Recognize and Safely Manage Dermatoses of Pregnancy
Although common in pregnancy, pruritus may bring more than discomfort to the mother. An expert reviews safe management of pruritic dermatoses unique to pregnancy.

By Mary Gail Mercurio, MD
Rochester, NY

The pregnant patient poses a unique challenge to the dermatologist. Pregnancy inevitably narrows the dermatologist’s treatment armamentarium, complicating the management of even the most common dermatologic diseases. Patients also commonly experience a plethora of physiologic and pathologic changes to the skin, resulting from the hormonal, immunologic, and vascular changes associated with pregnancy. We can classify the dermatologic effects of pregnancy into four categories:

- Physiologic changes
- Pre-existing dermatologic conditions affected by pregnancy
- Skin tumors affected by pregnancy
- Dermatoses unique to pregnancy

Hyperpigmentation, melasma, striae distensae, spider telangiectases, palmar erythema, nonpitting edema, varicosities, and hyperemia are several of the more common physiologic changes resulting from pregnancy. In addition to the physiologic changes, pregnancy may exacerbate certain pre-existing dermatoses such as atopic dermatitis, while other skin disease such as psoriasis and certain autoimmune diseases may improve during pregnancy. Certain skin tumors such as melanocytic nevi, keloids, and pyogenic granulomas may also develop or grow as a result of pregnancy.

Dermatologists, of course, are quite comfortable in recognizing and managing the numerous physiologic changes and skin tumors that may develop during pregnancy, but the recognition and management of dermatoses unique to pregnancy may not be as straightforward due to a relatively low incidence of these dermatoses. Pruritic urticarial papules and plaques of pregnancy (PUPPP), also known as polymorphic eruption of pregnancy, is the most common dermatosis of pregnancy, occurring in approximately one in 150 pregnancies. Although the etiology remains uncertain, some have hypothesized that skin distension may play a role, since the incidence of PUPPP appears to be higher in association with above-average maternal-fetal weight gain and in twin and triplet pregnancies. Another study has suggested that the presence of fetal cells in the maternal dermis or epidermis may be a contributing factor in PUPPP. Interestingly, among women who develop PUPPP, there is a male/female infant ratio of 2:1.

The onset of PUPPP typically occurs during the third trimester, although there have been reports of PUPPP first presenting in the postpartum period. PUPPP typically occurs in primigravidas and does not recur in subsequent pregnancies. True to its name, PUPPP or polymorphic eruption of pregnancy can have varying presentations. Most commonly, PUPPP initially presents as urticarial papules and plaques in the striae of the abdomen, and over the next several days, the plaques and papules spread to involve the trunk and extremities. Although less common, vesicles, purpura, targetoid, eczematous, or polycyclic lesions may develop. The disease usually spares the periumbilical region, face, palms, and soles, but a recent report suggests the possibility of extensive palmoplantar involvement.

Although PUPPP usually resolves within one week of delivery without posing any risk to mother or infant, the pruritus may be severe, causing significant discomfort to the mother. In fact, in at least one case, the severity of the pruritus necessitated early delivery. However, most patients respond well to topical corticosteroids, and in severe cases, systemic steroids. When used appropriately, moderate doses of corticosteroids pose minimal risk to the infant. However, whenever using these
agents during pregnancy, it is important to assess the neonate for adrenal insufficiency. In addition to corticosteroid therapy, oatmeal baths and bland emollients are safe treatment adjuncts that may provide temporary relief.

When a patient presents with what appears to be PUPPP, if there is any suspicion of herpes gestationis, it is important to rule out the latter diagnosis by direct immunofluorescence (DIF). In contrast to herpes gestationis, DIF results with PUPPP are negative.

**Herpes Gestationis**

Compared to PUPPP, herpes gestationis (HG) or pemphigoid gestationis is significantly less common, occurring in approximately one in 50,000 pregnancies. We classify HG as an autoimmune bullous disease, and its clinical, histologic, and immunologic features most closely relate to the more common autoimmune bullous disease, bullous pemphigoid, with both conditions having similar targets in the basement membrane zone. Very rarely, HG may develop in association with hydatidiform mole and choriocarcinoma, further confirmation of this disease’s hormonal milieu. Research has revealed that HG is associated with HLA-DR3, HLA-DR4, and HLA-B8, which indicates a predisposing immunologic profile in women with HG. Furthermore, HG’s association with HLA-DR3 and HLA-DR4 may also explain the fact that HG is more common in white women than in black women.15

The main target of this autoimmune condition is the basement membrane. It is thought that the presence of antigen BP180 in the placenta stimulates immunoglobulin G (IgG) antibodies; IgG binds to the cutaneous basement membrane and results in HG’s characteristic subepidermal vesicles.16 Typically, HG develops in the second or third trimester, initially presenting as pruritic, urticarial lesions on the abdomen. At first, the lesions may mimic PUPPP, but the urticarial plaques tend to rapidly develop into a generalized bullous eruption. In contrast to PUPPP, HG involves the umbilical region and tends to spread to the extremities and trunk, sparing the face, mucous membranes, palms, and soles.2 DIF aids in differentiating HG from PUPPP and will reveal a linear band of C3 with or without IgG at the basement membrane; a routine biopsy will reveal a subepidermal blister with a mixed infiltrate, often with many eosinophils. In addition, indirect immunofluorescence may also detect a complementing fixing antibody—the HG factor—in HG patients’ serum.

Although patients with mild disease may respond to topical steroid therapy, patients with severe disease will require 0.5–1mg/kg of prednisone, which should then be tapered based on the patient’s response. Studies also suggest that cyclosporine, intravenous immunoglobulin, and tetracyclines postpartum show promise as HG treatments.17 Inform patients, however, that the disease tends to flare at delivery or immediately postpartum in as many as 75 percent of HG cases, and be prepared to immediately increase the steroid dosage at that time.18 Interestingly, as many as 25 percent of HG cases do not present until after delivery.19 Most women experience resolution of the disease without scarring within several weeks following delivery, but recurrence with subsequent pregnancies is common. Patients also must be aware that a subset of women experience long-term recurrences of HG, often coinciding with their menstrual periods or with the use of oral contraceptives. In addition, HG increases a woman’s risk for developing Graves’ disease, which necessitates long-term follow-up with thyroid function studies.20

The risk HG poses to the fetus remains controversial, but most data indicate that HG does not increase fetal mortality. However, HG does increase the potential for premature birth or small for gestational age newborns.21 Additionally, in up to 10 percent of HG cases, transplacental passage of HG antibodies occurs, and the newborn may develop neonatal HG, which tends to be transient and self-limited.21

**Pruritic Folliculitis of Pregnancy**

Pruritic folliculitis of pregnancy (PFP) represents a somewhat uncommon pregnancy dermatosis that resembles the monomorphic acne that may result in association with oral corticosteroid therapy.22 However, some believe that PFP may be more common than thought and is often misdiagnosed as microbial folliculitis, which highlights the importance of cultures and stains to rule out an infectious etiology.2 It is also worthwhile to note that pityrosporum folliculitis has been misdiagnosed as PFP, which further suggests the importance of cultures to confirm the diagnosis.23 A routine biopsy generally shows folliculitis.

Although the pathogenesis of PFP remains unknown, we believe the pathogenesis is similar to that of steroid acne, but in the case of PFP, we believe the hormonal milieu is responsible for the acneiform lesions. Studies indicate serum androgen levels remain normal in women with PFP, but it is interesting to note that among women with PFP, there is a male to female infant ratio of 2:1.20,24

**Intrahepatic cholestasis of pregnancy appears to increase the risk for fetal distress, preterm delivery, and stillbirth, warranting increased fetal surveillance.**
PFP typically develops in the second or third trimester and presents as generalized red, follicularly based papules widely disseminated on the chest, face, and back. Although PFP tends to be asymptomatic, some patients do report pruritus. The pregnant state of the woman limits our treatment options for PFP, but acceptable and often beneficial treatment options include topical erythromycin, benzoyl peroxide, topical steroids, and UVB therapy. PFP is a self-limited disease that does not pose a risk to mother or infant and tends to resolve two to three weeks after delivery.

**Prurigo of Pregnancy**

Prurigo of pregnancy (PP) represents the least characterized pregnancy dermatosis. It is a diagnosis of exclusion, and it is particularly important to perform liver function studies, including serum bile acids, to rule out intrahepatic cholestasis of pregnancy (discussed below). Other conditions to rule out include scabies, arthropod bites, drug eruptions, and allergic reactions. The histopathology of PP is nonspecific and typically demonstrates inflammation with superficial excoriation; DIF is negative.

PP occurs in an estimated one in 300 pregnancies, and although reports suggest PP can occur in all trimesters, it typically presents in the second half of pregnancy. Patients commonly present with discrete, excoriated papules on the extremities and occasionally on the abdomen. Interestingly, PP appears to be more common in women with a history of atopic dermatitis, which supports the theory that PP is a pregnancy-related variant of AD. The fact that women with PP often have increased serum levels of immunoglobulin E (IgE) further supports this theory.

Treatment is symptomatic, and topical emollients and topical midpotency corticosteroids often provide sufficient relief of PP symptoms. In some cases, however, systemic antihistamines may be necessary. Improvement of PP ensues soon after delivery and does not appear to pose any risk to mother or fetus.

**Intrahepatic Cholestasis of Pregnancy**

Of all the dermatoses discussed, intrahepatic cholestasis of pregnancy (ICP) poses the greatest risk to the fetus and therefore requires prompt recognition and management. ICP remains relatively uncommon in the US, occurring in approximately one in 10,000 pregnancies. The incidence of ICP appears to be higher among women with a family history of ICP, which suggests a genetic predisposition, in twin pregnancies, and in certain regions outside the US, such as Chile and Scandinavia. Although we do not fully understand the pathogenesis of ICP, we believe that high estrogens levels interfere with the normal hepatic excretion of bile acids and subsequently interfere with bile salt transport.

While pruritus is common in pregnancy and often thought to be a physiologic effect of pregnancy, ICP represents the severe end of the pruritus spectrum, and it is critical to assess any pregnant patient who reports severe pruritus for ICP. Typically developing in the third trimester, ICP presents as a
Dermatoses of Pregnancy

generalized pruritus that tends to be most severe on the palms and soles and tends to intensify at night, although the pruritus is constant. Unlike the other dermatoses discussed, no lesions or rash are present in ICP patients; exacerbations are the only cutaneous finding. In a small number of patients, jaundice may also be present. Studies indicate the severity of pruritus in ICP patients correlates with elevated serum levels of bile salts, while another study suggests the early onset of the pruritus may also indicate a higher risk for spontaneous preterm delivery.29,30

Liver function studies are key to confirming the diagnosis, and neither routine biopsy nor immunofluorescence aid diagnosis. The predominant finding in ICP is elevated serum bile acids, but other laboratory findings include increased bilirubin and elevated serum alkaline phosphatase and transaminase levels. A recent study has shown that a glutathione S-transferase (GSTA) level may be a more specific and sensitive serum indication of hepatic dysfunction in women with ICP.31 It is important to rule out other causes of liver function abnormalities, particularly hepatitis C virus, since recent studies suggest an association between ICP and hepatitis C virus.32,33

First-line treatment for ICP is bland antipruritic agents and UVB light therapy; ion-exchange resins, such as cholestyramine, may be a more specific and sensitive serum indication of hepatic function abnormalities. Bile acid levels were found to be constant in a small number of ICP patients as well as with the use of oral contraceptives. In addition, ICP increases a woman’s risk of developing gallbladder disease.

Although controversial, fetal risk remains an area of concern, for ICP appears to increase the risk for fetal distress, preterm delivery, and stillbirth, warranting increased fetal surveillance.34,35 The risk for fetal death appears to increase after 36 weeks’ gestation. A recent study has shown that bile acid levels greater than or equal to 40 micro/L correlate with an increased incidence of fetal complication rates.36

Expect the Unique

Without doubt, the pregnant patient poses a unique challenge to the dermatologist. Although the pregnancy dermatoses we discussed are not widespread in pregnancy, prompt recognition and management are important to reduce any maternal discomfort and minimize any potential risk to the fetus. Topical and systemic corticosteroids—all used in moderation—represent effective, low-risk treatment options for PUPPP, HG, PP, and PFR, while UVB therapy and bland antipruritics represent acceptable treatment options for ICP.