

DERMATOSES OF PREGNANCY

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CONFLICTS OF INTEREST

No Relevant Conflicts of Interest

June 2017- sat on a Young Dermatology Advisory Board for AbbVie Pharmaceuticals

LEARNING OBJECTIVES

- **Identify normal physiologic cutaneous changes that are observed during pregnancy**
- **Identify the most common dermatoses that occur during pregnancy and their associated maternal-fetal risks**
- **Understand a basic systemic approach to pruritus in pregnant women and develop confidence in treating pregnant women**

OUTLINE

- **History of pregnancy associated dermatoses**
- **Physiology changes during pregnancy**
 - Pigmentary, Hair, Nail, Glandular, Connective Tissue, Vascular
- **Dermatoses of Pregnancy**
 - Pemphigoid gestationis
 - Polymorphic eruption of pregnancy
 - Atopic eruption of pregnancy
 - Intrahepatic cholestasis of pregnancy
 - Impetigo herpetiformis
 - Autoimmune progesterone dermatitis
 - Preexisting skin conditions during pregnancy
 - Common infections in pregnancy
- **Approach to the pregnant woman with pruritus**

HISTORY OF PREGNANCY DERMATOSES

- **1872 – Milton described “herpes gestationis”**
- **1904 - Besnier coined term “prurigo gestationis” for all dermatoses other than pemphigoid gestationis**
- **1941 – Costello changed term to “prurigo gestationis of Besnier”; estimated an incidence of 2% of all pregnancies**
- **1962 – Bourne characterized “toxaemic rash of pregnancy” for patients with intensely pruritic papules/plaques in late pregnancy**
- **1962 – Spangler et al. reported on a series of women with similar symptoms as above but also reported biochemical changes in the women (i.e. elevated urinary HCG, etc.); “papular dermatitis”**
 - **Spangler’s papular dermatitis was reported to be associated with high fetal wastage – now discredited**

HISTORY CONTINUED

- **1968 – Nurse divided patients with non-pemphigoid gestationis pregnancy eruptions into early and late forms**
 - “Early” form was found to be similar to Spangler’s papular dermatitis and those entities were reclassified as prurigo of pregnancy
 - “Late” form overlapped with Bourne’s toxaemic rash of pregnancy and has since been described as pruritic urticarial papules and plaques of pregnancy, now polymorphic eruption of pregnancy
- **Atopic Eruption of Pregnancy added**
- **Intrahepatic cholestasis of pregnancy classically absent because there were no primary lesions**

PHYSIOLOGIC CHANGES DURING PREGNANCY

- **PATHOGENESIS**

- Variable
- Hormonal changes seen during pregnancy
 - Increase in estrogen, progesterone, melanocyte stimulating hormone
- Weight gain and redistribution of volume

PHYSIOLOGIC CHANGES DURING PREGNANCY

• PIGMENTARY CHANGES

- Hyperpigmentation
 - Up to 90% of patients
 - Classically areolae, linea nigra, nipples, genital skin
- Melasma (“mask of pregnancy”)
 - Up to 70% of patients
 - Centrofacial, malar, mandibular
- Pathogenesis
 - Elevated serum levels of melanocyte stimulating hormone and estrogen
 - Melasma a result of excessive melanin deposition in epidermis & dermal macrophages
- Treatment
 - Sunscreen!
 - Often resolves postpartum, may recur with subsequent and OCPs



PHYSIOLOGIC CHANGES DURING PREGNANCY

• HAIR CHANGES

- Hirsutism
 - Tends to regress postpartum
- Postpartum telogen effluvium
 - Many patients notice thickening of hair during pregnancy due to prolonged anagen phase
 - With the stress of pregnancy/delivery, increased numbers of telogen hairs leading to telogen effluvium
 - Notice loss of approx. 10-20% hair
 - Lasts 1-5 mo., can last up to 15 mo.
- Postpartum patterned/androgenetic alopecia
 - Much less common than telogen effluvium
 - May not ever return to normal



PHYSIOLOGIC CHANGES DURING PREGNANCY

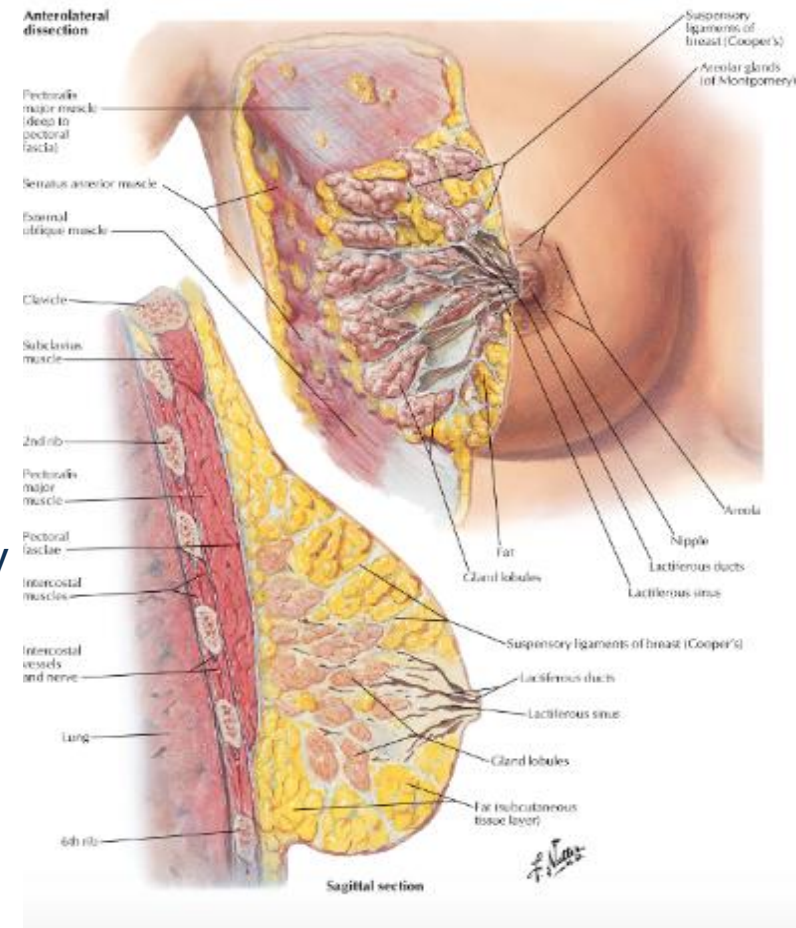
- **NAIL CHANGES**

- No nail changes are pathognomonic – all are loosely associated with pregnancy
 - Pathogenesis unclear
- Subungual hyperkeratosis
- Distal onycholysis
- Transverse grooving
- Brittleness

PHYSIOLOGIC CHANGES DURING PREGNANCY

GLANDULAR CHANGES

- Eccrine function increases (except on palms)
 - Leads to miliaria, hyperhidrosis, dyshidrotic eczema
- Increased sebaceous function
 - Acne gravidarum
 - Tends to flare in early pregnancy but otherwise often improves
 - Montgomery gland enlargement
 - Sebaceous glands of areolae
- Decreased apocrine function (incompletely understood)
 - Do see improvement in Fox-Fordyce disease and hidradenitis suppurativa



PHYSIOLOGIC CHANGES DURING PREGNANCY

- **CONNECTIVE TISSUE CHANGES**

- Striae gravidarum
 - Up to 90% of patients, can resolve or at least become less apparent over time
 - Hormonal and physiologic stretching are factors in development
 - Familial tendency exists; less common in Asian and African American women



PHYSIOLOGIC CHANGES DURING PREGNANCY

• VASCULAR CHANGES

- Result from distention & instability of vessels and new vessel formation
- Most pronounced during third trimester – most regress after delivery
- Examples:
 - Spider angiomas, palmar erythema, non-pitting edema, varicosities, vasomotor instability, purpura, gingival hyperemia/hyperplasia, pyogenic granulomas, hemorrhoids



PHYSIOLOGIC CHANGES DURING PREGNANCY

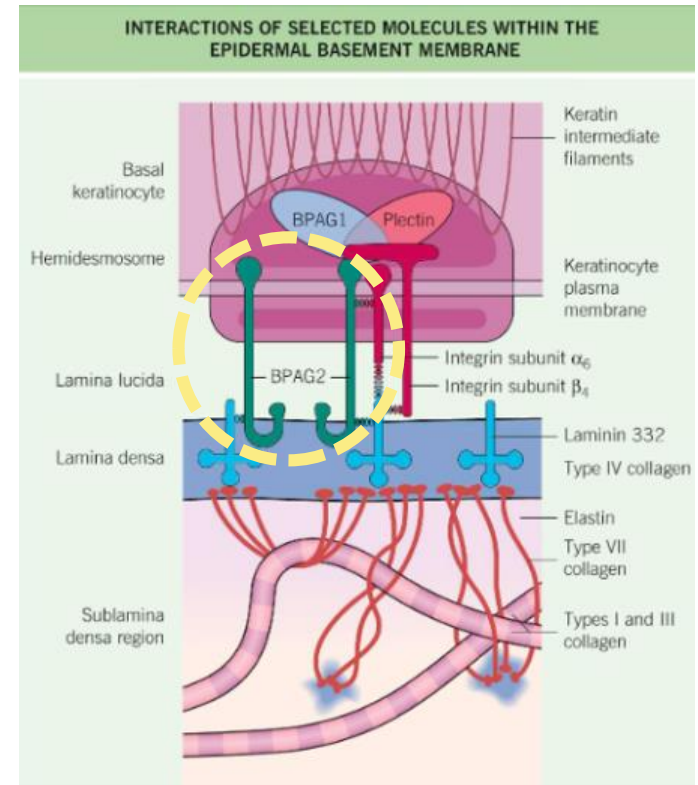
- **VASCULAR CHANGES CONT'D**
 - Jacquemier-Chadwick sign
 - Erythema of vagina and vestibule due to distention of vasculature
 - Goodell's sign
 - Bluish discoloration of the cervix resulting from increased vascularity

PEMPHIGOID GESTATIONIS

- **History**
 - 1872 – Milton – “herpes gestationis”
 - Little more known about condition until immunofluorescence techniques were developed in 1973

PEMPHIGOID GESTATIONIS

- **Pathogenesis**
 - Antibodies against IgG1 subclass directed against BPAG2/180kDa/Collagen XVII
 - Induces deposition of C3 along the DEJ
 - Unknown what initiates development of antibodies
 - Increase in HLA DR3/DR4
 - Increased expression of MHC class II antigens within the villous stroma of chorionic villi



PEMPHIGOID GESTATIONIS

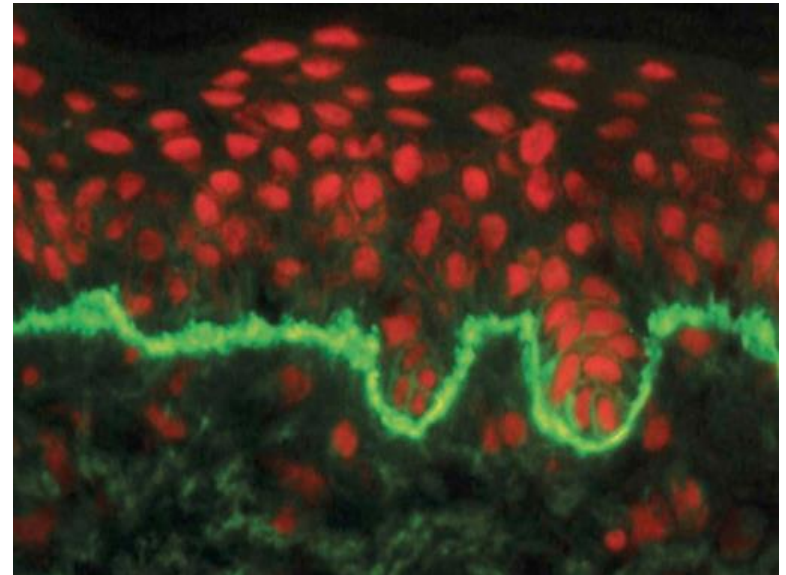
- **Clinical**
 - Late pregnancy/immediate postpartum most common (1:1700-1:50,000 pregnancies)
 - Can resolve during gestation but often flares again with delivery
 - Abrupt onset of erythematous, pruritic, urticarial papules, plaques and vesicles/bullae
 - Almost immediate involvement of umbilicus
 - Spares mucous membranes

PEMPHIGOID GESTATIONIS



PEMPHIGOID GESTATIONIS

- **Histopathology (lesional skin)**
 - Subepidermal vesicle
 - Only actually seen in small subset of patients
 - Spongiosis with eosinophils
- **Direct Immunofluorescence (perilesional skin)**
 - Linear C3 along BMZ



PEMPHIGOID GESTATIONIS

- **Differential diagnosis**
 - Polymorphous eruption of pregnancy (PEP)
 - Can be very difficult
 - Immunofluorescence and BP180-NC16A ELISA are important

PG



PEP



Usefulness of BP180 NC16a Enzyme-Linked Immunosorbent Assay in the Serodiagnosis of Pemphigoid Gestationis and in Differentiating Between Pemphigoid Gestationis and Pruritic Urticarial Papules and Plaques of Pregnancy

Ann Marie Powell, MB, MRCPI; Yohko Sakuma-Oyama, MD; Noritaka Oyama, MD, PhD; Sandra Albert, MD, DNB; Balbir Bhogal, BSc; Fumio Kaneko, MD, PhD; Takeji Nishikawa, MD, PhD; Martin M. Black, MD, FRCP, FRCPath

Background: Pemphigoid gestationis (PG) is a rare pregnancy-associated subepidermal immunobullous disease that targets hemidesmosomal proteins, particularly BP180. Clinically, PG can resemble the eruption known as polymorphic urticarial papules and plaques of pregnancy (PUPPP), and accurate differentiation between these 2 pruritic pregnancy dermatoses has important implications for fetal and maternal prognoses. Results of epitope mapping studies show that IgG autoantibodies in up to 90% of PG serum samples target the well-defined membrane-proximal NC16a domain of BP180.

Objective: To examine the usefulness of a commercially available NC16a domain enzyme-linked immunosorbent assay in the serodiagnosis of PG and in the differentiation of PG from PUPPP.

Participants: A total of 412 women consisting of pre-

treatment patients with PG (n=82), patients with PUPPP (n=164), and age- and sex-matched controls (n=166).

Methods: All serum samples were assayed in duplicate. Receiver operating characteristic analyses were performed to determine a cutoff value for the diagnosis of PG and for differentiation from PUPPP and controls.

Results: A cutoff value of 10 enzyme-linked immunosorbent assay units was associated with specificity and sensitivity of 96%.

Conclusions: The NC16a enzyme-linked immunosorbent assay is highly sensitive and highly specific in differentiating PG from PUPPP, and it is potentially a valuable tool in the serodiagnosis of PG.

Arch Dermatol. 2005;141:705-710

PEMPHIGOID GESTATIONIS

- **Treatment**

- Goal: relieve symptoms
- Topical corticosteroids combined with emollients
 - Mild to moderate potency in limited quantities
- Systemic antihistamines can be used
- Oral corticosteroids often required
 - Prednisolone is treatment of choice – inactivated in the placenta
 - Recommended dosing: 0.5 mg/kg daily
 - Taper dose once blister formation is stopped, though may need to increase taper if flare with delivery

PEMPHIGOID GESTATIONIS

- **Maternal/fetal risk**
 - Maternal
 - Tends to recur in subsequent pregnancies
 - Often earlier and more severe
 - Can flare with menstruation and with OCP use
 - Increased risk for Graves disease
 - Fetal
 - Small percentage of newborns with mild skin involvement from passage of maternal antibodies (IgG)
 - Resolves spontaneously within weeks
 - Increased risk prematurity and SGA

POLYMORPHIC ERUPTION OF PREGNANCY

- **Synonyms:**
 - Pruritic urticarial papules and plaques of pregnancy (PUPPP)
 - Bourne's "toxaemic rash of pregnancy"
 - Nurse's "late onset prurigo" of pregnancy
 - Toxic erythema of pregnancy

POLYMORPHIC ERUPTION OF PREGNANCY

- **History**

- 1979 – Lawley et al. – coined term PUPPP
 - Found to overlook the later polymorphous feature that occurs with the rash
- 1982 – Holmes and Black– proposed PEP in Great Britain because PUPPP did not describe full clinical spectrum

- **Incidence**

- Approx. 1 in 160 pregnancies (much more common than Pemphigoid gestationis)
- Primiparous women, multi-gestation pregnancies
- No autoimmune or HLA association

POLYMORPHIC ERUPTION OF PREGNANCY

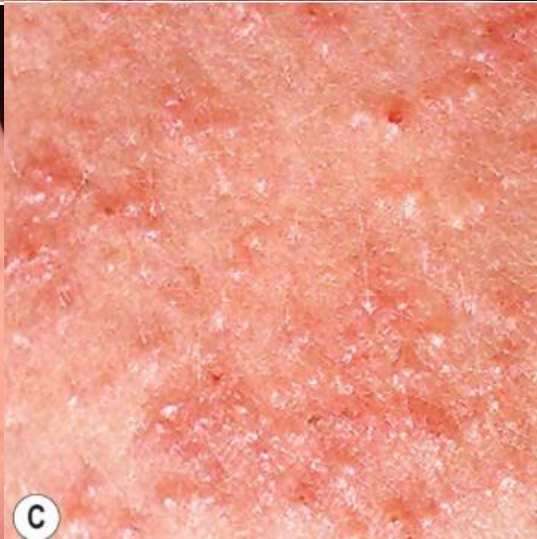
- **Pathogenesis**

- Remains unknown
- Association with increased maternal weight gain and multiple-gestation pregnancies
 - Potentially a result of the rapid stretching of skin leading to damage of connective tissue
 - Lesions begin within abdominal striae and later generalize
- Other theories
 - Increased hormonal levels with multiple gestations leading to increased vascularity and collagen damage

POLYMORPHIC ERUPTION OF PREGNANCY

- **Clinical**
 - Erythematous papules and plaques initially seen in striae but sparing the umbilicus
 - Extremely pruritic
 - Generalizes in a few days – spares face, palms/soles
 - Polymorphic features develop
 - Erythema, targetoid lesions, vesicles, eczematous changes
 - Lesions resolve over 1 month

POLYMORPHIC ERUPTION OF PREGNANCY



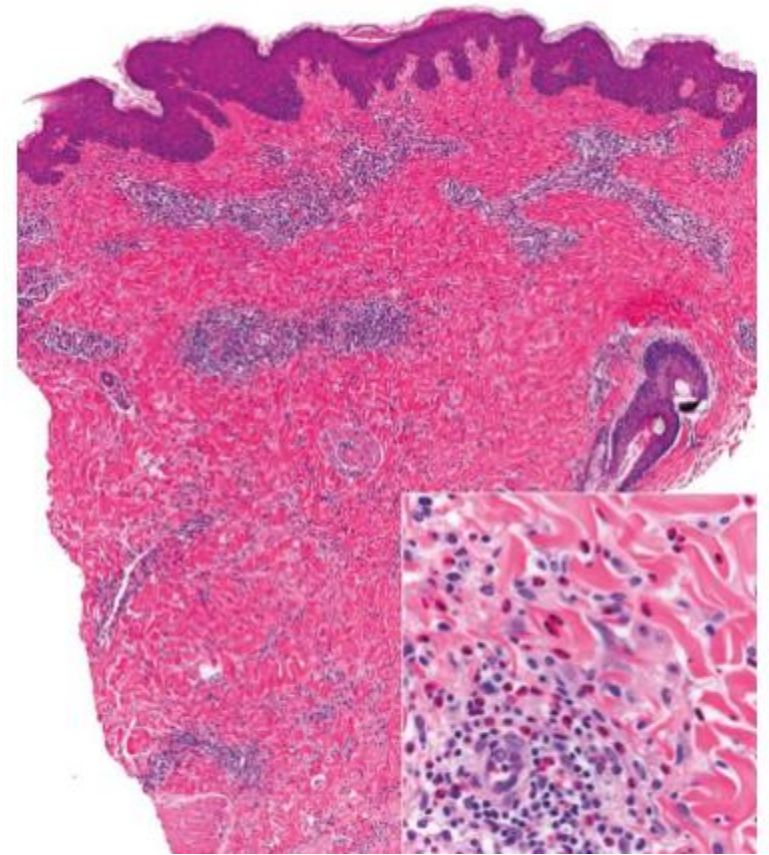
POLYMORPHIC ERUPTION OF PREGNANCY

- **Histopathology**

- Findings vary depending on stage of disease
 - Acute – more spongiosis
 - Mixed infiltrate with eosinophils
 - Dermal edema often seen to some extent

- **Immunofluorescence**

- Both direct and indirect negative



POLYMORPHIC ERUPTION OF PREGNANCY

- **Differential diagnosis**
 - Pemphigoid gestationis
 - Drug eruption

POLYMORPHIC ERUPTION OF PREGNANCY

- **Treatment**
 - Symptomatic with topical steroids and oral antihistamines
 - Rarely oral corticosteroids are required
 - Self-limited course

POLYMORPHIC ERUPTION OF PREGNANCY

- **Maternal/fetal risk**
 - Maternal
 - No significant risk of recurrence in subsequent pregnancies
 - Fetal
 - No health risks; no newborn skin changes

ATOPIC ERUPTION OF PREGNANCY

- **Synonyms**

- Prurigo of pregnancy
- Nurse's "early onset prurigo" of pregnancy
- Spangler's "papular dermatitis of pregnancy"
- Pruritic folliculitis of pregnancy
- Eczema in pregnancy

- **Definition**

- Exacerbation OR the first occurrence of eczematous/papular skin changes during pregnancy in atopic patients
 - Majority tend to be first occurrence (~80%) - often overlooked and lead to other differential diagnoses

ATOPIC ERUPTION OF PREGNANCY

- **History**
 - 1904 – Besnier – “prurigo gestationis” – prurigo was used to describe atopic dermatitis at that time
 - 1968 – Nurse – accompanying eczematous feature
 - 1983 – Homes & Black – first to describe it as a result of pregnancy-related pruritus in women with an atopic diathesis rather than a specific entity

ATOPIC ERUPTION OF PREGNANCY

- **Pathogenesis**
 - Maternal body lacks strong cell mediated immune function to prevent fetal rejection
 - Decreased TH1 response and increased TH2 response
 - Worsens already present TH2 imbalance in atopic patients

ATOPIC ERUPTION OF PREGNANCY

- **Clinical**
 - Appears early in pregnancy – often 1st trimester with 75% before the 3rd trimester
 - 80% patients experiencing new eczematous changes
 - 2/3 of patients develop eczematous lesions on classic “atopic sites”: face, neck, flexural surfaces
 - 1/3 of patients develop a papular eruption on trunk/extremities
 - Xerosis throughout

ATOPIC ERUPTION OF PREGNANCY



ATOPIC ERUPTION OF PREGNANCY

- **Histopathology**
 - Classic atopic findings – nothing specific to pregnancy changes
 - Spongiosis, acanthosis, erosion, \pm eosinophils
- **Direct immunofluorescence: negative**
- **Possible mild elevation serum IgE**

ATOPIC ERUPTION OF PREGNANCY

- **Differential diagnosis**
 - Polymorphous eruption of pregnancy
 - AEP has no association with striae, develops earlier
 - Intrahepatic cholestasis of pregnancy
 - AEP has normal serum bile acid levels
 - Other pruritic dermatoses – scabies, viral exanthem, drug eruptions

ATOPIC ERUPTION OF PREGNANCY

- **Treatment**

- Topical steroids \pm oral antihistamines
- Emollients, humectants, topical antipruritics
- Topical urea (10%), polidocanol, menthol – safe in pregnancy
- UVB therapy for severe disease
- Close monitoring for superimposed bacterial infections and treat as appropriate

ATOPIC ERUPTION OF PREGNANCY

- **Maternal/fetal risk**
 - Maternal risk: none
 - Fetal risk: none

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **History**
 - 1907 – First described by Keher
 - Confusion arose over time from describing a dermatological condition often without skin findings
 - Often missed prior to laboratory evaluation

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Epidemiology**
 - Most commonly seen in South America
 - Highest incidence in Bolivia and Chile
 - Rates as low as 0.1-1.5% described in Europe/North America with mild increased incidence in Scandinavia and Baltic states
 - Questionable genetic component given endemic clustering and positive family history
 - Mutation encoding ABCB4 gene encoding transport proteins necessary for bile excretion
 - Noted in multigestation pregnancies – possible hormonal component
 - Association with Hepatitis C virus infection

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Pathogenesis**
 - Elevated serum bile acids secondary to decreased excretion
 - Toxic bile acids can cause abnormal uterine contractions, vasoconstriction of chorionic veins and cross the placenta and cause impaired fetal heart function
 - Can lead to acute fetal anoxia

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Pathogenesis continued**
 - ABCB4 gene – encodes bile transporter proteins
 - Mutations
 - Non-pregnant patient: no symptoms
 - Pregnant patient: in setting of high sex hormones, transporters' capacity to secrete substances is exceeded and symptoms develop
 - Cholestatic effect of hormones
 - High estrogen alters hepatic cell membrane
 - Dietary factors
 - Selenium deficiency leads to formation of free radicals that damage hepatocyte structure and function

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

ORIGINAL ARTICLE

Hepatitis C infection and intrahepatic cholestasis of pregnancy: A systematic review and meta-analysis

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Available online 16 August 2016

Summary

Background/objectives: Hepatitis C virus (HCV) infection is a major cause of cirrhosis worldwide. Several studies have linked HCV infection to a higher risk of developing intrahepatic cholestasis of pregnancy (ICP), but some data demonstrates contradictory results. To further investigate the association and estimated risk of ICP in patients with HCV infection, we conducted this meta-analysis to summarize all available evidence.

Methods: This study consists of two meta-analyses. A literature search was performed using MEDLINE and EMBASE from inception to January 2016. The first study included observational studies that reported relative risks, odds ratios, or hazard ratios of the associations between HCV infection and risk of ICP. The second analysis included studies comparing the risk of later HCV infection in ICP patients with those without ICP. Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated using a random-effect, generic inverse variance method.

Results: Three studies were included in the first analysis. The pooled OR of ICP in HCV-infected pregnant women compared to non-HCV pregnant women was 20.40 (95% CI, 9.39–44.33, $I^2 = 55\%$). Two studies were included in the second analysis. The pooled OR of later HCV infection among ICP patients compared to non-ICP patients was 4.08 (95% CI, 3.13–5.31, $I^2 = 0\%$).

1. HCV downregulates expression of ABC transporter MRP2 in liver and, along with the hormonal changes, increases risk of ICP
2. Persistent viremia could induce direct cytotoxic effect in hepatocytes, leading to environment that facilitates ICP
3. ABCB11 genotype which is present in 40% of HCV-infected patients also renders the carrier to increase bile acid levels

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Clinical**
 - Patients often present in late pregnancy
 - Intense, generalized pruritus that begins with palms/soles
 - No specific primary lesions to ICP
 - Secondary changes from scratching i.e. excoriations, prurigo nodularis
 - Jaundice
 - Relatively uncommon; seen in ~10% of patients
 - If noted, usually prolonged and severe ICP with concomitant extrahepatic cholestasis
 - Pruritus persists until delivery

INTRAHEPATIC CHOLESTASIS OF PREGNANCY



INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Diagnosis**

- Confirmed by elevated total serum bile acids
 - Normal level in pregnancy 0-6 $\mu\text{mol/l}$
 - Levels >10 indicate ICP; levels >40 indicate severe disease/risk to fetus
- Serum transaminases may be elevated
 - Can be normal in ~30%
- If clinically jaundiced, direct bilirubin may be increased and prothrombin time prolonged
- No specific histopathologic findings – biopsies not routinely performed

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Treatment**

- Goal: reduction of serum bile acids
- Ursodeoxycholic acid (UDCA) remains treatment of choice
 - Corrects maternal serum bile acid profile
 - Decreases passage of maternal bile acids across placenta
 - Improves function of bile acid transport system
 - ADR: mild diarrhea (safe for mother and baby)
 - Recommended dosing: 15 mg/kg/day
 - Continue until delivery

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

- **Maternal/fetal risk**
 - Maternal:
 - If severe course with jaundice, can have steatorrhea and vitamin K deficiency
 - Increases risk for intra- and postpartum hemorrhage
 - Fetal: risk correlates with elevation in serum bile acid levels (especially if >40 $\mu\text{mol/l}$)
 - Premature births (20-60%)
 - Intrapartum fetal distress including abnormal fetal heart rate and meconium staining (20-30%)
 - Fetal loss (1-2%)

IMPETIGO HERPETIFORMIS

- **Epidemiology/pathogenesis**
 - Now recognized as a form of pustular psoriasis
 - Potentially induced by relative hypocalcemia of pregnancy and increase in progesterone in late pregnancy
 - Controversy as to whether this condition is specific to pregnancy or solely exacerbated by pregnancy
 - Exact prevalence unknown
 - Many women do not have a personal or family history of psoriasis
 - Some do progress to generalized pustular psoriasis later in life
 - Most commonly presents in the second half of pregnancy

IMPETIGO HERPETIFORMIS

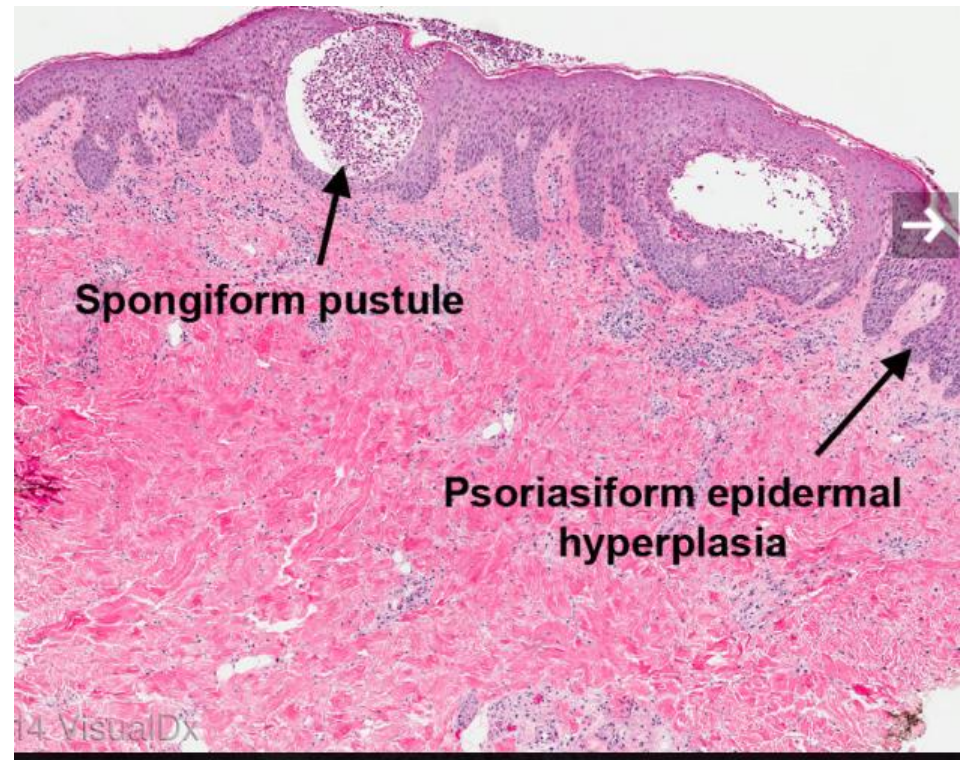
- **Clinical**
 - Erythematous plaques with circumferential rings of pustules first present in intertriginous areas and expand symmetrically to trunk/extremities
 - Often begins in flexures/groin
 - Head, hands, feet often spared
 - Plaques can enlarge and become eroded
 - \pm mucosal involvement (including esophagus)
 - Subungual involvement can lead to onycholysis
 - Systemic symptoms
 - Nausea, vomiting, diarrhea, chills, lymphadenopathy, seizure, delirium

IMPETIGO HERPETIFORMIS



IMPETIGO HERPETIFORMIS

- **Diagnosis**
 - Pathology
 - Parakeratosis, psoriasiform epidermal hyperplasia, intraepidermal pustules/vesicles,
 - Spongiform pustule with neutrophils in epidermis
 - Sterile pustules (cultures negative)
 - DIF negative



IMPETIGO HERPETIFORMIS

- **Treatment**
 - Low dose systemic corticosteroids
 - Caution if high doses are necessary, slow taper
 - Often resolves with delivery but can have a prolonged course
 - Postpartum treatment with oral retinoids
 - Case reports of treatment with parenteral calcium with vitamin D

IMPETIGO HERPETIFORMIS

- **Maternal/fetal risk**
 - Maternal
 - Systemic complications including fluid loss, electrolyte imbalance, sepsis
 - Hypocalcemia can lead to delirium, convulsions
 - If severe, risk of cardiac and renal failure
 - Tends to recur with subsequent pregnancies – often earlier and more severe
 - Can also recur with menstrual cycles
 - Fetal
 - Controversial reports of increased fetal morbidity
 - Potential risks include placental insufficiency, intrauterine fetal demise, low birth weight

AUTOIMMUNE PROGESTERONE DERMATITIS

- **Not a specific dermatosis of pregnancy – can first appear during pregnancy or post partum**
- **Clinical**
 - Cyclic flares of dermatitis that correspond to the luteal phase of the menstrual cycle
 - Various eczematous changes occur – urticarial, papulosquamous, erythema multiforme-like
- **Diagnosis**
 - Oral or IM progesterone challenge
- **Treatment**
 - Inhibit ovulation via estrogen containing preparations

AUTOIMMUNE PROGESTERONE DERMATITIS



PREEXISTING SKIN CONDITIONS

- **Atopic dermatitis**
 - More likely worsens
 - Irritant hand dermatitis and nipple eczema post partum
- **Psoriasis**
 - More likely to improve but chronic plaque psoriasis can worsen or develop during pregnancy
- **Chronic cutaneous lupus**
 - Not affected by pregnancy
- **SLE**
 - Cutaneous flares
- **Pemphigus variants**
 - Tends to flare

INFECTIONS IN PREGNANCY

- **Secondary to immunosuppressive effects of high levels of estrogen**
 - Candida vaginitis – occurs in over half of pregnant women
 - Trichomonas vaginitis– occurs in 60% of pregnant women with no adverse effects on fetus
 - Condyloma acuminata – can grow rapidly during pregnancy
 - Pityrosporum folliculitis – due to Malassezia furfur
 - Recurrent genital HSV – not increased frequency but significant risk to fetus
 - Fetal transmission 50% with first episode, 5% with recurrent
 - If clinically evident lesions at birth, >50% neonates get HSV
 - Progression to AIDS in HIV patients at higher rate

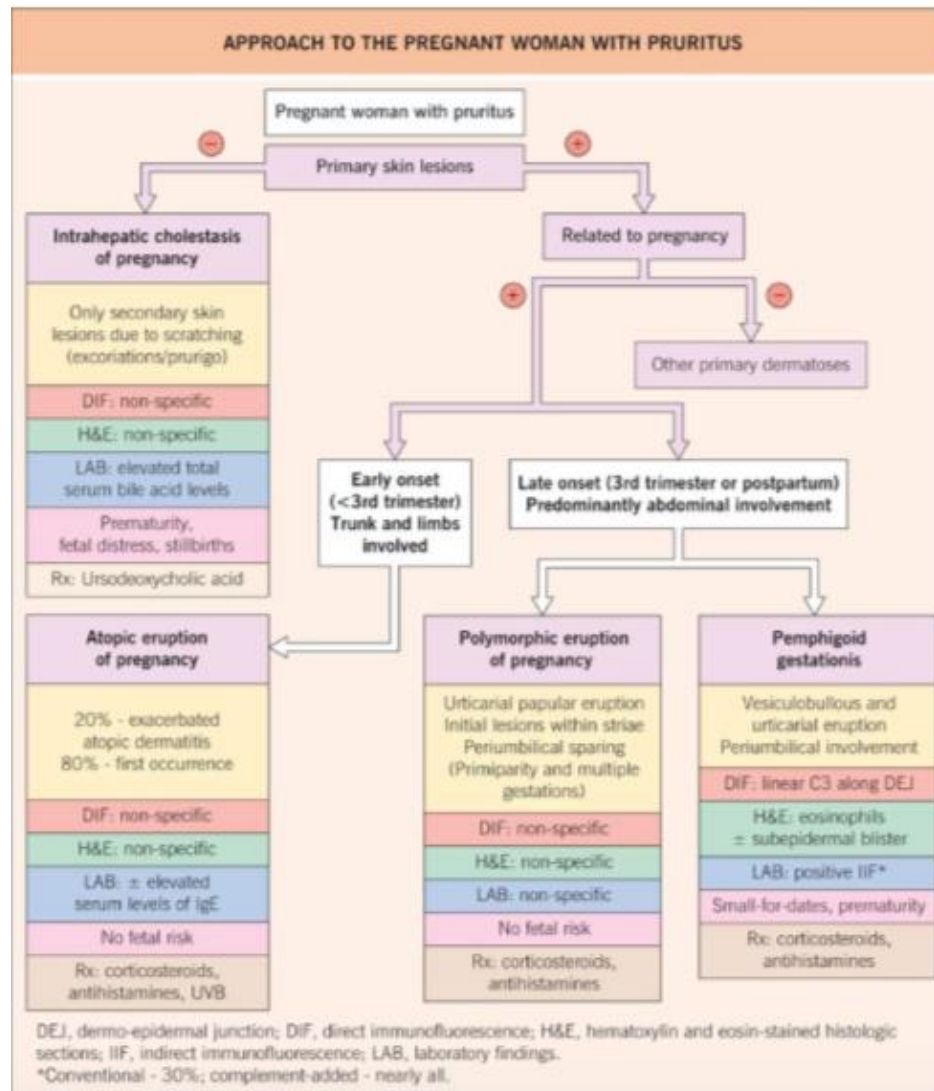
APPROACH TO A PREGNANT WOMAN WITH PRURITUS

- **Pruritus**
 - Major symptom of many of the pregnancy-related dermatoses
 - Can also be coincidental and be a symptom of another disorder
 - Scabies, urticaria, etc.
 - Needs full assessment due to maternal/fetal risks as previously described

APPROACH TO A PREGNANT WOMAN WITH PRURITUS

- **Hints indicating possible dermatosis of pregnancy**
 - Primiparity and multiple gestation – PEP
 - Early presentation (first trimester) – AEP
 - Abdominal involvement
 - Umbilical – HG
 - Periumbilical – PEP
 - Palm and sole pruritus – ICP

APPROACH TO A PREGNANT WOMAN WITH PRURITUS



APPROACH TO A PREGNANT WOMAN WITH PRURITUS

- **General treatment**
 - Mild to moderate topical steroids
 - Priority should be on not using super-potent topical steroids if not required
 - No real evidence on topical halogenated steroids vs. non-halogenated
 - Prednisolone
 - Inactivated by the placenta- first choice for systemic steroids
 - Prednisone
 - Can be used but associated with fetal macrosomia, gestational diabetes, premature rupture of membranes
 - Halogenated steroids, i.e. betametasone, dexamethasone, cross the placenta more quickly and should not be chosen unless necessary
 - Systemic antihistamines
 - 1st gen: Chlorpheniramine; 2nd gen: Cetirizine, Loratadine

TABLE 27.3 Special considerations for corticosteroid and antihistamine use during pregnancy²⁵.

SPECIAL CONSIDERATIONS FOR CORTICOSTEROID AND ANTIHISTAMINE USE DURING PREGNANCY	
Corticosteroids	
Topical	<ul style="list-style-type: none"> • Overuse of high-potency products can lead to systemic absorption and halogenated corticosteroids do cross the placenta; they may also add to the already considerable risk of striae • Class 6 and 7 corticosteroids are safest • Corticosteroids that have enhanced cutaneous metabolism, e.g. mometasone furoate, prednicarbate, methylprednisolone aceponate, can also be considered
Systemic	<ul style="list-style-type: none"> • Prednisolone is the systemic corticosteroid of choice for dermatologic indications as it is largely inactivated in the placenta (mother : fetus = 10 : 1) • During the first trimester, particularly between weeks 8 and 11, there is a possible (debated) slightly increased risk of cleft lip/cleft palate, especially if high doses prescribed and for >10 days; during this same period, a longer duration of therapy appears safe if dosages are <10–15 mg daily • If use is long-term and extends late into gestation, fetal growth should be monitored and the risk of adrenal insufficiency in the newborn should be addressed
Antihistamines	
Systemic	<ul style="list-style-type: none"> • During the first trimester, the classic sedating agents (e.g. chlorpheniramine, clemastine, dimethindene) are preferred • During the second and third trimesters, if a non-sedating agent is requested, loratadine and cetirizine are considered safe

Pregnancy Outcomes After Maternal Exposure to Topical Corticosteroids

A UK Population-Based Cohort Study

Ching-Chi Chi, MD, MMS, DPhil, FAAD; Shu-Hui Wang, MD, MS; Richard Mayon-White, MBBS, FRCP, FFPH; Fenella Wojnarowska, MA, DM, FRCP

IMPORTANCE Topical corticosteroids are indicated for pregnant women with skin conditions, but their safety in pregnancy is not fully understood.

OBJECTIVE To investigate whether maternal exposure to topical corticosteroids results in adverse pregnancy outcomes.

DESIGN Retrospective cohort study.

SETTING United Kingdom National Health Service.

PARTICIPANTS A total of 2658 pregnant women exposed to topical corticosteroid and 7246 unexposed pregnant women.

EXPOSURE Topical corticosteroids dispensed during pregnancy.

MAIN OUTCOMES AND MEASURES Orofacial cleft, low birth weight, preterm delivery, fetal death, low Apgar score, and mode of delivery.

RESULTS No associations of maternal topical corticosteroid exposure with orofacial cleft, low birth weight, preterm delivery, fetal death, low Apgar score, and mode of delivery were found in the primary analysis (adjusted risk ratio [RR], 1.85 [95% CI, 0.22-15.20] [$P = .57$]; 0.97 [95% CI, 0.78-1.19] [$P = .75$]; 1.20 [95% CI, 0.73-1.96] [$P = .48$]; 1.07 [95% CI, 0.56-2.05] [$P = .84$]; 0.84 [95% CI, 0.54-1.31] [$P = .45$]; and $P = .76$, respectively). Stratified analyses based on potency did not reveal any significant associations in most of these categories either, but an exploratory analysis showed a significantly increased risk of low birth weight when the dispensed amount of potent or very potent topical corticosteroids exceeded 300 g during the entire pregnancy (adjusted RR, 7.74 [95% CI, 1.49-40.11]; $P = .02$).

CONCLUSIONS AND RELEVANCE This study reassuringly showed no associations of maternal topical corticosteroid exposure with orofacial cleft, preterm delivery, fetal death, low Apgar score, and mode of delivery. With this study and all available evidence taken together, the risk of low birth weight seems to correlate with the quantity of topical corticosteroid exposure.

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Use of Corticosteroids in Early Pregnancy is Not Associated With Risk of Oral Clefts and Other Congenital Malformations in Offspring

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Corticosteroids are commonly used to treat inflammatory diseases. There is conflicting evidence regarding the association of corticosteroid use in pregnancy and congenital malformations in offspring. We conducted a prevalence study of 83,043 primiparous women who gave birth to a live-born singleton in northern Denmark, in 1999–2009. Through medical registries, we identified prescriptions for corticosteroids, congenital malformations, and covariates. Furthermore, we summarized the literature on this topic. Overall, 1449 women (1.7%) used inhaled or oral corticosteroids from 30 days before conception throughout the first trimester. Oral cleft in the offspring was recorded for 1 of the users (0.08%) and 145 of the nonusers (0.2%), prevalence odds ratio (OR) 0.47 [95% confidence interval (CI), 0.07–3.34]. The prevalence OR for congenital malformations overall was 1.02 (95% CI, 0.79–1.32). According to published studies, the use of corticosteroids in early pregnancy was associated with congenital malformations overall with relative estimates ranging from 0.8 (95% CI, 0.4–1.7) to 2.1 (95% CI, 0.5–9.6). For oral clefts, the ORs ranged from 0.6 (95% CI, 0.2–1.7) to 5.2 (95% CI, 1.5–17.1). We found no evidence of an association between use of corticosteroids in early pregnancy and risk of congenital malformations in offspring.

Keywords: congenital malformation, corticosteroids, epidemiology, oral clefts, pregnancy

CONCLUSION

- **Many normal physiologic changes occur during pregnancy and may be of concern to expectant mothers**
- **Several of the dermatoses of pregnancy are very common and benign, while few present risk to both mother and baby and need to be recognized early**
- **Treatment of these dermatoses, even symptomatically, is very important and can be done safely without posing significant risk to mother or baby**

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VisualDx: Photos borrowed for Pemphigoid Gestationis, Impetigo Herpetiformis and Autoimmune progesterone dermatitis.

QUESTIONS?