Dermatological Disorders of Pregnancy
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The following presentation represents the views of the speaker at the time of the presentation. This information is meant for educational purposes, and should not replace other sources of information or your medical judgment.
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Conflict Disclosures
I have NO conflicts to disclose

I am a member of GÉMOQ and NASOM

Some of the drugs or treatment modalities mentioned in this presentation are:
Dermatological creams in general
Oral prednisone
Set objectives

1. Evaluate a pregnant woman with cutaneous lesions and diagnose the major dermatoses specific to pregnancy (PUPPP, pemphigoid gestationis, atopic eruption of pregnancy, pustular psoriasis).
2. Decide when a biopsy is needed.
4. Plan the fetal follow-up required for gestational pemphigoid and advise the patient about possible neonatal lesion and risk of recurrence in a future pregnancy.
Your objectives?
My objectives

• Do NOT panic

• Remember what I know

• Think within a framework

• Know one set of creams
What do we already know?
Game 1: Pre-test
Problems with skin lesions in pregnancy

1. Recent changes in nomenclature

2. So many rashes look alike (at least to my Internal Medicine eyes)
Game 2: AKA

A. PUPPP

B. Pemphigoid gestationis

C. Pustular psoriasis

D. Atopic eruption of pregnancy
Classification of pruritic pregnancy-specific dermatoses

- Polymorphic eruption pregnancy (PEP)
- Atopic eruption of pregnancy (AEP)
  - Prurigo of pregnancy
  - Pruritic folliculitis of pregnancy
  - Eczema of pregnancy
- Intrahepatic cholestasis of pregnancy (ICP)
- Pemphigoid gestationis (PG)
How does the patient present?

• Oh and by the way, doctor....
• Referral for rash: Please assess... (HELP!)
• Referral for pruritus
• Systemic illness (and rash present on careful clinical exam)
• QUESTION**: What are the skin findings of the normal pregnant patient?
| Increased hormone levels                      | Hyperpigmentation                  |
|                                             | Spider angioma, telangiectasia, palmar erythema |
|                                             | Gingival hyperemia, pyogenic granuloma |
|                                             | Hypertrichosis, telogen effluvium     |
|                                             | Molluscum fibrosum gravidarum        |
| Vascular expansion                          | Oedema, varicosities                |
| Abdominal distension                       | Striae gravidarum                   |
| Glandular function                         | Miliaria, Hyperhydrosis             |
| Nails changes                               | Increased brittleness, onycholysis   |
|                                             | Transverse grooving                  |
Frameworks
<table>
<thead>
<tr>
<th>PRURITUS</th>
<th>Pregnancy-related</th>
<th>Unrelated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commonly turns out to be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Must NOT be missed</td>
<td></td>
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</tr>
</tbody>
</table>
## Proposed framework

<table>
<thead>
<tr>
<th>RASH</th>
<th>Pregnancy-related</th>
<th>Unrelated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commonly turns out to be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Must NOT be missed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Rash

• **Ddx: do not miss**
  – Pemphigoid gestationis
  – Pustular psoriasis
  – Drug reaction

• **Commonly turns out to be:**
  – PEP
  – Pregnancy-unrelated conditions
Pruritus

• **Ddx: do not miss**
  – Obstetric cholestasis
  – Early PG
  – Scabies!
  – Opioid withdrawal

• **Commonly turns out to be:**
  – Pruritus of pregnancy
  – Xerosis
Pruritus

- 20% reported pruritus as early as T1
- 44% developed a rash

High yield information

• Systemic features
• Type of rash*
  – Bulla are bad
  – (Bulla may arise LATER)
• Distribution
• Prior history
• Medication exposure and contacts
### Useful clues

<table>
<thead>
<tr>
<th></th>
<th>PEP</th>
<th>AEP</th>
<th>ICP</th>
<th>PG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primiparous</td>
<td>73%</td>
<td>44%</td>
<td>47%</td>
<td>48%</td>
</tr>
<tr>
<td>Multiple</td>
<td>16%</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>7%</td>
<td>34%</td>
<td>88%</td>
<td>9%</td>
</tr>
<tr>
<td>Early</td>
<td>3%</td>
<td>75%</td>
<td>20%</td>
<td>29%</td>
</tr>
<tr>
<td>Abdomen</td>
<td>98%</td>
<td>68%</td>
<td>36%</td>
<td>95%</td>
</tr>
<tr>
<td>Only pruritus (excoriations)</td>
<td>0</td>
<td>0</td>
<td>100%</td>
<td>0</td>
</tr>
</tbody>
</table>
PEP

• **Classical features:**
  – Primiparous, T3 or immediately pp
  – ? associated with males fetuses and Gest Diabetes
  – Starts within striae with **umbilical sparing**

• **Importance:**
  – More common 1:160 pregnancies
  – Must be distinguished from PG
PEP 2

• Maternal investigations:
  – Biopsy? Not diagnostic
  – Helps to rule-out PG

• Fetal investigations:
  – None in particular


PEP 3

• **Maternal management:**
  – Reassurance
  – Recurrence rare except if multiple gestation
  – Symptomatic:
    • Oral antihistamines
    • Topical corticosteroids
  – If severe:
    • Short course of prednisone 20-40 mg po qd in tapering doses

• **Fetal management:**
  – none
PEP 4

- Maternal complications:
  - none

- Fetal complications:
  - none
Pemphigoid gestationis

• **Classical features:**
  – Rare, autoimmune bullous disorder
  – T3 or early pp
  – Pruritus $\rightarrow$ papules $\rightarrow$ spread $\rightarrow$ bullae

• **Importance:**
  – Maternal impact
    • May recur earlier, risk of secondary infection
  – Fetal impact
    • Placental and fetal involvement
Pemphigoid gestationis 2

• Maternal investigations:
  – Biopsy? **YES** and must be **PERI**-lesional skin
  – With direct immunofluorescence

• Fetal investigations:
  – Fetal surveillance (growth, movements, well being)
  – Risk of prematurity and SGA
  – Prognosis generally good (10% with mild skin lesions)
Pemphigoid gestationis 3

• **Maternal management:**
  – Treatment varies with stage and severity
  – Mild pre-bullous
    • topical corticosteroids (+/- oral antihistamines)
  – All others
    • Oral prednisone 0.5-1.0 mg/kg/day
  – Unresponsive cases
    • Immunoapheresis, IVIG, azathioprine, dapsone

• **Fetal management:**
  – Follow growth curve
Pemphigoid gestationis 4

- **Maternal complications:**
  - Counseling on course and risk of recurrence

- **Fetal complications:**
  - SGA babies: if diagnosis in T1 or T2
  - Prematurity: if diagnosis in T2 and blisters present
  - 5-10% neonates with mild skin lesions with spontaneous resolution
Atopic eruption of pregnancy

- **Classical features:**
  - Common, starts early
  - Tends to recur
  - Triggered by pregnancy-specific immunological changes
  - Includes atopic dermatitis that can be aggravated by pregnancy

- **Importance:**
  - Most common dermatosis in pregnancy accounting for 50% of patients
  - 80% experience first signs of atopy
AEP 2

• Maternal investigations:
  – E-type AEP:
    • Affects typical atopic sites (face, neck, décolleté, and flexural surfaces)
  – P-type AEP:
    • Papular lesions (trunk and limbs with typical prurigo nodules)
  – Biopsy? Rarely required
  – ? w-up for obstetric cholestasis

• Fetal investigations:
  – None in particular
AEP 3

• **Maternal management:**
  – Treat underlying dry skin
  – Oral antihistamines
  – Topical corticosteroid cream
  – Short course oral prednisone in severe cases
  – Narrowband UVB safe for severe, early cases (folic acid supplementation)

• **Fetal management:**
  – None in particular
  – Probiotics in infancy RR=0.79 (0.71-0.88)

Pelucchi 2014)
AEP 4

• **Maternal complications:**
  – Rapid response to therapy
  – Resolves 2-3 months postpartum
  – Recurrence in subsequent pregnancies

• **Fetal complications:**
  – Certain heredity
Pustular psoriasis

• **Classical features:**
  – Rare >200 cases described
  – Systemic symptoms, **third** trimester, rapid resolution pp
  – Widespread tiny pustules on erythematous-squamous plaques
  – Exact etiology is not known but it is known to be triggered by hypocalcaemia, hypoparathyroidism, infections and stress.

• **Importance:**
  – Maternal complications (hypocalcemia)
  – Fetal impact
Pustular psoriasis 2

- **Maternal investigations:**
  - CBC, electrolytes (Ca++, Mg++), renal, LFTs, PTH
  - Urgent dermatology consult
  - ICU may be necessary
  - Biopsy: yes
  - Sterile cultures

- **Fetal investigations:**
  - Monitoring
Pustular psoriasis 3

• **Maternal management:**
  – Prednisone 20-30mg po daily
  – Supportive fluids, calcium
  – Refractory cases:
    • Prednisone 60-80mg po daily
    • UVA
    • Cyclosporine 50mg/kg/day.

• **Fetal management:**
  – Fetal monitoring
  – Early delivery
Pustular psoriasis 4

• **Maternal complications:**
  – Beware of bacterial superinfection
  – Dehydration
  – Electrolyte imbalance
  – Delirium, tetanic seizures from hypocalcemia

• **Fetal complications:**
  – Placental complications including IUFD
Classification of pregnancy-specific dermatoses (PSD)

- Polymorphic eruption pregnancy (PEP)
- Atopic eruption of pregnancy (AEP)
  - Prurigo of pregnancy
  - Pruritic folliculitis of pregnancy
  - Eczema of pregnancy
- Intrahepatic cholestasis of pregnancy (ICP)
- Pemphigoid gestationis (PG)
## Summary 1

<table>
<thead>
<tr>
<th>Classical features</th>
<th>Importance</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemphigoid gestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEP</td>
<td></td>
<td></td>
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<tr>
<td>Atopic eruption of pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pustular psoriasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstetric cholestasis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Summary 2

• Indications for biopsy
  ➢ Bullous lesions
  ➢ Unclear diagnosis
  ➢ Unwell patient
  ➢ Any other suspicious lesion
    • Do not miss melanoma
<table>
<thead>
<tr>
<th>Potency</th>
<th>Name</th>
<th>Vehicle</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Super high</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II High</td>
<td>Methylprednisolone aceponate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III High</td>
<td>Triamcinolone acetonide</td>
<td>O, C</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Bmethasone</td>
<td>O, C, L, F</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Amcinonide</td>
<td>C, L</td>
<td>0.1</td>
</tr>
<tr>
<td>IV Medium</td>
<td>Hydrocortisone</td>
<td>O</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>O, C</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>C, L, S</td>
<td>0.1</td>
</tr>
<tr>
<td>V Lower-mid</td>
<td>Hydrocortisone butyrate</td>
<td>O, C, L, S</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Fluticasone propionate</td>
<td>C, L</td>
<td>0.05</td>
</tr>
<tr>
<td>VI Low</td>
<td>Fluocinolone</td>
<td>C, S</td>
<td>0.01</td>
</tr>
<tr>
<td>VII Super low</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig 1. Therapeutic index of topical corticosteroids (modified from Luger et al.\textsuperscript{62}). BMV, betamethasone valerate; CP, clobetasol propionate; HC, hydrocortisone; HCB, hydrocortisone butyrate; MF, mometasone furoate; MPA, methylprednisolone acetate; PC, prednicarbate; TRI, triamcinolone acetonide.
Topical steroid creams

• Pregnancy
  1 systematic review (7 studies) + 2 studies since
  No increased risk of:
  – Cleft lip/palate or other malformations
  – Prematurity
  – SGA babies (except for 1 study at high doses)
  – IUFD

• Lactation
  Few studies; low excretion; careful if treating areola

Kirtschig *British J Dermatol* 2011
Ferreira *Grossesse et allaitement* 2nd Ed 2013
<table>
<thead>
<tr>
<th>Vehicle</th>
<th>Smooth, nonhairy skin; thick, hyperkeratotic lesions</th>
<th>Hairy areas</th>
<th>Palms, soles</th>
<th>Infected areas</th>
<th>Between skin folds; moist, macerated lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ointment</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Lotion</td>
<td></td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Solution</td>
<td>+++</td>
<td></td>
<td>+</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Gel</td>
<td>++</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foam</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

+: infrequently used; ++: acceptable vehicle; +++: preferred vehicle.
Adapted from Goldstein, BG, Goldstein, AO, Practical Dermatology 2nd ed, Mosby-Year Book, Inc, St. Louis, MO, 1997.
<table>
<thead>
<tr>
<th>Area</th>
<th>BID/1 week</th>
<th>TID/2 week</th>
<th>BID/4 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face and neck</td>
<td>15 g</td>
<td>45 g</td>
<td>60 g</td>
</tr>
<tr>
<td>Trunk</td>
<td>60 g</td>
<td>180 g</td>
<td>240 g</td>
</tr>
<tr>
<td>One arm</td>
<td>15 g</td>
<td>45 g</td>
<td>60 g</td>
</tr>
<tr>
<td>One leg</td>
<td>30 g</td>
<td>90 g</td>
<td>120 g</td>
</tr>
<tr>
<td>Hands and feet</td>
<td>15 g</td>
<td>45 g</td>
<td>60 g</td>
</tr>
<tr>
<td>Body</td>
<td>180 g</td>
<td>0.75 to 1 kg</td>
<td>1.25 to 2 kg</td>
</tr>
</tbody>
</table>

For children use one-third to one-half these amounts.

BID: two times per day; TID: three times per day.

Antihistamines

• Pregnancy:
  – Diphenhydramine 25-50mg po q 4-6 hours
  – Hydroxyzine 25mg po q 6-8 hours
  – Cetirizine 5-10mg po qd
  – Loratidine 10mg po qd

• Lactation:
  – Diphenhydramine: maximal dose=0.3% of pediatric dose
  – Loratidine: 1% of maternal dose
Table 2. Algorithmic approach to pregnant patients with pruritus.

Pruritus in pregnancy

Related to pregnancy (dermatoses of pregnancy)

- Early onset (before third trimester of pregnancy)
  - AEP
    - Involvement of trunk and extremities
    - 20% exacerbation
    - 80% first manifestation
    - DIF/IIF: negative
    - Histopathology: nonspecific
    - Elevated total IgE (20-70% of cases)
    - Topical corticosteroids ± oral antihistamines ± systemic corticosteroids ± UVB-treatment (in severe, generalized cases)
  - DIF/IIF: positive linear deposition of C3 (100%) ± IgG (30% of cases) along the BMZ
  - Histopathology: ± subepidermal blistering

- Late onset (third trimester or postpartum period)
  - PG
    - Predominant abdominal involvement
    - Papulo-urticarial rash
    - Later on: blisters
    - Umbilical involvement
    - DIF/IIF: negative
    - Histopathology: nonspecific
  - Systemic corticosteroids ± oral antihistamines ± immunoadsorption (in uncontrolled cases)

Unrelated to pregnancy (dermatoses coinciding with pregnancy)

- PEP
  - Predominant abdominal involvement
  - Papulo-urticarial rash, starting within striae distensae
  - Later on: polymorphous lesions
  - Umbilical sparing
  - DIF/IIF: negative
  - Histopathology: nonspecific
  - Laboratory tests: non-specific
  - Topical corticosteroids ± oral antihistamines ± systemic corticosteroids (in severe cases, short course)

- ICP
  - Intense generalized pruritus
  - No primary rash
  - Only secondary skin lesions due to scratching (excoriations, purigo nodules)
  - DIF/IIF: negative
  - Histopathology: nonspecific
  - Elevated serum bile acid levels ± elevated routine liver function tests
  - Ursodeoxycholic acid

AEP = atopic eruption of pregnancy, PG = pemphigoid gestationis, PEP = polymorphic eruption of pregnancy, ICP = intrahepatic cholestasis of pregnancy, DIF = direct immunofluorescence, IIF = indirect immunofluorescence, BMZ = basal membrane zone.
Set objectives

✓ Evaluate a pregnant woman with cutaneous lesions and diagnose the major dermatoses specific to pregnancy (PUPPP, pemphigoid gestationis, atopic eruption of pregnancy, pustular psoriasis).
✓ Decide when a biopsy is needed.
✓ Start treatment for dermatoses of pregnancy.
✓ Plan the fetal follow-up required for gestational pemphigoid and advise the patient about possible neonatal lesion and risk of recurrence in a future pregnancy.
Back to your objectives

• Further questions?
Game 3: Post-test
Extra learning

**Articles**

- Ambros-Rudolph *Ann Dermatol.* 23(3) 2011
- Kirtschig *British J Dermatol* 2011
- Sävervall *Derm Research and Practice* 2015
- Roth *Clinics in Dermatol* 2016;34:392-400.

**Cases and Modules**

*American College of Dermatology Module*
THANK YOU!
Intrahepatic cholestasis of pregnancy (ICP)

- **Prevalence:** 1:150 pregnancies

- **Hallmark features**
  - Pruritus palms and soles with rapid generalization
  - Icterus in 10%, steatorrhea is rare
  - Abnormal LFTs in 70% (AST/ALT > tbili)
  - Second and third trimester, multiple gestation
  - Resolves rapidly pp

- **IMPORTANCE:**
  - Measure bile acids and repeat LFT’s
  - Meconium, fetal arrhythmia, PTL, IUFD
  - Treatment includes delivery plan
  - Tends to recur next pregnancy and with OCP
ICP fetal impact

• Cardiotocographic abnormalities:
  – Reduced variability
  – Tachycardia, bradycardia
  – Fetal tachyarrhythmia (atrial flutter at 220-230bpm)

• Prematurity (up to 1/2)
• Intrapartal fetal distress (up to 1/3)
• Meconial staining of amniotic fluid
• IUFD (1/100)
Bile salts measurement

• Cholic acid, chenodeoxycholic acid, taurine, autotaxin

• Bile acids levels
  – Mild ICP <4 µmol/L
  – Moderate ICP 4-40
  – Severe ICP >40

• 1-2% increased risk for every 1 µmol/L above 40
ICP treatment

- RCT 2012 (BMJ 2012;344:e3799)
  - Ursodeoxycholic acid (UCDA) vs placebo
    - Less pruritus
    - ALT lower
  - Early delivery vs expectant
    - No difference in rate in c/s or major neonatal outcomes

- UDCA 10-15mg/kg/day bid or tid (max 2g/day)
- Diphenhydramine 25-50mg po q 4-6hrs
- Hydroxyzine 25mg po q 6-8hrs
Approach to fetal monitoring

- NO single intervention has been shown to predict or prevent adverse fetal outcomes
- Elective delivery at 37 or 38 weeks
- ? Monitoring
- PR interval
ICP standards

- RCOG guidelines 2011
- Leaflet for patient
- Infection screen: hepatitis A, B, C, EBV, CMV
- Autoimmune work-up: ANA, Anti-smooth muscle, AMA
- Serial LFTs q 1-2 weeks
- Liver ultrasound
- Delivery plan: maximum 38 weeks gestation
- Post-natal follow-up until normalization