# Cutaneous Manifestations of Internal Disease

Emily Reynolds, RN, MSN, FNP-BC, DCNP

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## Disclosures

I have no financial interests to disclose.

Some treatments I will talk about are “off-label.” However, they are generally accepted as treatments in the dermatology community with supporting evidence-based research.

## Objectives

- Describe various skin findings that are associated with different internal diseases.
- Identify a collage of cutaneous findings that could indicate genetic conditions such as neurofibromatosis or tuberous sclerosis.
- Identify cutaneous findings associated with malignancy or malignant genetic disorders.

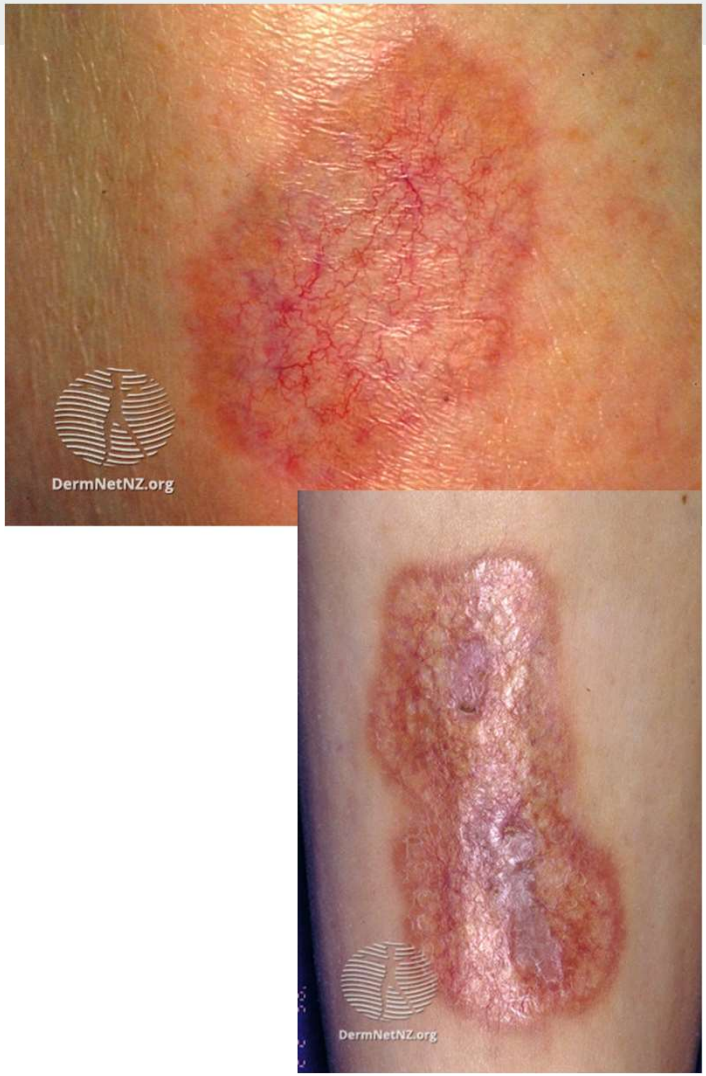
# Necrobiosis lipoidica

# Necrobiosis lipoidica

- Cause is unknown
- History of diabetes in about  75% of cases
- Granulomatous disorder - inflammatory granulomatous changes with collagen degradation on pathology
- Usually patients in their 30s-40s
- Females>Males
- Chronic

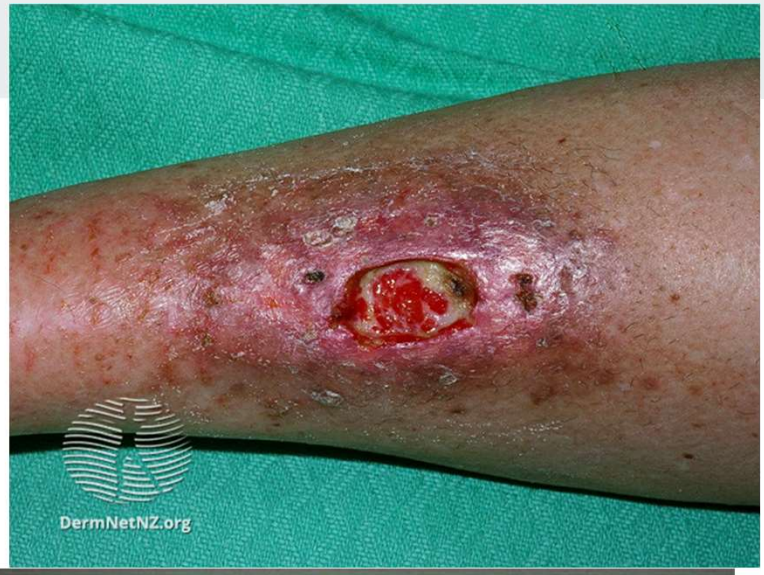
## Presentation

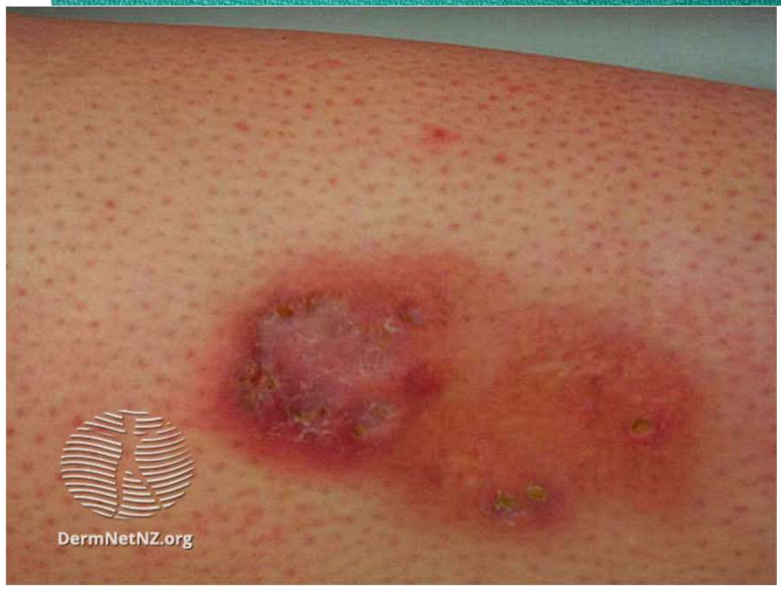
- Occurs mainly on the lower legs
- Yellowish and erythematous, shiny, smooth, patches or plaques
- May see central atrophy or ulcerations in the plaques
- Asymptomatic or tender



# DDX and Treatment

- DDX: Sarcoidosis, Granuloma Annulare, Pyoderma Gangrenosum
- Topical steroids (Clobetasol)
- Intralesional triamcinolone injections
- Tacrolimus ointment
- Case studies only: Pentoxifylline 400 mg three times a day x 1 month.
  - Some recommendations are to use this up to 6 mos:
    https://pubmed.ncbi.nlm.nih.gov/14759079/



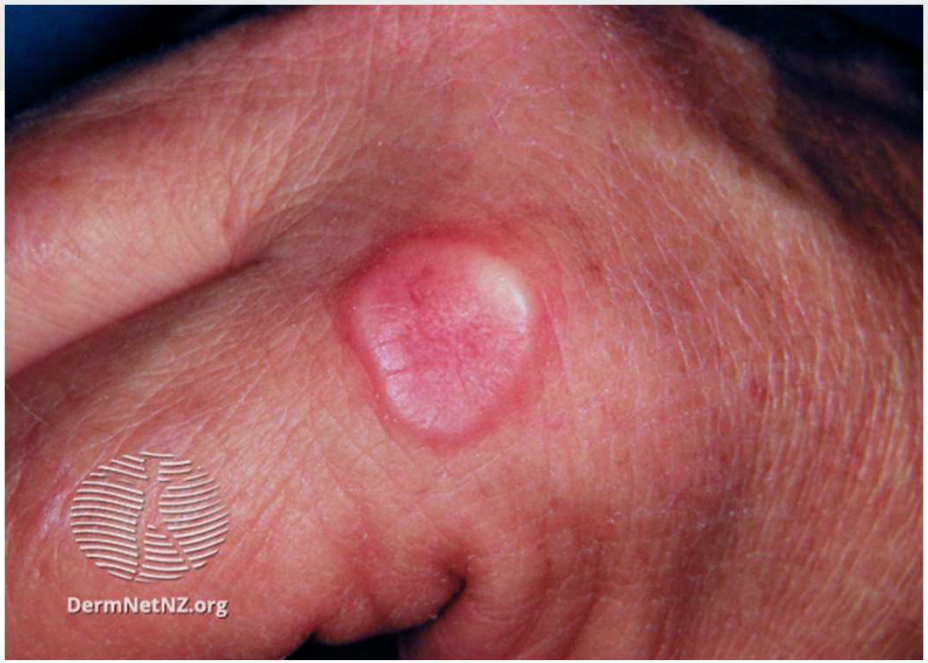
# Granuloma Annulare

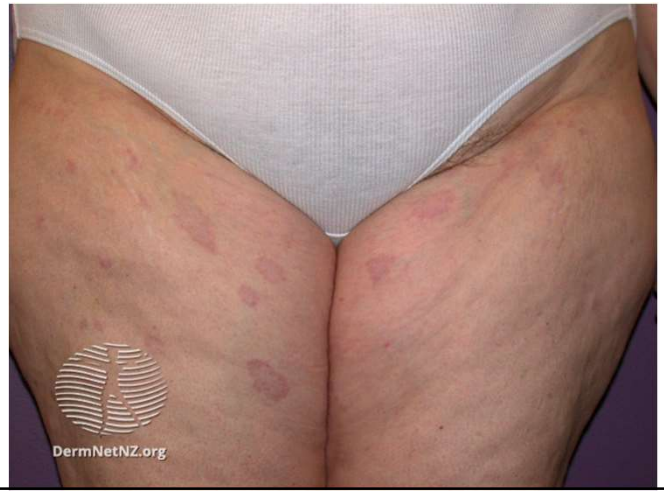
## Granuloma Annulare (GA)

- Can be associated with diabetes or autoimmune thyroiditis
- Generalized GA can be associated with HIV
- Females>males
- Can be chronic or resolve on its own over time (months to years)
- Most common locations: hands, elbows, forearms, feet, ankles
- Granulomatous disorder

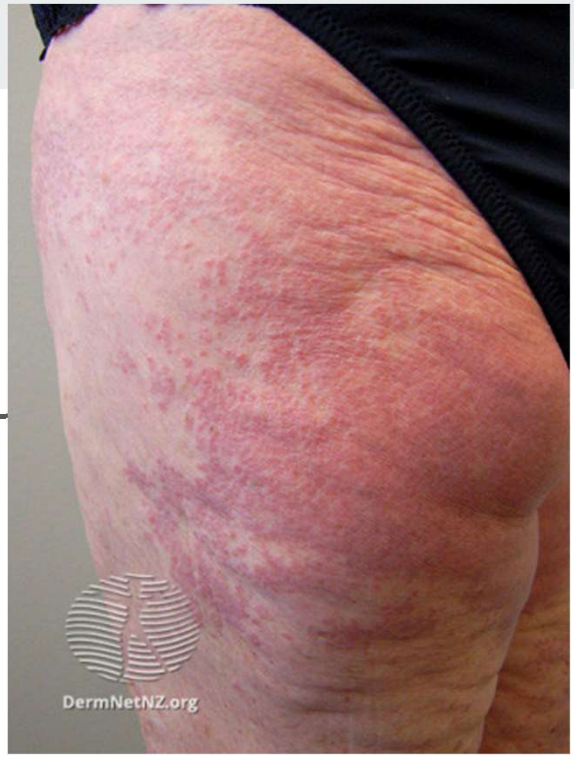
## Presentation

- Erythematous to violaceous or tan **smooth** annular plaques
- Interstitial GA can be violaceous or tan smooth thin plaques, barely palpable.
- DDX: NL, tinea, Erythema nodosum



# Treatment




Localized GA

- Clobetasol or other super high potency BID x 2-4 weeks, sometimes longer or can do 2 weeks, on 2 weeks off for several weeks.
- Intralesional Kenalog
- Do not treat these with LN2 even though some literature suggests it.

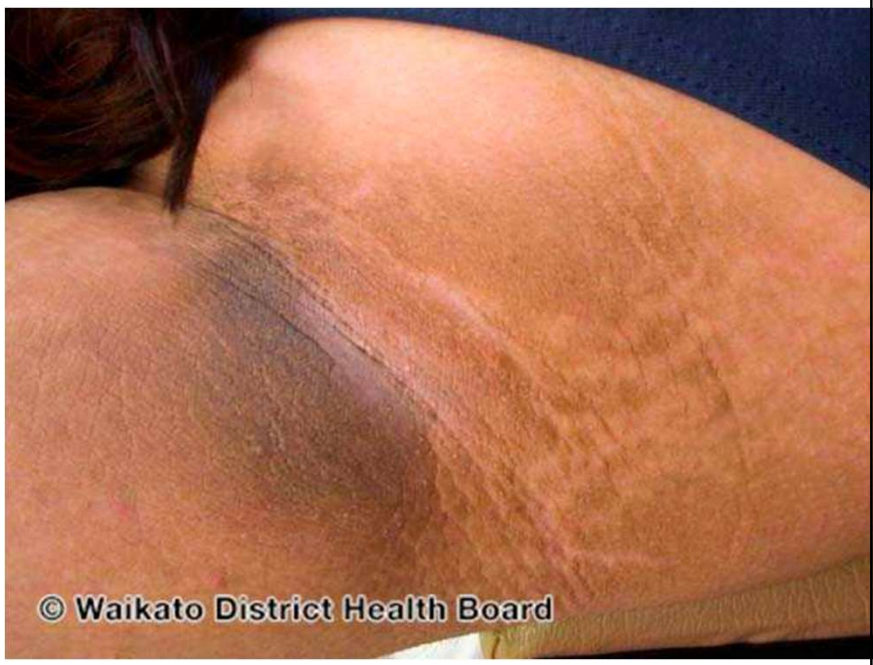
Disseminated GA

- Systemic steroids, isotretinoin, dapsone, methotrexate, hydroxychloroquine, TNF alpha inhibitors - nothing works well

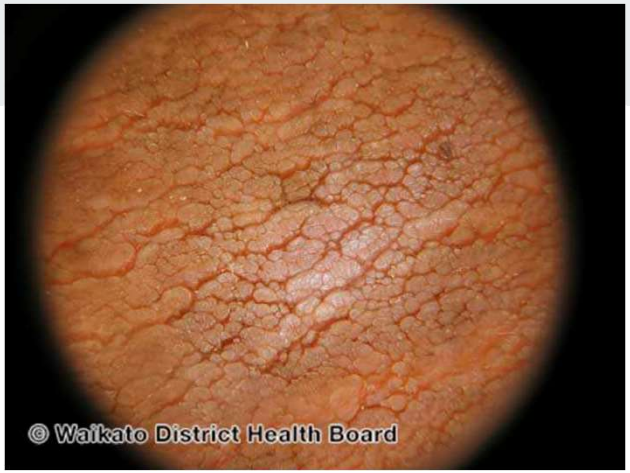
# Acanthosis nigricans

# Acanthosis nigricans

- Hyperpigmented, velvety smooth plaques
- Mainly affected flexural areas, mostly neck, axilla, groin.
- Most commonly related to an insulin resistance or hyperinsulinemia disorder:
  - Most commonly diabetes, PCOS, Obesity
- Medications that increase insulin may cause it: nicotinic acid, systemic steroids, estrogen, insulin, niacin, oral contraceptive pills, pituitary extract, triazinate, testosterone, aripiprazole



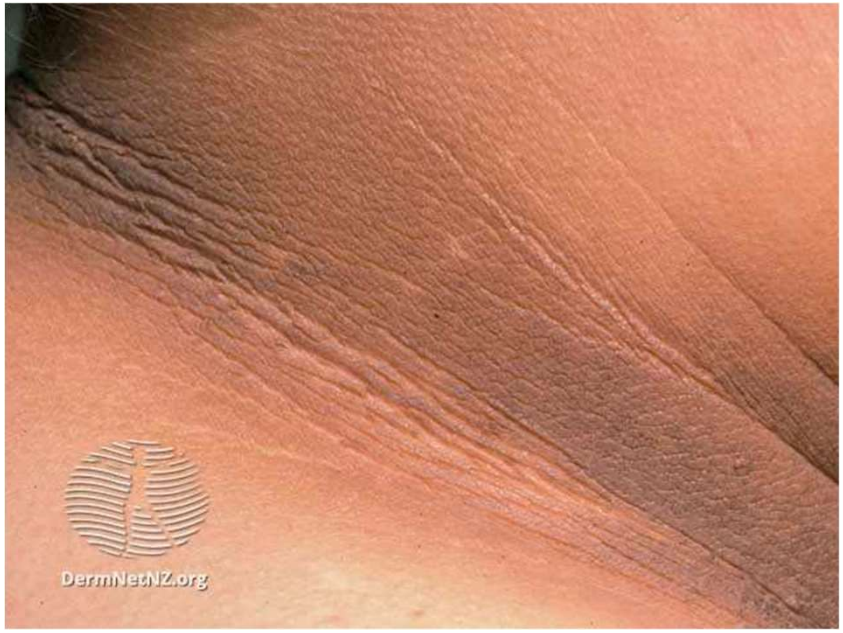
# Acanthosis nigricans




- Insulin can cross the dermal-epidermal junction.
- When a lot of insulin is in the DE junction, can see growth-stimulating effects
- It binds to type 1 insulin-like growth factor receptors (IGFRs) on keratinocytes → stimulates the proliferation of these cells = acanthosis nigricans.
- Affects African Americans, Latinos and Native Americans most frequently.
- Develops typically before age 40
- Rarely can be a sign of internal malignancy.
  - Typically, >40 yo, sudden onset, no history of hyperinsulinemia
  - Treatment: treat the malignancy

# Acanthosis nigricans

- DDX: Confluent and Reticulated Papillomatosis (CARP)
- Treatment:
  - weight loss, address the insulin resistance cause
  - 2% ammonium lactate cream
  - Tretinoin or other topical retinoid daily if tolerated
  - Calcipotriene cream twice daily for months



# Xanthomas

## Xanthomas Overview

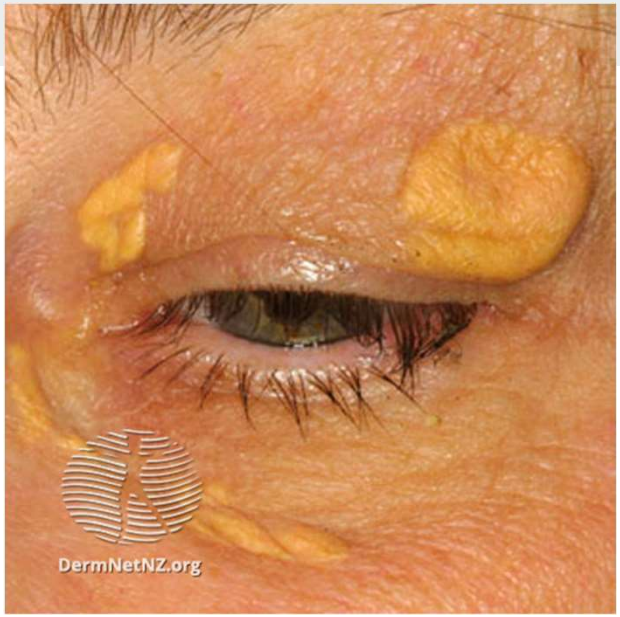
- In general can be a sign of hyperlipidemia of some kind
- Fat collections within dermal macrophages of the skin
- Types: eruptive, tuberous, tendinous, plane  and xanthelasma

## Types of Hyperlipidemia

- Type 1 - Low LDL, Low HDL, high triglycerides → Eruptive xanthomas (No risk of coronary artery disease)
- Type 2 - Low LDL clearance, high cholesterol → tendinous, tuberous, plane (+CAD risk)
- Type 3 - combined dyslipidemia or  hyperlipoproteinemia → Tuberous, plane, tendinous (+CAD risk)
- Type 4 - high VLDLs and high triglycerides → Eruptive (Frequently associated with ETOH use, obesity and DM, type 2)
- Type 5 - Low LDL, Low HDL and high triglycerides → Eruptive (can also be associated with DM)

# Xanthelasma

- AKA: xanthelasma palpebrarum
- Most common version that you will see clinically
- Mostly on the eyelids
- Yellow, soft, smooth plaques
- Only 50% of these patient have high cholesterol
- Treatment: trichloroacetic acid, laser ablation, surgical excision

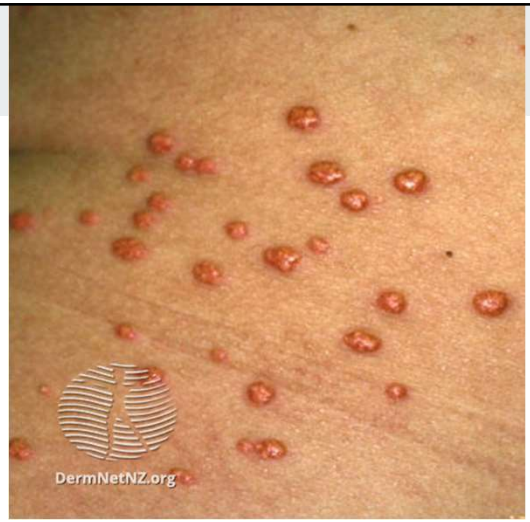


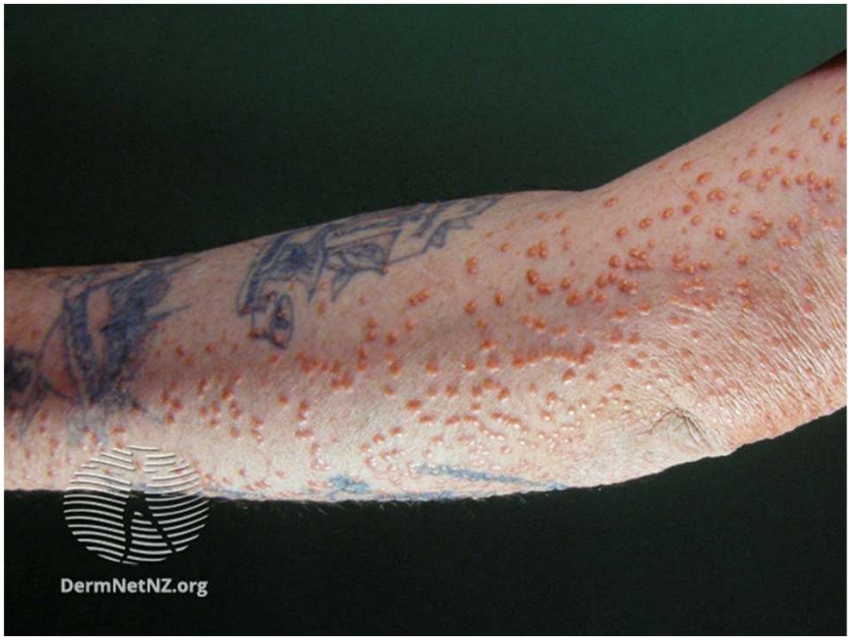

# Plane Xanthomas

- Yellow, soft, flat macules or smooth thin papules
- Locations: Anywhere but can involve the web spaces of the toes
- May or may not be associated with hyperlipidemia
- If found in the web spaces of the fingers/toes or creases of the fingers/toes, they are more likely to be associated with hyperlipidemia (Type 2 or 3)
- Rarely associated with monoclonal gammopathy

# Eruptive Xanthomas

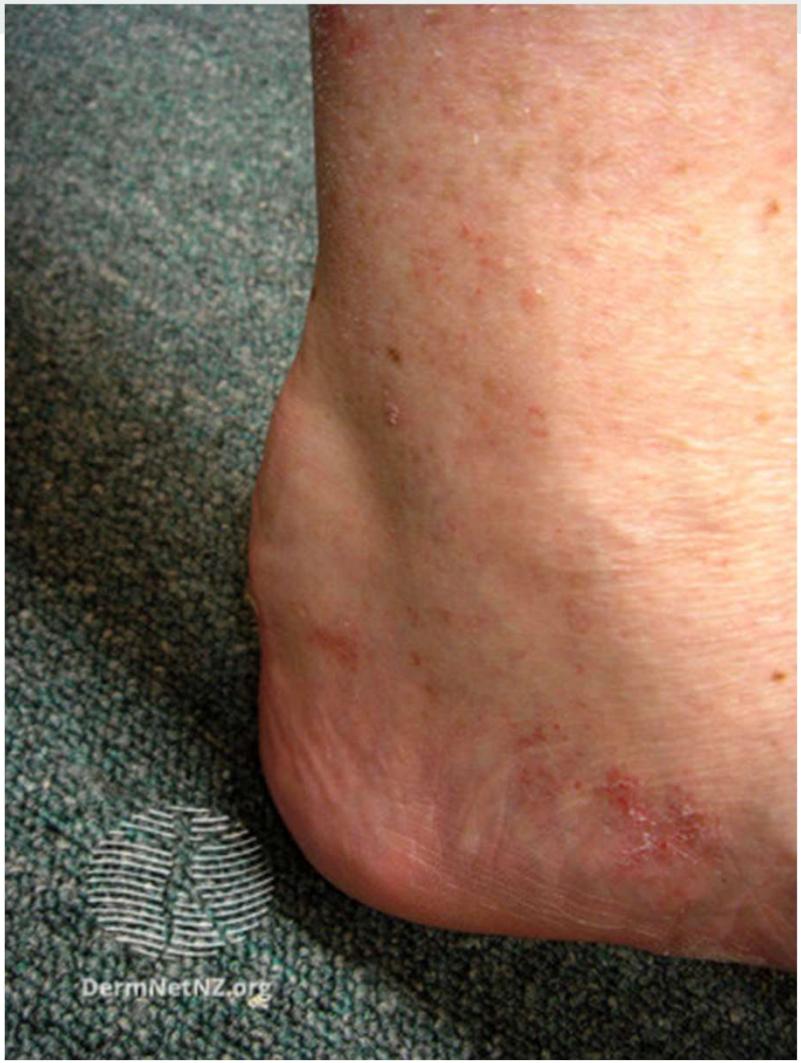
- Yellow to pink, smooth, discreet, scattered papules
- Typically on the extensor areas of the arms, legs, buttock but can be widespread
- Generally associated with high triglycerides (+3,000mg/dl) and/or poor DM control
- Treatment: treat the triglycerides and/or DM



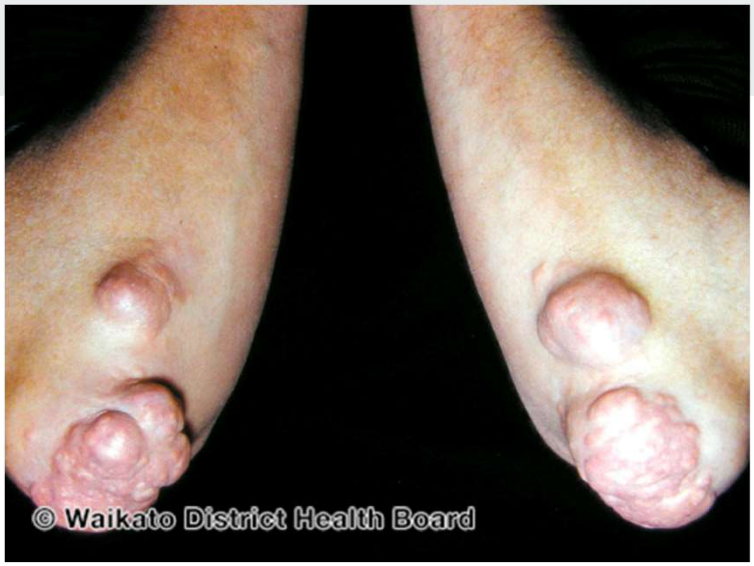
## Tendinous Xanthomas

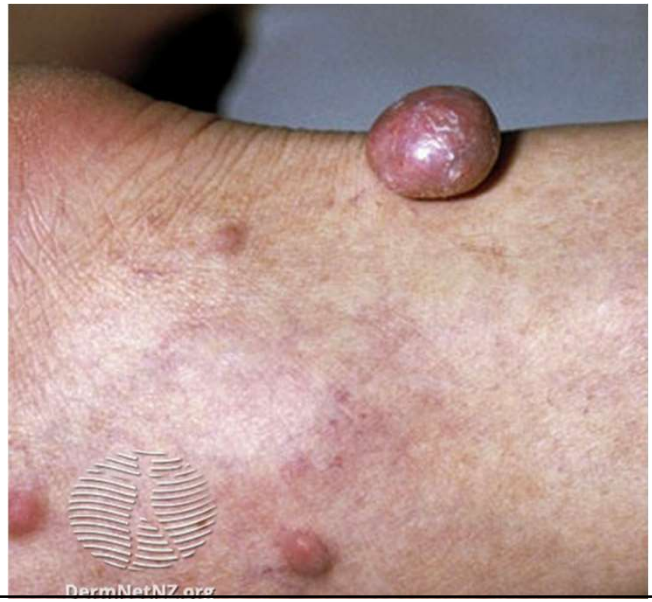
- Firm, smooth, yellow papules or nodules
- Locations: Achilles, extensor tendons of hands, knees or elbows
- Associated with Type 2 hyperlipidemia



## Tuberous Xanthomas

- Pink or tannish yellow nodules
- Locations: elbows and knees on the extensor aspects
- Type 2 or 3 Hyperlipidemia
- Resolve or improve with statin therapy



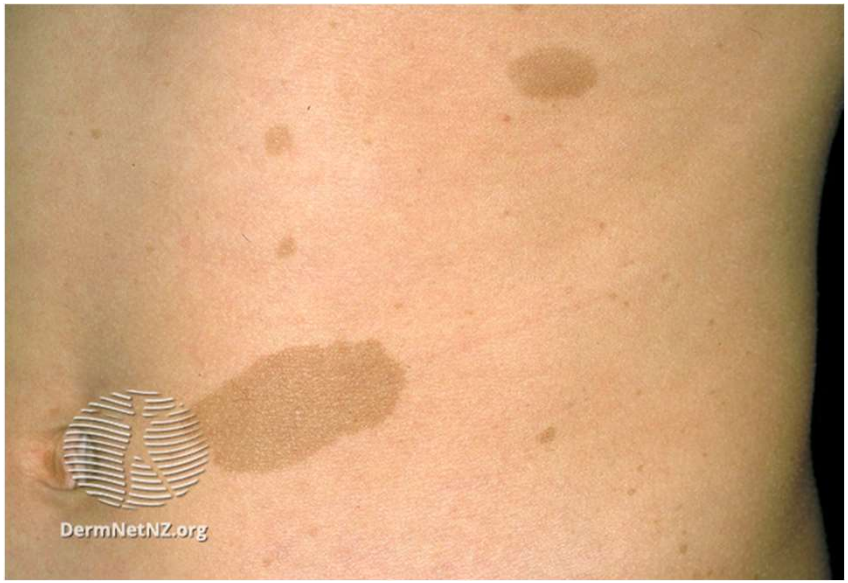
# Neurofibromatosis (NF)

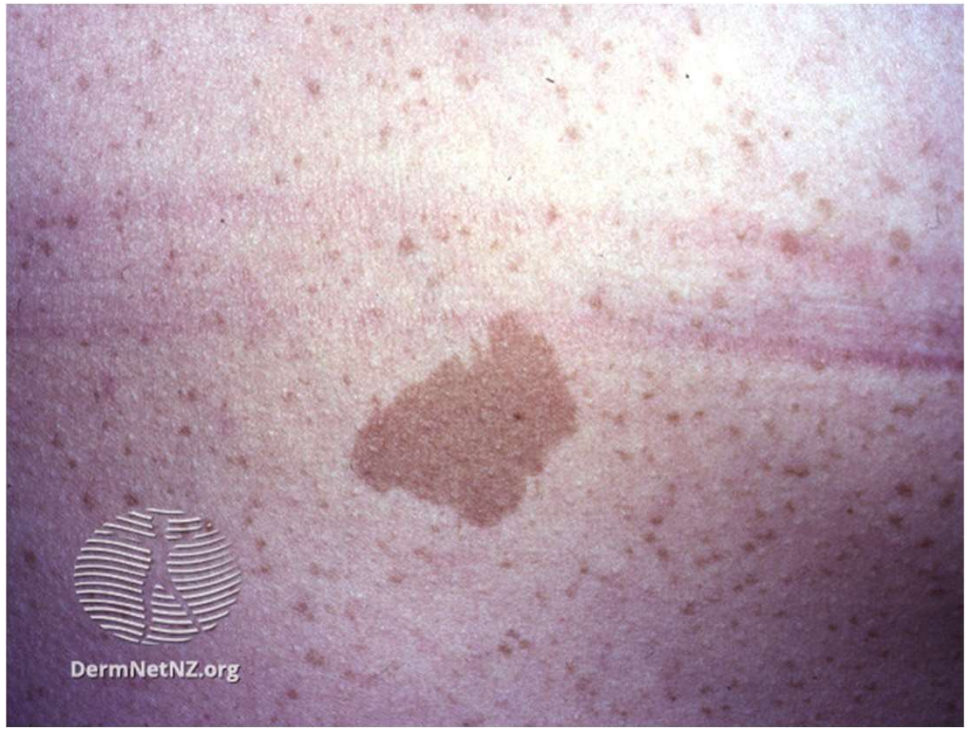
# Overview

- Genetic disorder - autosomal dominant
- Two general types:
  - NF 1
    - 1 in 3000 births
    - mutation on the neurofibromin gene of chromosome 17.
    - 3–15% increased risk for developing a malignant tumor
  - NF 2
    - 1 in 50,000 births
    - mutation on chromosome 22.

# NF 1

- Diagnostic characteristics:
  - 6 or more café-au-lait macules (CALM)
  - Axillary freckling or in the skin folds
  - Iris Lisch nodules
  - Multiple neurofibromas
  - Optical pathway glioma
  - Distinctive bone lesions
  - First degree relative with NF1



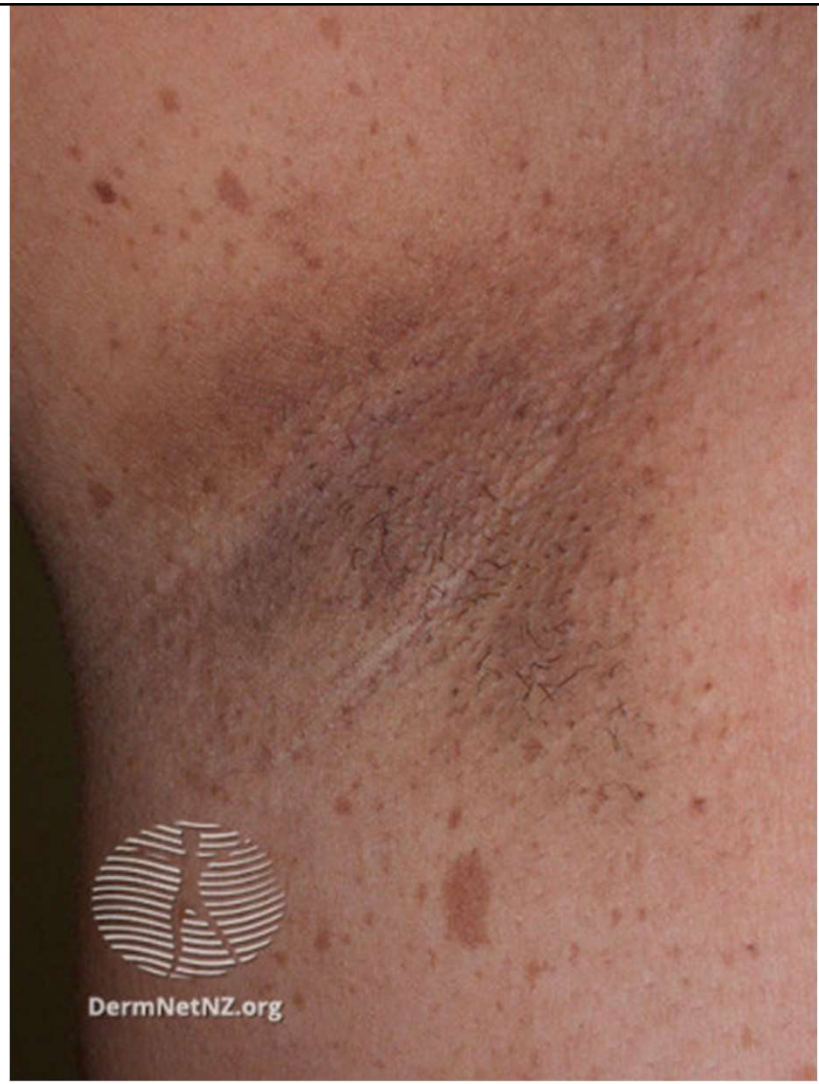




**CALM** - Tan to brown ovalish patches, >5mm

- Seen on many infants and children
- >6 is a warning sign for NF

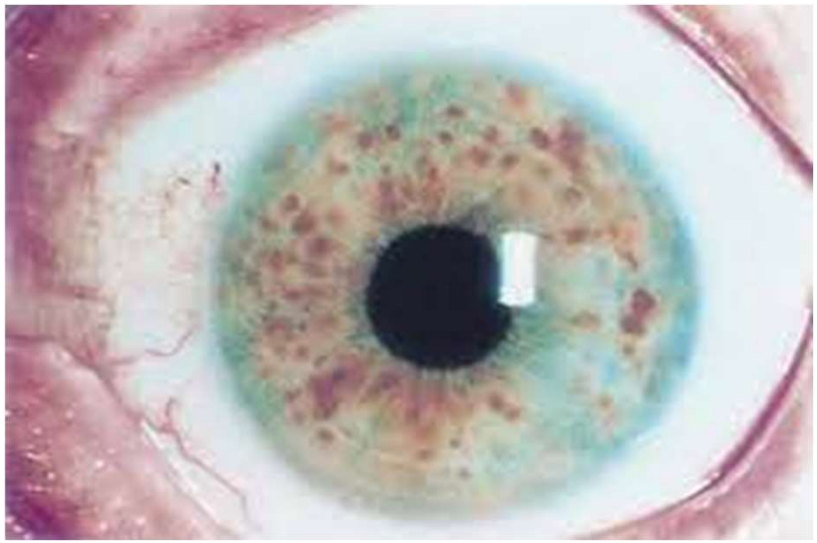
## Axillary Freckling

- Also known as Crowe sign
- Begins after puberty
- Can be seen in the groin fold or other skin folds



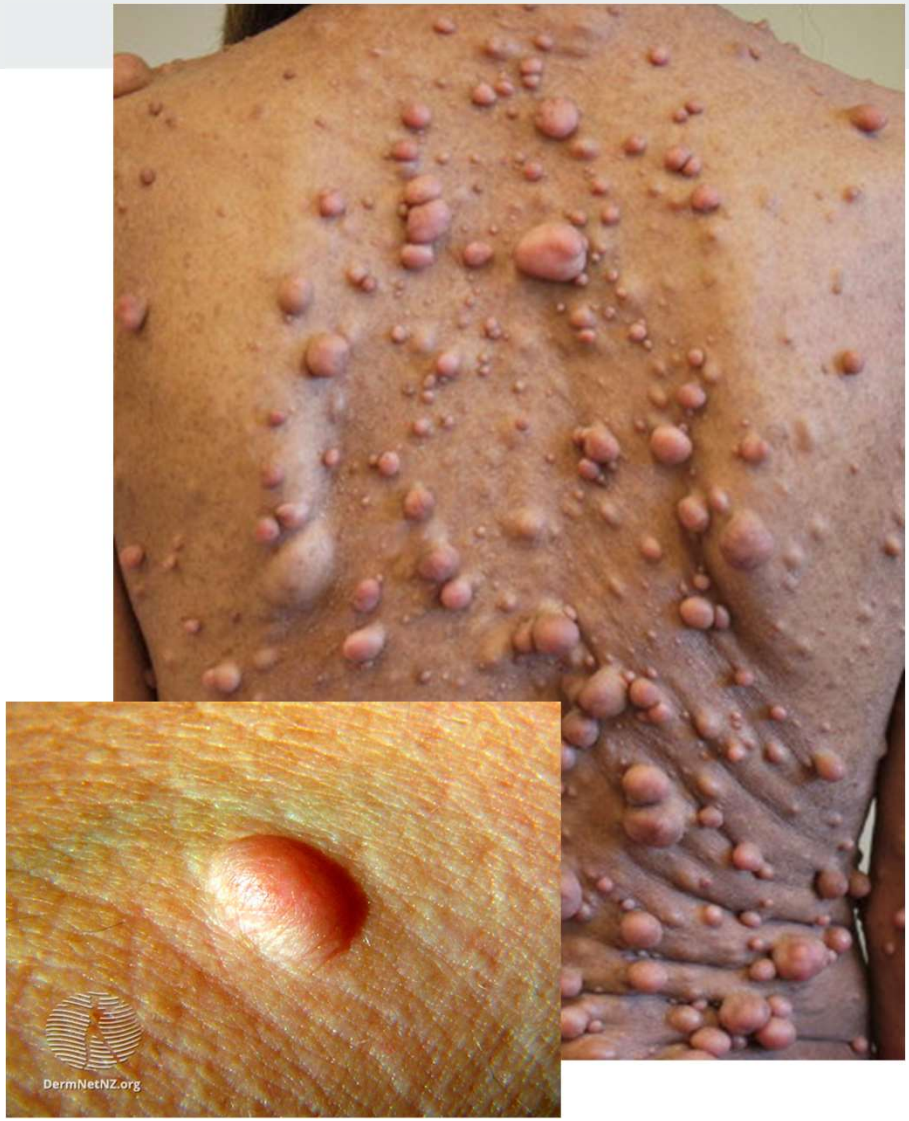
# Lisch Nodules

- Small, yellow tumours on the iris
- Occur after puberty
- Seen in 97-100% of patient with NF1
- Not harmful but help to confirm diagnosis



# Neurofibromas

- Develop along a nerve (3 types)
- **Cutaneous neurofibromas**: skin colored, fleshy papules
  - + buttonhole sign (they will invert when you push them with a finger.)
- **Subcutaneous neurofibromas**: deeper, may be tender but look like cutaneous NFs.
- **Plexiform neurofibromas**: bag-like fleshy nodule
  - can involve the nerve roots.
  - Some are invasive tumours within the skin, muscle, bone, and blood vessels
  - Plexiform seen only in NF 1



# NF1 - other signs

- Malformation bones below the knees and elbows and scoliosis
- Short stature, growth hormone deficiency
- Intellectual/learning and speech disabilities
- Optic nerve tumors →vision loss
- Hypertension
- Spinal or brain tumors → epilepsy
- GI  tract tumors
- Hearing impairment

## A note on malignancy

- Malignant peripheral nerve sheath tumors are types of sarcomas
- Occur in 8-16% of patients with plexiform neurofibromas

## NF2

- Multiple (often benign)  tumors occur on the brain and spinal cord
- Hearing loss is often the first symptom (tumor of the auditory nerve)
- Often not diagnosed until 20s
- No cutaneous manifestations

## Management

- Mainly supportive
- Refer pt to appropriate specialists for any symptoms (neurology, ophthalmology, audiology).
- Often managed by NF specialist or PCP
- Genetic counseling referral

# Tuberous Sclerosis

# Overview

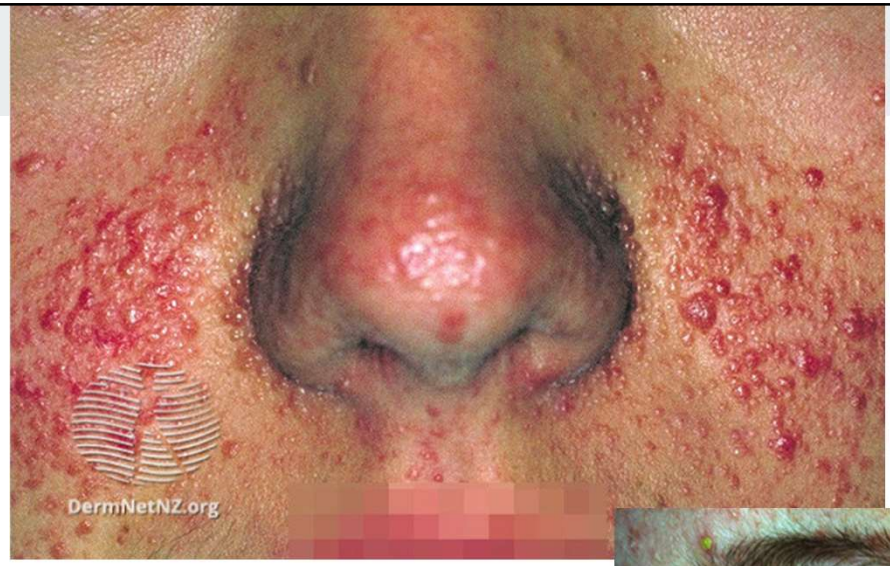
- Autosomal dominant genetic condition
- Tumors (aka hartomas) of the central nervous system, kidneys, heart, retina (and more)
- 1 in 6000 people
- 60% of cases are sporadic (no family history)
- Vogt Triad - epilepsy, angiofibromas and intellectual disability occurs in 25% of patients
- Intellectual disability - present in <50% of patients
- Also known as epiloia

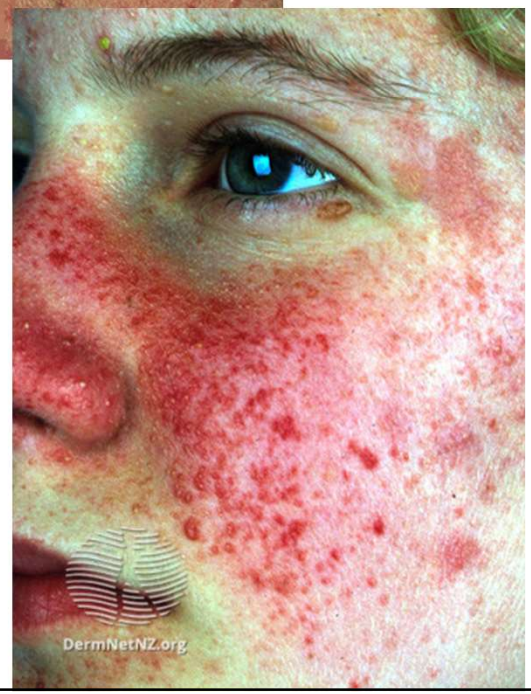
# Overview

- Hamartomas - benign tumors
  - composed of an overgrowth of the cells and tissues that normally occur in the affected area (brain, kidney hear, etc), including congenital nevi.
- Occurs from the mutation of  TSC1 (produces hamartin) and TSC2 (produces tuberin
- 33% cases are inherited
- 66% are due to mutations in early life, most often of TSC2
- Two thirds of people with tuberous sclerosis have skin findings

# Angiofibromas

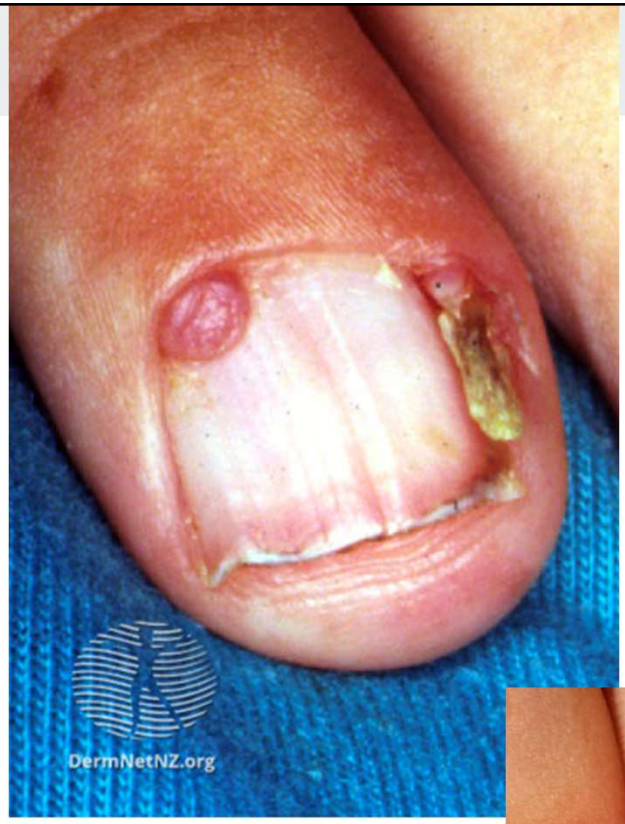
- Erythematous to violaceous firm papules
- Occur on nose and cheeks
- Benign
- Typically numerous in TS
- Begin around ages 3-10

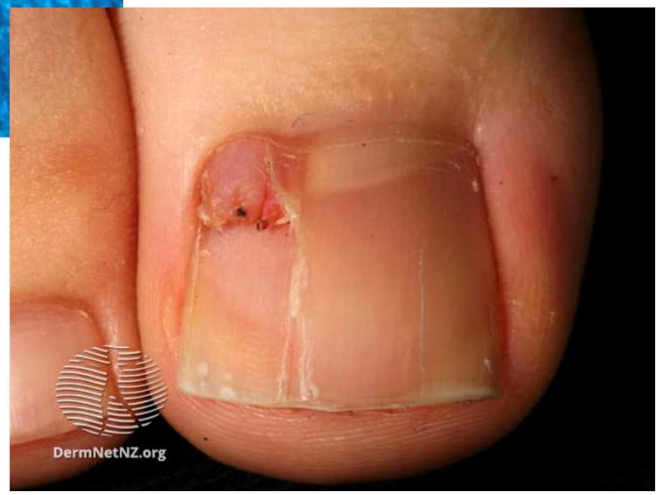


# Periungual Fibromas

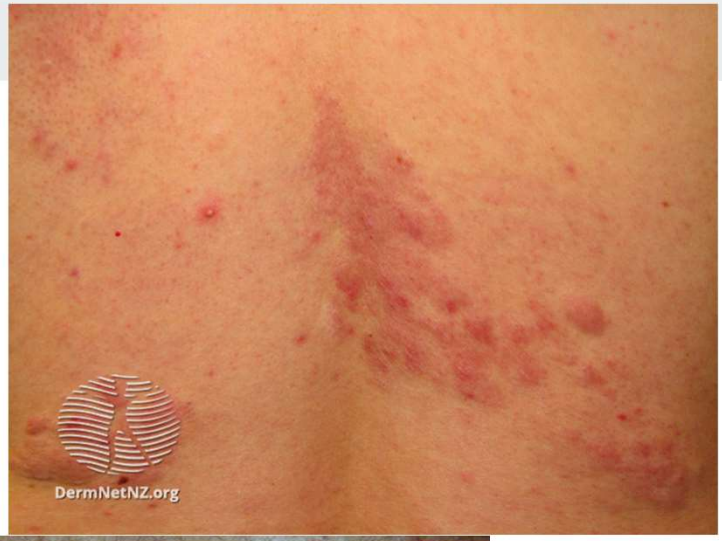
- Pink to skin colored, firm nodules
- Location: nail folds
- May see longitudinal groove of the nail plate, splinter hemorrhages or white streaks
- Occur in 50% of patients

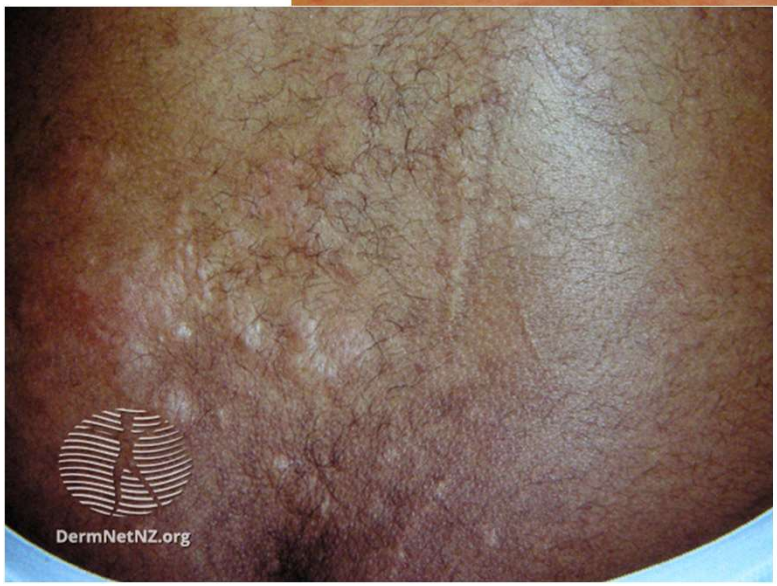


# Shagreen Patch

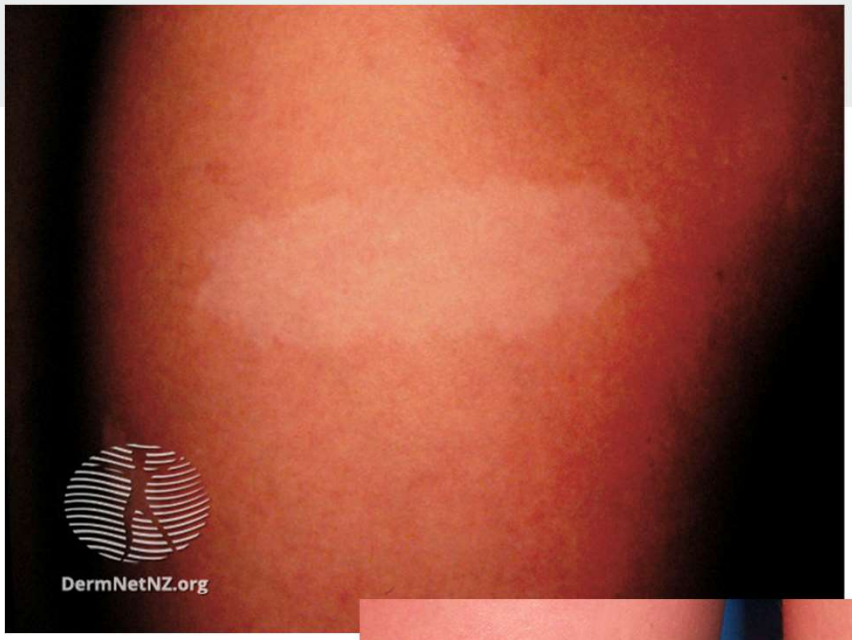
- Skin colored to orangish, thickened plaque
- Typically on the back
- Occurs in early childhood
- Occurs in 70% of patients
- Has a pig skin like texture

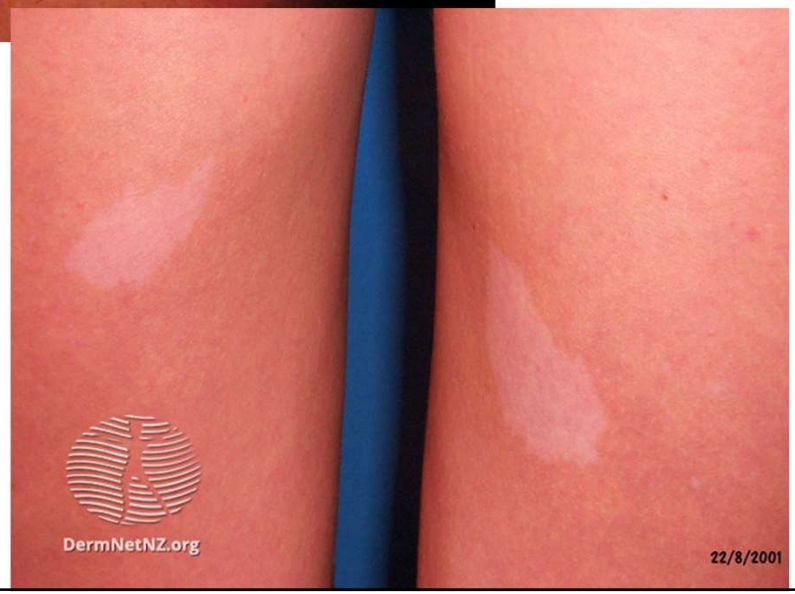


# Ash leaf marks

- Often present at birth on infancy
- Hypopigmented, confetti shaped patches
- 3 or more highly correlated with TS
- Location: arms, legs, trunk
- May also present as a white tuft of hair



# Other systemic signs

- Epilepsy - present in >70% of cases
- Behavioral diagnosis - intellectual disability/delay, ADHD, autism, depression, schizophrenia, anxiety
- Central nervous system lesions
- Kidney lesions - cysts, angiomyolipomas, renal cell carcinoma
- Cardiac rhabdomyomas
- Lungs - Lymphangioleiomyomatosis, Multifocal micronodular pneumonocyte hyperplasia
- Eye lesions

## Treatment

- Specialist referrals and follow up
- Genetic Counseling
- Angiofibromas can be treated with CO2 laser (fibrous lesions) or pulsed dye laser (for the more vascular lesions)

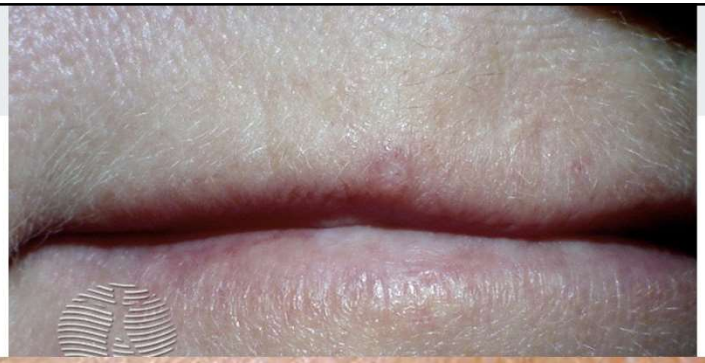
# Genetic Malignant Syndromes

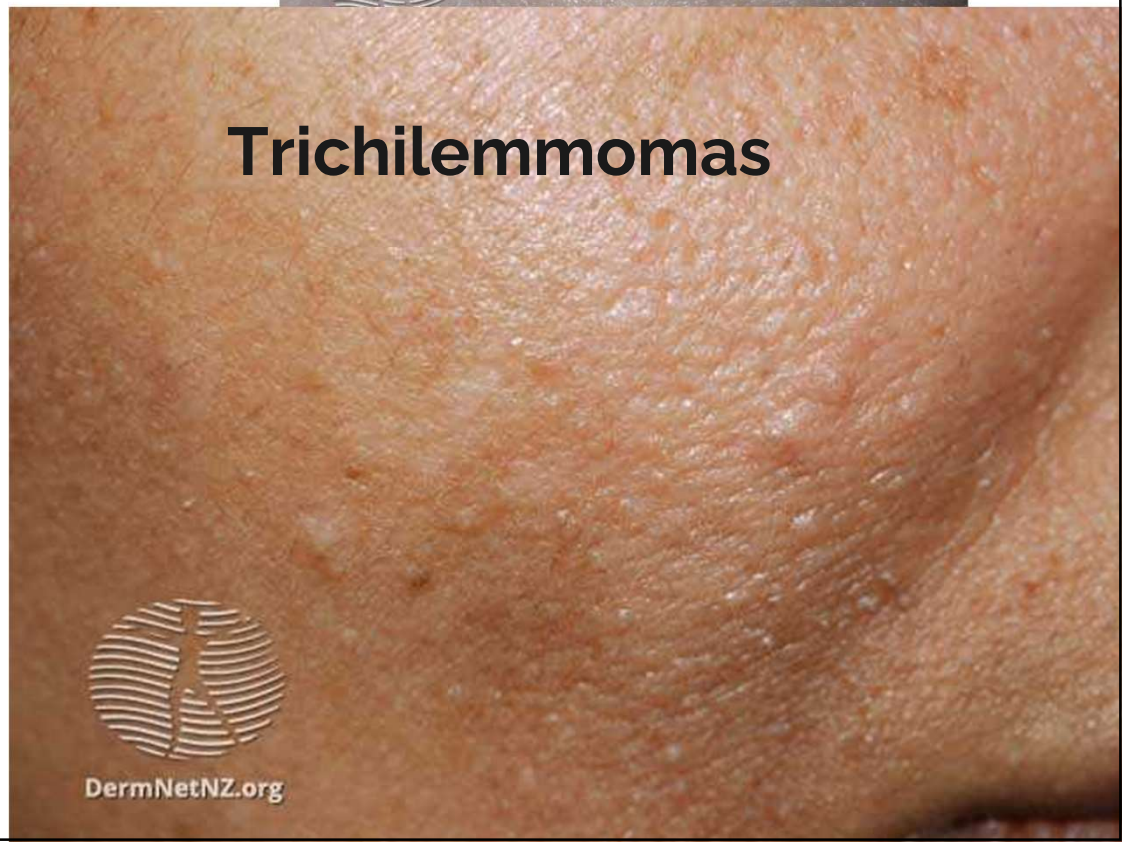
# Cowden Syndrome

# Cowden Syndrome

- Rare - 1 in 200K
- Autosomal dominant - but 45% of cases occur de novo
- Part of the *PTEN* Hamartoma Tumour Syndromes (PHTS)
  - Bannayan-Riley-Ruvalcaba syndrome
  - Proteus syndrome
  - Proteus-like syndrome
- Cutaneous manifestations occur in ages 20s and 30s
- More common in females


Mucosal papillomas
DermNetNZ.org




Trichilemmomas
DermNetNZ.org


Acral keratoses
DermNetNZ.org

# Cowden Syndrome Malignancies

- May see breast lesions, thyroid gland lesions, macrocephaly, autism, CNS disorders  and many other symptoms
- Associated with malignancies:
  - Breast Cancer
  - Thyroid cancer
  - Renal Cell Carcinoma
  - Endometrial Cancer
  - Colon Cancer

# Muir-Torre Syndrome (MTS)

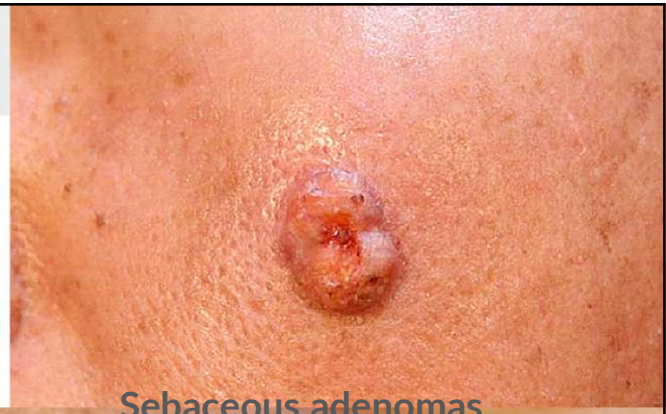
# Overview

- MTS is a rare variant of Lynch Syndrome which also called hereditary nonpolyposis colorectal cancer (HNPCC) syndrome.
  - MTS represents 1-2% of cases of Lynch Syndrome
- Characterised by one sebaceous tumor and one internal malignancy.
- Autosomal dominant
- Risk factors: sun exposure history, radiation therapy, transplant patients (due to immunosuppression drugs)
- Usually caused by a mutation in MLH1 or  MSH2 genes.

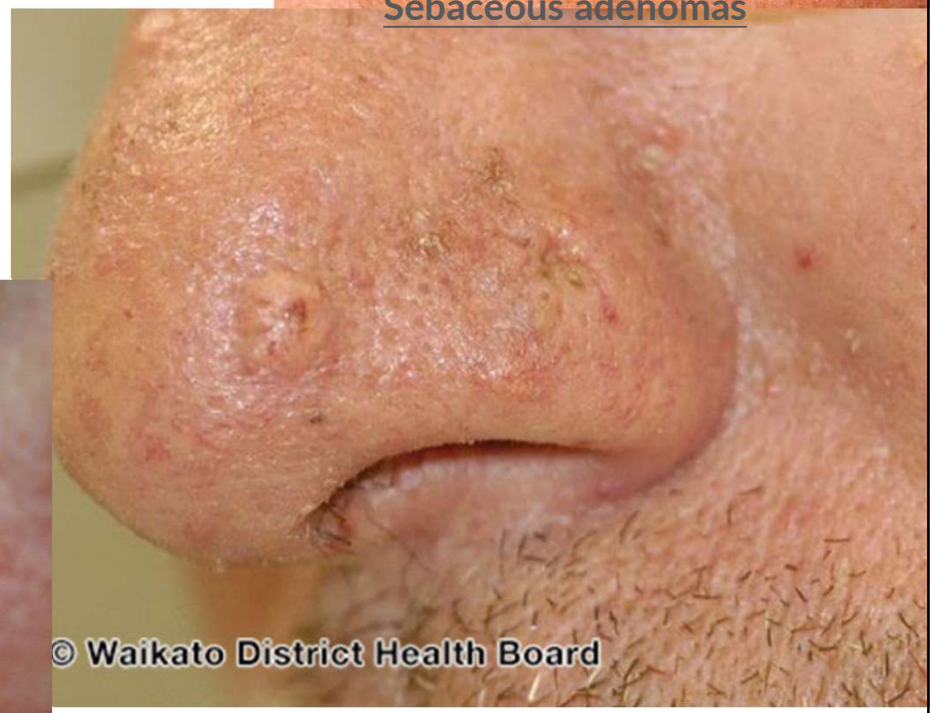
# Skin findings

~20% of patients - cutaneous findings are the first sign

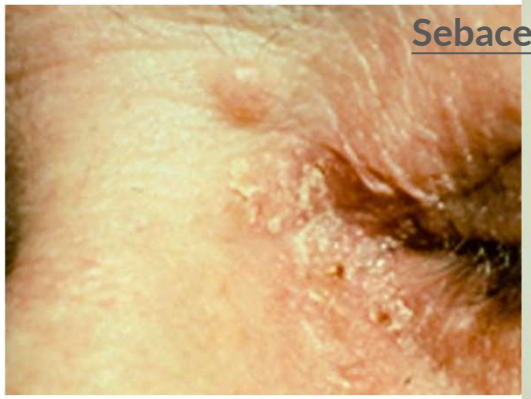
Sebaceous adenoma, sebaceoma, or sebaceous carcinoma

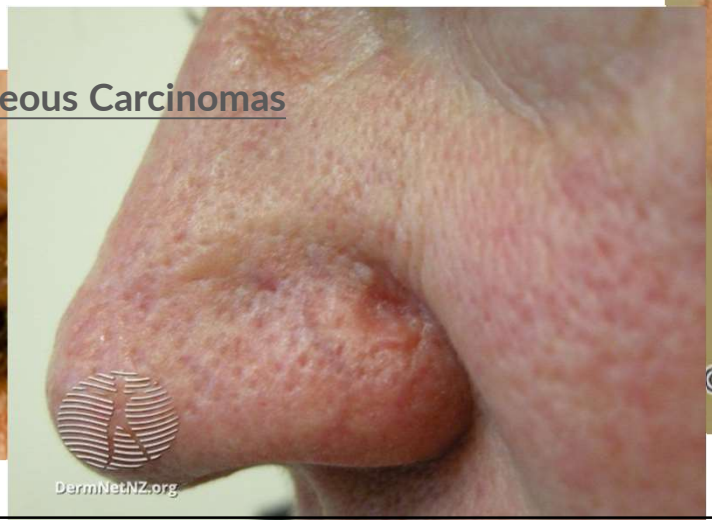


Sebaceous adenomas

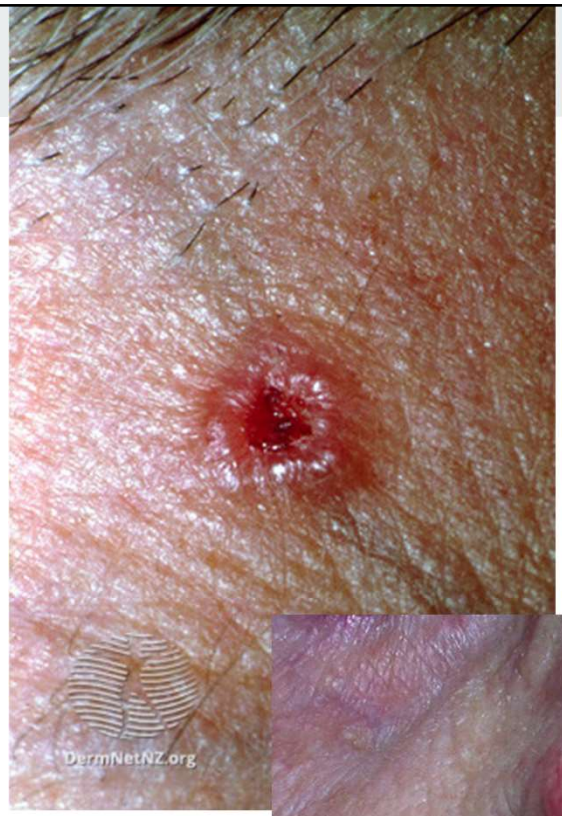


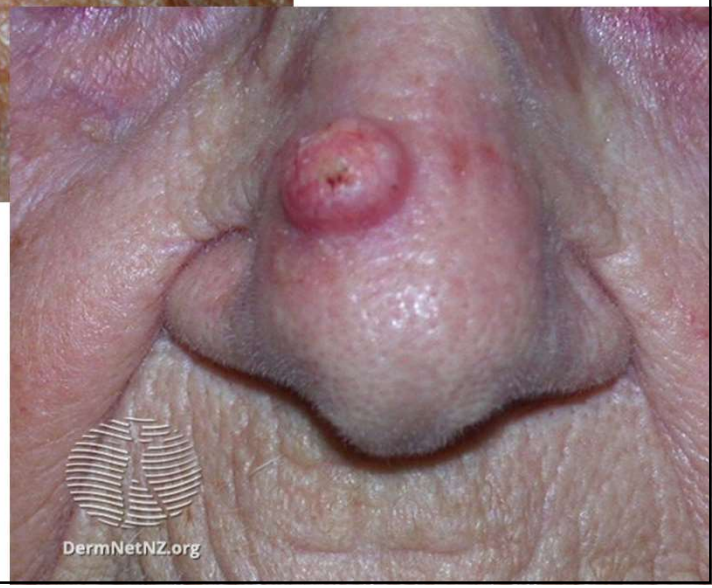

Sebaceous Carcinomas





# Skin Cancers




Basal Cell Carcinoma with follicular differentiation

Multiple Keratoacanthomas

# Internal Malignancies

- Colorectal - most common
- Others:  stomach, pancreas, endometrium, ovary, urological (renal pelvis, ureter, prostate), and brain
- Family history is important - often there is a history of one or more of these cancers and often before age 50
- Any patient with sebaceous adenoma or carcinoma on pathology should have a thorough review of family history of the above malignancies.

## Follow up

- Patients needs skin checks every 6 months to 12 months
- Depending on family history, patients need a colonoscopy every 1-2 years
- Patients should have genetic testing for confirmation
- Regular follow ups with GI, GYN, urology, and close monitoring with PCP.

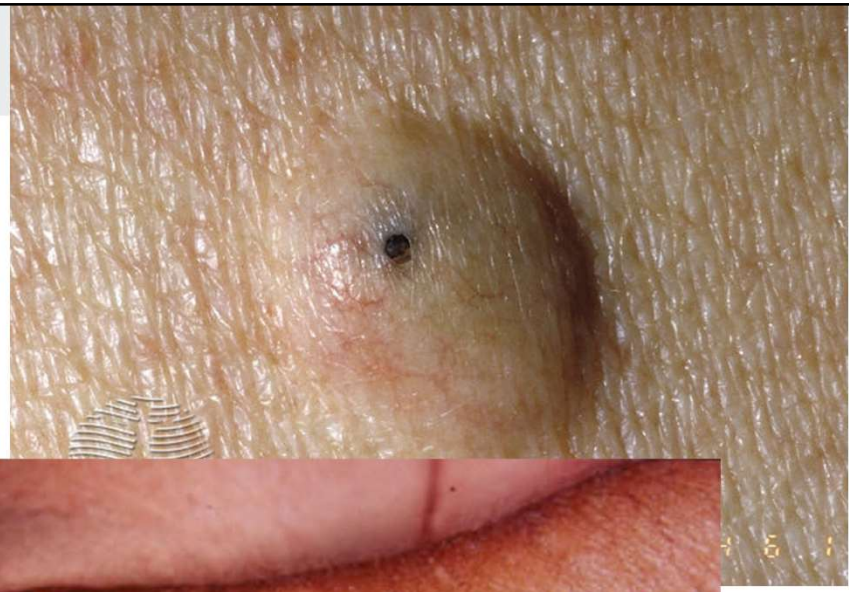
# Gardner Syndrome

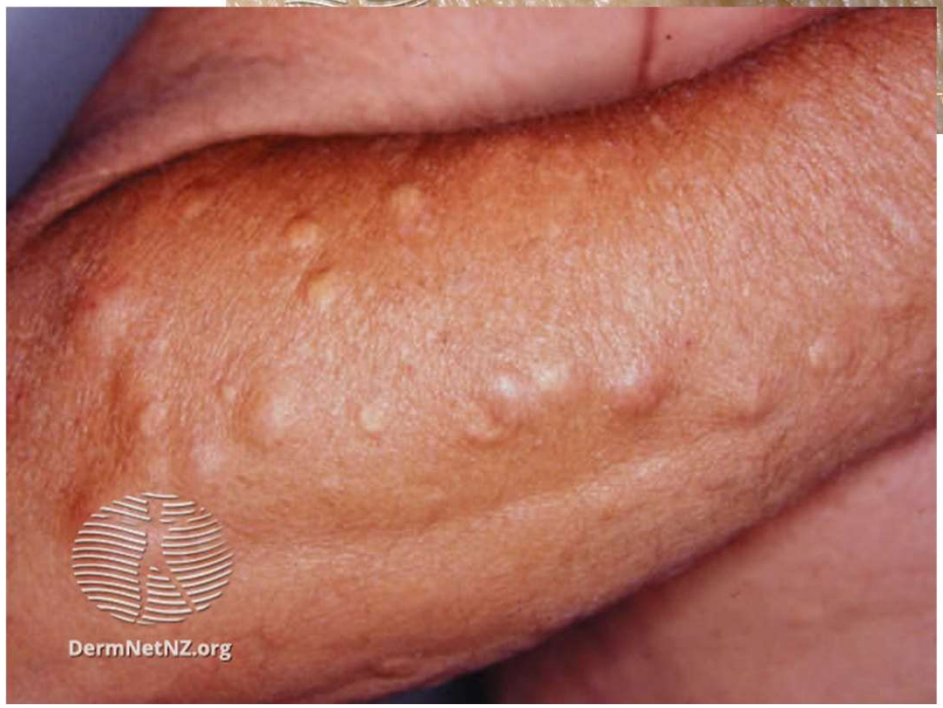
## Overview

- Variant of familial adenomatous polyposis (FAP)
- Rare, autosomal dominant, mutation of the *APC* gene on chromosome 5q22
- Usually diagnosed in the second decade of life
- Average age to develop malignancy is 39

# Cutaneous Findings

- Epidermal Inclusion cysts (scalp, neck, legs)
- Affects 35% of patients
- Multiple EICs can be a helpful sign





# Non Cutaneous Findings

- GI polyps - **most common sign**
  - Almost always transition to **colon cancer**
  - Affects >80% of patients
- Desmoid tumors - occurs mainly in the abdominal wall
- Osteomas - mainly in the jaw and skull
  - Often the first sign of Gardner's syndrome
- Pigmented lesions in the fundus of the eye - occurs in 80% of patients

# Malignancies

- Colon Cancer
  - Nearly certain to a occur by the age of 40
  - Multiple polyps (>100) found and a diagnosis of Gardner's leads to preventative colectomy
- Other associated malignancies:
  - Thyroid Cancer is fairly common as well - mostly in young women
  - Small bowel, pancreas, CNS, liver, bile ducts and stomach cancers can occur
- Genetic counseling is important.

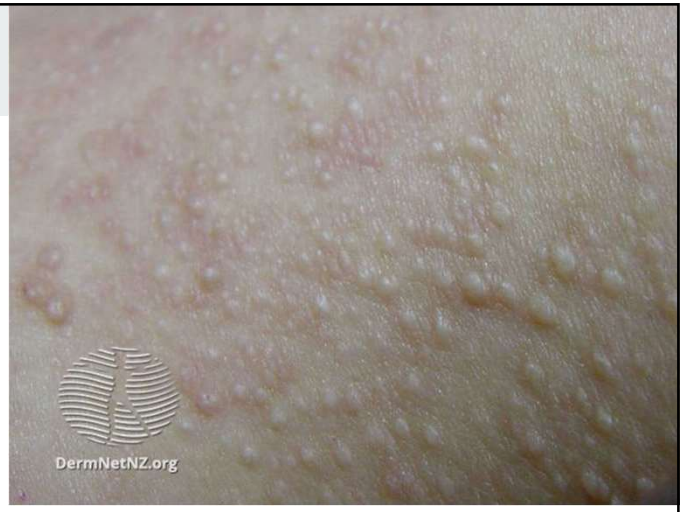
# Birt–Hogg–Dubé Syndrome

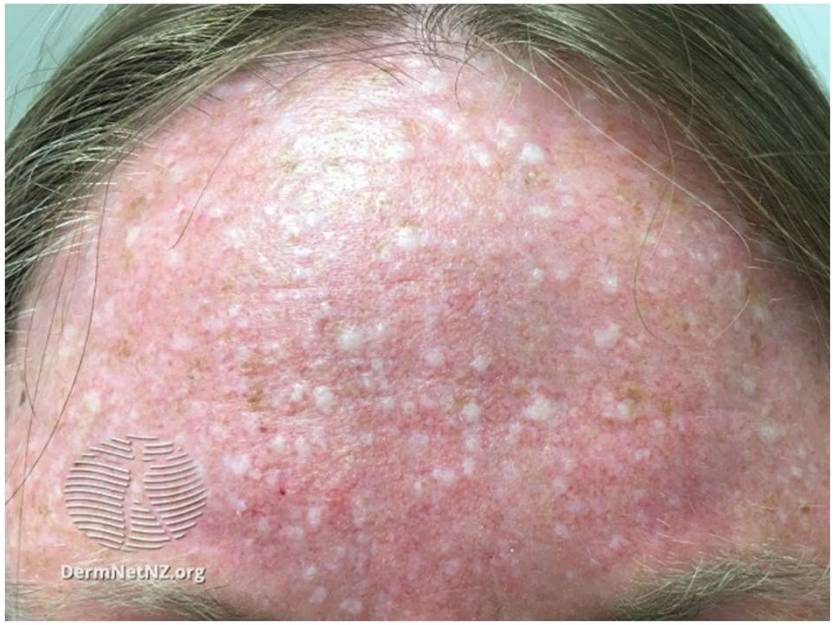
# Overview

- Rare
- Autosomal dominant - *FLCN* gene mutation
- Increased risk of melanoma
- Associated with renal carcinoma and spontaneous pneumothorax, lung cysts

# Cutaneous Findings

- Fibrofolliculomas (trichodiscomas) - 1-3 mm white or flesh colored, smooth papules
  - Bening hair follicle hartomas
- May be just a few or hundreds of lesions
- Acrochordons (skin tags) and angiofibromas can be other findings



# Evaluation

- Genetic Testing
- If positive → renal ultrasound and abdominal CT/ MRI, chest x-ray and colonoscopy
- Cutaneous treatment:
  - Dermabrasion
  - Laser therapy
  - Curettage/cautery or excision

# Other Conditions: Rare and Common

# Case Presentation

- 78 year old, caucasian male
- Presents with a history of nail discoloration that occurs intermittently
- Reports that it lasts for several months to years and then disappears
- No symptoms
- No specific changes of the nail plate
- Also develops discoloration of the fingertips

# Medical History

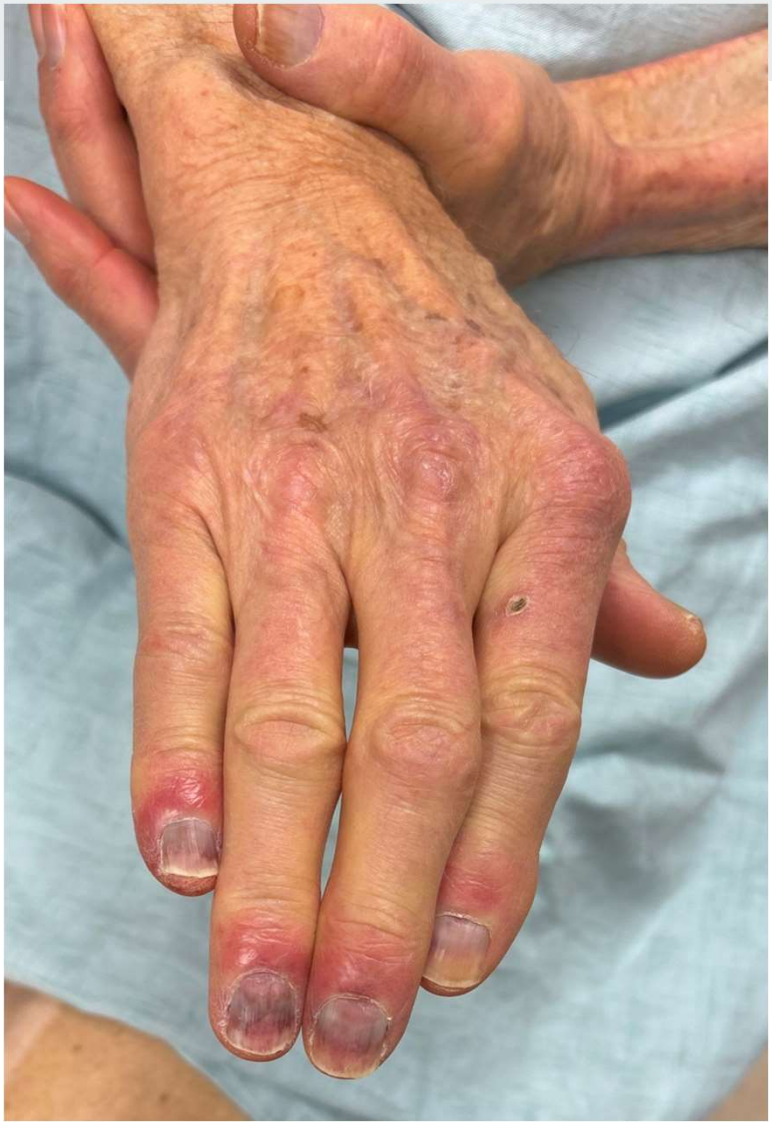
- Diabetes
- Septoplasty
- Hx of Non Melanoma Skin Cancer (many)
- Gout
- HTN
- Mandibular SCC, treated with excision and radiation
- Thrombocytopenia
- Colon Cancer
- **DVT**
- **MI**

# Medications

- Irbesartan
- Synthroid
- Famotidine
- Atorvastatin
- Testosterone
- Allopurinol
- Terazosin
- Amlodipine
- Ezetimibe
- Dyrenium
- clopidogrel

# Presentation

Diffuse violaceous erythema of the nail fold extending over the nail matrix  and diffuse erythrithronichia of the nail plates



# Presentation

Few violaceous smooth and scaly papules on the fingertips

# Differential Diagnoses???

## DDX

- Pernio or Chilblains
- Trauma
- Lupus
- Something weird

## Labs

- Elevated anticardiolipin antibodies
- Specifically: Beta 2-Glycoprotein IgG Antibody - 15
  - (normal range <7)

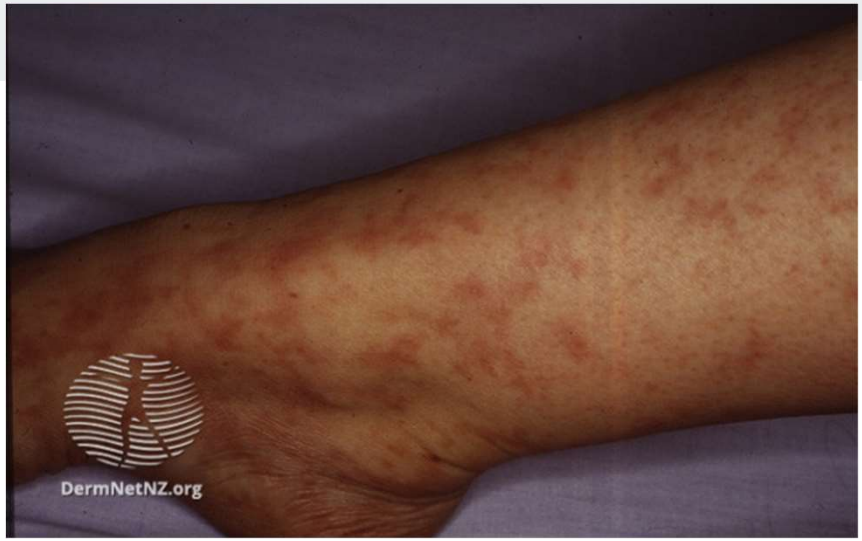
# Any Additional guesses?

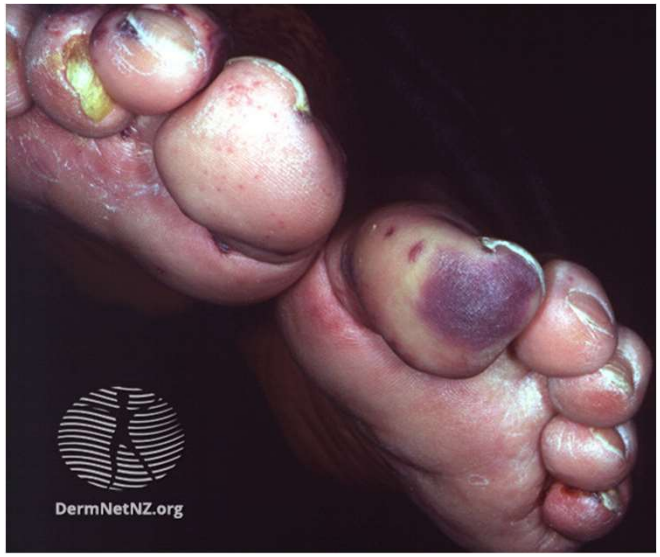
## Antiphospholipid syndrome

- Autoimmune disorder
- Makes patients clot more easily
  - venous or arterial thrombosis, MI, Pregnancy loss
- Will see elevated anticardiolipin antibodies (needs to be repeated 12 weeks apart)
  - possible elevated circulating lupus anticoagulant
    - May not have systemic lupus (the above is misleading)
- Risk factors: DM, obesity, smoking, pregnancy, surgery and genetic conditions that make patient hypercoagulable

# Cutaneous findings

- Livedo reticularis
- Cholesterol emboli
- Leg ulcers
- Superficial thrombophlebitis
- Splinter hemorrhages
- Vasculitis



# Systemic Symptoms

- Migraines
- Seizures
- CVA
- Dementia (multi-infarct type)
- Heart murmur
- Cardiac valve vegetations
- Blindness

# Labs

- aCL antibodies
- **Anti-beta-2 glycoprotein I antibodies**
- Activated partial thromboplastin time (aPTT)
- LA tests such as dilute Russell viper venom time (DRVVT)
- Complete blood cell count
  - Thrombocytopenia
  - Coombs-positive haemolytic anaemia

# Treatment

- REFER TO HEMATOLOGY
- Avoid smoking
- Avoid oral contraceptives
- Aspirin or blood thinners based on history

# Cutaneous Lupus Erythematosus (CLE)

## Overview

- 2-3 times more common than systemic lupus erythematosus (SLE)
- More common in women, presents in middle age, more common in skin of color
- Autoimmune disease - factors of genetics, environment, hormones play a role
- **20-50% of patients diagnosed with CLE will go on to develop SLE**
- Drug induced lupus
  - Most common: **Omeprazole**, calcium channel blockers, terbinafine, diuretics
  - Other classes of medications: chemotherapies, biologics, antiarrhythmics, ACEIs,NSAIDs,  antipsychotics, and antibiotics (and many more)
- SLE symptom screening: chest pain/SOB, oral ulcers, joint pain, fatigue, urinary symptoms, headaches, seizures, psychosis

## CLE Subtypes: Acute cutaneous LE (ACLE)

- Malar rash→ Broad erythema across nose and cheeks with scale.
  - induced by the sun, intermittent, non scarring but pigmentation changes can occur.
- Most likely to have SLE (~ 50 to 100%)
- Labs: ANA + in 95% of patients, often + anti-dsDNA and anti-Sm antibodies
- Need referral to Rheum ASAP
- Very important to ask about SLE symptoms in these patients.
- DDX: rosacea, photo dermatitis or drug eruptions, atopic dermatitis, or dermatomyositis
  - look at hands for gottron's papules or cuticle overgrowth as dermatomyositis path is very similar to ACLE.

## CLE Subtypes: Subacute Cutaneous LE (SCLE)

- Photodistributed → V distribution on chest and back, lesions on face, extensor arms/hands.
- Can be more annular lesions or present as scaly papules and plaques (psoriasiform)
- 30% develop SLE, but joint manifestations are most common.
  - Severe SLE disease occurs in only 10% of patients
- Often + anti- Ro/SSA antibodies
- DDX:
  - annular SCLE - granuloma annulare, drug eruption, erythema annulare centrifugum
  - Papulosquamous SCLE: psoriasis and photoallergic drug rashes

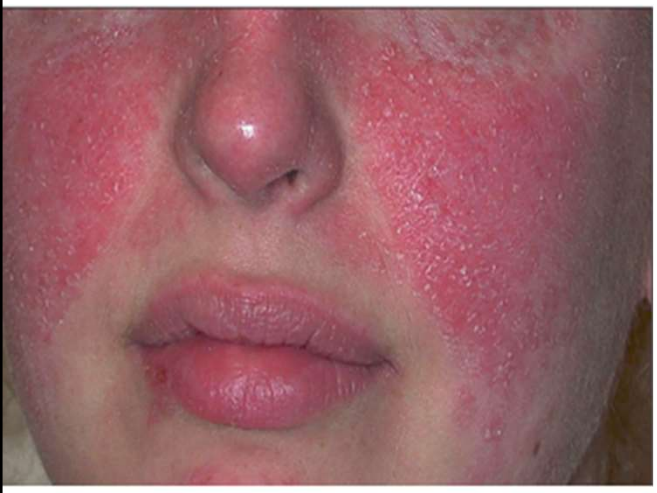
# CLE Subtypes: Chronic Cutaneous LE (CCLE)

- Includes: discoid Lupus, *LE profundus, chilblain LE, and LE tumidus*

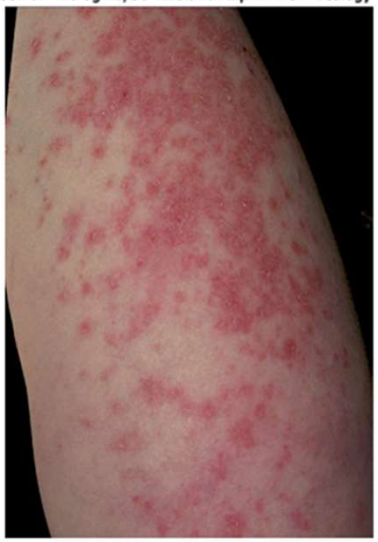
**Discoid Lupus (DLE):** Most common of CCLE

- Locations: head, neck, scalp, dorsal hands, forearms
- Well-defined, erythematous, scaly papules/plaques, coin-shaped.
  - Develop into scarred, atrophic, hypopigmented plaques or patches.
  - In the scalp, will see “carpet tacking” c/w follicular plugging.
- 5-10% develop SLE
- Can see koebnerization with sun or trauma.
- Can develop SCC in the lesions
- DDX: psoriasis, granuloma faciale, polymorphous light eruption eruption, and sarcoidosis

## Acute

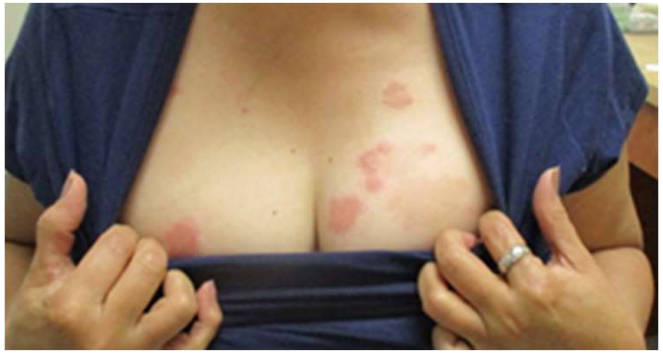


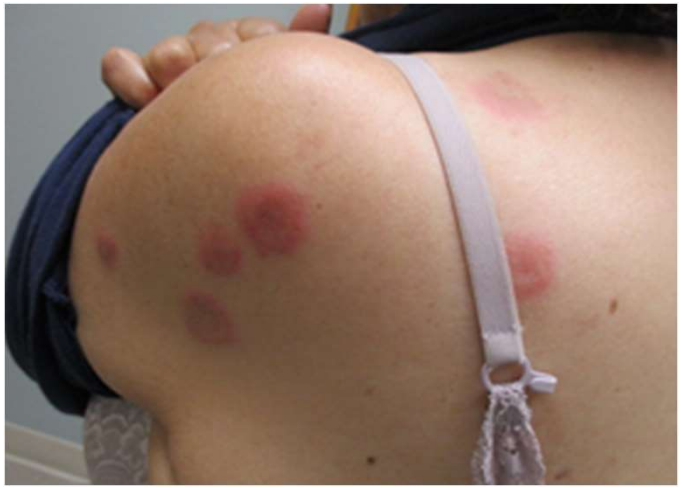




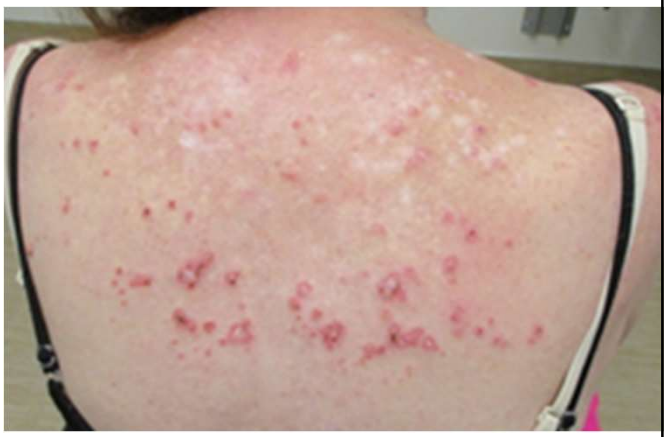


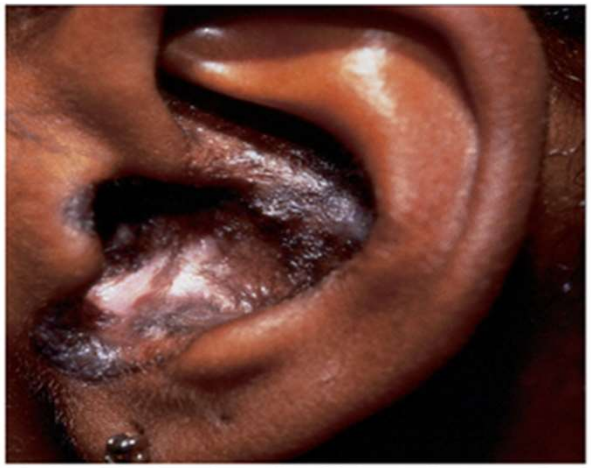
## Sub Acute





## Discoid





# Diagnosis

- Punch biopsy
- Direct immunofluorescence (DIF) biopsy discussed in literature.
  - Most of the time not necessary.
- Labs: Base on your level of suspicion for SLE per rheum guidelines
  - ANA (most important), anti-SSA/SSB, anti-dsDNA
  - CBC to evaluate for anemia, thrombocytopenia, or leukopenia
  - CMP/UA for renal abnormalities

## Treatment

- Prevention through strict sun protection → Mineral based sunscreens, UV protective clothing, vehicle window tinting, etc.
- Smoking Cessation!
- First line treatment: topical steroids
  - Low potency for face: hydrocortisone 2.5% BID, desonide 0.5%, triamcinolone 0.25% creams.
  - Mid to high potency for body i.e. trunk/extremities: triamcinolone 0.1% ointment, betamethasone 0.5% cream/oint or clobetasol 0.5% oint/cream.
  - Clobetasol or mometasone solution for the scalp.
  - Duration: 2-4 weeks, then recheck.
  - Consider alternating with tacrolimus or pimecrolimus
- Intralesional triamcinolone injections are helpful, especially on the scalp.

## Treatment cont.

- First line systemic treatment: *hydroxychloroquine, quinacrine, and chloroquine*
- **Hydroxychloroquine (Plaquenil)**: most commonly used. Studies show ~50% improvement rate.
  - Typical dose is 200 mg BID. Able to dose of up to 5-6.5 mg/kg/day.
  - Safer than chloroquine → lower incidence of retinopathy.
- All antimalarials take about 2-3 months to show efficacy.
- Side effects: skin rashes, GI upset, blue-gray skin discoloration, dizziness, HA, peripheral neuropathy, and ototoxicity.
  - Retinopathy → with hydroxychloroquine and chloroquine (~ 1%).
- Ophthalmology exams every 6-12 months. Most changes not seen until on drug for 5 years. Dose Dependent.

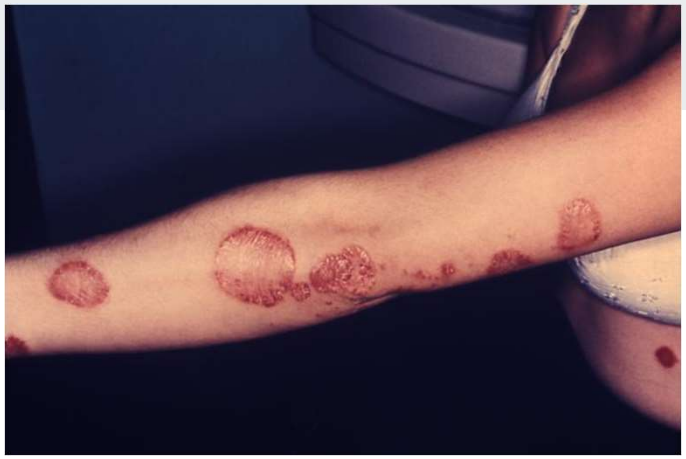
# Treatment cont.

Second line PO treatment

- Systemic corticosteroids
- Steroid sparing agents:
  - Methotrexate 7.5 to 25mg orally or SC once a week
  - Mycophenolate mofetil
  - azathioprine, cyclophosphamide, and cyclosporine
- Others: rituximab, dapsone, acitretin, IVIG
- All above meds managed by rheumatology unless you have specific rheumatology training and it fits into your scope.

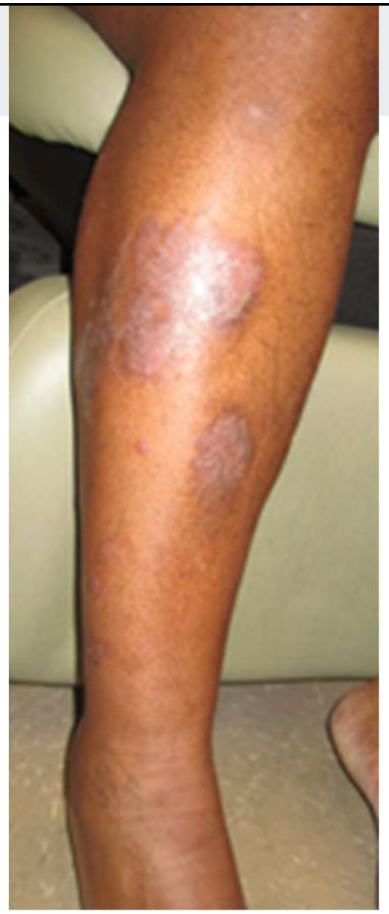
# Psoriasis

## Overview of Psoriasis (PSO)



- Affects 2% of people in the world
- Immune mediated disease→ activation of T-cells and dendritic cells which causes the release of inflammatory cytokines interleukin 17 (IL-17), IL-23, and tumor necrosis factor-alpha (TNF-α).
- ETOH intake and smoking rates are higher
- Psoriatic arthritis (PSA) occurs in ~30% of patient with PSO
  - ~65% of patient develop skin manifestations first, 19% develop joint pain first
- Ask about finger pain, swelling, sausage like digits, heel pain at every visit

## Clinical Presentation and Severity



- Pink to erythematous, well demarcated plaques, generally with micaceous or silvery scale.
- Guttate psoriasis - occurs with URI/strep
- Affects any part of the body.
  - Affects genitals in 60% of patients.
  - Nails, palms or soles
- Severity is distinguished by body surface area (BSA)
  - Mild = < 3%, Moderate = 3-10%, Severe = >10 %
- Diagnosis is clinical.
  - Biopsy can be helpful if not classic presentation or if not responding to TX.

## Comorbidities - SYSTEMIC DISEASES

- Metabolic syndrome, Heart disease (stroke and MI), Diabetes, Obesity
  - All likely encouraged by proinflammatory response of cytokines
  - Patients should have regular evaluation of weight, BP, Lipids, HgbA1c
- Higher rates of depression, anxiety
- Decreased quality of life, work productivity and sexual health
- Association with inflammatory bowel disease
- Increased malignancy risk:
  - lymphohematopoietic cancers (esp. cutaneous T-cell lymphoma), head/neck & digestive tract
  - Non Melanoma Skin CA - UVA therapy and possibly those on TNF blockers.

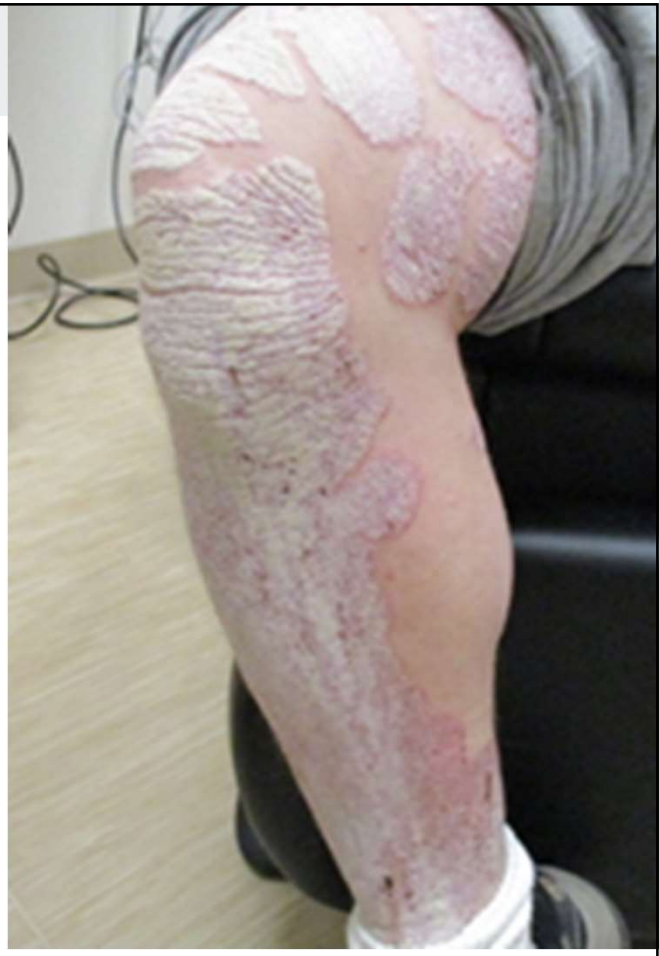
# Psoriasis Treatment Options: Review and Updates

# Treatment: Topical Steroid Tips

- Low potency for face, neck, genitalia, axilla:
  - hydrocortisone 2.5% BID, desonide 0.5%, triamcinolone 0.25% creams/ointments.
- Mid to high potency for body areas including trunk/extremities:
  - triamcinolone 0.1 or 0.5% cream/ointment, mometasone 0.1% cream/ointment, Betamethasone 0.5% cream/ointment
- Super or Ultra High potency for trunk/extremities, feet/**palmar** hands:
  - clobetasol 0.5% oint/cream, Augmented betamethasone dipropionate, Halobetasol.
- Scalp: mometasone solution, fluocinonide oil, Clobetasol solution
- Twice daily (once daily works for some), 2 weeks on, 2 weeks off→ recheck.
- Side effects: skin atrophy, steroid reliance or rebound effect, purpura, telangiectasia, striae, focal hypertrichosis, acne, rarely hypothalamic-pituitary-adrenal axis suppression (children)
- Maintenance therapy can be 1-2x/week

# Additional Treatment: Topical/Light

- Calcipotriene (Dovonex) 0.5% ointment, cream, solution
  - Daily to BID dosing
  - Ages 12 yo +
  - Vitamin D3 derivative
- Calcitriol ointment - BID
  - Binds to Vitamin D receptors
  - Not approved in peds
- Tapinarof (VTAMA) - naturally derived from worm poop
  - Daily application, can see resolution for up to 4 months
- Roflumilast (Zoryve) - topical PDE4 inhibitor
  - Good for intertriginous areas
  - Cream is only approved for PSO at this time
- UVB phototherapy - need access and time 2-3x/week



# Treatment: Biologics - TNF alpha inhibitors

- Etanercept (Enbrel)
  - FDA approved for PSO and PSA down to 4 years old
- Infliximab (Remicade): Infusion
- Adalimumab (Humira)
- Certolizumab (Cimzia) - approved during pregnancy
- All FDA approved for psoriasis and PsA
- Full response is seen 3-4 months after starting treatment
  - can consider dose increase if not responding

# Treatment: TNF alpha inhibitors

- TNFs alone do not increase risk of malignancy but combined with other meds (immunosuppressants) may play a role.
  - Avoid if patient has a history of CA.
- HIV +: ok if being treated with antivirals→ consult with pt's ID provider.
- Hep C: ok, Hep B: need treatment with antivirals, then OK
- Screen for MS, CHF, malignancy (esp. lymphoreticular), current infection
- Lab screening: CBC, CMP, TB, Hepatitis B and C, HIV case by case
  - Yearly: TB, per provider discretion CMP, CBC
- Side effects: injection site reaction, increased risk for infection, drug induced lupus, CHF exacerbation, hepatotoxicity mostly with infliximab, sometimes will see TNF alpha induced psoriasis
- Generally accepted as safe in pregnancy (Certolizumab)

# Treatment: Biologics - IL17a inhibitors

Secukinumab (Cosentyx) and Ixekizumab (Taltz), brodalumab (Siliq), bimekizumab (Bimzelx)

- Both FDA approved for PSO and PSA
  - Ixekizumab and Secukinumab - approved down to 6 yo for PSO
  - Can use in Hep B/C, HIV +, no evidence of increased risk for CA
  - SE: oral thrush, increased infection risk. **Contraindicated for IBD patients**
  - Screening: same as TNFs but can skip Hepatitis/HIV...maybe
- Brodalumab (Siliq) - IL17 and IL25 inhibitor - good efficacy data but has a black box warning for suicidal ideation, only prescribed through a restrictive program
- Newest: bimekizumab (Bimzelx) - really good data...may be the new go to in the IL 17 category but increased risk of candidiasis for SE

# Treatment: Biologics - IL23 inhibitors

Guselkumab (Tremfya), Risankizumab (Skyrizi), Tildrakizumab (Ilumya), Ustekinumab (Stelara)

- All are approved for psoriatic arthritis as well
- **EXCEPT** Tildrakizumab (Ilumya) - PSO only, no peds approval.
- Ustekinumab (Stelara) - IL23 and IL 12
  - PSO and PSA (and Crohn's) in 12+ yo patient
  - May be good for obese patients because it has a weight based dosing.
- Efficacy within 12 weeks (often faster)
- No evidence of increased malignancy risk, can use in Hep B/C, HIV + pts
- Side effects: increased risk for infections, increased ALT/AST (rare)
- Experts in immunology consider this the safest class

| BIOLOGIC | MOA | MAINTENANCE DOSING |
|---|---|---|
| etanercept | TNFi | every week |
| infliximab | TNFi | every 8 weeks |
| adalimumab | TNFi | every 2 weeks |
| certolizumab | TNFi | every 2 weeks |
| secukinumab | IL-17Ai | every 4 weeks |
| ixekizumab | IL-17i | every 4 weeks |
| brodalumab | IL-17RAi | every 2 weeks |
| bimekizumab | IL-17A/Fi | every 8 weeks |
| ustekinumab | IL-12/23i | every 12 weeks |
| guselkumab | iL-23i | every 8 weeks |
| tildrakizumab | IL-23i | every 12 weeks |
| risankizumab | iL-23i | every 12 weeks |

Compliments of Blauvelt, A. (2024, April.) *Cutaneous Immunology: Where the drugs fit in.* Society of Dermatology Nurse Practitioners. Kiawah Island, South Carolina.

# Treatment - Non Biologics

- Apremilast (Otezla)
  - Phosphodiesterase 4 (PDE4) inhibitor: decreases inflammatory responses of T helpers 1 and 17.
  - FDA approved for  mod to severe PSO and PSA
  - Dosing:  30 mg twice daily PO
    - Loading dose: 10 mg daily, titrated up by 10 mg per day over first 5 days.
    - Do not use with cytochrome P450 meds (rifampin, phenobarbital, carbamazepine, phenytoin)
  - **Efficacy - need to discuss with patients**
  - SE: diarrhea, nausea, URIs, headache
    - Ask about depression - occurs in 1% of patients
    - Weight loss in 5-10% of patients
  - Labs monitoring not necessary but can be considered.

# Treatment - Non Biologics

Deucravacitinib (Sotyktu)

- Tyrosine Kinase 2 - member of the JAK family
  - Shuts down the IL 12 and IL 23 pathway
- Thought to be safer than other JAKs (Jak1/Jak2)
- Not a immunosuppressive like other JAKS
- No black box warning
- Oral dosing: 6 mg daily
- Only approved for psoriasis
- Labs: TB, LFTs, CBC, lipids at baseline
- Then at 1 month, then 3 months, then every 3-6 mos
  - TB yearly

## Treatment - Non Biologics

- Methotrexate - most common, immunosuppressant, used for 50 years.
- Cyclosporine - immunosuppressant, steroid sparing
- Acitretin (Soriatane) - Retinoid
  - not for women of childbearing age
  - Best for palmar/plantar PSO

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