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The Skin as a Window to Diabetes Mellitus: Manifestations, Complications and Clinical Insights

Authors:

Aleksandra Kutaj [AK]

Ola.kutaj1@gmail.com

ORCID: https://orcid.org/0009-0001-5145-0752

Poznan University of Medical Sciences, Collegium Maius, Fredry 10, 61-701 Poznan

Zuzanna Adamowicz [ZA]

Zuzka.adamowicz@gmail.com

ORCID: https://orcid.org/0009-0003-9848-5359

Poznan University of Medical Sciences, Collegium Maius, Fredry 10, 61-701 Poznan

Abstract

Introduction and purpose

Diabetes mellitus (DM) is a chronic disease with rising global prevalence, affecting 8.3% of adults, many of whom remain undiagnosed. It impacts multiple organ systems, with skin manifestations often serving as early, visible signs of metabolic dysregulation. Conditions like acanthosis nigricans, xerosis, diabetic dermopathy, and necrobiosis lipoidica reveal

underlying metabolic issues and offer non-invasive tools for monitoring glycemic control. This article examines common dermatological signs of DM, their diagnostic value, and their role in disease management, highlighting prevention, treatment, and the importance of glycemic control for better patient outcomes.

Material and methods

This study is based on a comprehensive review of recent literature focusing on the skin manifestations and clinical implications of diabetes mellitus -related skin changes.

Description of the State of Knowledge

Hyperglycemia disrupts normal cellular processes in the skin, leading to impaired wound healing, increased oxidative stress, and inflammation. These pathological changes contribute to various dermatological symptoms, including xerosis, pruritus, erythema, and fibrosis. Skin changes, such as diabetic dermopathy, necrobiosis lipoidica, and recurrent fungal infections, are not only indicators of DM but also reflect glycemic control and disease severity. These manifestations can signal undiagnosed diabetes or poorly controlled blood glucose levels, offering a non-invasive method for disease monitoring.

Conclusions

Skin manifestations are vital diagnostic tools in diabetes care, providing early indications of metabolic imbalances and poor glycemic control. Their presence underscores the need for timely interventions, including lifestyle modifications, pharmacological treatments, and patient education. Dermatological assessments, particularly in resource-limited settings, offer an accessible approach to monitoring therapy effectiveness and predicting complications.

Keywords: Diabetes mellitus, skin manifestations, diabetic dermopathy, glycemic control, dermatological complications

1.Introductiona

Diabetes mellitus (DM) is a chronic and increasingly prevalent disease, affecting 8.3% of adults globally, with an alarming 46% of cases remaining undiagnosed [1]. As a multifaceted condition, DM impacts nearly every organ in the body and poses a wide range of serious health complications. Among these, skin conditions are some of the earliest and most visible signs of the disease, often signaling underlying metabolic imbalances.

Skin problems associated with diabetes, such as xerosis, pruritus, erythema, fibrosis, and swelling, are common, affecting up to 80% of individuals with the condition [2]. These dermatological issues not only disrupt daily life but can also significantly diminish patients' quality of life by causing discomfort, visible changes, and secondary infections if left untreated.

Importantly, the presence of certain skin symptoms can provide valuable diagnostic insights. They may help identify undiagnosed cases of diabetes or indicate poor blood sugar control, offering clinicians a non-invasive way to monitor the disease's progression or effectiveness of treatment [3]. Understanding these manifestations is crucial for improving both patient outcomes and quality of care.

In this article, we aim to highlight the skin manifestations of diabetes, emphasizing their importance in understanding the disease, improving diagnosis, and supporting better management strategies.

2.Pathophysiological Impact of Diabetes Mellitus on the Skin

Elevated glucose levels in diabetes negatively affect various cellular processes in the skin, such as proliferation, migration, and protein synthesis in keratinocytes and fibroblasts [4]. These disruptions are accompanied by increased endothelial cell apoptosis and inhibition of nitric oxide (NO) production due to the suppression of nitric oxide synthase (NOS) activity. Consequently, vascular function is impaired, leading to reduced vasodilation. Additionally, hyperglycemia compromises immune response mechanisms by weakening chemotaxis and phagocytosis in innate immune cells. Advanced glycation end products (AGEs) are formed through non-enzymatic glycation of proteins, lipids, and nucleic acids [5]. These molecules interact with intra- and extracellular proteins, such as type I collagen and epidermal growth factor receptor, impairing their biological functions. AGEs also bind to the RAGE receptor, triggering the NF-κB signaling pathway and promoting the production of proinflammatory cytokines. [6][7][8]. This cascade exacerbates oxidative stress and inflammation, further contributing to tissue damage in diabetes [9] .

3.The Most Common Skin Manifestations of Diabetes Mellitus

3.1 Acanthosis Nigricans – An Indicator of Insulin Resistance

Acanthosis nigricans (AN) is one of the most common dermatological manifestations of diabetes, often serving as an indicator of insulin resistance. This condition is more pronounced in individuals with darker skin tones, making it more prevalent among African Americans, Hispanics, and Native Americans [10].

The characteristic features of AN include symmetrical thickening of the skin in natural folds, especially in the armpits but also on the neck, areolas, elbows or umbilicus.The affected areas of skin become darker due to hyperkeratosis and increased proliferation of keratinocytes and fibroblasts under the influence of hyperinsulinemia [1].

The mechanism behind AN development is closely linked to excessive insulin activity. Hyperinsulinemia, a hallmark of insulin resistance, stimulates insulin receptors and insulin-like growth factor 1 (IGF-1) receptors on keratinocytes and fibroblasts, leading to abnormal growth and skin thickening [11].

The presence of acanthosis nigricans can serve as an important clinical diagnostic marker, indicating the need to evaluate insulin resistance and assess the risk of developing type 2 diabetes. This is particularly significant in children and young adults, where the presence of such skin changes should prompt further metabolic investigations [12].

Management of AN primarily involves addressing insulin resistance through weight loss, physical activity, and appropriate pharmacotherapy. The use of topical treatments, such as retinoids or keratolytic agents, can improve the appearance of the lesions, though their efficacy is limited without proper control of the underlying cause [13].

3.2 .*Diabetic Dermopathy – The Most Common Manifestation on the Lower Legs*

Diabetic dermopathy (DD) is the most common cutaneous manifestation of diabetes, observed in approximately 40% of patients with the disease [14]. It occurs more frequently in men and individuals over the age of 50 [15].The lesions present as small, round, brownish spots measuring 0.5–1.5 cm in diameter, typically located on the anterior surface of the lower legs. These spots result from vascular changes in the microcirculation and minor skin injuries that fail to heal properly due to metabolic disturbances and impaired repair mechanisms [16].

Diabetic microangiopathy, characterized by damage to small blood vessels, is the primary cause of diabetic dermopathy. Elevated glucose levels lead to non-enzymatic glycation of collagen, weakening the structure of blood vessel walls and causing tissue hypoxia. Additionally, reduced local immunity increases the risk of chronic inflammation in the affected areas [17] [18].

Although diabetic dermopathy is usually asymptomatic and does not require treatment, its presence may indicate advanced microangiopathic changes and suggest the need for more rigorous glycemic control. Patients should also be aware that these lesions can be the first visible sign of microcirculatory abnormalities, underscoring the importance of proper education and regular monitoring [19].

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3.3 Bullosis Diabeticorum – Rare but Characteristic

Bullosis diabeticorum also known as Diabetic blisters, are rare yet distinctive skin lesions occurring predominantly in patients with advanced diabetes. These lesions manifest as painless, well-demarcated blisters filled with clear fluid, appearing suddenly, most commonly on the feet, hands, or lower legs [20].

The exact etiology of these lesions remains unclear; however, it is believed that blisters result from a combination of diabetic neuropathy, microangiopathy, and local skin trauma. Vascular damage leads to local hypoxia and increased vessel wall permeability, which may promote blister formation. Diabetic blisters typically heal spontaneously within a few weeks without scarring [21].

Bullosis diabeticorum can recur over the years, with repeated episodes sometimes leading to ulceration and scarring. Secondary infections, marked by cloudy blister fluid, may arise and require treatment to prevent complications like cellulitis, abscess, or osteomyelitis. In severe cases, infections have resulted in amputations [22].Preventing secondary infections through proper hygiene and avoiding manipulation of blisters is crucial in treatment. Optimizing glycemic control is also important to reduce the risk of recurrence.

Recognizing bullosis diabeticorum is essential, as the presence of these lesions may indicate advanced diabetes with microangiopathic complications. This should prompt a thorough

assessment of the patient's metabolic status and the implementation of appropriate therapeutic measures .

3.4 Xerosis and puritus

The skin is among the organs most frequently affected by diabetes complications. High blood glucose levels lead to dehydration and dysfunction of sweat glands, resulting in decreased epidermal hydration [23]. Xerosis can affect any area of the skin and is characterized by flaking and scaling, often associated with advanced disease [24].

Itching often accompanies skin dryness and results from both metabolic changes and diabetic neuropathy. Damage to nerve fibers, reduced blood flow in microcirculation, and increased levels of pro-inflammatory cytokines contribute to this symptom [25]. Itching may affect large skin areas or be limited to specific sites, such as the lower limbs. The discomfort of these symptoms often negatively impacts patients' quality of life.

It is important in clinical practice to pay attention to symptoms like skin dryness and itching, as they may indicate inadequate glycemic control or developing complications. Early recognition and treatment of these symptoms, such as with emollients containing polidocanol or menthol, can provide relief to patients and improve their comfort. In more severe cases, interventions like topical corticosteroids, intralesional corticosteroids or oral therapies, including antihistamines or antidepressants may be required. Ultraviolet phototherapy is also an option for refractory cases [14].

4. Skin changes associated with diabetes mellitus cimplications

4.1 Necrobiosis lipoidica

Necrobiosis lipoidica (NL) is a chronic dermatological condition more frequently observed in patients with type 1 diabetes, although it can also occur in individuals without the disease. It is estimated that NL develops in 0.3–1.6% of diabetic patients, making it a rare but significant complication [1]. Among patients diagnosed with NL, diabetics account for 65% of cases [26]. It primarily affects women between the fourth and sixth decades of life [27].

The characteristic lesions are well-demarcated yellow-brown patches or plaques, often with central atrophy and telangiectasias. These lesions are commonly located on the anterior surface of the lower legs, typically affecting both limbs, though they can also appear in other locations [15][28].

The pathogenesis of NL is multifactorial and is is characterized by collagen degradation, granuloma formation, lipid deposition, and thickening of blood vessel walls.. Telangiectasias and painful ulcerations develop in advanced stages, affecting about 30% of cases. The condition is believed to stem from an immunologically mediated vascular disorder, especially in diabetic patients. Key vascular changes include thickened vessel walls, fibrosis, and endothelial proliferation, causing dermal ischemia and hypoxia. Reduced collagen production, disrupted fibril structure, and immune deposits at blood vessels further contribute to lesion development [29].

Treatment of NL involves both topical and systemic therapeutic strategies. Glucocorticoids, calcineurin inhibitors, and occlusive dressings for ulcers are commonly used. Additionally, glycemic control is essential to limit the progression of the lesions.

4.2 Insulin Lipodystrophy – A Problem at Injection Sites

Insulin-induced lipodystrophy is a common complication of insulin therapy, affecting approximately 25–55% of patients undergoing insulin treatment [30] It manifests as lipoatrophy (LA) or, more frequently, lipohypertrophy (LH) which affects approximately 27% of people with diabetes [14] at sites of repeated insulin injections.

LA results from inflammatory processes and immune reactions to insulin, leading to the degradation of local adipose tissue. The prevalence of LA has significantly decreased with the advent of purified and recombinant insulin forms, now affecting an estimated 3.6% of patients using insulin injections [31].

In contrast LH is characterized by tumor-like lumps of adipose tissue that are both visible and palpable at insulin injection sites. This condition arises due to the lipogenic effects of repeated insulin exposure, promoting proliferation and hypertrophy of adipocytes [32]. These

localized fatty deposits not only alter the aesthetic appearance of the injection site but also impair the physiological function of insulin.

When insulin is administered into tissue affected by LH, its absorption becomes unpredictable, leading to poor glycemic control. This can result in excessive glucose variability and an increased risk of hypoglycemia. Despite its clinical significance, the underlying pathophysiology of LH remains poorly understood [33]. This complication has clinical significance as it affects insulin absorption, leading to glucose level fluctuations and challenges in maintaining stable metabolic control. Preventive measures include rotating injection sites, avoiding the reuse of needles, and employing proper injection techniques.

4.3. Fungal and Bacterial Infections

Patients with diabetes are particularly susceptible to skin infections, both bacterial and fungal. This increased vulnerability is primarily due to hyperglycemia, which impairs the function of immune cells, such as neutrophils and macrophages, thereby reducing the body's ability to combat infections effectively [34].

Fungal Infections

Fungal infections, particularly candidiasis caused by Candida albicans, frequently affect skin folds, including the axillae and groin. In diabetic individuals, these infections are often recurrent and difficult to manage. Dermatophyte infections, such as tinea pedis, are also common and can result in chronic skin lesions. If untreated, such conditions may escalate into more severe complications, including diabetic foot syndrome [35].

Bacterial Infections

Bacterial infections, including boils and abscesses, are most commonly caused by Staphylococcus aureus. These infections can progress to cellulitis or systemic complications, particularly if glycemic control is poor. Moreover, diabetic patients are at a higher risk of developing severe infections such as necrotizing fasciitis or septicemia [36].

Management of fungal and bacterial infections in diabetic patients involves antifungal or antibiotic therapy, tailored to the type and severity of the infection.Effective glycemic control plays a crucial role in reducing the recurrence of infections and enhancing the overall immune response. Preventive measures, such as maintaining good skin hygiene and promptly addressing minor skin injuries, are also essential in minimizing infection risks [37].

4.4. Diabetic Foot Syndrome – A Serious Complication

Diabetic Foot Syndrome (DFS) represents one of the most severe complications of diabetes, resulting from a combination of neuropathic and vasculopathic changes in the lower extremities. This condition significantly impacts patients' quality of life and is a major cause of morbidity and hospitalization among individuals with diabetes [38]. The prevalence of DFS ranges from 4% to 10% with most cases involving men and patients over the age of 60.

DFS commonly begins with calluses and dry skin caused by diabetic neuropathy. In advanced stages, chronic ulcers and foot deformities develop. Between 15% and 25% of patients with diabetes will experience ulcers during their lifetime [39].Neuropathic ulcers, which are typically painless due to sensory nerve damage, are the most frequent type. Ischemic ulcers, associated with peripheral vascular disease, are less common but often painful [40]. Ulcers are most often located on areas exposed to trauma, such as the toes, forefoot, and heels. If untreated, these ulcers may lead to secondary infections, gangrene, or osteomyelitis, potentially necessitating limb amputation [41]. Fungal infections, particularly between the toes, may also exacerbate ulcer progression.

The development of diabetic foot syndrome (DFS) involves a complex interplay of mechanisms, including peripheral neuropathy, ischemia caused by atherosclerosis, and delayed wound healing. Hyperglycemia, a hallmark of diabetes, plays a pivotal role in these processes. Elevated blood glucose levels drive the formation of advanced glycation end-products (AGEs), which result from non-enzymatic reactions between glucose and proteins or lipids. AGEs accumulate in tissues, exacerbating oxidative stress, chronic inflammation, and cellular dysfunction [42].

Neuropathy diminishes sensory and motor functions, reducing patients' ability to perceive injuries and contributing to abnormal gait patterns, which increase the risk of ulcer formation.

Autonomic nerve damage also decreases sweating, resulting in dry, fissured skin prone to infection. Concurrently, arterial atherosclerosis impairs blood flow, exacerbating tissue hypoxia and ulceration.

Management of DFS requires a multidisciplinary approach emphasizing prevention and treatment of active ulcers. Preventive strategies include daily foot inspections, proper hygiene, and the use of specialized footwear to reduce pressure on vulnerable areas [43].
Antibiotic therapy is necessary for infected ulcers, while severe ischemia may require revascularization procedures [44]. Early identification and intervention are crucial to reducing the risk of severe complications, including amputations.

5. Skin Manifestations and Glycemic Control

Skin changes can be among the first visible signs suggesting the development of diabetes [45], even before classic symptoms such as polyuria, excessive thirst, or weight loss appear. These changes not only serve as early indicators of diabetes but also act as a tool for monitoring its control. Regular observation of a patient's skin condition allows physicians to assess the effectiveness of the current diabetes therapy.

On the other hand, recurrent skin infections, such as candidiasis , may suggest insufficient metabolic control [46]. Persistent changes like diabetic dermopathy or necrobiosis lipoidica lesions could signal poorly controlled diabetes, necessitating medical intervention.

Another indicator is the presence of ulcers in diabetic foot syndrome. The emergence of new ulcers or difficulties in their healing may point to prolonged uncontrolled blood glucose levels Early identification of these symptoms can be crucial, enabling the timely implementation of preventive measures such as lifestyle modifications, pharmacological treatment, or intensive patient education.

Skin manifestations are particularly useful for patients with limited access to advanced laboratory tests. In such cases, assessing skin changes can serve as a simple and accessible tool for evaluating therapy effectiveness and predicting the risk of further complications

6.Summary

Diabetes mellitus is a chronic condition that affects multiple organs, with the skin often exhibiting some of the earliest signs of metabolic imbalance. Common skin issues associated with diabetes, such as dryness, itching, redness, and swelling, can significantly impact patients' daily lives and overall quality of life, especially if left untreated and complicated by secondary infections.

These dermatological symptoms are not only clinical concerns but also valuable diagnostic tools, offering non-invasive insights into undiagnosed diabetes or poor blood sugar control. Early recognition of these manifestations plays a crucial role in improving disease management, monitoring treatment effectiveness, and supporting better health outcomes.

The article highlights the need for an interdisciplinary approach to diabetic care, emphasizing the integration of dermatological assessments into routine management to address skin complications and enhance patients' well-being.

Author's contribution:
Conceptualization, supervision and project administration- AK; ZA
Methodology- AK; ZA
Software, validation, formal analysis, investigation, resources, writing original draft preparation- AK; ZA
Writing review editing and visualization- AK; ZA

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References:

1. Mendes, Adriana Lucia et al. “Diabetes mellitus and the skin.” Anais brasileiros de dermatologia, vol. 92, no. 1, 2017, pp. 8-20. doi:10.1590/abd1806-4841.20175514.
2. David, Pascaline et al. “A Comprehensive Overview of Skin Complications in Diabetes and Their Prevention.” Cureus, vol. 15, no. 5, e38961, 13 May 2023. doi:10.7759/cureus.38961.
3. Labib A, Rosen J, Yosipovitch G. “Skin Manifestations of Diabetes Mellitus.” Endotext, MDText.com, Inc., updated 2022 Apr 21.
4. Blakytny, R., & Jude, E. B. (2009). Altered Molecular Mechanisms of Diabetic Foot Ulcers. The International Journal of Lower Extremity Wounds, 8(2), 95–104. https://doi.org/10.1177/1534734609337151
5. Palimeri S, Palioura E, Diamanti-Kandarakis E. Current per- spectives on the health risks associated with the consumption of advanced glycation end products: recommendations for dietary management. Diabetes Metab Syndr Obes. 2015;8:415–26. doi:10.2147/DMSO.S63089
6. Blakytny R, Jude EB. Altered molecular mechanisms of diabetic foot ulcers. Int J Low Extremity Wounds. 2009;8(2):95–104. doi:10.1177/1534734609337151.
7. Stern D, Yan SD, Yan SF, Schmidt AM. Receptor for advanced glycation endproducts: a multiligand receptor magnifying cell stress in diverse pathologic settings. Adv Drug Deliv Rev. 2002;54(12):1615–25.
8. Gkogkolou P, Böhm M. "Diabetes mellitus and its dermatological footprint: Exposing skin manifestations and their clinical significance." J Dtsch Dermatol Ges. 2014;12:847–864.
9. HuH,JiangH,RenH,HuX,WangX,HanC.AGEsand chronic subclinical inflammation in diabetes: disorders of immune system. Diabetes Metab Res Rev. 2015;31(2):127–37. doi:10.1002/dmrr.2560
10. Karadağ, A. S., You, Y., Danarti, R., Al-Khuzaei, S., & Chen, W. (2018). Acanthosis nigricans and the metabolic syndrome. Clinics in Dermatology, 36(1), 48–53. https://doi.org/10.1016/j.clindermatol.2017.09.008
11. Angelidi, Angeliki M et al. “Severe insulin resistance syndromes.” The Journal of clinical investigation vol. 131,4 (2021): e142245. doi:10.1172/JCI142245

12. Mukhtar, Q., Cleverley, G., Voorhees, R. E., & McGrath, J. W. (2001). Prevalence of acanthosis nigricans and its association with hyperinsulinemia in New Mexico adolescents. https://doi.org/10.1016/s1054-139x(00)00217-2
13. Patel, Nupur U et al. “Current treatment options for acanthosis nigricans.” Clinical, cosmetic and investigational dermatology vol. 11 407-413. 7 Aug. 2018, doi:10.2147/CCID.S137527).
14. Lima, A. L., Illing, T., Schliemann, S., & Elsner, P. (2017). Cutaneous Manifestations of Diabetes Mellitus: A Review. American Journal of Clinical Dermatology, 18(4), 541–553. https://doi.org/10.1007/s40257-017-0275-z
15. Pal, R. S., Wal, P., Pal, Y., & Wal, A. (2019). Recent Insights On Diabetic Dermopathy. The Open Dermatology Journal, 13(1), 8–12. https://doi.org/10.2174/1874372201913010008
16. Goldenberg, G., & Fitzpatrick, J. E. (2013). Cutaneous manifestations of diabetes mellitus and thyroid disease. In Endocrine Secrets, Sixth Edition (pp. 444-452). Elsevier Inc.. https://doi.org/10.1016/B978-1-4557-4975-1.00064-4
17. Madonna, R., Pieragostino, D., Balistreri, C. R., Rossi, C., Geng, Y.-J., Del Boccio, P., & De Caterina, R. (2018). Diabetic macroangiopathy: Pathogenetic insights and novel therapeutic approaches with focus on high glucose-mediated vascular damage. Vascular Pharmacology, 107, 27–34. https://doi.org/10.1016/j.vph.2018.01.009
18. Berbudi, A., Rahmadika, N., Tjahjadi, A. I., & Ruslami, R. (2020). Type 2 Diabetes and its Impact on the Immune System. Current Diabetes Reviews, 16(5), 442–449. https://doi.org/10.2174/1573399815666191024085838
19. Baselga Torres, E., & Torres-Pradilla, M. (2014). Cutaneous manifestations in children with diabetes mellitus and obesity. Actas dermo-sifiliograficas, 105(6), 546–557. https://doi.org/10.1016/j.ad.2013.11.014
20. Larsen, Kirsten et al. “Incidence of bullosis diabeticorum--a controversial cause of chronic foot ulceration.” International wound journal vol. 5,4 (2008): 591-6. doi:10.1111/j.1742-481X.2008.00476.x
21. Gupta, V., Gulati, N., Bahl, J., Bajwa, J., & Dhawan, N. (2014). Bullosis Diabeticorum: Rare Presentation in a Common Disease. Case Reports in Endocrinology, 2014, 1–3. https://doi.org/10.1155/2014/862912

22. Chouk, C., & Litaiem, N. (2024). Bullosis Diabeticorum. In StatPearls. StatPearls Publishing.
23. Man, Mao-Qiang et al. “Alterations in epidermal function in type 2 diabetes: Implications for the management of this disease.” Journal of diabetes vol. 14,9 (2022): 586-595. doi:10.1111/1753-0407.13303
24. Stingeni, Luca et al. “Xerosis in Patients with Type 2 Diabetes: An Italian Multicentre Study.” Acta dermato-venereologica vol. 101,10 adv00577. 26 Oct. 2021, doi:10.2340/actadv.v101.263
25. Nirenjen, S et al. “Exploring the contribution of pro-inflammatory cytokines to impaired wound healing in diabetes.” Frontiers in immunology vol. 14 1216321. 27 Jul. 2023, doi:10.3389/fimmu.2023.1216321
26. Kowzan-Korman, A., Rosińska-Więckowicz, A., Olek-Hrab, K., Czarnecka-Operacz, M., & Silny, W. (2009). Case reportNecrobiosis lipoidica diabeticorum – a case report. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii, 26(2), 104-109.
27. Jelinek JE. The skin in diabetes. Diabet Med. 1993;10:201–213. doi:10.1111/j.1464-5491.1993.tb00048.x
28. Lepe, K., Riley, C. A., Hashmi, M. F., & Salazar, F. J. (2024). Necrobiosis Lipoidica. In StatPearls. StatPearls Publishing.
29. Nihal, A., Caplan, A. S., Rosenbach, M., Damsky, W., Mangold, A. R., & Shields, B. E. (2023). Treatment options for necrobiosis lipoidica: a systematic review. International journal of dermatology, 62(12), 1529–1537. https://doi.org/10.1111/ijd.16856
30. Saberi, S., Esfandiari, N.H., MacEachern, M.P. et al. Detemir plus aspart and glulisine induced lipoatrophy: 2015 literature review and report of a new case.Clin Diabetes Endocrinol 1, 10 (2015). https://doi.org/10.1186/s40842-015-0013-5
31. Kadiyala, P., Walton, S., & Sathyapalan, T. (2014). Insulin induced lipodystrophy. British Journal of Diabetes, 14(4), 131. https://doi.org/10.15277/bjdvd.2014.036
32. Tian, Tiffany et al. “Lipohypertrophy and Insulin: An Update From the Diabetes Technology Society.” Journal of diabetes science and technologyvol. 17,6 (2023): 1711-1721. doi:10.1177/19322968231187661

33. Xu, Xiao-Han et al. (“Lipohypertrophy: prevalence, clinical consequence, and pathogenesis.” Chinese medical journal vol. 134,1 47-49. 17 Aug. 2020, doi:10.1097/CM9.0000000000000970)
34. Berbudi, Afiat et al. “Type 2 Diabetes and its Impact on the Immune System.” Current diabetes reviews vol. 16,5 (2020): 442-449. doi:10.2174/1573399815666191024085838
35. Rodrigues, Célia F et al. “Candida sp. Infections in Patients with Diabetes Mellitus.” Journal of clinical medicine vol. 8,1 76. 10 Jan. 2019, doi:10.3390/jcm8010076
36. Casqueiro, J., Casqueiro, J., & Alves, C. (2012). Infections in patients with diabetes mellitus: A review of pathogenesis. Indian journal of endocrinology and metabolism, 16 Suppl 1(Suppl1), S27–S36. https://doi.org/10.4103/2230-8210.94253
37. Zhou, K., & Lansang, M. C. (2024). Diabetes Mellitus and Infection. In K. R. Feingold (Eds.) et. al., Endotext. MDText.com, Inc.
38. Tuttolomondo, Antonino et al. “Diabetic foot syndrome: Immune-inflammatory features as possible cardiovascular markers in diabetes.” World journal of orthopedics vol. 6,1 62-76. 18 Jan. 2015, doi:10.5312/wjo.v6.i1.62
39. Amin, Noha, and John Doupis. “Diabetic foot disease: From the evaluation of the "foot at risk" to the novel diabetic ulcer treatment modalities.” World journal of diabetes vol. 7,7 (2016): 153-64. doi:10.4239/wjd.v7.i7.153).
40. McDermott, Katherine et al. “Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers.” Diabetes care vol. 46,1 (2023): 209-221. doi:10.2337/dci22-0043
41. Armstrong, David G et al. “Diabetic Foot Ulcers: A Review.” JAMA vol. 330,1 (2023): 62-75. doi:10.1001/jama.2023.10578
42. Kim, J. H. (2023). Investigating Diabetic Foot Pathophysiology and Amputation Prevention Strategies through Behavioral Modification. Journal of Wound Management and Research, 19(3), 167–172. https://doi.org/10.22467/jwmr.2023.02747
43. Frykberg R. G. (2002). Diabetic foot ulcers: pathogenesis and management. American family physician, 66(9), 1655–1662.
44. Hingorani, A., LaMuraglia, G. M., Henke, P., Meissner, M. H., Loretz, L., Zinszer, K. M., Driver, V. R., Frykberg, R., Carman, T. L., Marston, W., Mills, J. L.,

& Murad, M. H. (2016). The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. Journal of Vascular Surgery, 63(2), 3S—21S. https://doi.org/10.1016/j.jvs.2015.10.003

45. Reschke, F., Biester, T., von dem Berge, T., Jamiolkowski, D., Hasse, L., Dassie, F., Maffei, P., Klee, K., Kordonouri, O., Ott, H., & Danne, T. (2023). Skin manifestations in rare types of diabetes and other endocrine conditions. Endocrine connections, 12(7), e220410. https://doi.org/10.1530/EC-22-0410
46. Talapko, Jasminka et al. "Candida albicans-The Virulence Factors and Clinical Manifestations of Infection." Journal of fungi (Basel, Switzerland) vol. 7,2 79. 22 Jan. 2021, doi:10.3390/jof7020079