Pruritus affects up to 20% of pregnant women.\textsuperscript{1,2} Pruritus can be sufficiently severe to affect sleep and quality of life, and might lead to or worsen depression.\textsuperscript{3} Although it is commonly caused by dry skin, it can also indicate an underlying condition unique to pregnancy. The dermatoses of pregnancy include pruritic urticarial papules and plaques of pregnancy (PUPPP), intrahepatic cholestasis of pregnancy (ICP), pemphigoid gestationis (PG), and atopic eruption of pregnancy.\textsuperscript{4}

It is important for physicians to be familiar with these conditions in order to differentiate among those that can be managed symptomatically and those that require further investigation. Some of these conditions should be evaluated and managed by a multidisciplinary team that includes an obstetrician or a maternal-fetal medicine specialist, a family physician, a dermatologist, and sometimes a gastroenterologist (Figure 1).\textsuperscript{5}

**Dermatoses unique to pregnancy**

**Pruritic urticarial papules and plaques of pregnancy.** Pruritic urticarial papules and plaques of pregnancy is a benign, self-limited pruritic inflammatory disorder. It might also be referred to as *polymorphic eruption of pregnancy*, *toxemia of pregnancy*, or *prurigo of pregnancy*. The incidence of PUPPP is about 1 in 160 pregnancies (0.6%), with most cases occurring in first pregnancies in the third trimester or immediately postpartum. It also occurs more frequently in women pregnant with multiples and seldom recurs in subsequent pregnancies.\textsuperscript{4}

**Clinical presentation:** The lesions of PUPPP are typically urticarial papules that coalesce into plaques and spread from the abdomen to the buttocks and thighs. About 50% of the time the lesions develop as microvesicles overlying the striae cutis distensae (stretch marks).\textsuperscript{5} This skin eruption starts on the abdomen, usually within
the striae, and classically spares the umbilical area, palms, soles, and face. The sparing of the umbilical area helps to differentiate PUPPP from PG early on. The striae first become itchy, then erythematous, and finally urti-
carial. Patients are very uncomfortable and the pruritus often interferes with sleep. The lesions are rarely exco-
riated.

Diagnosing PUPPP: Initially, PUPPP might be con-
fused with PG; however, sparing of the umbilicus pro-
vides the best clue to diagnosis, as PG lesions usually
cluster around the umbilicus. Other disorders that might be confused with PUPPP include atopic dermatitis and contact or irritant dermatitis.

To make a diagnosis, a history and physical examina-
tion are necessary, as there are no systemic symptoms. Results of laboratory studies, including histology, serol-
ysis, and immunofluorescence, are not specific.

Treatment: Pruritic urticarial papules and plaques of pregnancy is a self-limiting disorder without serious
consequences to the mother and fetus. The mean dura-
tion of the eruption is 6 weeks and it remits within days
of delivery. Recurrence is rare as it usually occurs in first
pregnancies. Symptomatic treatment with mild to potent
topical corticosteroids and antihistamines are the main-
stay for treating PUPPP. Relief within 24 to 72 hours is
normally seen. Oil baths and emollients are also helpful
for relief of pruritus. In cases in which the diagnosis of
PUPPP is not clear, referral to a dermatologist should be
considered.

Intrahepatic cholestasis of pregnancy. Although ICP
is a pruritic condition in pregnancy that involves only
secondary skin changes, it is included in the classifica-
tion of dermatoses of pregnancy because identifying this
disease early is important to minimize potential adverse
fetal outcomes. Intrahepatic cholestasis of pregnancy is also called idiopathic jaundice of pregnancy, obstetric
cholestasis, and pruritus gravidarum. It is caused by the
disruption of hepatic bile flow during pregnancy. The
prevalence of ICP in North America is 0.5% to 1%, but it is
particularly common in Scandinavia and South America,
with the highest rates in Chile (15% to 28%). It runs in
families and tends to recur in subsequent pregnancies.

Clinical presentation: Intrahepatic cholestasis of
pregnancy presents in the second or third trimester with
the sudden onset of severe pruritus that starts on the
palms and soles and quickly becomes more generalized.
The pruritus persists throughout pregnancy and is worst
at night. The secondary lesions involve linear excoria-
tions and excoriated papules and develop secondary to
scratching. Jaundice occurs in about 10% of patients and
is due to concomitant extrahepatic cholestasis, often
accompanied by dark urine and clay-coloured stools.
These patients are at risk of developing steatorrhea with
malabsorption of fat-soluble vitamins, including vita-
min K, which might lead to bleeding complications and
cholelithiasis.

Pathophysiology: Intrahepatic cholestasis of preg-
nancy is a hormonally triggered cholestasis. It presents
in genetically predisposed women in late pregnancy
who have a defect in the excretion of bile acids resulting
in elevated bile acid levels in the serum. This leads to
severe pruritus in the mother and, as toxic bile acids can
pass into fetal circulation, might have deleterious effects
on the fetus owing to acute placental anoxia and card-
diac depression. A family history of the disorder is pres-
ent in half of cases, and cases with a familial component
tend to be more severe.

Diagnosis: Diagnosis is usually made based on the
characteristic symptom of pruritus starting from the
palms and soles that is not accompanied by a rash. The
diagnosis can be confirmed by demonstrating a rise in
total serum bile acid levels. In healthy pregnancies, total
serum bile acid levels in the third trimester of up to
11.0 µmol/L are accepted as normal. In women with ICP,
the presence of total serum bile acid levels of more than
40.0 µmol/L is associated with a higher risk of adverse
fetal outcomes. There might also be a mild increase
in liver transaminase levels including aspartate amino-
transferase and alanine aminotransferase levels; this
increase might only appear weeks after the onset of pru-
ritis. Steatorrhea with subsequent vitamin K deficiency
might also be noted. Close surveillance of prothrombin
time might be needed. Ultrasound examination of the
liver and serologic tests might be necessary to exclude
other diagnoses such as cholelithiasis and viral hepatitis.

Treatment: The aim of treatment is to reduce serum
bile acid levels. Ursodeoxycholic acid is the treatment
of choice, as it improves maternal pruritus, decreases
liver transaminase and bile acids levels, and might also
reduce the rate of adverse fetal outcomes, although this
latter effect is debatable. A dose of 15 mg/kg daily or
1 g daily is administered until delivery.

Before ursodeoxycholic acid treatment, cholestyr-
amine was used to treat ICP. However, this drug can
cause vitamin K deficiency, which might already occur
with this disorder. Antihistamines might also improve
maternal symptoms.

Elective delivery around weeks 36 to 38 has been rec-
ommended, as stillbirths tend to cluster around weeks
37 to 39. Some authors suggest that labour induction
at 37 weeks is indicated only in cases of severe ICP
(defined as total serum bile acid levels of more than
40 µmol/L).

Prognosis: The prognosis for the mother is gener-
ally good. Pruritus regresses spontaneously within days
to weeks after delivery but can recur with subsequent
pregnancies or while using hormonal contraception.
Figure 1. Diagnostic approach to pruritus in pregnancy

Pruritus in pregnancy

Without rash

ICP

Only secondary skin lesions due to scratching (excoriations or prurigo)

Related to pregnancy

Unrelated to pregnancy

Coinciding diseases

Early onset (before third trimester)
Trunk and limbs involved

Late onset (third trimester or postpartum)
Predominant abdominal involvement

Without rash

ICP

Only secondary skin lesions due to scratching (excoriations or prurigo)

Related to pregnancy

Unrelated to pregnancy

Coinciding diseases

Early onset (before third trimester)
Trunk and limbs involved

Late onset (third trimester or postpartum)
Predominant abdominal involvement

IMF: nonspecific
H and E: nonspecific
Laboratory: elevated total serum bile acid levels
Prematurity, fetal distress, stillbirths


*PUPPP is also referred to as PEP.
Adapted with permission from Ambros-Rudolph et al.
If jaundice and vitamin K deficiency occur, there is an increased risk of intrapartum and postpartum hemorrhage.

This condition has been associated with adverse fetal outcomes including preterm labour, meconium in the amniotic fluid, fetal distress, and fetal demise. Importantly, some have reported that fetal demise in ICP is the result of a sudden event and might occur despite a previously normal fetal heart rate tracing. Indeed, there is no evidence that close fetal monitoring in cases of ICP is effective in preventing fetal death. As a result, it has been recommended that labour be induced by 36 to 38 weeks. Prompt diagnosis, specific therapy, and close obstetric monitoring are essential. Consultation with a gastroenterologist in equivocal or severe cases is recommended.

**Pemphigoid gestationis.** Pemphigoid gestationis is a self-limited autoimmune bullous disorder that presents after the 20th week of gestation and might only appear in the postpartum period.

Historically, PG was referred to as herpes gestationis, a term that was coined in 1872 by Milton because of the characteristic “creeping” blister formation. However, this term might be misleading as this condition has no association with the herpes virus, and it is now referred to as pemphigoid gestationis. It is a relatively rare condition, with an estimated incidence of 1 in 10,000 pregnancies.

**Clinical presentation:** Pemphigoid gestationis presents with intense pruritus that can precede the skin lesions. The characteristic rash begins with pruritic, urticarial, erythematous papules and plaques around the umbilicus and extremities. As the disease progresses, the lesions develop into tense blisters. The face, palms, and soles are spared and there is mucous membrane involvement about 20% of the time. Commonly, PG flares around the time of delivery but regresses spontaneously after delivery.

The pathophysiology is similar to that of bullous pemphigoid and involves immunoglobulin G directed at a 180-kDa hemidesmosome transmembrane glycoprotein. **Diagnosis:** A skin biopsy is necessary to make the diagnosis. Direct immunofluorescence of perilesional skin is the criterion standard in the diagnosis of PG. It shows linear complement C3 deposition along the dermoepidermal junction, and biopsy results are characteristically negative for this in the other dermatoses of pregnancy.

The main differential diagnosis is PUPPP, especially early in the disease before the formation of the tense blisters. Thus, skin biopsy is indicated in suspected cases of PUPPP with an unusual and severe presentation that does not respond to routine therapy.

**Prognosis:** The natural course is characterized by exacerbations and remissions during pregnancy, with frequent improvement in late pregnancy followed by a flare-up at the time of delivery. Lesions usually resolve within weeks to months. It tends to recur in subsequent pregnancies at an earlier gestational age and with increasing severity. It might also recur with menstruation or hormonal contraception. There is an increased risk of other autoimmune diseases, in particular Graves disease.

Pregnancies affected by PG are considered high risk because there is an association with an increase rate of adverse fetal outcomes, such as preterm births and low birth weight. Because of passive transfer of the maternal autoantibodies to the fetus, about 10% of newborns might develop mild skin lesions that resolve spontaneously within days to weeks.

**Treatment:** Treatment aims to control pruritus and to prevent blister formation. In cases of mild pre-blistering state, topical corticosteroids with oral antihistamines might be sufficient. All other cases require systemic steroids—typically 20 to 60 mg of prednisone a day. The prednisone dose should be increased in time to prevent the flare that commonly occurs at delivery.

**Atopic eruption of pregnancy.** Atopic eruption of pregnancy is an umbrella term recently coined by Ambros-Rudolph to include prurigo of pregnancy, pruritic folliculitis of pregnancy, and eczema in pregnancy. Although in the literature they are described as separate entities, the lack of clinical distinction between these disorders led to the recently coined term.

These are benign pruritic conditions of pregnancy that include eczematous or papular lesions in patients with a history of atopy.

**Pathogenesis:** These conditions are thought to be triggered by pregnancy-specific immunologic changes—a reduced cellular immunity and reduced production of Th1 cytokines compared with the dominant humoral immunity and increased secretion of Th2 cytokines.

**Clinical presentation:** Most patients (80%) experience atopic skin changes for the first time or after a long remission (since childhood). Most women present with widespread eczematous changes affecting typical atopic sites such as the face, neck, chest, and the flexural surfaces of the extremities, while one-third have papular lesions. These include small erythematous papules disseminated on the trunk and limbs, and typical prurigo nodules located on the shins and arms.

**Diagnosis:** The clinical history and physical examination are key to making the diagnosis. Histopathology is nonspecific and varies with the clinical type and stage of the disease. Direct and indirect immunofluorescence results are negative. Laboratory tests can reveal elevated...
pruritus in pregnancy requires taking a thorough history and complete physical examination. Laboratory studies such as liver transaminase levels, serum bile acid levels, and in selected cases skin biopsy might be indicated in order to determine the most likely diagnosis. The dermatoses of pregnancy should be considered in the differential diagnosis of pruritus and managed accordingly. An accurate diagnosis must be made owing to the fact that some of these conditions are associated with an increased risk of adverse fetal outcome. The treatments described for the above conditions are considered safe in pregnancy.

**Competing interests**
None declared

**References**