Cutaneous Manifestations of Systemic Diseases

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Objectives

- To highlight the relation between skin manifestations and common systemic disorders
- To understand various skin clues and their importance in investigating and managing different systemic disease

Cutaneous manifestations of endocrine diseases

- Diabetes mellitus
- Thyroid diseases
- Cushing's syndrome
- Addison's disease

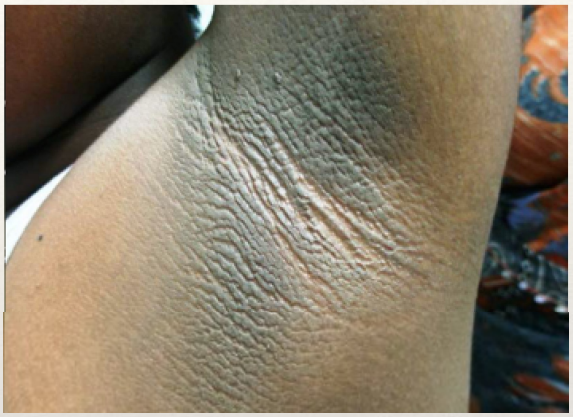
Diabetes Mellitus

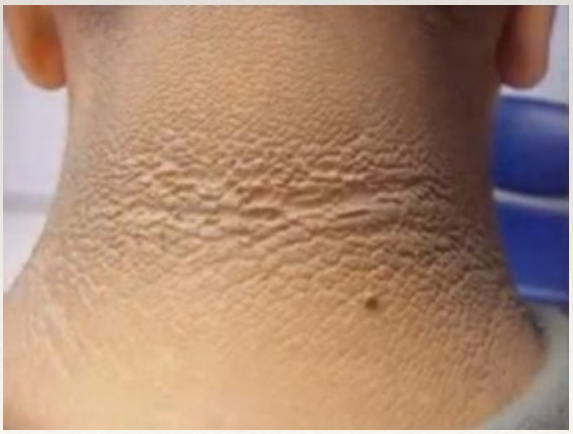
Diabetes Mellitus

- Acanthosis Nigricans
- Acrochordrons " skin tags"
- Diabetic Dermopathy
- Necrobiosis Lipodica Diabeticorum
- Bullous Diabeticorum
- Scleredema Diabeticorum
- Acquired Perforating Dermatosis
- Bacterial and Fungal infections

Acanthosis Nigricans

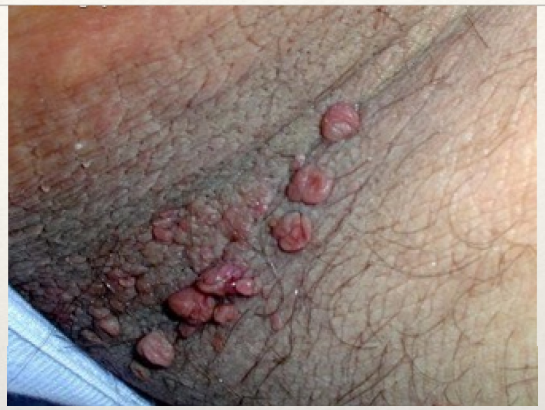
- A skin condition characterized by hyperpigmented velvety plaques in body folds and creases
- It's an indicator of insulin resistance
- High concentrations of insulin stimulate keratinocytes and dermal fibroblasts through high affinity binding to insulin-like growth factor 1 (IGF-1)
- Treatment- weight reduction and reducing insulin resistance

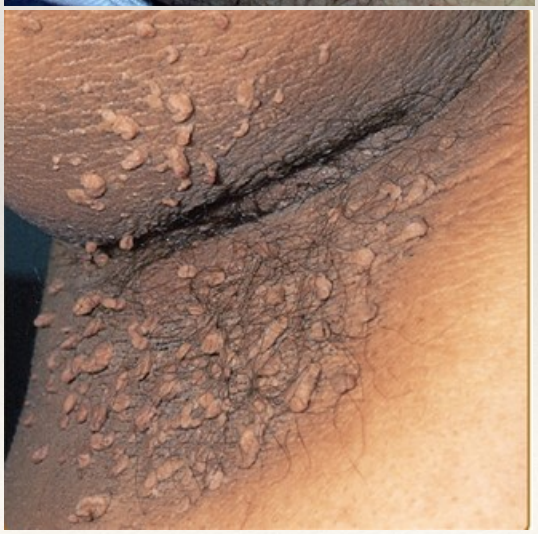




Acrochordrons " Skin Tags"

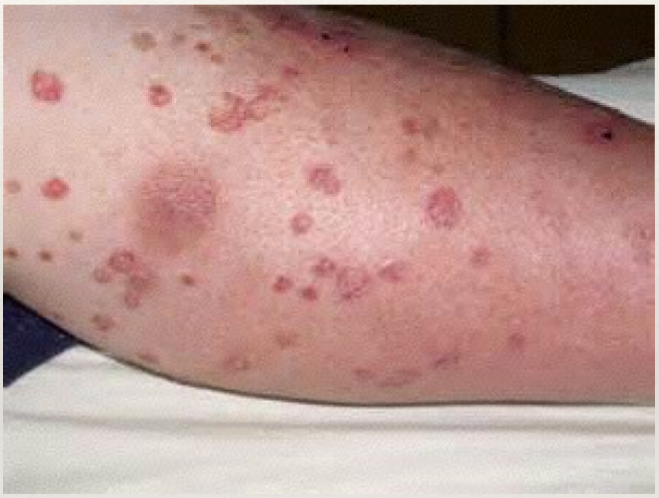
- Small, skin colored, pedunculate papules commonly occur on the neck and also frequently seen in the axilla and on the eyelids.
- Mostly associated with obesity and insulin resistance
- May be related to the growth hormone-like activity of insulin
- If numerous, usually on top of acanthosis nigricans





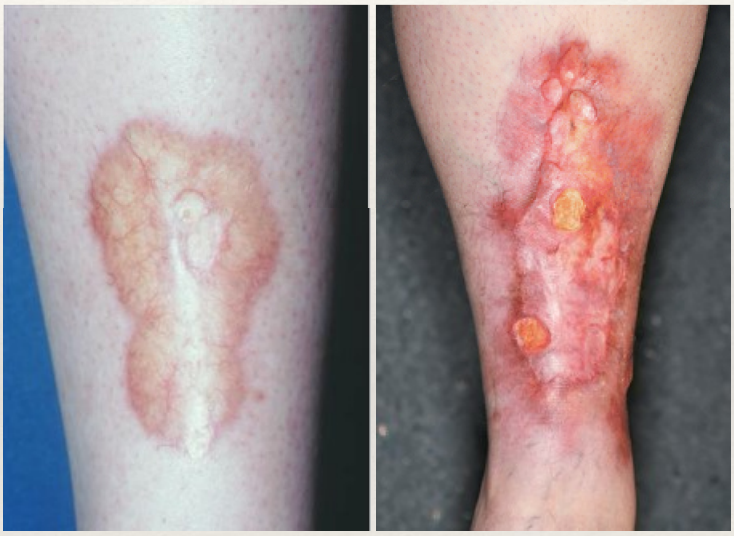
Diabetic Dermopathy

- Most common cutaneous sign of diabetes
- starts as red papules, that progress to atrophic, hyperpigmented papules and plaques on the shins
- Possibly related to diabetic neuropathic and vascular complications
- They usually do not require treatment and tend to go after a few years with improved blood glucose control



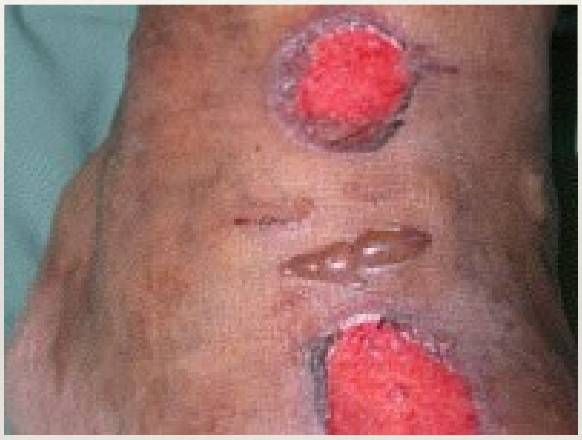
Necrobiosis Lipodica Diabeticorum

- Start as erythematous papules over the pretibial area, and evolve into yellowish-brown plaques, with dilated blood vessels and central epidermal atrophy
- Sometimes they ulcerate
- Histopathology shows a granulomatous reaction
- Treatment-topical and intralesional steroids, tacrolimus, phototherapy, cyclosporine



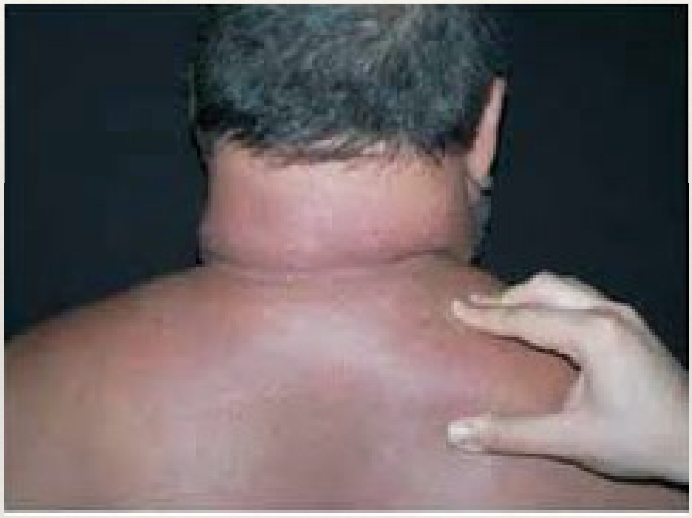
Bullous Diabeticorum

- Rare
- Distinct marker of diabetes
- Spontaneous blister-like lesions on the hands and feet
- Heals spontaneously without scarring



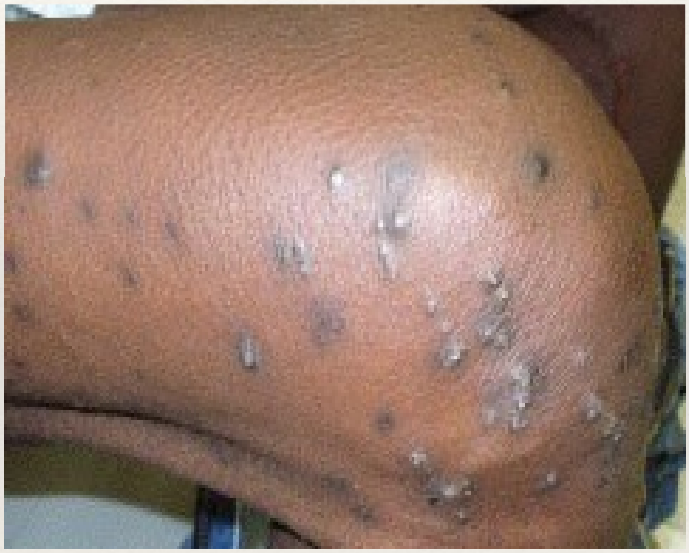
Scleredema Diabeticorum

- More common in males, often obese, with longstanding, uncontrolled diabetes, that have frequently suffered complications of diabetes (neuropathy, nephropathy, retinopathy, atherosclerosis)
- Presents as woody induration and thickening of the skin of the mid upper back, neck, and shoulders
- Control of diabetes does not affect the course of scleredema



Acquired Perforating Dermatosis

- It's a skin disorder occurring in patients with chronic renal failure, diabetes mellitus, or both
- They are characterized by the transepidermal elimination of both collagen and elastic fibers
- Pathogenesis is unknown
- They present as 2 to-10 mm, firm, hyperkeratotic, often umbilicated papules occurring on the trunk and extremities
- Treatment- topical keratolytics, phototherapy, topical/systemic retinoids, topical/intralesional steroids, oral antihistamines, cryotherapy



Bacterial and Fungal infections

- Patients with uncontrolled DM and ketosis are more susceptible to develop severe systemic and cutaneous infections

Bacterial infections

- Usually caused by staphylococcus aureus and beta-hemolytic streptococci: styes, folliculitis, fruncles, carbuncles, infections around the nails, impetigo, erysipelas, cellulitis, and necrotizing fasciitis
- Corynebacteria minutissimum- erythrasma
- Pseudomonas aeruginosa- malignant otitis externa

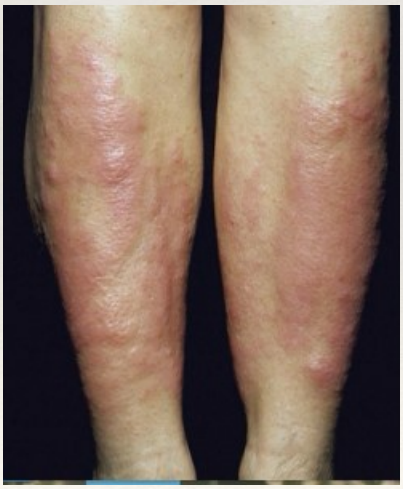
Fungal infections

- Candida- often occur in warm, moist folds of the skin, (under the genitocrural folds, nail folds, web spaces of fingers and toes, corners of the mouth, armpits)
- Tinea pedis, tinea cruris, tinea corporis, onychomycosis,
- Rhinocerebral mucormycosis- extensive, life threatening infection, beginning in the nasal passages and spreading into the orbit and cerebrum

Thyroid Diseases

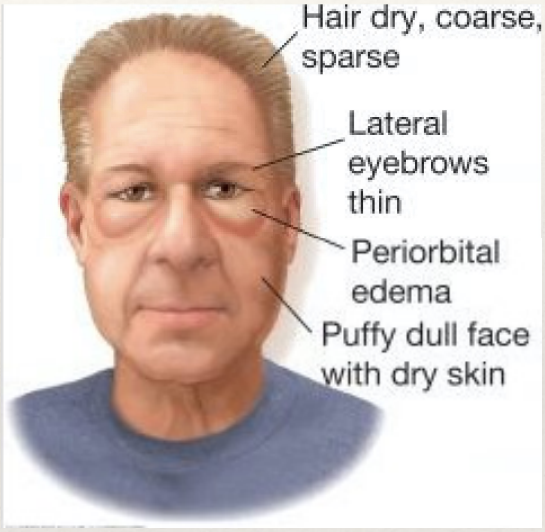
Hyperthyroidism

- Warm, moist skin
- Palmoplantar hyperhidrosis
- Pruritis
- Diffuse, non-scarring alopecia
- Facial flushing
- Hyperpigmentation of the skin/vitiligo
- Nail changes- plummers nails —> concave contour and distal onycholysis
- Pretibial myxedema- it's the most characteristic feature of thyrotoxicosis, presents as shiny, waxy papules and plaques that has an orange-skin appearance on the chin of the tibia



Hypothyroidism

- Coarse, rough, dry skin
- Pallor
- Pruritis
- Carotenemia
- Diffuse hair loss
- Loss of the lateral 1/3 of the eyebrow
- Myxedematous facies
- Autoimmune diseases- vitiligo, alopecia areata



Cushing's Syndrome

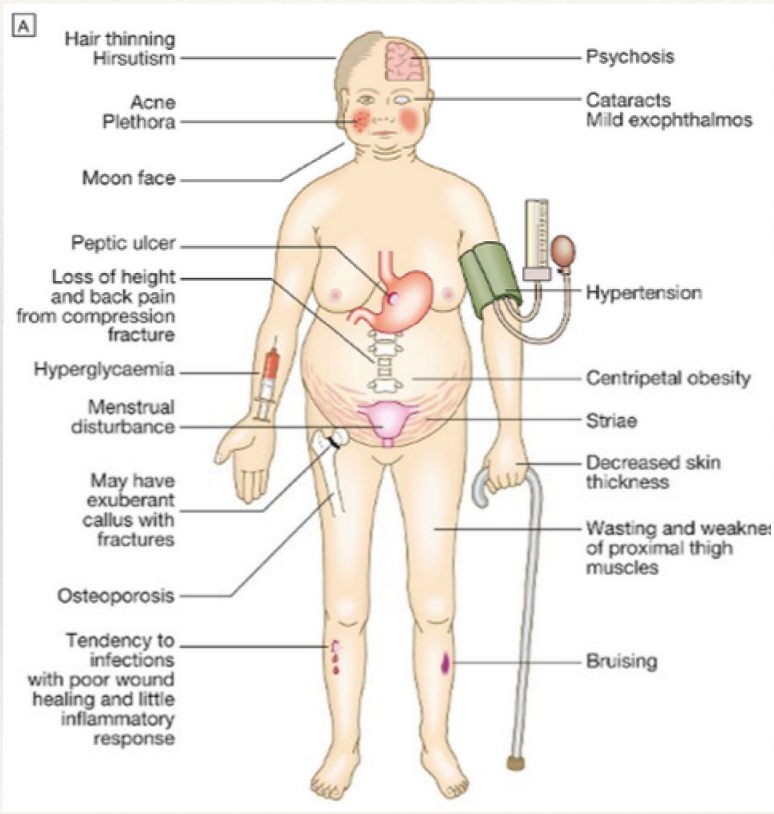
- Cushing's syndrome occurs when there is an excess of cortisol in the body
- Causes:
    - The pituitary gland releasing too much ACTH
    - The adrenal glands releasing too much cortisol
    - Patients taking large doses of glucocorticoids (e.g. asthma, RA)

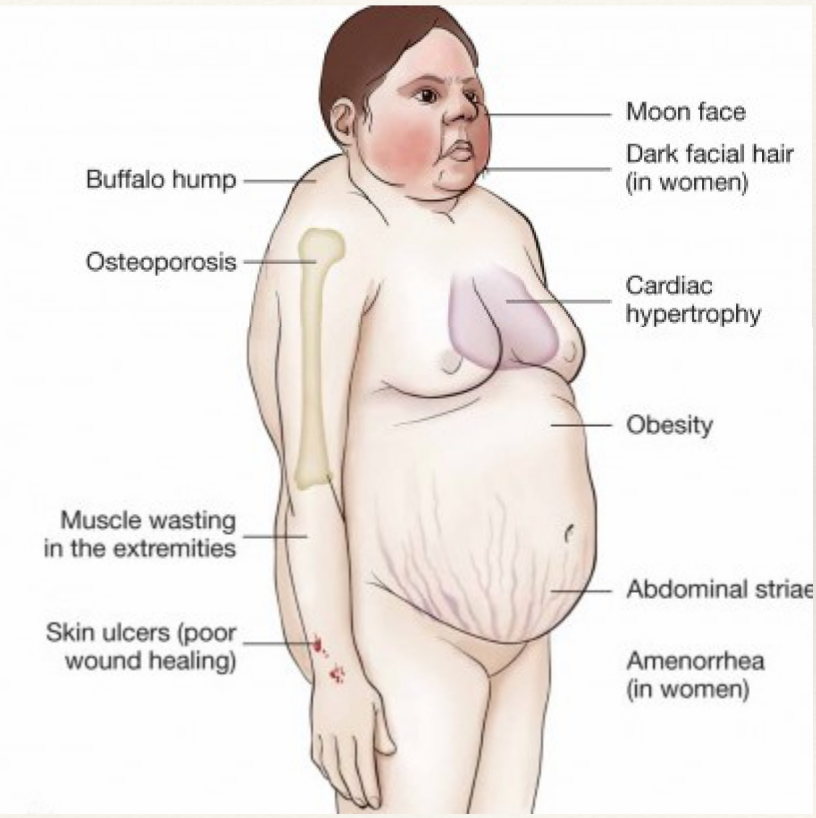
Normal or high blood ACTH levels- pituitary adenomas " **Cushing's disease**", ectopic ACTH syndrome

Low blood ACTH levels- medications that contain glucocorticoids (prednisone) mimics effects of cortisol. Inhaled or topical forms, can cause Cushing's syndrome

- Weight gain
- Skin changes -thin, fragile skin, increased susceptibility to infections, poor wound healing, striae, redistribution of fat (moon faces, buffalo hump, central obesity), hirsutism, acne
- Menstrual irregularities
- Muscle loss and weakness
- Osteoporosis
- Glucose intolerance
- High blood pressure
- Cardiovascular disease
- Psychological symptoms
- Hypercoagulability

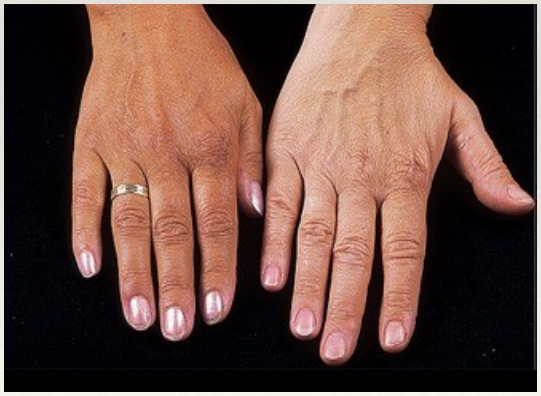
Cushing's Syndrome





Addison's Disease

- Adrenocortical insufficiency due to the destruction or dysfunction of the adrenal cortex
- Hyperpigmentation of the skin & mucous membranes is considered a hallmark of Addison's disease
- Oral mucous membrane hyperpigmentation is pathognomonic for the disease
- The hyperpigmentation is caused by high levels of circulating ACTH that binds to the **melanocortin 1** receptor on the surface of dermal melanocytes

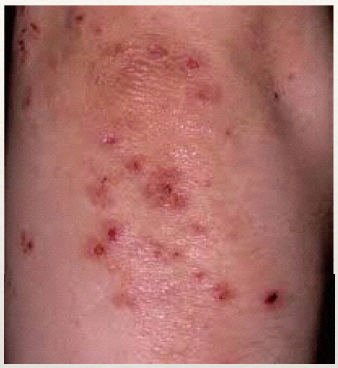


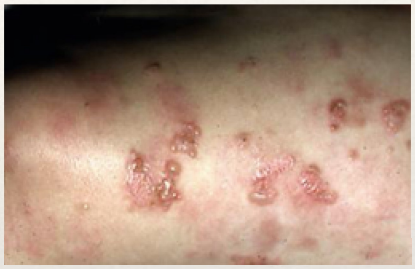
Cutaneous Manifestations of Gastrointestinal Diseases

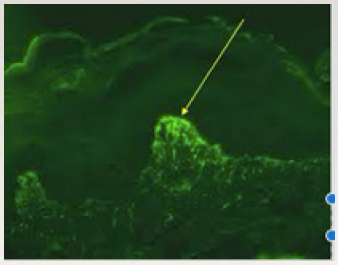
- Dermatitis herpetiformis
- Acrodermatitis enteropathica
- Pyoderma gangrenosum
- Peutz Jeghers syndrome
- Porphyria cutanea tarda
- Hemochromatosis
- Liver cirrhosis

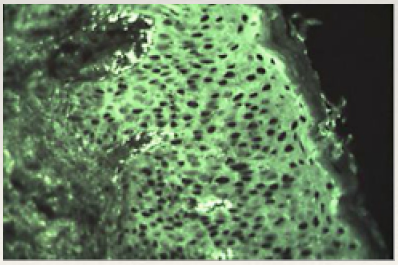
Dermatitis Herpetiformis

- An autoimmune blistering disorder that is often associated with a gluten-sensitive enteropathy
- Small, severely pruritic, clustered vesicular papules or plaques that are symmetrically distributed over the extensor surfaces (elbows, knees, buttocks and shoulders)
- Worsening of the disease with dietary intake of gluten
- Is considered as the cutaneous manifestation of celiac disease (also known as " gluten sensitive enteropathy" caused by the inability to absorb gluten from the diet)
- Direct immunofluorescence of precessional skin shows granular IgA deposits in dermal papillae



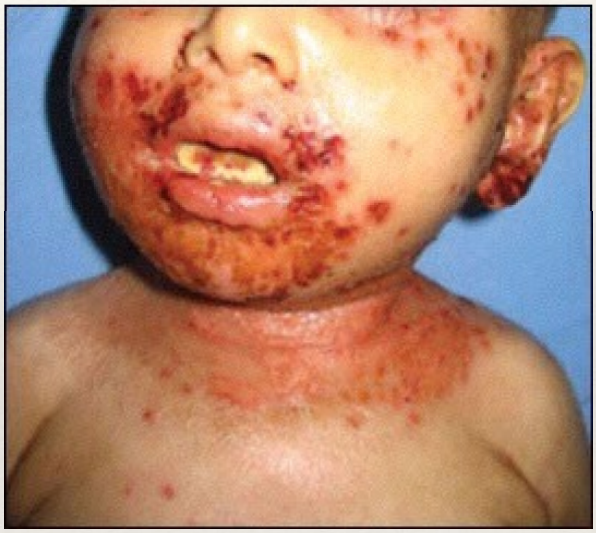






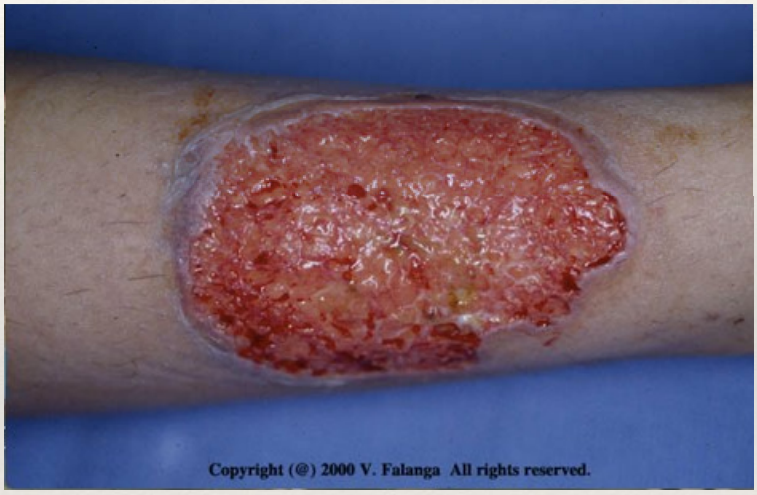
Acrodermatitis Enteropathica

- A rare autosomal recessive disorder that impairs dietary zinc absorption in the jejunum and ileum
- The features of the disease usually starts manifesting as an infant is weaned from breast milk
- Characterized by periorificial and acral **dermatitis**, **alopecia**, and **diarrhea**
- Scaly erythematous patches and plaques similar to atopic dermatitis, but progress to vesicles, crusts, erosions, and pustules on the acral, preioral and perianal areas
- Treatment- lifelong dietary zinc supplementation



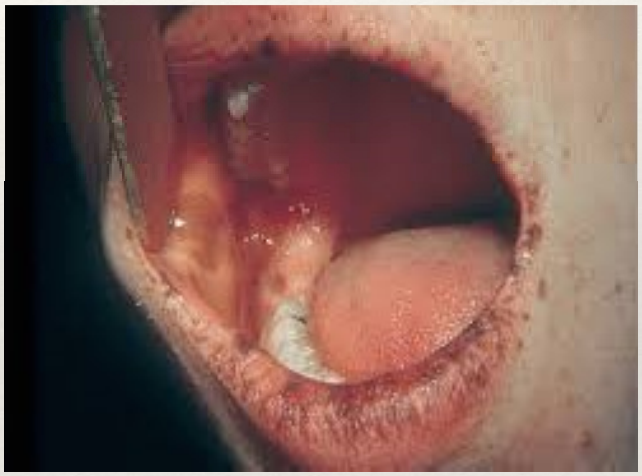
Pyoderma Gangrenosum

- Painful ulcerative lesion with a well-defined undermined violaceous border
- Starts as a small red papule or pustule, that subsequently burst and expand to form a large non-infectious ulcer
- +ve pathergy test
- Mostly associated with ulcerative colitis. Also associated with Crohn's disease, rheumatoid arthritis, and leukemia
- Surgery is contraindicated



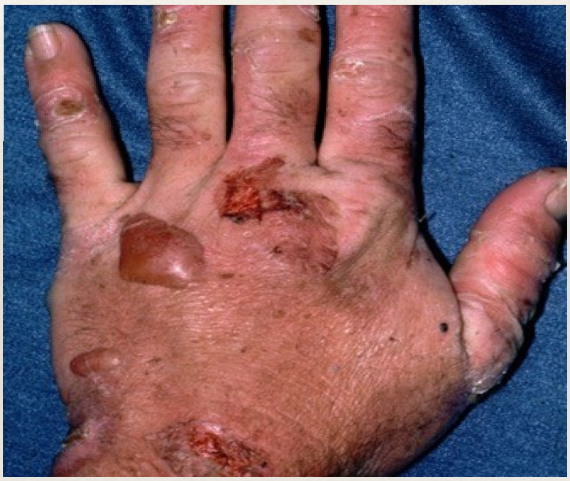
Peutz-Jeghers Syndrome

- Autosomal dominant disorder characterized by hyperpigmentation of the skin and mucous membranes along with intestinal hamartomatous polyps (mostly jejunum)
- The skin findings first appear in infancy or early childhood, and involve brown macules on the lips and buccal mucosa
- It entails a significant overall increased lifetime risk of intestinal and extraintestinal malignancy as well as increased risk of malignancy in younger individuals



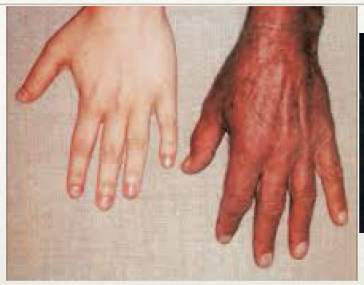
Porphyria Cutanea Tarda

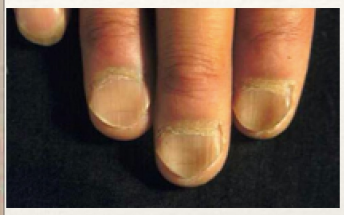
- Porphyria is a group of inherited metabolic disorder resulting from a deficiency of an enzyme in the heme production pathway resulting the overproducing of toxic heme precursors
- Porphyria cutanea tarda is the most common porphyria occurring in adults
- Results from " uroporphyrinogen decarboxylase" deficiency
- Photosensitivity, skin fragility of sun-exposed skin after mechanical trauma, leading to erosions and bullae typically on the hands and other skin exposed areas
- Healing of crusted erosions and bullae leaves milia, hyperpigmentation, and atrophic scars
- Facial hypertrichiosis
- Frequently associated with hepatitis C infection
- Treatment- the goal is to reduce serum ferritin levels to the lower limit of the reference range (avoid iron supplementation, phlebotomy, hydroxychloroquine), sun avoidance

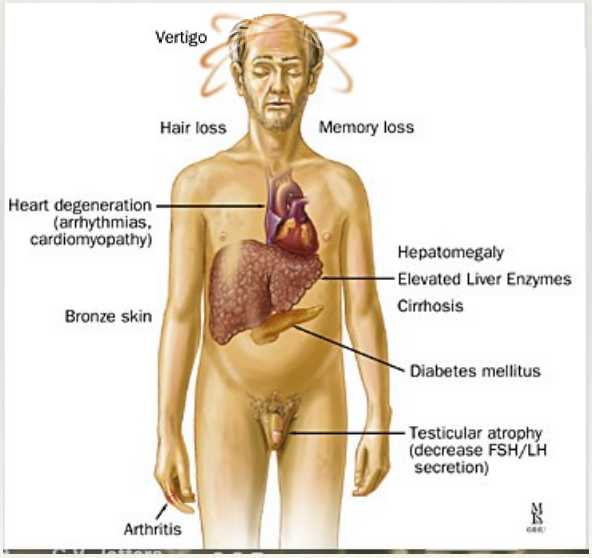


Hemochromatosis

- It's an autosomal recessive disorder characterized by the abnormal accumulation of iron in several organs leading to organ toxicity
- Cutaneous pigmentation- is one of the earliest signs of the disease, most pronounced on sun-exposed skin, particularly the face, brownish bronze or, at times, slate gray
- Other skin changes- ichthyosis-like changes, koilonychia, and hair loss (mostly over pubic area)
- Treatment- the goal of therapy is to remove the iron before it can produce irreversible damage
  - phelebotomy
  - chelation therapy
  - surgery indicated when there is :
    1. end-stage liver disease/hepatocellular carcinoma
    2. severe arthropathy

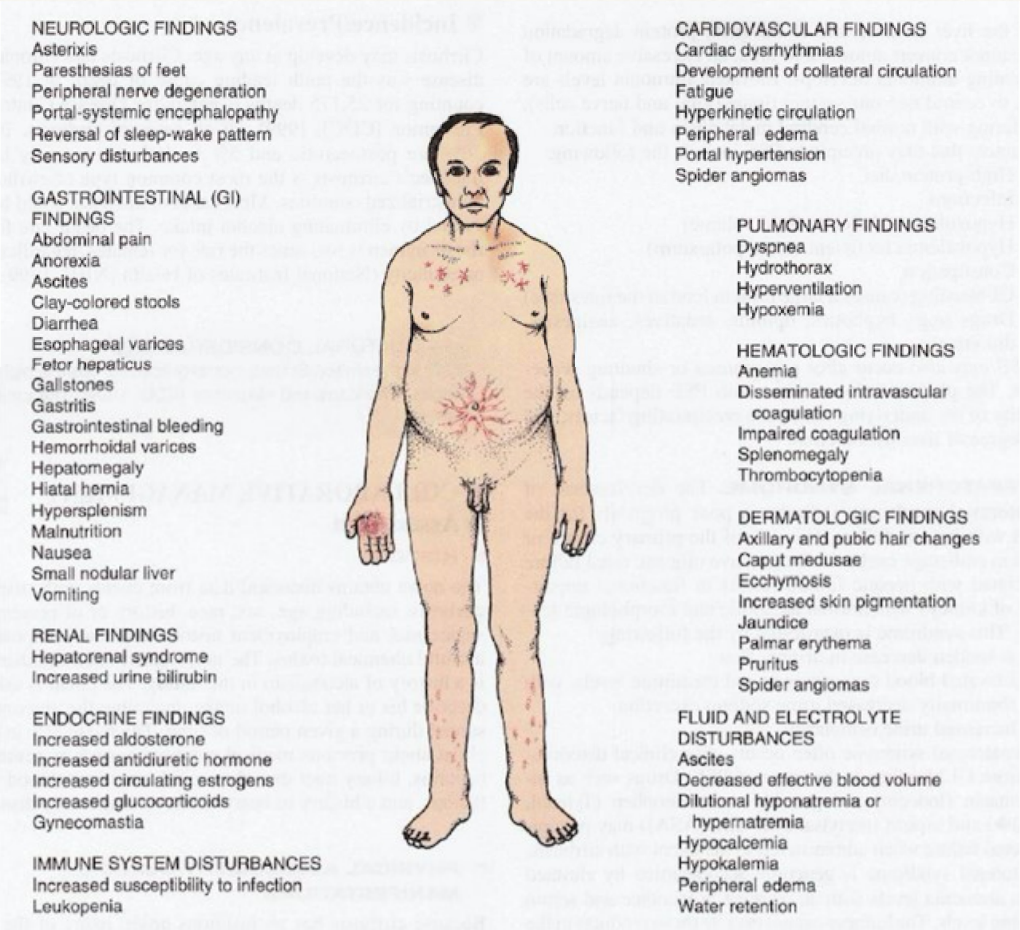






Liver Cirrhosis

- Jaundice
- Pruritis
- Spider angioma
- Palmar erythema
- Purpura
- Petechiae
- Caput medusa
- Loss of body hair



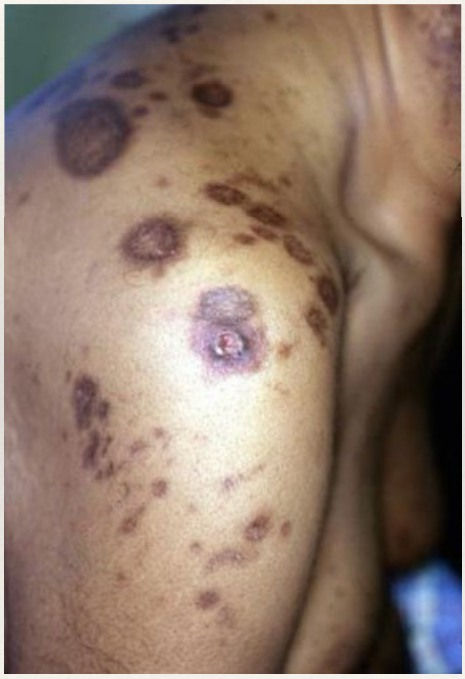
Cutaneous Manifestations of Renal Disease

- Manifestations associated with uremia
- Nephrogenic systemic fibrosis

Manifestations associated with uremia

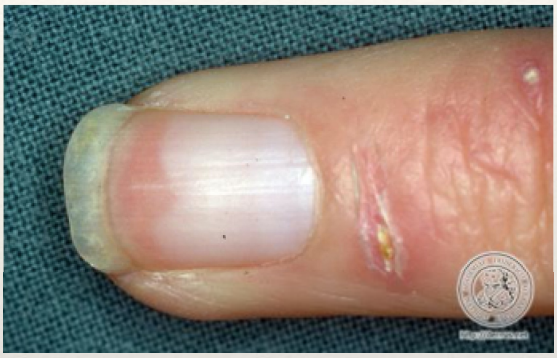
- **Xerosis:**
  - occurs in 50-90% of dialysis patients
  - some develop acquired ichthyosis
  - the exact cause of xerosis in ESRD is unknown
  - Many patients respond to routine use of emollients

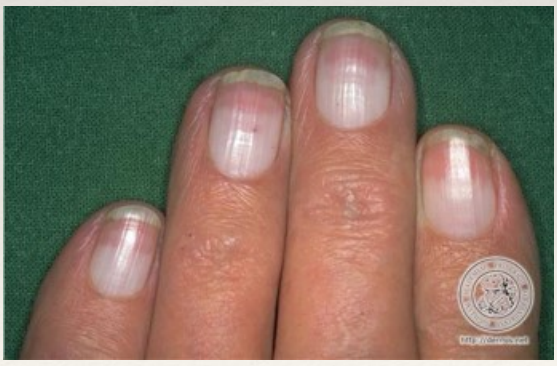
- **Pruritus:**
  - uremia is the most common metabolic cause of pruritus
  - pruritus affects 15-49% of patients with CRF, and 50-90% of the dialysis population
  - cutaneous manifestations of pruritus include excoriations, prurigo nodularis, lichen simplex chronicus
  - resolves after transplantation
  - treatment- sedating antihistamines, emollients, phototherapy, thalidomide, gabapentin



Manifestations associated with uremia

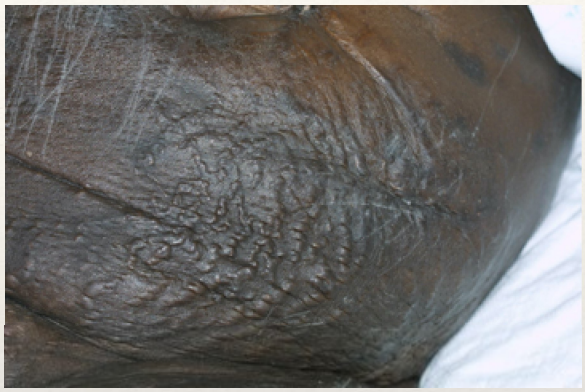
- **Half-and-Half nails:**
  - Although not pathognomonic for renal failure, it occurs in around 40% of patients on dialysis
  - Disappears several months after successful renal transplantation
  - Dark (reddish-brown) distal band and a white proximal band
  - more commonly involves fingernails, but could be seen on toenails

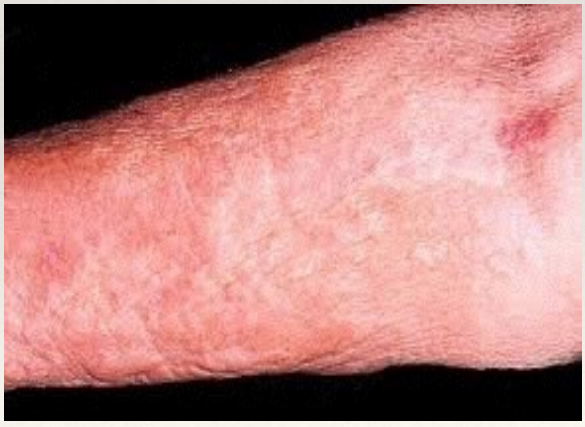




Nephrogenic Systemic Fibrosis

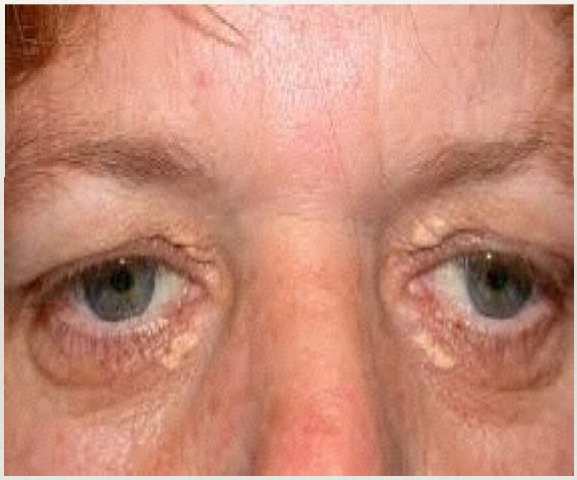
- It's a disease of fibrosis of the skin and internal organs similar to scleroderma
- It's caused by **gadolinium** exposure used in imaging patients who have **renal insufficiency**
- Large areas of thick, indurated skin with fibrotic nodules and plaques on the extremities and trunk
- Treatment- extracorporeal photopheresis, immunosuppressive therapy, phototherapy, IVIG, topical steroids





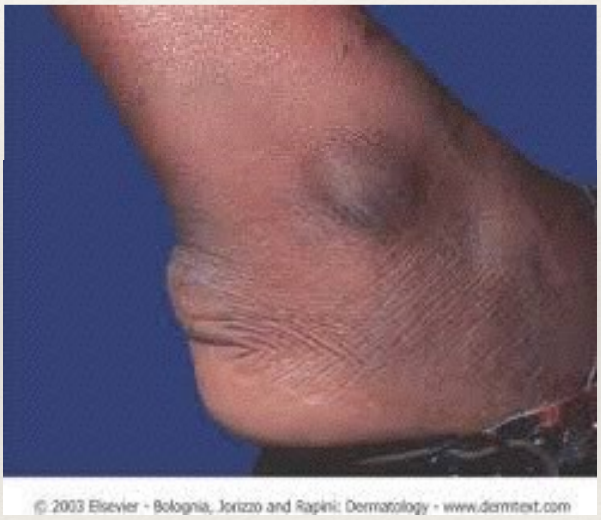
Cutaneous Manifestations of Hyperlipidemia

- **<u>Xanthelasma Palpebrarum:</u>**
  - most common cutenaous xanthoma
  - occurs most commonly near the inner canthus, more often on the upper eyelid than the lower lid
  - Asymptomatic and usually bilateral and symmetric
  - Can be associated with any type of primary hyperlipoproteinemia, but can also occur without hyperlipidemia
  - Treatment- surgical excision, Co2 laser ablation, chemical cauterization (tricoloroacetic acid), electrodesiccation, cryotherapy



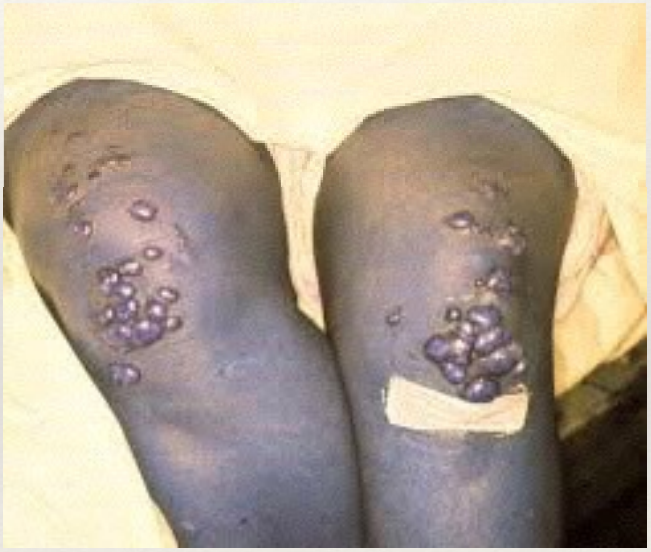
Cutaneous Manifestations of Hyperlipidemia

- **Tendinous Xanthomas:**
  - Commonly seen on the Achilles tendon, followed by the hands, feet, elbows , and knees
  - The least responsive to treatment
  - Mostly seen in patients with familial hypercholesterolemia



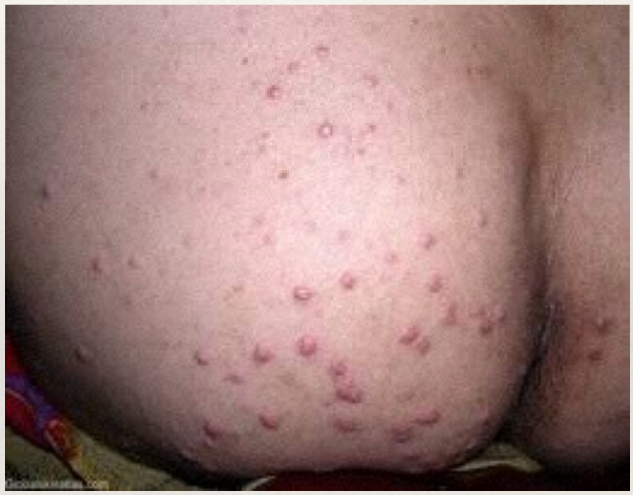
Cutaneous Manifestations of Hyperlipidemia

- **Tuberous Xanthomas:**
  - firm, nontender, cutaneous and subcutaneous yellowish nodules on the extensor surfaces
  - Mostly associated with familial dyslipoproteinemia
  - May resolve after months of treatment with lipid lowering agents



Cutaneous Manifestations of Hyperlipidemia

- **Eruptive Xanthomas:**
  - painless, yellowish papules on an erythematous base, that present as grouped lesions on the trunk, elbows, and buttocks
  - Usually associated with hypertriglyceridemia
  - could be seen in poorly controlled diabetes and acute pancreatitis
  - usually resolves in few weeks after therapy



Cutaneous Manifestations of Hyperlipidemia

- **Planar Xanthomas:**
  - elevated cutaneous yellowish-orange deposits on planar creases
  - usually associated with dysbetalipoproteinemia