SPECIFIC DERMATOSES OF PREGNANCY
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Disclosure
- I have no relationships with commercial interests to disclose relevant to the content of this CME activity.
- Some medications discussed are off-label (not approved for indications being discussed).

Specific Dermatoses of Pregnancy


Specific Dermatoses of Pregnancy (DPs): Why all the confusion?
- Which dermatoses actually are actually specific for pregnancy?
- Many synonyms used historically and classifications
- Variable clinical presentations, but all pruritic

Confusion...
- Uncommon or rare
- Not always definitive diagnostic test
- Treatment options limited
- Onset sometimes postpartum

Current Classification of DPs
- Based upon largest study of DPs to date
- 505 patients over 10 years with pruritic dermatoses during pregnancy from 2 university centers
- PMH, morphology of skin eruption, labs, dermatoses during other pregnancies or postpartum

Current Classification of DP

- Polymorphic Eruption of Pregnancy (PEP) (Pruritic and Urticarial Papules and Plaques of Pregnancy)
- Pemphigoid Gestationis (PG)
- Atopic Eruption of Pregnancy (AEP) - eczema in pregnancy, prurigo of pregnancy, pruritic folliculitis of pregnancy
- Intrahepatic Cholestasis of Pregnancy (ICP)

Lehrhoff S, Pomeranz MK. Dermatologic Ther 2013;26:274-84

Case Report

- A 28 year-old primigravida, 25 weeks’ gestation, 1-week hx itchy rash on arms and legs, spreading to trunk. No similar eruption before, no one in close contact has a similar rash
- No personal h/o atopy, but states that her mother had eczema as a child
- No medical problems prior to or during pregnancy, only on prenatal vitamins
- On OTC antihistamine with mild relief of itching

DP's: Key Points

- Epidemiology
- Pathogenesis
- Clinical presentation, including timing of onset during pregnancy
- Diagnosis including laboratory evaluation, if needed
- Differential dx
- Treatment
- Maternal/fetal risk, if any
- Recurrence in subsequent pregnancy
**Atopic Eruption of Pregnancy**

**Papular Dermatitis of Spangler Nurse’s Early Prurigo Prurigo Gestationis Prurigo of Pregnancy Pruritic Folliculitis of Pregnancy Eczema in Pregnancy**

**AEP** includes previous categories ([EP, PP, PFP]) due to overlapping clinical and histologic features from 2-center study of 505 pregnant women with pruritic dermatoses (Ambros-Rudolph CM et al. J Am Acad Dermatol 2006;54:395-404.)

**Epidemiology:** Most common pruritic dermatosis of pregnancy (50%); in 75% onset before 3rd trimester (mean 18 wks); personal or family hx of atopy

**Pathogenesis:** pregnancy-induced immunologic Th2 cytokine shift (increased production IL-4, IL-10)

**Diagnosis:** clinical, eczematous (E-type) or papular (P-type)

120 with diffuse eczematous plaques face, neck, chest, flexural aspects extremities (48%)

52 with flare of existing atopic dermatitis (21%)

79 with diffuse small erythematos papules on trunk and limbs and typical prurigo nodules shins/arms (31%)

E-type (2/3)

P-type (1/3)

**In E-type, 80% have eczema for 1st time or recurrence after long remission (childhood)**

**In P-type, if no personal or family hx of atopy, may have AD minor features – such as KP, white dermatographism, Dennie Morgan infraorbital folds, etc.**

251 pregnant patients with pruritic eczematous or papular eruption and in patients with personal or family hx atopy (other DPs excluded)

**Diagnosis:** usually clinical; often serum levels of IgE, eosinophilia

**Culture:** if pustules; typically bacterial cultures sterile

**Histology:** non-specific and correlates to clinical findings (eczematous vs. papular vs. folliculitis)

**Differential dx:** PG, PEP, ICP, bacterial folliculitis

**Treatment:** topical corticosteroids, antihistamines (diphenhydramine, chlorpheniramine)

**Maternal/Fetal Prognosis:** excellent; infant may develop atopy

**Recurrence:** likely in mother, especially if atopic hx

**Case Report**

A 31 yr-old primigravida, 19 weeks’ gestation, presented with a 1-week hx pruritic eruption starting on the neck and chest and spreading to extremities and sides of her abdomen. Tried OTC hydrocortisone cream with mild improvement. No similar eruption in the past.

PMH: asthma and seasonal allergies. No meds.

FH: Sister has eczema

ROS: negative.
A 25 yr-old primigravida, 31 weeks' gestation, severely pruritic skin eruption, starting on her abdomen. Triamcinolone 0.1% cream bid was prescribed, but eruption worsened and spread to her extremities. Liver function tests were normal. A lesional biopsy for histology and biopsy for perilesional DIF were taken.
Pemphigoid Gestationis (aka Herpes Gestationis)

- **Epidemiology**: Rare; 1:50,000 pregnancies; genetic component - increased risk in those with HLA-DR3 and HLA-DR4.
- **Pathogenesis**: Circulating complement-fixing IgG1 antibodies ("HG factor") bind to BPAG2 (BP180) in hemidesmosomes of BMZ.
- Abnormal expression of MHC class II antigens within placenta, exposure of placental BPAG2 to maternal immune system (foreign antigen) triggers local immune response to placental BMZ. IgG1 antibodies cross-react with BPAG2 in BMZ of skin.

- **Clinical Presentation**: Usually onset 2nd or 3rd trimester, up to 25% immediate postpartum.
- Intensely pruritic urticarial papules and plaques, start on abdomen and involve umbilicus, progression to tense herpetiform vesicles and bullae with spread to extremities.
- Usually spares face, mucous membranes, palms and soles.

- **Diagnosis**: Histology and DIF.
- **Histology (lesional)**: Subepidermal blister or dermal edema (prebullous stage), perivascular mixed infiltrate with variable eosinophils.
- **DIF (perilesional)**: In all cases linear C3 along DEJ; IgG ~ 30% of the time.
- IIF is + in 30-100% cases; Anti-BP180 NC16A Ab level by ELISA for dx: 97% sensitivity, 100% specificity (JAAD 2017;76:560)/disease activity.
- **Differential Dx**: Early PEP vs. PEP (look for umbilical involvement in PEP vs. periombilical and lesions in striae in PEP), drug eruption, DH, EM, bullous LE, urticaria.
**Pemphigoid Gestationis**
- **Treatment:** usually systemic steroids (0.5 - 1 mg/kg/d prednisone, increase if no response after few days) +/- antihistamines; taper very slowly (weeks) if no new vesicles
- May increase dose near due date anticipating postpartum flare
- Refractory cases during pregnancy may need addition of IVIG, plasmapheresis, cyclosporine
- **Postpartum flares triggered by OCPs or menses** treated with prednisone +/- azathioprine, hydroxychloroquine, dapsone, cyclosporine

**Maternal/Fetal Prognosis:** increased risk for prematurity and SGA infants, especially in more severe disease
- Transient bullous eruption in ~10% infants due to placental Ab transfer
- Mother with increased risk for autoimmune disorders (Grave’s Disease)
- **Recurrent:** likely (only ~ 8% “skip pregnancies”) and often with earlier onset and more severe disease

**Polymorphic Eruption of Pregnancy**
- **Why PEP vs. PUPPP?**
- **PEP** utilized since more than ½ of patients present with features in addition to urticarial papules/plaques:
  - Eczematous lesions (22%)
  - Vesicles (17%)
  - Nonurticarial erythema (6%)
  - Targetoid lesions (6%)

**Epidemiology:** ~ 1/160 deliveries, 2nd most common of DPs
**Pathogenesis:** unknown, potential triggers include rapid, late abdominal skin distention with striae distensae/excessive maternal weight gain→connective tissue damage and subsequent immune response
**Clinical Presentation:** Onset in late 3rd trimester (≥ 35 wks gestation), usually primigravidas (or in multigravidas in the 1st pregnancy that goes to term); increased risk multiple gestation pregnancies and may present earlier; may unusually present postpartum
Polymorphic Eruption of Pregnancy

- **Clinical Presentation, cont’d**: pruritic edematous and erythematous papules and plaques typically starting within striae distensae and/or on abdomen with umbilical sparing
- May spread to proximal thighs, extremities, and trunk over days, typically sparing face, palms and soles, and mucosa
- Variable morphology of lesions: targetoid, small vesicles, widespread erythema, eczematous plaques

- **Diagnosis**: May be made clinically; if in doubt about PG; biopsy for path, DIF
- Labs typically normal
- Histology non-specific; correlates with morphology of skin lesions (mild spongiosis, perivascular lymphocytic infiltrate, with dermal edema)
- **Differential Dx**: PG, contact dermatitis, drug eruption, viral exanthem, EM, etc

- **Treatment**: topical steroids and antihistamines; may consider short-course systemic steroids in particularly severe cases
- **Maternal/Fetal Prognosis**: excellent; eruption usually resolves with delivery or over 4 weeks, no danger to mother or infant
- **Recurrence**: typically does not recur in subsequent pregnancies, except in some cases of multigestation pregnancy

Intrahepatic Cholestasis of Pregnancy (aka Pruritus Gravidarum, Obstetric Cholestasis)

- **Epidemiology**: incidence in Araucania, Chile approximately 20% vs. <1% in North America
- **Pathogenesis**: genetic, environmental, and hormonal influences
- **Genetic component significant**: more common in 1st degree relatives and familial clustering observed
- Mutations in ABCB11 gene (bile salt exporter pump) and ABCB4 gene (phosphatidylcholine transport into biliary canaliculi) (Dixon et al. Am J Gastroenterol 2014;109:76-84)
**Intrahepatic Cholestasis of Pregnancy**

- **Pathogenesis, cont’d**: increased steroid levels at end of pregnancy decrease export of bile salts/transport of other bile components, accounting for increased incidence of ICH in multiple gestation pregnancies.
- **Clinical Presentation**: 3rd trimester onset of severe pruritus of hands and feet, then becoming more generalized.
- Typically no primary lesions – excoriations, prurigo nodules later on shins, forearms.

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**Intrahepatic Cholestasis of Pregnancy**

- Jaundice in only 10% – typically these are most severe cases.
- Nausea, RUQ discomfort.
- **Diagnosis**: Most sensitive marker = fasting serum bile acids > 11 micromol/L; bile acids > 40 micromol/L often indicator of more severe disease.
- Increased transaminases, increased GGT, +/- hyperbilirubinemia.

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<thead>
<tr>
<th>Condition</th>
<th>Onset</th>
<th>Diagnosis</th>
<th>Maternal Risk</th>
<th>Fetal Risk</th>
<th>Recurrence Subsequent Pregnancy</th>
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<tbody>
<tr>
<td>AIP</td>
<td>before 3rd trimester</td>
<td>clinical or mild IgE testing</td>
<td>No</td>
<td>No</td>
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<tr>
<td>PIP</td>
<td>3rd trimester if pruritus is severe</td>
<td>clinical IgE testing</td>
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<tr>
<td>PG</td>
<td>24 and 28th week</td>
<td>biopsy &amp; DIF for r/o PG</td>
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<tr>
<td>ICP</td>
<td>late 2nd and 3rd trimester</td>
<td>total serum bile acids &gt;11 μmol/L, meconium staining, meconium aspiration, stillbirth unusual</td>
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