January 6, 2011

To the Staff and Faculty of Banner Good Samaritan Medical Center,

ABOUT THIS FILE

The talk at Grand Rounds this morning was about wound pathergy and when not to operate. The slides in this file are the presentation exactly as given. Unfortunately, I have not yet written any commentary or annotations for each slide. However, most of the content of this presentation was based on a previous case review that I wrote for one of the journals. That case was of post-operative wound pathergy attributed to post-splenectomy thrombocytosis. That review and today's presentation are nearly identical in content, both focused on pathergy, just presented in a slightly different order, and with a difference in emphasis on surgery versus thrombocytosis. Over the next few weeks, I will write text explicitly for the slides and presentation given today, so if you are interested, check back. In the meantime, I have appended the original review, which should enable you to read about most of what was presented today.

- Marc E. Gottlieb, MD -

PRINCIPLES OF SURGERY

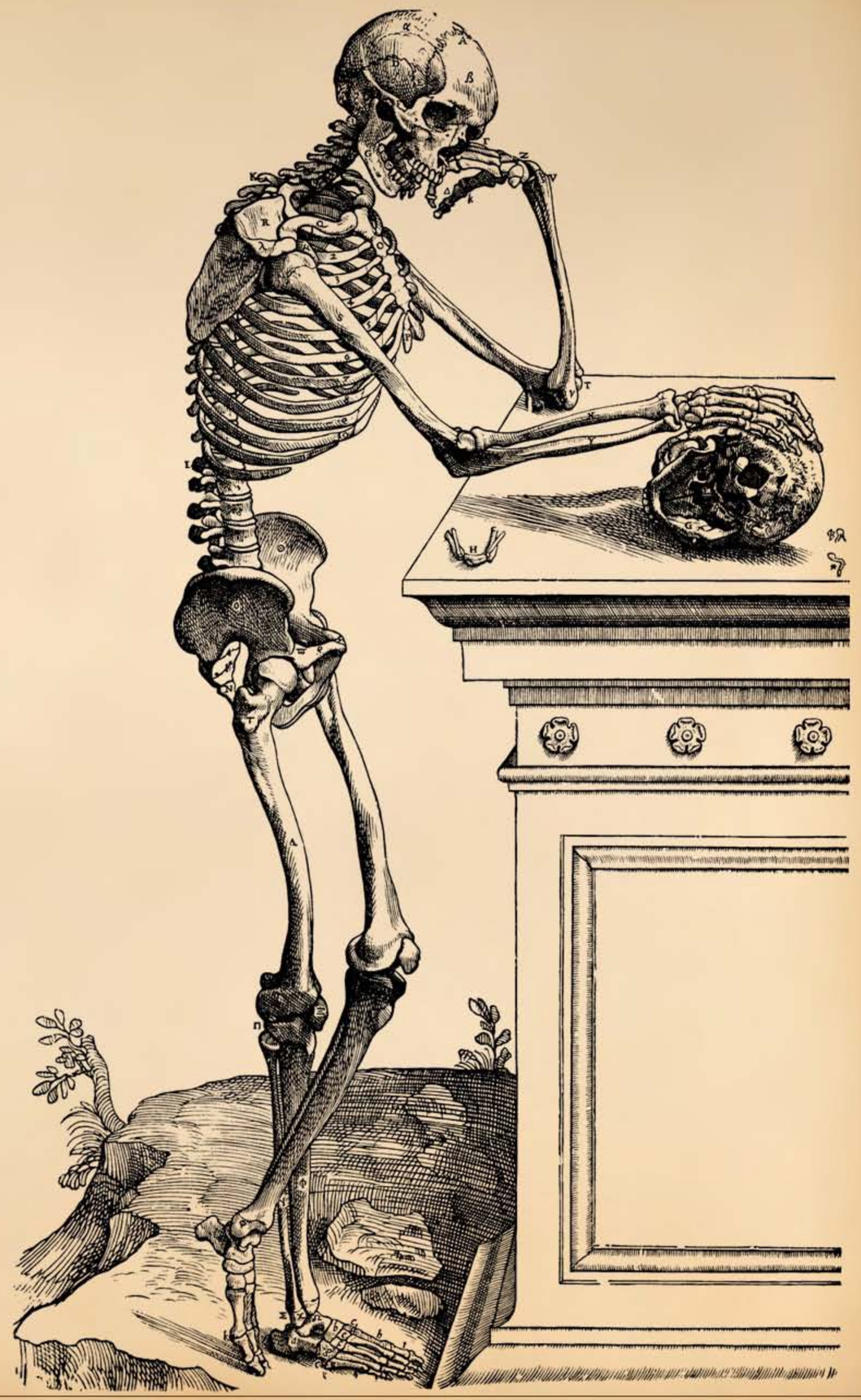
WOUND PATHERGY

(WHEN NOT TO OPERATE)

SITUATIONS TO AVOID THAT WILL CAUSE NECROSIS, DEHISCENCE, WOUND FAILURE, & RELATED COMPLICATIONS

Marc E. Gottlieb, MD, FACS
Phoenix, Arizona

arimedica.com
2011

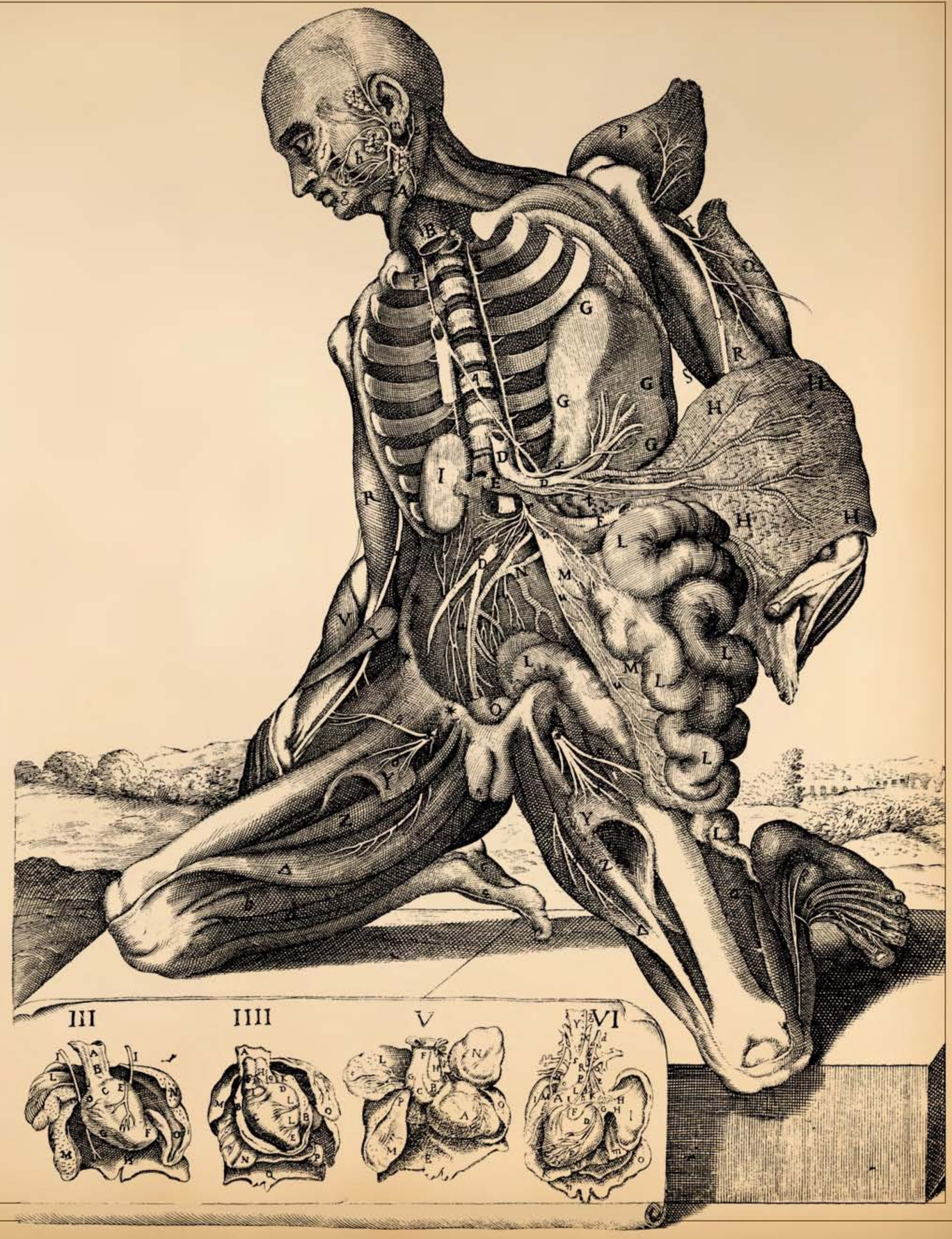


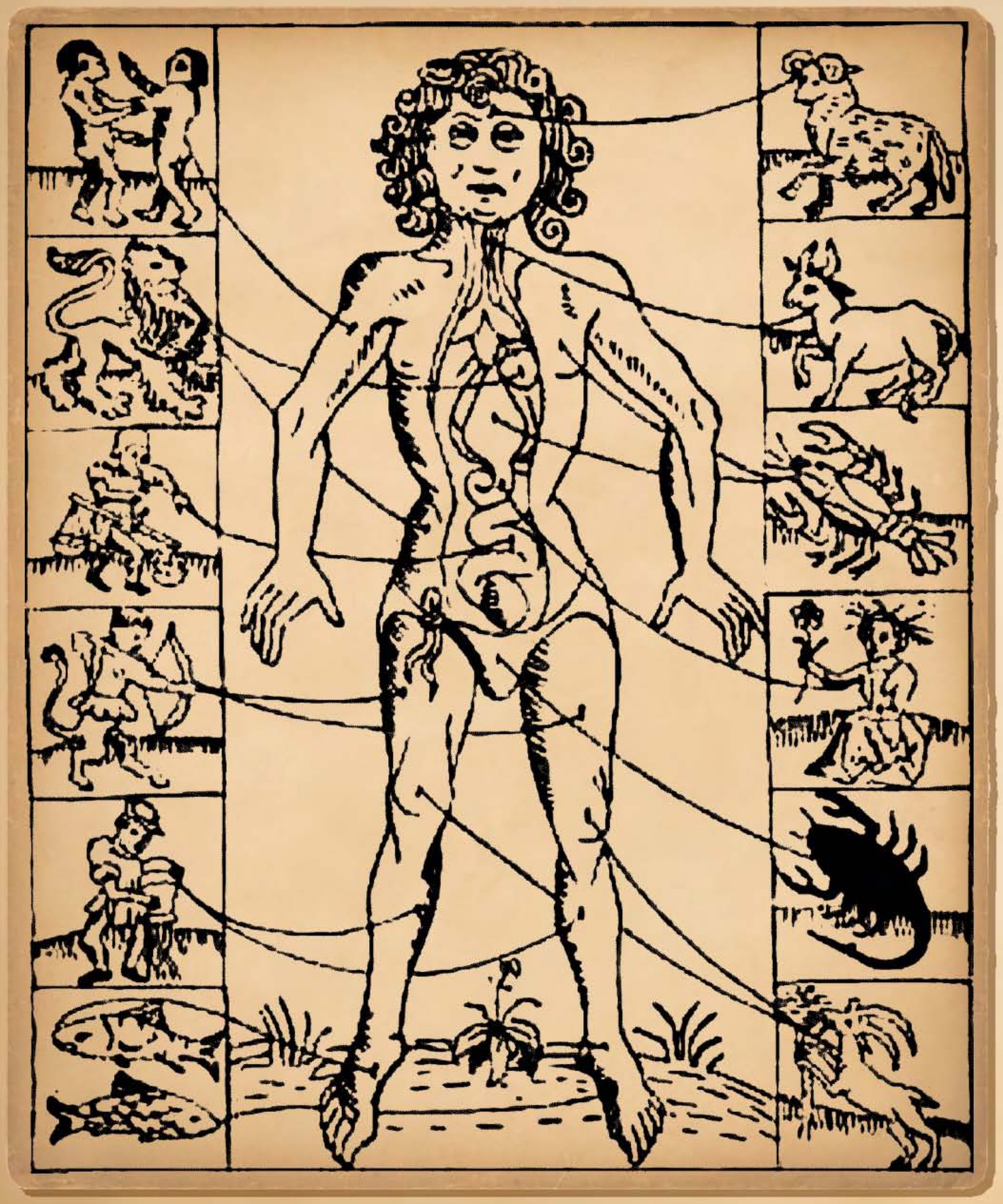
WHEN NOT TO OPERATE

X

General Health & Co-Morbidity

When the risks of complications and instabilities are high due to cardiovascular, pulmonary, hepatic, renal, endocrine, metabolic, and other active diseases and general disorders.





WHEN NOT TO OPERATE

2

Astrology, the Black Arts, & Divine Improvidence

The notion we all clandestinely acknowledge but no one will admit to.

WHEN NOT TO OPERATE

3

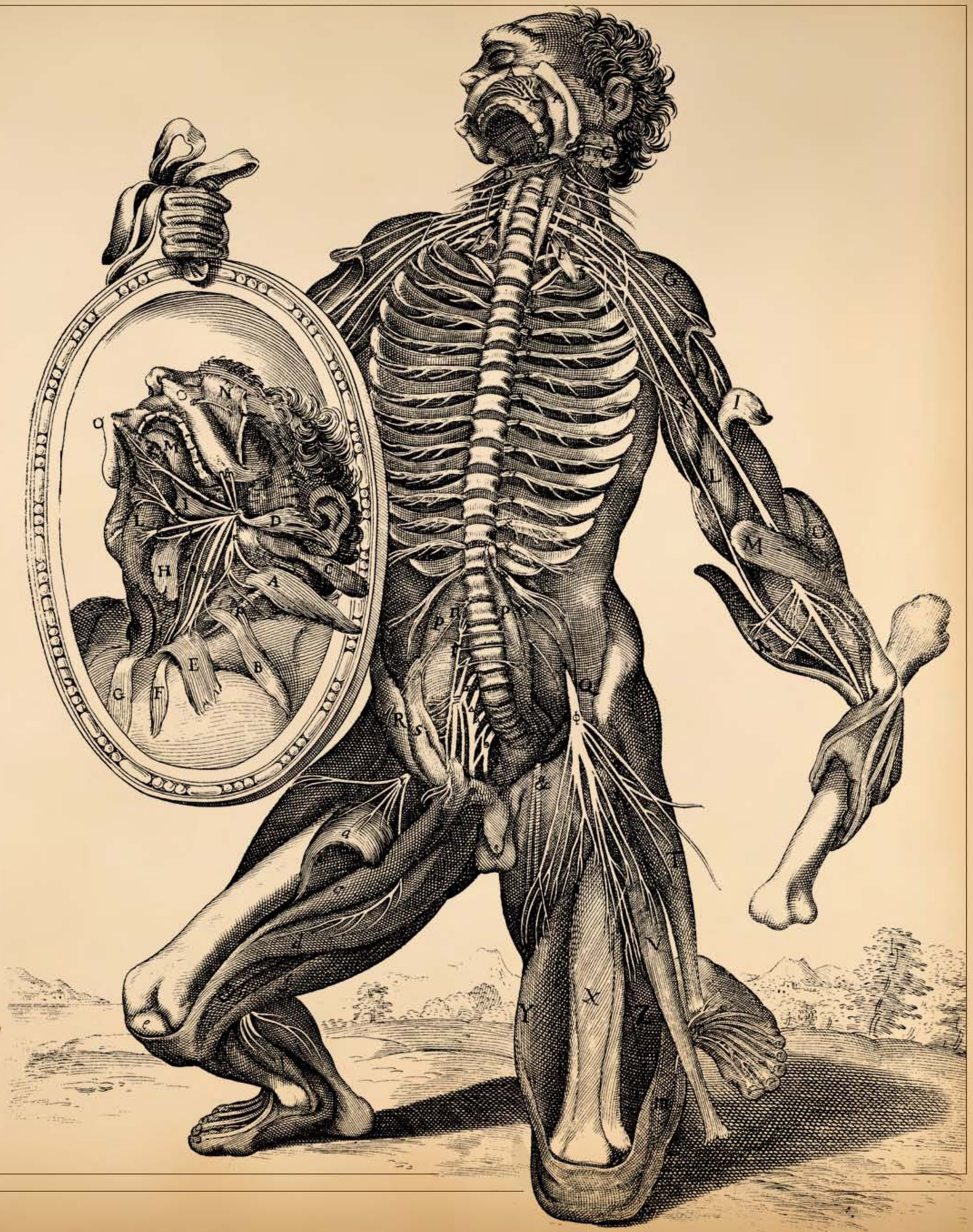
Failed Wounds & Failed Surgery due to Repetitive Trauma and Imprudent Care

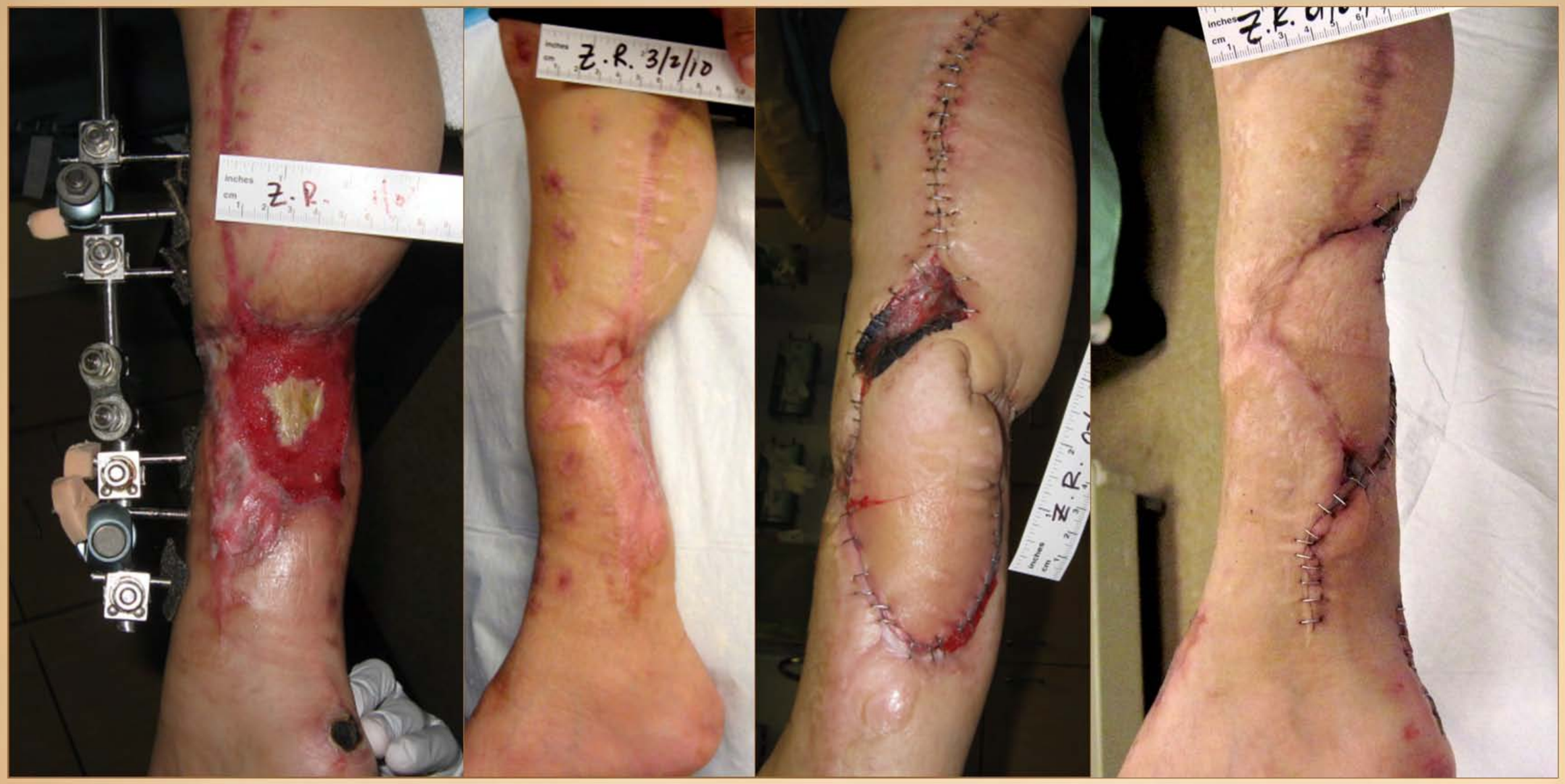
Doing too much too soon too often.

Separating debridement and control from repair and reconstruction.

The quintessential importance of patience, prudence, planning, proper care.

The quintessential importance of the biology of injury, inflammation, and wound healing.





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Separating debridement and control from repair and reconstruction.

The quintessential importance of patience, prudence, planning, proper care.

The quintessential importance of the biology of injury, inflammation, and wound healing.

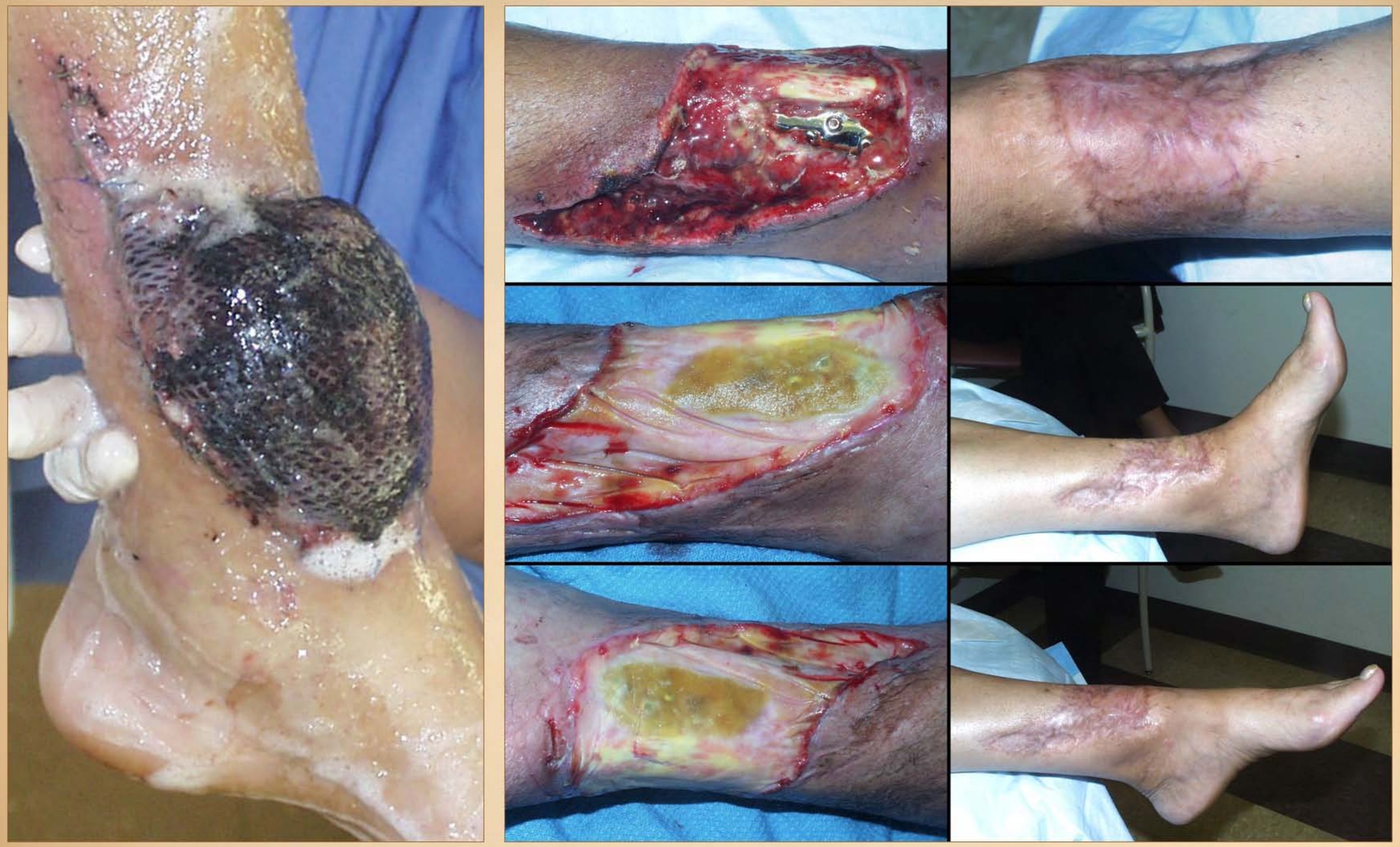
Staged reconstruction.

The Law of Countable Destiny

Multiple procedures: small successes versus big catastrophe.

Not everything this week or this year – resident care versus real care.

Don't be greedy. Live to fight another day.



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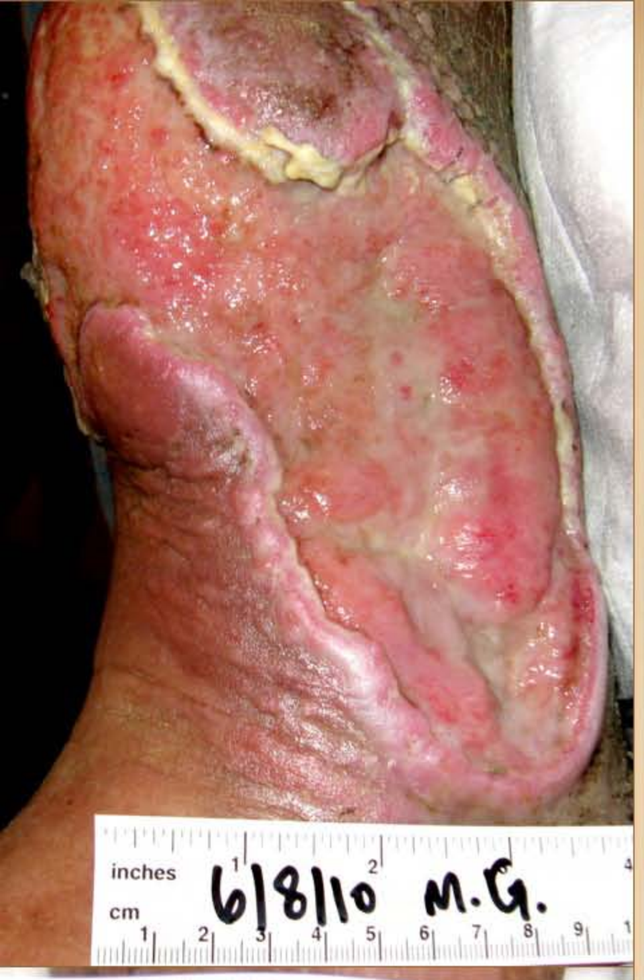

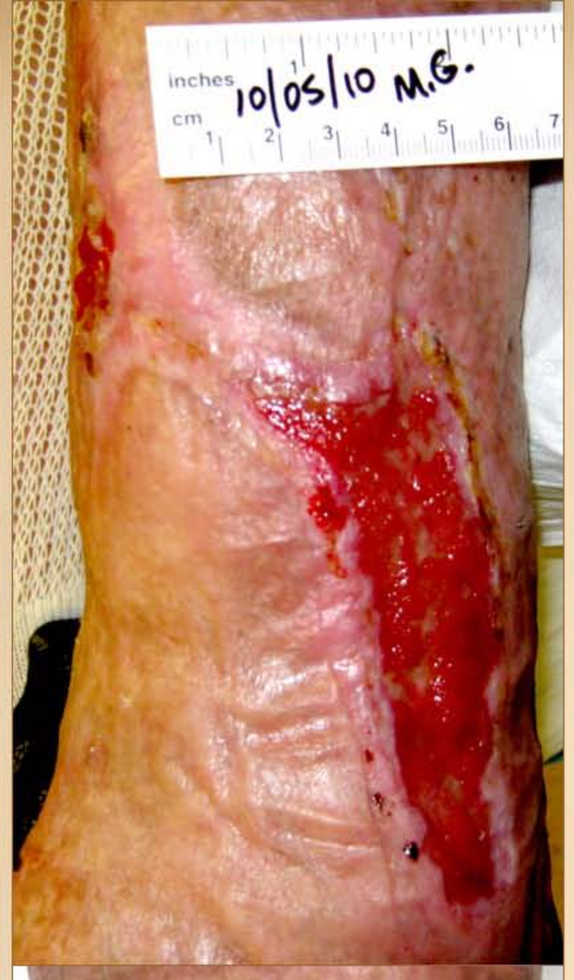

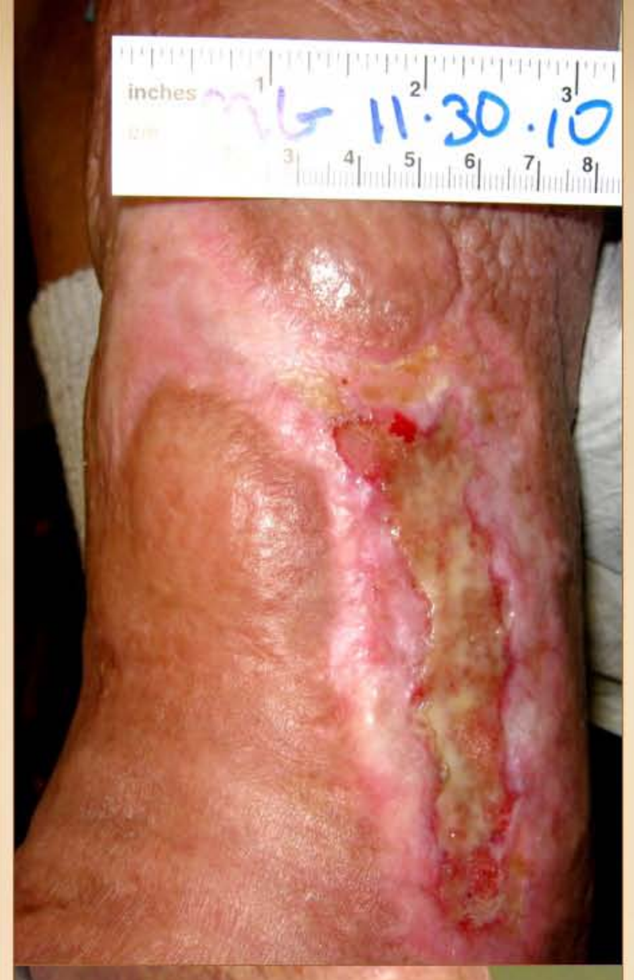

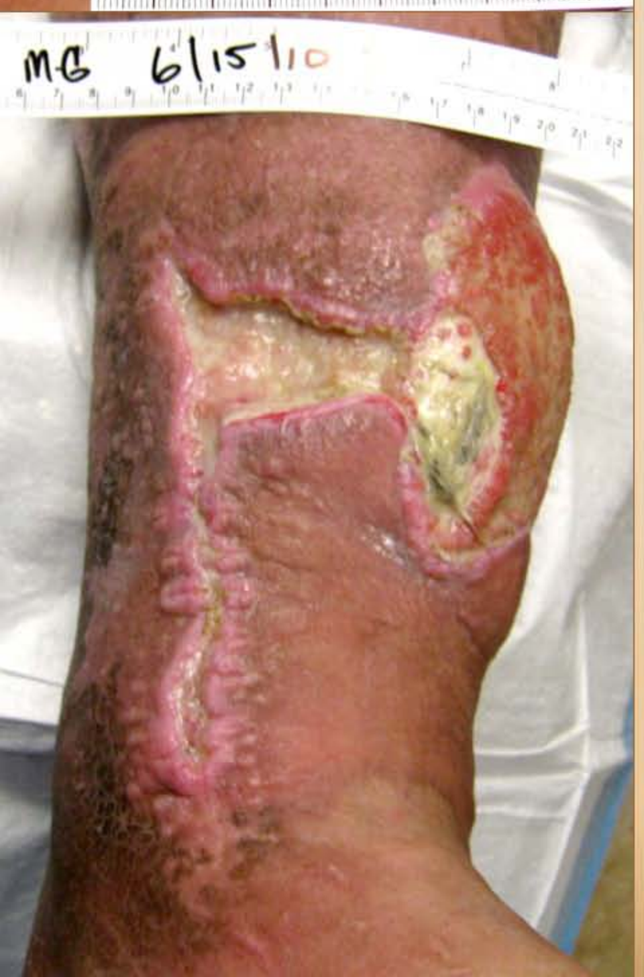

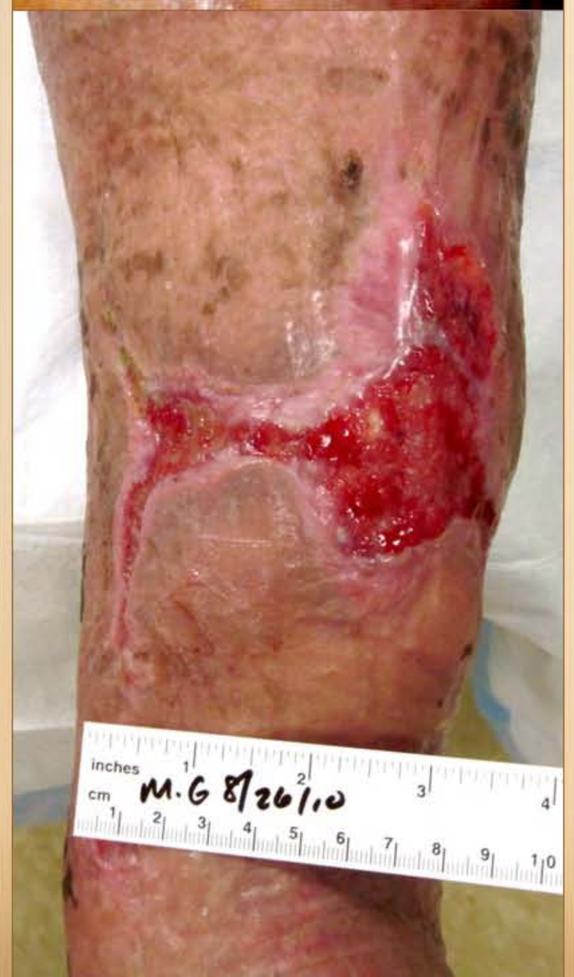

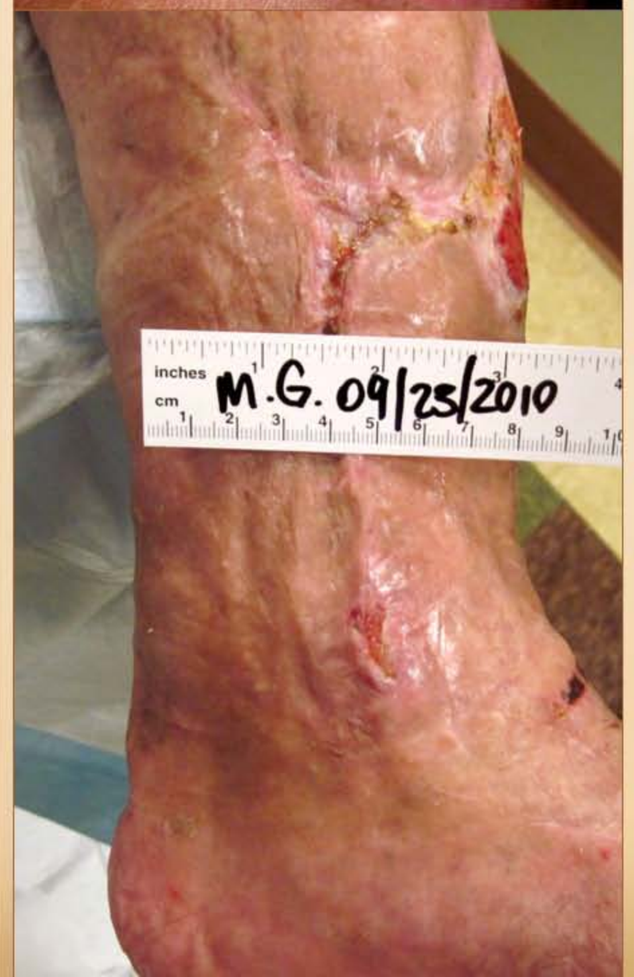

Doing
too much
too soon
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Separating
debridement and control
from repair and reconstruction.

Quintessentially important:
patience, prudence,
planning, proper care.

Quintessentially important:
the biology of injury,
inflammation, wound healing.

NECROSIS & ULCERATION - TWO GENERAL PATHOLOGIES & PATTERNS

THROMBO-INFARCTIVE

Macro-occlusive

Micro-occlusive

Micro-angiopathies

Hemopathologies

Hypercoagulable / Coagulopathic

INFLAMMATORY-LYTIC

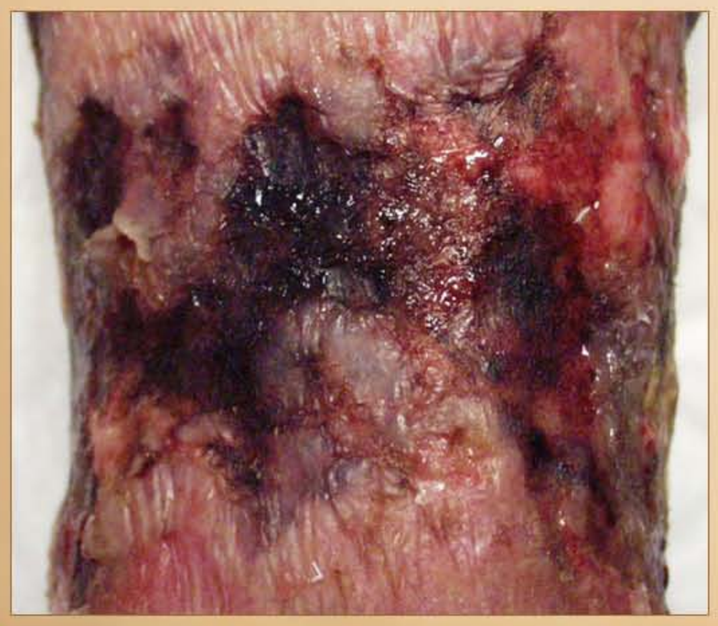
Inflammatory

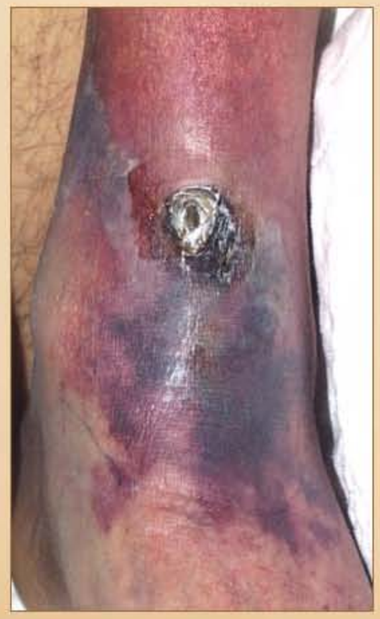
Autoimmune

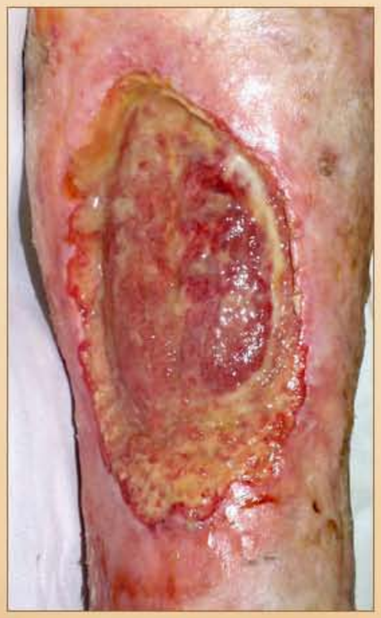
Atopic, Suppurative

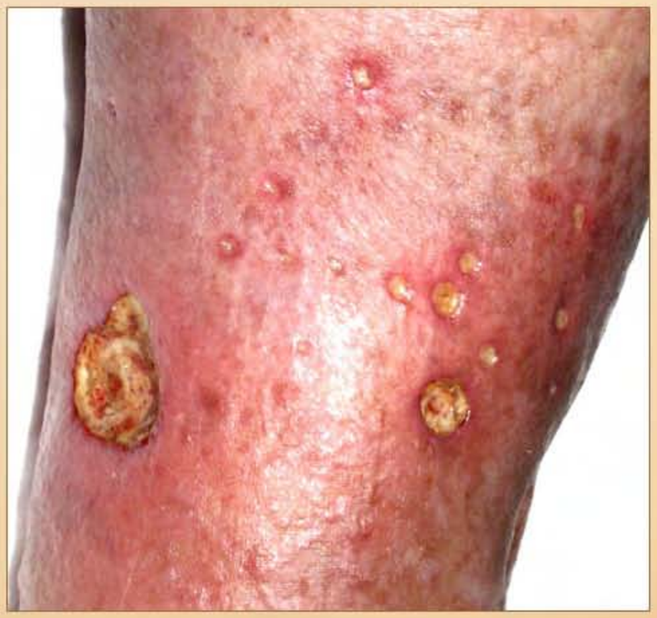
Connective Tissue Disorders

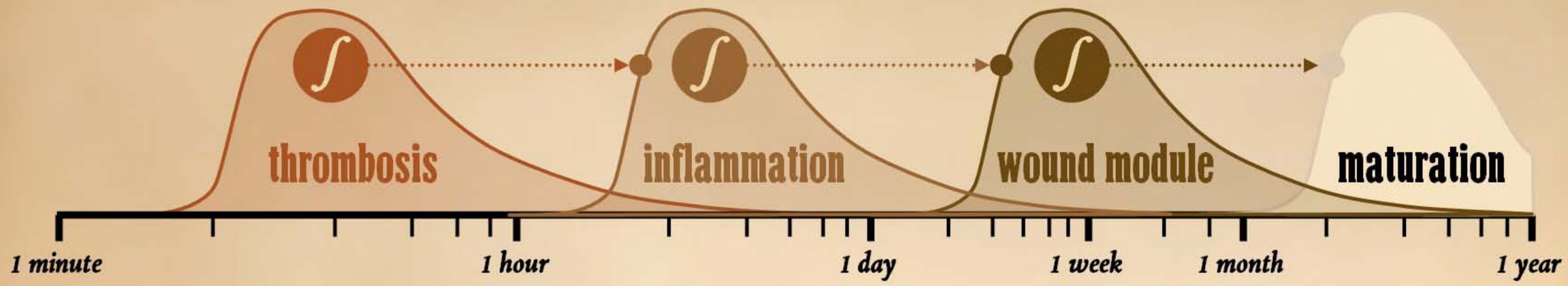
Lymphoreticular / Reticuloendothelial



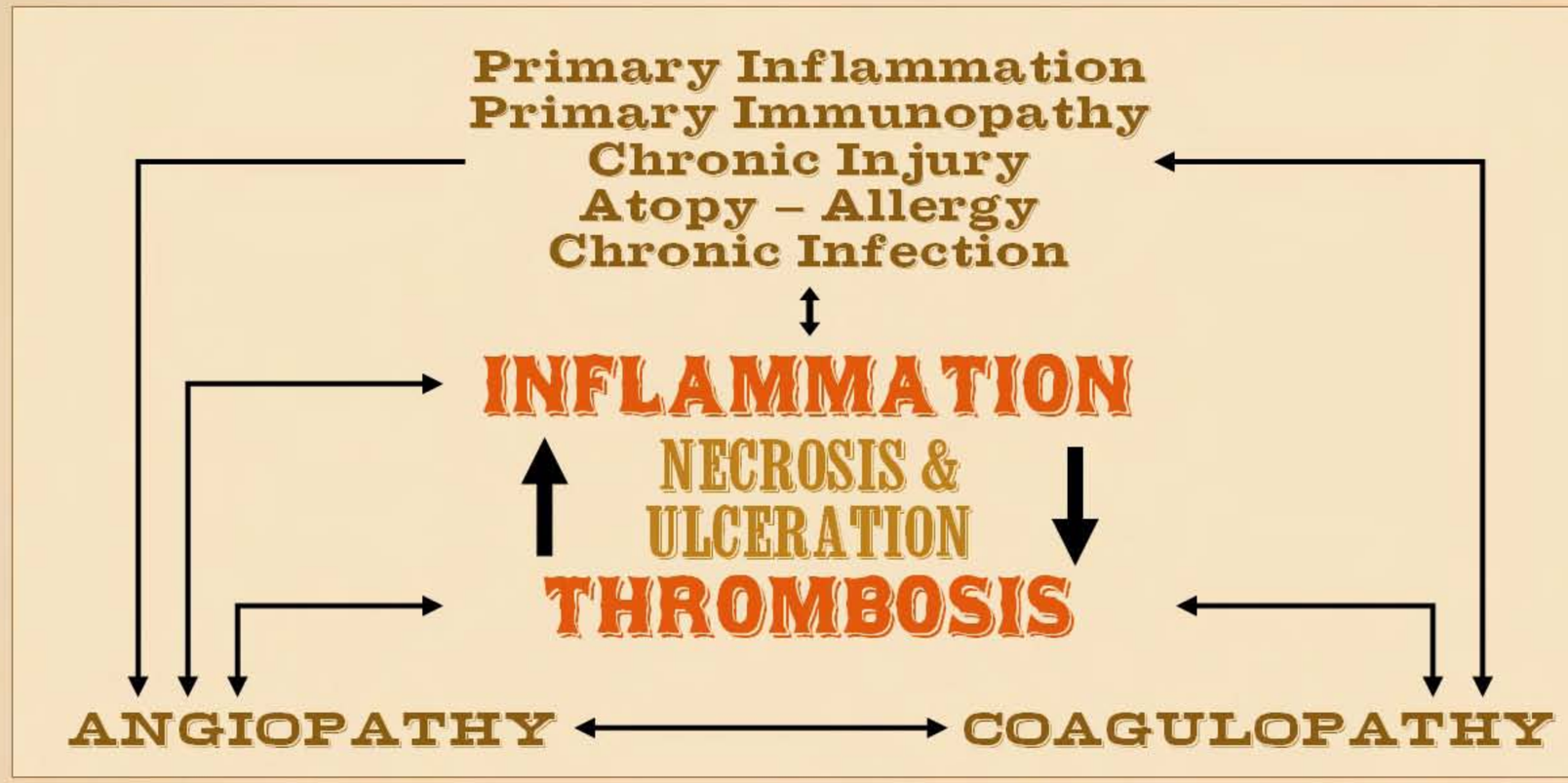




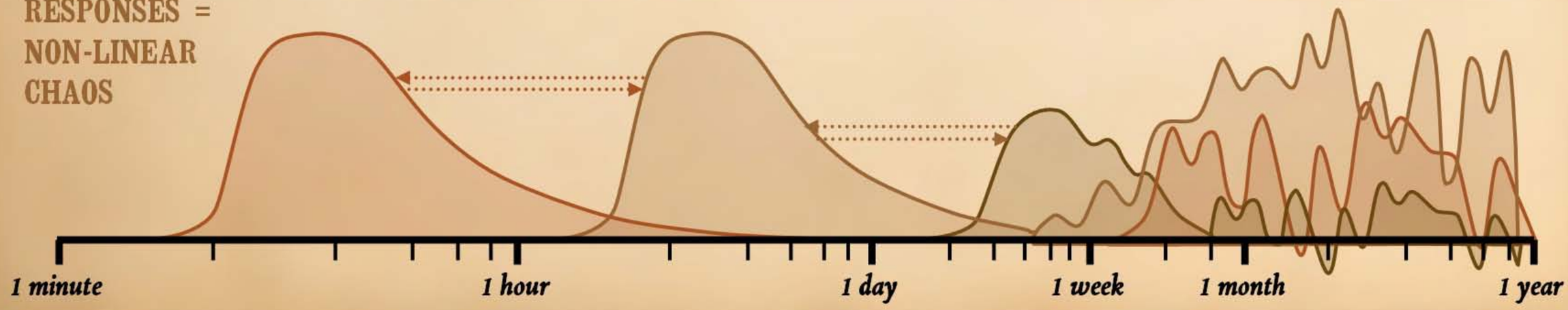


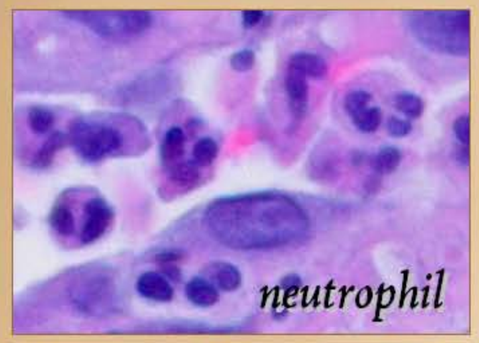


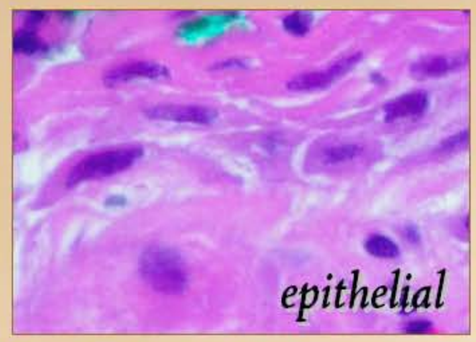
NORMAL HEALTHY RESPONSES = SEQUENTIAL LINEAR ONE-SHOTS

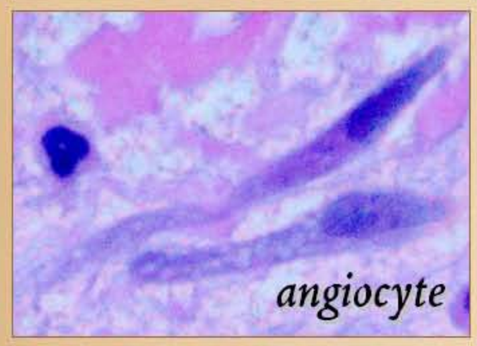


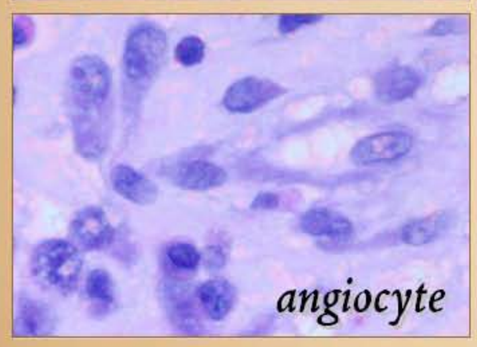
CHRONIC PATHOLOGICAL RESPONSES = NON-LINEAR CHAOS

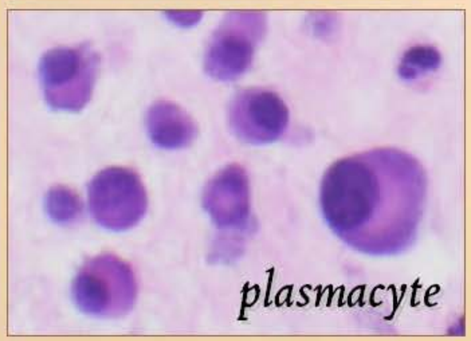


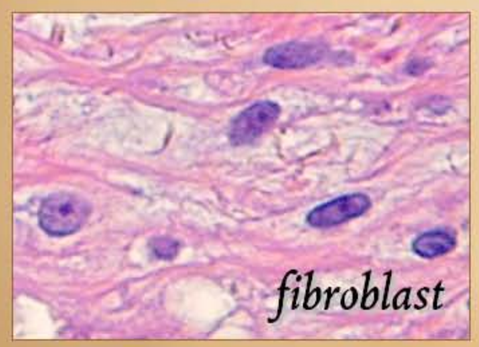


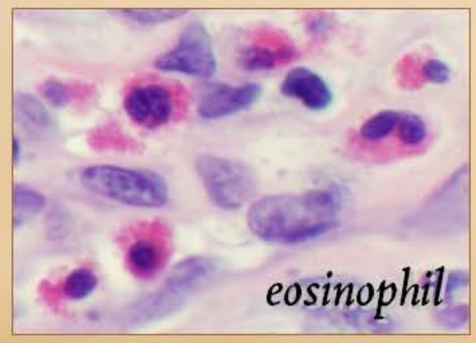












CELLULAR AUTOMATA

Wound Self-Assembly & Stromal Reorganization

The wound is a cellular self-organizing automatic system.
It is made of real biological cells. Their deterministic interactions are epitomized in the Main Control Loop.

Each cell - monocyte, angiocyte, fibroblast, keratinocyte –
has an assigned job. If allowed to function properly, stromal rebuilding & wound closure are automatic and correct.

When pathological, self-organization is disturbed or fails.
Wound healing is then disrupted - because wound healing is nothing more than the self-organization of these cells.

Problems happen when chronic inflammatory cells appear.
They disturb the function & organization of the cells meant to be there, arresting or disrupting their intended organization.

In the chronic chaotic intrinsically pathological wound,

NOT ONE OF THESE CELLS IS INTRINSICALLY PATHOLOGICAL.

Each cell and cell type is intrinsically correct or healthy, trying to do what it is meant to do. If it is failing, it is because it is being besieged, restrained, or deprived by another of these cells.

Are there intrinsic disorders of the repair cells? No. See the website & text.

These are not divergent wounds - they are not ulcerating and getting worse. They are just not healing. What is disrupted is ONLY the aggregate organization and self-assembly.

THE PHYSICS AND PATHOLOGY OF WOUNDS

ARIMEDICA

www.arimedica.com

Marc E. Gottlieb, MD, FACS

Phoenix, AZ

1

The Wound as a System and a Controlled Machine

The wound module, the wound control loop, wound pathology, and the basic dynamics of healthy and impaired wounds.

2

Auto-Immunopathy and the Intrinsic Disease of Wound Healing

The cellular and histopathological basis of intrinsic wound failure wound chronicity: chronic inflammation, wound autoimmunopathy, and the 3-population wound.

3

Chronicity and the Physics of Wound Failure

The physics of wound failure and chronicity: N-body dynamics and chaos, population logistics, cellular automata and self-organization.

PRINCIPLES OF SURGERY – WHEN NOT TO OPERATE

Situations to avoid that will cause necrosis, dehiscence, wound failure, & related complications

Preceding examples show effects of repetitive & sustained injury, inflammation & lysis, thrombosis & infarction in patients who are otherwise healthy, where the injury is due solely to surgical trauma.

What happens when patients have endogenous diseases or disorders that trigger, sustain, perpetuate, alter, and activate inflammation & lysis, thrombosis & infarction?

These are the disorders which will complicate your surgery, causing necrosis, dehiscence, & wound failure, and interdicting the good results you and your patient had hoped for.

Vasculopathies • Hematopathologies • Coagulopathies • Immunopathies • Cvd-Ctd

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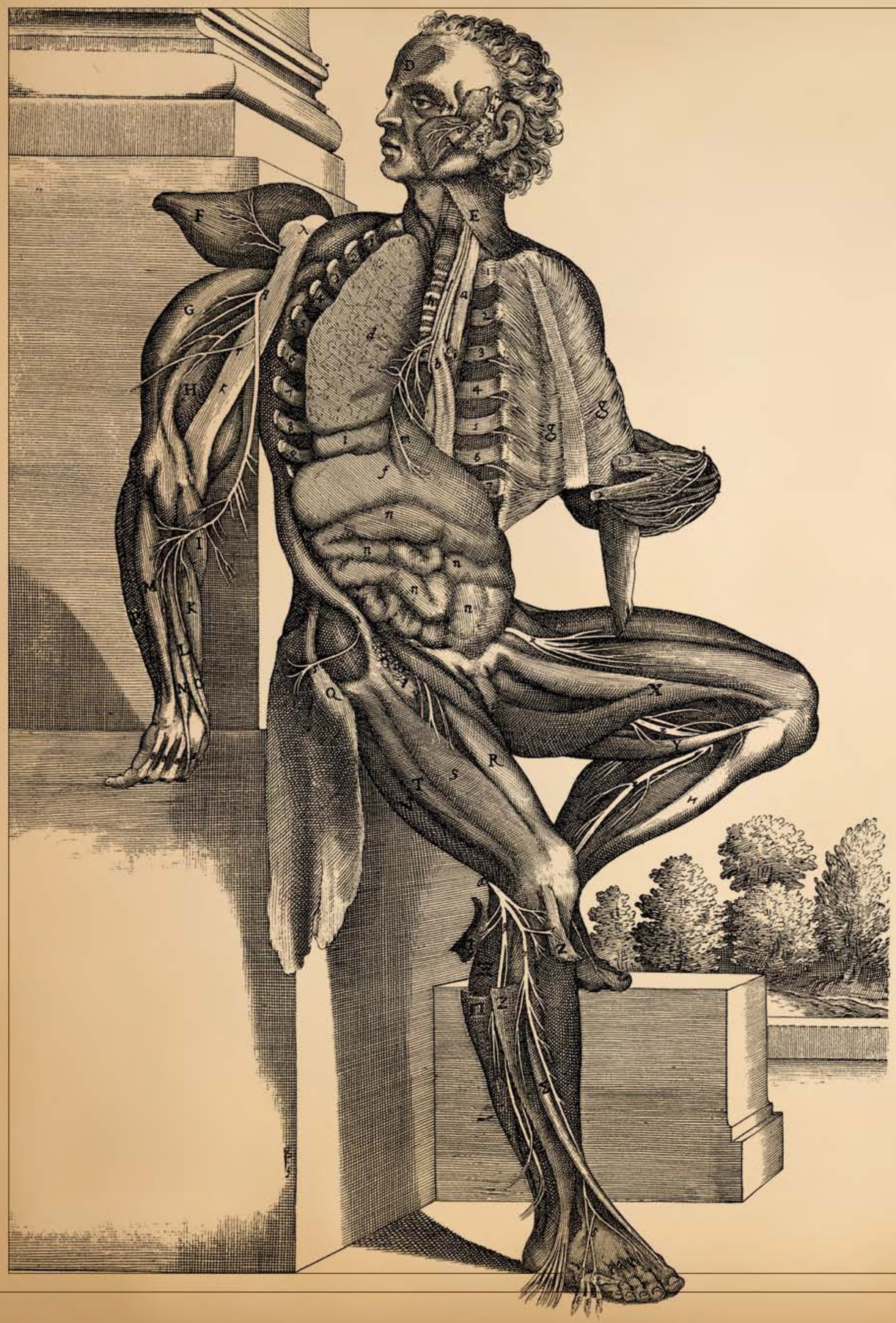
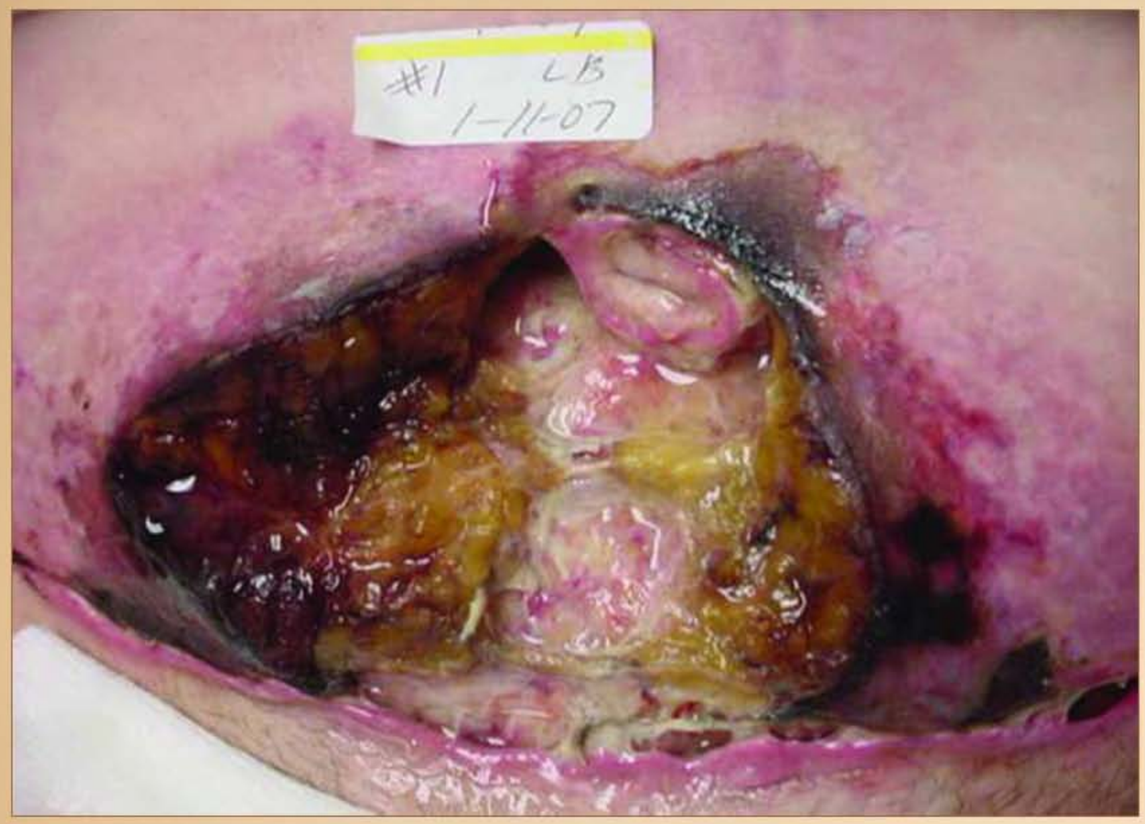


WHEN NOT TO OPERATE

4

Wound & Surgery Failure, Wound Pathergy Due to a Priori Pathology

Diseases and disorders of blood, coagulation, blood vessels, connective tissues, immunity, inflammation.



INDEX CASE

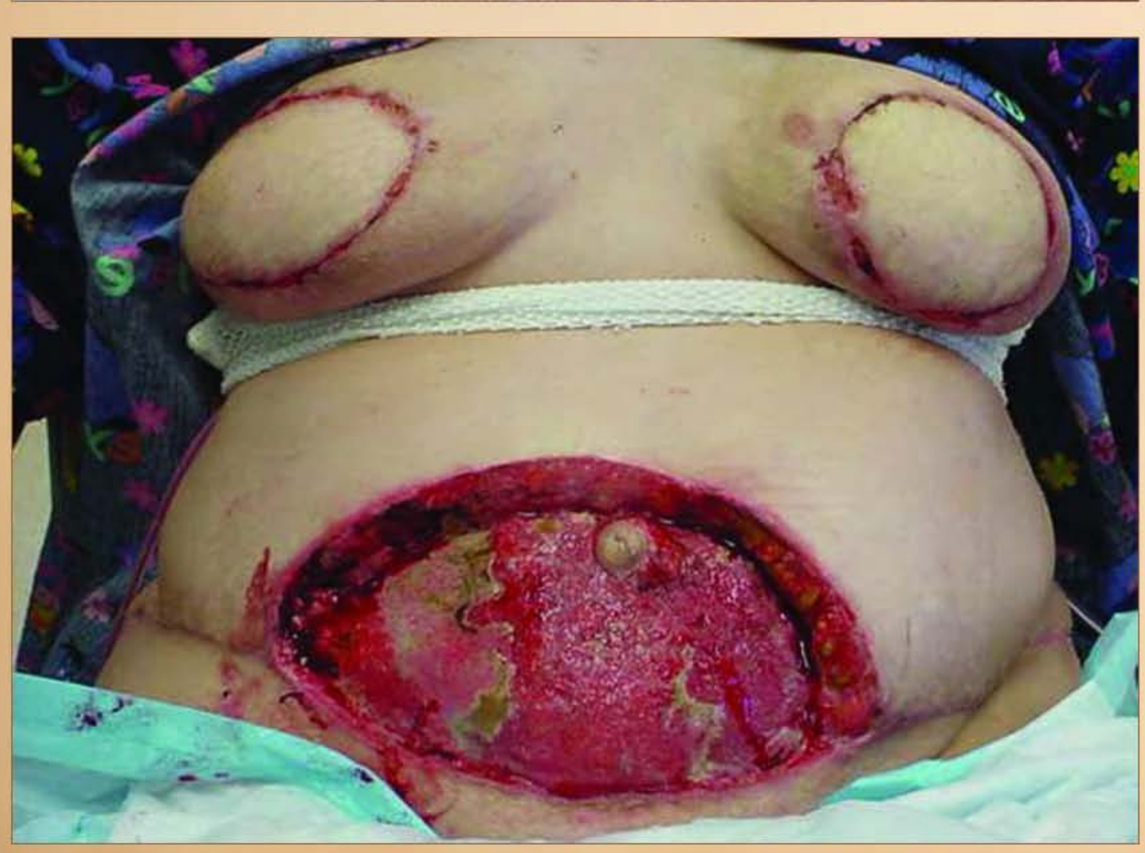
Breast reconstruction with complications.

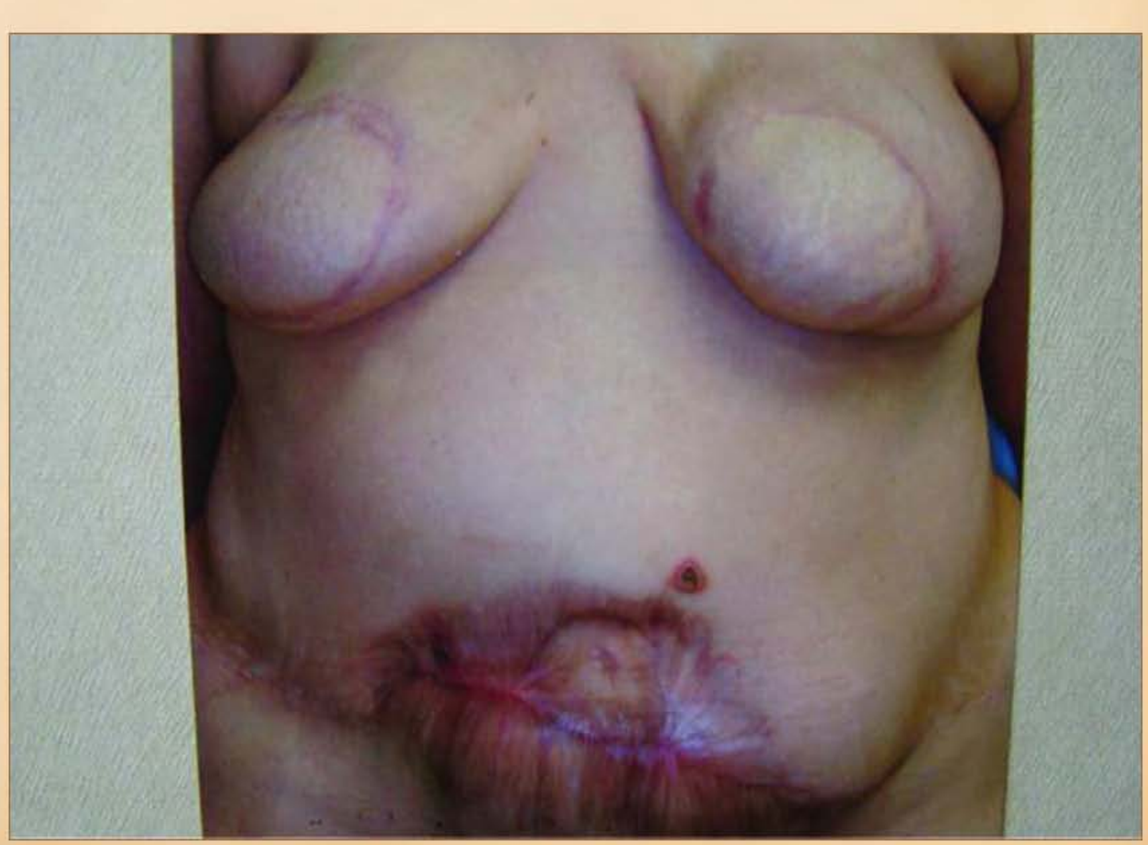
Traumatic splenectomy 12 years prior.

Plt 350K/mm^3 before surgery

Plt 1690K/mm^3 post-op peak

Wound complications attributed to post-splenectomy thrombocytosis.





WHEN NOT TO OPERATE - GENERAL INTENT OF THIS PRESENTATION

**Trauma, surgery, and wounds can be complicated by ischemic (thrombo-infarctive)
and by immunopathic (inflammatory-lytic) events that will cause
tissue necrosis, ulceration, wound bursitis & dehiscence, and wound healing failure.**

These undesirable, and usually unanticipated events are collectively known as "wound pathergy".

**Such events are due to diseases that might be missed, overlooked, or ignored until it is too late,
but which are all treatable, and the pathergy avoidable.**

Vasculopathies • Hematopathologies • Coagulopathies • Immunopathies • Cvd-Ctd

**Pathergy results from the
mutually interdependent
self-perpetuating triad of**

INJURY — THROMBOSIS - INFLAMMATION

SET 1 – INTRODUCTION

Ulcers due to Thrombocytosis

Nominal thrombocytosis: platelet count > 400,000, > 600,000, > 1,000,000.
Primary / essential thrombocytosis: a myeloproliferative disorder (cf. cml, pcv, myelofibrosis).
Secondary thrombocytosis: reactive after other pathology (trauma-surgery, infection-inflammation, cancer, misc).

Post-splenectomy: 80% incidence of transient, persistent, or incidental thrombocytosis.
Thrombosis with thrombocytosis is a recognized phenomenon, but the incidence is low.
Thrombotic & embolic complications of post-splenectomy thrombocytosis are only 5%.
Myeloproliferative primary thrombocytosis: benign with Rx, thrombosis-embolism incidence only 10-15%.

PLATELETS

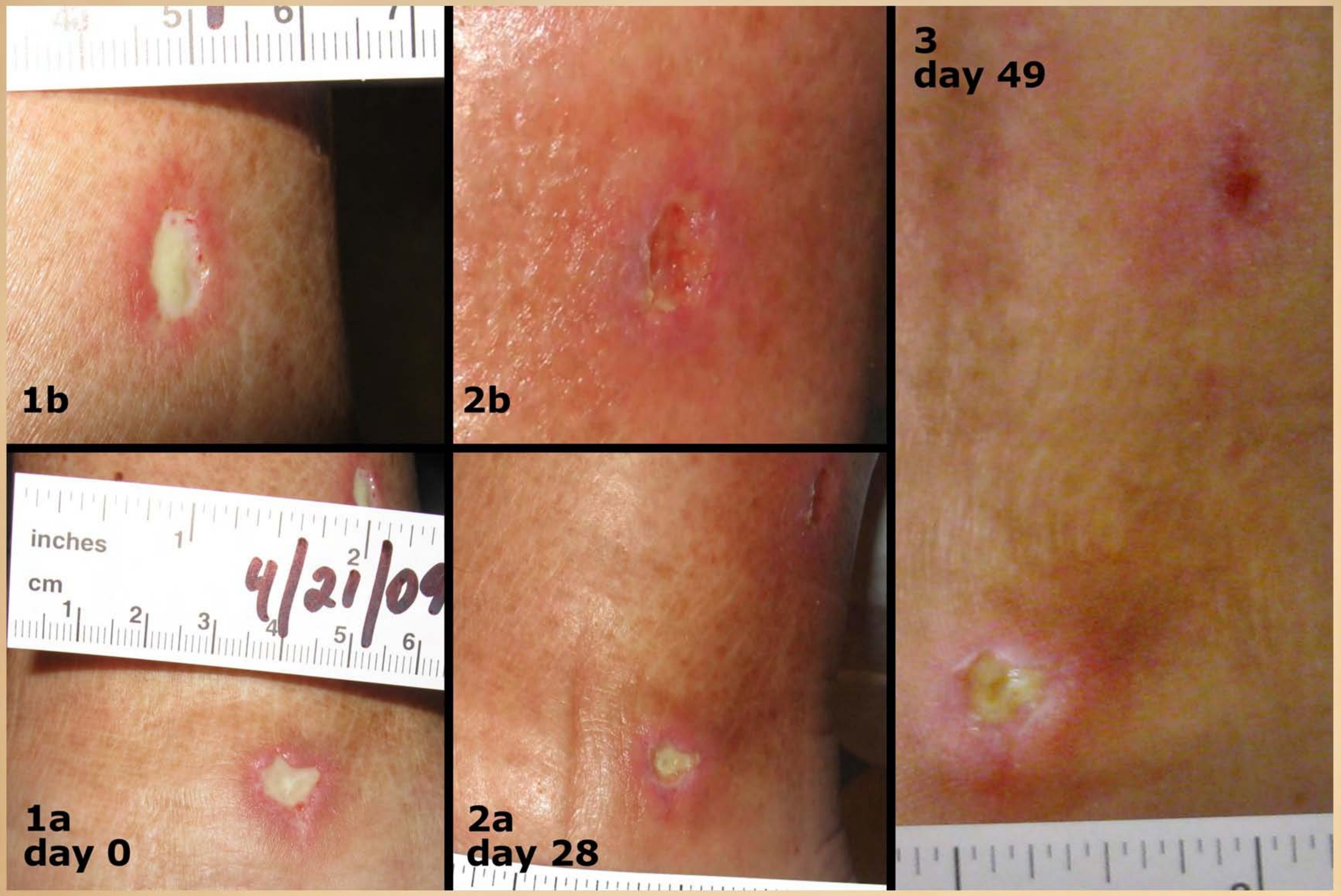
Not just dust and debris, not just a passive "log jam". Active elements with complex functions programmed to respond to acute events: adhere and aggregate, trigger thrombosis, trigger inflammation, effects on vessels themselves, initiation of wound repair, highly interconnected to various proteins with multimodal roles.

Not always "on" and active; in "standby" awaiting a trigger. When high, random adhesion-aggregation-thrombosis unlikely during baseline "healthy" status, explaining benign low thrombosis statistics. High counts more relevant during morbid or trigger states (inflammation, trauma, surgery) when platelet events are accelerated or amplified.

Thrombosis not linearly related to platelet count; risks & responses not predictable by raw counts. "Standby" counts irrelevant until a trigger. Once triggered, activation & thrombosis is strongly non-linear & self-amplifying. High counts can potentially increase sensitivity or amplify or accelerate the response, but not in mappable ways.

Surgery-trauma is an immediate complex trigger – activate & upregulate platelets & thrombosis. This is the primary intent of this system. "High" counts in numerical bounds in the injured area is healthy. But the process can leach into general circulation, and in unhealthy patients, keeping events regulated in safe physiological limits is less certain.

Thrombocytosis raises risk in principle, but complications not predictable on counts alone, especially under 1 million. Pathergy after thrombocytosis can be causal or coincidental. Prior benign history is no guarantee of safety, with serious consequences on proper provocation. However, do not assume causality and ignore proper eval & diagnosis.



#1: 67 m essential thrombocytosis

Thrombocytosis & wound pathergy: real (the complication has occurred) or potential (a risk for pending surgery). Proper active or preemptive treatment depends on proper diagnosis. What is the differential diagnosis? Relevant items to consider in evaluating such a patient or situation are:

(1) platelet count per se
(2) the cause of the thrombocytosis and associated pathologies
(3) presence or absence of triggers and acute disease
(4) intrinsic disorders of platelet dysfunction
(5) the possibility of an unrelated or coincidental pro-thrombotic or micro-occlusive disorder

Differential Diagnosis of Wound Pathergy Platelet Problems

(1) Simple thrombocytosis: Yes, this case could have been nothing more than one among that 5% of patients who gets thrombotic complications of simple or post-splenectomy thrombocytosis. However, this does not relieve the obligation of proper evaluation and correct diagnosis. Even if just benign thrombocytosis, the higher the counts, the more relevant to preemptively treat before surgery, especially for counts above 1,000,000.

(2) Myeloproliferative disorder: Splenectomy or hyposplenism can be coincidental, irrelevant, and misleading – the thrombocytosis could be early, forme fruste, or established MPD. Myeloproliferative disorders and all disorders of the formed blood elements have risk of wound pathergy, infarction, and chronic ulceration. Attributing transient thrombocytosis to impaired splenic clearance may miss an underlying disorder of greater significance.

(3) Concurrent acute illness and triggers: In simple thrombocytosis, post-operative pathergy is the exception not the rule, so concurrent active illnesses and sensitizers must be considered: acute inflammatory or thrombotic states due to pathogens, allergens, immunogens, trauma; metabolic imbalances of renal, hepatic, endocrine or pharma effects; hemo-pathological states due to blood, bone marrow, and reticuloendothelial disorders or due to cancer (Trousseau).

(4) Intrinsic platelet dysfunction: Most disorders cause hemorrhage (e.g. von Willebrand, hemophilia, Glanzmann, drug effects). In comparison, the science and clinicals of platelet hyperactivity syndromes is wanting – either they are few & infrequent, or we have yet to learn to recognize them (e.g. "sticky platelet syndrome"). Function can be assessed by "aggregation studies". Demonstrable alterations are more significant than diagnostic monikers.

SET 2: PATHERGY

AND PATHOLOGICAL WOUND COMPLICATIONS

"Pathergy" general meaning – an abnormal or exaggerated response to an injury or challenge.

1920's – a rapid or excessive response to allergens.

1930's – Behçet's disease – an intense inflammatory and ulcerative response to minor trauma.

1990's – unexpected or disproportionate adverse response of wound to injury (debridement and surgery).

The injury-induced necrosis of pyoderma gangrenosum is a paradigm.

In modern parlance, "pathergy" means "unexpected acute wound failure" – implying inflammation, infarction, necrosis, tissue lysis, wound bursitis, dehiscence, & other undesirable events not due to obvious causes (infection, macrovascular ischemia, excess mechanical load), especially if unanticipated, exaggerated, or a consequence of treatment or of injury-triggered flare-up of an underlying disease.

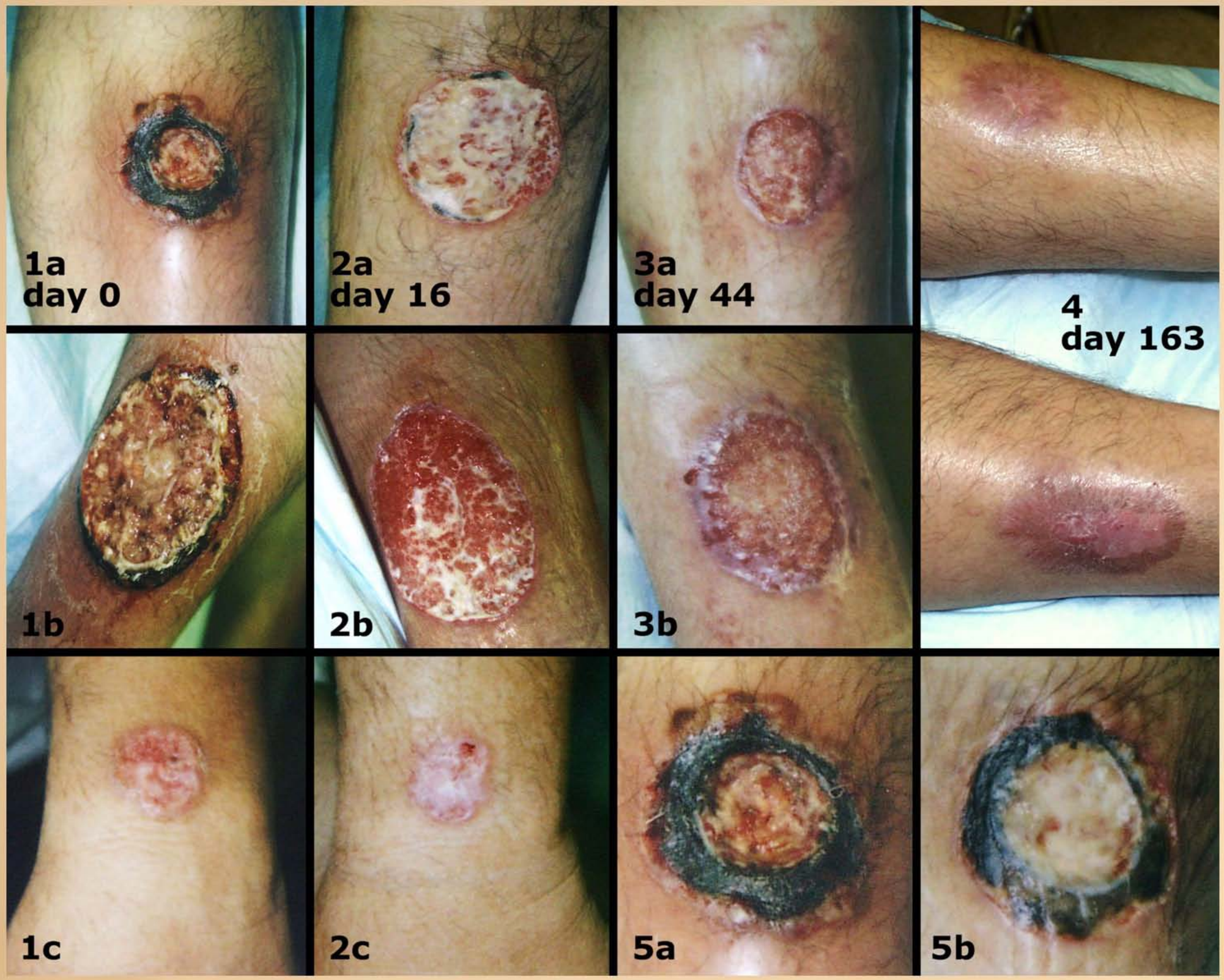
PATHERGY

Prone to occur with any condition of *severe ischemia* or *severe inflammation*, including:

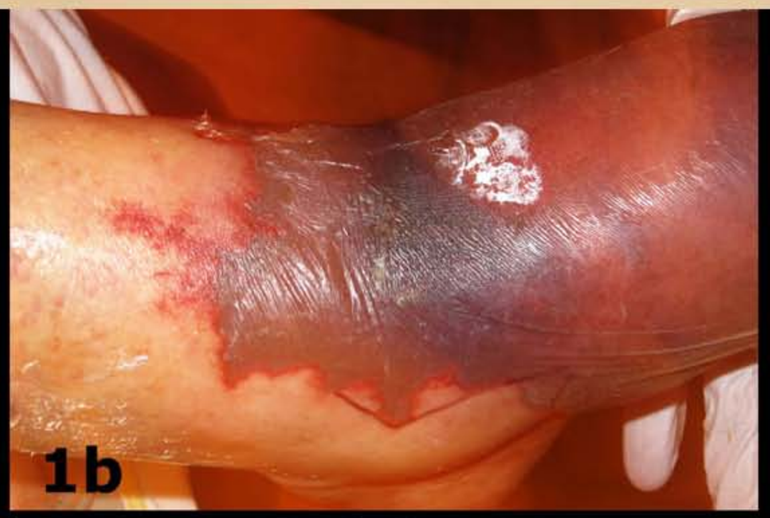
(1) athero- and other macro-occlusive arterial diseases, traumatic devascularization, other states of gross hypoperfusion or flow stasis.
(2) hypercoagulable, microthrombotic, formed-element hematopathologies, dysproteinemias, and other micro-occlusive disorders
(3) autoimmune vasculitis and angiopathies, and the various active immunopathies, including connective tissue disorders, panniculopathies, inflammatory dermatoses, and any similar disease of immunity and inflammation.

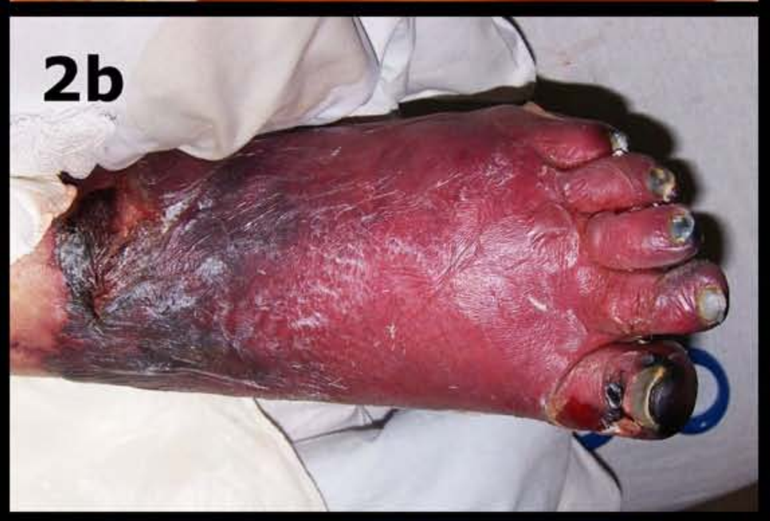
Pathogenic pathways to wound failure mediated in many ways, including acute neutrophilic inflammation, complement & lymphocyte activation, abnormal cytokine profiles, protease activation, platelet-mediated thrombosis, and coagulation-mediated thrombosis. In sick hosts or wounds, these events lead to ischemic infarction, inflammatory tissue lysis, or both, i.e. necrosis and ulceration.

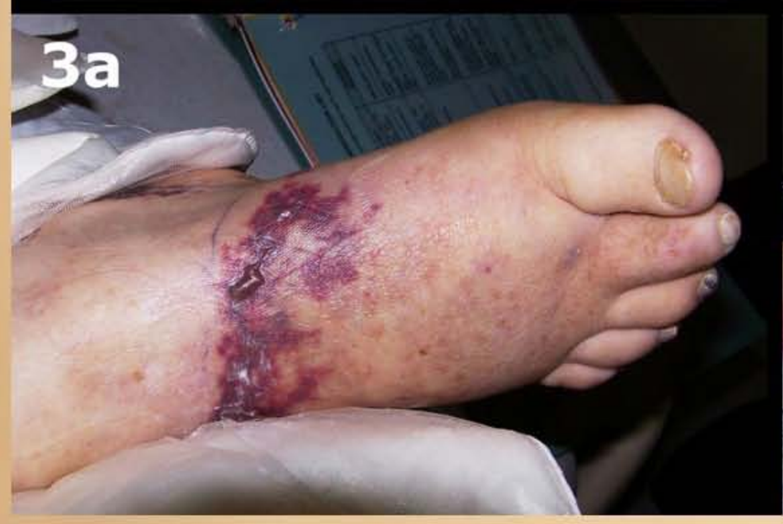
The mutually interdependent triad of *injury-thrombosis-inflammation* is of central importance – the response to injury that, while necessary to contain primary damage and prepare for repair, is nonetheless inherently destructive. Healthy wounds & hosts weather injury-thrombosis-inflammation as acute events wax then wane. Sick wounds & hosts cannot accommodate the secondary injury created by this triad, and when the system is unbalanced, then secondary injury, i.e. necrosis and ulceration, can become significant.

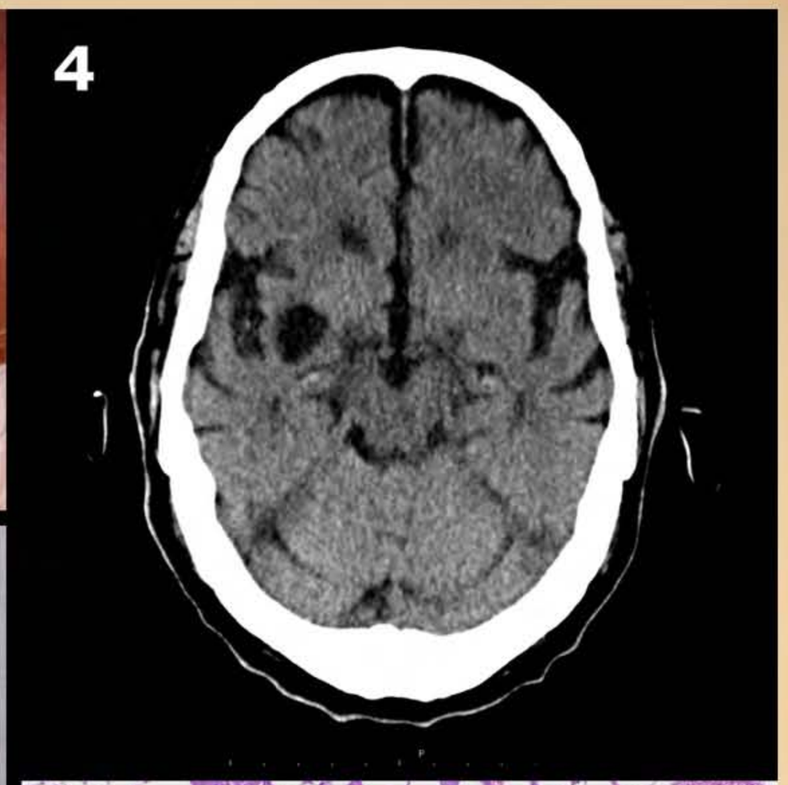


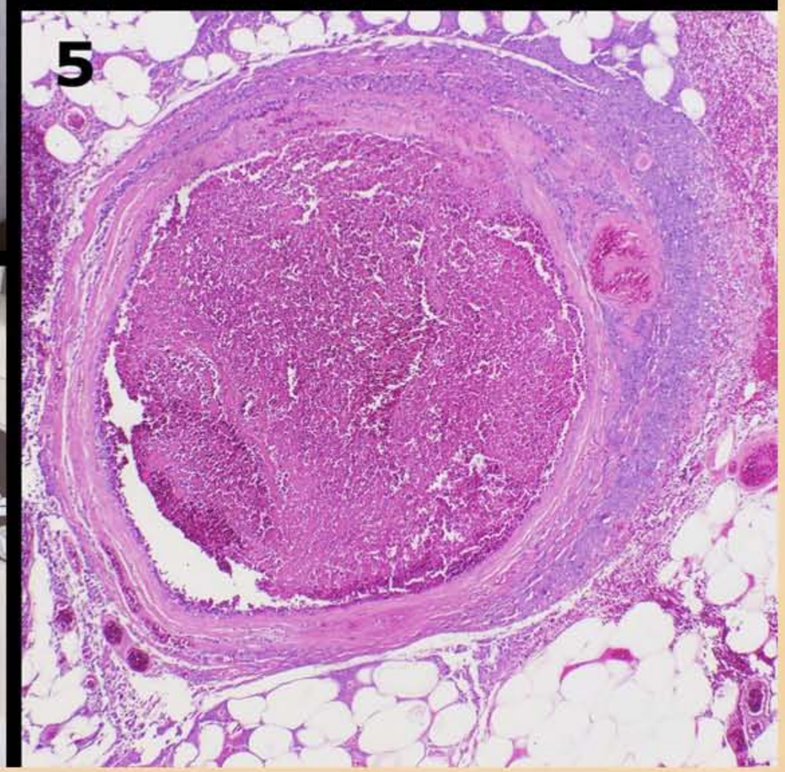
#2: 45 m pyoderma gangrenosum





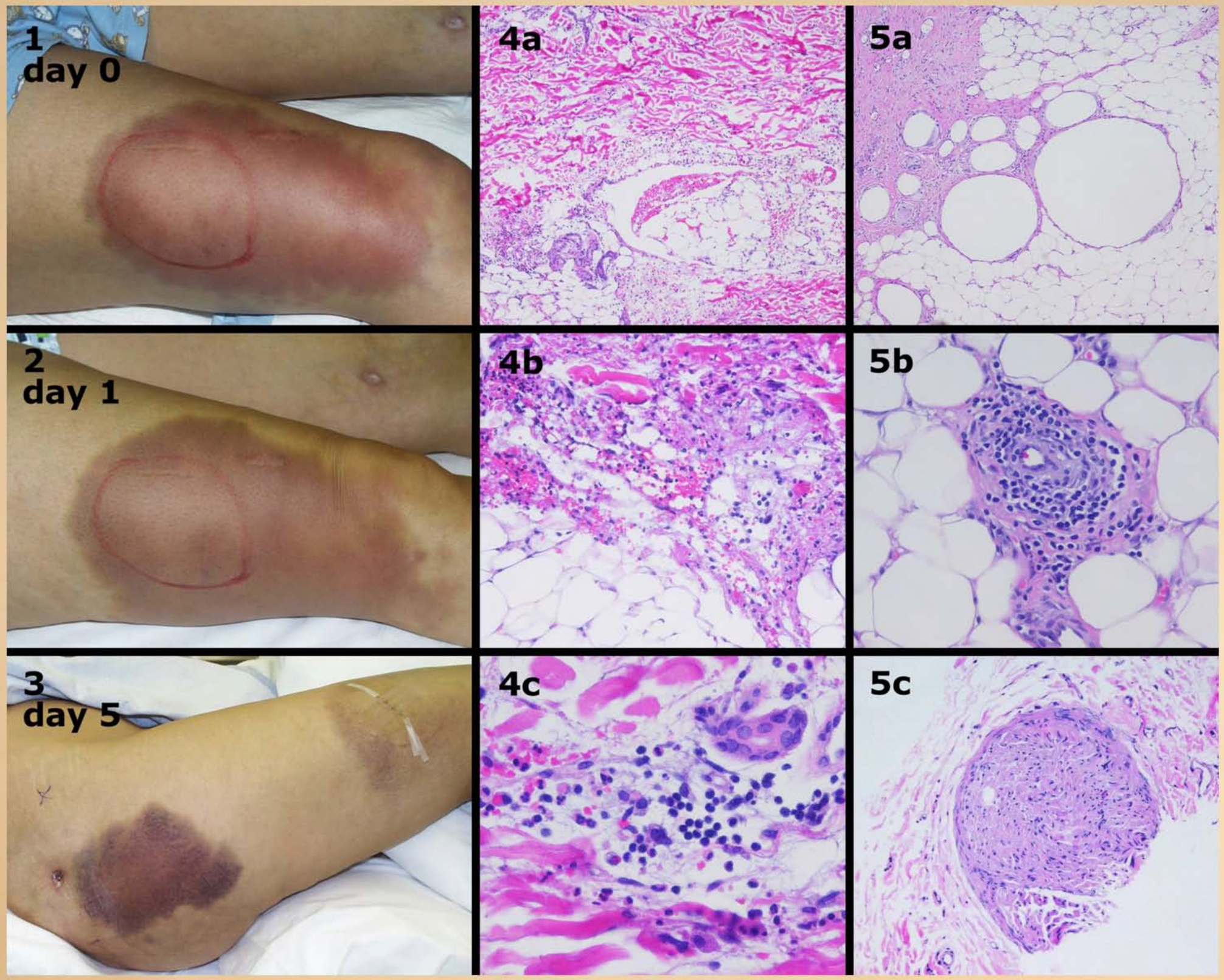




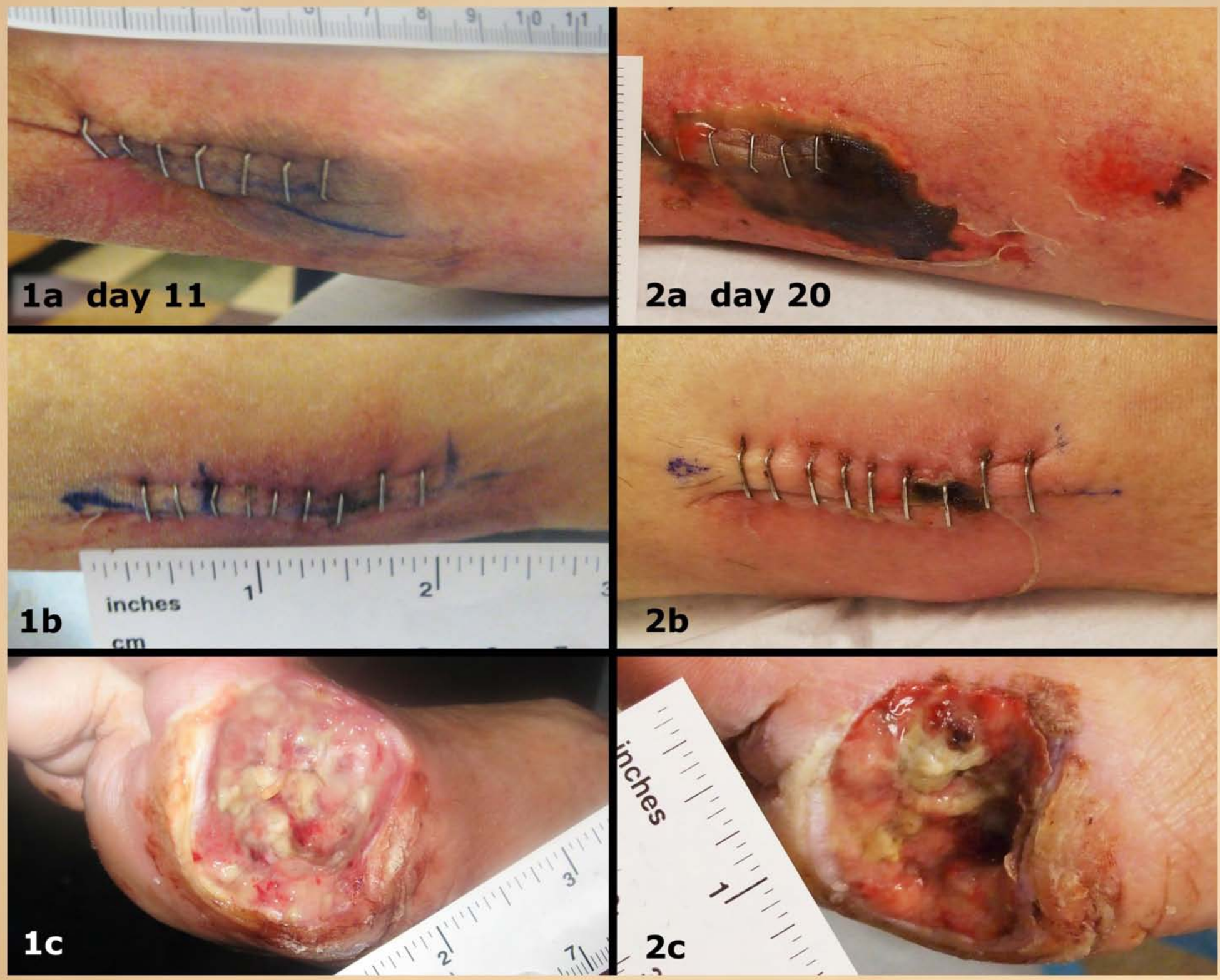


#3: 80 m hypercoagulable state

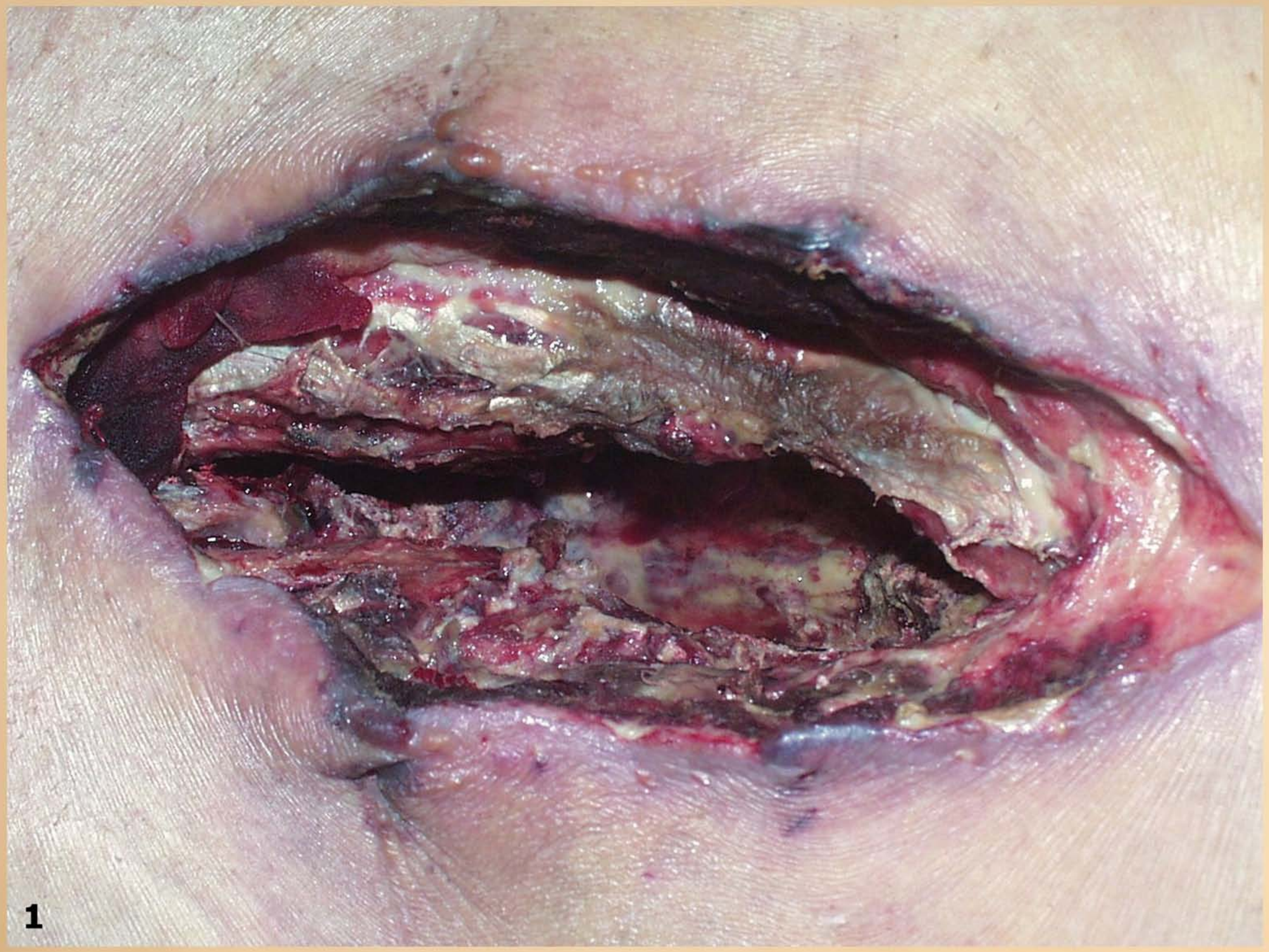
D



#4: 43 f Behçet's syndrome

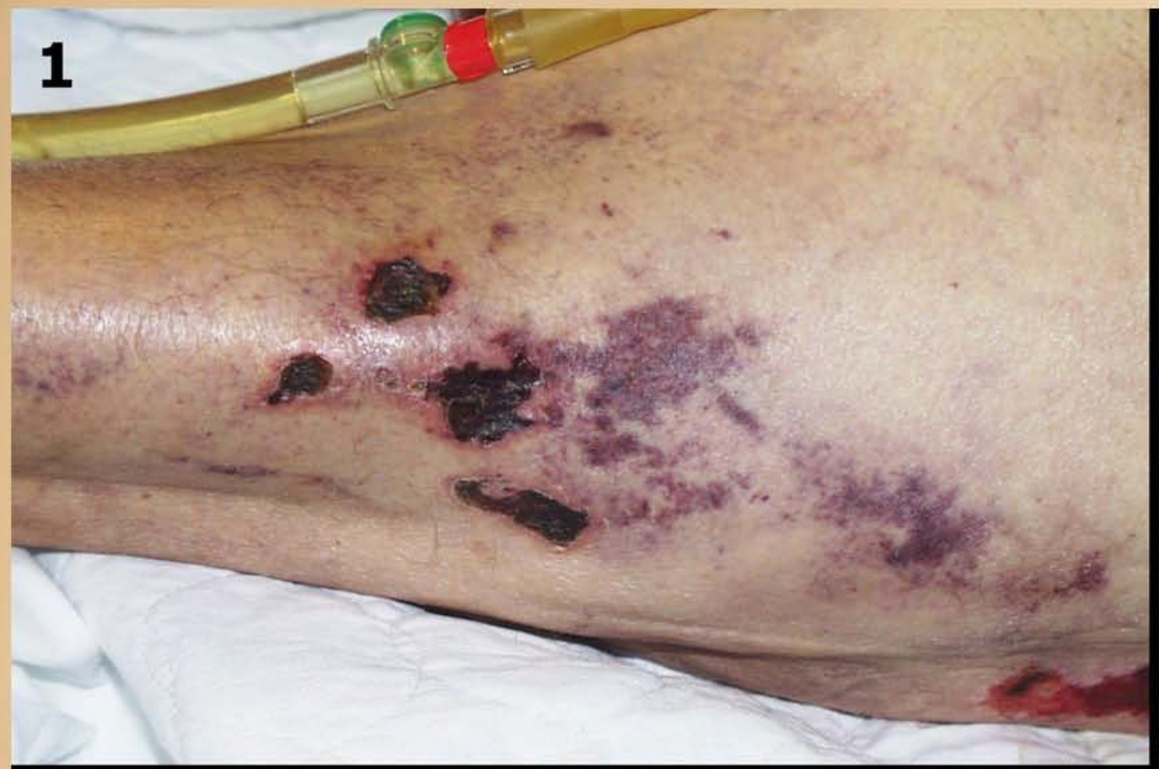


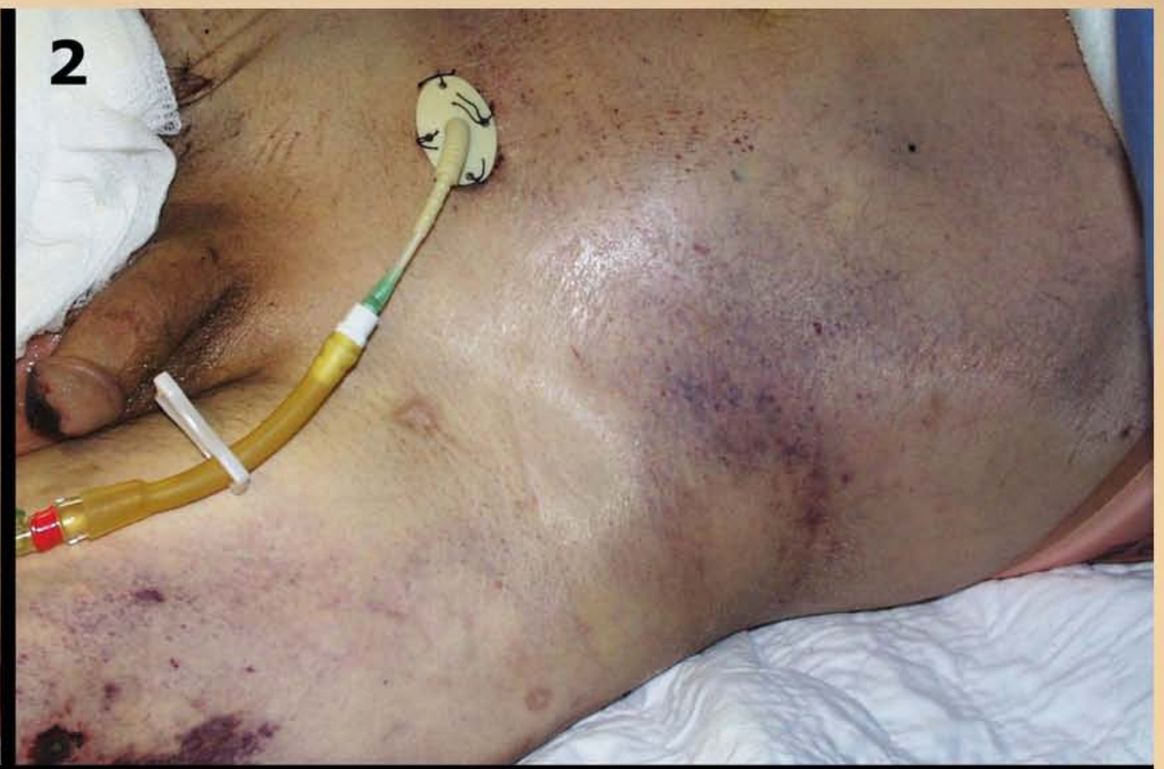
#5: 57 f Trousseau's syndrome

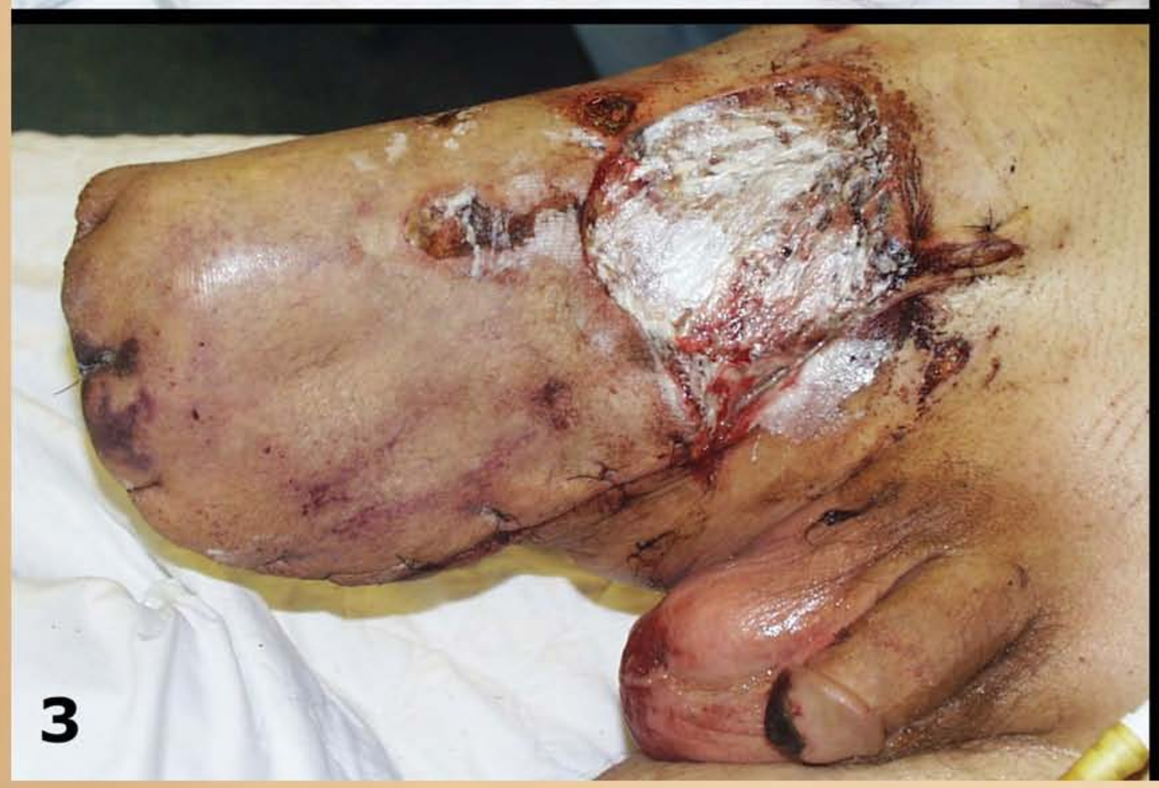


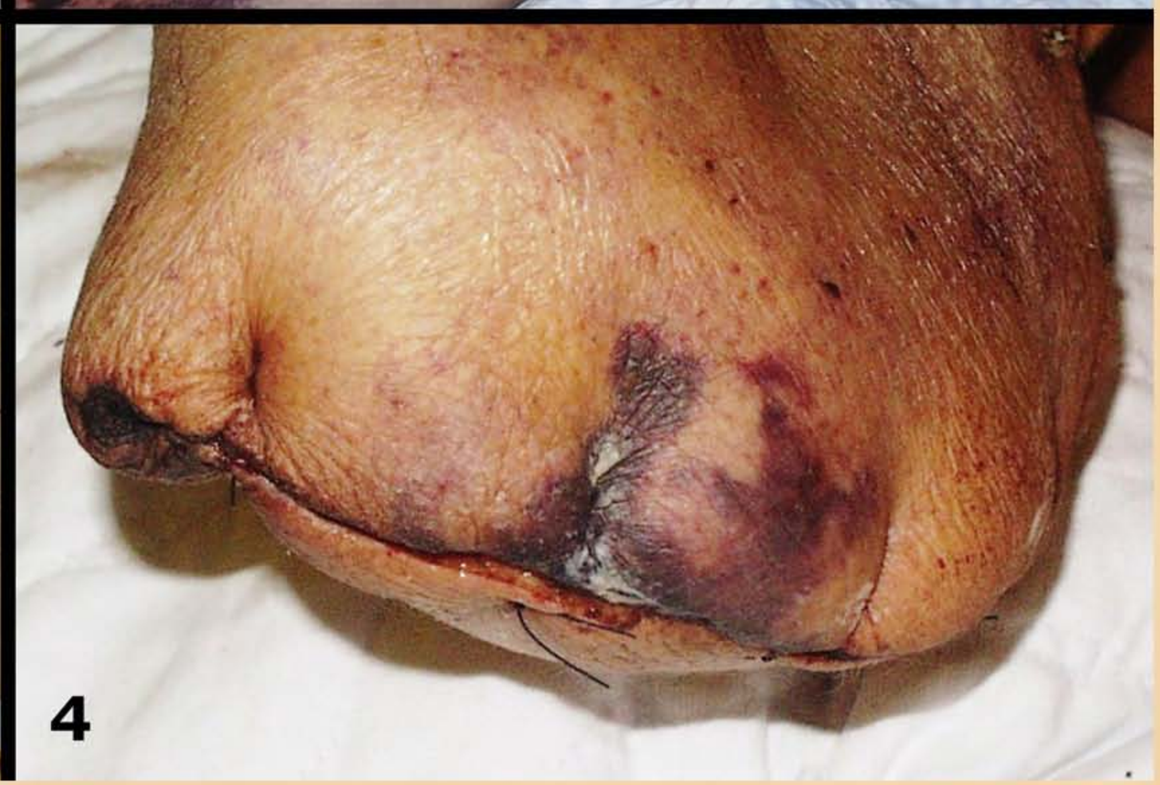
#6: 63 f rheumatoid and hypercoagulopathy

D









#7: 58 m apc resistance - hypercoagulability

D

ISCHEMIC & THROMBO-INFARCTIVE DISORDERS

Disorders of Greater Vascular System: Blood Vessels, Blood, Thrombosis & Coagulation

Pathergy occurs with *severe ischemia* & *severe inflammation*:
(1) macro-occlusive arterial diseases, devascularization, hypoperfusion.
(2) micro-occlusive disorders due to blood vessels, blood, thrombosis.
(3) autoimmunopathies, connective tissue disorders, inflammatory states.

NOMENCLATURE OF THROMBO- & MICRO-OCCLUSIVE DISORDERS

macrovasculopathies	blood & coagulation normal **vessel macro-occlusion**	disorders of the coagulation system intrinsic: the prethrombotic disorders extrinsic: examples - estrogens, cancer
hemodynamic disorders	vessels, blood, & coagulation normal **fluid dynamics abnormal**	Examples: arteriovenous malformations vascular compression, atrial fibrillation
endo-vasculopathies (intrinsic & luminal)	blood & coagulation normal **vessels abnormal**	Examples: small vessel atherosclerosis thromboangiitis, alloplastic implants
exo-vasculopathies (extrinsic & mural)	blood & coagulation normal **vessels abnormal**	Examples: calcium-phosphate disorders, immunopathies & connective tissue disorders
non-hypercoag hemopathologies	vessels & coagulation normal **blood abnormal**	Examples: red cell & platelet abnormalities, hemoglobinopathies, dys- & cryoproteinemias
hypercoagulability	vessels & blood normal **coagulation abnormal**	disorders of the coagulation system intrinsic: the prethrombotic disorders extrinsic: examples - estrogens, cancer

Set 3: Micro-Occlusive and Ulcerogenic Disorders

Vasculopathies

VASCULOPATHIES & ISCHEMIC DISORDERS - PATHERGY & WOUND FAILURE

The effects of arterial ischemia, acute and chronic, are familiar, even if most surgeons do not explicitly think about it in the terms of "wound failure" and "pathergy".

Syndromic risks are of common experience:

an amputation that infarcts then requires higher amputation
a saphenous donor site that dehisces or necroses
sternal necrosis after use of the mammary artery
flap necrosis with hematopathologies
flaps distal to a vascular lesion
etc

Strategies and methods for treating or preempting problems are well developed.

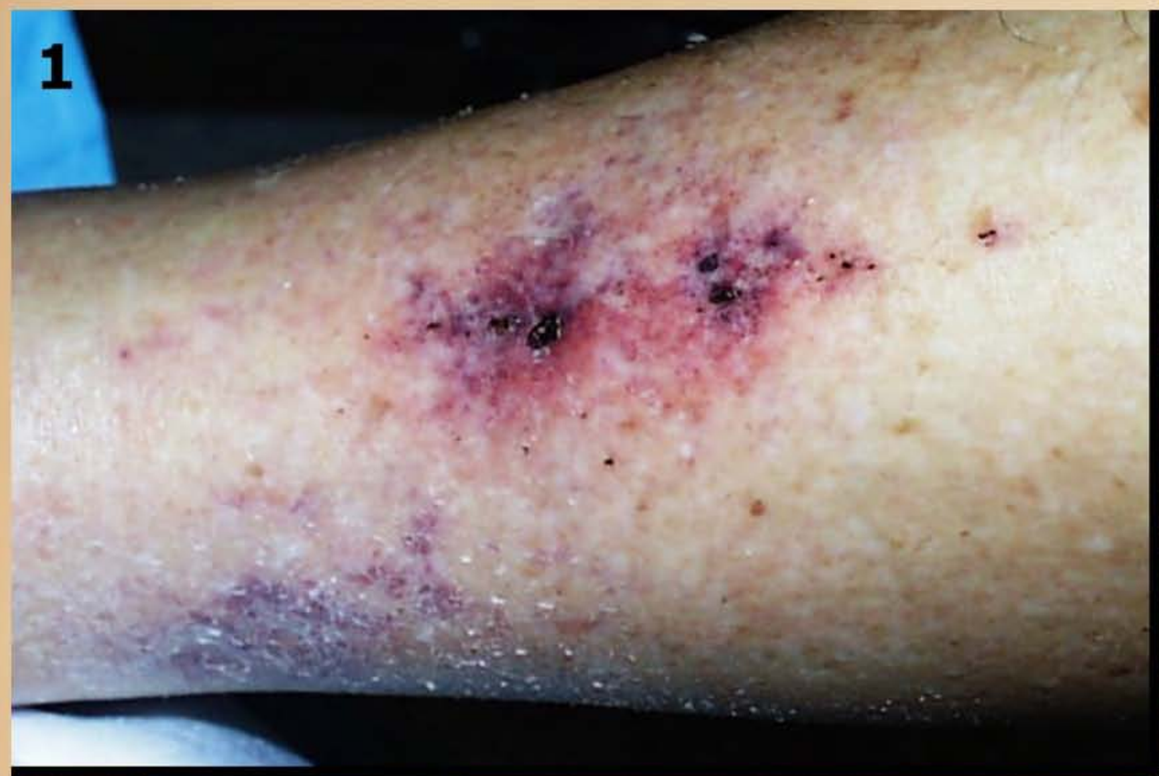
Revascularization techniques
Pharmacological support
Hyperbaric oxygen

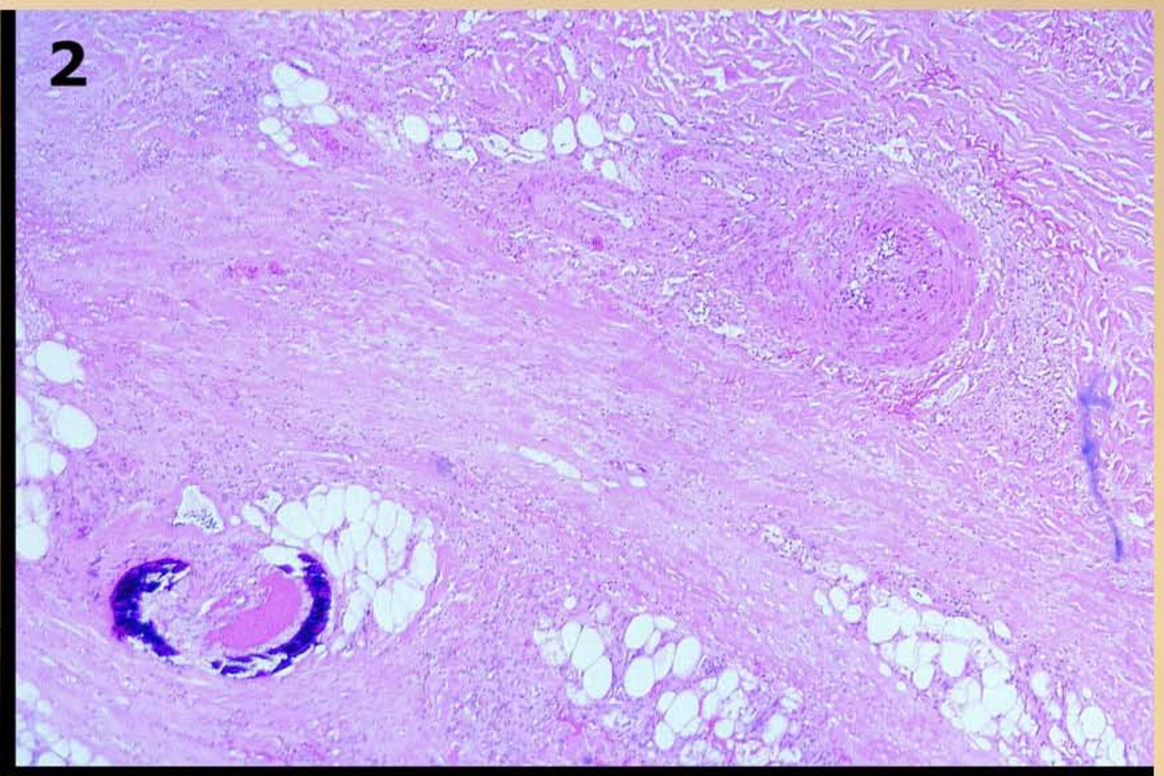
Macro and degenerative arterial diseases
atherosclerosis
arteriosclerosis obliterans
medial calcific a.s. (Monckeberg's)
fibromuscular hyperplasia's
lupus-crst angiopathy

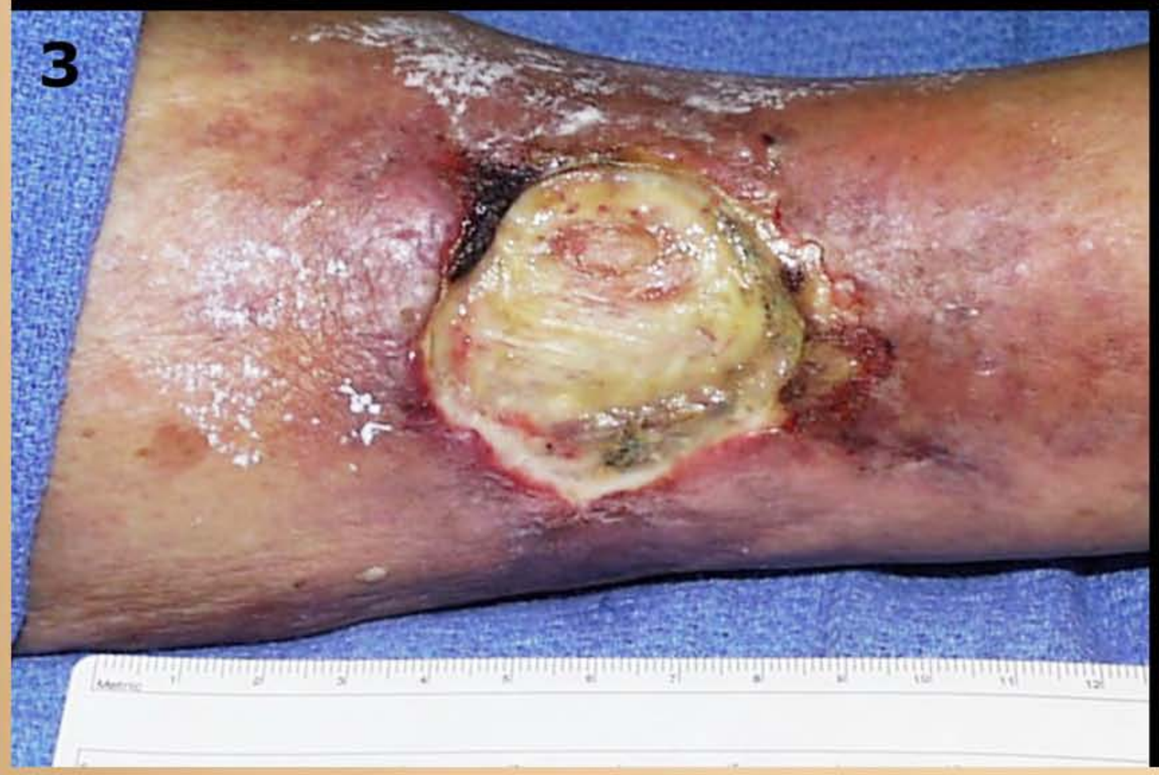
Micro and immunopathic vasculitides
polyarteritis nodosa
leukocytoclastic
autoimmune
giant cell
temporal
thromboangiitis
Behcet's
Takayasu's
lupus-crst
hypersensitivity
venous

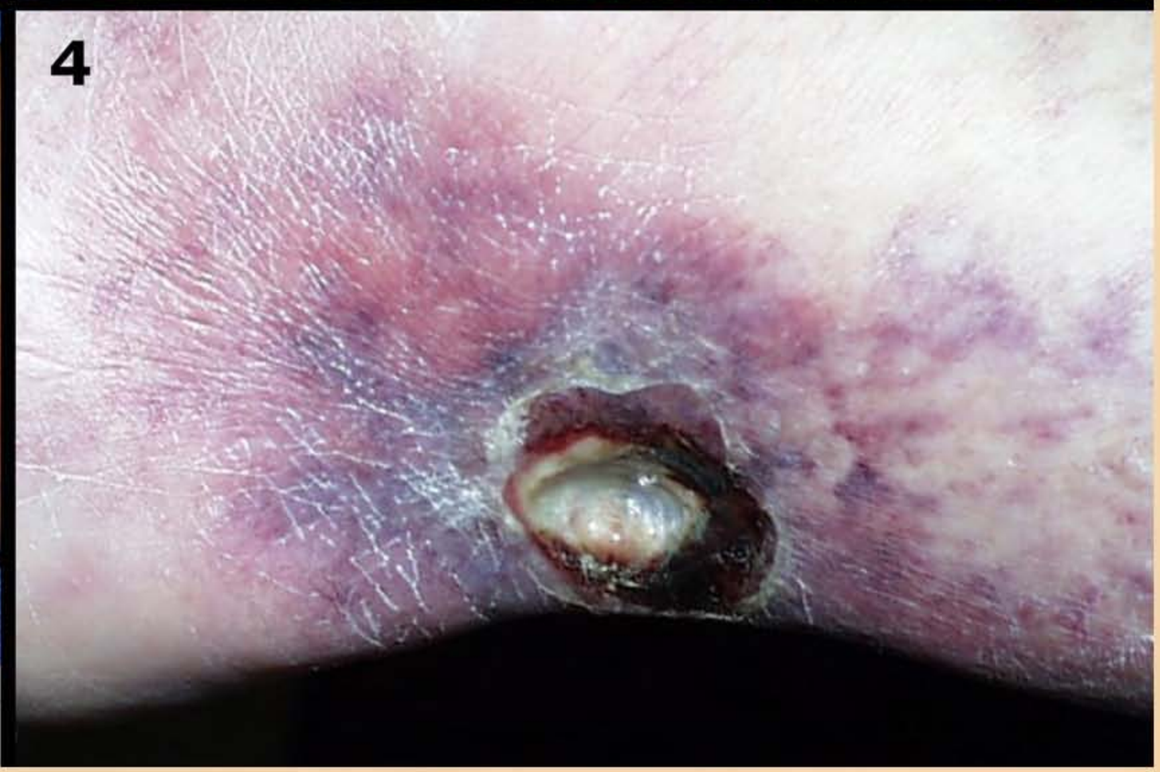
Metabolic and miscellaneous
hyperparathyroidism - calciphylaxis
diabetes
amyloid

. . . etc.



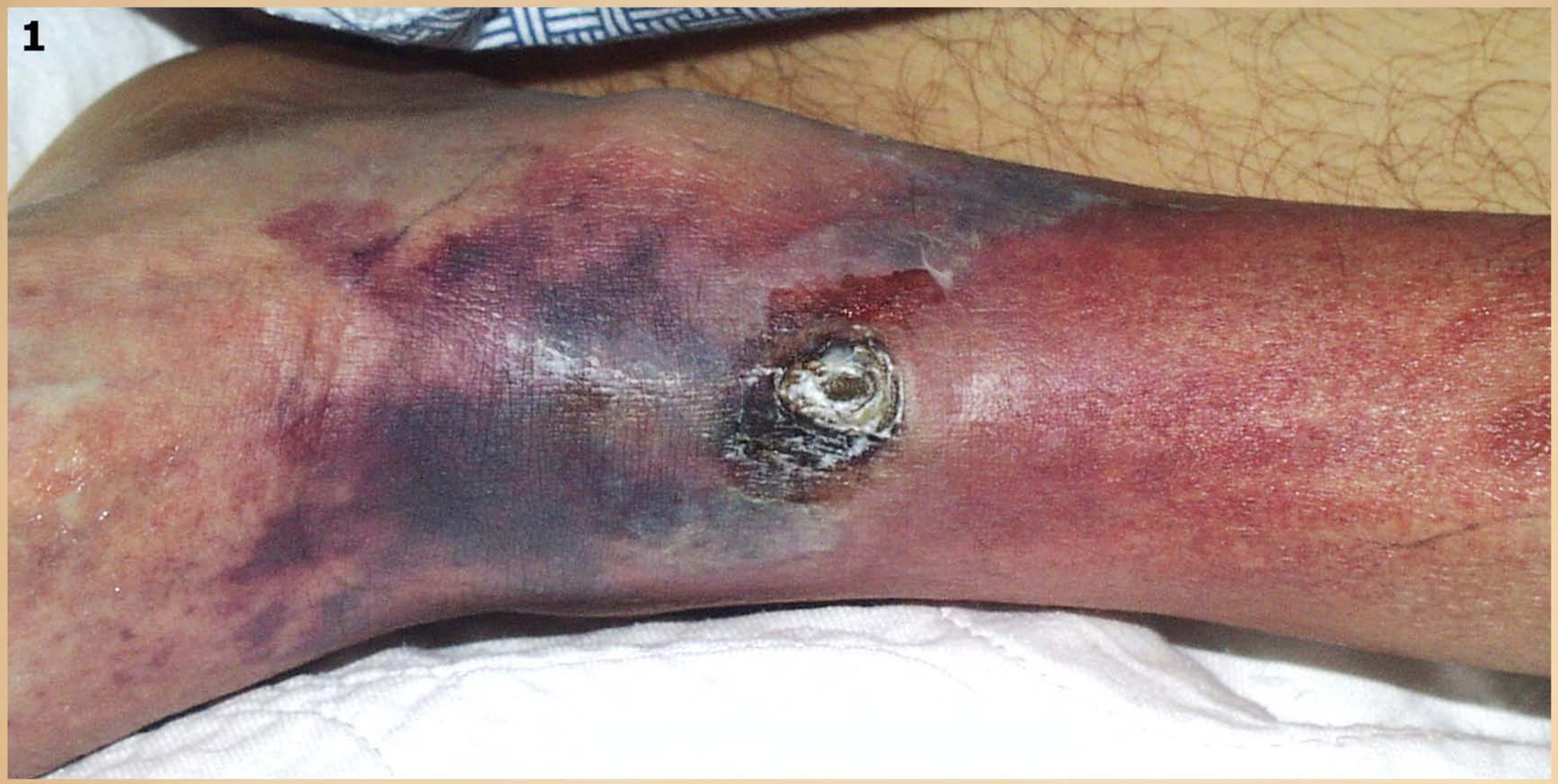




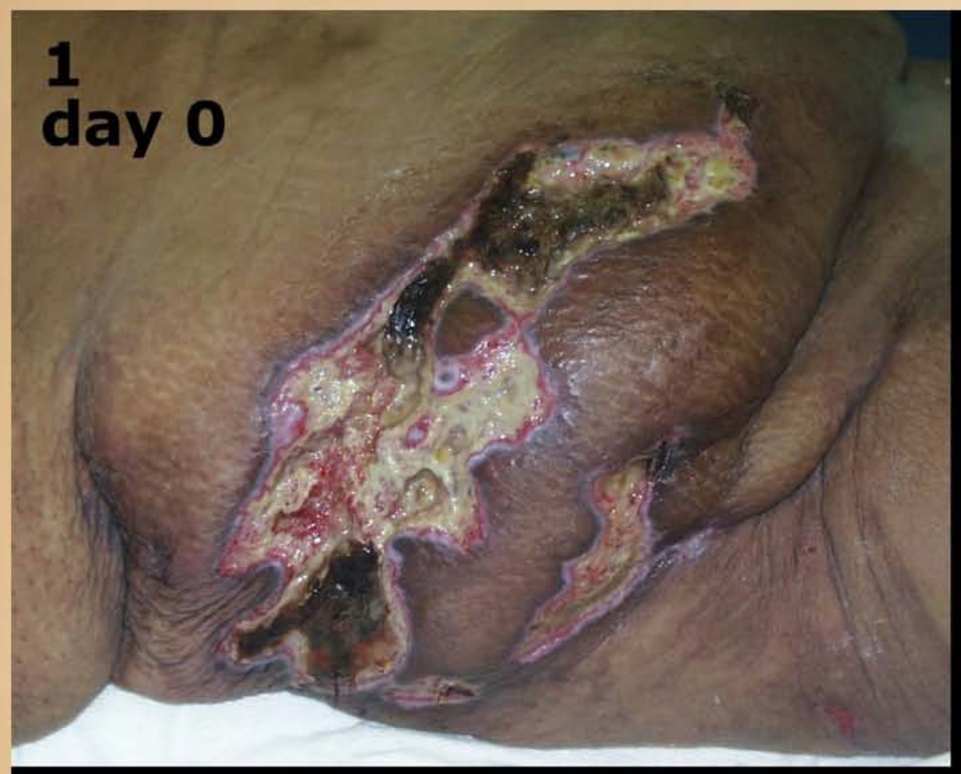


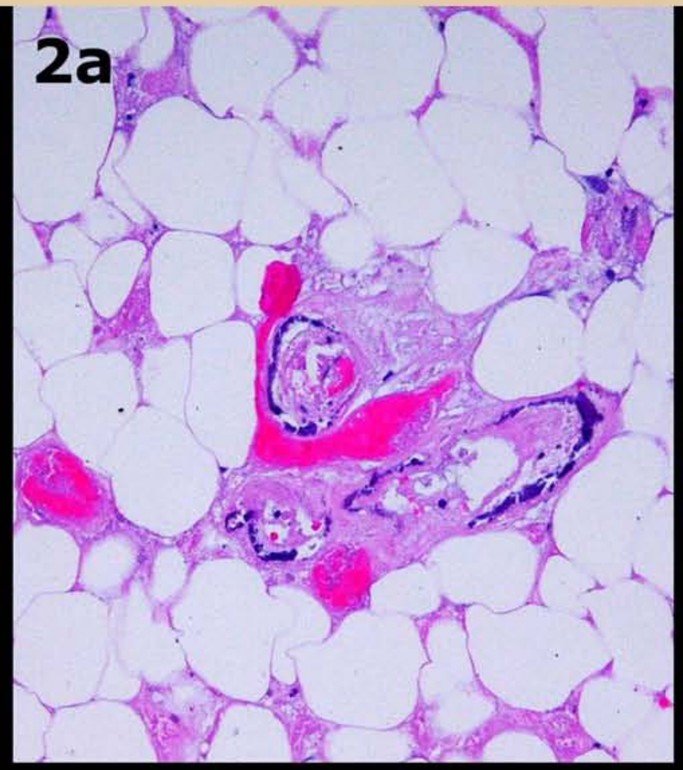
#8: 78 m aso-pvod

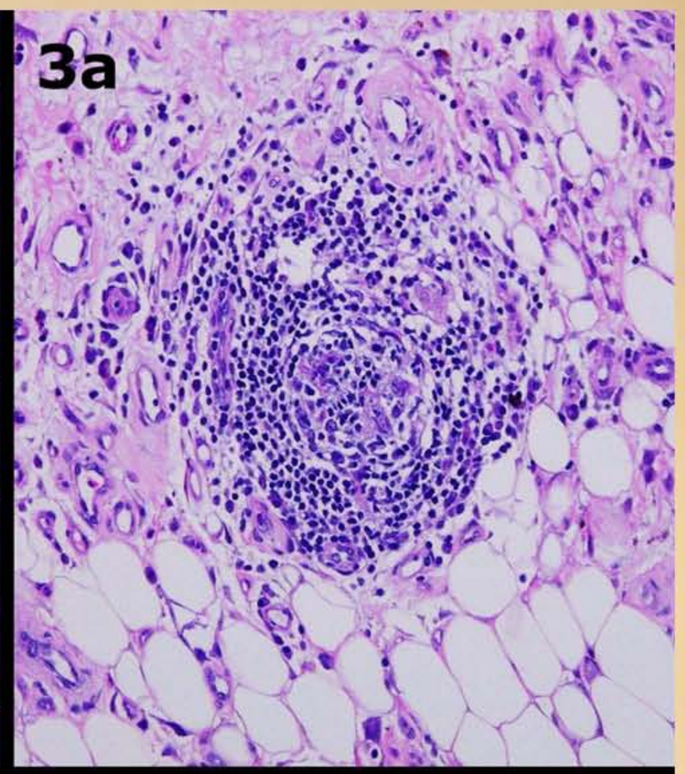
D

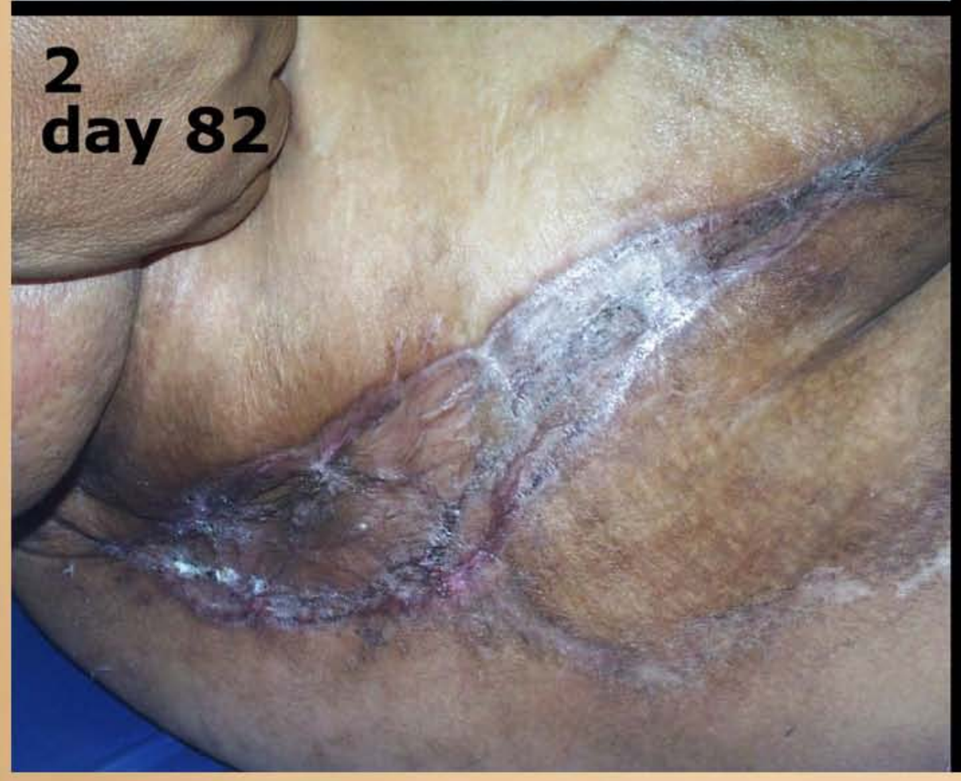


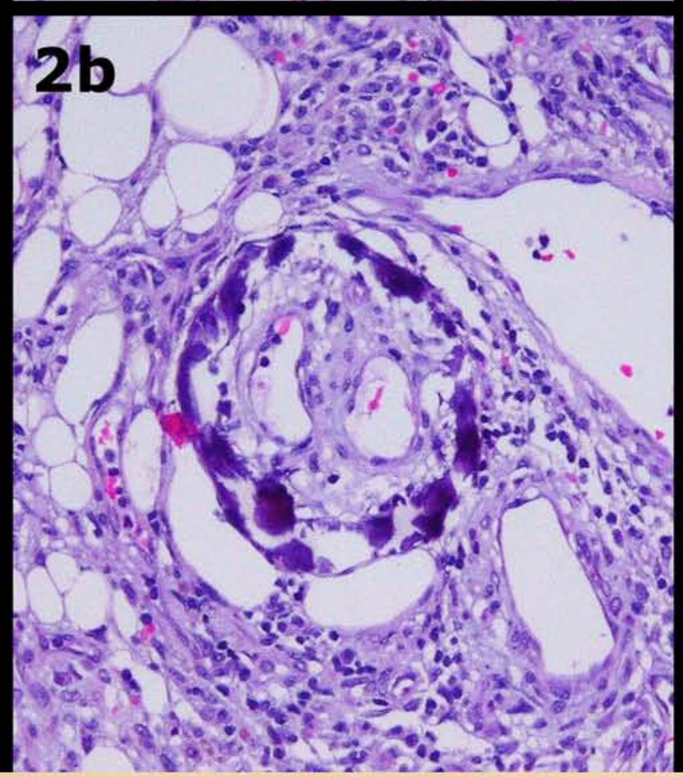
#9: 47 m diabetes with aso-pvod

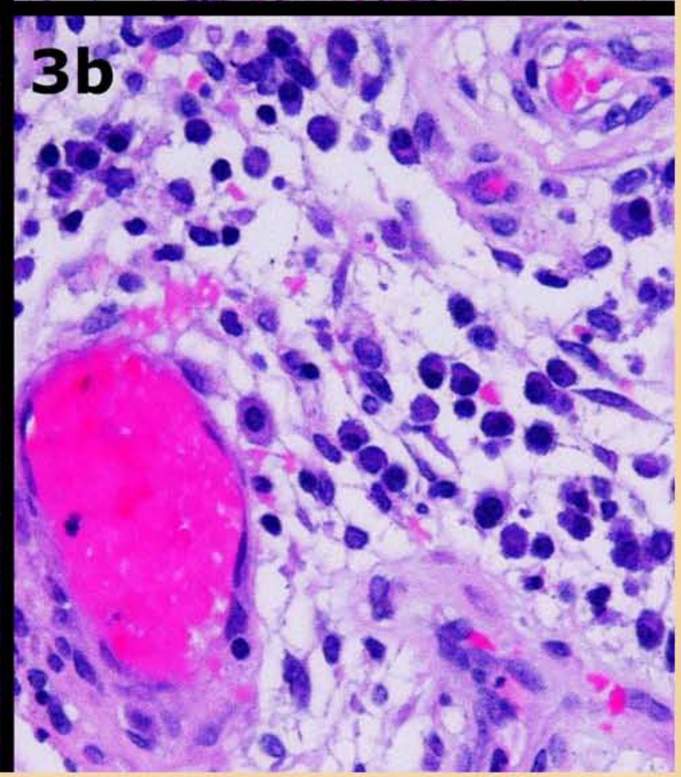












#10: 51 f dm-esrd-pth with calciphylaxis

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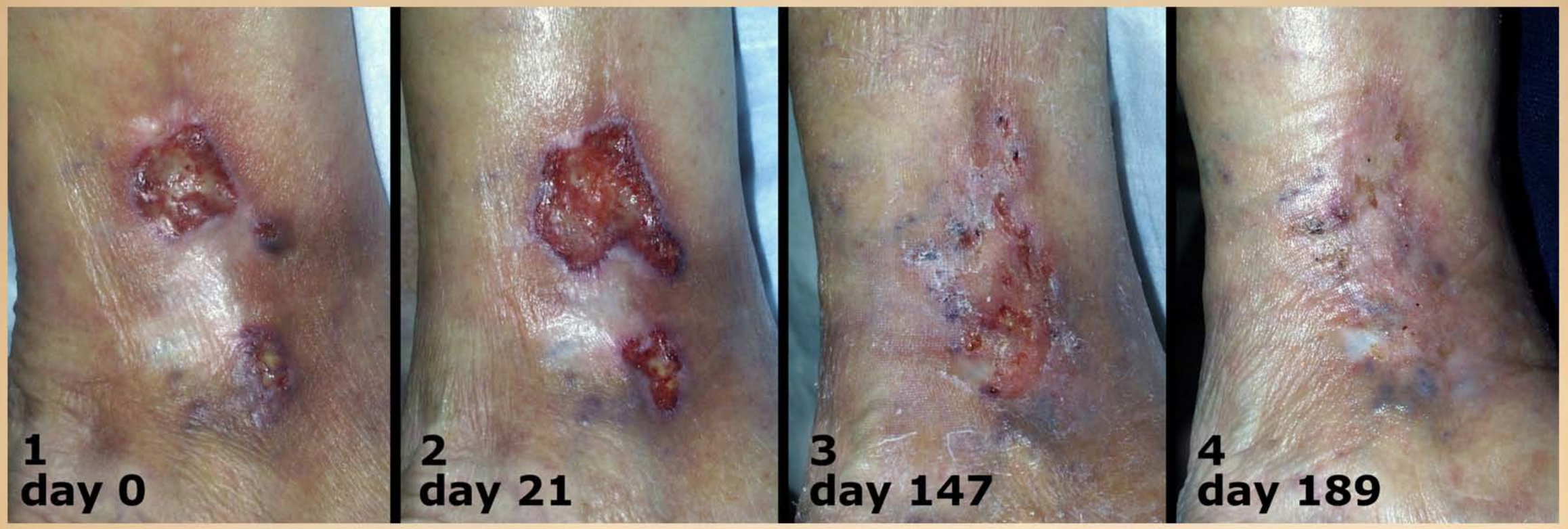
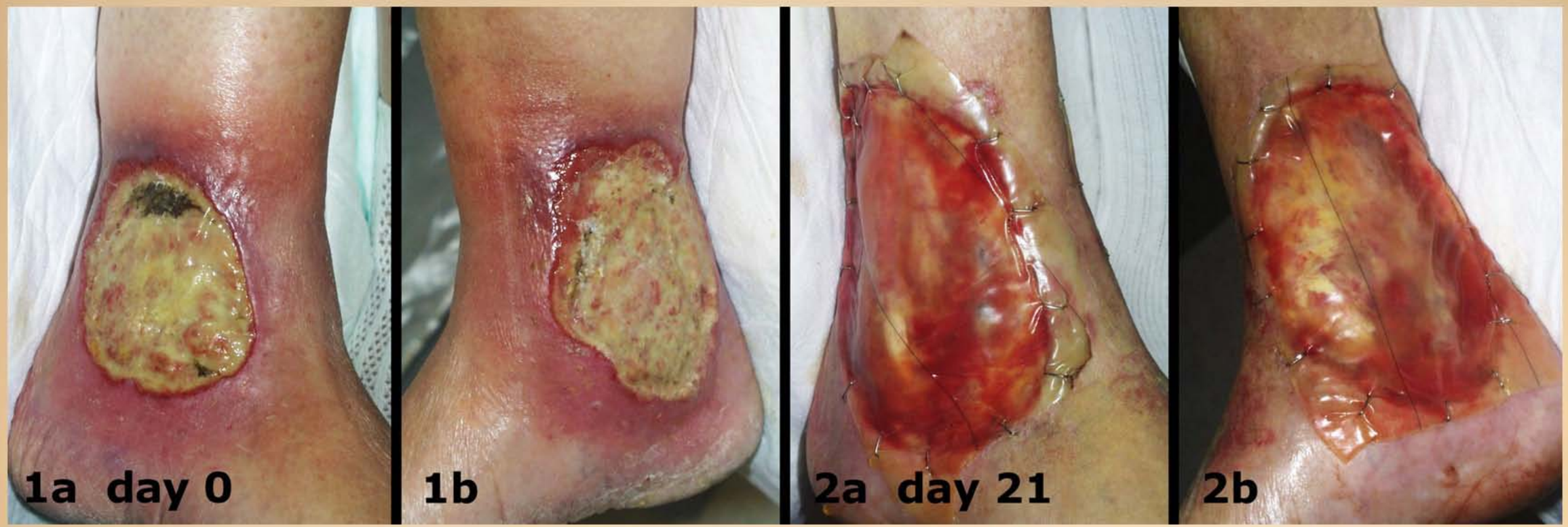
Set 4: Micro-Occlusive and Ulcerogenic Disorders

Hematopathologies

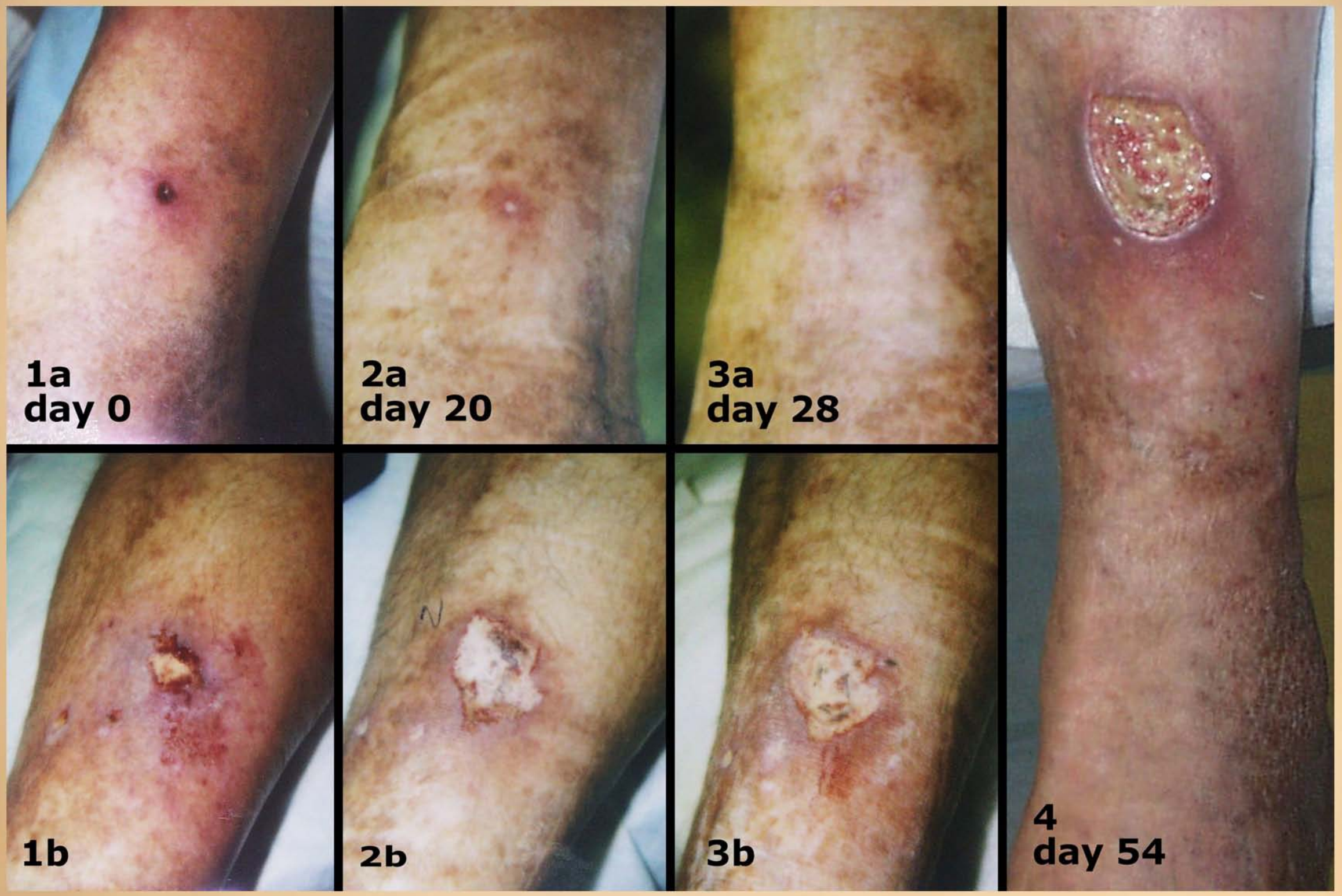


#11: 88 f hereditary spherocytosis



#12: 72 m polycythemia vera and anticardiolipins

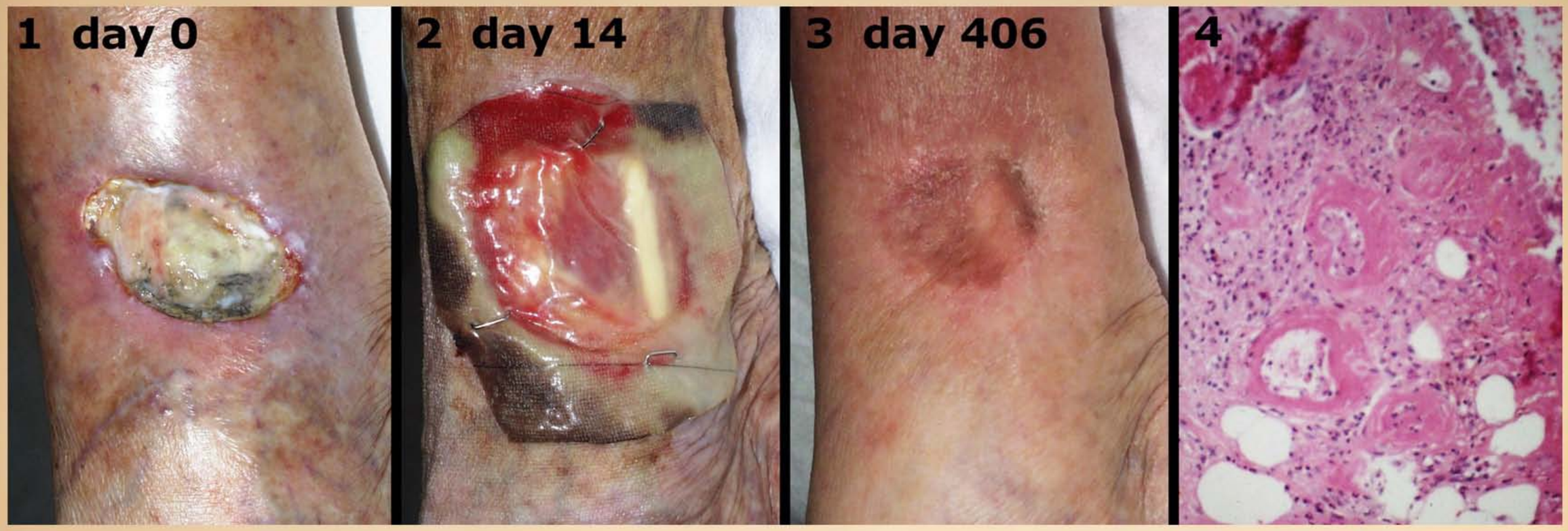
D



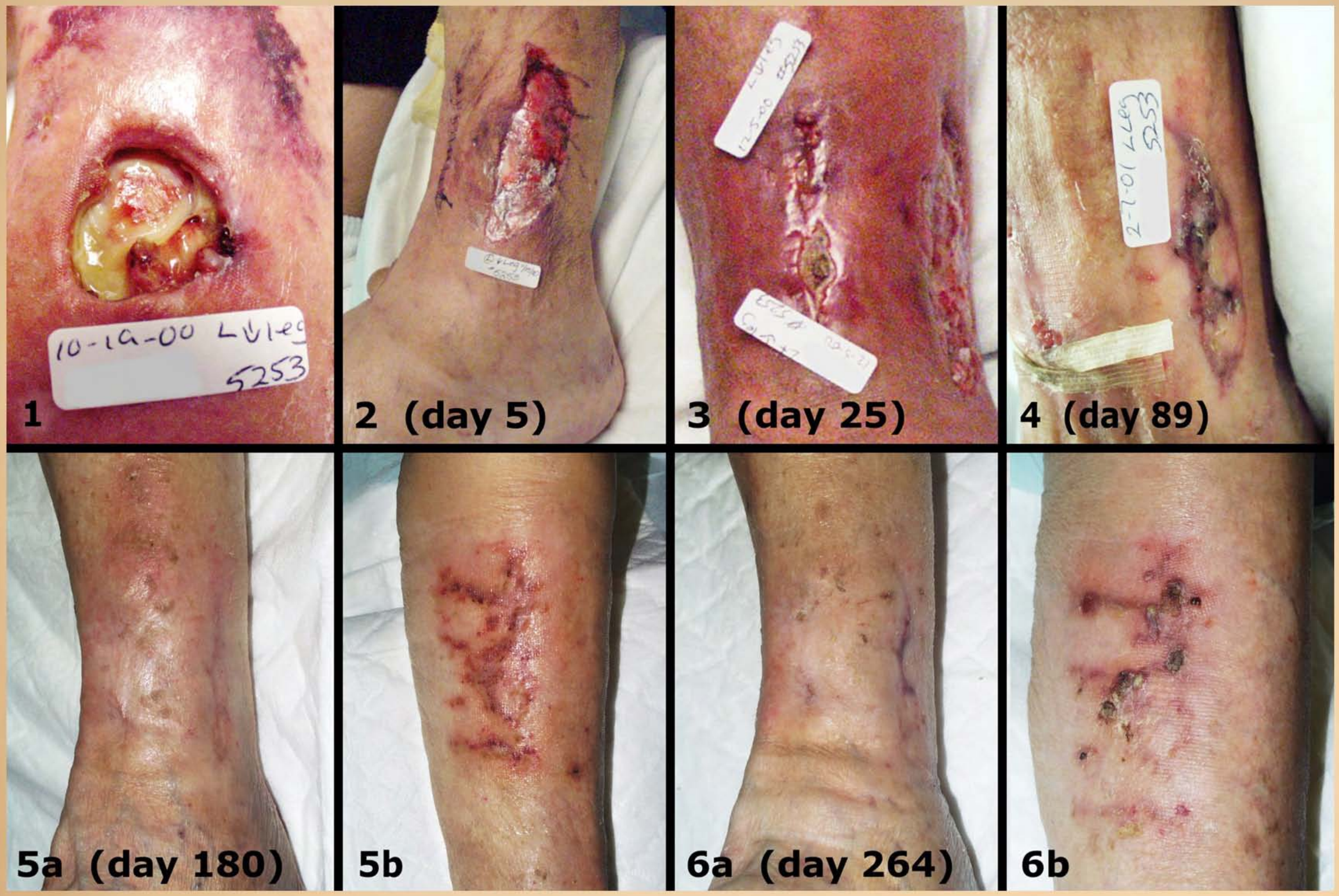
#13: 54 m polycythemia vera and f-V Leiden

Set 5: Micro-Occlusive and Ulcerogenic Disorders

Hypercoagulopathies



#14: 69 f hypercoagulopathy (protein C and cryoglobulins)



#15: 72 f hypercoagulopathy (anticardiolipins)

IMMUNOPATHY • SET 6 • INFLAMMATION

Auto-Immune Disorders & Wound Pathergy

AUTO-IMMUNOPATHY & INFLAMMATION - PATHERGY & WOUND FAILURE

Auto-immunopathies and connective tissue disorders deserve special emphasis.

Strongly correlated with hypercoagulable states.

The immunity & coagulation duality causes both inflammatory-lytic and thrombo-infarctive effects.

These disorders are among the most significant causes of chronic ulceration and impaired wound healing

These disorders are among the most under-appreciated causes of wound pathergy and surgical complications.

In any patient with a major wound pathergy event, it is essential to evaluate for connective tissue and hematological disorders.

Classic Connective Tissue Disorders
- rheumatoid
- lupus
- sjögren's
- scleroderma - crst
- poly- & dermatomyositis
- ankylosing spondylitis
- behçet's
- wegener's
- sarcoidosis
- fam. med. fever
- mctd (mixed)
- uctd (undifferentiated)

Vasculitides
- polyarteritis nodosa
- leukocytoclastic
- autoimmune
- giant cell
- hypersensitivity
- thromboangiitis
- venous

Fibro-adipose Panniculopathies
- weber-christian
- erythema nodosum
- nodular fasciitis
- eosinophilic
- lympho-plasmacytic
- necrobiosis lipoidica

Fibrous Panniculopathies & Myopathies
- synovitis & arthropathies
- polyserositis
- polymyalgia rheumatica

Inflammatory Dermatoses
- eczema
- pyoderma gangrenosum
- erythema nodosum
- pemphigus / pemphigoid
- sweet's

Visceral
- crohn's
- ulcerative colitis
- bowel-derma-arthritis (badas)
- autoimmune hepatitis & biliary
- autoimmune thyroiditis
- autoimmune diabetes
- rheumatic carditis
- autoimmune neuropathies
- autoimmune myopathies
- myasthenia gravis
- multiple sclerosis
- autoimmune sialoadenitis
- autoimmune nephritis
- autoimmune pneumonitis

Miscellaneous
- granulomatous disorders
- drug eruptions & lupus

. . . and Many Others

Concept of a common autoimmune disease

MCTD – UCTD - NCTD

UNDERSTANDING HOW IMMUNOPATHIES AFFECT WOUND HEALING

PREDICATES

All mesenchymal stroma is composed of 2 cell types (& their derivative structures):
fibroblasts, angiocytes

Wound healing, the mesenchymal wound module, depends on 2 cell types:
fibroblasts, angiocytes

The target of mesenchymal autoimmune attack is the collagen-vascular stroma, i.e.
fibroblasts, angiocytes

1

CVD - CTD AS THE DISEASES OF WOUND HEALING

Basic syllogism :

A

Diseases that affect collagen-vascular connective stroma
ipso facto affect the mesenchymal wound module.

B

The autoimmune CVD-CTD diseases are diseases
that affect the collagen-vascular connective stroma.

Therefore, the CVD-CTD are diseases of wound healing.

2

INTRINSIC WOUND CHRONICITY AS A CVD - CTD

Basic syllogism :

A

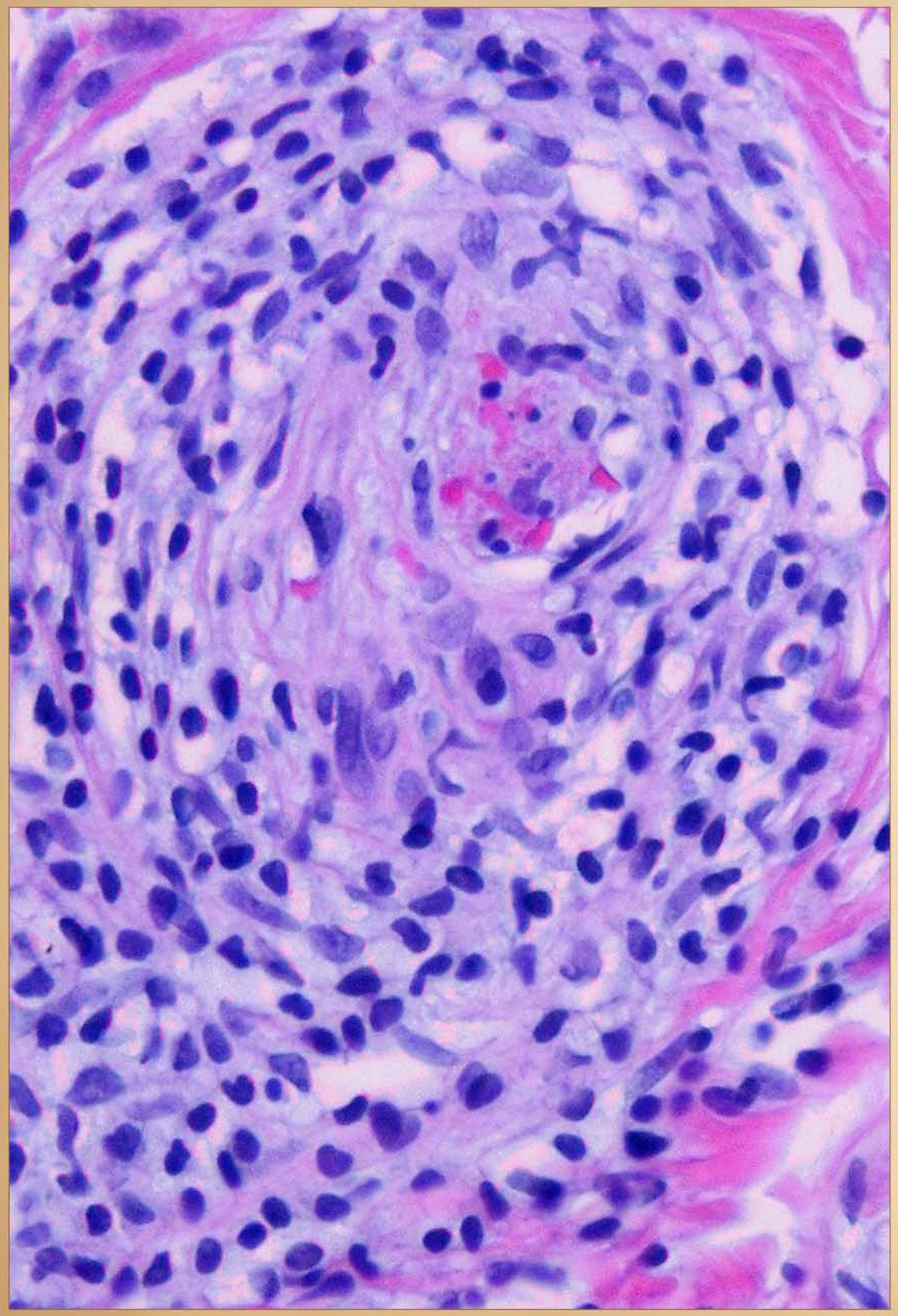
Autoimmune diseases that affect the
collagen-vascular stroma are the CVD-CTD.

B

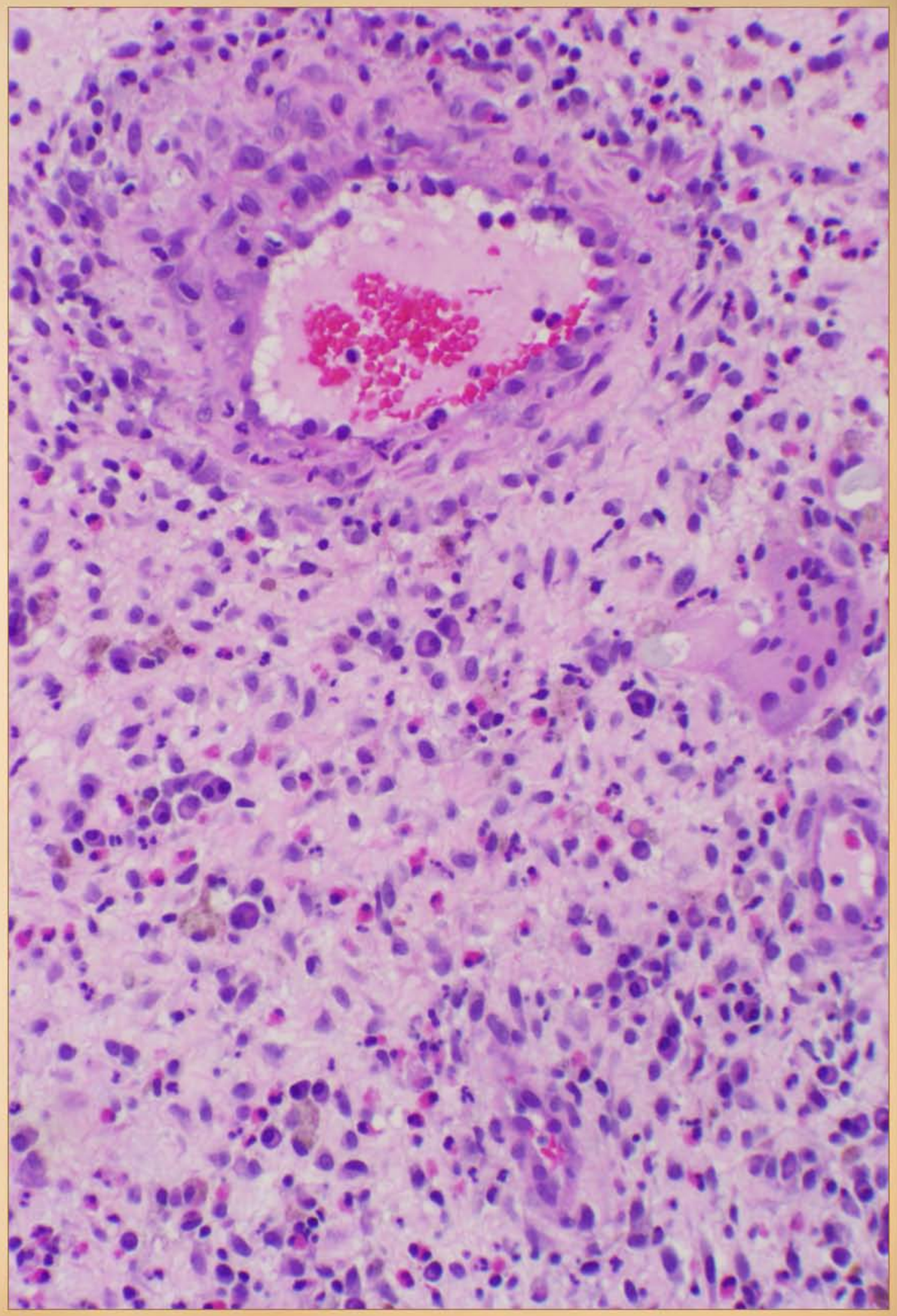
Intrinsic lymphoid wound chronicity is an autoimmune disorder
that affects the collagen-vascular connective stroma.

Therefore, intrinsic wound chronicity is a CVD-CTD.

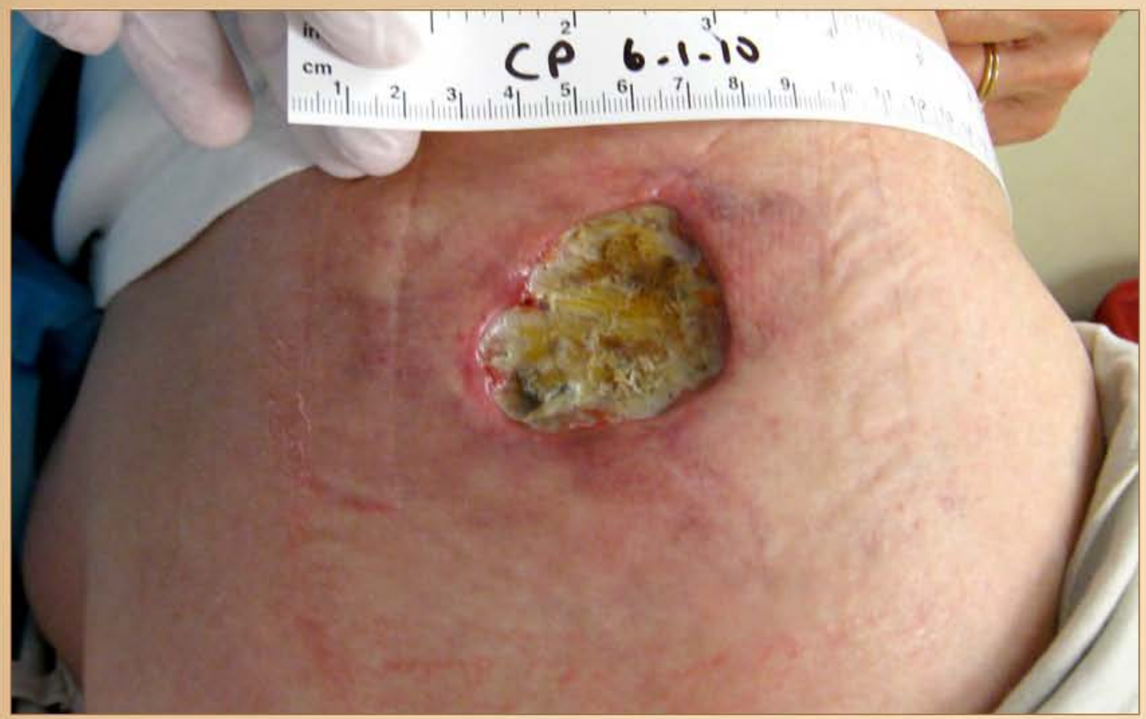
74 f; advanced rheumatoid arthritis; hypercoagulopathy; chronic leg ulcers

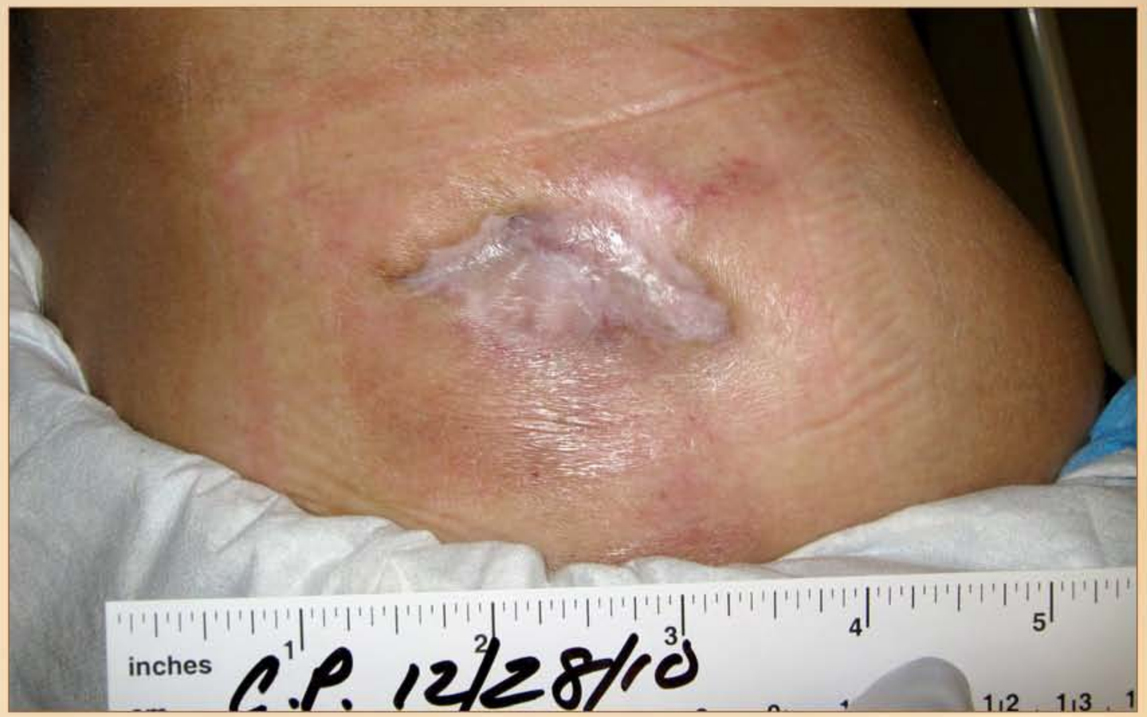


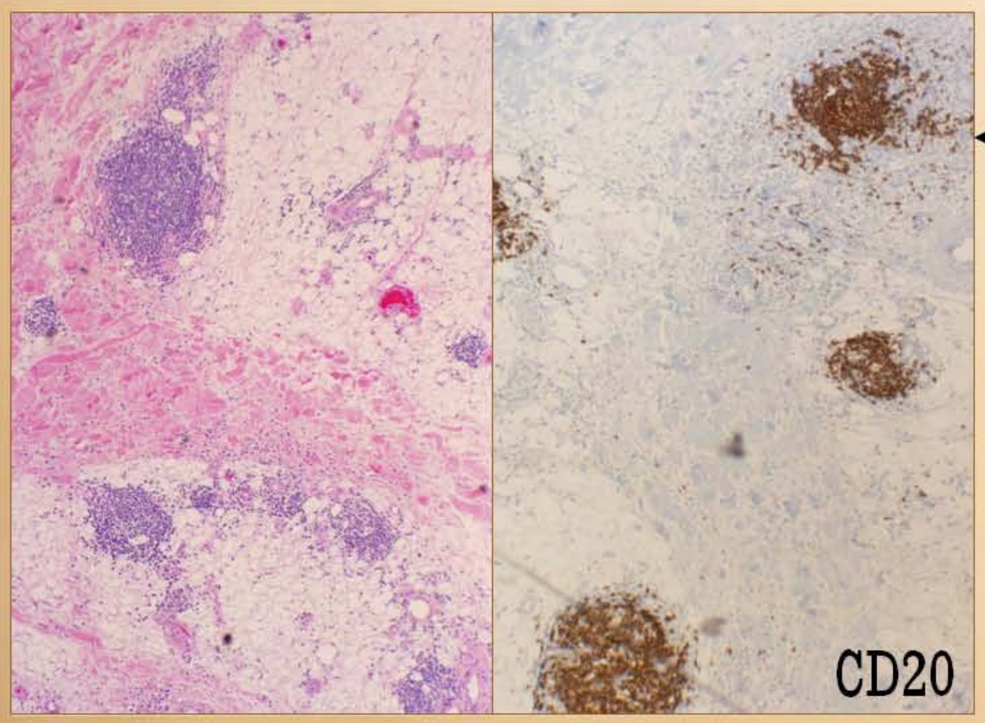
33 m; spine injury paraplegia; pemphigoid; pressure & diffuse pemphigoid ulcers

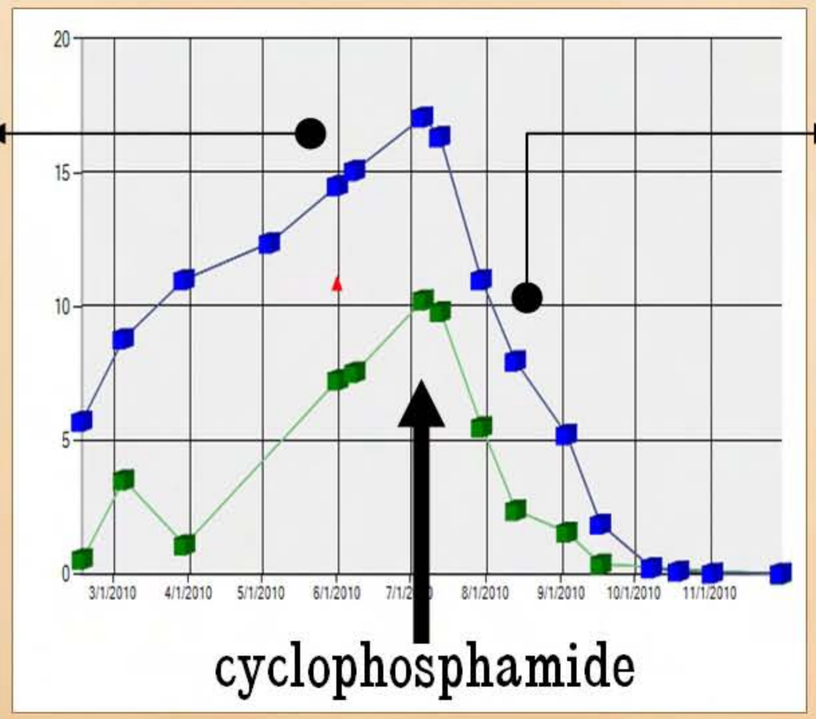


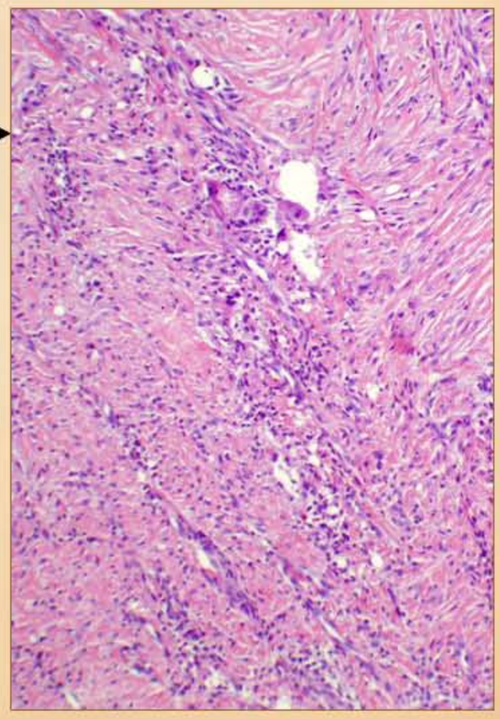
AUTO-IMMUNOPATHY & WOUND FAILURE - RESOLUTION WITH ANTI-IMMUNE RX

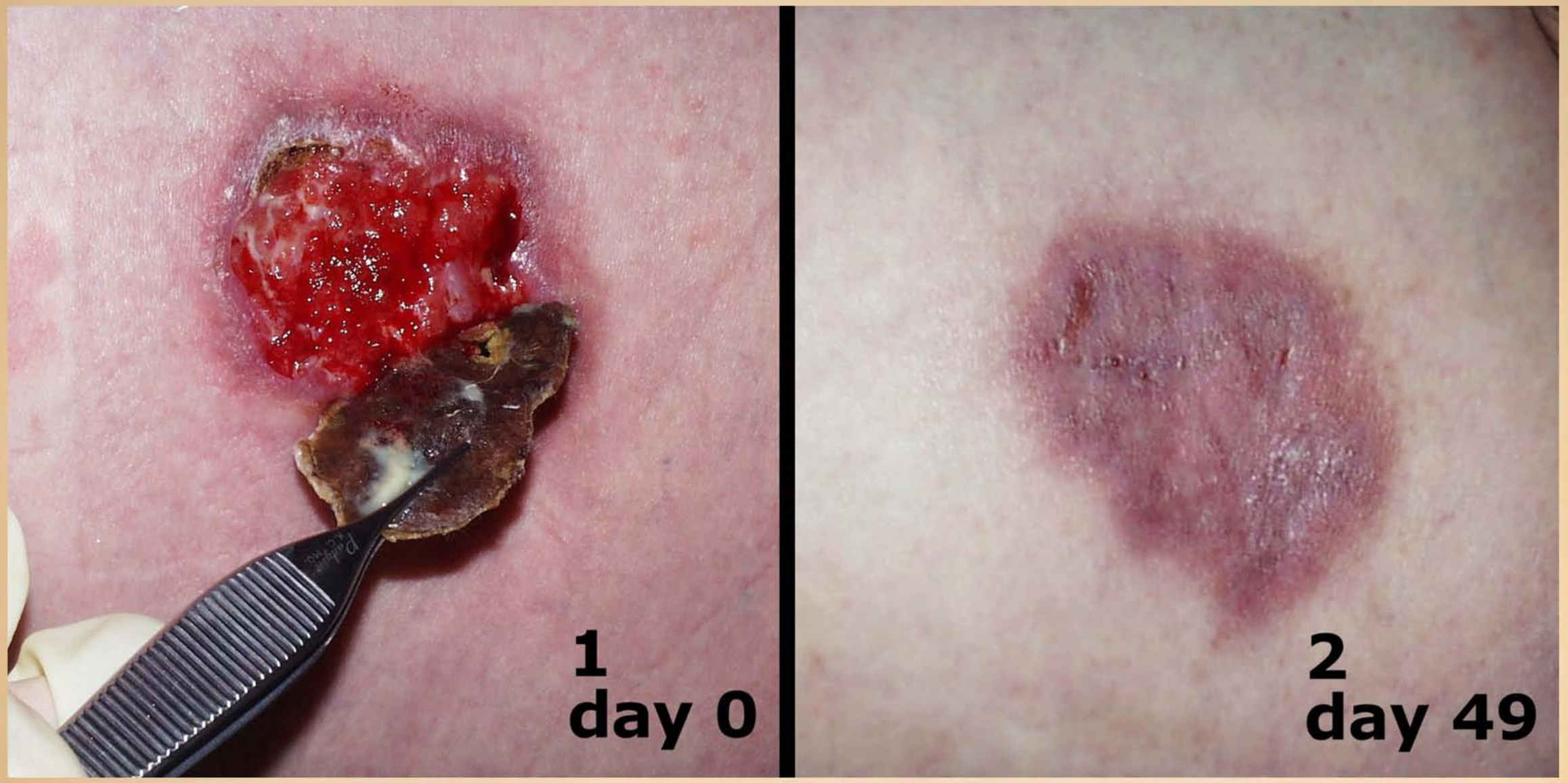




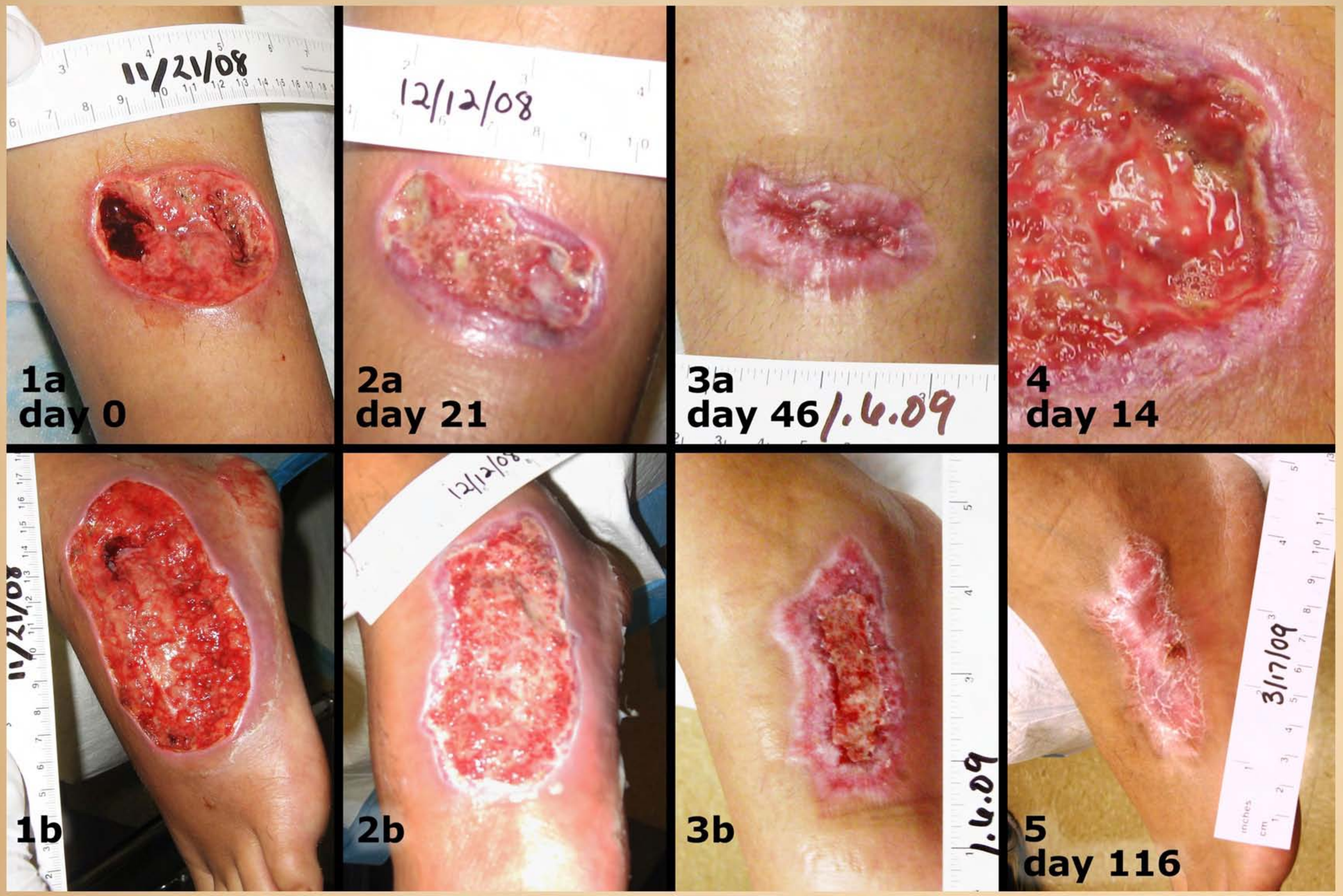








#16: 50 f pyoderma gangrenosum



#17: 26 f pyoderma gangrenosum

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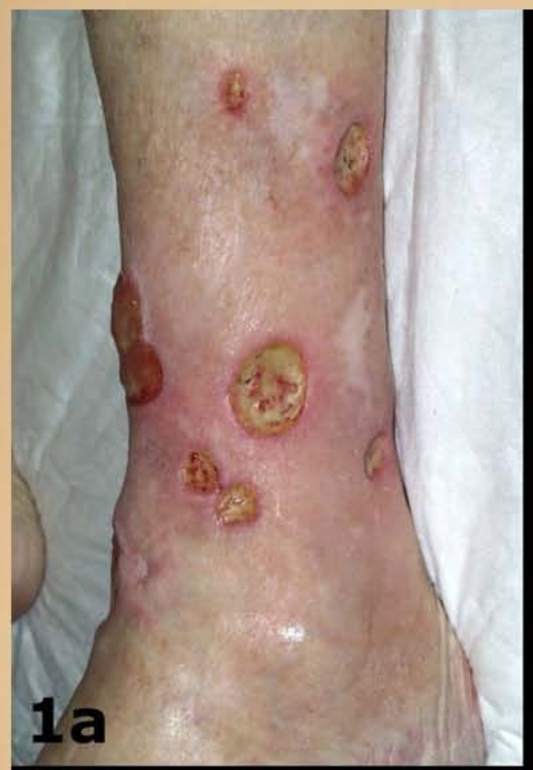
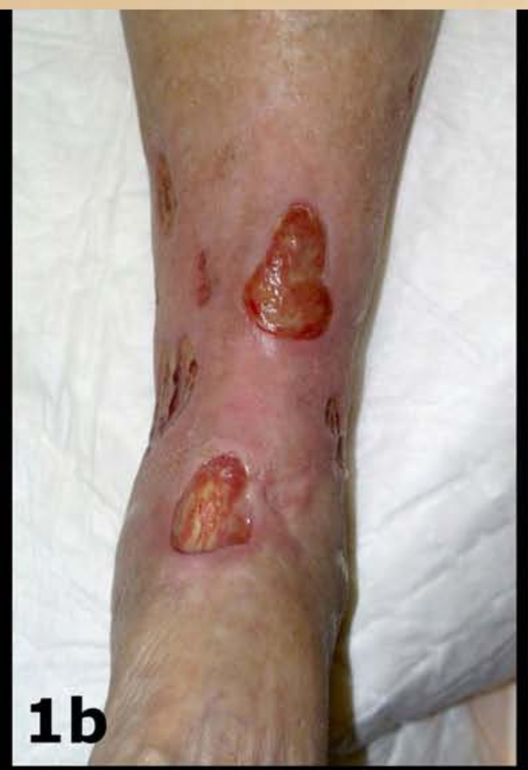
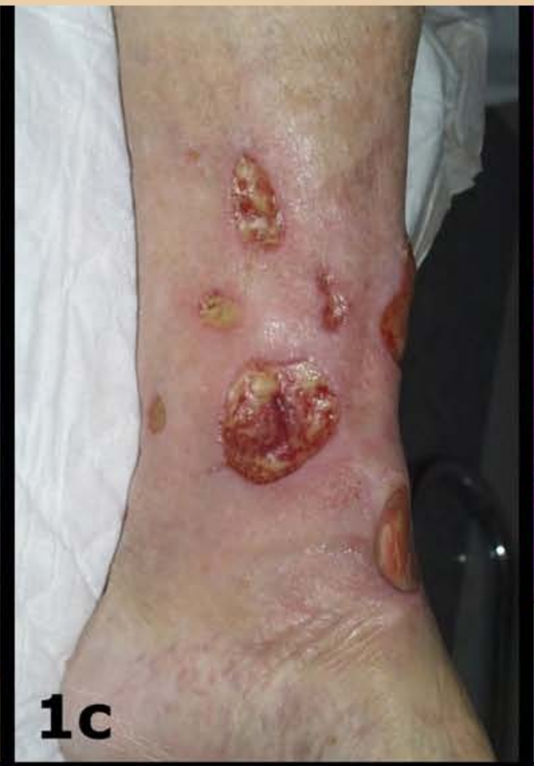
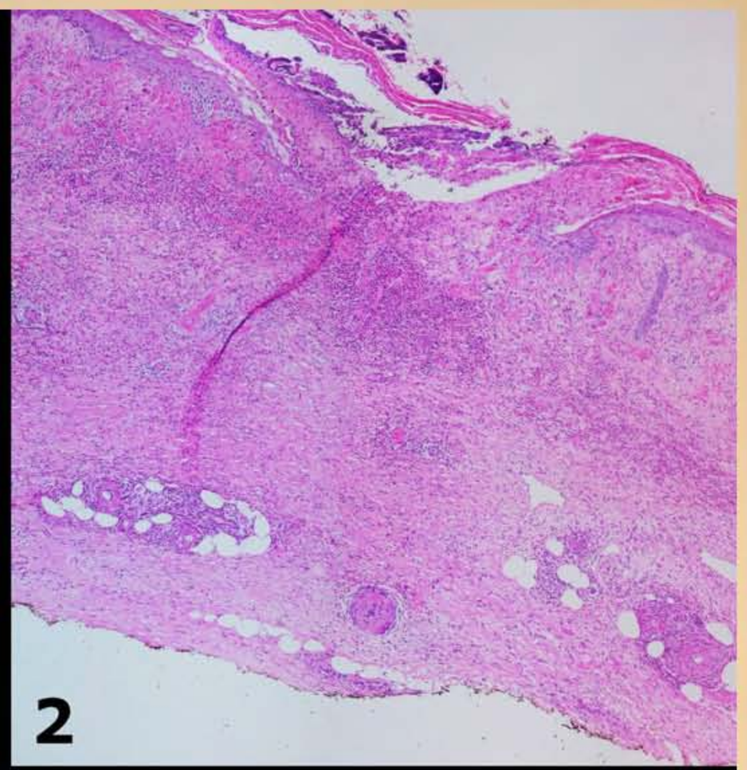


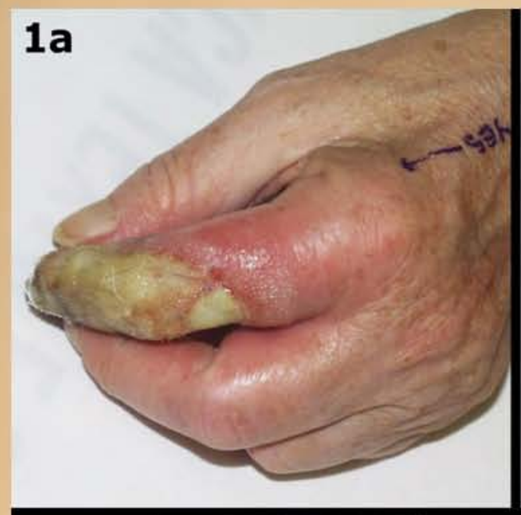


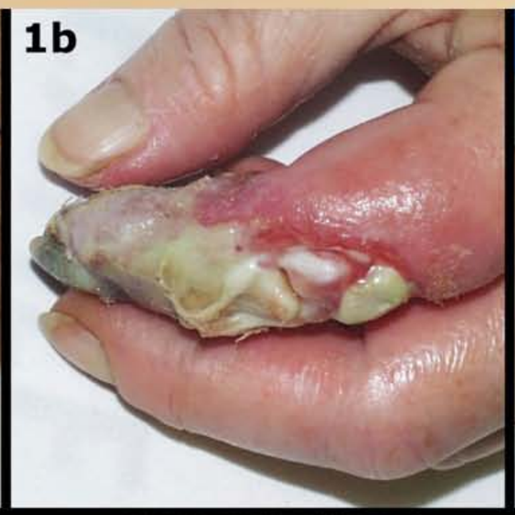


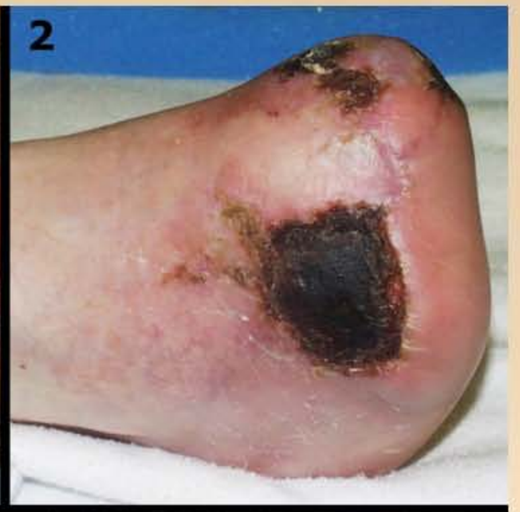


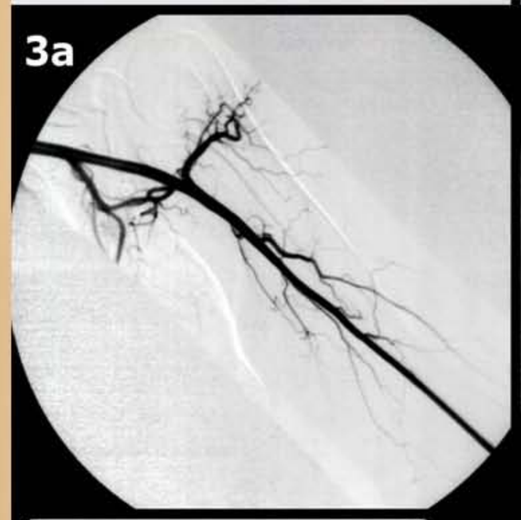
#18: 85 f polyarteritis nodosa

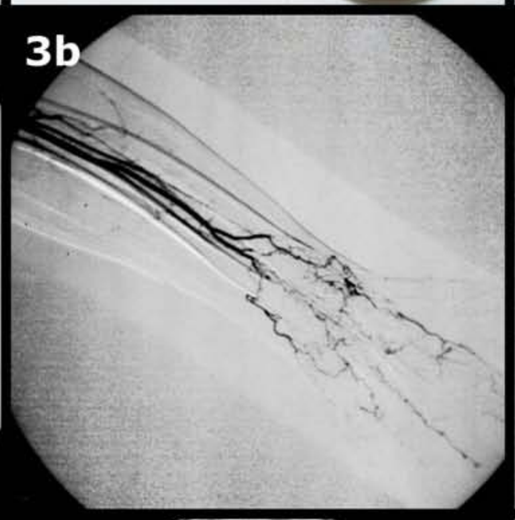
D

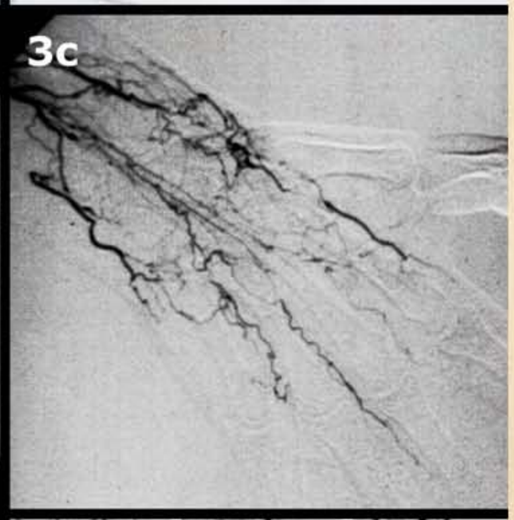


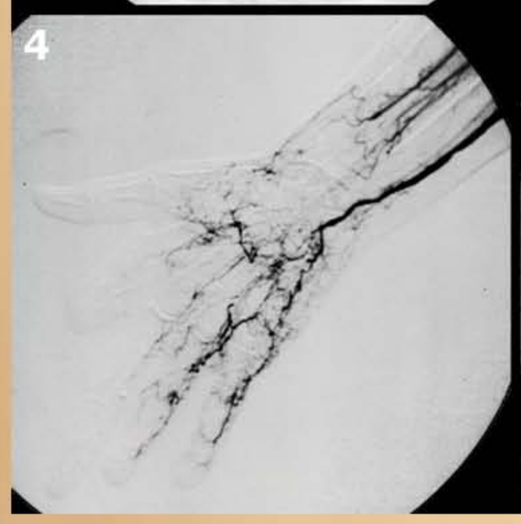


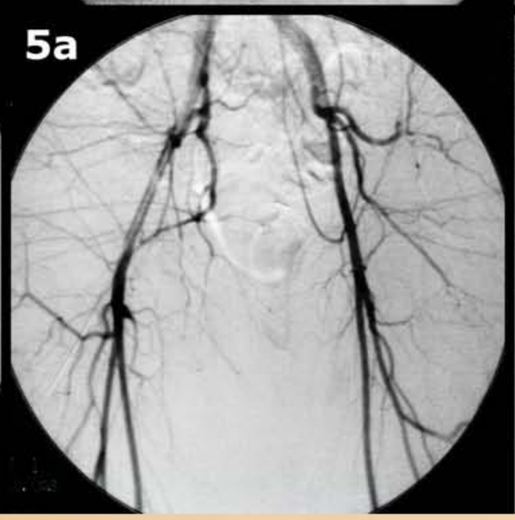


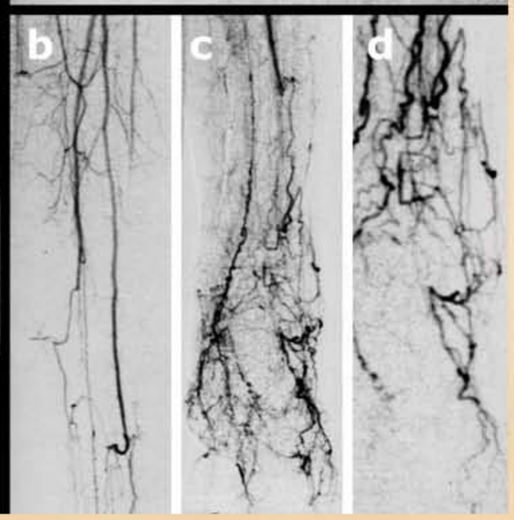


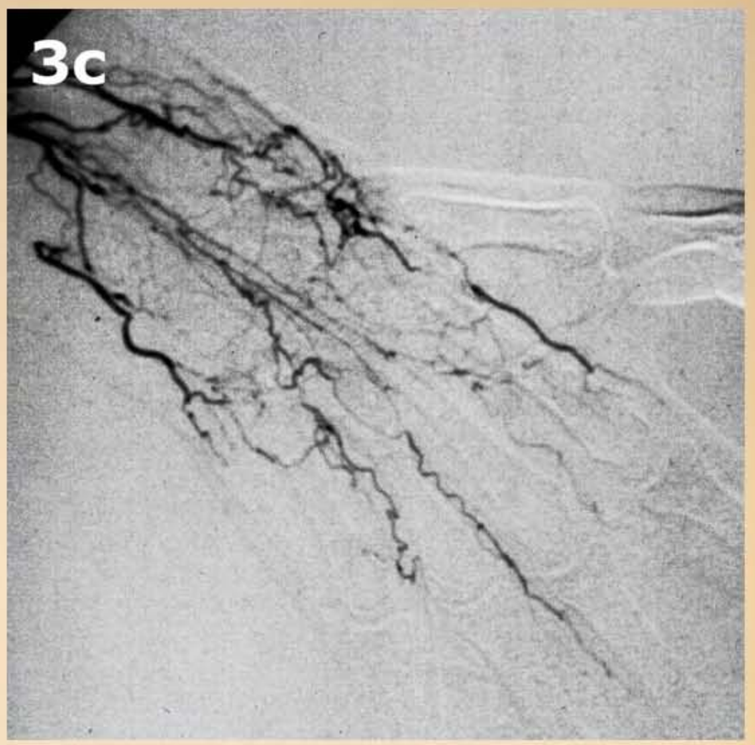


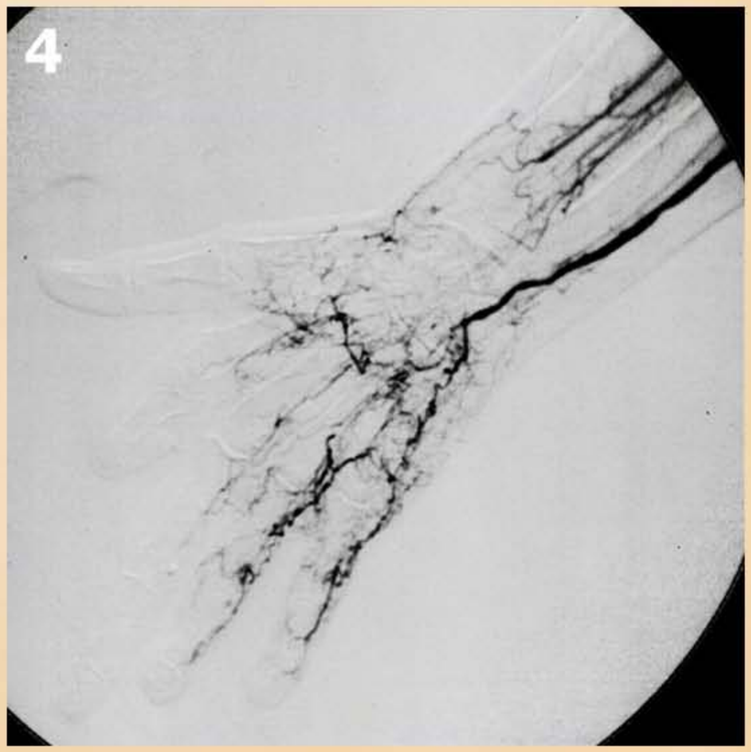




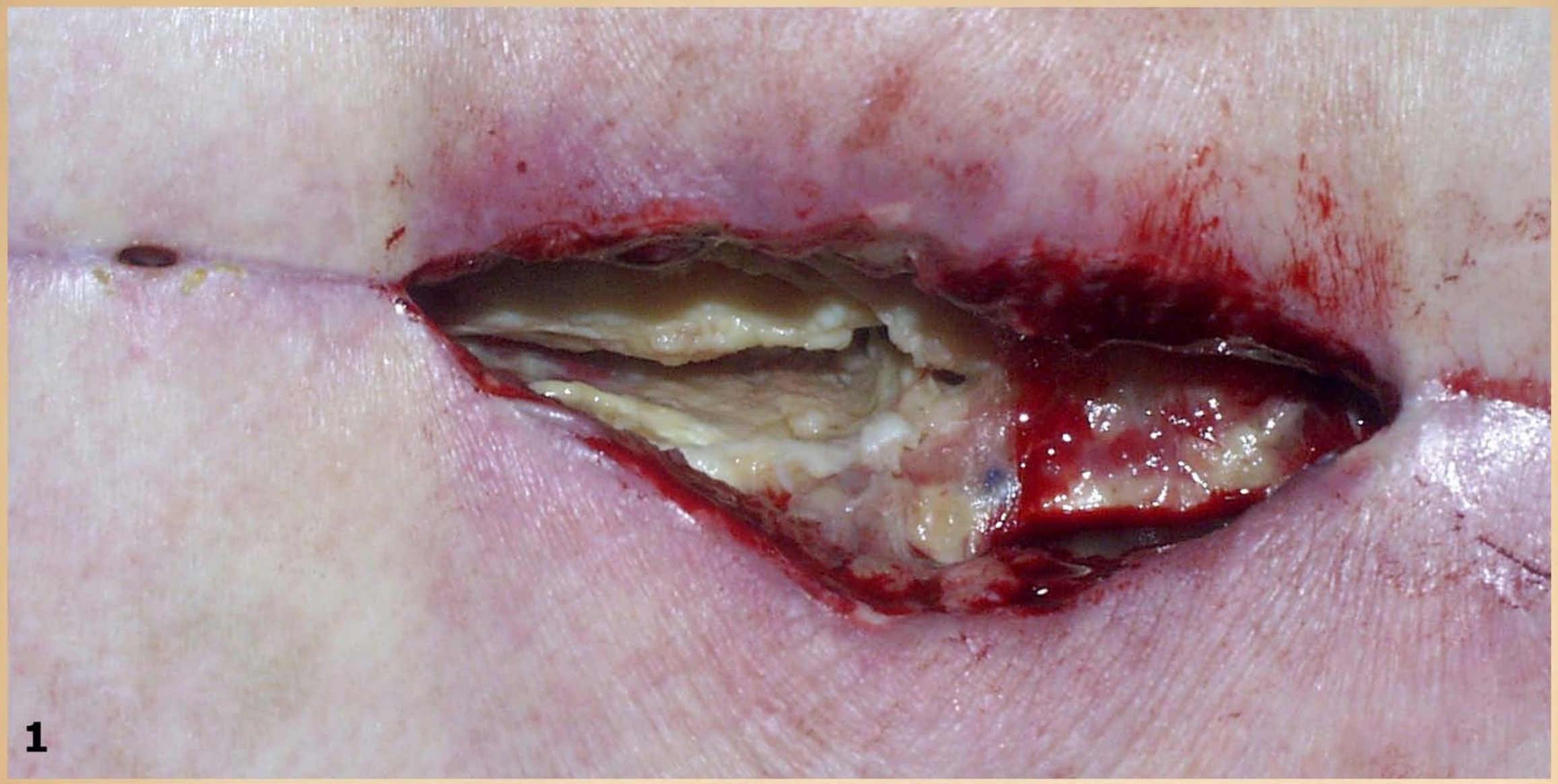




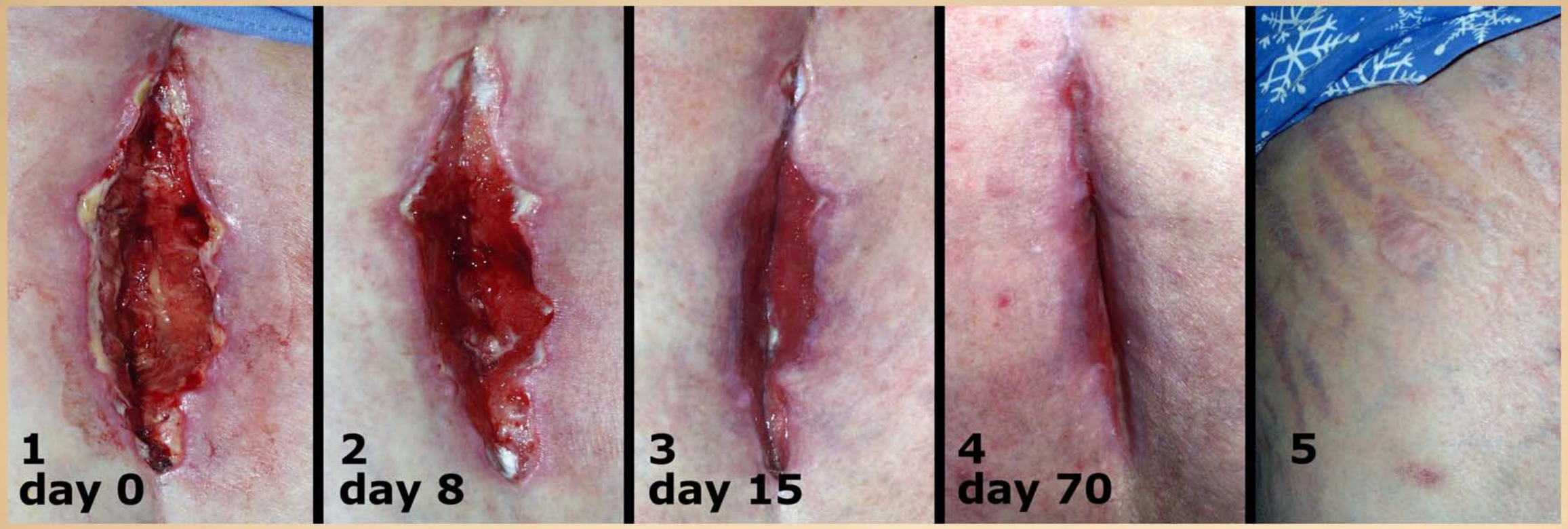




#19: 58 f scleroderma-crest



#20: 67 f rheumatoid & f-V Leiden



#21: 41 f pemphigus

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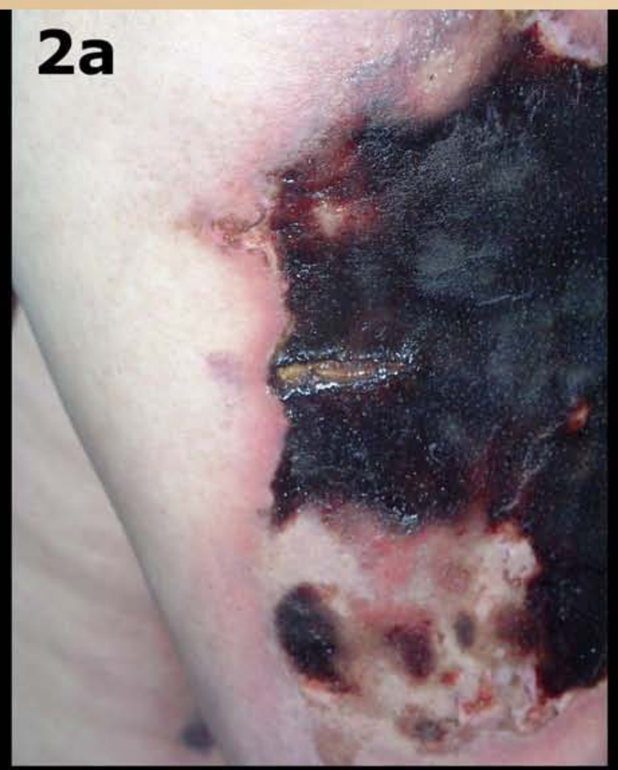

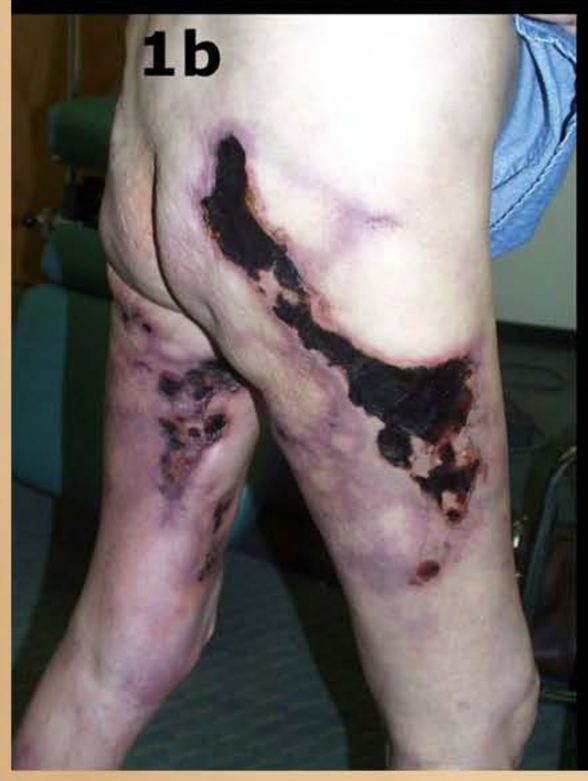

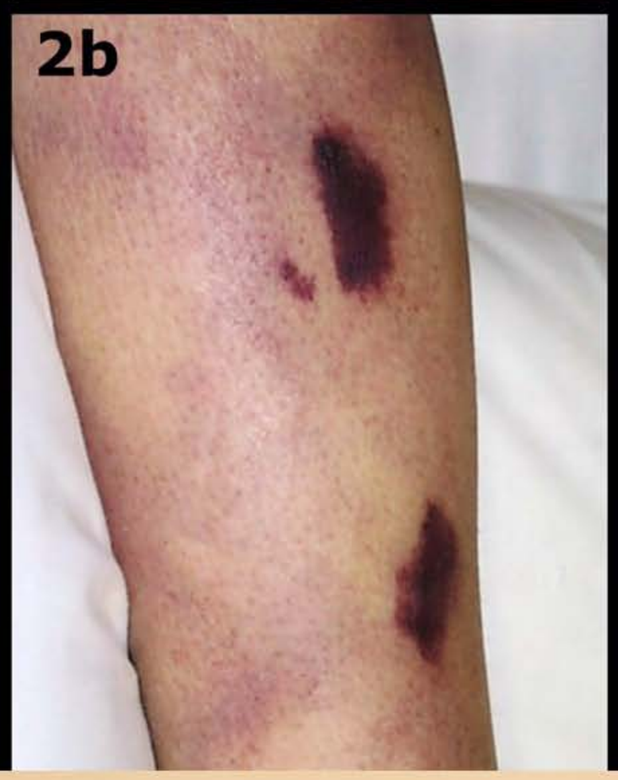

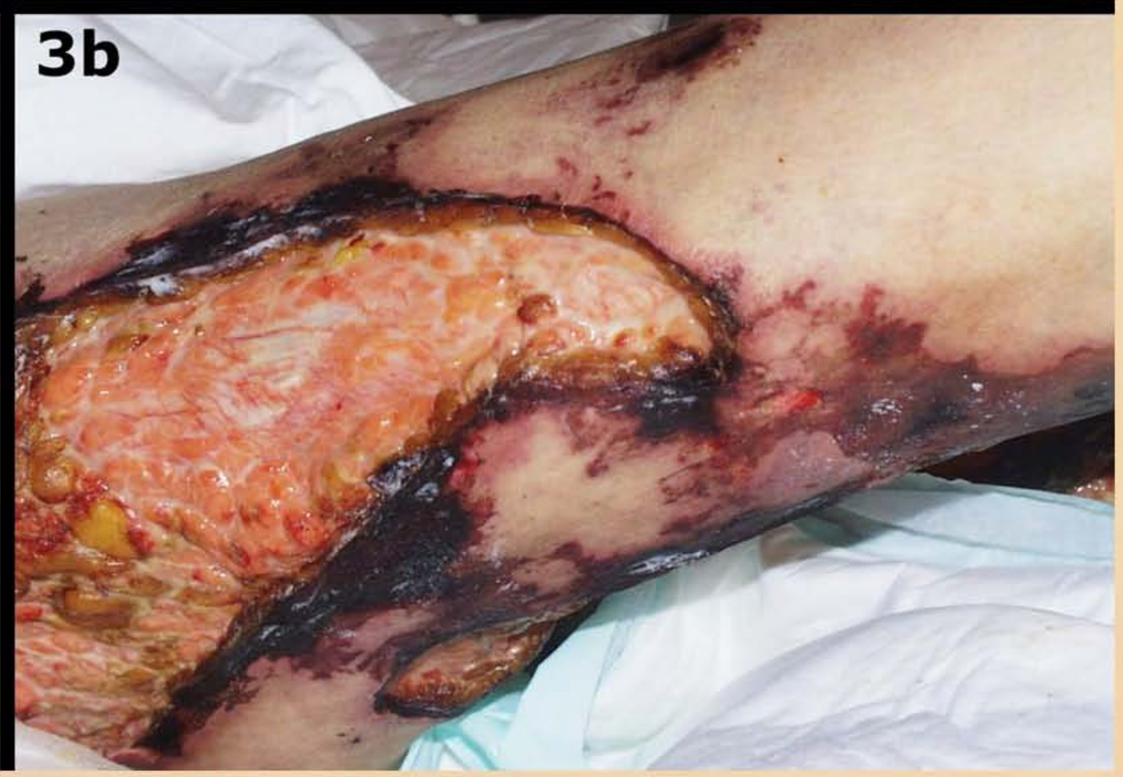

#22: 35 f acute lupus

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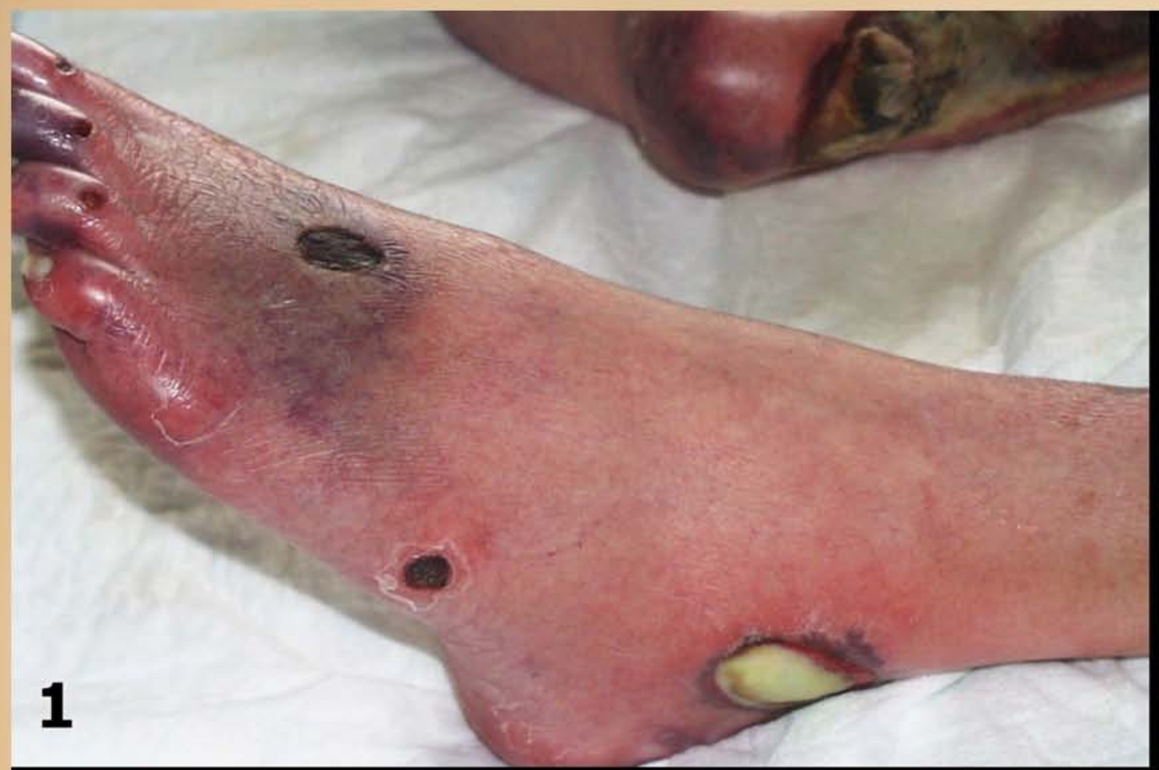
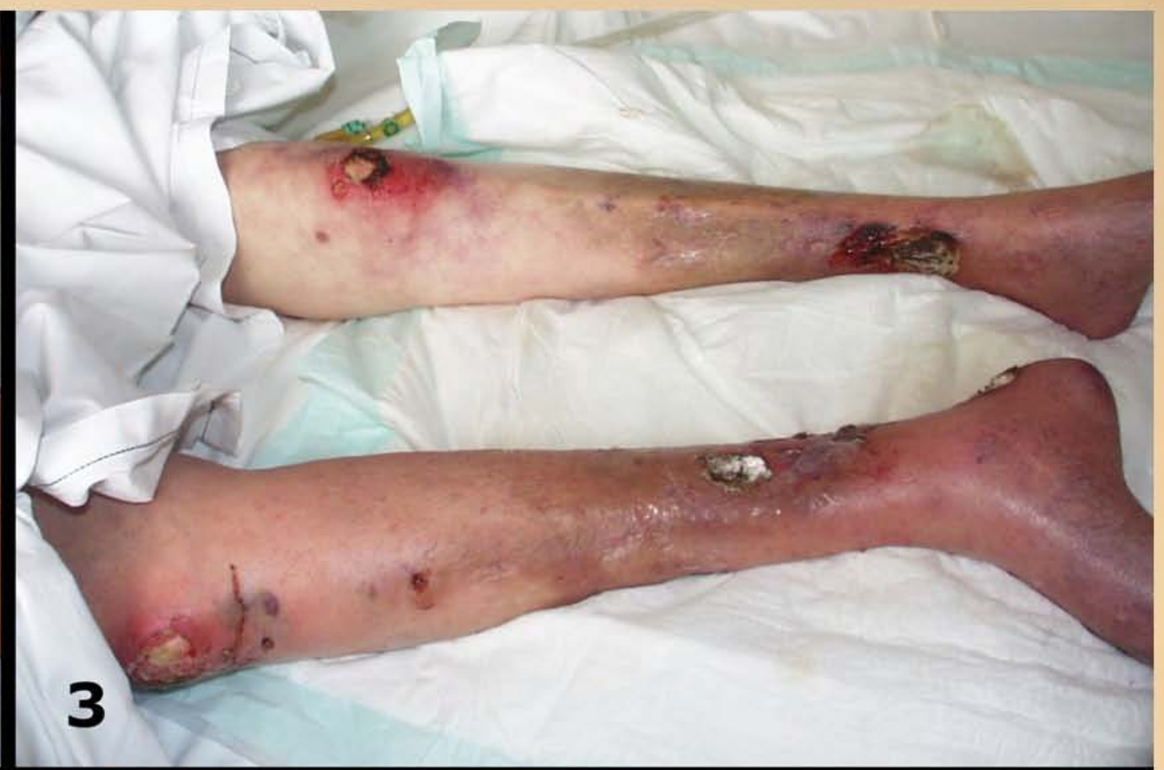
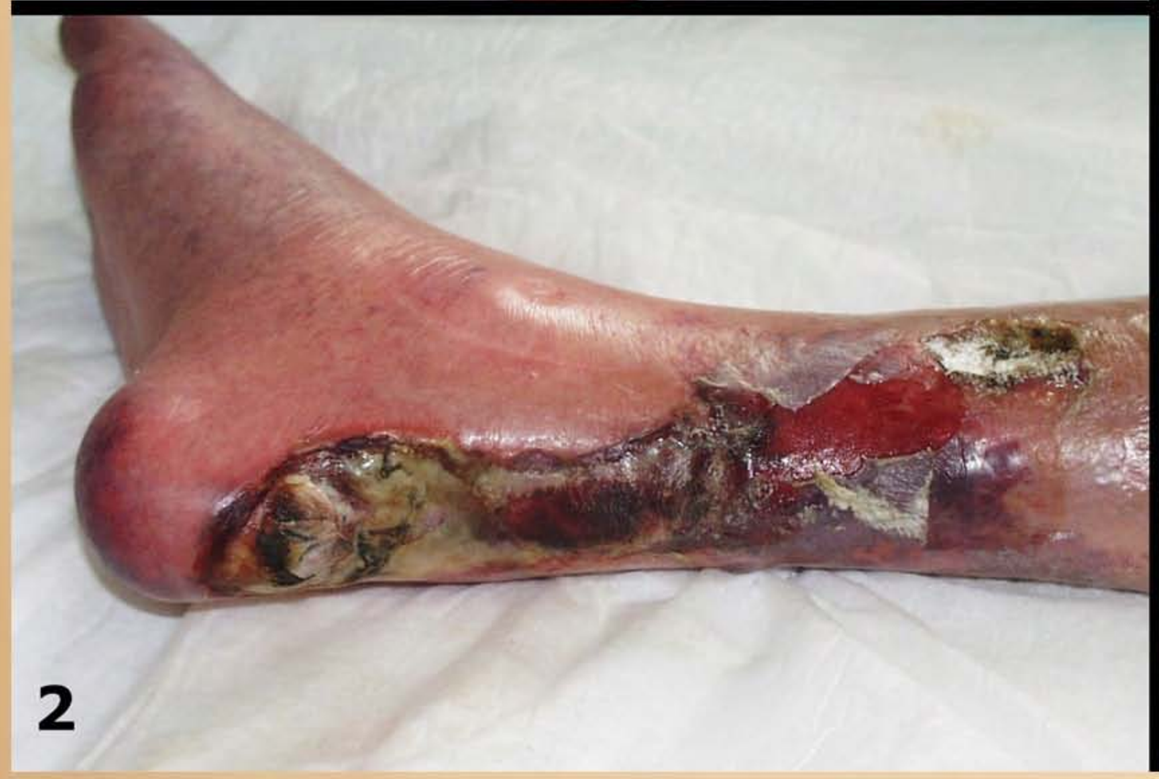
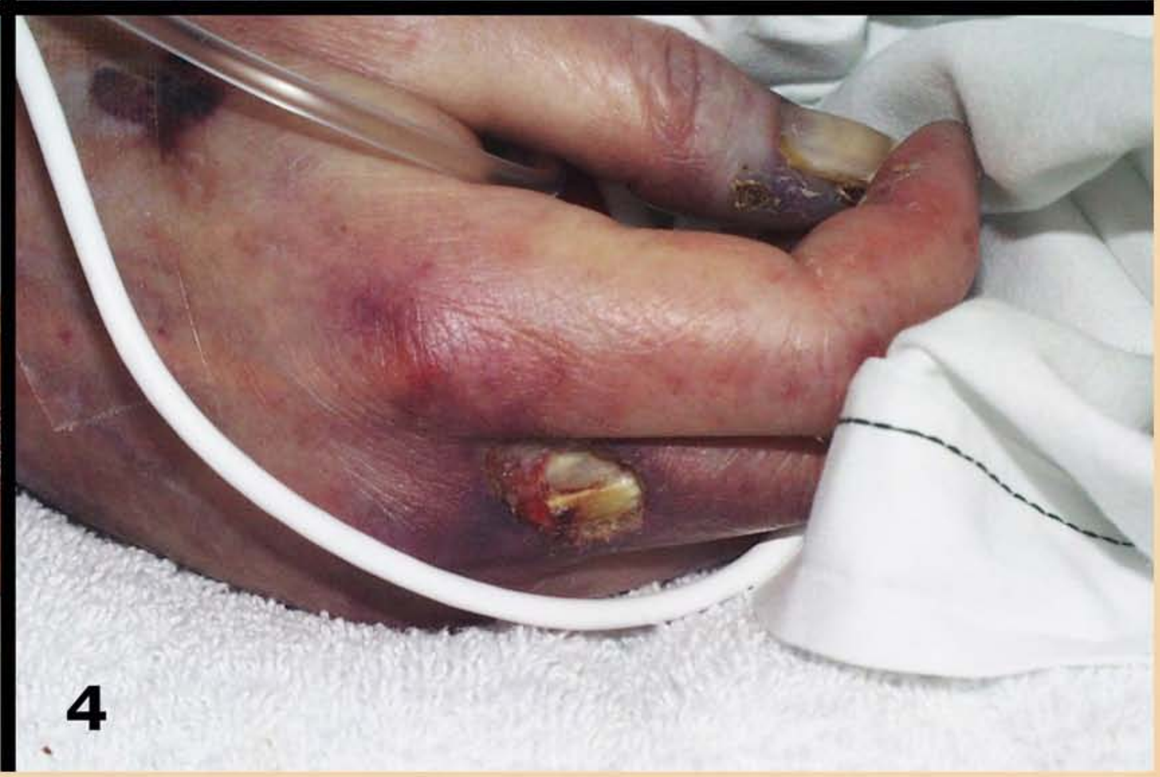






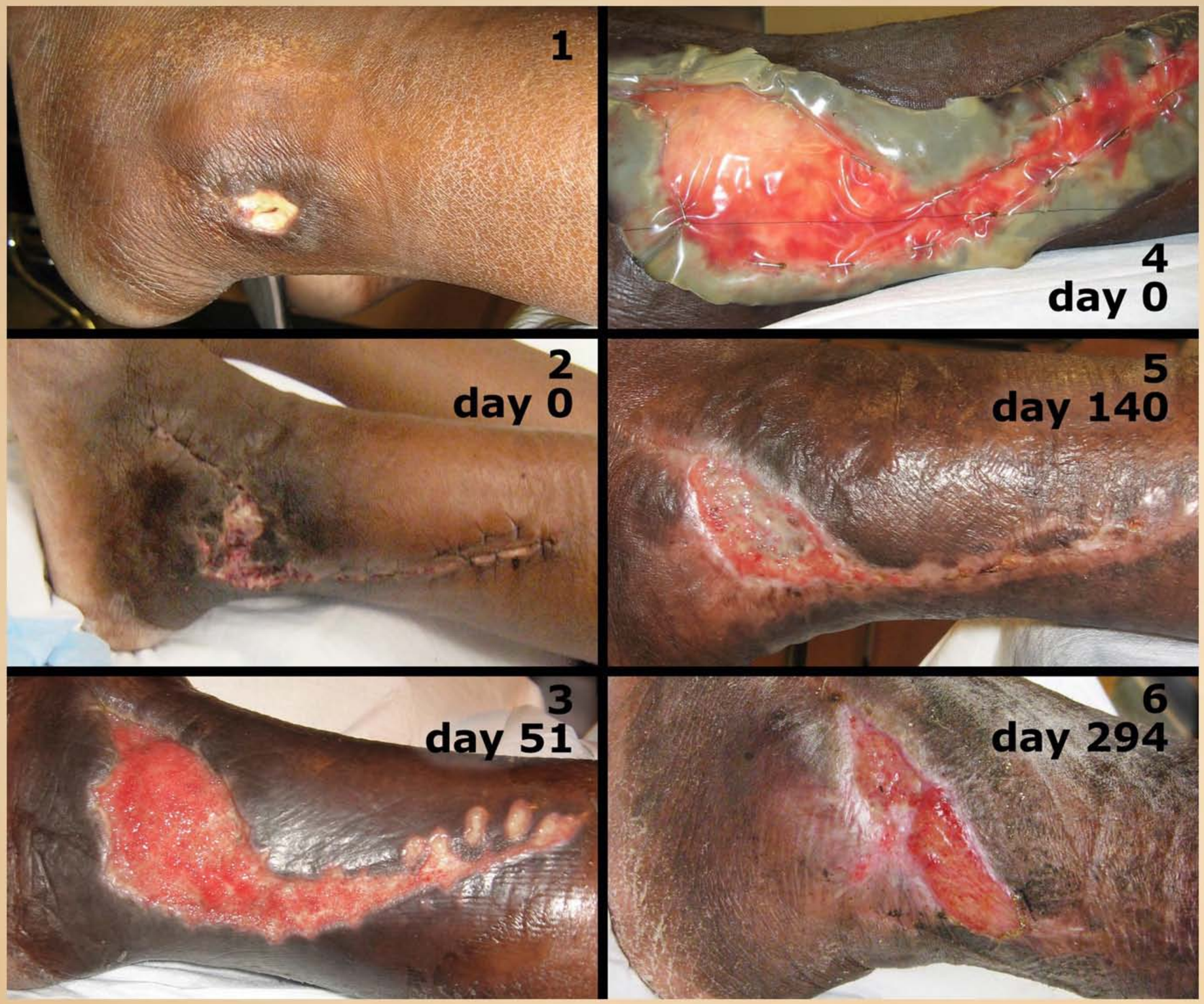


#23: 47 f Behçet's syndrome

D

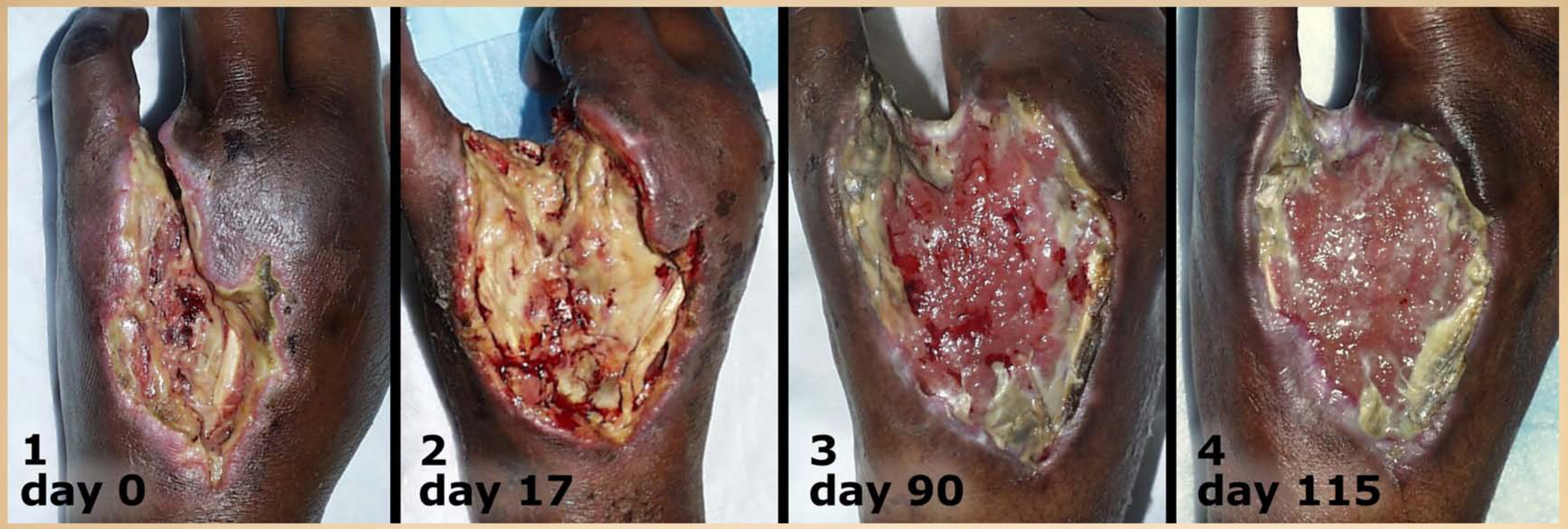
SET 7 - THE MESSAGE

PROSCRIPTION AGAINST SURGERY



#24: 33 f sickle disease

#25: 64 m aso-pvod



#26: 51 m aso-pvod

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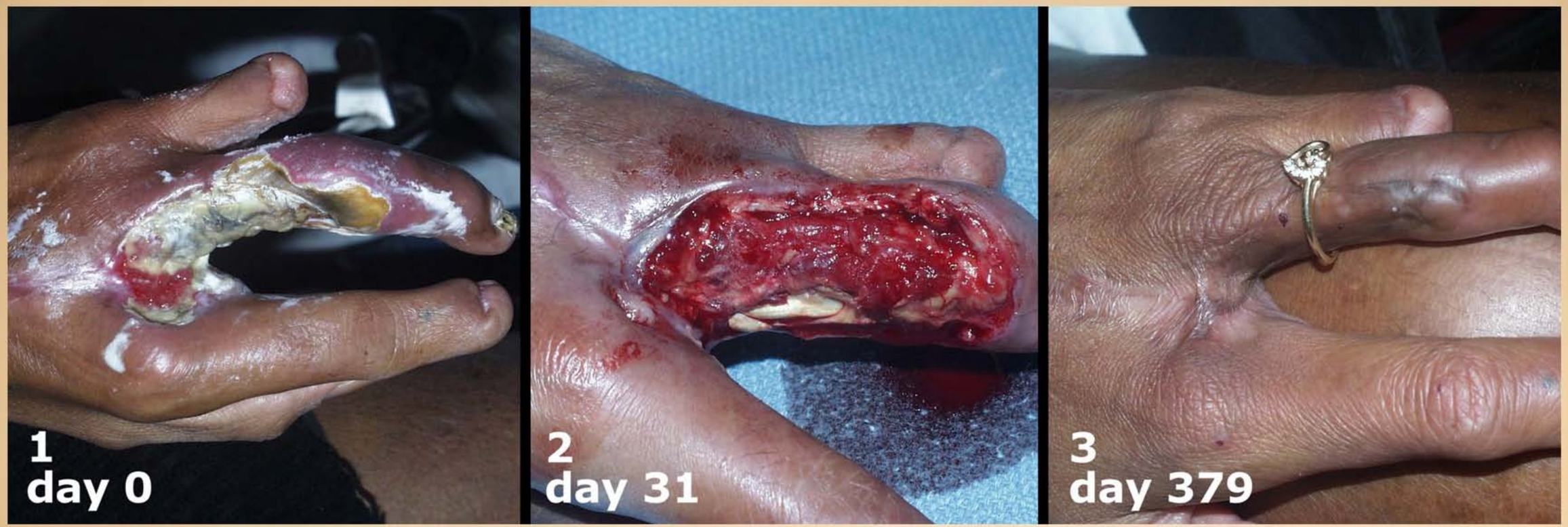
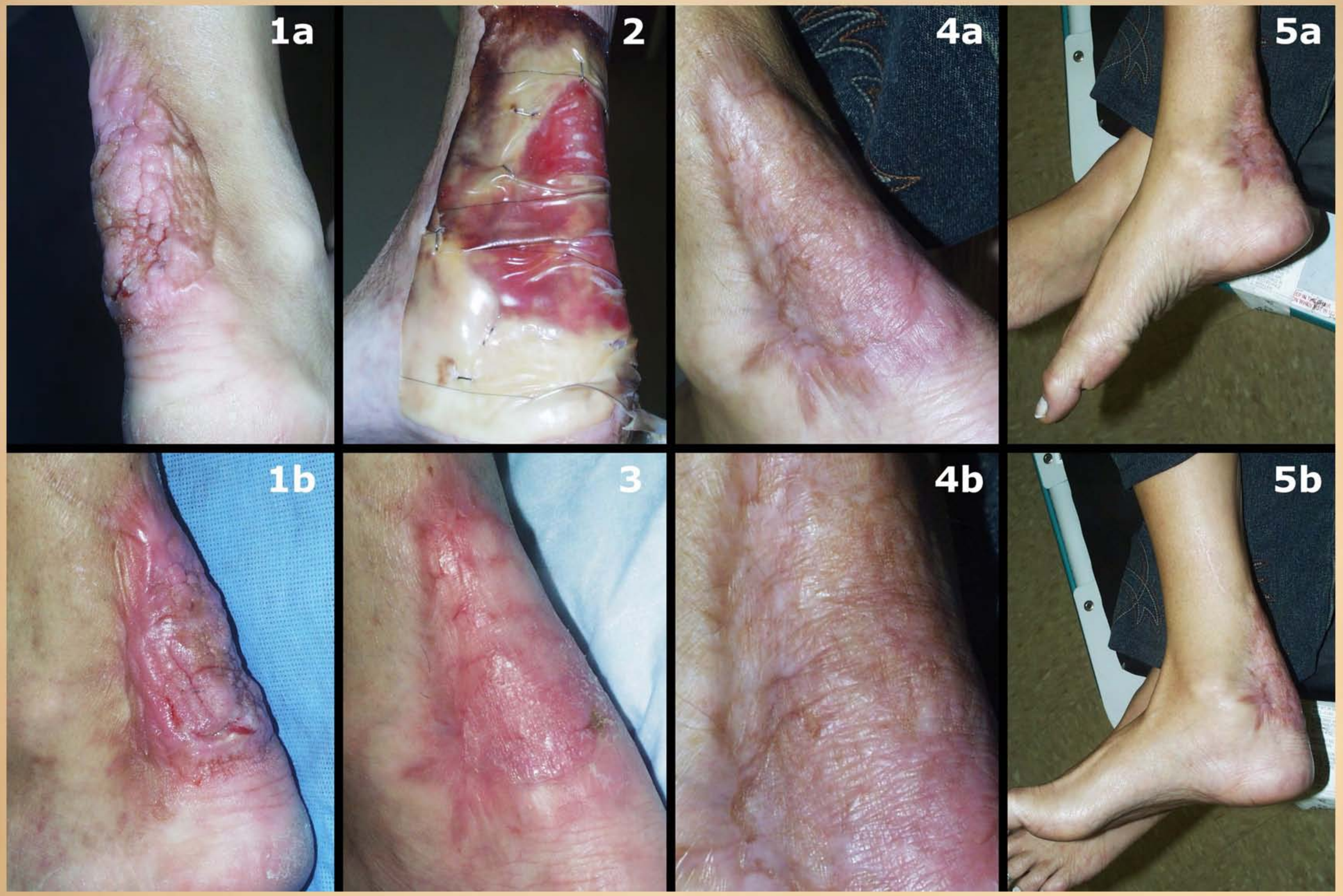
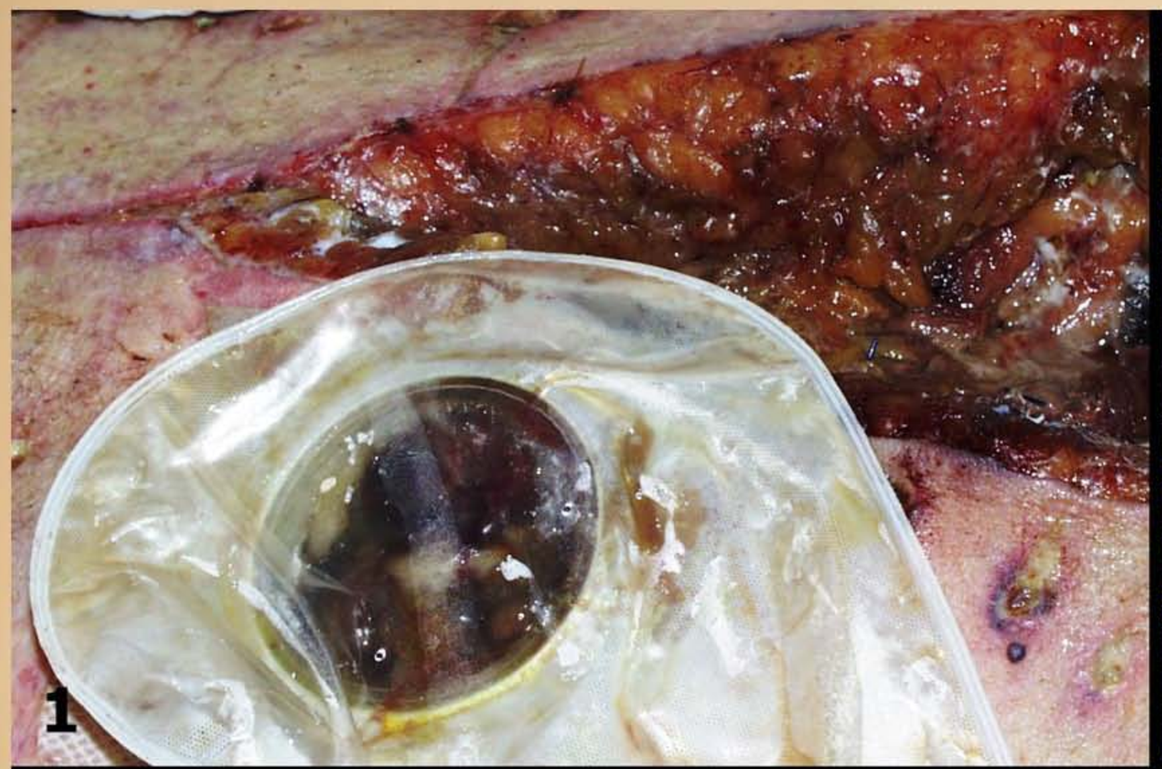
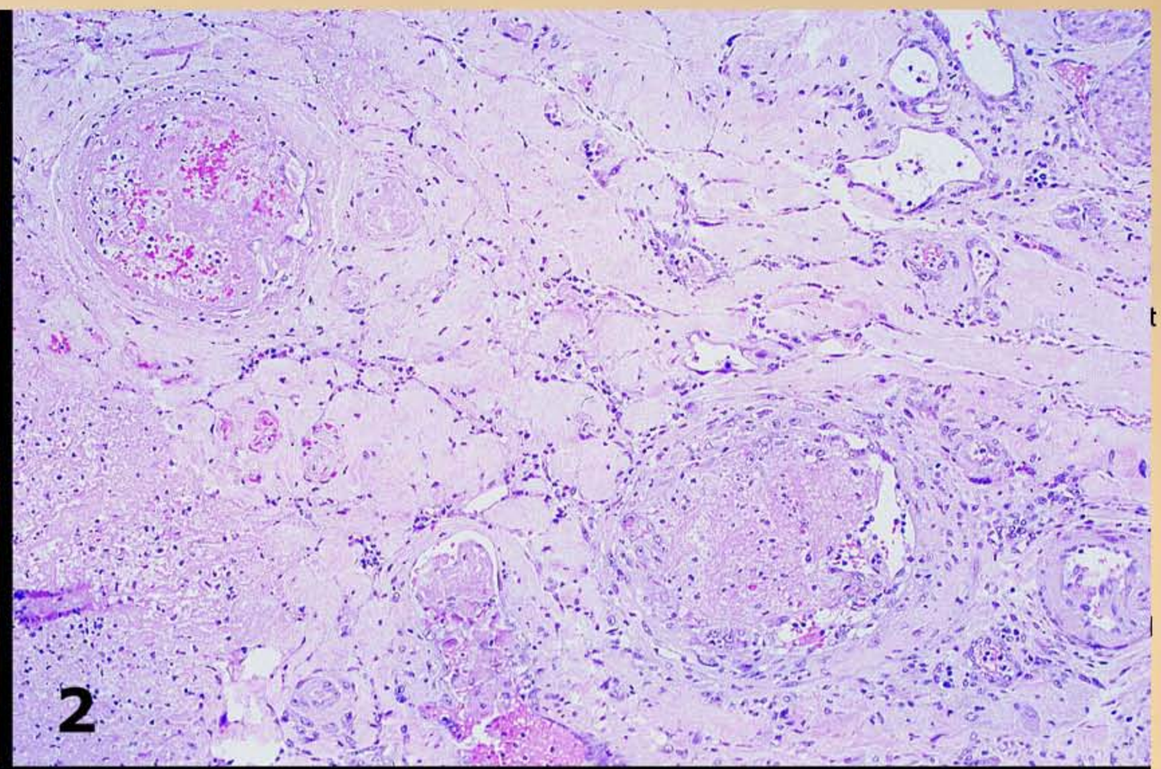


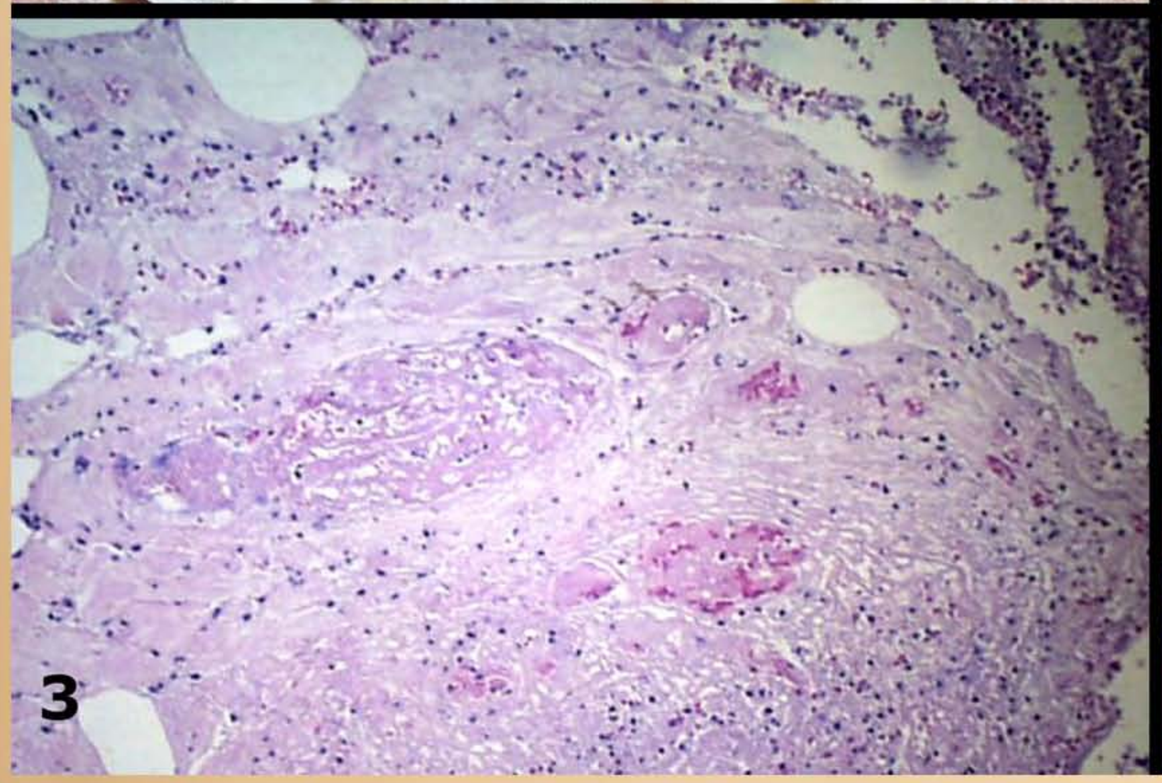
#27: 42 f aso-pvod

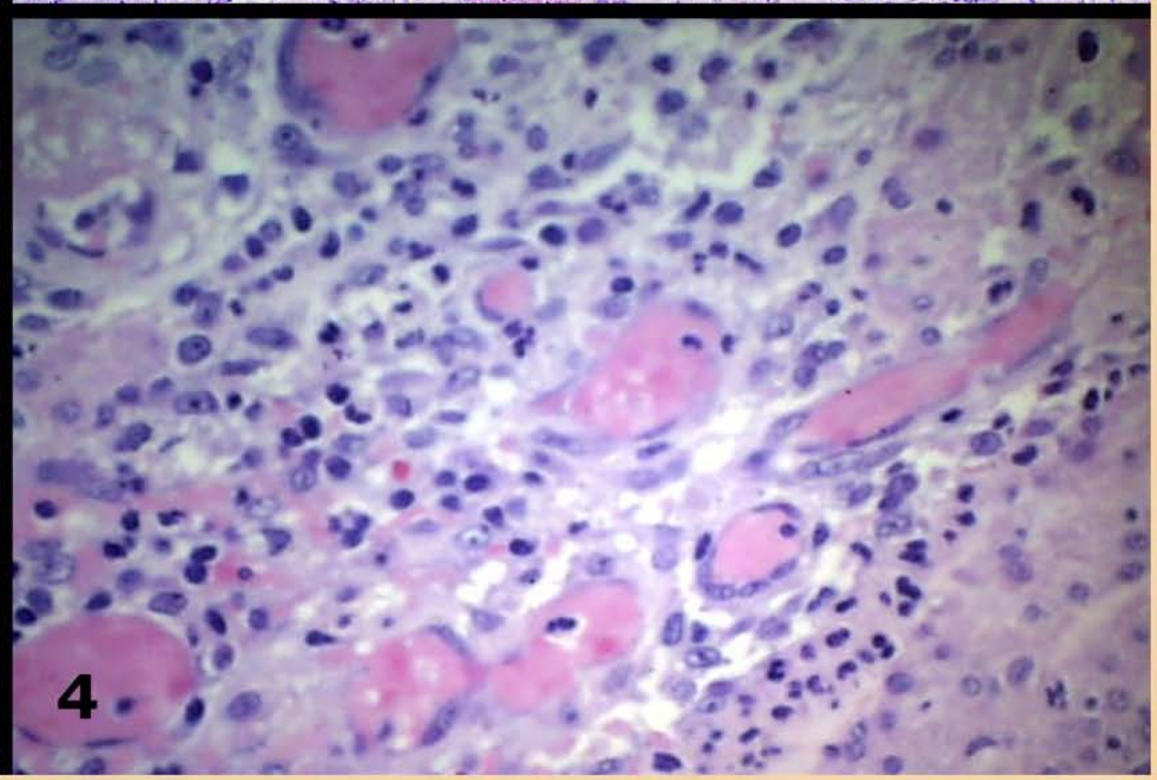


#28: 44 f hypercoagulopathy (anticardiolipins)









#29: 66 m hypercoagulopathy (apc deficient)

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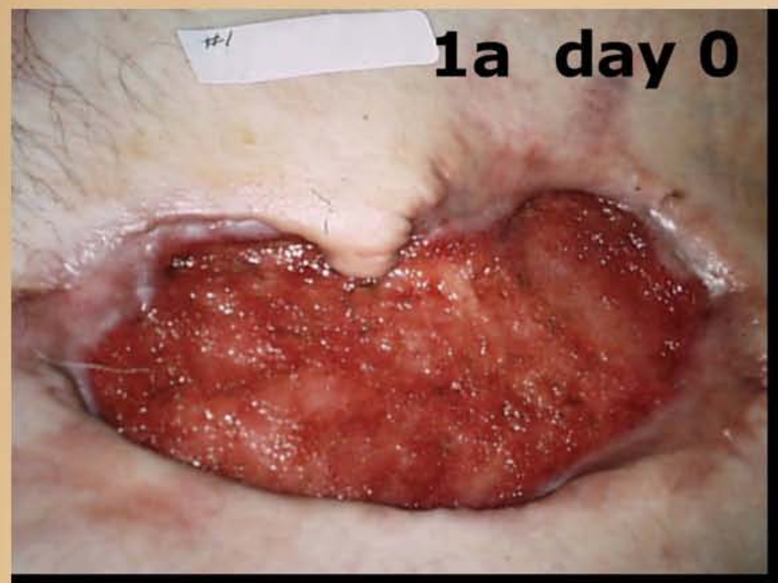
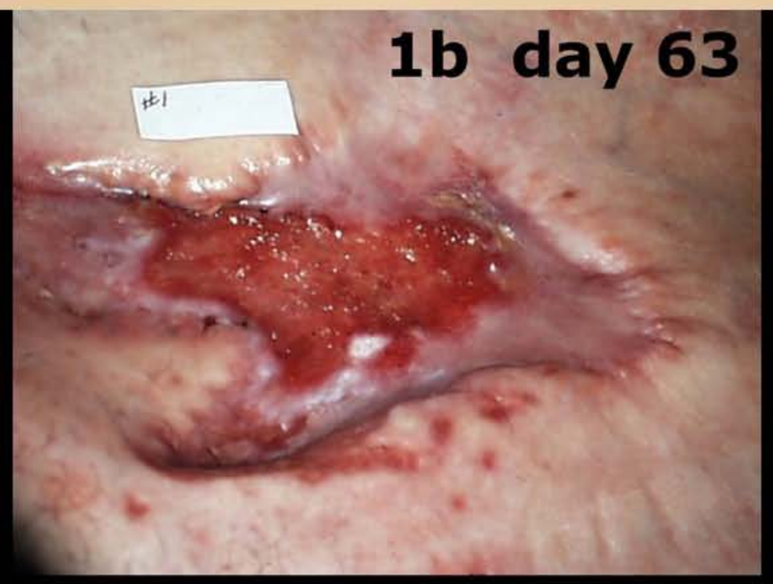
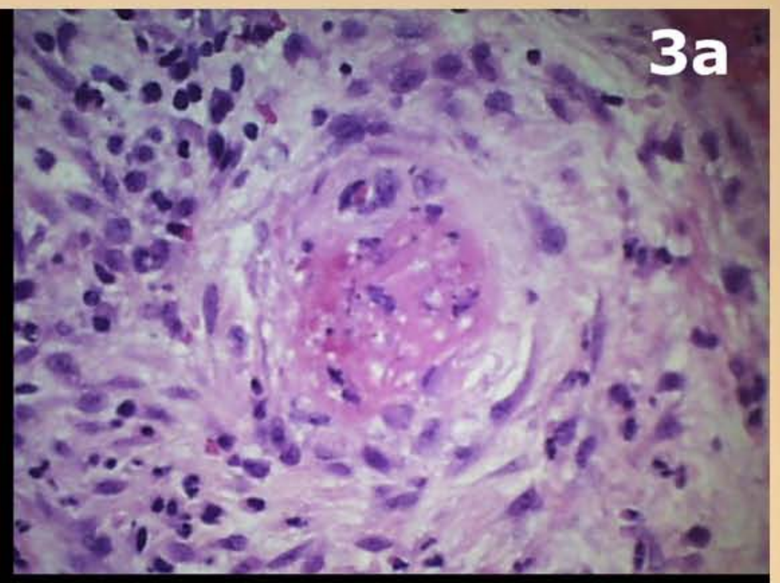
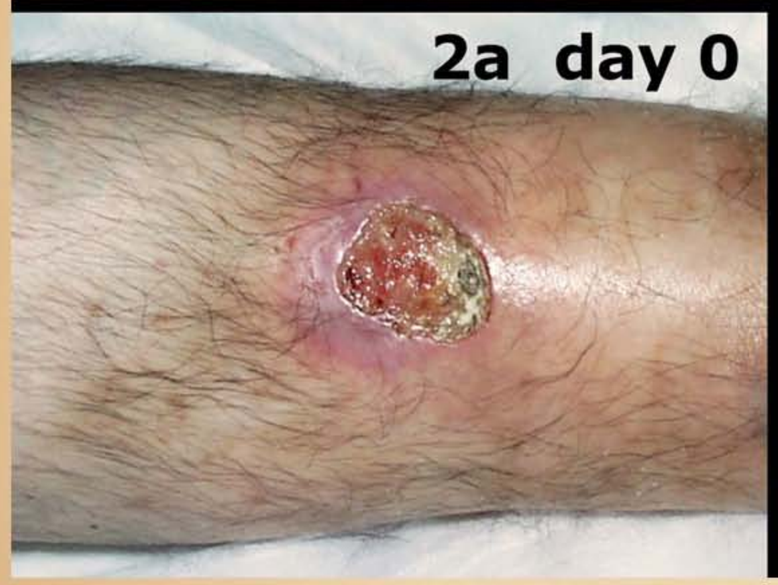
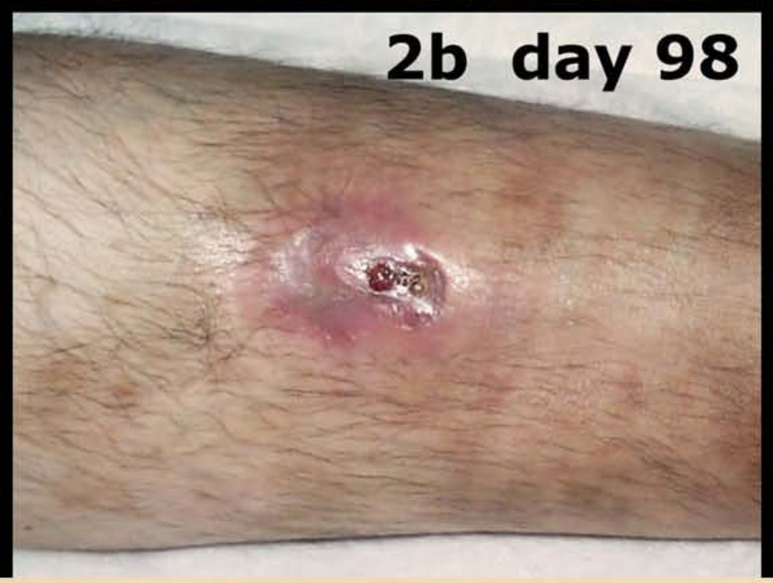
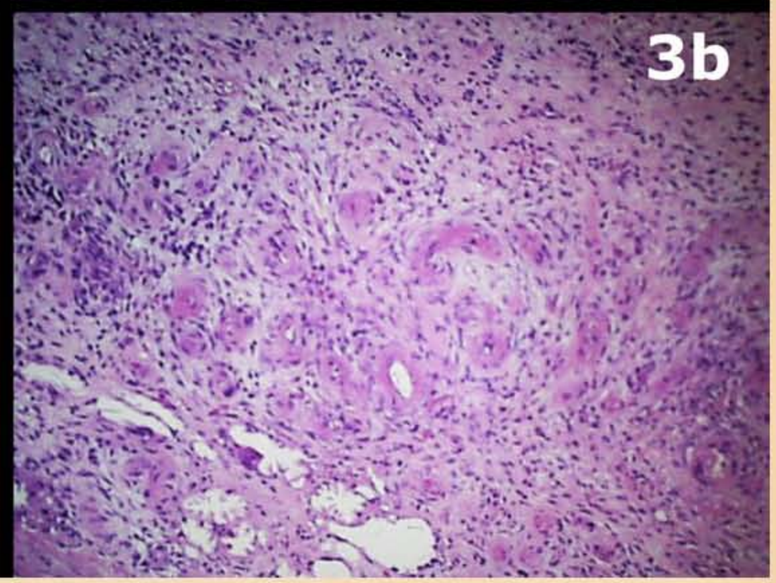












#30: 34 m lupus and hypercoagulopathy (anticardiolipins)

D

PATHERGY, IMMUNOPATHIC, & ISCHEMIC DISORDERS - DIAGNOSIS & EVALUATION

Any patient who has a wound pathergy complication without an obvious cause warrants a thoughtful evaluation for the potential associated or underlying diagnoses.

The majority of items can be ruled out by basic history and physical examination. Many of these diagnoses can be made on positive criteria by history and physical alone.

For confirmation, or to clarify the items that remain on a differential, laboratory evaluation usually resolves the diagnosis easily enough.

LABORATORY

Standard screens or panels for hematological, auto-immune, inflammatory, and coagulopathic disorders are important.

Microvascular measures, such as transcutaneous pO2, laser doppler, or multi-spectral reflectance imaging can confirm the presence of micro-occlusive states.

Histology is crucial in cases of trauma- or surgery-induced wound pathergy, revealing thrombosis, inflammatory patterns & profiles, vasculitis & other vasculopathies, panniculopathies & dermatoses, immune complex fixation, and many other relevant pathological alterations.

PATHERGY, IMMUNOPATHIC, & ISCHEMIC DISORDERS - TREATMENT & MANAGEMENT

Therapies for these cases are twofold:

1 - Those that control the causes of the stasis, ischemia, inflammation, infarction.
2 - Those that protect and promote survival of the affected tissues.

Remember, these events have a highly interconnected physiology . . . e.g. . . .
If platelets are the primary problem, then controlling platelets means not just interfering with their own intrinsic function, but also blocking the secondary events that they initiate, such as plasma coagulation and inflammation.

1 - Antiplatelet Rx:	***short acting inhibitors*** (aspirin, clopidogrel), ***long term suppressants*** (hydroxyurea, anagrilide), ***immediate platelet clearing modalities*** (plasmapheresis)
2 - Anticoagulant Rx:	***heparin*** (raw heparins and low molecular weight variants), ***dicoumarol derivatives*** (warfarin being the only one in modern use), ***factor-specific inhibitors*** (fondaparinux, argatroban)
3 - Blood rheology Rx:	***rheological drugs*** (lmw dextran, pentoxifylline, mannitol), ***viscosity lowering modalities*** (phlebotomy to reduce red cell mass, plasmapheresis to remove proteins)
4 - Anti-inflammatory Rx:	***high potency steroids*** (prednisone, methylprednisolone), ***non-steroidals*** (nsaid's), ***misc*** (sulfasalazine)
5 - Anti-immune Rx:	***antimetabolites*** (cyclophosphamide, azathioprine, hydroxyurea, etc.), ***mycotics, etc.*** (cyclosporine, mycophenolate, tacrolimus, rapamycin, etc), ***monoclonal antibodies*** (anti-tnf, anti-CD20, etc.)
6 - Circulation restoring Rx:	***procedures*** (procedural revascularization, thrombolysis), ***vasodilators and other vasoactive pharma*** (sympatholytic and autonomic agents, nitrates, prostanoids, ca+channel blockers, numerous others)
7 - Tissue survival Rx:	***hyperbaric oxygen*** (to support cell survival and basic metabolism in ischemic areas), ***reperfusion protectants*** (many putative agents: mannitol, allopurinol, tocopherols, misc anti-oxidants, etc., etc.)
8 – Wound and tissue Rx:	***topical care*** (hygiene, silver or sulfa based topicals or permissible alternatives, judicious debridement), ***edema control*** (elevation, compression), ***wound closure or protection with non-autogenous skin substitutes*** (alloplastic, semibiological, cadaveric, living).

(This list is not exhaustive, just illustrative, and there are many additional pharmaceuticals, novel and competitor.)

In wound pathergy cases, surgery must be avoided, delayed, or approached with caution and proper preparation.

Even indiscriminate debridement and biopsies carry risk.

Redo and repeat operations, especially when done not for the primary disease,
but rather for consequences of the pathergy are almost certain to cause more problems

- When wound and soft tissue pathologies are present, the simple rules of "cut-and-sew" are invalidated.
- Pathergy events and complications must be explicitly and directly acknowledged and managed, not ignored.
- Without proper preparation, more surgery means more thrombosis and inflammation, augmenting the adversity.
- With explicit pathergy-oriented management, these risks and consequences are manageable and surgery can be successful.

"On post-op day 18, the patient underwent operative debridement of her abdominal and chest wounds with primary closure of the breast wounds . . . over the next several weeks, the wounds deteriorated again . . ."

Never ignore the risks of wound pathergy related to hematological, immune, and related micro-occlusive disorders.

- Without proper preparation and peri-operative care, indiscriminate surgery will simply trigger more of the same.
- Recognize risks and pre-empt those risks by proper planning and treatment before the next operation.

"Over the next 2 weeks, both the mastectomy and abdominal skin flaps underwent progressive necrosis as the platelet count rose to 1390 thou/cm . . . and aspirin therapy was instituted."

No workup or therapy done for the thrombocytosis other than aspirin.

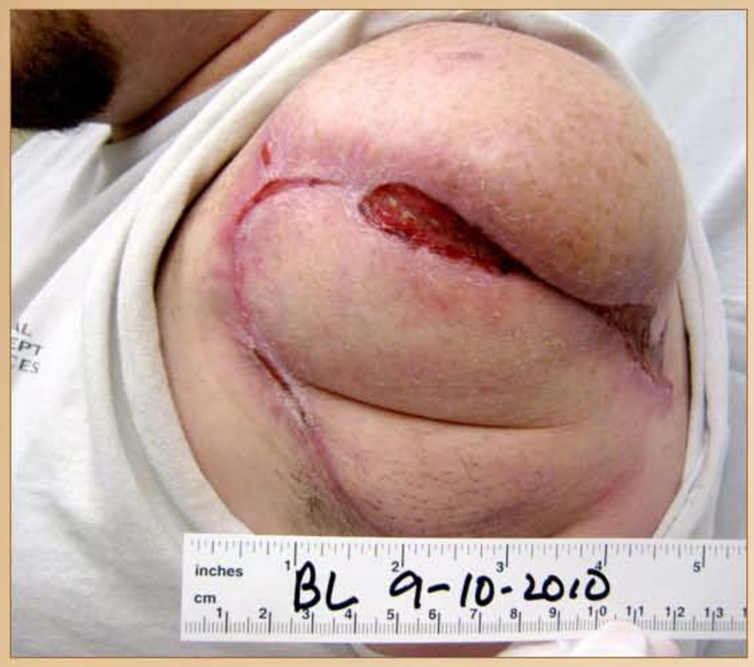
Do not passively capitulate to the disease & its damage – take an active aggressive approach to controlling pathergy.

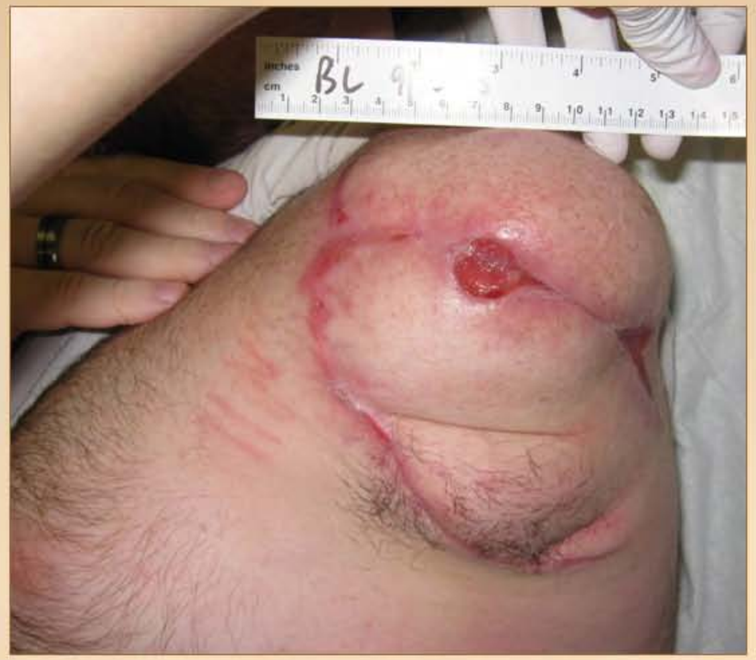
- For incidental thrombocytosis without problems, aspirin would have sufficed as prophylaxis against platelet complications.
- But this patient had significant complications for which repeat trouble is predictable – thorough workup & treatment were needed.
- Platelets per se not the whole story – they trigger coagulation, then flow stasis causes more thrombosis, so anti-coagulation was needed.
- The crucial inter-relationship between platelets, thrombosis, & inflammation means that steroids should have been used.
- Hyperbaric oxygen and anti-oxidant & rheological drugs would have minimized necrosis in the ischemic flaps and wounds.
- Plasmapheresis for acute control of blood counts and viscosity, and even simple phlebotomy hemodilution might have helped.

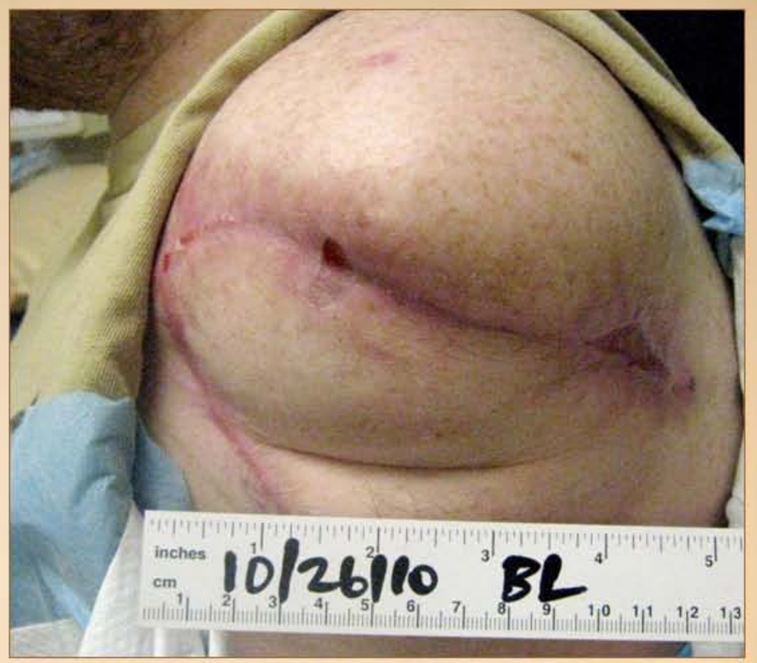
"Once both thrombocytosis and platelet activation occur, antiplatelet activation drugs are recommended [quote from a referenced article] . . . Should this patient ever require surgery in the future, a platelet activation profile study might be a valuable tool to assess the potential need for aggressive platelet therapy."

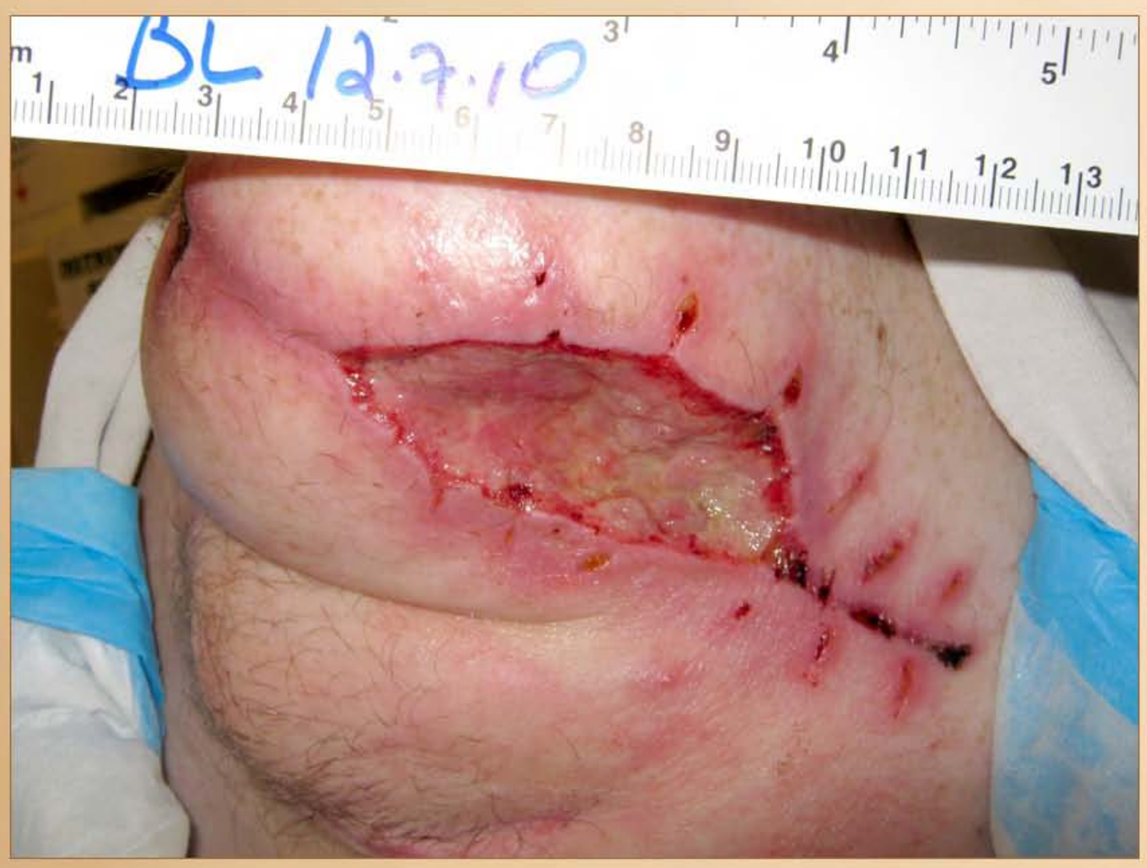
No, the patient needs that evaluation and treatment planning now.

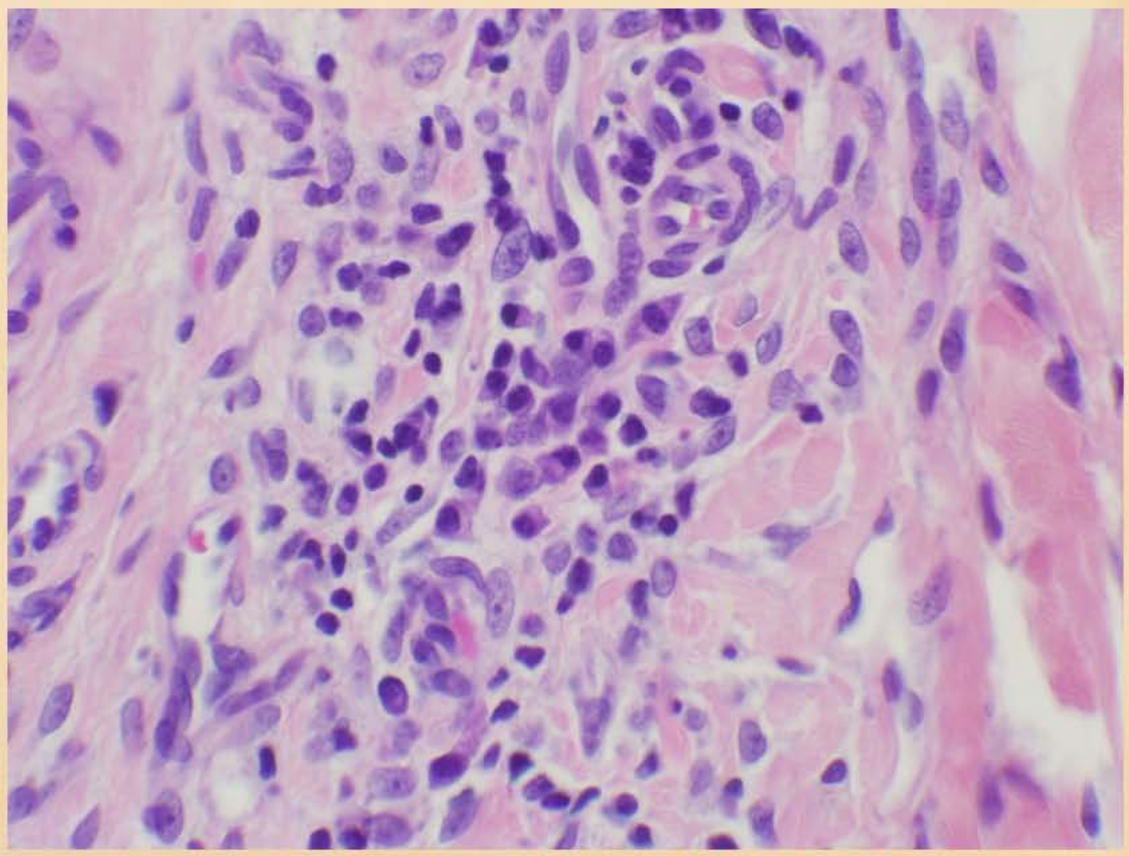
This is precisely the morbid event, with life-and-limb threat, that mandates pre-emptive evaluation, diagnosis, & treatment planning:
(1) to rule out a more significant underlying problem
(2) regardless of specific diagnosis, to be prepared so that similar events can be prevented with future trauma or surgery.











31 m traumatic amputation, reulceration after neurectomy

PATHERGY & WOUND FAILURE - SURGICAL STRATEGIES FOR REAL PATIENTS & SITUATIONS

NEVER - do repair & reconstruction concurrent with drainage & debridement - NEVER.

Try to anticipate, pretreat, preempt problems.
When trouble happens, treat and control quickly.

Aggressively treat the underlying diseases and disorders – all patients.
Treat as required with steroids and/or anticoagulants – many or most patients – be neither timid nor stingy.
Ancillary Rx as appropriate for specific indications (e.g. hbo, miscellaneous pharmaceuticals, etc.)

Close with Integra, Biobrane, matrices, judicious flaps, etc.
Avoid grafts and simple repairs.
Proper hygiene, topical care, and edema control for remaining open wounds.

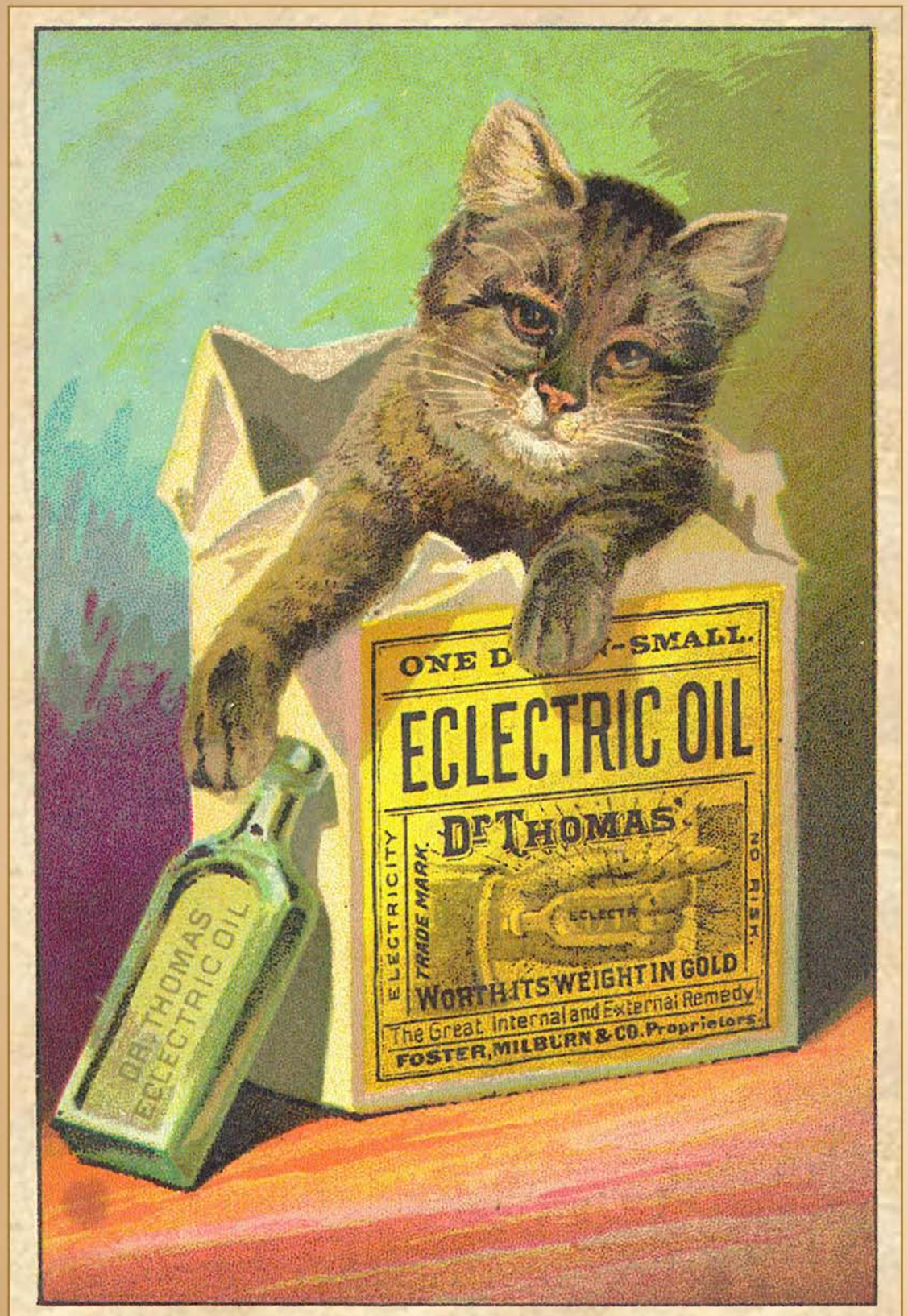
When Surgery Must Be Done

When surgery is emergent and unplanned and must be done now.
Adhere to surgery principles above, treat underlying disease, treat with steroids, anticoagulants, etc.

When surgery is mandatory and urgent but not emergent, and short preparation and planning can be done.
Assess & treat state of disease or risks, pre- or concurrent treatment with steroids, anticoagulants, etc.

When surgery is "elective" but important, and long term planning and preparation can be done.
Thorough "tune-up" of disease, pretreatment with steroids, anticoagulants, etc.

When surgery is non-vital or not medically indicated.
Don't do it – or mind every p&q of deliberate judicious management .



PATHERGY, WOUND FAILURE, & SURGERY

SUMMARY

Wound pathergy will undermine your surgery, wounds, & patients.

It is a mistake to trivialize the significance of such events, and then to be complacent about misdiagnosis and inadequate treatment.

Recognize and respect wound pathergy and cease any more surgery until the problem is worked up and treated.

Respect and preemptively deal with underlying vascular, blood, thrombotic, inflammatory, & autoimmune diseases & complications.

Always be cognizant of the injury-thrombosis-inflammation triad, understand its implications, and understand how to treat and correct it when it is on the wrong attractor.

Indiscriminate surgery will have complications, and then more indiscriminate obsessive surgery will have even more problems, and the wounds will become "locked in" to a state of intrinsic pathology that cannot correct itself.

Some operations must be done, even in these patients, and they can be done safely, with good wounds and outcomes, as long as certain principles and details of pre-, intra-, and post-op care are applied.

These patients have latent risks due to chronic diseases. Pathergy and wound complications will become manifest if the patient is stressed or injured again. These patients need a proper diagnosis and reserve plan of care to be implemented at those future times.

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Phoenix, AZ

PRINCIPLES OF SURGERY

WOUND PATHERGY

(WHEN NOT TO OPERATE)

SITUATIONS TO AVOID THAT WILL CAUSE NECROSIS, DEHISCENCE, WOUND FAILURE, & RELATED COMPLICATIONS

Marc E. Gottlieb, MD, FACS
Phoenix, Arizona

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