COMMON RHEUMATOLOGY CONDITIOINS

Dr. Wong Woon-Sing Raymond

31st March 2012

Common Rheumatology Conditions

- Lupus and other related autoimmune disorders
- Rheumatoid arthritis and other synovial disorders
- Ankylosing spondylitis and other spondyloarthropathies
- Vasculitides
- Osteoarthritis and related disorders
- Gout and other crystal deposition arthropathies
- Septic arthritis and other infection related rheumatic diseases

Common characteristics of rheumatic diseases

- Unknown pathogenesis
- Variation in presentation
- Tendency to exacerbations and remissions
- Chronic nature of disease
- Variable response to treatment

SYSTEMIC LUPUS ERYTHEMATOSUS

SLE

- It is an autoimmune disease affecting mainly the younger population
- Most patients are nowadays grouped under the care of either rheumatologists or nephrologists
- Knowledge on the clinical presentation, immunopathogenesis, treatment and complication has advanced tremendously in the past decade

Demographic characteristics and prevalence

- SLE in Chinese is at least twice as common as the European Caucasians
- Exact prevalence in HK is unknown but roughly estimated to be about 0.06%
- Underestimation is likely because patients being seen in the private sector are not included
- It mainly affects women of child bearing age
- The female predominance is consistent among different ethic groups, female to male rate being 8.6 to 1
- Mean age is 30.5 $\pm$ 13 years

Clinical Presentation

- The butterfly rash, though the hallmark of SLE, is uncommon in actual clinical practice
- More frequently, patients present with erythematous rash of different morphologies on the face and the forehead associated with photosensitivity
- A common presentation is fatigue, systemic upset, low grade fever, facial rash, arthritis/arthralgia, mild alopecia together ↓ with leucocyte, ↑ ESR but normal CRP
- Some patients may present with acute organ dysfunction which necessitate hospitalization

Clinical Presentation

- Is a clinically heterogeneous disease
- No two patients are exactly alike and the same patients may develop different features at different time points
- Apparently 3 distant patterns of clinical manifestations have been identified
  - One subset with predominant musculoskeletal/cutaneous involvement
  - One subset with predominant and rather serious renal disease
  - One subset with heterogeneous presentation involving multiple organs

Criteria for the Classification of SLE

SLE may be classified if 4 or more of the following disorders are present

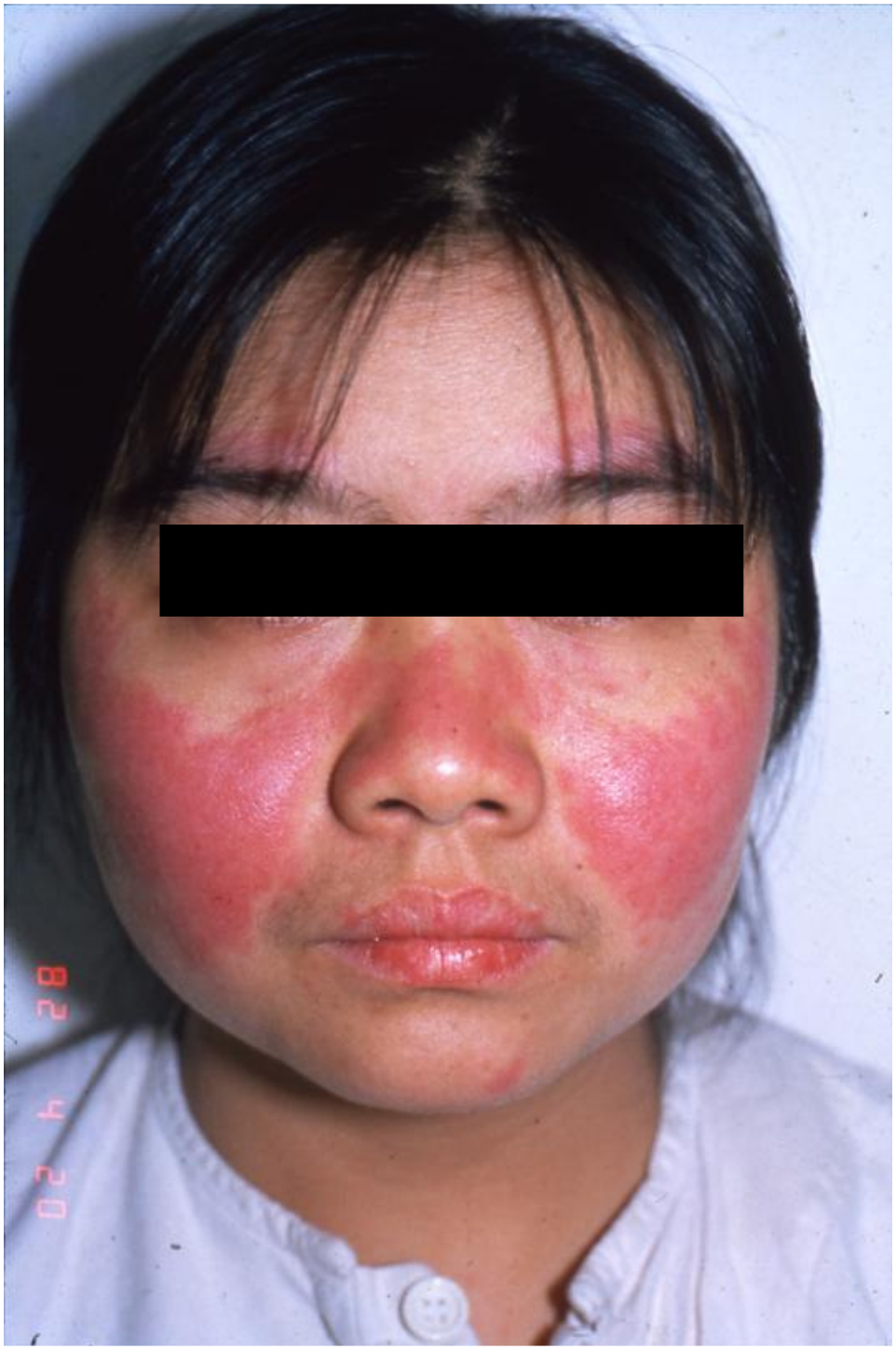
1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcer
5. Arthritis
6. Serositis
7. Renal disorder
8. Neurologic disorder
9. Haematologic disorder
10. Immunologic disorder
11. Antinuclear antibody

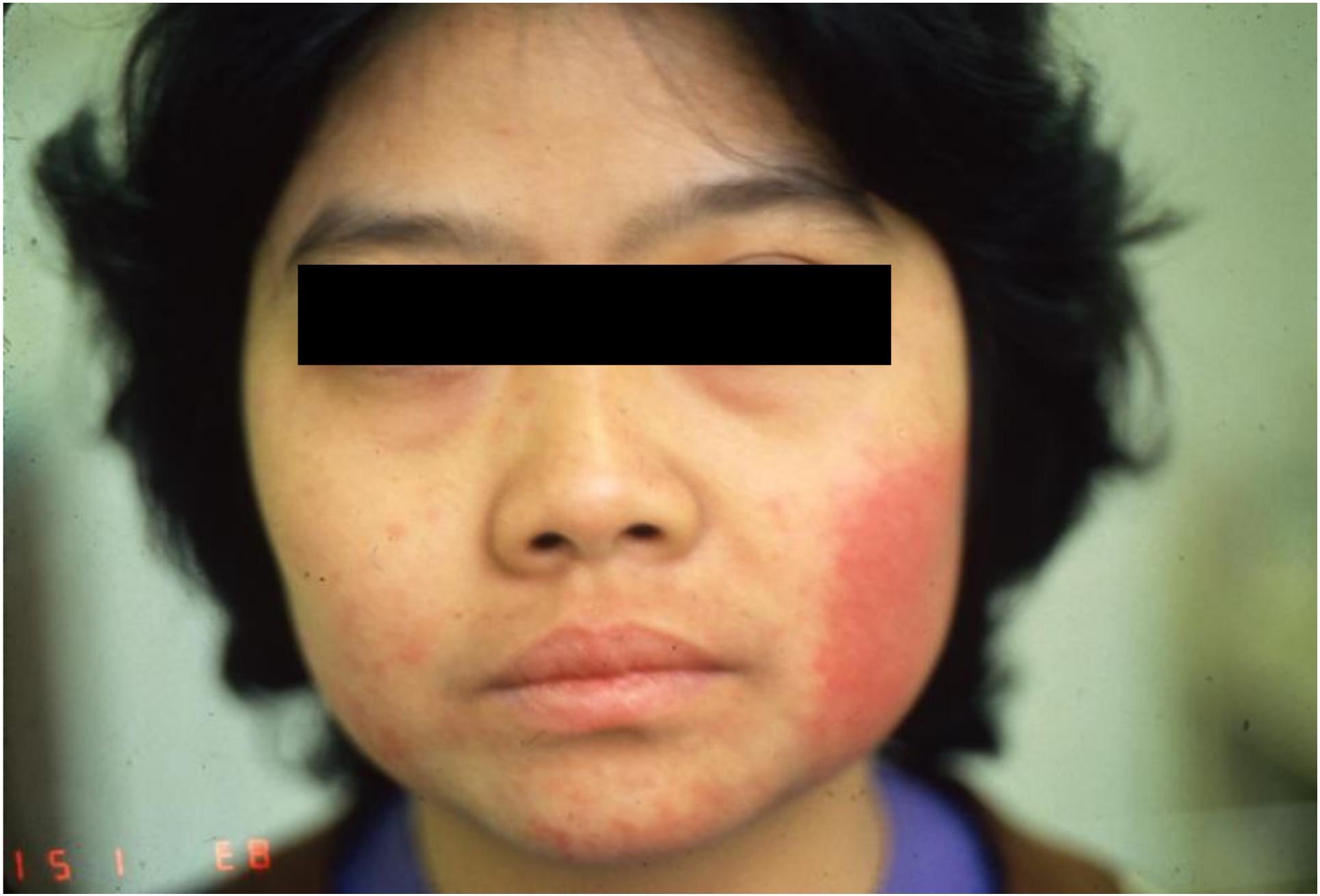
Cutaneous Manifestations in Lupus Erythematosus

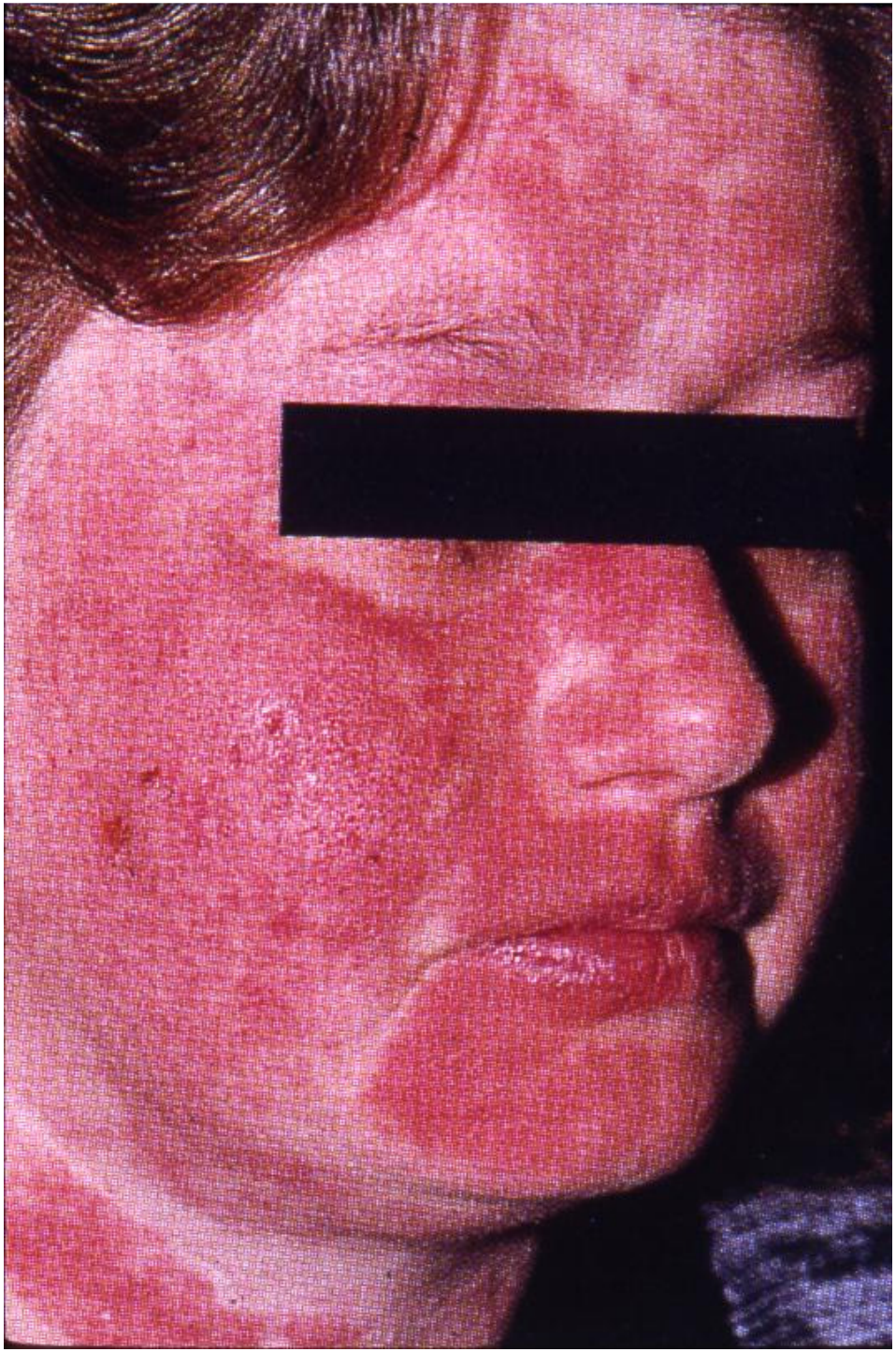
- Specific
- Non-specific

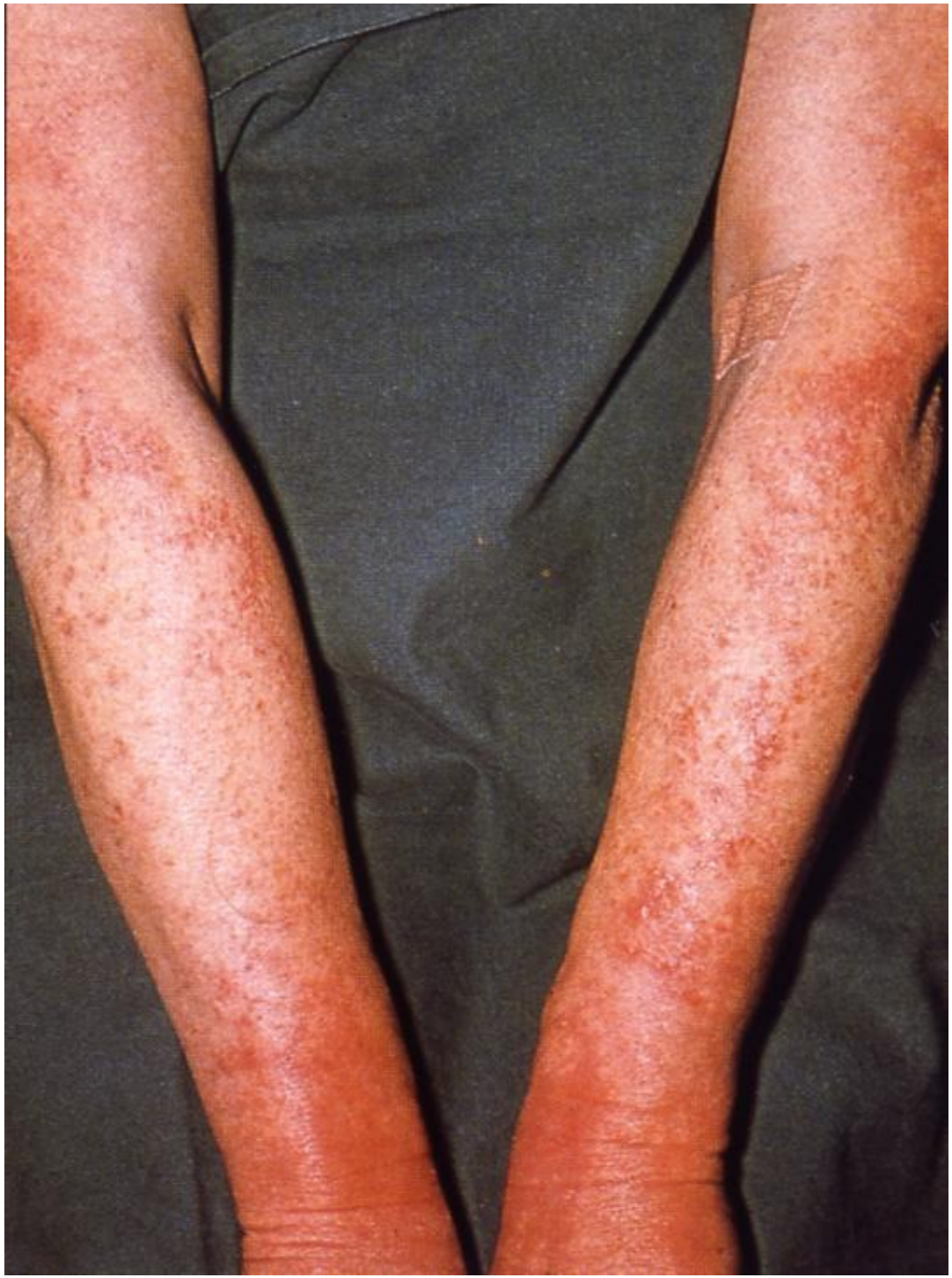
Cutaneous Manifestations in Lupus Erythematosus

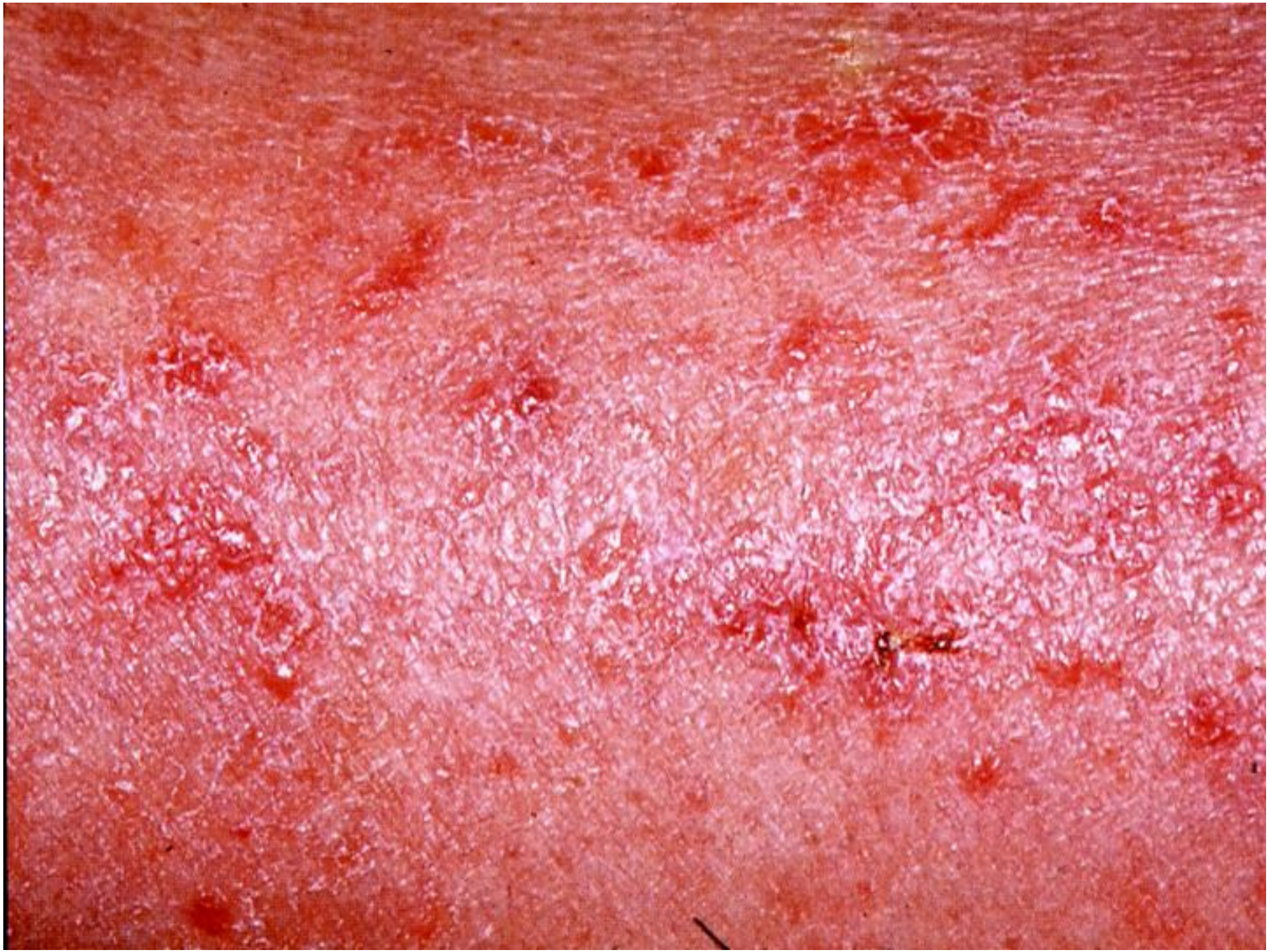
- **Specific**
  - –Discoid
  - –Subacute cutaneous
    - Papulosquamous
    - Annular/polycyclic
  - – Malar rash

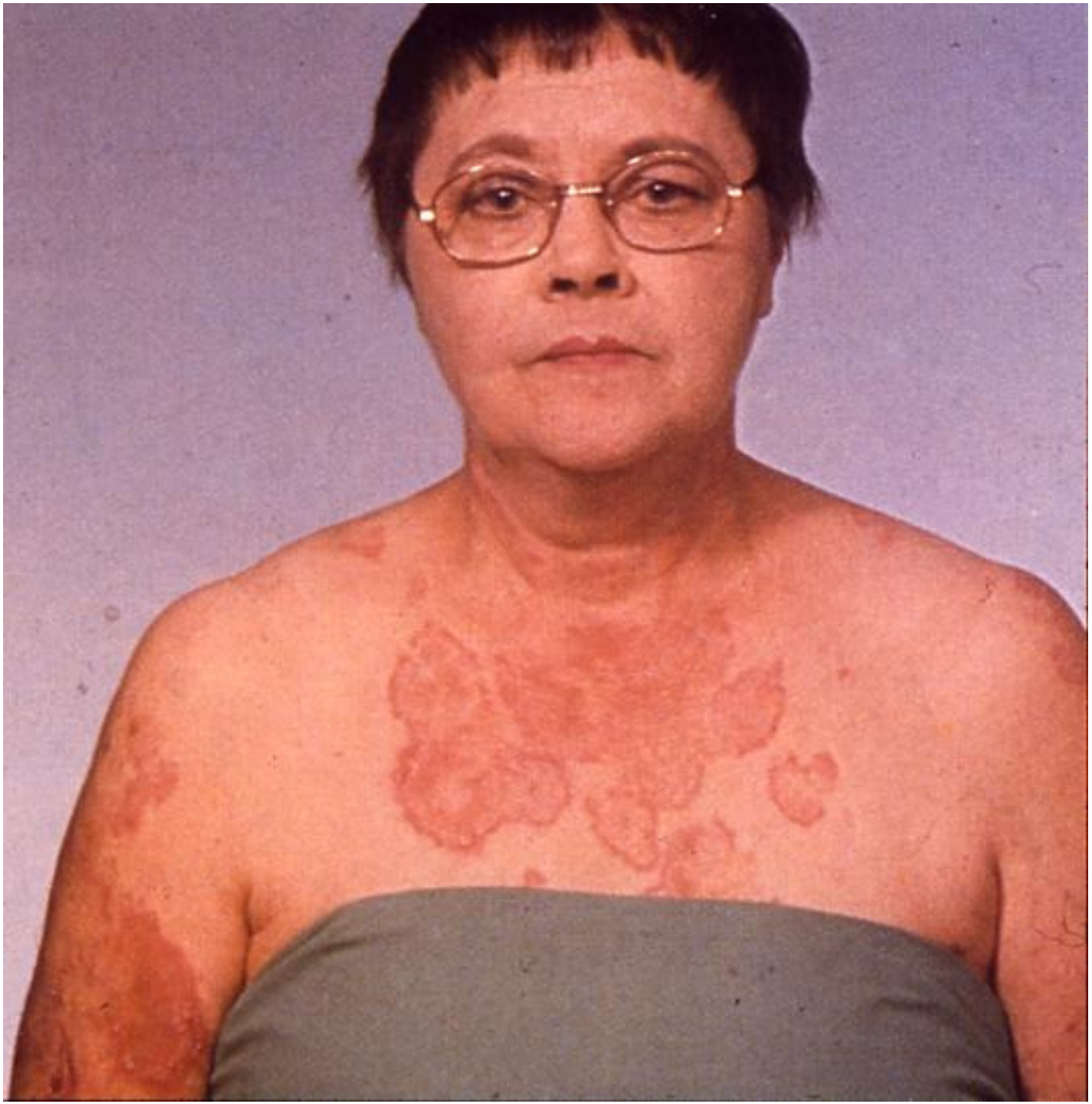

82 4 20

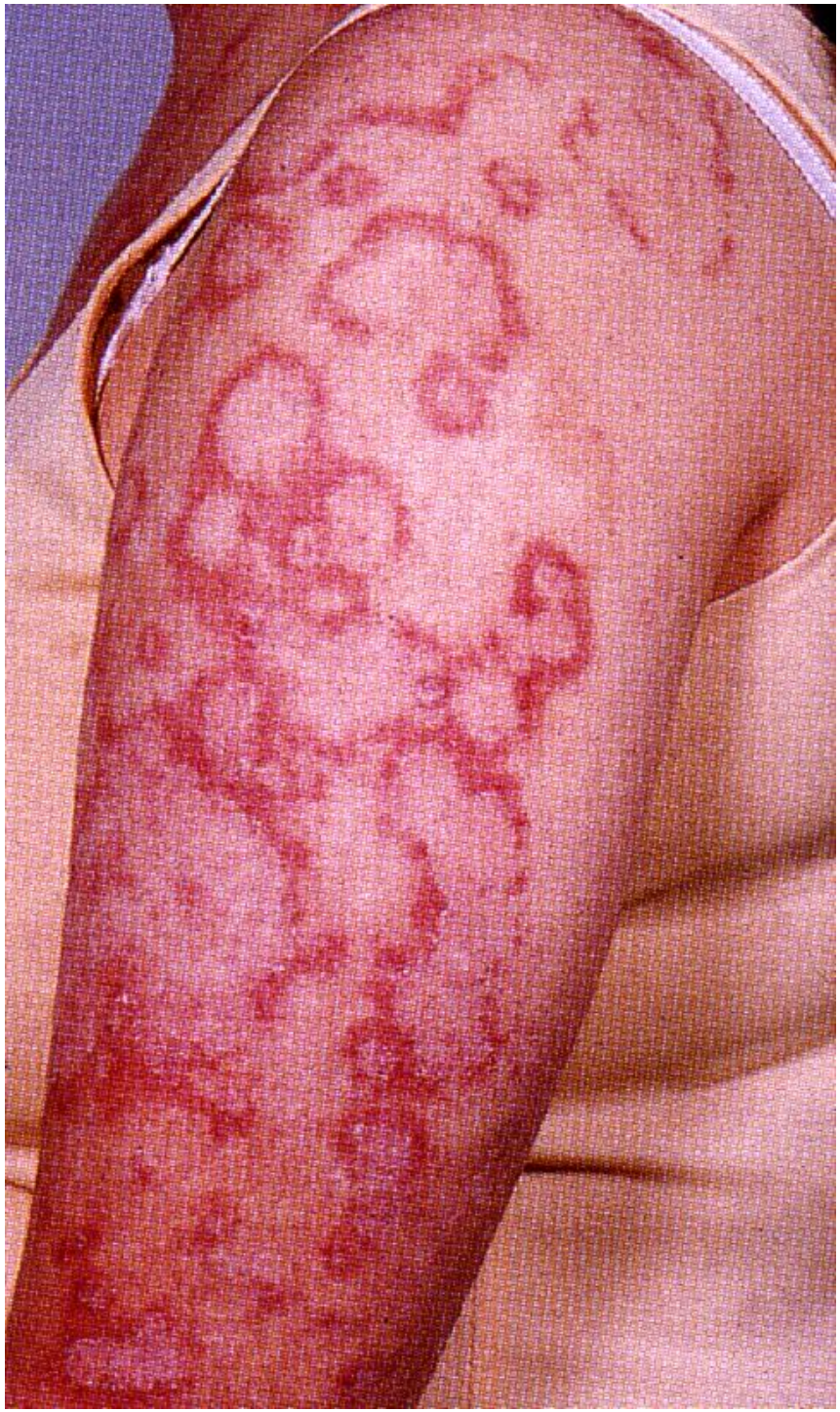


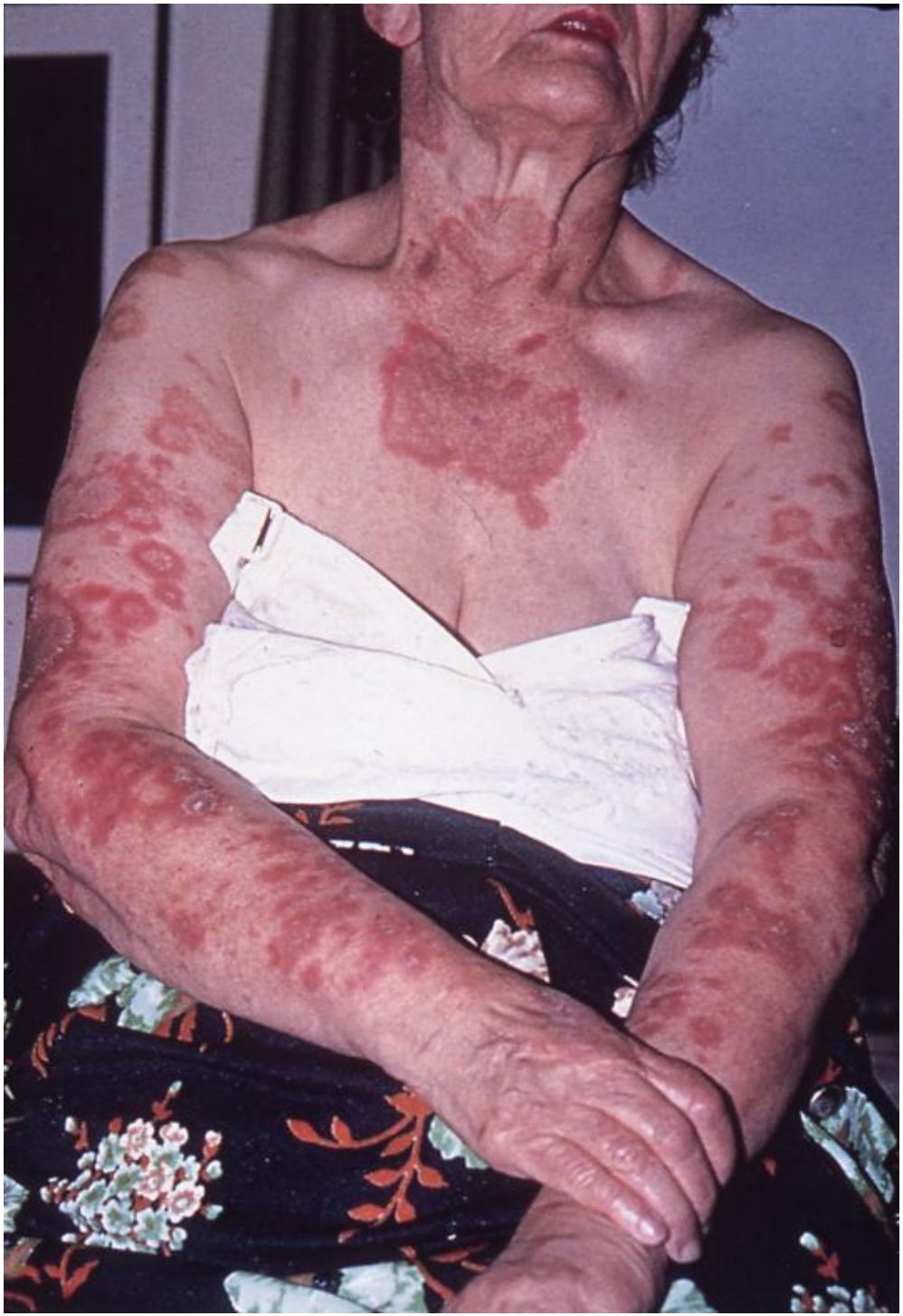


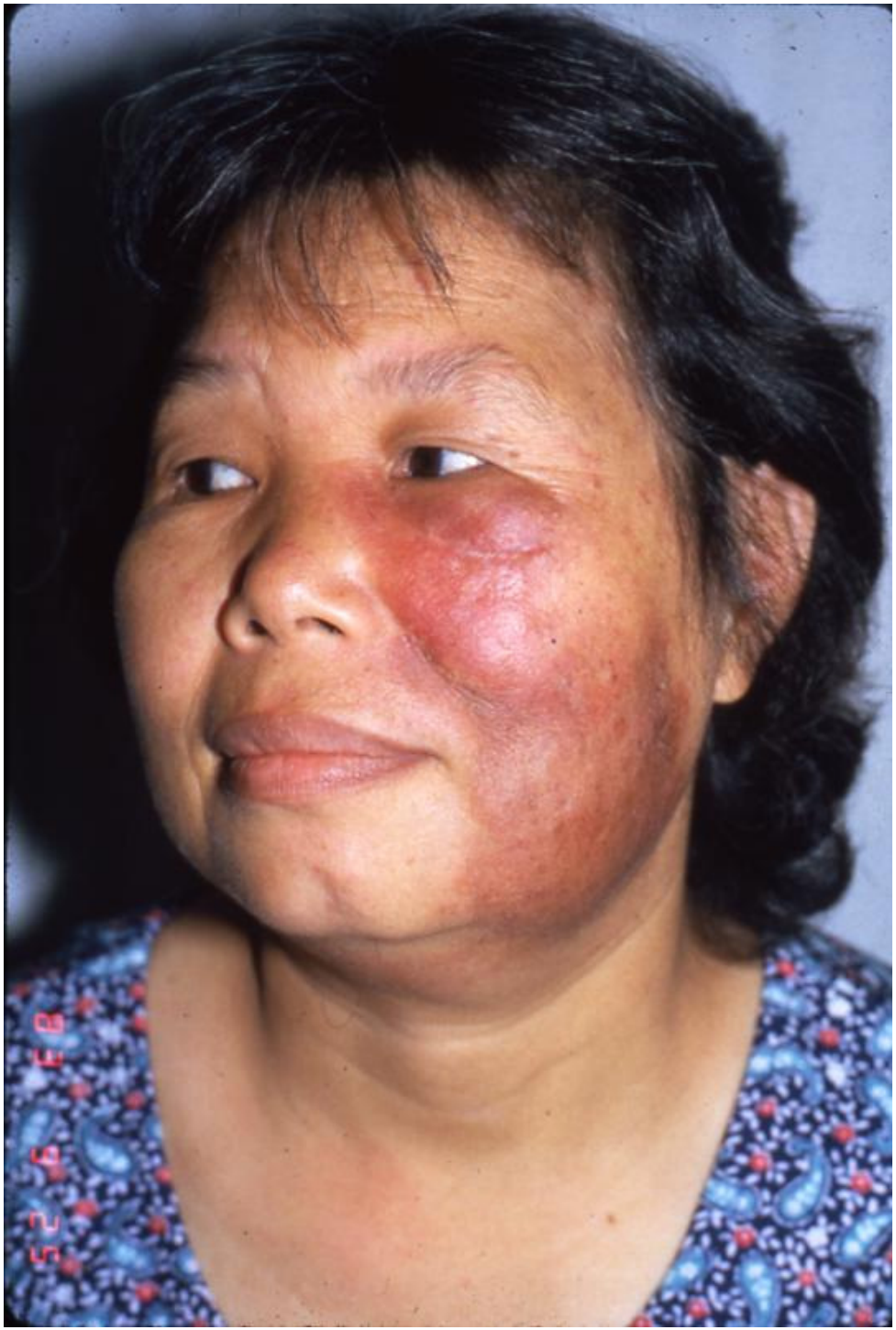


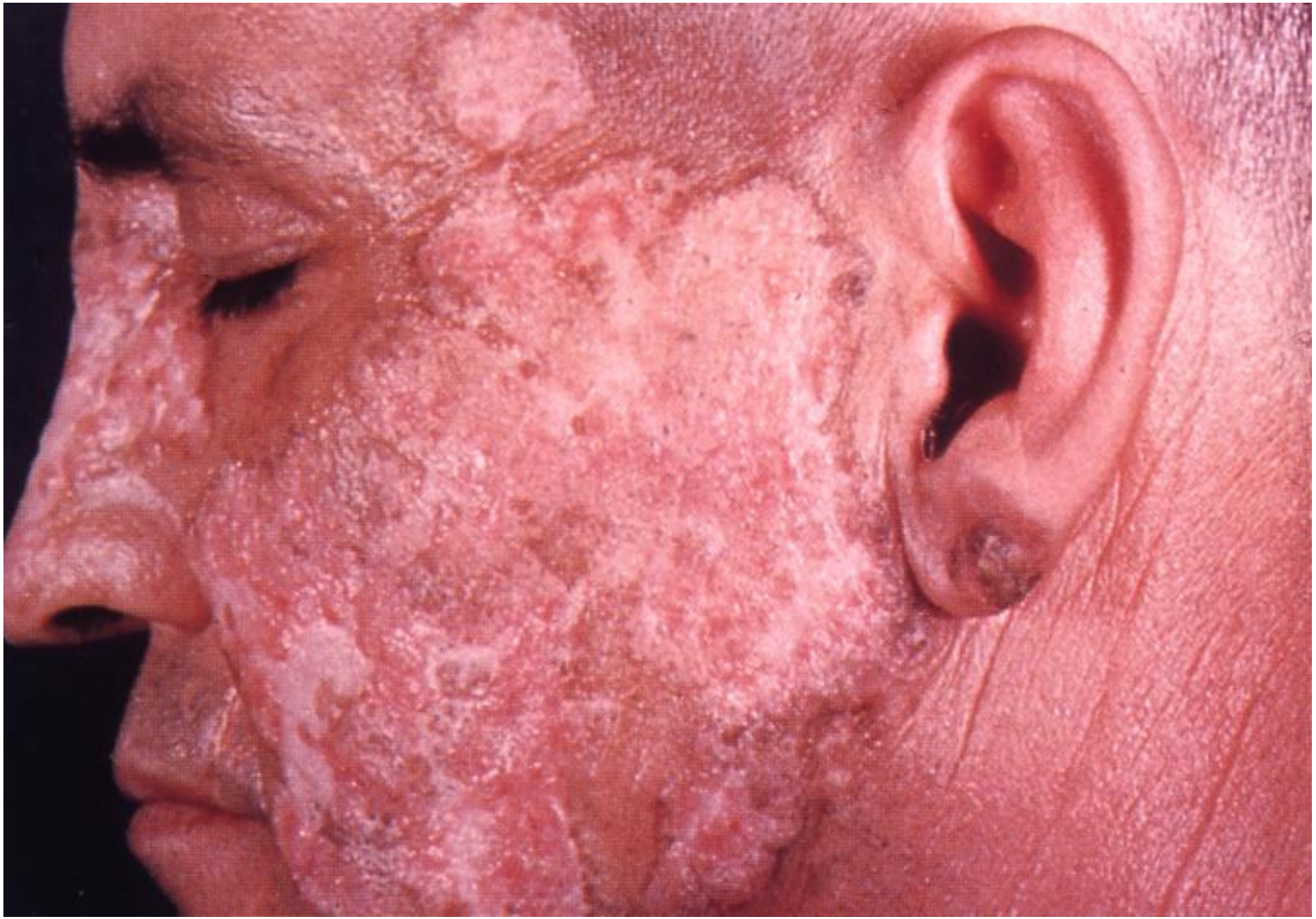








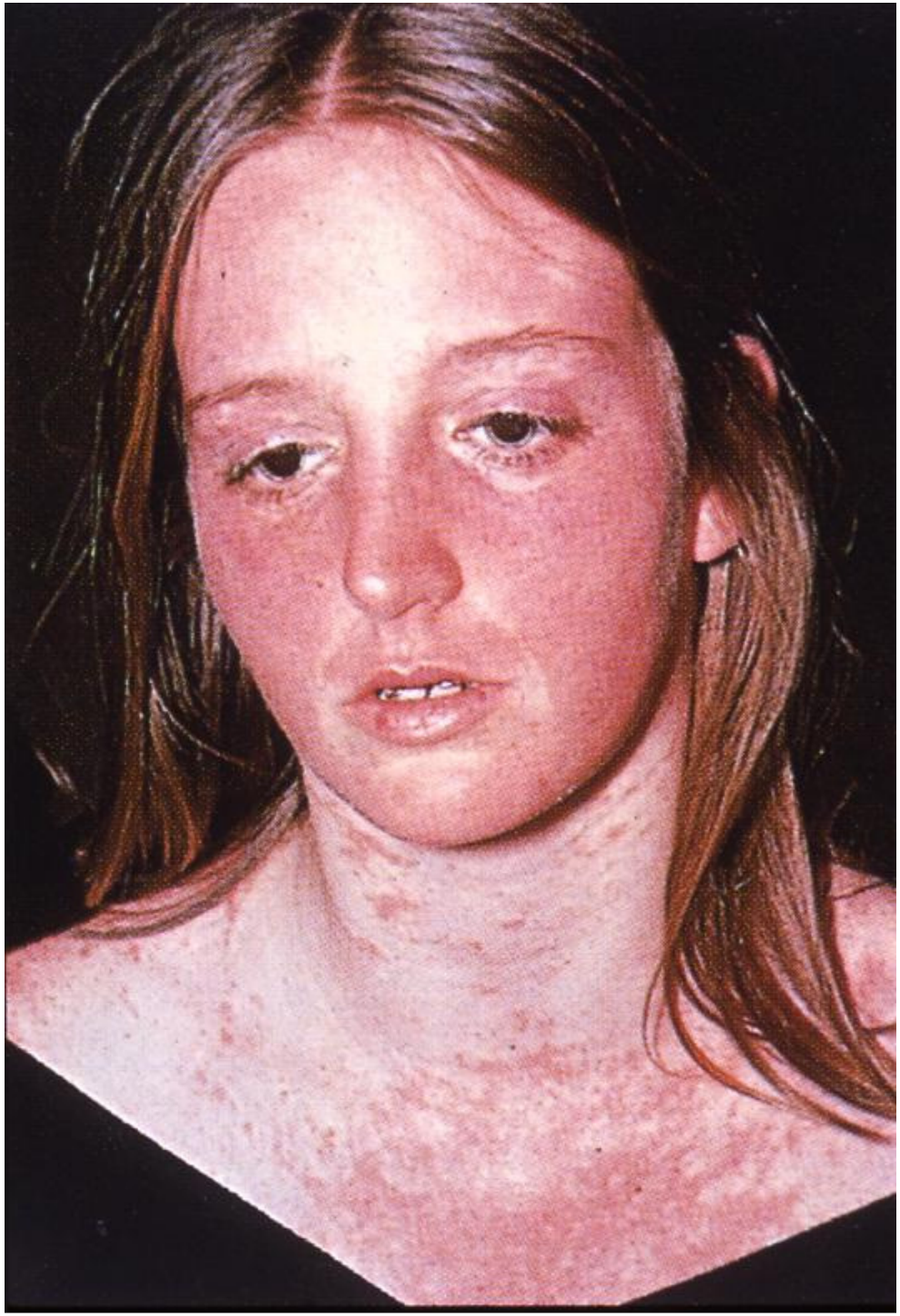


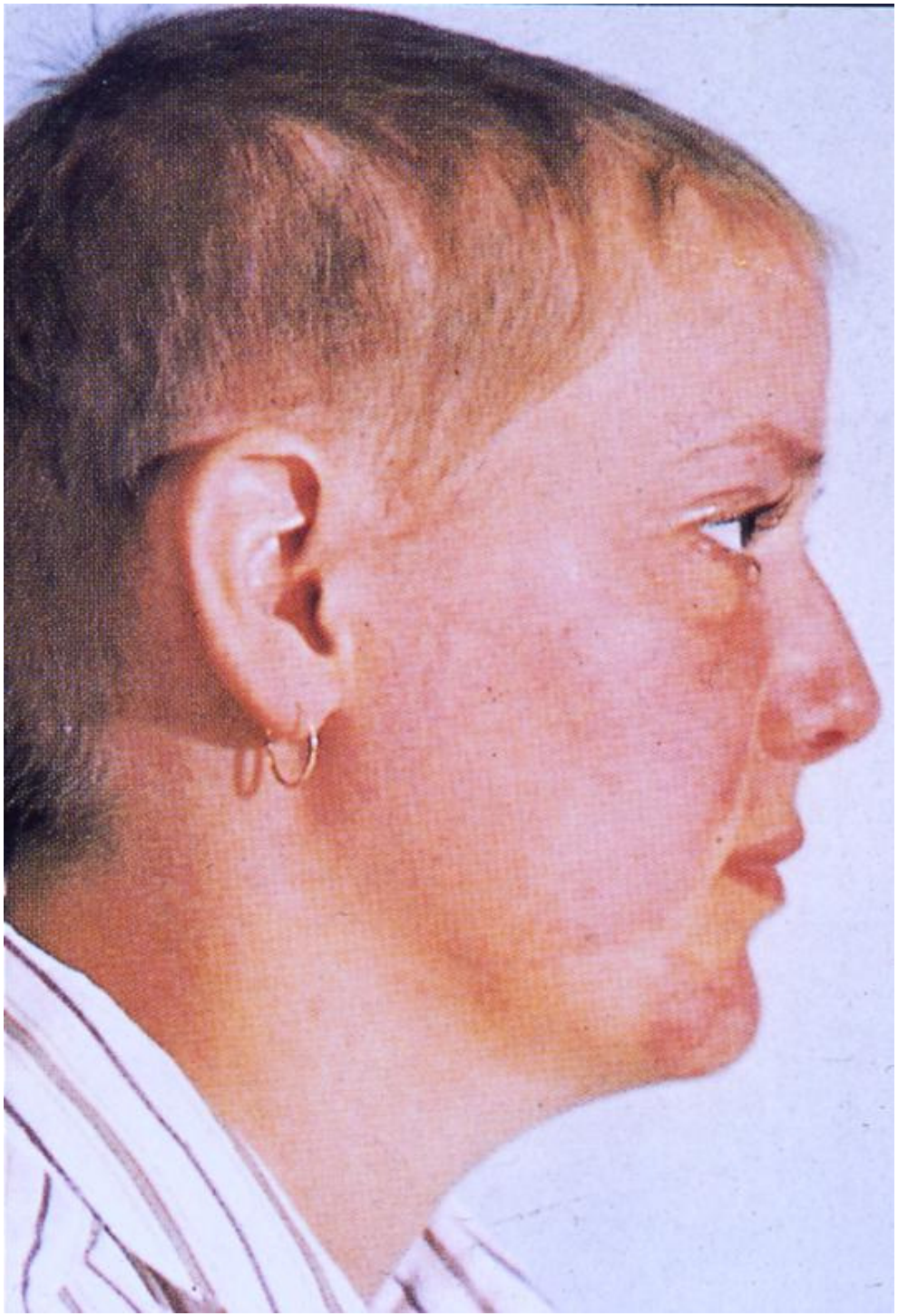


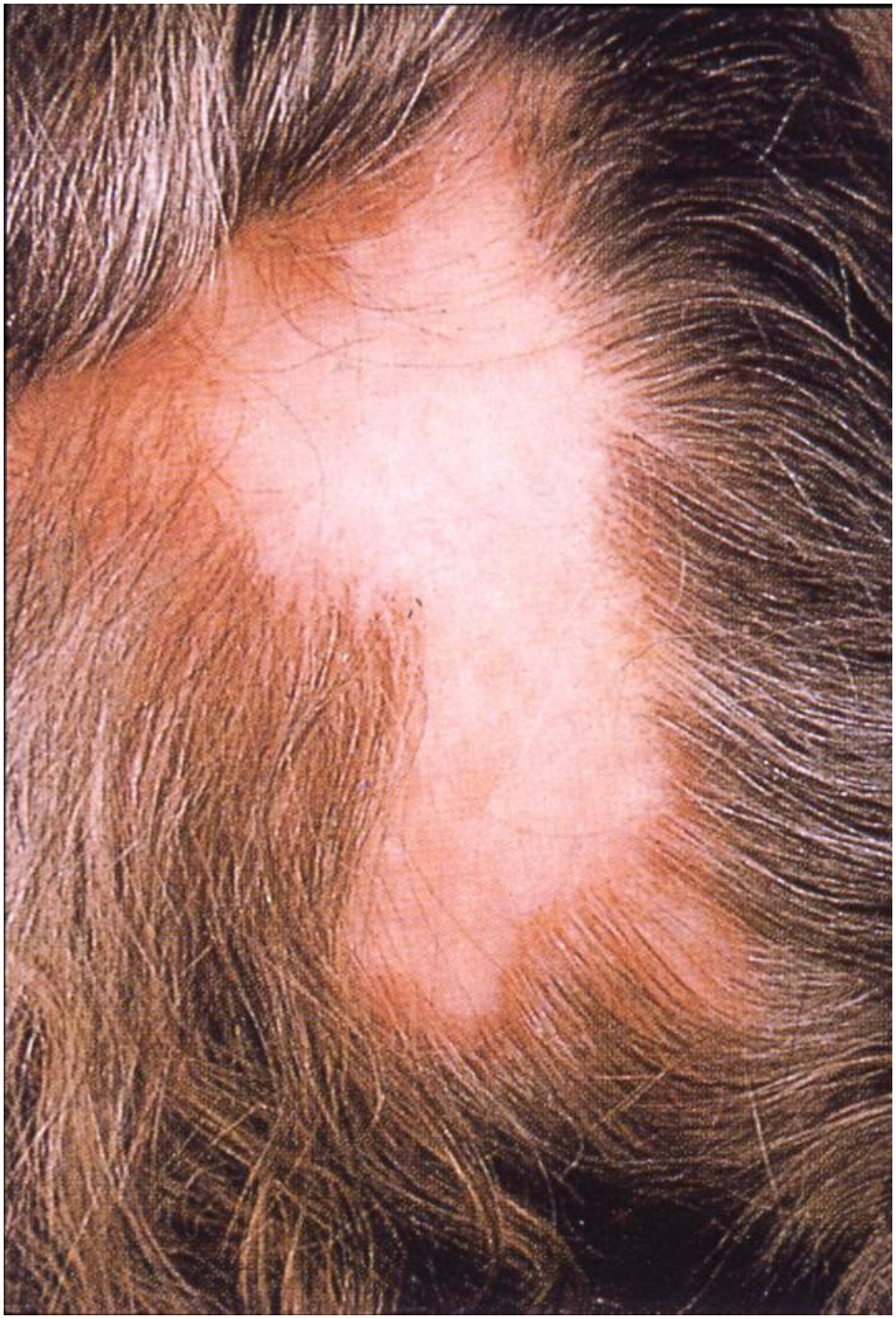
Cutaneous Manifestations in Lupus Erythematosus

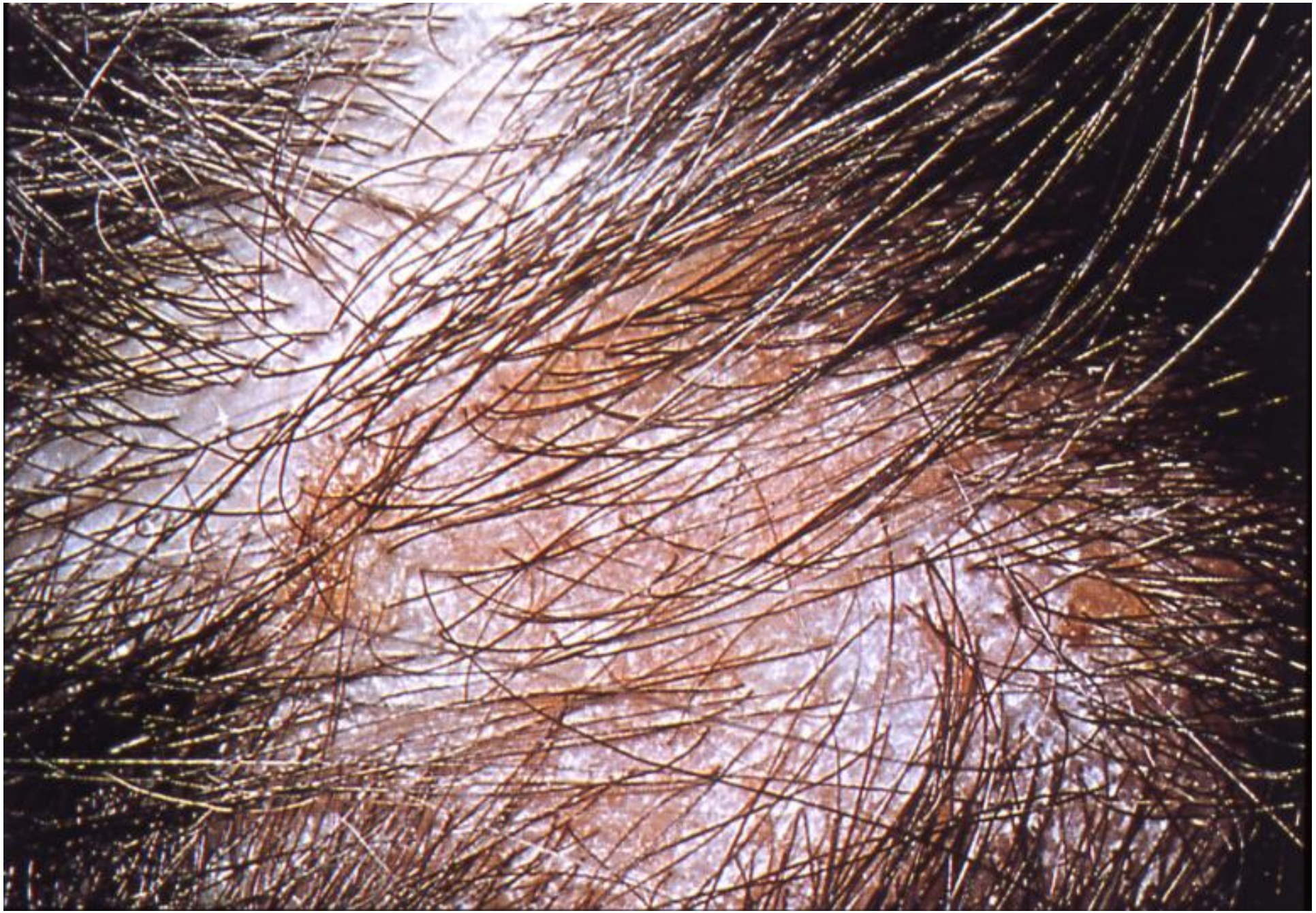
Nonspecific Lesions

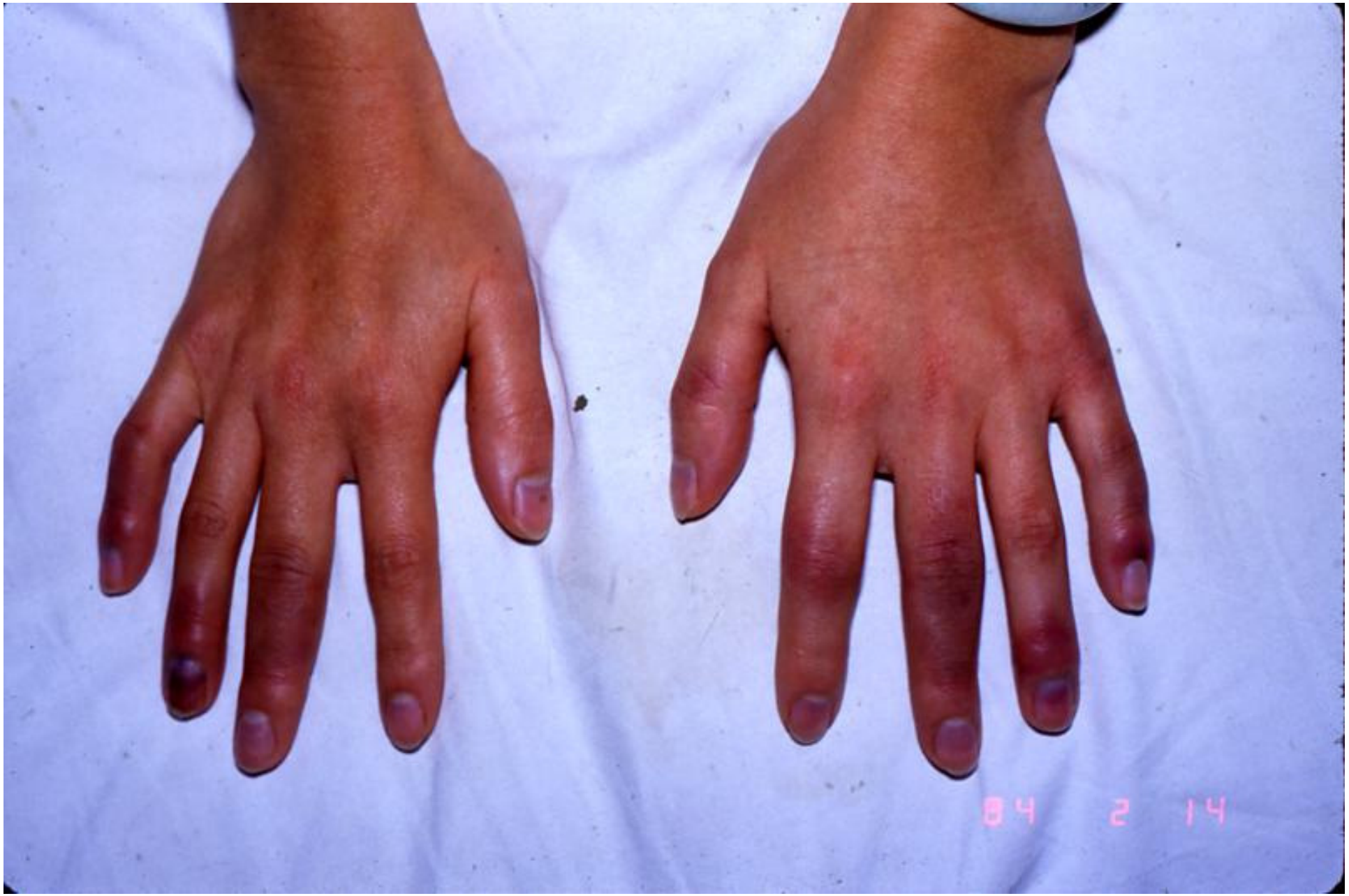
- Photosensitivity
- Alopecia
- Raynaud's phenomenon
- Livedo reticularis
- Bullous
- Lupus panniculitis
- Vasculitis
- Urticaria-like vasculitis
- Oral ulcerations
- Nail changes

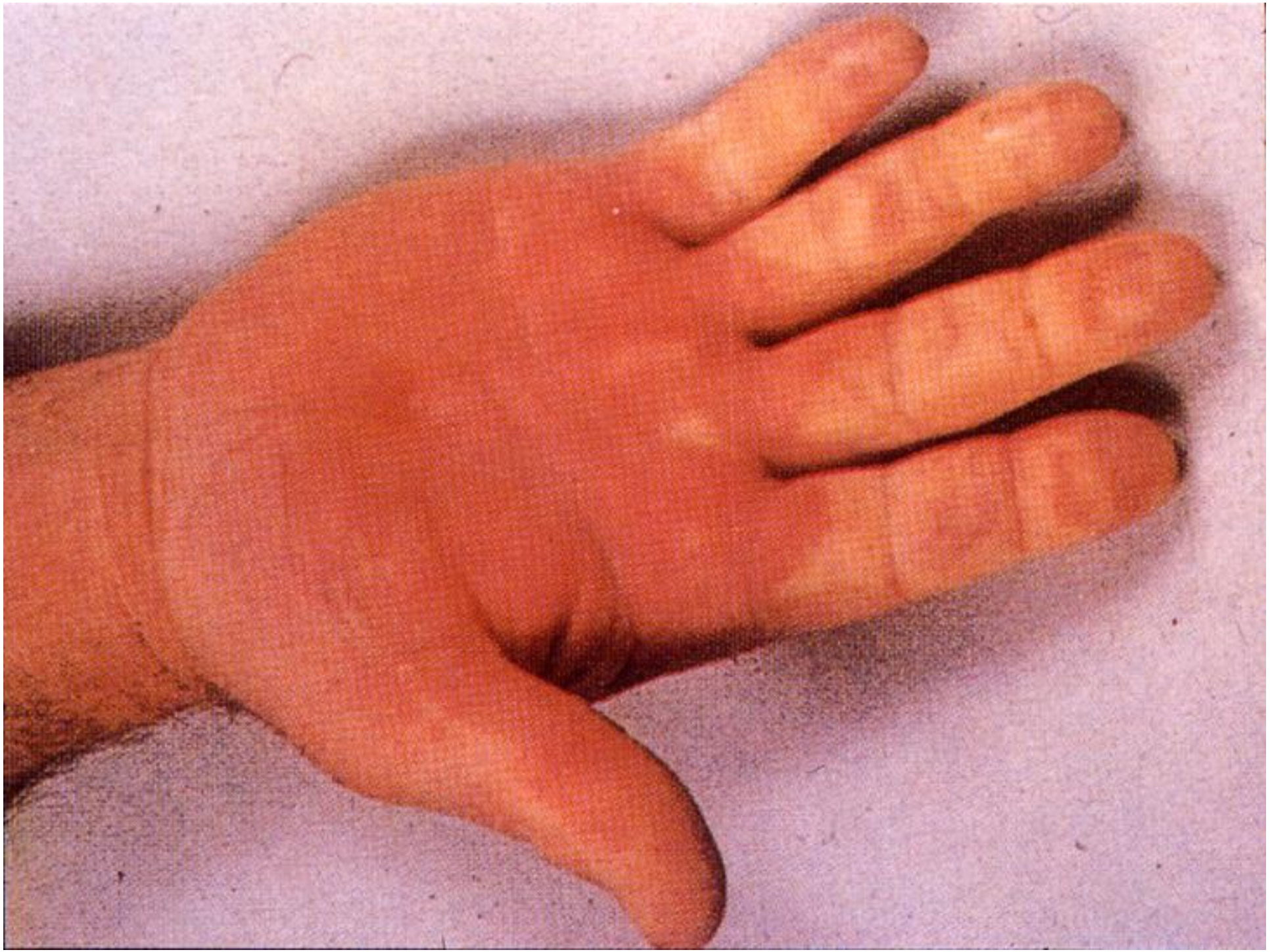


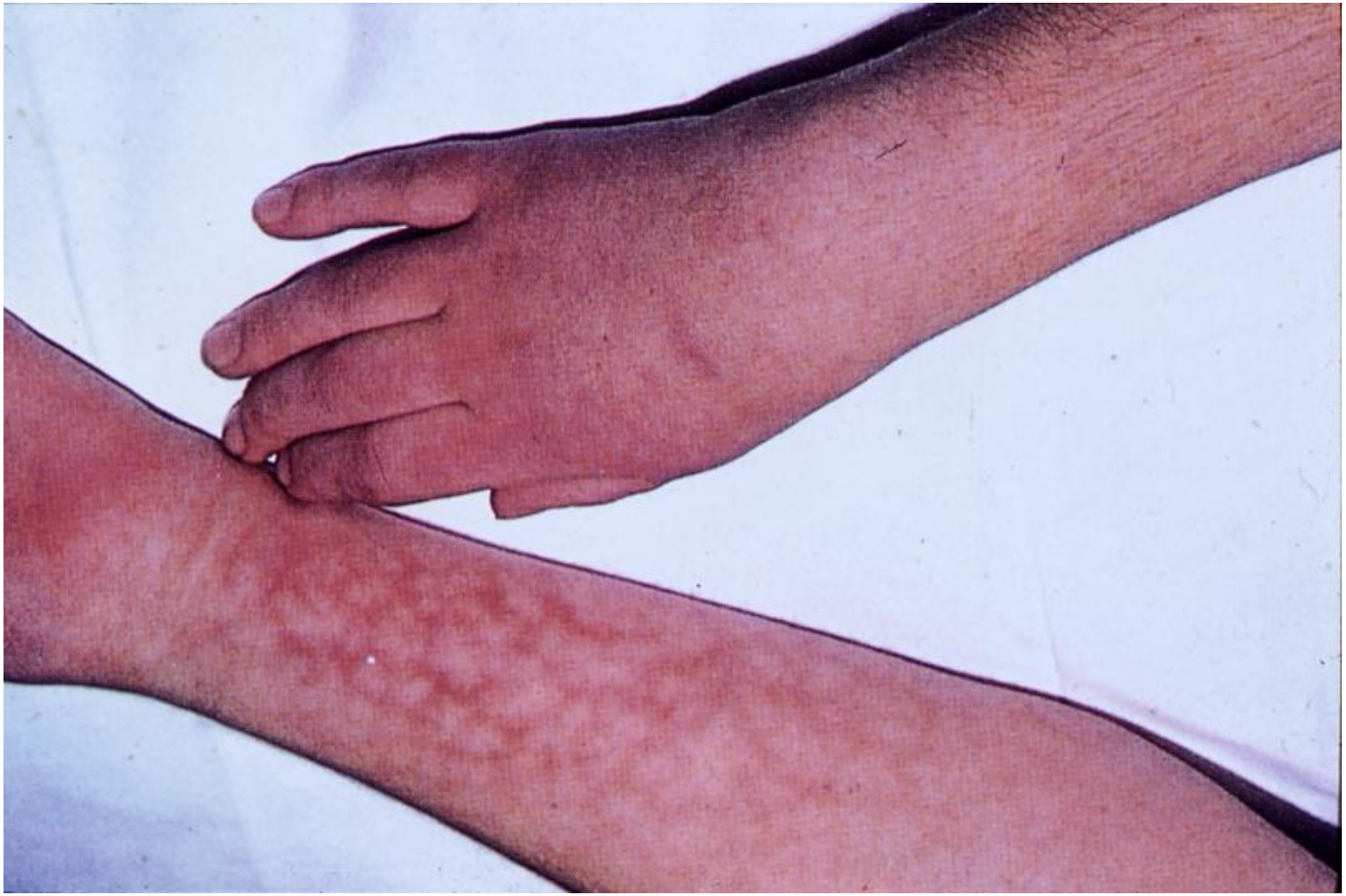


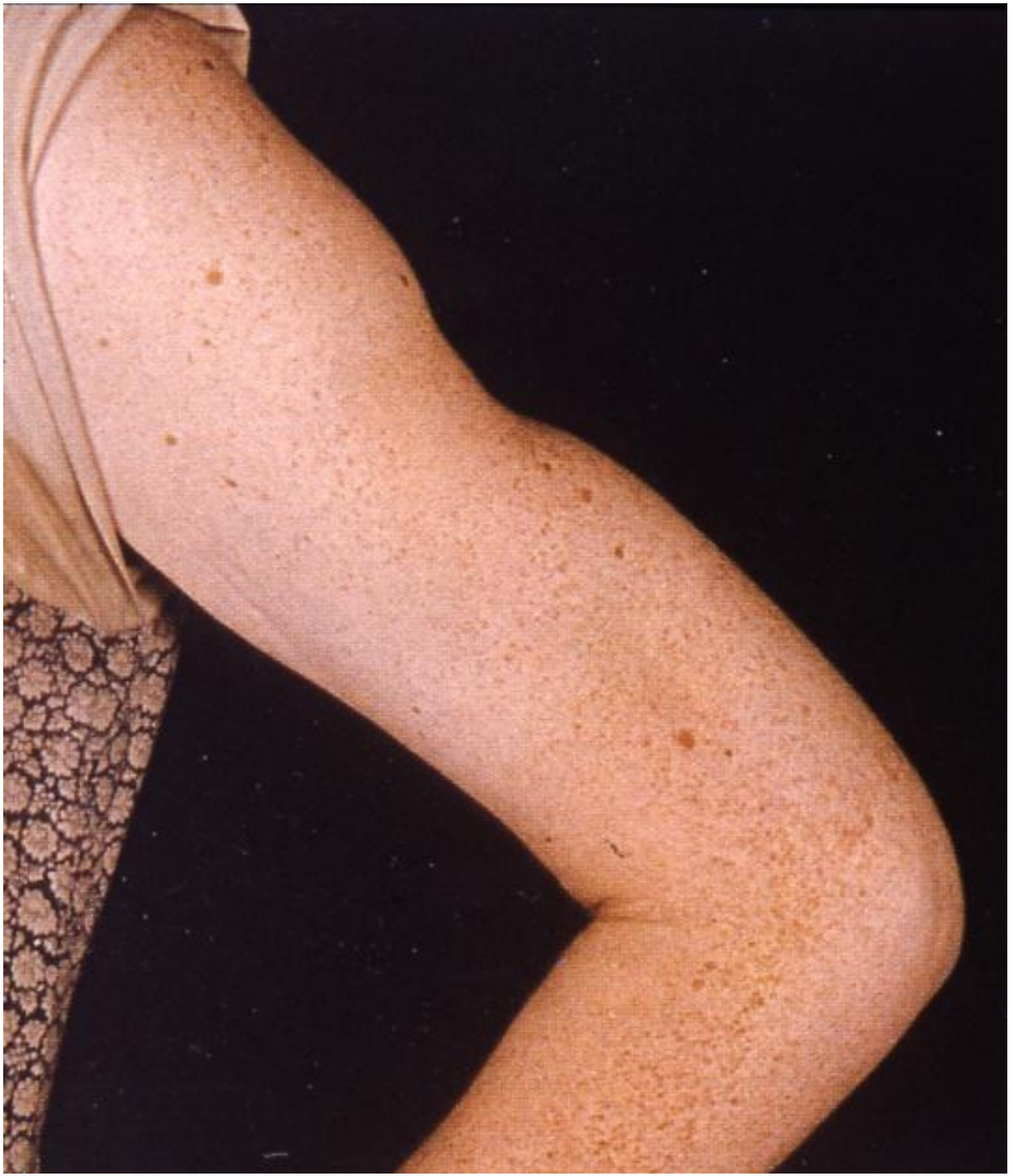


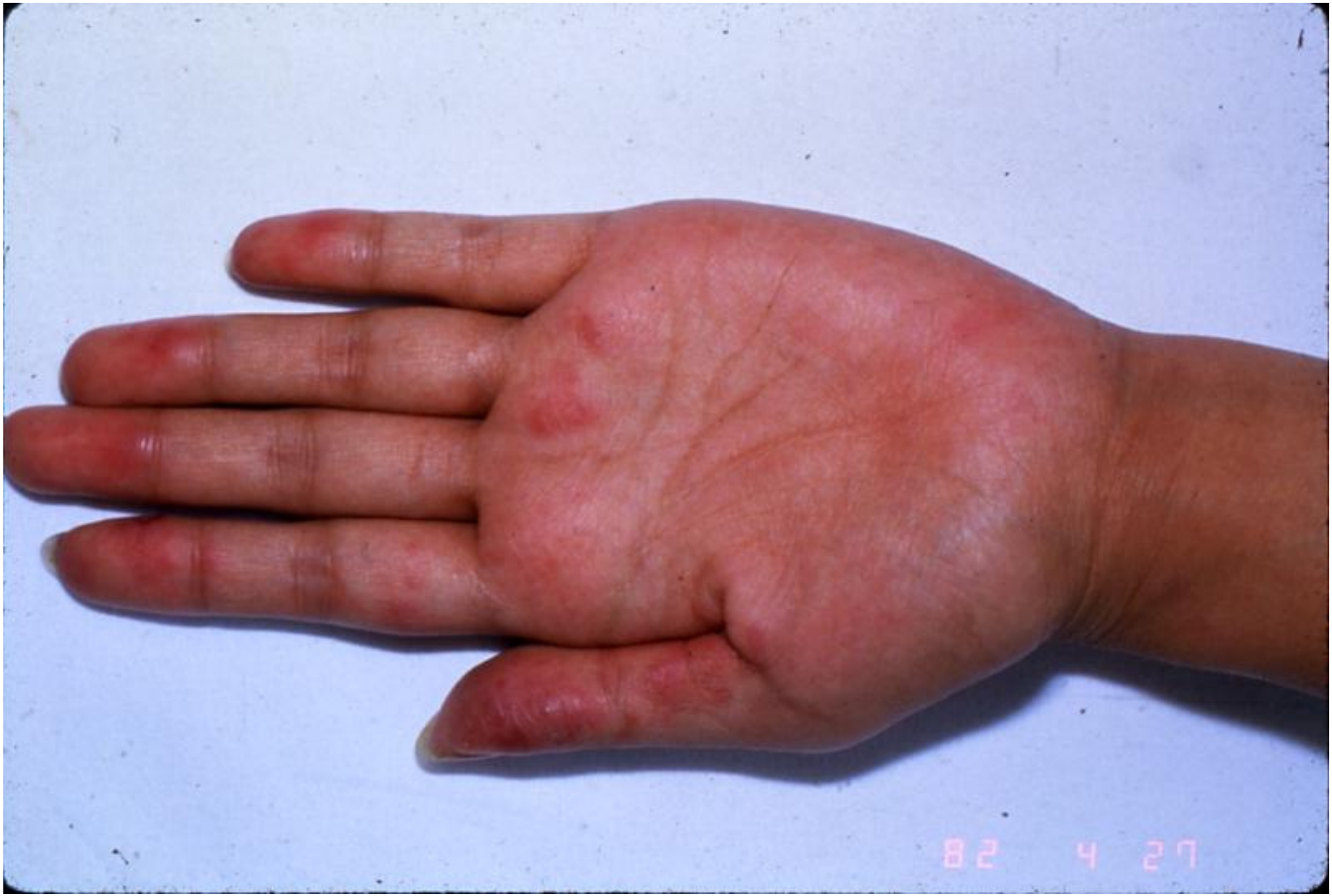


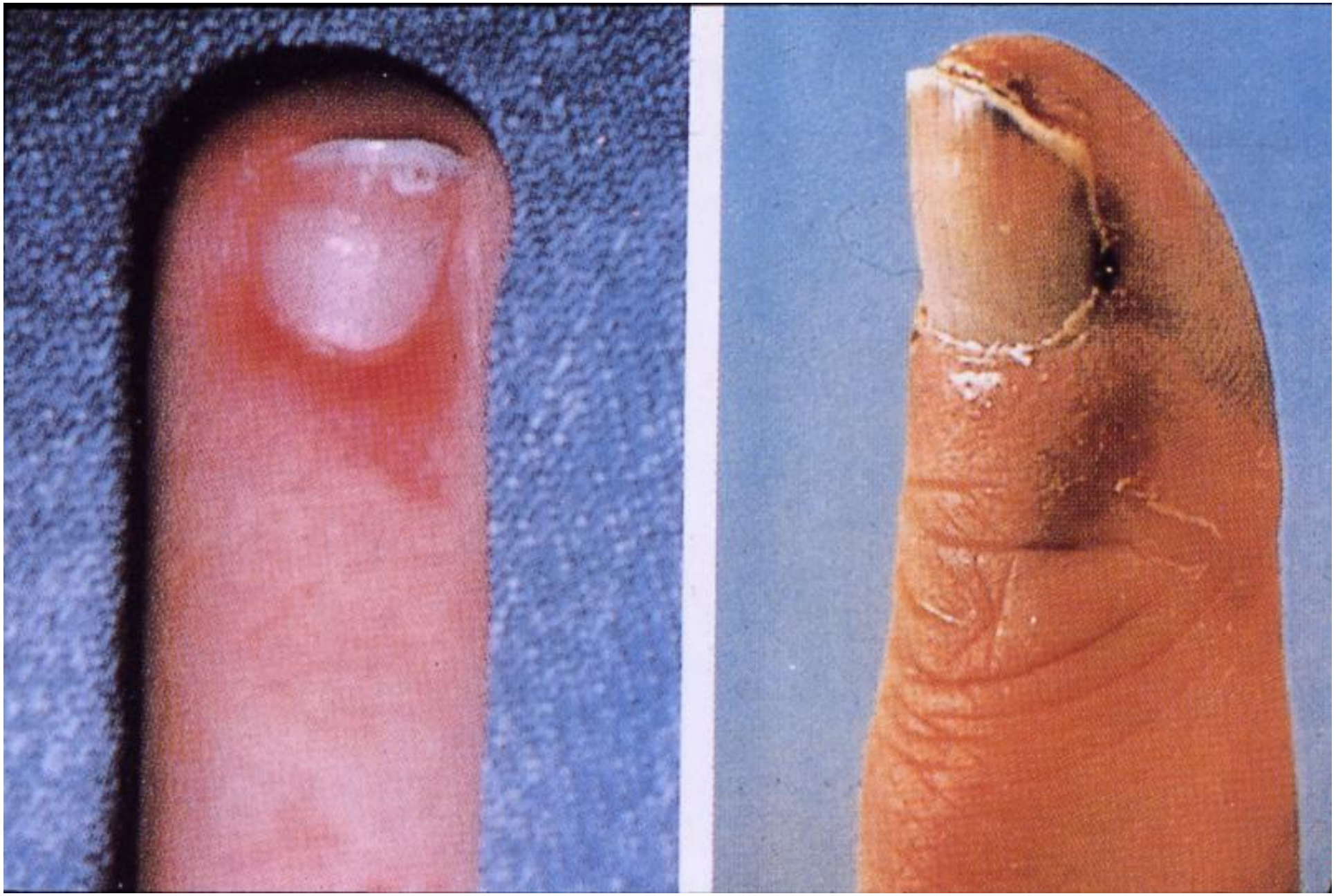

84 2 14

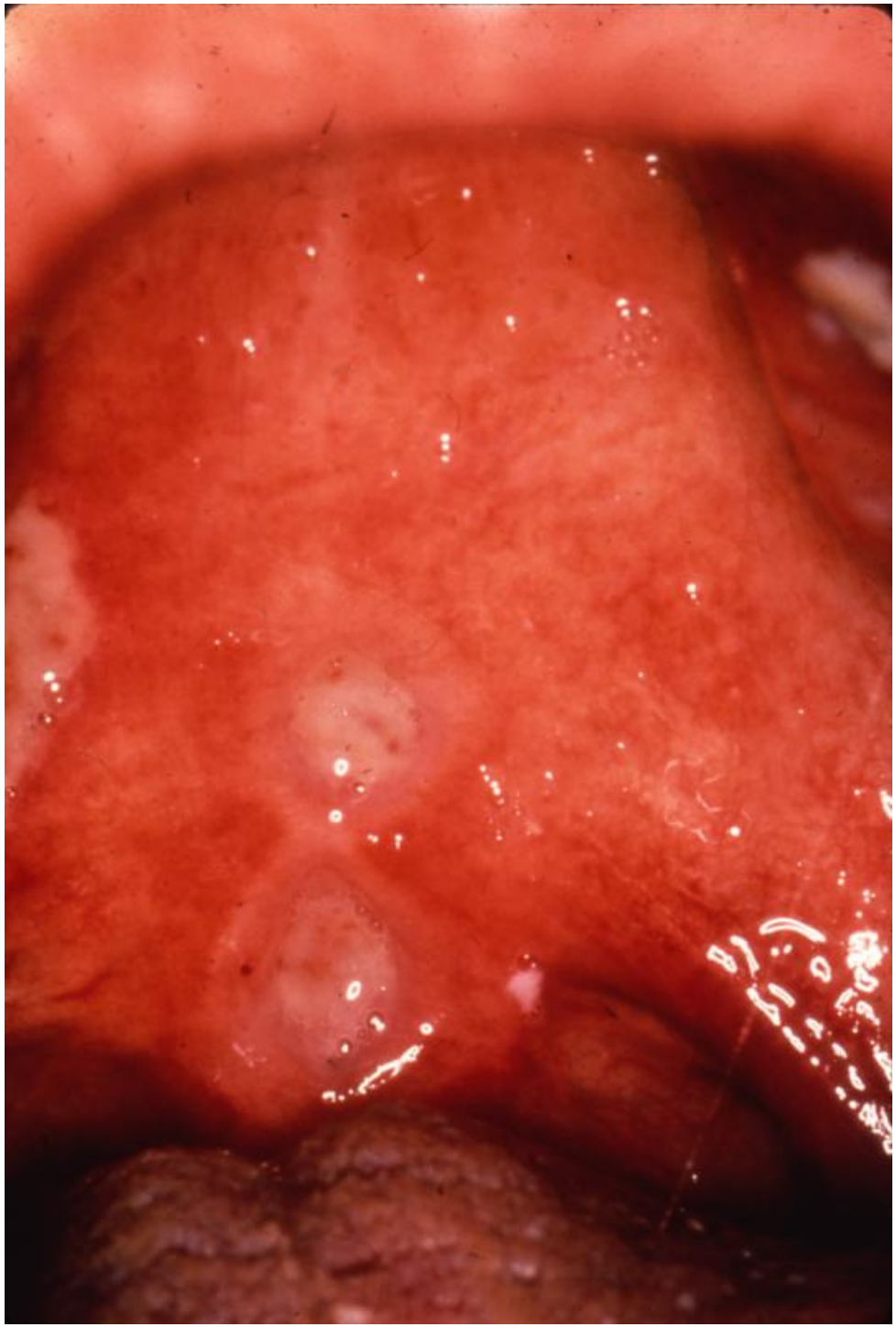




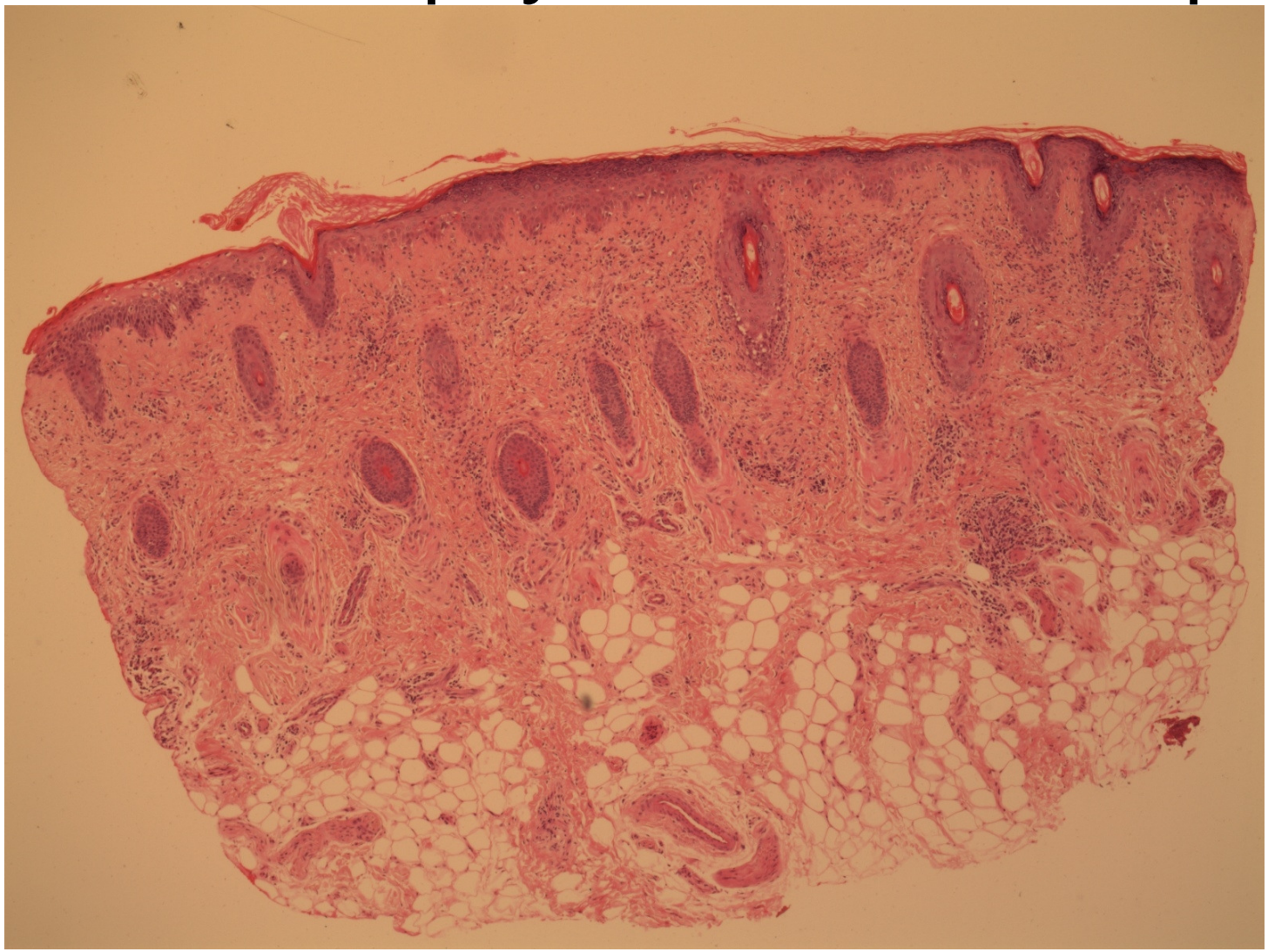



82 4 27





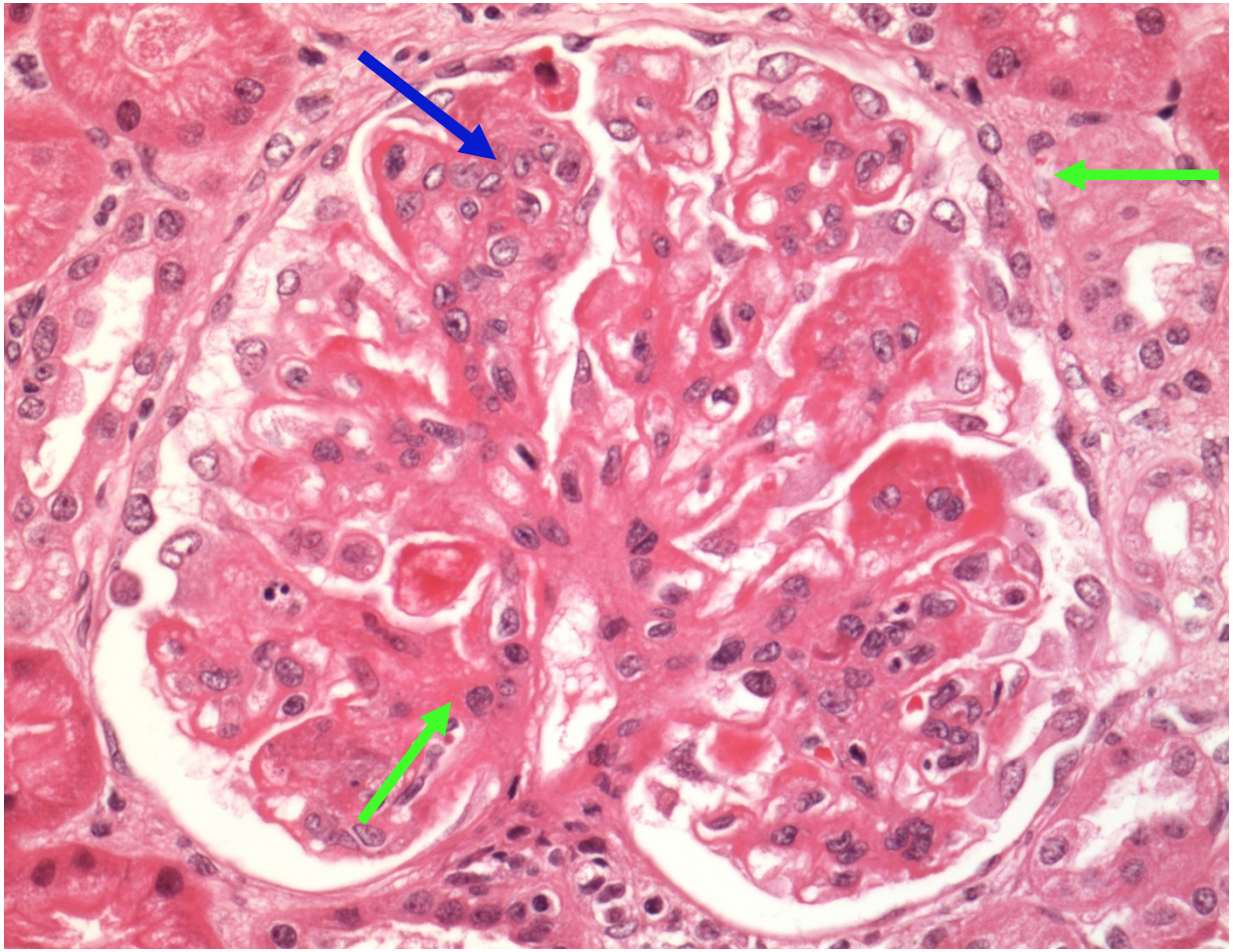
Skin biopsy : cutaneous Lupus



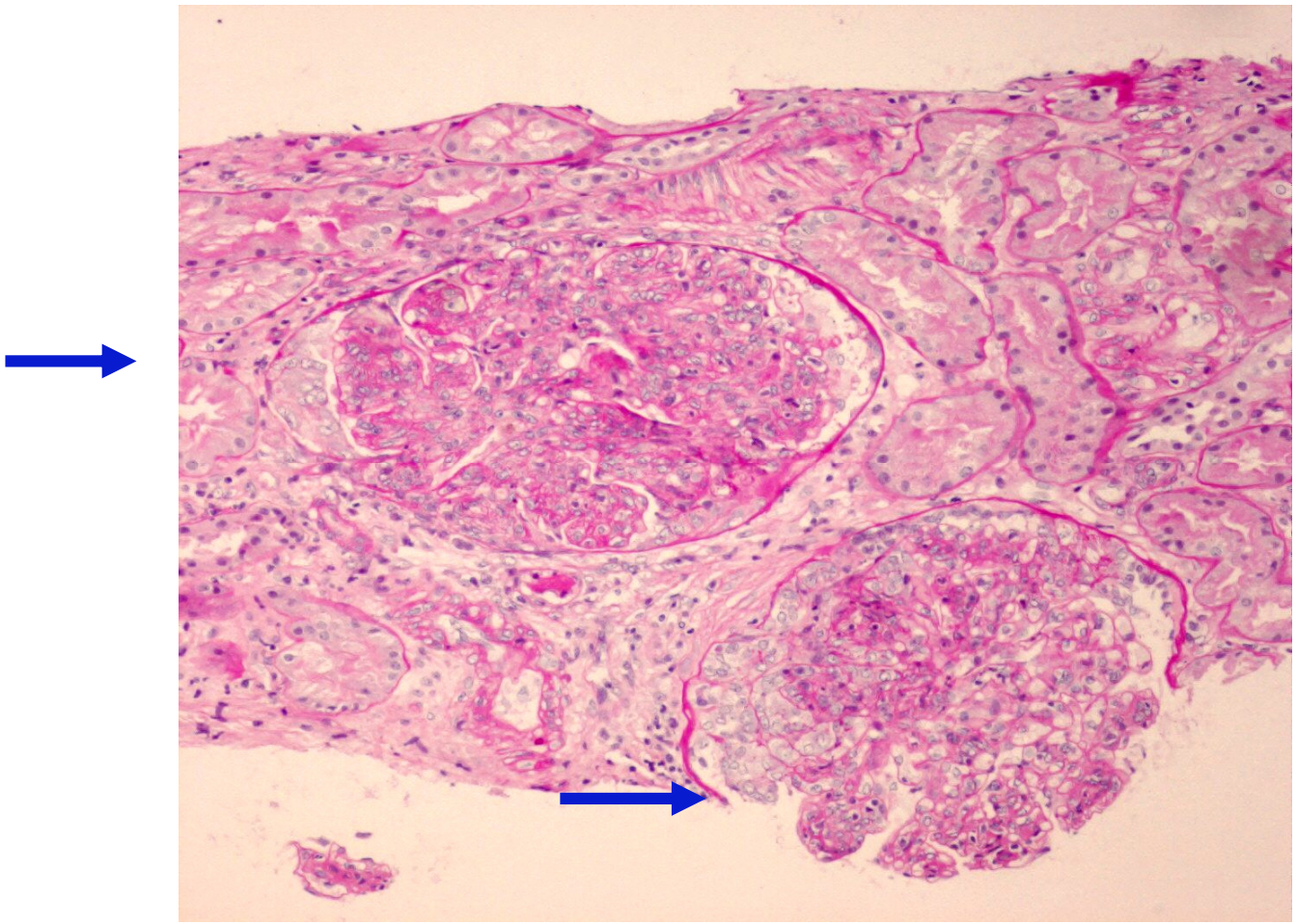
Renal Manifestations in SLE

- Present in about 50-70% patients
- Patients may be asymptomatic
- Abnormal urinalysis
    - Haematuria
    - Casts
    - Pyuria
    - Proteinuria
- Hypertension
- Nephrotic syndrome
- Renal failure

Mesangioproliferation (blue arrow) & Immune complex hyaline deposits (green arrows)



Crescentic Glomeruli



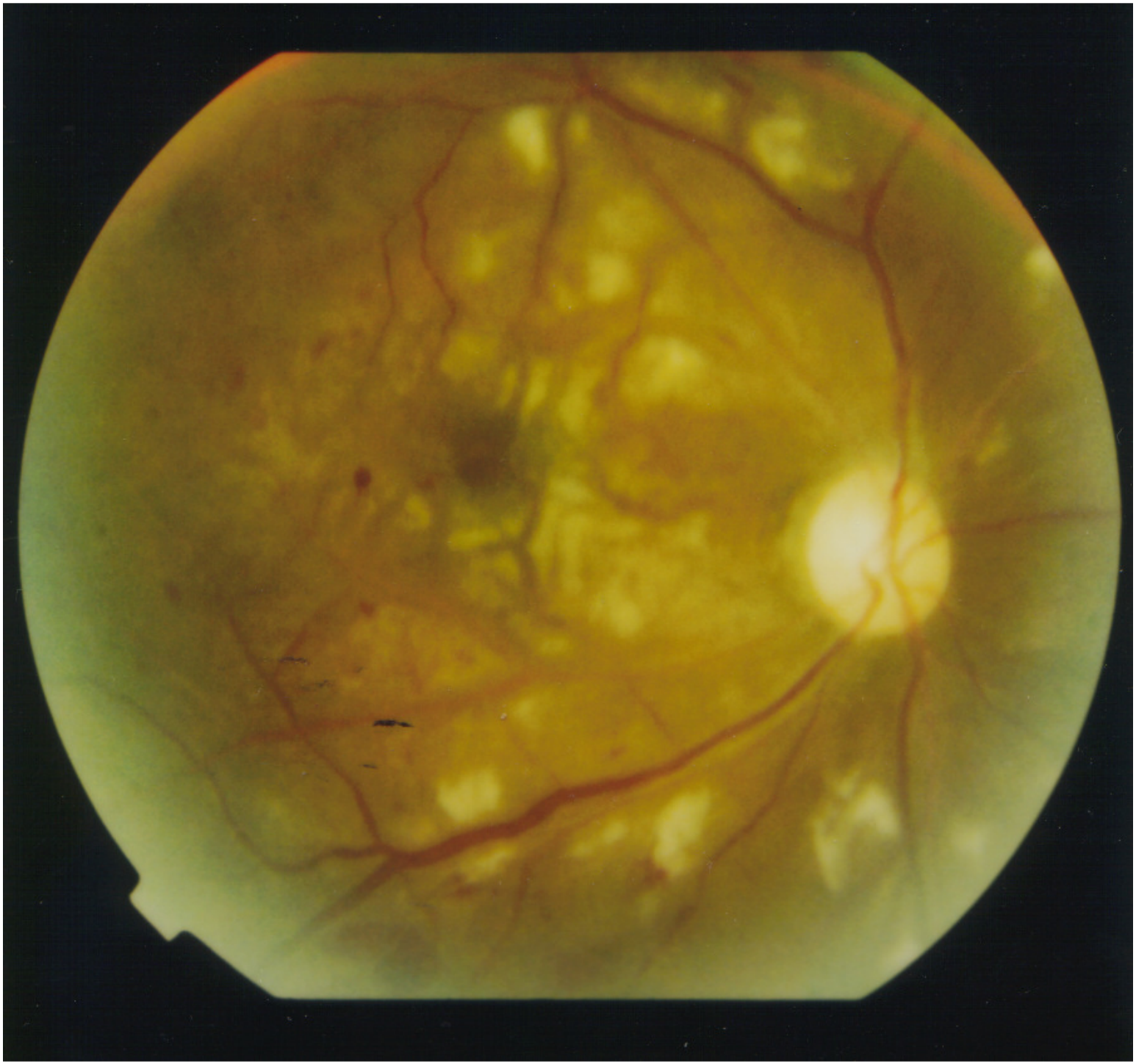
The ACR nomenclature of 19 neuropsychiatric syndromes in SLE

Central nervous system

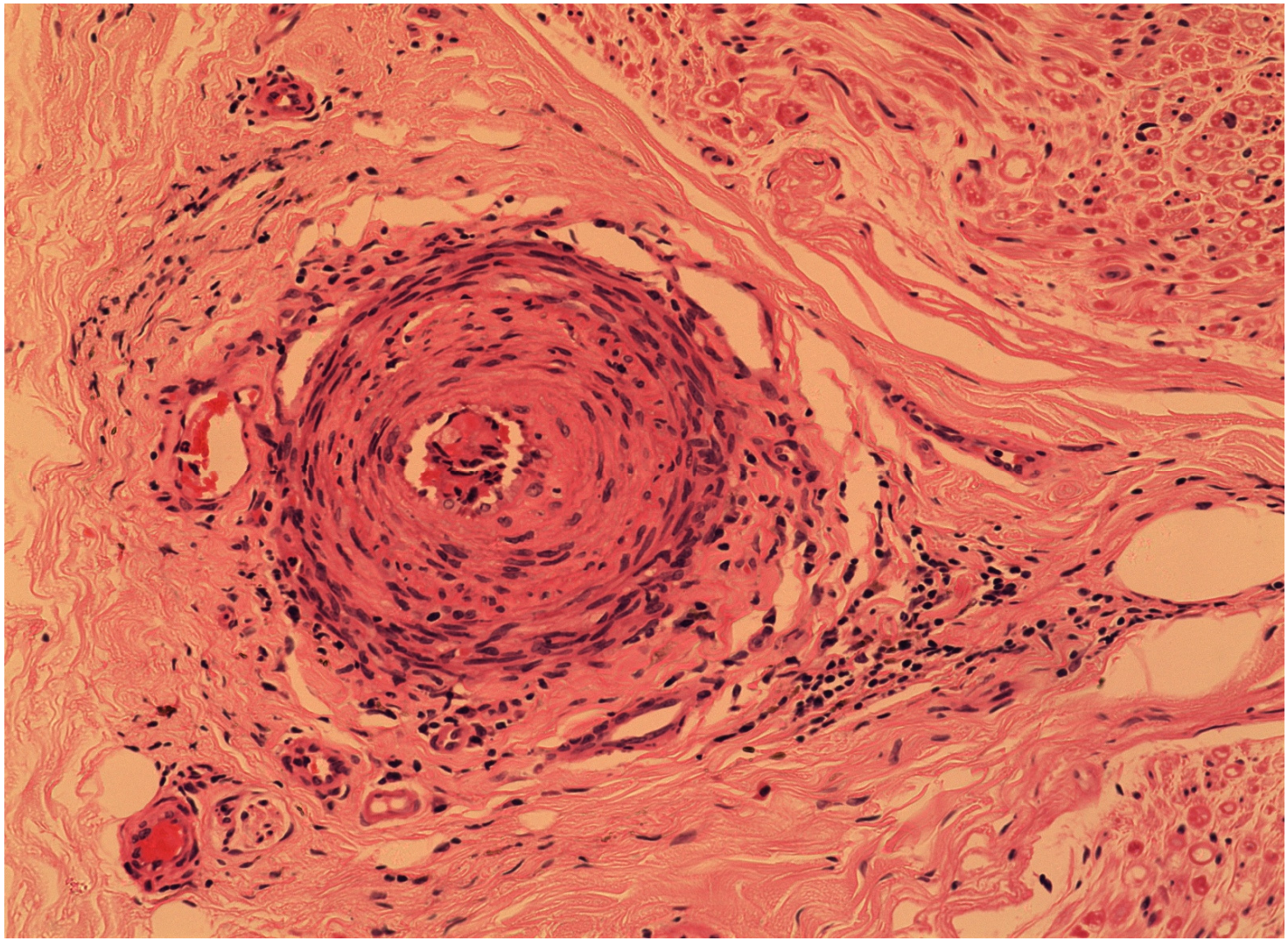
Aseptic meningitis
Cerebrovascular disease
Demyelinating syndrome
Headache
Movement disorder
Myelopathy
Seizure disorder
Acute confusional state
Anxiety disorder
Cognitive dysfunction
Mood disorders
Psychosis

Peripheral nervous system

Gullain-Barre syndrome
Autonomic neuropathy
Mononeuropathy (single/multiplex)
Myasthenia gravis
Cranial neuropathy
Plexopathy
Polyneuropathy



Nerve-Biopsy Vasculitis

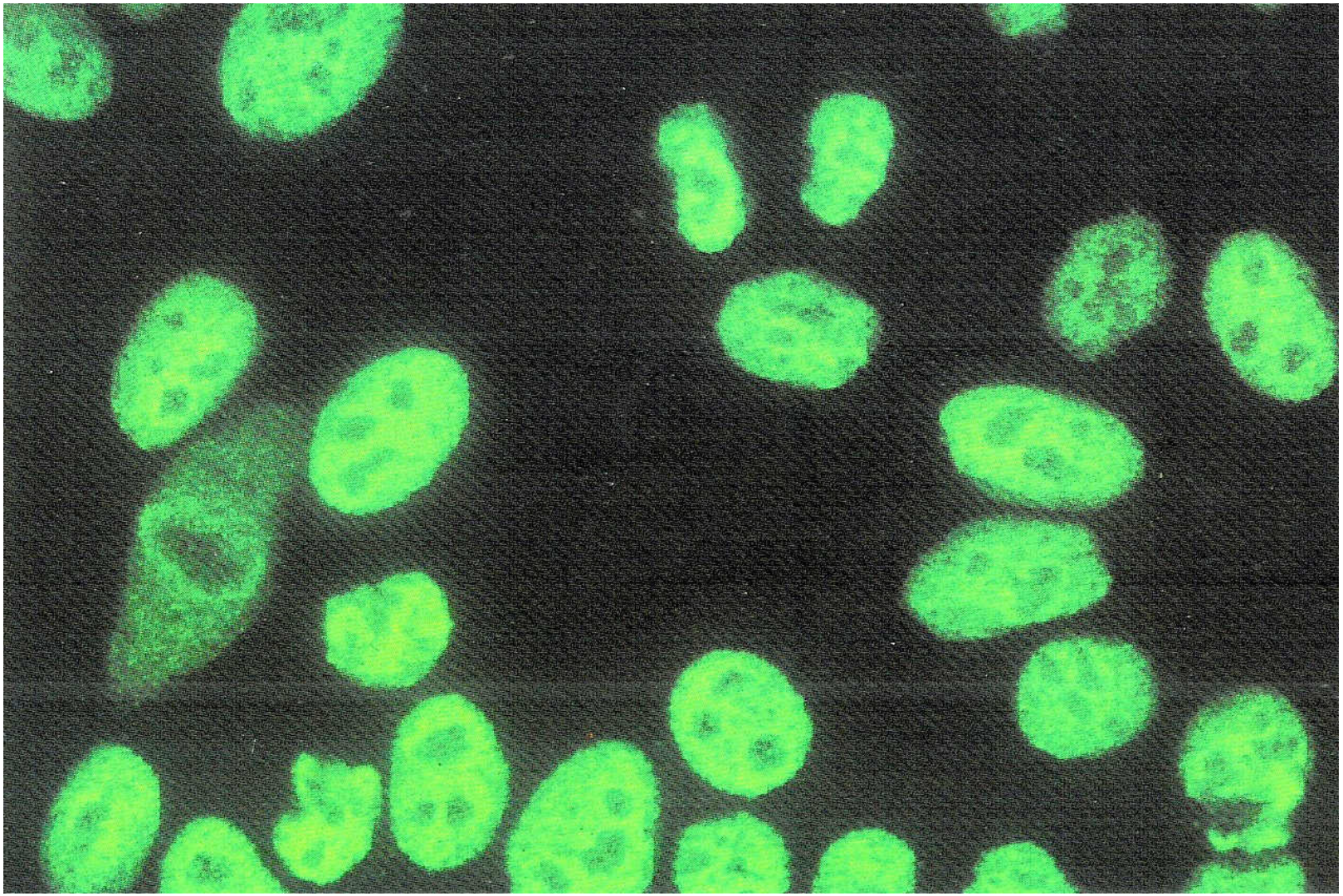


Autoantibodies in SLE

- A myriad of autoantibodies can be seen in patients with SLE
- Some of these autoantibodies can be present up to 9.4 years before the diagnosis of SLE
- The number of such “occult” autoantibodies may increase just before onset of the disease
- The actual chances of developing SLE in individuals with the “occult” autoantibodies is unknown but probably not more than 2.5%

Autoantibodies in SLE

- ANA is present in almost all untreated SLE patients
- It is a sensitive but non-specific marker
- Anti-dsDNA and anti-Sm are specific lupus antibodies
- titre of anti-dsDNA correlates with disease activity
- Anti-Sm is steroid resistant and persists throughout the whole course of illness
- Anti-Ro and anti-La antibodies are associated with photosensitivity, subacute cutaneous lupus and sicca symptoms
- Maternal 52 kD anti-Ro increases the risk of congenital heart block in the fetus



Autoantibodies in SLE

- In SLE, isolated presence of anti-nRNP; a characteristic antibody for undifferentiated connective tissue disease (formally called mixed connective tissue disease) is associated with Raynaud's phenomenon and less chance of renal involvement
- Anti-phospholipid antibodies (anti-cardiolipin antibodies, ACA and lupus anticoagulant) are present in up to 1/3 of local SLE patients at any time of the disease course
- A high titre of the anti-cardiolipin antibodies and persistently positive test results are more clinically significant
- β2 glycoprotein I antibody is a more specific anti-phospholipid antibody
- Anti-ribosomal P antibody has been associated with certain neuropsychiatric manifestations such as psychosis and depression
- Its clinical usefulness is limited by the low sensitivity

Mortality in SLE

- The survival of SLE patients has improved tremendously in the past few decades
- The cumulative 5 year and 10 year survival of local SLE patients is 92% and 83% respectively
- The improved survival is due to
  - Increased awareness and earlier diagnosis of the disease and its complications
  - More judicious use of immunosuppressive therapy
  - Availability of more powerful anti-microbial therapy

Morbidity in SLE

- This is contributed by irreversible damage of organ function as a result of refractory disease manifestations and complications of treatment
- Common morbidities include:
  - Musculoskeletal complications e.g. avascular bone necrosis, osteoporotic fracture
  - Uncontrolled renal disease
  - Sequel after cerebrovascular and cardiovascular events
  - Cyclophosphamide induced ovarian failure

Management of SLE

- Management plan has to be individualized
- It depends on a number of factors e.g.
  - Severity of involvement
  - Reversibility of the clinical manifestations
  - Nature of pathology : inflammatory or non-inflammatory
- Team approach and patient education are of paramount important
- An optimal management plan should include primary and secondary precaution of morbidities such as osteoporosis and thrombosis

Conventional Therapy for Cutaneous LE

- Photoprotection
- Topical Steroids
- Intralesional Steroids
- Antimalarial Drugs

Conventional Therapy for Cutaneous LE

Photoprotection

- To avoid sun exposure especially between 10am to 3pm
- To wear protective clothing and broad rimmed hats
- To apply sunscreen with a sun protective factor of 15 or higher

Conventional Therapy for Cutaneous LE

Photoprotection

- Both ultraviolet A and ultraviolet B may induce lesions in photosensitive individuals
- Broad spectrum sunscreens may offer better protection
- Patients should take protective measures during prolonged car travel

Conventional Therapy for Cutaneous LE

Topical Steroids

- Commonly prescribed to treat cutaneous LE
- To minimize the risks of atrophy, the potency of the corticosteroid preparation is tailored to the location of the lesions being treated

  i.e. low potency for facial lesions

  medium potency for the trunk and extremities

  high potency for palms and soles

Conventional Therapy for Cutaneous LE

Topical Steroids

- They are probably of limited value in the treatment of widespread DLE and in most patients with SCLE
- Application over large body surface may lead to significant specific absorption with its associated toxicity

Conventional Therapy for Cutaneous LE

Intralesional Steroids

- They are useful in the treatment of localized disease or individual DLE lesions, particularly over the face, scalp, palms and soles
- When lesions are too numerous, injection of intralesional steroids is not a safe or practical approach

Conventional Therapy for Cutaneous LE

Antimalarial Drugs

- Their effectiveness in the treatment of cutaneous LE has been well established
- Response rates generally exceed 80% for both DLE and SCLE
- The most commonly used agents are hydroxychloroquine sulphate,chloroquine phosphate and quinacrine hydrochloride

Therapy for Lupus Nephritis

- Milder forms of lupus nephritis (class 1,2,3 and mild class 5) can be treated with steroid, using Azathioprine as the steroid sparing drug
- Angiotensin converting enzyme inhibitors (ACEI) are also helpful adjuncts
- Class 4 and severe class 5 require more aggressive induction regime consisting of steroid and cyclophosphamide, mycophenolate, or calcineurin inhibitors

Therapy for Lupus Nephritis

- Cyclophosphamide can either be given orally or by intravenous pulses
- Recent randomized controlled trials have shown MMF to be equally efficacious as cyclophosphamide but with less toxicities such as ovarian failure or major infection
- However, long term data on MMF beyond 5 years are still not available
- The evidence for the efficacy of calcineurin inhibitors is less strong
- They are indicated in patients intolerant of other immunosuppression because of cytopenia
- Of the 2 calcineurin inhibitors, tracolimus is preferred to cyclosporin A because of lower incidence of hypertension, ginginval hyperplasia and hyperlipidaemia

Therapy for Neuropsychiatric Lupus

- Optimal treatment is less clearly defined for lack of controlled trials
- Certain manifestations eg. headache, anxiety and depression require symptomatic treatment only
- Aggressive immunosuppressive regimes are indicated for severe cases
- A combination of high dose steroid and an extended course of IV cyclphosphamide or sequential daily oral cyclphosphamide and azathioprine has been used
- Pulse steroid is indicated for rapidly progressive neurological disease

Novel Therapeutic Modalities for SLE

- Newer immunosuppresive agents
  - Mycophenolate mofetil
  - Tacrolimus
  - Leflunomide
- Hormones
  - Dehydroepiandrosterone
- B cell depletion
  - Fludarabine, rituximab, epratuzumab, belimumab
- B cell toloerogen
  - LJP394 – Riquent
- Blockade of the co-stimulatory pathways
  - Abatacept
- Neutralization of cytokines
  - IL-10, TNF, IL-6
- Anti-complement
  - Anti-C5b (eculizumab)
- Immunoablative cyclophosphamide $\pm$ stem cell rescue

Conclusion

- The knowledge on pathogenesis and clinical management of SLE has advanced over the past few decades
- There is an increasing number of RCTs to determine better and safer therapies
- Novel therapeutic agents are undergoing multicentre trials
- Primary and secondary prevention of disease and treatment related morbidities is equally important
- It is hoped that the outcome of SLE can continue to improve in the next decade

RHEUMATOID ARTHRITIS

Rheumatoid Arthritis

- It is the most common connective tissue disease
- It is the most important in socioeconomic terms since it is a chronic, aggressive and disabling disease
  - It affects people in the prime of life
  - 50% of the affected individuals would be unable to hold full time employment
  - 10% of the victims might become chairbound
- It might also shorten the life span of affected patients by 7 years for male patients and 5 years for female patients

Rheumatoid Arthritis : Epidemiology

- a disease of modern time : first case described in 1800
- of variable prevalence, ranging from 0.1% to 5.3%
- annual incidence : 30/100,000
- females affected 3 times more than males
- peak incidence is between the 4th and the 6th decades
- geographical distribution :
  - ⇧ reported in some native American population
  - lowest rates in oriental population and rural Africans
- ± familial aggregation of rheumatoid arthritis
- ⇧ incidence of rheumatoid factor in first degree relatives
- genetic associations : HLA-DR4 and HLA-DR1

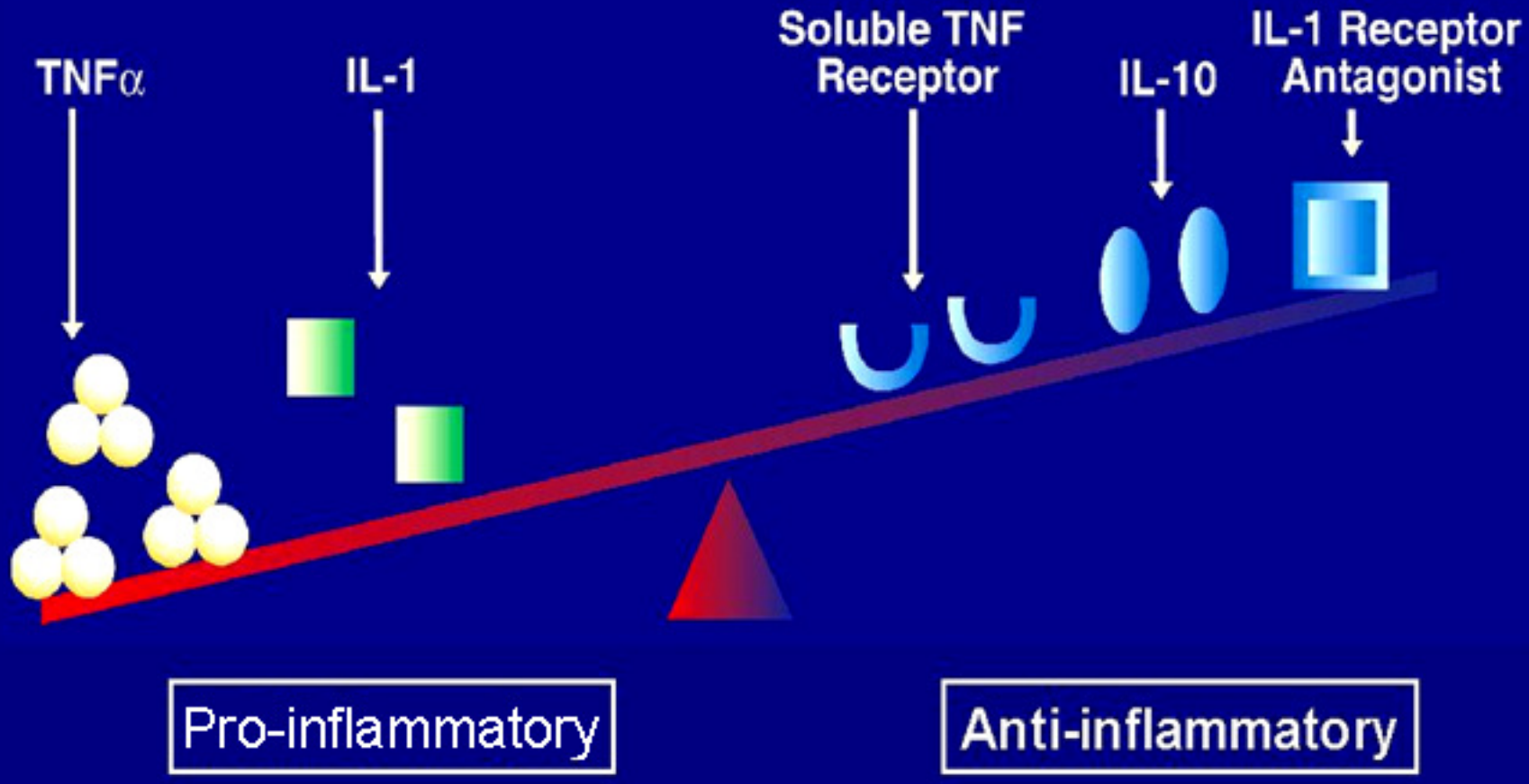
Rheumatoid Arthritis : Aetiology

- Unknown
- Probably induced in genetically predisposed individuals by many different arthritogenic agents
- Interrelationships of infectious agents, genetics, and autoimmunity
- Candidate viruses include herpes viruses eg. EB virus, rubella virus and parvovirus
- Candidate bacterias include mycoplasma, mycobacteria and various enteric organisms

Rheumatoid Arthritis : Aetiology

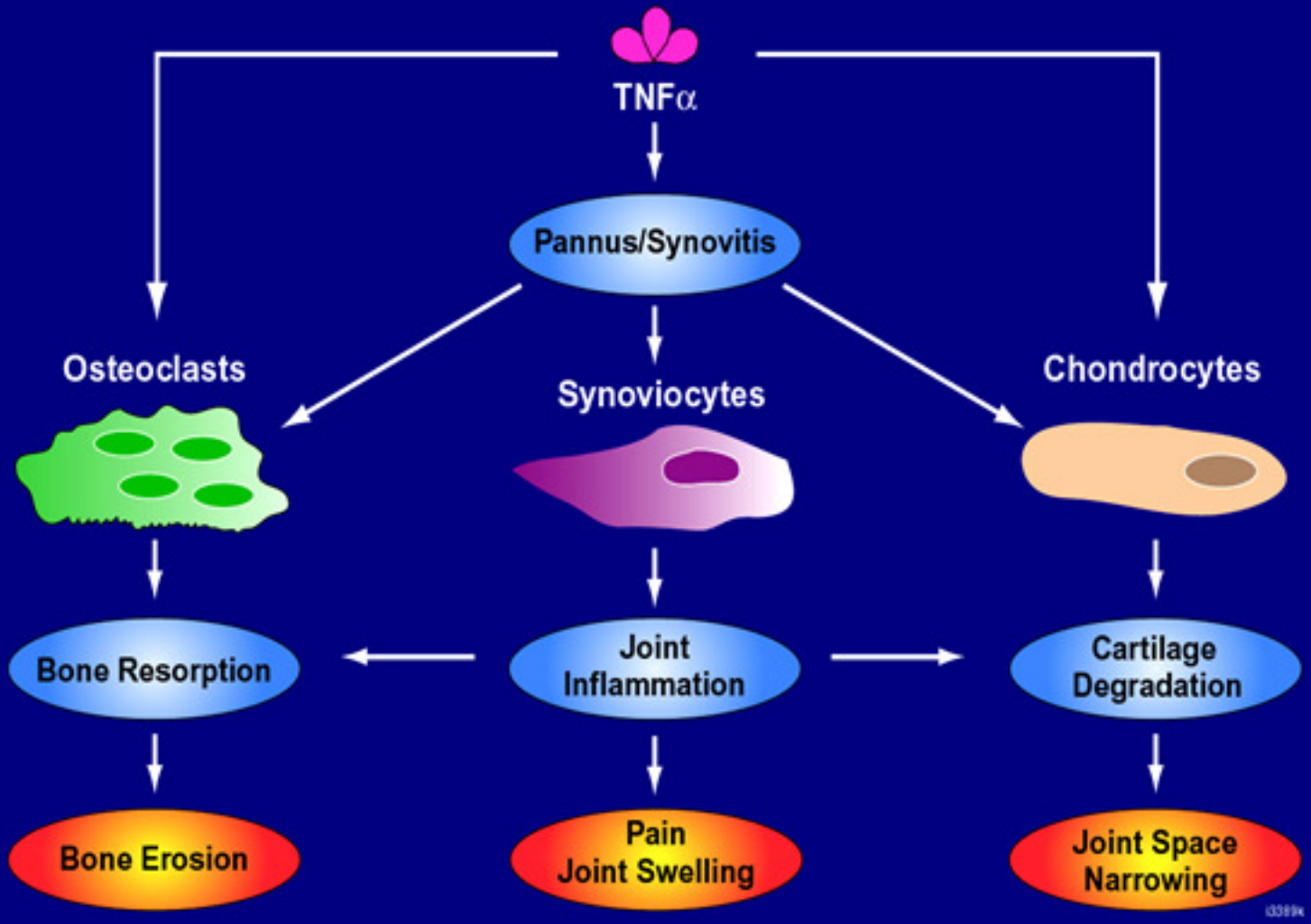
- The third hypervariable regions of the beta chains of HLA-DR1 and DR4 influence susceptibility to disease
- Rheumatoid factors may play a role in amplifying rheumatoid inflammation but they are not a primary triggering or aetiologic factor
- Immunoglobulin genes, in addition to the MHC, influence disease susceptibility to RA

Disequilibrium of Cytokines in Joints of Patients with Rheumatoid Arthritis



Feldmann M, et al. Rheumatoid Arthritis. *Cell.* 1996; 85:307-10.

Central Role of TNFα in RA

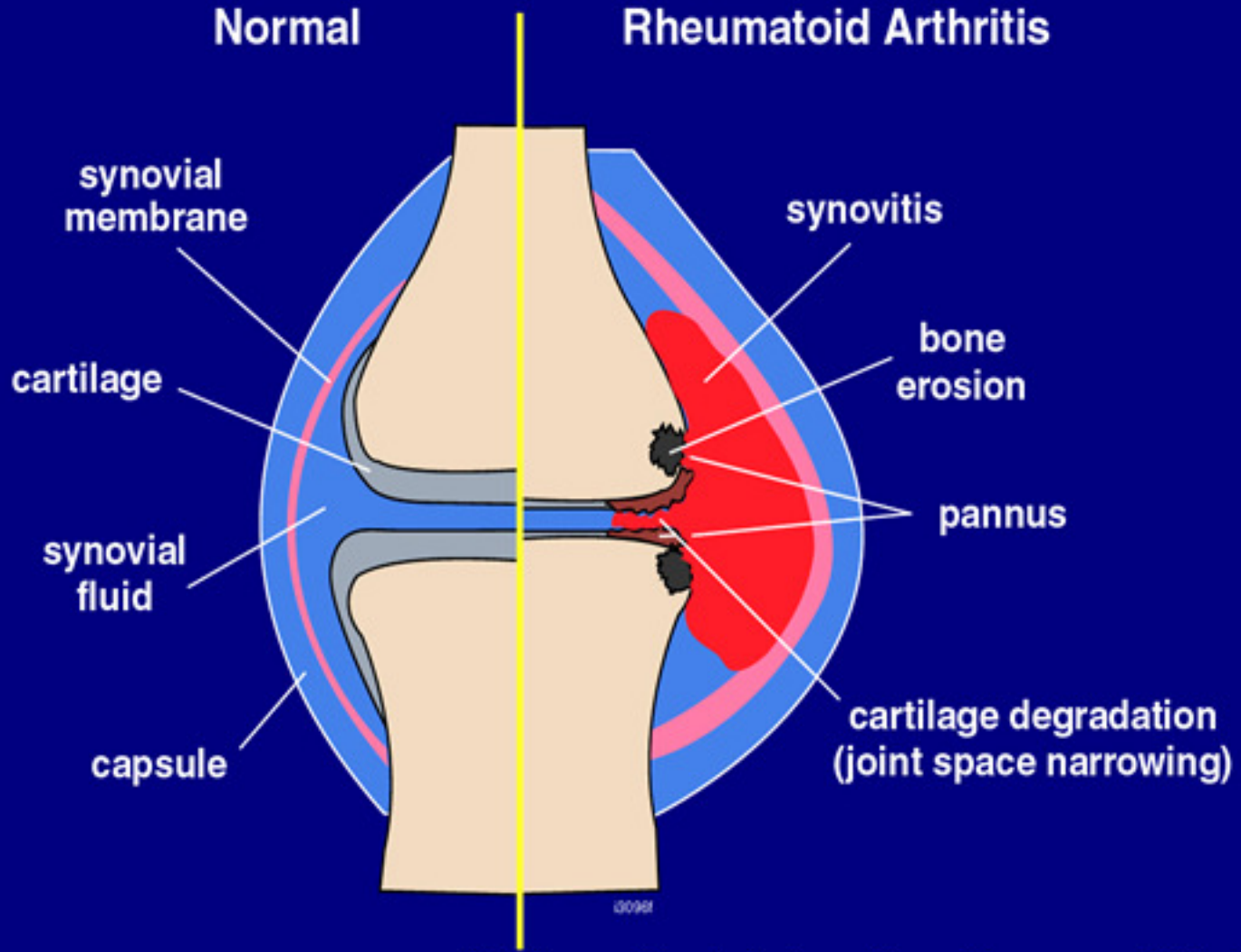


Kirwan JR, *J Rheumatol.* 1999; 7:720-725.

Rheumatoid Arthritis : Pathological Changes

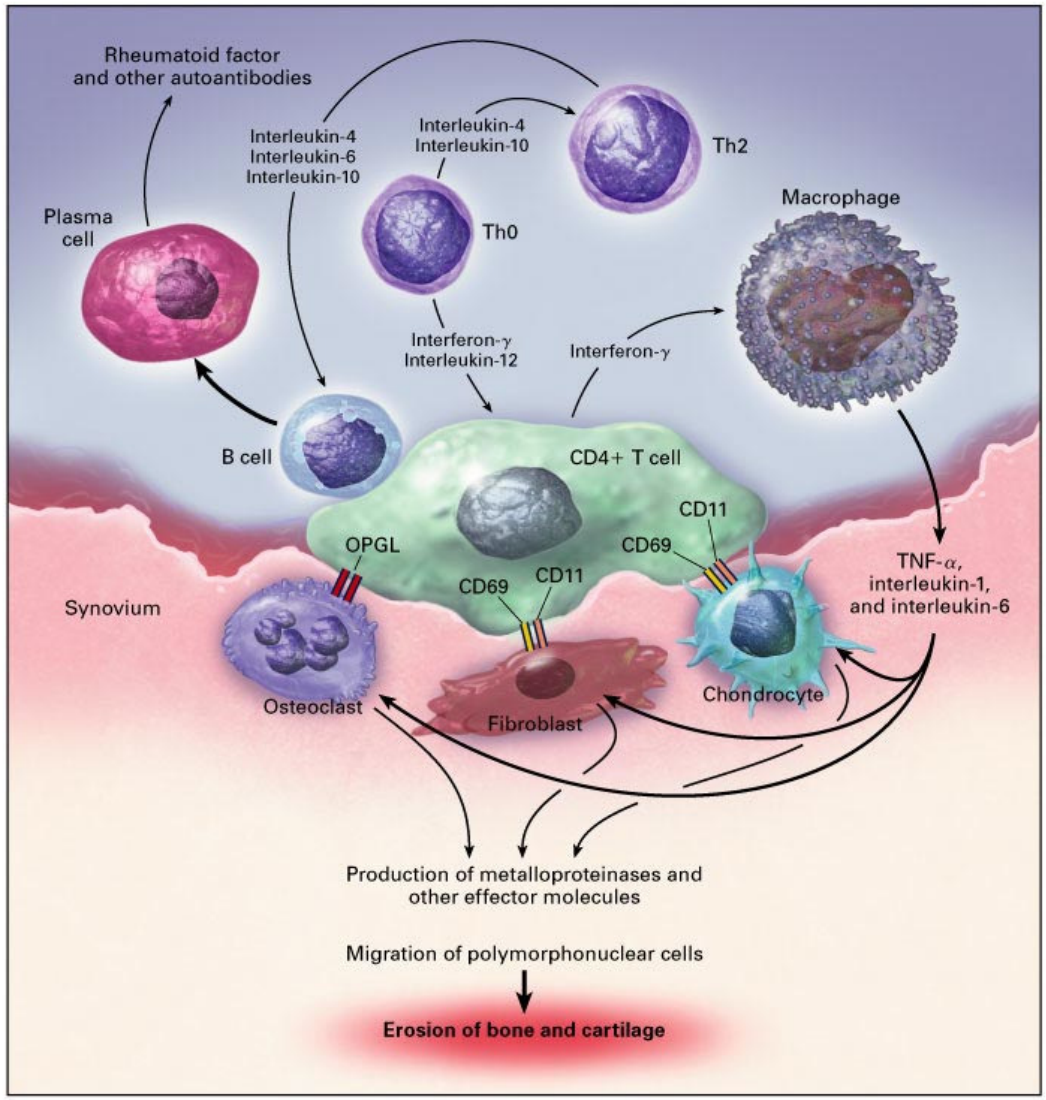
- Oedema of synovium
- Vascular congestion and dilatation
- Cellular infiltrates (lymphocytes and plasma cells)
- Hyperplasia and hypertrophy of synovial lining cells
- Villous hypertrophy
- Pannus (granulation) formation

The Pathology of Rheumatoid Arthritis



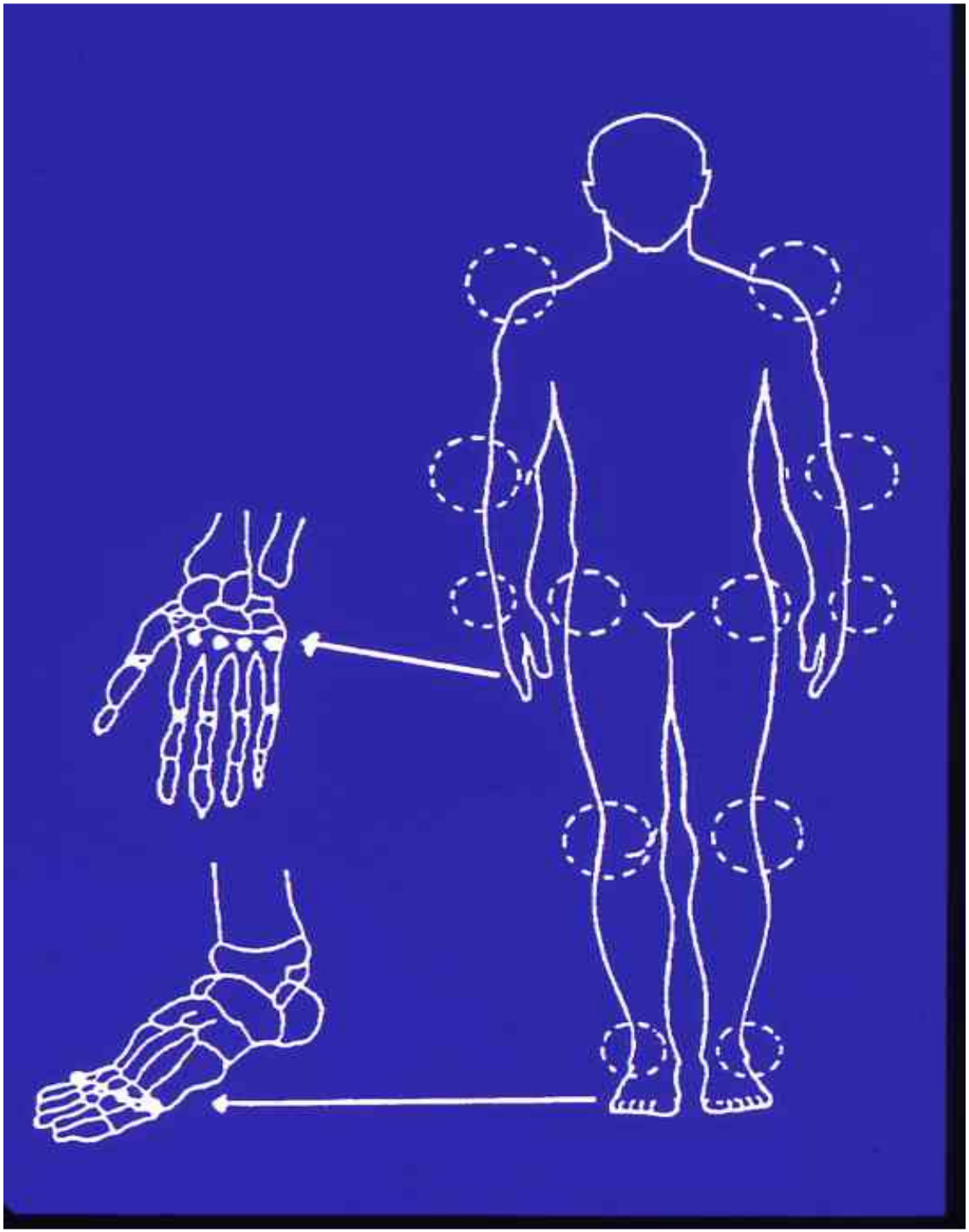
Feldmann M, et al. *Annu Rev of Immuno.* 1996; 14:397-440.

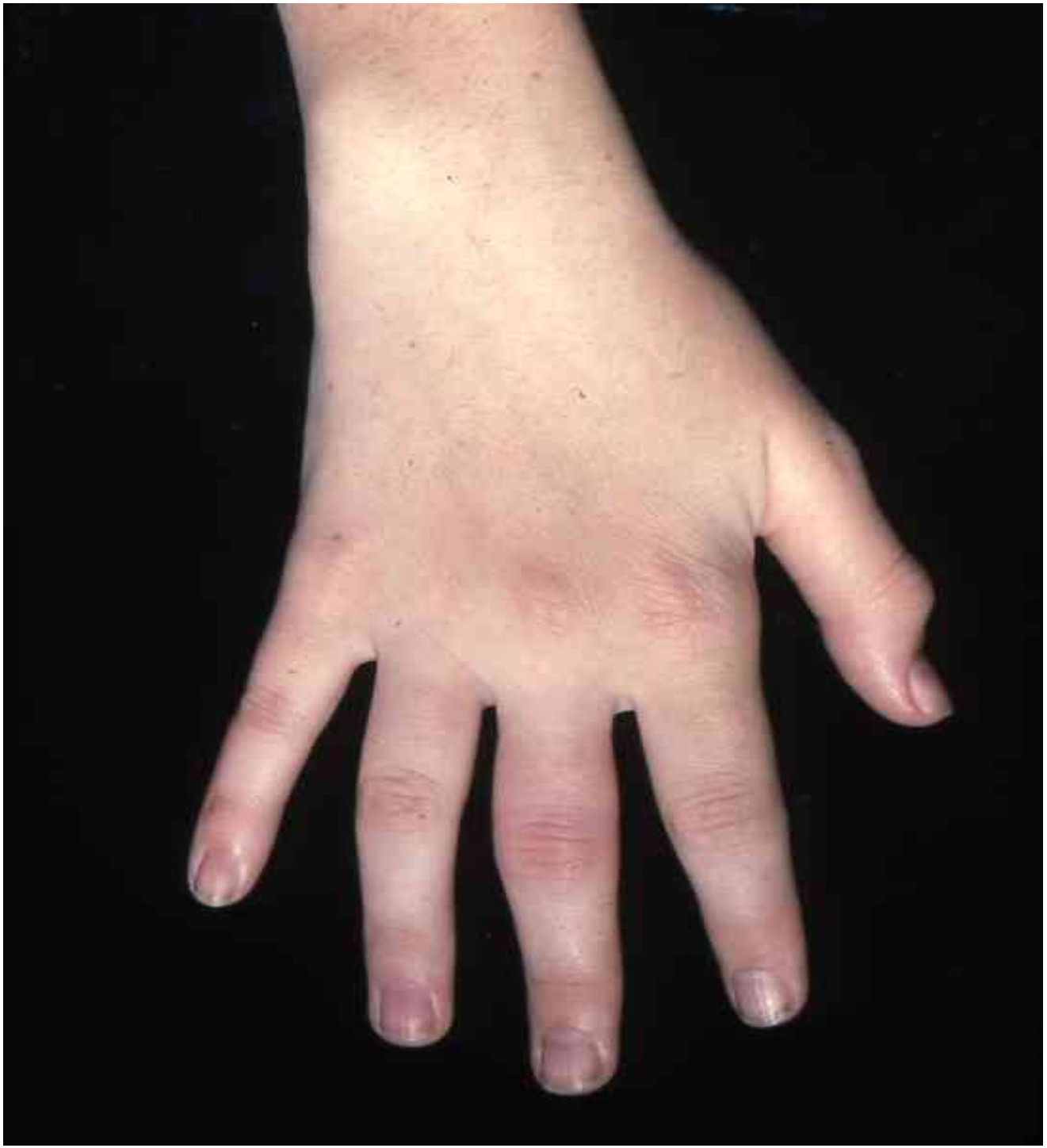
Self-sustaining inflammation in the RA pannus

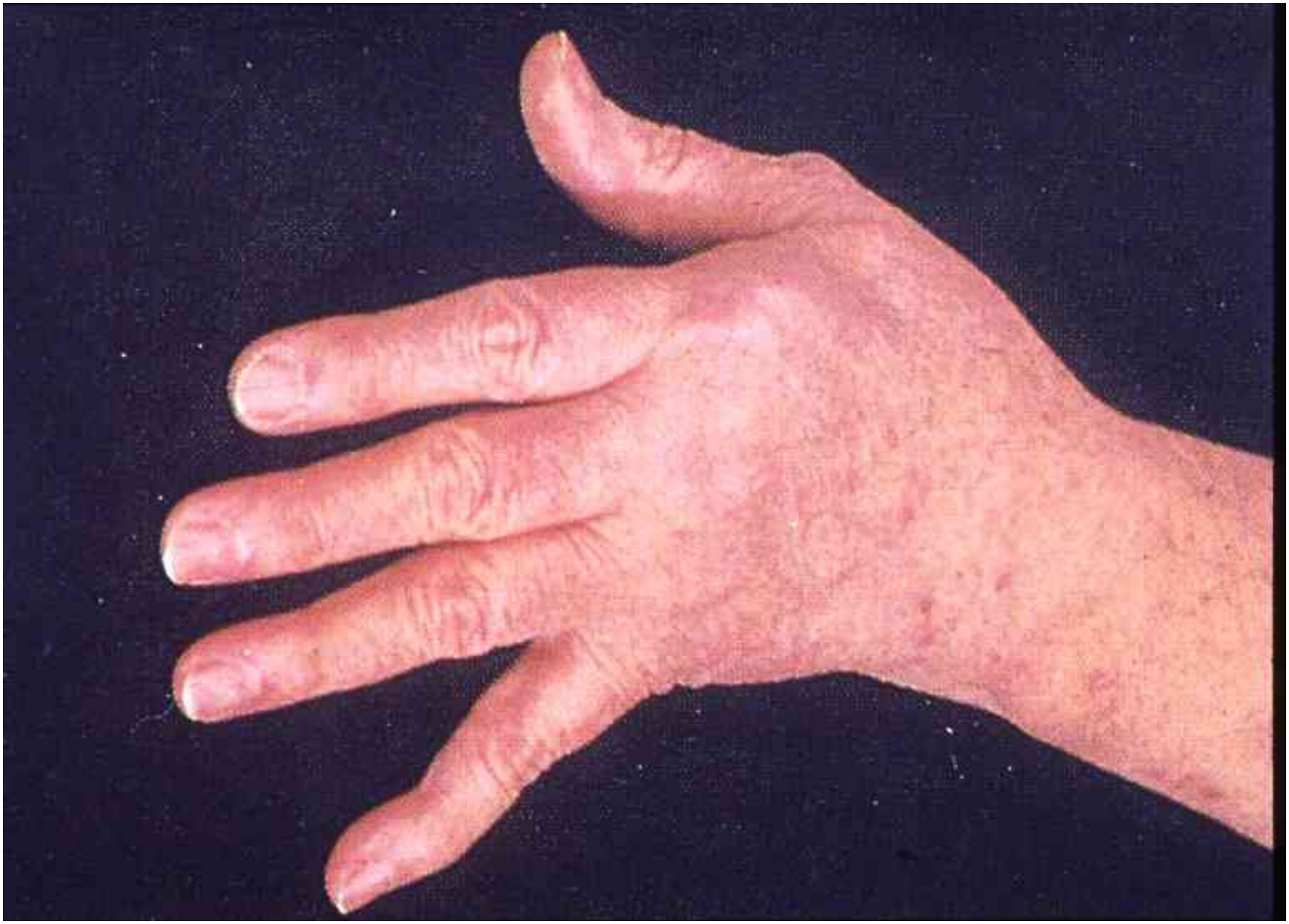


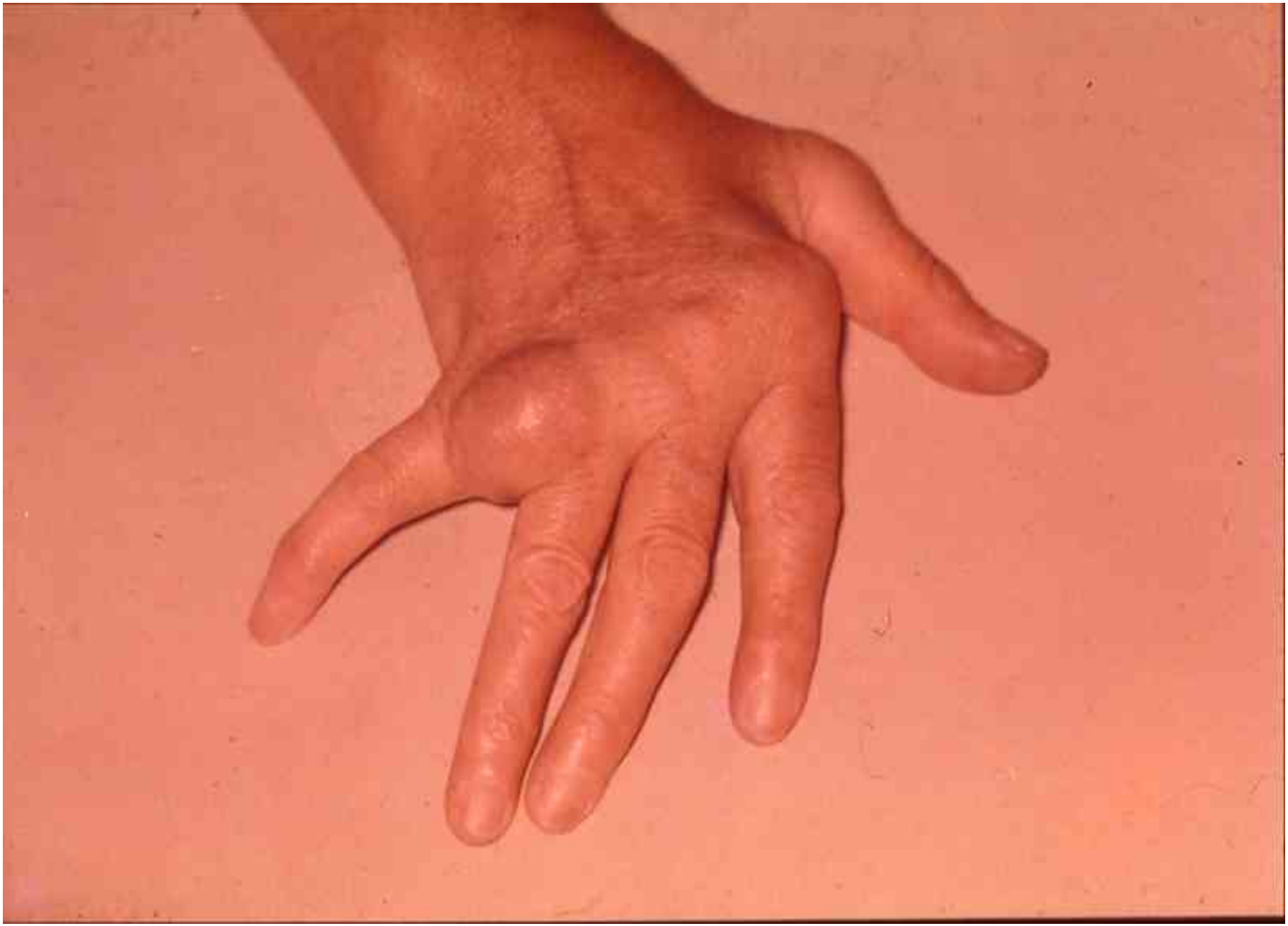
Rheumatoid Arthritis : Articular Features

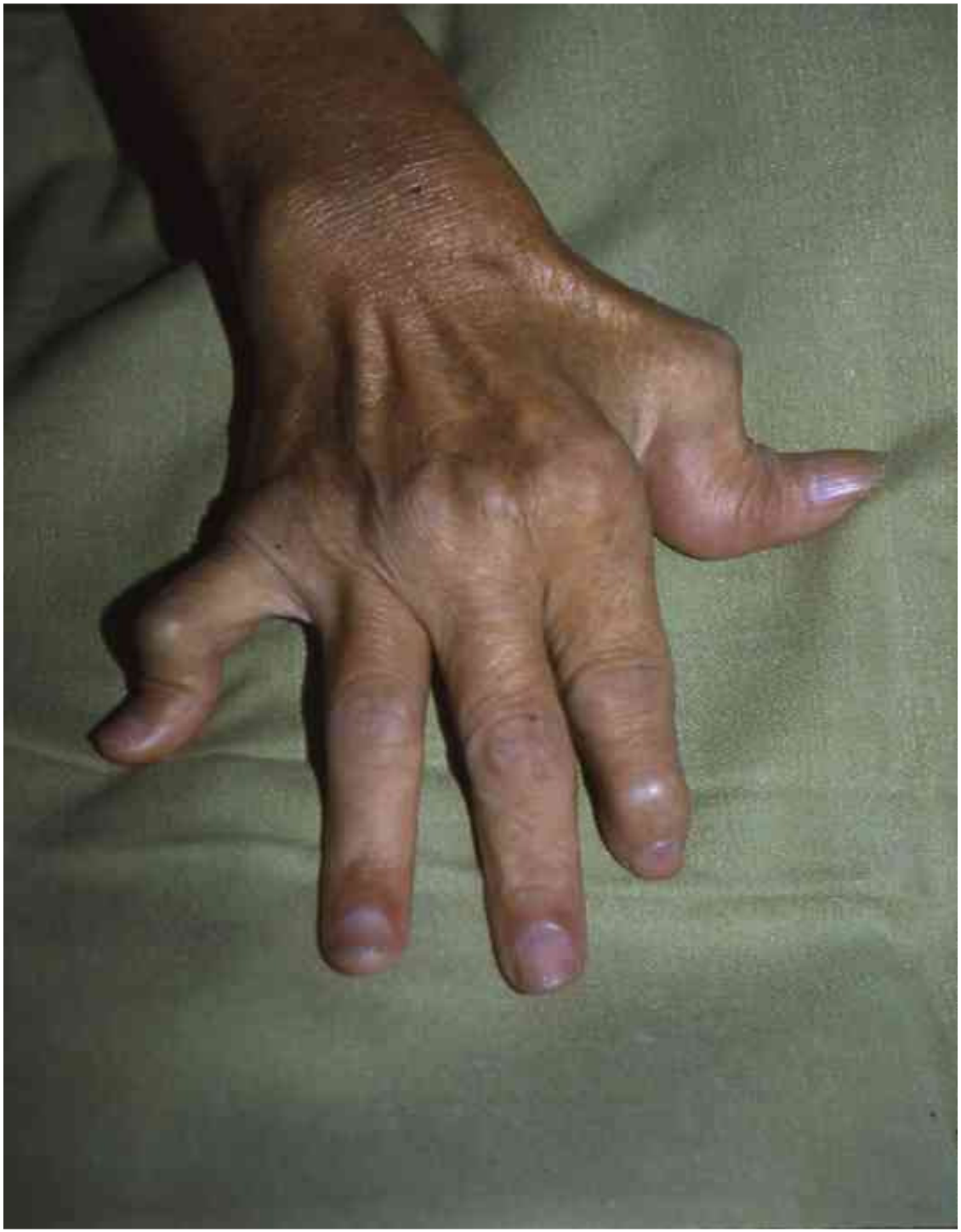
- manifested clinically by pain, stiffness, limitation of movement and signs of inflammation
- insidious symmetrical polyarthritis is the commonest mode of presentation
- asymmetrical onset in not uncommon
- total number of affected joints usually reaches plateau after the first year
- Proximal interphalangeal (PIP) joints and metacarpophalangeal (MCP) joints are most commonly involved
- involvement of tendons and ligament with spontaneous rupture is common
- Typical deformities include : swan neck deformity, button hole deformity and Z deformity of thumb

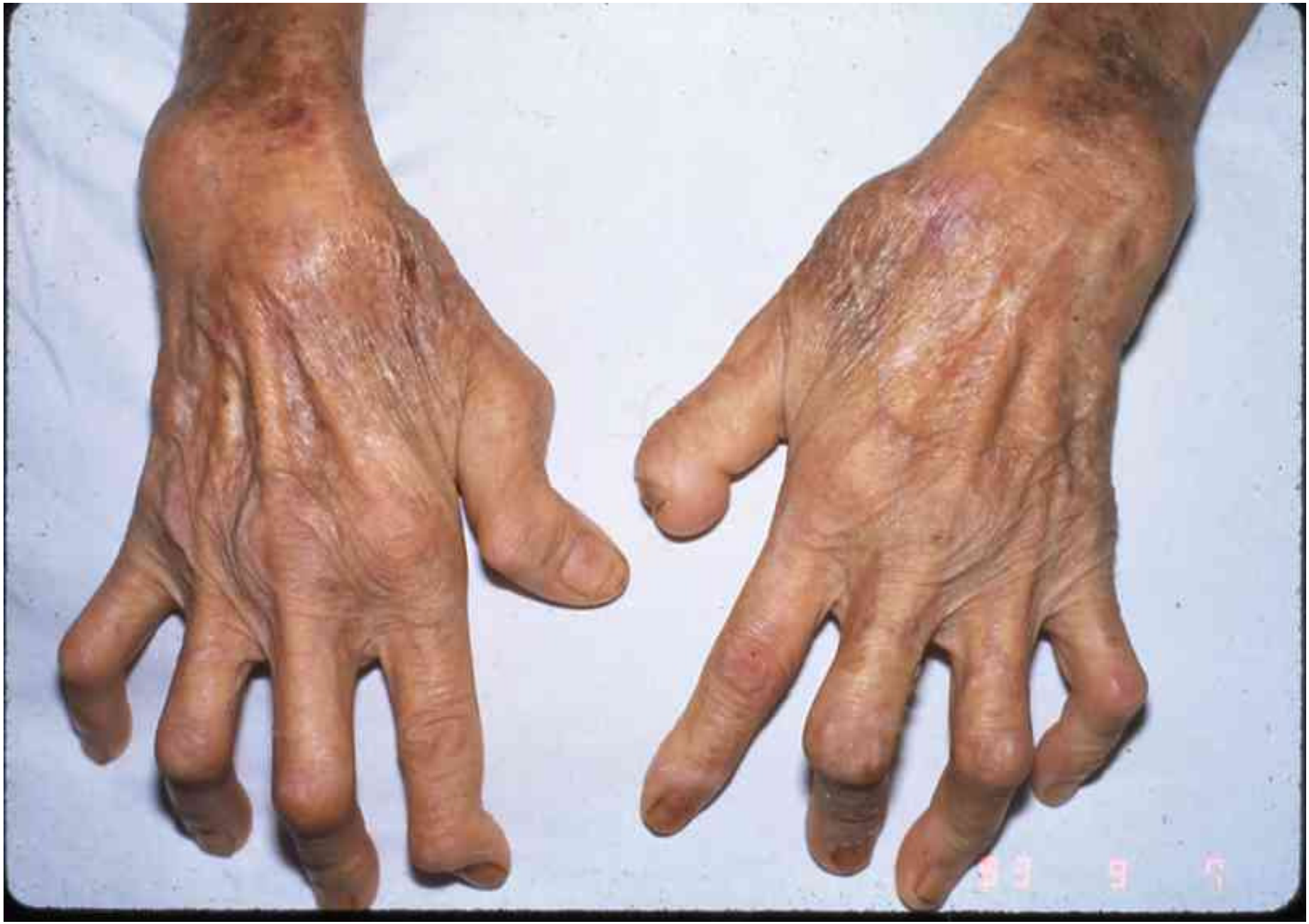


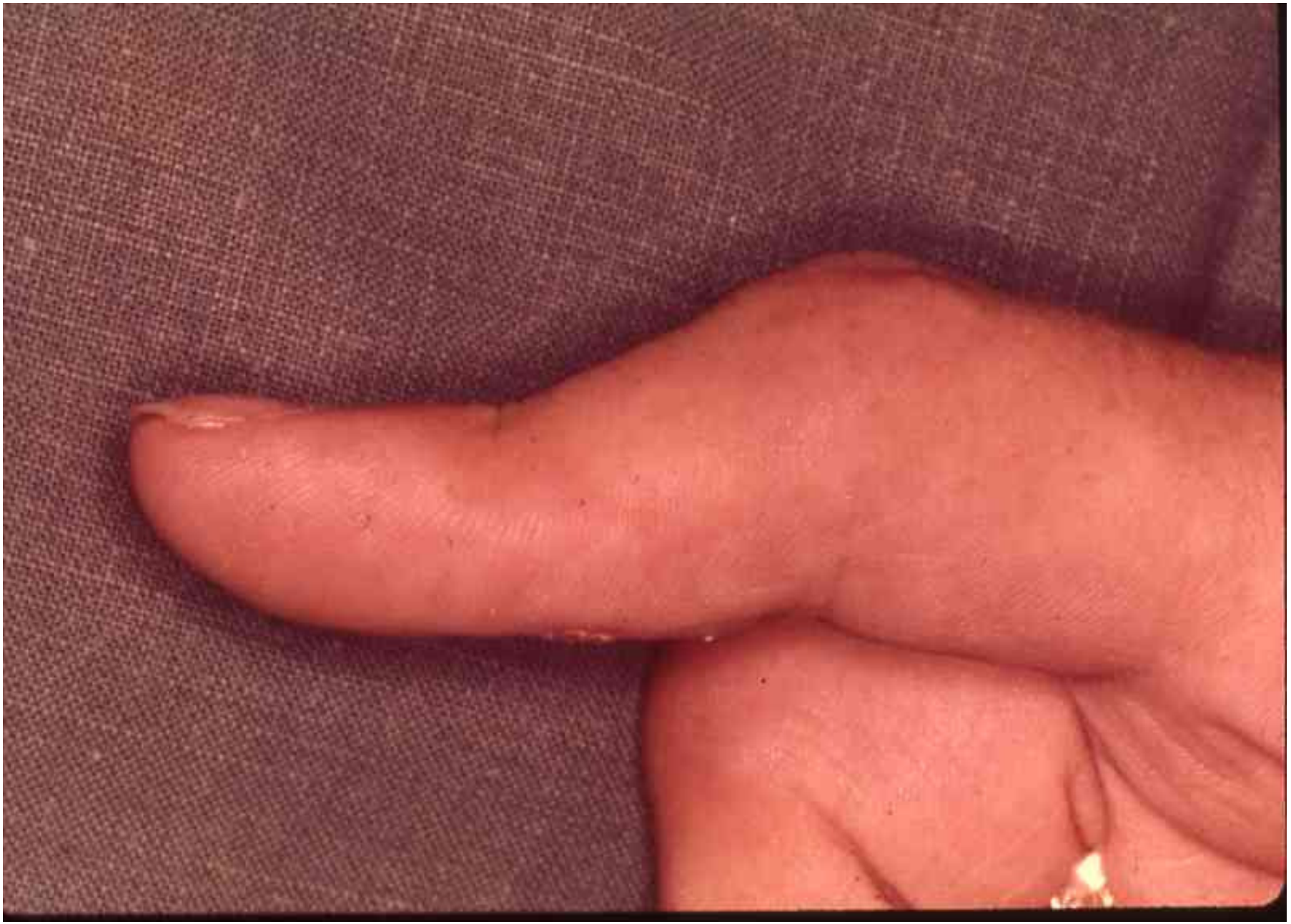


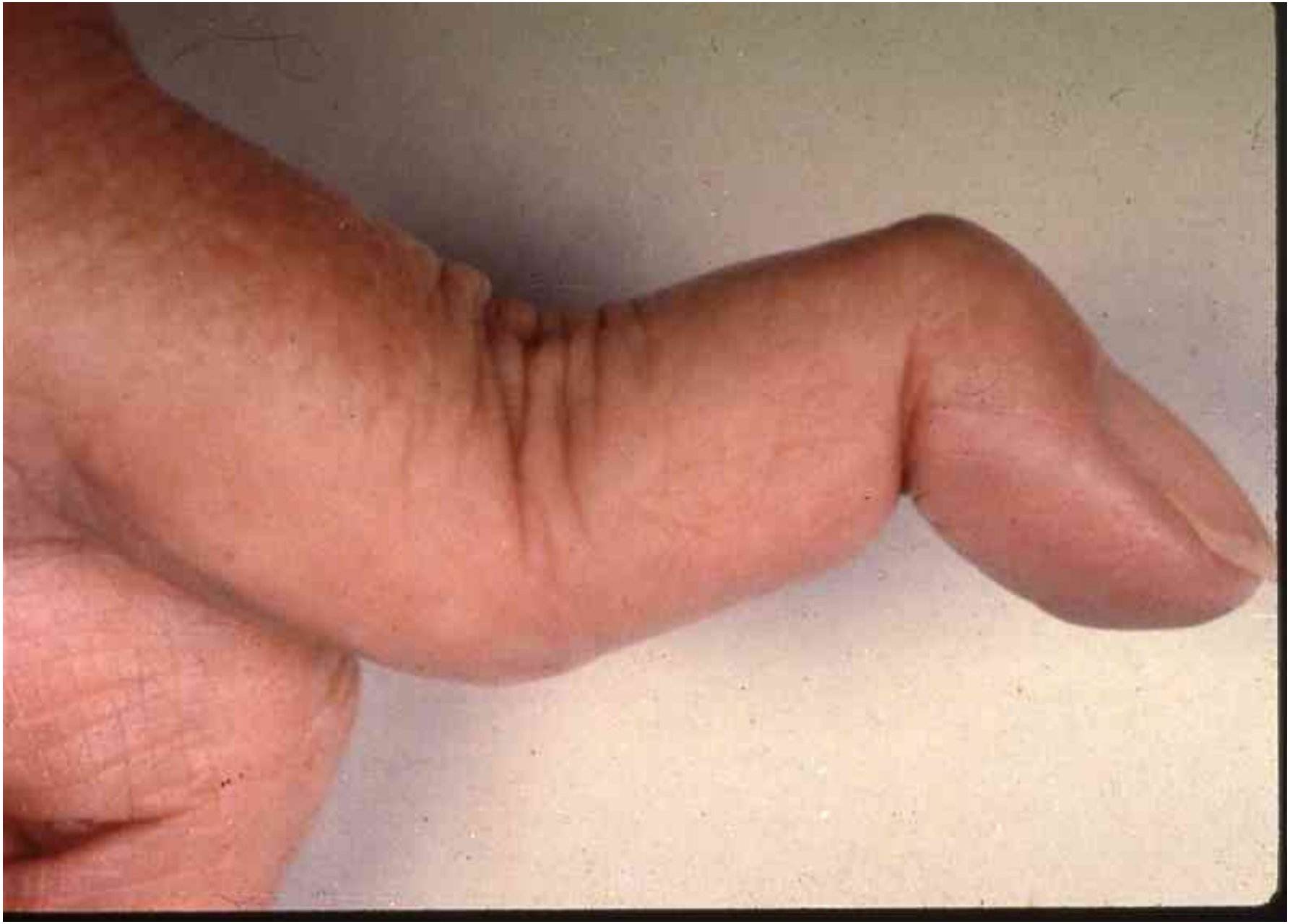






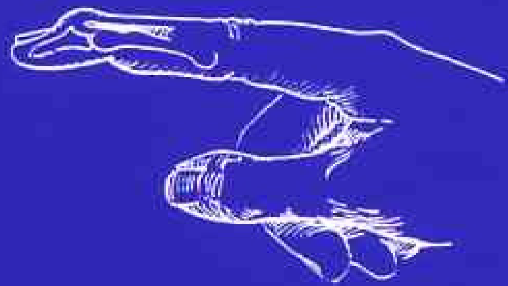






鹅颈畸形

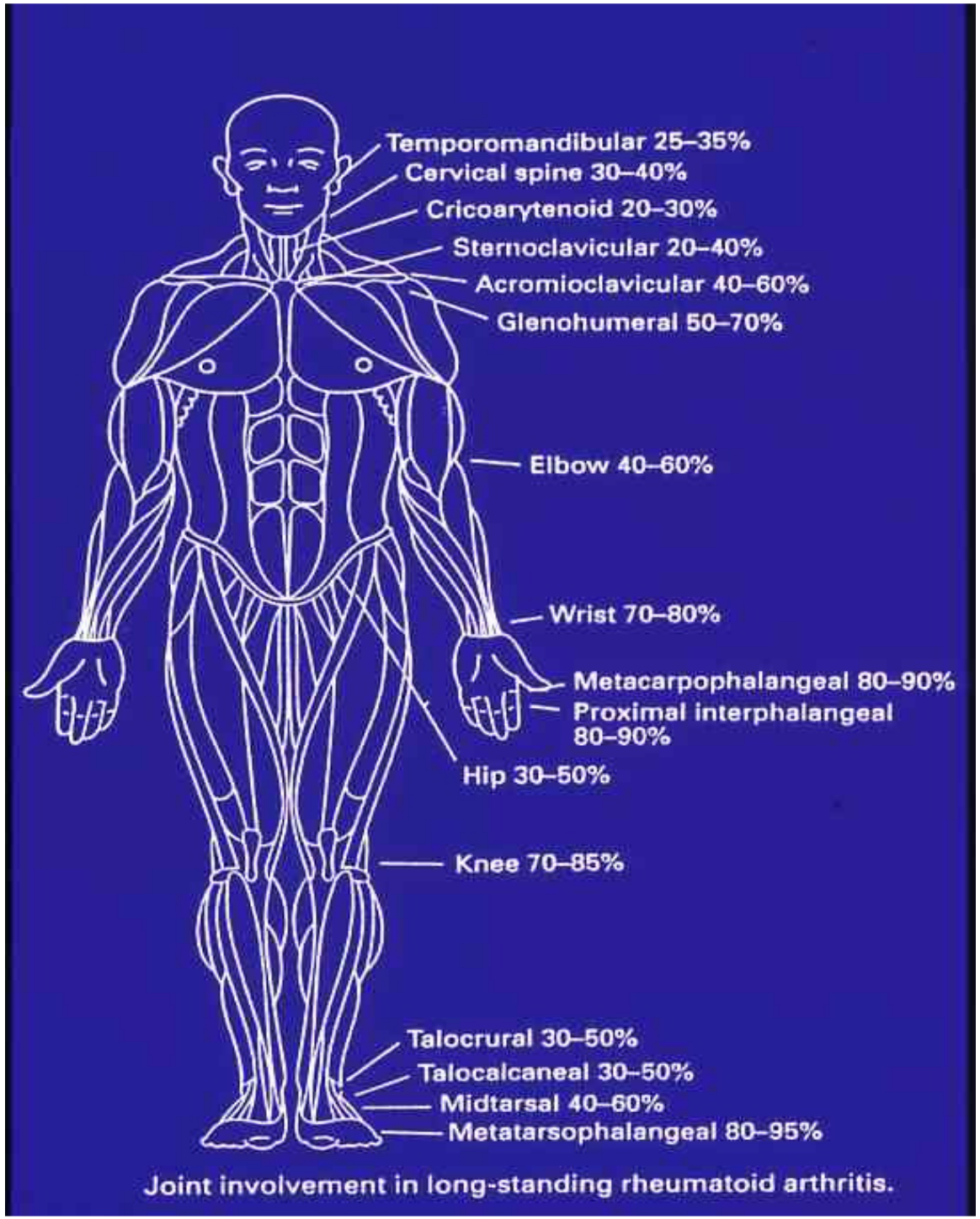
纽扣花畸形



锤状指

Course of Rheumatoid Arthritis

- Intermittent
- Long clinical remissions
- Progressive disease



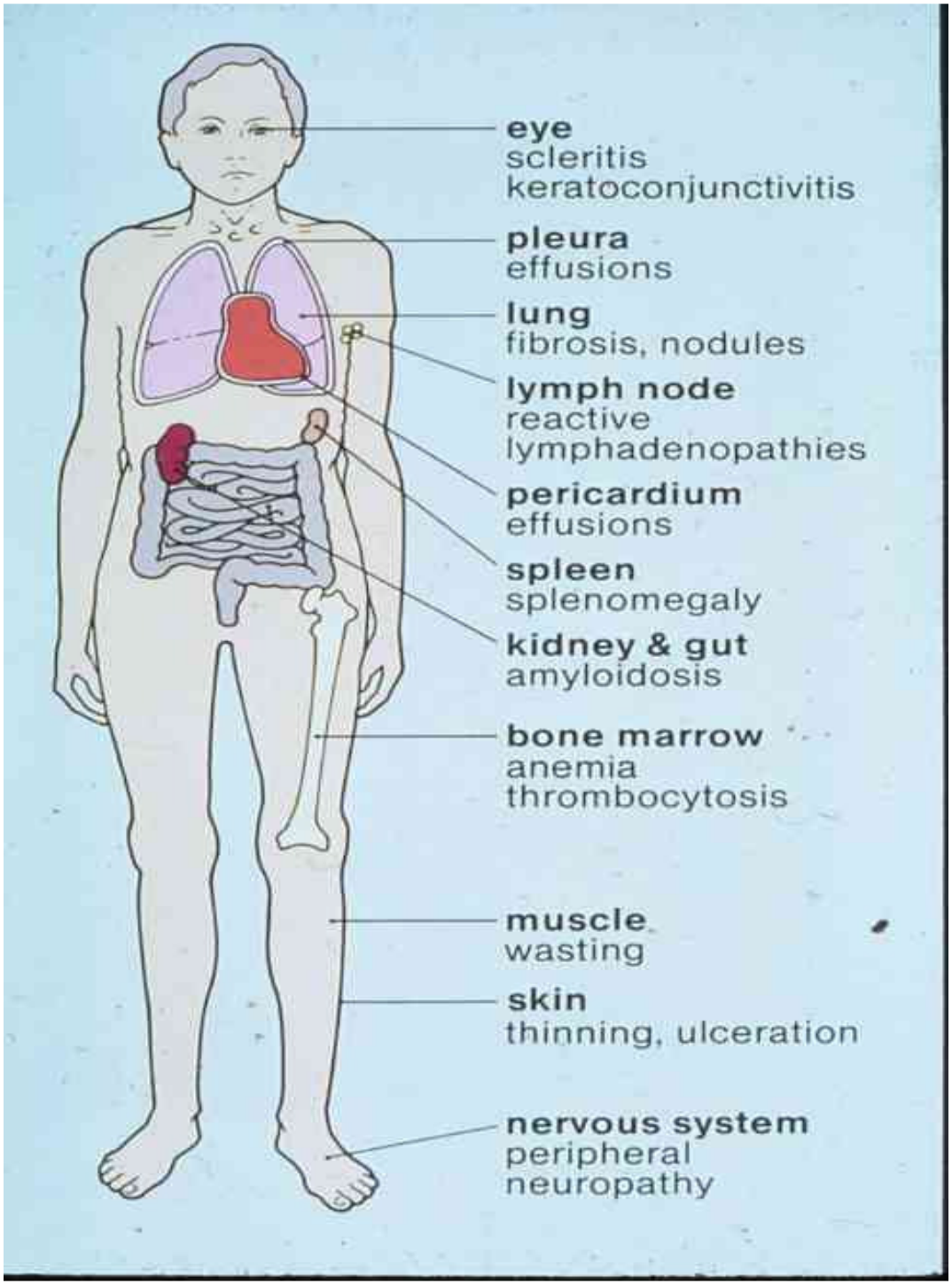
Joint involvement in long-standing rheumatoid arthritis.

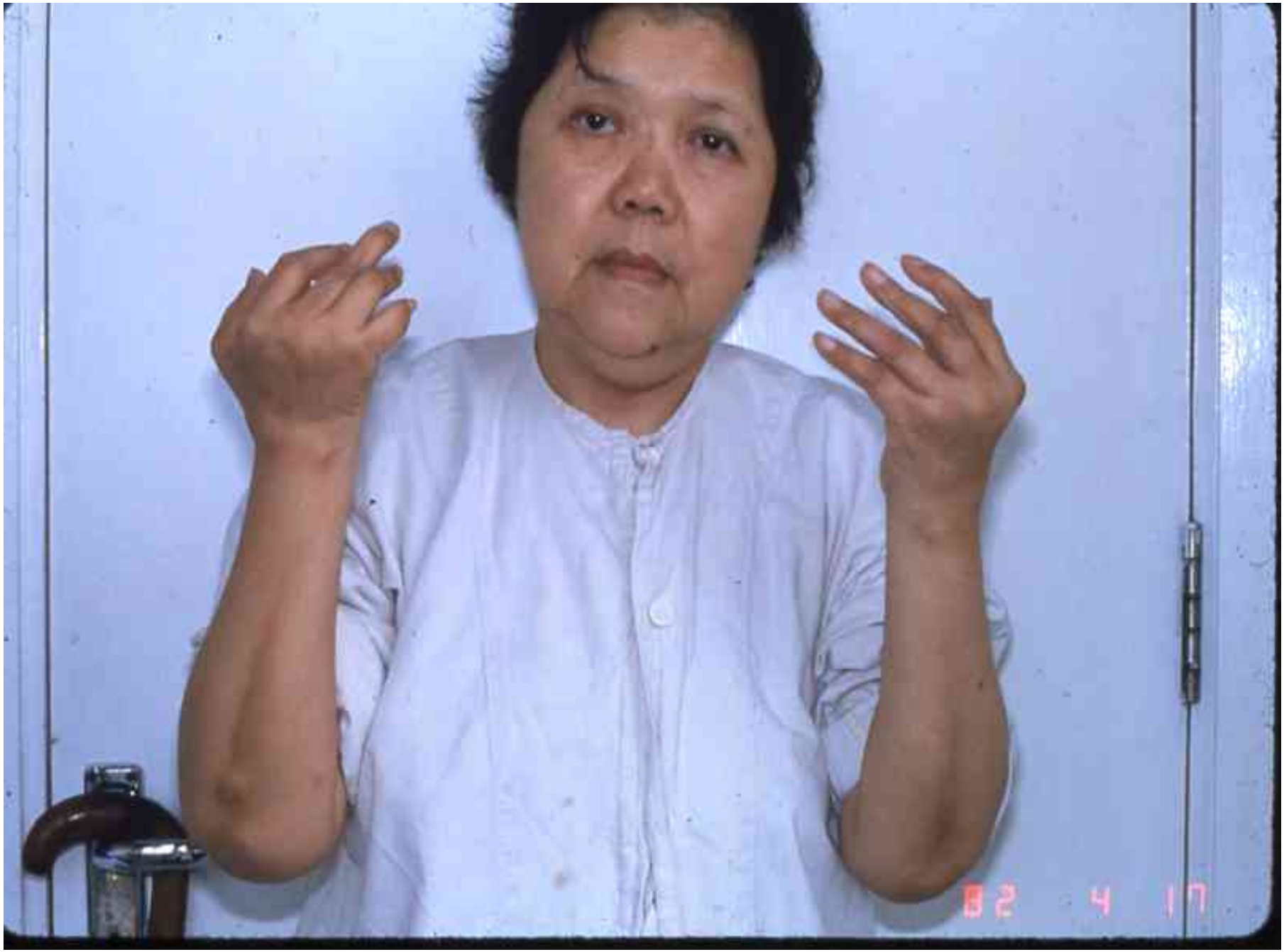
Rheumatoid Arthritis : Extraarticular Features

1. Systemic
   Fever, malaise, myalgia, weight loss
2. Rheumatoid nodules
   Commonest on extensor surfaces and pressure areas
3. Haematological
   Anaemia, thrombocytosis, neutropenia
   splenomegaly, Felly's syndrome
   lymphadenopathy
4. Vasculitis
   Nail fold and finger pulp infarcts
   chronic leg ulcers and gangrene
5. Eye
   Keratoconjunctivitis sicca, Sjogren's syndrome
   scleromalacia perforans
   scleritis and episcleritis

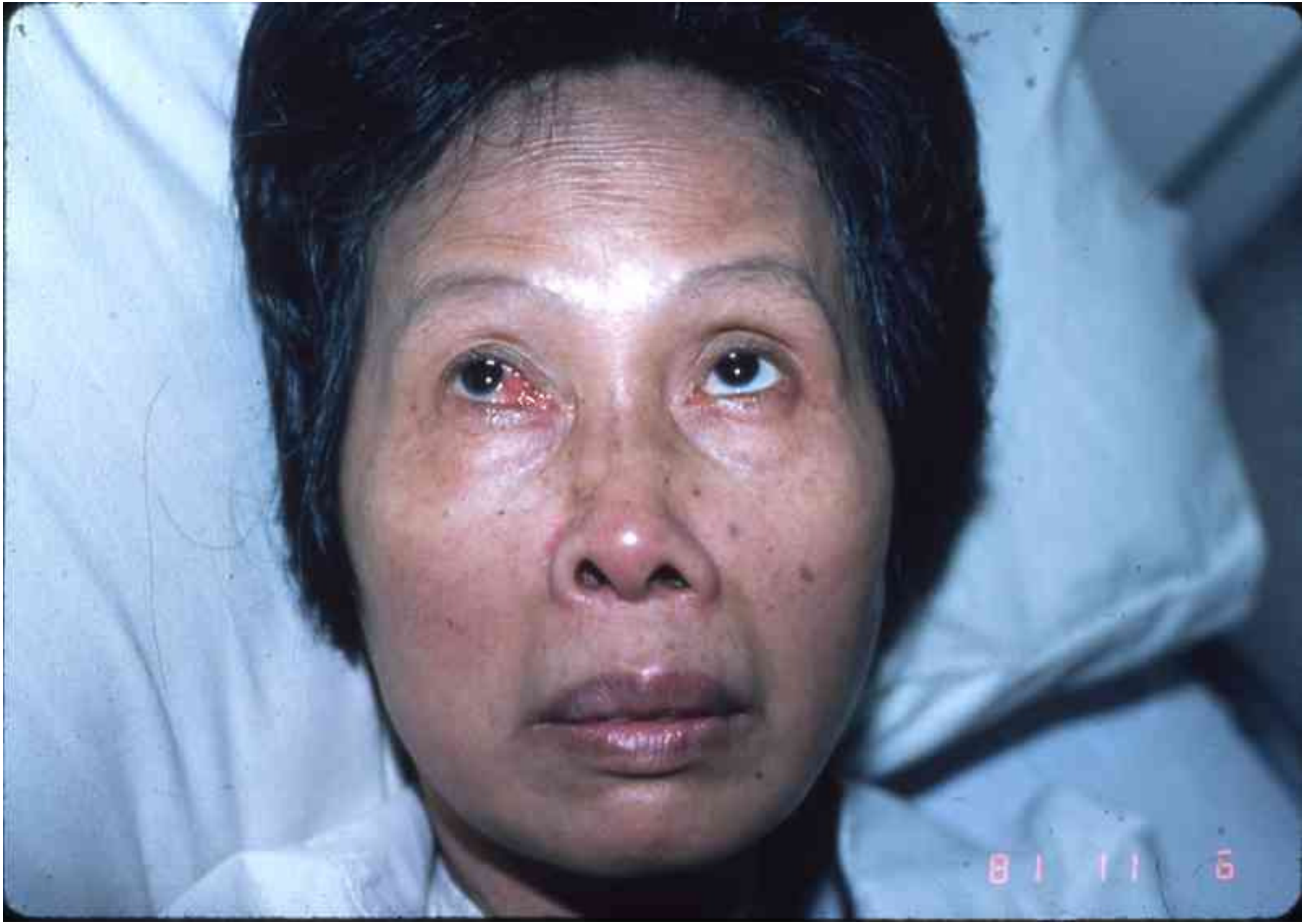
Rheumatoid Arthritis : Extraarticular Features

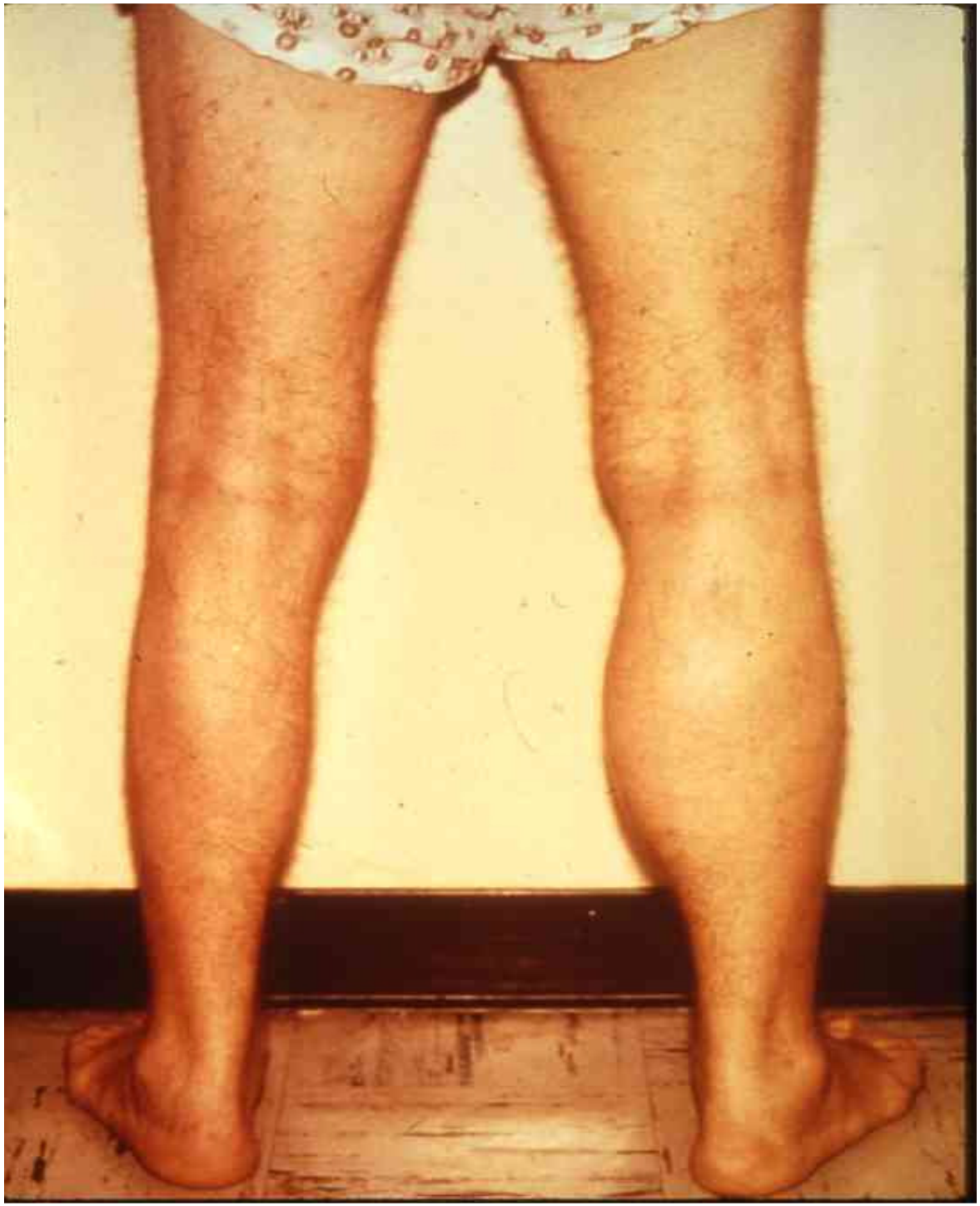
6. Heart
   Pericarditis,
   cardiomyopathy and conduction defects, valvular granuloma
7. Lungs
   Pleurisy $\pm$ pleural effusion
   Interstitial fibrosis
   Pulmonary nodules
   Caplan's syndrome
8. Nervous system
   Entrapment neuropathy
   Peripheral neuropathy
   Mononeuritis multiplex
   Autonomic neuropathy
   Cervical myelopathy


eye
scleritis
keratoconjunctivitis
pleura
effusions
lung
fibrosis, nodules
lymph node
reactive
lymphadenopathies
pericardium
effusions
spleen
splenomegaly
kidney & gut
amyloidosis
bone marrow
anemia
thrombocytosis
muscle
wasting
skin
thinning, ulceration
nervous system
peripheral
neuropathy


82 4 17


15 12 21


81 11 6



Rheumatoid Arthritis Laboratory Features

- Anaemia of chronic inflammatory disease
- Neutropenia in Felty's syndrome
- Thrombocytosis
- Reversed albumin/globulin ratio
- Raised ESR
- Raised CRP

Rheumatoid Arthritis Laboratory Features

- Positive RF in 80%
- Positive ANA in 20%
- Decreased complements with extraarticular features
- Presence of circulating immune complexes
- Typical radiological abnormalities
- Typical synovial fluid abnormalities and synovial histology
- Typical histological nodule changes

Rheumatoid factor

- An autoantibody against IgG
- Positive in 70% of RA patients – not sensitive
- Present in many other rheumatic and non-rheumatic diseases – not specific
- High levels usually indicate poor prognosis in RA patients

Causes of Positive Rheumatoid Factors

1. Rheumatic diseases
2. Normal, healthy individuals
3. Acute viral infections
4. Parasitic infestations
5. Chronic inflammatory diseases
6. Neoplasms
7. Other hyperglobulinaemic states

Anti-CCP

- Anti-cyclic citrullinated peptide
- High specific for RA (>90%)
- predictive of progressive and erosive disease
- Allow early diagnosis (precede clinical presentation of RA by years)
- Not sensitive (~50%)
- sensitivity a little better if screen together with RF

1987 Revised Diagnostic Criteria for the Classification of Rheumatoid Arthritis

- Morning stiffness of at least one hour*
- Arthritis in at least three joints areas^ with swelling or fluid*
- Arthritis of hand joints (at least one area swollen in a wrist, MCP, or PIP joint)*
- Symmetric joint swelling and involvement*
- Subcutaneous nodules
- Radiographic changes typical of RA
- Positive rheumatoid factor

* specified criteria that must be present for at least 6 weeks

^ right or left proximal interprhalangeal (PIP), metacarpophalangeal (MCP), wrist, elbow, knee, ankle and metatarsophalangeal (MTP) point

2010 Rheumatoid Arthritis Classification Criteria

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

Applicable to patients:

1. who have at least 1 joint with definite clinical synovitis (i.e. swelling)
2. whose synovitis not better explained by another disease

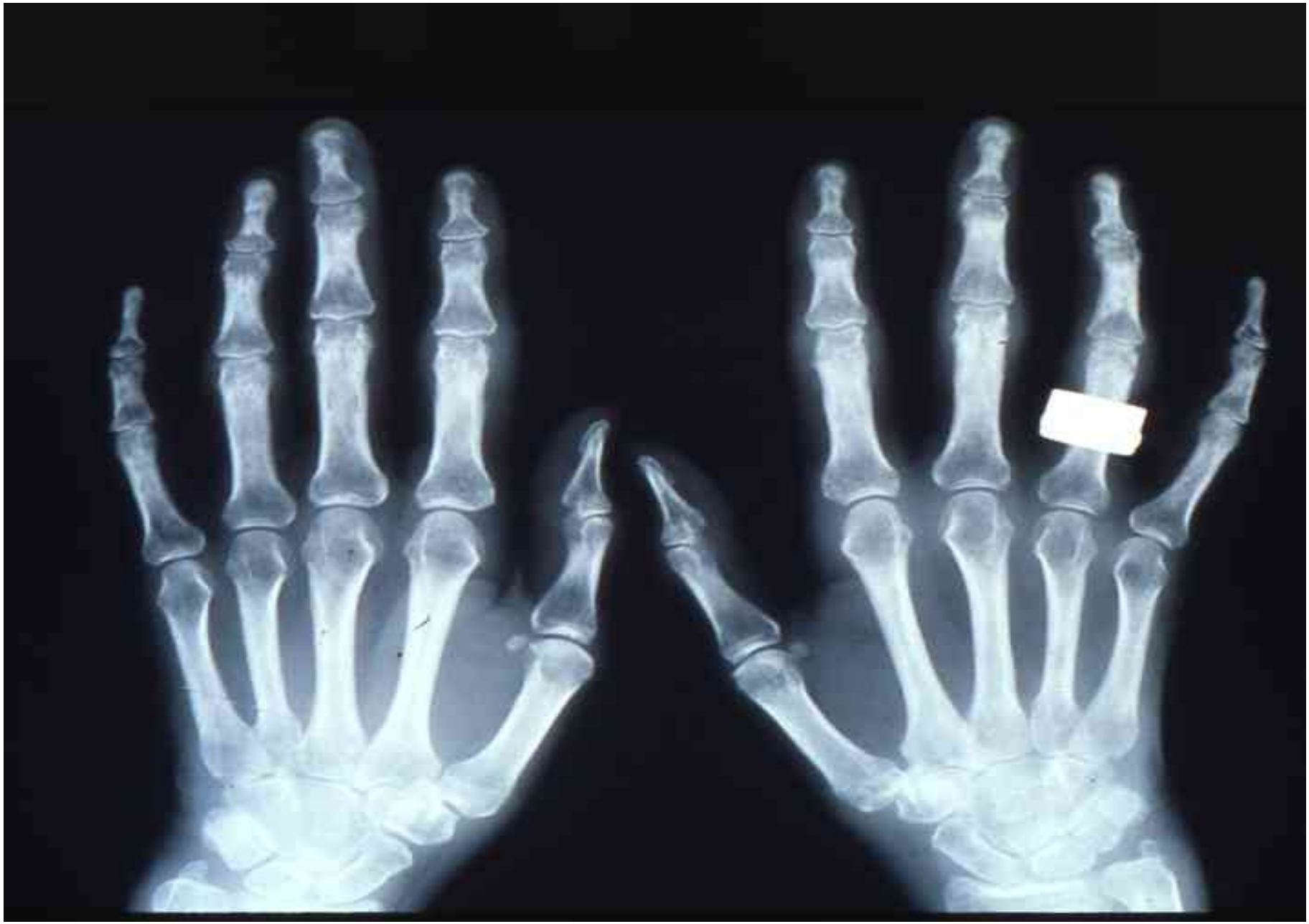
2010 Rheumatoid Arthritis Classification Criteria

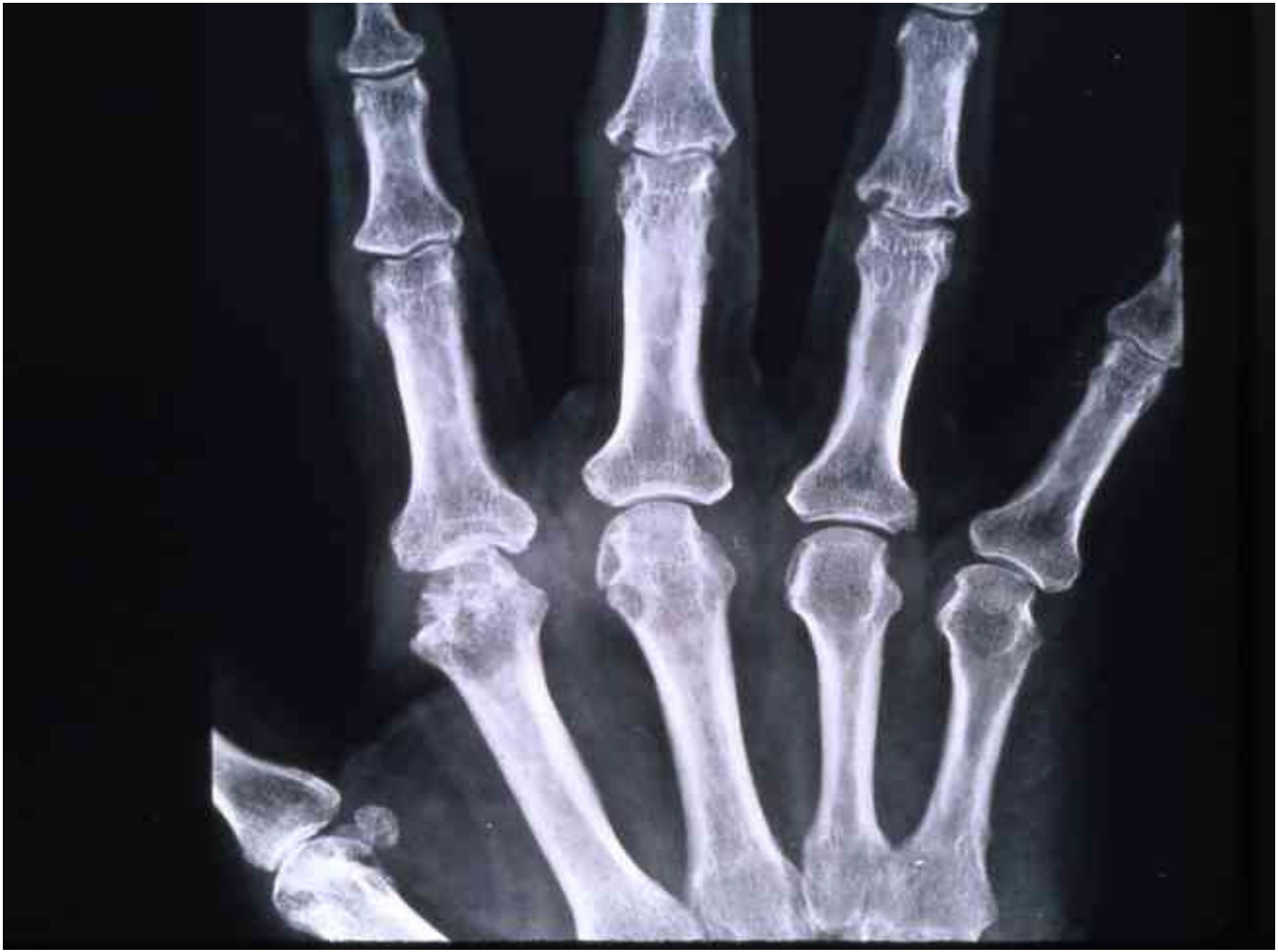
A total score of ≥ 6/10 is needed for classification of a patient as having definite RA

	Score
A. Joint involvement	
• 1 large joint	0
• 2-10 large joints	1
• 1-3 small joints	2
• (with or without involvement of large joints)	
• 4-10 small joints	3
• (with or without involvement of large joints)	
• >10 joints	5
• (at least 1 small joint)	
B. Serology (at least 1 test result is needed for classification)	
•Negative RF and negative ACPA	0
•Low-positive RF or low-positive ACPA	2
•High-positive RF or high-positive ACPA	3

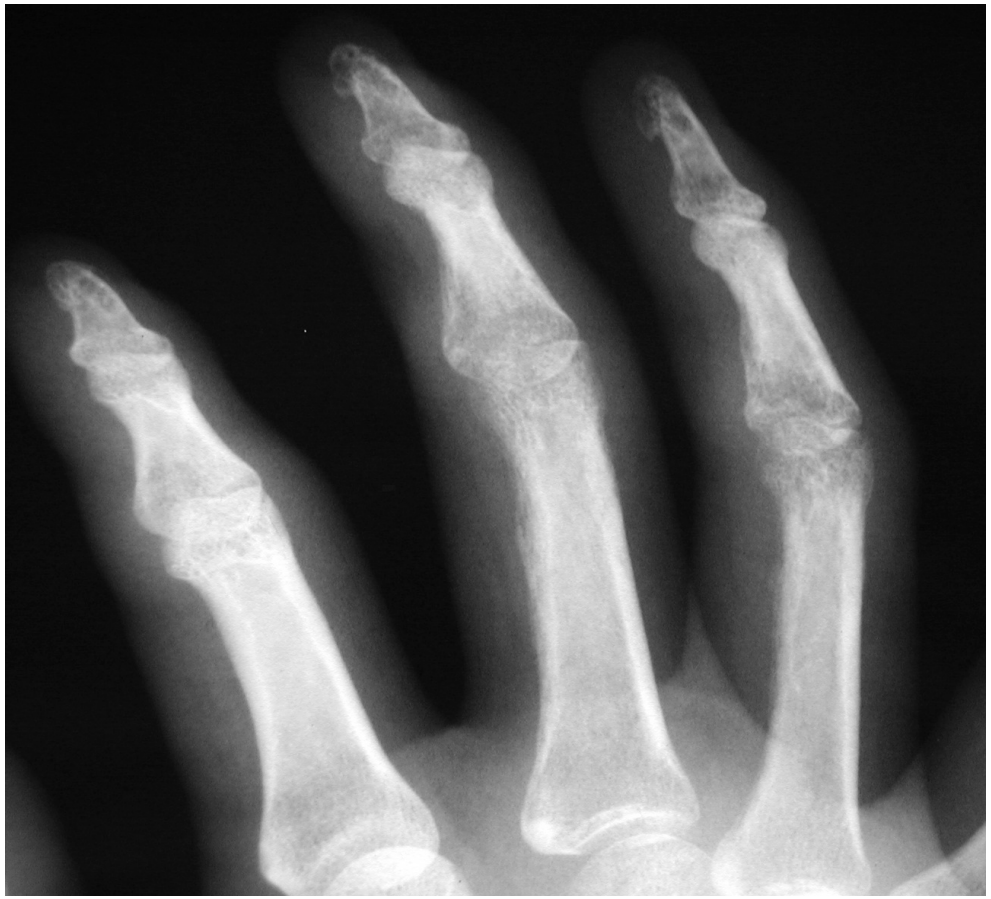
2010 Rheumatoid Arthritis Classification Criteria

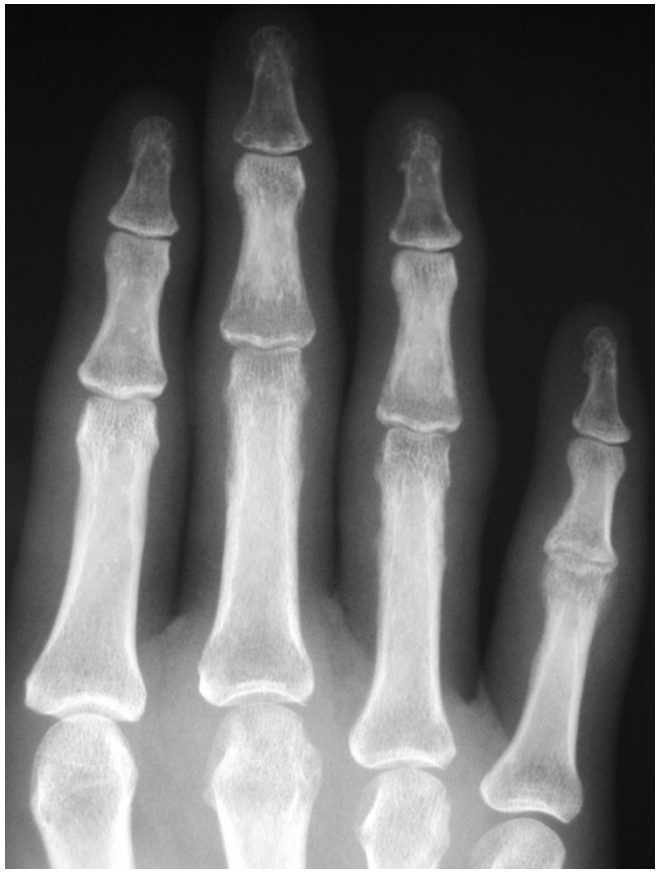
	Score
C. Acue-phase reactants (at least 1 test result is needed for classification) Normal CRP and normal ESR Abnormal CRP or normal ESR	 0 1
D. Duration of symptoms < 6 weeks > 6 weeks	 0 1
“Large joint” refers to shoulders, elbows, hips, knees and ankles *“Small joints” refers to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth meta sophalangeal joints thumb interphalangeal joints, and wrists.*	



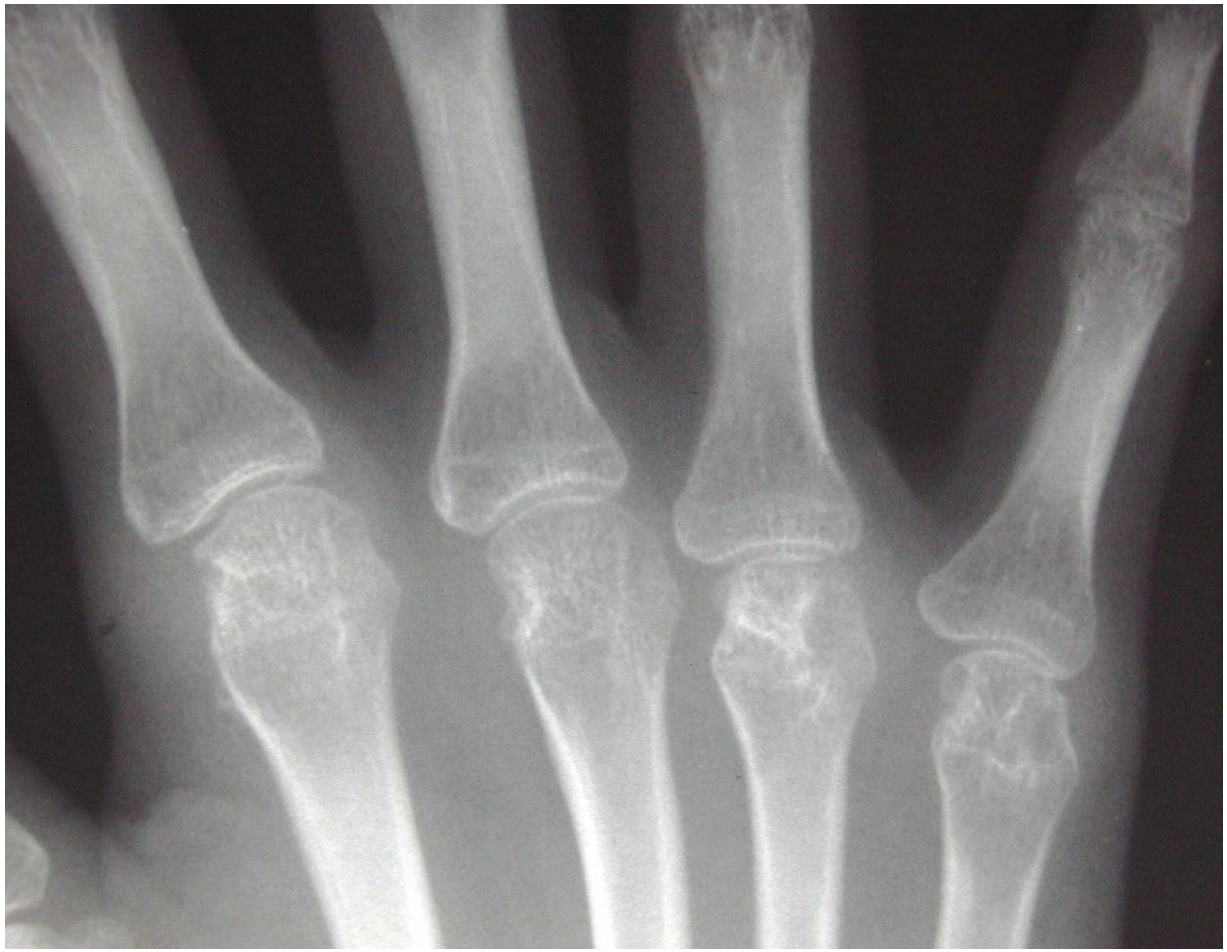


RHEUMATOID ARTHRITIS

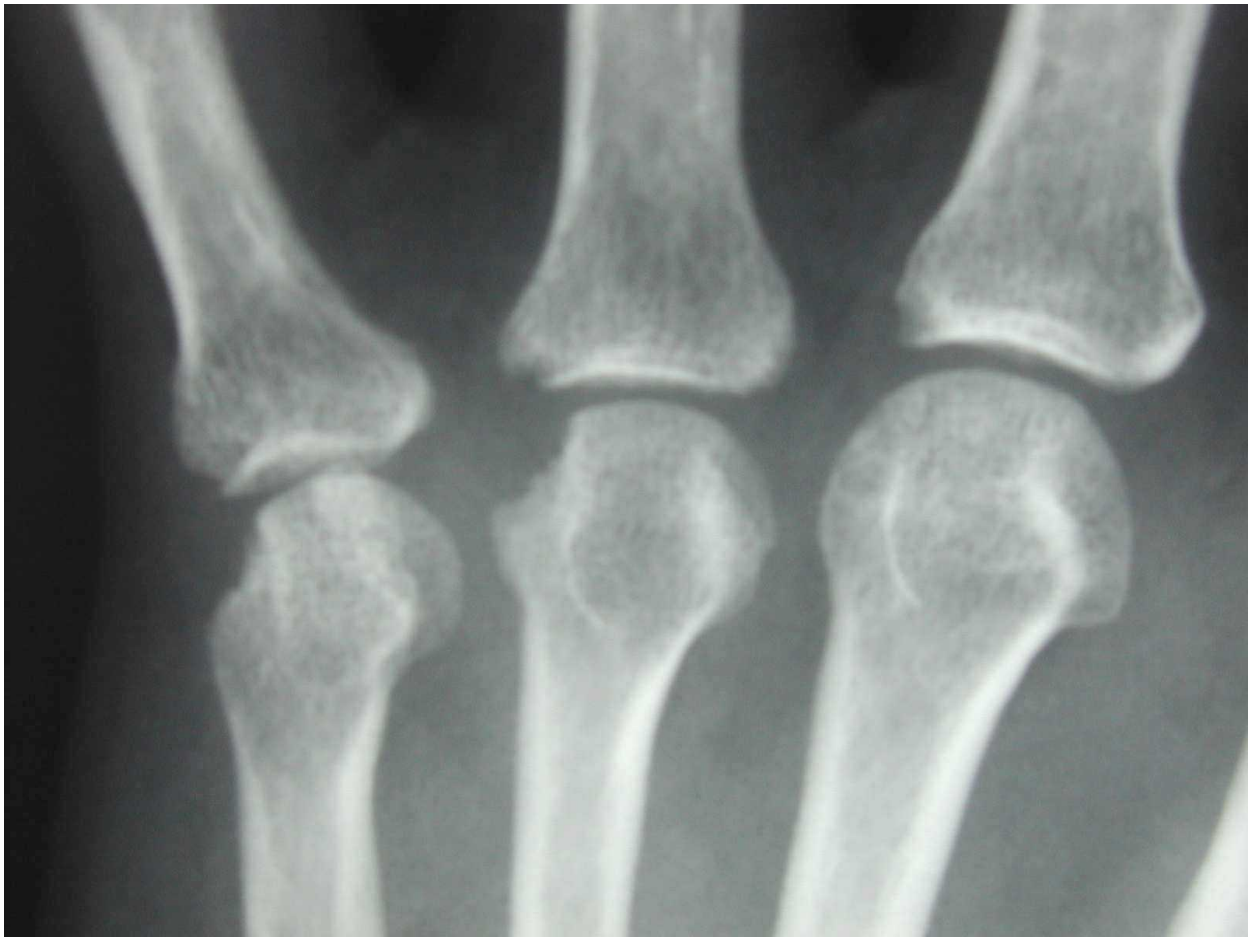




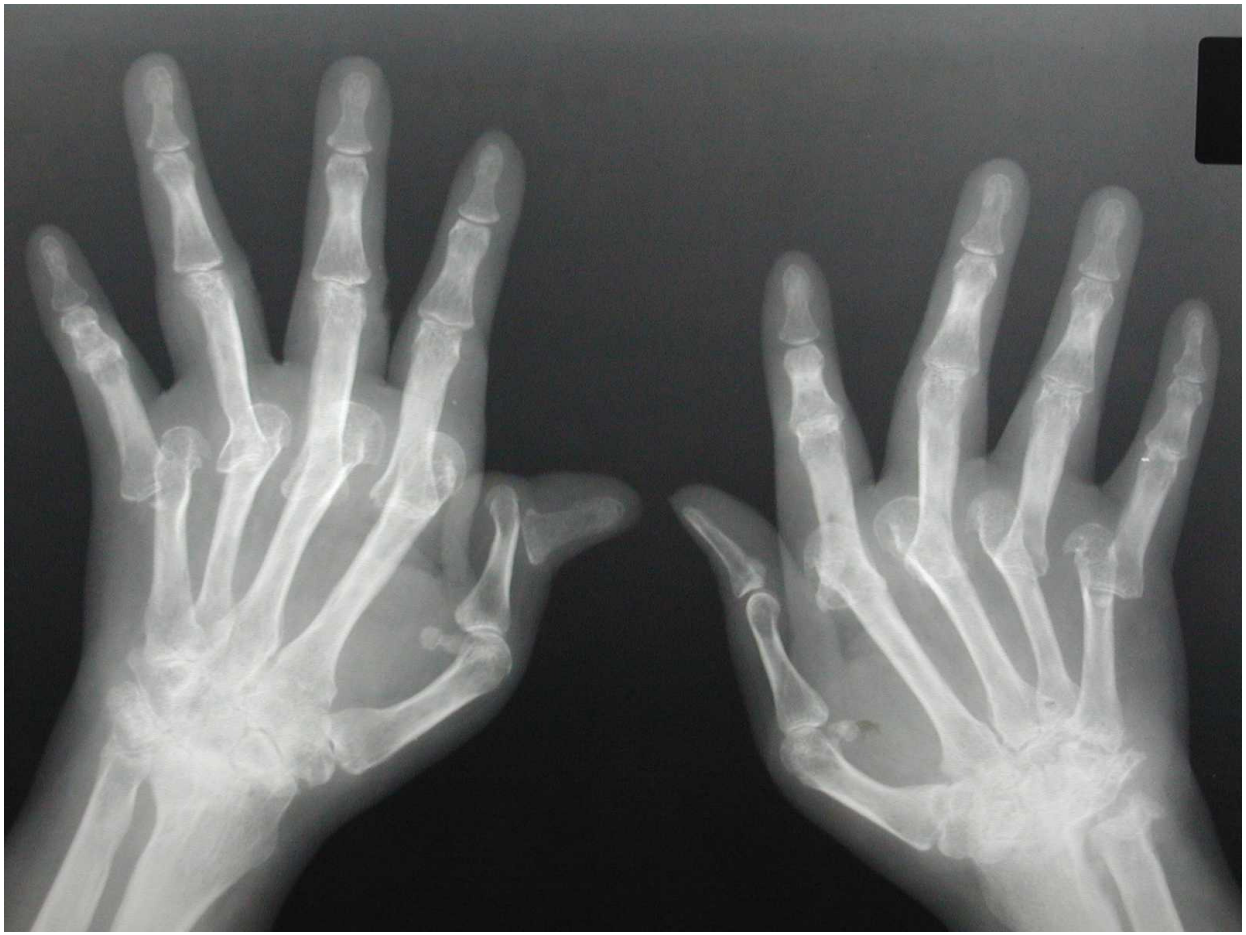
RHEUMATOID ARTHRITIS



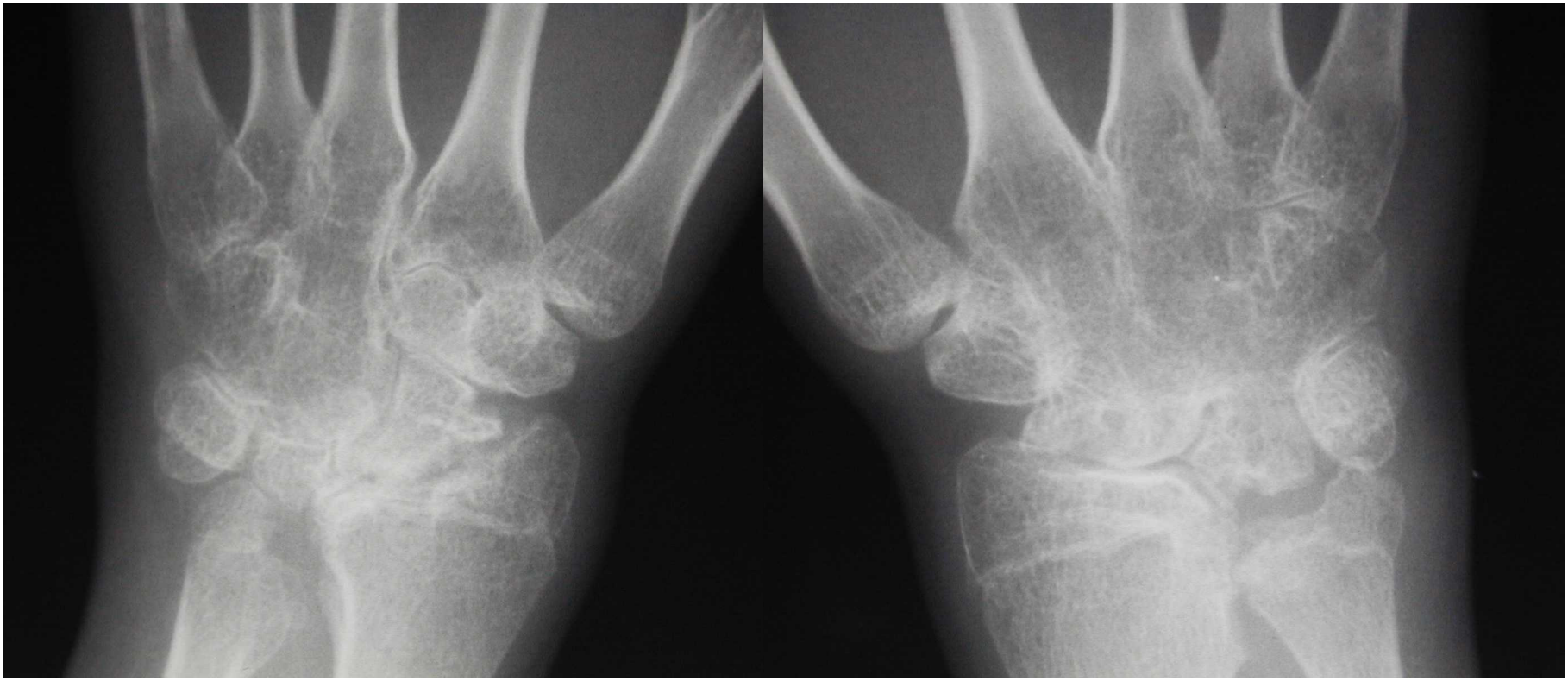
RHEUMATOID ARTHRITIS

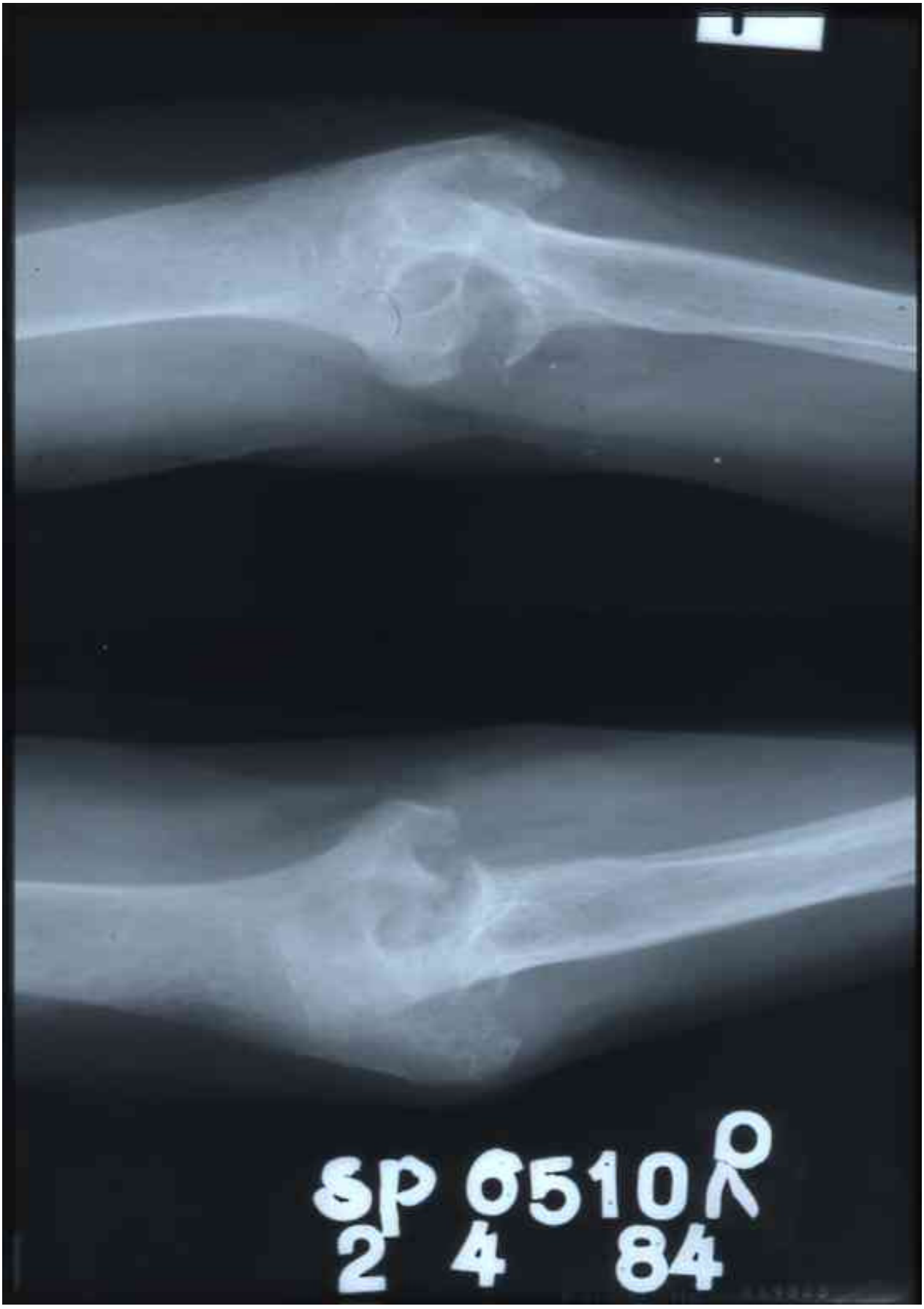


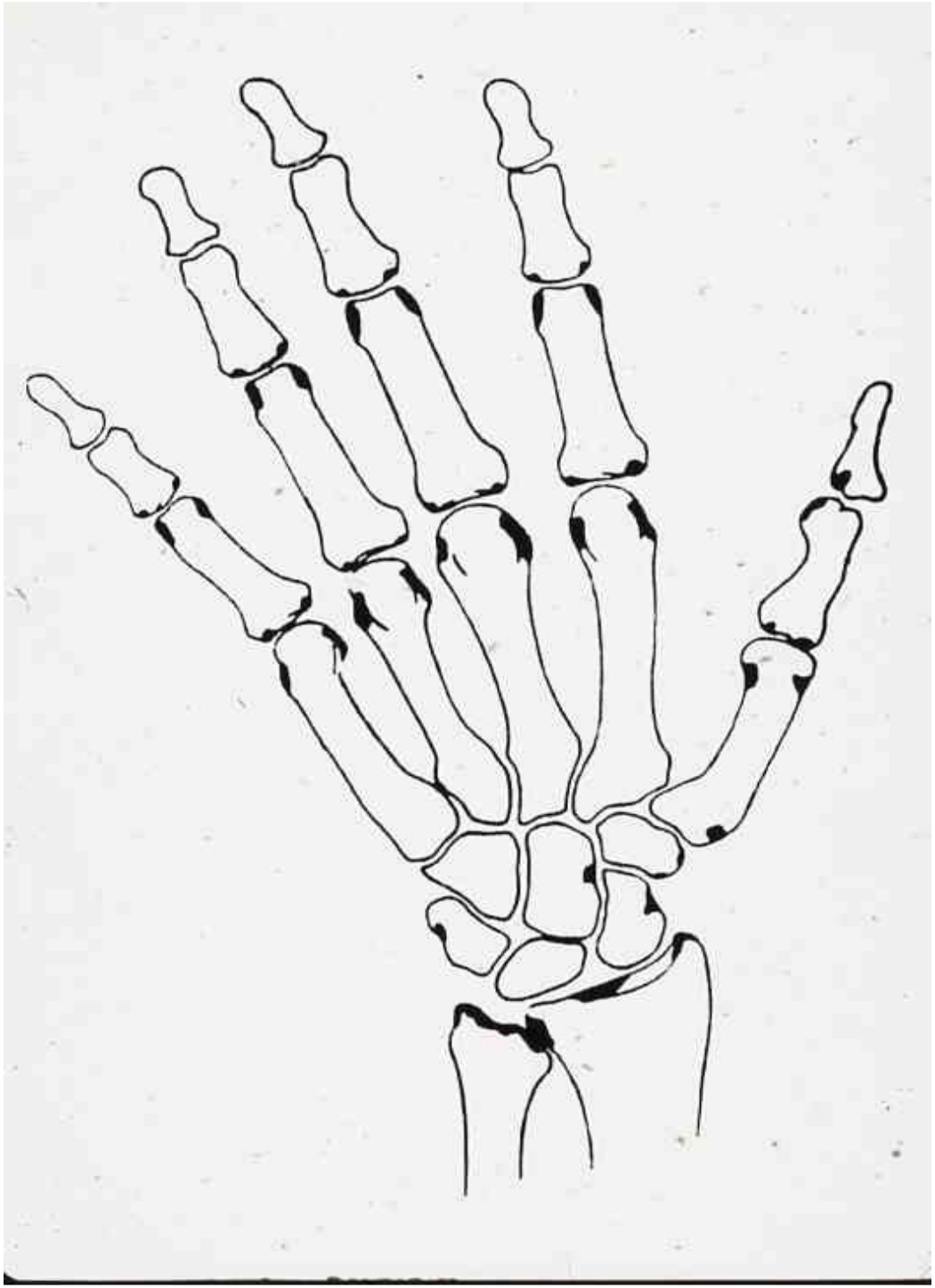
RHEUMATOID ARTHRITIS

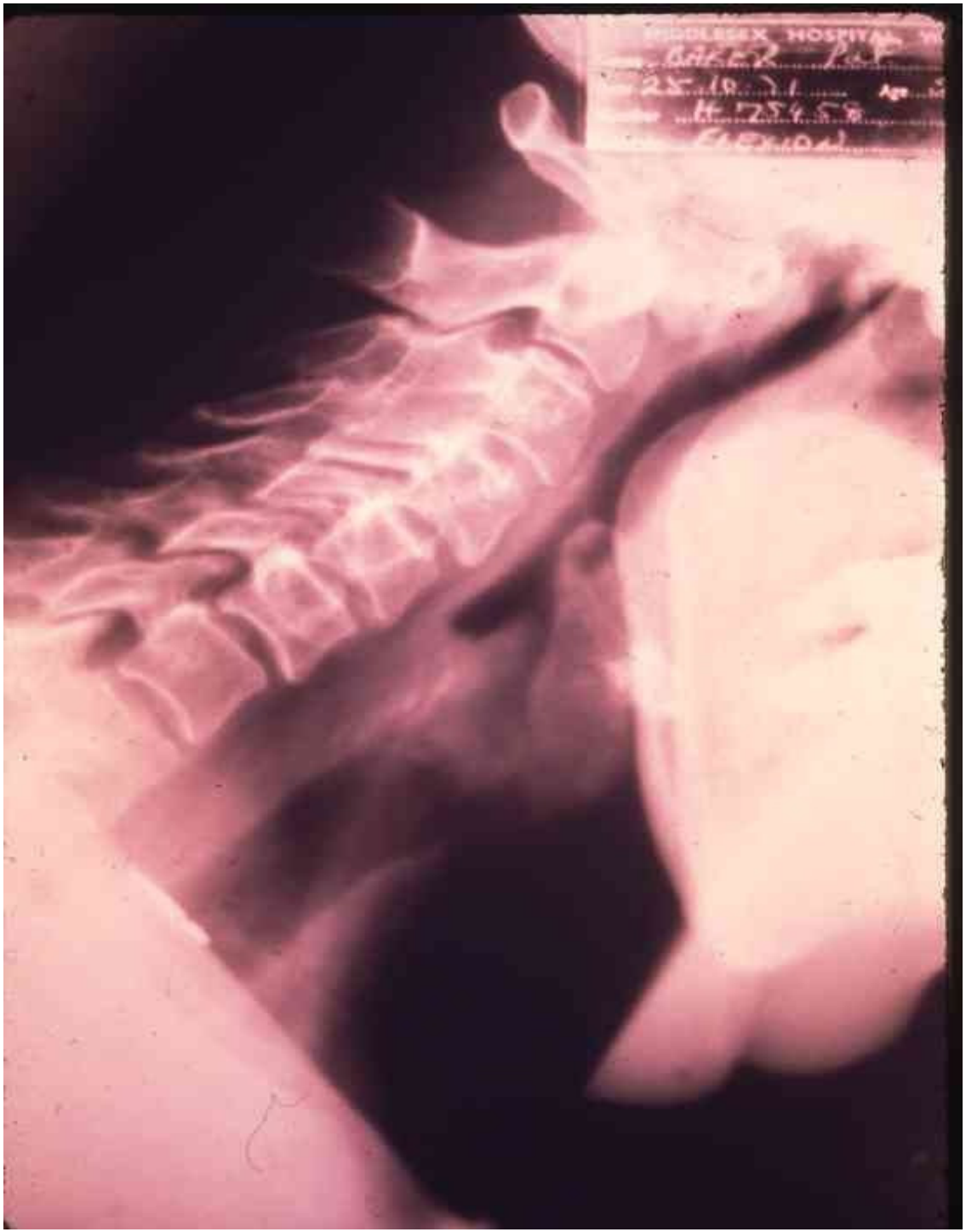


RHEUMATOID ARTHRITIS

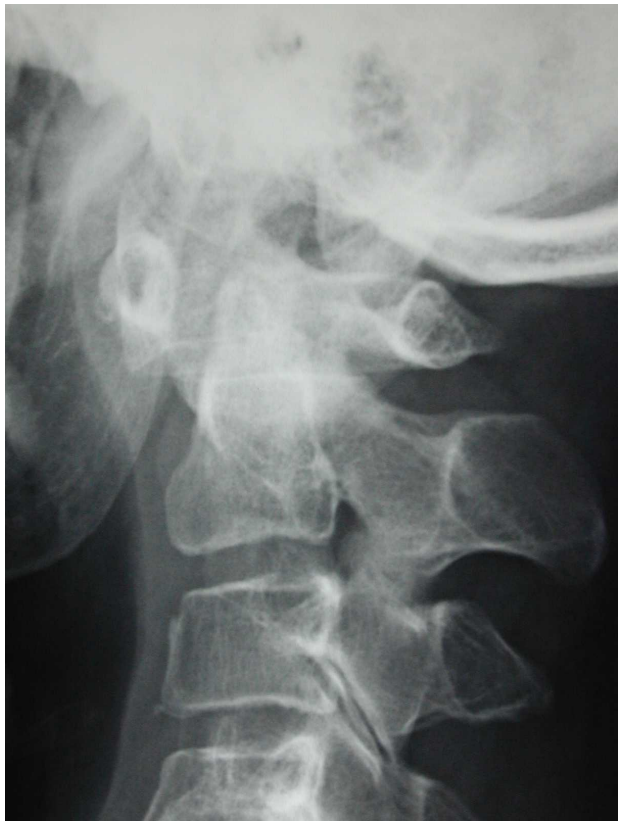


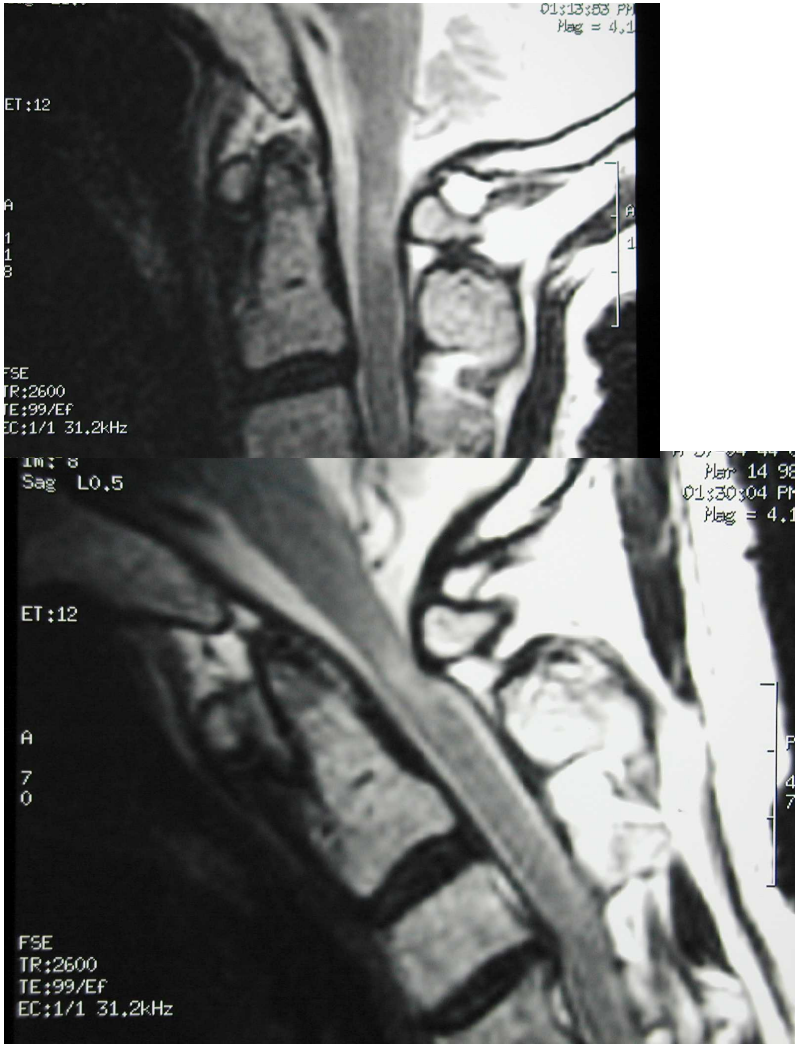

SP 0510 R
2 4 84




MIDDLESEX HOSPITAL
BAKER P.
H. 7254.58

RHEUMATOID ARTHRITIS





Assessment of Disease Activity in Rheumatoid Arthritis

- Articular indices
- Pain scales
- Functional capacity indices
- Biochemical measurements
- Radiologic assessment
- Questionnaires on disability and life-impacts

Rheumatoid Arthritis
Objectives of Management

- Relief of pain
- Reduction or suppression of inflammation
- Minimising side effects
- Preservation of muscle and joint function
- Return to a desirable and productive life
- Treatment of extraarticular manifestations and complications

Rheumatoid Arthritis
Logistics of Management

Supportive Therapy

- Education of patients and family : adaptation and counselling
- Rest
- Physiotherapy : pain relief, rest and relaxation, exercise programme
- Occupational therapy : advice on correct/appropriate use of joints in daily life, aids to daily living and splints
- Rehabilitation service

Rheumatoid Arthritis
Logistics of Management

Drug Therapy

- Drugs form only one part of the management
- Effective drug prescribing is dependent on accurate assessment before and after commencing therapy
- Use less toxic drug whenever possible

Pharmacotherapy of RA

- Pain relief :

  Simple analgesics

  Nonsteroidal antiinflammatory drugs (NSAIDs)

  COX-II inhibitors
- Conventional disease modifying antirheumatic drugs (DMARDs)
- Biologic agents
- Corticosteroids

Nonsteroidal anti-inflammatory drugs

- Main tool for relieving symptoms and signs of inflammatory arthritis
- Less effective in osteoarthritis and non-articular rheumatic complaints
- No disease remitting effect
- Potentially toxic
- No obvious drug of choice
- Variation in response is greater between patients than between drugs

Ways to Reduce NSAID Induced Gastropathy

↑ prescription threshold
↑ caution with patients at risk
use of less toxic NSAIDs
concommitant antacid administration
to take with meals
H2 antagonist
Prostaglandin analogues
Mucosal protecting agents
proton pump inhibitors

The COX-Concept

- All NSAIDs inhibit cyclooxygenase (COX), the enzyme which converts arachidonic acid to prostaglandins
- Inhibition of COX produces both the therapeutic and characteristic side effects of NSAIDs
- Recently, it is discovered that COX exists in two forms : COX-1 and COX-2

The COX-Concept

- COX-1 is responsible for the production of prostaglandins with general “housekeeping” functions e.g. gastroprotective role and maintenance of renal perfusion
- COX-2 is responsible for the production of prostaglandins at sites of tissue inflammation
- If COX-2 enzyme is selectively inhibited, it is possible to minimize the side effects while maintaining the efficacy of NSAIDs

Available COX-2 inhibitors

- Celecoxib
- Rofecoxib (withdrawn Sept 2004)
- Etoricoxib

Conventional disease modifying anti-rheumatic drugs

- Hydroxychloroquine
- Methotrexate
- Salalzopyrine
- Leflunomide
- Parenteral gold
- Penicillamine
- Oral gold
- Azathioprine
- Cyclosporine A

Drug	Approximate time to benefit	Usual maintenance dose
Sulfasalazine	1-2 months	2gm twice daily
Methrotrexate	1-2 months	7.5-15mg/week
Axathioprine	2-3 months	50-150mg/day
Hydroxchloroquine	2-4 months	200-300mg nocte
D-penicillamine	3-6 months	25-0-750mg daily
Injectable gold	3-6 months	20-40mg IM every 2-4 wks
Oral gold	4-6 months	3mg twice daily

Rheumatoid Arthritis
Disease Modifying Anti-rheumatic Drugs

- No immediate anti-inflammatory effect
- Modes of action largely unknown
- Needs at least two months to act
- Efficacy cannot be predicted for the individual patient
- Needs to be given on a long term basis
- Potentially highly toxic
- Majority of patients cannot be maintained on the same DMARD because of either side effects or lack of efficacy

Rheumatoid Arthritis
Indications for Disease Modifying Drugs

- Persistence of active synovitis
- Deteriorating functional capacity due to active synovitis
- Increasing number of affected joints
- Development or increase in number of radiological erosions
- Development of extra-articular features

Biologic agents in treatment of RA

- Tumor Necrosis Factor (TNF) α blockers
  - Etanercept (Enbrel)
  - Infliximab (Remicade)
  - Adalimumab (Humira)
  - Golimumab
  - Certolizumab pegol
- Interleukin-1 receptor antagonist
  - Anakinra
- Anti-CD 20 antibody
  - Rituximab (MabThera)
- IL-6-receptor blockade
  - Tocilizumab (Actemra)
- T-cell co-stimulation blocker
  - Abatacept (Orencia)

TNF-blocking agents in RA

- Results of randomized placebo controlled trials have shown that both agents significantly decrease the progression of cartilage destruction, especially when combined with methotrexate
- Their side effects profiles appear to be acceptable, although rare cases of lupus like diseases and of severe infections have been reported
- Their long-term safety and continuing - efficacy remain to be determined

Timing is critical

The use of DMARDs should not be delayed beyond 3 months for established RA patient who in spite of adequate treatment with NSAIDs has:

- Ongoing joint pain
- Significant morning stiffness or fatigue
- Active synovitis
- Persistent elevation of ESR or CRP

Window of opportunity

- RA patient with active polyarticular disease & +ve RF have >70-% probability of developing joint damage or erosion within 2 years of the onset of disease
- 90% of joint erosion occurring in the first 2 years
- Sensitive imagining modalities (e.g. MRI) detect erosions within 4 months after onset of the disease
- Rate of BMD loss is higher in patients with early RA

Rheumatoid Arthritis
Use of Local Steroid

- Useful adjunct to treatment
- Most useful when only a few joints are inflammed
- Intra-articular or peri-articular injection
- Effect usually last for weeks to months
- Not to be repeated within 3 months
- Not to inject the same joint more than 3-4 times in a year
- Exclude the presence of septic complication
- Use of long acting preparation
- Beware of possible systemic side effect

Rheumatoid Arthritis
Use of Systemic Steroid

- As a bridging therapy -
  - to allow earlier return to work
  - to facilitate rehabilitation programme

  Given orally at low dosage (eg. 5-10mg/day)

  Given parenterally (eg. depot methylprednisolone 80-120mg IMI)
- For control of systemic/extra-articular manifestations
- ? as a disease modifying drug of articular disease
- Beware of various undesirable side effects
- Possibility of difficulty in weaning off

GOUT

Clinical Features of Gout

1. Asymptomatic Hyperuricaemia
2. Acute Gouty Arthritis

   M:F 8:1

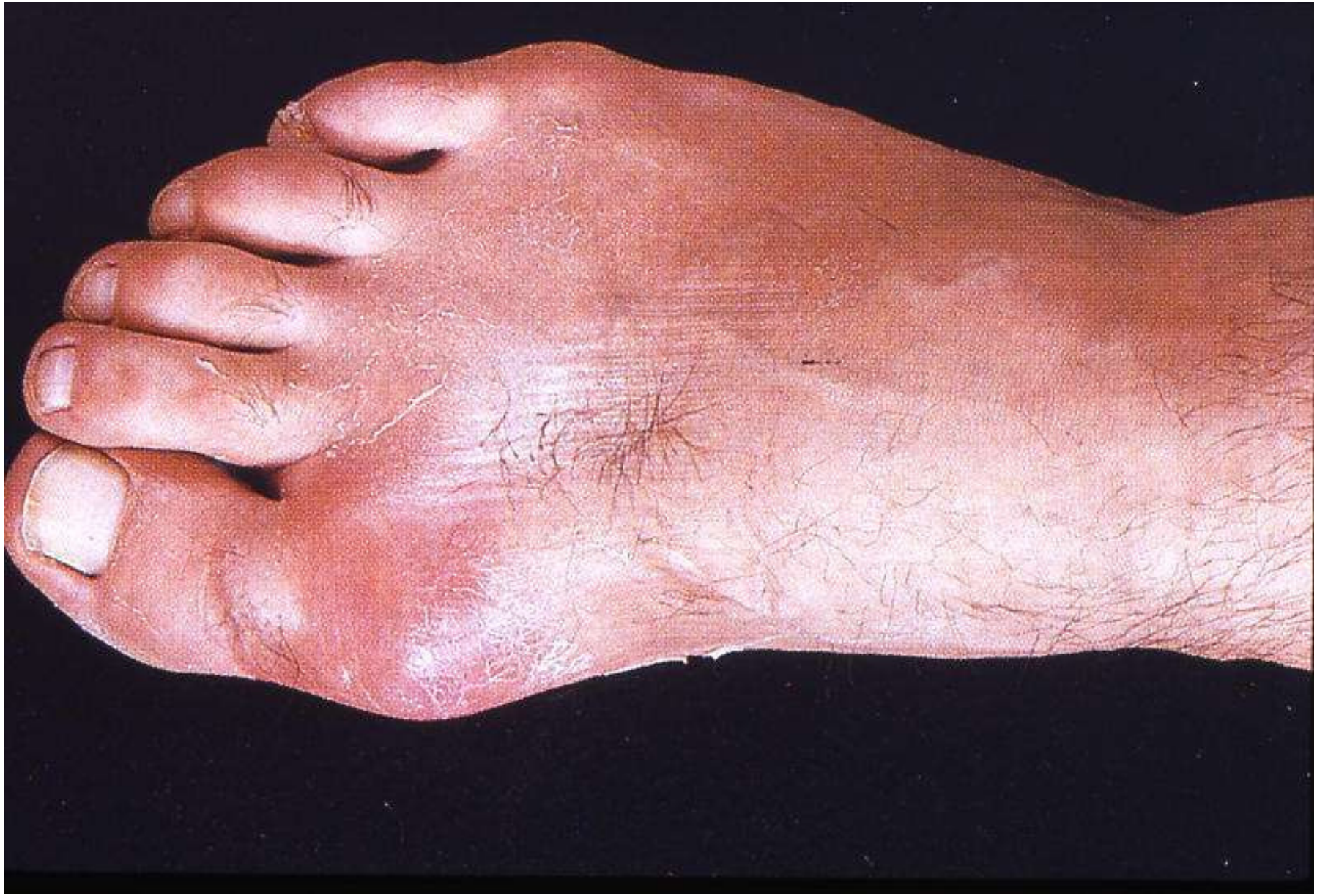
   Commonest 30 to 60 years of age

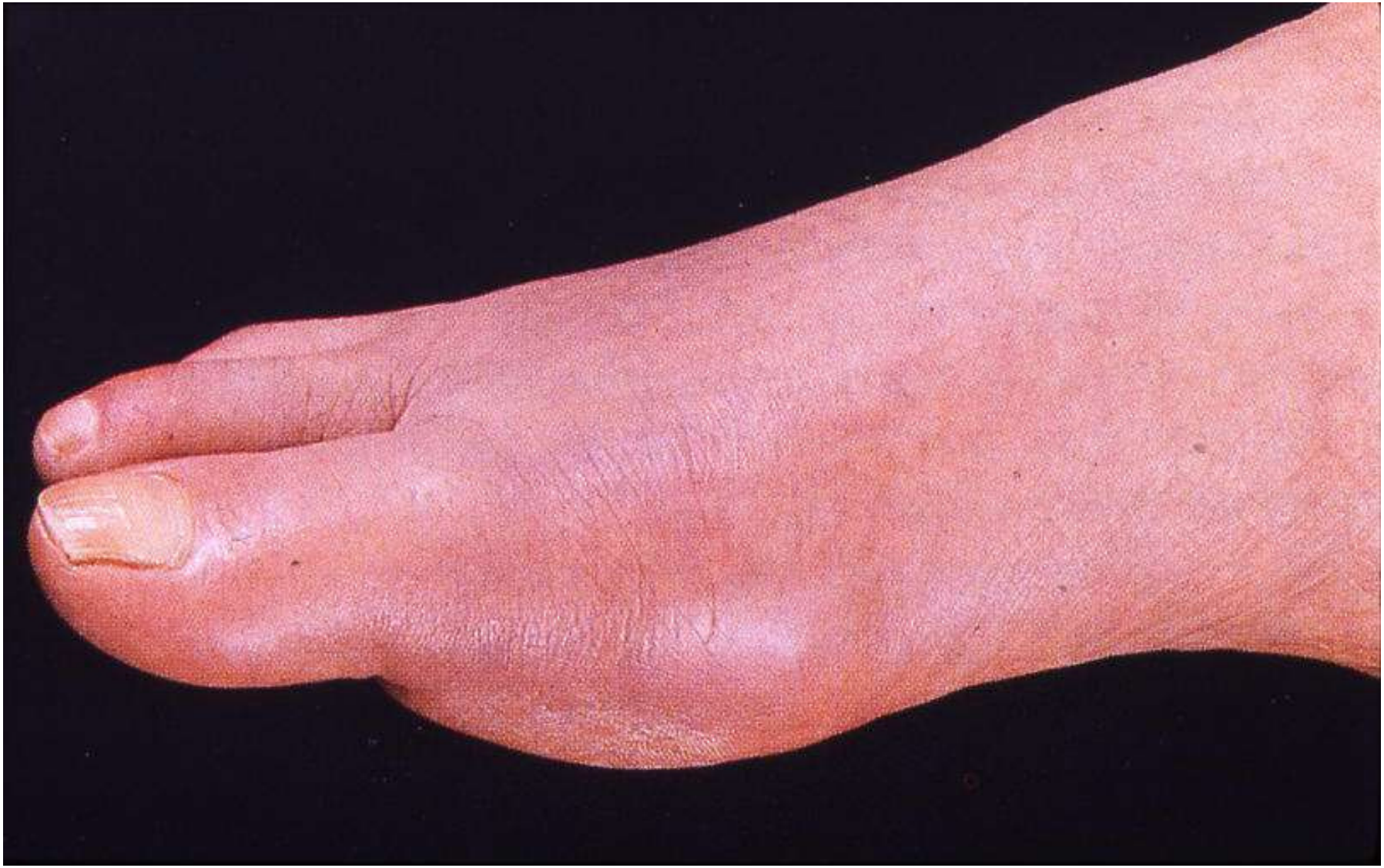
   Initially monoarticular

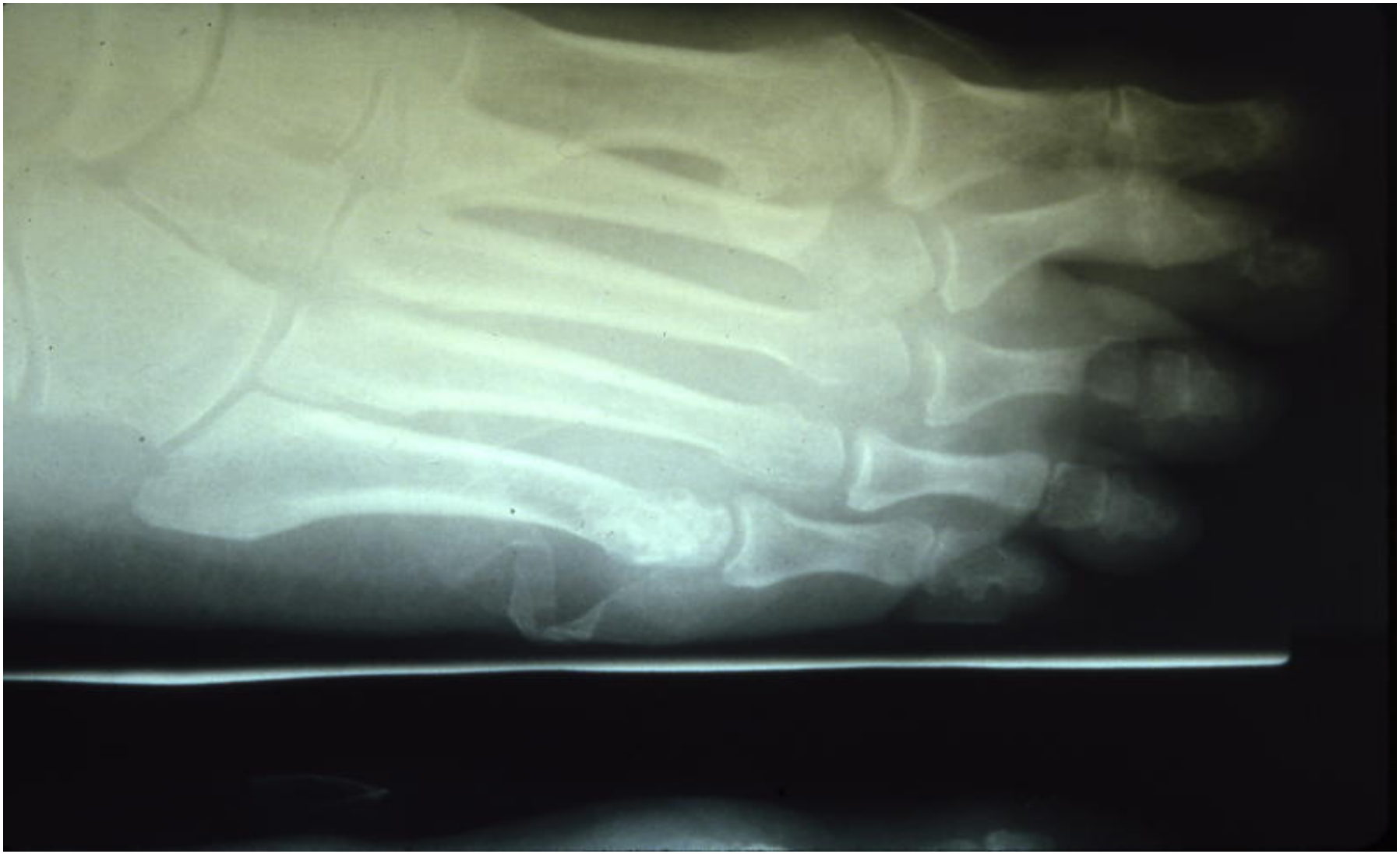
   MP joint of big toe affected first in 20%

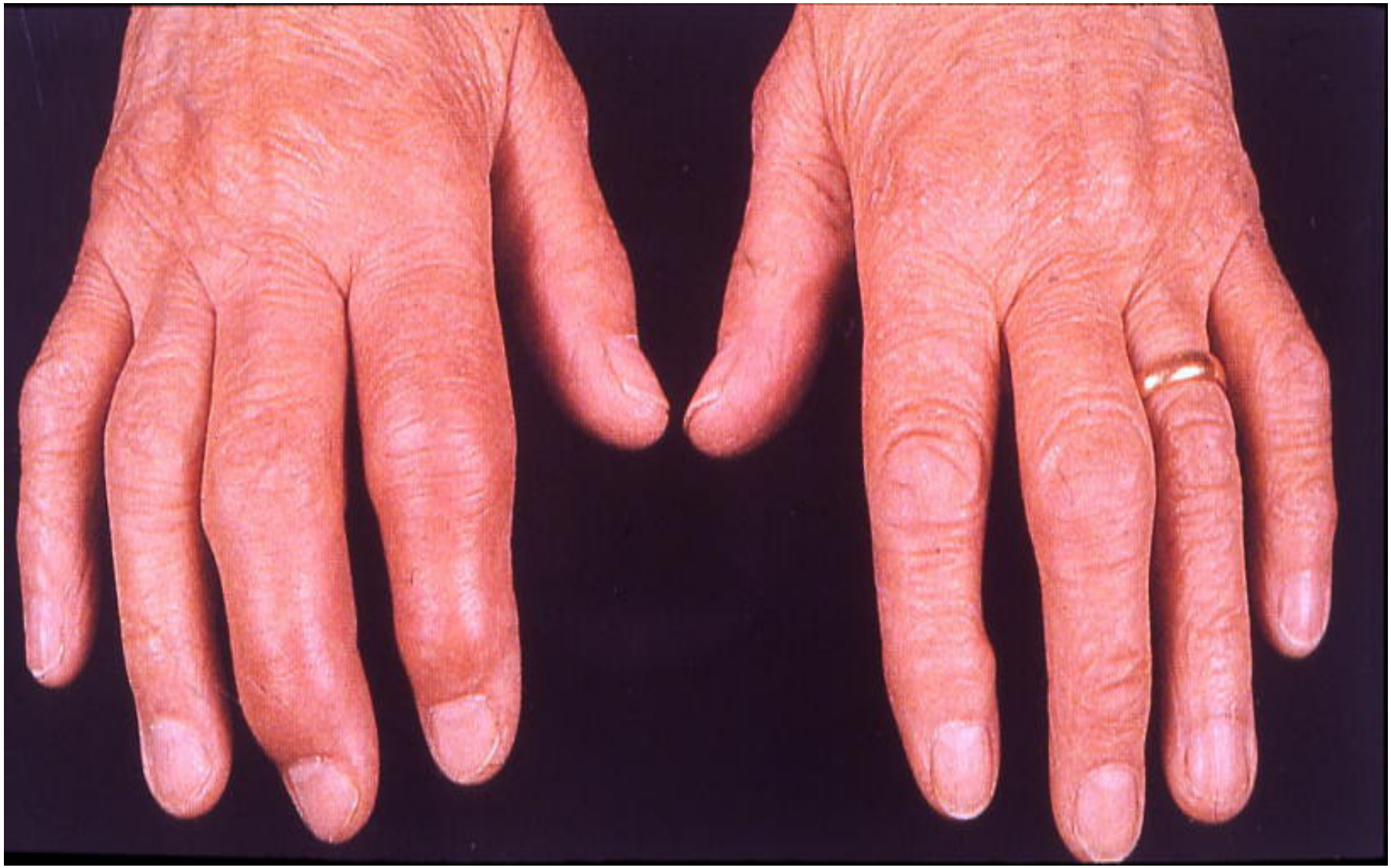
   Fever, leucocytosis

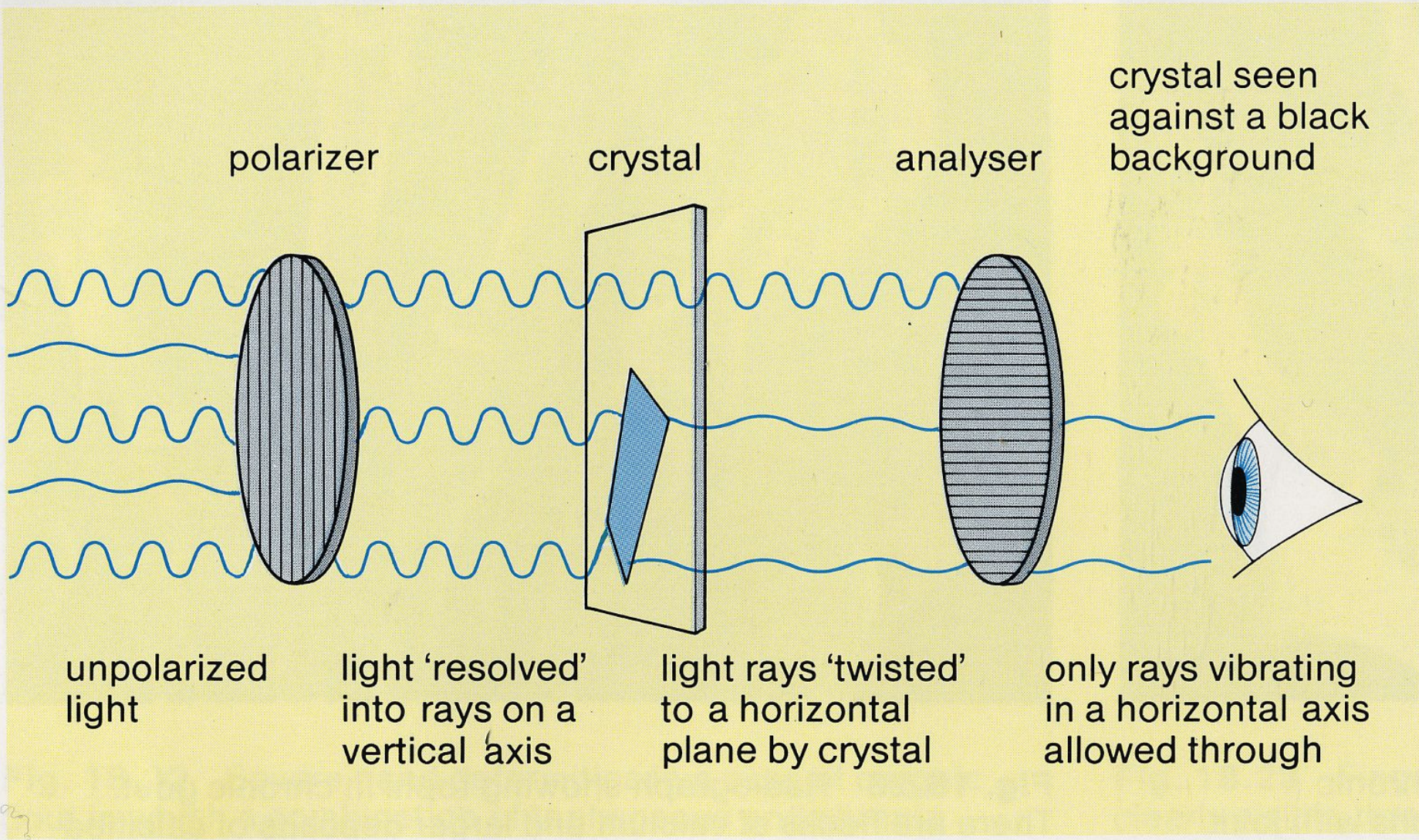
   Pruritus & desquamation of overlying skin











Simplified scheme of the principles behind the use of polarized light microscopy, showing a birefringent crystal altering the vector of plane polarized light, allowing it to pass through the analyser and be seen at the microscope eye piece.

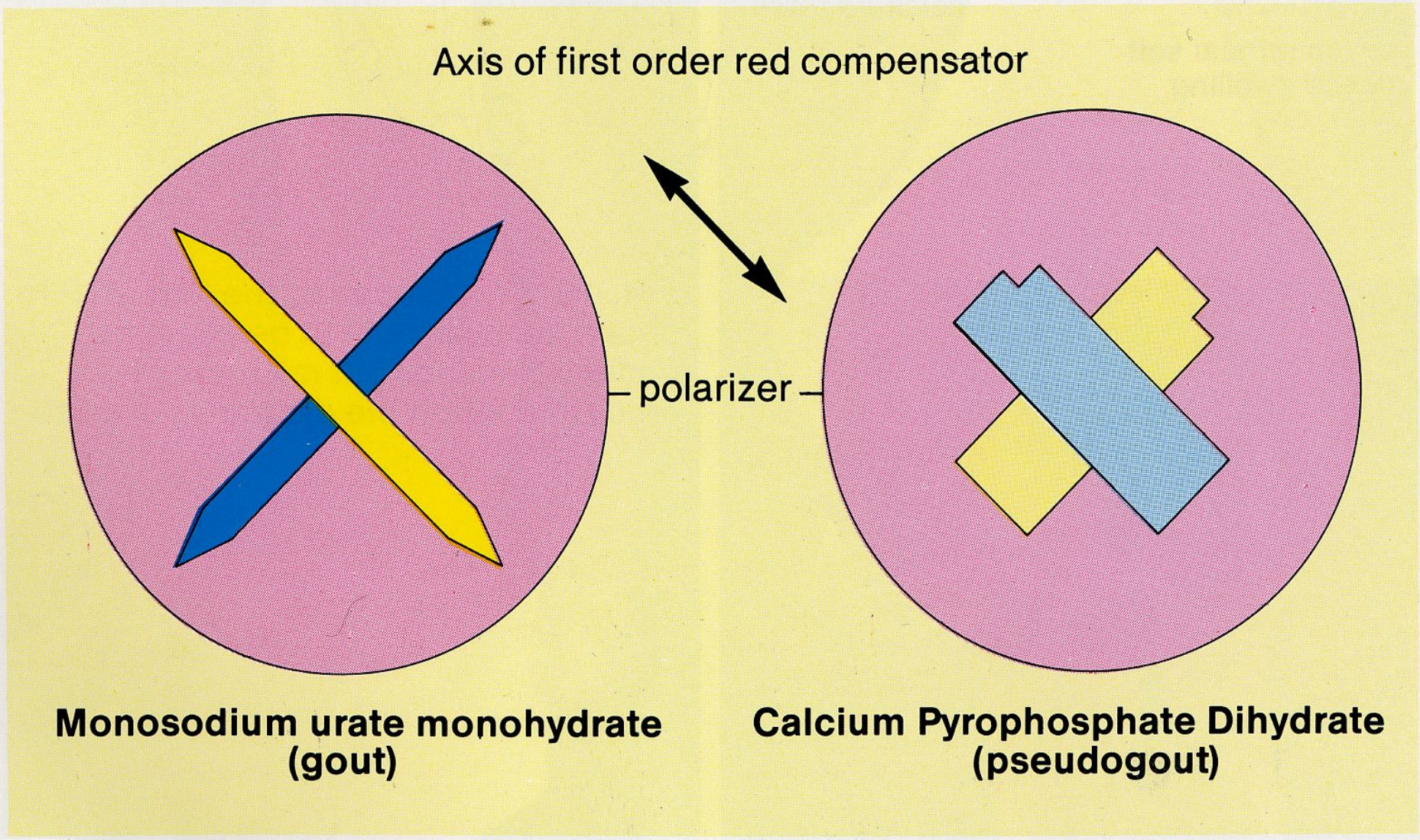
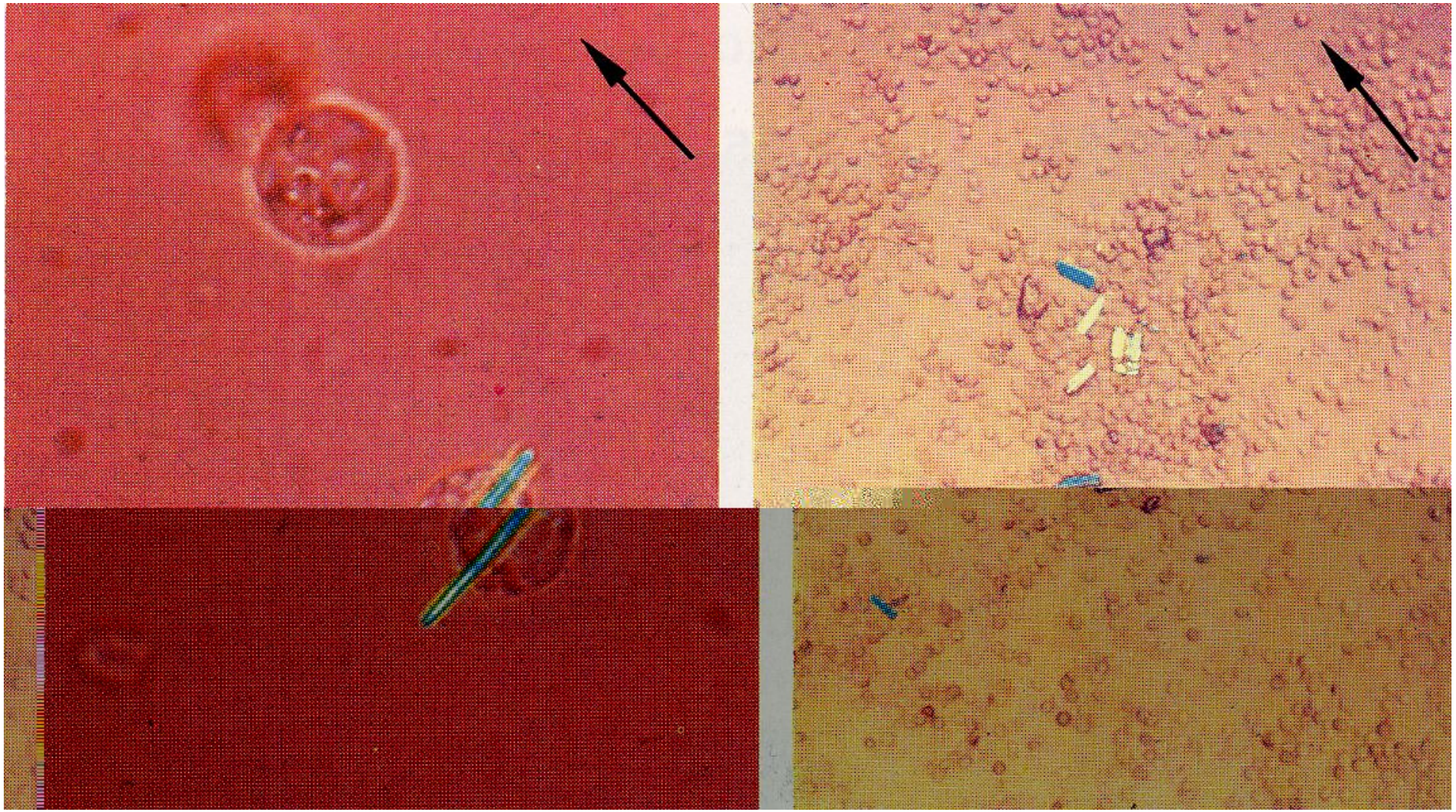


Diagram to show the different morphology, and sign of birefringence of urate and pyrophosphate crystals. Birefringence can be detected by a color shift to blue (positive) or yellow (negative) when the long axis of the crystal is aligned with the optical axis of a first order red compensator.



ERROR: syntaxerror
OFFENDING COMMAND: %ztokenexec_continue

STACK:

-filestream-