Dermatology- New, old, off label and emerging trends for treatment

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Conflicts of interest

I will be discussing off label treatments for some multiple conditions

Consultant and speaker- Johnson and Johnson

What dermatologists can offer for wounds

Consult on diagnosis of wounds/ulcers

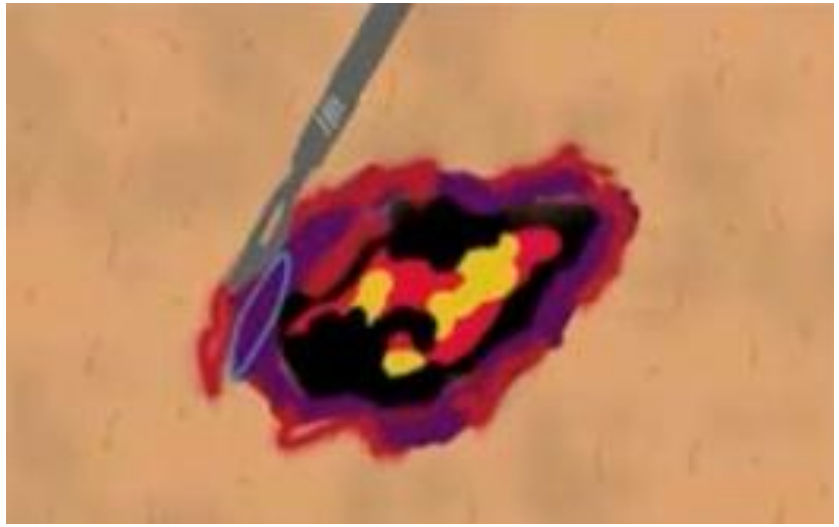
- Often getting diagnosis correct more important than wound dressings
  - e.g. antibiotics for “bilateral lower leg cellulitis”→ stasis dermatitis + acute LDS
  - Antibiotics for pyoderma
  - HS managed as recurrent abscess with incision and drainage
  - Calciphylaxis managed as pyoderma

Assist with performing biopsies

- More tissue the better→ incisional biopsy
- Often punch biopsy inadequate specimen/sampling error

Consult on off label treatment options..

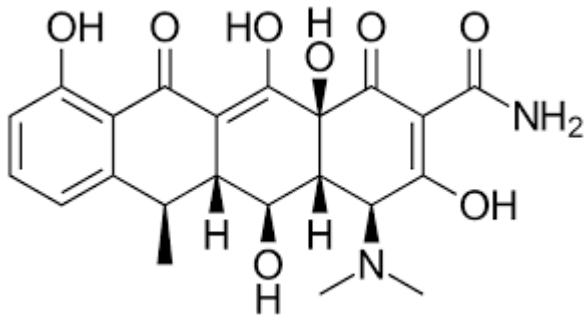
- More to come…

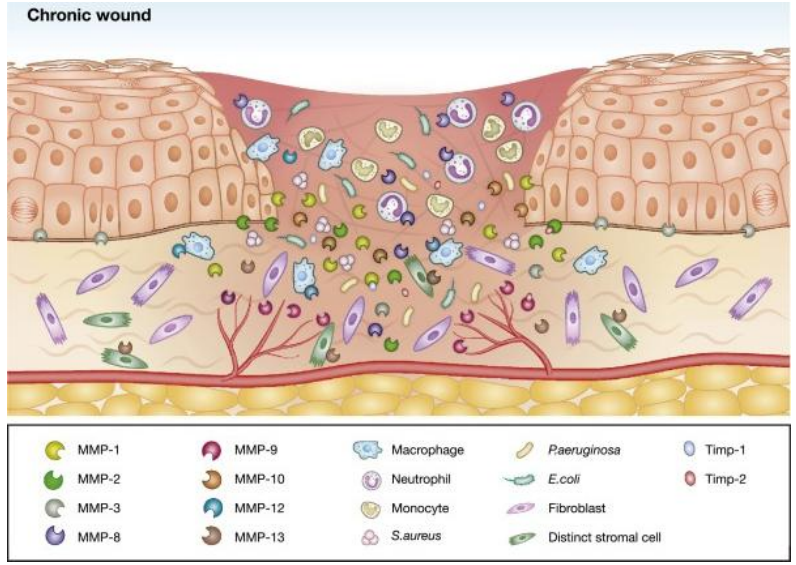


Old solutions for wounds

Oral doxycycline

- Doses 50mg daily to 100mg daily (can be BD divided doses)
- Apart from antimicrobial activity (bacteriostatic)…
- Very useful anti-inflammatory effect
  - **Inhibits**
    - Matrix metalloproteinases- ‘sculptors’ of chronic wound
    - Neutrophil migration
    - Proinflammatory cytokine production
    - Granuloma formation
- Cheap and few drug interactions

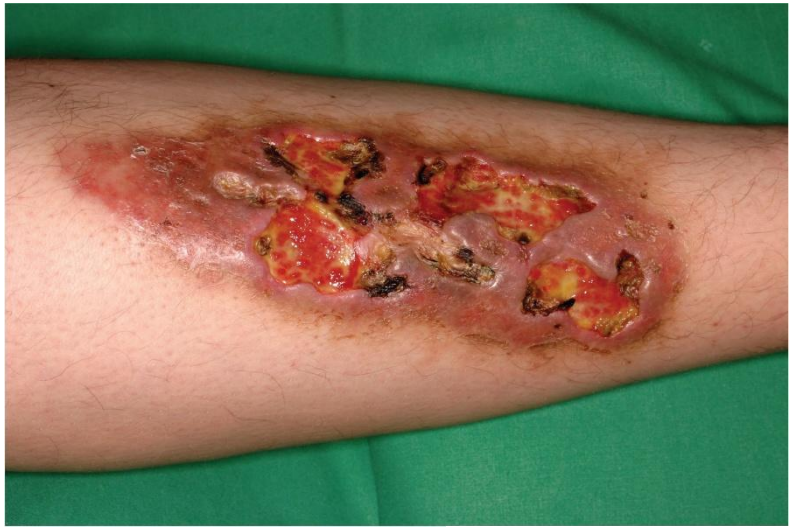




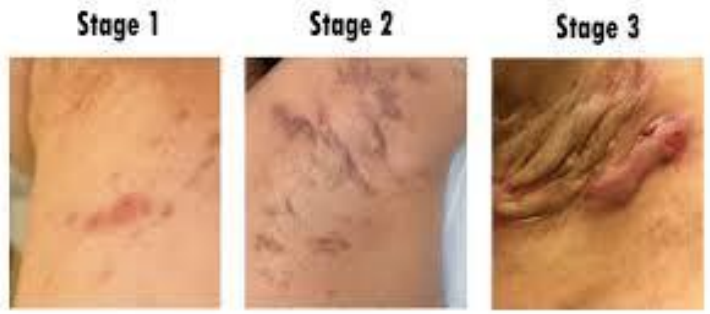
Old solutions for wounds

Oral doxycycline

- **Many indications!!!**
  - Pyoderma
  - Sweets/neutrophilic conditions
  - Hidradenitis suppurativa
  - Lipodermatosclerosis
  - Immunobullous
  - Granulomatous
  - Necrobiosis lipoidica



- Often used as an adjunctive agent alongside other systemic therapy

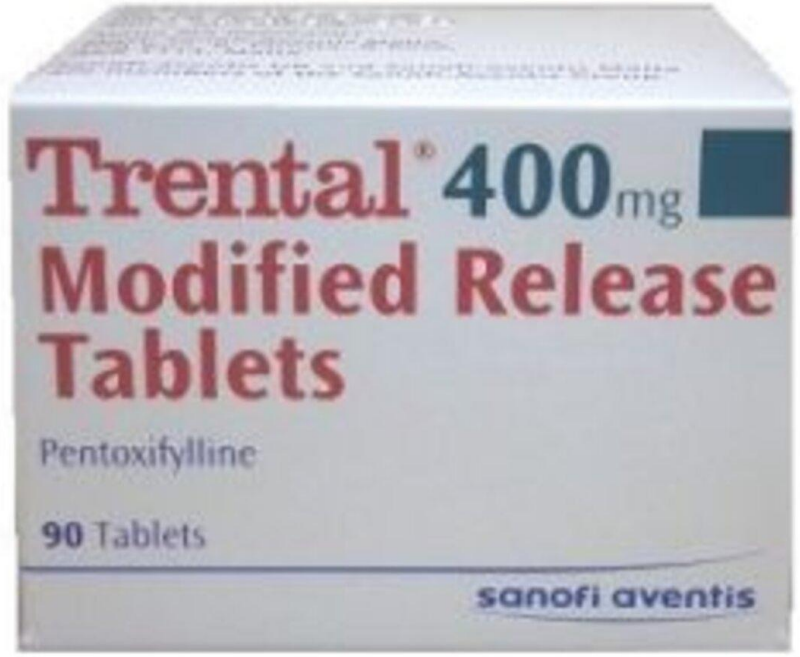


Old solutions for wounds

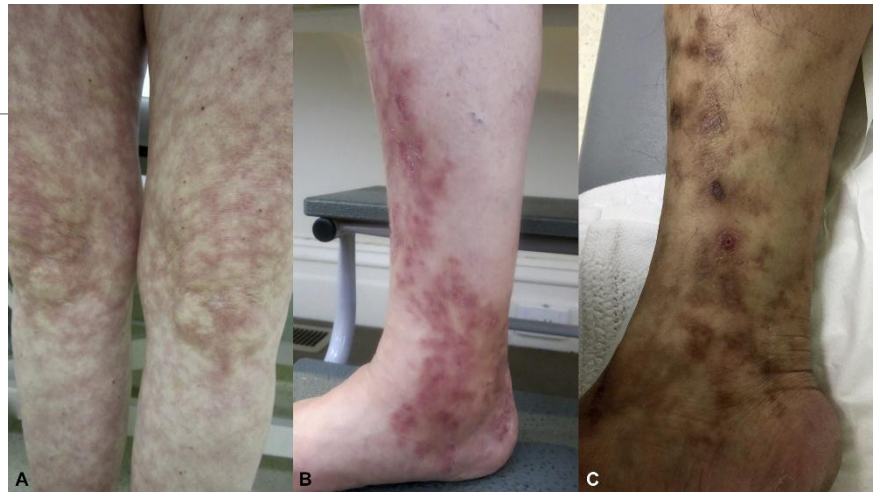
Pentoxifylline

- Anti TNF alpha inhibition
- Phosphodiesterase inhibitor
- Anti-neutrophilic
- Allows more malleable RBCs for small vessel perfusion
- Mild antiplatelet activity

- Dose 400mg daily → TDS



Old solutions for wounds



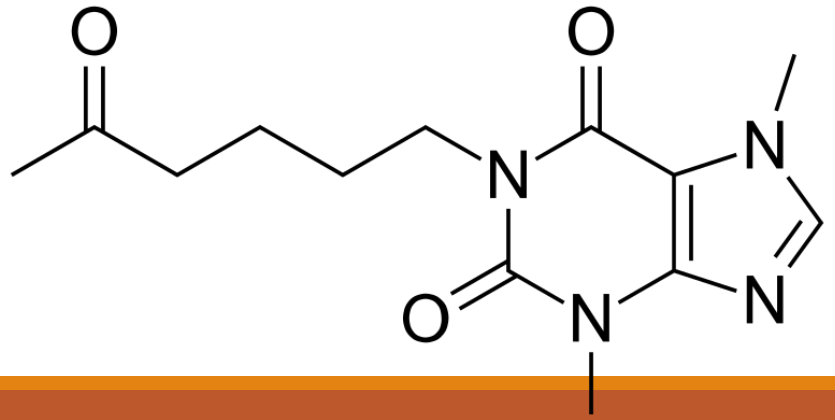
Pentoxifylline

- **Indications**
  - Venous (stasis) ulcer
  - Livedoid vasculopathy/Lymphocytic thrombophilic arteritis
  - Lipodermatosclerosis
  - Necrobiosis lipoidica

Some cost through community pharmacies (50 tabs $40)- not covered by PBS

- Most hospital pharmacies help subsidise cost for outpatients

GI upset, headache/flushing most common side effects



New solutions for wounds

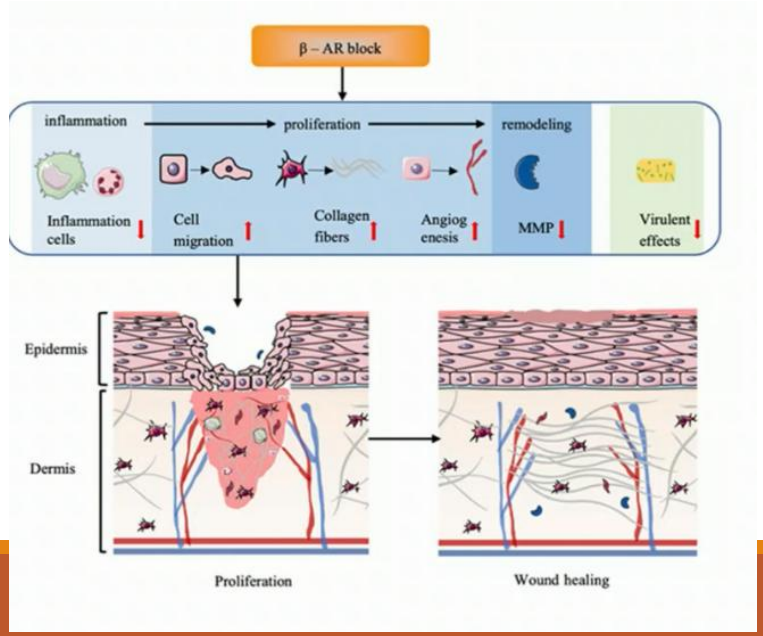
Topical timolol 0.5% eye drops

- apply 1 drop per 1-2 cm squared, Finger as a paint brush

Keratinocytes express abundant b2-adrenergic receptors-play role in cutaneous homeostasis

Benefits

- increase extracellular signal-regulated kinase phosphorylation and keratinocyte migration and thus accelerate skin wound re-epithelialization
- Reduce anti-inflammatory cytokine production
- Increase collagen fibre deposition
- Improve angiogenesis
- Inhibit MMP overexpression



New solutions for wounds

Topical timolol

- Very safe – used for many years for infantile haemangioma
- Minimal systemic absorption even in infants

- Data exists for
  - Diabetic ulcer
  - Venous ulcers
  - Mixed ulceration (arteriovenous)

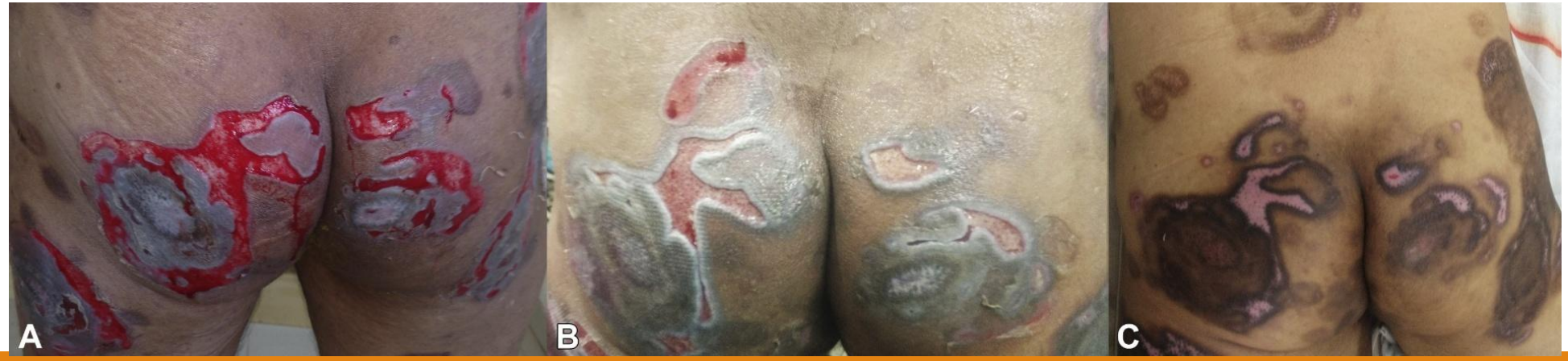
Prospective non-randomized observational study:	Multi-center retrospective case series:	Prospective randomized controlled Phase 2 trial:	Phase 3 trial:	Phase 3 trial:
Timolol maleate 0.5% (1 drop per 2 cm of wound perimeter) improved healing in chronic diabetic and venous leg ulcers by promoting keratinocyte migration (N=60)[1].	**Timolol maleate** 0.5% (1 drop per cm^2) was effective and safe for recalcitrant wounds of various etiologies[2] (N=39).	**Timolol maleate** gel showed benefit and safety for hard-to-heal venous leg ulcers (VLU) [3] (N=43).	FDA-approved ocular **timolol maleate** gel is currently being tested in a double-blind, randomized controlled trial for diabetic foot ulcers [4] (N=35).	Randomized, double-blind topical application of **esmolol 14% gel** (β1 -selective blocker) with SOC demonstrated a significant proportion of ulcer closure within a 12-week treatment period in patients with diabetic foot ulcers[5] N=140

1.Thomas B et al. J Vasc Surg Venous and Lym Dis 2017
2. Cahn BA et al, J Drugs Dermatol. 2020
3.Baltazard T. et al, Ann Dermatol Venereol 2021
4. Kaur R.et al , ClinicalTrials.gov ID NCT03282981
5.Rastogi A et al. JAMA Network Open.2023

New solutions for wounds

Topical insulin in the treatment of nonhealing erosions and ulcers of pemphigus vulgaris

- 0.5 to 1 mL insulin (Actrapid human insulin 40 IU/mL sprayed over each ulcer using an insulin syringe. Ulcers were then covered with sterile gauze.
- Repeated BD
- benefit for leg ulcers in case reports
- ↑ vascular endothelial growth factor, transforming growth factor b1, and Ki-67→angiogenesis and granulation tissue formation



New solutions for wounds- Biologics

Mainly case series and case report data

No RCT or higher level of evidence data

Off label ($$$) requires compassionate support from hospital and pharmaceutical company

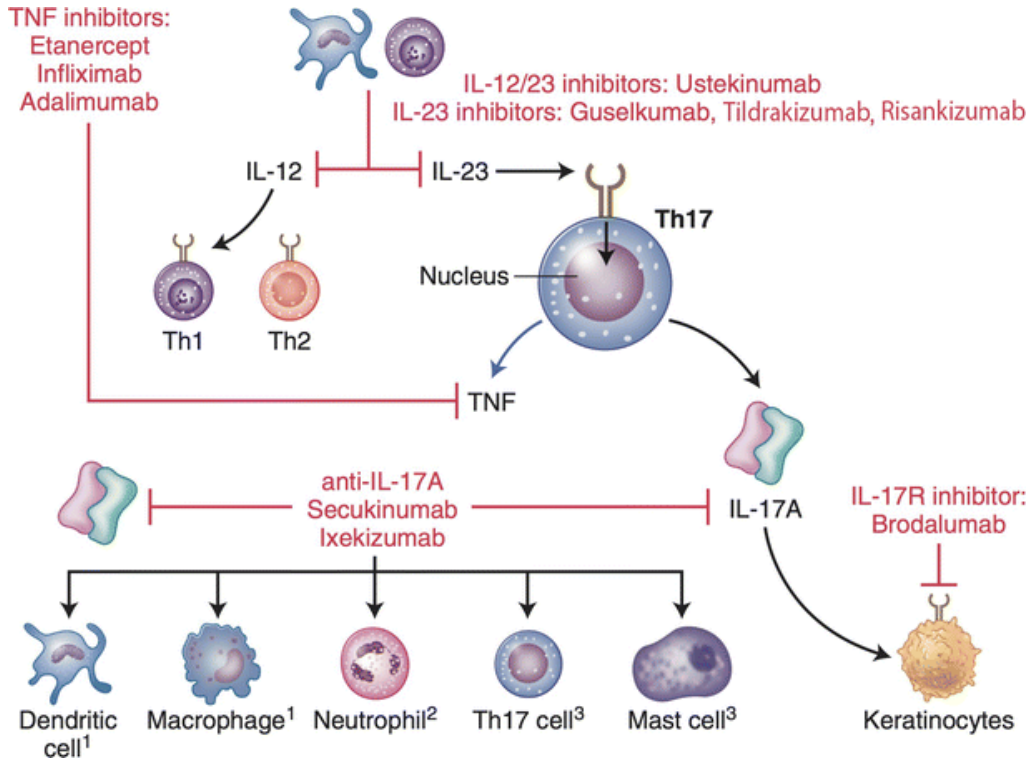
Generally added or substituted when conventional immunosuppression not efficacious/contraindicated

- Main settings
  - Pyoderma Gangrenosum + other neutrophilic
  - Ulcerative NLD/LDS

New solutions for wounds- Biologics

Classes of biologics most frequently used

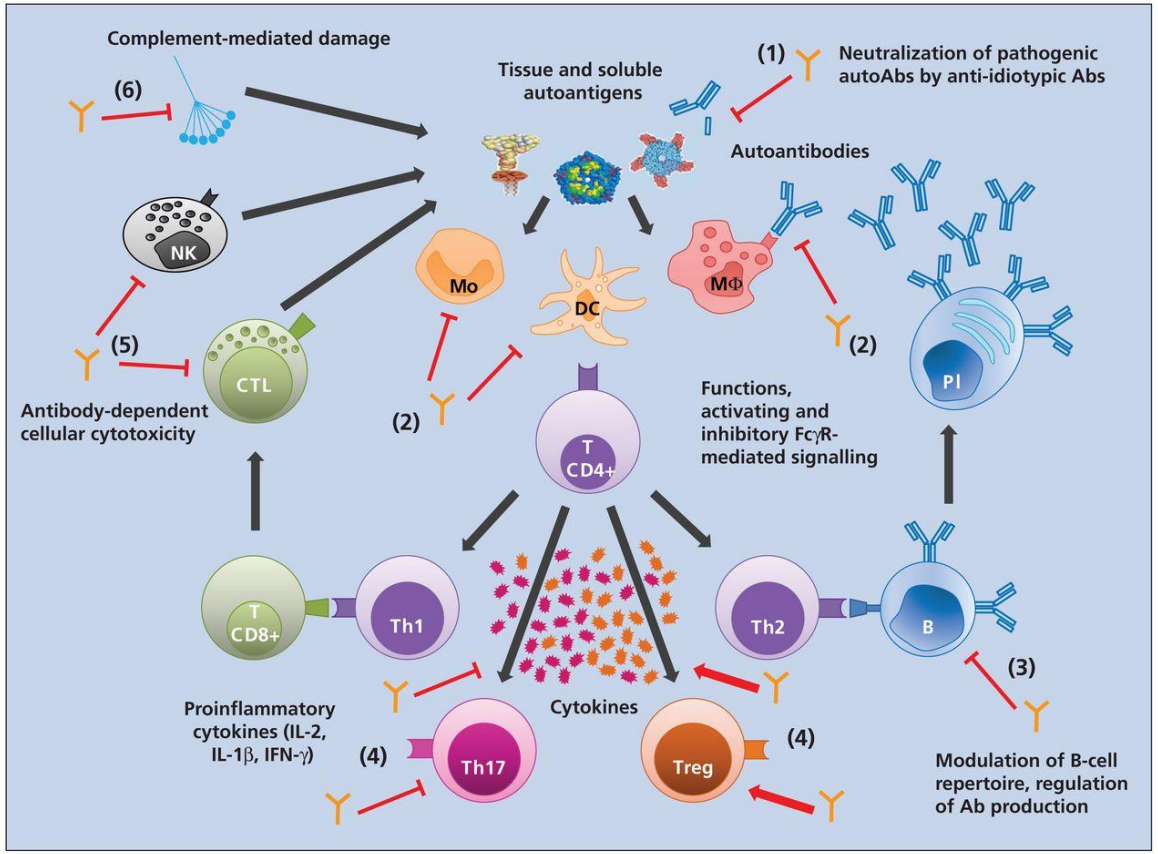
- Anti- TNF alpha
  - Infliximab – IV infusion and now subcut form available
  - Adalimumab- subcut
- Anti IL12/23
  - Ustekinumab- subcut and IV loading
- Anti IL23
  - guselkumab, tildrakizumab etc



New solutions for wounds- IVIg

Intravenous immunoglobulin

- Blood product- plasma with immunoglobulin separated
- Pooled from many donors !!
- Expensive $$$$
- Accessed via hospital – IV infusion
  - Approval from BloodStar (Red Cross)
  - Only certain indications such as Pyoderma/refractory immunobullous/autoimmune etc



Issues with sorbolene/aqueous creams

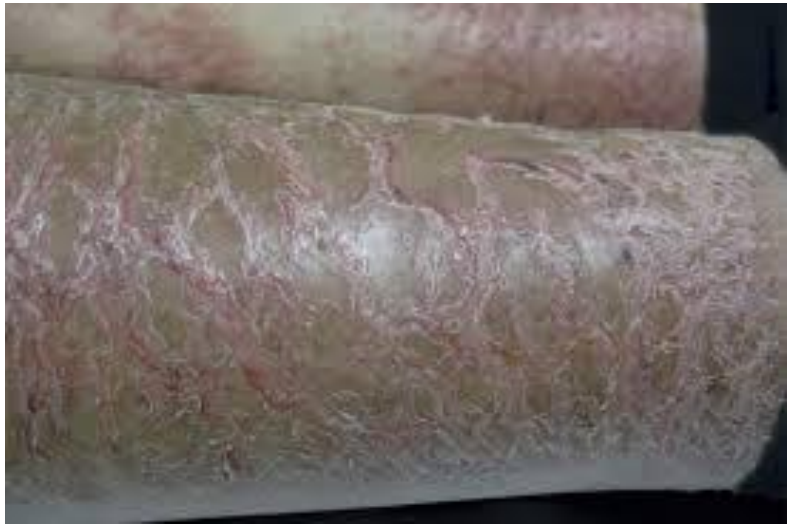
Inspissated cream!- leaving on cream and not removing excess/residue

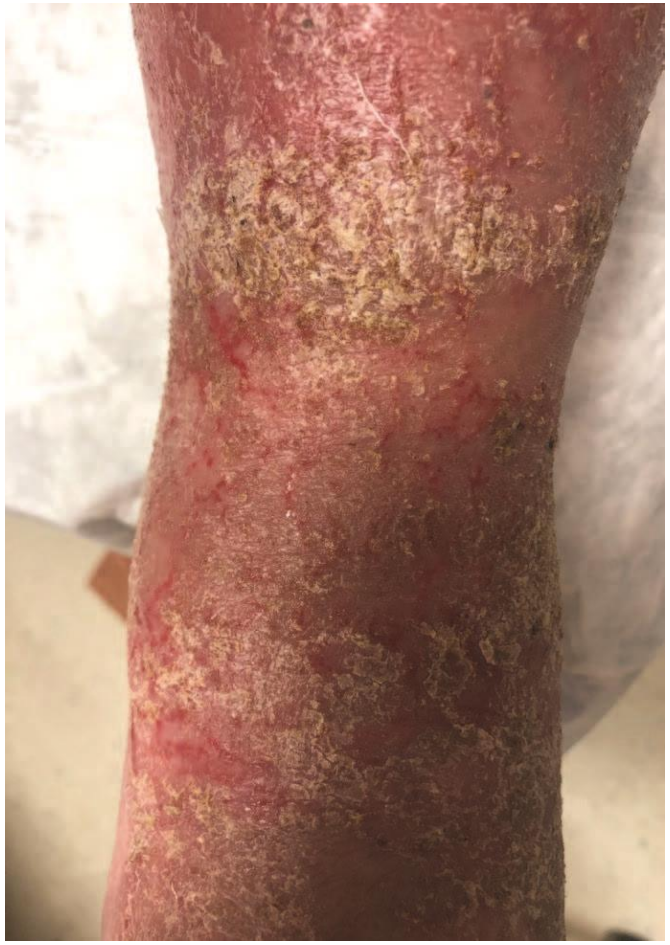
Fragrances + preservatives- Allergic contact dermatitis risk!!

pH not optimised for skin- pH for both higher!

Poor quality moisturisers

- Many better on market
  - Ceramide containing- CeraVe, QV with ceramides, Cetaphil
  - Silicone containing- Strata CTX





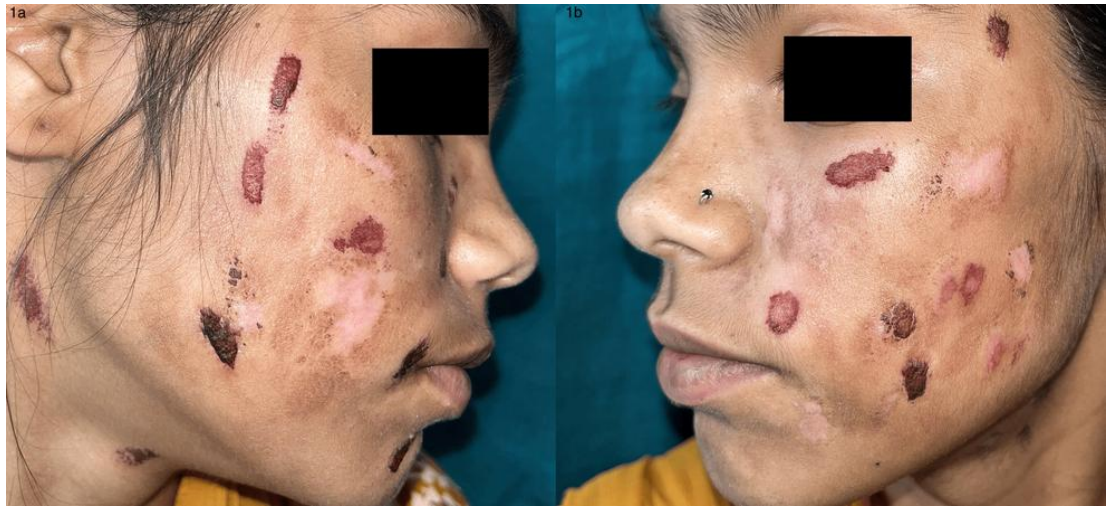
Dermatitis artefacta

A modern epidemic!

Especially in post COVID mental health pandemic

Patients self induce skin lesions as maladaptive response to psychological stress

- Clues
  - Unusual / geometric shapes
  - Linear
  - Co-existent mental health
  - Location on body that can be reached
  - Heal when under supervision/occlusive dressing



Dermatitis artefacta

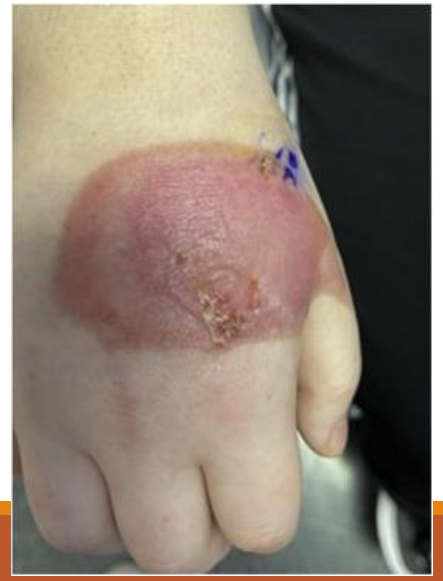
Often patients deny having created lesions

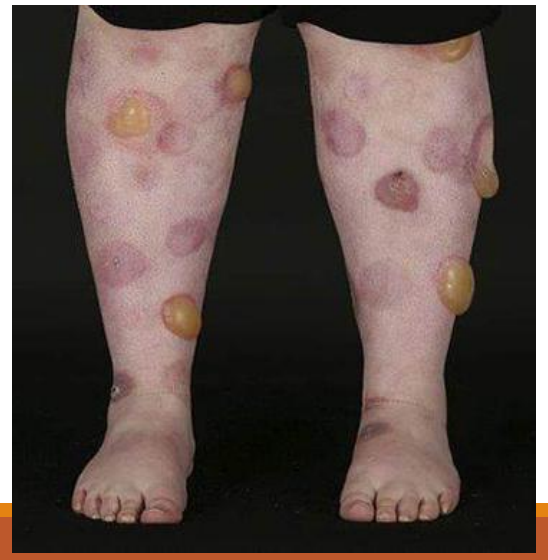
In adults often poor prognosis

In my personal experience limited psych support

- Have even had psychiatrists support patients insistence for “missed” organic diagnosis

In many cases require biopsies, bloods, cultures to exclude differentials





Skin decontamination

Dilute vinegar soaks- antipseudomonal 1:10 water

Bleach and hypochlorous acid-

- 1/2 cup(125 mL) of demineralised water with 1/4 cup (60 mL) of white vinegar
- Slowly add 1/2 teaspoon (2.5 mL) of baking soda while stirring the solution until no further bubbles are produced.
- Finally add two teaspoons (10 mL) of Milton sanitising solution.
- 0.04% hypochlorous acid solution has a pH of approximately 5, similar to the pH of the skin.
  - stored away from direct sunlight.
- liquid or gel can be made by adding a small amount of xanthan gum or gelatine powder Potassium permanganate- dilute to light rose- astringent and antimicrobial

Burrows solution- aluminium acetate 3-15%- astringent and antimicrobial

Prontosan costly

BlastX- risk of allergic and irritant contact dermatitis

- PEG & Benzalk Chloride

A case for call to action

- Acute wards, outpatients and EDs under more and more pressure
  - Tight budgets and increasing healthcare costs with an ageing population,
  - >1000 patients under management in Barwon Health alone with chronic wounds,

  - Wound care clinician involvement becomes even more important!

A case for call to action

- 49 year old male
- Referred for inpatient dermatology consultation by wound care nurse
- Admitted under colorectal team **multiple months** in acute hospital!!!
- Perforated sigmoid diverticulitis → multi quadrant peritonitis→sepsis
- Multiple attempts to re-approximate wound due to suspected dehiscence
- Concern from wound nurse of pathergy/PG response prompted referral
- Suicidal and medically deteriorating

- Distant history of GPA in remission, however repeat bloods post derm consultation
  - cANCA >200 with signs of PG on biopsy with necrotizing granuloma in lungs
- Treatment
  - topical corticosteroids to wound edge, IVIg, IV methylprednisolone 500mg x3 followed by rituximab 1g two weeks apart and weaning prednisolone
  - Promptly discharged within 1.5 weeks to rehabilitation

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Thank you