

Dermatoses of pregnancy

George Kroumpouzou, MD,^a and Lisa M. Cohen, MD^{b,c} *Boston, Massachusetts*

The dermatoses of pregnancy can be classified into the following 3 groups: physiologic skin changes in pregnancy, dermatoses and cutaneous tumors affected by pregnancy, and specific dermatoses of pregnancy. Correct diagnosis and classification are essential for the treatment of these disorders, when necessary. Laboratory investigations are required when the diagnosis remains in question despite a careful history and thorough physical examination. A discussion with the pregnant woman about the nature of her skin condition, and the possible fetal risks associated with it, is imperative. (J Am Acad Dermatol 2001;45:1-19.)

Learning objective: At the conclusion of this learning activity, participants should be familiar with the dermatoses of pregnancy and the proposed classification of them into 3 main categories. Participants should also have a better understanding of the current knowledge of these conditions to aid in evaluating the patient with a pregnancy dermatosis.

During pregnancy profound immunologic, metabolic, endocrine, and vascular changes¹ occur, which make the pregnant woman susceptible to changes of the skin and appendages, both physiologic and pathologic. Recognition of these changes is important for correct classification and appropriate treatment when necessary. The classification and nomenclature of pregnancy dermatoses have been controversial.²⁻⁴ This review suggests a simplified classification of the pregnancy dermatoses into the following 3 categories: physiologic skin changes in pregnancy, dermatoses and cutaneous tumors affected by pregnancy, and dermatoses only occurring in pregnancy, such as intrahepatic cholestasis of pregnancy and specific dermatoses of pregnancy. This article discusses the current knowledge of these conditions and the evaluation of the patient with a pregnancy dermatosis.

PHYSIOLOGIC SKIN CHANGES IN PREGNANCY

Pregnancy-related skin changes are most likely caused by the hormonal changes associated with

Abbreviations used:

BMZ:	basement membrane zone
DIF:	direct immunofluorescence
HG:	herpes gestationis
HSV:	herpes simplex virus
ICP:	intrahepatic cholestasis of pregnancy
IH:	impetigo herpetiformis
PFP:	pruritic folliculitis of pregnancy
PP:	prurigo of pregnancy
PUPPP:	pruritic urticarial papules and plaques of pregnancy
SLE:	systemic lupus erythematosus

pregnancy.³ They have also been called physiologic skin changes or skin changes of endocrine origin.⁵⁻⁷ However, other authors³ consider that the so-called physiologic changes may be pathologic when severe. The conditions to be discussed are summarized in Table I.

Pigmentary changes

Pigmentary changes of pregnancy include hyperpigmentation and melasma. Hyperpigmentation is common during pregnancy and may be seen in up to 90% of pregnant women.⁸ The physiology of hyperpigmentation may be related to elevated serum levels of melanocyte-stimulating hormone, estrogen, and possibly progesterone.⁷⁻⁹ Mild generalized hyperpigmentation is usually seen with accentuation of normally hyperpigmented areas such as the areo-

From the Department of Dermatology, Boston Medical Center, Boston University School of Medicine^a; the Division of Dermatology, Children's Hospital, Harvard Medical School^b; and the Department of Dermatology, New England Medical Center, Tufts University School of Medicine.^c

Reprint requests: Lisa M. Cohen, MD, 51 Winchester St, Suite 205, Newton Highlands, MA 02461. E-mail: lcohen@cohenderm.com.

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Fig 1. Extensive melasma of the malar cheeks, glabella, and upper cutaneous lip.

lae, nipples, genital skin, axillae, and inner thighs. Darkening of the skin adjoining the areolae results in so-called secondary areolae, whereas darkening of the linea alba is called linea nigra.¹⁰ Occasionally, hyperpigmentation of freckles, nevi, and scars occurs.¹¹

Melasma (chloasma) is common in pregnancy ("mask of pregnancy") and has been reported in up to 70% of pregnant women³ and in 5% to 34% of nonpregnant women taking oral contraceptives⁷ (Fig 1). This type of irregular hyperpigmentation is observed in 3 clinical patterns¹²: centrofacial, malar, and mandibular. This type of hyperpigmentation results from excessive melanin deposition in the epidermis (70%), dermal macrophages (10%-15%), or both (20%) and can be clinically demonstrated by Wood's lamp examination. This examination will show enhancement of color contrast if the excess melanin is located in the epidermis but no enhancement if melanin is located only in the dermis.

Elevated estrogens, progesterone, and melanocyte-stimulating hormone levels^{9,12,13} are thought to cause melasma of pregnancy. Ultraviolet and visible light may worsen melasma or allow it to persist.^{12,14} In most cases, gestational melasma will resolve postpartum. The condition may recur in subsequent pregnancies or with the use of oral contraceptives. Epidermal melasma is responsive to treatment, whereas the dermal type is more difficult to treat. Preparations containing hydroquinone, topical corticosteroids, and tretinoin are useful for persistent cases of epidermal melasma.¹⁵ Sunscreen and proper patient education are critical for long-term success.

Hair and nail changes

Some degree of hirsutism is seen in all women, especially on the face, and less often on the arms, legs, and back. This excessive hair is caused by the

Table I. Physiologic skin changes in pregnancy

Pigmentary
Hyperpigmentation
Melasma
Hair
Hirsutism
Postpartum telogen effluvium
Postpartum male-pattern alopecia
Nail
Subungual hyperkeratosis
Distal onycholysis
Transverse grooving
Brittleness
Glandular
Increased eccrine function
Increased sebaceous function
Decreased apocrine function
Connective tissue
Striae
Vascular
Spider telangiectases
Palmar erythema
Nonpitting edema
Varicosities
Vasomotor instability
Gingival hyperemia
Hemorrhoids
Mucous membrane
Gingivitis
Jacquemier-Chadwick sign
Goodell's sign

Adapted from Wong RC, Ellis CN. Physiologic changes in pregnancy. *J Am Acad Dermatol* 1984;10:929-40.

endocrine changes of pregnancy and regresses within 6 months postpartum.¹¹ When severe hirsutism occurs, androgen-secreting tumors of the ovary, luteomas, lutein cysts, or polycystic ovary disease should be excluded.¹⁶

Although prolonged anagen phase on the scalp has been shown,¹⁷ the anagen to telogen ratio has varied in previous studies.¹⁸ Postpartum, an increased number of hairs enters the telogen phase, which leads to shedding³ (telogen effluvium) (Fig 2). This shedding generally lasts 1 to 5 months but may not cease until 15 months postpartum.⁶ Other hair changes during pregnancy include a mild frontoparietal recession reminiscent of male-pattern alopecia^{3,6} that may not normalize after pregnancy⁵ and a diffuse thinning in some women in the later months of pregnancy that may be due to inhibition of anagen hairs.¹

Nail changes in pregnancy include transverse grooving, brittleness, distal onycholysis, and subungual hyperkeratosis.^{3,10} The pathogenesis of these nail changes is unclear.



Fig 2. Telogen effluvium that developed 3 months after delivery, with characteristic temporal recession and thinning.

Glandular changes

Increased eccrine and sebaceous function and decreased apocrine function have been reported.^{1,3} Increased eccrine function is observed during pregnancy, except on the palms where it is diminished.¹⁹ This may contribute to the increased incidence of miliaria, hyperhidrosis, and dyshidrotic eczema in pregnancy.^{3,6} The increase in eccrine function has been associated with increased thyroid activity.¹¹ However, apocrine activity appears to decrease during pregnancy, although the evidence is conflicting,¹¹ which may explain the clinical improvement of pre-existing Fox-Fordyce disease and hidradenitis suppurativa.^{3,20,21} The diseases may rebound postpartum.¹⁰ Some authors^{3,8} postulate that sebaceous gland activity increases in the third trimester, possibly because of increased circulating estrogen, a finding which has not been verified by others.¹¹ The effect on acne is unpredictable, but in many patients acne develops for the first time during pregnancy.¹⁰ During gestation, the sebaceous glands on the areolae enlarge and appear as small brown papules called Montgomery's glands or tubercles.¹¹

Connective tissue changes

Striae distensae (*striae gravidarum*) develop in up to 90% of women during the sixth and seventh months of pregnancy.⁸ Striae are uncommon in Asian and African American women, and there seems to be a familial tendency. They appear as pink or purple atrophic bands on the abdomen and sometimes on the breasts, thighs, and inguinal areas. Hormonal⁸ (adrenocortical hormones, estrogen, relaxin) and physical¹ factors (stretching secondary to increase in the abdominal girth) play a role in the development of the striae. There seems to be an association between the development of striae and maternal weight gain and fetal birth weight, and some authors²²



Fig 3. Extensive spider telangiectases of the trunk.

believe that stretch is the only factor in striae gravidarum. Postpartum the lesions change to pale atrophic lines that are less apparent but may never disappear completely.

Vascular changes

Vascular changes result from distention, instability, and proliferation of vessels and regress postpartum. Early in pregnancy, the vasculature of the vestibule and vagina distends, which is clinically manifested as erythema (Jacquemier-Chadwick sign), whereas increased vascularity of the cervix causes a bluish discoloration known as Goodell's sign.²³ Other vascular changes^{1,3} include spider telangiectases (Fig 3), palmar erythema, nonpitting edema, varicosities, vasomotor instability, purpura, and gingival hyperemia. Spider telangiectases⁸ (spider angiomas, spider nevi, nevi aranei) are observed in areas drained by the superior vena cava, such as around the eyes. These are seen in 67% of white patients, appear between the second and fifth months of pregnancy, and resolve within 3 months postpartum. Palmar erythema¹⁰ is often seen and usually accompanies the development of vascular spiders. Although slight hypothenar redness occurs, which may simulate liver palms, a pattern of more diffuse, mottled hyperemia has also been recognized.¹¹

Nonpitting edema^{11,23} of the face, eyelids, and extremities is observed in at least half of all pregnant women. The swelling is most pronounced in the early morning and disappears during the course of the day. It is important to differentiate this condition from edema of other origins, such as preeclampsia. Varicosities¹¹ appear in 40% of patients and result from increased venous pressures in the femoral and pelvic vessels caused by the gravid uterus. Thrombosis⁸ occurs in fewer than 10% of pregnant women, whereas other severe complications such as throm-

Table II. Cutaneous disorders and tumors affected by pregnancy

Inflammatory	Infectious	Autoimmune
Atopic dermatitis*	Fungal (<i>Candida</i> , <i>Pityrosporum</i>)	SLE
Psoriasis	Herpesvirus (HSV, VZV)	Systemic sclerosis
Chronic plaque*	AIDS	Dermatomyositis/polymyositis
Pustular (impetigo herpetiformis)	Leprosy	Pemphigus vulgaris/vegetans/foliaceus
Acne vulgaris*	Protozoan (<i>Trichomonas</i>)	Rheumatoid arthritis*
Fox-Fordyce disease*	Condyloma acuminatum	
Hidradenitis suppurativa*		
Urticaria		

Modified from Winston GB. Skin diseases aggravated by pregnancy. J Am Acad Dermatol 1989;20:1-13.

VZV, Varicella zoster virus.

*May improve during pregnancy.

bophlebitis are quite rare. Vasomotor instability³ manifested as facial flushing, pallor, hot and cold sensations, cutis marmorata of the legs, worsening of pre-existing Raynaud's phenomenon, dermatographism, and urticaria¹¹ are common during pregnancy. Purpuric lesions⁶ are common on the legs in the second half of pregnancy.

Hyperemia of the gums is seen in virtually all pregnant women^{6,10} with varying degrees of severity and may be associated with gingivitis¹ (pregnancy gingivitis, marginal gingivitis, papillomatous hypertrophy of the gums). It develops in the third trimester of pregnancy and progressively resolves postpartum. The condition may be severe in patients with pre-existing periodontal disease, poor dental hygiene, nutritional deficiencies, and local irritative factors. Proliferation of capillaries within the hypertrophied gingiva may be seen in association with severe gingivitis and results in a granuloma gravidarum or pregnancy epulis (see "Skin Diseases Affected by Pregnancy").

SKIN DISEASES AFFECTED BY PREGNANCY

The immunologic, endocrine, metabolic, and vascular changes of pregnancy make the pregnant woman susceptible to aggravation or less often to improvement of certain skin diseases.²⁴ The skin diseases and tumors affected by pregnancy are summarized in Table II.

Inflammatory disorders

Atopic dermatitis is more likely to worsen than remit in pregnancy.^{25,26} The exacerbation is partly attributed to the pruritus of pregnancy. Nevertheless,

remission of the disease has been reported in up to 24% of cases.²⁵ The condition may also present for the first time in pregnancy in a person with an atopic diathesis. Irritant hand dermatitis and nipple eczema may be seen postpartum.⁴ Urticaria may be adversely affected by pregnancy.^{27,28} The effects of pregnancy on acne vulgaris, hidradenitis suppurativa, and Fox-Fordyce disease have been previously discussed.

Chronic plaque psoriasis is the most common type of psoriasis to develop or worsen in pregnancy,²⁹ whereas pustular psoriasis is seen less often.³⁰ Psoriasis is more likely to improve than worsen; 40% to 63% of pregnant women with psoriasis improve during pregnancy, whereas only 14% worsen.^{31,32} This may be attributed to the high levels of interleukin 10 in pregnancy,³³ a cytokine which has a favorable effect on the course of the disease.^{34,35} Psoriatic arthritis has been reported to develop or worsen during pregnancy, and 30% to 45% of women had onset of psoriatic arthritis either postpartum or perimenopausally.³⁶

Impetigo herpetiformis (IH), a rare variant of generalized pustular psoriasis, has been reported in pregnancy.³⁷⁻⁴⁰ It is often associated with hypocalcemia^{41,42} or low serum levels of vitamin D.⁴³ Pregnant women with IH usually have no personal or family history of psoriasis. The onset occurs most commonly in the last trimester of pregnancy, but it has been reported as early as the first month. IH often persists until delivery and occasionally long afterward.³⁹ It has been associated with severe systemic symptoms such as malaise, fever, delirium, diarrhea, vomiting, and symptoms of tetany.³

IH is manifested as symmetric, erythematous patches that show grouped pustules at their mar-

Metabolic	Connective tissue	Tumors	Miscellaneous
Porphyria cutanea tarda Acrodermatitis enteropathica	Ehlers-Danlos syndrome Pseudoxanthoma elasticum Anetoderma	Pyogenic granuloma Skin tag Hemangioma Hemangioendothelioma Glomus tumor Dermatofibroma Dermatofibrosarcoma protuberans Leiomyoma Keloid Desmoid tumor Neurofibroma Melanocytic nevus Melanoma	Sarcoidosis* Erythema nodosum Erythrokeratoderma variabilis Bowenoid papulosis Mycosis fungoides Erythema multiforme Tuberous sclerosis Acanthosis nigricans Hereditary hemorrhagic telangiectasia

gins. The lesions start in the intertriginous or flexural areas and extend centrifugally, occasionally covering large skin areas.³⁹ The mucous membranes, including the esophagus, may show erosive or circinate lesions while the face, hands, and feet are spared. The skin lesions may form crusted or vegetative plaques resembling those of pemphigus vegetans or condylomata acuminata.³⁸ Subungual pustules may cause onycholysis.³⁹ Postinflammatory hyperpigmentation is regularly seen.

The histopathologic findings show changes of pustular psoriasis, and direct immunofluorescence (DIF) is negative. The laboratory findings include leukocytosis, elevated erythrocyte sedimentation rate, and occasionally hypocalcemia or decreased vitamin D levels secondary to hypoparathyroidism.⁴¹ Pus from the lesions is sterile, as are blood cultures, except in cases of superinfection. IH can be differentiated from impetigo, subcorneal pustular dermatitis, dermatitis herpetiformis, and herpes gestationis on the basis of clinical history, triggering factors, association with systemic illness, negative bacteriology, and negative DIF.

Many authors^{39,40} consider IH as an outbreak of psoriasis, triggered by an altered metabolic state such as pregnancy or hypocalcemia. Because hypocalcemia exacerbates generalized pustular psoriasis⁴² and can be secondary to hypoalbuminemia (often observed in pregnancy),⁴⁴ IH most likely represents a variant of psoriasis. Furthermore, patients with latent hypoparathyroidism may become hypocalcemic because of the increased demands for calcium in the last trimester of pregnancy.³⁹ Nevertheless, claims exist that IH may be a distinct entity.^{45,46}

IH is controlled with systemic corticosteroids, usually effective at a relatively low dose of 15 to 30 mg/day of prednisone.³⁸ At times, doses up to 60 mg/day are necessary to control the eruption.⁸ In superinfected cases, appropriate systemic antibiotics should be administered. Responses to parenteral calcium with vitamin D have been reported.⁴¹ Serum calcium and albumin levels should be followed and replacement therapy undertaken if necessary. Several authors have successfully treated the condition with postpartum administration of oral retinoids^{47,48} or PUVA.⁴⁹ Risks during pregnancy include tetany, seizures, and delirium. Remission is seen postpartum, but recurrence in successive pregnancies may occur^{39,50} with earlier onset and increased morbidity.⁴⁵ Stillbirth and placental insufficiency have been reported even when the disease was controlled with corticosteroids.⁵⁰

Infections

The increased incidence of certain infections in pregnancy has been attributed to the immunosuppressive effects of high serum levels of estrogens.⁵¹ These include a decrease in cell-mediated immunity, neutrophil function, and activity of natural killer cells, as well as impairment of local antibody responses. *Candida* vaginitis can be seen in up to 56% of pregnant women, and the organism can be cultured from up to 50% of neonates born to infected mothers.⁸

Trichomonas is seen in up to 60% of pregnant women but has no adverse effects on the fetus.⁸ *Pityrosporum* folliculitis caused by the yeast *Malassezia furfur* occurs with greater frequency in

pregnant women.⁵² Systemic fungal infections such as blastomycosis^{53,54} and coccidioidomycosis⁵⁵ have been reported in pregnant women, but their true incidence in pregnancy is unknown. Condylomata acuminata⁵⁶ can grow rapidly during pregnancy and may block the birth canal.

Recurrent genital herpes simplex virus (HSV) infection is not exacerbated in pregnancy but is of critical interest because of its relation to fetal morbidity and mortality. The frequency of transmission of HSV infection to the neonate is approximately 50% for primary infections of the mother and 5% for recurrent infections.⁵⁷ More than half of infants born to mothers with clinically evident vaginal lesions will acquire neonatal HSV infections, and a significant number will die or have neurologic sequelae.⁵⁸ Primary HSV infection that occurs after the 26th week of pregnancy is rare but may result in disseminated disease with the mortality rate approaching 50% for mother and fetus.⁵⁹ Varicella can be complicated with maternal pneumonia (14%), maternal death (3%), premature labor, or congenital varicella syndrome if the primary infection occurs during the first trimester.⁶⁰ Herpes zoster infection does not cause complications to the mother or fetus.⁶¹

Progression to AIDS develops in 45% of HIV-positive pregnant women within 2 years of their pregnancies,⁶² an attack rate much higher than is usually seen in the same period for HIV-positive, nonpregnant women. Nevertheless, recent studies⁶³ do not show any effect of pregnancy on the early progression of HIV disease. In cohort studies^{64,65} of HIV-infected women with mild to moderate immunosuppression, pregnancy did not accelerate progression to AIDS or death. Most of the women with AIDS investigated were not suspected of having the disease until their offspring developed AIDS after delivery. The source of AIDS infection in most cases was intravenous drug use or transmission of infection from a husband who was an intravenous drug user.⁶² Opportunistic infections have a high maternal mortality,^{66,67} but the number of cases is too small to conclude that the death rate due to opportunistic infections is increased in pregnant women with AIDS. Increased maternal and fetal mortality,⁶⁸ intrauterine growth retardation, prematurity, and a dysmorphic syndrome⁶⁹ have been reported. AIDS will develop in a high percentage of infants within 16 months of birth.

One third of patients with leprosy will experience an exacerbation of disease during pregnancy or within the first 6 months of lactation.⁷⁰ The type 1 lepra reaction increases in frequency during the first trimester of pregnancy,⁷¹ then declines until delivery, whereupon it again increases sharply. The type 2 reac-

tion increases in frequency with peaks in the first and third trimesters and the first 9 months of lactation.⁷² Many patients have erythema nodosum leprosum almost continuously from the third trimester through several months postpartum. Leprosy is associated with a high incidence of infant mortality, and low birth weights and small placentae have been documented.⁷³ Up to 20% of children born to mothers with leprosy will develop leprosy by puberty.⁷³

Autoimmune disorders

Chronic cutaneous lupus is not affected by pregnancy,⁷⁴ but debate exists as to whether flares of systemic lupus erythematosus (SLE) are more common in pregnancy. Although reports of increased rate of lupus flares in pregnancy have been published,⁷⁵ other studies^{76,77} have determined that the outcome may be more favorable. Pregnancy is well tolerated by mothers in remission for at least 3 months before conception, except those with nephropathy or cardiopathy. If conception occurs during the active stage of SLE, approximately 50% of patients will worsen during pregnancy, and a few will die or experience permanent renal damage.^{77,78} Patients whose SLE first appears during pregnancy have a high frequency of severe manifestations.⁷⁶ Nevertheless, postpartum remission and successful subsequent pregnancy occur in more than two thirds of cases.

Cutaneous flares are the most common manifestation of SLE in pregnancy, followed by arthritis.⁴ Painful vasculitic lesions on the extremities are the most common skin lesions. The effects of SLE on fetal outcome correlate with the severity of maternal lupus.⁷⁹ Premature birth occurs in 16% to 37% of pregnancies and spontaneous abortion may occur 2 to 4 times more than normal. Neonatal lupus⁸⁰ is a rare syndrome seen in babies of mothers most often with circulating anti-Ro(SS-A) antibodies and can lead to congenital heart block or a photodistributed skin eruption. The antiphospholipid antibody syndrome⁸¹ presents with thrombosis, recurrent miscarriage, livedo reticularis, migraine, stroke, and/or thrombocytopenia.

The course of systemic sclerosis is not significantly altered by pregnancy, and the fetal outcome is relatively unaffected by the disease. In one report,⁸² 39% of women experienced worsening of their symptoms, whereas 22% improved. Cutaneous sclerosis has been shown to be alleviated in some reports,⁸³ whereas in others,⁸⁴ patients had an increased risk of preeclampsia, hypertension, and renal failure, leading to maternal death. Polymyositis/dermatomyositis can be detrimental to both mother and fetus.⁸⁵ A flare of the heliotrope rash or proximal muscle weakness (or both) may occur in half of

affected persons. Fetal loss due to spontaneous abortion or stillbirth or neonatal death secondary to immaturity occurs in more than half of the cases.

Pemphigus variants vulgaris, vegetans, or foliaceus^{86,87} may present or worsen during pregnancy, especially in the first or second trimester. The clinical presentation may mimic herpes gestationis, and immunofluorescence studies are essential for confirmation of the diagnosis. Fetal transmission of the disease may occur from transplacental transfer of IgG antibodies. Blisters of neonatal pemphigus normally resolve within 2 to 3 weeks postpartum.⁸⁸ Many cases of pemphigus in pregnancy resulted in stillbirth, and the stillborn infants had skin lesions with immunofluorescence findings consistent with the disease. The cause of fetal death is multifactorial and may be due to the skin disease, maternal drug ingestion, intercurrent infection, and/or placental insufficiency.

Metabolic disorders

Porphyria cutanea tarda is adversely affected by estrogen; therefore one might expect exacerbation of the disease in pregnancy. Although the results of previous reports have been inconsistent,⁸⁹ a clinical exacerbation has been noticed⁹⁰ during the first trimester, coinciding with a rise in serum estrogen and a high rate of porphyrin excretion. Later in pregnancy, as fetal iron requirements rise and blood volume increases, the skin disease improved, and a concomitant fall in serum iron and urinary porphyrins occurred. The disease did not adversely affect fetal prognosis.

Acrodermatitis enteropathica flares during pregnancy, as serum zinc levels decline early in gestation.⁷⁸ In some patients the disease is recognized in pregnancy, but it may be misdiagnosed as impetigo herpetiformis or herpes gestationis, unless serum zinc is measured. Most often, the patient had a non-specific skin eruption during childhood that reappeared during pregnancy with progressive worsening until delivery and rapid clearing postpartum.⁹¹ Most pregnancies have produced normal offspring. In a few cases⁹² of untreated maternal acrodermatitis enteropathica, anencephaly, and achondroplastic dwarfism with neonatal death have been reported.

Connective tissue disorders

Patients with Ehlers-Danlos syndrome types I (classic or gravis) and IV (ecchymotic or arterial) are likely to have complications during pregnancy.²⁴ Pregnant women are susceptible to postpartum bleeding, rupture of major vessels (especially in type IV), poor wound healing, uterine lacerations, bladder and uterine prolapse, and abdominal hernias.⁹³



Fig 4. Characteristic pyogenic granuloma of the lingual surface of the gingiva that developed in pregnancy.

A favorable outcome of pregnancy with normal vaginal delivery has been reported for patients with type II⁹⁴ (mitis) and type X⁹⁵ (fibronectin abnormality). Reports of pregnancy in each type of Ehlers-Danlos syndrome are not available.

Pregnancy may aggravate the vascular complications of pseudoxanthoma elasticum.⁹⁶ The main complication is gastrointestinal bleeding, but repeated epistaxis and congestive heart failure with ventricular arrhythmia have also been reported. Intrauterine growth retardation and placental abnormalities have been reported,⁹⁷ but the data on the fetal risk are scarce. Anetoderma of Jadassohn has been reported¹⁰ in a patient during the first month of pregnancy, but the association with pregnancy may be coincidental.

Cutaneous tumors

Tumors may appear for the first time, enlarge, or increase in number during pregnancy (Table II). The pyogenic granuloma of pregnancy,¹¹ also called granuloma gravidarum, pregnancy tumor, or pregnancy epulis is a proliferation of capillaries within the gingiva that appears between the second and fifth months of pregnancy in 2% of pregnant women. It is a deep-red or purple nodule that may be seen between adjacent teeth or on the buccal or lingual surface of the marginal gingiva (Fig 4). The histopathologic features are identical to pyogenic granuloma. Postpartum, spontaneous shrinkage of the mass occurs³ so that surgical intervention is usually not necessary.

Molluscum fibrosum gravidarum¹⁰ is the name given to soft fibromas or skin tags that appear during the later months of pregnancy and partially or completely disappear postpartum. They vary in size and color and can be localized to the face, neck, upper chest, and beneath the breasts. The association of

Table III. Dermatoses of pregnancy

Conditions occurring only in pregnancy
ICP
Specific dermatoses of pregnancy
HG
PUPPP
PP
PFP

pregnancy with hemangioma, hemangioendothelioma, and glomus tumor reflects the effects of gestational hormones on the vascular structures.³ Large hemangiomas resulting in arteriovenous shunting and high-output cardiac failure have been reported¹⁰; these lesions regressed postpartum. Hemangioendotheliomas may occur around the eyes, breast, or umbilicus; are surrounded by dilated veins; and are associated with hyperpigmentation in other skin areas. New glomangiomas may occur in successive pregnancies.

Dermatofibromas, leiomyomas, and keloids may develop or grow rapidly during pregnancy.⁸ Cases of accelerated growth of dermatofibrosarcoma protuberans during pregnancy have been reported.⁹⁸ Desmoid tumors may develop in the rectus abdominis muscle,⁸ whereas neurofibromas may enlarge or arise de novo during pregnancy. Plexiform neurofibromas⁹⁹ may enlarge rapidly. This is often associated with complications such as massive hemorrhage within the tumor. In most cases, a partial regression of the lesion occurred postpartum. Patients with neurofibromatosis may experience severe vascular complications during pregnancy, such as hypertension and renal artery rupture.¹⁰⁰

Melanocytic nevi may develop, enlarge, or darken during pregnancy.^{10,101,102} Histologically, they may have larger melanocytes, increased melanin, and fully developed dendrites. Other studies,¹⁰³ however, did not show any histopathologic changes in melanocytic nevi of pregnant women. An increase in estrogen and progesterone receptors has been demonstrated,¹⁰⁴ perhaps explaining the pigmentary changes observed in the nevi of pregnant women.¹⁰ A mild degree of histopathologic atypia has been reported,¹⁰⁵ and it has been suggested¹⁰⁶ that pregnancy is associated with increased rate of dysplastic nevus change. The data to support an increased risk of malignant transformation within nevi during pregnancy are insufficient.

The relationship between pregnancy and malignant melanoma has been debated. An unfavorable effect of estrogens on melanoma has been suggested by reports^{107,108} of rapid growth of tumors, appearance of multiple primaries, cases of malignant trans-

formation of congenital and dysplastic nevi during pregnancy, and regression of metastases after delivery. On the other hand, there is evidence¹⁰⁹ that multiparity confers a protective effect in the development of melanoma and that women with melanoma have a better prognosis than men. Most authors¹¹⁰ have found that melanomas that develop during pregnancy are diagnosed at a more advanced stage than melanomas in nonpregnant women, resulting in shorter disease-free survival. Whether this difference is caused by a delay in diagnosis or by acceleration of tumor growth during pregnancy remains unclear. No differences in the histologic type or site of melanoma were found between pregnant and nonpregnant women. Recent studies¹¹¹ show that, although the melanomas arising during pregnancy are thicker, these are not associated with a less favorable prognosis. Grin, Driscoll, and Grant-Kels¹¹² reviewed controlled clinical trials to assess the effect of pregnancy on the prognosis of melanoma and showed that pregnancy does not influence the 5-year survival rates.

Miscellaneous disorders

Sarcoidosis is one of the skin conditions that often decreases during pregnancy.^{113,114} Exacerbation or new onset of erythema nodosum,^{115,116} erythrokeratoderma variabilis,¹¹⁷ bowenoid papulosis,¹¹⁸ mycosis fungoides,¹¹⁹ erythema multiforme,^{120,121} tuberous sclerosis,^{122,123} acanthosis nigricans,¹²⁴ and hereditary hemorrhagic telangiectasia¹²⁵ has been reported.

DERMATOSES OF PREGNANCY

Dermatoses of pregnancy include conditions that occur exclusively during pregnancy, such as intrahepatic cholestasis of pregnancy, and specific dermatoses of pregnancy^{126,127} (Table III).

Conditions occurring only in pregnancy

Intrahepatic cholestasis of pregnancy (ICP) is seen in the third trimester of pregnancy in 70% of cases¹²⁸ (mean, 31 weeks) and is due to a mild form of intrahepatic bile secretory dysfunction. The incidence varies from 0.02% to 2.4% of pregnancies.¹²⁸ The condition was particularly common at one time in Chile and Scandinavia (3%-14%),¹²⁹ a finding now attributed to dietary factors.¹³⁰ The incidence is much lower in the United States (1/1293 to 1/146 deliveries) and Canada (Vancouver, 1/217).¹³⁰ The features of ICP¹³¹ are (1) generalized pruritus with or without jaundice, (2) absence of primary skin lesions, (3) biochemical abnormalities consistent with cholestasis, and (4) resolution after delivery. Recurrence with subsequent pregnancy occurs in 40% to 50% of patients.

ICP may be subdivided^{130,131} according to those patients with hyperbilirubinemia (cholestatic jaundice of pregnancy) and those with pruritus and biochemical abnormalities but without hyperbilirubinemia (prurigo gravidarum). For a diagnosis of ICP to be established, there must be no history of exposure to hepatitis viruses or hepatotoxic drugs.³⁹ Icteric cholestasis of pregnancy must be differentiated from other causes of jaundice.³ Finally, pruritus secondary to concurrent cutaneous disease or other specific gestational dermatoses must be excluded.

ICP is associated with elevated serum bile acids (mean, 1349 μ g/100 mL), predominantly cholic acid, and mild abnormalities of the liver function tests, including elevated cholesterol, triglycerides, phospholipids, alkaline phosphatase, 5'-nucleotidase, and lipoprotein X.¹²⁹ Occasionally, there is mild to moderate bilirubin elevation (2-5 mg/dL in jaundiced patients).¹²⁹ The serum levels of bile acids correlate with the severity of pruritus. Malabsorption of fat secondary to cholestasis can lead to weight loss and vitamin K deficiency in severe cases.³⁹ Skin biopsy findings are nonspecific, whereas liver biopsy reveals changes of mild cholestasis, namely, dilated bile canaliculi, staining of parenchyma with bile pigments, and minimal inflammation.¹³² As stated by Haemmerli¹³³ in 1966, "cholestasis is clinically marked, biochemically moderate and histologically minimal."

Many aspects of the pathophysiology of ICP remain unclear, and there is debate as to whether the condition is physiologic or pathologic ("pregnancy is cholestatic").¹³⁴ The condition has been associated¹³⁵ with HLA subtypes A31 and B8, and a Mendelian dominant inheritance has been proposed. Genetic factors are also suggested from epidemiologic studies,¹²⁹ a positive family history in up to 50% of cases,¹³¹ and occurrence of ICP in twin pregnancies.¹³⁶ Estrogens interfere with the diffusion of fluid across the canalicular membrane of the hepatocyte and subsequently with hepatic bile acid secretion.³⁹ Progestins inhibit hepatic glucuronyl-transferase, thereby reducing the clearance of estrogens and amplifying their effects.¹²⁹ Moreover, it has been postulated that "predisposed" women may have altered estrogen metabolism in the liver, resulting in reduced biliary volume and excretion of these compounds.¹²⁹ Whether the aforementioned abnormalities are causal or secondary to cholestasis is unknown.

These changes may play a role in the high prevalence of gallstones in ICP-affected women.³⁹ There appear to be no maternal risks associated with ICP, other than those associated with deficiency of vitamin K in severe cases (uterine and intracranial hem-

orrhage).¹³¹ Fetal risks include an increased tendency for fetal distress, stillbirth, and preterm delivery.¹³⁷ Examination of the placenta often reveals nonspecific abnormalities (degenerative changes, edematous villi, infarcts), which may contribute to fetal hypoxia.¹³⁸

The pruritus associated with mild cholestasis responds to bland antipruritic emollients, soothing baths, primrose oil, and topical antipruritics.^{4,131} Epomediol¹³⁹ and silymarine¹⁴⁰ may be helpful in controlling the pruritus in mild ICP. S-denosyl-L-methionine has been shown to have beneficial effects on both pruritus and biochemical alterations in patients with mild ICP.¹⁴¹ More severe cases have been treated with ion-exchange resins, such as cholestyramine or ursodeoxycholic acid^{39,131} or ultraviolet B therapy^{4,131} with variable results. Cholestyramine needs to be administered for several days before pruritus is alleviated and does not affect the biochemical abnormalities of ICP.¹³² Ursodeoxycholic acid given orally at a dose of 15 mg/kg per day for 3 weeks controls both the pruritus and the biochemical abnormalities and may decrease the risk of adverse fetal outcome.¹⁴² Other authors have successfully treated severe ICP with oral corticosteroids.¹⁴³ If ICP lasts for several weeks, vitamin K absorption may be impaired, leading to a prolonged prothrombin time. The prothrombin time should therefore be routinely monitored and intramuscular vitamin K administered as necessary.

Specific dermatoses of pregnancy

Specific dermatoses of pregnancy include those skin diseases that result directly from the state of gestation or the products of conception¹²⁷ (see Table III).

Herpes gestationis (HG) (also known as "pemphigoid gestationis") is the most well-defined dermatosis of pregnancy and the most important to diagnose. The incidence of HG in North America is estimated as 1 in 50,000 pregnancies¹⁴⁴ and in the United Kingdom 1 in 40,000 pregnancies.¹⁴⁵ The condition typically develops during the second or third trimester (mean onset, 21 weeks) but has been reported in the first trimester. It starts with the sudden onset of intensely pruritic, urticarial lesions (Fig 5) on the abdomen in half of the cases.^{146,147} The lesions rapidly progress to a generalized bullous eruption (Fig 6), sparing the face, mucous membranes, palms, and soles.^{144,148}

The clinical presentation and course of HG are variable. The disease often resolves during the later part of gestation and flares at the time of delivery.¹⁴⁹ Exacerbation at delivery or immediately postpartum is classic, occurring in 75% of cases.¹³¹ Occasionally,

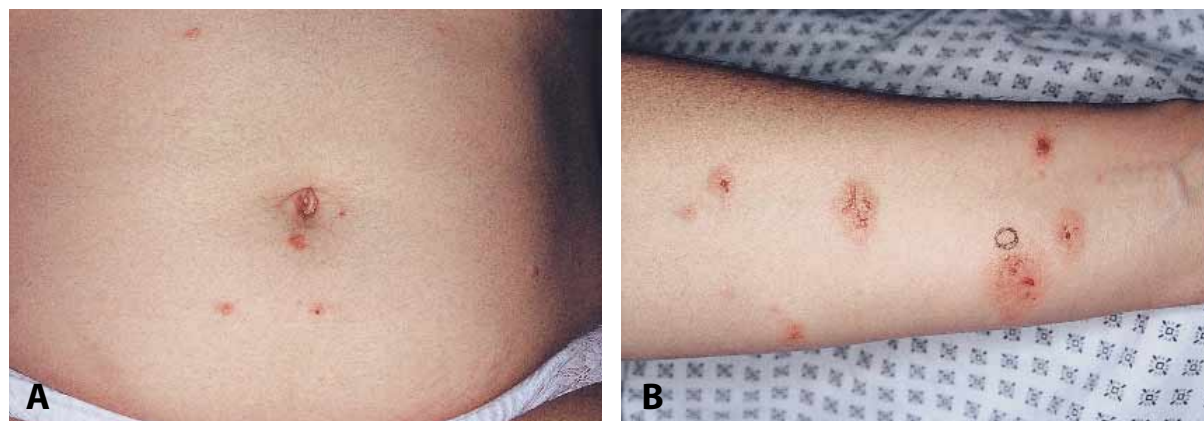


Fig 5. A and B, Unusual presentation of HG characterized by small urticarial papules and papulovesicles in a 4-month pregnant woman.



Fig 6. Characteristic tense bullae on erythematous base in a patient with HG.

the disease may present within hours of parturition. Most patients experience spontaneous regression over weeks to months postpartum. In two cases, a protracted postpartum course and conversion to bullous pemphigoid were reported.¹⁵⁰ Recurrence with menses or with subsequent use of oral contraceptives has often occurred. The disease may be less severe in subsequent pregnancies, and disease-free pregnancies have been reported.^{146,151}

HG has been associated with autoimmune diseases, particularly Graves' disease.¹⁵² Increased serum antithyroid and anti-gastric parietal cell antibodies¹⁵² and acute phase reactants have been reported. Serum eosinophilia¹⁵³ and anti-basement membrane zone (BMZ) antibody levels¹⁵⁴ do not correlate with the severity of disease. Histopathologic examination reveals a subepidermal vesicle with perivascular lymphocytes and eosinophils^{144,148} or a nonspecific, mixed cellular infiltrate with numerous

eosinophils. DIF of perilesional skin shows C3 with or without IgG in a linear band along the BMZ, the sine qua non of the disease¹³¹ (Fig 7). In salt-split skin specimens, the antibody binds to the roof of the vesicle. Indirect immunofluorescence is generally negative, but it may reveal the capacity to fix complement to the BMZ.

HG is the only specific dermatosis of pregnancy for which the origin is known. From the late 1970s there has been speculation on the autoimmune nature of the disease, and investigative efforts focused on the identification of the serum factor (HG factor) that binds to the BMZ. DIF shows IgG deposits in 25% of cases, but in almost all cases when indirect complement-added immunofluorescence is used.^{155,156} The antibody belongs to the IgG1 subclass¹⁵⁵ and the antigen is a 180-kd protein (bullous pemphigoid antigen 2, BPAG2).^{157,158} Epitope mapping has demonstrated that HG autoantibodies bind a common antigenic site within the noncollagenous domain (NC16A) of the transmembrane 180-kd HG antigen.^{159,160} Serum HG antibodies activate complement via the classic pathway,^{131,161} with subsequent chemoattraction of eosinophils and degranulation,¹⁶² which may dissolve the junction between epidermis and dermis. Nevertheless, antibody titers and DIF for C3 may remain positive even after clearance of the skin lesions, raising speculation that factors other than antibody to BPAG2 may contribute to blister formation in HG.¹⁶³

Associations with HLA antigens DR3 (61%-80%), DR4 (52%), or both (43%-50%) have been reported.¹⁵³ Furthermore, DR3 was found to be in linkage disequilibrium with the C4 null allele, with subsequent increase of the latter.¹⁶⁴ The striking finding of anti-HLA antibodies in all persons with a history of HG¹⁶⁵ raised speculation about a possible immuno-

logic insult against placental antigens during gestation.¹⁶⁶ The HG antibody was found to bind to the amniotic basement membrane,¹⁶⁷ and a higher frequency of major histocompatibility complex class II antigens within the villous stroma of chorionic villi associated with an increased number of lymphocytes was found.¹⁶⁸ These findings support a hypothesis that the disease is due to an immunologic response against class II antigens¹⁶⁹⁻¹⁷¹ of paternal haplotype¹⁷² at the placental BMZ, which then cross-reacts with the skin.

The differential diagnosis of HG includes allergic contact dermatitis, drug eruption, and pruritic urticarial papules and plaques of pregnancy (PUPPP, see below). It may be difficult to distinguish the prebullous urticarial lesions in HG from the urticarial lesions of PUPPP, but the two diseases have a different clinical course and can be distinguished by immunofluorescence studies. The cornerstone of treatment in HG is systemic corticosteroids.¹⁷³ Most patients respond to 0.5 mg/kg of prednisone daily. Doses higher than 80 mg daily are exceptional, although doses up to 180 mg daily have been used.¹⁵³ Because postpartum exacerbations are common, some authors¹⁷⁴ suggest an increase in the corticosteroid dose temporarily in the early postpartum period. Some patients with mild prebullous HG may respond to topical corticosteroids combined with a systemic antihistamine suitable for use in pregnancy.¹⁷⁵ Alternatives to systemic corticosteroids (dapsone, sulfapyridine, pyridoxine, or cyclosporine) or adjuvants (methotrexate, azathioprine, cyclophosphamide, or gold) have been tried.^{131,148,174-176} None, with the exception of cyclosporine,¹⁷⁶ are useful before delivery. Their use in postpartum, non-nursing patients has been reported, with mixed results.¹³¹ Dapsone is now contraindicated because it is ineffective and can cause hemolytic disease of the neonate.^{148,174} Pyridoxine is similarly unhelpful.¹⁴⁸ Plasmapheresis^{148,175} can be considered in severe cases. Ritodrine,¹⁷⁷ a β -agonist used for the treatment of premature labor, was successful in one patient. Chemical oophorectomy with goserelin¹⁷⁸ has been effective in one case of severe long-standing HG. Early delivery may be required in intractable cases.

There is no maternal risk in HG other than symptomatic complaints. An increased risk of Graves' disease and other autoimmune diseases has been reported¹⁵² for patients with a history of HG. Neonatal HG has been reported¹⁷⁹ in up to 10% of cases, but the disease is mild and self-limited. Most studies^{153,180} show a tendency for small-for-gestational-age infants and prematurity, which is not altered by the use of systemic corticosteroids. Nevertheless, no increase in fetal morbidity or mortality has been noted.¹⁸¹

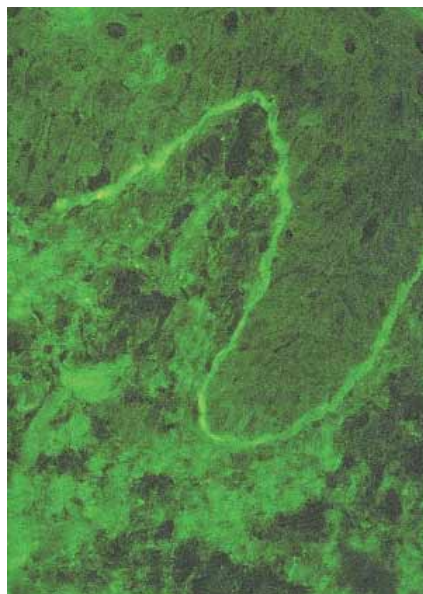


Fig 7. Intense linear C3 deposition along BMZ in a patient with HG. (Courtesy of Miguel Staderker, MD, Boston, Mass.)

Pruritic urticarial papules and plaques of pregnancy

PUPPP is the most common of the gestational dermatoses, affecting between 1 in 130 and 1 in 300 pregnancies.¹⁸² Many different names have been applied to this condition, including "toxemic rash of pregnancy,"¹⁸³ "Nurse's late prurigo of pregnancy,"¹⁸⁴ "toxemic erythema of pregnancy,"¹⁸⁵ and "polymorphic eruption of pregnancy."^{2,145,186} The terminology has been confusing as a result of the variable clinical presentation of the condition. The term *pruritic urticarial papules and plaques* was coined by Lawley et al¹⁸⁷ (1979), who reported a specific pruritic eruption in 7 pregnant women.

PUPPP occurs classically in primigravidas in the third trimester of pregnancy (mean onset, 35 weeks) or occasionally postpartum and does not usually recur in subsequent pregnancies or with oral contraceptives. In exceptional cases, familial occurrence was reported.¹⁸⁸ The mean duration of the eruption is 6 weeks,¹⁸⁹ although it is rarely severe for more than 1 week. The eruption usually begins in the striae on the abdomen and shows periumbilical sparing^{187,190,191} (Fig 8). The eruption is polymorphous, most commonly with erythematous, urticarial papules and plaques (Fig 9), but occasionally with vesicles, purpura, targetoid (Fig 10) or polycyclic lesions.^{191,192} The rash then spreads over a few days to involve the thighs, buttocks, breasts, and arms. The face, palms, and soles are commonly spared.^{191,193} When widespread, PUPPP may resemble a toxic erythema. As it resolves, it may take on an eczematous appearance.



Fig 8. Early PUPPP shows small urticarial papules within erythematous striae.

Histopathologic examination shows a spongiotic dermatitis with a perivascular or upper dermal inflammatory cell infiltrate^{193,194} (Fig 11). Focal epidermal changes such as parakeratosis, exocytosis, and mild acanthosis may be seen. There may be a striking number of eosinophils,¹⁹³ and differentiation from the early, prebullous phase of HG can be difficult. Serologic and immunofluorescence tests are usually negative^{187,191,194} and help to distinguish this disorder from HG. Ambiguous findings of C3 deposition in blood vessel walls and linear or granular C3 at the dermoepidermal junction have been reported in some cases.^{187,192,195} Zurn et al¹⁹⁶ reported circulating IgM anti-BMZ antibodies in 5 patients with PUPPP; however, the specificity of this observation has been debated.¹⁹⁷

The origin of PUPPP has not been established. Serology and DIF are normal,¹⁹⁰ and no immunologic abnormalities have been found.¹⁹⁸ Associations with preeclampsia, autoimmune disorders, or HG have not been reported. Hormonal abnormalities have not been consistently reported. Vaughan Jones et al¹²⁷ recently reported a decrease in serum cortisol in patients with PUPPP. The clinical presentation suggests a hypersensitivity reaction.³⁹ The role of estrogens or progesterone, or both, has been addressed in one patient who had persistent pruritus during 2 months of breast-feeding and 9 successive menstrual periods, and in two patients with recurrent episodes of urticaria while breast-feeding.³⁹ Some authors^{199,200} speculate that rapid abdominal wall distention in primigravidas may cause damage to connective tissue in



Fig 9. Characteristic urticarial papules and plaques involving the lower abdomen and thighs in a patient with PUPPP. Note prominent linea nigra.



Fig 10. Targetoid lesions in patient with PUPPP.

the striae and trigger the inflammatory response of PUPPP. Studies supporting this hypothesis show that PUPPP is related to abnormal weight gains in the mother and fetus¹⁹⁹ and to twin pregnancy²⁰¹ (13/114 cases, 1 triplets); however, this relationship has been debated.^{127,202} Other authors²⁰³ speculated that during the aging of the placenta in the third trimester, a substance is released into the maternal circulation that may trigger fibroblast proliferation.

A biopsy for DIF should be done when necessary to differentiate PUPPP from the urticarial form of HG.²⁰⁴ Drug rashes need to be excluded. Viral exanthems are usually seen within the context of associated symptoms. PUPPP is distinguished from pruritic folliculitis of pregnancy²⁰⁵ (see below) on the basis of the follicular nature of the lesions and histopathologic features of folliculitis in the latter. Prurigo of pregnancy¹⁸⁴ begins earlier in pregnancy, lacks urticarial lesions, persists throughout pregnancy,

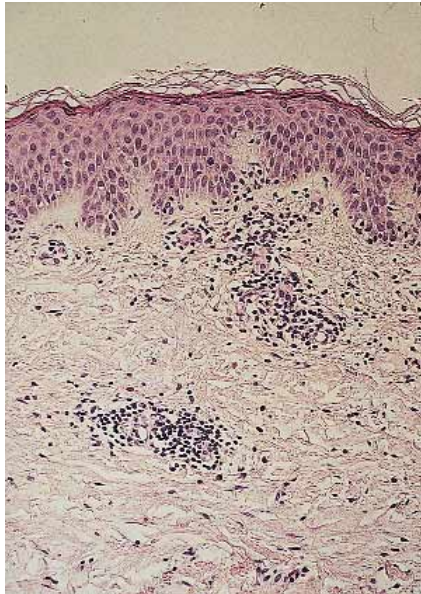


Fig 11. Photomicrograph of biopsy specimen from patient with PUPPP that reveals mild spongiosis and a superficial perivascular inflammatory cell infiltrate with numerous eosinophils.

and may recur with subsequent pregnancies. Differentiation between PUPPP and ICP¹²⁹ is feasible through a detailed clinical history, absence of primary skin lesions in ICP, serology, and recurrence in subsequent pregnancies in ICP.

The condition is harmless to the fetus and mother, but pruritus may be severe and intractable. The mother should be reassured that the eruption will resolve after delivery. In view of the self-limited nature of PUPPP, symptomatic treatment is all that is usually required. Antipruritic topical medications (menthol, doxepin), antihistamines, and topical corticosteroids usually control the pruritus.¹³¹ A short course of oral prednisone is effective and safe in severe cases.^{127,202,206} One of us has successfully treated several patients with PUPPP using UVB therapy (L. Cohen, unpublished observation). Early delivery in cases of intractable pruritus¹²⁷ has been debated.^{207,208}

Prurigo of pregnancy

Prurigo of pregnancy (PP) comprises the previously described “Besnier’s prurigo gestationis,”²⁰⁹ “Nurse’s early prurigo of pregnancy,”¹⁸⁴ and “papular dermatitis of Spangler.”²¹⁰ These conditions have extensive clinical overlap,²¹¹ and the pathogenesis has not been identified in any of them. It has been debated²¹² whether “linear IgM dermatosis of pregnancy” described by Alcalay et al²¹³ should be classified as a distinct entity or may be a variant of PUPPP³⁹ or PP.¹³¹ The incidence of PP is 1 in 300 pregnancies.



Fig 12. Typical follicular erythematous papules on the abdomen in patient with PFP.

PP has been reported in all trimesters of pregnancy. The lesions consist of erythematous papules and nodules on the extensor surfaces of the extremities and occasionally on the abdomen, similar to those seen in prurigo nodularis of nonpregnant women.^{4,131} They may be crusted or excoriated. The condition runs a protracted course through gestation and may last for weeks to months postpartum. Recurrence during subsequent pregnancies is variable.

Results of serologic tests are normal, and the histopathologic features are nonspecific, showing a chronic inflammatory cell infiltrate in the upper dermis with occasional epidermal changes. DIF is negative. The cause of PP is unknown. The condition may be related to an atopic background or ICP or both.²¹⁰ Several patients with PP have elevations in serum IgE,¹²⁷ which is consistent with the theory that PP arises as a result of pruritus gravidarum in women with an atopic predisposition.^{127,210} The differential diagnosis comprises other specific dermatoses of pregnancy and pruritic dermatoses unrelated to pregnancy. Arthropod bites, scabies, and drug eruptions need to be excluded. The treatment is designed to alleviate symptoms with mid-potency topical corticosteroids and antihistamines.^{39,131} The maternal and fetal prognosis is excellent,^{4,131} the birth weight normal,¹²⁷ and the condition usually resolves postpartum.

Pruritic folliculitis of pregnancy

Pruritic folliculitis of pregnancy (PFP) was first described by Zoberman and Farmer²⁰⁵ in 1981. The authors reported a pruritic eruption in 6 pregnant

women that resolved spontaneously at delivery or in the postpartum period. The lesions were generalized, erythematous, follicular papules, which developed from the fourth to the ninth month of gestation (Fig 12). There was no morbidity to the mother or fetus, with the exception of one study that showed reduction in fetal birth weight.¹²⁷ The histopathologic features are those of a sterile folliculitis, and DIF is negative. Since the original article by Zoberman and Farmer, there have been several subsequent reports.^{2,182,215-220} The condition seems to be more common than previously thought, and it is likely that many cases of PFP are misdiagnosed as microbial folliculitis. The differential diagnosis of PFP includes an infectious folliculitis and a specific dermatosis of pregnancy such as PUPPP, HG, and PP. Cultures and special stains can exclude microbial folliculitides.

The origin of PFP remains unknown. Some authors consider PFP to be a form of steroid acne.^{215,217} There is no evidence of any immunologic or hormonal abnormalities in this condition.¹²⁷ In one patient, hormonal levels were normal for gestational age,²¹⁸ whereas in another case, increased levels of androgens were found.²¹⁷ Association with intrahepatic cholestasis has been reported.²¹⁹ Some authors²¹¹ have suggested that PFP and PP should be included within the spectrum of "polymorphic eruption of pregnancy." Although the eruption is mostly asymptomatic and usually resolves after delivery, some authors have successfully treated patients with PFP with topical corticosteroids,¹²⁷ benzoyl peroxide,^{215,217} or UVB therapy.²²⁰

EVALUATION OF THE PATIENT WITH A PREGNANCY DERMATOSIS

A detailed history, medical history, and physical examination are imperative for correct diagnosis and treatment of a pregnancy dermatosis. The physician should inquire about the patient's gestational age, parity, possibility of twin pregnancy, dermatoses in previous pregnancies, and family history of a pregnancy dermatosis. The duration of the eruption and the associated symptoms should be clarified. The physician should also inquire about dietary habits, history of atopy, connective tissue diseases, autoimmune diseases, and recent drug intake.

The physical examination should focus on the distribution and morphology of the lesions. Involvement of striae is seen commonly in PUPPP but not in other dermatoses. Nodular lesions on the limbs are commonly seen in PP, whereas a follicular distribution is characteristic for PFP or acne. Urticarial lesions suggest PUPPP or HG, whereas vesicular lesions can be seen in HG, herpes simplex/zoster, eczema, and occasionally in PUPPP.

Laboratory work-up should be directed by the constellation of clinical findings. Most authors advocate skin biopsy of lesional skin and DIF if the diagnosis is in question or to exclude HG. Because of the clinical overlap among specific dermatoses of pregnancy and the risk of fetal distress associated with ICP, some authors¹⁸² have suggested a routine laboratory work-up in all cases of pruritic dermatoses of pregnancy, including determination of serum transaminase levels, total biliary salts, and DIF. Other authors²⁰⁴ disagree, given the unnecessary costs of this expensive work-up. We believe that serologic and histopathologic investigations are only necessary when the diagnosis is in question, despite a careful history and physical examination.

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Answers to CME examination

Identification No. 801-107

July 2001 issue of the Journal of the American Academy of Dermatology

Questions 1-32, Kroumpouzos G, Cohen LM. *J Am Acad Dermatol* 2001;45:1-19.

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|-------|-------|
| 1. e | 17. d |
| 2. e | 18. e |
| 3. b | 19. d |
| 4. a | 20. e |
| 5. e | 21. c |
| 6. d | 22. a |
| 7. a | 23. c |
| 8. b | 24. b |
| 9. e | 25. a |
| 10. a | 26. c |
| 11. d | 27. c |
| 12. b | 28. a |
| 13. c | 29. b |
| 14. b | 30. e |
| 15. d | 31. b |
| 16. a | 32. c |

Answer sheets are bound into the Journal for US, Canadian, and life members. Request additional answer sheets from American Academy of Dermatology, Member Services Department, PO Box 4014, Schaumburg, IL 60168-4014. Phone 847-330-0230; E-mail: tsmith@aad.org

CME examination

Identification No. 801-107

Instructions for Category I CME credit appear in the front advertising section. See last page of Contents for page number.

Questions 1-32, Kroumpouzou G, Cohen LM. J Am Acad Dermatol 2001;45:1-19.

Directions for questions 1-32: Give single best answer.

1. A 30-year-old woman presents with hyperpigmentation of the malar areas during her 8th month of pregnancy. You should tell her that
 - a. this is rare, occurring in fewer than 10% of pregnant women
 - b. this condition may also occur in association with oral contraceptives
 - c. this condition may develop in the centrofacial, malar, or mandibular areas
 - d. this condition does not usually recur with subsequent pregnancies
 - e. b and c
2. In patients with melasma, Wood's light examination may be helpful to determine
 - a. whether there is destruction of melanocytes
 - b. where in the skin the excessive melanin deposition is located
 - c. what form of treatment will be effective
 - d. whether ultraviolet radiation has played a role in the development of the lesions
 - e. b and c
3. The usual course of postpartum telogen effluvium is to
 - a. last less than 1 month
 - b. last 1 to 5 months
 - c. last more than 1 year
 - d. last indefinitely
 - e. none of the above; it does not occur postpartum
4. The histopathologic features of granuloma gravidarum are those of a
 - a. benign vascular proliferation
 - b. malignant vascular proliferation
 - c. infectious granuloma
 - d. sarcoidal granuloma
 - e. palisading granuloma
5. What clinical factor(s) appear(s) to contribute to the development of striae distensae?
 - a. Familial tendency
 - b. Racial predilection
 - c. Hormones
 - d. Increased abdominal girth
 - e. All of the above
6. A woman presents in her 4th month of pregnancy with spider telangiectases and palmar erythema. You should tell her that
 - a. the lesions will regress before delivery
 - b. the lesions occur most commonly on the lower abdomen
 - c. she should be examined for evidence of hepatitis
 - d. these findings are common and not of concern
 - e. she has an increased risk of thrombosis
7. Hyperemia of the gums may lead to
 - a. gingivitis
 - b. increased salivation
 - c. dry mouth
 - d. discoloration of the teeth
 - e. abnormality of the buccal and labial mucosa
8. Alleviation of Fox-Fordyce disease and hidradenitis suppurativa during pregnancy is believed to be due to
 - a. increased apocrine function
 - b. decreased apocrine function
 - c. increased eccrine function
 - d. decreased eccrine function
 - e. decreased sebaceous function
9. Montgomery's tubercles develop as a result of
 - a. enlargement of the apocrine glands
 - b. decreased size of the apocrine glands
 - c. enlargement of the eccrine glands
 - d. decreased size of the eccrine glands
 - e. enlargement of the sebaceous glands
10. The main complication occurring in pregnant patients with pseudoxanthoma elasticum is
 - a. gastrointestinal bleeding
 - b. epistaxis
 - c. congestive heart failure

- d. ventricular arrhythmia
 - e. fetal death
11. The most common form of psoriasis to develop or worsen in pregnancy is
 - a. psoriatic arthritis
 - b. pustular psoriasis
 - c. guttate psoriasis
 - d. chronic plaque psoriasis
 - e. psoriasis involving the nails
 12. Which of the following conditions is most likely to improve during pregnancy?
 - a. HIV infection
 - b. Psoriasis
 - c. Atopic dermatitis
 - d. Urticaria
 - e. Dyshidrotic eczema
 13. A 34-year-old woman develops erythematous patches, which contain grouped pustules at their margins. The lesions began in flexural and intertriginous areas and have spread to involve extensive areas of the body. What laboratory test is most likely to be abnormal?
 - a. Red blood cell count
 - b. Vitamin K level
 - c. Serum calcium level
 - d. Culture from a pustule
 - e. Direct immunofluorescence
 14. Which of the following statements is true about the prognosis of impetigo herpetiformis?
 - a. It does not recur in subsequent pregnancies.
 - b. It usually responds to low doses of systemic corticosteroids.
 - c. There is no risk of fetal morbidity or mortality.
 - d. It has been associated with pustules in the newborn.
 - e. There are no significant complications other than cutaneous involvement.
 15. Impetigo herpetiformis is believed to represent a variant of
 - a. bacterial impetigo
 - b. herpes simplex virus infection
 - c. dermatophyte infection
 - d. pustular psoriasis
 - e. connective tissue disease
 16. In genital herpesvirus infection in pregnancy, the risk of transmission to the neonate is approximately
 - a. 50% for primary infection of the mother
 - b. 100% for primary infection of the mother
 - c. 50% for recurrent infection of the mother
 - d. 100% for recurrent infection of the mother
 - e. none of the above; herpesvirus infection in pregnancy is of no consequence
 17. In pregnancy, melanocytic nevi may
 - a. lose their estrogen and progesterone receptors
 - b. regress
 - c. show histopathologic features indistinguishable from melanoma
 - d. enlarge or darken
 - e. develop halos around them
 18. A woman in her third month of pregnancy develops a pigmented lesion on the leg, which is highly suspect for melanoma. You should tell her that
 - a. she should consider terminating the pregnancy
 - b. the high estrogen state of pregnancy confers a better prognosis
 - c. the lesion need not be removed until after delivery because nevi mimic melanoma in pregnancy
 - d. melanomas that develop during pregnancy are diagnosed at an earlier stage than those in non-pregnant women
 - e. pregnancy does not appear to influence 5-year survival
 19. A woman in her third trimester develops generalized pruritus without a rash. Which is most likely to be abnormal?
 - a. Skin biopsy specimen for light microscopy
 - b. Skin biopsy specimen for direct immunofluorescence
 - c. Blood test for hepatitis C
 - d. Blood test for serum bile acids
 - e. Liver biopsy
 20. Intrahepatic cholestasis of pregnancy has been associated with
 - a. HLA-A31 and HLA-B8
 - b. positive family history in half of the cases
 - c. high prevalence of gallstones in affected women
 - d. decreased hepatic bile acid secretion
 - e. all of the above
 21. Which of the following conditions is a manifestation of intrahepatic cholestasis of pregnancy?
 - a. Uterine hemorrhage due to thrombocytopenia
 - b. Pruritic papules and plaques
 - c. Fetal distress due to placental abnormalities
 - d. Liver failure
 - e. None of the above; there are no complications
 22. A patient in her 24th week of pregnancy develops pruritic urticarial plaques and scattered bullae. The most important diagnostic test is
 - a. skin biopsy for direct immunofluorescence
 - b. bacterial culture from one of the bullae
 - c. culture for herpesvirus infection
 - d. blood test for syphilis
 - e. serum eosinophil count
 23. Which of the following statements is true in patients with herpes gestationis?
 - a. Serum eosinophilia and anti-basement membrane zone antibody correlate with the severity of disease.
 - b. The antibody belongs to the IgG2 subclass.
 - c. The antibody may remain positive even after clearance of the skin lesions.
 - d. Indirect immunofluorescence is usually positive.
 - e. IgM is the most common immunoreactant found on direct immunofluorescence.

24. What is the most common outcome for a patient with herpes gestationis?
 - a. Complete resolution at the time of delivery
 - b. Exacerbation at the time of delivery
 - c. Complete resolution immediately before delivery
 - d. Exacerbation immediately before delivery
 - e. Complete resolution only with treatment
25. What is the importance of paternal major histocompatibility complex class II antigens in the pathogenesis of herpes gestationis?
 - a. The paternal antigens within the placenta stimulate the maternal immune response.
 - b. The paternal antigens cross the placenta and cross-react with the skin.
 - c. The paternal antigens are located within the lamina lucida of the skin.
 - d. The paternal antigens are synonymous with herpes gestationis factor.
 - e. None; the paternal antigens play no role in the pathogenesis of herpes gestationis.
26. Which dermatosis of pregnancy has lesions that have a predilection for the striae?
 - a. Herpes gestationis
 - b. Prurigo of pregnancy
 - c. Pruritic urticarial papules and plaques of pregnancy
 - d. Impetigo herpetiformis
 - e. Pruritic folliculitis of pregnancy
27. Which dermatosis of pregnancy occurs most often in primigravidas during the third trimester and is associated with an increased incidence of twin pregnancy?
 - a. Herpes gestationis
 - b. Prurigo of pregnancy
 - c. Pruritic urticarial papules and plaques of pregnancy
 - d. Impetigo herpetiformis
 - e. Pruritic folliculitis of pregnancy
28. Which dermatosis of pregnancy frequently recurs after delivery with the use of oral contraceptives?
 - a. Herpes gestationis
 - b. Prurigo of pregnancy
 - c. Pruritic urticarial papules and plaques of pregnancy
 - d. Impetigo herpetiformis
 - e. Pruritic folliculitis of pregnancy
29. A 31-year-old woman with a history of atopic dermatitis presents in the second trimester with excoriated erythematous papules and nodules on the extensor surfaces of the extremities. The most likely diagnosis is
 - a. herpes gestationis
 - b. prurigo of pregnancy
 - c. pruritic urticarial papules and plaques of pregnancy
 - d. impetigo herpetiformis
 - e. pruritic folliculitis of pregnancy
30. Which inflammatory cell is notably elevated or increased in lesions of herpes gestationis?
 - a. Neutrophil
 - b. Plasma cell
 - c. Lymphocyte
 - d. Mast cell
 - e. Eosinophil
31. The most effective treatment of herpes gestationis is
 - a. topical corticosteroids
 - b. systemic corticosteroids
 - c. dapsone
 - d. methotrexate
 - e. PUVA
32. Which of the following will most reliably distinguish pruritic urticarial papules and plaques of pregnancy from herpes gestationis?
 - a. Location of the lesions on the body
 - b. Gestational age of the patient at onset of the eruption
 - c. Results of direct immunofluorescence
 - d. Eosinophil count
 - e. The presence or absence of vesicles