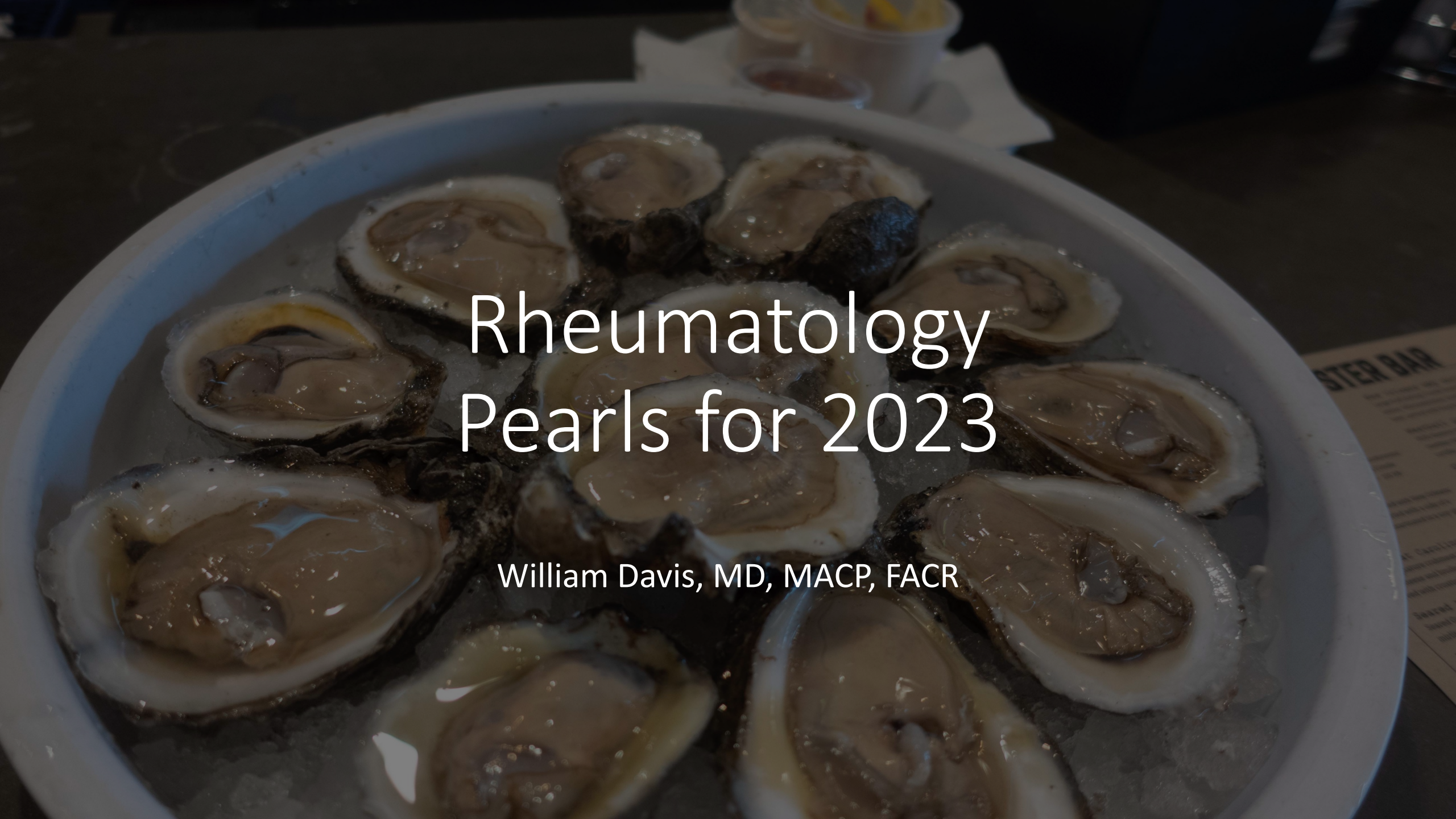


Rheumatology Pearls for 2023

William Davis, MD, MACP, FACR

Disclosures

Consultant

- ANI Pharma
- Aurinia Pharma
- Janssen

Research

- Abbvie
- Amgen

- Gout & Hyperuricemia
- Systemic Lupus Erythematosus
- Systemic Vasculitis

Gout

Mr RR

- 80 y/o M with glioblastoma multiforme admitted for seizures
- PMH:
  - HTN
  - HLP
  - DM
  - CKD3
  - CAD s/p PCI
  - AAA s/p repair
- Meds:
  - Amlodipine
  - Escitalopram
  - Fenofibrate
  - Gabapentin
  - Lacosamide
  - Levetiracetam
  - Losartan
  - Metoprolol
  - Pantoprazole
  - Pravastatin
  - Silodosin

Mr RR (Cont)

- He is admitted and neurology commences changes in anti-convulsant therapy
- Hospital day 4 - c/o painful R great toe
- R 1st MTP is swollen, red, warm; he is limping on it

- Does he have gout?
- How can we treat it?

SPECIAL ARTICLE

2015 Gout Classification Criteria

An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative

Tuhina Neogi,[1] Tim L. Th. A. Jansen,[2] Nicola Dalbeth,[3] Jaap Fransen,[4] H. Ralph Schumacher,[5] Dianne Berendsen,[4] Melanie Brown,[6] Hyon Choi,[1] N. Lawrence Edwards,[7] Hein J. E. M. Janssens,[4] Frédéric Lioté,[8] Raymond P. Naden,[9] George Nuki,[10] Alexis Ogdie,[5] Fernando Perez-Ruiz,[11] Kenneth Saag,[12] Jasvinder A. Singh,[13] John S. Sundy,[14] Anne-Kathrin Tausche,[15] Janitzia Vaquez-Mellado,[16] Steven A. Yarows,[17] and William J. Taylor[6]

This criteria set has been approved by the American College of Rheumatology (ACR) Board of Directors and the European League Against Rheumatism (EULAR) Executive Committee. This signifies that the criteria set has been quantitatively validated using patient data, and it has undergone validation based on an independent data set. All ACR/EULAR-approved criteria sets are expected to undergo intermittent updates.

The American College of Rheumatology is an independent, professional, medical and scientific society which does not guarantee, warrant, or endorse any commercial product or service.

ACR/EULAR gout classification criteria

Step 1: Entry criterion	At least 1 episode of swelling, pain, or tenderness in a peripheral joint or bursa	(only apply criteria below to those meeting this entry criterion)
Step 2: Sufficient criterion	Presence of MSU crystals in a symptomatic joint or bursa (i.e., in synovial fluid) or tophus	(if met, can classify as gout without applying criteria below)
Step 3: Criteria (to be used if sufficient criterion not met)		
Clinical		
Pattern of joint/bursa involvement during symptomatic episode(s) ever	Ankle *or* midfoot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint	1
	Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)	2

ACR/EULAR gout classification criteria

Characteristics of symptomatic episode(s) ever		
• Erythema overlying affected joint • Cannot bear touch or pressure to affected joint • Great Difficulty with walking in inability to use affected joint	One characteristic Two characteristics Three characteristics	1 2 3
Time course of episode(s) ever	One typical episode	1
Presence (ever) of ≥2, irrespective of anti-inflammatory treatment		2
• Time to maximal pain <24 hours • Resolution of symptoms in ≤14 days • Complete resolution (to baseline level) between symptomatic episodes	Recurrent typical episodes	2

ACR/EULAR gout classification criteria

Clinical evidence of TOPHUS	Present	4
Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (e.g., Achilles)		
Laboratory		
Serum urate, ideally during intercritical period; highest value irrespective of timing	< 4 mg/dL 6 - < 8 8 - < 10 ≥ 10	-4 +2 +3 +4
Synovial fluid analysis of symptomatic joint or bursa	MSU negative	-2

ACR/EULAR gout classification criteria

Imaging		
Imaging evidence of urate deposition in (ever) symptomatic joint or bursa	Present by either ultrasound or dual energy Computed tomography (DECT)	4
Imaging evidence of gout related joint damage: conventional radiography of the hands and/or feet demonstrates at least 1 erosion	Present	4

http://goutclassificationcalculator.auckland.ac.nz

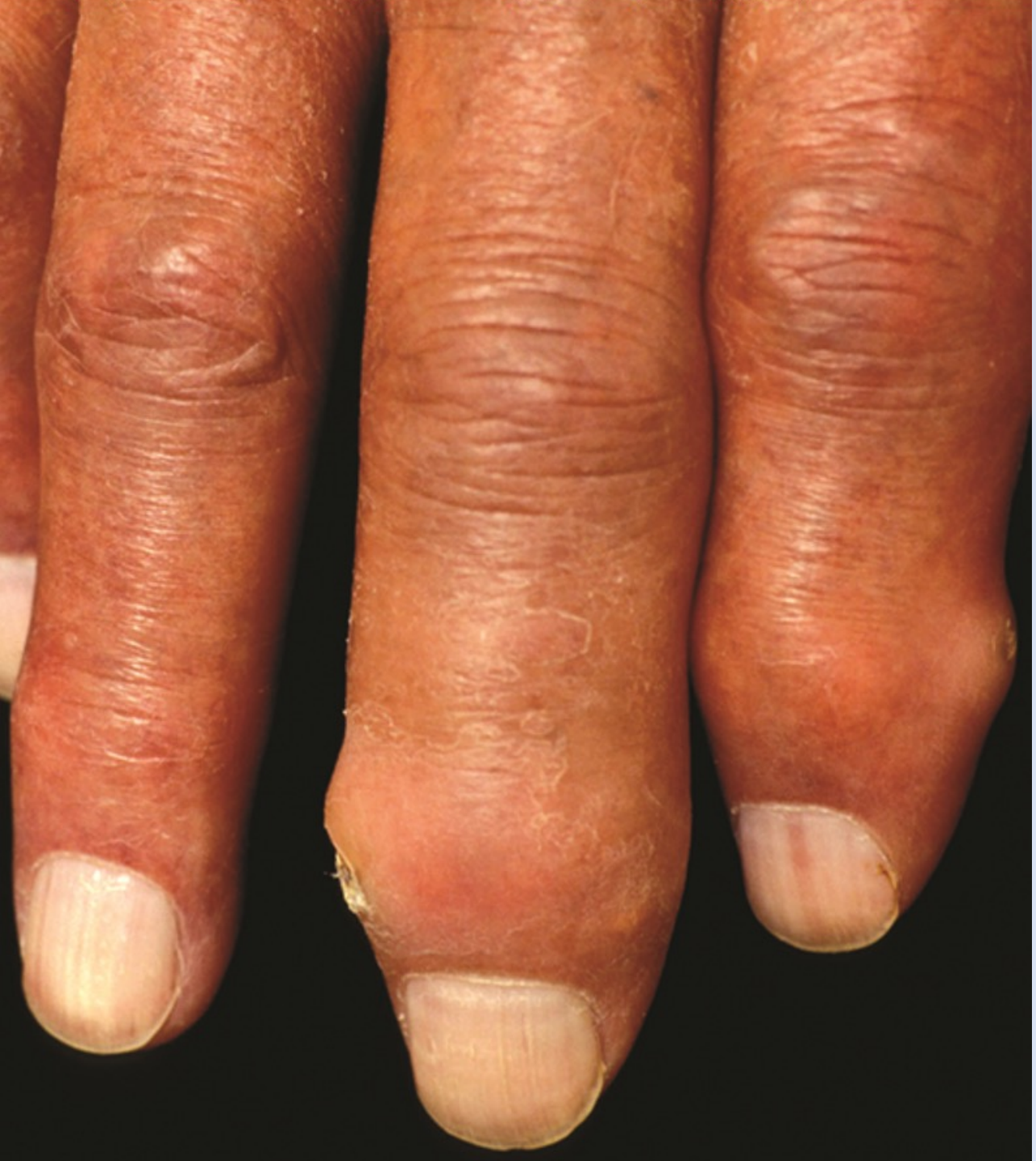
https://goutclassificationcalculator.auckland.ac.nz/

• MTP 1	2
• 3 characteristics	3
• Erythema	
• Can't bear touch	
• Difficult to walk	
• Typical episode (<24 hours to maximal pain)	1
• Serum urate 6 - <8	1
• Total	8

Subject meets criteria for gout classification (score ≥8)

Gout: Presentation

- Acute intermittent gout
  - Great toe (podagra): 50% of initial attacks
  - Other joints include forefoot, ankles, knees, fingers, wrist, elbow
  - Nocturnal onset
  - Fever, erythema, swelling, significant pain
- Intercritical gout: asymptomatic period between attacks



Gout: Presentation

Chronic recurrent gout

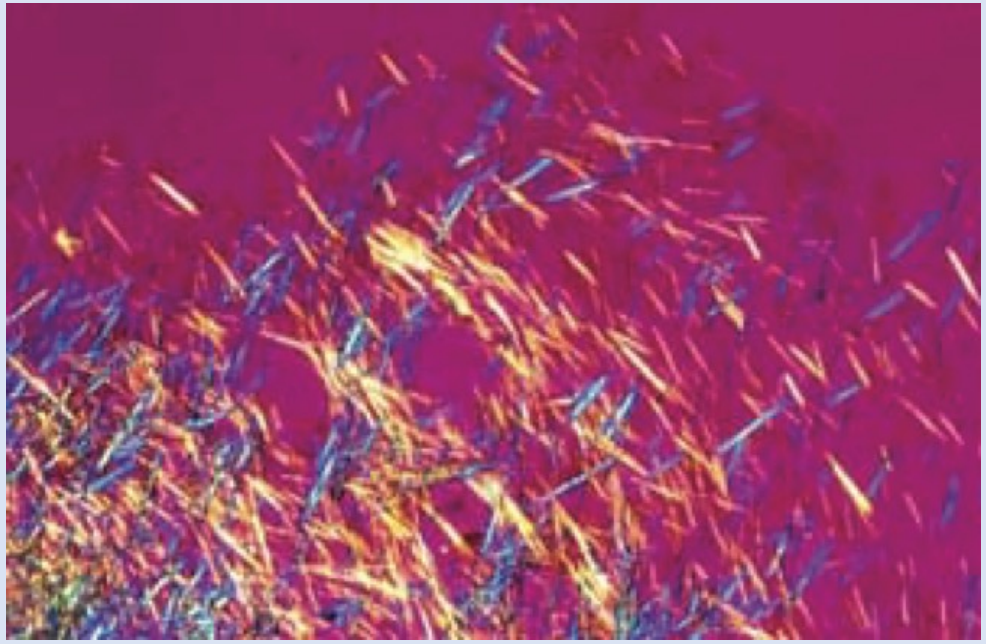
- Increasingly severe/frequent attacks
- Arthritis may become persistent, polyarticular
- Soft tissue involvement (cellulitis mimic, bursitis)

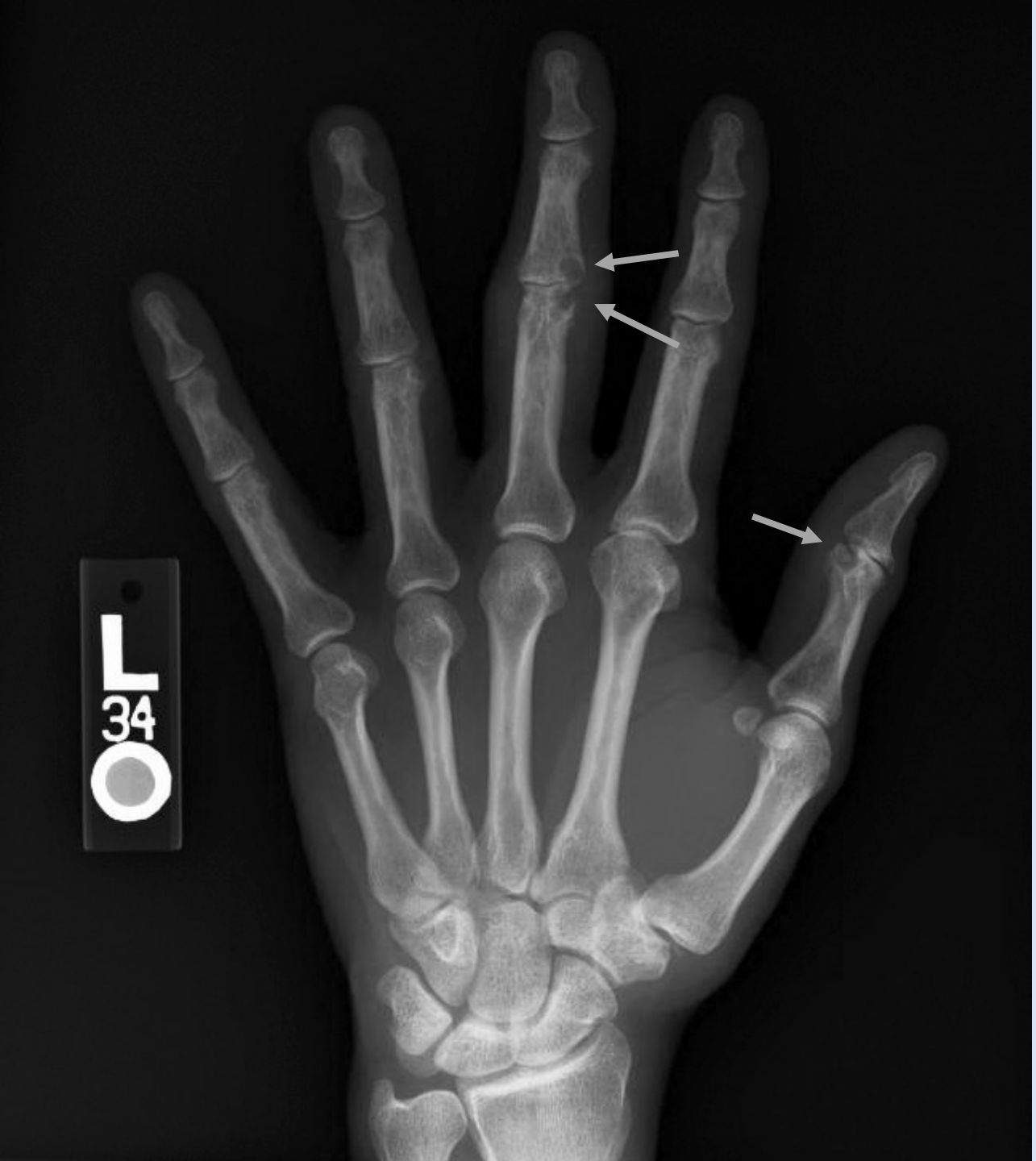
Chronic tophaceous gout

- Chronic recurrent gout + tophi
- Tophi on extensor elbows, Achilles tendon, fingers

Gout: Synovial Fluid Testing

- WBCs >2000-100,000/µL
  - Neutrophil predominance
- Urate crystal
  - Needle-shaped, negatively birefringent
- Acute gout
  - Intracellular (leukocyte) crystals
- Intercritical gout
  - Extracellular crystals
- Gram stain and culture
  - Diagnose concomitant infection





Gout: Testing

Serum urate levels

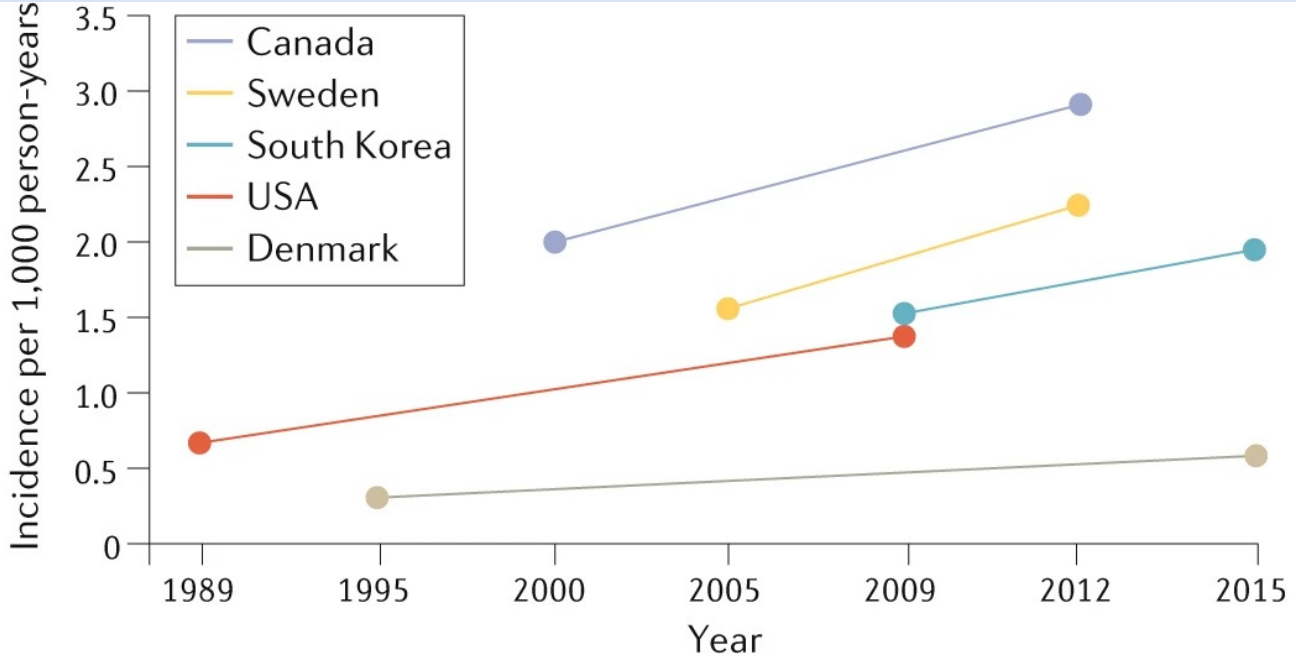
- Not helpful in acute gout

↑ C-reactive protein, ESR, WBC

- Nonspecific findings

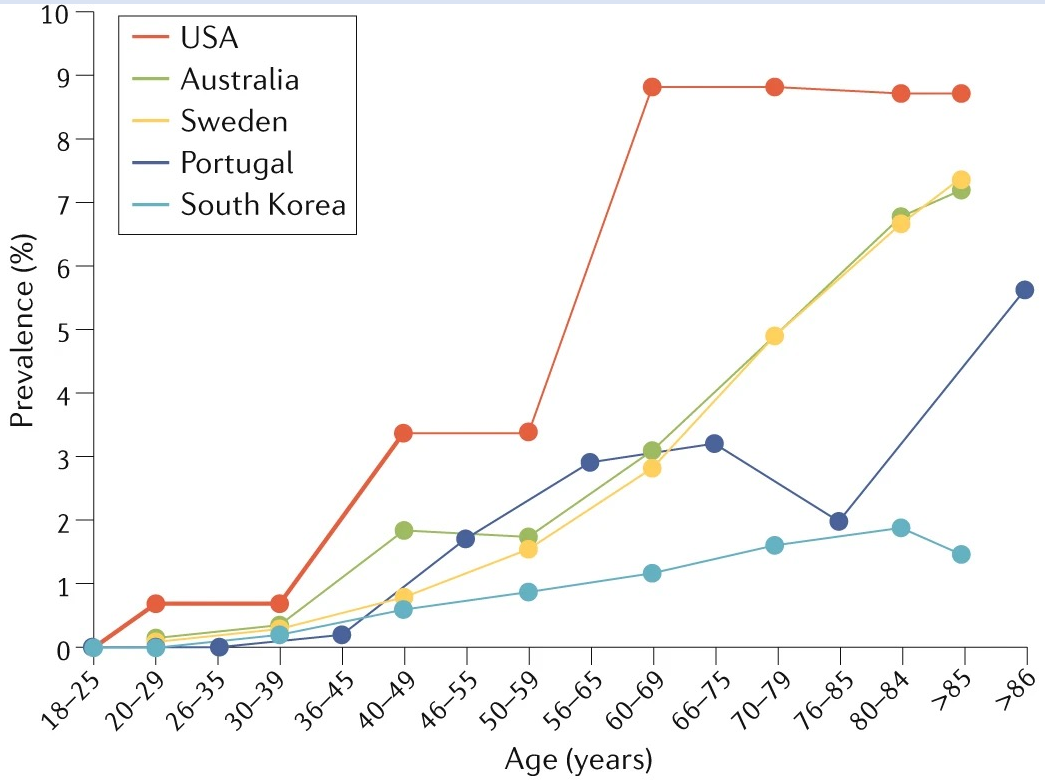
Imaging

- Uncertain diagnosis or arthrocentesis not possible
- Ultrasound → double contour sign
- Dual-energy CT → MSU deposits
- Plain films (chronic gout) → erosions with overhanging cortical bone



Location	Incidence per 1,000 person-years in indicated year						
	1989	1995	2000	2005	2009	2012	2015
Canada			2			2.9	
Sweden				1.55		2.24	
South Korea					1.52		1.94
USA	0.67				1.37		
Denmark		0.32					0.58

Dehlin, M., Jacobsson, L. & Roddy, E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nat Rev Rheumatol* **16**, 380–390 (2020). https://doi.org/10.1038/s41584-020-0441-1



Location	Prevalence (%) in indicated age range (years)							
	20–29	30–39	40–49	50–59	60–69	70–79	80–84	>85
USA	0.7	0.7	3.4	3.4	8.8	8.8	8.7	8.7
Australia	0.08	0.33	1.84	1.68	3.03	4.9	6.72	7.19
Sweden	0.06	0.27	0.8	1.54	2.83	4.89	6.61	7.38
South Korea	0.03	0.2	0.59	0.85	1.15	1.59	1.9	1.49

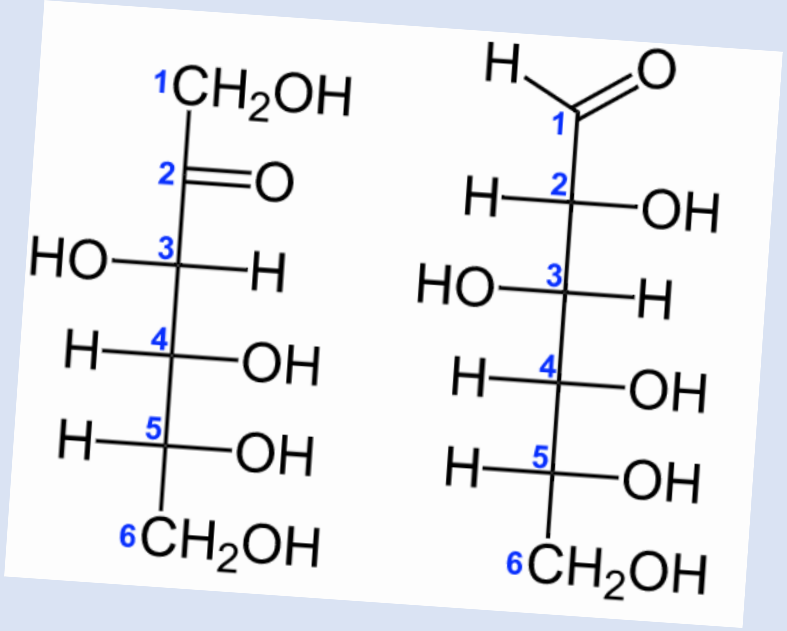
Location	Prevalence (%) in indicated age range (years)							
	18–25	26–35	36–45	46–55	56–65	66–75	76–85	>86
Portugal	0	0	0.2	1.7	2.9	3.2	2	5.6

Conditions Associated With Gout

- Age
- Male or post- menopausal
- Obesity
- Western diet (red meat, seafood and shellfish, fructose, sugar-sweetened soft drinks and alcoholic drinks (particularly beer))
- Diuretics

<u>Comorbidities:</u>

- HTN, DM, HLP, CKD
- Gout ↔ ASCVD

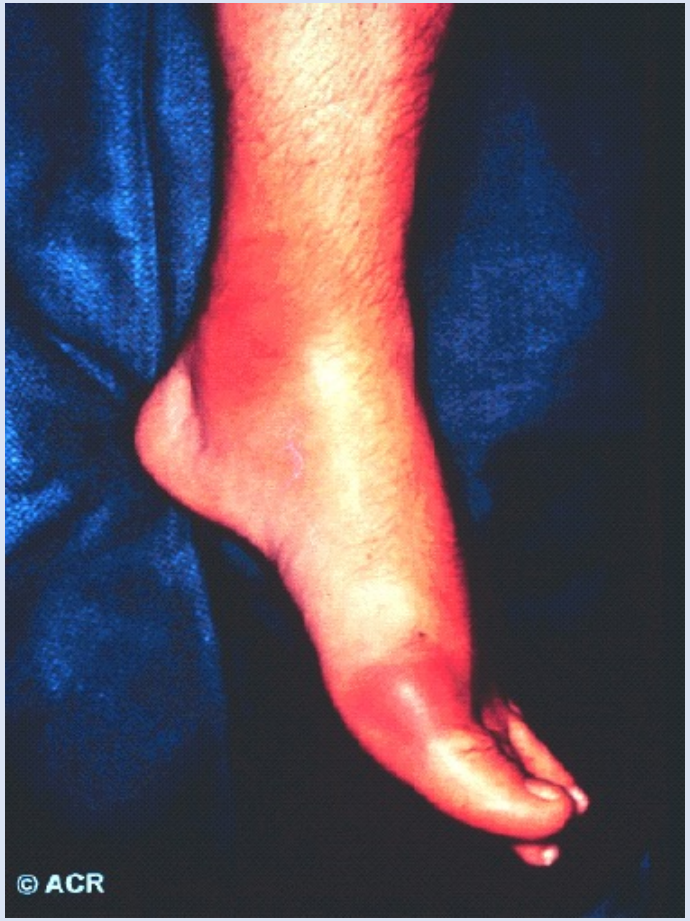


Precipitants of Acute Gout

- Alcohol binge
- Sepsis
- Myocardial Infarction
- Acute severe illness
- Trauma, surgery
- Dehydration

Acute Gout

- Microcrystal release
- IgG coating of crystal
- Adhesion molecule activation
- Neutrophil diapedesis, chemotaxis, phagocytosis
- Inflammasome



Arthritis Care & Research
Vol. 0, No. 0, June 2020, pp 1–17
DOI 10.1002/acr.24180

American College of Rheumatology
Empowering Rheumatology Professionals

Gout flare management

- Using **colchicine, NSAIDs, or glucocorticoids** (oral, intraarticular, or intramuscular) as appropriate first-line therapy for gout flares over IL-1 inhibitors or adrenocorticotropic hormone (ACTH) is strongly recommended for patients experiencing a gout flare.
- Given similar efficacy and a lower risk of adverse effects, **low-dose colchicine** over high-dose colchicine is strongly recommended when colchicine is the chosen agent.
- Using an **IL-1 inhibitor** over no therapy (beyond supportive/analgesic treatment) is conditionally recommended for patients experiencing a gout flare for whom the above anti-inflammatory therapies are either ineffective, poorly tolerated, or contraindicated.

Colchicine: Mechanism of Action

- Reduces monocyte eicosanoid release; Inhibits phospholipase A2
- Inhibits phagocytosis by interfering with microtubules
- Alters neutrophil adhesion, motility, and chemotaxis

Colchicine Toxicity

Acute

- Nausea, vomiting
- Abdominal pain, cramping
- Diarrhea/ hemorrhagic gastroenteritis

Chronic

- Myelosuppression
- Neuromyopathy
- Alopecia
- Amenorrhea, dysmenorrhea
- Oligospermia, azospermia

Colchicine for Acute Gout

YES!

- Colchicine 0.6 mg
  - 2 tablets at onset of attack
  - 1 tablet one hour later

NEVER!!!

- Colchici .6 mg
  - On ourly un ain abates or ent lops di ea
  - No exceed g
- Intraven 0.5-1 mg

NSAID

- NSAID gastropathy
- Renal hemodynamics
- Platelet inhibition
- Drug interactions

Risk Factors for NSAID-associated Upper Gastrointestinal Tract Complications

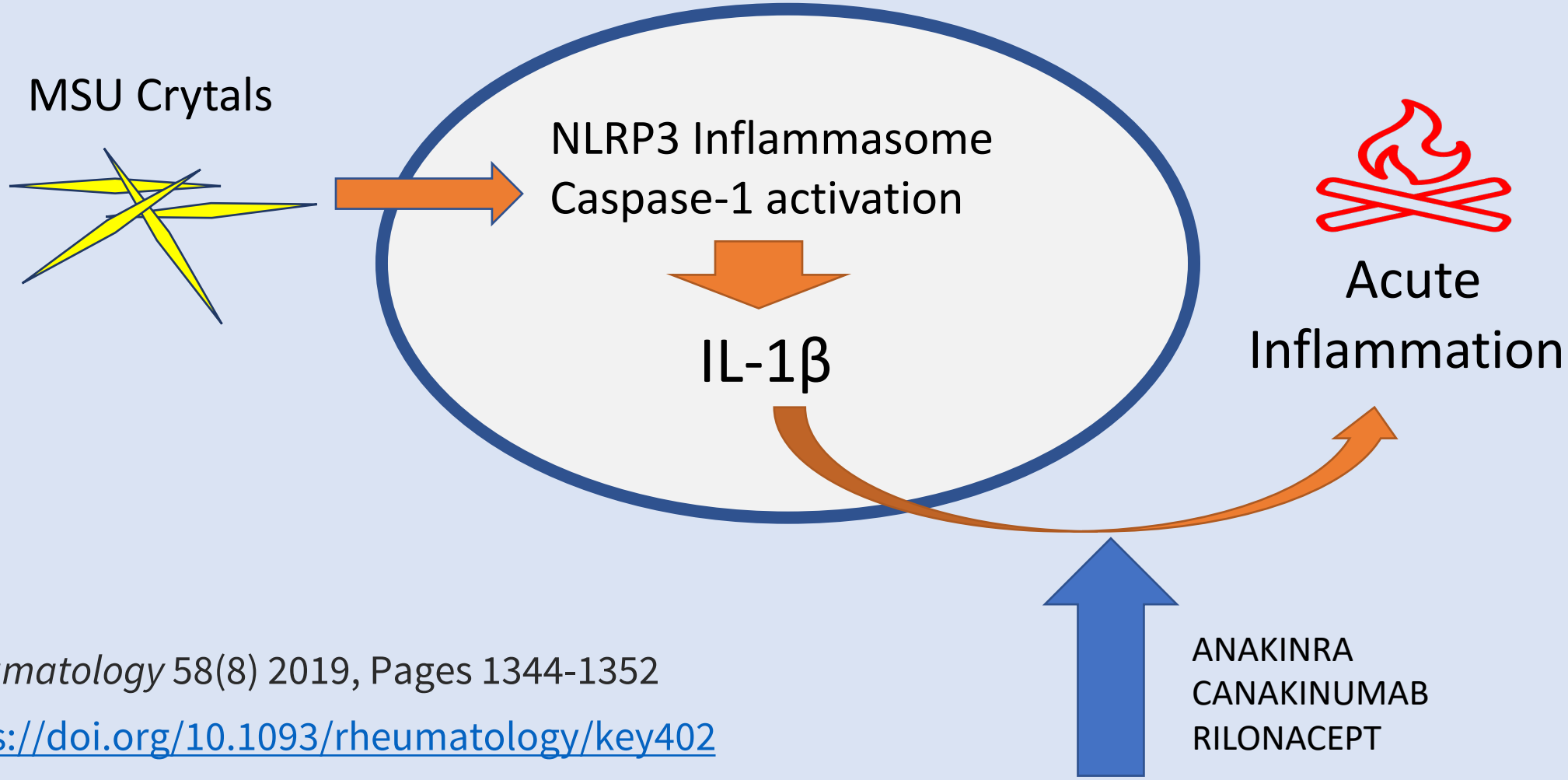
- Older age
- Previous peptic ulcer disease
- Previous gastrointestinal bleeding
- History of cardiovascular disease
- Concomitant corticosteroid
- Presence of co morbidity
- Use of H2 blockers

Corticosteroids

- Oral
- Intra-articular
- Intramuscular
- Intravenous

- ACTH / adrenocorticotropic hormone

Anti-IL1 and acute gout



Rheumatology 58(8) 2019, Pages 1344-1352
https://doi.org/10.1093/rheumatology/key402

ANAKINRA (Kineret®)
IL-1 Receptor Antagonist (IL-1RA)

FDA Indications

- Rheumatoid arthritis
- Deficiency of IL-1RA
- Neonatal onset, multisystem Inflammatory Disease (NOMID)

Non-FDA Uses

- Familial Mediterranean Fever
- Pericarditis
- Adult Still Disease
  - Macrophage Activation Syndrome
- Gout
  - 100 mg once daily x 3-5 days

Anakinra

- Injection site reactions
- Hypersensitivity/allergic reactions
- Infections
- Neutropenia (1-3 months)

<u>Other IL-1 inhibitors</u>

Canakinumab
Rilonacept

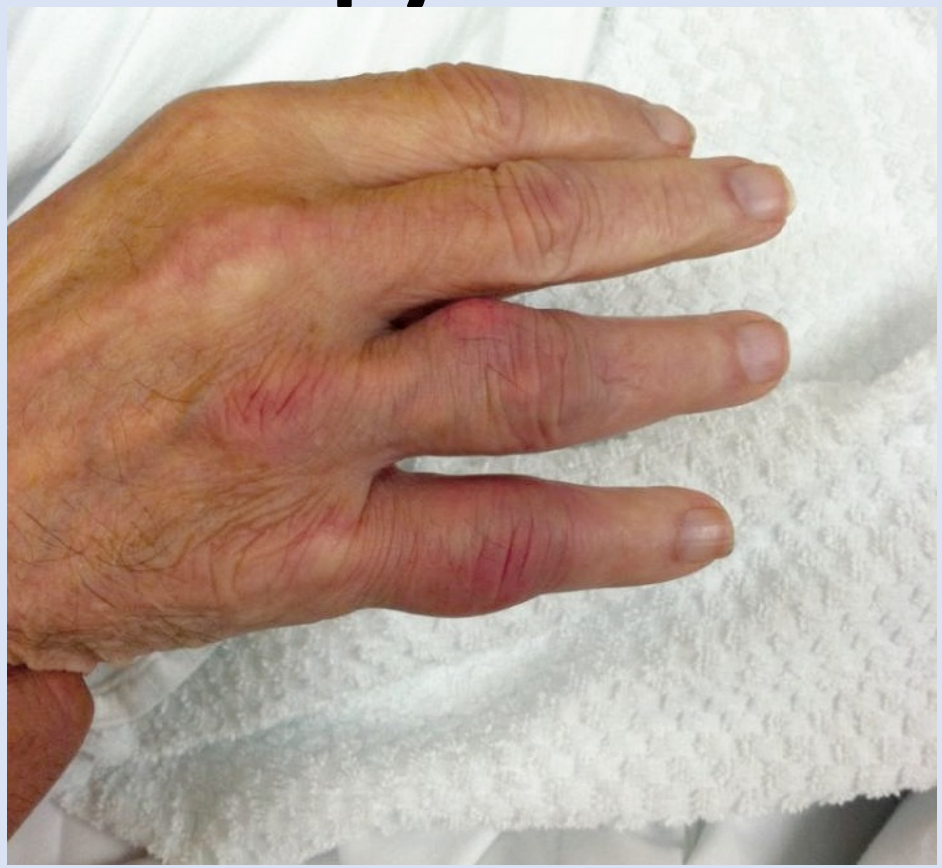
Saag *Arthritis Rheum* 2021

Gout: Treatment

- Discontinue diuretics; consider losartan (uricosuric)
- Weight loss, alcohol reduction
- Specific dietary restrictions (insufficient evidence)
- Acute gout treatment; consider comorbidities/drug interactions
  - Glucocorticoids (oral, intra-articular, or intramuscular)
  - NSAIDs
  - Low-dose colchicine
  - Anakinra (IL1-RA)

Hyperuricemia: Allopurinol Therapy

- First-line therapy
  - Decrease dosage in CKD
- Indications
  - ≥2 attacks in a year
  - 1 attack + stage ≥3 CKD or nephrolithiasis, serum urate level >9 mg/dL
  - Tophi
  - + Radiographic signs of chronic gout
- Concomitant low-dose colchicine, NSAIDs, or prednisone



Hyperuricemia: Other Therapy

- Febuxostat → patients intolerant of allopurinol; boxed warning
- Probenecid → possibly combined with allopurinol
- IV pegloticase → severe recurrent or tophaceous gout
  - Oral drug failure
  - Risk for severe allergic reactions
- Serum urate level target <6 mg/dL

Systemic Lupus Erythematosus

34 F admitted for fatigue, fever, arthralgia after missing dialysis.

Hospitalized 1 week ago with central line infection. She left hospital AMA after line changed.

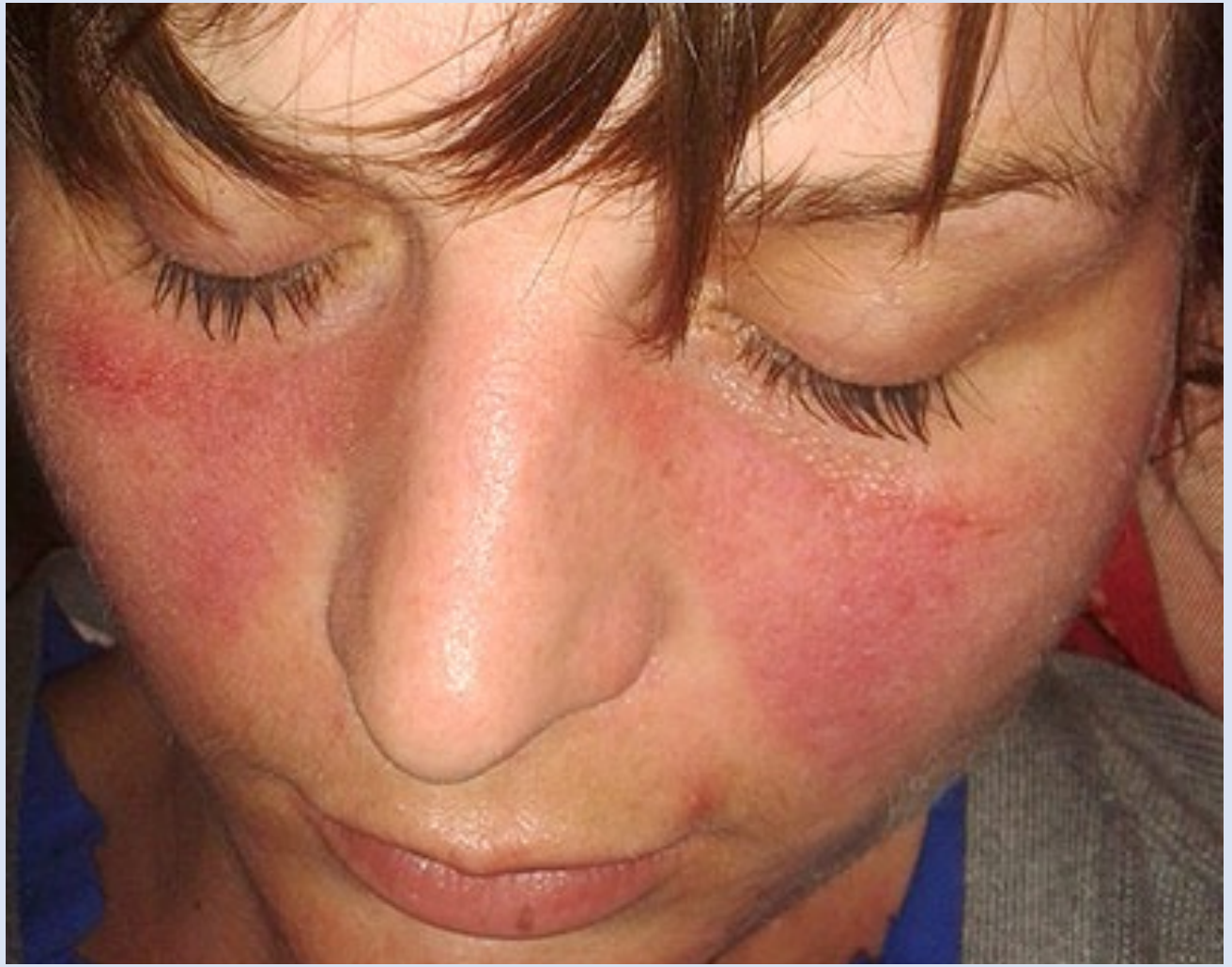
SLE dx 5 years previous when presented with fever, arthritis, RPGN, +ANA/DNA, low C3/C4. She was treated with prednisone and MMF and HCQ.

She developed ESRD 2 years ago and has been off of all lupus meds for 6 months.

She has T 101.6, BP 160/110, HR 90

PE notable for diffuse erythematous rash on sun exposed areas

Lab WBC 3.0, Hgb 9.2, Plate 123, K 6.9, Alb 2.8



https://en.wikipedia.org/wiki/Lupus#/media/File:Lupusfoto.jpg

Systemic Lupus Erythematosus: Classification Criteria

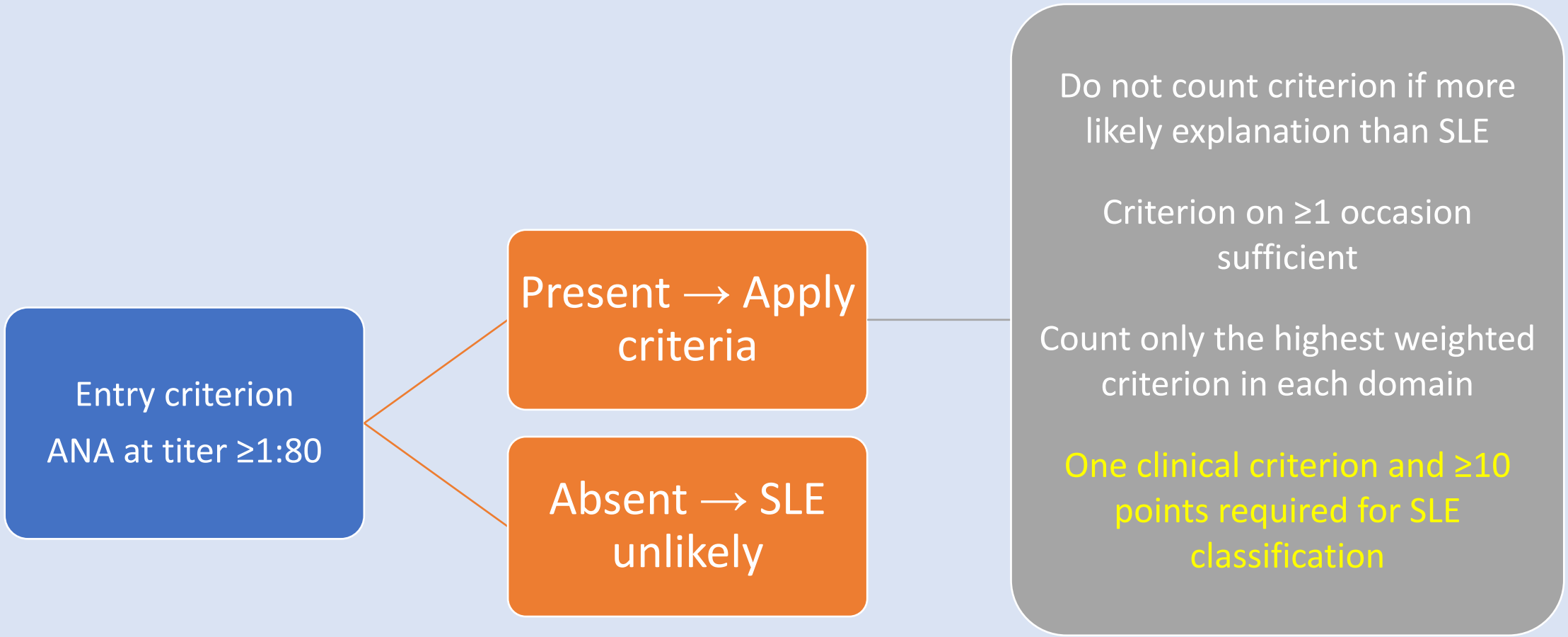
	American College of Rheumatology (ACR) Classification Criteria
1971	Criteria for classification of SLE developed
1982	Revised ACR Classification
1997	Revision of Revised Classification
2012	SLICC Classification Criteria
2019	ACR/EULAR Classification Criteria

SLICC – Systemic Lupus International Collaborating Clinics

EULAR – European League Against Rheumatism

Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78:1151-1159. [PMID: 31383717] doi:10.1136/annrheumdis-2018-214819.

Systemic Lupus Erythematosus: Classification Criteria



Information from BMJ: Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78:1151-1159. [PMID: 31383717] doi:10.1136/annrheumdis-2018-214819.

Systemic Lupus Erythematosus: Classification Criteria

Clinical Domain	Criteria	Points
Constitutional	Fever	2
Hematologic	Leukopenia	3
	Thrombocytopenia	4
	Autoimmune hemolysis	4
Neuropsychiatric	Delirium	2
	Psychosis	3
	Seizure	5
Mucocutaneous	Nonscarring alopecia	2
	Oral ulcers	2
	Subacute cutaneous or discoid lupus	4
	Acute cutaneous lupus	6
Serosal	Pleural or pericardial effusion	5
	Acute pericarditis	6
Musculoskeletal	Joint involvement	6
Renal	Proteinuria >0.5 g/24 h	4
	Renal biopsy class II or V lupus nephritis	8
	Renal biopsy class III or IV lupus nephritis	10

Immunology Domain	Criteria	Points
Antiphospholipid antibodies	Anticardiolipin antibodies *or* Anti-β_2-glycoprotein I antibodies *or* Lupus anticoagulant	2
Complement proteins	Low C3 *or* low C4	3
	Low C3 *and* low C4	4
SLE-specific antibodies	Anti-dsDNA antibody or Anti-Smith antibody	6

One clinical criterion and ≥10 points required for SLE classification

Information from BMJ: Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78:1151-1159. [PMID: 31383717] doi:10.1136/annrheumdis-2018-214819.

Systemic Lupus Erythematosus: Diagnosis

- ANA IFA >95% sensitive (not specific)
- Assays for anti-dsDNA and anti-Sm antibodies are highly specific
- Disease activity markers can be helpful in some cases
  - Anti-dsDNA positively correlated
  - Complement negatively correlated
  - ANA titers do not correlate

Systemic Lupus Erythematosus: Assessment

- Constitutional
- Musculoskeletal
- Mucocutaneous
- Serosal (pleuro-pericardial)
- Renal
- Neuropsychiatric

<u>Non-inflammatory</u>

- Fibromyalgia
- Headaches
- Corticosteroid induced complications
  - Infection
  - Avascular necrosis
  - Diabetes
  - Et al

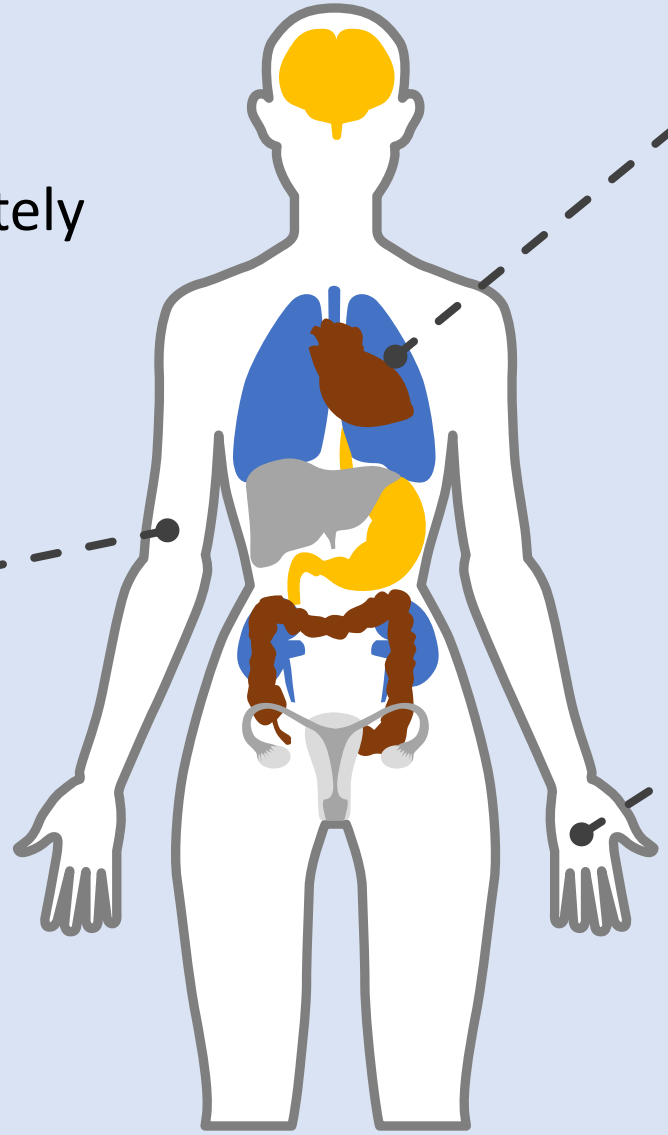
Systemic Lupus Erythematosus: Treatment

Prevention of SLE flares

- Hydroxychloroquine indefinitely in most patients
  - Pregnancy safe

Photosensitive cutaneous lupus

- Sun protection, topical glucocorticoids, hydroxychloroquine



Treat ASCVD risk factors in all patients

- CAD is common cause of death

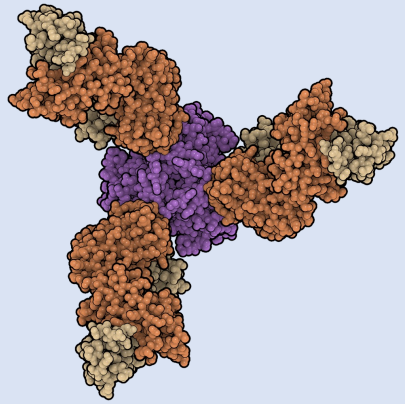
Arthritis

- NSAIDs & hydroxychloroquine

Systemic Lupus Erythematosus: Treatment

- Proliferative glomerulonephritis
  - IV cyclophosphamide **or**
  - Mycophenolate, glucocorticoids
- Any severe or life-threatening disease
  - High-dose glucocorticoids and cyclophosphamide, azathioprine, or mycophenolate
- Glucocorticoid therapy (prednisone ≥2.5 mg/d for ≥3 months)
  - Risk assessment for osteoporosis → periodic BMD
  - Consider prophylactic bisphosphonate

Systemic Lupus Erythematosus: New Therapies



Belimumab:

Monoclonal antibody against **B-cell Activating Factor (BAFF)**

- Adjunct to standard therapies for SLE complications
- Not proven for neuropsychiatric disease

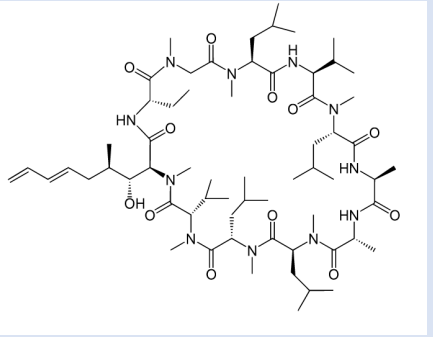
Anifrolumab:

Monoclonal antibody against **Type 1 Interferon receptor**

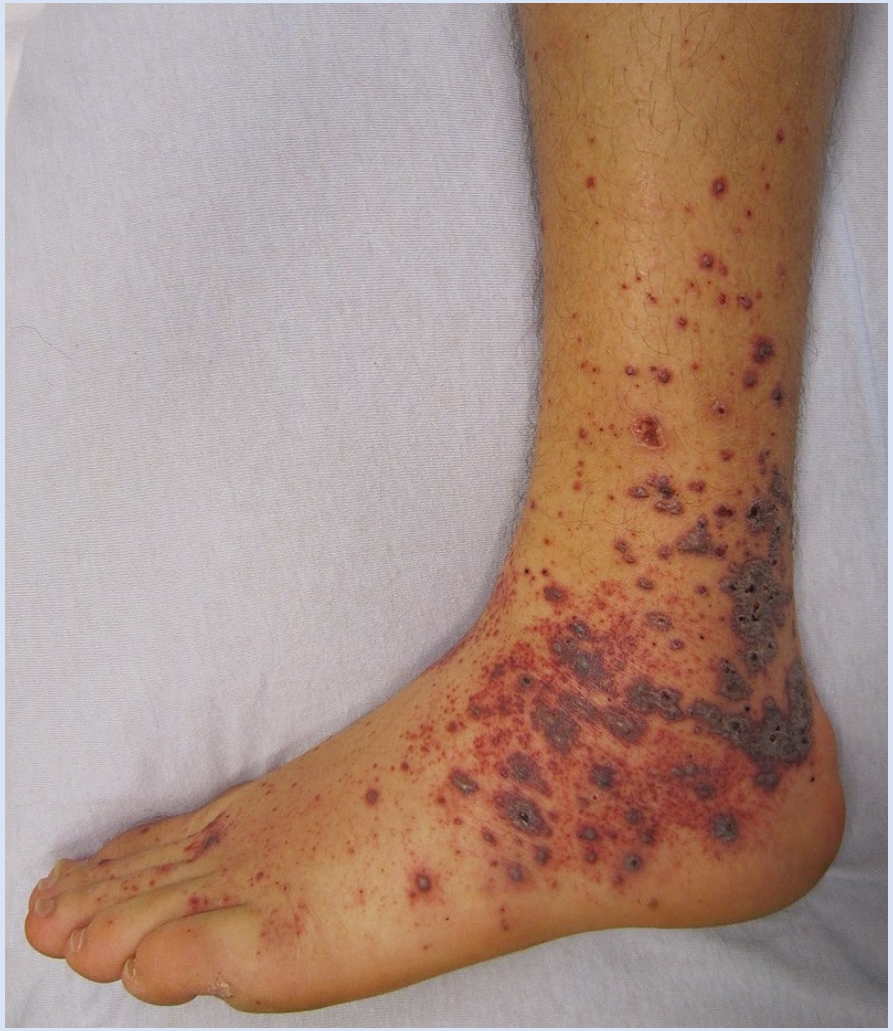
- Adjunct to standard therapies for moderate to severe lupus
- Not proven for severe glomerulonephritis or neuropsychiatric disease

Voclosporin: **Calcineurin inhibitor**

- Adjunct therapy for lupus nephritis



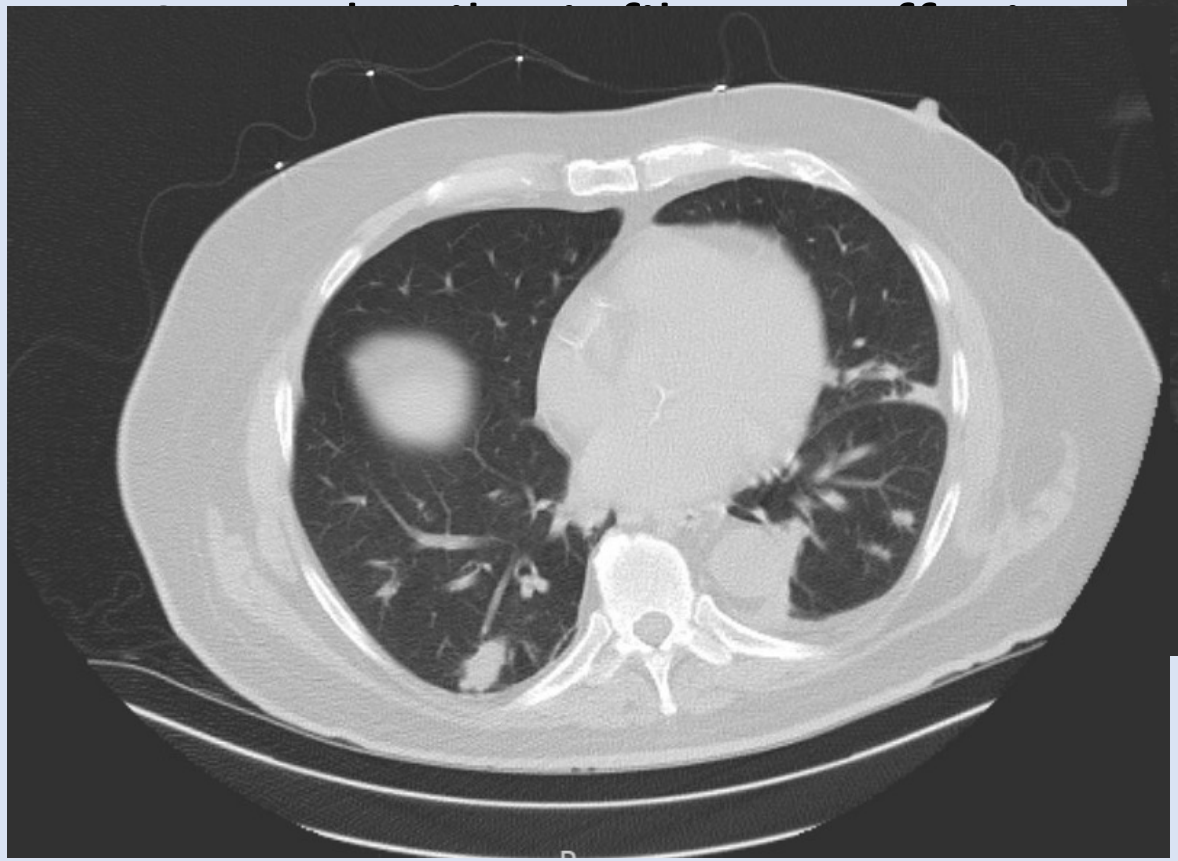
Systemic Vasculitis

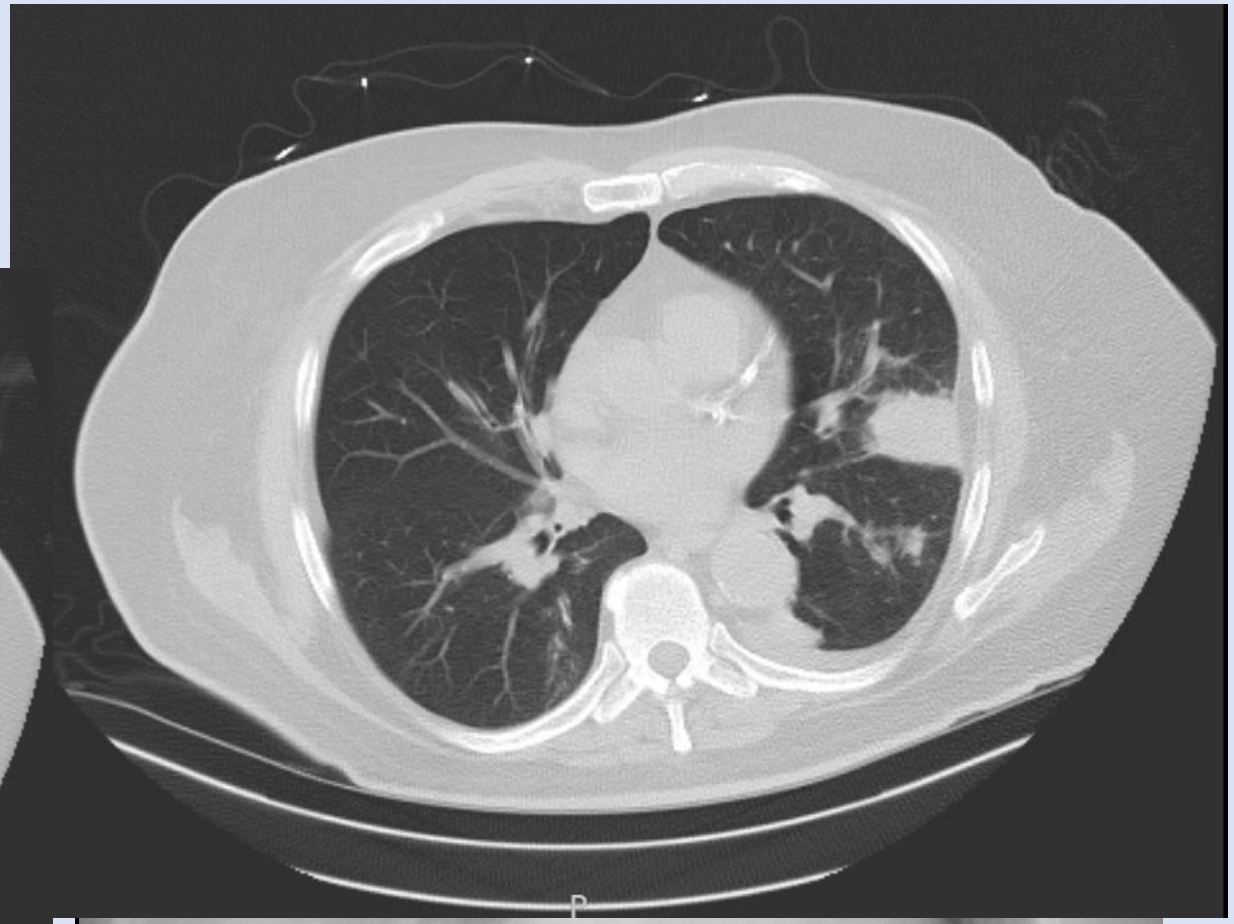


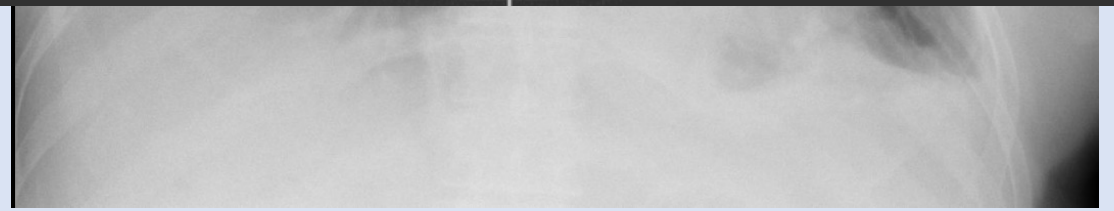
HT

- 80 y/o M
- Admitted with 1 month hx of fatigue, malaise, intermittent fever, weight loss
- PMH
  - CAD with stent
  - HTN
  - Non-smoker
- PE: normal VS x HR 100
  - Cachectic M, appears ill
- Lab: normal WBC, normocytic anemia, Cr 0.6, Alb 2.8, CRP 25

HT







HT

- Empiric, broad spectrum antibiotics
- IR biopsy performed
- While waiting for biopsy results he develops intermittent hemoptysis, SaO2 87%

HT

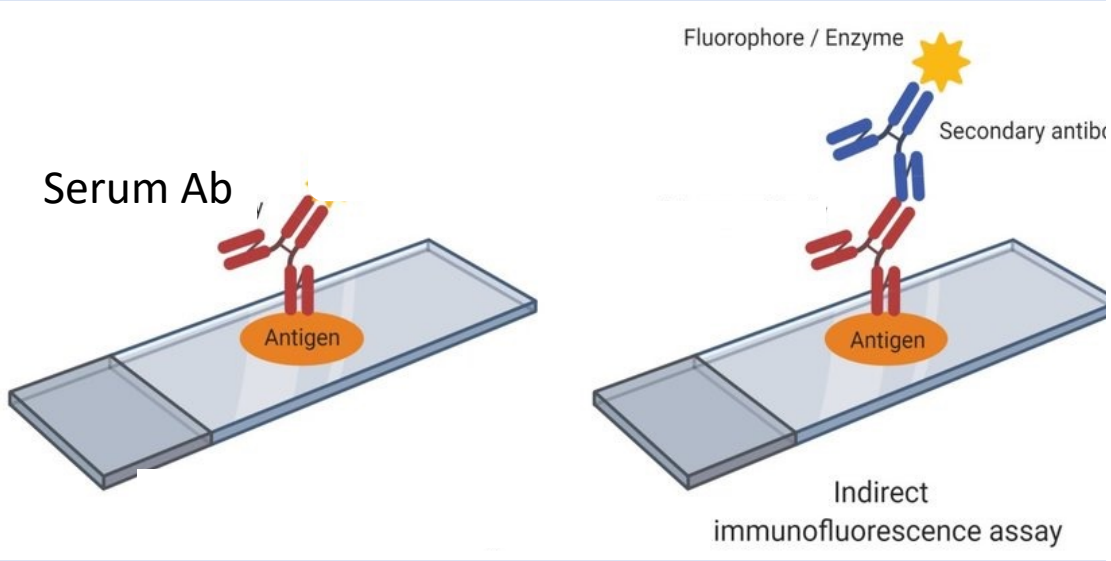
- ESR 67
- U/A: 8 RBC, Tr Protein
- ANCA 1:80, PR3 > 8
- Lung biopsy:
  - Necrotizing granulomatous inflammation
  - Negative for neoplasm

ANCA-Associated Vasculitis

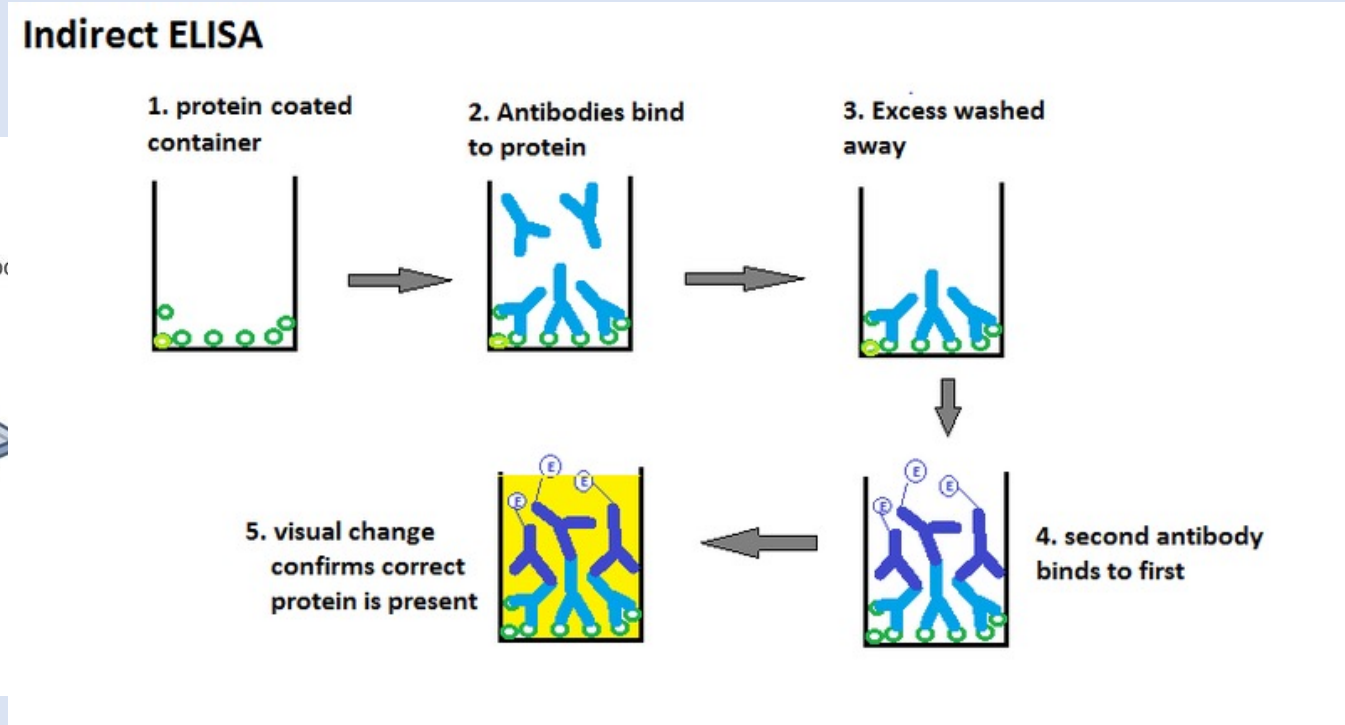
- Granulomatosis with polyangiitis – GPA
- Microscopic polyangiitis – MPA
- Eosinophilic granulomatosis with polyangiitis - EGPA

ANCA, PR-3, MPO

- ANCA – Indirect Immunofluorescence



- PR-3, MPO – ELISA



ANCA-Associated Vasculitis

- Granulomatous Polyangiitis
  - Upper respiratory tract
  - Lower respiratory tract
  - Glomerulonephritis
- PR3 positive 90%

- Microscopy Polyangiitis
  - Pulmonary vasculitis
  - Glomerulonephritis
  - Cutaneous
  - Mononeuritis multiplex
- MPO positive 60-80%

Alveolar hemorrhage can occur suddenly in either GPA or MPA

Small-Vessel Vasculitis – Eosinophilic Granulomatosis with Polyangiitis

- Presentation
  - Asthma (~100%) & eosinophilia (95%)
  - Pulmonary infiltrates/hemoptysis, skin, renal involvement, mononeuritis multiplex
- Diagnosis
  - p-ANCA, anti-myeloperoxidase antibody assays (50%)
  - Kidney or lung biopsy

Differential diagnosis

- Anti-GBM disease / Goodpasture
- Systemic lupus erythematosus
- Cocaine/levamisole drug use
- Granulomatous infections, Infective endocarditis
- Atrial myxoma, Cholesterol emboli syndrome
- Lymphoma, para-neoplastic syndrome

Arthritis & Rheumatology
Vol. 0, No. 0, Month 2021, pp 1–18
DOI 10.1002/art.41773

American College of Rheumatology
Empowering Rheumatology Professionals

2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis

Sharon A. Chung,[1] Carol A. Langford,[2] Mehrdad Maz,[3] Andy Abril,[4] Mark Gorelik,[5] Gordon Guyatt,[6] Amy M. Archer,[7] Doyt L. Conn,[8] Kathy A. Full,[9] Peter C. Grayson,[10] Maria F. Ibarra,[11] Lisa F. Imundo,[5] Susan Kim,[1] Peter A. Merkel,[12] Rennie L. Rhee,[12] Philip Seo,[13] John H. Stone,[14] Sangeeta Sule,[15] Robert P. Sundel,[16] Omar I. Vitobaldi,[17] Ann Warner,[18] Kevin Byram,[19] Anisha B. Dua,[7] Nedaa Husainat,[20] Karen E. James,[21] Mohamad A. Kalot,[22] Yih Chang Lin,[23] Jason M. Springer,[3] Marat Turgunbaev,[24] Alexandra Villa-Forte,[2] Amy S. Turner,[24] and Reem A. Mustafa[25]

Severe disease:

- Alveolar hemorrhage
- Glomerulonephritis
- Central nervous system vasculitis
- Mononeuritis multiplex
- Cardiac involvement
- Mesenteric ischemia
- Limb/digit ischemia

Non-severe disease:

- Rhinosinusitis
- Asthma
- Mild systemic symptoms
- Uncomplicated cutaneous disease
- Mild inflammatory arthritis

Five-Factor Score (FFS)

- Developed for EGPA
  - Creatinine >1.58 mg/dL
  - Proteinuria >1 g/day
  - CNS involvement
  - Gastrointestinal involvement
  - Myocardial involvement

- When applied to GPA and MPA, proteinuria is excluded
- 5-year survival
  - 0 91%
  - 1 79%
  - ≥2 60%

Cohen P. *Arthritis Rheum* 2007

Remission Induction

- For patients with active, severe GPA/MPA, we conditionally recommend treatment with **rituximab** over cyclophosphamide for remission induction.
- In patients with active, severe GPA/MPA with active glomerulonephritis / active alveolar hemorrhage, we conditionally recommend ***against*** adding **plasma exchange** to remission induction therapies.
- For patients with active, severe GPA/MPA, either IV pulse glucocorticoids or high-dose oral glucocorticoids may be prescribed as part of initial therapy.
- For patients with active, severe GPA/MPA, we conditionally recommend a **reduced-dose glucocorticoid regimen** over a standard-dose glucocorticoid regimen for remission induction

2021 AMERICAN COLLEGE OF RHEUMATOLOGY/VASCULITIS FOUNDATION GUIDELINE FOR ANCA-ASSOCIATED VASCULITIS

- Induction
  - Solumedrol followed by prednisone
  - Rituximab vs cyclophosphamide
  - +/- Plasmapheresis

- Questions
  - How much prednisone?
  - What is the risk of plasmapheresis?
  - What precautions for infection?

IV Pulse Methylprednisolone for induction in severe ANCA associated Vasculitis (BMC Nephrol 2019;20:58)

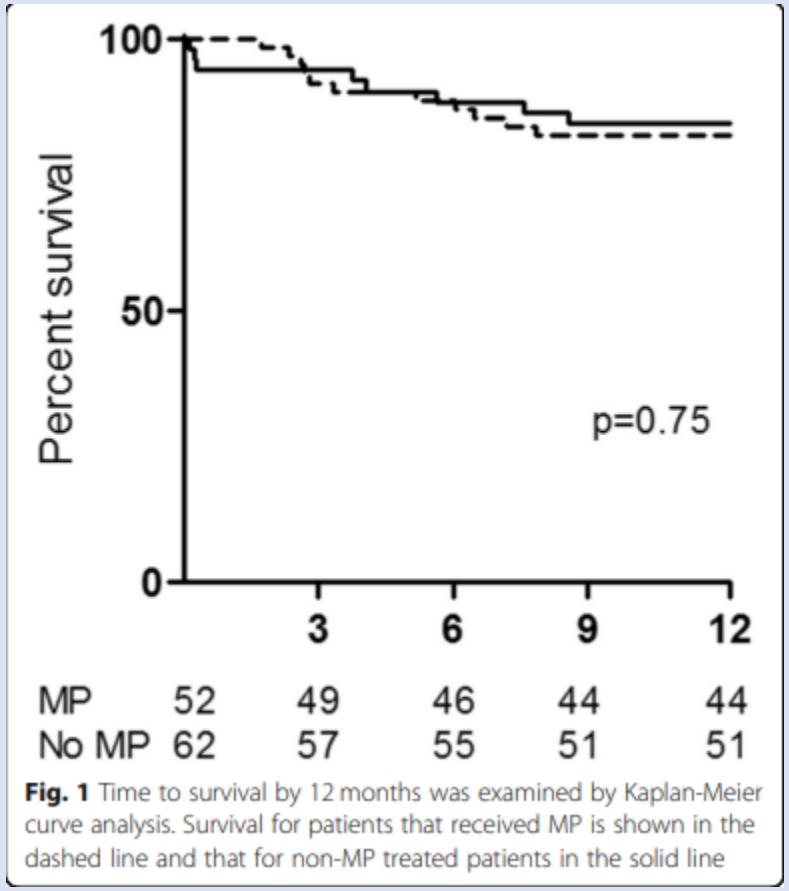


Fig. 1 Time to survival by 12 months was examined by Kaplan-Meier curve analysis. Survival for patients that received MP is shown in the dashed line and that for non-MP treated patients in the solid line

IV Pulse Methylprednisolone for induction in severe ANCA associated Vasculitis (BMC Nephrol 2019;20:58)

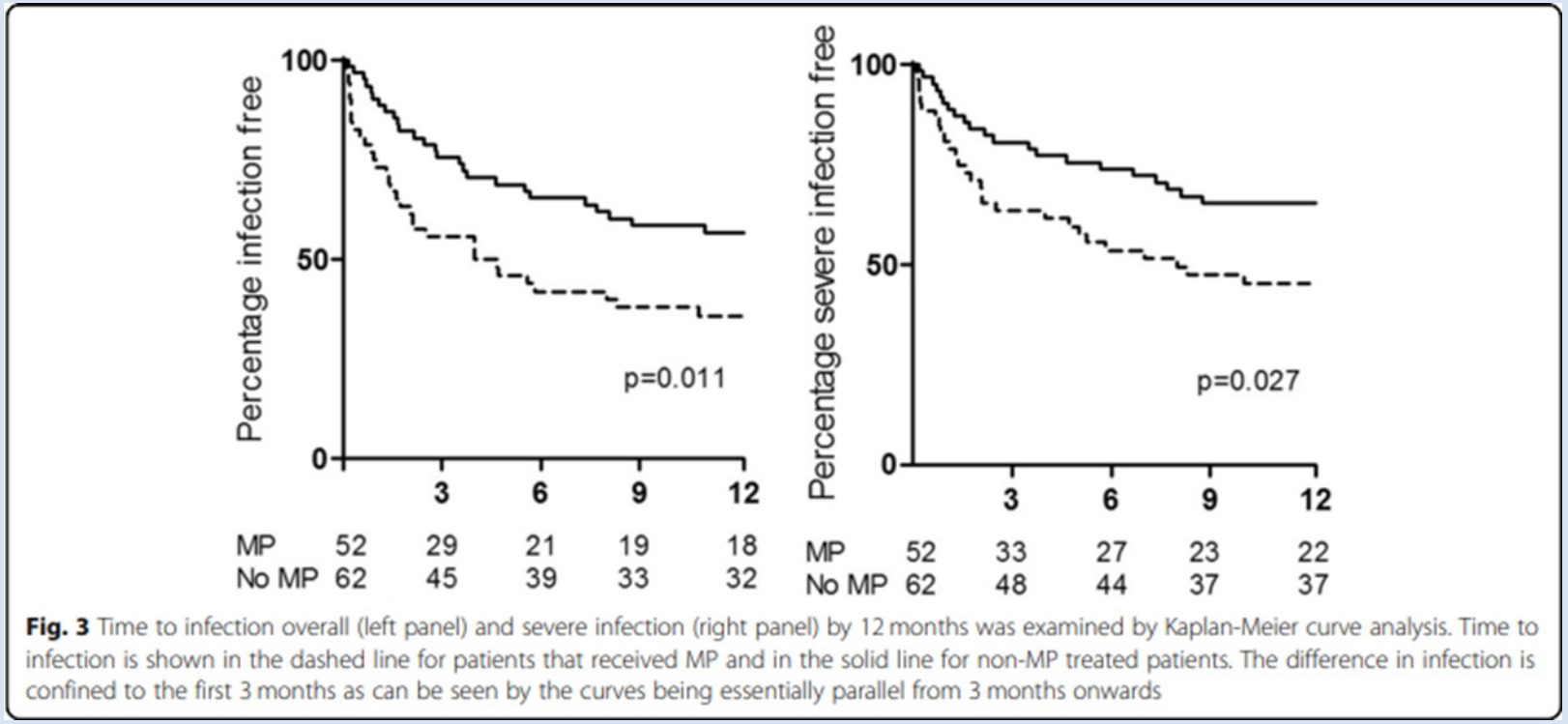


Fig. 3 Time to infection overall (left panel) and severe infection (right panel) by 12 months was examined by Kaplan-Meier curve analysis. Time to infection is shown in the dashed line for patients that received MP and in the solid line for non-MP treated patients. The difference in infection is confined to the first 3 months as can be seen by the curves being essentially parallel from 3 months onwards

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

- *Among patients with severe ANCA-associated vasculitis, the use of plasma exchange **did not reduce** the incidence of death or ESKD.*
- *A reduced-dose regimen of glucocorticoids was **noninferior** to a standard-dose regimen with respect to death or ESKD.*

for the PEXIVAS Investigators*

NEJM 2020;382:622-31

Complications of Plasma Exchange

- Central catheter
- Hypotension
- Fluid overload or non-cardiogenic pulmonary edema
- Decreased plasma proteins
- Coagulopathy
- Thrombocytopenia
- Immunoglobulin immunodeficiency
- Removal of protein bound drugs

Prednisone – Reduced Schedule

Week	Standard (50-75 kg)	Reduced dose (50-75 kg)
	Pulse	Pulse
1	60	60
2	60	30
3-4	50	25
5-6	40	20
7-8	30	15
9-10	25	12.5
…	…	…

NEJM 2020;382:622-31

ANCA Associated Vasculitis

- Beware pulmonary hemorrhage
- Check for glomerulonephritis

- Intravenous (Pulse) solumedrol followed by prednisone
- (Plasmapheresis)
- Rituximab