



Dermatoses of Pregnancy

Christina M. Ambros-Rudolph

I do not have any relevant relationships with industry.

*Scuola Dermatologica Sergio Chimenti – Tecnologia e Innovazione Terapeutica in Dermatologia
Roma, ITALIA, 26-27 Oct 2018*

ambros-rudolph@mozartpraxis.at

Skin Manifestations in Pregnancy

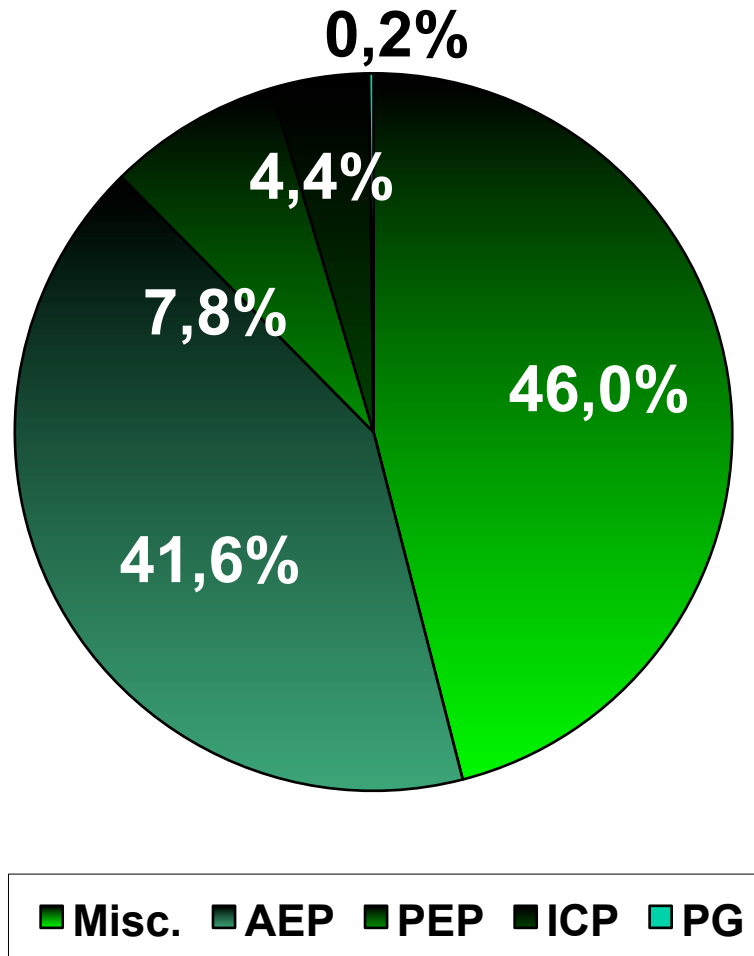
Immunological, hormonal, metabolic, and vascular alterations during pregnancy may lead to:

- „Physiological“ skin changes
(Hyperpigmentation, melasma, varicose veins, palmar erythema, spider nevi, hair and nail alterations, striae distensae)
- Changes in pre-existing dermatoses
(Psoriasis, lupus erythematosus; Th1 – Th2 imbalance)
- **Specific dermatoses of pregnancy → 30-50%**
- *Miscellaneous dermatoses coinciding with pregnancy*



Dermatoses in Pregnancy

Dermatologic Pregnancy Clinic, Dept. of Dermatology, Medical University Graz

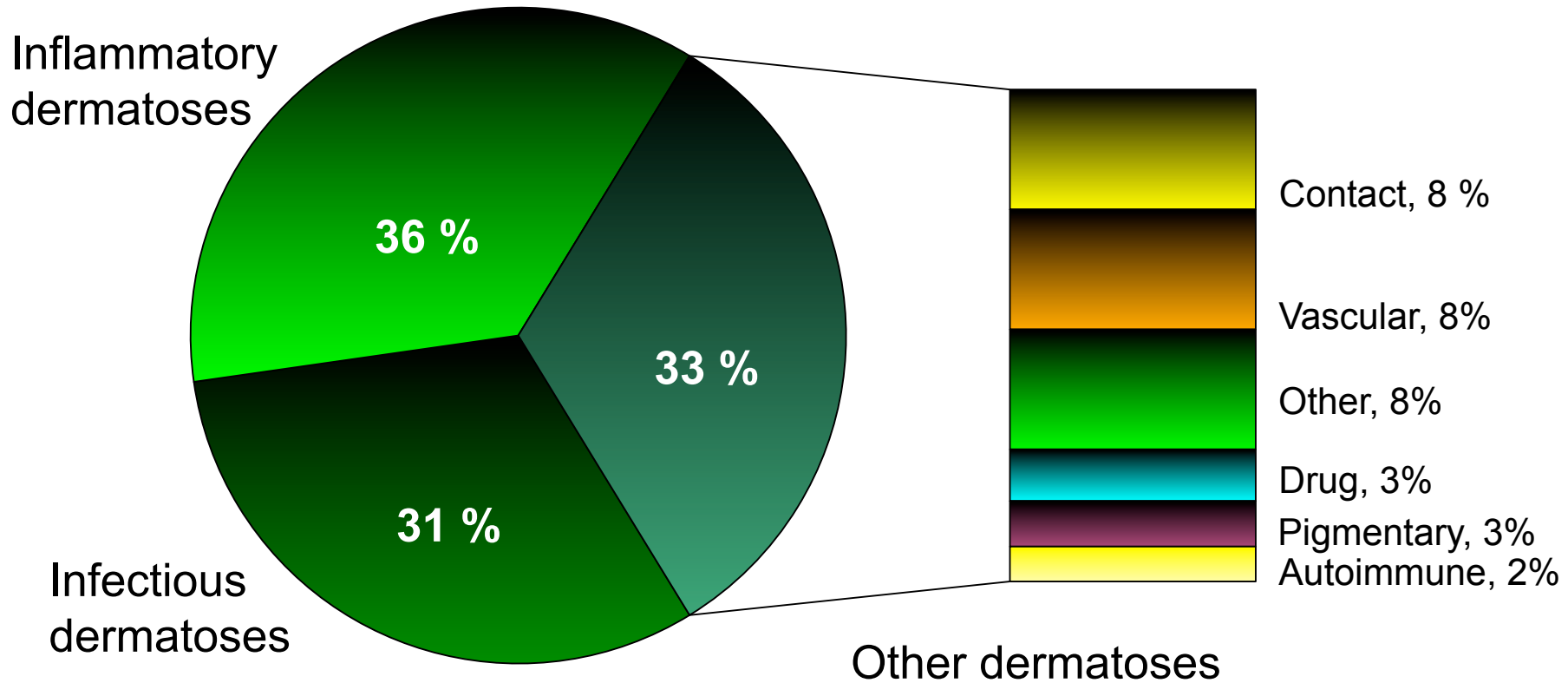


Graz, 2000-2013, n=574

- Specific dermatoses 54%
 - Atopic eruption of pregnancy (AEP, 41.6%)
 - Polymorphic eruption of pregnancy (PEP, 7.8%)
 - Intrahepatic cholestasis of pregnancy (ICP, 4.4%)
 - Pemphigoid gestationis (PG, 0.2%)
- Miscellaneous dermatoses 46%

Miscellaneous Dermatoses

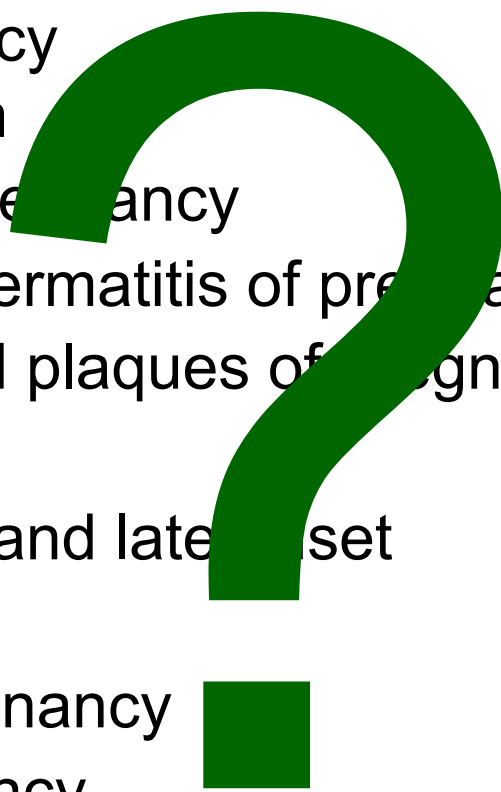
Dermatologic Pregnancy Clinic, Dept. of Dermatology, Medical University Graz



N= 264

Specific Dermatoses of Pregnancy

- Heterogeneous group of inflammatory dermatoses exclusively associated with pregnancy and/or the postpartum period
- **PRURITUS**

- Herpes (Pemphigoid) gestationis
 - Impetigo herpetiformis
 - Prurigo gestationis
 - Pruritus (Prurigo) of pregnancy
 - Pruritus (Prurigo) gravidarum
 - Intrahepatic cholestasis of pregnancy
 - Autoimmune progesterone dermatitis of pregnancy
 - Pruritic urticarial papules and plaques of pregnancy
 - Toxaemic rash of pregnancy
 - Prurigo of pregnancy - early and late onset
 - Toxic erythema of pregnancy
 - Polymorphic eruption of pregnancy
 - Papular dermatitis of pregnancy
 - Pruritic folliculitis of pregnancy
- 

New Classification

Dermatosis	Abb.	Incid.	Classification
Pemphigoid gestationis	PG	1:2.000- 1:50.000	Holmes & Black Shornick Ambros-Rudolph et al.
Polymorphic eruption of pregnancy	PEP (PUPPP)	1:160-1:200	Holmes & Black Shornick Ambros-Rudolph et al.
Intrahepatic cholestasis of pregnancy	ICP	1:50-1:5.000	Shornick Ambros-Rudolph et al.
Atopic eruption of pregnancy	AEP	1:5-1:20	Ambros-Rudolph et al.

Classifications: Holmes & Black (1983), Shornick (1998), Ambros-Rudolph et al. (2006)

AEP – a new term

The specific dermatoses of pregnancy revisited and reclassified: Results of a retrospective two-center study on 505 pregnant patients

Christina M. Ambros-Rudolph, MD,^a Robert R. Müllegger, MD,^a Samantha A. Vaughan-Jones, MD,^b
Helmut Kerl, MD,^a and Martin M. Black, MD, FRCP, FRCPath^b
Graz, Austria, and London, United Kingdom

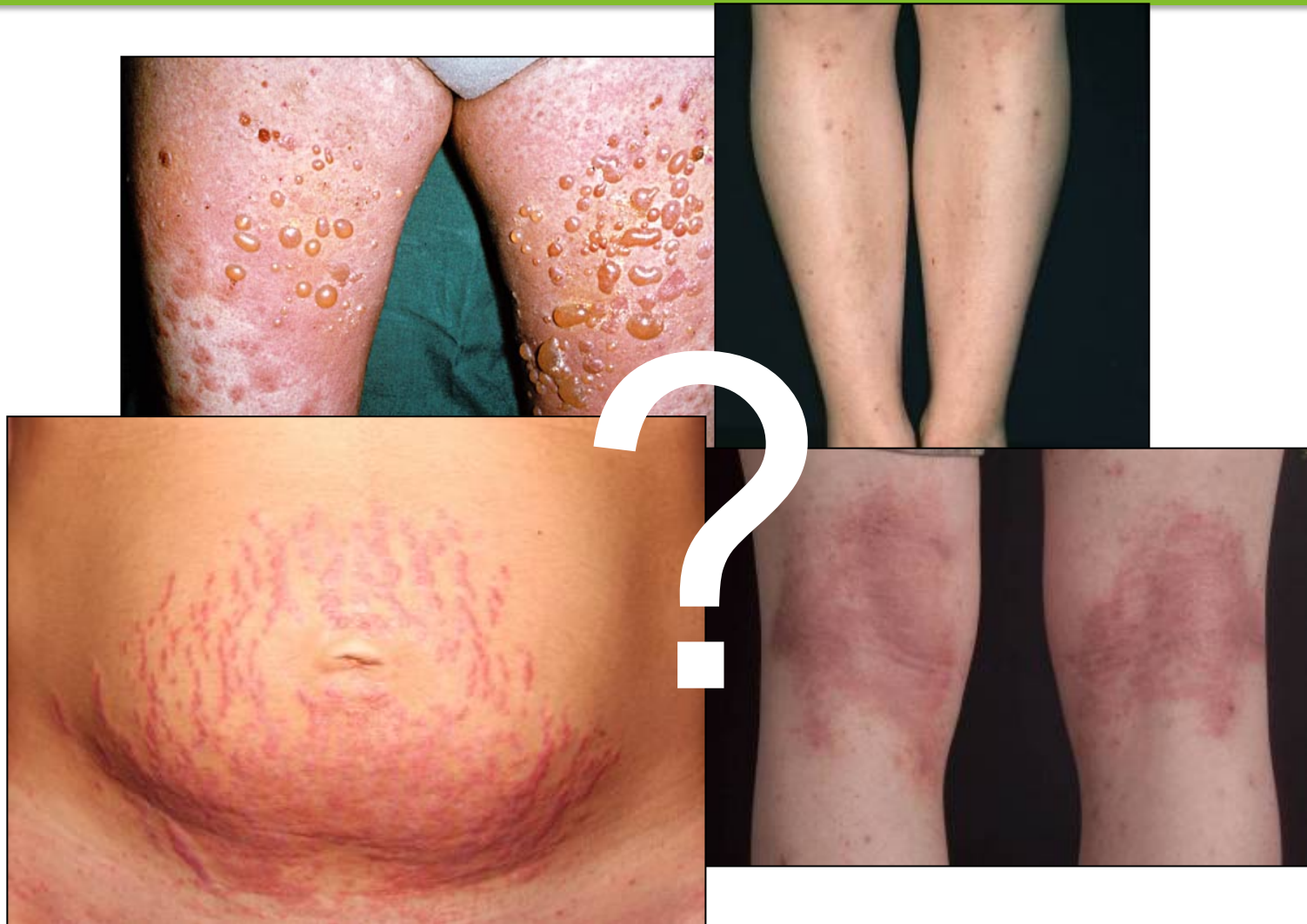
Objectives: We sought to evaluate the frequency and clinical characteristics of pruritic dermatoses in pregnancy and to assess a rationalized classification.

Methods: Data of 505 pregnant patients seen at two university-based dermatologic hospitals (1994-2004) were retrospectively studied.

Results: Diagnoses included eczema in pregnancy (49.7%), polymorphic eruption of pregnancy (PEP) (21.6%), pemphigoid gestationis (PG) (4.2%), intrahepatic cholestasis of pregnancy (ICP) (3%), prurigo of pregnancy (0.8%), pruritic folliculitis of pregnancy (0.2%), and miscellaneous dermatoses (20.6%). Eczema in pregnancy, prurigo of pregnancy, and pruritic folliculitis of pregnancy showed considerable overlap and were summarized as atopic eruption of pregnancy (AEP). While PEP, PG, and ICP presented in late pregnancy, AEP started significantly earlier. Primigravidae and multiple gestations were characteristic for PEP, abdominal involvement for PEP and PG, and a history of affected pregnancies for ICP.

Limitations: This was a retrospective study.

Conclusion: We propose classifying the dermatoses of pregnancy as PG, PEP, AEP, and ICP. Stereotypic immunofluorescence and laboratory findings are diagnostic of PG and ICP, whereas distinct clinical characteristics facilitate discrimination between PEP and AEP. (J Am Acad Dermatol 2006;54:395-404.)



Diagnostic “Clues”

	PG	PEP	ICP	AEP
Primigravidae, %	48	73^a	47	44
Multiple gestations, %	0	16^a	0	1
Previously affected pregnancies, %	9	7	88^b	34
Early onset (< 3rd trimester), %	29	3	20	75^c
Abdominal involvement, %	95^d	98^d	36	68
Pruritus as sole presenting sx, %	0	0	100	0
Only secondary skin changes, %	0	0	100	0

N=401

χ^2 test;

^a $p < .001$ vs. PG, ICP und AEP

^b $p < .001$ vs. PG, PEP und AEP

^c $p < .001$ vs. PG, PEP und ICP

^d $p < .001$ vs. ICP und AEP

PRURITUS in PREGNANCY

without RASH

with RASH

ICP

Only secondary skin lesions due to scratching (excoriations / prurigo)
IMF: non-specific
H&E: non-specific
LAB: elevated total serum bile acid levels
Prematurity, fetal distress, stillbirths
Ursodeoxycholic acid



Intrahepatic Cholestasis of Pregnancy

Key features

Syn.: Pruritus (Prurigo) gravidarum, obstetric cholestasis

- Genetically linked, hormonally triggered reversible cholestasis
- Incidence: 0,02 - 2,4% (++) Bolivia, Chile), runs in families
- III. Trimester; pruritus and **secondary** skin changes
- Impaired hepatic bile acid excretion
 - Mother: pruritus
 - Fetus: cardiodepression, vasoconstriction of placental vessels
 - ➔ **prematurity and stillbirths (19-60%; 1-2%), fetal distress (22-33%)**



Intrahepatic Cholestasis of Pregnancy

Clinical characteristics

- Generalized pruritus
- Exclusively secondary skin changes (due to scratching!)
- Excoriations – prurigo nodularis: correlation between severity of skin changes and duration of pruritus
- Icterus only seen in patients with concomitant extrahepatic cholestasis (10%)

Intrahepatic Cholestasis of Pregnancy

Investigations

- **Laboratory findings**
 - **Elevated total serum bile acid levels ($>11\mu\text{mol/l}$)**
 - \pm Elevation of: ASAT, ALAT, GGT, bilirubin, (AP)
- H&E: non-specific; IMF: negative

Bile acid levels

- Normal range: $0-6\mu\text{mol/l}$
- Increased fetal risk: $>40\mu\text{mol/l}$

→ The higher the bile acids, the higher the fetal risk!!



Intrahepatic Cholestasis of Pregnancy

Prognosis

- Risk for bleeding complications (vit K deficiency) in both mother and child (10%, concomitant extrahepatic cholestasis!)
- Pruritus stops quickly after delivery
- Recurrence with oral contraception and in subsequent pregnancies (70%)

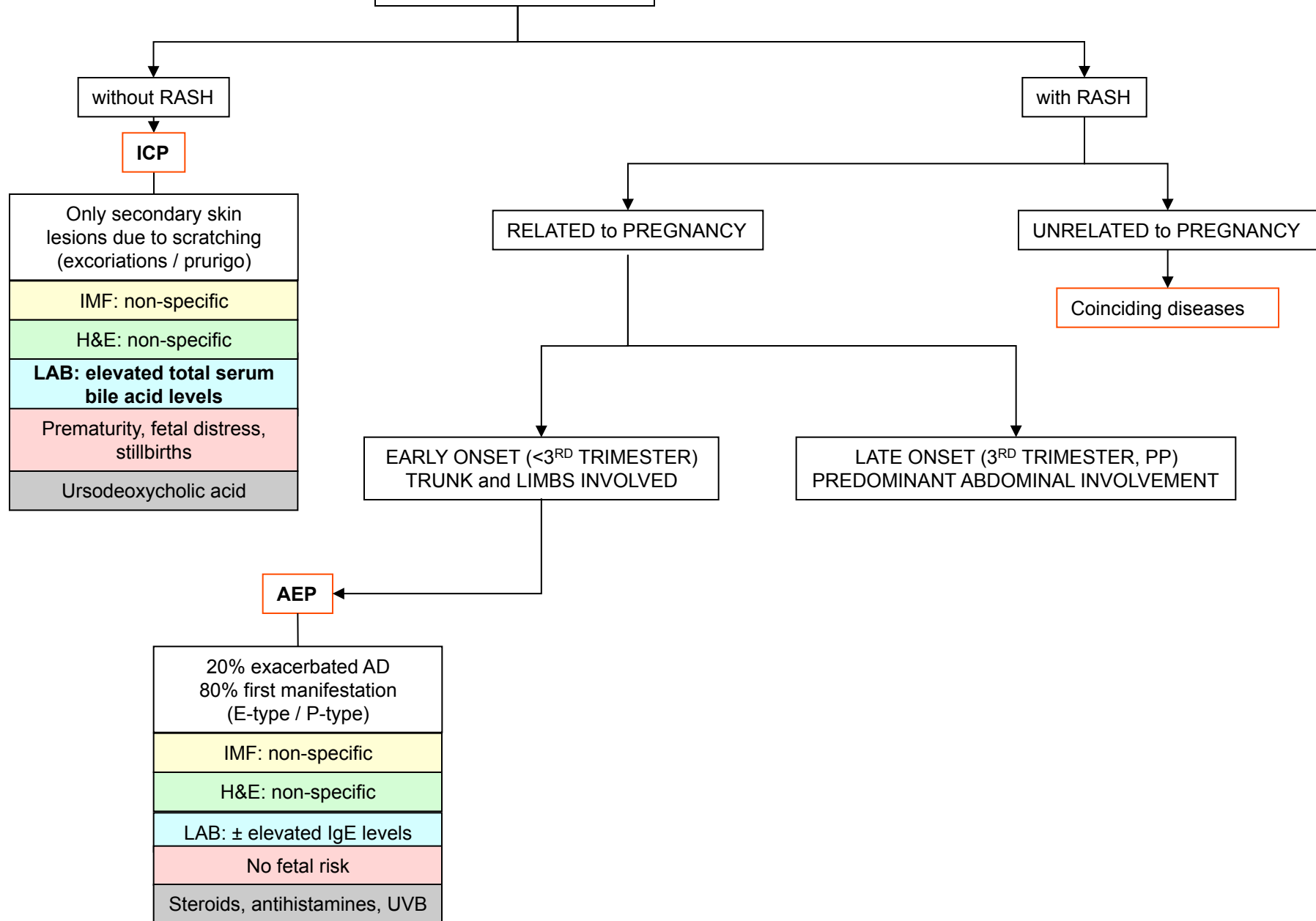
Intrahepatic Cholestasis of Pregnancy

Therapy

Ursodeoxycholic acid (UDCA)	First-line treatment for ICP Naturally occurring, non-toxic bile acid Dosage: 15mg/kg/d or 1g/d No side effects (occasional mild diarrhea) Significant reduction of prematurity and stillbirths CAVE: Approved only for treatment of PBC – Off-label-use!
Concomitant measures	Close obstetric surveillance (weekly CTG monitoring from 34 wks onwards)



PRURITUS in PREGNANCY



Atopic Eruption of Pregnancy

Key features

Syn.: Prurigo of pregnancy, pruritic folliculitis of pregnancy

- Skin changes in patients with atopic diathesis
- Exclusion of other specific pregnancy-associated or not pregnancy-associated dermatoses
- Most frequent pruritic condition in pregnancy (50%), 75% < III. trimester
- Pathogenesis: ? Triggered by Th1 → Th2 Shift
 - Pregnancy biases T cell immunity towards a type-2 T-helper response (↓ IL-2, IFN- γ and IL-12 vs. ↑ IL-4, IL-10), important for continuation of a normal pregnancy

Atopic Eruption of Pregnancy

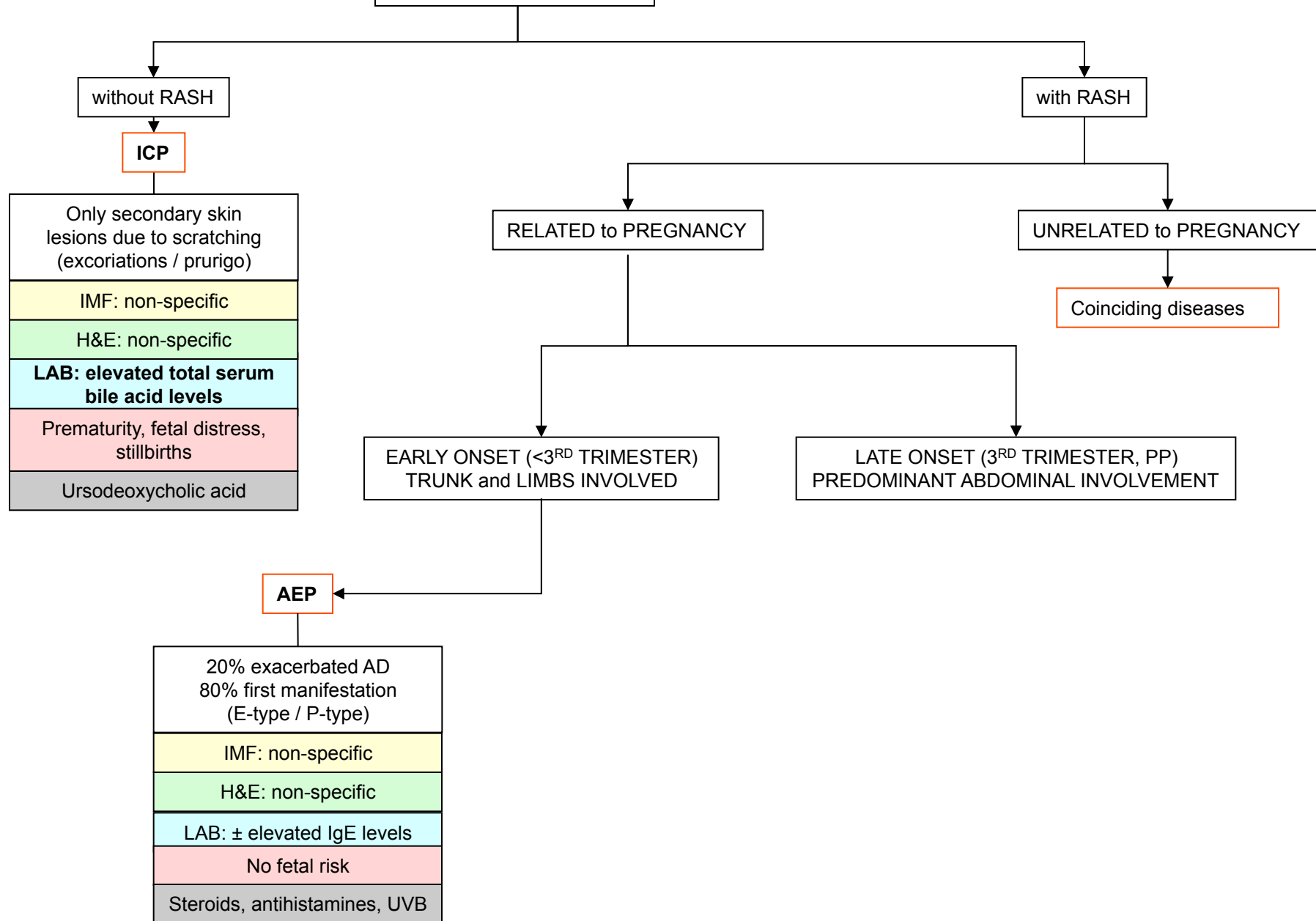
Clinical characteristics

Onset Mean, SD (Range)	I. and II. trimester 18 ± 9w (2 – 39w)	191 (75%)
Morphology	Exacerbation of atopic dermatitis First manifestation of atopic skin changes <ul style="list-style-type: none">- Eczematous lesions (E-type AEP) 120 (48%)- Tiny papular lesions (H&E: ± folliculitis), prurigo nodules (P-type AEP) 79 (31%)	52 (21%) 199 (79%)
Laboratory findings (N=143) Median (range)	Elevated serum IgE levels 156 kU/L (2-2000kU/L)	101 (71%)
Obstetric parameters	Primiparae Single pregnancies	111 (44%) 249 (99%)

N=251



PRURITUS in PREGNANCY



Atopic Eruption of Pregnancy

Therapy

Symptomatic treatment

- Topical corticosteroids, \pm systemic antihistamines
- Light therapy (UVB)
- Basic treatment with emollients
 - Antipruritic additives (urea 3-10%, polidocanol, menthol)
 - Oil baths, showering oils
- Bacterial / viral superinfection
 - Penicillins, cephalosporins
 - Acyclovir

Corticosteroids

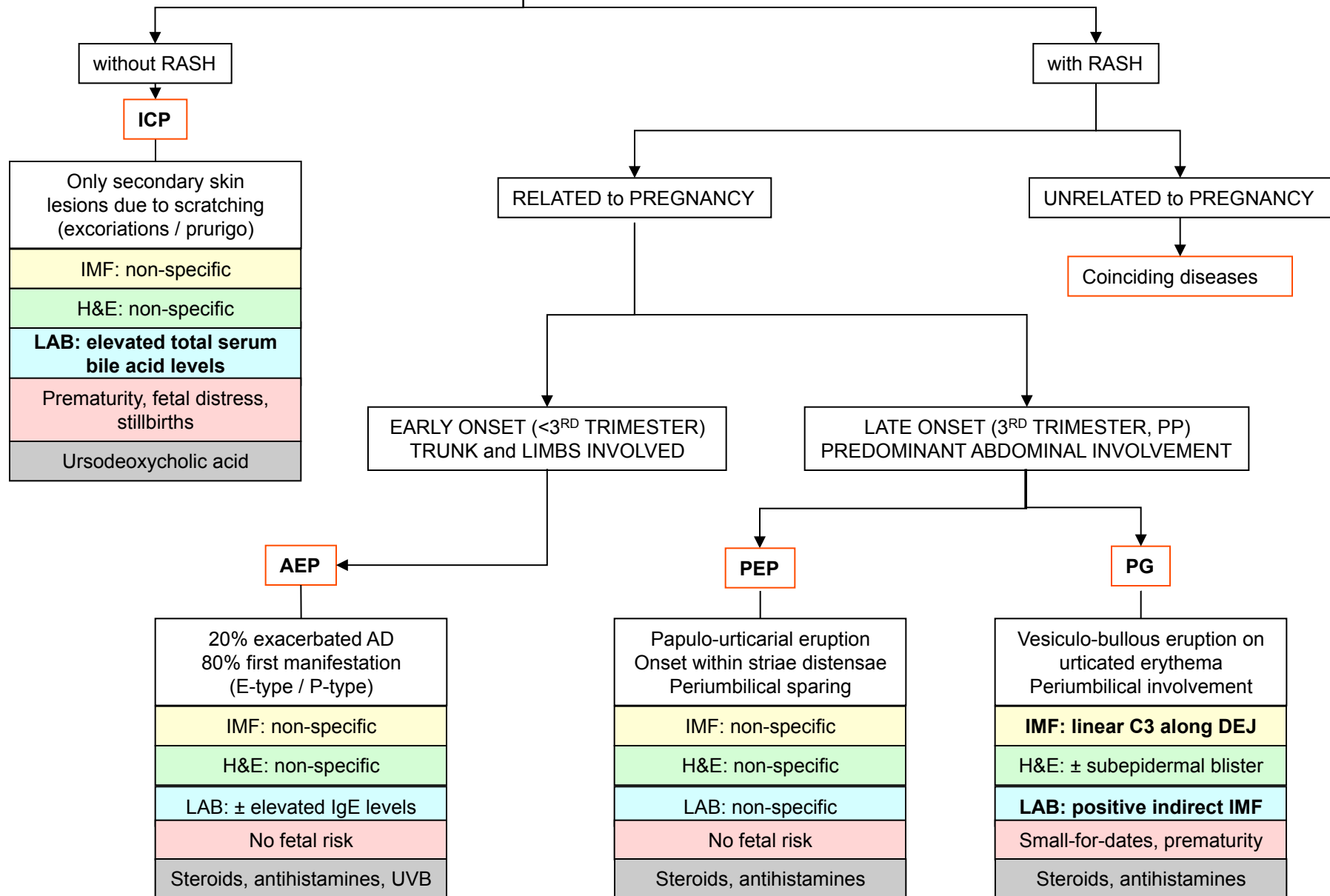
Topical	Mild to moderate potent agents ; if potent agents are needed: total amount applied: <300g
Systemic	<p>Steroid of choice: prednisone/prednisolone</p> <p>Largely inactivated in the placenta (10:1)</p> <p><i>I. trimester: (8-11 weeks gestation)</i></p> <p>? Risk for cleft lip / cleft palate</p> <p>For longer administration: <10-15mg/d</p> <p><i>II.-III. trimester:</i></p> <p>CAVE: High-dose long-term therapy may lead to growth retardation and adrenal insufficiency in the newborn</p>



Antihistamines

I.-III. trimester:	No increased risk for teratogenicity or malformations!
Sedating 1 st gen. agents	Chlorpheniramine, diphenhydramine, dimetindene maleat Caution last 4 weeks (uterine contractions, withdrawal symptoms, retrolental fibroplasia in premature infants)
Non-sedating 2 nd gen. agents	1 st choice: loratadine 2 nd choice: cetirizine

PRURITUS in PREGNANCY



Polymorphic Eruption of Pregnancy

Key features

Syn.: Pruritic urticarial papules and plaques of pregnancy (PUPPP)

- Self-limited, benign inflammatory dermatosis
- Incidence: 1:160-1:200
- (Late) III. trimester, postpartum (15%)¹
- Primigravidae (70%), multiple gestations (13%), excessive maternal weight gain (78%)
- Pathogenesis: ? abdominal distension



Polymorphic eruption of pregnancy

Clinical characteristics

- Pruritic urticarial papules and plaques
- Starting on the Abdomen, within striae distensae
- Umbilical sparing!
- Polymorphous morphology including target lesions, erythema, vesicles (due to heavy spongiosis) and eczematous changes

Polymorphous morphology in 51%



Target lesions / Erythema, 6%

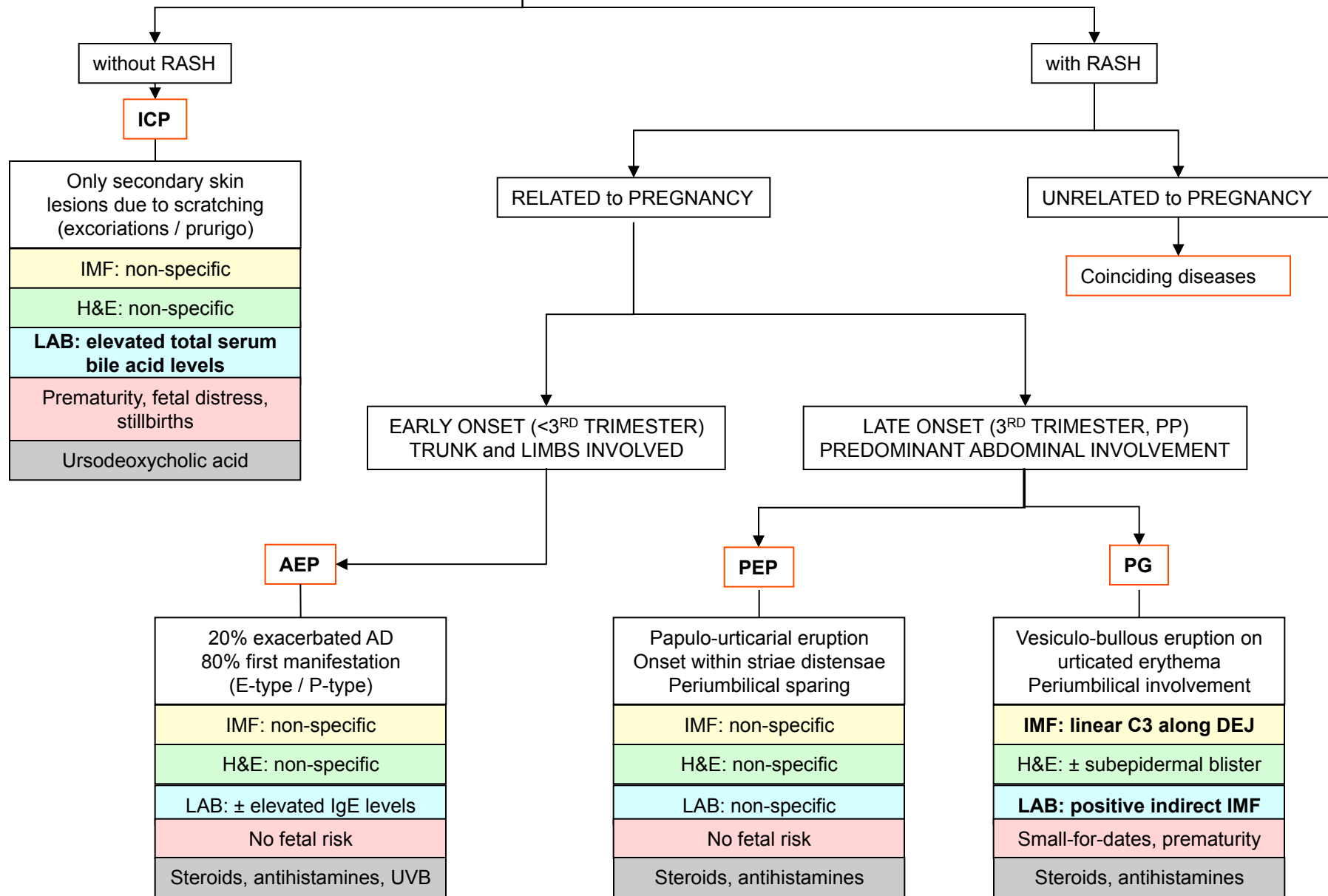


Vesicles, 17%



Eczematous changes, 22%

PRURITUS in PREGNANCY



Pemphigoid gestationis

Key features

Herpes gestationis

- Hormonally triggered, vesiculo-bullous autoimmune disease
- Incidence: 1:2.000-1:50.000; HLA DR3 and DR4
- Onset: II. and III. trimester; trophoblastic tumors
- **Autoantibodies are primarily directed against placenta matrix AG, corresponding to the 180 kDa BP-AG2 (type XVII collagen) in the skin**

Pemphigoid gestationis

Clinical characteristics

- Papular-urticarial rash
- Often starting on the abdomen
- Typically involving the umbilical area
- No association to striae distensae
- Development of tense blisters within days to weeks

Pemphigoid gestationis

Investigations

- Laboratory findings: non-specific
- Histopathology
 - Spongiosis, \pm subepidermal blister formation
 - Dermal edema, perivascular lymphohistiocytic infiltrate with numerous eosinophils
- **Immunofluorescence**
 - **DIF: linear C3 deposition at BMZ (+ IgG in 25-30%)**
 - **IIF: positive (30-100%)**
- **BP180 NC16a ELISA: positive (80-100%), monitoring**

Pemphigoid gestationis

Prognosis

- **Risk for 'small-for-date babies' and prematurity**
 - No association with corticosteroid treatment but disease severity!¹
 - Early start and blister formation¹
- **Mild cutaneous affection of the newborn in 10%**
- Pre-partum: improvement; post-partum: flare in 75%
- Self-limited; recurrence with menstruation, hormonal contraception, and subsequent pregnancies

¹Chi CC et al., BJD 2009.

PRURITUS in PREGNANCY

