

Skin diseases seen in diabetes mellitus

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Diabetes mellitus (DM) is the most common endocrine disorder, expected to affect 5.4% of the world population by the year 2025. DM is characterized by high serum glucose levels and by disturbances of carbohydrate and lipid metabolism and resultant long term systemic complications. DM has replaced syphilis of pre-antibiotic days as the great clinical imitator with a wide array of signs and symptoms affecting every organ of the body. The incidence of cutaneous disorders in diabetic patients varies between 30% and 71% according to different authors. Cutaneous manifestations of DM generally

appear subsequent to the development of the disease, but may be the first presenting signs or may even precede the primary disease manifestations by many years in some diabetics. We provide a concise review of the various dermatologic disorders encountered in diabetic patients.

Key words: diabetes mellitus, cutaneous, manifestations

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Diabetes mellitus (DM) is the most common endocrine disorder, expected to affect 5.4% of the world population by the year 2025.¹ In Kuwait, the age-standardized incidence rate for Type 2 diabetes in Kuwaiti children aged 0 to 14 years is 20.9; this incidence is high compared to the values in neighboring Arab countries and appears to be increasing.² About 15% of the adult Kuwaiti population has Type 2 diabetes.³

DM is characterized by high serum glucose levels and by disturbances of carbohydrate and lipid metabolism and resultant long term systemic complications. DM has replaced syphilis of pre-antibiotic days as the great clinical imitator, with a wide array of signs and symptoms affecting every organ of the

body. It is not surprising that the skin is not only affected in DM, but the manifestations of diabetes of the skin are numerous and varied.

The incidence of cutaneous disorders in diabetic patients varies between 30% and 71% according to different authors.⁴⁻⁷ Cutaneous manifestations of DM generally appear subsequent to the development of the disease, but may be the first presenting signs, or even precede the primary disease manifestations by many years in some diabetics. The prevalence of cutaneous disorders does not seem to differ between Type 1 and Type 2 DM patients. It has been noted, however, that Type 2 patients develop more frequent skin lesions associated with infections, whereas the Type 1 patient is associated with more autoimmune-type cutaneous lesions.¹

Cutaneous findings in DM can be classified into four categories: (1) skin diseases with strong association and others with less distinct association with DM, (2) cutaneous infections, (3) dermatologic disorders related to diabetic complications, and (4) skin conditions related to diabetic treatment.¹ Although the table below is not meant to be complete, it contains most of the manifestations seen. It is the purpose of this review to outline the major dermatologic manifestations of diabetes.

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Table. Skin diseases seen in diabetes mellitus**I. Skin diseases with strong association and other conditions with less distinct association with DM**

- Diabetic dermopathy
- Necrobiosis lipoidica
- Diabetic thick skin
- Yellow skin
- Diabetic bullae
- Acanthosis nigricans
- Eruptive xanthomas
- Perforating disorders
- Pigmented purpuric dermatoses
- Granuloma annulare
- Rubeosis facie
- Lichen planus
- Vitiligo

II. Skin infections

- Fungal
 - Tinea pedis
 - Onychomycosis
 - Candidal angular cheilitis
 - Candidal balanitis
 - Candidal intertrigo
- Bacterial
 - Folliculitis
 - Furunculosis
 - Carbuncles
 - Ecthyma
 - Cellulitis
 - Erysipelas
 - Erythrasma

III. Skin diseases related to diabetic complications

- Diabetic macroangiopathy
- Diabetic microangiopathy
- Diabetic neuropathy

IV. Skin diseases related to diabetes treatment

- Sulfonylurea-related skin lesions
- Insulin lipohypertrophy
- Insulin lipoatrophy
- Insulin allergic reactions

Skin Diseases with Strong Association and other Conditions with Less Distinct Association with Diabetes Mellitus

Diabetic Dermopathy

Diabetic dermopathy is considered to be the most common cutaneous manifestation in DM.⁸ It has also been referred to as *pigmented pretibial papules* and *shin spots*. It is seen with the greatest frequency in geriatric men.

The lesions begin as small, dull red, scaly papules and small plaques. They develop into

characteristic multiple, bilateral, circumscribed, round or oval, shallow pigmented scars and/or atrophic hyperpigmented brownish macular lesions with a fine scale, on the pretibial areas.^{9,10}

Although the origin is unclear, previous mechanical trauma or infection may be a precipitating factor. Histologically, early lesions show edema of the papillary dermis, extravasated erythrocytes, and a mild lymphocytic infiltrate.¹¹

The lesions are asymptomatic and require no treatment.

Necrobiosis Lipoidica Diabeticorum (NLD)

NLD is the best known cutaneous marker of DM, although only 0.3% - 1.6% of all patients with DM will have NLD.^{7,12,13} Necrobiosis lipoidica is not confined to diabetics, with almost one third of patients with this cutaneous disorder being nondiabetic.^{9,12} However, patients with necrobiosis lipoidica who had not been diagnosed as diabetic should always be evaluated for DM: NLD may precede the onset of DM in approximately 15% of patients by an average of 2 years; in 25% of patients, both diseases appear concomitantly and in the remainder, NLD appears after DM has been established.¹⁴ NLD occurs most commonly in the third to fourth decade, with the majority of patients being women.

The characteristic lesion of NLD is a slowly enlarging, irregularly contoured plaque; the border is often slightly elevated and has a reddish blue periphery.¹⁵ The central area, at first erythematous, becomes yellow or sclerotic, and resembles glazed porcelain. The plaque often atrophies further and may soften and become entirely brown. Visible telangiectasiae on the surface are common in older lesions (Fig. 1a, 1b; all figures appear on page 39 as Appendix). The histopathologic features observed are degeneration of collagen throughout the dermis, histiocytes in a palisaded arrangement around the degenerated collagen, and obliterative granulomatous vasculitis.^{9,10,14}

The pathogenesis of NLD is still not certain. However, diabetic microangiopathy associated with neuropathy may contribute to the necrobiosis of collagen.¹⁶

The lesions resolve spontaneously in approximately 13% to 19% of cases after 6 to 12 years.^{14,17} Treatment is usually conservative. Protection from injury is important. Topical, injected, and systemic steroids, pentoxifylline, aspirin, dipyridamole and skin grafting have been tried with varying success.¹

Diabetic Thick Skin

Diabetics have been observed to have thicker skin than non-diabetics.¹ There are three forms of diabetic thick skin: (1) scleroderma-like skin changes of the fingers and the dorsum of the hand associated with still joints and limited mobility; (2) clinically inapparent but measurable increased skin thickness as compared with controls, and (3) scleredema adutorum (Buschke).⁹

The thickness is commonly observed on the dorsum of the fingers, palms and soles, and the posterior thorax and neck (Fig. 2). The skin over the fingers and the dorsum of the hand has a shiny appearance, is not easily tented and may appear pebbled (Huntley's papules on the interphalangeal joints), especially the knuckles or rough over the extensor surfaces of the hand. The thickened skin can lead to limited mobility of the hands. This condition has been described in 8% to 50% of patients with Type 1 DM.^{9,18-20} This limitation of joint mobility, in combination with the waxy appearance of the tight skin, is now termed *limited joint mobility and waxy skin syndrome*.²¹

Scleredema adutorum of DM is characterized by a marked increase in dermal thickness on the back and posterior upper neck in older, obese Type 2 diabetic patients with a *peau d'orange* appearance of the involved area.^{7,22-24}

Histologically, the dermis is thickened, with large, swollen collagen bundles separated by clear spaces and small amounts of acid mucopolysaccharides.

The pathogenesis of diabetic thick skin is not clearly known. Possible explanations include the non-enzymatic glycosylation of collagen, which makes it less soluble,²⁵ collagen hydration secondary to polyol accumulation,²⁶ and nonenzymatic glycosylation of albumin resulting in endothelial cell extravasation contributing to the pathogenesis of diabetic microangiopathy.²⁷

There is no known treatment for these conditions.

Yellow Skin

Approximately 2% to 5% of diabetic patients are reported to have a yellow hue to their skin; the cause of this remains in dispute.⁷ The condition is unrelated to hypercarotenemia.²⁸ Possible causes include nonenzymatic glycosylation of dermal collagen and other proteins that eventually become yellow.⁹ This condition is asymptomatic, and has no effective treatment.

Diabetic Bullae

The appearance of spontaneous blisters that are usually confined to the hands and feet in adult men is a rare but specific event in DM.¹⁶ The bullae are often bilateral and contain a clear, sterile, serous fluid with a noninflammatory base. They heal spontaneously within 2 to 5 weeks.^{9,29} Sometimes the bullae are hemorrhagic and heal with atrophy and scarring.

Histologically, the biopsy specimen shows subepidermal cleavage without acantholysis.^{9,30} The type associated with atrophy and scarring shows cleavage below the dermoepidermal junction.¹

Acanthosis Nigricans

Although it may be familial and benign, acanthosis nigricans has long been recognized as a cutaneous marker for systemic conditions such as endocrinopathies (including DM) and malignancy.¹⁵ More recently it has been considered to be a marker for insulin resistance.³¹ The characteristic lesion is a symmetric, brown thickening of the skin. As it continues to thicken, the lesion may develop a leathery, verrucous, papillomatous appearance, with the involved area ranging from small to extensive (Fig. 3a, 3b). Typical locations are the axillae, groin, neck, beltline, umbilicus, mouth and areolae of the breasts, as well as flexural areas. Histopathologic examination shows marked hyperkeratosis and papillomatosis and only mild acanthosis and hyperpigmentation. The lesions are generally asymptomatic and do not require treatment. Retinoic acid may be effective in asymptomatic patients.

Eruptive Xanthomas

Eruptive xanthomas associated with DM are accompanied by hyperlipidemia. The eruption is that of multiple, firm, yellow, waxy papules, ranging from 1 to 4 mm in diameter, appearing in crops on the extensor surfaces, pressure points, and antecubital and popliteal surfaces (Fig. 4a, 4b).³² They may show Koebner's phenomenon. Histopathologic examination of a biopsy specimen reveals lipid-laden histiocytes and a mixed lymphoneutrophilic inflammatory cell infiltrate in the dermis. With correction of hyperlipidemia the lesions involute, sometimes with post-inflammatory hyperpigmentation, and occasionally with scars.

Perforating Disorders

These unusual lesions consist of a transepidermal expression of degenerative material, typically collagen or elastin. The condition is seen almost exclusively in patients with end-stage diabetic nephropathy.³³ The eruption is characterized by hyperkeratotic papules 2 to 10 mm in diameter, often with a keratotic plug. Koebner's phenomenon may occur, and severe pruritus and rubbing can bring about coalescence of papules into plaques. Lesions occur primarily on the legs but may also be found on the trunk and face.

Histologically, perforating dermatoses appear as epidermis encircling a plug of degenerative material (collagen or elastin) with nuclear debris and neutrophils.¹

These lesions have little tendency for spontaneous resolution. Ultraviolet B light has been helpful when used in combination with topical anti-pruritic agents and topical retinoic acid.¹⁰

Pigmented Purpuric Dermatoses

Approximately 50% of patients with diabetic dermopathy, and most with a history of cardiac decompensation, develop *pigmented purpuric dermatoses*, which appear as orange-tannish patches with cayenne pepper spots over the anterior tibial area (Fig. 5a, 5b). These lesions are the result of extravasation of erythrocytes in the superficial vascular plexus.^{9,34}

Granuloma Annulare

Granuloma annulare is another necrobiotic disorder like NLD, which in its localized form

mainly affects nondiabetics but in its generalized form has been associated with DM, occurring in approximately 0.5% to 10% of such patients.^{24,35} The lesions are usually asymptomatic. The characteristic lesion is a ring of small, firm, flesh-colored, sometimes reddish, papules (Fig. 6a, 6b). Histologically, granuloma annulare appears as a focal degeneration of collagen in the upper and mid-dermis, with surrounding palisading histiocytes and multi-nuclear giant cells.¹⁰ No treatment is usually required because the lesions are primarily asymptomatic and frequently resolve spontaneously. Should the lesions become a cosmetic problem and require treatment, they may be injected with corticosteroids.

Rubeosis Faciei

Individuals with DM are prone to develop a reddish complexion secondary to venous engorgement of the superficial vessels of the face. It has been reported in 3% to 59% of patients with diabetes.³⁶ There is no definitive treatment.

Lichen Planus

Lichen planus, possibly an autoimmune related disorder, occurs in 1.6% to 3.8% of the diabetic population.^{24,37,38} Also, an increased incidence of diabetes and abnormalities of insulin response to glucose challenge have been reported in patients with lichen planus. Some dermatologists support the concept of two types of lichen planus, one of an immunologic, the other of a metabolic defect linked to diabetes.³⁹

Lichen planus presents as pruritic, flat-topped, violaceous papular lesions over the flexor aspects of the forearms and wrists, lower legs and lower back (Fig. 7a, 7b). Mucous membranes, including the mouth and genitalia, are involved in two thirds of patients. Typical histologic findings include hyperparakeratosis, with hypergranulosis, acanthosis, and a saw tooth appearance of rete pegs. Antihistamines, topical corticosteroid ointments, and retinoids all have been used to treat lichen planus.

Vitiligo

This autoimmune disorder may appear alone or with increased frequency in Type 1 DM; it is

noted rarely in Type 2 diabetic patients. This is a disease of diminished or absent melanocyte function and manifests as macular areas of depigmentation, most often seen periorificially and on the extensor aspects of extremities (Fig. 8a, 8b). It is asymptomatic. Treatment of vitiligo can be attempted with high potency corticosteroids, but the condition can persist for years or even decades.

Skin Infections Associated with Diabetes Mellitus

As a group, skin infections occur in 20% to 50% of diabetics.^{7,38} The incidence of cutaneous infections in DM shows a close correlation to the mean blood glucose levels. The other predisposing factors for infections in DM are impaired microcirculation, hypohidrosis, and suppression of cell-mediated immunity, especially in ketotic patients.⁴⁰ They are seen more frequently in Type 2 diabetic patients. The infectious lesions may be divided into fungal infections and bacterial infections.

Fungal Infections

Candida infections may be early indicators of undiagnosed DM. *Candida* paronychia commonly involves the nailfold; there may be erythema, swelling, pain, and loss of cuticle (Fig. 9a, 9b). *Candida* infections of the female genitalia accompanied by pruritus vulvae and lesions in the inframammary area and other skin folds are common findings in women with DM. *Candida* balanitis, balanoposthitis, and phimosis may be the presenting manifestations of DM in men (Fig. 10, 11).⁴⁰ Angular stomatitis and median rhomboid glossitis are oral manifestations related to *Candida* infections in diabetics. Treatment for these infections can be accomplished with nystatin powder or ointment applied topically, and sometimes with systemic antifungal agents.

Dermatophyte infections do not show an increased prevalence in diabetics. However, tinea pedis can act as a portal of secondary bacterial invasion and should be treated promptly in diabetics.⁴¹

Bacterial Infections

Common bacterial infections of the diabetic skin, usually caused by *Staphylococcus aureus*

and β -hemolytic streptococci, include impetigo, folliculitis, furunculosis, carbuncles, ecthyma, cellulitis, and erysipelas (Figs. 12-15).⁴⁰ In addition to suitable systemic antibiotic treatment, glycemic control and debridement of devitalized tissues may be indicated. Erythrasma, caused by *Corynebacterium minutissimum* is manifested by tan-red, fine, scaly patches in intertriginous areas (Fig. 16). Extensive erythrasma occurs with increased frequency in obese patients with DM.⁴⁰ Topical or systemic erythromycin is curative.

Cutaneous Complications Associated With Diabetes Mellitus

Macroangiopathy

Atherosclerosis of the arteries of legs in diabetics results in skin atrophy, hair loss, coldness of the toes, nail dystrophy, pallor on elevation, and mottling on dependence.⁴²

Microangiopathy

The role of diabetic microangiopathy is not completely understood. The signs of microangiopathy may include diabetic dermopathy, pigmented purpuric dermatoses, erysipelas like erythema, NLD and diabetic foot.^{9,43} Other signs of diabetic microangiopathy include cutaneous reactive hyperemia and reduced capillary flow on cold or warm challenge of patients with DM, as measured by laser Doppler flowmetry.⁴⁴⁻⁴⁶ The nail changes associated with microangiopathy include Beau's lines, pterygium, splinter hemorrhages, and yellow nail discoloration.⁴⁷

Neuropathy

The cutaneous manifestations of autonomic neuropathy in DM are disturbances in sweating and peripheral hyperemia with erythema, edema, and atrophy.¹⁷

The combination of motor and sensory neuropathy along with mechanical factors and microangiopathy plays a major role in the development of the diabetic foot.⁴³ This condition is characterized by mal perforans, Charcot's foot, and claw toes, in addition to gangrene.

Cutaneous Reactions to Diabetic Treatment

Sulfonylureas, especially the first generation agents like chlorpropamide and tolbutamide, may be associated with hypersensitivity-related cutaneous manifestations of a maculopapular eruption, a morbilliform eruption, erythema, or urticaria-like lesions. These often disappear with continuation of the sulfonylurea therapy. Photosensitivity reactions, lichenoid lesions, and rosacea-like eruptions are also seen. Second generation sulfonylureas rarely cause cutaneous side-effects.⁴⁸

Lipoatrophy and lipohypertrophy, jointly referred to as lipodystrophy, are also related to diabetic therapy. Lipoatrophy occurs at the site of insulin injections, presenting as a depressed circumscribed area of skin (Fig. 17), reflecting possibly a localized immune reaction to the insulin, with associated loss of subcutaneous fat. Lipoatrophy is rarely seen now with the introduction of purified human insulin. Insulin lipohypertrophy presents as soft dermal nodules, often at the site of frequent injections. This is thought to be caused by the lipogenic actions of insulin occurring chronically at the same site.¹⁰

Insulin allergy may be seen in patients receiving insulin injections. It may manifest as a wheal and flare at the injection site or as generalized urticaria or, rarely, anaphylaxis. The newer purified insulins have made these skin side-effects very rare.^{1,10}

References

1. Paron NG, Lambert PW. Cutaneous manifestations of diabetes mellitus. *Prim Care* 2000;27:371-83.
2. Shaltout AA, Moussa MA, Qabazard M, Abdella N, Karvonen M, Al-Khawari M, et al. Further evidence for the rising incidence of childhood Type 2 diabetes in Kuwait. *Diabet Med* 2002;19:522-5.
3. Akanji AO. Diabetic dyslipidaemia in Kuwait. *Med Princ Pract* 2002;11:47-55.
4. Braverman I. Cutaneous manifestations of diabetes mellitus. *Med Clin North Am* 1971;55:1019-29.
5. Hall SE, Sibbald RG. The skin in diabetes mellitus, In: Pickup JC, Williams G, editors. *Chronic complications of diabetes*. Oxford: Blackwell Scientific Publications;1994: p.250-9.
6. Jelinek JD. Skin disorders associated with diabetes mellitus, In: Rifkin H, Porte D, editors. *Ellenberg and Rifkin's Diabetes Mellitus: Theory and Practice*. New York: Elsevier;1990: p.838-49.
7. Yosipovitch G, Hodak E, Vardi P, Shraga I, Karp M, Sprecher E, et al. The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications. *Diabetes Care* 1998;21:506-9.
8. Bernstein JE. Cutaneous manifestations of diabetes mellitus. *Curr Concepts Skin Dis* 1980;1:3-10.
9. Huntley AC. Cutaneous manifestations of diabetes mellitus. *Dermatol Clin* 1989;7:531-46.
10. Sibbald RG, Landolt SG, Toth D. Skin and diabetes. *Endocrinol Metab Clin North Am* 1996;25:463-72.
11. Bauer M, Levan NE. Diabetic dermangiopathy: a spectrum including pretibial pigmented patches and necrobiosis lipoidica diabetorum. *Br J Dermatol* 1970;83:528-35.
12. Muller SA. Dermatologic disorders associated with diabetes mellitus. *Mayo Clin Proc* 1966;41:689-703.
13. Muller SA, Winkelman RK. Necrobiosis lipoidica diabetorum: A clinical and pathological investigation of 171 cases. *Arch Dermatol* 1966;93:272-81.
14. Braverman IM. *Skin signs of systemic disease*. Philadelphia: WB Saunders;1981: p. 654-64.
15. Jelinek JE. Cutaneous manifestations of diabetes mellitus. *Int J Dermatol* 1994;33:605-16.
16. Perez MI, Kohn SR. Cutaneous manifestations of diabetes mellitus. *J Am Acad Dermatol* 1994;30:519-31.
17. Huntley AC. The cutaneous manifestations of diabetes mellitus. *J Am Acad Dermatol* 1982;7:427-55.
18. Fitzcharles MA, DUBY S, Waddell RW, Banks E, Karsh J. Limitation of joint mobility (cheiroarthropathy) in adult noninsulin-dependent diabetic patients. *Am Rheum Dis* 1984;43:251-7.
19. Garza-Elizondo MA, Diaz-Jouanen E, Franco-Casique JJ, Alarcon-Segovia D. Joint contractures and scleroderma-like skin changes in the hands of insulin-dependent juvenile diabetes. *J Rheumatol* 1988;10:797-800.
20. Rosenbloom AL. Limited joint mobility in insulin dependent childhood diabetes. *Eur J Pediatr* 1990;149:380-8.

21. Rosenbloom AL, Silverstein JH. Connective tissue and joint disease in diabetes mellitus. *Endocrinol Metab Clin North Am* 1996;25:473-83.
22. Cole GW, Headley J, Skowsky R. Scleroderma diabeticorum: A common and distinct cutaneous manifestation of diabetes mellitus. *Diabetes Care* 1983;6:189-92.
23. Hanna W, Friesen D, Bombardier C, Gladman D, Hanna A. Pathologic features of diabetic thick skin. *J Am Acad Dermatol* 1987;16:546-53.
24. Jelinek JE. The skin in diabetes. *Diabet Med* 1993;10:201-13.
25. Buckingham BA, Uitto J, Sandborg C, Keens T, Roe T, Costin G, et al. Scleroderma-like changes in insulin dependent diabetes mellitus: clinical and biochemical studies. *Diabetes Care* 1984;7:163-9.
26. Eaton PR. The collagen hydration hypothesis: a new paradigm for the secondary complications of diabetes mellitus. *J Chron Dis* 1986;39:753-66.
27. Williams SK, Devenny JJ, Bitensky MW. Micropinocytic ingestion of glycosylated albumin by microvessels: possible role in pathogenesis of diabetic microangiopathy. *Proc Natl Acad Sci USA* 1981;78:2393-7.
28. Hoerer E, Dreyfuss F, Herzberg M. Carotenemia, skin color, and diabetes mellitus. *Acta Diabetol Lat* 1975;12:202-7.
29. Rocca F, Pereyrae E. Phlyctenular lesions in the feet of diabetic patients. *Amer Diet Assoc* 1963;12:220-2.
30. Toonstra J. Bullosis diabeticorum: Report of a case with review of the literature. *J Am Acad Dermatol* 1982;13:799-805.
31. Kahn CR, Flier JS, Bar RS, Archer JA, Gorden P, Martin MM, et al. The syndromes of insulin resistance and acanthosis nigricans. Insulin-receptor disorders in man. *N Eng J Med* 1976;294:739-45.
32. Cruz PO, East C, Berstreser PR. Dermal, subcutaneous and tendon xanthomas: diagnostic markers for specific lipoprotein disorders. *J Am Acad Dermatol* 1988;19:95-111.
33. Rapini RP. Acquired perforating dermatosis: Evidence for combined transepidermal elimination of both collagen and elastic fibres. *Arch Dermatol* 1989;125:1074-8.
34. Lither F. Purpura, pigmentation, and yellow nails of the lower extremities in diabetes. *Acta Med Scand* 1976;199:203-8.
35. Muhlemann MF, Williams DRR. Localized granuloma annulare is associated with insulin-dependent diabetes mellitus. *Br J Dermatol* 1984;111:325-9.
36. Gitelson S, Wertheimer-Kaplinski N. Color of the face in diabetes mellitus: Observations on a group of patients in Jerusalem. *Diabetes* 1965;14:201-8.
37. Lozada-Nur F, Luangjarmekorn L, Silverman S Jr, Karam J. assessment of plasma glucose in 99 patients with oral lichen planus. *J Oral Med* 1985;40:60-1.
38. Romano G, Moretti G, Di Benedetto A, Giofre C, Di Cesare E, Russo G, et al. Skin lesions in diabetes mellitus: Prevalence and clinical correlations. *Diabetes Research and Clinical Practice* 1998;39:101-6.
39. Lisi P, Giommoni U. A study on the carbohydrate metabolism in lichen planus patients in time. *Ann Ital Dermatol Clin* 1983;37:29-33.
40. Meurer M, Szeimies RM. Diabetes mellitus and skin diseases. *Curr Probl* 1991;20:11-23.
41. Lugo-Somolinos A, Sanchez JL. Prevalence of dermatophytosis in patients with diabetes. *J Am Acad Dermatol* 1991;26:408-10.
42. Haroon TS. Diabetes and skin: a review. *Scott Med J* 1974;19:257-67.
43. Grunfeld C. Diabetic foot ulcers: etiology, treatment, and prevention. *Adv Intern Med* 1991;37:103-32.
44. Tur E, Yosipovitch G, Bar-On Y. Skin reactive hyperemia in diabetic patients: a study by laser Doppler flowmetry. *Diabetes Care* 1991;14:958-62.
45. Rendell M, Bamisedun O. Diabetic cutaneous microangiopathy. *Am J Med* 1992;93:611-8.
46. Mitchell WS, Winocour PH, Gush RJ, Taylor LJ, Baker RD, Anderson DC, et al. Skin blood flow and limited joint mobility in insulin-dependent diabetes mellitus. *Br J Rheum* 1989;28:195-200.
47. Greene RA, Scher RK. Nail changes associated with diabetes mellitus. *J Am Acad Dermatol* 1987;16:1015-21.
48. Wilkin JK. Flushing reactions: Consequences and mechanisms. *Ann Intern Med* 1981;95:468-76.

CME/CPD Questions

After you have completed reading the article *Skin diseases seen in diabetes mellitus*, take the test given below. Circle T (True) or F (False) in the answer sheet (page 54) to show the correct answer to each question. Questions 11 to 20 are related to the content in this article.

11. Cutaneous manifestations of diabetes mellitus are seen only with Type 2 diabetes mellitus.
12. Cutaneous manifestations of diabetes develop only subsequent to the development of diabetes mellitus.
13. Diabetic dermopathy manifests with painful ulcers.
14. Necrobiosis lipoidica is seen only in diabetics.
15. Diabetic patients may develop waxy skin and limited joint mobility.
16. Diabetic bullae show acantholysis as in pemphigus vulgaris.
17. Acanthosis nigricans seen in diabetics is never a marker for insulin resistance.
18. The perforating disorder seen in diabetics does not show Koebner's phenomenon.
19. Granuloma annulare and necrobiosis lipoidica are both necrobiotic disorders.
20. Cutaneous infections are seen more frequently in Type 1 diabetic patients compared to Type 2 patients.