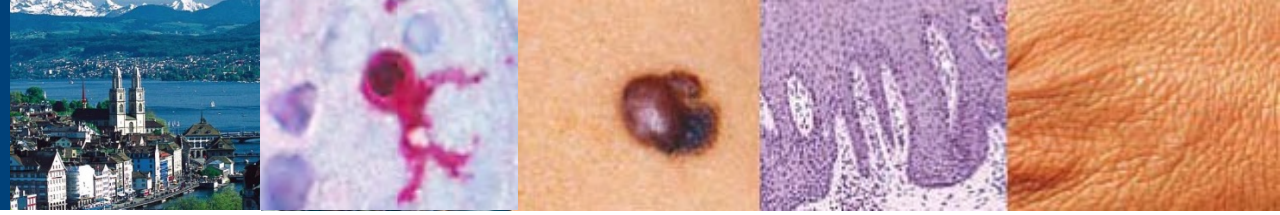
2024-10-24
IBDnet nurse workshop
Technopark Zürich



Blickdiagnose Haut

Worauf sollte bei IBD-Patienten geachtet werden?

Antonios Kolios
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Dermatologist, Clinical Immunologist, Allergologist

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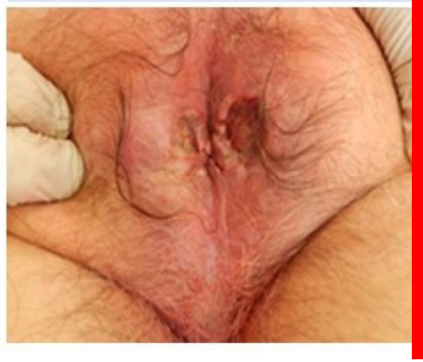
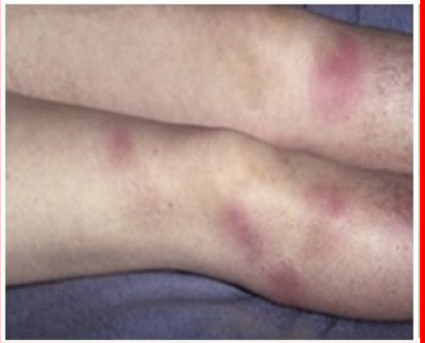
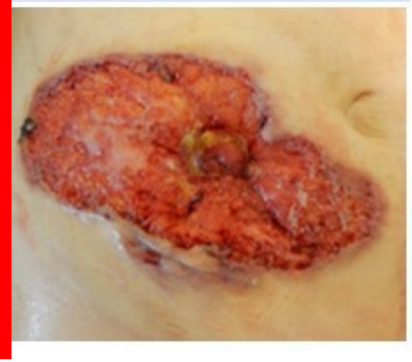
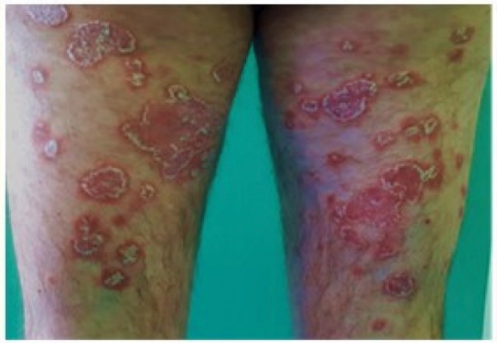
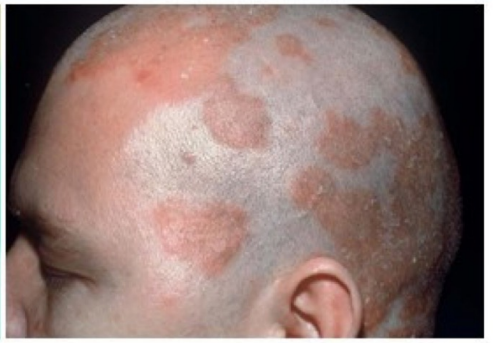
Dermatologic manifestations in IBD

Specific manifestations	Disorders associated with inflammatory bowel disorders	Reactive manifestations	Muco-cutaneous conditions secondary to treatment of inflammatory bowel disorders	Cutaneous manifestations secondary to nutritional malabsorption
Continuous/contiguous Crohn's disease Metastatic Crohn's disease	Aphthous stomatitis Erythema nodosum Psoriasis Epidermolysis bullosa acquisita	Pyoderma gangrenosum Sweet's syndrome Bowel-associated dermatosis-arthritis syndrome Aseptic abscess ulcers Pyodermatitis-pyostomatitis vegetans SAPHO syndrome PAPA syndrome	Adverse muco-cutaneous reactions (injection site reactions, infusion reactions, paradoxical reactions, eczematiform and psoriasiform reaction, life-threatening disorders) Cutaneous infections Cutaneous malignancies	Stomatitis Glossitis Angular cheilitis Pellagra Scurvy Purpura Acrodermatitis enteropathica Phrynoderma Seborrheic-type dermatitis Hair and nail abnormalities
				

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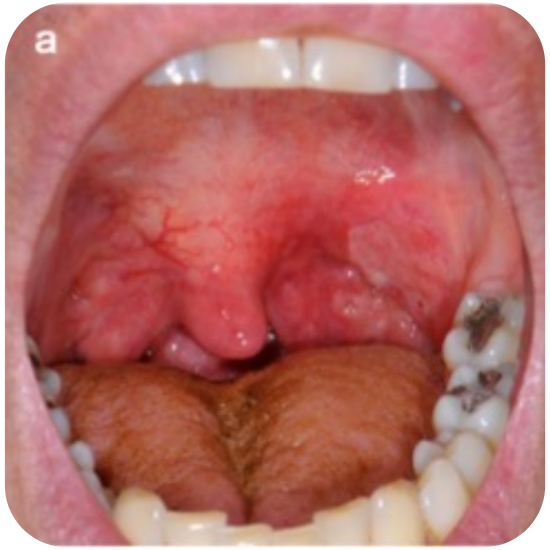
Antonelli E et al., *J Clin Med,* 2021

Aphthous stomatitis

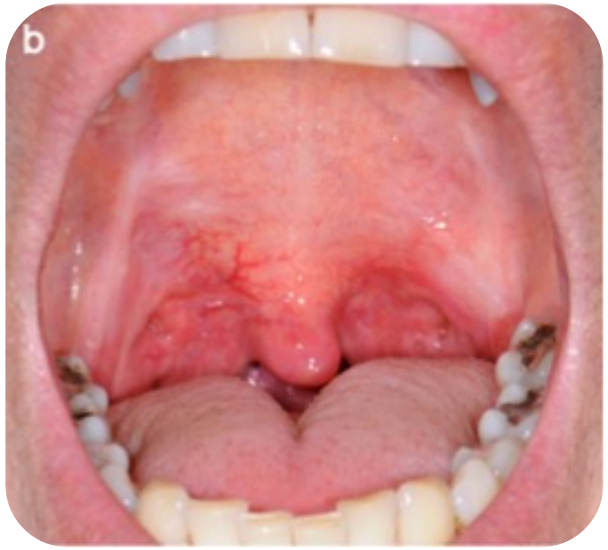
Small molecules in precision medicine – apremilast in aphthous stomatitis

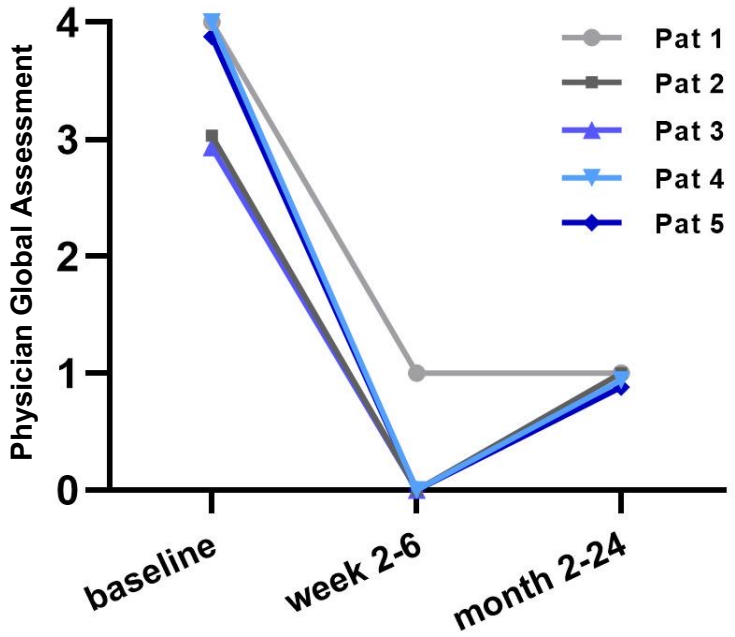
The NEW ENGLAND JOURNAL of MEDICINE

Prior treatment



During treatment



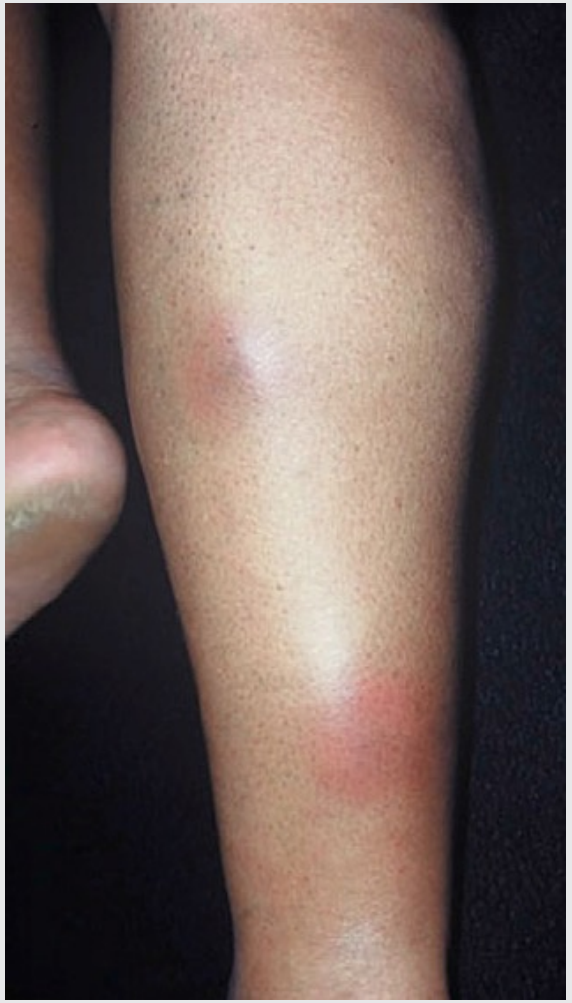


Kolios AGA et al., *N Engl J Med,* 2019

Erythema nodosum

Erythema nodosum

- Begleitet von mit Fieber, Unwohlsein, Arthralgien
- **Löfgren Syndrom**: E. nodosum, Fieber, hiläre Lymphadenopathie
  - Häufigste unspezifische Manifestation
  - 10-20% mit Sarkoidose assoziiert
- Schmerzhafte, hellrote, 0.5– mehrere Centimeter messende, subkutane Knoten, idR symmetrisch an Vorderkante der Unterschenkel, Abheilung unter Hyperpigmentierung
- Tage bis Wochen
- Gute Prognose auch für Systembefall



Motswaledi MH et al., Australasian Dental Association 2014

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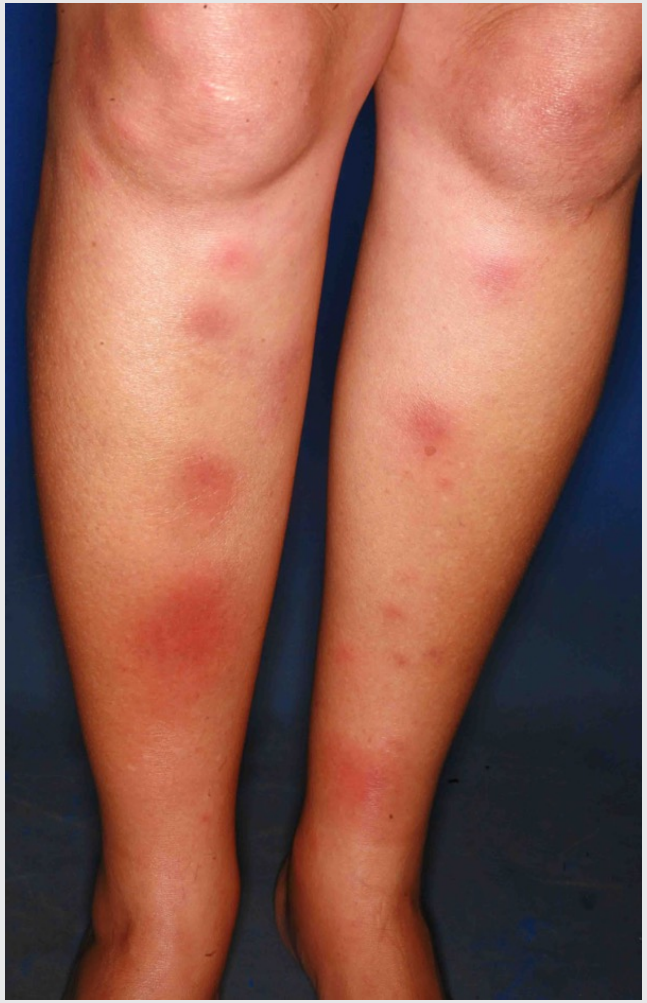

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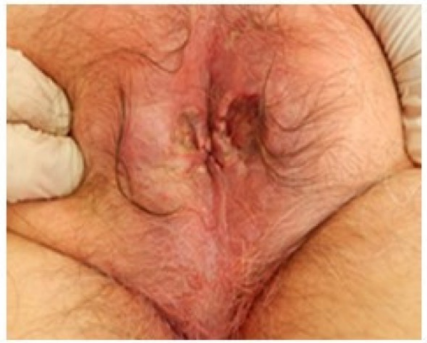
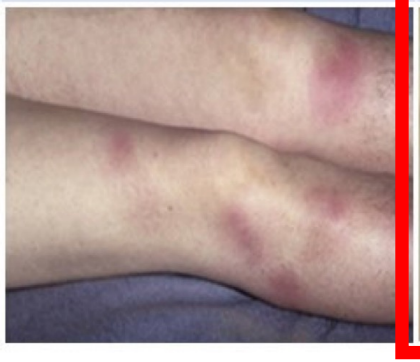
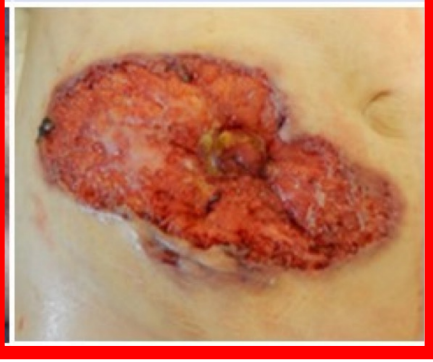
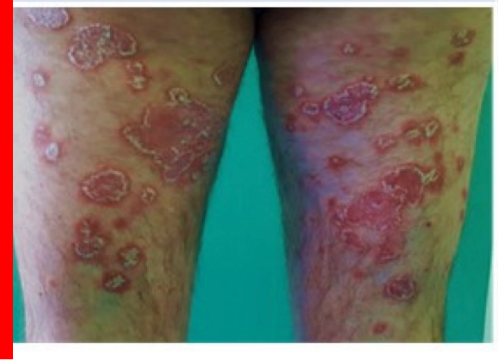
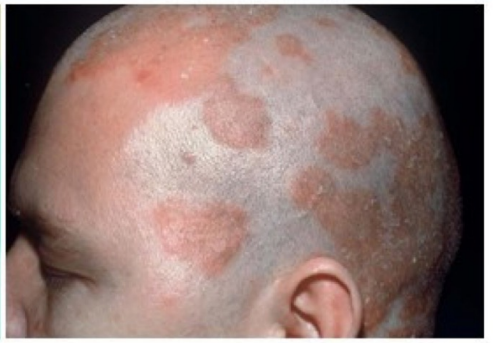

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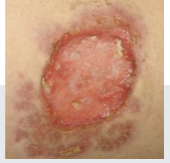
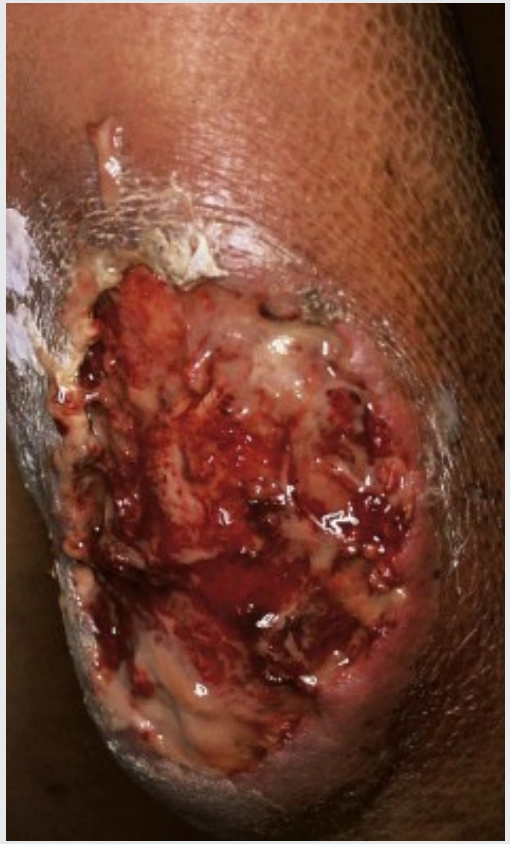
Antonelli E et al., *J Clin Med,* 2021

Pyoderma gangrenosum

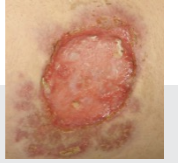


Pyoderma gangraenosum (PG)

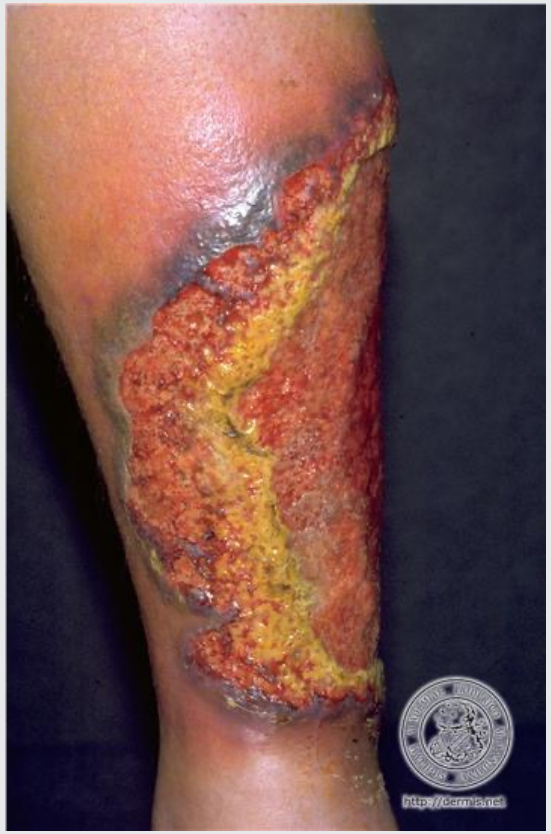
- Seltene, solitäre oder multiple, chronisch-wiederkehrende, schmerzhafte, polyzyklische, ulzerierende, neutrophile Dermatitis
- Häufig assoziiert mit **Systemerkrankungen**
- Epidemiologie:
  - 0,3-1,0/100.000, Frauen gehäufter
  - 3.-6. Lebensjahrzehnt
- Pathogenese: unklar
  - Unzureichende Deaktivierung von Neutrophilen
  - Überreagibilität der Neutrophilen (myeloproliferative Erkrankungen)
  - Vermehrte Zyotkinfreisetzung: TNF-α, IL-6, IL-8, ggf. IL-16, IL-1β?
  - Autoinflammatorischen Syndrome:
    PAPA-Syndrom -> Mutationen im PSTPIP1 Gen



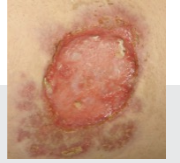
Klinik



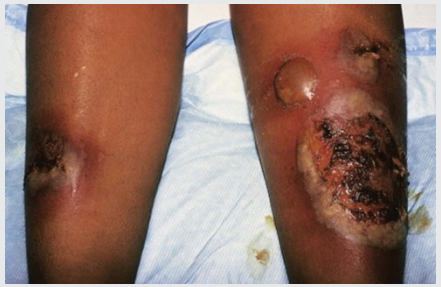
- Schmerzhafte, *nicht infektiöse* bedingte Ulzera mit blaulividem, ödematös aufgeworfenem, unterminiertem, druckdolentem Rand, serpiginöser Kontur und einem schmierig-nekrotischem Grund ohne viel Granulation
- Initial: schmerzhafte Pusteln nach Bagatelltraumen
- Pathergie-Phänomen: **20-50%** der Pat.
- Prädilektionsstellen: Beine, peristomal, seltener Stamm, Kopf, Nacken
  - Kinder: Gesäss, Perinealregion, Kopf und Hals
- Extrakutaner Befall:
  - Gelenke, Lunge, Herz, ZNS, GIT (Leber, Pancreas, Milz), Augen

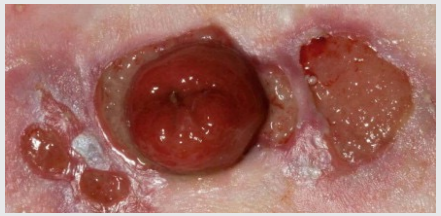


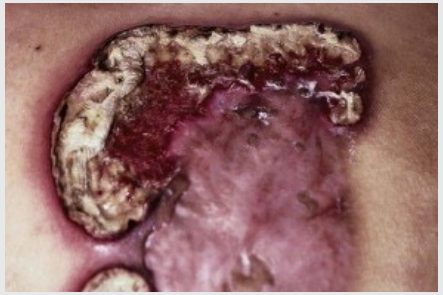
Varianten



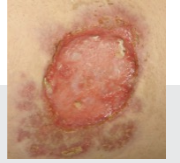
- **Chronisch ulzerierend**: *langsam* progredient
  - Vorwiegend schmerzhafte Pusteln ohne ausgeprägte Ulzeration
  - Häufig mit CED assoziiert (M. Crohn)
- **Vesikulobullös**: *rapid* progredient
  - Bevorzugt Gesicht und obere Extremität, bes. Handrücken
  - Assoziiert mit hämatologischen Erkrankungen (Leukämie) und HIV
- **Peristomal**
  - Post-OP progressive Gangrän
  - **CAVE**: schnelle Tiefenzunahme bis Faszie
- **Chronisch vegetierend**
  - Nicht assoziiert mit Systemerkrankung
    - › Ggf. Paraproteinämie
  - Oberflächlich granulomatös, meist ohne lividen und unterminierten Rand



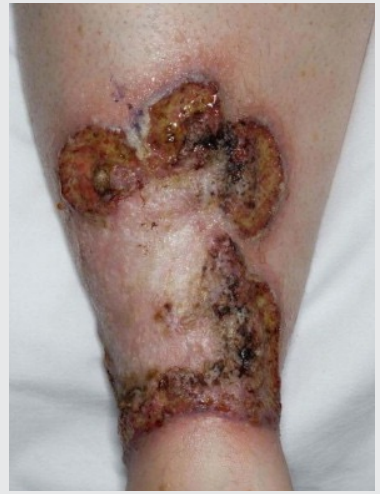


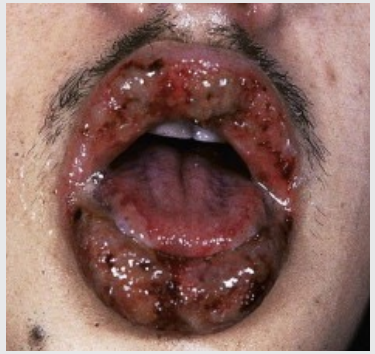


Assoziierte Erkrankungen



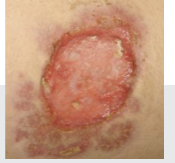
- Häufig:
  - **Arthritiden** (bis 37%)
  - **CED**, M. Crohn (15-20%)
  - Myeloproliferative Erkankungen
  - Paraproteinämien, meist IgA (ca. 15%)
- Seltener:
  - Solide maligne Tumore
  - Hepatopathien (Hepatitis C, PBC)
  - Sarkoidose
  - HIV, Hypocomplementämie
  - SLE
  - Autoinflammatorische Syndrome: PAPA, Hypercalprotectinämie





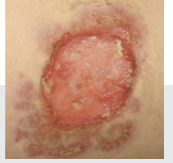
Binus AM et al, Br J Dermatol. 2011 Dec;165(6):1244-50. doi: 10.1111/j.1365-2133.2011.10565.x.
Dermatology, 3rd Edition, J. Bolognia

Therapy of mild disease



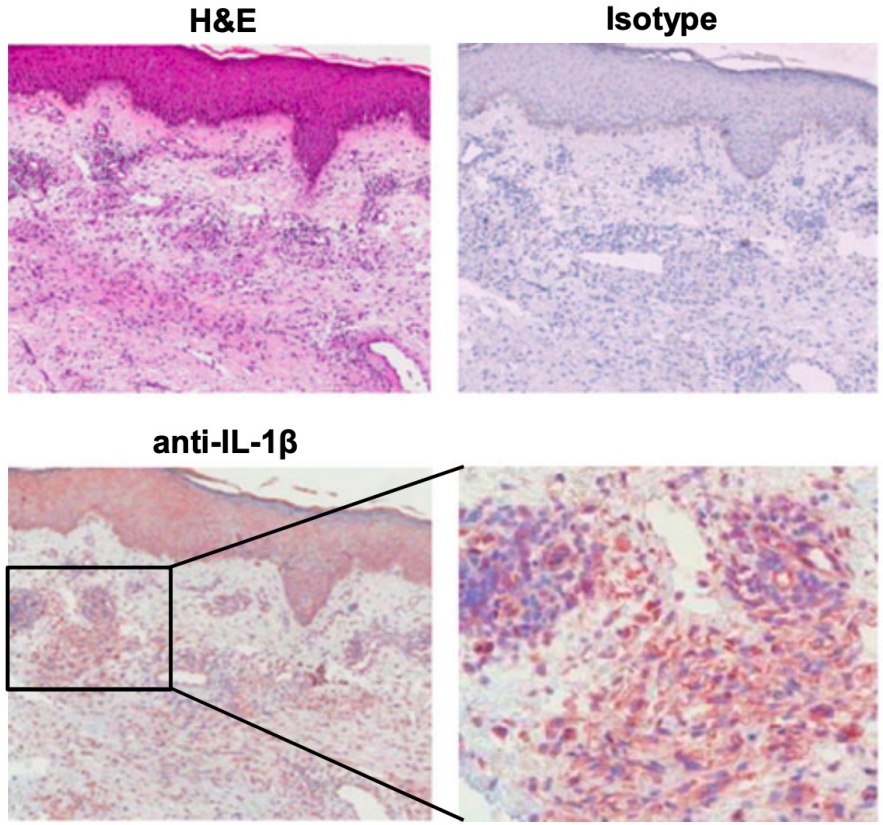
Superpotent topical corticosteroids	
Intralesional corticosteroids	
Topical tacrolimus	
Oral antibiotics (e.g. sulfonamides, minocycline)	
Colchicine	0.6 mg po thrice daily
Dapsone	50–150 mg po daily
Clofazimine	100–400 mg po daily
Other (e.g. oral potassium iodide, intralesional cyclosporine, topical cromolyn sodium, nicotine patch or cream)	

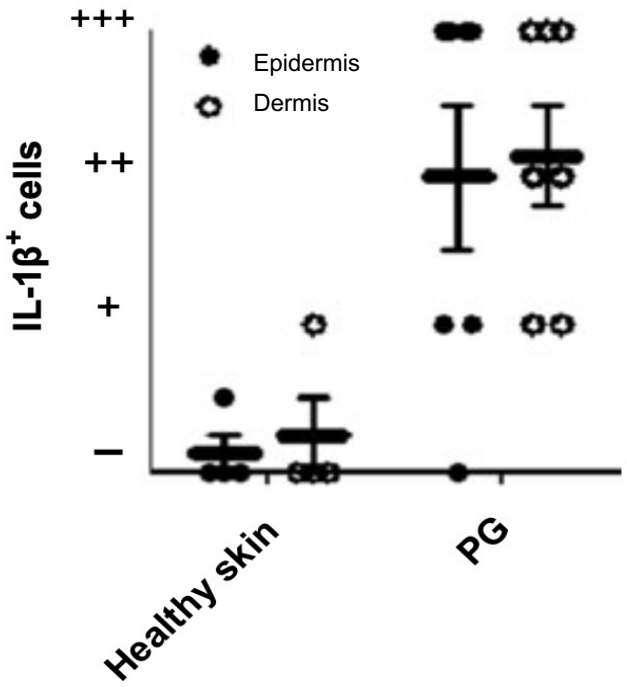
Therapy of severe disease



Prednisone	60–120 mg po daily usual starting dose (including split-dose), with taper to alternate days
Methylprednisolon i.v. Stosstherapie	1g/d für 3-5 Tage
Thalidomide	50–150 mg po nightly
Cyclosporine	2.5–5 mg/kg po daily
Tacrolimus	0.1–0.2 mg/kg po daily
Biologicals	IFX, ADA, ETA, UST, **Canakinumab**, Anakinra, Visilizumab
Methotrexat	2.5–25 mg po or IM weekly
Azathioprin	50–100 mg po twice daily
Mycophenolat mofetil	1–1.5 g po twice daily
Cyclophosphamid	Variable oral (50–200 g daily) or IV pulse (500–1000 mg monthly) dosing
Chlorambucil	4–6 mg po daily
IVIg	2–3 g/kg IV monthly (given over 2–5 consecutive days)
Granulocytenapherese, Plasmapherese	
Totale Colectomie	(schwere Fälle von C. ulcerosa)

Biolocials in precision medicine – Canakinumab in Pyoderma Gangrenosum





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Kolios AGA et al., *Br J Dermatol,* 2015

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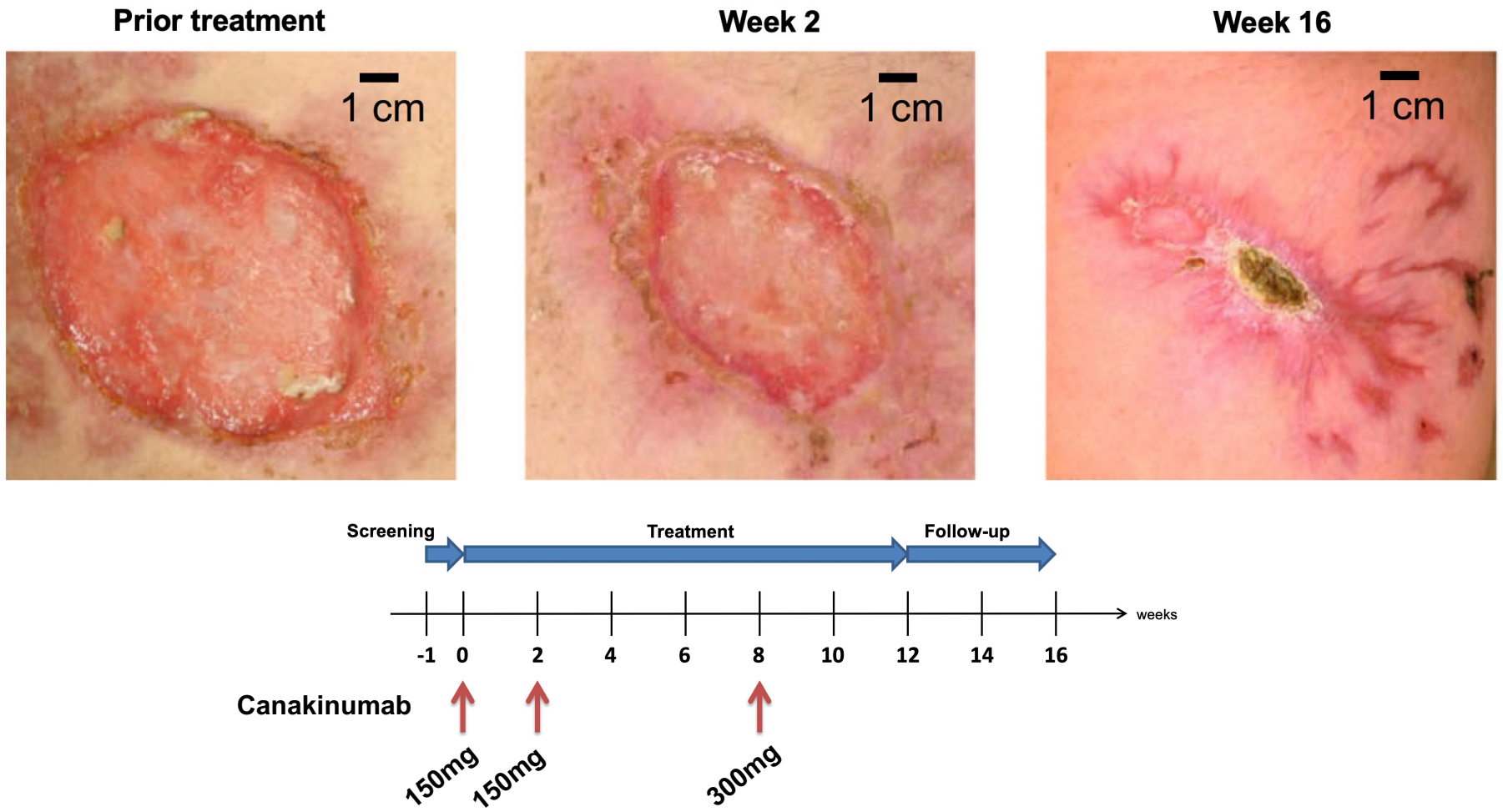

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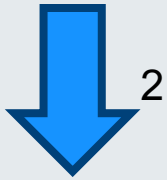
Kolios AGA et al., *Br J Dermatol,* 2015

Case report

- 50y/o male
- Medical history: IBD (indeterminate colitis affecting the sigmoid colon) since 5 months
- Therapies:
  - oral sulfasalazine ineffective
  - flare of colitis: 50 mg prednisone daily
  - Azathioprine 50 mg once daily was started 3 weeks after flare of colitis

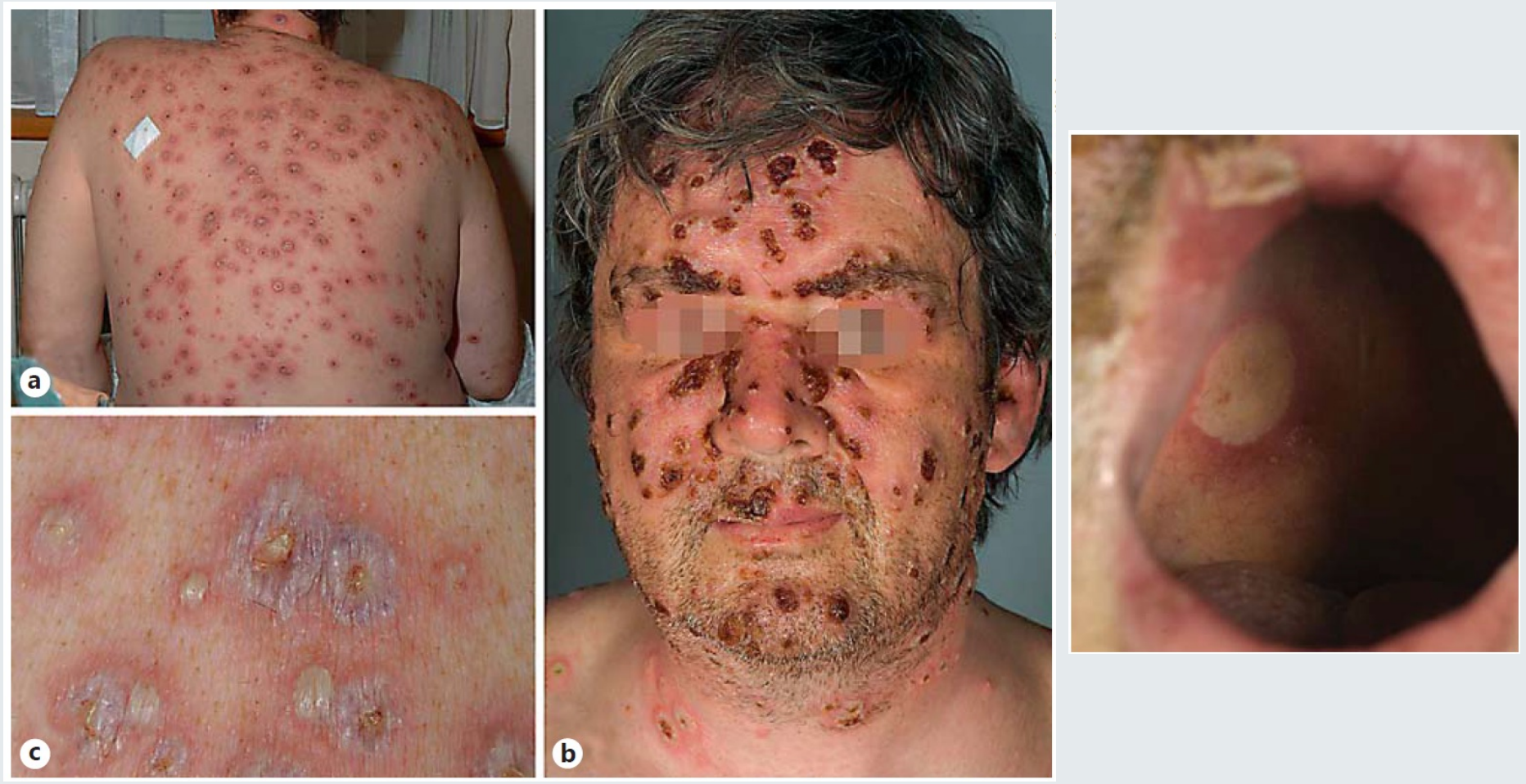


2 weeks later

- Emergency Unit Department of Dermatology:
  - Diffuse pustular and necrotizing skin eruption
  - Large aphthous orally
  - Fever 39.6°C
  - Neutrophilia 20.000/µL, CRP 193mg/L

Imhof L et al, Dermatology. 2015;230(4):293-8.

Case report – AzA-induced Sweet syndrome



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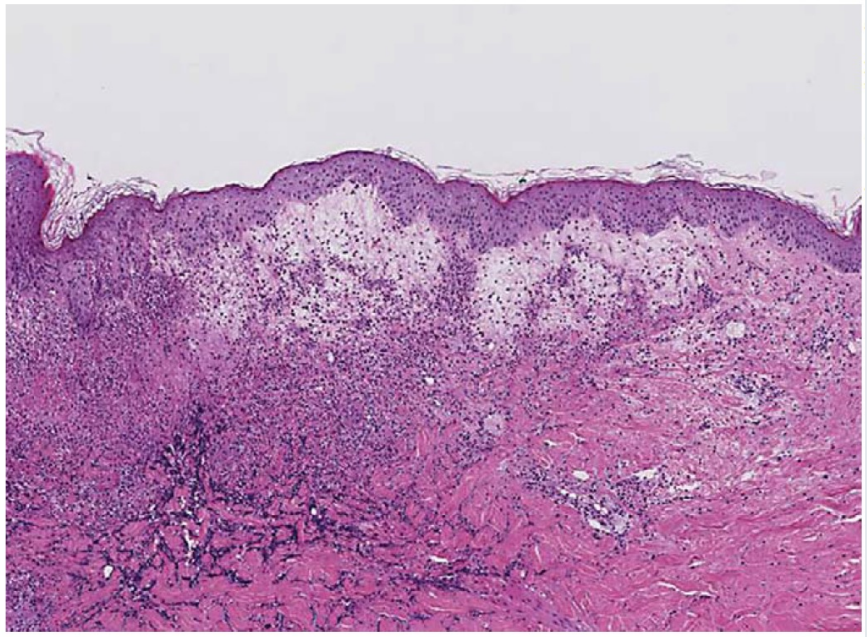
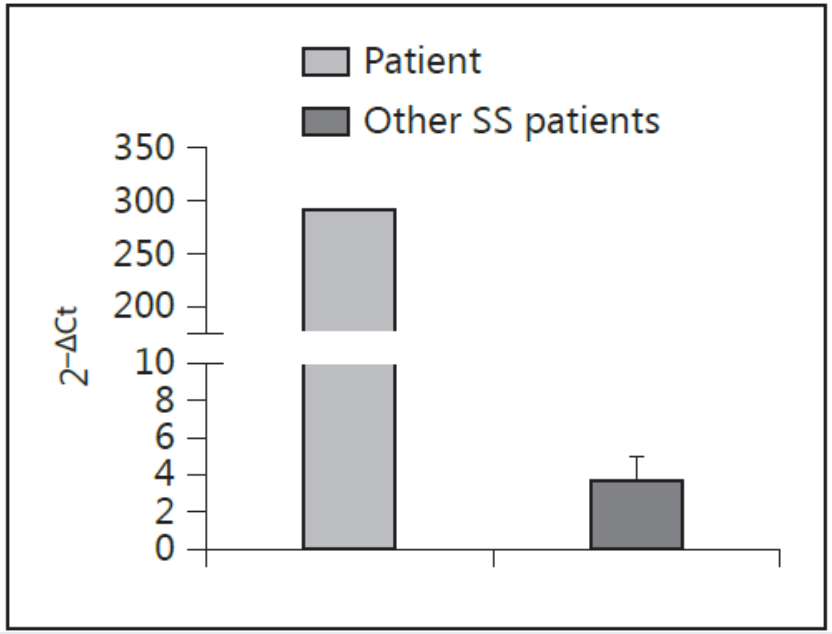
Case report



Skin biopsy taken on the upper back showing marked superficial edema with florid neutrophilic infiltration of the whole dermal thickness. Hematoxylin and eosin, x100.



Analysis of IL-1β mRNA levels by quantitative RT-PCR in the patient's skin biopsy and healthy control skin

Imhof L et al, Dermatology. 2015;230(4):293-8.

Immune-mediated reactions: Azathioprine

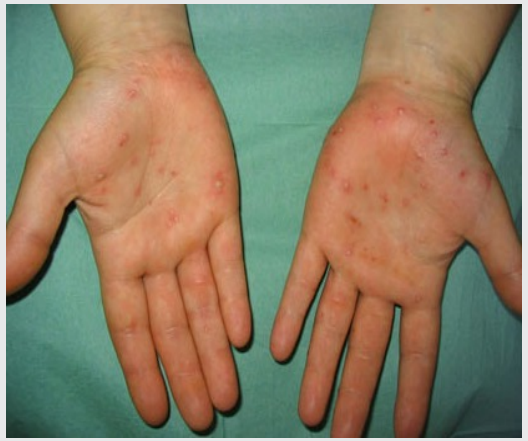
Cutaneous findings	No. of patients	Reference Nos.	Time of onset after starting AZA (days)	Underlying disease	Recurrence of side effects with rechallenge	TPMT level	Concurrent use of steroids	Elevated WBC	Sex (# of patients) average age
Sweet's syndrome	12	1-8	5-28	Crohn's disease UC SLE Myasthenia gravis	7/12	5/12 – N 7/12 – NR	10/12	10/12	M(9)/F(3) 46
Erythema nodosum	3	9	8-14	Crohn's disease	2/3	3/3 – N	3/3	3/3	M(1)/F(2) 47
Small-vessel vasculitis	7	1-13	8-46	RA Crohn's disease Wegener's Renal transplant	4/7	1/7 – N 6/7 – NR	1/7	3/7	M(2)/F(5) 56
Acute generalized exanthematous pustulosis	3	9, 14	16-18	Crohn's disease Urticaria Pemphigus foliaceus	1/3	2/3 – N 1/3 – NR	3/3	3/3	M(2)/F(1) 37
Nonspecific	8	10, 15-21	5-20	MCTD Demyelinating disease Psoriatic arthritis RA Vasculitis Wegener's MS	5/8	1/8 – N 7/8 – NR	4/8	3/8	M(4)/F(4) 47
None	34	21-36	3-25	MS Organ transplant Crohn's disease Vasculitis* Urticaria Other†	15/34	1/34 – N 33/34 – NR	5/34	7/34	M(16)/F(5) NR (18) 47
Total	67		3-46	IBD (18) Neurologic (15) Connective tissue (14) Transplant (6) Vasculitis (5) Other (9)	34/67	13/67 – N 54/67 – NR	26/67	29/67	M(34)/F(20) NR (13) 47

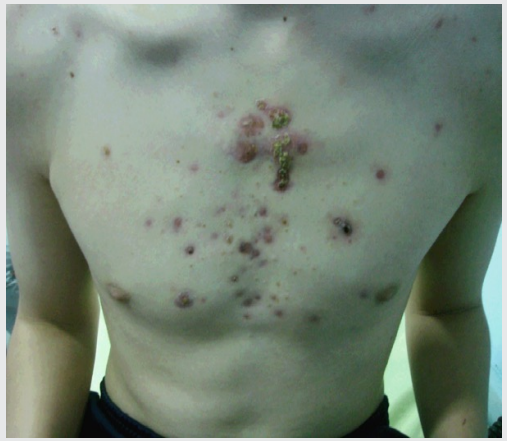
Bidinger JJ et al. J Am Acad Dermatol. 2011 Jul;65(1):184-91.

SAPHO

SAPHO Syndrom
Haut-Knochen-**Gelenk** Erkrankung

- **Synovitis**
- **Akne**
- **Pustulose**
- Hyperostose
- Osteitis

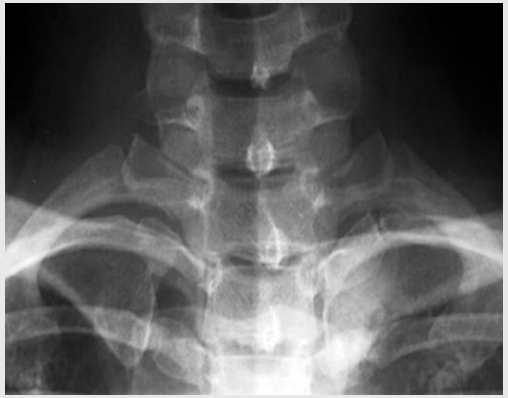




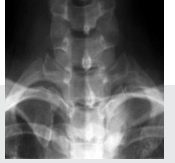
Sterile Knochenentzündung

+

Pustulöse Dermatose



SAPHO



Neutrophilen-mediierte Autoimmun-Erkrankung durch Mikroorganismen getriggert und erhöhter Chemotaxis für Neutrophile

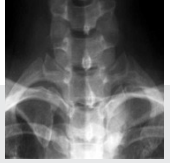
Osteoartikulär: Synovitis, arthrosteitis (knöcherne Strukturen der Gelenke), aseptische Osteomyelitis

Prädilektion: Sternum, Clavikulae, Rippen, Wirbelsäulre, Becken

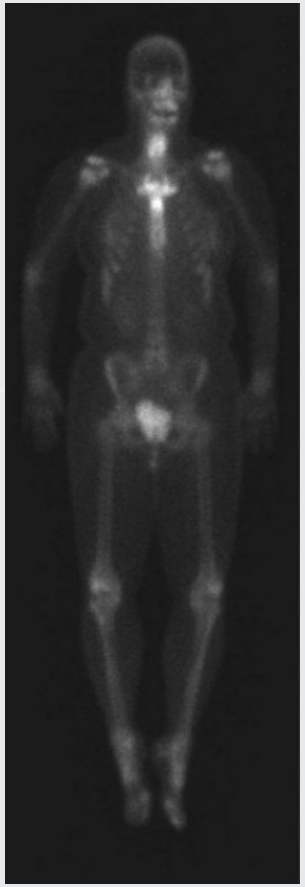
Gelenk-Knochen: periodischundulierend, keine Korrelation mit dem Verlauf der Hautbeteiligung

CAVE: Kinder mit Majeed Syndrom oder DIRA können SAPHO entwickeln

Therapie



Variable Wirksamkeit	NSAIDs
	Colchicin
	Sulfasalazin
	Orale Antibiotika (Doxycyclin, Azithromycin, Clindamycin)
Stärkere Wirksamkeit	Methotrexat (20 mg p.o./ Woche)
	Corticosteroide (intralesional/ p.o.)
	Bisphosphonate
	TNF-α Inhibitoren



CAVE: Isotretinoin als zur Behandlung der Akne kann einen Schub auslösen

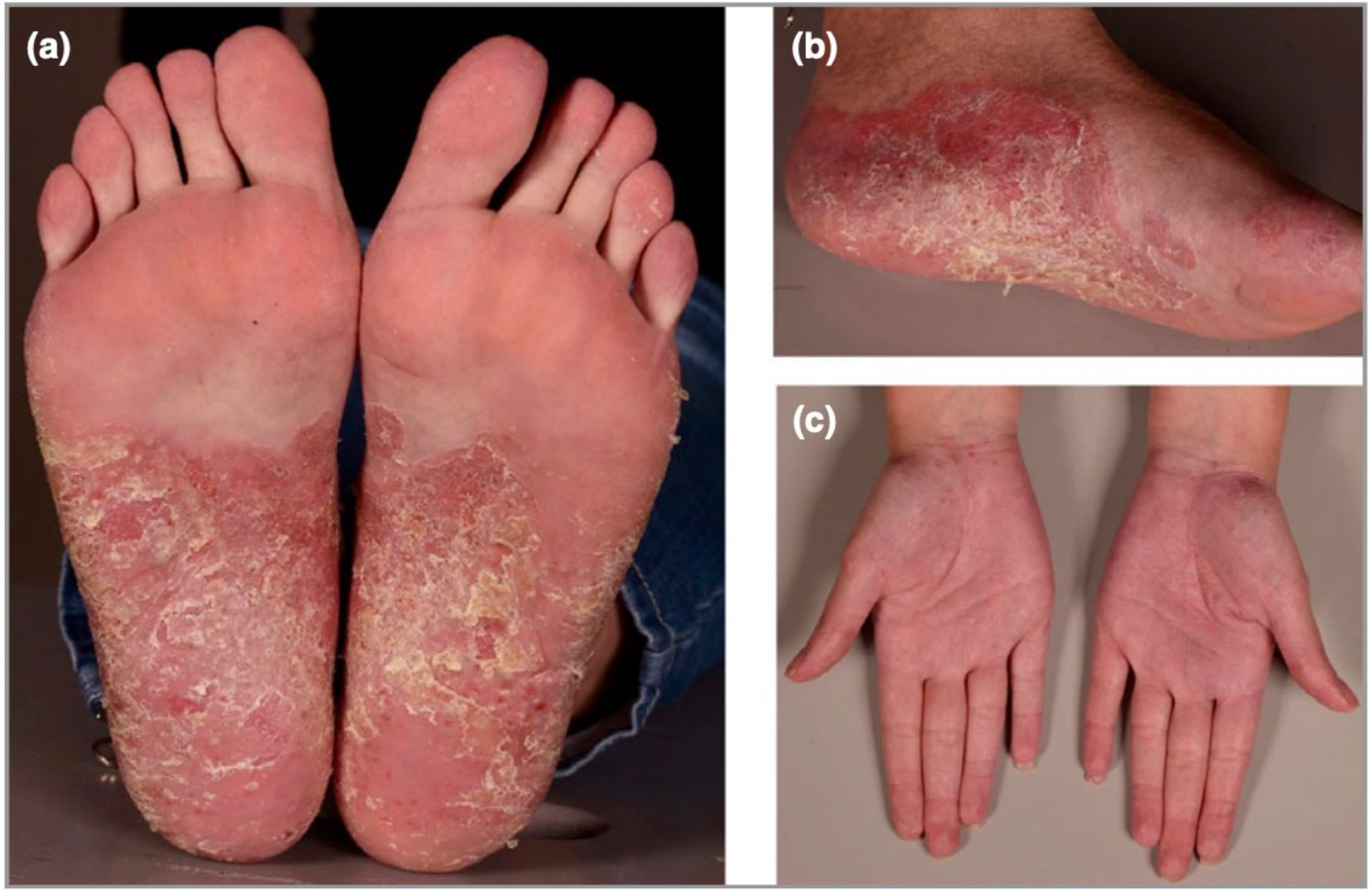
CASE REPORT: THERAPY

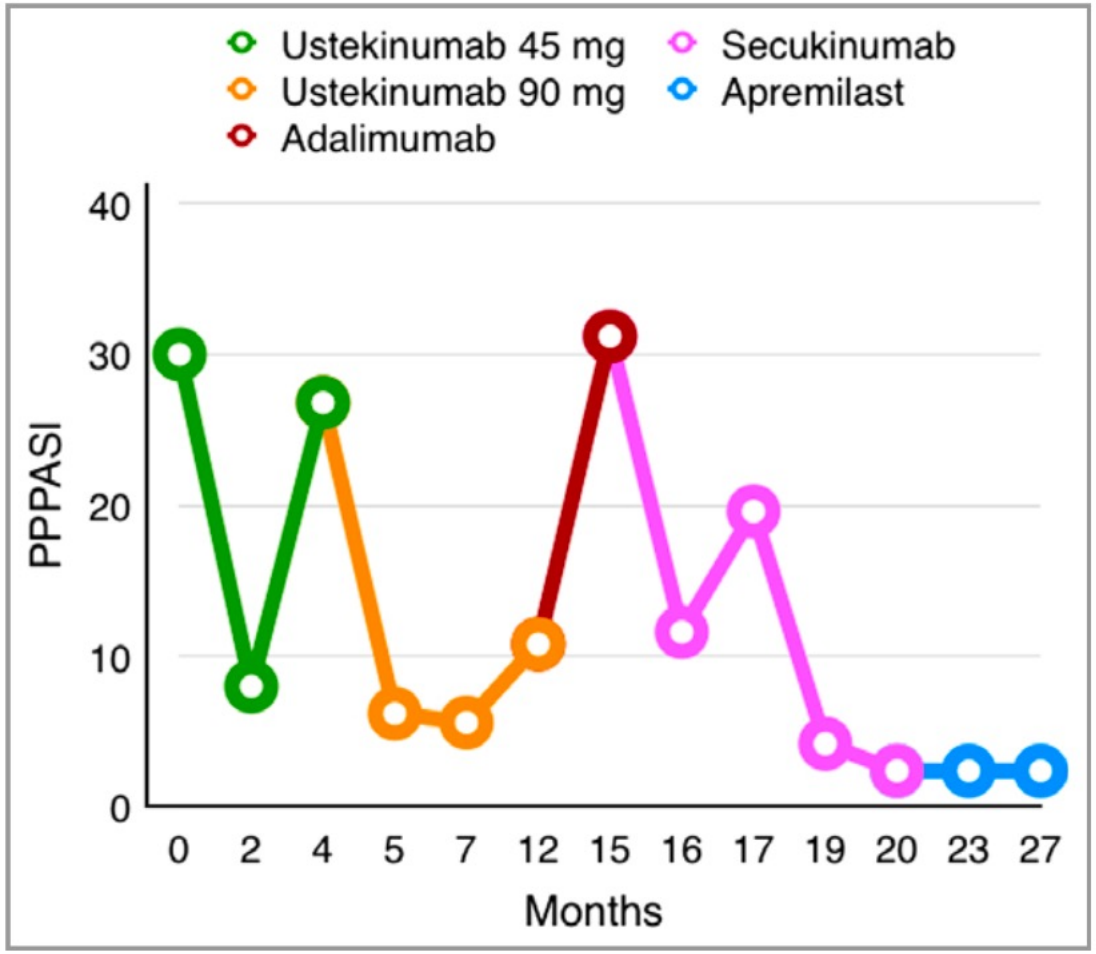
BJD
British Journal of Dermatology

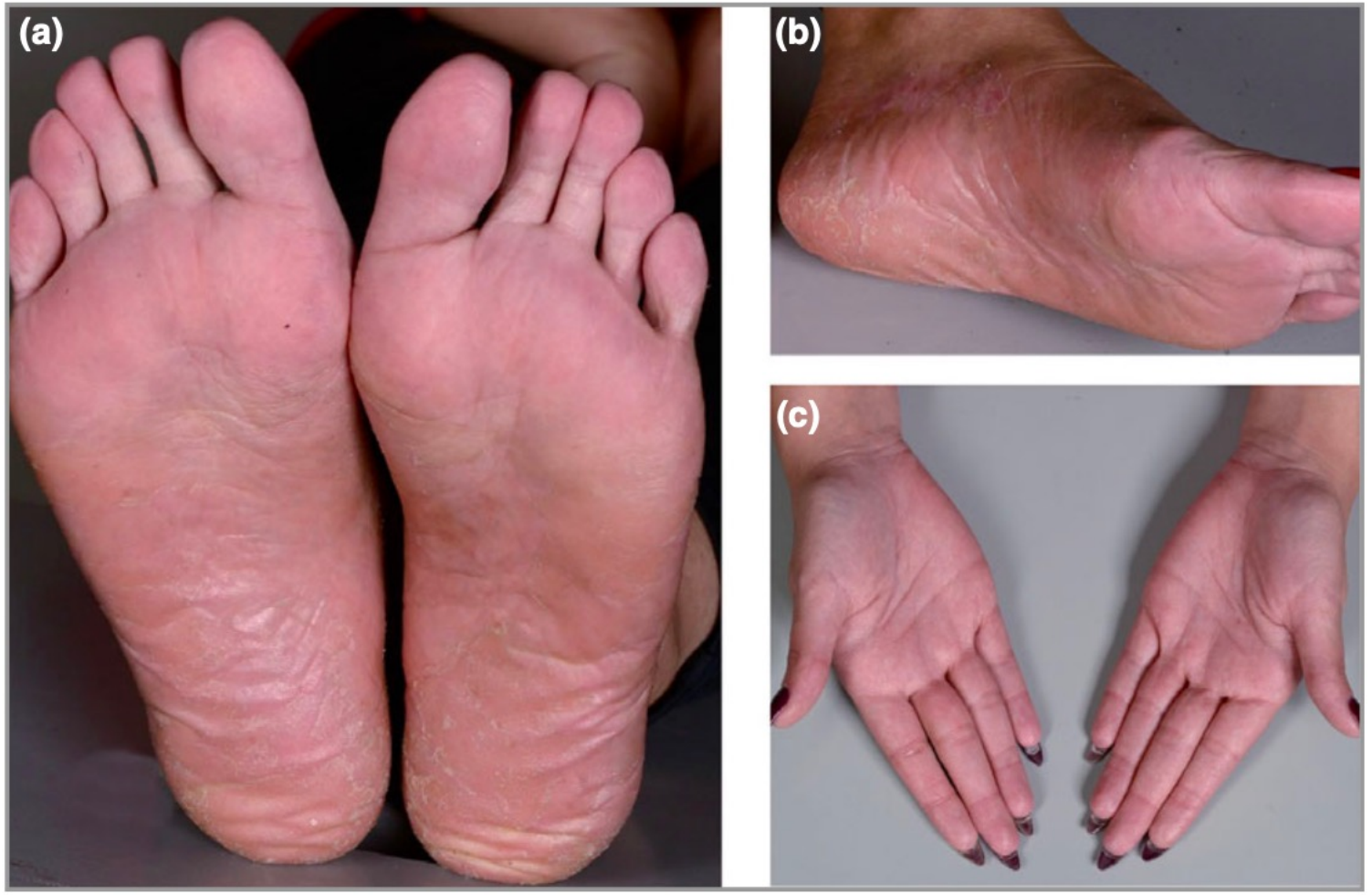
Successful treatment of SAPHO syndrome with apremilast

S. Adamo,[1] J. Nilsson,[1] A. Krebs,[2] U. Steiner,[1] A. Cozzio,[3] L.E. French[4] and A.G.A. Kolios[1,4]

Departments of [1]Immunology, [2]Rheumatology and [4]Dermatology, University Hospital Zurich, Switzerland
[3]Department of Dermatology, Venerology and Allergology, Kantonsspital St. Gallen, Switzerland

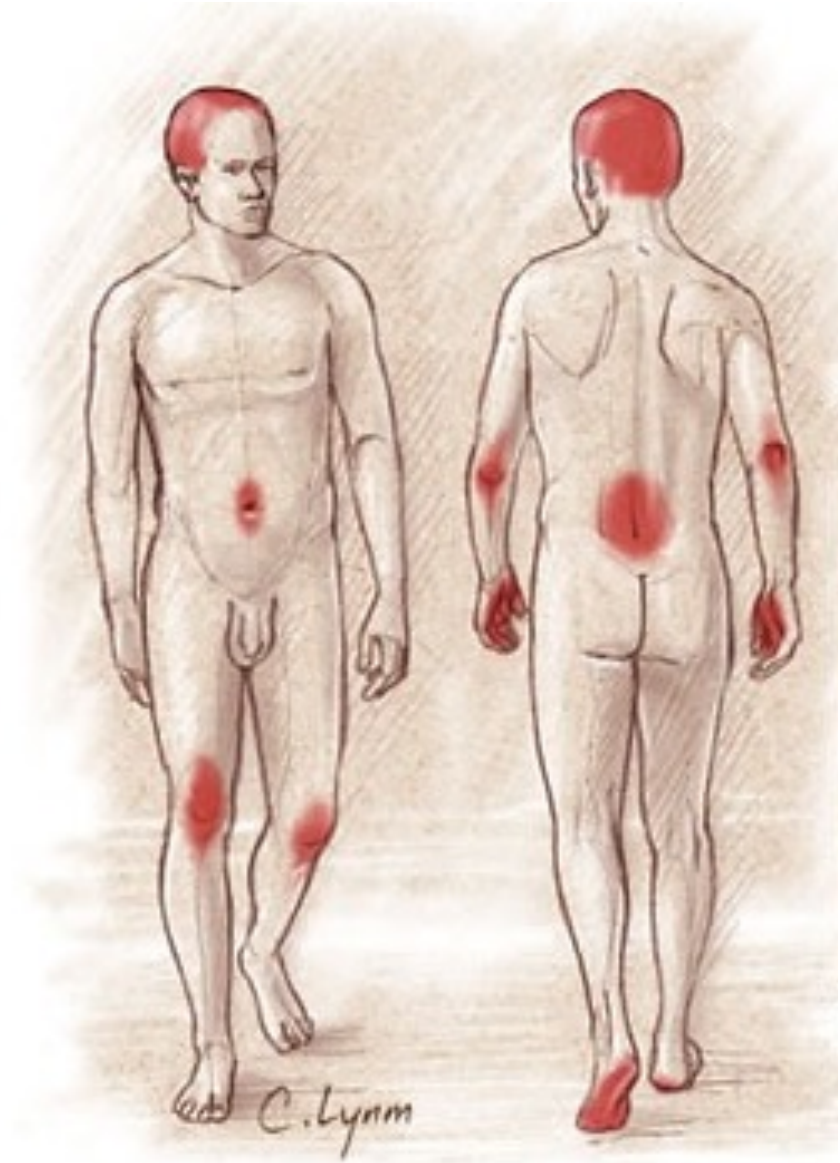

(a)
(b)
(c)


Ustekinumab 45 mg
Ustekinumab 90 mg
Adalimumab
Secukinumab
Apremilast
PPPASI
40
30
20
10
0
0 2 4 5 7 12 15 16 17 19 20 23 27
Months

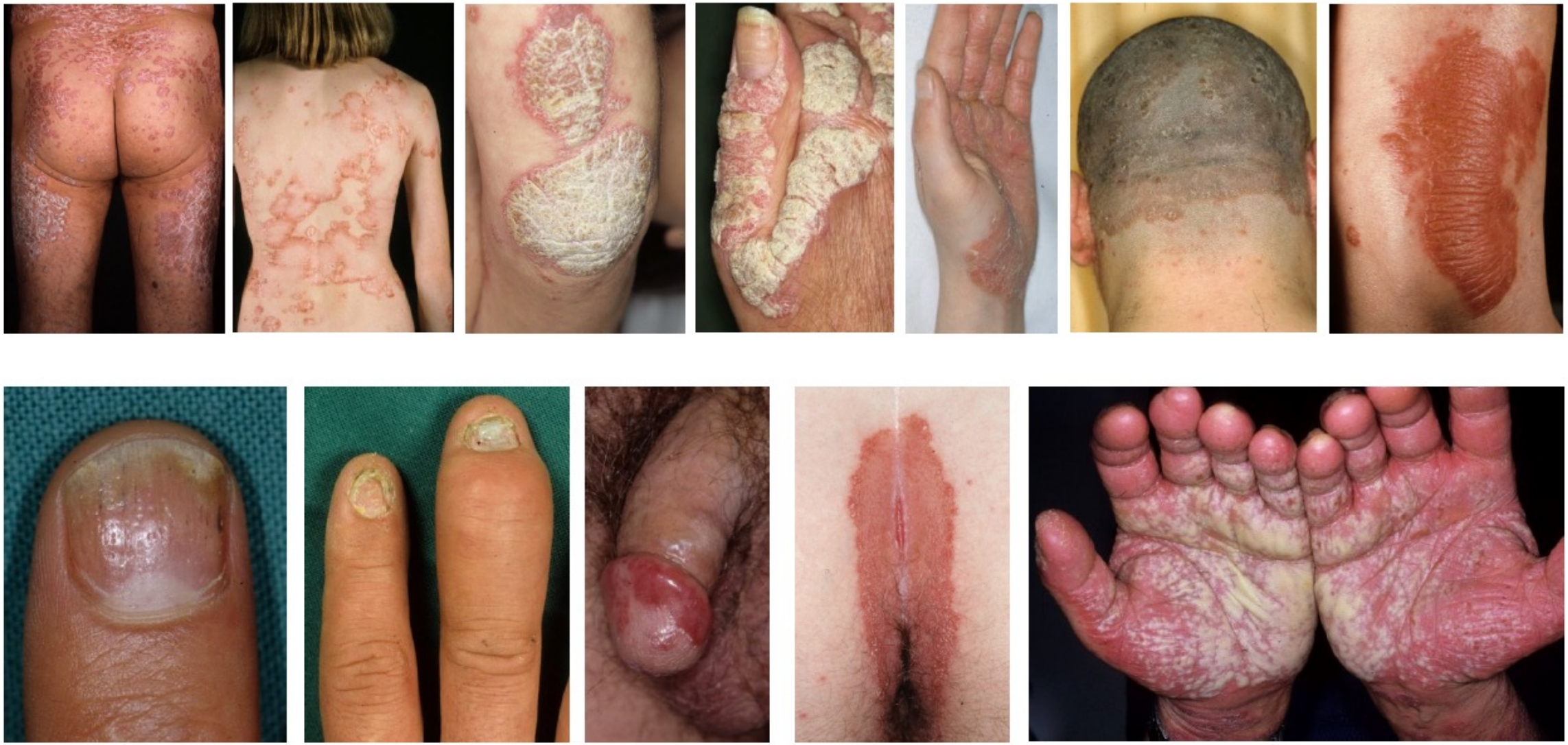

(a)
(b)
(c)

Psoriasis

Psoriasis vulgaris (Plaque-Psoriasis)



Psoriasis vulgaris (Plaque-Psoriasis)



Psoriasis vulgaris (Plaque-Psoriasis)

Consensus Guidelines

Dermatology

Dermatology
DOI: 10.1159/000445681

Received: March 20, 2016
Accepted: March 20, 2016
Published online: June 21, 2016

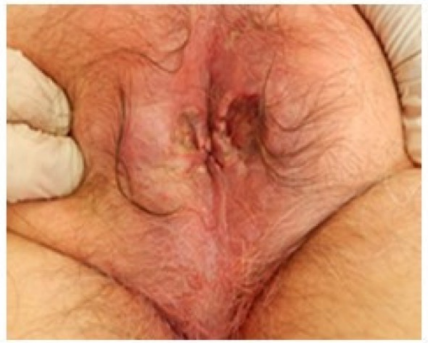
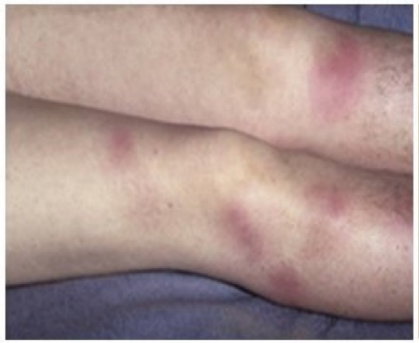
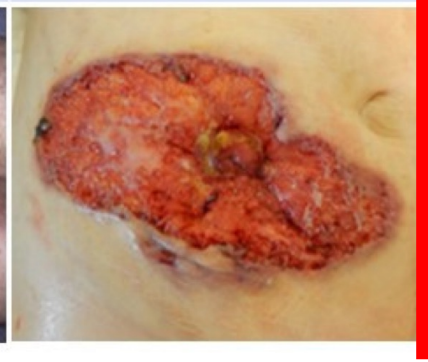
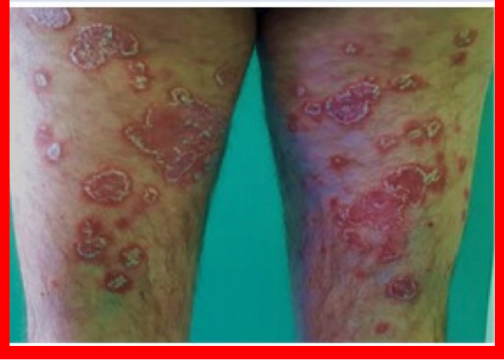
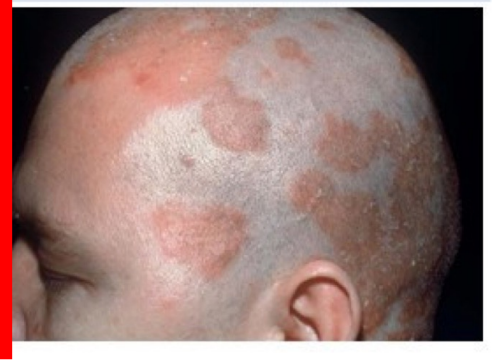
Swiss S1 Guidelines on the Systemic Treatment of Psoriasis Vulgaris

Antonios G.A. Kolios[a, b] Nikhil Yawalkar[c] Mark Anliker[d] Wolf-Henning Boehncke[e]
Luca Borradori[c] Curdin Conrad[f] Michel Gilliet[f] Peter Häusermann[g] Peter Itin[g]
Emmanuel Laffitte[e] Carlo Mainetti[h] Lars E. French[a] Alexander A. Navarini[a]

Departments of [a]Dermatology and [b]Immunology, Zurich University Hospital, Zurich, [c]Department of Dermatology, Bern University Hospital, Bern, [d]Department of Dermatology and Allergies, St. Gallen Cantonal Hospital, St. Gallen, [e]Division of Dermatology and Venereology, Geneva University Hospital, Geneva, [f]Department of Dermatology and Venereology, Lausanne University Hospital, Lausanne, [g]Department of Dermatology, Basel University Hospital, Basel, and [h]Department of Dermatology, Regional Hospital of Bellinzona, Bellinzona, Switzerland

Kolios AGA et al., *Dermatology*. 2016

Dermatologic manifestations in IBD

Specific manifestations	Disorders associated with inflammatory bowel disorders	Reactive manifestations	Muco-cutaneous conditions secondary to treatment of inflammatory bowel disorders	Cutaneous manifestations secondary to nutritional malabsorption
Continuous/contiguous Crohn's disease Metastatic Crohn's disease	Aphthous stomatitis Erythema nodosum Psoriasis Epidermolysis bullosa acquisita	Pyoderma gangrenosum Sweet's syndrome Bowel-associated dermatosis-arthritis syndrome Aseptic abscess ulcers Pyodermatitis-pyostomatitis vegetans SAPHO syndrome PAPA syndrome	Adverse muco-cutaneous reactions (injection site reactions, infusion reactions, paradoxical reactions, eczematiform and psoriasiform reaction, life-threatening disorders) Cutaneous infections Cutaneous malignancies	Stomatitis Glossitis Angular cheilitis Pellagra Scurvy Purpura Acrodermatitis enteropathica Phrynoderma Seborrheic-type dermatitis Hair and nail abnormalities
				

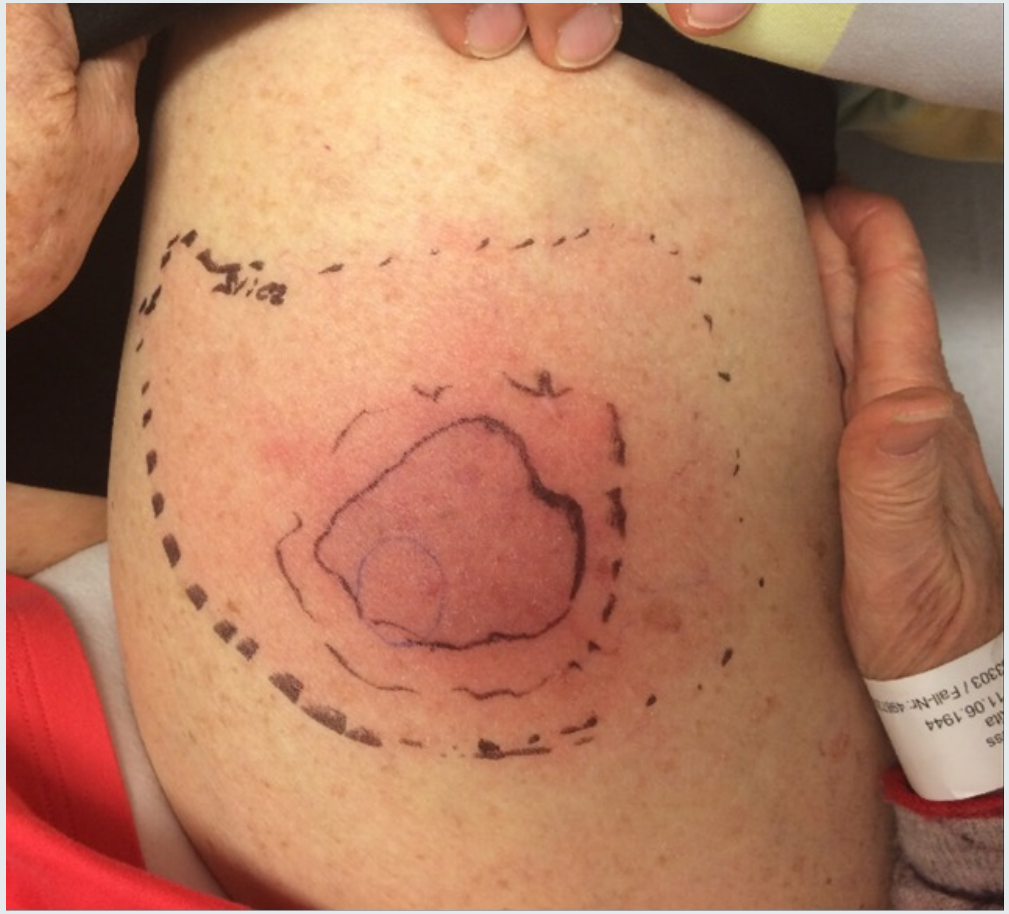
University of Zurich[UZH]

Antonelli E et al., *J Clin Med,* 2021

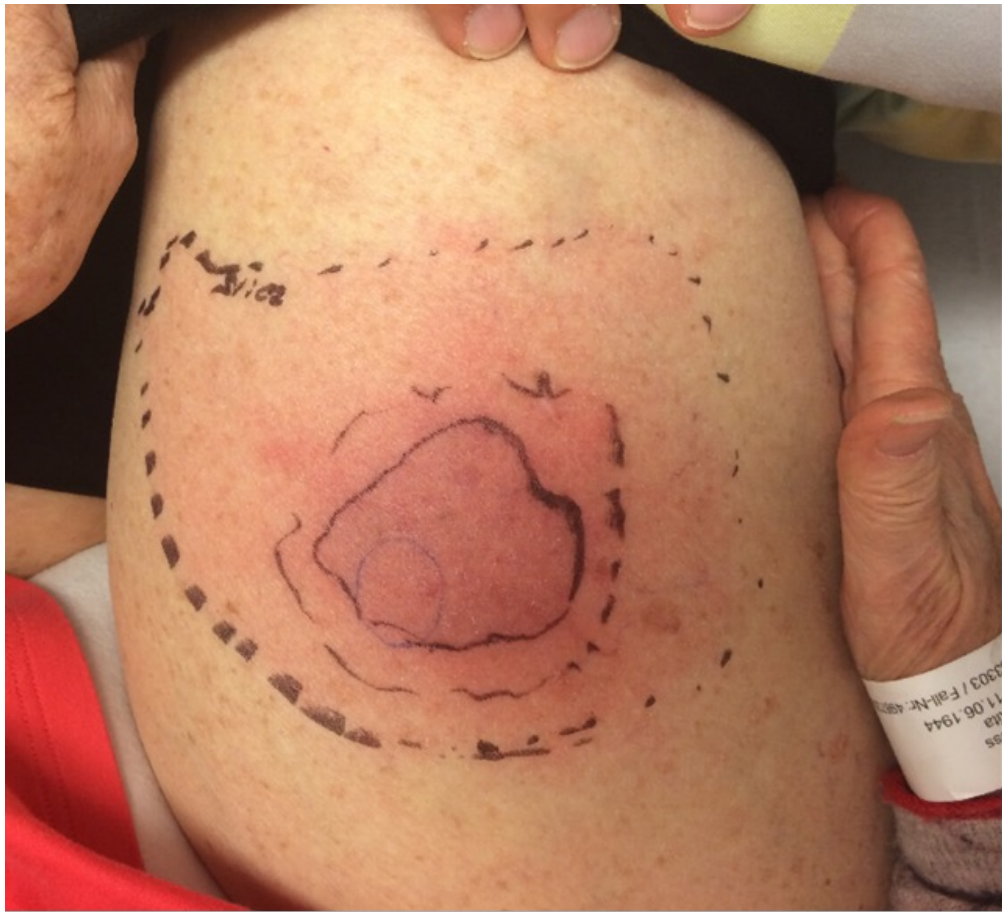
Case report: RH

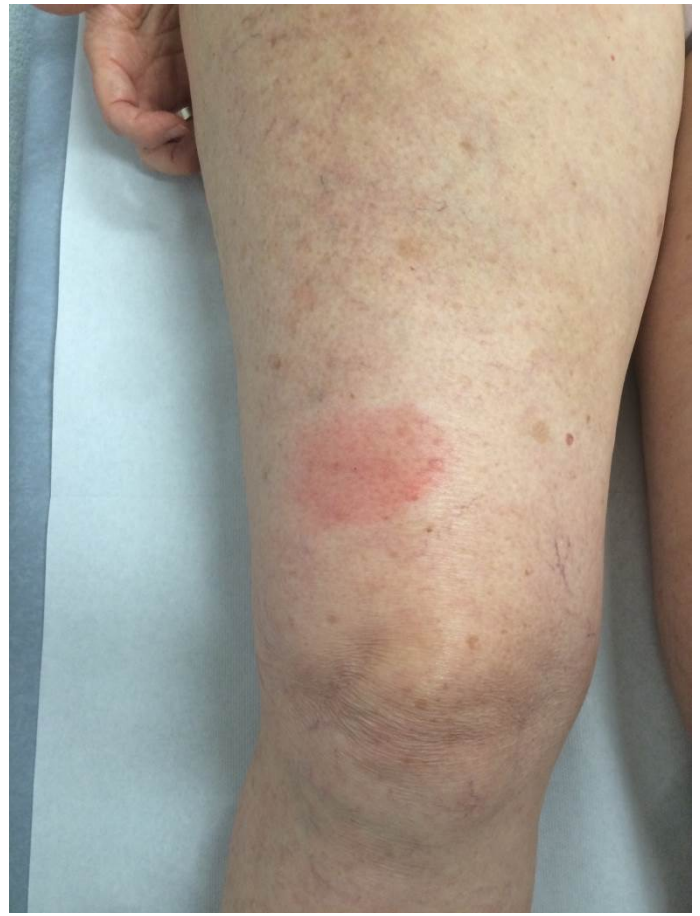
- 82 y/o patient with suspicious autoinflammatory polyserositis
- Colchicine 1mg/d and prednisone 15mg not satisfactory
- Attempt: anakinra 100mg s.c.
  - 1st day: ok, improvement of symptoms and decrease of CRP / IL-6
  - 2nd day: ok, improvement of symptoms and decrease of CRP / IL-6
  - 3rd day: erythema at injection site
  - 4th day: growing erythema, heat, swelling at injection site accompanied by fever and flu like symptoms

Case report – Injection site reaction to anakinra



Case report – Omalizumab-assisted desensitization to Anakinra





kutanen Nebenwirkungen Biologika

Side effects during biologicals, e.g. TNFi treatment

- **Injection site reactions**
- **Infusion reactions**
- **Infectious complications**
  - Bacterial: cellulitis, erysipelas, abscess
  - Viral: HSV, VZV, CMV, HPV, MC
  - Fungal: Candida species
- **Immune-mediated and toxic complications**
  - Psoriasiform eruptions
  - Lupus like-syndrome
  - Cutaneous vasculitis
  - Erythema multiforme
  - Stevens Johnson syndrome
  - Toxic epidermal necrolysis
- **Skin cancers**
  - Non-melanoma skin cancer
    - Basal cell carcinoma
    - Squamous cell carcinoma
  - Melanoma

Mocci G. et al., *J Crohns Colitis,* 2013
Moustou AE et al., *J Am Acad Dermatol,* 2009

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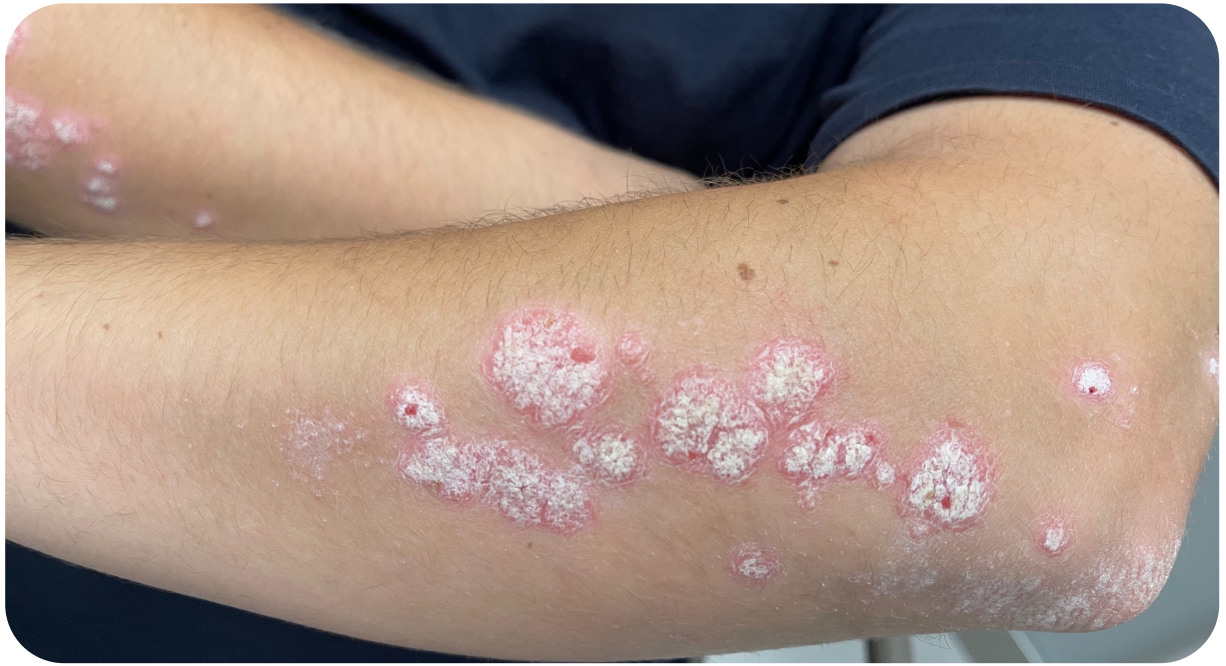
Mocci G. et al., *J Crohns Colitis,* 2013
Moustou AE et al., *J Am Acad Dermatol,* 2009

Psoriasiform eruptions – clinical manifestations



TNFi-associated psoriasiform eruptions in about **3%**

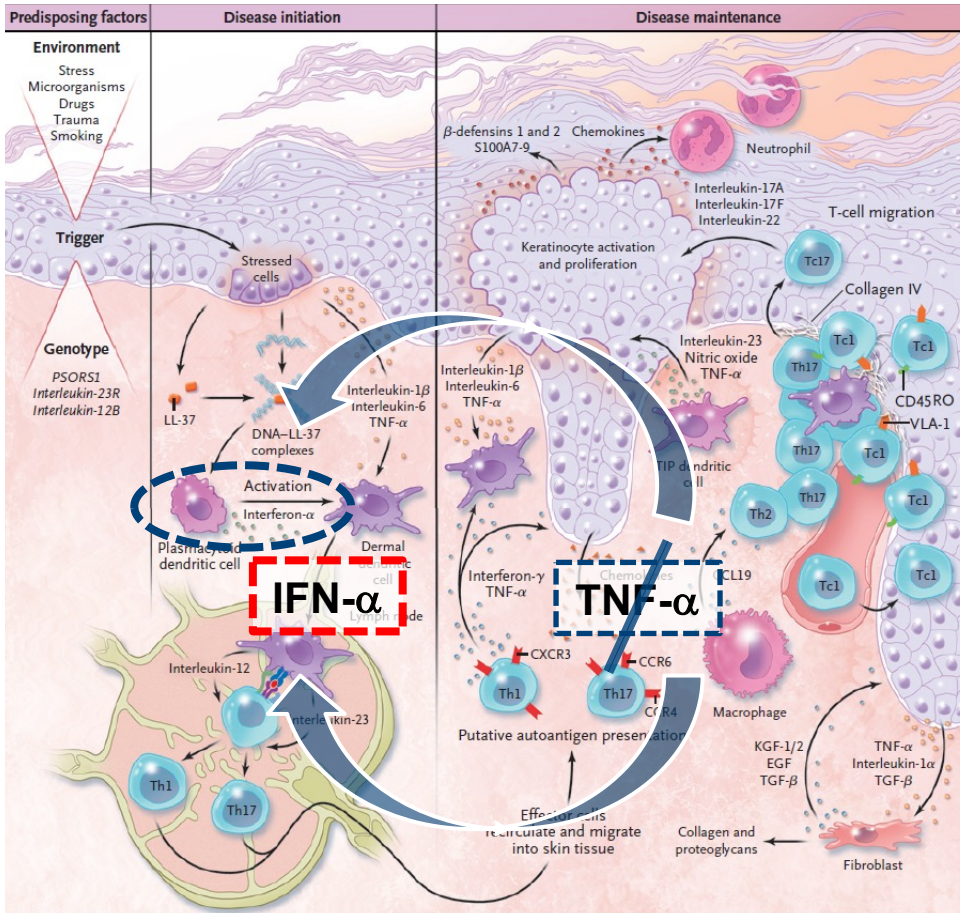
Clinical manifestations:

- plaque-type psoriasis (21-61%)[1-4]
- palmoplantar pustular psoriasis (29-56%)[1-4]
- scalp psoriasis (21%)[3]
- generalized pustular psoriasis (12%)[3]
- erythrodermic psoriasis (4%)[3]
- inverse psoriasis (4%)[3]

University of Zurich[UZH]

[1] Denadai R et al., *J Crohn's and Colitis*, 2013
[2] Shmidt E et al., *J Am Acad Dermatol*, 2012
[3] Wollina U et al., *Am J Clin Dermatol*, 2008
[4] Kip et al., *Inflamm Bowel Dis*, 2013

Psoriasiform eruptions – INF-α imbalance

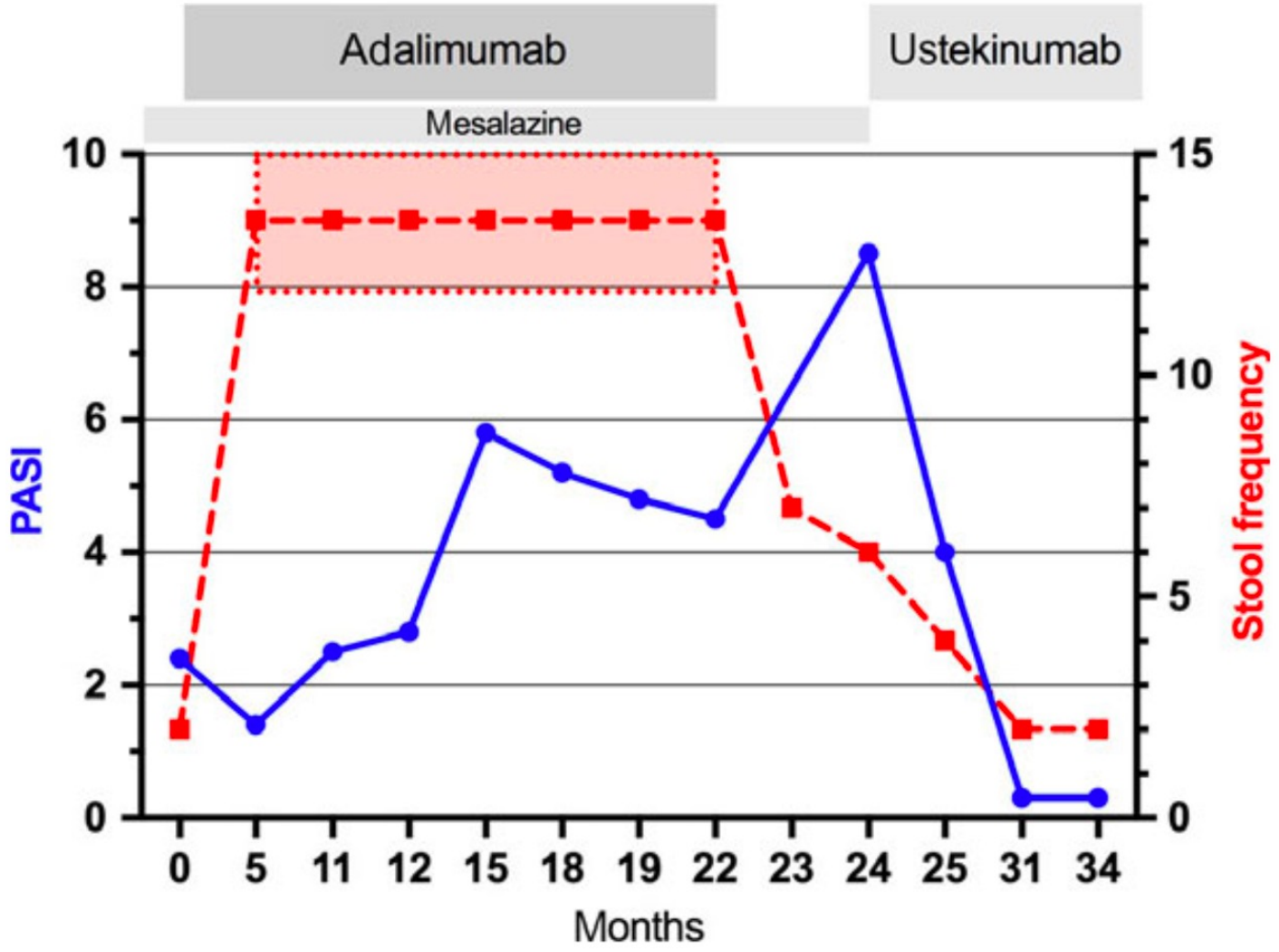


University of Zurich[UZH]

Palucka AK et al. *PNAS*. 2005
Conrad C et al, *Poster ESDR* 2012

Psoriasis. Nestle FO et al. *N Engl J Med*. 2009
Ma HL et al. *Arthritis Rheum*. 2010

Case II – ??



Kolios AGA et al., *Brit J Dermatol*, 2019

Case II – ??

CASE REPORT: THERAPY

BJD
British Journal of Dermatology

Paradoxical ulcerative colitis during adalimumab treatment of psoriasis resolved by switch to ustekinumab

A.G.A. Kolios,[1,2] L. Biedermann,[3] A. Weber,[4] A.A. Navarini,[2] J. Meier,[5] A. Cozzio[6] and L.E. French[2]

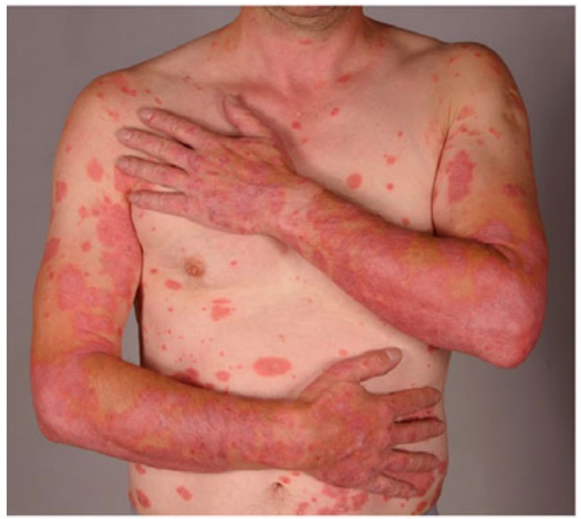
Departments of [1]Immunology, [2]Dermatology, [3]Gastroenterology and Hepatology and [4]Pathology and Molecular Pathology; Zurich University Hospital, Zurich, Switzerland

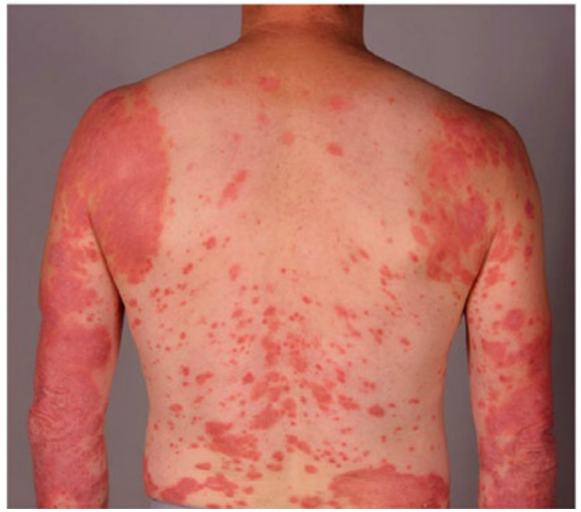
[5]Ambulante Gastroenterologie Baden AG, Baden, Switzerland

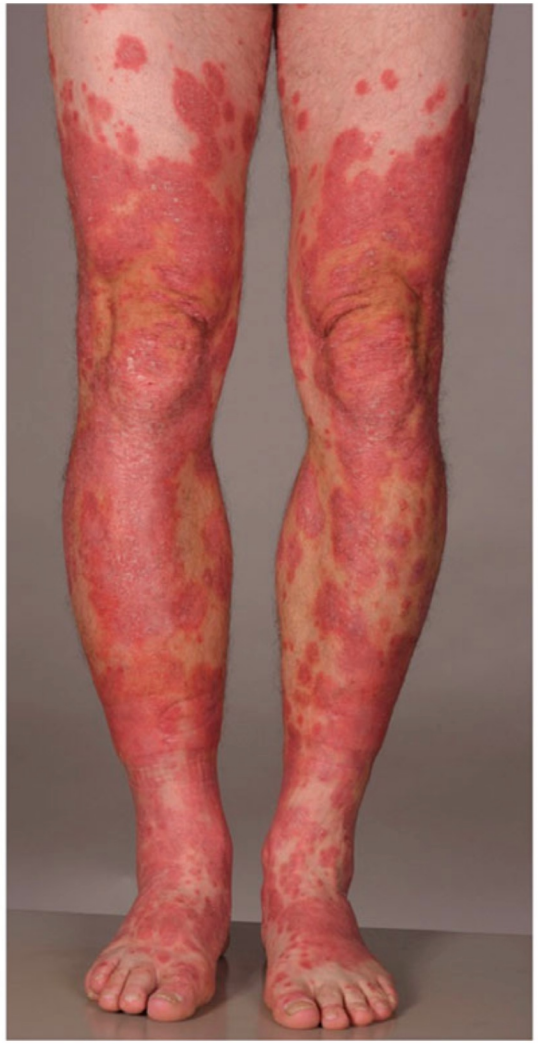
[6]Department of Dermatology and Allergology, Kantonsspital St Gallen, St Gallen, Switzerland

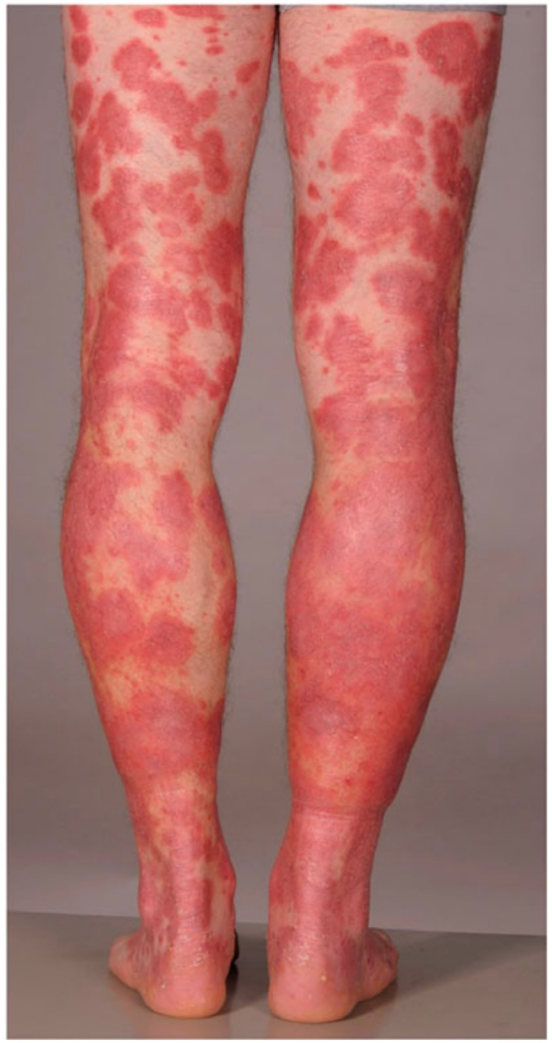
Kolios AGA et al., *Brit J Dermatol*, 2019

Case II – paradoxcial ulcerative colitis (PUC)









Kolios AGA et al., *Brit J Dermatol*, 2019

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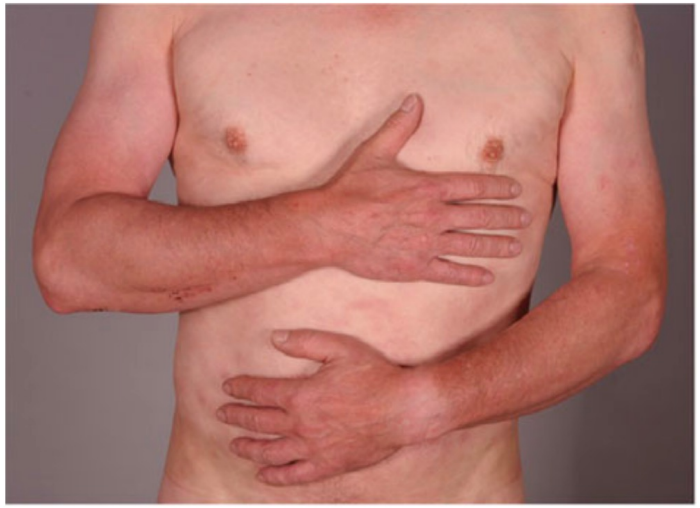
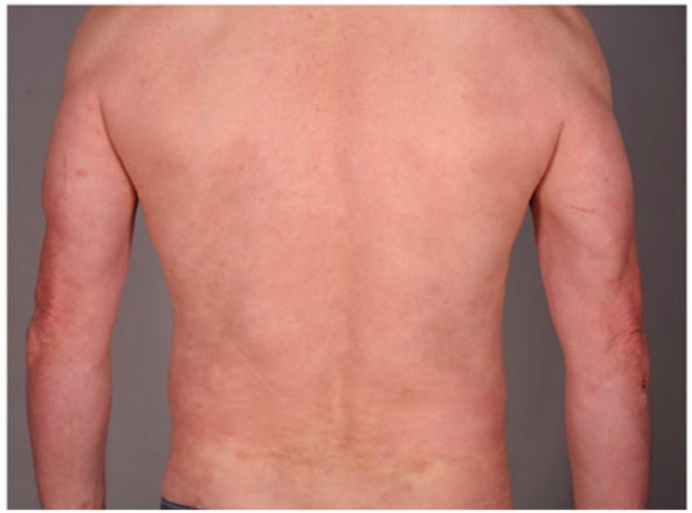
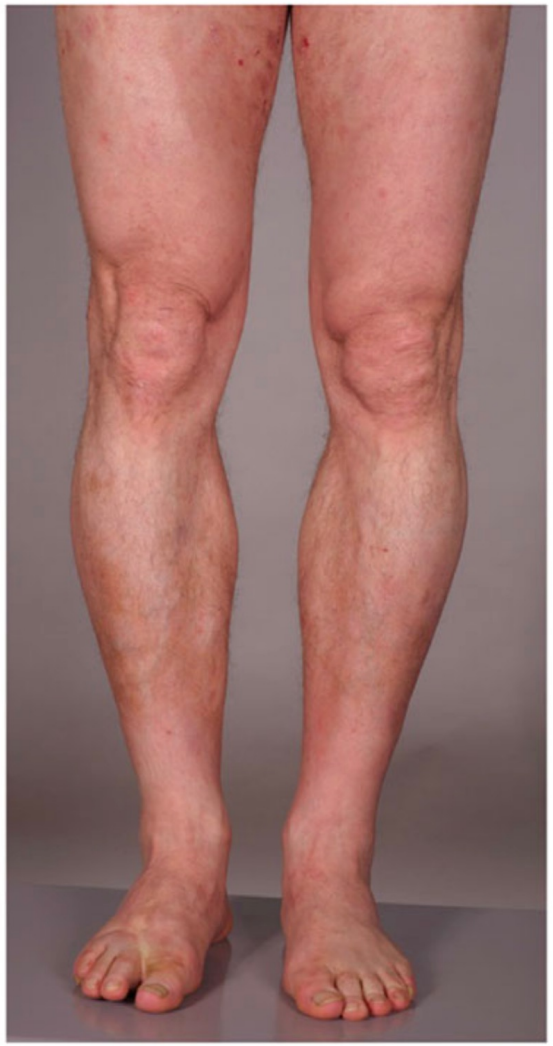
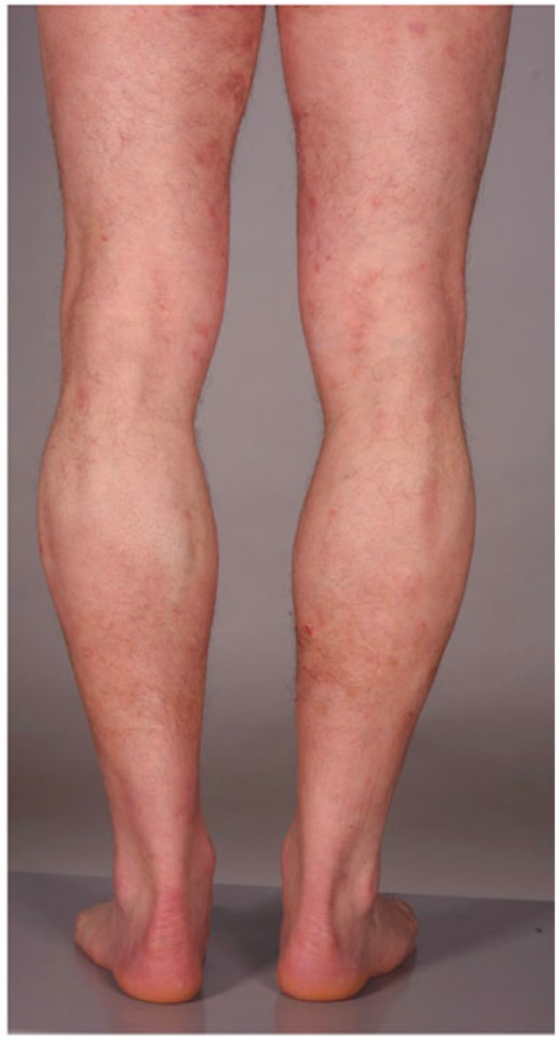








University of Zurich[UZH]

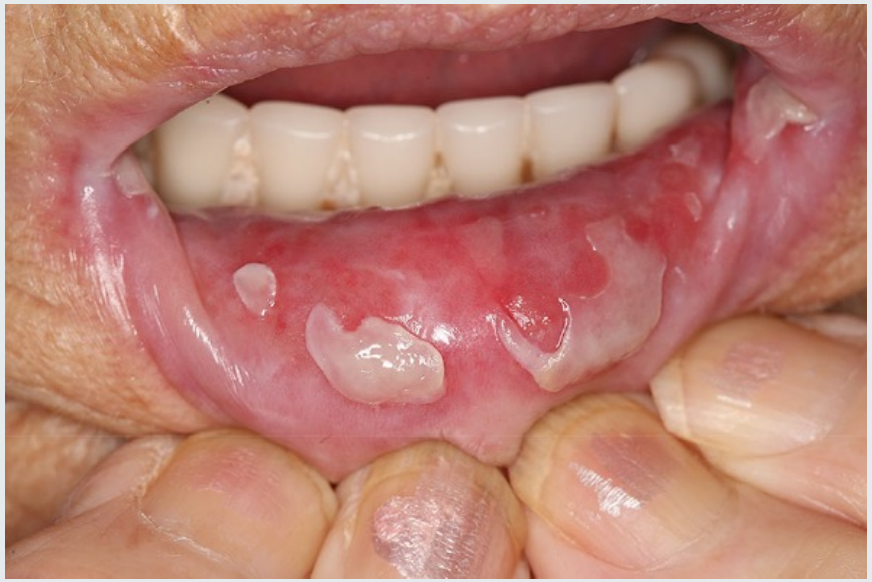
Kolios AGA et al., *Brit J Dermatol*, 2019

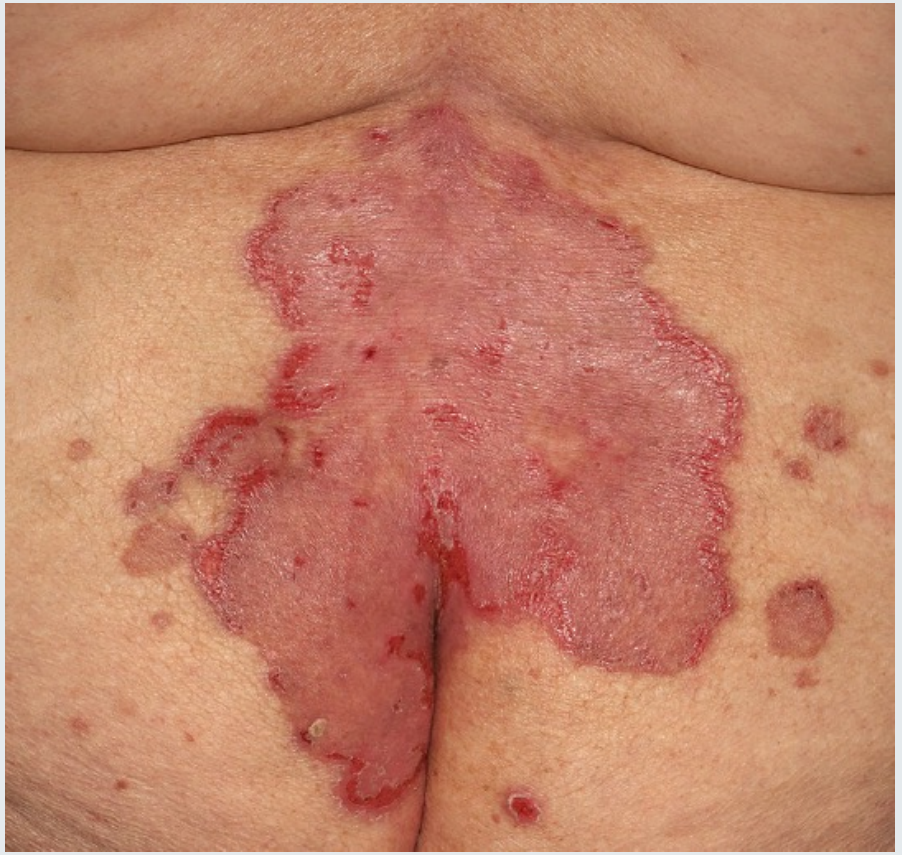
Case report

- 83y/o female with plaque type psoriasis
- Since 10 years under MTX, now 25mg weekly
  - folic acid 5mg once weekly, cumulative dose >7g
- Oral ulceration since 3 weeks followed by painful worsening of psoriasis since 2 weeks
- Comorbidities: aHT, congestive cardiac failure, no new medication
- Blood:
  - MTX not detectable
  - kidney function normal
  - leucocytes/erythrocytes normal, low platelet 109 (normal 150-400x10^9/L)

Weidmann A et al., Dermatol Ther (Heidelb) (2014) 4:145–156

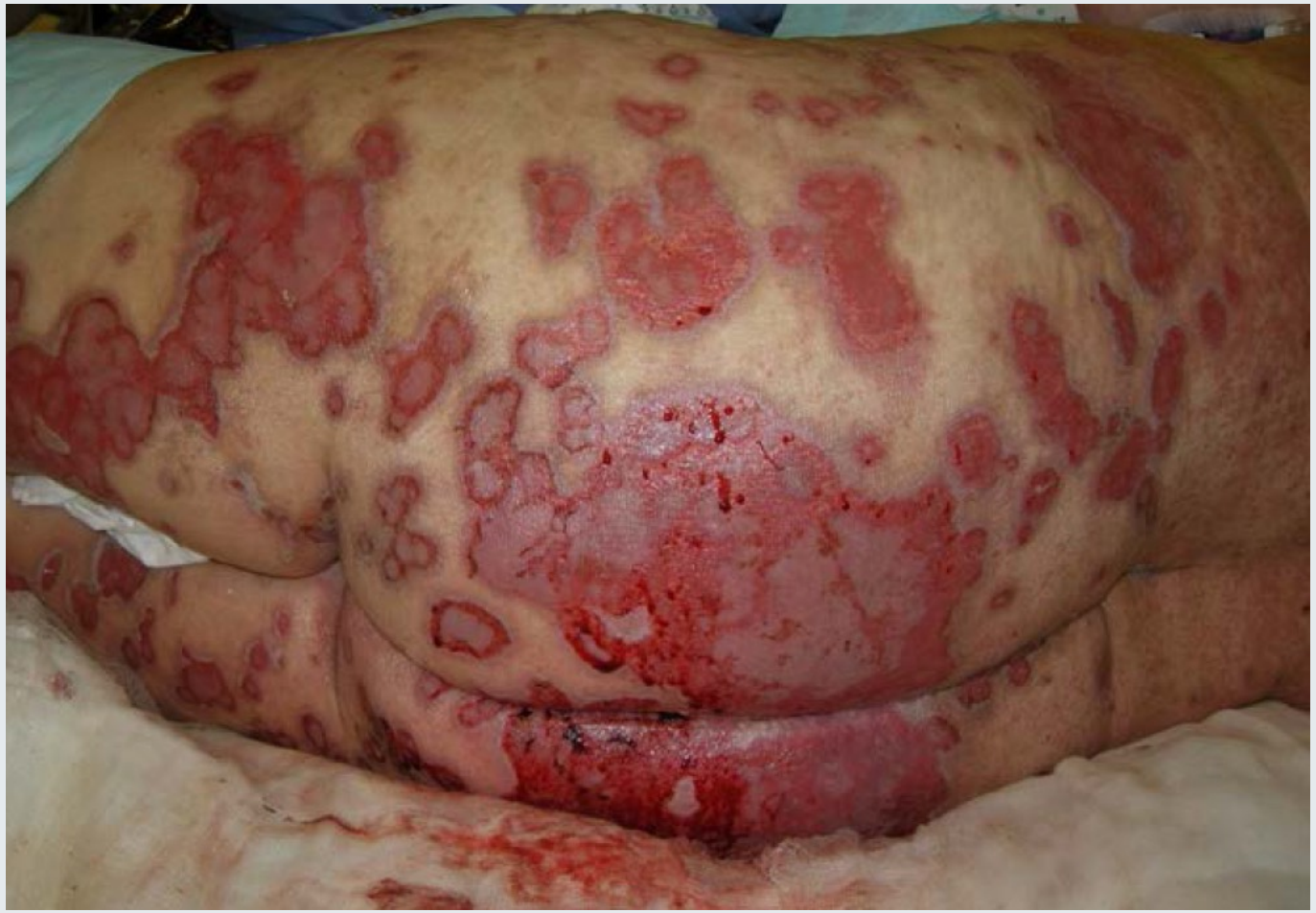
Case report





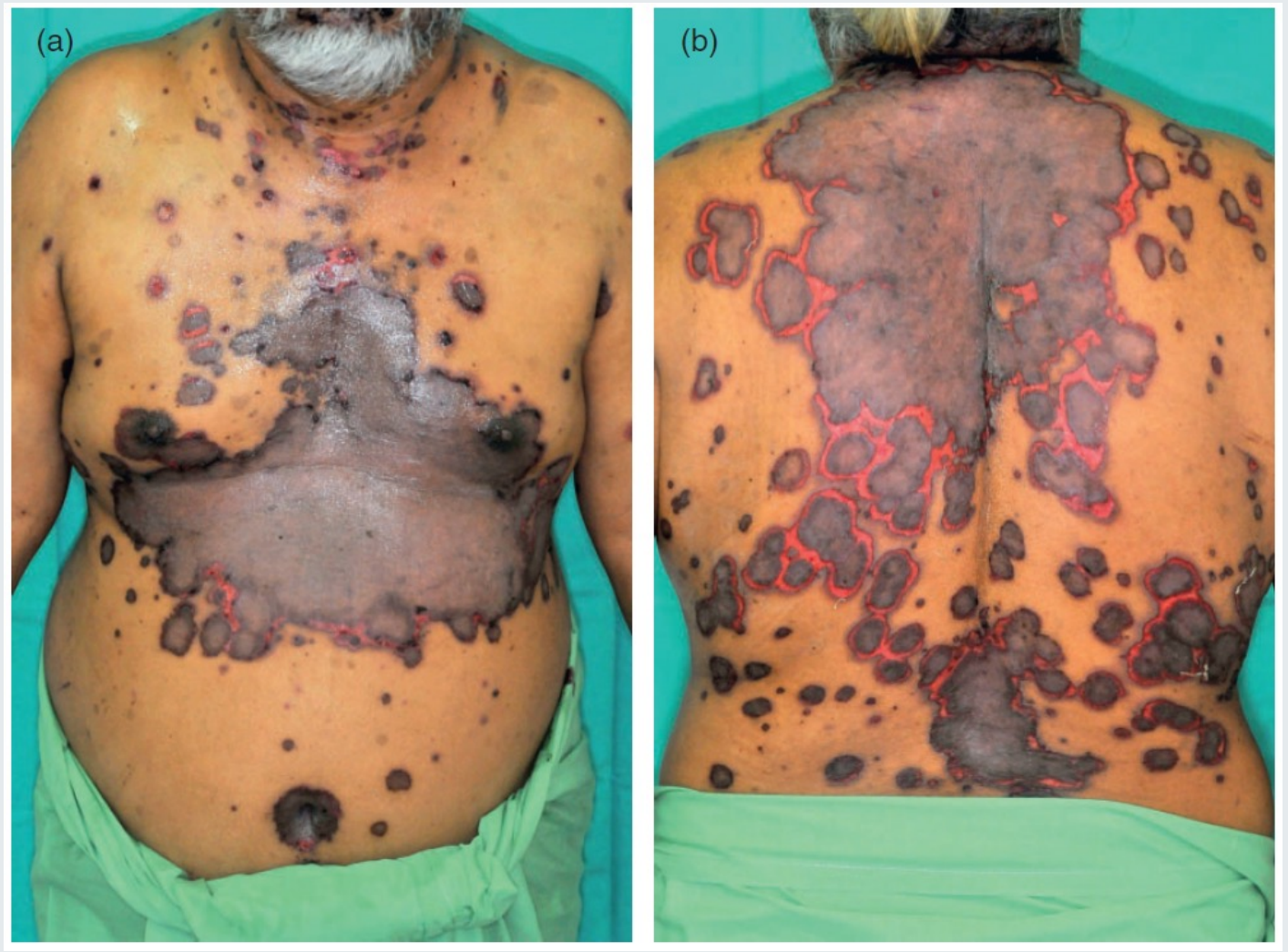
Weidmann A et al., Dermatol Ther (Heidelb) (2014) 4:145–156

MTX-induced skin ulceration



Shiver MB et al., Dermatol Online J. 2014 Jul 15;20(7).

MTX-induced skin ulceration

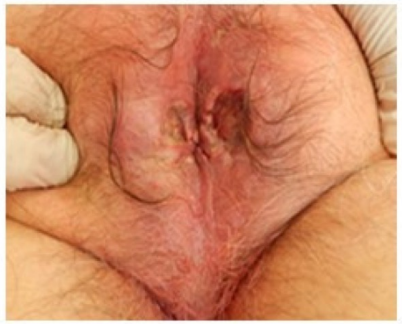
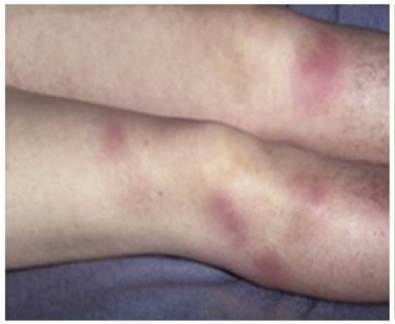
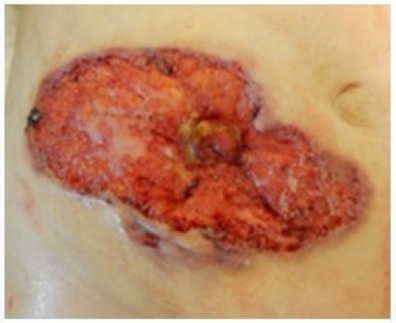
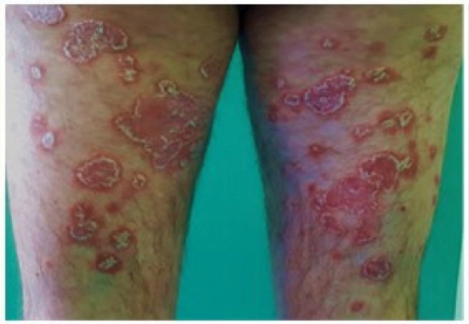
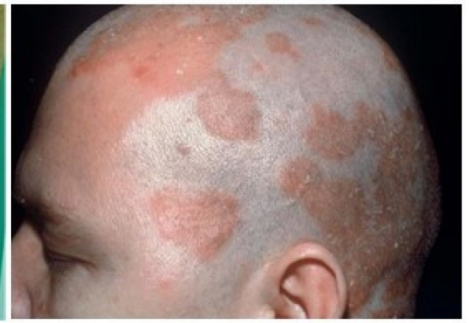


Wong S et al., Australasian Journal of Dermatology (2012) 53, 81–83

Immunosuppressive drugs in Dermatology

Cutaneous side effects	Infections	Immune-mediated reactions
Azathioprine	• Viral, fungal and bacterial very often in tranplanted (62,3%) and • occasional patients without immunosuppression • atypical infections, reactivation VZV, hepatitis B and others	Sweet syndrome, Erythema nodosum, Small-vessel vasculitis, AGEP / SJS / TEN
Ciclosporin	• Bacterial, fungal, viral, parasites, opportunistic infections • Activation of polyoma virus (BK- and JC)	Hypertrichosis, gingival hyperplasia, sebaceous hyperplasia
Cyclophosphamide	• Viral, bacterial, fungal, protozoa, reactivation of latente infections (TBC, JCV, PcP), Strongyloides	Dermatitis, SJS / TEN, hyper-/ hypopigmentation esp. palmar and nails, urticaria, hyperhidrosis, stomatitis, alopecia
Methotrexate	• 58% infections incl. opportunistic infections (PcP, Listeria meningitis, disseminated herpes zoster, M. avium, systemic fungal infections)	Photosensitivity, alopecia, oral ulcers, necrosis of psoriatic plaques, accelerated rheumatoid nodulosis
Mycophenolate mofetil	• Bacterial, fungal, viral, opportunistic infections • Incl. CMV-Sepsis (20%) influenza, meningitis, endocarditis, tuberculosis, atypical mycobacterial infection	

Take home message

Specific manifestations	Disorders associated with inflammatory bowel disorders	Reactive manifestations	Muco-cutaneous conditions secondary to treatment of inflammatory bowel disorders	Cutaneous manifestations secondary to nutritional malabsorption
Continuous/contiguous Crohn's disease Metastatic Crohn's disease	Aphthous stomatitis Erythema nodosum Psoriasis Epidermolysis bullosa acquisita	Pyoderma gangrenosum Sweet's syndrome Bowel-associated dermatosis-arthritis syndrome Aseptic abscess ulcers Pyodermatitis-pyostomatitis vegetans SAPHO syndrome PAPA syndrome	Adverse muco-cutaneous reactions (injection site reactions, infusion reactions, paradoxical reactions, eczematiform and psoriasiform reaction, life-threatening disorders) Cutaneous infections Cutaneous malignancies	Stomatitis Glossitis Angular cheilitis Pellagra Scurvy Purpura Acrodermatitis enteropathica Phrynoderma Seborrheic-type dermatitis Hair and nail abnormalities
				

Antonelli E et al., *J Clin Med,* 2021

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