Pyoderma gangrenosum – using the PARACELSUS score instead of biopsies:

Caroline Fife, MD

6-12-2024: 2:00 -2:30

Disclosure

I have no relevant financial relationships with ineligible companies, whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

I do have a CONFESSION –
I AM NOT A DERMATOLOGIST.

This presentation is from the standpoint of a wound care clinician.

Pyoderma Gangrenosum (PG)

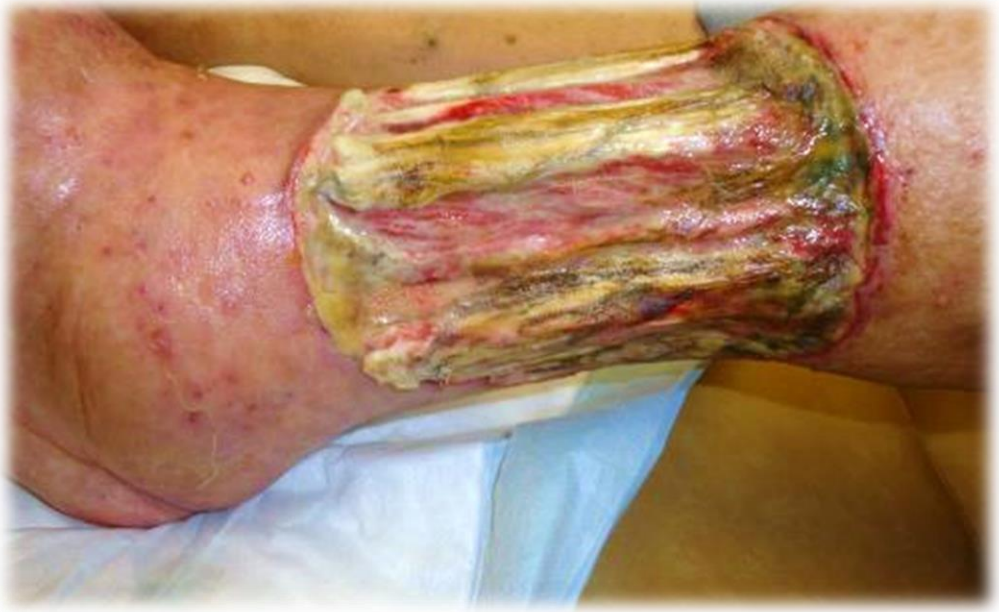
L88 – Pyoderma gangrenosum

- PG is autoinflammatory disorder that involves an **abnormal immune response** of neutrophils (neutrophilic dermatosis) which causes progressive tissue necrosis.
  - Usually presents as an extremely painful erythematous lesion which rapidly progresses to a blistered or necrotic ulcer; often a ragged undermined edge with a violaceous/erythematous border.
- Can occur on *any* part of the body (including genitals and eyes), but most often affects the legs.
- Can be triggered by trauma ("pathergy") and made worse by "debridement."
- About 50% of cases are associated with a systemic inflammatory condition: ulcerative colitis, Crohn's disease, polyarthritis (an inflammation of several joints together), gammopathy, vasculitis, leukemia, and other conditions.
- "Rare": Incidence is thought to be approximately 1:100,000
  - ~1% of patients in the USWR are diagnosed with PG (but likely most cases are missed)

Pyoderma gangrenosum - Autoimmune Association Pyoderma gangrenosum – a guide to diagnosis and management - PMC (nih.gov)

Bad Disease with Bad Associations

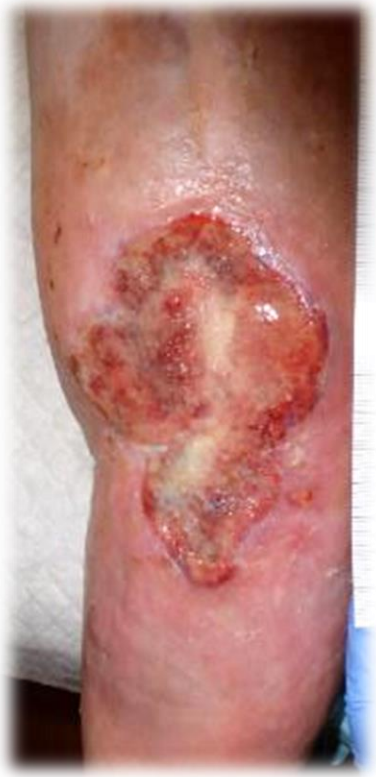
- Inflammatory bowel disease/Ulcerative colitis/Crohn's disease
- Rheumatoid arthritis/psoriatic arthritis, etc.
- Myelocytic and Hairy cell leukemia
- Myelofibrosis
- Myeloid metaplasia
- Solid tumors (paraneoplastic syndrome)
  - Colon
  - Sarcoma
  - Others



Limb threatening PG as a paraneoplastic syndrome of myosarcoma (Photo C. Fife, MD, do not use without permission)

The many presentations of PG

- Main types of PG
  1. Classic ulcerative form; most often occurs in the legs
  2. Granulomatous (may be more superficial) – slow progression, presents with verrucous and ulcerative lesions
  3. Peristomal (~15% of all cases)
  4. Pustular
  5. Malignant



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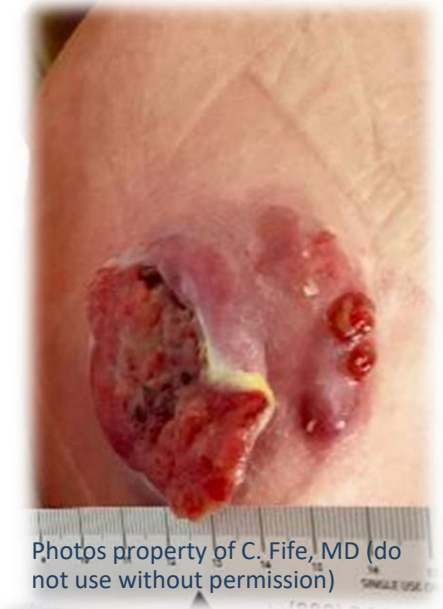

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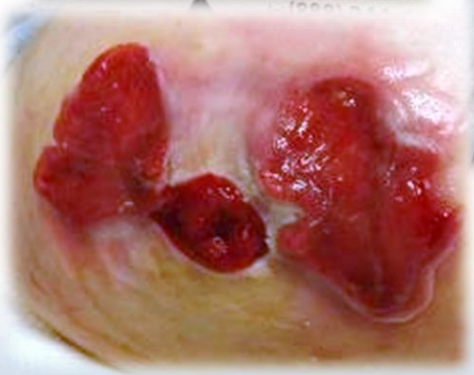

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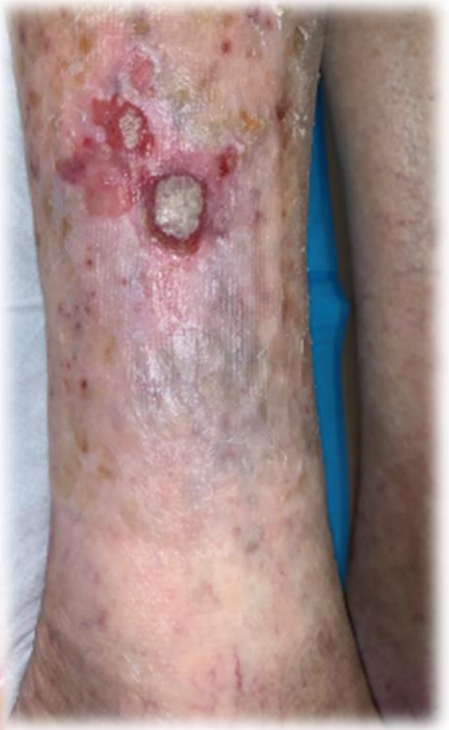

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Pyoderma gangrenosum – a guide to diagnosis and management - PMC (nih.gov)

The many presentations of PG

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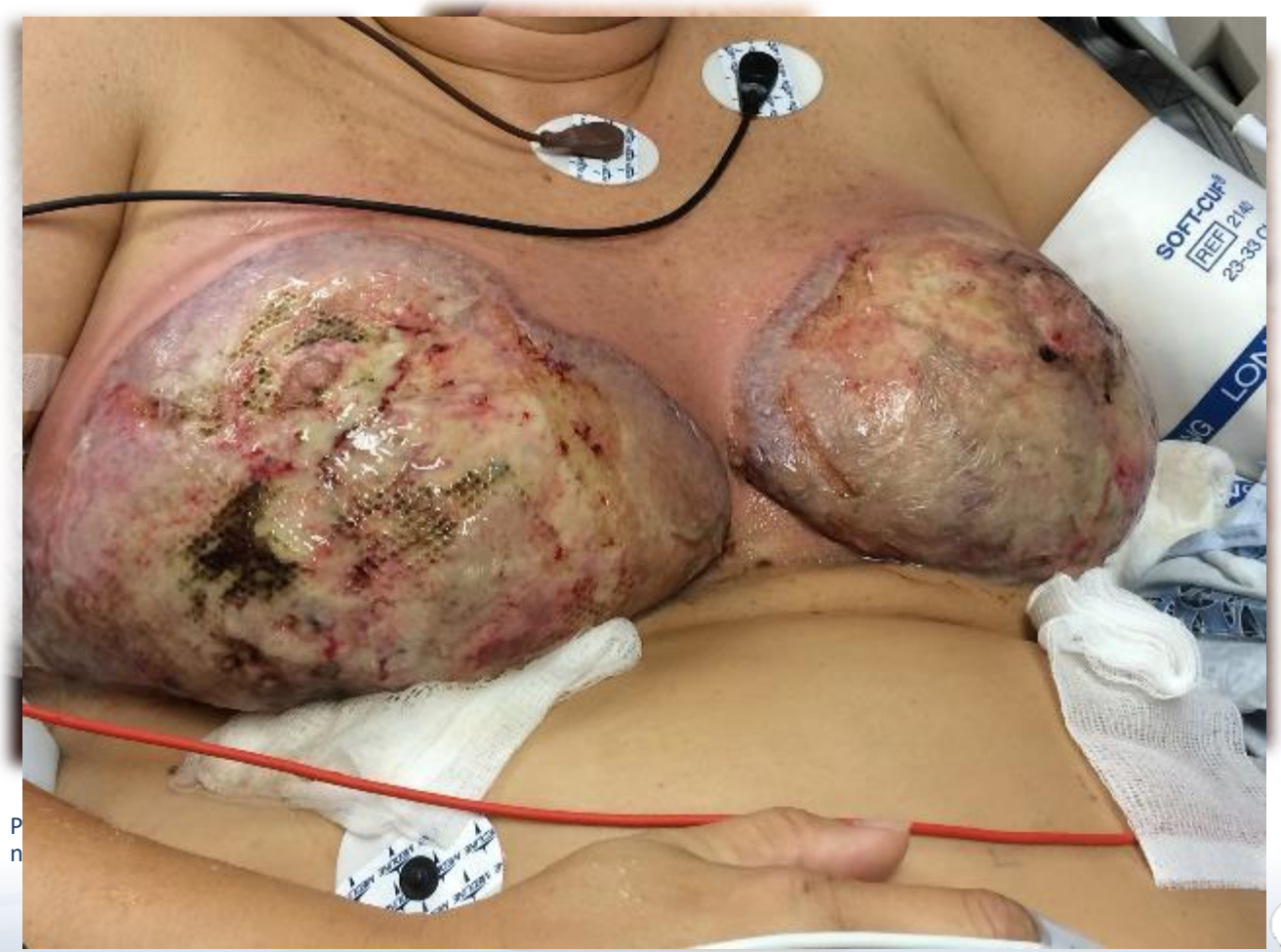

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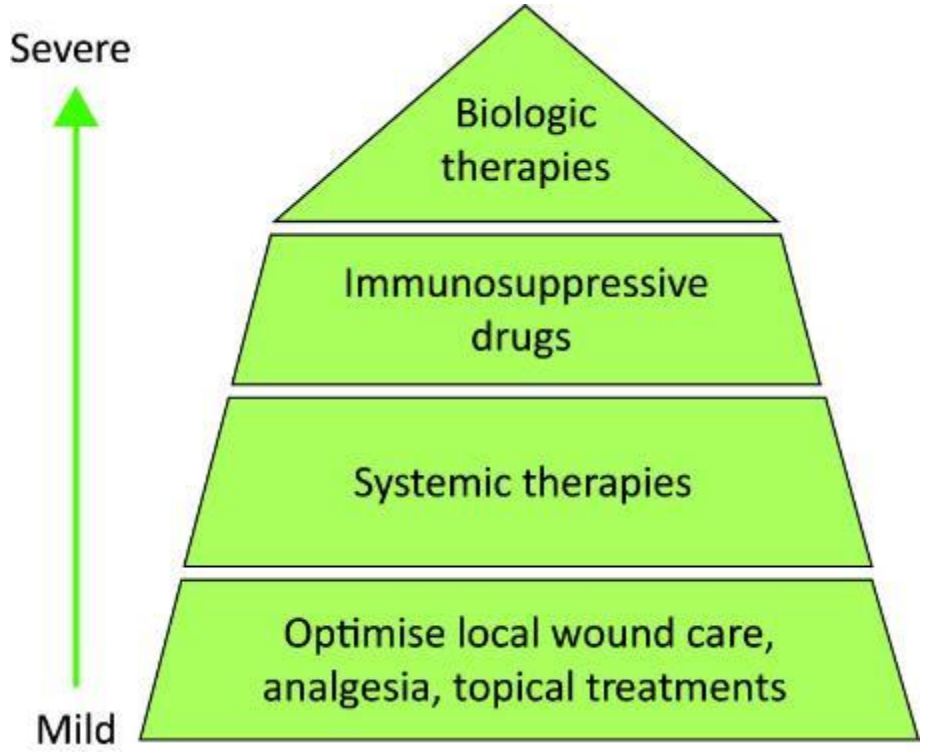
PG Treatment

- Largely Anecdotal
- **THIS IS A SYSTEMIC DISEASE THAT REQUIRES SYSTEMIC TREATMENT**
- **Systemic steroids response can be diagnostic**
- Intralesional steroids are helpful in isolated lesions, but topical steroids are of almost no use
- In mild cases, topical tacrolimus and cyclosporin may be useful.
- Wound care practitioners see more of this than dermatologists

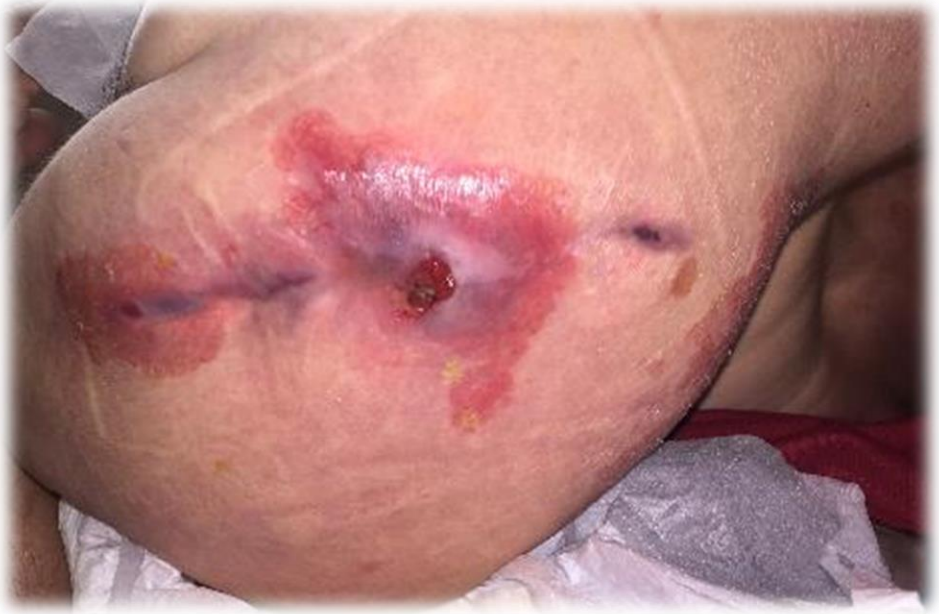


Pyoderma gangrenosum – a guide to diagnosis and management - PMC (nih.gov)

A screaming patient should be a hint

The “Debridement Disgrace”

- A hallmark of pyoderma gangrenosum is pathergy, which is the appearance of new lesions at sites of trauma, including surgical wounds.
  - It is also possible to diagnose PG from the PTSD signs of patients who have been to a wound center for debridement . . .. .



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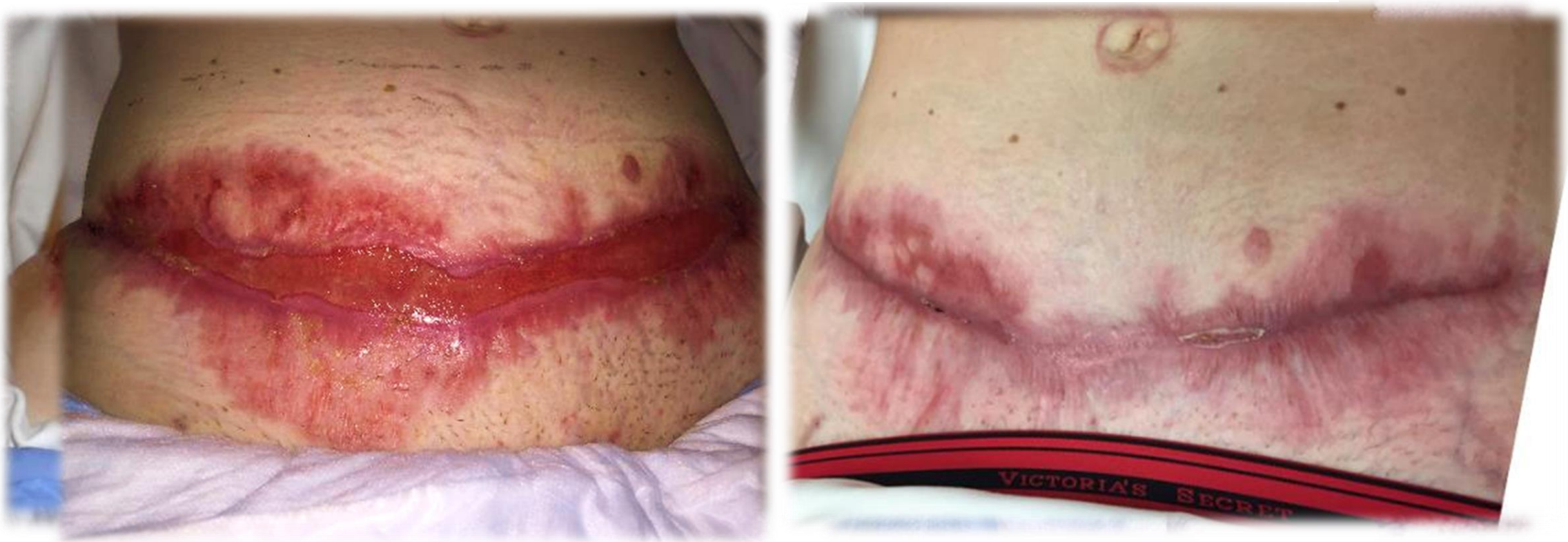
PG forming in an operative wound

30 y.o woman developed PG after an abdominoplasty which went unrecognized. She underwent NPWT for the wound breakdown and was told to “stop screaming” about the pain. She responded to systemic steroids making a dramatic improvement after only one week.



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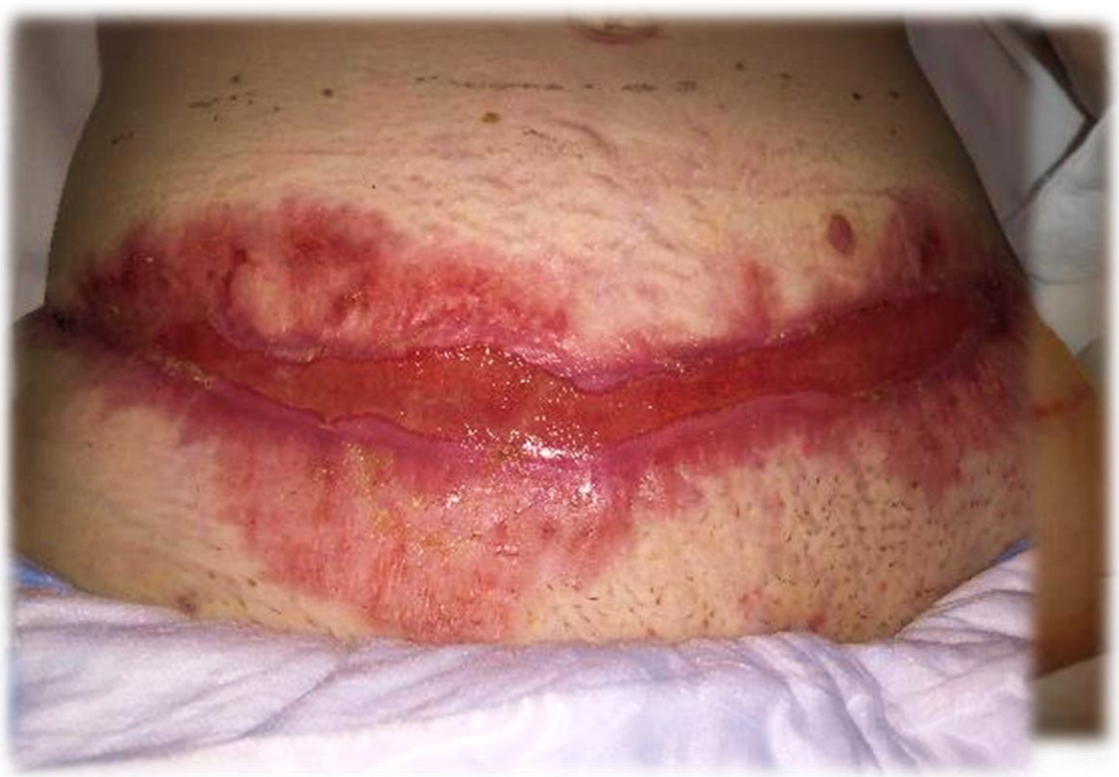

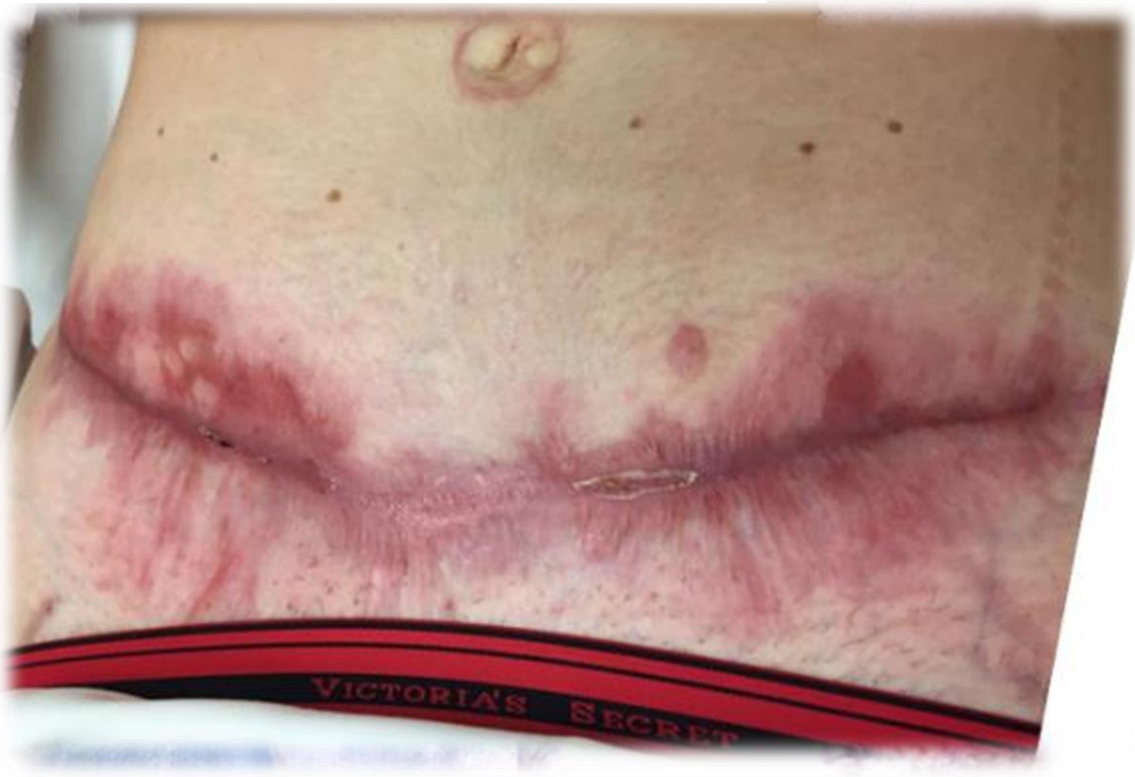

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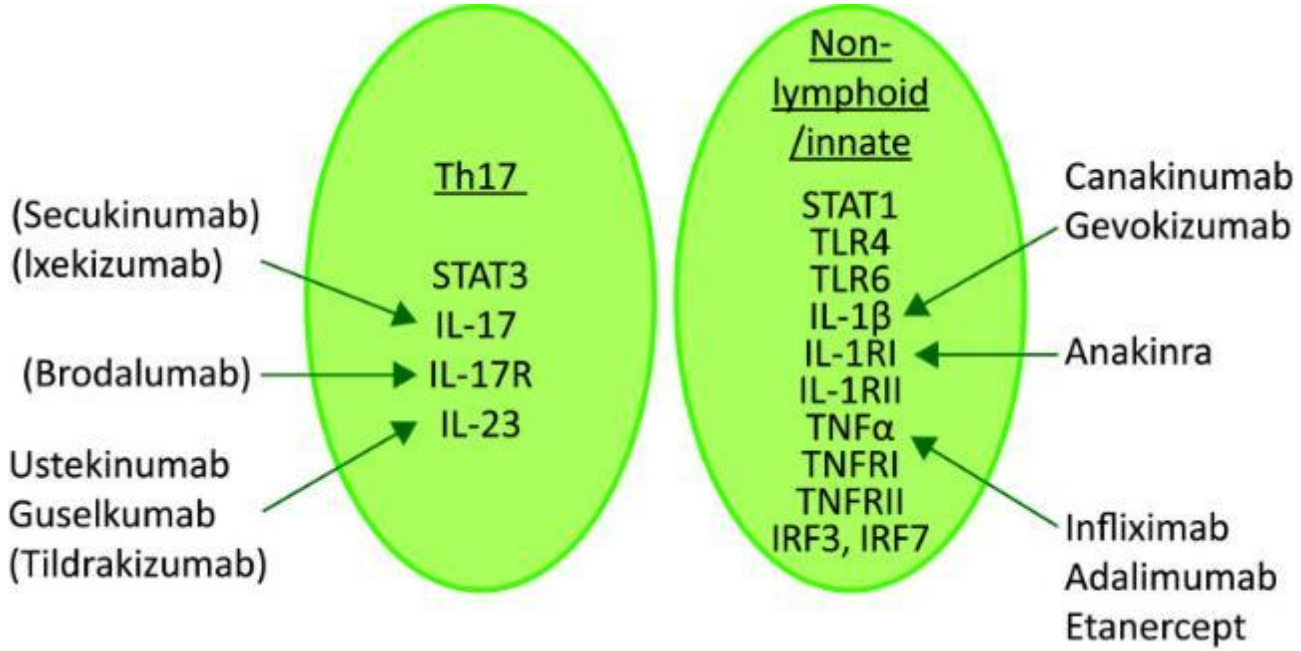
Treatment for PG

While I get the patient who isn't responding referred to an expert for biologic therapy . . .

- Call their rheumatologist or gastroenterologist
- DO NOT DEBRIDE
- Check for undiagnosed disease
  - Colonoscopy
  - Blood work for Rheumatoid disease or cancer
- **I know my limitations:**
  - Systemic steroids (start with 60 mg)
  - Dapsone (get a G6-PD level and CBC first)
  - Intralesional Kenalog
  - Topical Tacrolimus and Cyclosporin



Biologic therapy for PG targeting various cytokines

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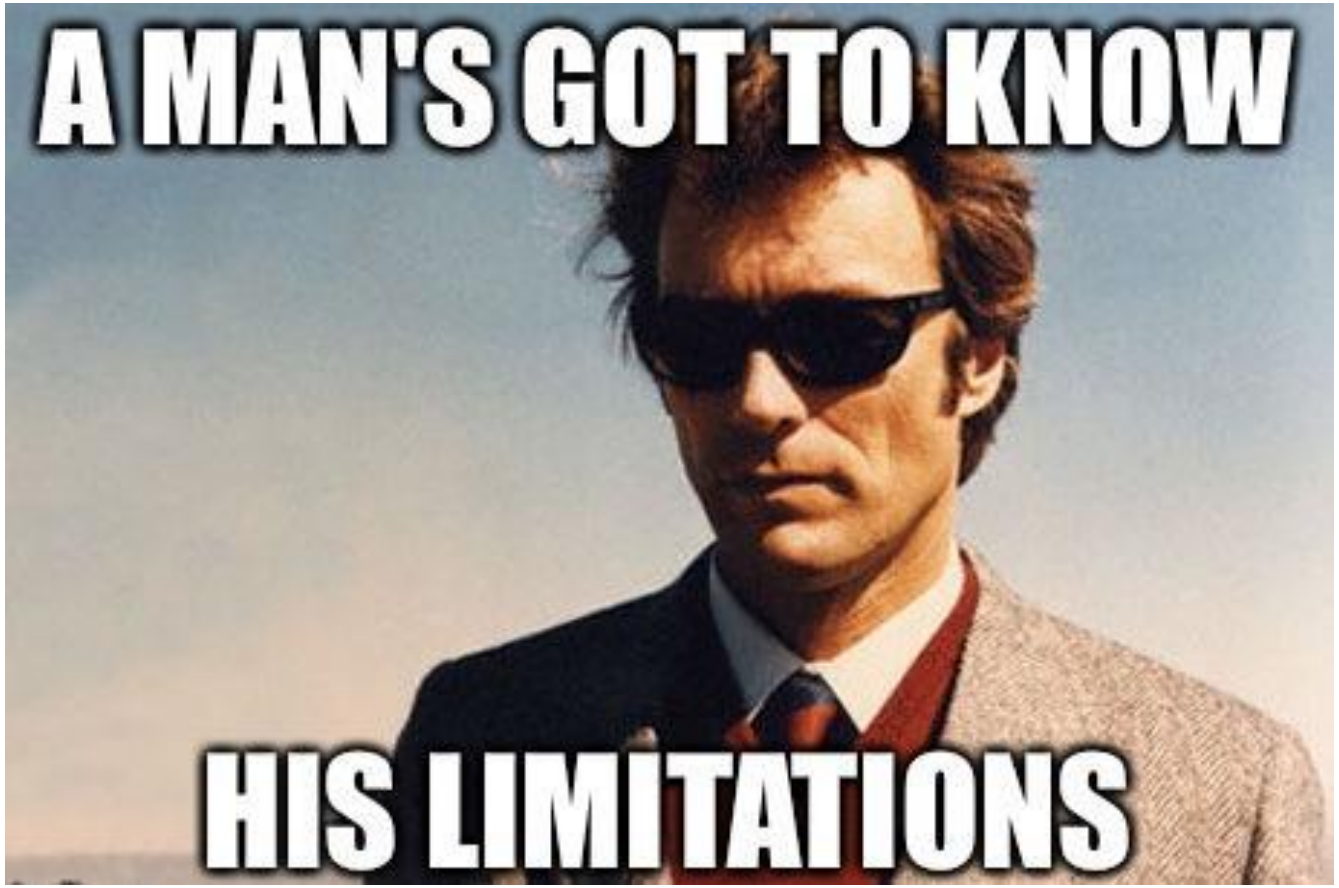


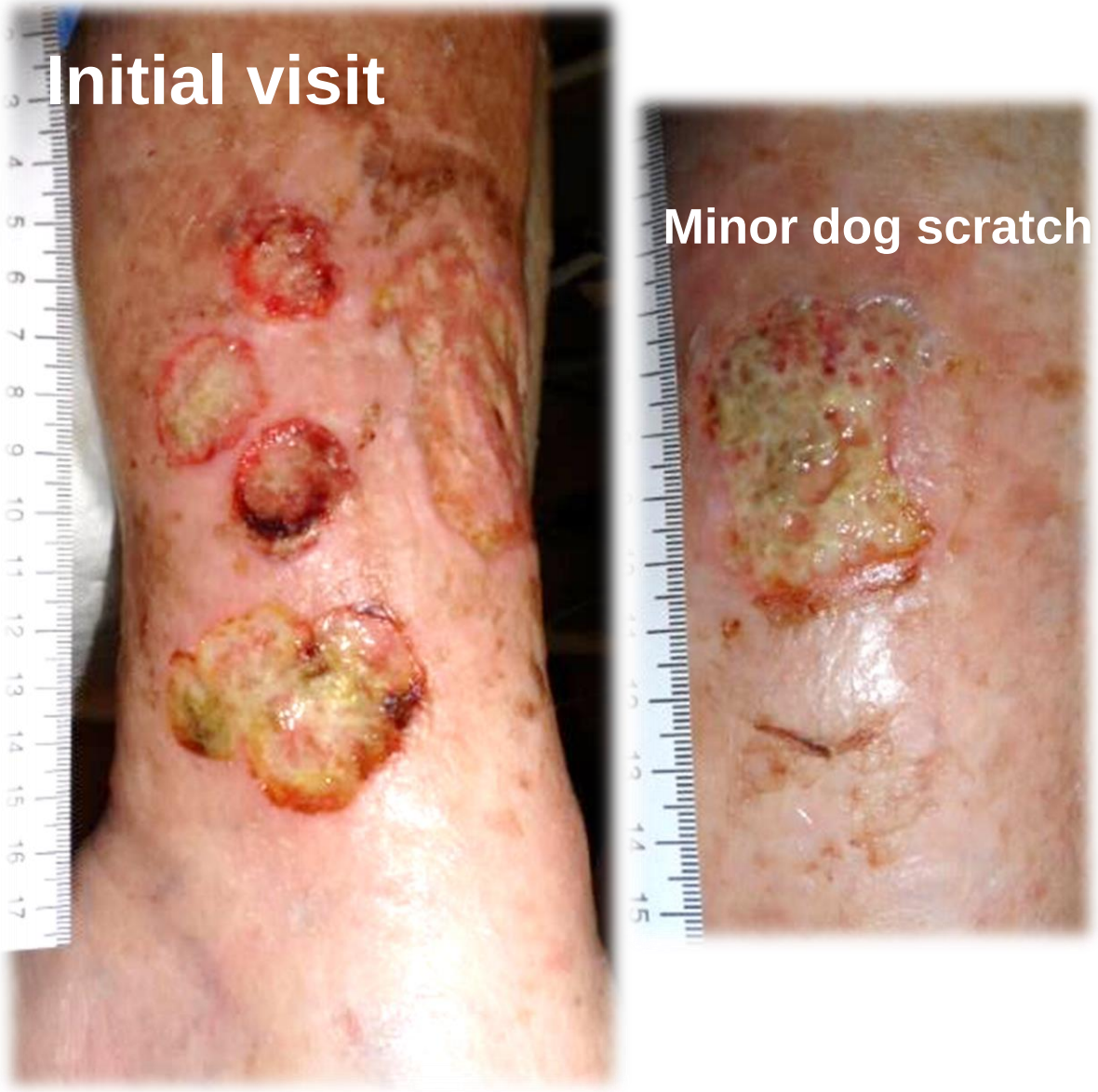
Debridement Disgrace

These excruciatingly painful left leg lesions began after a minor scratch five month earlier. **New lesions developed in response to debridements at another wound center.** She had a new and rapidly enlarging anterior shin lesion on the other leg that formed after a minor scratch from her dog. Of note, she had "bird fancier's lung" from her parrot.

Her first tearful question was, "Are you going to debride this?"

Biopsy did not show pyoderma. Dramatic improvement after 4 weeks on high dose prednisone (60 mg) which completely stopped her pain.

In consultation with her pulmonology and dermatology, she's transitioned to Cyclosporine.



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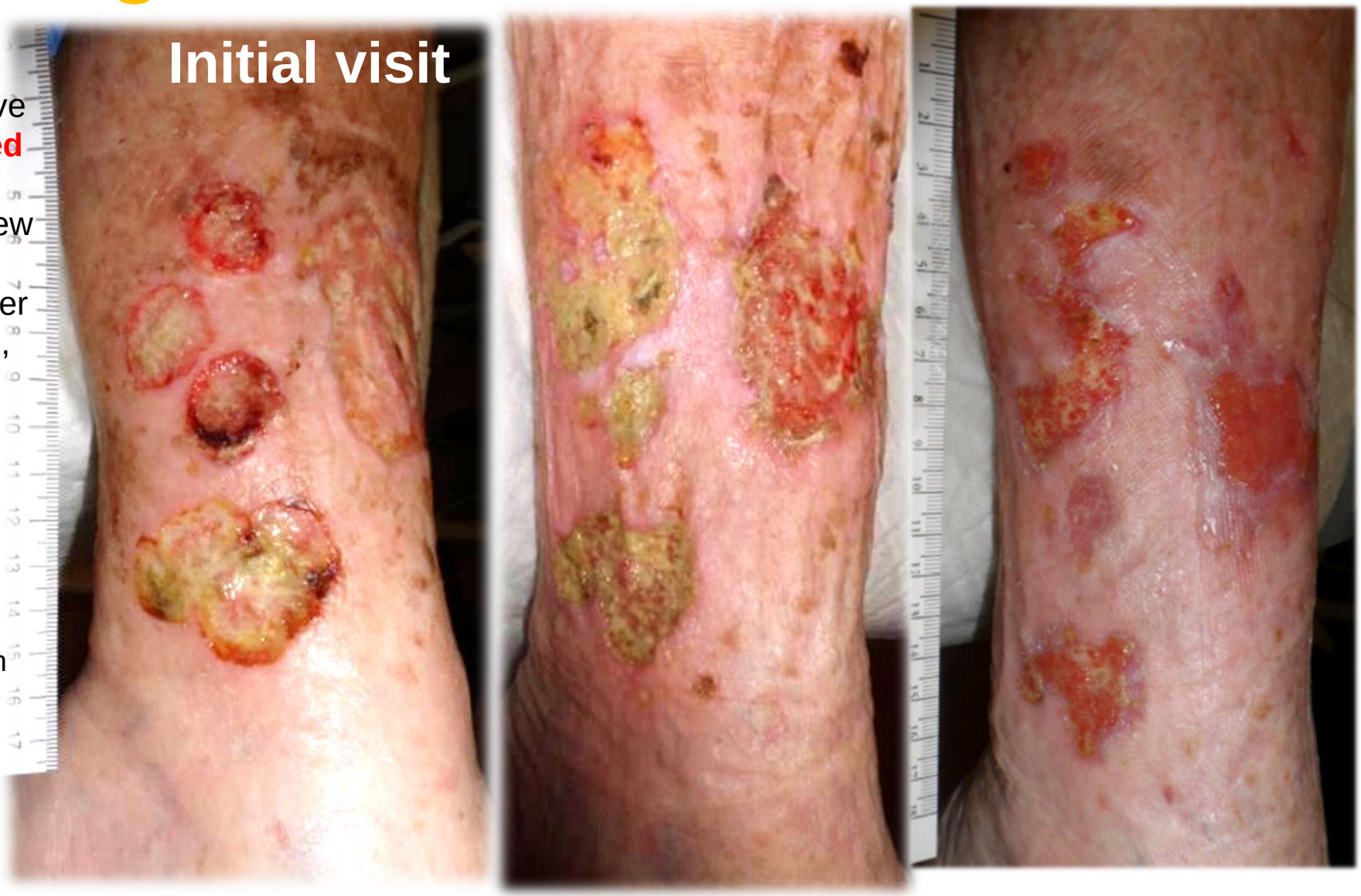


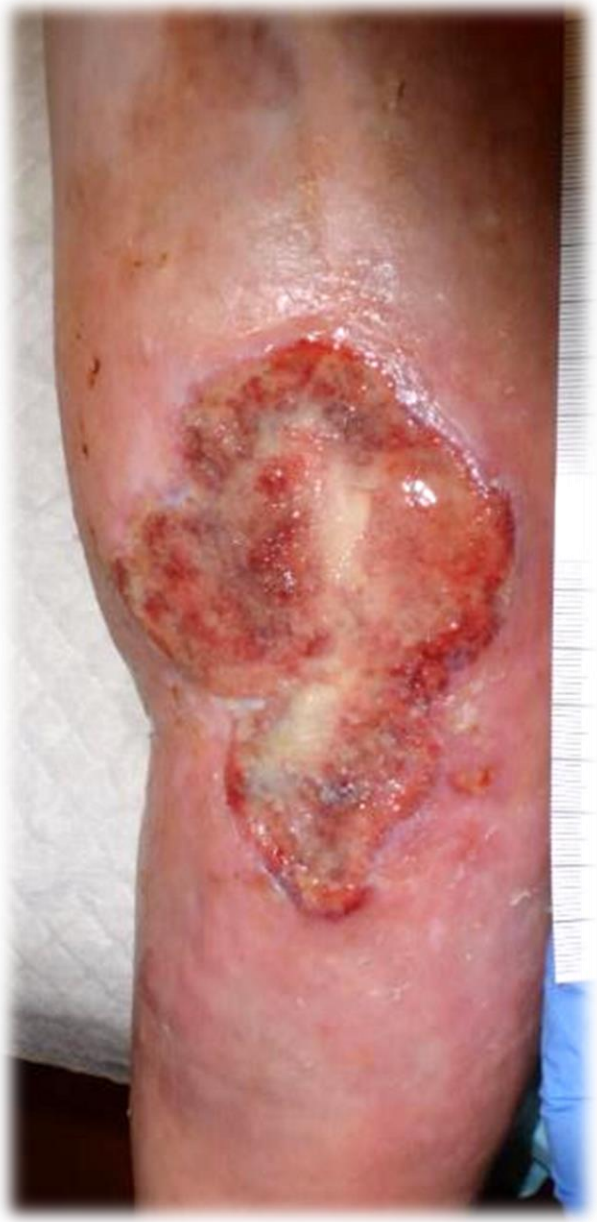
Rapid response to stopping debridement and starting prednisone.

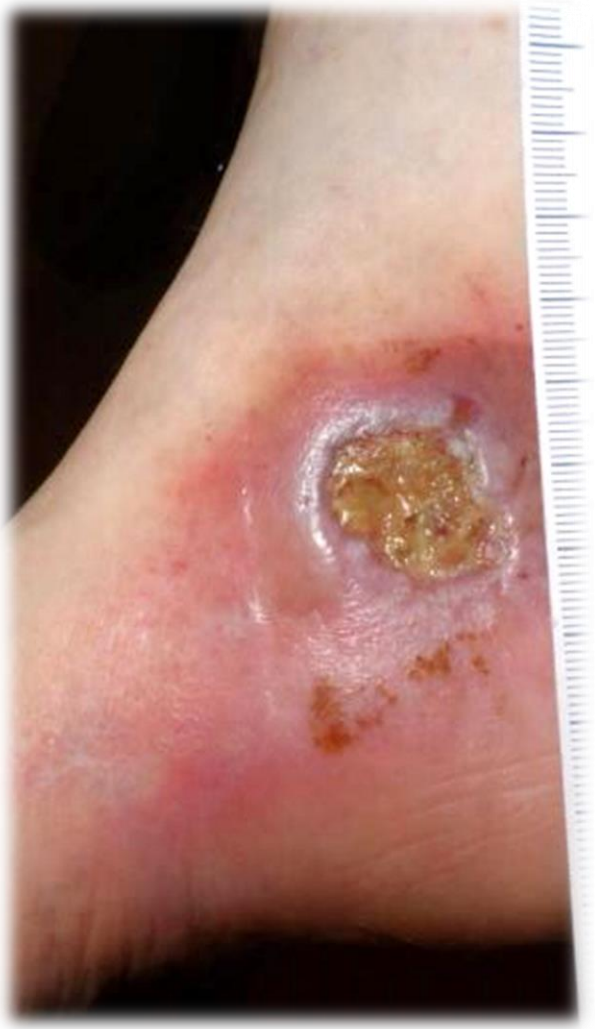
Debridement Disgrace

48 y.o. man with mild mental retardation: excruciatingly painful left shin ulcer began 10 years earlier after a go-cart accident. A new, contralateral ankle ulcer has rapidly enlarged since he was stung by a wasp. He has no arterial disease, and his X-rays show no osteomyelitis.

He has been treated elsewhere with serial debridements and venous ablation which made him worse.

Closed with prednisone and dapsone.





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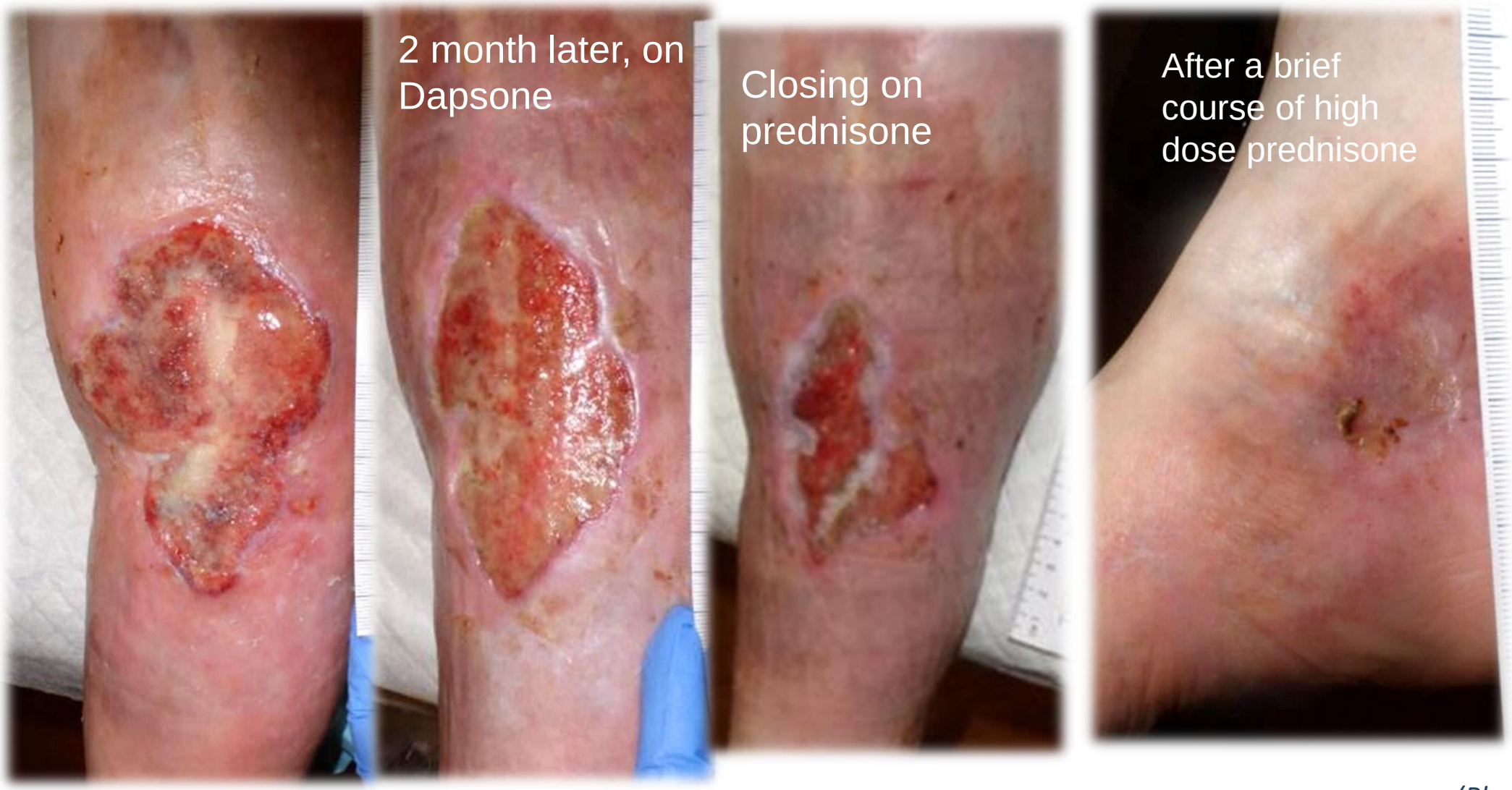
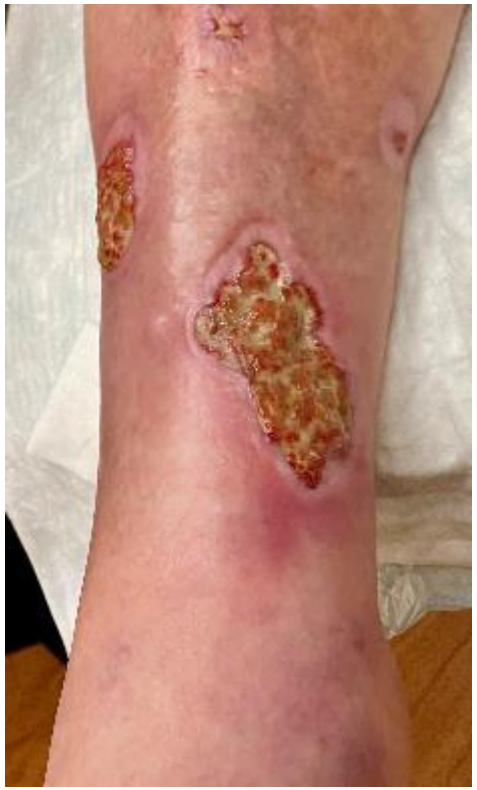
Debridement Disgrace

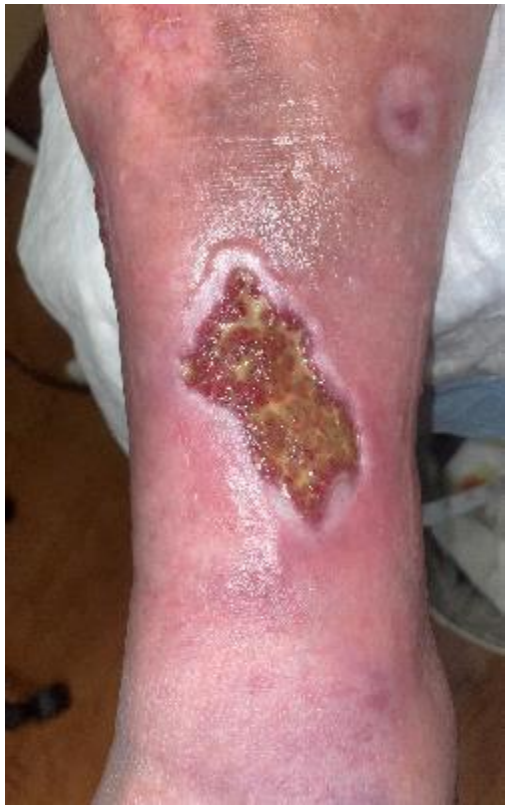


(Photos, C. Fife, MD)

It can be hard to find a dermatologist to help

When the biopsy was negative, the academic dermatologist told him it was “vascular.”





67-year-old man with well-controlled diabetes and multiple, bilateral, irregularly irregular, painful lesions which had all been made worse by the “serial debridements” performed at another wound center. Wounds improved when he stopped going to the wound center.

He was s/p a colostomy performed for inflammatory bowel disease (IBD), had hidranitis supprativa (HS), and scars on his face from cystic acne.

A biopsy performed at a respected academic dermatology program was unhelpful and the dermatologist told him it was “vascular.”

I diagnosed him with “PASH” for Pyoderma gangrenosum, Acne, and “Supprativa Hidradenitis,” first identified in 2012. Dramatic improvement with one week of prednisone, which also improved his HS.

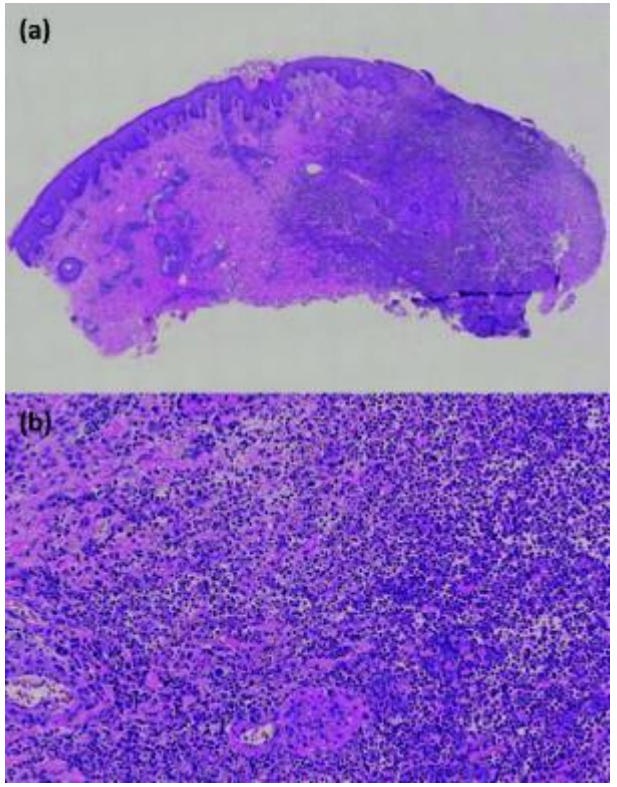
A month later he died of COVID.

1. J Am Acad Dermatol. 2012 Mar;66(3):409-15. Pyoderma gangrenosum, acne, and suppurative hidradenitis (PASH)–a new autoinflammatory syndrome distinct from PAPA syndrome.
2. Cugno M, Borghi A, Marzano AV. PAPA, PASH and PAPASH syndromes: pathophysiology, presentation and treatment. Am J Clin Dermatol. (2017) 18:555–62. doi: 10.1007/s40257-017-0265-1.
3. Marzano AV, Ceccherini I, Gattorno M, Fanoni D, Caroli F, Rusmini M, et al. Association of pyoderma gangrenosum, acne, and suppurative hidradenitis (PASH) shares genetic and cytokine profiles with other autoinflammatory diseases. Medicine (Baltimore). (2014) 93:e187.
4. CASE REPORT article, Front. Med., 24 March 2022 Sec. Dermatology; Pyoderma Gangrenosum, Acne, and Hidradenitis Suppurativa Syndrome: A Case Report and Literature Review.

PG is a diagnosis of Exclusion

Do not trust the biopsy.

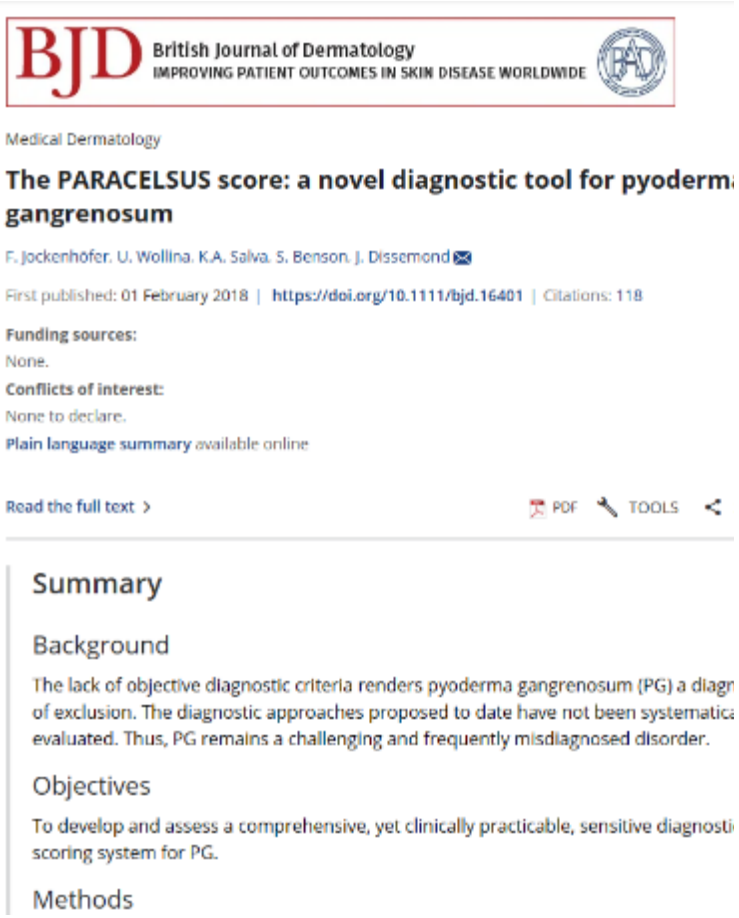
- PG can be mistaken for other conditions, such as infection, cancer, or vasculitis.
- **The purpose of a biopsy is really to rule out another etiology and not to diagnose PG**
  - **Biopsies have a high false negative rate, particularly in indolent cases**
  - **NOT providing a trial of steroids in a patient with classic signs because the biopsy is negative is bad clinical practice.**
- There is something more reliable than a biopsy!



Histological findings with an intense neutrophilic infiltrate, neutrophilic pustules and abscess formation

Pyoderma gangrenosum – a guide to diagnosis and management - PMC (nih.gov)

Comparison of 3 major diagnostic criteria



BJD British Journal of Dermatology
IMPROVING PATIENT OUTCOMES IN SKIN DISEASE WORLDWIDE

Medical Dermatology

The PARACELSUS score: a novel diagnostic tool for pyoderma gangrenosum

F. Jockenhöfer, U. Wollina, K.A. Salva, S. Benson, J. Dissemond

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None to declare.
Plain language summary available online

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Summary

Background

The lack of objective diagnostic criteria renders pyoderma gangrenosum (PG) a diagn of exclusion. The diagnostic approaches proposed to date have not been systematica evaluated. Thus, PG remains a challenging and frequently misdiagnosed disorder.

Objectives

To develop and assess a comprehensive, yet clinically practicable, sensitive diagnosti scoring system for PG.

Methods

	Mayo	Delphi consensus	PARACELSUS
Journal Invest Dermatol (2021)	N=47 (PG)	Retrospective	Dx agreed upon blind review
	Sensitivity: 74%	**Sensitivity: 74%**	**Sensitivity: 89%**
Br J Dematol (2022)	N=157 (PG and mimickers)	Multicenter	Dx by academician
		Sensitivity:32% **Specificity:57%**	**Sensitivity: 99%** **Specificity: 60%**
		PPV: 76% **NPV: 16%**	**PPV: 93%** **NPV: 95%**
JAMA Dermatol (2023)	N=162 (PG and mimickers)	PubMed cases	Dx by authors
	Sensitivity:86 % **Specificity: 70%**	**Sensitivity: 88%** **Specificity:90%**	**Sensitivity: 96%** **Specificity: 5%**

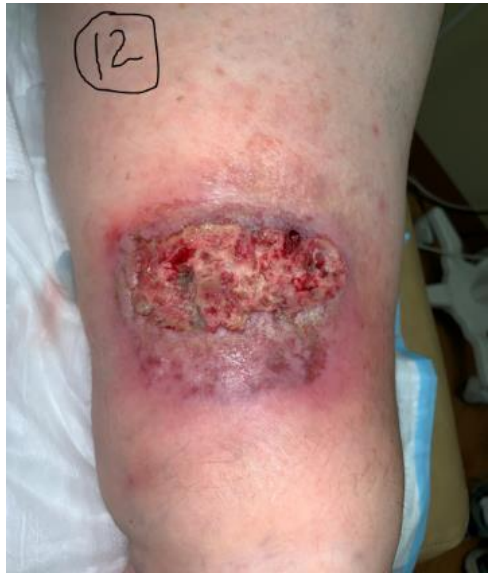
The PARACELSUS score: a novel diagnostic tool for pyoderma gangrenosum - Jockenhöfer - 2019 - British Journal of Dermatology - Wiley Online Library

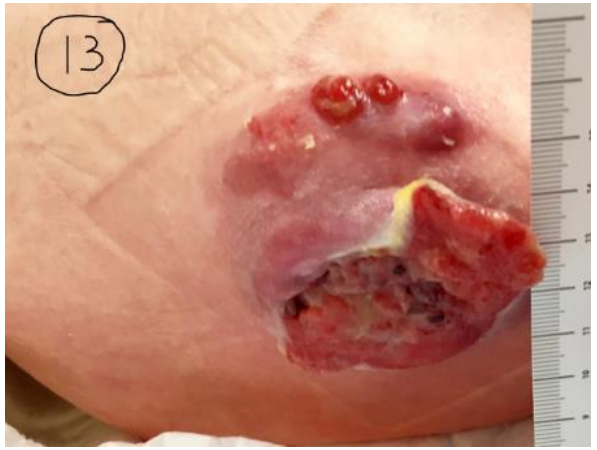
Both major criteria + at least two minor criteria

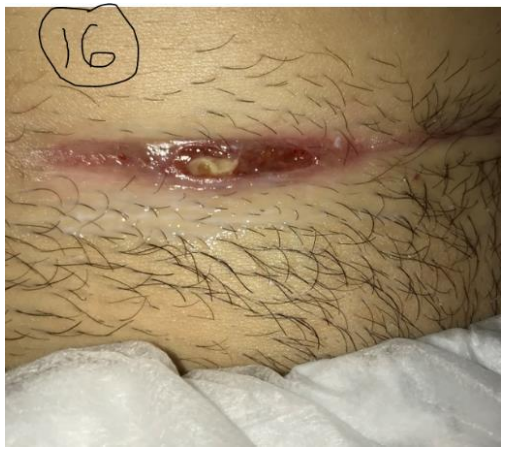
How did it perform?

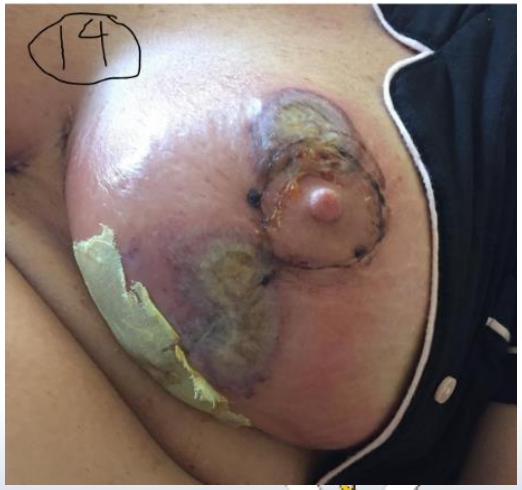
If I'd used the PARACELSUS score before I tried steroids, all these cases would have had a score of at least 10- which is enough to start a trial of immune suppression.

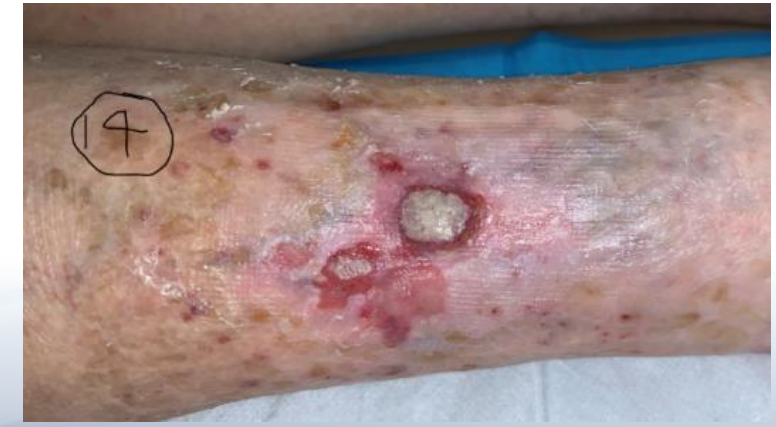
- **Major criteria (3 points for any of the criteria below):**
  1. Progressive course of disease
  2. Absence of relevant differential diagnosis
  3. Reddish-violaceous wound border
- **Minor criteria (2 points for any of the criteria below):**
  1. Amelioration due to immunosuppressant
  2. Characteristically bizarre ulcer shape
  3. Extreme pain (>4)
  4. Localized pathergy
- **Additional Criteria (1 point for any of the criteria below)**
  1. Suppurative inflammation in histopathology
  2. Undermined wound margin
  3. Associated systemic disease











UNDERSEA & HYPERBARIC MEDICAL SOCIETY

Maybe you can use the PARACELSUS tool to get support for a trial of steroids from other physicians who probably have less experience with PG than you do . . . .

Because you can NOT trust a biopsy for the diagnosis of PG.