Drug eruptions

Drug eruptions

5% of all dermatoses

15% of drug side effects

- skin changes
- mucosal involvement
- pruritus
- paraesthesia, pain

Classification of drug reactions

According to the time of onset of symptoms

- early (up to 1 hour)
- late (over 1 hour from the application of the drug)

Hypersensitivity drug exanthema

According to the involvement of immune mechanisms

- allergic:

- antibody mediated

- cell mediated

- non-allergic

- drug interaction with immune receptor of p-i concept cells

- pseudo allergic - anaphylactoid - no sensitization required

Allergic reactions according to Coombs and Gell

Type I. Anaphylactic - IgE antibodies
urticaria (nonsteroidal antirheumatic drugs)

Type II. Cytotoxic - antibody dependent
thrombocytopenic purpura

Type III. Immunocomplex
drug vasculitis

Type IV. T cell mediated
IVa allergic contact dermatitis
IVb DRESS, maculopapular rash
IVc TEN, fixed drug rashes
IVd AGEP

Hypersensitivity drug rashes
According to the mechanism of cell activation

- reaction triggered by a hapten-carrier complex
- reaction based on the pharmacological interaction of the drug with cell immune receptors
- pseudoallergic reaction resulting from stimulation or inhibition of inflammatory cell receptors and enzymes

Hypersensitivity drug rashes
According to severity

- mild reactions
- severe, life-threatening reactions with possible organ involvement (anaphylactic shock, SCARs)

Drug rashes from other causes

- Overdose
- Cumulation
- Pharmacological side effects
- Drug interactions
- Microbial imbalance – dysmicrobia

Clinical signs

- Exfoliative erythroderma
- Haemorrhagic coumarin necrosis
- Alopecia diffusa toxica
- Acneiform eruptions
- Provocation of skin diseases
- Pigmentation (amiodarone)

History and diagnosis of drug rashes

History:

- Drugs – targeted questions on: medications, vitamins, contraception, sedatives, laxatives, hypnotics, analgesics, inhalation, anaesthesia, external medications
- Complementary and alternative medicine, self-medication
- Food influences – ask about: dyes, fragrances, flavours, preservatives, tonics, artificial sweeteners
- Previous drug reactions
- Exposure - whether the substance (or a similar substance) has been administered in the past
- Timing – onset of rash and administration of the drug (5-10 days from commencing the drug)

Exclusion of other causes - other dermatoses, skin manifestations infectious and systemic diseases

History and diagnosis of drug rashes

Elimination test – regression confirms the diagnosis

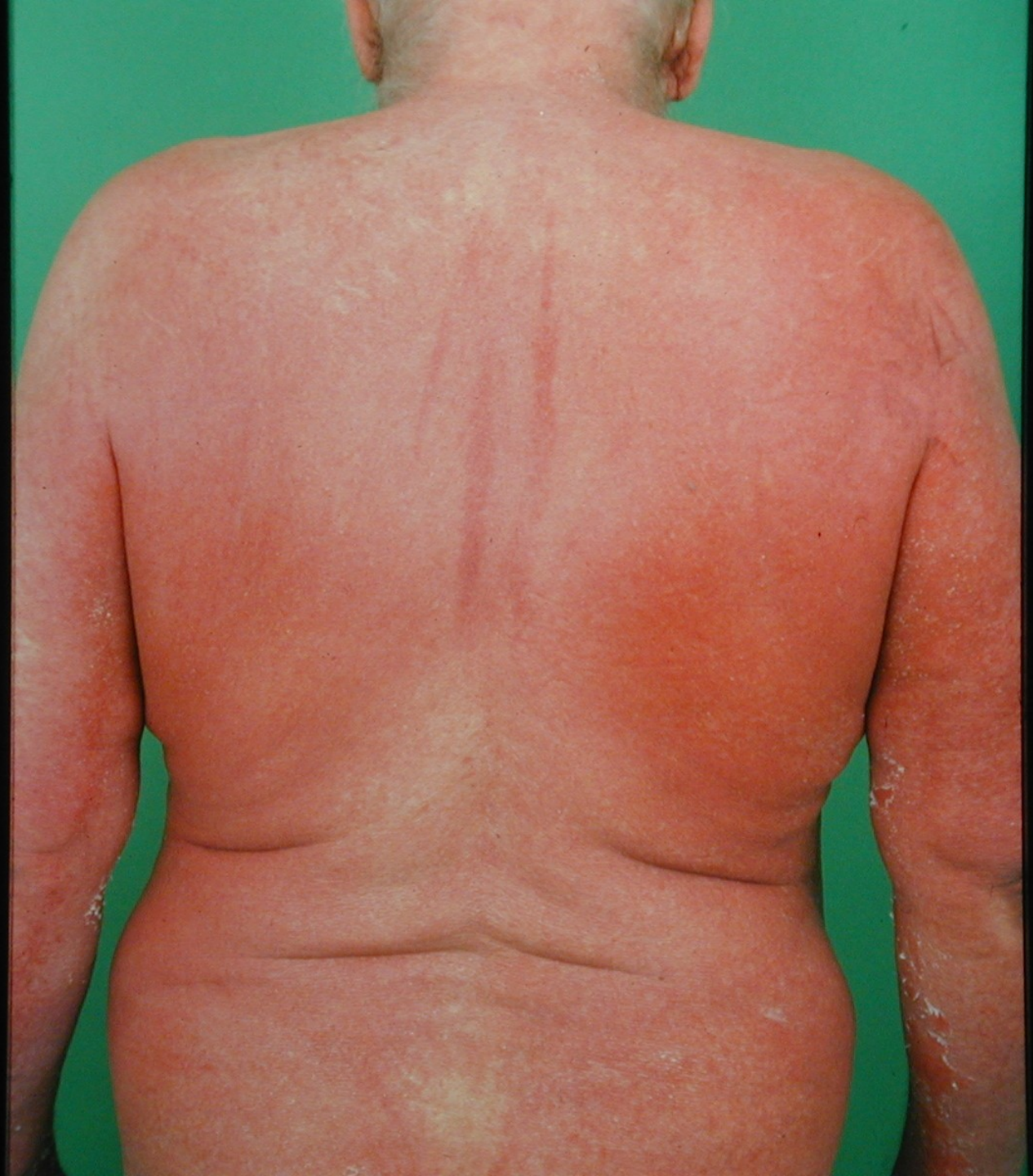
Reexposure test – recurrence confirms the diagnosis

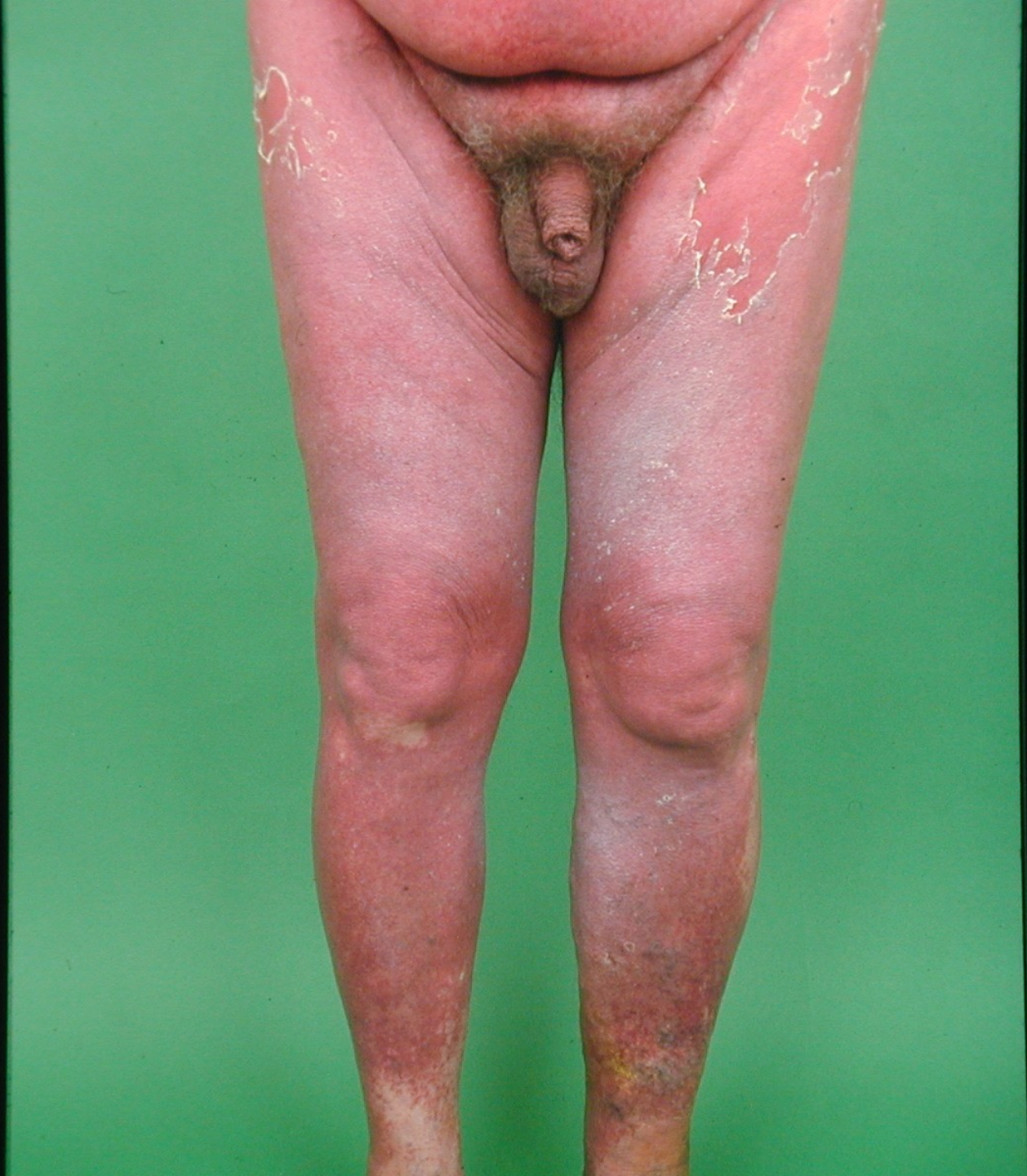
Laboratory tests:

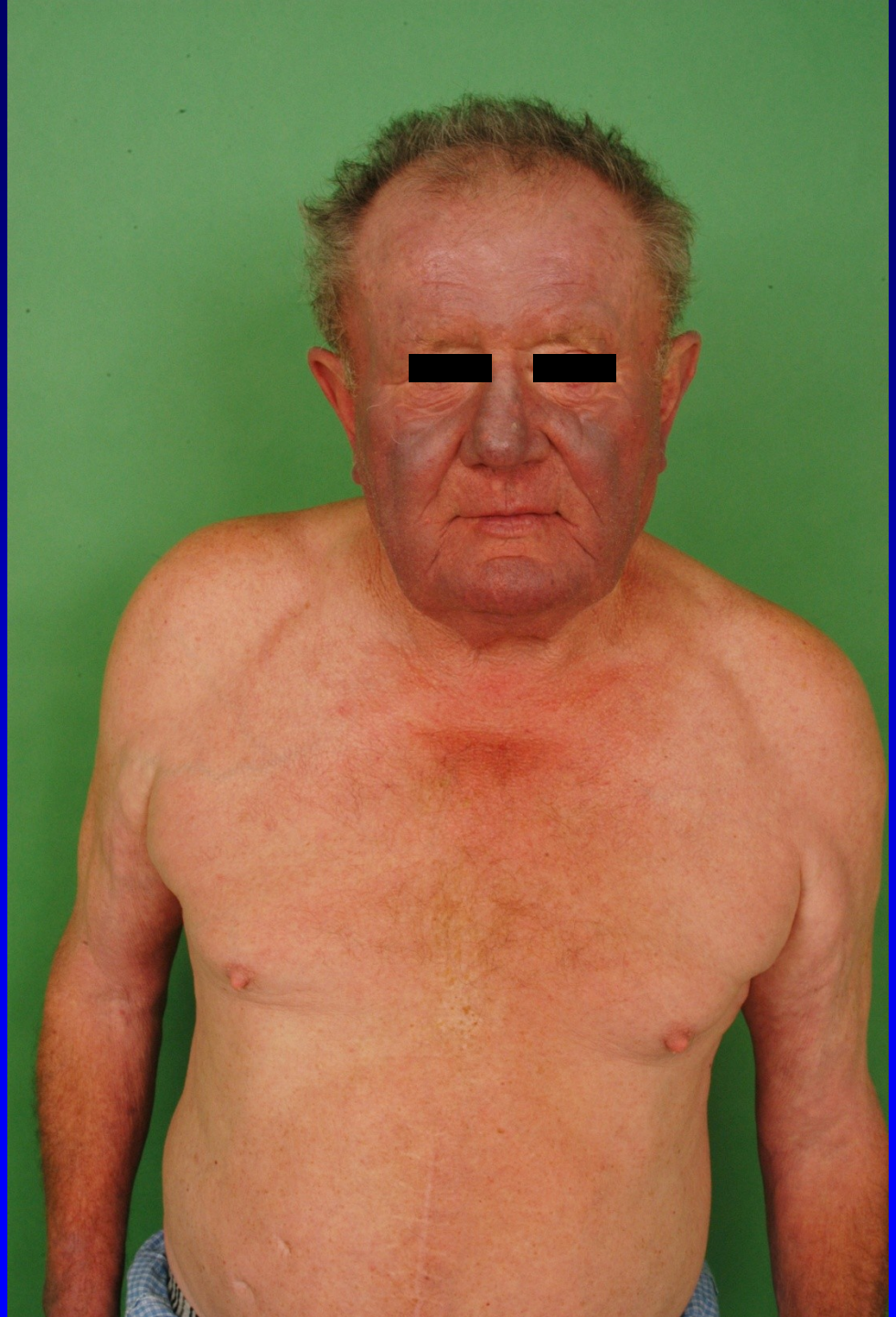
- In vivo:
  - Intradermal (scarification) in anaphylactic type I reactions
  - Epicutaneous in a type IV hypersensitivity reaction (fixed drug rash)
- In vitro:
  - RAST (penicillin)
  - Other: lymphocyte transformation test, etc.

When more than one drug is given at the same time, the drug likely responsible is:

- The drug with a higher risk of rash
- The drug administered last







Drug rashes according to clinical findings

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- acute generalised exanthematous pustulosis (terbinafine)
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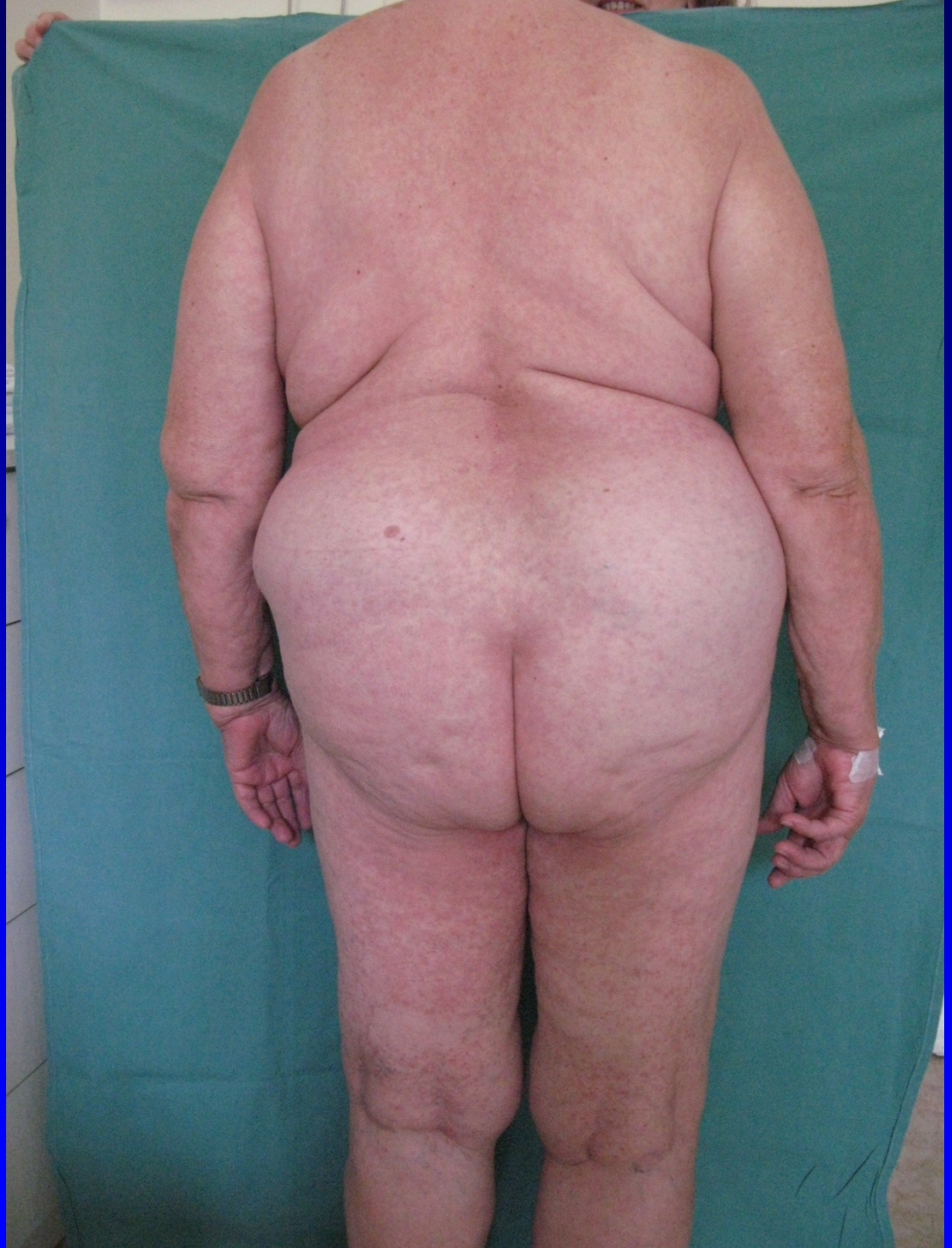

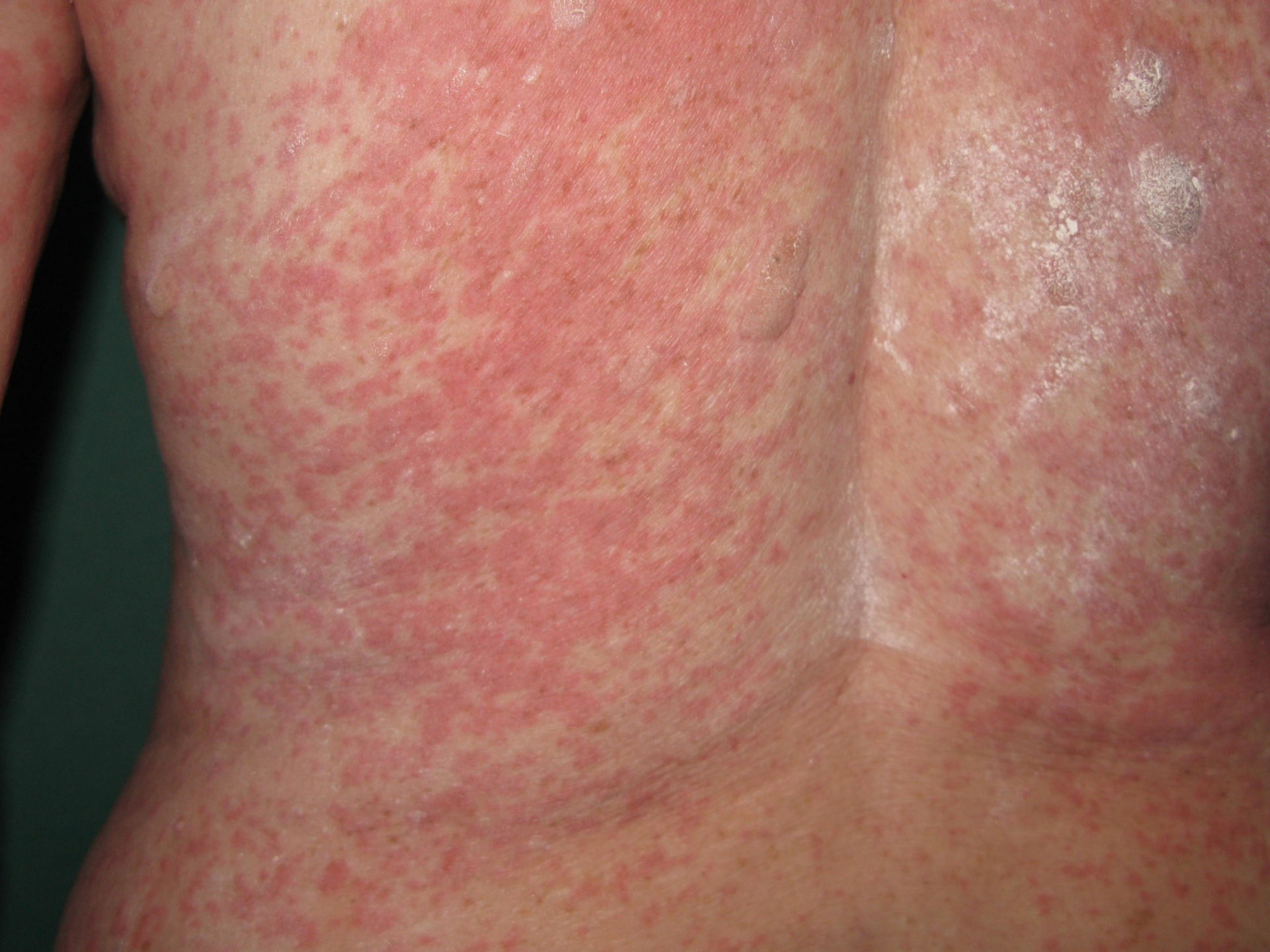

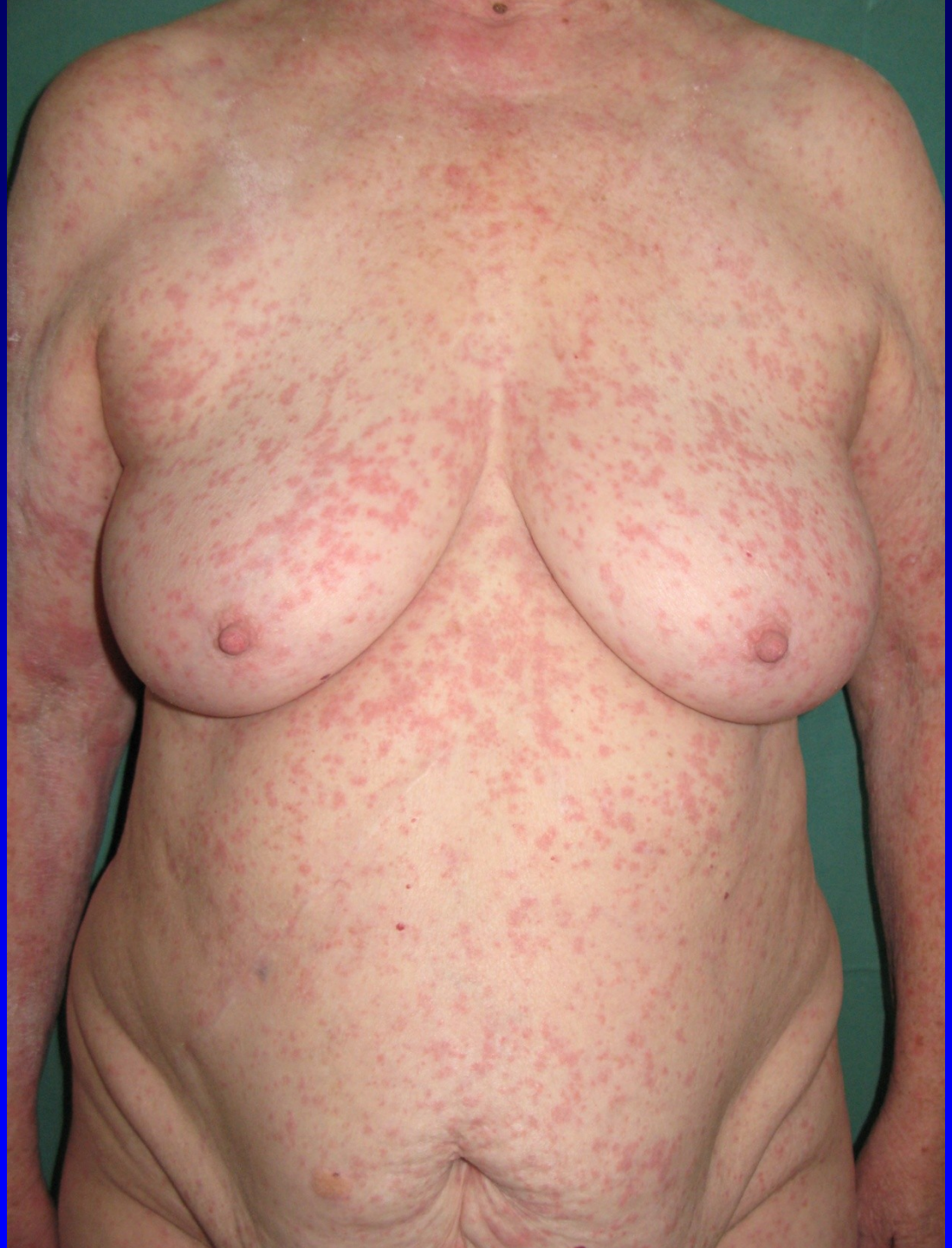

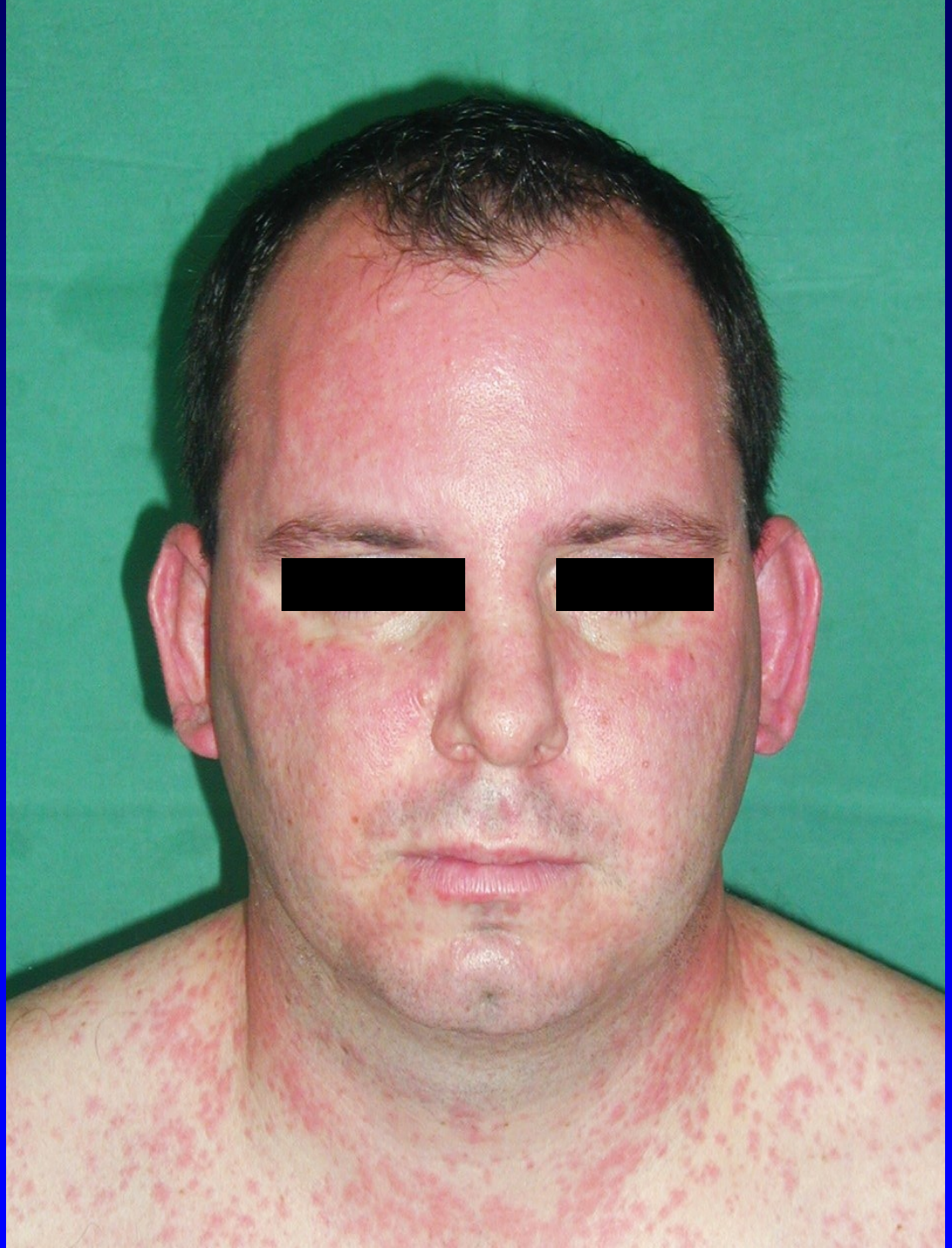

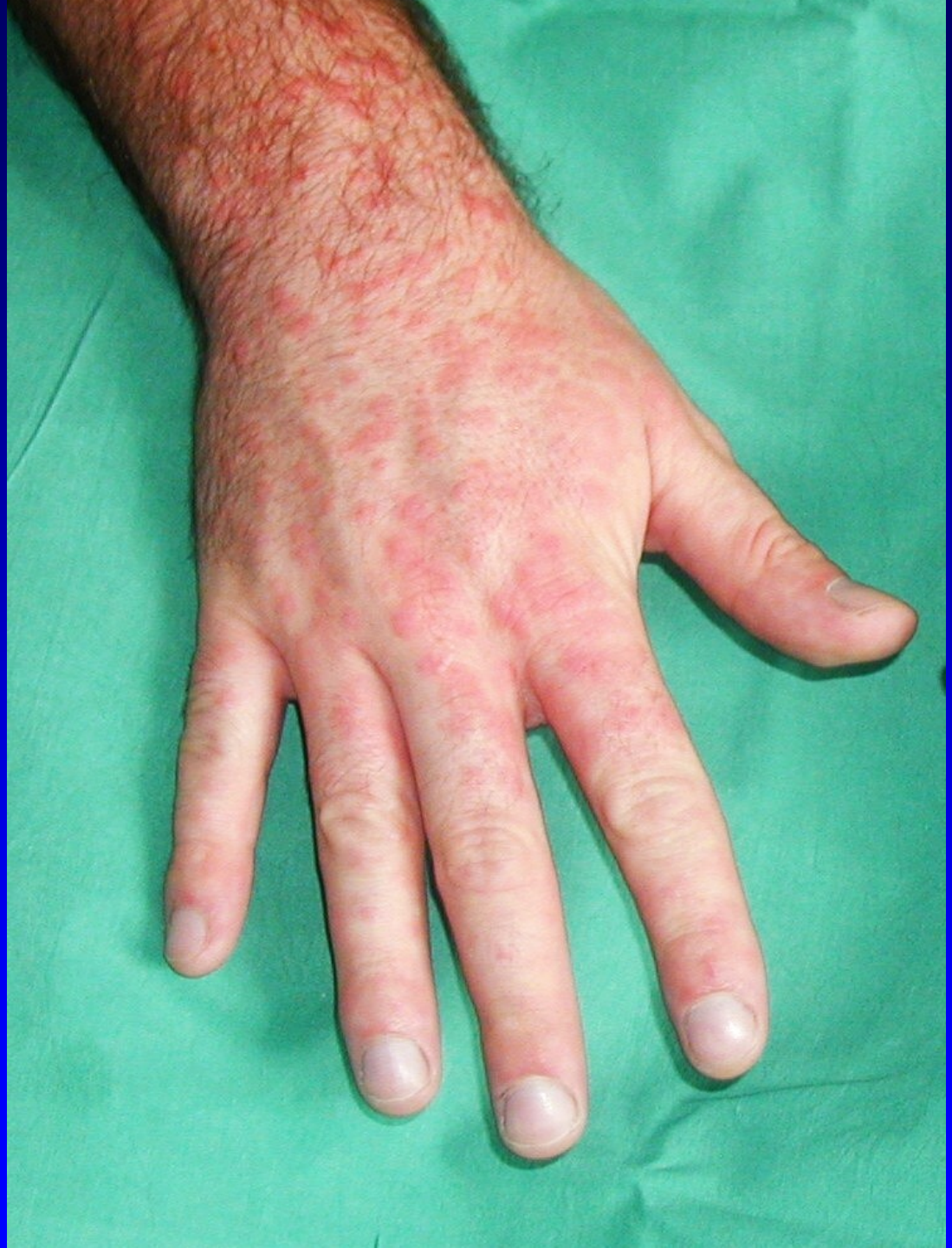

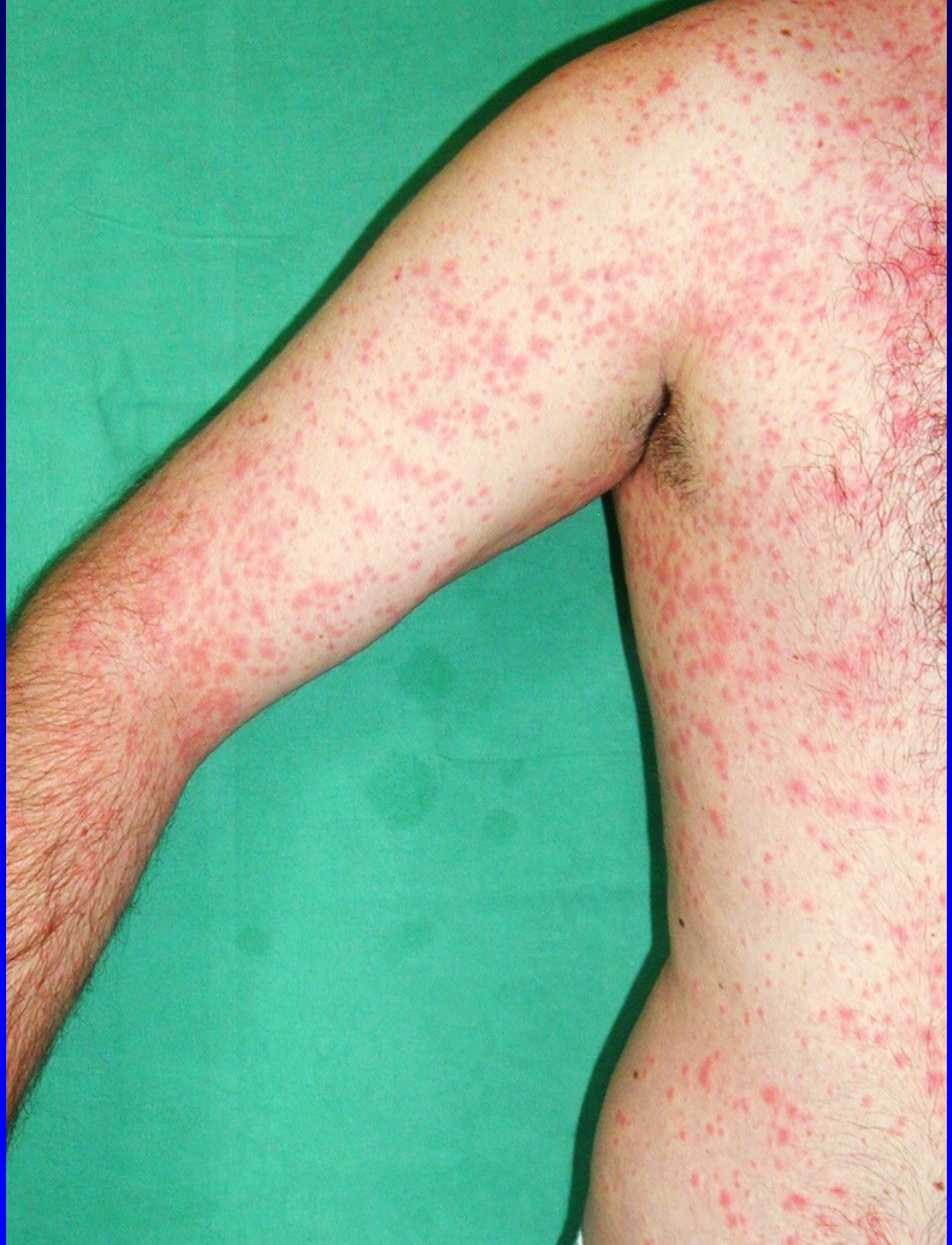

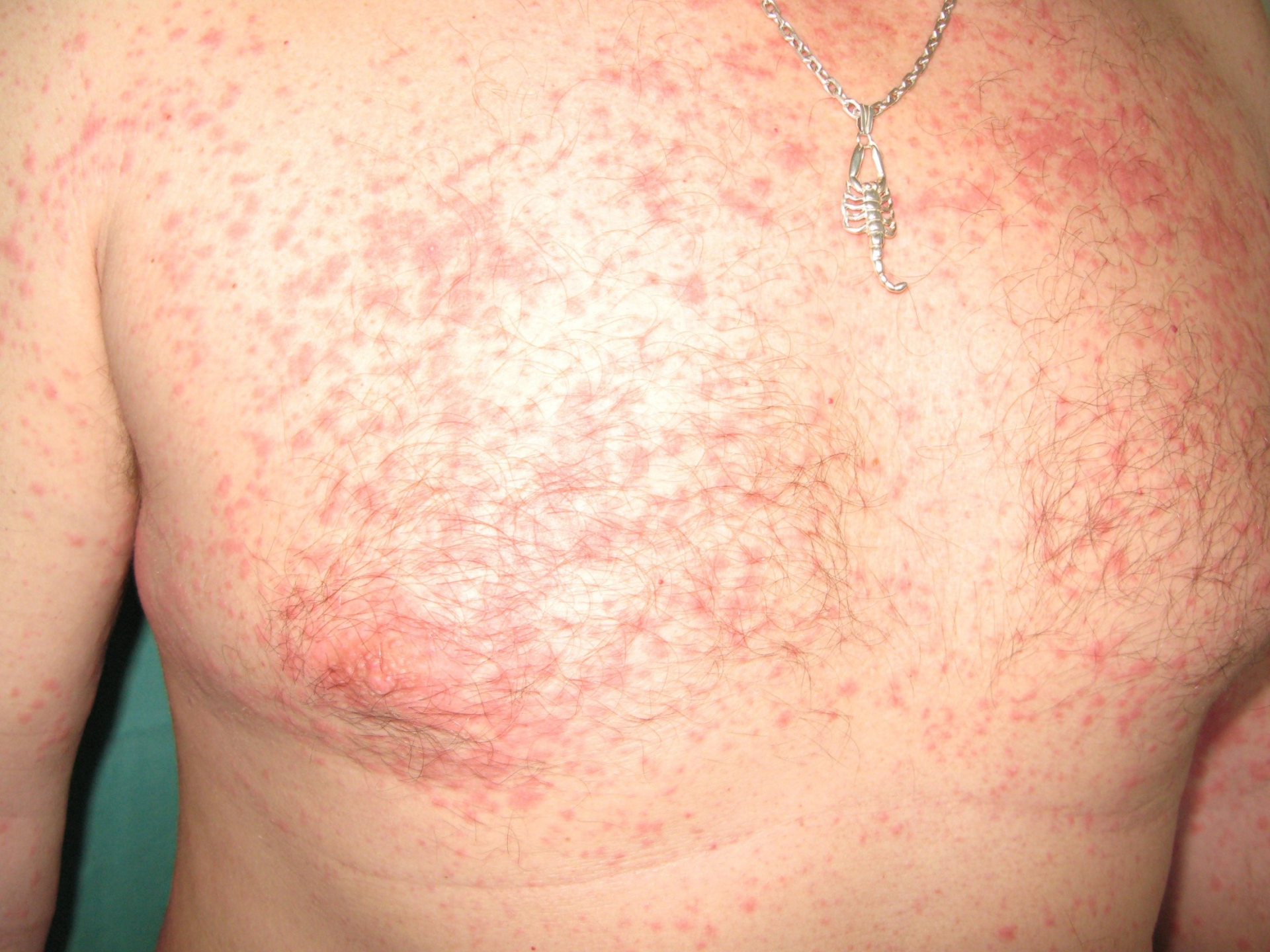

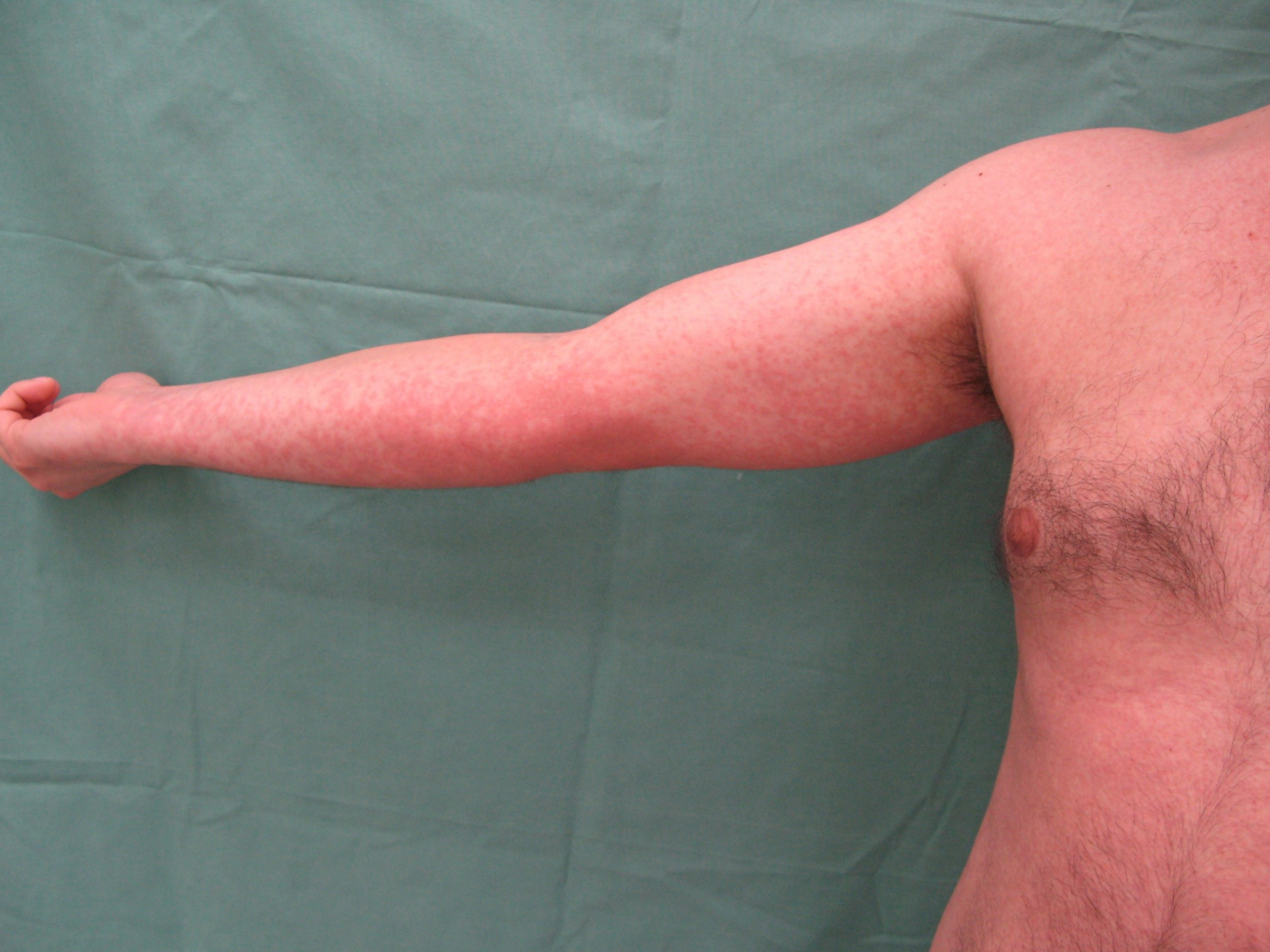

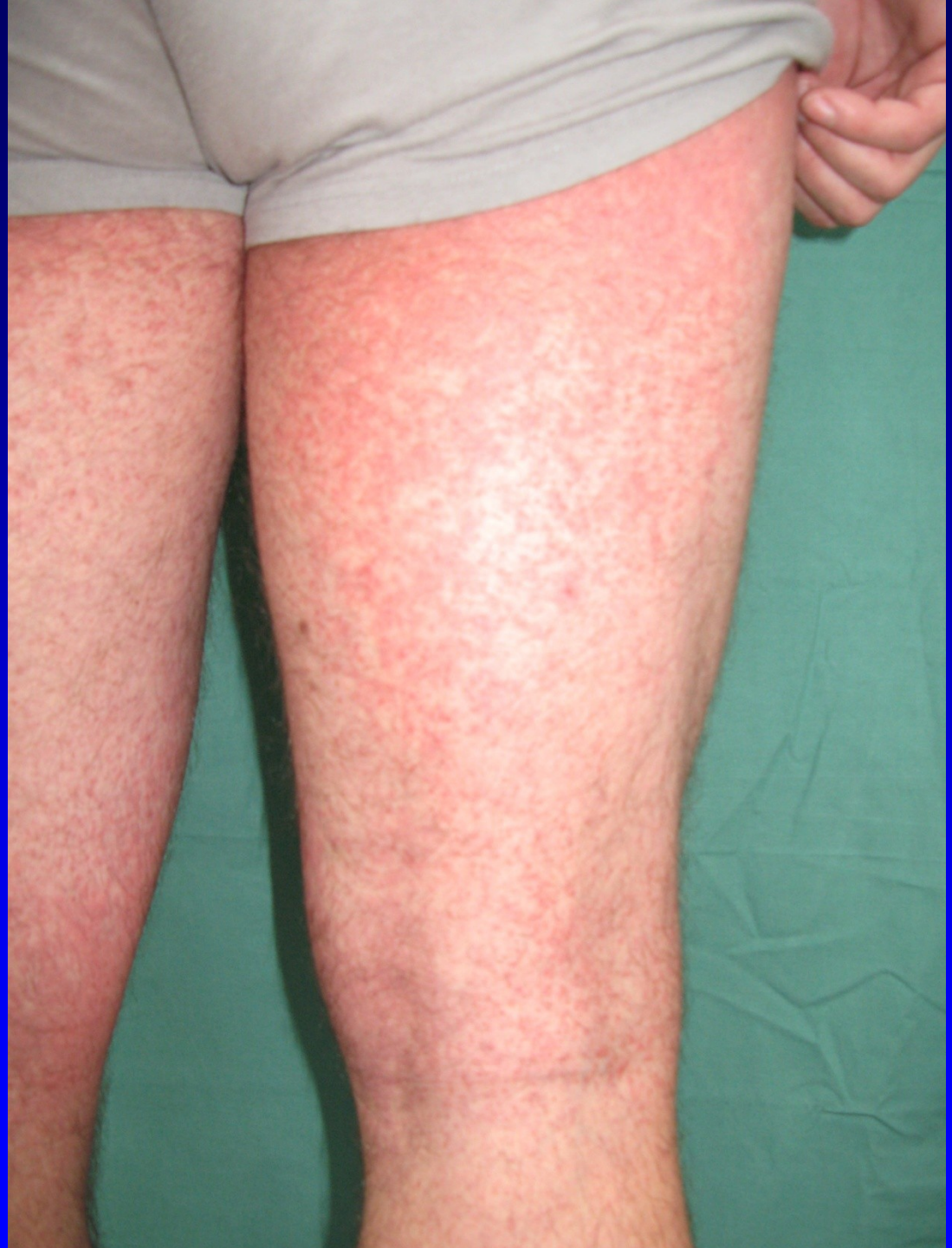

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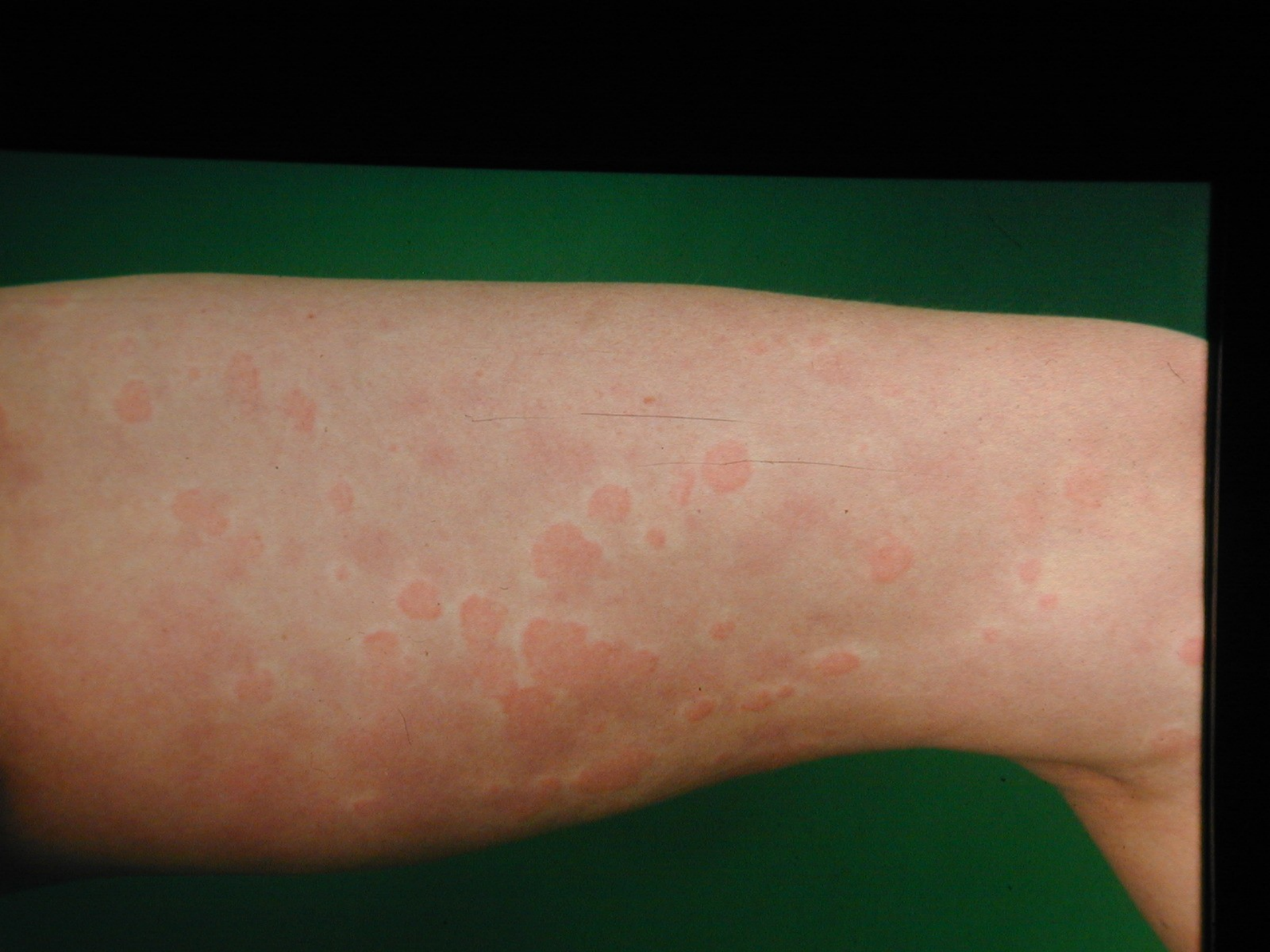
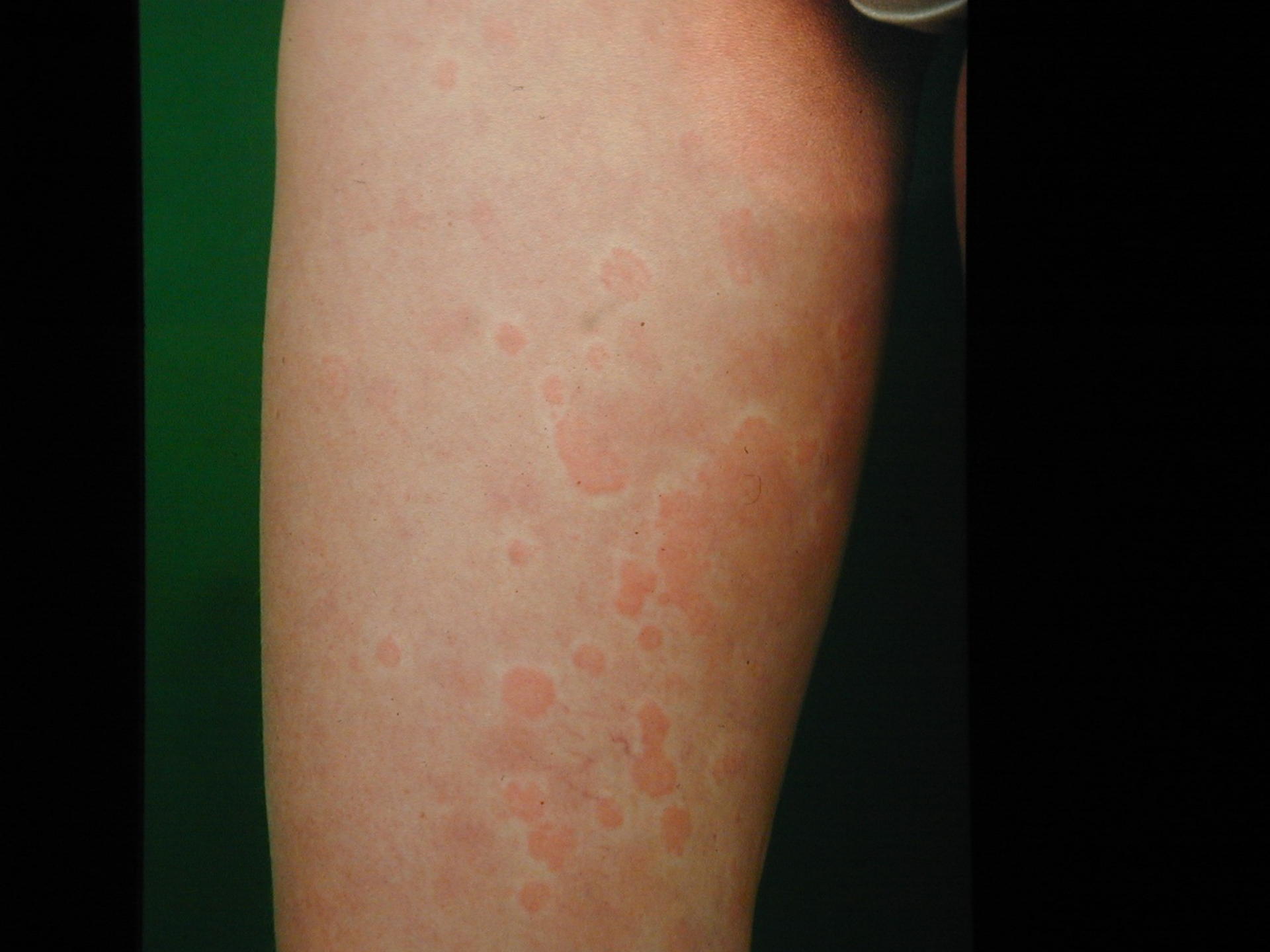
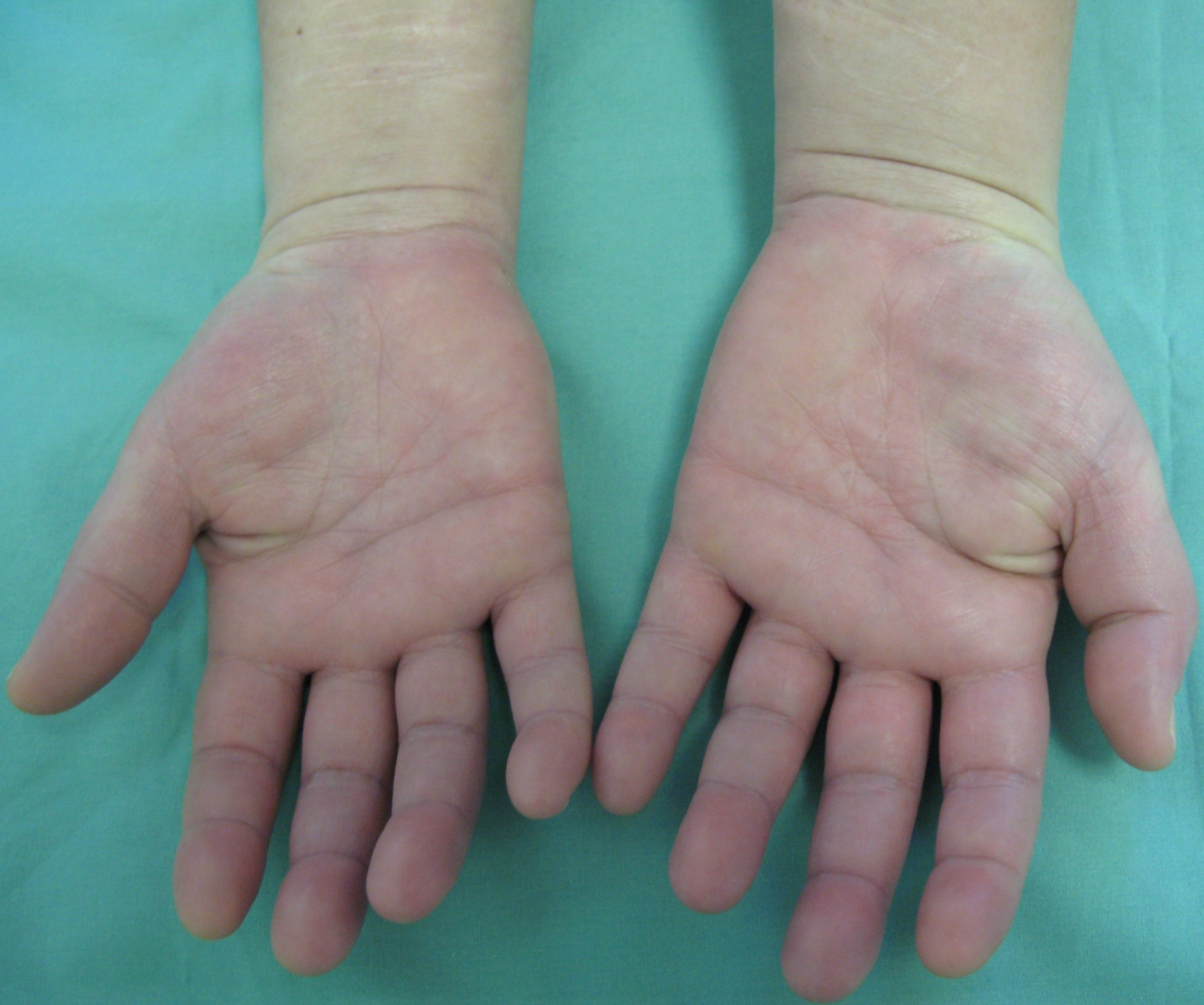
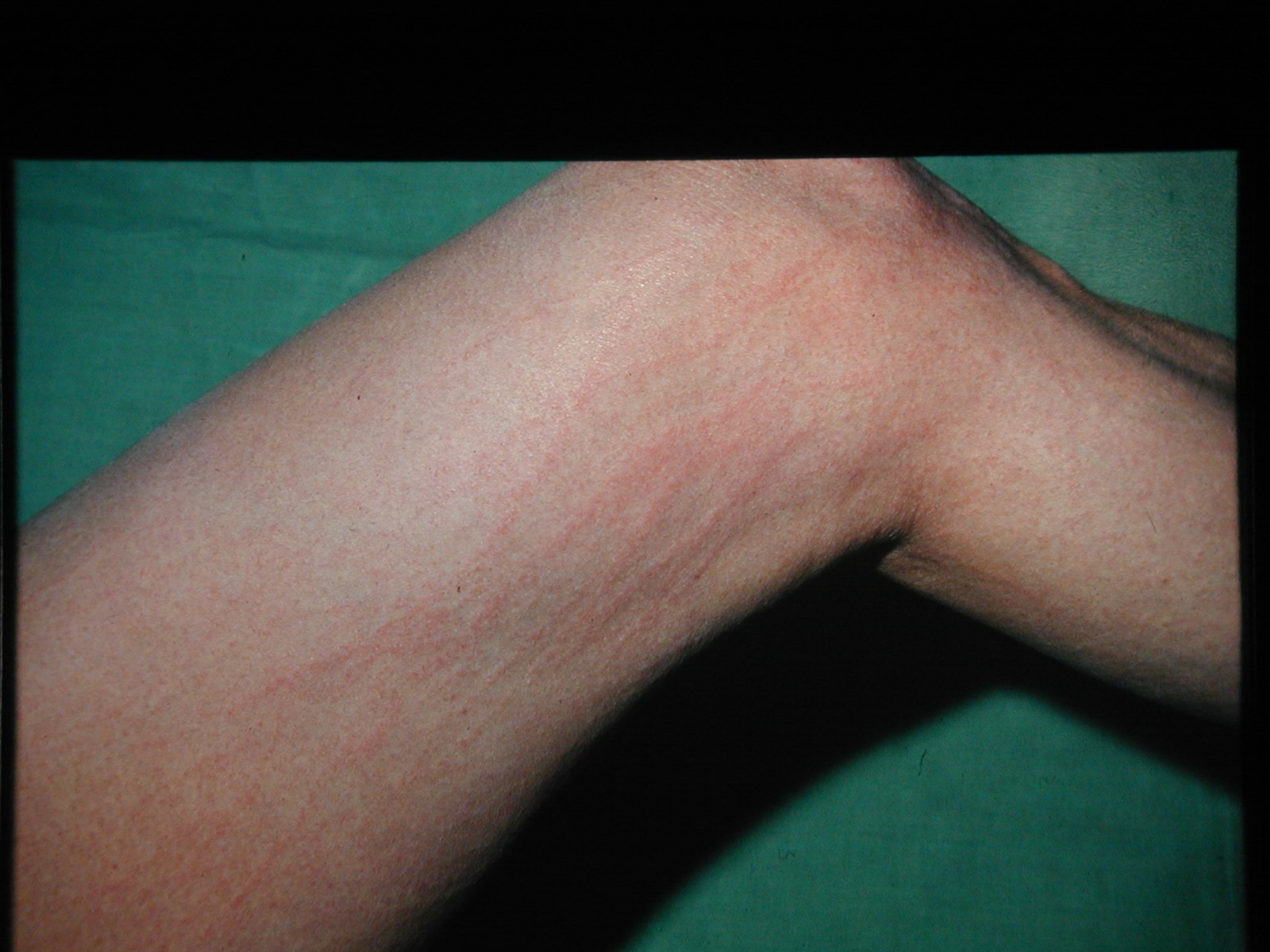
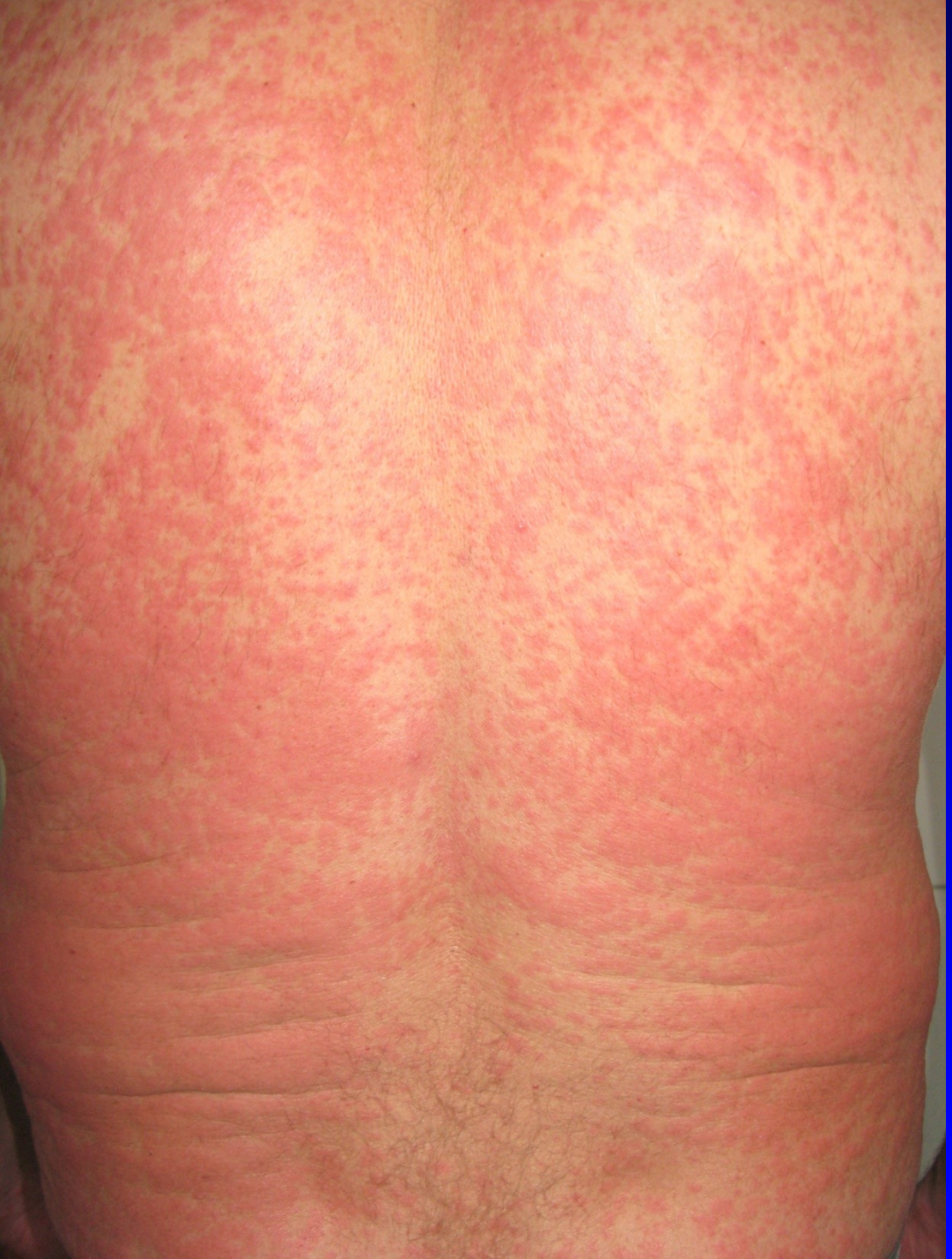


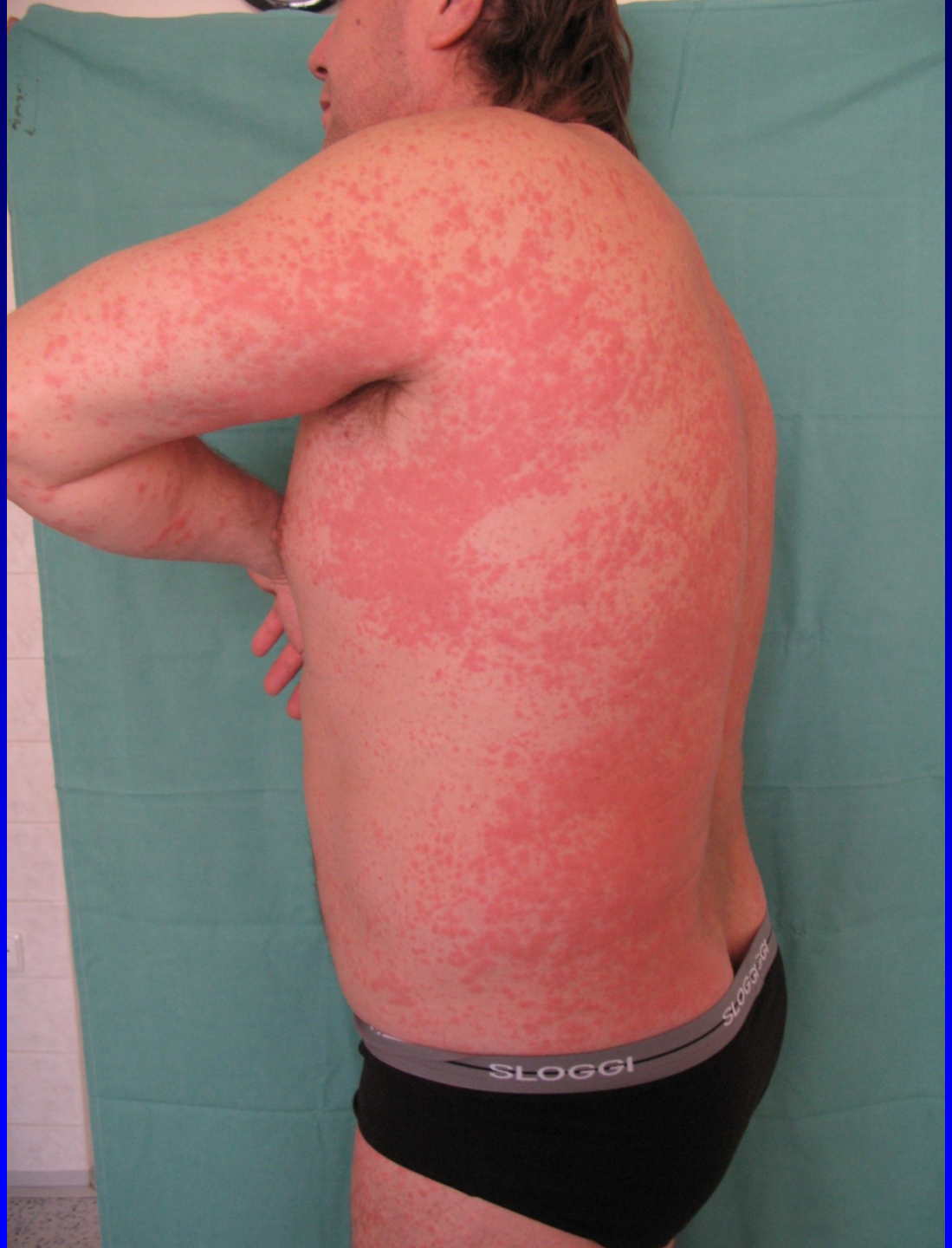








Maculo-urticarial
(penicillin)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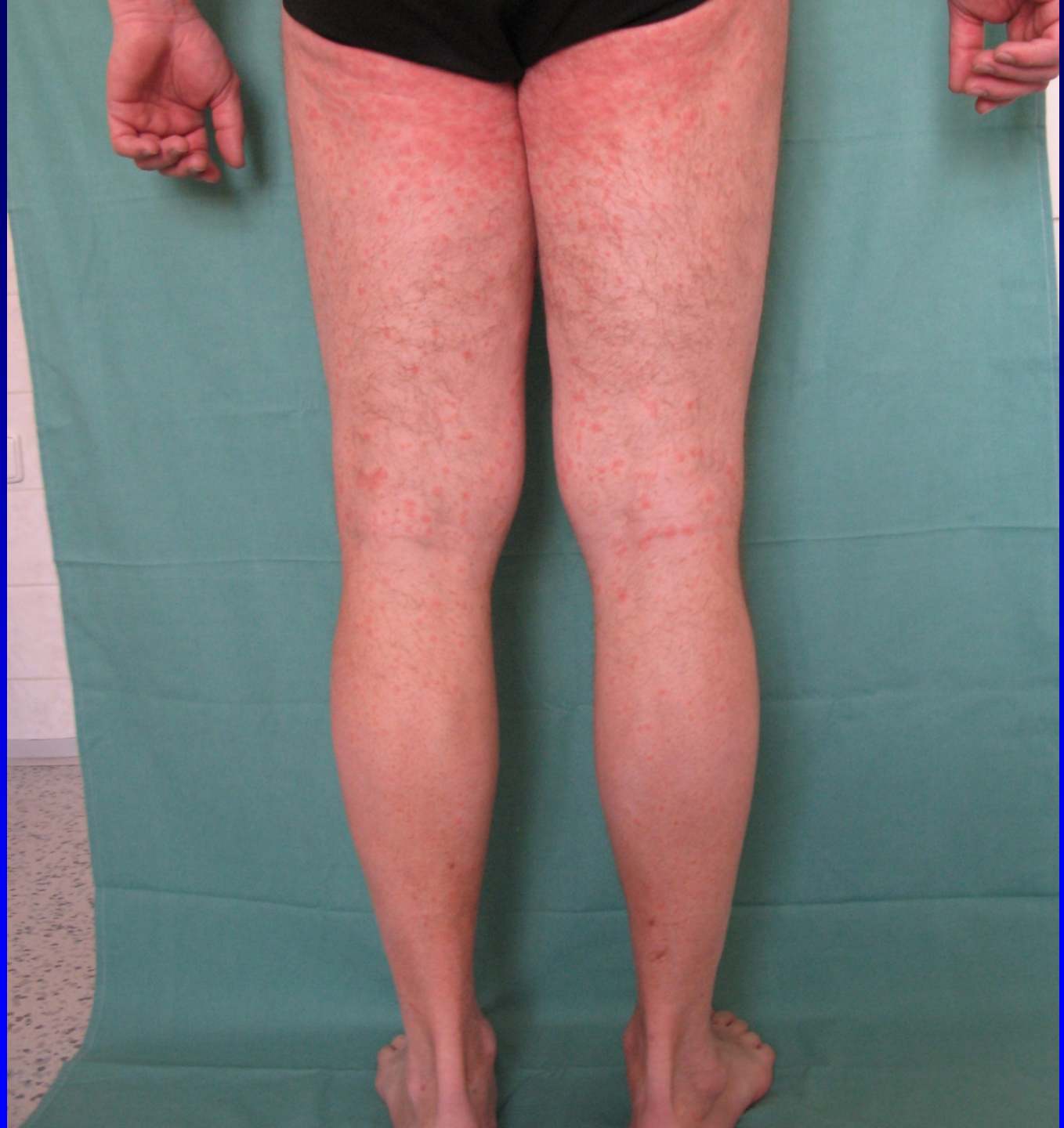

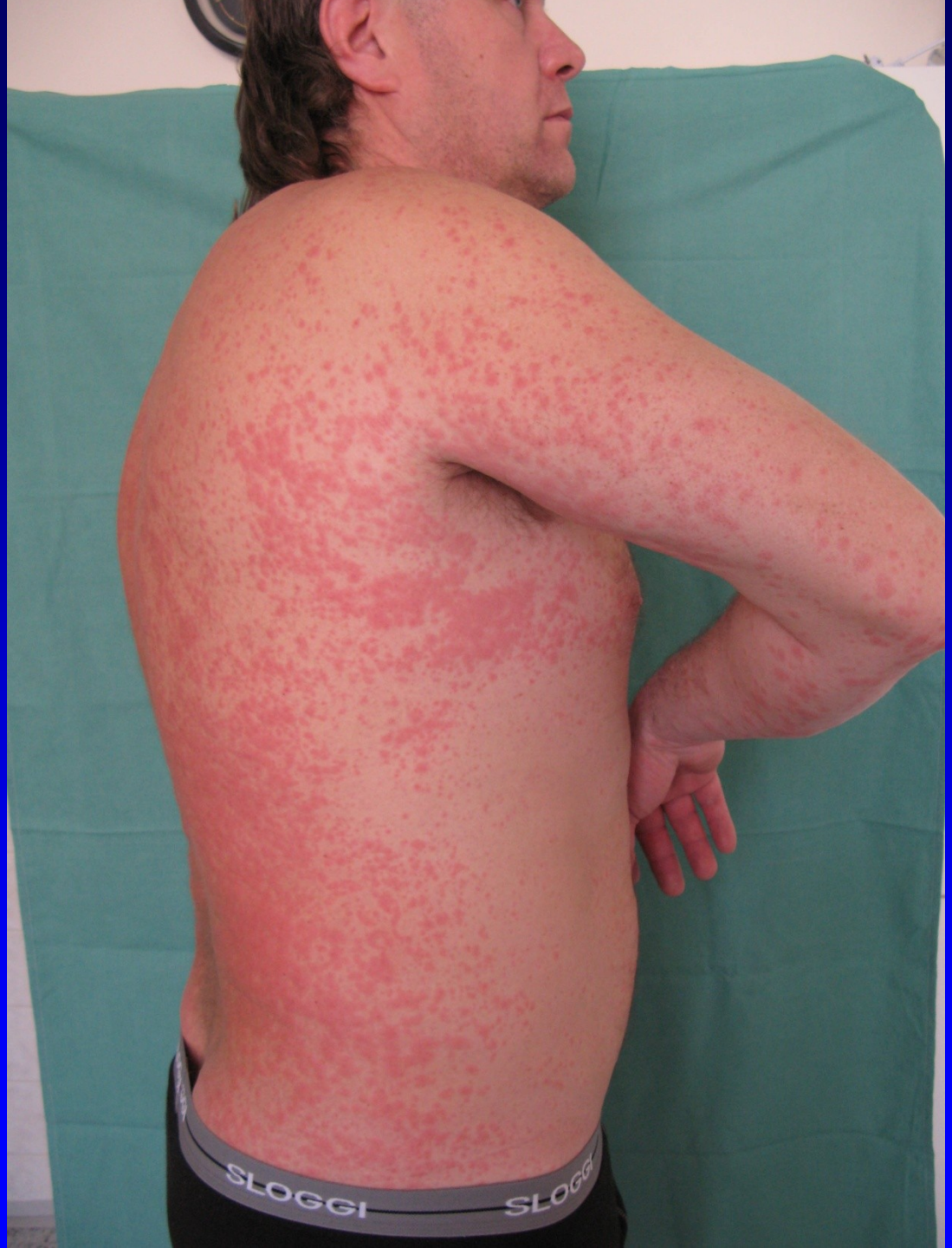
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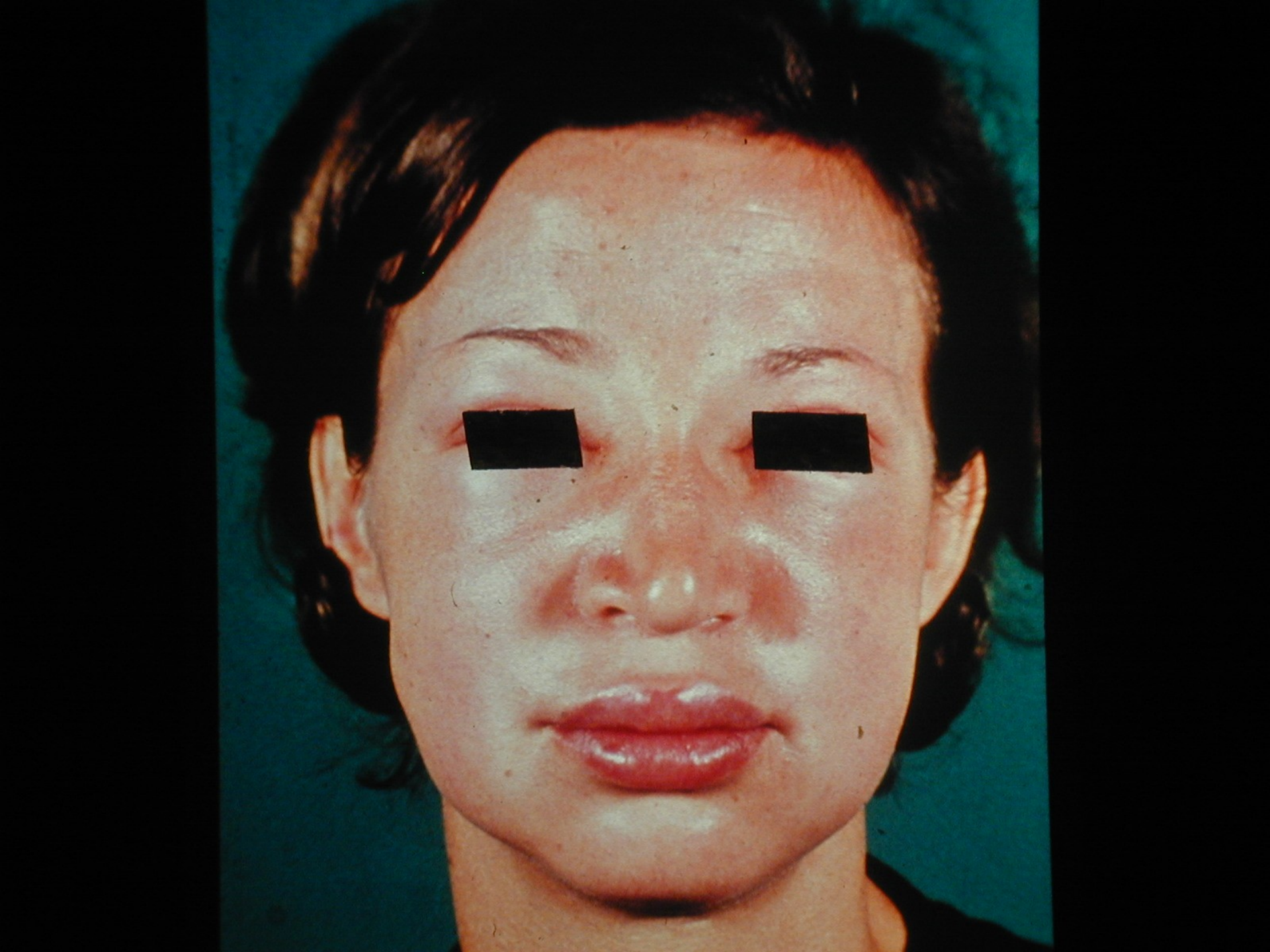

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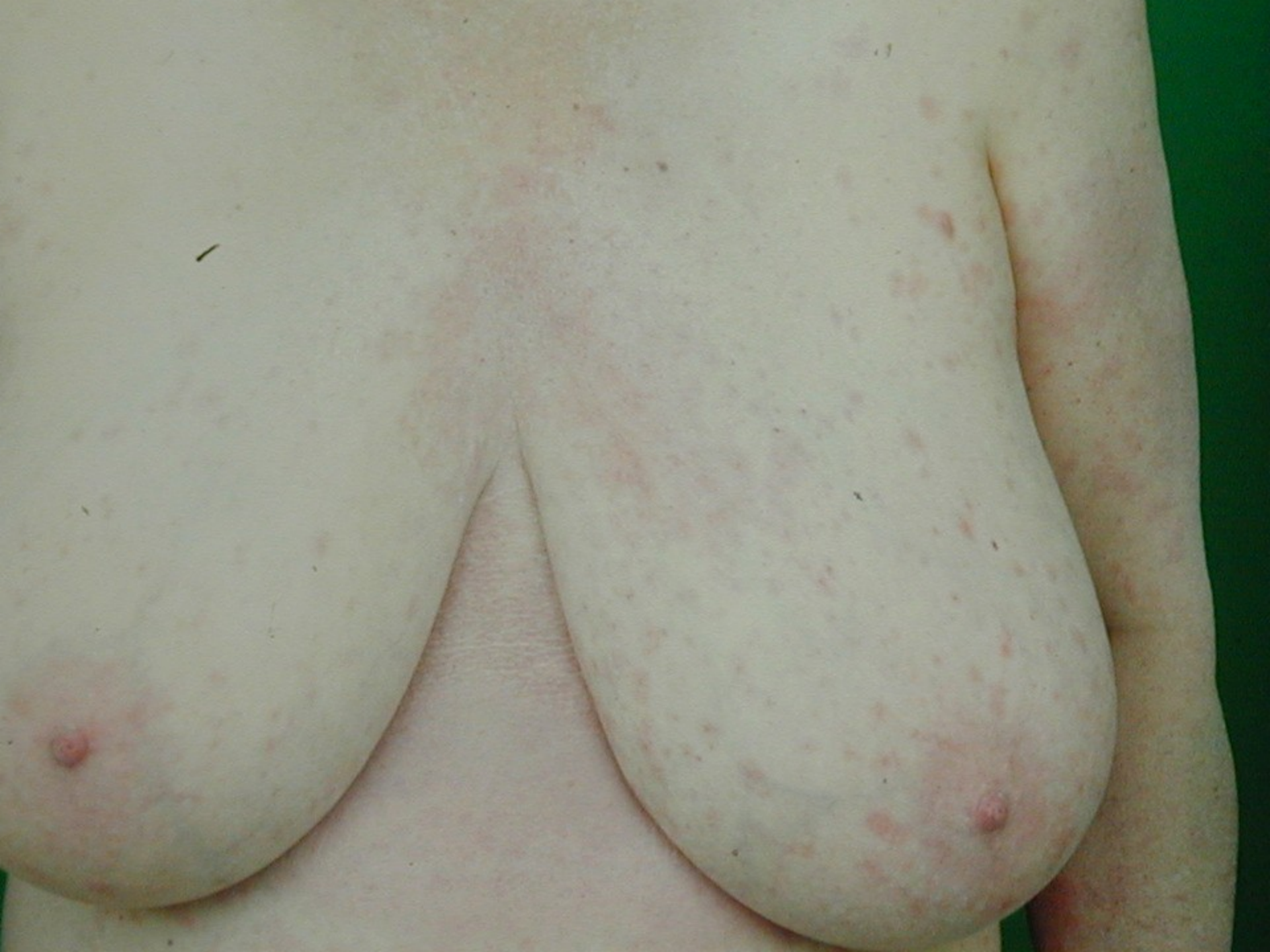

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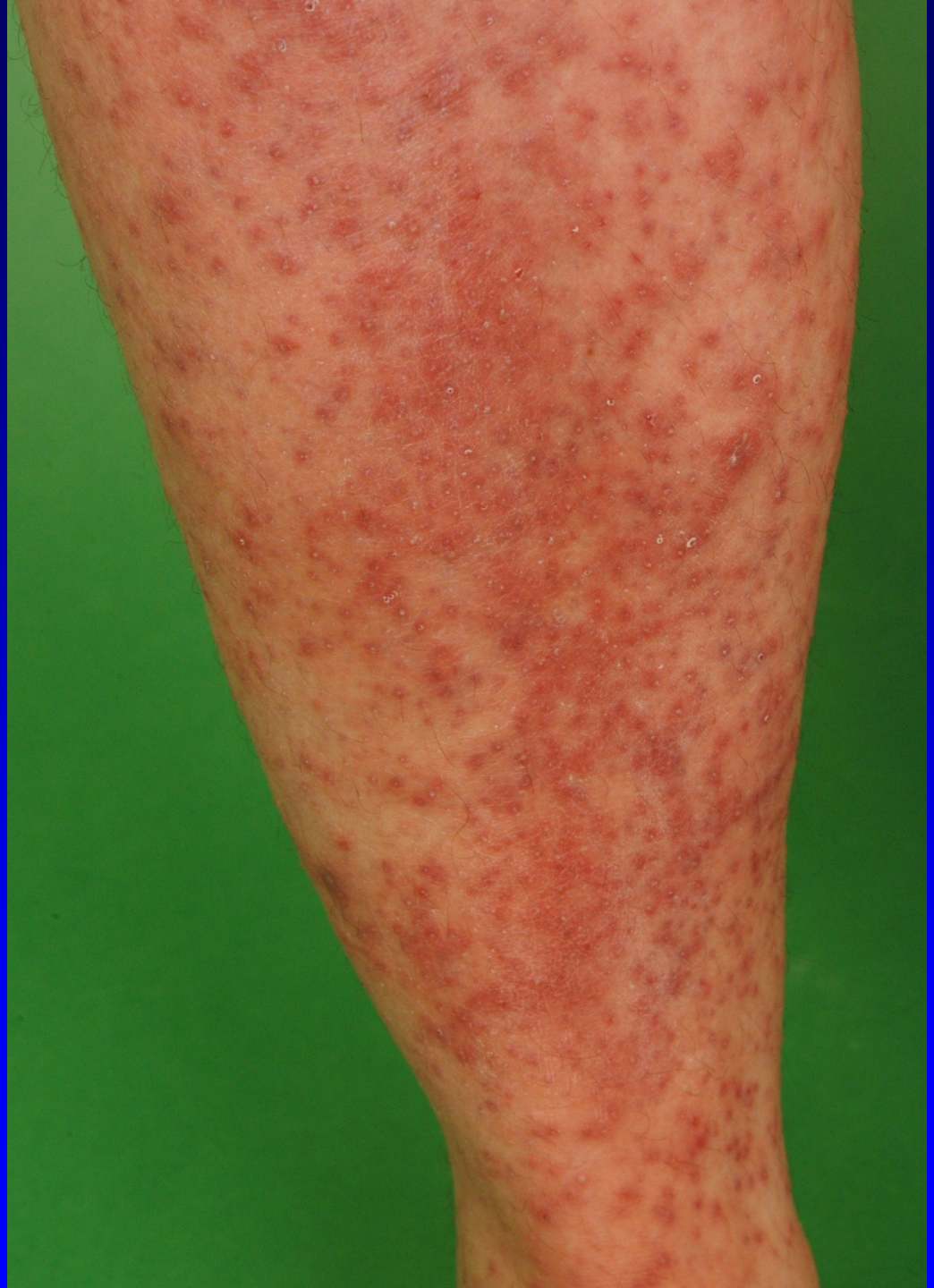

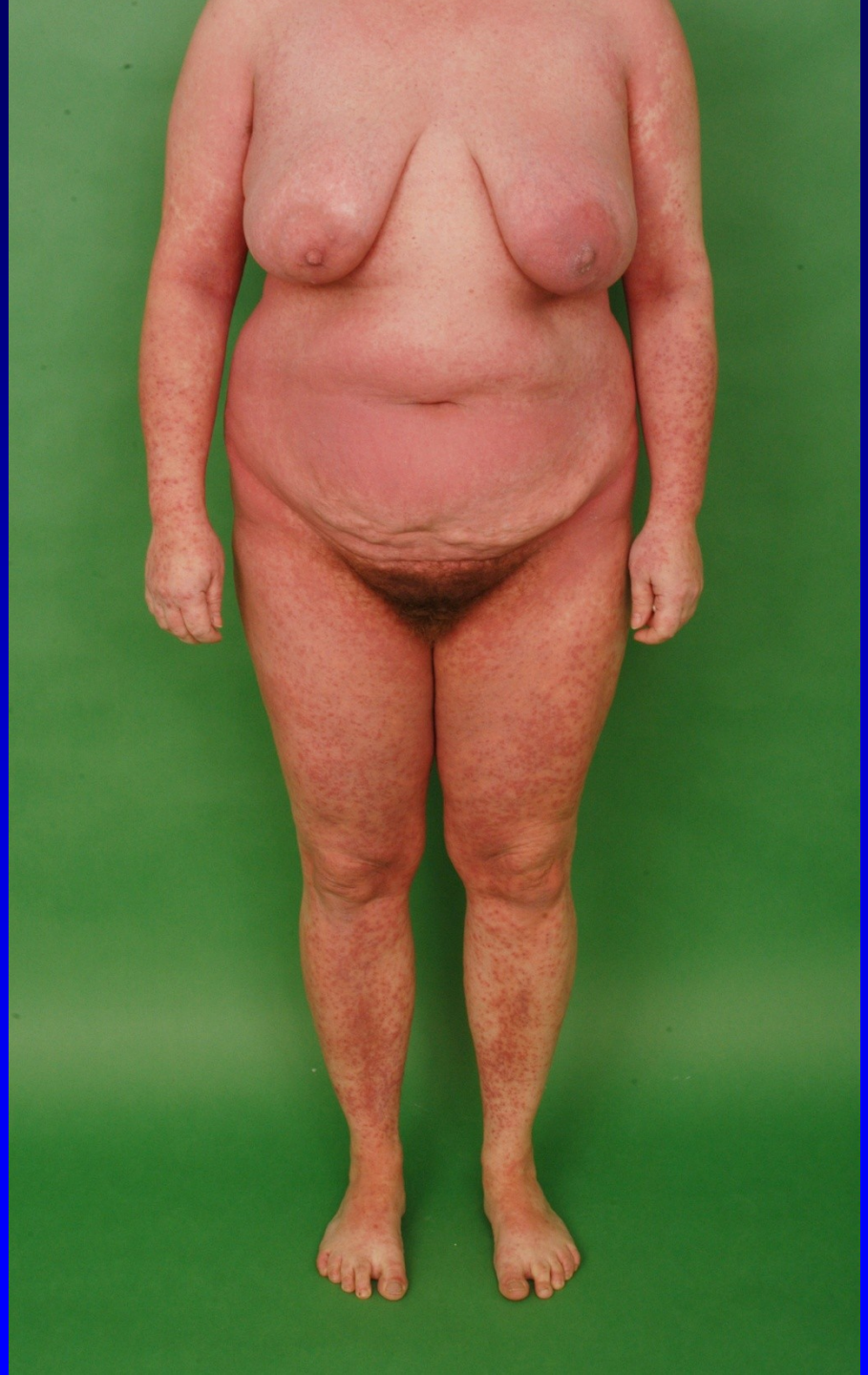

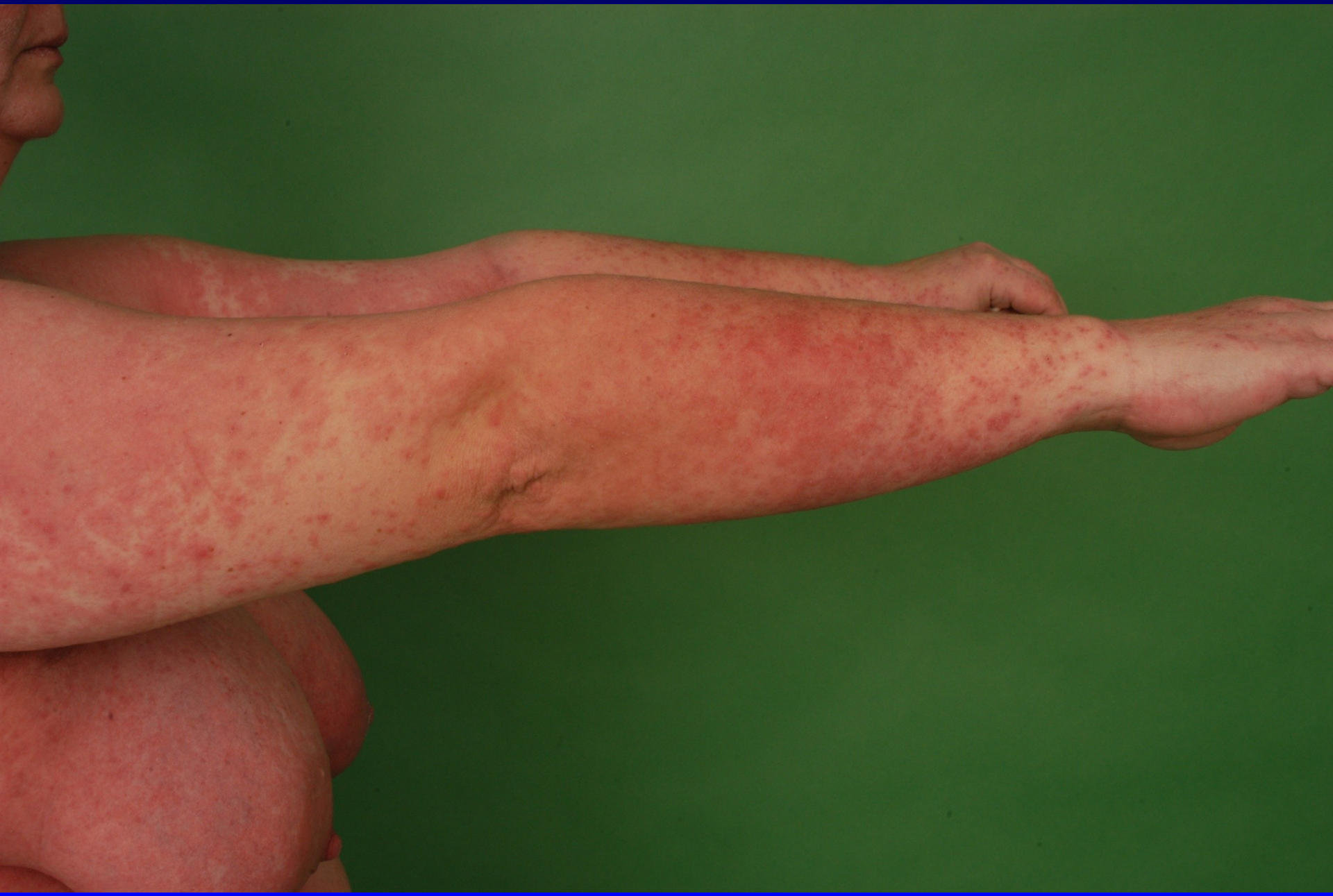

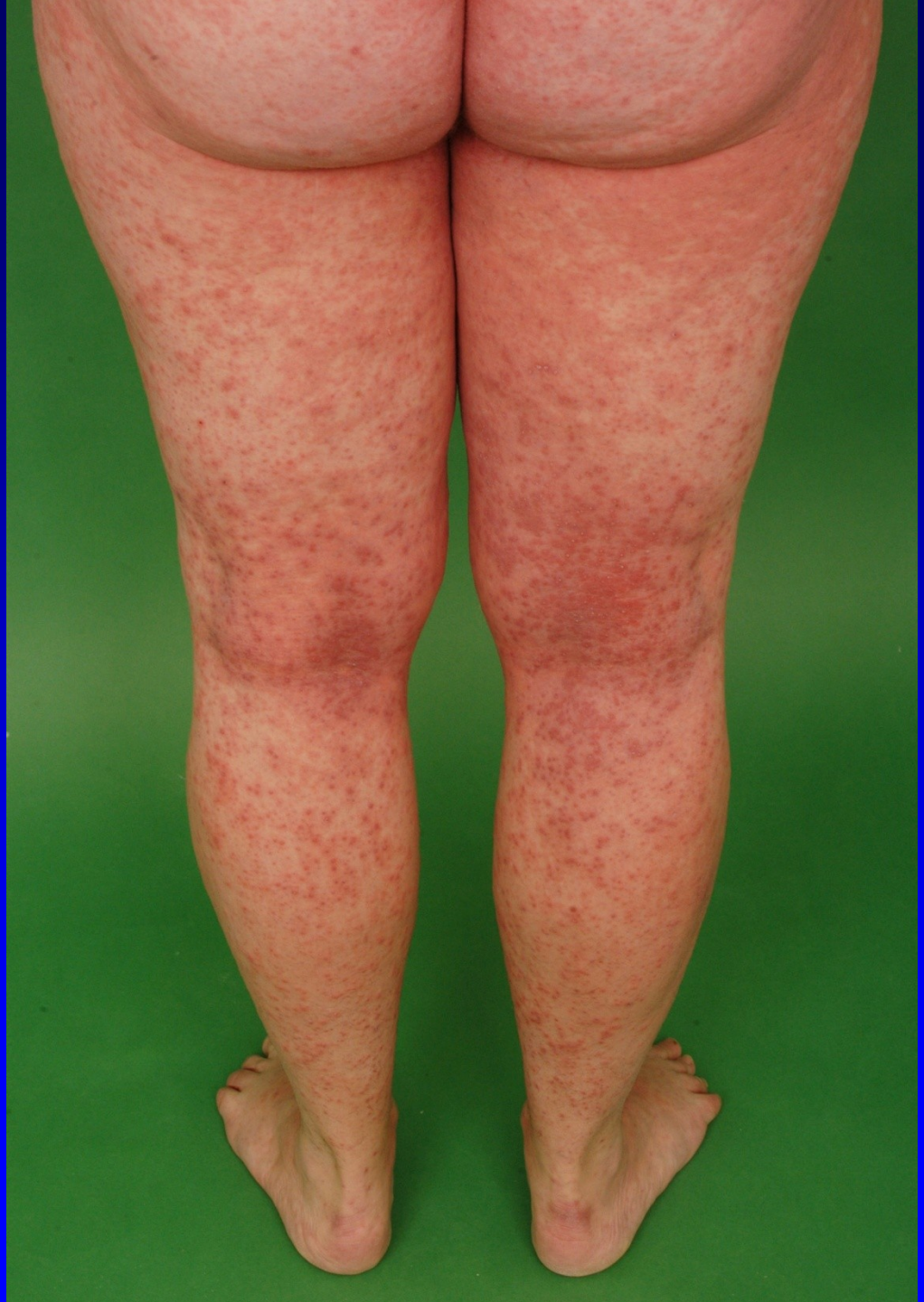

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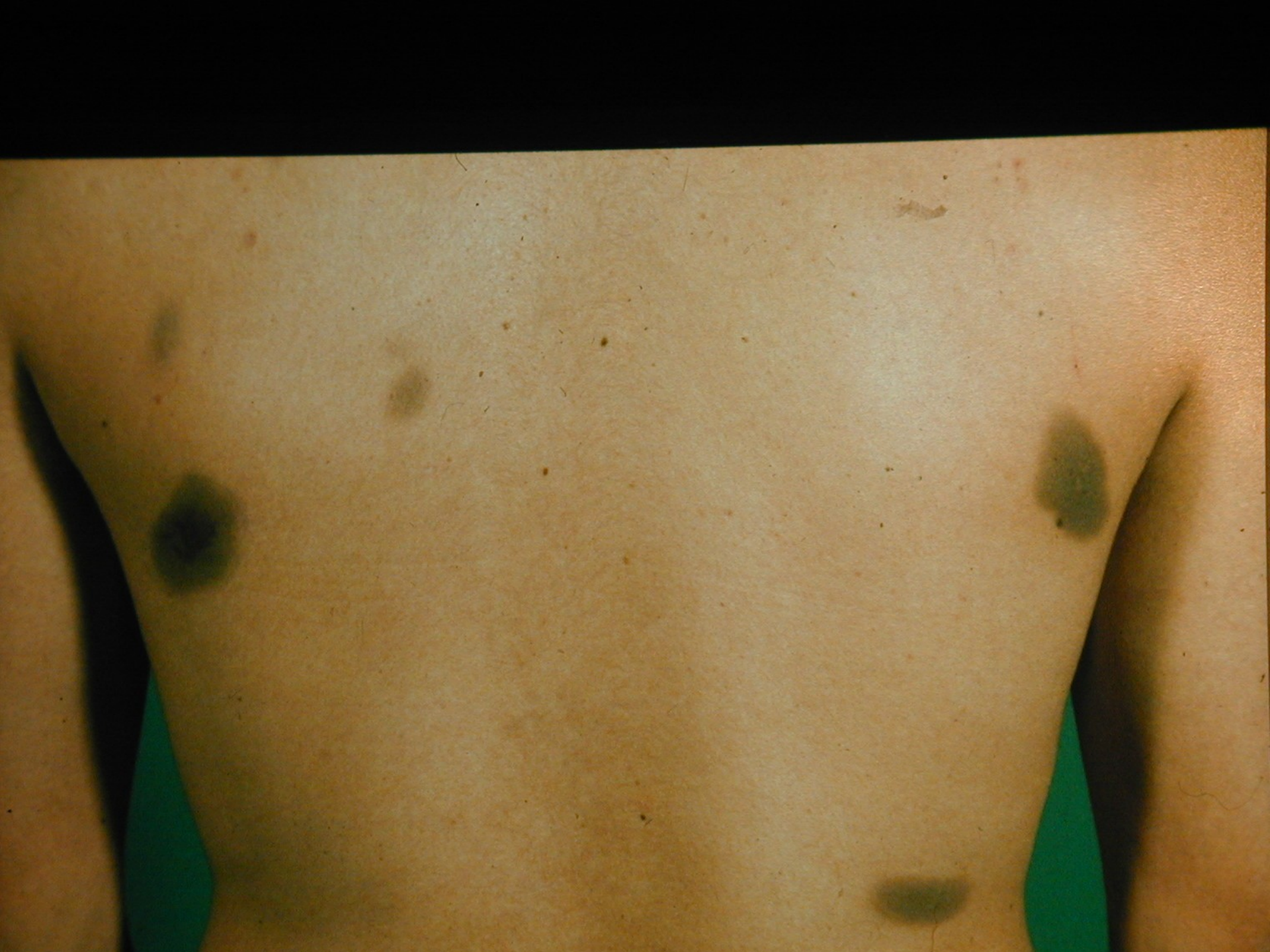

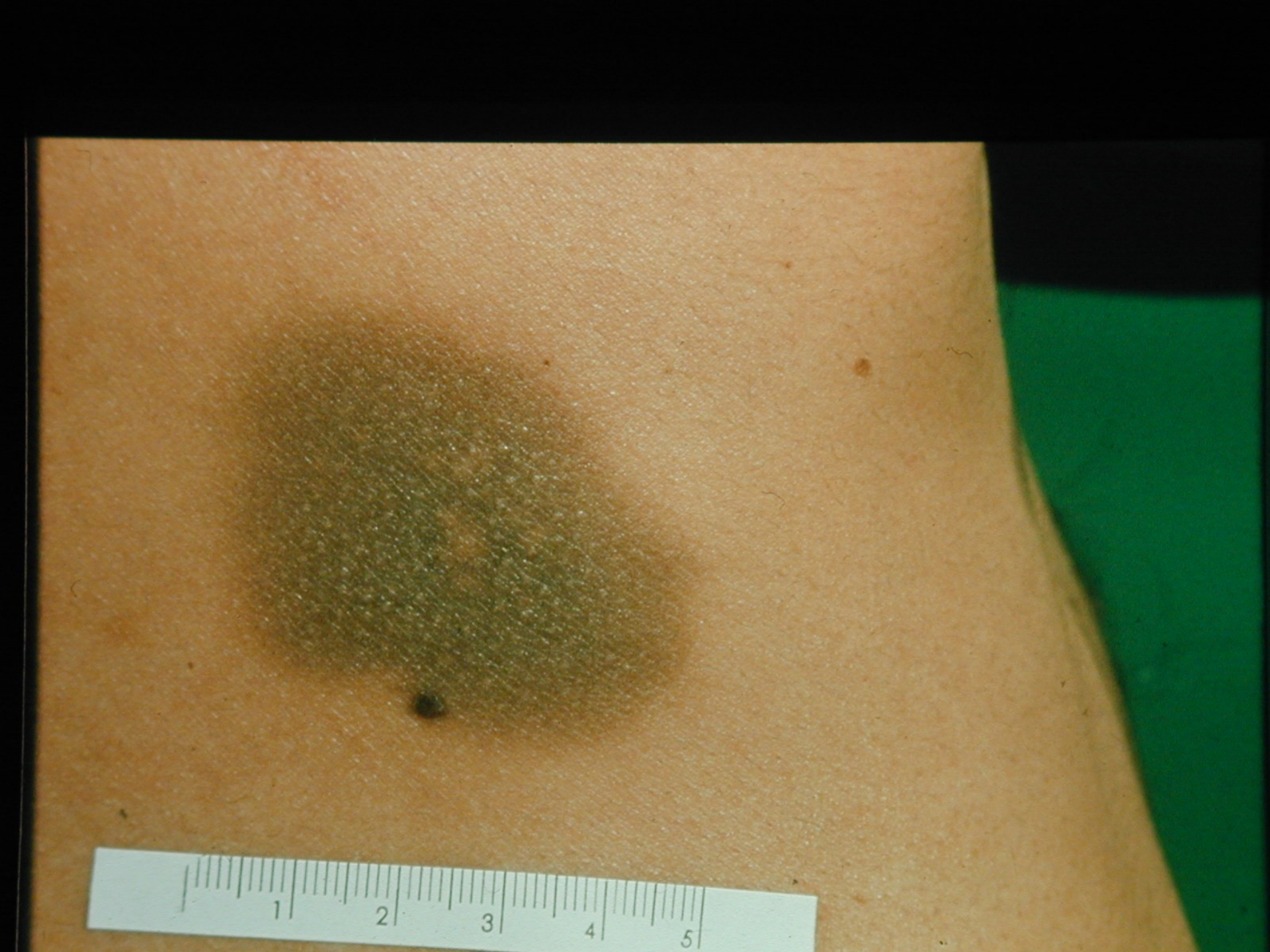
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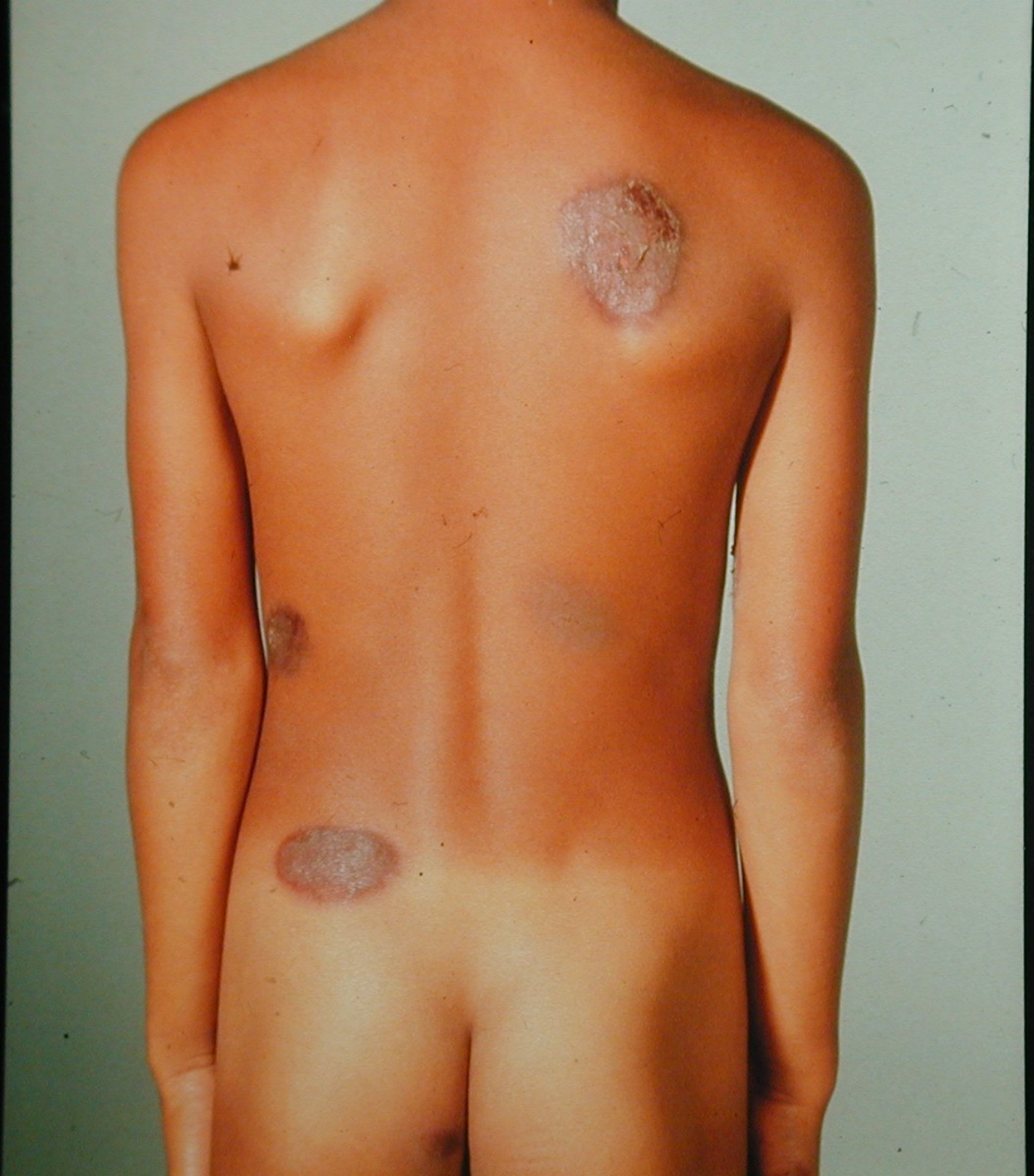

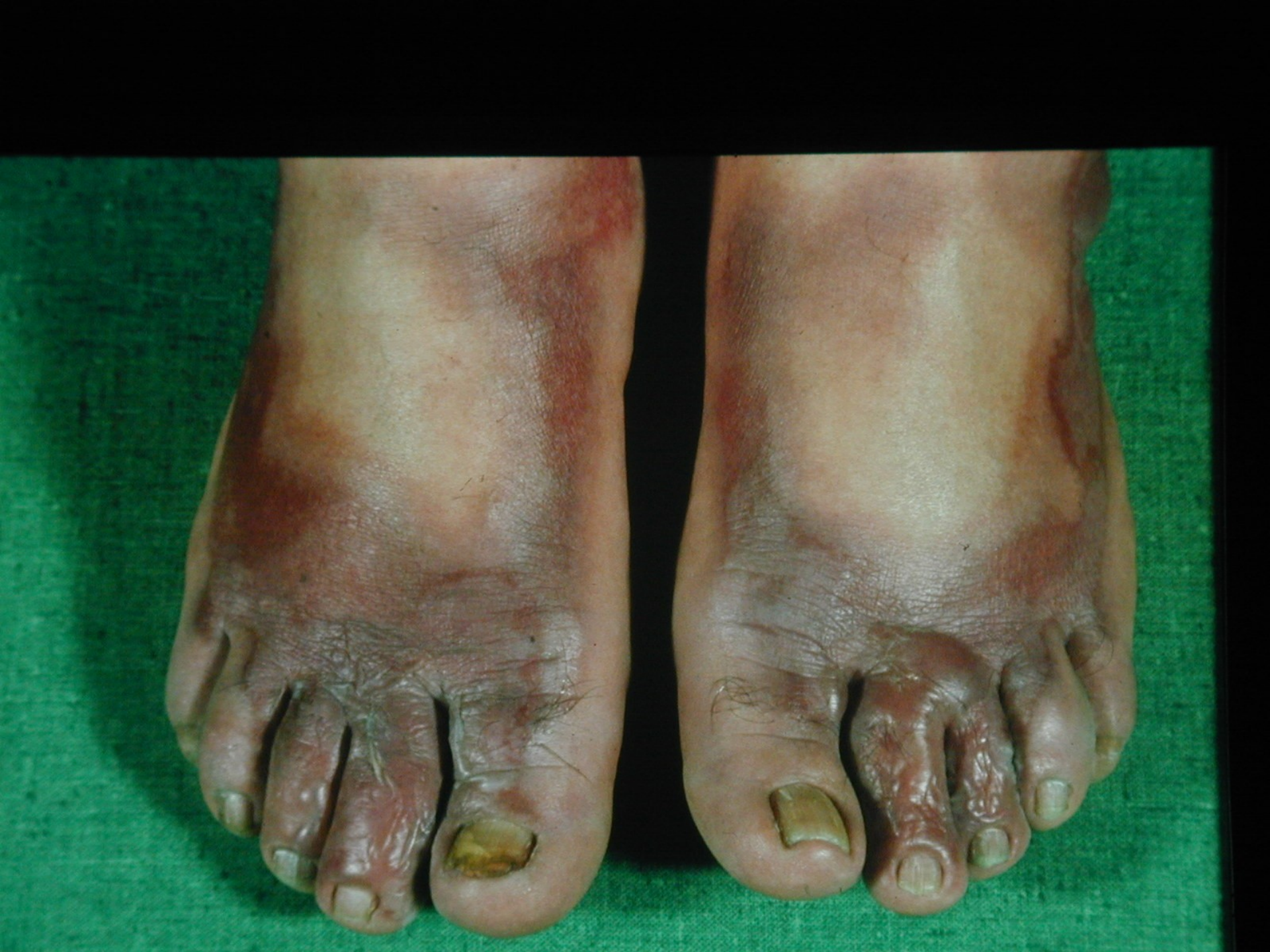

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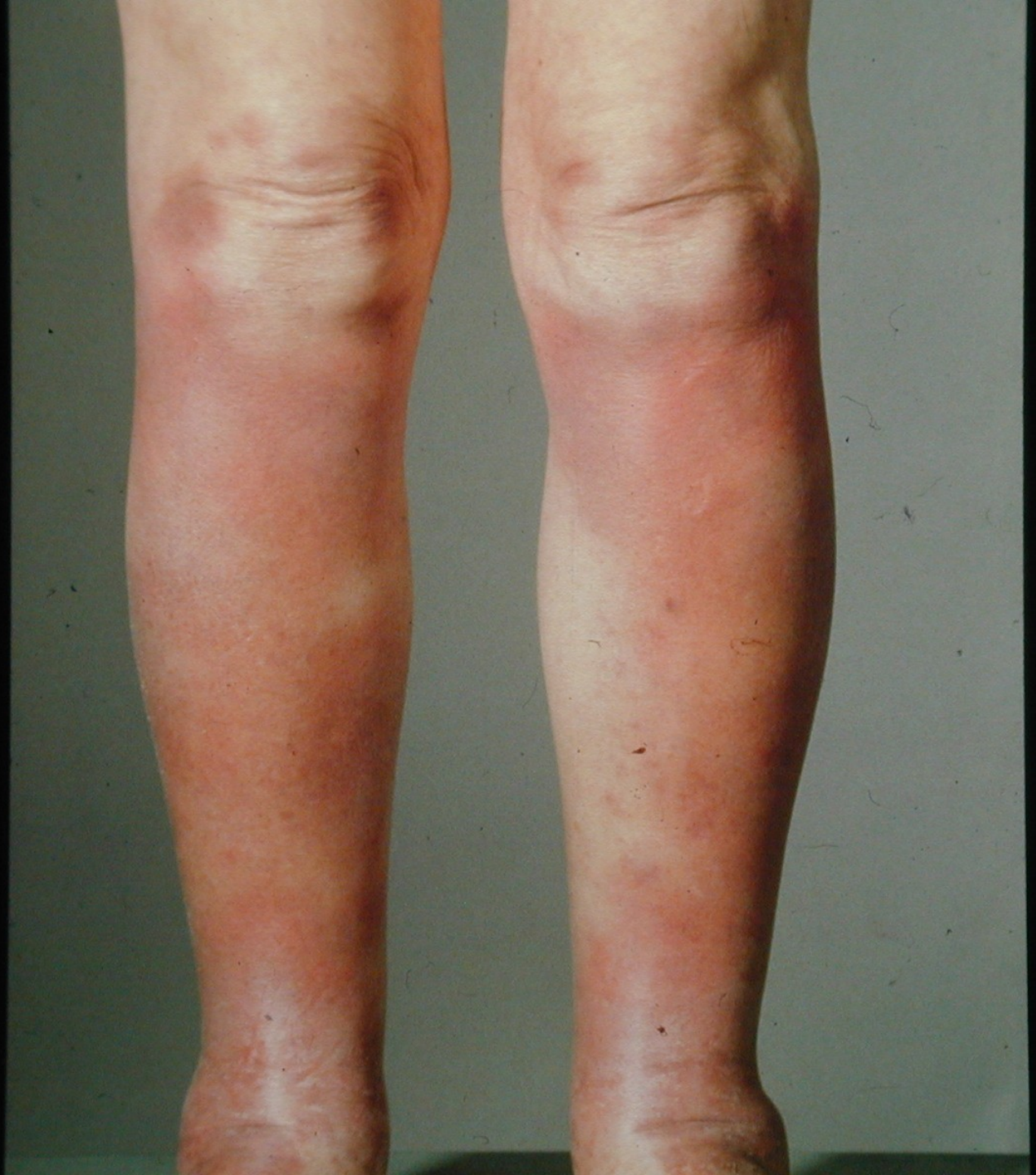
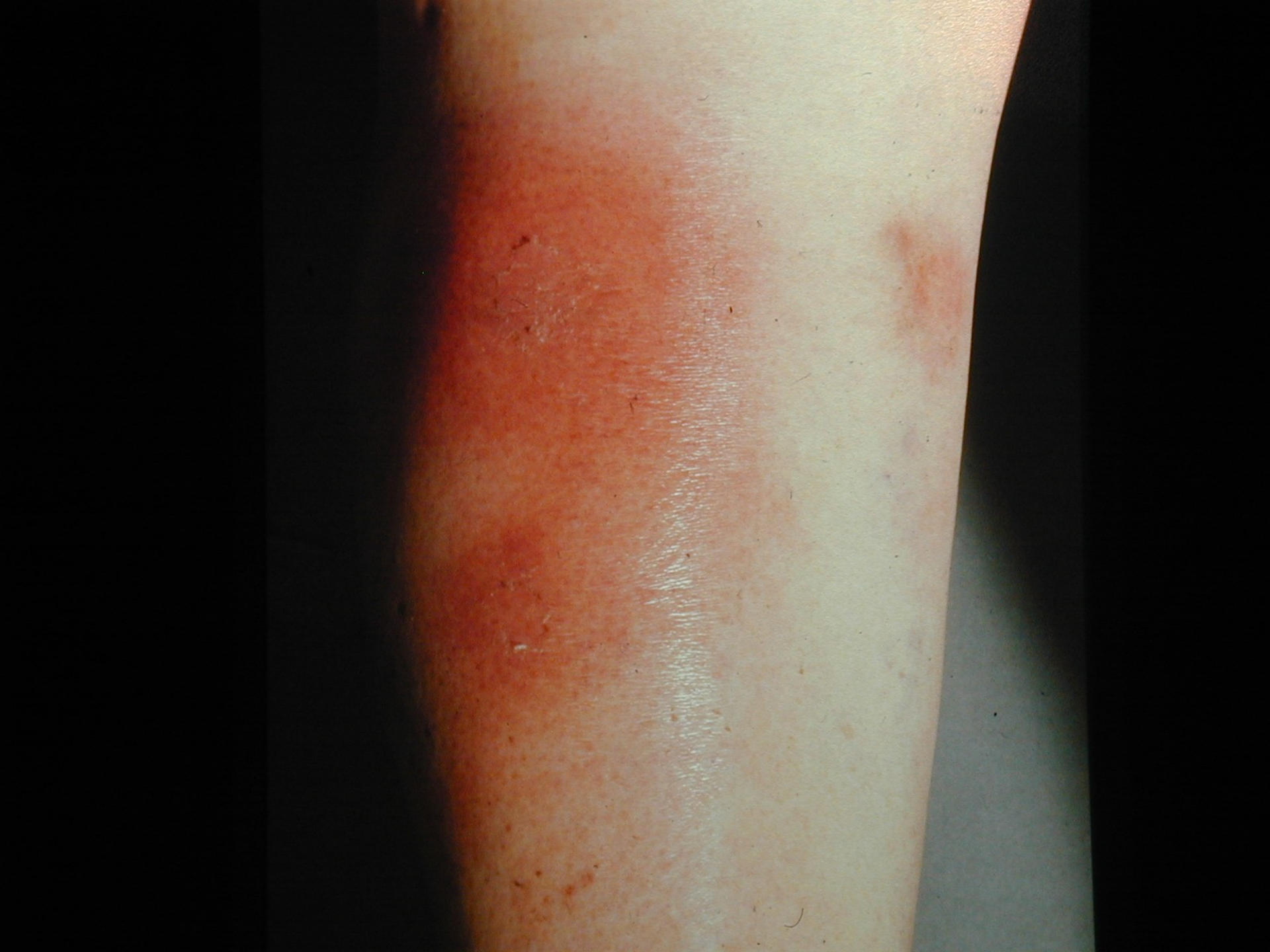
Erythema nodosum

multifactorial etiology:
infections, drugs, sarcoidosis, others

Allergic reactions - II. type
- IV. type tuberculin

most common: contraceptives, sulfonamides





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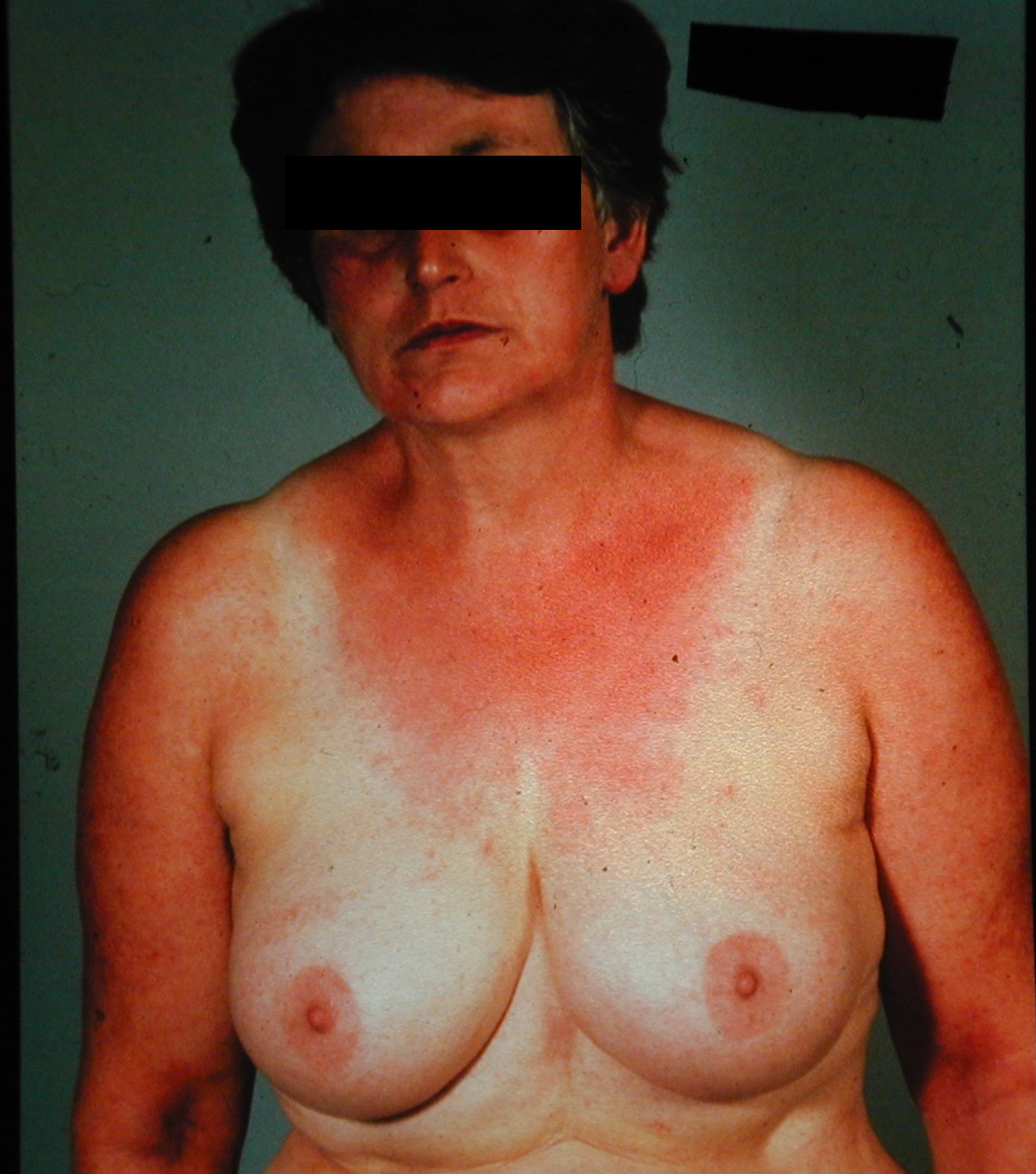
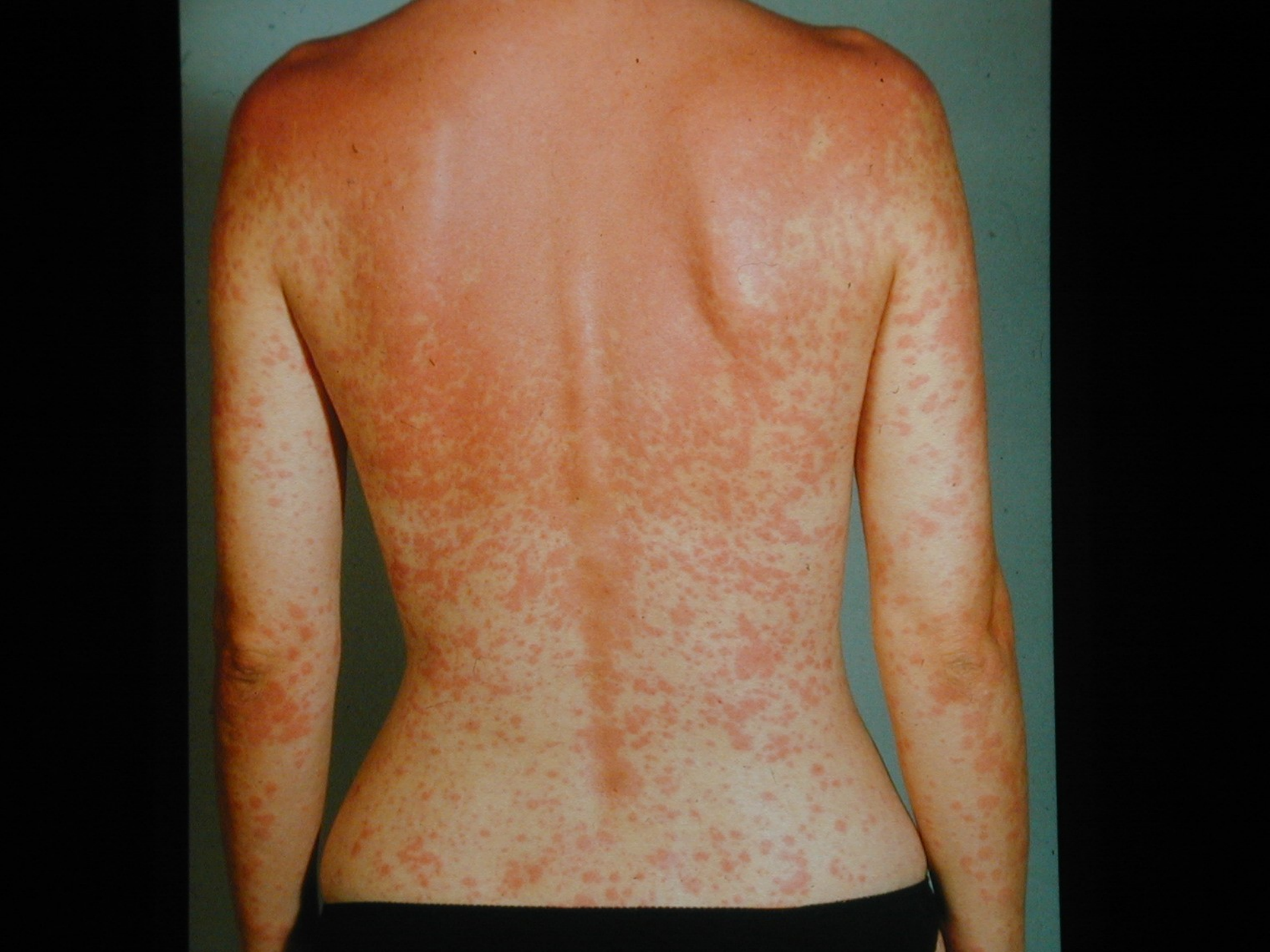
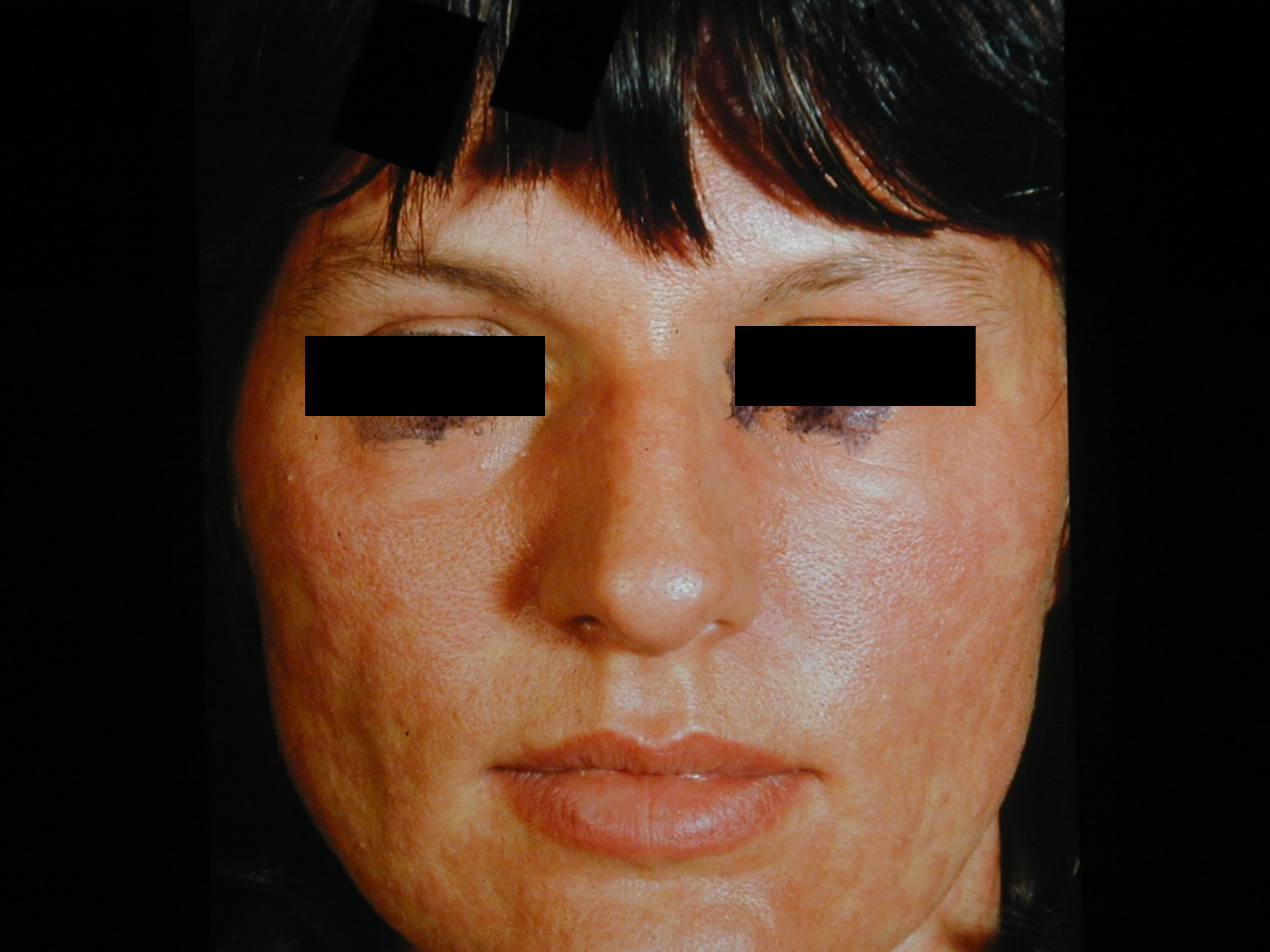
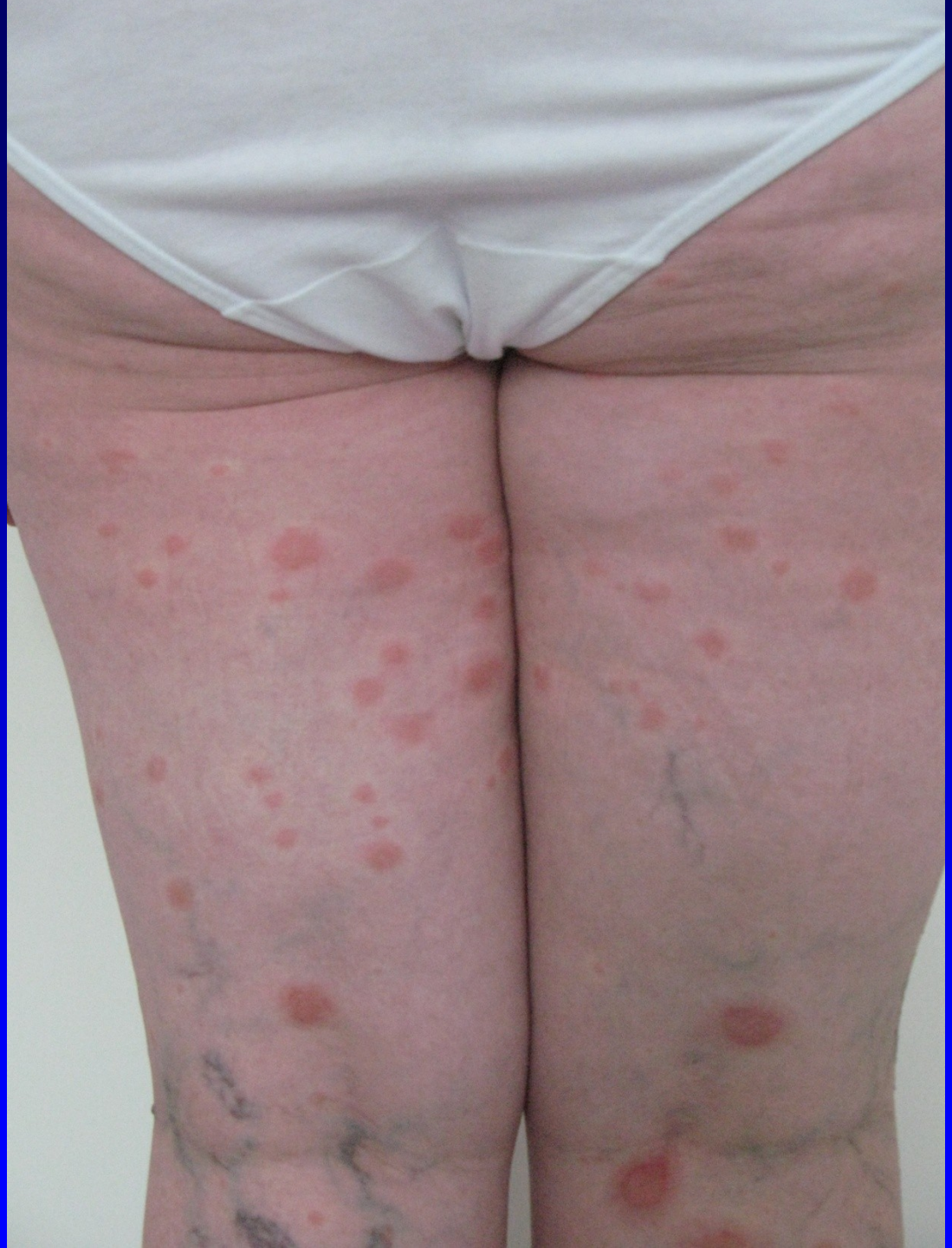


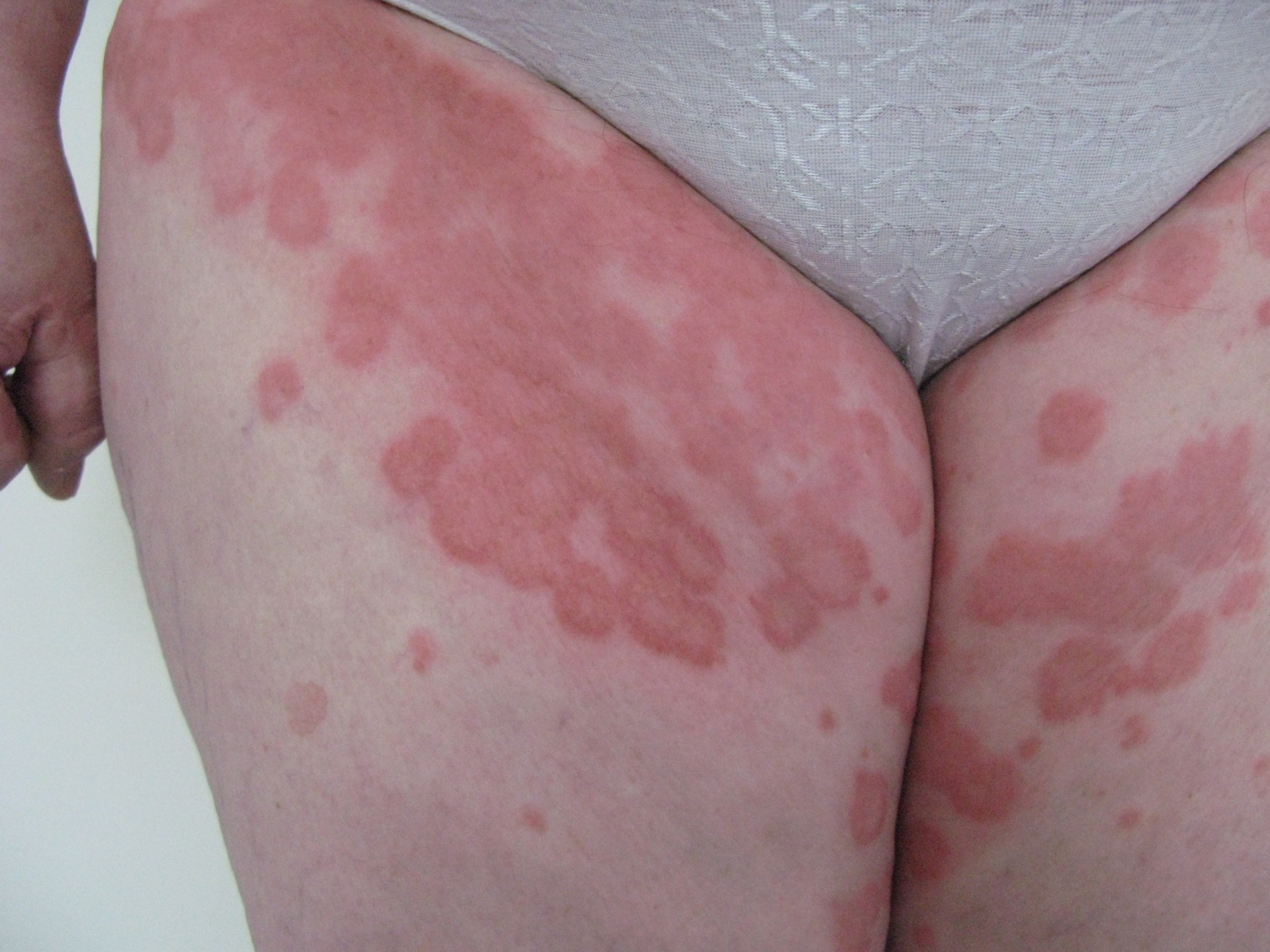




Erythema multiforme

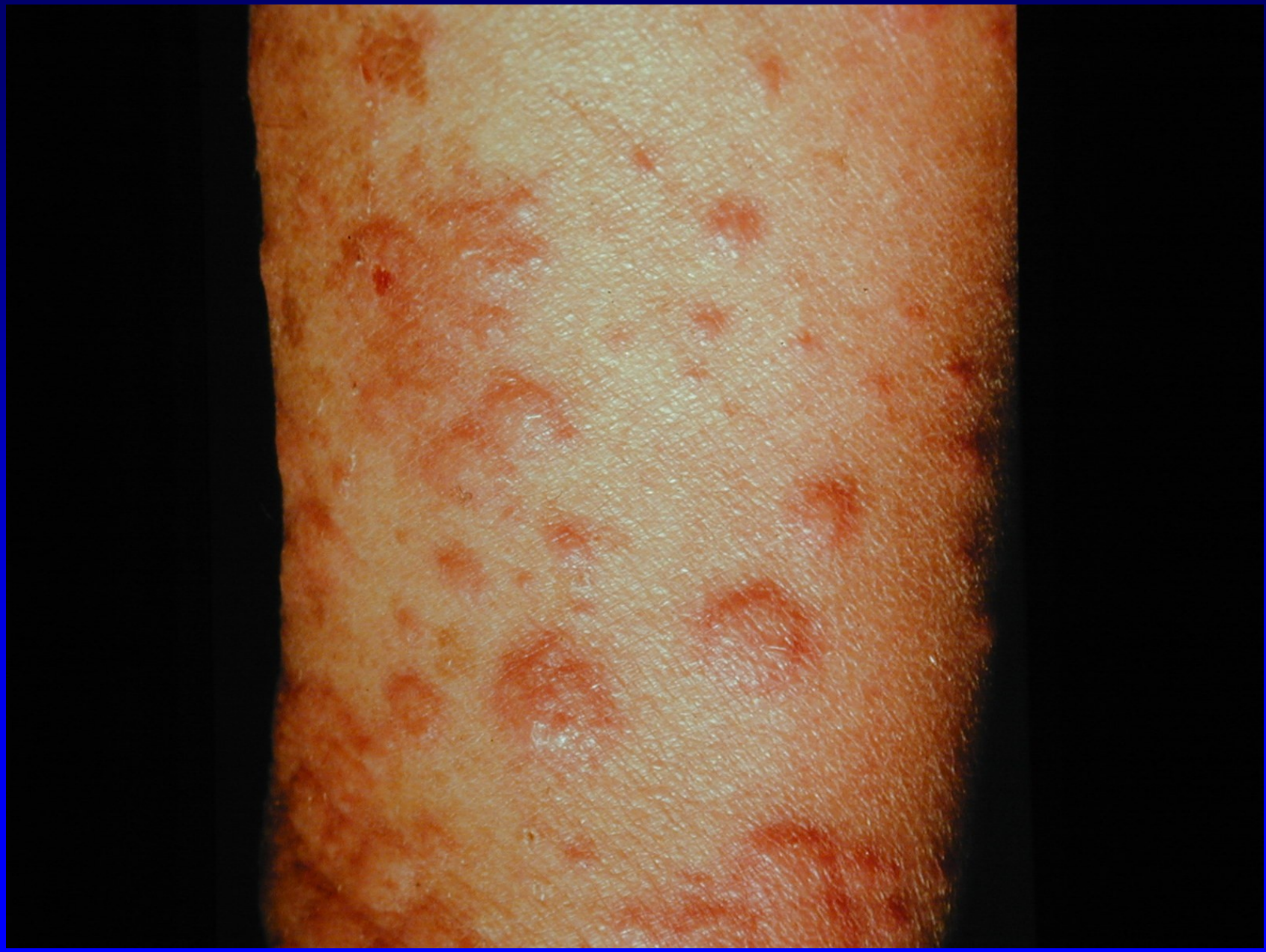
- multifactorial etiology: infections, drugs, neoplasia, autoimmune disease, idiopathic
- forms: **minor**
  - target lesions
  - up to 2 cm in size
  - symmetrical in acral distribution
  - most commonly HSV
  - mortality 0

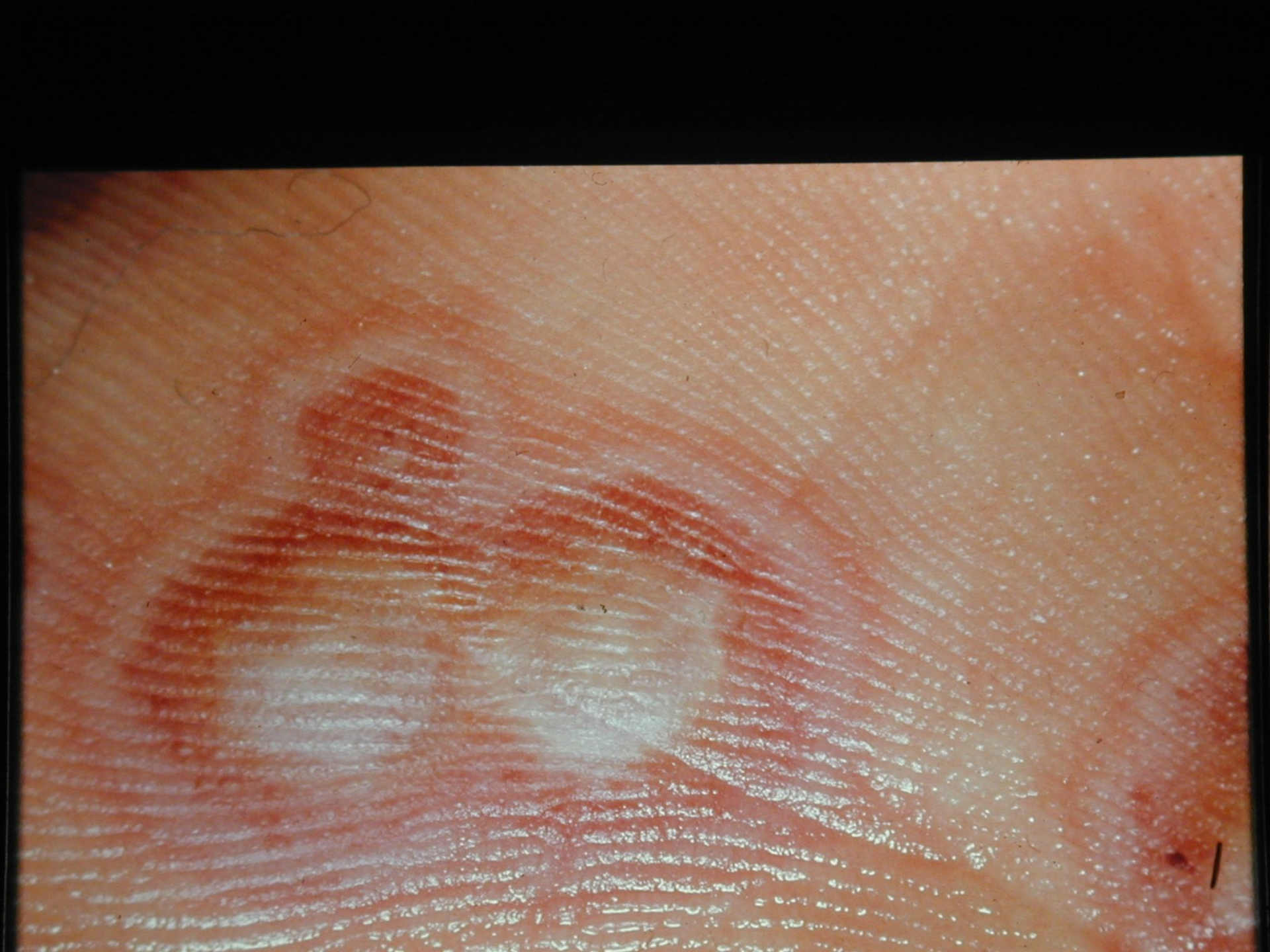


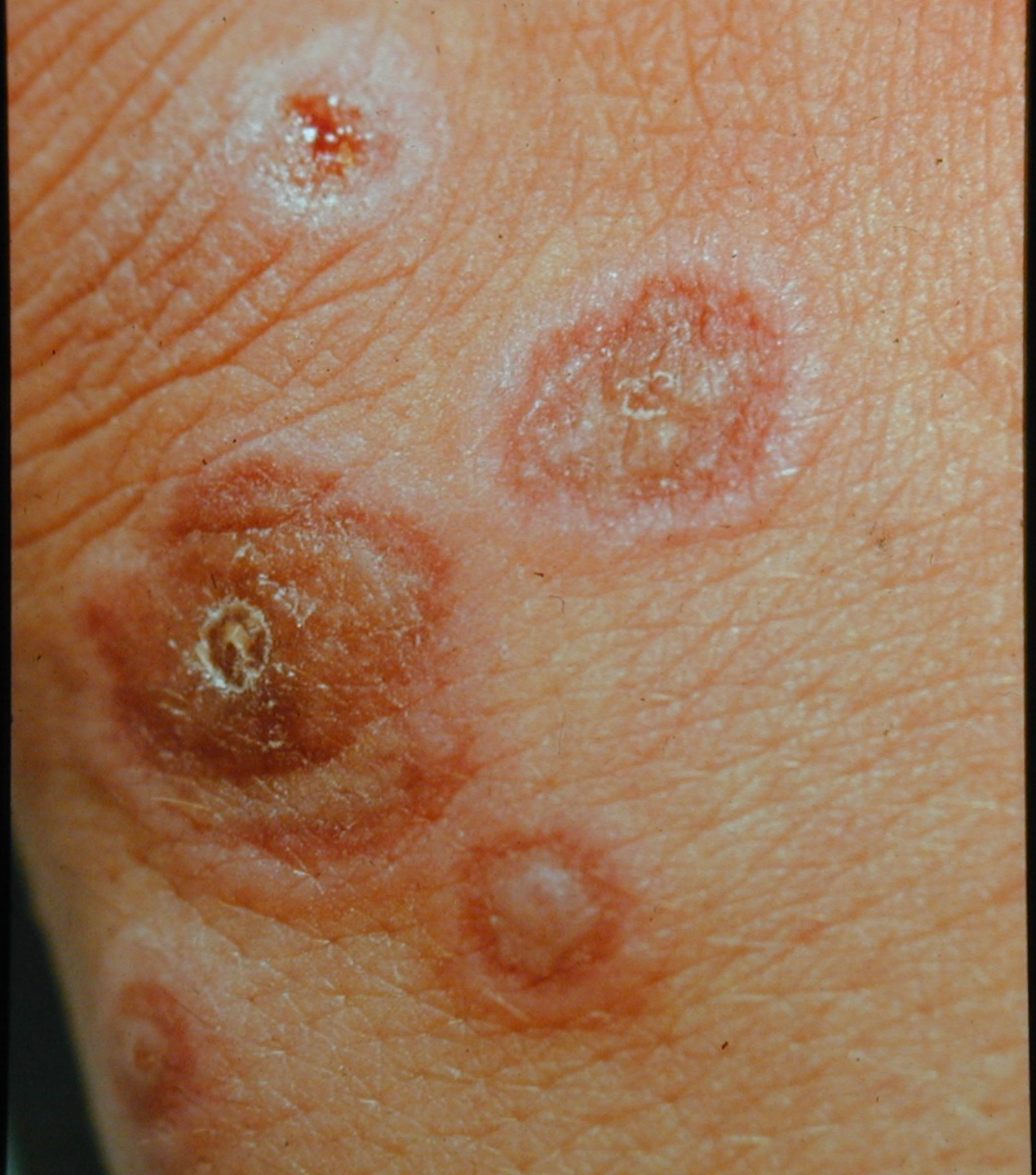


major

- target lesions with blisters
- acral distribution and torso
- blisters < 10 % surface
- most commonly HSV, mycoplasma
- mortality 1 %

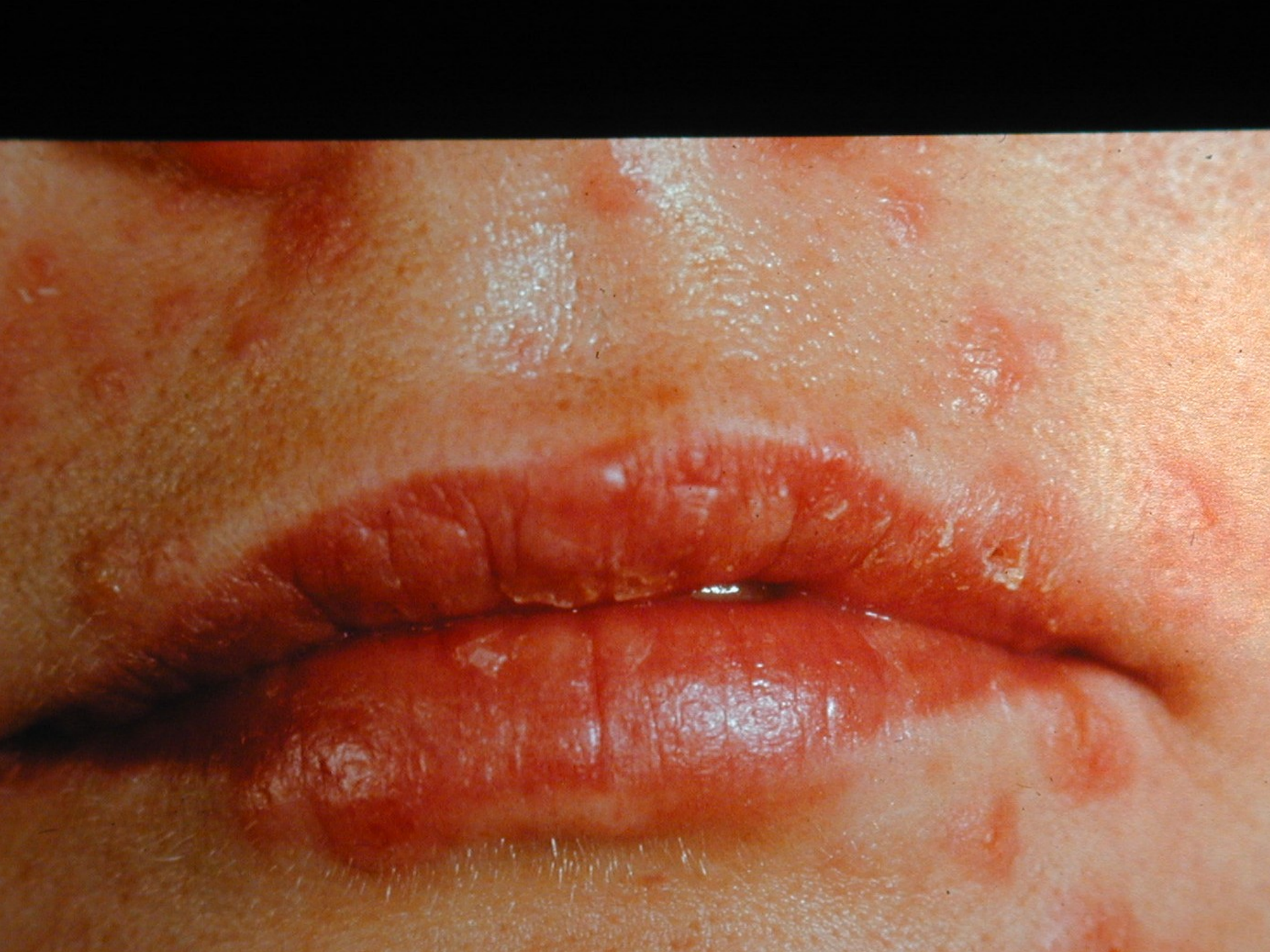


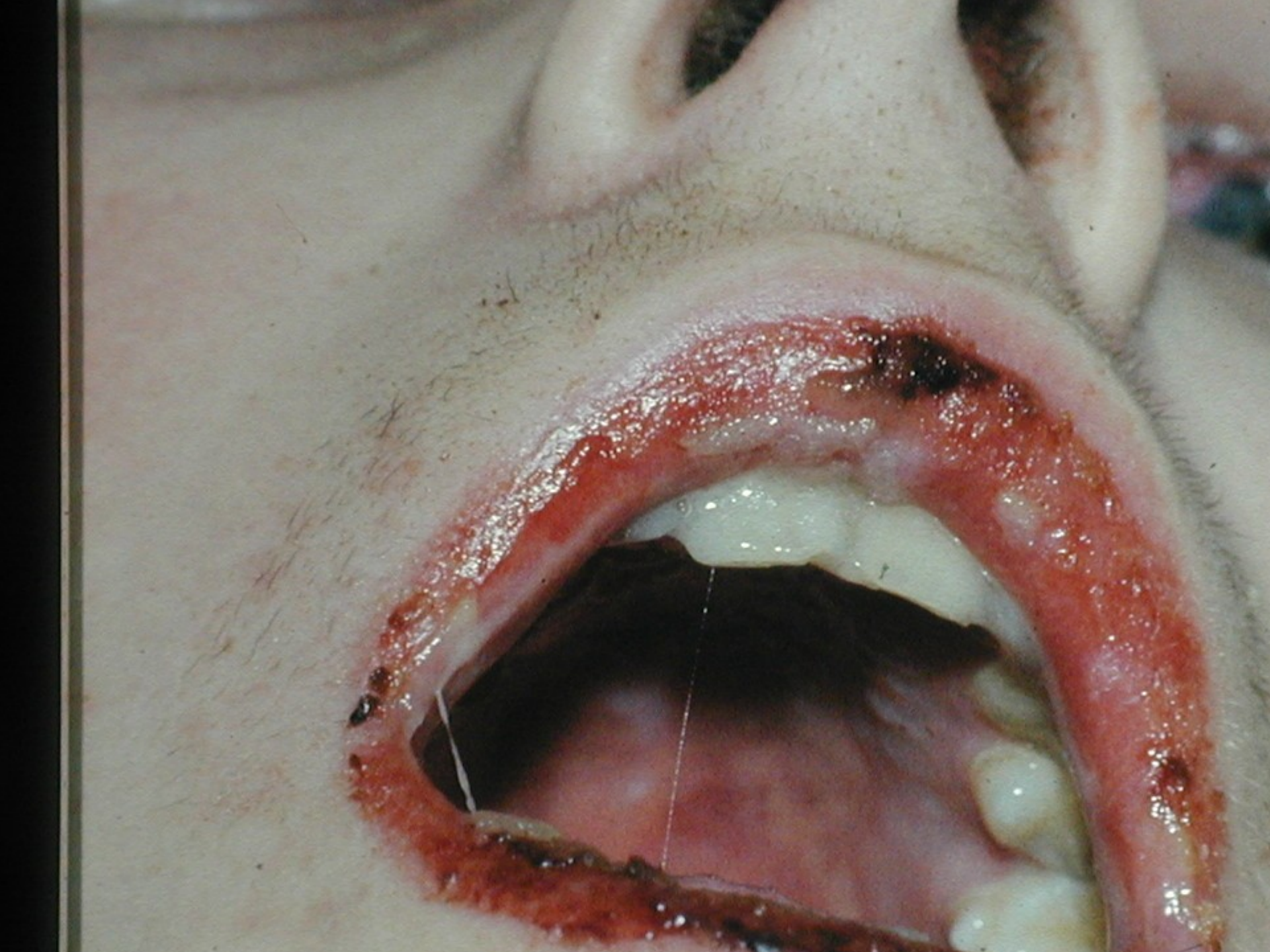




Stevens-Johnson Syndrome (SJS)

- atypical target lesions
- primarily the torso
- blisters < 10 % suface
- mucosal involvement
- possible systemic symptoms
- most commonly drugs
- mortality 6 %





Toxic epidermal necrolysis (TEN, Lyell's syndrome)

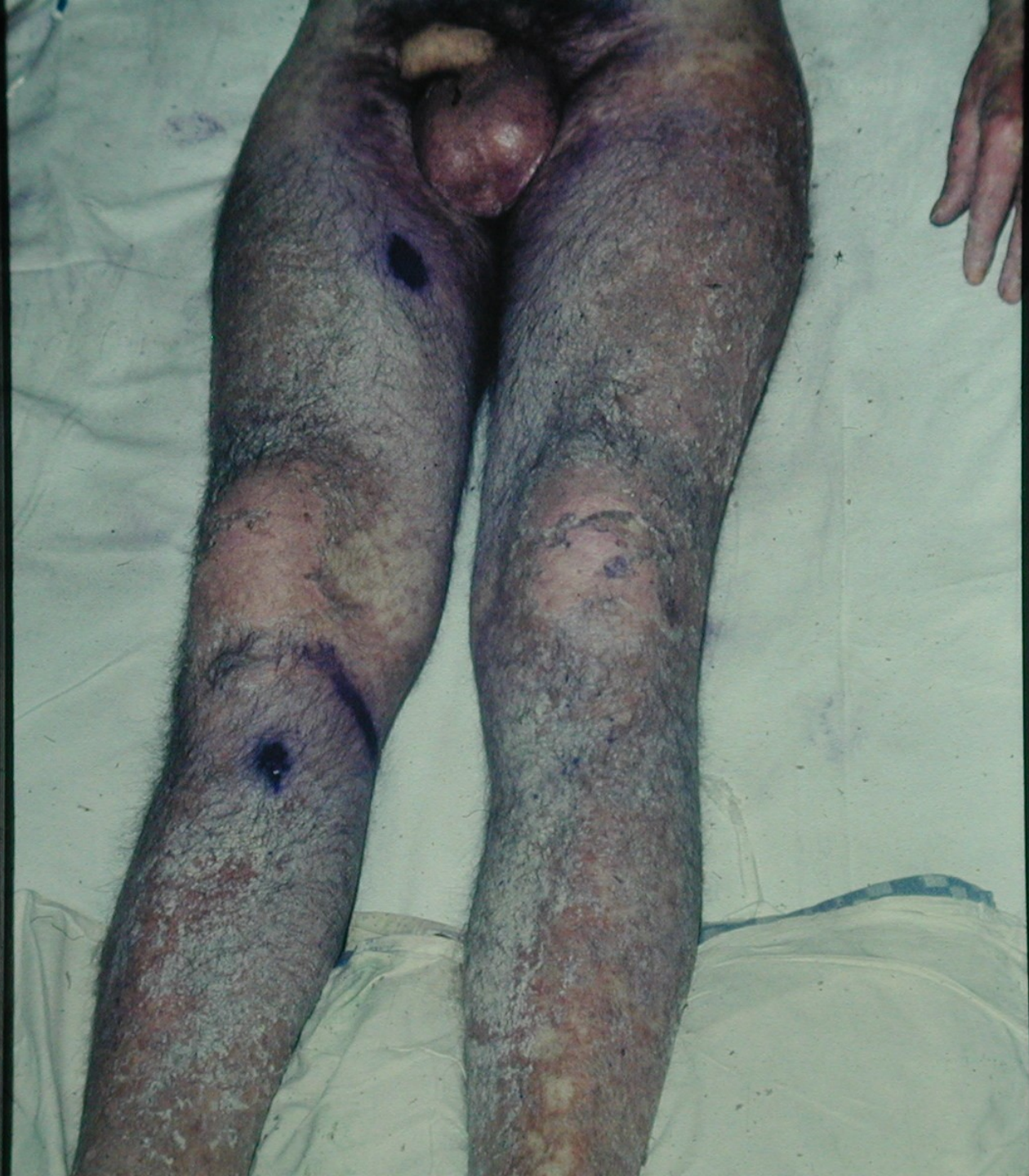
- cell-mediated cytotoxic immune response directed against epidermal antigens with high TNF α production → keratinocyte necrosis
- drug (metabolite) binding to keratinocytes
- necrosis of the entire epidermis

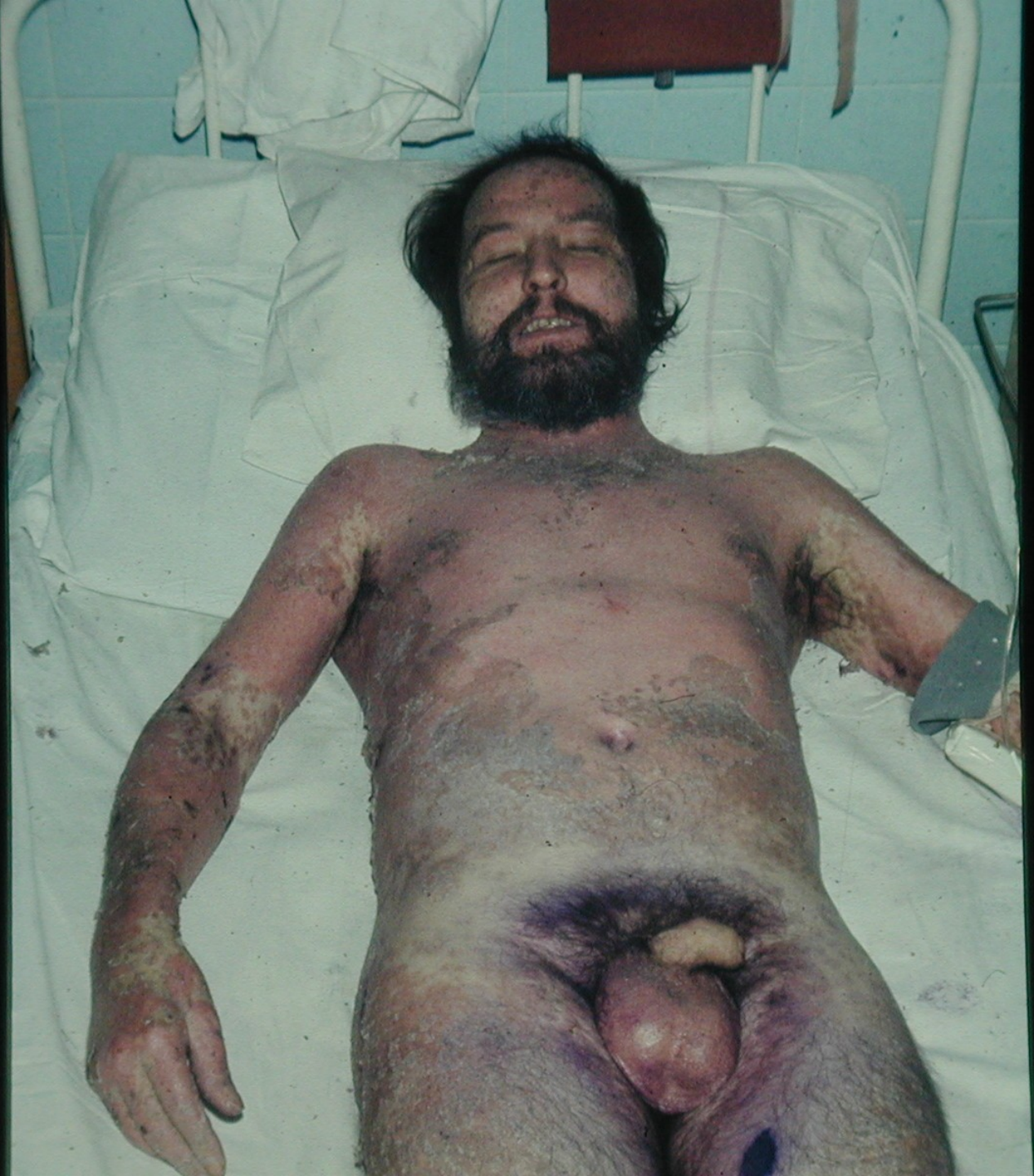
Transitional form SJS / TEN

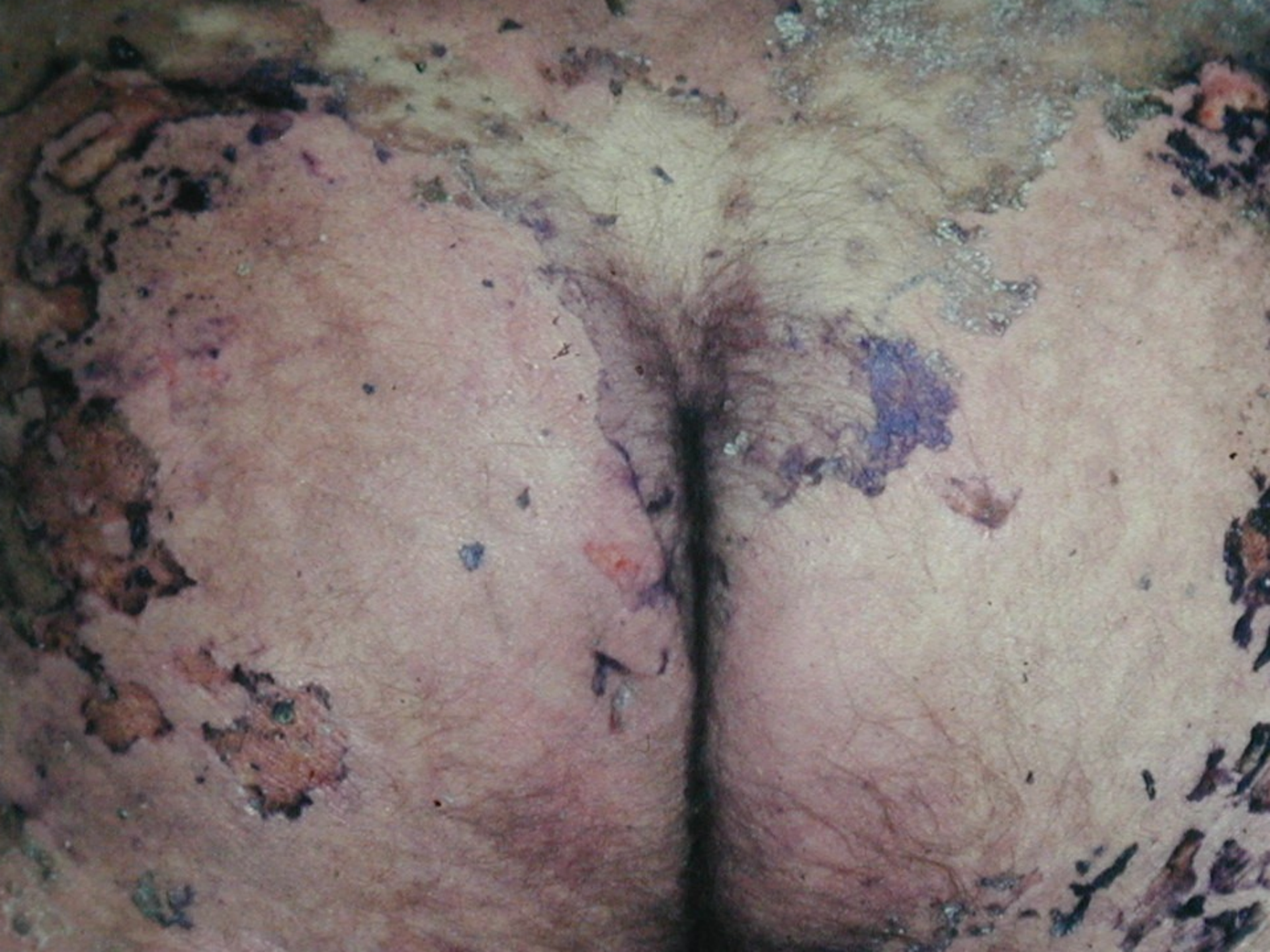
- atypical target lesions
- mucosal involvement
- blisters 10 - 30%
- systemic symptoms
- mortality 25 %

TEN

- rapidly merging erythema
- linear separation of the epidermis
- positive Nikolsky phenomenon
- mucosal involvement
- severe general condition (fever, impaired consciousness, glomerulonephritis, pneumonia and hepatitis)
- mortality 40% (septicemia, gastrointestinal bleeding, renal failure, electrolyte imbalance)







TEN
most commonly triggering drugs

- sulfonamides
- trimethoprim - sulfamethoxazole
- carbamazepine
- phenytoin
- phenobarbital
- non-steroidal anti-inflammatory drugs
- allopurinol
- aminopenicillins

Differential diagnosis of severe drug eruptions

Disease	Location	Target lesions	Mucous membranes	blisters % surface	mortality %
EM minor	acral	typical		0	0
EM major	acral, torso	typical	+	< 10	1
SJS	torso	atypical	++	< 10	6
SJS/TEN	torso	atypical	++	10-30	25
TEN	torso	atypical	++	> 30	40

EM = Erythema multiforme
SJS = Stevens-Johnson syndrome
TEN = Toxic epidermal necrolysis

Conclusion

- Drug rashes are usually mild, but in rare instances can be life-threatening (with mucosal involvement and organ failure)
- Drug rashes occur most often within a few days of starting a new drug, but sometimes even after weeks or months of use
- In addition to drugs, other potential triggers - food, vitamins, food supplements, herbal preparations, self-medication and infectious diseases should be considered.