AA-Amyloidosis

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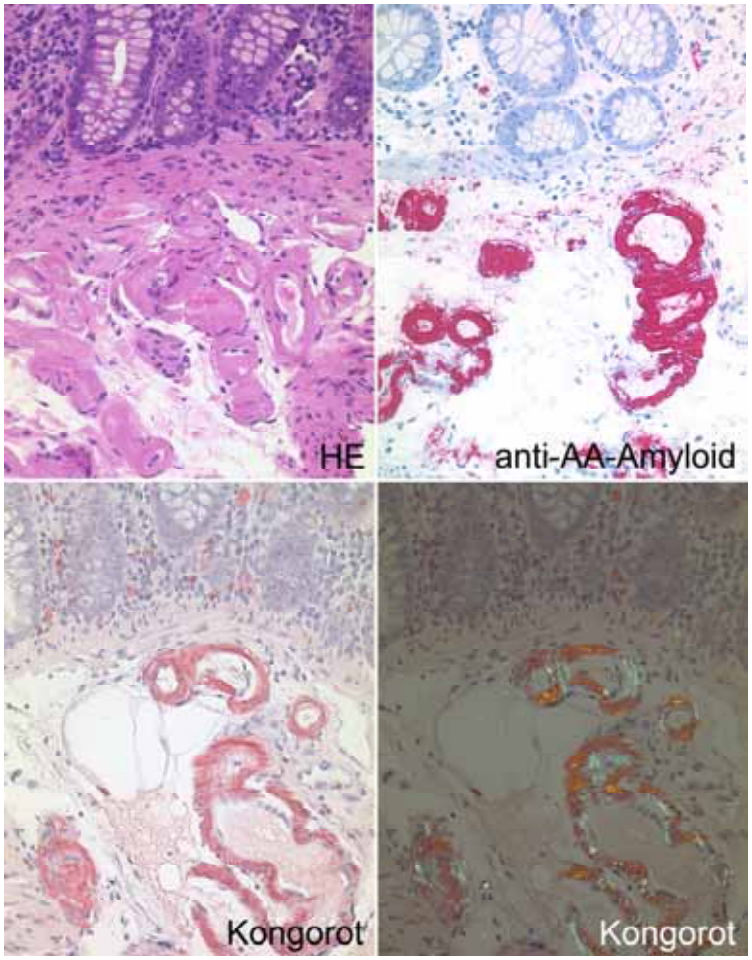
AA-Amyloid in deep rectal biopsy



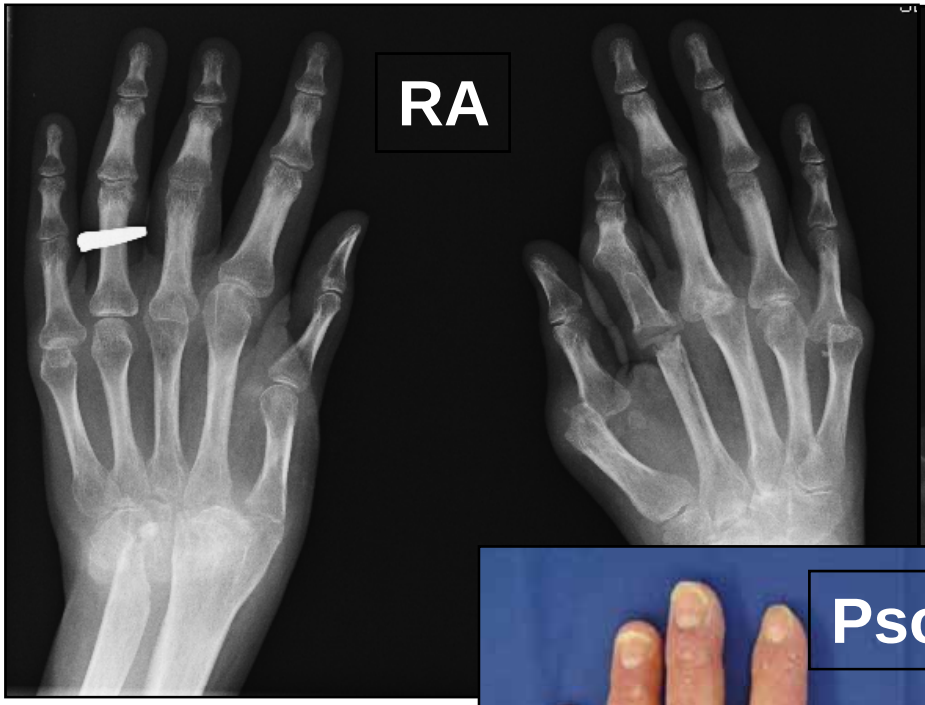
(Prof. Röcken, Charite, Berlin)

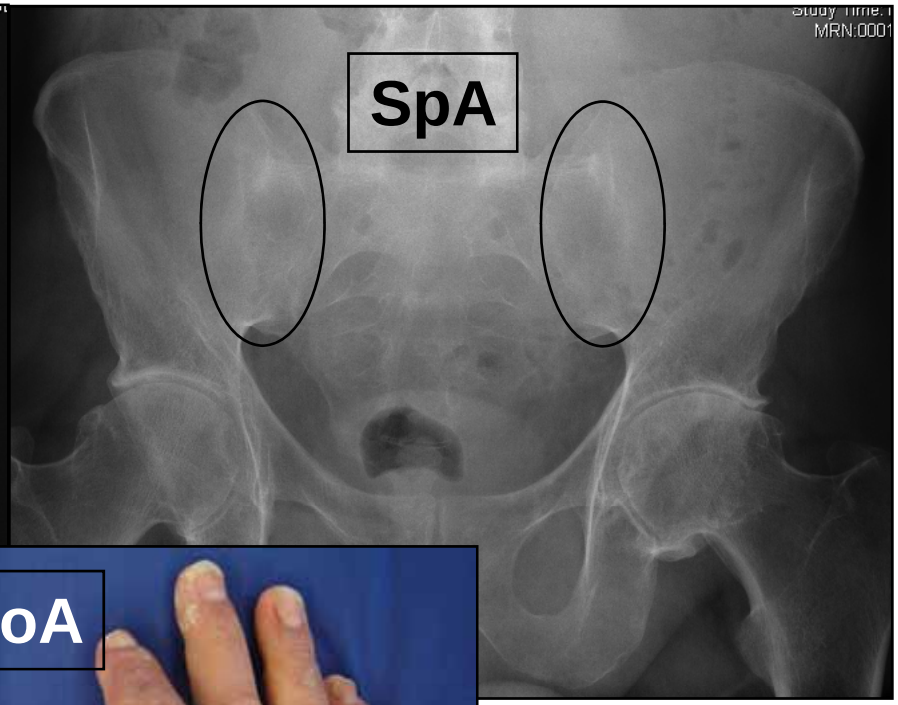
secondary AA-Amyloidosis

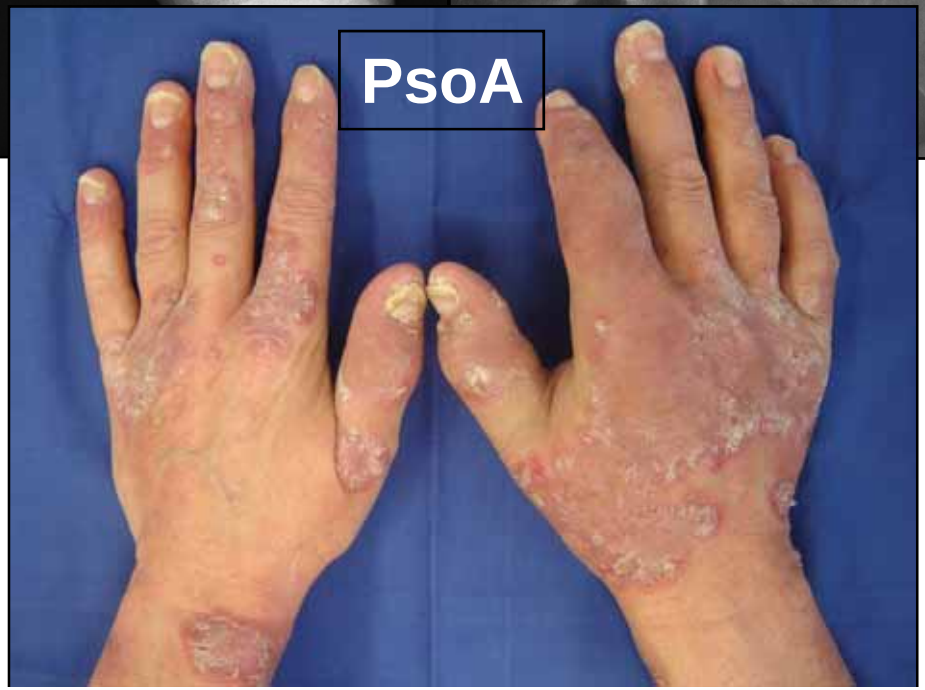
can be associated with any chronic-inflammatory disease

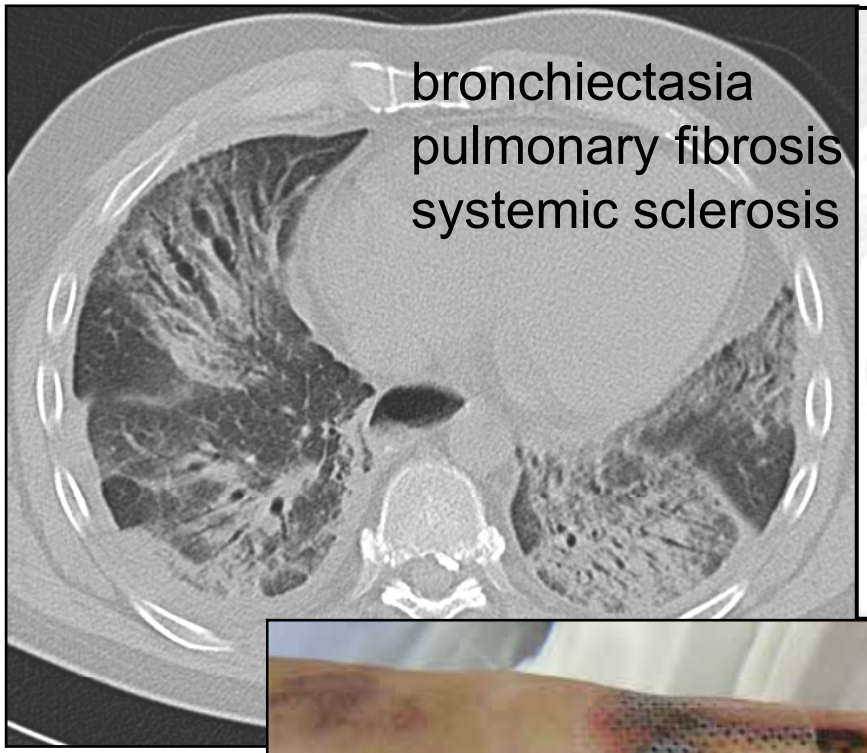
rheumatoid diseases:

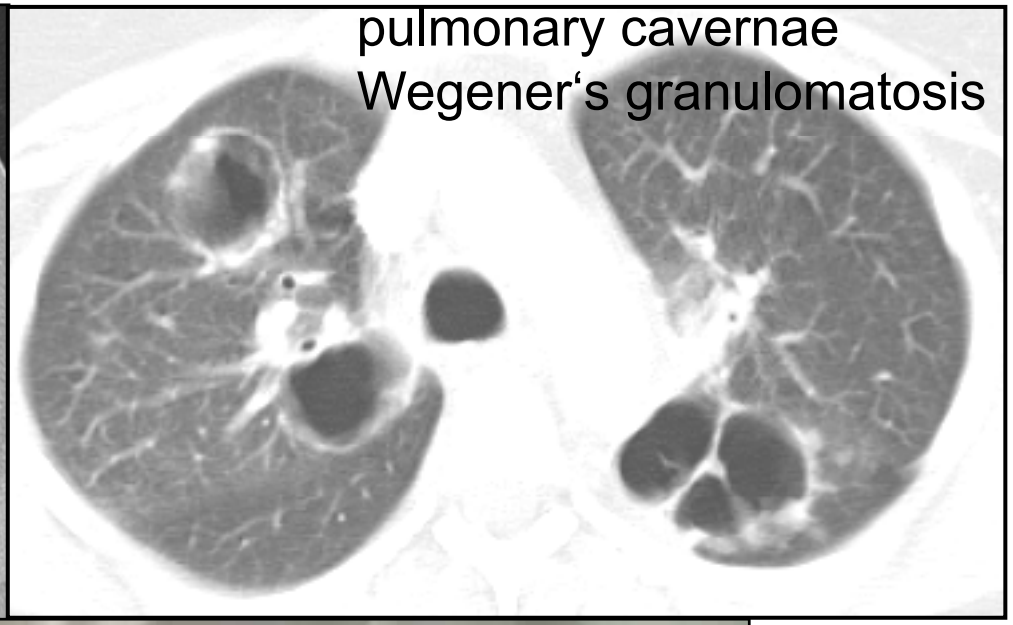
rheumatoid arthritis
juvenile idiopathic arthritis
ankylosing spondylitis (Bechterew)
psoriatic arthritis
connective tissue diseases, vasculitis

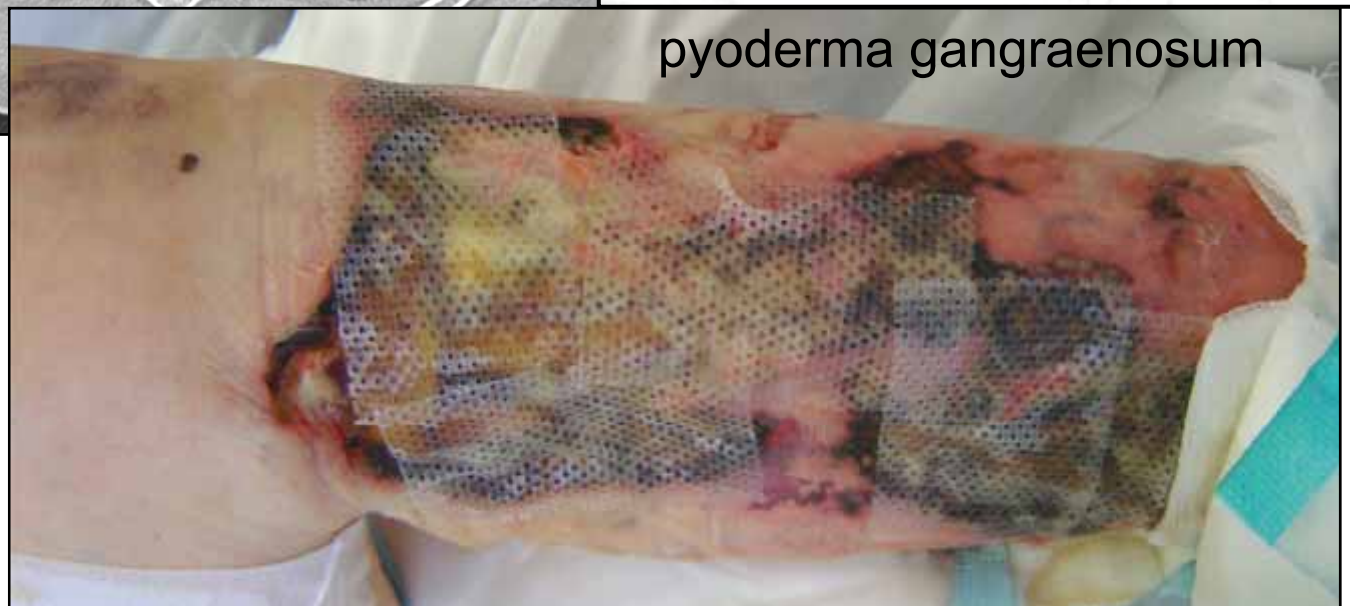

RA


SpA
MRN:0001


PsoA


bronchiectasia
pulmonary fibrosis
systemic sclerosis


pulmonary cavernae
Wegener‘s granulomatosis


pyoderma gangraenosum

secondary AA-Amyloidosis

can be associated with any chronic-inflammatory disease

rheumatoid diseases:
rheumatoid arthritis
juvenile idiopathic arthritis
ankylosing spondylitis (Bechterew)
psoriatic arthritis
connective tissue diseases, vasculitis

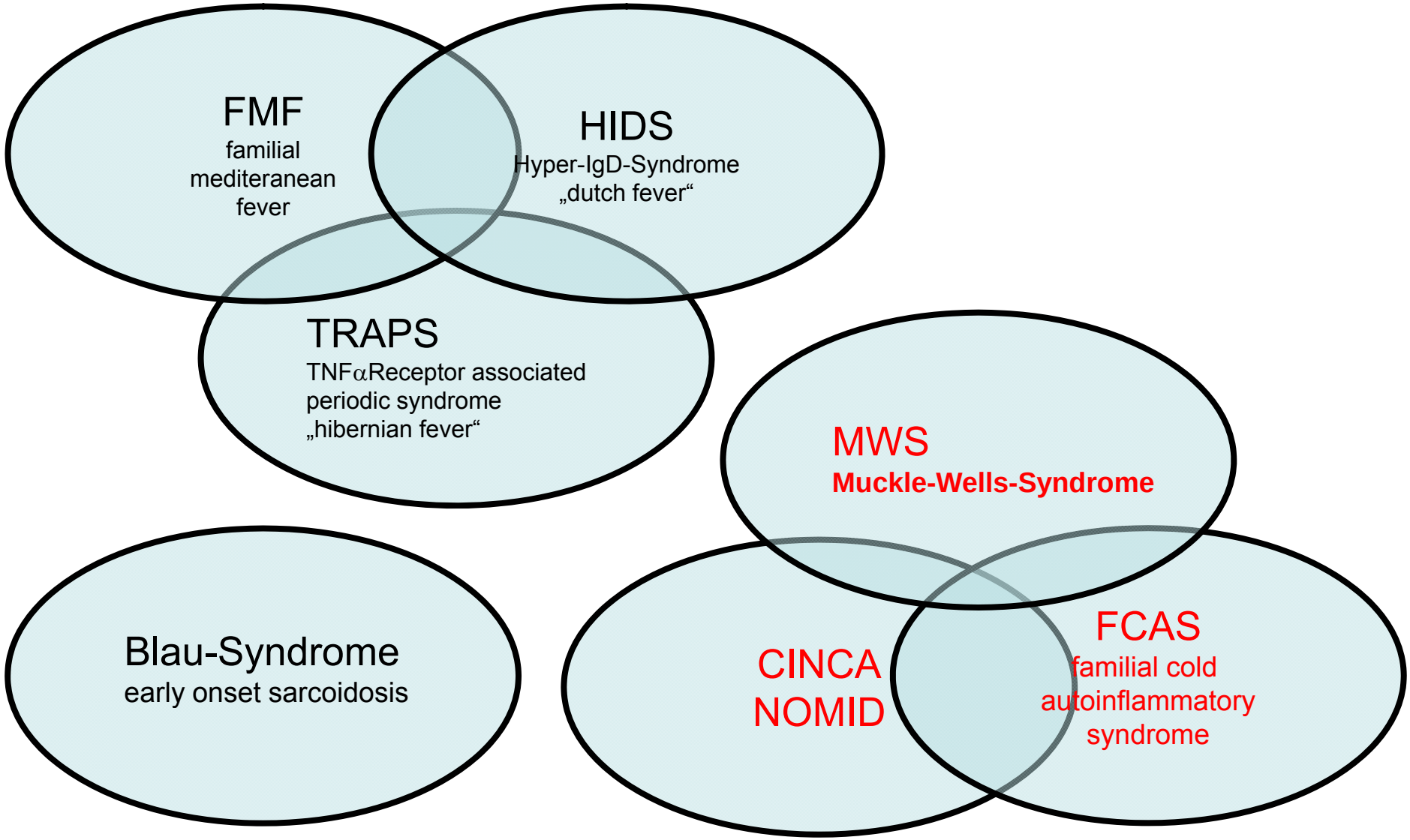
periodic fever syndromes

gastrointestinal diseases:
Crohn‘s disease, Colitis ulcerosa, Whipple‘s disease

chronic pulmonary diseases:
COPD, mucoviszidosis, bronchiektasia

chronic infections:
infected ulcers, decubiti, osteomyelitis, skin abscesses, tuberculosis

periodic fever syndromes



CAPS : **C**ryopyrin-**a**ssociated **p**eriodic **s**yndrome :

FCAS : **f**amilial **c**old **a**utoinflammatory **s**yndrome = FCU

MWS : **M**uckle-**W**ells-**S**yndrome

CINCA: **c**hronic **i**nflammatory **n**euro-**c**utaneous **a**rthritis syndrome

NOMID: **n**ewborn **o**nset **m**ultisystemic **i**nflammatory **d**isease

1st episode < 1. year

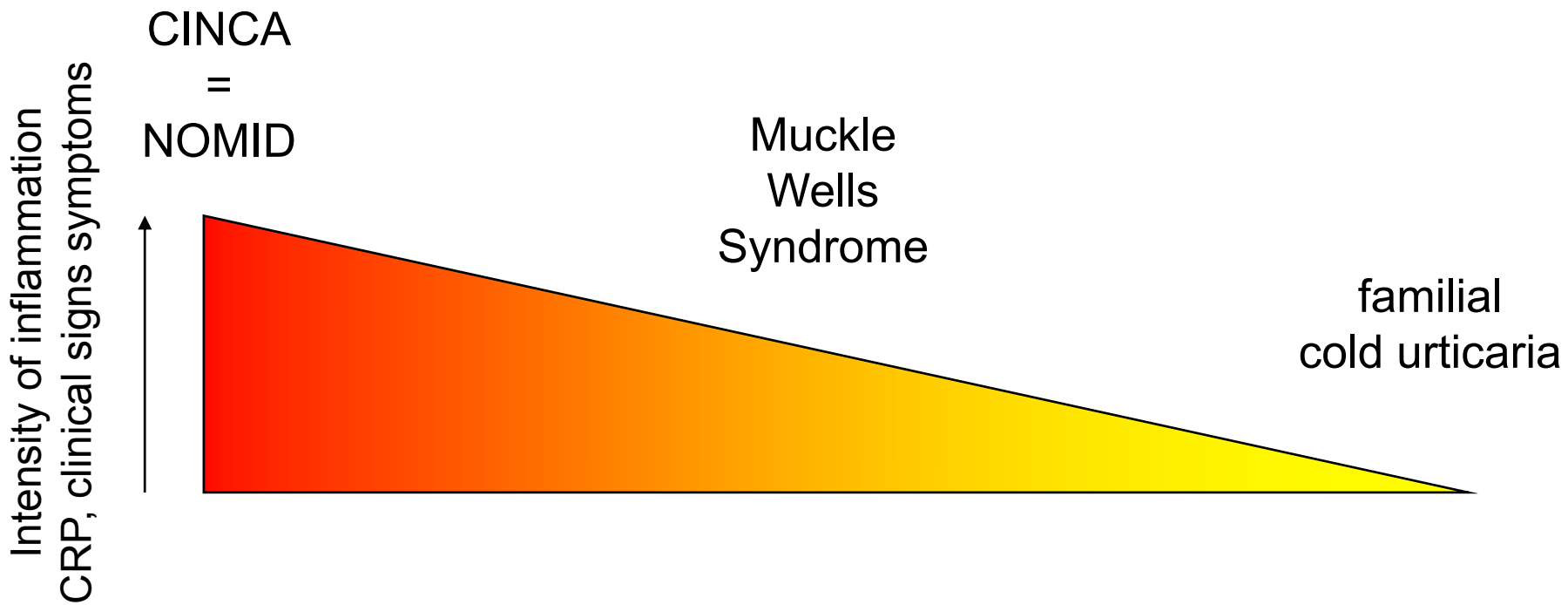
variable fever episodes, arthralgia, arthritis

Urticaria ca. 2-3h after cold exposition

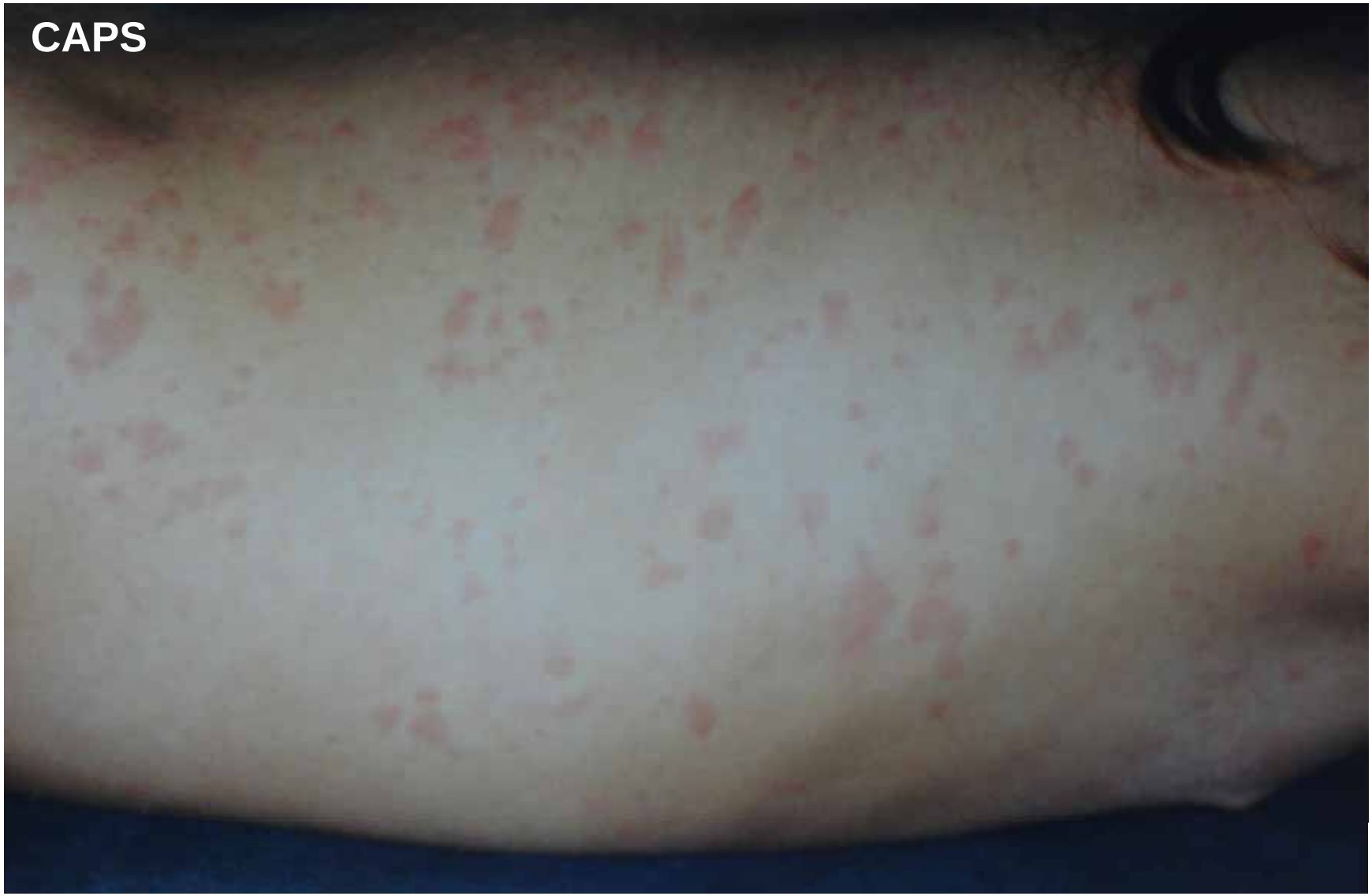
CNS involvement: sterile meningtitis, cephalgia, nausea and vomiting
transient-permanent hearing loss

AA amyloidosis

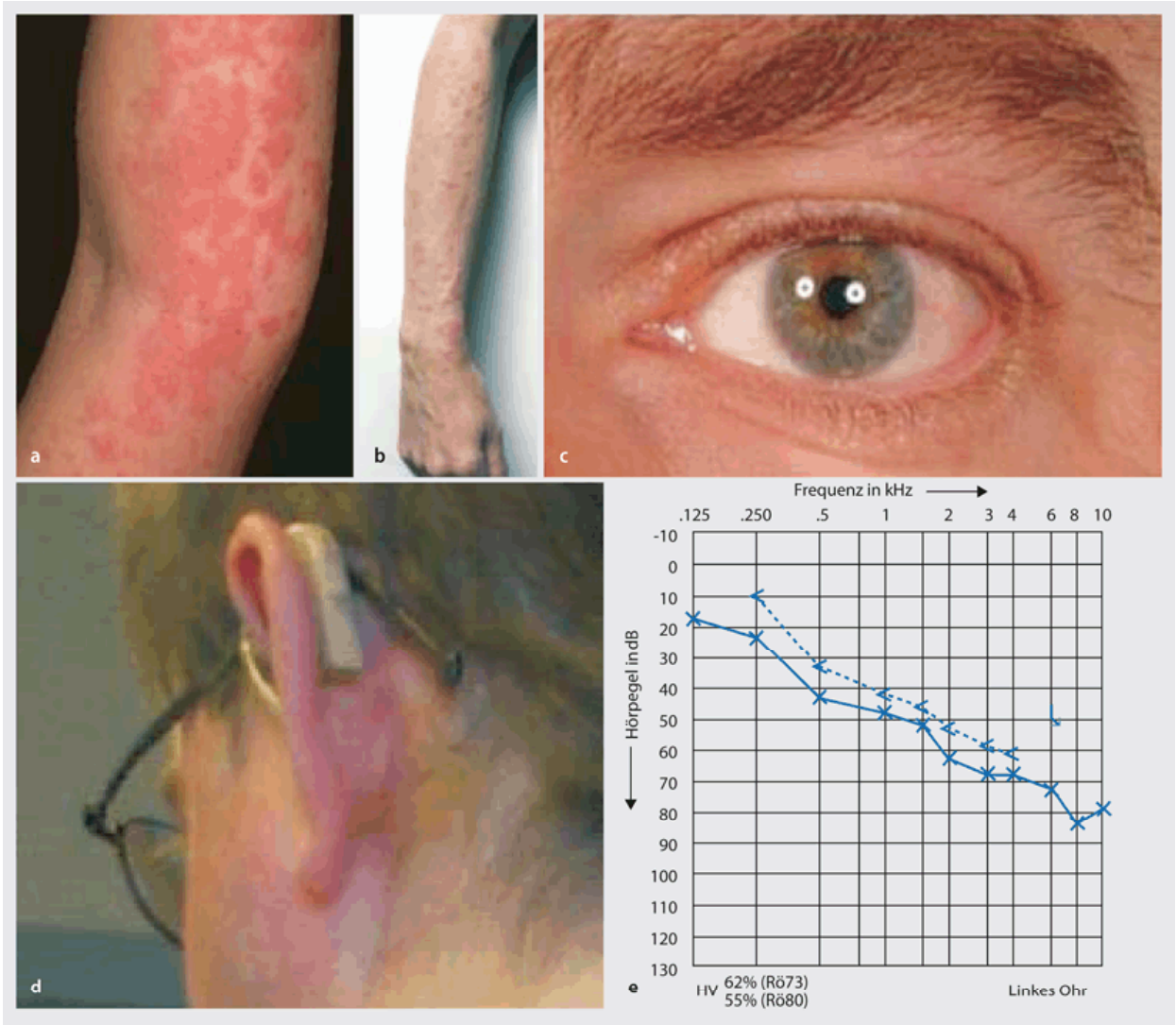
clinical spectrum of CIAS1 = NLRP3 mutations



CAPS

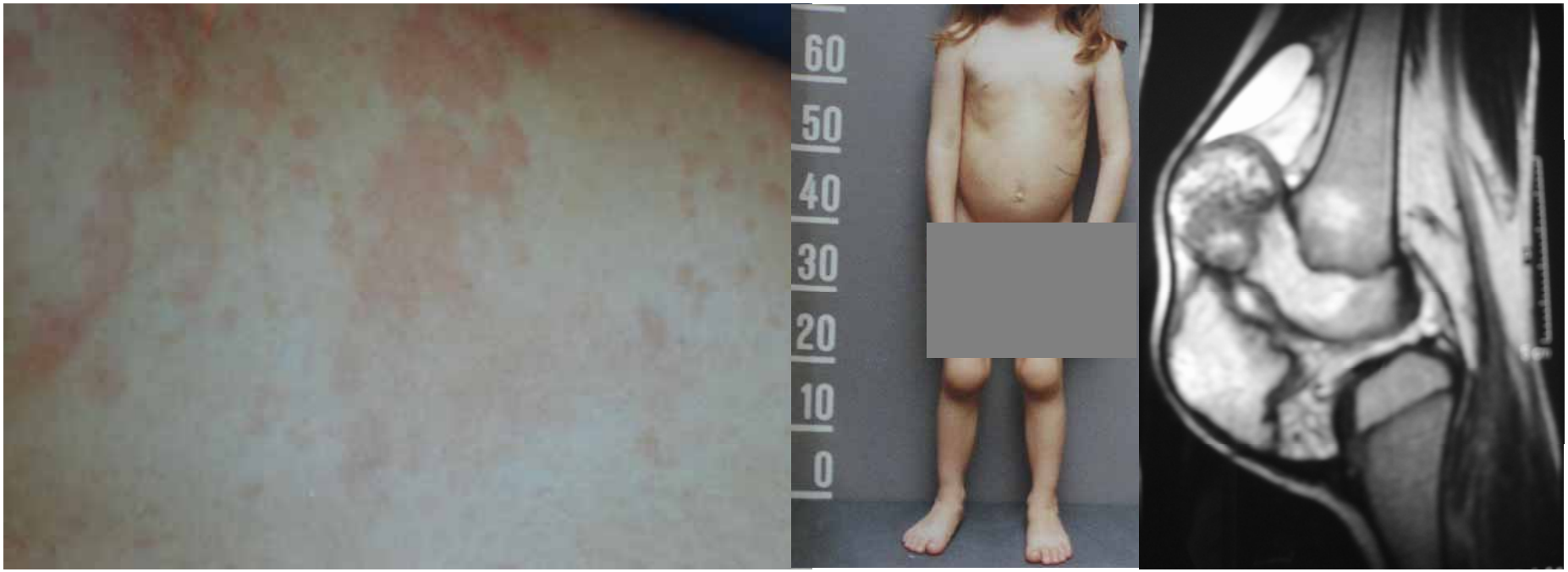


CAPS



Kötter I, **Schedel J**, **Kümmerle-Deschner JB**.
Periodic fever syndrome/autoinflammatory syndrome. Z Rheumatol 2009

CAPS : FCAS / MWS / CINCA-NOMID:



ASC=apoptosis-associated speck like protein containing a CARD
BBCC=B box and a coiled coil
SPRY=B30.2 domain
NACHT=NAIP, CIITA, HETE and TP-1 : NOD1,2, IPAF, NALPs
PAMP=pathogen-associated molecular pattern

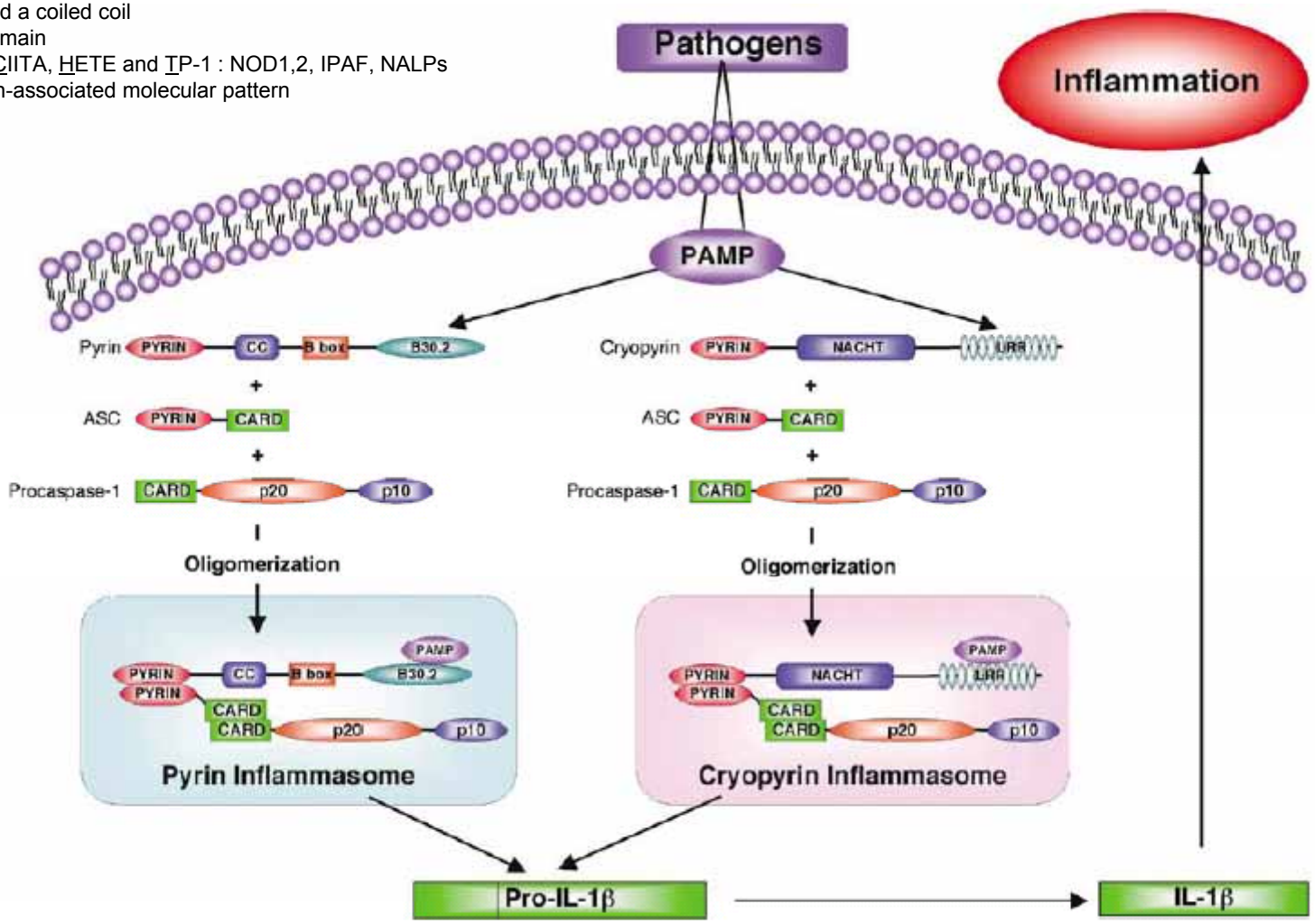
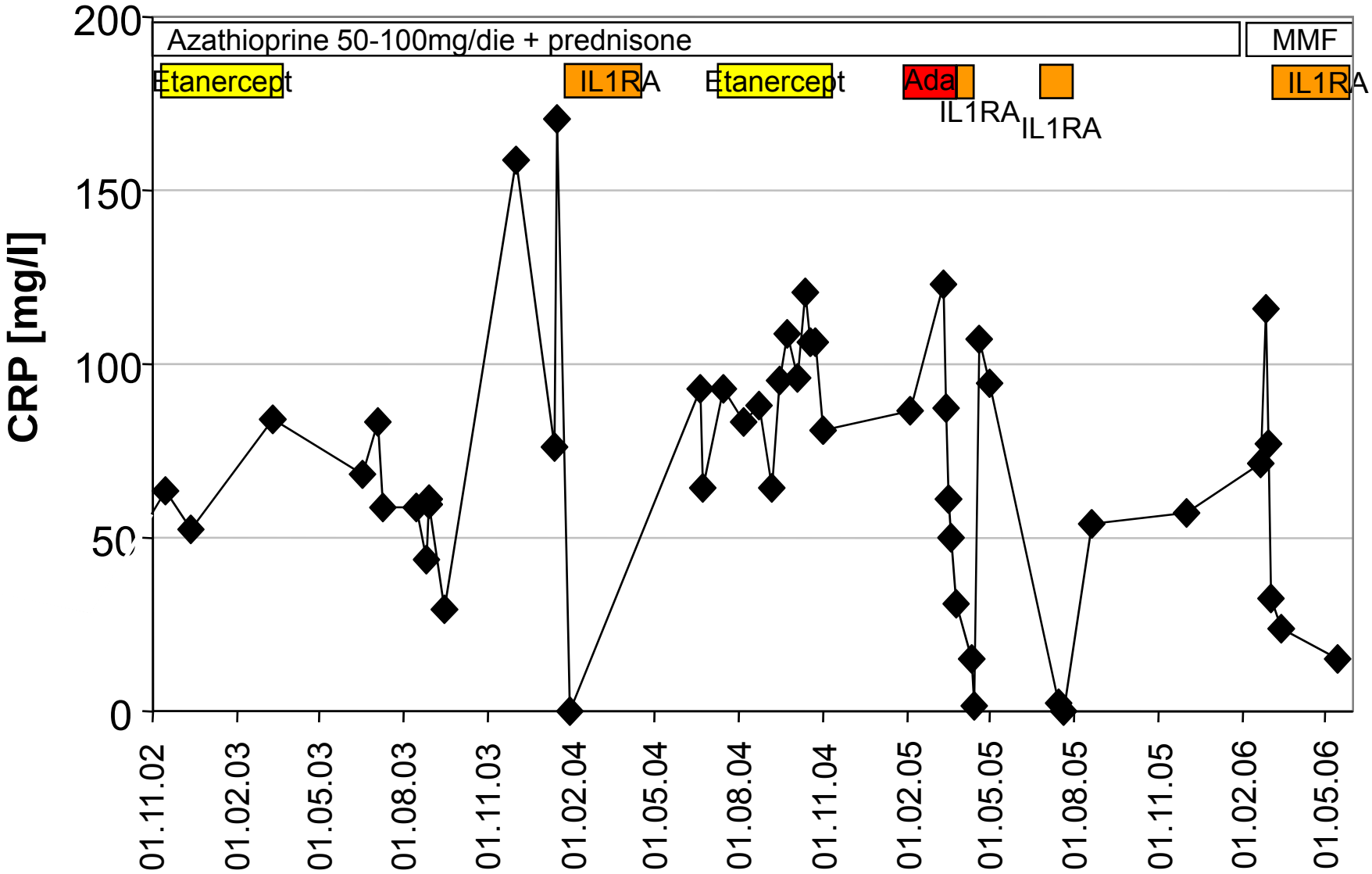


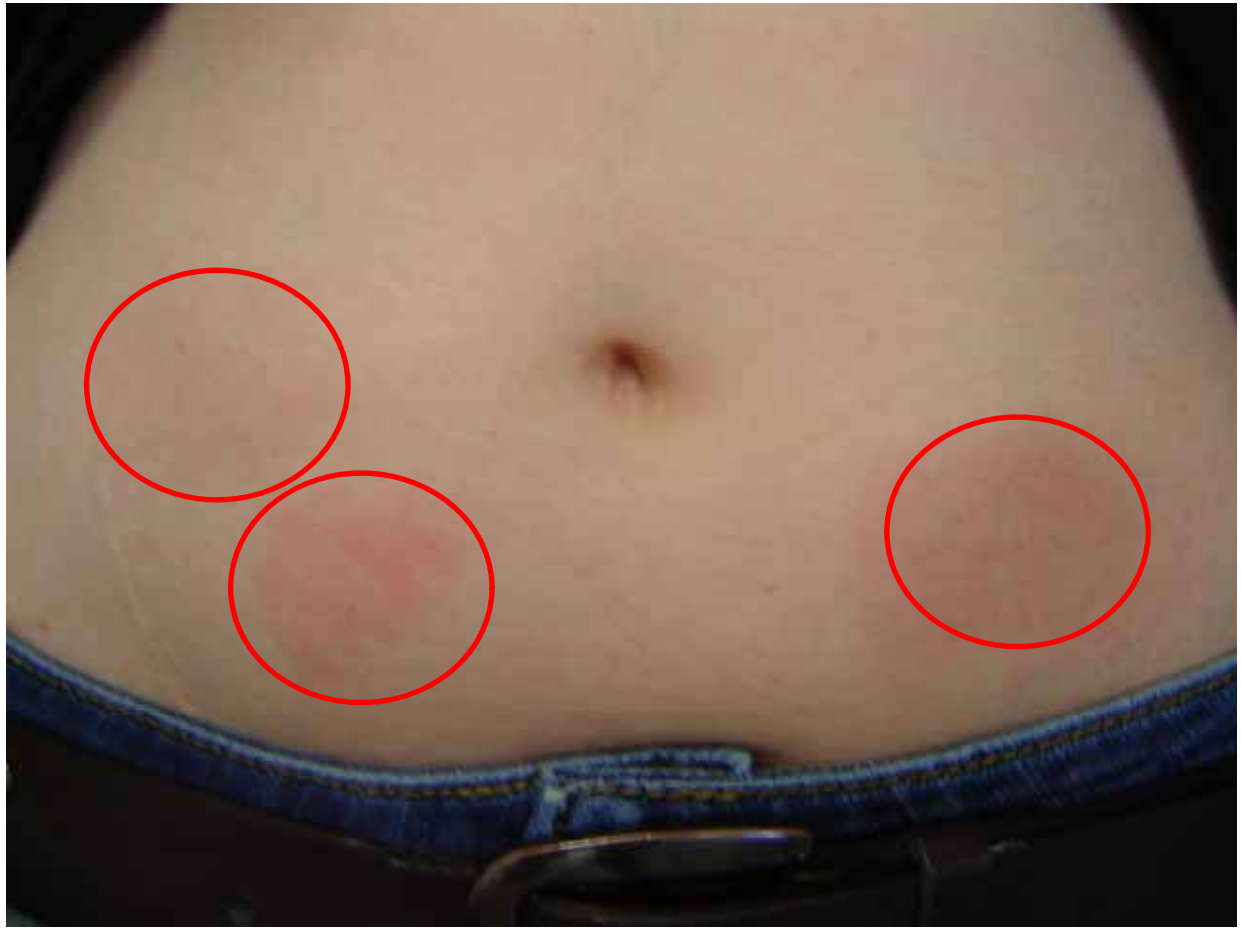
Figure 8 A hypothetical model illustrating the formation of the cryopyrin and pyrin inflammasomes in response to pathogen infection. Recognition of PAMPS by the LRR or B30.2 domains of cryopyrin or pyrin proteins leads to recruitment and oligomerization of ASC and procaspase-1 into two distinct inflammasome complexes. These complexes are then capable of processing pro-IL-1β into the mature IL-1β, which induces inflammation after its release from the infected cell

Yu et al, Cell Death Differ, 2006

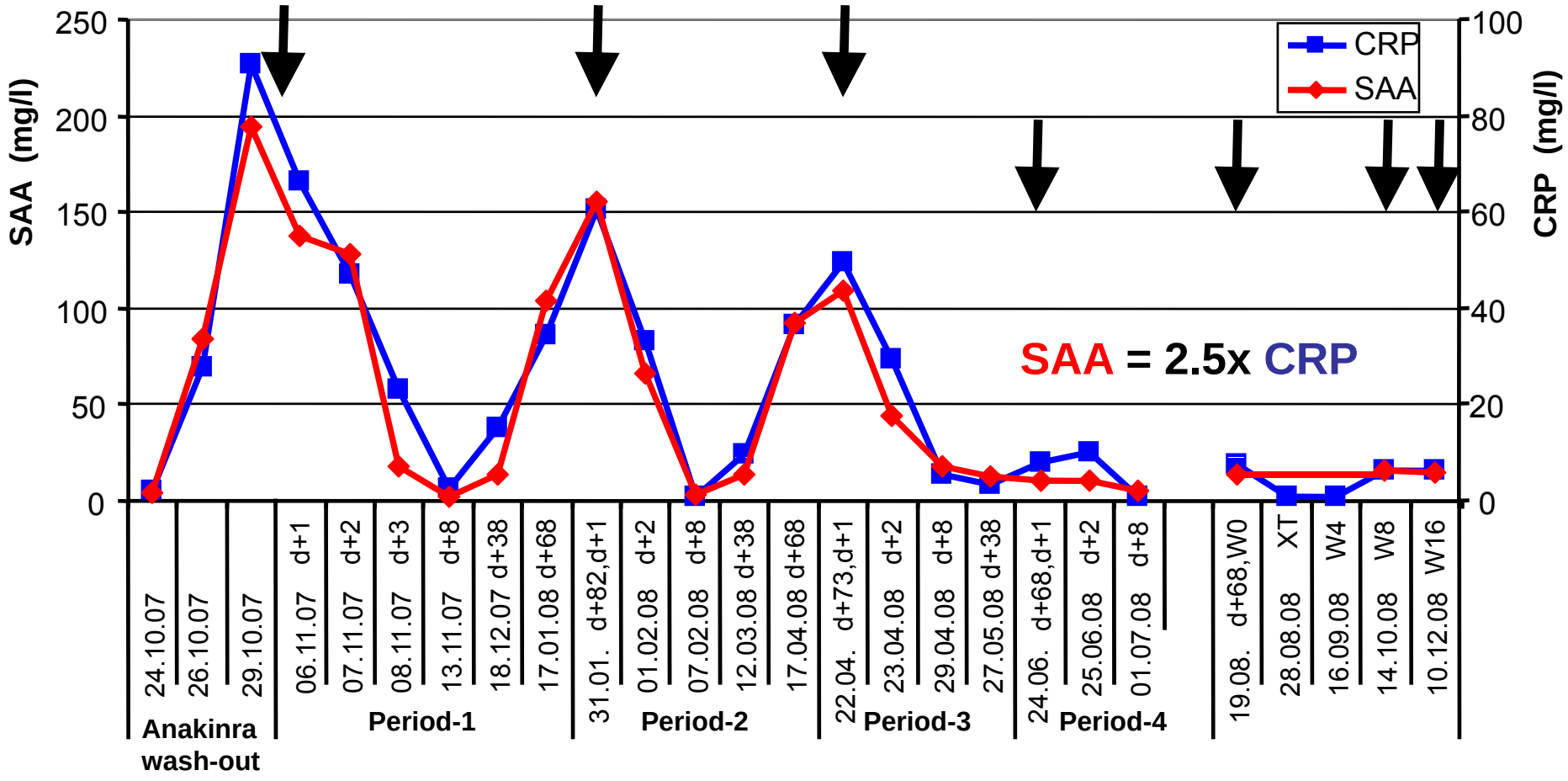
Patient with CINCA



local reactions to anakinra (Kineret®)



MWS-CINCA overlap syndrome treated with Canakinumab (anti-IL1β)

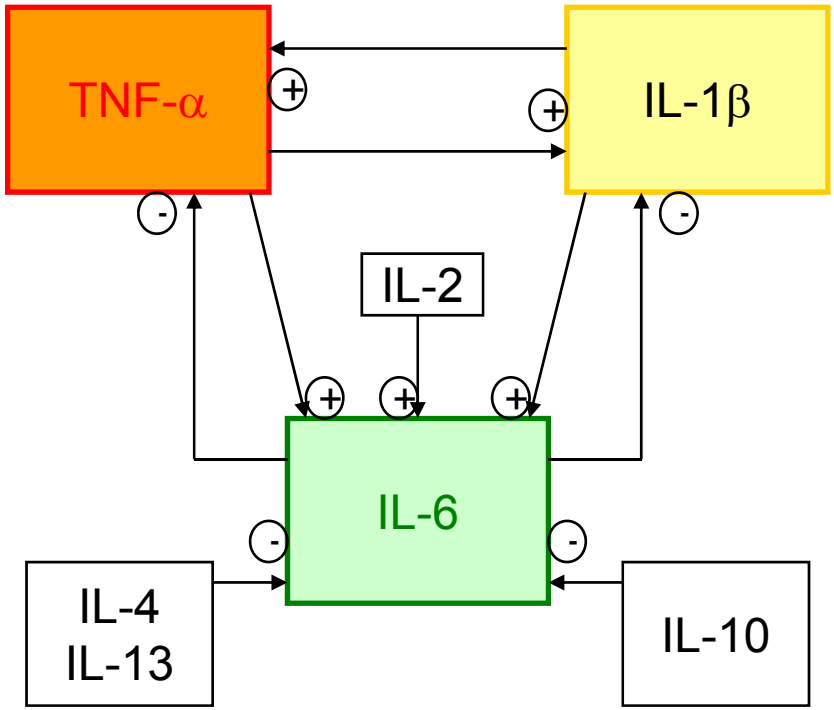


ACZ885-A2102

ACZ885-D2306

Therapeutic targets in chronic inflammatory diseases

the cytokine network



the role of IL-6 in the cytokine network
Th1-cytokines induce IL-6, Th2-cytokines inhibit IL-6.
Adapted from Tackey et al., Lupus 2004.

	Target	Type of drug
Etanercept	TNF-α	TNF-Receptor-IgG-construct
Infliximab	TNF-α	chimeric monoclonal antibody
Adalimumab	TNF-α	human monoclonal antibody
Golimumab	TNF-α	human monoclonal antibody
Certolizumab	TNF-α	pegylated Fab2- antibody fragment
Anakinra	IL-1β	recombinant human IL-1-Receptorantagonist
Rilonacept	IL-1β	IL-1-Receptor-IgG-construct, IL-1-trap
Canakinumab	IL-1β	human monoclonal antibody
Tocilizumab	IL-6R	humanized monoclonal antibody
Rituximab	CD20	chimeric monoclonal antibody, B cell depletion
Abatacept	B7	CTLA4-IgG-construct, blocks costimulation

Summary / Conclusion:

AA amyloidosis (AAA) is a rare long term complication of chronic inflammatory diseases

screening procedures reveal a higher incidence of AAA

treatment with biologics probably reduce the risk for AAA and inhibit progression of manifest AAA