taste, then “park” the gum between gum and cheek
  - Rechew every few minutes and park again on other side
  - Chew each piece for 30 minutes; 1 every 1-2 hrs
  - 1st 6 weeks: fixed schedule, then use ad libitum
- Dose:
  - Use 2mg if smoke 1-24 cig/day
  - Use 4mg if smoke >24 cig/day
- Max 24 pieces/day
- Taper dose slowly; use for 3 months; consider maintenance for 6 months
- Don’t eat or drink anything but water while chewing
- Side effects: mouth and jaw soreness, dyspepsia
- 4 mg strength delays weight gain

Nicotine Inhaler (Rx)

- Plastic device that looks like cigarette
  - Insert cartridges (4mg each)
  - 20 minutes of active puffing = full 4 mg
  - Can use until craving gone (partial cartridge) then put away until needed again
  - No special inhalation technique
  - Delivery decreased if < 40 degrees F
- 6 month abstinence rate: 24.8%
- Decrease use after 3 months, use for up to 6 months
- Side effects: cough, mouth/throat irritation
Efficacy

Medications shown to be more effective than the nicotine patch alone (should consider these first if possible and/or not contraindicated): (DHHS; PHS)

- Varenicline
- Combination of nicotine patch plus ad libitum short-acting NRT

Patient Case 16

GG is a 27 y/o woman who wants to quit smoking. She is only interested in NRT (not “pills”). Has only tried quitting cold turkey in the past; was unsuccessful. Smokes 1 ppd; 1st cigarette is 1 hr after waking up. Which is most appropriate?

A. Patch 21/14/7 (4 wk/2 wk/2 wk)
B. Inhaler 6 cartridges/day (regularly x 6wk then ad libitum)
C. Gum 4mg (max 10/day) (regularly x 6wk then ad libitum)
D. Patch (21/14/7 4 wk/2 wk/2 wk) plus nicotine gum 2mg ad libitum

Choice A & B are OK, but combination therapy should be considered first.

Nicotine Lozenge (OTC)

- 6 month abstinence rate:
  - 23.6 – 24.2%
- Directions:
  - Suck on lozenge and move from side to side in mouth until dissolves; do not chew
- Side effects: throat irritation, hiccups, stomach discomfort, nausea

- Dose:
  - Use 2mg if 1st cigarette is ≥ 30 min after waking
  - Use 4mg if 1st cigarette is < 30 min after waking
  - Use on fixed schedule for 1st six weeks then decrease frequency for 3 mo. Use
  - May use maintenance for 6 mo.
  - 4 mg strength delays weight gain

Nicotine nasal spray (Rx)

- Two sprays = 1 mg nicotine
- Spray 1 spray in each nostril
- Use for maximum of 6 mo.
- 6 month abstinence rate: 26.7%
- Side effects: nasal irritation (94% get moderate-severe symptoms)

Practice Management

- Asthma or COPD, key issues to consider in MTM:
  - Inhaler technique
  - Controller versus rescue inhalers
  - Complex medical regimens, oxygen
  - Triggers (asthma)
  - How often using rescue medication (asthma)
  - Exercise-induced symptoms (asthma)
  - Does patient have asthma action plan (asthma)
  - Is patient monitoring his/her condition (e.g., symptoms, SABA use, peak flow monitoring, if applicable)

Practice Management

- Developing a new Asthma/COPD/Smoking Cessation service: key issues to consider:
  - Who else should be on the team (MD, RN, counselor for smoking cessation, respiratory therapist, someone to perform spirometry)
  - What resources would be needed to start a practice/clinic (spirometry, carbon monoxide monitor, placebo inhaler, holding chambers, etc.)
  - Identify criteria to evaluate the success of a service/clinic in asthma, COPD, or smoking cessation (quality measures)
  - Certification: Certified Asthma Educator (AE-C)
Asthma Quality Measures  (Specific for Pharmacy)
- Documentation of asthma severity classification
- Use of inhaled corticosteroids for persistent asthma
- Provision of asthma action plans
- Patients have been educated on managing their asthma and avoiding triggers
- Influenza vaccines given
- Smoking cessation counseling completed
- Number of full SABA canisters used in past 3 months
- Number (or %) of patients who have been taught how to use a MDI or DPI by a health professional

Asthma Quality Measures  (Specific for Pharmacy)
- Daily symptom burden
  - Frequency of symptoms and beta-agonist use (per week)
  - Number of days of (or free from) asthma symptoms in past month
  - Days with nocturnal symptoms in past month
  - Number of school/work days missed in past month
  - Frequency of urgent care or acute office visits
  - Frequency of ED visits or hospitalization

COPD Quality Measures  (Specific to Pharmacy)
- Pneumococcal vaccination
- Influenza vaccination
- Number (or %) of patients who received smoking cessation counseling
- Number (or %) of patients prescribed long-acting bronchodilators in patient group B
- Number (or %) of patients prescribed inhaled corticosteroids in patient groups C and D

Patient Advocacy
- For asthma and COPD, all inhalers are brand name and not available generically
- Patient assistance programs are available from manufacturers www.rxassist.org
- Ventolin HFA available in smaller canister on the $4 programs of some retail pharmacies
  - Cost: $8 per canister (60 puffs/canister instead of 200)
- Generic albuterol and ipratropium nebulizer solutions are also available for $4 a month.
- Coupons available from some manufacturers websites

Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

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