Treatment of Infections and Infestation in the Pregnant Patient

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

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F126: The Pregnant Pause
Treatment of Infections and Infestation in the Pregnant Patient

DISCLOSURES

UpToDate®: Author, Royalties
Allergan, Beiersdorf, UCB: Advisory Board, Honoraria
Allergan: Speaker, Honoraria
Medical Therapy in Pregnancy: Resources

- Drugs in Pregnancy and Lactation
  - A Reference Guide to Fetal and Neonatal Risk
  - Third Edition

- Drugs During Pregnancy and Lactation
  - Treatment Options and Risk Assessment
  - Third Edition
Welcome to MotherToBaby

MotherToBaby, a service of the non-profit Organization of Teratology Information Specialists (OTIS), is dedicated to providing evidence-based information to mothers, health care professionals, and the general public about medications and other exposures during pregnancy and while breastfeeding. Talk directly to the experts behind the most up-to-date research! Find a MotherToBaby affiliate near you by clicking on the map above, or call us toll-free: 1-866-628-6847.
Infant Risk Center
AT TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

The Infant Risk Center representatives are available to answer your questions:

MONDAY - FRIDAY
8 A.M. CST - 5 P.M. CST

Call us at 806.352.2519
or visit us online at:

mommymeds.com

爸爸需要更多信息或建议？
Call the IRC or Visit our forums
The following scale is used to rate the safety of each drug. If you have questions about any of these ratings, please call the InfantRisk Center.

### Pregnancy

- **Safest**
  - Minimal or no risk to the fetus.

- **Safer**
  - Benefits are likely to exceed risk.

- **Probably Safe**
  - No data available, risk to fetus cannot be ruled out.

- **Possibly Hazardous**
  - Human trials suggest risk, weigh carefully against benefits.

- **Hazardous**
  - Major risk likely to exceed benefits.

- **Unknown**
  - There is no data or information available.

### Lactation

- **L1 - Compatible**
  - No to extensive data suggest there is little or no risk to a breastfeeding infant. Thus the possibility of harm is remote.

- **L2 - Probably Compatible to Compatible**
  - Limited to extensive data suggests there are only limited risks to a breastfeeding infant.

- **L3 - Probably Compatible**
  - No or limited data suggest this drug may be compatible in breastfeeding mothers. However no studies in humans are available. Use only if the risk is justified.

- **L4 - Possibly Hazardous**
  - No or significant data suggests there may be a possible risk to a breastfeeding infant, but the benefits from use in breastfeeding women may be acceptable despite the risk.

- **L5 - Hazardous**
  - No to significant data suggests that his product is potentially hazardous to a breastfeeding infant. Avoid if at all possible.

- **Unknown**
  - There is no data or information available.
The Itchy Pregnant Patient

- Pregnancy dermatoses
- Atopic dermatitis
- Contact dermatitis
- Drug eruption
- Pityriasis rosea
- Psoriasis

- Primary pruritus
  - Malignancy (Hodgkin, NHL)
  - Hepatobiliary disease
  - Hepatitis C
  - HIV

- Scabies, lice
- Viral exanthem
- Dermatophyte infection
- Folliculitis - bacterial, candidal, *Pityrosporum*
- Secondary bacterial infection
- Arthropod bite reaction
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Most Common Infections in Pregnancy

- 600 pregnant women
- Outpatient OB/GYN appointment
- Detailed history, complete PE, dermatologic exam
- +/- Skin biopsy

<table>
<thead>
<tr>
<th>Infection</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>21%</td>
</tr>
<tr>
<td>Tinea versicolor</td>
<td>6%</td>
</tr>
<tr>
<td>Scabies</td>
<td>2.8%</td>
</tr>
<tr>
<td>Dermatophytosis</td>
<td>1.5%</td>
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</table>

Vulvovaginal Candidiasis

- 70-75% at least 1 episode in lifetime
  - 40-50% at least 1 recurrence

- Up to 50% of pregnant women affected

- ↑ risk with advanced gestation, higher gravidity

- ~$1 billion per year in US (OTC meds)
Vulvovaginal Candidiasis Pathogenesis

- Estrogen = essential
  - Increased glycogen content of vaginal epithelium
  - $E_2$-dependent squamous differentiation
- ↑ adherence of yeast cells to vaginal mucosa
- Suppression of protective normal bacterial flora
### Vulvovaginal Candidiasis Clinical Presentation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Pruritus</td>
<td>Erythema</td>
</tr>
<tr>
<td>Pain, burning</td>
<td>Edema (labia minora)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Fissuring</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>Adherent discharge</td>
</tr>
<tr>
<td></td>
<td>(pseudomembranes)</td>
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<tr>
<td></td>
<td>Erosion/ulcer</td>
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</table>
Microbiology

• 80-90% azole-sensitive *Candida albicans*

• 10-20% non-albicans *Candida* spp.
  – Increasing over time
  – Most common: *Candida glabrata*
    • Non-dimorphic (budding only)

• Antifungal susceptibility testing available
Vulvovaginal Candidiasis and the Fetus

- **Neonatal candidosis**
  - Vertical transmission during passage through birth canal
  - Limited to skin, mucous membranes (genital, oral cavity)
  - ↑ risk systemic infection in LBW, immunosuppressed
  - Onset few days after birth

- **Congenital candidosis**
  - Ascending infection *in utero*
  - Generalized papulopustular skin eruption, pneumonia, sepsis
  - Onset shortly after birth (within 12 hours)
VVC Treatment During Pregnancy

• Acute episode:
  – If + pseudohyphae on KOH, no culture necessary
  – Clotrimazole 1% cream PV qhs for 7 days
  – Miconazole 2% cream PV qhs for 7 days
    • Imidazoles more effective than nystatin
    • 7 day course more effective than 4 days
    • 14 day course NOT more effective than 7 days
  – Nystatin cream, 100,000U tablets

• Recurrent:
  – Obtain culture, consider antifungal susceptibility testing
Risks of Oral Fluconazole

• Miscarriage
  – National Danish registry, cohort of 1.4 million pregnancies
  – 4 unexposed pregnancies: 1 fluconazole exposed pregnancy
  – 150-300mg between 7-22wga
  – Risk of spontaneous abortion: HR 1.48 (CI 12.3-1.77)
  – Risk of stillbirth: HR 1.32 (CI 0.82-2.14)

  – Risk of fluconazole vs topical azoles
    • Spontaneous abortion: HR 1.62 (CI 1.25-2.07)
    • Stillbirth: HR 1.18 (CI 0.64-2.16)

Risks of Oral Fluconazole

- Teratogenicity
  - Cleft palate, skull abnormalities, congenital heart disease
  - High doses (400-800mg/day)
  - Prolonged duration (weeks+)
  - Maximal risk at 6wga

- No increased risk of congenital anomalies with single-dose 150mg in 1st trimester

Scabies in Pregnancy

• 2-6% of all skin disease in pregnancy
• Clinical presentation identical to non-pregnant
  – Crusted scabies is rare

• Not associated with negative pregnancy outcomes

• Critical to differentiate from other causes of pruritus
  – Intrahepatic cholestasis, pregnancy dermatoses

Scabies in Pregnancy: Treatment

• Permethrin 5% cream
  – ≤ 2% systemic absorption rate
  – May cross placenta, rapidly metabolized
  – Animal studies 200-400mg/kg/day oral → no fetal harm, mutagenicity

  – Prospective studies in pregnant women
    • 1/4 exposed during 1st trimester
    • No difference in spontaneous abortion, major malformation, preterm delivery, birth weight, stillbirth

Mylton OT et al. BJOG 2007; 114: 582.
Scabies in Pregnancy: Treatment

- 2nd line: Precipitated sulfur

- 3rd line:
  - Crotamiton 10% lotion: no safety studies in pregnancy
  - Malathion 0.05%: percutaneous absorption ≤ 8%
    - Possible shortened gestation, preterm delivery

Scabies in Pregnancy: Oral Ivermectin

- **Animal studies**
  - Doses that caused maternal toxicity
  - Fetal malformations in rabbits: cleft palate, exencephaly, clubbed forepaws

- **Human studies** (oncocerciasis, filariasis)
  - Liberia, 203 children: no ↑ in birth defects
  - Cameroon, 100 pregnant women: no ↑ in abortion, congenital malformation, stillbirth

- Considered safe to use in lactation
Tinea

• Superficial fungal infection

• Dermatophyte (boxcar hyphae, no spores)
  – *Trichophyton rubrum*
  – *Trichophyton mentagrophytes*
  – *Epidermophytum floccosum*

• Autoinoculation from feet, nails
Tinea in Pregnancy: Treatment

• 1st line:
  – Clotrimazole
  – Miconazole
  – Ciclopirox
  – Oxiconazole
  – Naftifine (over small areas)

• Not recommended
  – Econazole (aromatase inhibition), ketoconazole
Tinea in Pregnancy: Treatment

- **Oral fluconazole**
  - Risk of teratogenicity at higher doses (400-800mg)

- **Oral itraconazole**
  - May disrupt estrogen production

- **Oral terbinafine**
  - Limited safety data
  - No teratogenicity observed in animals or humans
Pityriasis Rosea in Pregnancy

• Overall incidence: 6.8 per 1000 dermatology patients
• Females slightly more common than males
• Pregnancy more common than general population (18% vs 6%)
• 1950: 1st report of coincident PR in pregnancy
• 2001: Detection of HHV-6, -7 DNA in plasma, WBCs

Pityriasis Rosea in Pregnancy

- 2008: 1st report of potential concerns in 38 pregnant women with PR
- Updates to case series: 2014 (N=61), 2018 (N=76)
- 14/61 (23%) preterm delivery
- 8/61 (13%) miscarriage
- PR onset prior to 15wga: 8/14 (57%) miscarriage
- Neonatal hypotonia

Pityriasis Rosea in Pregnancy

- Predictors of adverse outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>p value</th>
</tr>
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<tr>
<td>Early onset of PR (before 15wga)</td>
<td>0.0017</td>
</tr>
<tr>
<td>Enanthem</td>
<td>0.0392</td>
</tr>
<tr>
<td>PR body surface area involvement (&gt;50%)</td>
<td>&lt; 0.004</td>
</tr>
<tr>
<td>Constitutional symptoms (fatigue, headache, loss of appetite, insomnia)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HHV6 viral load (plasma)</td>
<td>&lt; 0.0001</td>
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Acyclovir for Pityriasis Rosea

• Systematic review, meta-analysis
• 7 studies, N=324: 159 +acyclovir, 165 controls

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<th>Treatment</th>
<th>Risk Ratio (Complete Regression)</th>
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<tr>
<td>Acyclovir vs placebo (week 1)</td>
<td>5.72 (CI 2.36-13.88)</td>
</tr>
<tr>
<td>Acyclovir + symptomatic treatment vs symptomatic treatment alone (week 4)</td>
<td>1.46 (CI 0.93-2.29)</td>
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• Acyclovir 400mg po TID x 7 days
  – As effective, better tolerated than 800mg po 5x/day

The Dermatology Foundation has supported & advanced my research – and patient care.