


# Dermatological manifestations in endocrine disorders

## Manifestações dermatológicas de distúrbios endócrinos

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### Abstract

This article reviews the dermatological manifestations that frequently arise in endocrine disorders, encompassing conditions such as diabetes mellitus, acromegaly, polycystic ovary syndrome, hypothyroidism, Addison's disease, among others. It explores the interactions between the endocrine system and the skin, highlighting how hormonal imbalances can result in a variety of skin symptoms. With a comprehensive approach, it offers important clinical insights for dermatologists and endocrinologists, aiming at a better understanding and an accurate diagnosis of these conditions.

**Keywords:** Skin manifestations. Endocrine system diseases. Dermatology.

### Resumo

Este artigo revisa as manifestações dermatológicas que frequentemente surgem em distúrbios endócrinos, abrangendo condições como diabetes mellitus, acromegalia, síndrome dos ovários policísticos, hipotireoidismo, doença de Addison, entre outras. Explora as interações entre o sistema endócrino e a pele, destacando como desequilíbrios hormonais podem resultar em uma variedade de sintomas cutâneos. Com uma abordagem abrangente, oferece insights clínicos importantes para dermatologistas e endocrinologistas, visando uma melhor compreensão e diagnóstico preciso dessas condições.

**Palavras-chave:** Manifestações dermatológicas. Doenças do sistema endócrino. Dermatologia.

### Introduction

The skin, the largest organ in the human body<sup>1</sup>, performs mechanical, immunological, and antimicrobial protection functions and participates in thermal regulation and sensory perception. It also has a rich network of hormone receptors and is therefore sensitive to hormonal changes, which can result in a wide variety of skin manifestations that represent a diagnostic challenge for general practitioners, endocrinologists, and dermatologists<sup>2</sup>.

Endocrine disorders can lead to significant changes in the skin and phanera and may serve as clinical markers of these underlying conditions. Cutaneous changes associated with these disorders can range from very mild to very severe, vary from non-specific to specific to the underlying disease, and may appear early or late in the course of these diseases<sup>3</sup>.

By understanding the complex interrelationships between the skin and the endocrine system, in several situations, health-care professionals can identify underlying

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endocrine disorders early and provide appropriate and effective treatment, which can significantly improve the quality of life and life-span of these patients<sup>4</sup>. This is particularly important in situations where these cutaneous alterations represent paraneoplastic manifestations of aberrant hormonal production by tumor cells<sup>5</sup>.

## Acromegaly

Acromegaly is a rare and chronic disease that results from the overproduction of growth hormone (GH) after the closure of the bone epiphyses<sup>6</sup>. It is mainly caused by pituitary adenomas, which produce excess GH and is characterized by an increase in blood levels of GH and insulin-like growth factor type 1 (IGF-1)<sup>7</sup>.

The characteristic signs and symptoms of acromegaly are related to increased levels of GH and IGF-1, which results in the overgrowth of soft tissues and organs, with subsequent clinical manifestations, such as enlargement of the extremities (hands and feet), tongue, jaw, facial changes (protruding forehead and enlarged nose), joint pain, sleep disturbances, voice changes, among others.

## Dermatological manifestations

The excess GH can cause an increase in skin thickness, which is due to the increase of dermal collagen, and not to the expansion of the epidermis due to the proliferation and maturation of keratinocytes<sup>8</sup>. In addition, these patients may have swollen skin due to the accumulation of glycosaminoglycans in the dermis, which is more prominent on the face, hands, and feet<sup>9</sup>. Skin tags, which are usually related to insulin resistance and diabetes mellitus (DM), are present in most individuals affected by acromegaly. It is unclear if its appearance is due to excess GH and IGF-1 or if it is a consequence of another metabolic dysregulation<sup>10</sup>. Excessive sweating is found in 50% to 88% of patients, due to the trophic effect of GH on the cutaneous sweat glands, as well as growth of the periglandular nerves<sup>11</sup>.

## Hypothyroidism

Hypothyroidism with low amounts of thyroid hormones results in a lower metabolic rate<sup>12</sup>. The most common causes are Hashimoto's thyroiditis, treatment of hyperthyroidism, surgical removal of the thyroid, or the use of certain medications, such as methimazole, propylthiouracil, and amiodarone<sup>13</sup>. If not properly treated, it can lead to weight gain, fatigue, constipation, depression, infertility,

heart disease, and decreased cognitive function. Treatment is done with thyroid hormone replacement<sup>14</sup>.

## Dermatological manifestations

Dry, cold, and rough skin, due to decreased blood flow and secretion from the acinar glands, in response to a drop in thyroid hormones, are the most common manifestations, resulting in flaking, itching, and hypersensitive skin<sup>14</sup>. Changes in skin pigmentation are also observed. Pallor may occur due to decreased cutaneous blood supply, a yellowish coloration is usually due to increased serum carotene levels, and also cutaneous hyperpigmentation can be observed when hypothyroidism is associated with primary adrenal insufficiency<sup>15</sup>.

There may also be weakening of the nails, which become brittle, fragile and prone to flaking. This is due to hypothermia caused by hypothyroidism, resulting from a decrease in metabolic rate, which leads to a compensatory secondary vasoconstriction. Vasoconstriction decreases blood flow, with a deficit in the supply of nutrients and oxygen to skin structures, causing slow growth and brittle nails<sup>16</sup>.

The hair may also become coarse, brittle, dry, develop slow growth, and eventually lead to alopecia<sup>17</sup>.

In addition, myxedema may occur in the lower limbs, a soft and painless edema, giving the skin a thick and flaccid appearance, especially on the face, periorbital region, hands, and feet which results from the infiltration of the skin with glycosaminoglycans with associated water retention<sup>18</sup>.

## Hyperthyroidism

The most common causes of hyperthyroidism are Graves' disease<sup>19</sup>, and hyperfunctioning thyroid nodules<sup>20</sup>. It can lead to a number of complications, including unintentional weight loss, tachycardia, palpitations, anxiety, tremors, muscle weakness, irritability, insomnia, heat intolerance, exophthalmos, cardiovascular, bone, and fertility changes<sup>21</sup>.

## Dermatological manifestations

Among the most common dermatological manifestations are warm, moist, and smooth skin. Heat is due to increased cutaneous blood flow and peripheral vasodilation, resulting from increased metabolism and may be accompanied by hyperhidrosis<sup>22</sup>. The skin may appear thin, soft, and fragile, becoming more susceptible to

injuries and bruises, because of the decrease in the keratin layer. Diffuse or generalized alopecia (Fig. 1) may also be found<sup>23</sup>.

Nails can present with onycholysis, also called Plummer's nails, which comprises the separation of the nail from the nail bed, and onychodystrophy, which involves changes in the shape and texture of the nails. Some patients may develop cutaneous hyperpigmentation, especially in the areas exposed to the sun. The mechanism is related to cortisol deficiency, due to its accelerated degradation that occurs in these patients, which leads to an increased production of pro-opiomelanocortin (POMC), a prohormone that is subsequently cleaved into adrenocorticotrophic hormone (ACTH) and melanocyte-stimulating hormone (MSH). Elevated serum levels of MSH stimulate increased melanin synthesis, which leads to hyperpigmentation<sup>24</sup>.

If the cause of hyperthyroidism is Graves' disease, periorbital edema and protrusion of the ocular globe may also be found. This is due to the enlargement of the eye muscles, caused by inflammation due to the accumulation of inflammatory cells and proliferation of fibroblasts in the interstitial tissue. Thus, this muscle enlargement ends up impairing the venous drainage of the orbital contents, causing periorbital and conjunctival edema<sup>25</sup>.

Other autoimmune diseases affecting the skin can also be observed more frequently in these patients, namely, vitiligo and chronic urticaria<sup>26</sup>.

### Polycystic ovary syndrome (PCOS)

It affects women of reproductive age and is characterized by hormonal changes that generally lead to the formation of multiple cysts in the ovaries, hyperandrogenism, weight gain, and fertility disorders<sup>27</sup>. Although not yet fully understood, the causes of polycystic ovary syndrome PCOS are associated with genetic and hormonal factors, associated with insulin resistance<sup>28</sup>. Complications such as menstrual irregularities, infertility, obesity, type 2 DM, cardiovascular disease, and mood disorders can occur. Diagnosis is based on clinical criteria, laboratory tests, and imaging<sup>29</sup>.

### Dermatological manifestations

Several alterations can be found in affected patients, such as hirsutism<sup>29</sup> and acne, resulting from hyperandrogenism<sup>30,31</sup>. This is due to the fact that androgens



**Figure 1.** Alopecia in a patient with hyperthyroidism (source: Lauro de Souza Lima Institute).

are the main hormonal regulators of hair growth and sebum production and secretion. In women with PCOS, excess androgen production by the ovaries increases serum levels of testosterone and dihydrotestosterone which interact with androgen receptors in hair follicles and promote differentiation from fleece hair (small, thin, and poorly pigmented) into terminal hair (thick, long, and pigmented)<sup>32</sup> and enhance the activity of sebaceous glands. Hirsutism occurs mainly in the genital area and can progress along the medium line, groins, lumbar region, face, chin, intermammary region, and around the nipples<sup>33</sup>. Acne in PCOS affects especially the face, but also the neck, upper trunk, and back regions.

Acanthosis *nigricans* (Fig. 2), characterized by dark, thick patches of skin, can also be found, especially in areas of body folds, such as the neck, armpits, and groin. It is strongly related to insulin resistance present in PCOS, with excessive production of insulin and IGF-1, which leads to increased stimulation of keratinocytes and fibroblasts<sup>29</sup>.





**Figure 2.** Acanthosis nigricans in a patient with polycystic ovary syndrome (source: University Hospital of Coimbra).



**Figure 3.** Hyperpigmentation on the lips of a patient with Addison's disease (source: University Hospital of Coimbra).

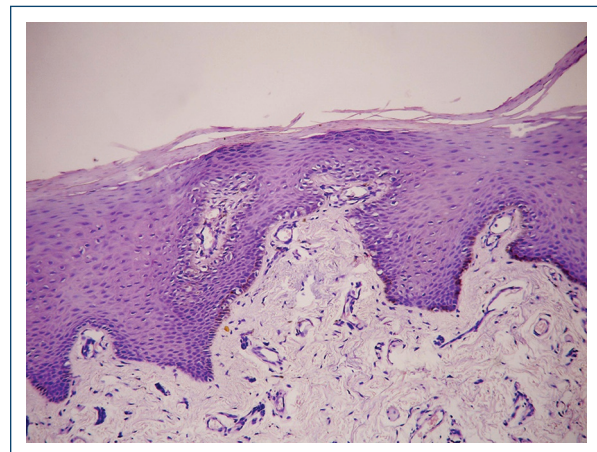
## Addison's disease

Addison's disease, also known as primary adrenal insufficiency, is a rare condition<sup>34</sup> resulting mainly from autoimmune destruction of these glands or infections, such as tuberculosis<sup>35</sup>. Addison's disease can lead to serious complications such as fluid and electrolyte imbalance, hypotension, chronic fatigue, weight loss, dizziness, and, in extreme cases, adrenal crisis or Addisonian crisis, a potentially life-threatening medical emergency<sup>36</sup>. Treatment involves replacing deficient adrenal hormones such as cortisol and aldosterone<sup>37</sup>.

### Dermatological manifestations

Cutaneous hyperpigmentation (Fig. 3) is the most characteristic finding, occurring in about 90% of patients<sup>35</sup>, which is a consequence of cortisol deficiency and increased production of POMC and MSH by the hypophysis. Elevated MSH results in increased melanin synthesis in basal melanocytes (Fig. 4), causing hyperpigmentation<sup>36</sup>. This hyperpigmentation is most common in sun-exposed areas and in skin folds, such as joints and scars. The color varies from light brown to dark brown and can be more intense on mucous membranes, such as gums, tongue, cheeks, and lips<sup>38</sup>.

Vitiligo, in unequal areas and often bilateral, may be present in 10% to 20% of patients with Addison's disease with autoimmune etiology, due to the autoimmune aggression of melanocytes<sup>39</sup>.



**Figure 4.** Histopathology (H and E  $\times 40$ ) of basal melanocytes of a patient with Addison's disease (source: University Hospital of Coimbra).

## Cushing's syndrome

It is a condition that results from excessive exposure to high levels of cortisol<sup>40</sup>, which plays an important role in regulating metabolism, the immune system, and stress<sup>41</sup>. The causes of Cushing's syndrome can be varied, including the use of exogenous corticosteroids, tumors in the adrenal glands or pituitary gland, and, in rare cases, cortisol-producing tumors in other organs<sup>42</sup>.

The complications of this syndrome can be serious and compromise several systems of the body. In addition to weight gain, patients may have redistribution of body fat, with accumulation in the abdomen and face,

with a decrease in fat tissue in arms and legs<sup>40</sup>. Other signs and symptoms may include muscle weakness, increased blood pressure, emotional changes, menstrual irregularities in women, and sexual dysfunction in men. In addition, these patients may have osteoporosis and DM<sup>41</sup>.

### **Dermatological manifestations**

One of the most prevalent manifestations is the presence of stretch marks in various regions of the body, such as the abdomen, thighs, arms, and breasts<sup>42</sup> (Fig. 5), which are reddish or purplish in the acute phase and become thinner and whitish over time<sup>43</sup>. Their presence is related to the reduction in skin elasticity caused by excess cortisol, which decreases the production of collagen and elastin, important components for skin integrity. High levels of cortisol can also inhibit cell regeneration and proper skin healing. When the skin is thin, it is more vulnerable to injury, and may present frequent bruising<sup>44</sup>.

Another common skin manifestation when the cause is a pituitary tumor producing high levels of ACTH is hyperpigmentation, which can develop in sun-exposed areas, as well as in skin folds, armpits, groin, and neck. The skin in these areas may become darker, and the coloration may vary from light brown to dark brown<sup>45</sup>.

Cushing's syndrome can also lead to the development of oily skin and monomorphic papular acne, due to the hyperstimulation of the sebaceous glands caused by cortisol. Facial erythema and flushing can also be found, especially on the cheeks and nose, a condition known as facial erythema<sup>46</sup>.

### **Hypopituitarism**

Hypopituitarism is a rare condition that can occur due to damage or dysfunction in the pituitary gland itself or in the surrounding structures, due to the presence of pituitary tumors, traumatic injuries, infections, inflammations, and complications after cranial surgeries or radiation therapy or post-partum (Sheehan syndrome)<sup>47</sup>.

The clinical manifestations of this disease can be diverse, such as excessive fatigue, unintentional weight loss, muscle weakness, menstrual disorders in women, sexual dysfunction in men, changes in growth and development in children, hypotension, stress intolerance, and metabolic disorders, among others<sup>48</sup>.



**Figure 5.** Stretch marks in a patient with Cushing's syndrome (source: University Hospital of Coimbra).

### **Dermatological manifestations**

Dermatologic findings depend on which glands are compromised and which hormones are insufficient. In case of insufficiency in the production of thyroid-stimulating hormone the skin may become dry, cold, and rough, due to the resulting hypothyroidism, with all the clinical manifestations of this disease<sup>4</sup>.

In addition, the decrease in the production of gonadotropins follicle-stimulating hormone, and luteinizing hormone results in secondary hypogonadism in men and women, with a consequent decrease in body hair and also alopecia, since sex hormones are essential for the maintenance of hair and hair follicles<sup>44</sup>.

### **DM**

DM is characterized by altered insulin secretion and varying degrees of peripheral insulin resistance, causing hyperglycemia and abnormal glycosylation of several molecules, namely, hemoglobin (HbA1C) whose levels are accurately related to the glycemic control<sup>49</sup>. Initial symptoms are related to hyperglycemia and include polydipsia, polyphagia, polyuria, and blurred vision. Late complications include vascular disease, peripheral neuropathy, kidney disease, and predisposition to infections<sup>50</sup>. Most complications can be postponed or prevented with adequate glycemic control<sup>51</sup>.

There are two main types of DM: type 1 and type 2 DM.

Type 1 DM is an autoimmune disease in which the immune system attacks and destroys insulin-producing pancreatic beta cells, leading to absolute insulin

deficiency<sup>49</sup>. Type 2 DM, on the other hand, is characterized by insulin resistance and/or deficiency<sup>50</sup>. While type 1 DM usually develops at younger ages and cannot be prevented, type 2 DM generally occurs in people older than 45 years and is strongly associated with obesity, physical inactivity, and family history, and can often be prevented or delayed with lifestyle changes<sup>49</sup>.

### **Dermatological manifestations**

Diabetic dermopathy is present in about 40% of patients and is often related to some DM-related chronic complication, such as kidney disease, retinopathy, or neuropathy<sup>52</sup>. The disease tends to appear in the lower extremities and in older men and can result from minor trauma<sup>53</sup>. It is characterized by painless, and rarely itching, atrophic and hyperpigmented macules, located on the anterior region of the legs. They are oval or round, depressed, shiny, irregularly contoured, sometimes bilateral but with asymmetrical distribution<sup>54</sup>.

Skin infections occur in 20-50% of patients with DM<sup>55</sup>, particularly in those with type 2 DM. Overall, they are associated with poor glycemic control. Several factors favor the onset of infections in these patients, mainly those with chronic vascular or neurological complications. Alterations in immune response are frequently found, especially reduced neutrophil chemotaxis and phagocytosis, with increased adhesion between epithelial cells and pathogens (such as *Candida albicans* in the oral and vaginal mucosa and *Escherichia coli* in the urinary tract)<sup>56</sup>.

Acanthosis nigricans often precedes the diagnosis of hyperglycemia, is characterized by dark, thick patches of skin, and is most often found in areas of body folds, such as the neck, armpits, and groin. It is strongly related to insulin resistance, which promotes the excessive production of IGF-1, which leads to hyperstimulation of keratinocytes and fibroblasts. The result is the appearance of hyperkeratosis and epidermal papillomatosis, which can be observed in histopathological analysis. Hyperkeratosis is mainly responsible for the clinical manifestation<sup>28</sup>.

Vulvovaginal candidiasis is a prevalent disorder found in women with DM (Fig. 6), especially in those with poor glycemic control, and is a frequent cause of vulvar pruritus<sup>56</sup>. It is clinically manifested by erythema of the genital area (with or without fissures) and satellite pustules. It is sometimes accompanied by whitish vaginal discharge. Its pathophysiology is related to the immune deficit of individuals with DM since they present inhibition of neutrophil activity, which increases the proliferation, adhesion, and virulence of this microorganism<sup>57</sup>.



**Figure 6.** Groin candidiasis in a type 1 diabetic patient with poor glycemic control (source: University Hospital of Coimbra).

Diabetic foot is the most devastating of DM-related complication. It is usually due to a combination of vasculopathy, neuropathy, and mechanical trauma, which occurs in 15-25% of all people with DM, and in about a quarter of these patients can lead to the onset of infections and osteomyelitis, which can lead to amputation of the affected limb<sup>58</sup>. It is generally due to an unnoticed trauma to cutaneous areas with neuropathy and calluses, such as on the soles of the feet and tips of toes. The healing process is generally seriously compromised, due to hyperglycemia, impaired chemotaxis, cell proliferation, and migration<sup>59</sup>. In addition, the increase in pro-inflammatory chemokines hinders wound healing, leading to the appearance of plantar ulcers. The presence of neuropathy and vasculopathy in these feet can cause muscle atrophy and bone deformation, with important changes in bone architecture, causing the collapse of the arch of the foot, a condition called Charcot foot.

Chronic pruritus is a common manifestation of DM, occurring in 3-49% of patients, significantly affecting their quality of life<sup>60</sup>. Diabetic polyneuropathy with sweating dysfunction due to sympathetic nervous system impairment may play a role in the pathogenesis of pruritus in these patients<sup>61</sup>.

Vitiligo (Fig. 7), is found in 2-10% of patients with type 1 DM<sup>62</sup>, occurring spontaneously with a progressive course. Its pathophysiology is related to autoimmune mechanisms, an intrinsic characteristic of this type of DM<sup>63</sup>.

Necrobiosis lipoidica (Fig. 8) affects 0.3-1.2% of all patients with DM, with a higher prevalence in women than





**Figure 7.** Vitiligo in a patient with type 1 diabetes (source: Lauro de Souza Lima Institute).



**Figure 8.** Necrobiosis lipoidica in a patient with type 2 diabetes (source: University Hospital of Coimbra).

in men, and is commonly located in the ventral area of the legs, often with symmetrical distribution<sup>64</sup>. It usually begins with erythematous papules, which slowly evolve into a brownish-yellow plaque with atrophic center and telangiectasia. In up to 35% of patients, lesions may ulcerate and present secondary bacterial infections. The pathophysiological mechanisms are still unknown, but the histopathology of the lesions shows degeneration of dermal collagen with a palisading granulomatous inflammatory infiltrate under an atrophic epidermis<sup>65</sup>. Glycemic control has no significant effect on the evolution of these lesions, and no study has convincingly proven the efficacy of the various types of drugs used in the treatment of necrobiosis lipoidica, namely, topical or intralesional corticosteroids injected into the lesion edges, and also ultraviolet A<sup>66</sup>.

## Conclusion

The cutaneous manifestations associated with endocrine disorders are varied and may serve as valuable clinical markers for these underlying conditions. Understanding the complex interactions between the skin and the endocrine system is crucial for early identification

of endocrine disorders and providing appropriate treatment. The examples covered in this narrative review article highlight how dermatological examination can play a key role in the detection and management of endocrine diseases, significantly improving the quantity and quality of life of patients. Therefore, collaboration between dermatologists, endocrinologists, and general practitioners is essential for effective diagnosis and treatment of these complex and often underdiagnosed conditions.

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## Conflicts of interest

None.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

## References

- Gilaberte Y, Prieto-Torres L, Pastushenko I, Juarraz Á. Anatomy and Function of the Skin. *Nanoscience in Dermatology*. Netherlands: Elsevier Inc.; 2016. p. 1-14.
- Demirkesen C. Skin manifestations of endocrine diseases. *Turk Patoloji Derg*. 2015;31:145-54.
- Gazdanova AA, Gorodetskaya GI, Perkov AV, Starodub MV, Urtaev SR, Prokopenko DV, et al. Cutaneous manifestations of endocrine disorders. *Klin Dermatol Venerol*. 2022;21:230-7.
- Lause M, Kamboj A, Faith EF. Dermatologic manifestations of endocrine disorders. *Transl Pediatr*. 2017;6:300-12.
- Silva JA, Mesquita KC, Igreja AC, Lucas IC, Freitas AF, Oliveira SM, et al. Paraneoplastic cutaneous manifestations: concepts and updates. *An Bras Dermatol*. 2013;88:9-22.
- Colao A, Grasso LF, Giustina A, Melmed S, Chanson P, Pereira AM, et al. Acromegaly. *Nat Rev Dis Primers*. 2019;5:20.
- Timoner FR, Paschoal LH, Oshiro RR, Zanini M, Paschoal FM. Aspectos dermatológicos da acromegalia. *An Bras Dermatol*. 2005;79:491-4.
- Póvoa G, Martins Diniz L. O sistema do hormônio de crescimento: interações com a pele. *Growth hormone system: skin interactions*. *An Bras Dermatol*. 2011;86:1159-65.
- Kanaka-Gantenbein C, Kogica C, Abdel-Naser MB, Chrousos GP. Skin manifestations of growth hormone-induced diseases. *Rev Endocr Metab Disord*. 2016;17:259-67.
- Resende M, Bolfi F, Nunes VS, Miot HA. Prevalence of dermatologic disorders in 15 patients with acromegaly. *An Bras Dermatol*. 2012;87:166-8.
- Nabarro JD. Acromegaly. *Clin Endocrinol (Oxf)*. 1987;26:481-512.
- Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. *Lancet*. 2017;390:1550-62.
- Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JL, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American association of clinical endocrinologists and the American thyroid association. *Endocr Pract*. 2012;18:988-1028.
- Heymann WR. Cutaneous manifestations of thyroid disease. *J Am Acad Dermatol*. 1992;26:889-902.
- Langan SM, Smeeth L, Hubbard R, Fleming KM, Smith CJ, West J. Bullous pemphigoid and pemphigus vulgaris - incidence and mortality in the UK: population based cohort study. *BMJ*. 2008;337:a180.
- Rosenberg A, Lipner SR. Nail changes associated with thyroid disease. *Cutis*. 2022;110:E8-12.
- Hussein RS, Atia T, Bin Dayel S. Impact of thyroid dysfunction on hair disorders. *Cureus*. 2023;15:e43266.
- Baldini E, Odorisio T, Tuccilli C, Persecchino S, Sorrenti S, Catania A, et al. Thyroid diseases and skin autoimmunity. *Rev Endocr Metab Disord*. 2018;19:311-23.
- Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American thyroid association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016;26:1343-421.
- Kahalay GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH. 2018 European thyroid association guideline for the management of graves' hyperthyroidism. *Eur Thyroid J*. 2018;7:167-86.
- Burch HB, Cooper DS. Management of graves disease a review. *JAMA*. 2015;314:2544-54.
- Leal JM, de Souza GH, de Marsillac PF, Alexandre Carlos Gripp, Serviço de Dermatologia, Hospital Universitário Pedro Ernesto, et al. Manifestações cutâneas associadas a doenças sistêmicas. *An Bras Dermatol*. 2021;96:627-87.
- Andrade VA, Gross JL, Maia AL. Tratamento do hipertireoidismo da doença de graves. *Arq Bras Endocrinol Metabol*. 2001;45:609-18.
- Hangaard G, Kirkeby K, Lingjaerde P. The pigmentation of thyrotoxic patients. *Acta Med Scand*. 1963;174:257-9.
- Carter JA, Utiger RD. The ophthalmopathy of Graves' disease. *Annu Rev Med*. 1992;43:487-95.
- Missaka RF, Penatti HC, Silveiras MR, Nogueira CR, Mazeto GM. Autoimmune thyroid disease as a risk factor for angioedema in patients with chronic idiopathic urticaria: a case-control study. *Sao Paulo Med J*. 2012;130:294-8.
- Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertil Steril*. 2018;110:364-79.
- Witchel SF, Oberfield S, Rosenfield RL, Codner E, Bonny A, Ibáñez L, et al. The diagnosis of polycystic ovary syndrome during adolescence. *Horm Res Paediatr*. 2015;83(6): 376-89.
- Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2013;98:4565-92.
- Archer JS, Chang RJ. Hirsutism and acne in polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol*. 2004;18:737-54.
- Lucky AW, Henderson TA, Olson WH, Robisch DM, Leibold M, Swinyer LJ, et al. Effectiveness of norgestimate and ethinyl estradiol in treating moderate acne vulgaris. *J Am Acad Dermatol*. 1997;37:746-54.
- Yilmaz B, Yildiz BO. Endocrinology of hirsutism: from androgens to androgen excess disorders. *Front Horm Res*. 2019;53:108-19.
- Matheson E, Bain J. Hirsutism in women. *Am Fam Physician*. 2019;100:168-75.
- Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, et al. Diagnosis and treatment of primary adrenal insufficiency: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2016;101:364-89.
- Erichsen MM, Løvås K, Skinningsrud B, Wolff AB, Undlien DE, Svartberg J, et al. Clinical, immunological, and genetic features of autoimmune primary adrenal insufficiency: observations from a Norwegian registry. *J Clin Endocrinol Metab*. 2009;94:4882-90.
- Kong M, Jelkoate W. Eighty-six cases of Addison's disease. *Clin Endocrinol (Oxf)*. 1994;41:757-61.
- Barnett AH, Espiner EA, Donald RA. Patients presenting with Addison's disease need not be pigmented. *Postgrad Med J*. 1982;58:690-2.
- Figueiredo Gatti R, Medeiros Prohmann C, Araújo Dantas C, Barcelos E Silva L, Marçal Machado T, Rodrigues de Oliveira Mattar F, et al. Hiperpigmentação na doença de Addison: relato de caso. *J Port Soc Dermatol Venerol*. 2017;75:169-72.
- Zelissen PM, Bast EJ, Croughs RJ. Associated autoimmunity in Addison's disease. *J Autoimmun*. 1995;8:121-30.
- Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. *Lancet*. 2015;386:913-27.
- Pivonello R, De Leo M, Cozzolino A, Colao A. The treatment of cushing's disease. *Endocr Rev*. 2015;36:385-486.
- Chabre O. Syndromes de cushing: physiopathologie, étiologie et principes thérapeutiques. *Press Med*. 2014;43:376-92.
- Rodrigues AC, Perez CL, Silva DP. Influência do cortisol nas disfunções estéticas. *Rev Saúde Foco*. 2019;11:20-38.
- Stratakis CA. Skin manifestations of Cushing's syndrome. *Rev Endocr Metab Disord*. 2016;17:283-6.
- Rosenberg EM, Hahn TJ, Orth DN, Deftos LJ, Tanaka K. ACTH-secreting medullary carcinoma of the thyroid presenting as severe idiopathic osteoporosis and senile purpura: report of a case and review of the literature. *J Clin Endocrinol Metab*. 1978;47:255-62.
- Mountjoy KG. The human melanocyte stimulating hormone receptor has evolved to become "super-sensitive" to melanocortin peptides. *Mol Cell Endocrinol*. 1994;102:R7-11.
- Raj R, Elshimy G, Mishra R, Jha N, Joseph V, Bratman R, et al. Dermatologic manifestations of endocrine disorders. *Cureus*. 2021;13:e18327.
- Schneider HJ, Aimaretti G, Kreitschmann-Andermahr I, Stalla G, Ghigo E. Seminar hypopituitarism. *Lancet*. 2007;369:1461-70.
- Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet*. 2017;389:2239-51.
- ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. Classification and diagnosis of diabetes: standards of care in diabetes - 2023. *Diabetes Care*. 2023;46:S19-40.
- Nathan DM, Bennett PH, Crandall JP, Edelstein SL, Goldberg RB, Kahn SE, et al. Does diabetes prevention translate into reduced long-term vascular complications of diabetes? *Diabetologia*. 2019;62:1319-28.
- Ahmed I, Goldstein B. Diabetes mellitus. *Clin Dermatol*. 2006;24:237-46.
- Kiziltan ME, Benbir G. Clinical and nerve conduction studies in female patients with diabetic dermopathy. *Acta Diabetol*. 2008;45:97-105.
- Morgan AJ, Schwartz RA. Diabetic dermopathy: a subtle sign with grave implications. *J Am Acad Dermatol*. 2008;58:447-51.



55. Mendes AL, Haddad V, Miot HA. Diabetes mellitus and the skin. *An Bras Dermatol*. 2017;92:8-20.
56. Foss NT, Polon DP, Takada MH, Foss-Freitas MC, Foss MC. Skin lesions in diabetic patients. *Rev Saude Publica*. 2005;39:677-82.
57. Nyirjesy P, Sobel JD. Genital mycotic infections in patients with diabetes. *Postgrad Med*. 2013;125:33-46.
58. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers. *JAMA*. 2005;293:217-28.
59. Blakytyn R, Jude EB. Altered molecular mechanisms of diabetic foot ulcers. *Int J Low Extrem Wounds*. 2009;8:95-104.
60. Ko MJ, Chiu HC, Jee SH, Hu FC, Tseng CH. Postprandial blood glucose is associated with generalized pruritus in patients with type 2 diabetes. *Eur J Dermatol*. 2013;23:688-93.
61. Sun P, Chen C, Kuo C, Lin H, Chan R, Kao M, et al. Impaired microvascular flow motion in subclinical diabetic feet with sudomotor dysfunction. *Microvasc Res*. 2012;83:243-8.
62. Lechleitner M, Hoppichler F, Kaser S. Autoimmunerkrankungen bei Type 1 Diabetes. *Wien Klin Wochenschr*. 2016;128:S201-3.
63. Amer AA, Gao XH. Quality of life in patients with vitiligo: an analysis of the dermatology life quality index outcome over the past two decades. *Int J Dermatol*. 2016;55:608-14.
64. Lowitt MH, Dover JS. Necrobiosis lipoidica. *J Am Acad Dermatol*. 1991;25:735-48.
65. Sibbald C, Reid S, Alavi A. Necrobiosis lipoidica. *Dermatol Clin*. 2015;33:343-60.