Minor conditions: Practical applications of pharmacist prescribing laws

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Objectives

• Describe the pathophysiology of motion sickness, lice, cold sores, and uncomplicated urinary tract infections
• Determine the differential diagnosis and referral criteria for motion sickness, lice, cold sores, and uncomplicated urinary tract infections
• Compare and contrast pharmacologic options for treatment of motion sickness, lice, cold sores, and uncomplicated urinary tract infections
• Counsel on non-pharmacologic interventions for motion sickness, lice, cold sores, and uncomplicated urinary tract infections
• Discuss workflow considerations for pharmacist prescribing in community pharmacy
• Complete an appropriate community pharmacy-based physical assessment for motion sickness, lice, cold sores, and uncomplicated urinary tract infections

Plan for today

• For each disease state:
  — Pathophysiology
  — Differential diagnosis (factors to consider for treatment and referral)
  — Physical exam refresher
  — Treatment options and patient education
  — Practice with physical exam and application to cases
• Workflow considerations

Disclosures

• The planners and presenter of this presentation have disclosed no conflict of interest, including no relevant financial relationships with any commercial interests
Motion Sickness

- Physiologic responses to motion by sea, car, train, air, and virtual reality immersion
- Can affect all people with functional vestibular systems
- Conflicting vestibular, visual, and proprioceptive inputs
  - e.g. Looking at an apparently unmoving ship cabin wall while sensing the ship rolling

Risk Factors

- Age:
  - Children aged 2 – 12 years are especially susceptible
  - Adults > 50 years are less susceptible
- Sex:
  - Females are more susceptible
  - Pregnancy, hormone replacement, menstruation
- Poor ventilation (fumes, smoke, CO)
- Emotional factors (fear, anxiety)
- Those prone to migraine headaches

Clinical Presentation

- Characteristic manifestations:
  - N/V/retching
  - Sweating/cold sweats
  - Vague abdominal discomfort
- Other symptoms/preceding symptoms:
  - Yawning
  - Hyperventilation
  - Salivation
  - Somnolence
  - Dizziness
  - Headache
  - Fatigue
  - Confusion

Differential diagnosis

- Exclusions: Symptoms caused by factors or disease states other than motion sickness
  - e.g. concussion, vestibulopathies, vestibular migraine
  - Ototoxic drugs
- Refer if present:
  - Atypical symptoms (e.g. true vertigo; excessive vomiting)
  - Symptom onset without motion
  - New-onset motion sickness

PHYSICAL EXAM FINDINGS

TREATMENT
Prevention

• Nonpharmacological interventions:
  – Acupressure
  – Avoidance of triggers
  – Optimize positioning to reduce motion or motion perception
  – Reducing sensory input
  – Limit alcoholic and caffeinated beverages
  – Avoiding smoking
  – Adding distractions
  – Adaptation

• Pharmacologic:
  – Scopolamine
  – Antihistamines:
    • Dimenhydrinate
    • Diphenhydramine
    • Meclizine
    • Cyclizine
  – Anti-dopaminergic drugs
    • Promethazine, metoclopramide
    • Ginger

Scopolamine

• Transderm-Scop®, generic
• Dose: 1.5mg/72 hours
• Apply 4 hours before effect is required
  – Best if 12 hours before
• Replace every 72 hours as needed
  – Remove old patch
• Adverse effects: anticholinergic
• Effectiveness:
  – Better than placebo
  – No better than antihistamines

Antihistamines

• Dimenhydrinate (Dramamine®, Driminate™, Motion Sickness)
  – Adults, children >12 yrs: 50-100mg every 4-6 hrs (max 400mg/day)
  – 6 to 12 yrs: 25-50mg every 6-8 hrs (max 150mg/day)
  – 2 to 5 yrs: 12.5-25mg every 6-8 hrs (max 75mg/day)
  – Chewable tablet
• Meclizine (Dramamine Less Drowsy®, Travel Sickness)
  – Adults, children >12 yrs: 25-50mg every 24 hrs
• Diphenhydramine
  – Adults: 25-50mg every 4-8 hrs
  – Children ≥12 yrs: 25-50mg every 4-6 hrs
  – 6 to 11 yrs: 12.5-25mg every 4-6 hrs
  – 2 to 5 yrs: 6.25mg every 4-6 hrs

Antidopaminergic Drugs

• Usually reserved for those that fail transdermal scopolamine and antihistamines
• Potentially more sedating than antihistamines
• Side effects:
  – Anticholinergic
  – Sedation
  – Extrapyramidal effects
• Promethazine (Phenergan®)
  – Adults: 25mg, 30-60 minutes prior to departure, 25mg BID
  – Children >2 yrs: 0.5mg/kg (max 25mg), 30-60 minutes prior to departure, every 12 hours PRN
APPLICATION TO CASES

Ectoparasites

- Head lice
  - Pediculus humanus capitis
- Body lice
  - Pediculus humanus corporis

Head Lice

- Life cycle of head louse:
  - Adults: one month
  - Female lays 7-10 eggs (nits) per day
  - Nits hatch in eight days, releasing nymphs
  - Nymphs require eight days to mature
- Transmission:
  - Direct contact
  - Louse do not fly, jump or use pets as vectors

Lice Presentation

- Chief complaint: scalp pruritus
  - Caused by reaction to louse saliva
  - If first infestation, sensitivity to saliva may take 4-6 weeks to develop
- Tickling sensation
  - “Something moving on head”
- Asymptomatic
- Primary finding: nits at proximal end of hair shafts
  - Height of nits above scalp indicates duration of infestation
    - 1 cm = 1 month

Differential diagnosis

- Itching not always present and not a sure-fire indicator of head or body lice
- Scalp:
  - Seborrheic dermatitis
  - Atopic dermatitis
  - Dandruff
  - Key: Presence of nits near to scalp or live lice
- Body:
  - Scabies
  - Atopic or contact dermatitis
  - Secondary pruritis
  - Key: Presence of nits or live lice on body or clothing
Physical exam findings

• Scalp: Distinguish nits from hair casts (seborrheic dermatitis, psoriasis) and piedra
  – Nits difficult to dislodge
  – Looking for multiple nits within ¼ inch from scalp
• Body: Distinguish from scabies (scabetic burrows, erythema)
  – Co-infection possible (refer)

Physical exam refresher

• Equipment: Magnifying glass, nit comb, comb, and gloves
• Inspection (Body lice and nits): Examine along seams of clothing
• Wet comb: Apply hair lubricant (e.g. conditioner), comb or brush hair to remove tangles, comb hair with nit comb, examine comb after each stroke, repeat nit comb for entire scalp

Treatment Overview

• Guidelines: The American Academy of Pediatrics
• Confirm presence of living lice
• Nits > 6.5mm from the scalp w/o nymphs or adults?
  – Treatment not necessary
• Topical pediculicides are the most common initial treatments
• Wet combing is sometimes used as an alternative
• Oral pharmacologic therapy if refractory
• Do not need to withhold children from school!!
• Treat family members
• Wash clothing/ bedding in hot water
FDA Approved Treatment Options

- Permethrin 1% (Nix®, Nix creme rinse*)
- Pyrethrins 0.3%/piperonyl butoxide 4% (RID®)
- Malathion 0.5% (Ovide®)
- Ivermectin (Sklice®)
- Spinosad (Natroba®)

Permethrin 1% (Nix, Nix creme rinse)

- Synthetic pyrethroid
- Less allergenic than pyrethrins
  - Ok to use if patient has chrysanthemum allergy
- Reported adverse effects:
  - Pruritus
  - Erythema
  - Edema

Permethrin 1% (Nix, Nix creme rinse)

- Directions:
  - Shampoo hair, towel dry, apply rinse to hair, leave on x 10 minutes, rinse
  - Remove nits with nit comb
  - Repeat if live lice after 7-10 days of initial therapy
  - 9 days is preferred based on the life cycle of lice

Pyrethrins 0.3%/piperonyl butoxide 4% (RID)

- Manufactured from chrysanthemum
- Avoid if allergy to chrysanthemum or “plants”
- Available in shampoo or mousse formulations
- Directions:
  - Apply to dry hair, leave on for 10 minutes, rinse
  - No residual pediculicidal activity after washing:
    - 20%-30% of eggs remain viable after treatment
    - Will likely need to repeat in 7-10 days
  - Efficacy has decreased substantially due to resistance

Malathion 0.5% (Ovide)

- Organophosphate (cholinesterase inhibitor)
- Highly ovicidal
  - Single application usually sufficient
- Consider use if pyrethroid resistance present
- Directions:
  - Apply lotion to dry hair, allow hair to dry, rinse after 8-12 hours, shampoo hair and rinse, use a nit comb
  - May repeat in 7-9 days
- Concerns:
  - Highly flammable (78% isopropyl alcohol)
    - Avoid hair dryers, curling irons and smoking
    - Contraindicated in children < 2 yrs

Ivermectin 0.5% Lotion (Sklice®)

- Anthelmintic agent
- Increases chloride ion permeability of muscle cells
  - Paralysis and death of lice
- Generally well tolerated
  - Potential ocular irritation, dry scalp, burning sensation
- Directions:
  - Apply to dry hair and scalp, rinse after 10 minutes
  - Only need one application
Spinosad (Natroba)

- Spinosyn A + spinosyn D (5:1)
- Broad spectrum of activity against many insects
- Ovicidal and pediculicidal
- Appears to be more effective than permethrin
  - Cure rate at 14 days: 84.6% vs. 44.9% (NNT 3)
- Directions:
  - Apply to dry hair, saturate scalp and work outward
  - Rinse 10 minutes after application
  - May repeat in 7 days if live lice present

Choosing an Agent

- Resistance patterns
- Age restrictions
- Cost
- Application requirements
  - Malathion must be left in for 8-12 hours
  - Malathion is malodorous
  - Malathion is flammable and may cause respiratory depression if ingested

Topical Pediculicides

<table>
<thead>
<tr>
<th>Product</th>
<th>Availability</th>
<th>Formulations</th>
<th>Age Restrictions</th>
<th>Cost Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permethrin (Nix®)</td>
<td>OTC</td>
<td>liquid or lotion</td>
<td>&lt; 2 months</td>
<td>$</td>
</tr>
<tr>
<td>Pyrethrins + piperonylbutoxide (Rite®)</td>
<td>OTC</td>
<td>Shampoo or mousse</td>
<td>&lt; 2 years</td>
<td>$</td>
</tr>
<tr>
<td>Malathion (Ovide®)</td>
<td>Rx</td>
<td>Lotion</td>
<td>&lt; 6 years</td>
<td>$$$$</td>
</tr>
<tr>
<td>Ivermectin (Sklice®)</td>
<td>Rx</td>
<td>Lotion</td>
<td>&lt; 6 months</td>
<td>$$$$</td>
</tr>
<tr>
<td>Spinosad (Natroba®)</td>
<td>Rx</td>
<td>Suspension</td>
<td>&lt; 6 months</td>
<td>$$$$</td>
</tr>
</tbody>
</table>

APPLICATION TO CASES

COLD SORES (HERPES LABIALIS)

Herpesviruses Overview

- Eight types of herpesviruses that infect humans
- All herpesviruses remain latent within specific host cells
  - May subsequently reactivate at any time
- Do not survive long outside of host:
  - Transmission usually requires intimate contact
  - Virus can reactivate without causing symptoms
  - Asymptomatic shedding
HSV Types

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Other Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV 1</td>
<td>Human herpesvirus 1</td>
</tr>
<tr>
<td>HSV 2</td>
<td>Human herpesvirus 2</td>
</tr>
<tr>
<td>Varicella-zoster</td>
<td>Human herpesvirus 3</td>
</tr>
<tr>
<td>Epstein-Barr</td>
<td>Human herpesvirus 4</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Human herpesvirus 5</td>
</tr>
<tr>
<td>Human herpesvirus 6</td>
<td>Roseola infantum</td>
</tr>
<tr>
<td>Human herpesvirus 7</td>
<td>Roseola infantum</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>Human herpesvirus 8</td>
</tr>
</tbody>
</table>

Oral Herpes

- Primarily caused by HSV1
  - Can be caused by HSV2, although less frequent
- Rash of skin and mucous membranes (primarily lips)
- Prodrome of tingling, itching, and burning
  - Oral and perioral lesions
- Contagious to those not previously infected, immunosuppressed
- Primary outbreak: herpetic gingivostomatitis
- Recurrent episodes: herpes labialis

Differential diagnosis

- Inclusion/exclusion from BOP (see handout)
- Differentiate from:
  - Aphthous ulcers (canker sores)
  - Bacterial pharyngitis (strep throat)
  - Syphilis (chancre is typically painless)
  - Stevens-Johnson Syndrome
  - Herpes infection somewhere other than mouth

Physical exam findings

- Location
- Appearance
- Past medical history

Non-HSV-1 Mouth Sores

Treatment options
Management Overview

- Education:
  - Contagious nature of virus
  - Modes of transmission
- Self-limited infection: treatment needed?
- Antiviral medications?
  - Immunocompromised or frequent outbreaks
  - Moderate-severe cases of primary infection
  - May improve symptoms and prevent recurrence
    - Do not cure infection (lifelong latency)

Management Overview

- Prompt initiation of antivirals:
  - Within 48-72 hours
- Potential benefits:
  - Fever reduction (1 vs 3 days)
  - Shorten duration ~ 1 day
  - Reduced viral shedding (1 vs 5 days)
- Strategies:
  - Episodic therapy
  - Chronic suppressive therapy
  - No treatment

Antivirals

- Acyclovir (Zovirax®)
- Valacyclovir (Valtrex®)
- Famciclovir (Famvir®)
- Mechanism of action:
  - Inhibit replication of human herpesviruses
  - Inhibit viral DNA synthesis

Acyclovir Mechanism of Action

- Prodrug of acyclovir → converted to acyclovir
- Pharmacokinetics:
  - Renally eliminated (dose adjustment required)
  - Low bioavailability
- Adverse effects:
  - Nephrotoxicity: ↑BUN/SCr, crystallization in renal tubules
    - Hydration is key
  - GI: N/V, ↑LFTs
  - Neurotoxicity: lethargy, tremors, confusion, hallucinations, seizures

Valacyclovir (Valtrex®)

- Prodrug of acyclovir → converted to acyclovir
- Pharmacokinetics:
  - Renally eliminated
  - Better bioavailability over acyclovir
  - Longer half-life than acyclovir
- Adverse effects:
  - Headache, dizziness, depression
  - GI: N/V, diarrhea
  - Renal toxicity (less than that of acyclovir)
Famciclovir (Famvir®)

- Rapidly converted to active compound - penciclovir
- Pharmacokinetics:
  - Renally eliminated
  - Better bioavailability over acyclovir
  - Longer half-life than acyclovir
- Adverse effects:
  - Headache, dizziness, fatigue
  - GI: N/V, diarrhea

HSV-1 Topical Treatment

- Acyclovir (Zovirax®)
  - Apply 5x/day x 4 days
- Acyclovir + hydrocortisone 1% (Xerese®)
  - Apply 5x/day x 5 days
  - Hydrocortisone to decrease inflammation
- Penciclovir (Denavir®)
  - Apply every 2 hours while awake x 4 days
- Docosanol 10% (Abreva®)
  - Apply 5x/day until lesions healed (max 10 days)
  - Efficacy similar to topical antivirals
  - Blocks virus from entering cells

Episodic Treatment

- Must be initiated quickly!
- Oral:
  - Acyclovir: 200 or 400mg five times daily x 5 days
  - Valacyclovir: 2g twice daily x 1 day
  - Famciclovir: 750mg twice daily x 1 day or 1500mg as a single dose
- Topical:
  - Benefit = modest
  - Must be applied at first sign of symptoms

What can pharmacists prescribe for?

- Active cold sore
- Short-term prevention

APPLICATION TO CASES

UNCOMPLICATED URINARY TRACT INFECTION
Background

- Epidemiology:
  - Affects ~150 million people worldwide annually
  - ~50% of women will have a UTI in their lifetime
  - 25% of women with first episode of cystitis report recurrent UTI within 6 months
- Incidence:
  - 15.2% for women aged 17–39
  - 11.4% for premenopausal women (aged 40–59)
  - 9.7% for postmenopausal women (aged 60–79)

Risk Factors

- Sexual intercourse
- Spermicide use
- Diaphragm contraception use
- Frequent or recent sexual activity
- Previous UTI
- Family history of UTI in first-degree female relative
- Increasing parity
- Diabetes mellitus
- Postmenopausal
- Others

Pathogenesis

- Female urethra is short, external one third is often colonized
- Bacteria from bowel or vagina colonize periurethral mucosa
- Bacteria ascend through the urethra to bladder
  - Can ascend to the kidneys (pyelonephritis)
- Once in the bladder, bacteria can colonize and cause infection
- Pathogens:
  - Escherichia coli causes 75-95% of uncomplicated UTIs
  - Klebsiella pneumoniae
  - Enterococcus faecalis
  - Proteus mirabilis
  - Staphylococcus saprophyticus
  - Streptococcus agalactiae

Signs and Symptoms

- Dysuria
- Frequency
- Urgency
- Suprapubic pain
- Gross hematuria – less common
- Dysuria + frequency w/o vaginal discharge = highly predictive
  - Probability > 90%

Differential diagnosis

- Inclusion/exclusion from BOP (see handout)
- Differentiate from:
  - Complicated UTI
  - Pyelonephritis or systemic illness
  - Pelvic inflammatory disease
  - Sexually transmitted disease
- Eliminate possibility of pregnancy

Physical exam findings

- Eliminate:
  - Symptoms suggesting anything other than uncomplicated UTI
  - Systolic hypotension (<100mmHg)
  - Tachypnea (>25 breaths per minute)
  - Tachycardia (>100 BPM)
  - Oxygenation <90%
  - Body temperature >103°F
Physical exam refresher

• Vitals
  – Breaths per minute
    • Assess alone or with pulse
    • Watch sternum
    • Count inhalations for 20 seconds (x3) or 30 seconds (x2)
  – Pulse oximetry
    • Devices
    • Potential sources of error
  – Pulse
    • Taken with pulse oximetry and automated BP cuff
    • Refer to handout for refresher on manual pulse confirmation

• Temperature
  – Selection of type of thermometer
    • Oral
    • Aural/Tympanic
    • Temporal
  – Legal considerations
• Example thermometer uses

Physical exam refresher

• Blood pressure devices
  – Meter selection
  – Cuff selection
• Blood pressure measurement
  – Patient positioning
  – Obtaining the measurement
  – Refer to handout for refresher on manual blood pressure assessment

TREATMENT

Treatment Guidelines

• Guidelines:
  – Infectious Disease Society of America:
    https://academic.oup.com/cid/article/52/5/e103/388285874161261
    • Published March, 2011
  – American College of Obstetricians and Gynecologists:
    https://www.acog.org/~/media/Practice-Bulletins/Committee-on-Practice-Bulletins/
    Gynecology/Public/pb091.pdf?dmc=1&ts=20170908T1409079422
    • Published March, 2008

• Choice should be individualized:
  – Allergies, resistance patterns, availability, cost
• Prescribe a recommended antimicrobial:
  – Nitrofurantoin monohydrate/macrocystals
  – Trimethoprim-sulfamethoxazole
  – Fosfomycin
• If a recommended antimicrobial cannot be prescribed:
  – Fluoroquinolones
  – β-lactams
Nitrofurantoin

- **Dose:**
  - Nitrofurantoin monohydrate/macrocrystals (Macrobid®)
    - 100mg BID x 5 days
  - Nitrofurantoin monohydrate (Macrodantin®)
    - 50-100mg every 6 hours x 5 days
- **First line agent**
  - Minimal resistance and propensity for collateral damage
- **Does not cover** *P. mirabilis*
- **Not effective for** pyelonephritis

Nitrofurantoin

- **Avoid if** CrCl < 30 mL/minute
- **Adverse effects:**
  - Discolors the urine brown
  - N/V/D
  - Macrystaline preparation is better tolerated
  - Acute pneumonitis
    - Fears, chills, cough, dyspnea, chest pain, pulmonary infiltration, eosinophilia
    - May occur within hours-days
    - Symptoms usually resolve after discontinuation
  - Interstitial pulmonary fibrosis
    - Chronic therapy

Trimethoprim-Sulfamethoxazole (Bactrim®)

- **Dose:**
  - 160/800mg (1 DS tablet) BID x 3 days
- **Avoid if:**
  - Local resistance rates ≥20%
  - Used for UTI within the previous 3 months
  - Concomitant ACE-I or ARB therapy
    - Increase in serum K+ → cardiac dysrhythmias, sudden cardiac death
- **Drug interactions**
  - Inhibits CYP2C9, CYP2C8; substrate of CYP2C9 (major)
    - Warfarin: Potential three-fold increase in INR
  - Photosensitivity/ Stevens-Johnson
  - Drug-induced hepatitis
  - Aseptic meningitis
  - Drug interactions

Trimethoprim-Sulfamethoxazole (Bactrim®)

- **Adverse effects:**
  - N/V/D
  - Renal: hyperkalemia, interstitial nephritis, acute tubular necrosis
  - Photosensitivity/ Stevens-Johnson
  - Drug-induced hepatitis
  - Aseptic meningitis
  - Drug interactions

Fosfomycin (Monurol®)

- **Dose:**
  - 3g as a single dose
- **First line agent**
  - Minimal resistance and propensity for collateral damage
- **Activity against** VRE, MRSA, ESBL producing Gram negative rods
- **Efficacy:** compared to other 1st line agents
  - Clinical cure rates comparable
  - Bacterial efficacy rates slightly lower
- **Not uniformly available**
- **Susceptibility data** not uniformly available
Fosfomycin (Monurol®)

- **Administration:**
  - Mix with 3-4oz (90-120 mL) of cool water
  - Do not administer in dry form or mix in hot water
  - Orange flavored

- **Adverse effects:**
  - Diarrhea > nitrofurantoin
  - Headache
  - Dizziness
  - Hypokalemia
  - Large sodium load: 14.4 mEq of sodium/gm of fosfomycin

**OPTIONS IF PREFERRED AGENTS ARE NOT APPROPRIATE**

**β-Lactams**

- **Agents:**
  - Amoxicillin-clavulanate (Augmentin®) 500mg BID
  - Cefdinir (Omnicef®) 300mg BID
  - Cefpodoxime (Vantin®) 100mg BID
  - Cefadroxil (Duricef®) 500mg BID
  - Others

- **Duration:** 5-7 days
- **Avoid ampicillin and amoxicillin: high rates of resistance**
- **Alternative agents:**
  - Efficacy: lower clinical cure rate in clinical trials
  - More adverse effects as compared to other first line agents

**Fluoroquinolones**

- **Agents:**
  - Ciprofloxacin 250mg BID or 500mg ER every day
  - Levofloxacin 250mg every day
  - Ofloxacin 200mg BID

- **Duration:** 3 days
- **Alternative agents:**
  - Propensity for collateral damage
  - Increasing rates of resistance
  - Should be reserved for important uses other than cystitis
  - Adverse drug events
  - Drug interactions

**Agent Dose Adverse Events**

| Nitrofurantoin microcrystals | 100mg BID x 5 days | Urine discolored, anorexia, nausea, vomiting, hyperglycemia, peripheral neuropathy, hepatitis, hemorrhagic uremia, and pulmonary reactions |
| Nitrofurantoin monohydrate | 50-200mg every 6 hours x 5 days | |
| Fosfomycin | 3g as a single dose | Diarrhea, nausea, vomiting, rash, and hypokalemia |
| Trimethoprim-sulfamethoxazole | 160/800mg (1 DS tablet) BID x 3 days | Rash, photosensitivity, nephrotoxicity, vertigo, nausea and vomiting, pyrexia, headache, urticaria, rheumatoid arthritis, and stomatitis |
| Amoxicillin-clavulanate | 500mg BID | Nausea, vomiting, diarrhea, hypoglycemia, rash, urticaria |
| Cefadroxil | 500mg BID | |
| Cefpodoxime | 500mg BID | |
| Ciprofloxacin | 250mg BID x 3 days | Rash, confusion, seizures, dermatitis, headache, fever, hyperglycemia, hypokalemia, hypotension, Achilles tendon rupture, aortic dissection, and peripheral neuropathy |
| Levofloxacin | 250mg once daily x 3 days | |
| Ofloxacin | 200mg BID x 3 days | |
Workflow considerations

- Form considerations
  - Patient intake
  - Patient assessment
  - Referral
  - Follow-up and communications with PCP

- Physical workflow considerations
  - Do all patients come to patient evaluation room?
  - Who takes what actions when during workflow? (What can technicians handle, what must be done by pharmacist?)