

## DERMATOZE DE SARCINĂ

## DERMATOSES OF PREGNANCY

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### Rezumat

Sarcina poate fi insotita de modificari fiziologice sau patologice la nivelul pielii. Unele dintre ele sunt influentate de profilul hormonal diferit la femeia gravida. Modificarile fiziologice pot fi pigmentare, vasculare, modificari ce tin de fanere sau modificari structurale ale pielii. Dermatozele care pot afecta femeia gravida se impart in doua categorii. Prima categorie este cea a bolilor care apar pentru prima oara in sarcina si sunt specifice sarcinii. A doua categorie este cea a bolilor preexistente sarcinii, care isi modifica evolutia in timpul acesteia.

**Cuvinte cheie:** sarcina, melasma, herpes gestationis, impetigo herpetiformis, prurigo de sarcina.

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### Summary

The pregnancy can be adjoined by physiological or pathological changes in the skin. Some of them are determined by particular hormonal profile of pregnancy. Physiologic changes can be pigmentary, vascular, hair and nails changes and structural changes of the skin. The dermatoses that can appear in the pregnant women fall in two categories. The first category is that of diseases that appear for the first time in pregnancy and are specific to pregnancy. The second category is that of preexisting conditions, that get better or worse during pregnancy.

**Key-words:** pregnancy, melasma, herpes gestationis, impetigo herpetiformis, prurigo of pregnancy

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### Introduction

Pregnancy is one of the most beautiful moments in a woman's life. In this period occurs many hormonal, immunologic and metabolic reactions. Because of this variations, pregnant women experiences different changes and some of this can induce cutaneous disorders known as the dermatoses of pregnancy. Their exact pathogenesis is unknown. This skin changes can be divided in: physiologic changes, dermatoses specific to pregnancy and diseases exacerbated or improved during pregnancy.(1)

### A. Physiologic changes (2)

Are represented by:

#### 1. Pigmentary lesions:

- melasma;
- pigmentations of nipples, areolae and linea alba;
- darkening of nevi and ephelides.

#### 2. Vascular lesions:

- palmar erythema;
- spider angioma;
- tumors (pyogenic granulomas, glomus tumors);

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- varicose veins;
  - cutis marmorata.
3. Hair and nails lesions:
- hirsutisme;
  - telogen effluvium;
  - nails changes.
4. Structural changes of the skin:
- striae gravidarum;
  - molluscum fibrosum gravidarum.

**Melasma**, named also the mask of pregnancy, is a specific hypermelanosis more pronounced in darker-skinned women which usually appears in the second trimester of pregnancy. It is localized more often over the forehead, cheeks and upper lip. There is a clear hormonal influence as melasma can be produced or exacerbated by oral contraceptives. The exposure to ultraviolet radiation worsens the hyperpigmentation. It usually regresses by one year after delivery but in persistent forms it needs treatment (topical: hydroxycloquine, tretinoin, non-ablative laser therapy)(3).

**Palmar erythema** develops in the first trimester of pregnancy. It is caused by hyperestrogenemia which characterizes the pregnancy. Clinically it's characterized by erythema of the thenar and hypothenar eminences. It usually disappears after delivery (3).

**Spider nevi** appears more common in white women at the end of first trimester of pregnancy. It is localized on the draining areas of the superior vena cava, meaning especially on the face, and upper limbs. They usually disappear after delivery but when they persist a treatment by electrocauterisation or laser ablation can be needed (3).

**Pigmentations of the nipples**, areolae and lineae albae appear early during pregnancy and they are sometimes adjoined by slight hyperpigmentation of other areas such as axillae and inguinal region. Linea alba becomes linea nigra and also the secondary areolae appears. After delivery, the hyperpigmentation tends to disappear, but usually the skin does not return to the original colour. (4)

**Darkening of nevi and ephelides** can become more intense in pregnancy, may enlarge or can appear new ones. It's recommended a strict surveillance concerning this nevus because we don't know for sure in what measure the

estrogen hormones are implicated in progress towards melanoma (2).

**Pyogenic granuloma** is a tumor consisting of vascular tissue most frequent in trauma areas. It can affect the pregnant women. The clinical appearance is a red-purple sessile or pedunculated tumor located on the face, mucous membranes or digits, soft on palpation, covered with crusts. The treatment consists in surgical excision deep enough (to prevent the recurrence) (5).

**Varicose veins** affect up to 40% of pregnant women. Venous dilation can appear on the calf, in the rectum or vagina. They are caused by hormonal changes and increased abdominal pressure. When venous dilations occur, legs must be elevated. Usually, the varicosities remit after delivery, but in some cases, sclerotherapy is needed (6).

**Cutis marmorata** is a transitory blushing as a response to cold because of the increased estrogen levels which leads to vasomotor instability. It is localized on the lower extremities and usually regresses after delivery (7).

**Telogen effluvium** can appear as a consequence of pregnancy. A great number of hairs enter in telogen phase, so the hair shedding increases. The excessive hair shedding usually stops in a few months and hair density comes back to normal. (8)

**Hirsutisme** is observed early in pregnancy, more pronounced on the face and arms. It usually disappears at six months after delivery (2).

**Nails** become more fragile and soften, with an increased growth, distal onycholysis and subungual keratosis (2).

**Striae gravidarum** it's a very frequent problem in pregnancy and is localized on the abdomen, breast, arms, buttocks and thighs. It seems to be related more with genetic factors and less with body mass index (9).

**Molluscum fibrosum** is a soft tissue fibroma, skin-colored, or hyperpigmented, can reach a few centimeters in size and appears frequently during pregnancy. The treatment consists in electrocautery or cryotherapy (10).

## B. Dermatoses specific to pregnancy

These are represented by four classes of inflammatory dermatoses: pemphigoid (herpes) gestationis, polymorphic eruption of pregnancy, prurigo of pregnancy and pruritic folliculitis of pregnancy (9).

**Herpes gestationis** appears especially in the late period of pregnancy. The pathophysiology of this bullous disease consists in appearance of autoantibodies (Ig G1) against NC 16 segment of BP 180, which are met in a genetic predisposed women. The placenta may play a major role. There are important associations with other autoimmune diseases such as: Grave's disease, Hashimoto thyroiditis, pernicious anemia. The patients present severe pruritus followed by urticaria-like and bullous lesions eruption located on the abdomen, palms and soles. The diagnosis is made using direct immunofluorescence. The autoantibodies can be detected in serum with indirect immunofluorescence. This disease can predispose to premature delivery and small for gestational age child. The treatment is used in order to ameliorate pruritus and prevent new blister formation. It includes glucocorticoids in small doses (prednisone 20-60 mg/orally) (11).

**Polymorphic eruption of pregnancy** (figure 1) is known also as pruritic urticarial papules and plaques of pregnancy (PUPPP). It appears in the third trimester and affects mainly the primigravidae. It is considered to appear as a consequence of damage to connective tissue caused by abdominal distension or by fetal antigens. The tegumentary eruption is represented by erythematous papules which evolves into urticarial plaques. It is located on the abdomen, buttocks, thighs and rarely involves the face, breast or palms. In general, this dermatose does not require any treatment. In some cases, a high-potency topical steroid may relieve the pruritus. Only the severe cases need a short course of oral prednisone (12).

**Prurigo of pregnancy** (prurigo Besnier) is a disorder which appears in the second trimester of pregnancy. It is characterized by pruritic, erythematous papules that are seen in symmetric distribution, especially on the trunk and extensor surfaces of the extremities. It is suspected to be associated with atopy, taking into account that

many women have increased titers of immunoglobulin E. This prurigo of pregnancy is often confused with scabies, but does not respond to antiscabetic agents. In order to treat this condition, topical steroids are administered in association with antihistamines (12).

A particular form of prurigo is represented by **cholestasis of pregnancy**. Cholestasis of pregnancy is a disease characterized by cholestasis that appears during second or third trimester of pregnancy. The etiology is unknown, but hormonal changes that appear during pregnancy in one organism which is predisposed can lead to cholestasis. The clinical presentation is with pruritus that begins usually in second or third trimester. The pruritus can be accompanied by jaundice or others systemic manifestations. In the first place the pruritus is localized on palms and soles. The symptoms disappears after birth, but they can appear during contraceptives intake. In severe cases can develop hemorrhage from



Figure 1. Pruritic urticarial papules of pregnancy appeared 5 days before delivery

Figura 1. Papule urticariene pruriginoase ale sarcinii au apărut 5 zile înainte de livrare

vitamin K deficiency. Fetal complications are prematurity and fetal death. The laboratory tests show elevation of serum bile acids, bilirubin and AST. The symptomatic treatment consist of cholestiramine and the pathogenic treatment (which ameliorate the symptoms to) is the ursodeoxicolic acid (13).

**Pruritic folliculitis of pregnancy** is characterized by an follicular, papular eruption, which on skin biopsy shows evidence of follicular involvement. Pruritic folliculitis of pregnancy typically develops in the second half of pregnancy. It resolves spontaneously within 2 to 3 weeks after delivery. Pruritic folliculitis of pregnancy is typically treated like mild acne. Benzoyl peroxide (10%) and hydrocortisone acetate 1% have been used with some success. Antibiotics are not needed (12).

### C. Diseases that modify their evolution during pregnancy

There are a few dermatological conditions that can improve during pregnancy. However, this improvement is not present in every case, there are situations when the disease can even get worse or remain unchanged. One example of disease that can improve during pregnancy is psoriasis and one example of disease that usually get worse is lupus erythematosus. Diseases that usually get worse are also the viral and fungal infections<sup>14</sup>.

**Psoriasis** is one of the dermatological diseases that can get better during pregnancy<sup>14</sup>. Psoriasis is a disease characterized by papulo-scuamous lesions distributed in areas of extension (knees, elbows). The pathophysiology of this disease is very complex and poorly understood, but it is known that reflects an interplay between genetic predisposition, immunologic factors, nervous system function and environmental factors. The immune system seems to play the major role in pathogeny; it was found that both innate and adaptive immune system interact and develop a complicated chain of events, which leads to psoriatic lesions. The dendritic cells, which probably lose their tolerance inductive capacity, activates a T-cell response, characterized by secretion of cytokines

(the most important are IL23, IL22, IL17, TNF- $\alpha$ , IFN- $\gamma$ ) and proinflammatory molecules such as eicosanoids. Hormonal changes may play an important role in the pathological process. In a genetically predisposed person, at one time of her life, may act one aggressive factor like stress, medication or infection, which determine the lesions to occur. The lesions remit but usually they appear again. This disease can present in the following clinical forms:

- Psoriasis vulgaris (red plaques, presenting scales, on the extensor surfaces)
- Generalized pustular psoriasis can develop from other forms and manifests as pustules on the trunk and extremities, which develop on erythematous skin
- Annular pustular psoriasis appears as pustules that develop in multiple annular erythematous lesions. It resembles



Figure 2. *Impetigo herpetiformis* (week 28 of pregnancy)  
Figura 2. *Impetigo herpetiforma* (săptămâna 28 de sarcină)

impetigo herpetiformis, but it persists after delivery.

- Impetigo herpetiformis (figure 2) appears in the third trimester of pregnancy and then disappears after delivery. There are pustules distributed in an annular pattern, similar to annular pustular psoriasis. Hypocalcemia can occur.

- Gutate psoriasis ( papules on the trunk)15

Psoriasis can manifest as arthritis and the clues for the diagnosis are enthesitis, onychodystrophy, distal interphalangeal involvement, sacroiliitis or spondyloarthritis, isolated involvement of the joints and enthesitis (16).

There are some improvements in 30-40 % of cases, the rest is distributed between unimproved cases and worsened cases. During pregnancy the systemic treatment is best to be avoided, the best choice is topical treatment, using topical corticosteroids, topical calcipotriene, topical anthralin and UVB2.

**Erythema nodosum** is an inflammatory disease that affects the subcutaneous tissue. It is associated with many other conditions such as infections, systemic illnesses and drug administration. It is useful to emphasize that in category of drugs that produce erythema nodosum are the contraceptives. For this reason and because erythema nodosum can appear during menses it is believed that hormonal changes during pregnancy can be a trigger for this illness. Clinical presentation is with erythematous nodules on the anterior surface of shins. The lesions are tender and usually last weeks. Systemic symptoms and signs can appear. Erythema nodosum appears in the first or second trimester of pregnancy. The treatment is represented by NSAIDs, but not in the third trimester (14).

**Human papilloma viruses infections.** Human papilloma viruses can infect the genital integumentum. The disease can have both apparent and subclinical evolution because of the capacity of the virus to persist in the basal layer of the skin. Some of the viral subtypes (16 and 18) are associated with the risk of malignant genital tumors. Genital warts present as smooth, pale, pink, papules or tumors in the genital or anal area. They have irregular surface and can coalesce to form bigger masses. The infection of

the newborn can occur independently of the route of delivery. In pregnancy podophyllotoxin is contraindicated, the electrocautery is the procedure of choice (17).

**Lupus erythematosus** is one of the most common autoimmune disorders that affect young women in the reproductive years. For most women with lupus a successful pregnancy is possible. During pregnancy or several weeks to months after delivery, women may experience lupus for the first time or may experience a worsening of its symptoms. They have 10% chances to end in miscarriage and if it occurs in the first trimester of pregnancy the cause can be due to active lupus and if it occurs later the cause is antiphospholipid antibody syndrome, in spite of treatment with heparin and aspirin. All women with lupus, even if they do not have a previous history of miscarriage, should be screened for antiphospholipid antibodies, both the lupus anticoagulant and anticardiolipin antibody. Another risk is the preterm birth due to pre-eclampsia and premature rupture of membranes, active lupus, high dose prednisone, and renal disease. The most important maternal risk, that of a lupus flare, is an excess of renal and hematologic flares, and fewer arthritis flares. About 3% of babies born to mothers with lupus will have neonatal lupus. This lupus consists of a temporary rash and abnormal blood counts. Neonatal lupus usually disappears by the time the infant is 3-6 months old and does not recur. About one-half of babies with neonatal lupus are born with a heart condition. This condition is permanent, but it can be treated with a pacemaker. A pregnant woman with lupus can be treated with prednisone, azathioprine, heparin, hydroxychloroquine (Plaquenil) (18, 19).

**Scleroderma** is an autoimmune affection including systemic and localized forms. Because scleroderma is a multisystem disease and complications do occur women with diffuse scleroderma are at greater risk for developing serious cardiopulmonary and renal problems early in the disease. However they should be encouraged to delay pregnancy until the disease stabilizes. All patients who become pregnant during this high-risk time should be monitored extremely carefully. The main problem which

develops is renal failure with signs of preeclampsia in the third trimester that must be treated aggressively with ACE inhibitors. Another risks are maternal death, or miscarriage, or high risk of premature and small infants (small for date).

**Dermatomyositis** is one of the most common forms of the idiopathic inflammatory myopathy, with an incidence of 1-9 cases per million per year. The disease is rare during pregnancy, and there are no available epidemiological data on pregnancy and dermatomyositis. Anyway, there are described two types of pregnancy-related DM. In the first type, the disease is provoked during pregnancy and tends to improve after delivery. In the second type, the onset is in the postpartum period. The symptoms and signs are usually non-specific: slight fatigue and periungual erythema. The risks in pregnancy are premature delivery and fetal mortality. The recommended treatment is corticotherapy, but it can have adverse effects. Therefore, the pregnant patients can be treated with intravenous immune globulin, with good fetal outcome. (20)

**Pemfigus vulgaris** is a bullous disease characterized by intraepidermal formation of blisters on the skin or mucous membranes. The disease is characterized by the presence of antibodies against desmoglein 1 and 3 and clinical manifestations are mucosal erosions, flaccid blisters and erosions in the skin. The treatment consists of corticotherapy, but treatment with intravenous immunoglobulins seems to be a new, safer approach (21, 22).

**Acne** during pregnancy can be mild, moderate or severe. It can be induced, pronounced or attenuated by the pregnancy. The increased levels of androgens are responsible for acne breakouts, which can appear any time in these nine months. Usually, the acne associated with pregnancy resolves on its own a few months later or after delivering. Treatments considered safe and recommended include: azelaic acid, benzoyl peroxide, salicylic acid (in low concentrations only) and erythromycin. A series of treatments can induce fetus malformations and need to be avoided: isotretinoin, topical retinoids, tetracycline and its derivatives (doxycycline and minocycline) (23).

**Pitiriazis rosea** is a papulosquamous disorder of a viral etiology. There are multiple erythematous-squamous patches that involves the trunk (parallel with skin lines). Usually this appearance is preceded by a large erythematous-squamous patch. The evolution is usually self limited. The therapy is represented by mid-potency topical corticosteroids. The pregnancy dose not affect the evolution of this disease (24).

In pregnancy **the medication** must be very carefully chosen. The number of the drugs prescribed to a pregnant women must be reduced. The topical agents are preferred, as they have a diminished absorption. If systemic therapy is used, oral administration is preferred. The drugs that can not be used during pregnancy are retinoids, estrogens, danazol, flutamide, methotrexate, thalidomide. The drugs that can damage and must be avoided as far as possible are azathioprine, colchicine, cyclophosphamide, busulfan, penicillamine and NSAIDs (22). The lists above presented are not exhaustive.

If during pregnancy appears a infection that must be treated with antibiotics, then penicillins are the first choice. From macrolides, the drugs of choice are spiramycin and erythromycin. Antibiotics that must be avoided are: sulfonamides in the third trimester, metronidazole (especially in systemic administration), tetracyclines (can produce dental and bone malformations), aminoglycosides, fluoroquinolones and chloramphenicol. In topical administration neomycin, bacitracin and fusidic acid can be used. Antifungal therapy is best to be topical and the substances used are imidazoles and nystatin. Antiviral therapy using acyclovir is controversial, but when needed is applied. Podophillin is best to be avoided. Antiparasite medication consist of diethanolamine, permethrin and benzoin benzoate. Corticosteroid therapy can be used during pregnancy, but if are used big doses the best is to have a pediatrician consult before delivery. The antihistamines can be used in pregnancy in topical administration. The recommendation in systemic administration is chlorpheniramine (23).

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Conflict de interese  
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