PAIN IN RHEUMATOLOGY

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Contents

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The current Medicine

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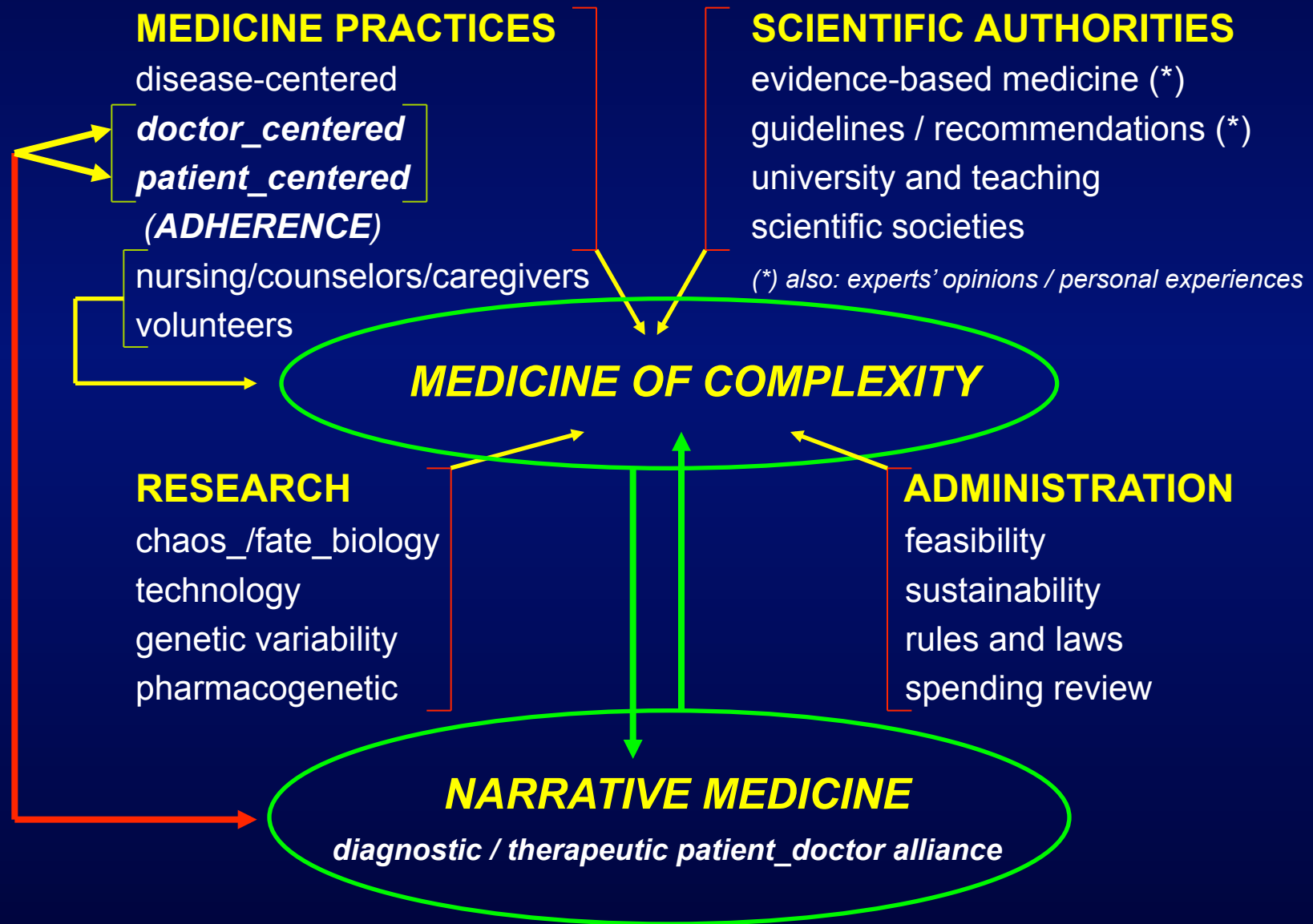

Medicine of Complexity and Narrative Medicine

Medicine of Complexity	*the modern Medicine*
Narrative Medicine	*a new way towards an olistic approach to Patient and its clinical situation*

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Coaccioli S.

Medicine of Complexity: the Modern Internal Medicine

Clin Ter 2010: 161(1):9-11

Complexity bears its methodological and doctrinal contribution to the general health and medical assistance management, as well as to the clinical context and medical training.

The science of complexity has suggested as alternative model in which the disease as well as the patient's general well-being are the result of a complex interaction between various elements of the entire system, dynamic and unique, of the individual.

Coaccioli S.

The Narrative Medicine: modern communication between Patient and Doctor

Clin Ter 2011;162(1)

In the Modern Medicine the ability to communicate represents a true and unique operative methodology which is the basis of Narrative Medicine.

This type of approach does not represent an alternative to the traditional model, but rather expands its boundaries while preserving its scientific base: where the feelings, expectations, and desires of the Patients and his interpretation of the disease, more or less obvious, are read in the broad context in which the Patient himself exhibits.

The Modern Narrative Medicine is a holistic approach to the complexity of the method known as the most effective and most efficient – not only in the patient-centred medicine, but also in the improvement of services rendered to the human being as well as the society at large.

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The Anamnesis of Pain

- Pain History
- Hystory of Previous Health Problems
- Psychiatric Comorbidities
- Psychosocial Factors
- Risk of Addiction
- Assessment and Function
- Goals
- Physical Exsamination
- Follow-up Visits

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The Anamnesis of Pain: *pain history*

- Details of **pain hystory** and **associated symptoms**
- Details of **previous consults and investigation**
- **Previous treatments** tried and details of **outcomes**
- **Current medications**, including OTC medications and other (complementary medicine) treatments

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The Anamnesis of Pain: *previous health problems*

- Comorbidities that could influence the manifestation of pain syndrome (dementia, diabetes *et al*.)
- Comorbidities that could influence treatment (renal failure, CV diseases, sleep disturbance)

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The Anamnesis of Pain: *psychiatric comorbidities*

- Anxiety
- Depression
- Bipolar disorders
- Post-traumatic stress disorder (PTSD)
- Adult attention deficit hyperactivity disorder (ADHD)

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The Anamnesis of Pain: *assessment of function*

- To determine the impact of pain on a person's life and provide a baseline for follow-up assessment
- It should cover all the relevant areas and usually includes impact of pain on domains such as employment, social, recreational, family, or home responsabilities.
- It should assess self care, sleep, and ideally evaluate the overall quality of life.

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The Anamnesis of Pain: *follow-up visits*

- To review goals achievement
- To review «homework»
- Need to document (the five As):
  - ***Analgesic response***
  - ***Activity response***
  - ***Aberrant drug related behaviour***
  - ***(new) Action plan of care***

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The Anamnesis of Pain: *methodology*

The format for documentation of a multidimensional pain assessment is recommended.

It serves to ensure that all the various dimensions of pain have been assessed and serves to facilitate communication with the patients as well as the other clinicians.

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Contents

1. The Communication between the Physician and the Patient
2. Anamnesis of Pain: Techniques, Methods, and Strategies

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3. Pain: methodology of investigation

- *Chronology*
- *Topography*
- *Characteristics*
- *Associated symptoms*
- *QoL and ADL*
- *Red flags*

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4. Take-Home Messages

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Pain. Methodology of Investigation: *Cronology*

- The arise of pain (acute *vs* chronic)
- How long pain persists
- Is pain recurrent ?
- Is pain persistent ?
- Is pain present during day-time ?
- Is pain present during night-time ?
- The excercise get better the pain / reduce the pain ?
- The excercise make worse the pain / increase the pain ?

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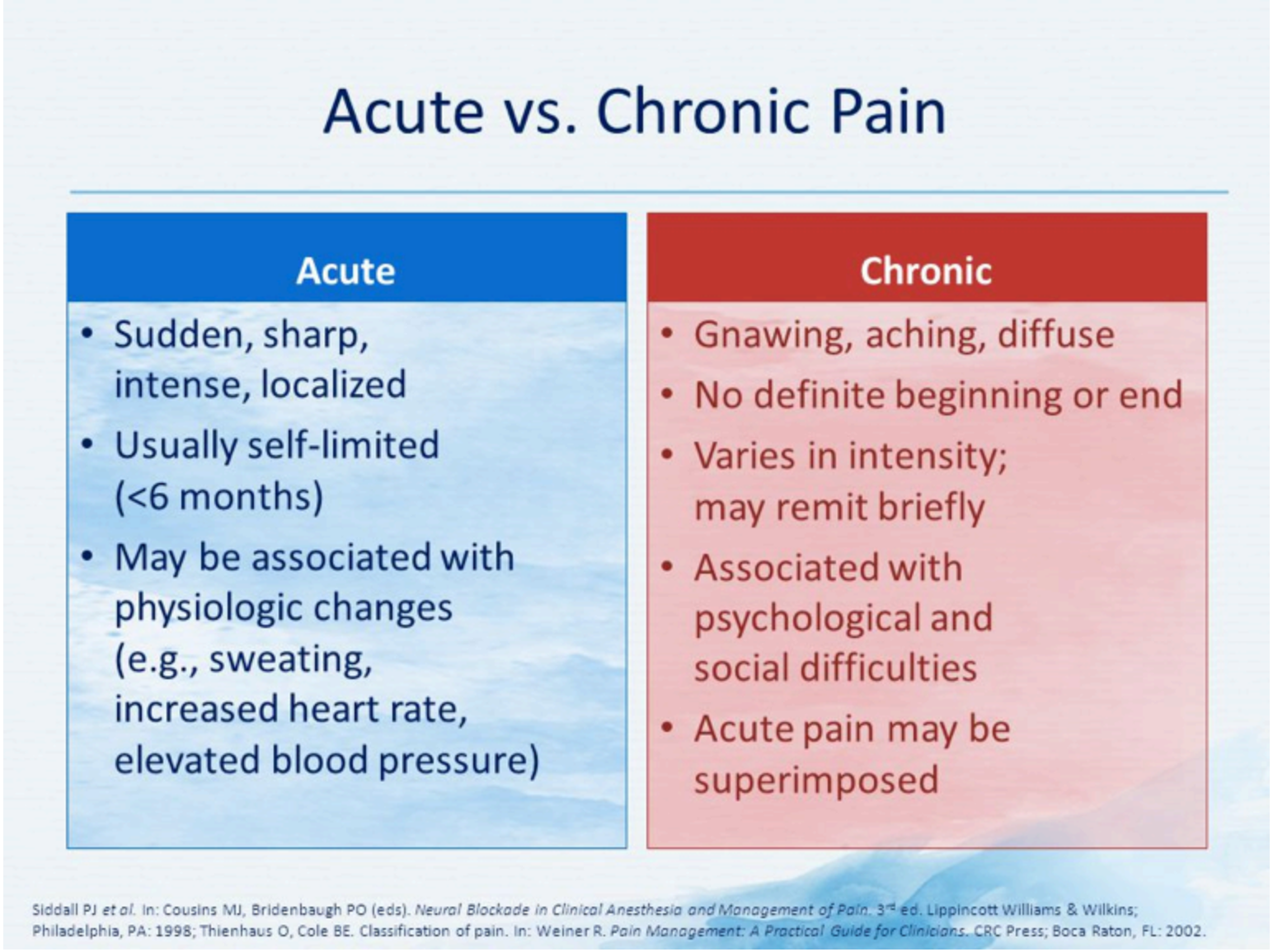
Pain. Methodology of Investigation: *Cronology*



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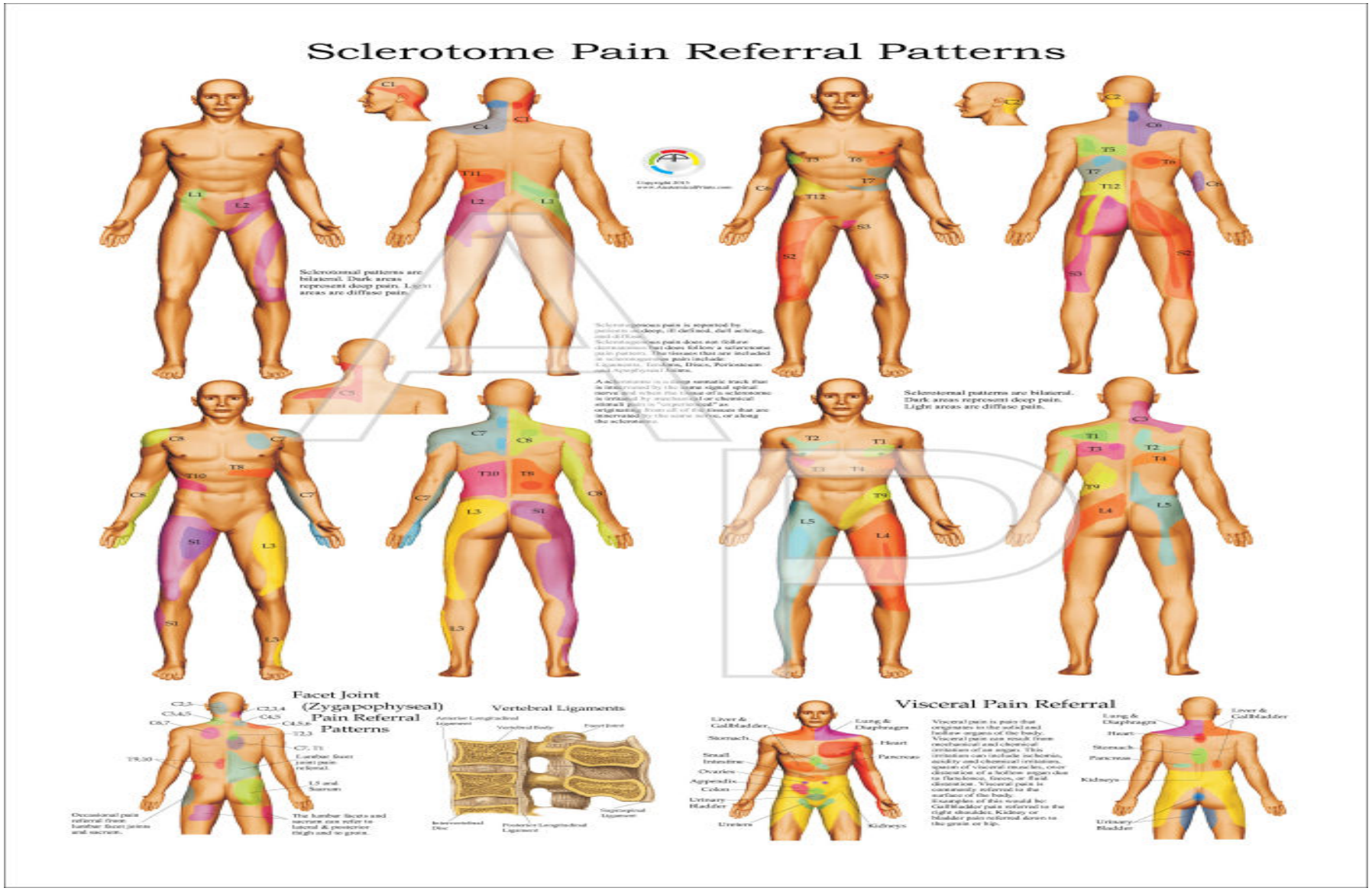
Pain. Methodology of Investigation: *Topography*



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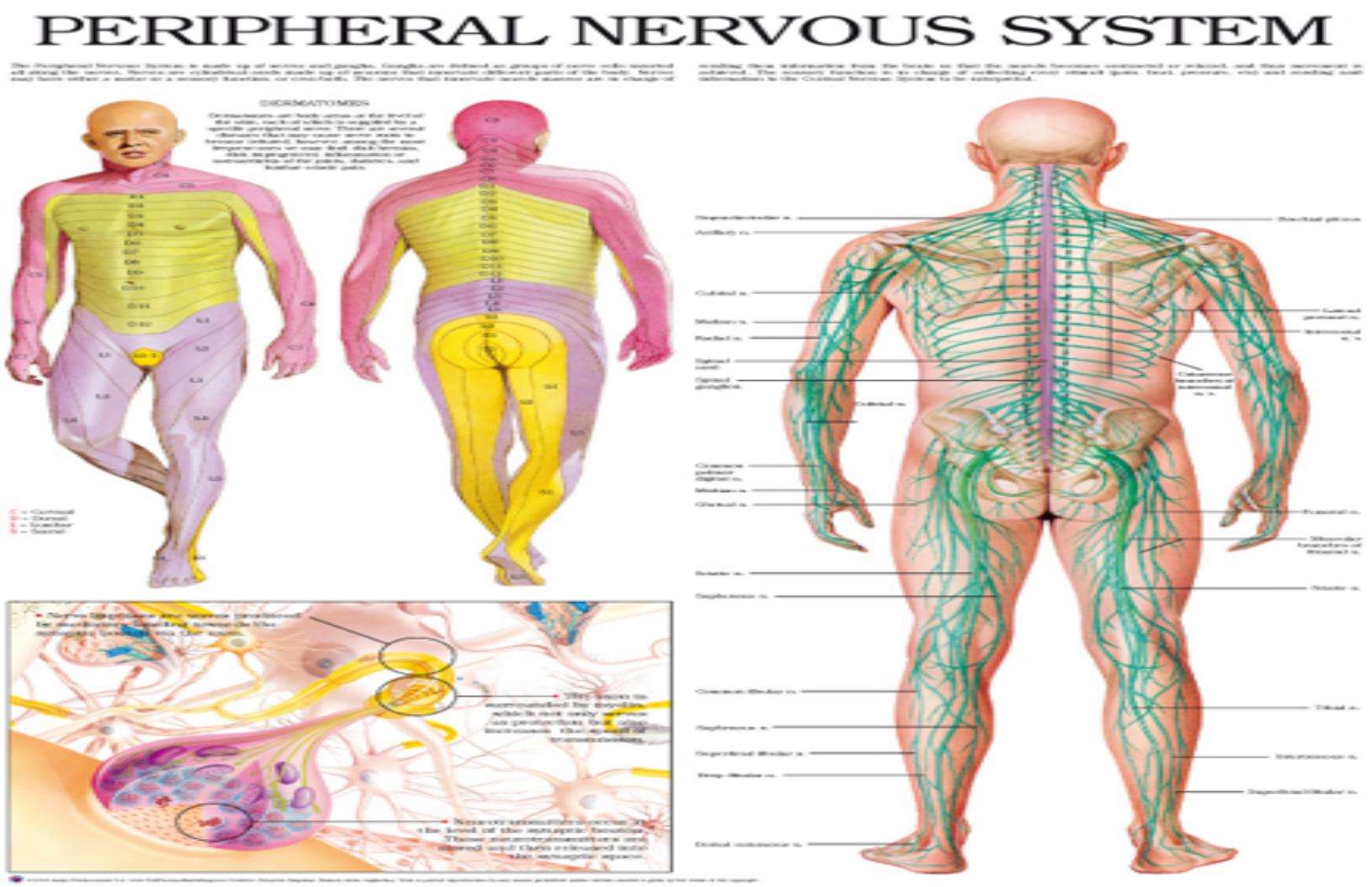
Pain. Methodology of Investigation: *Topography*



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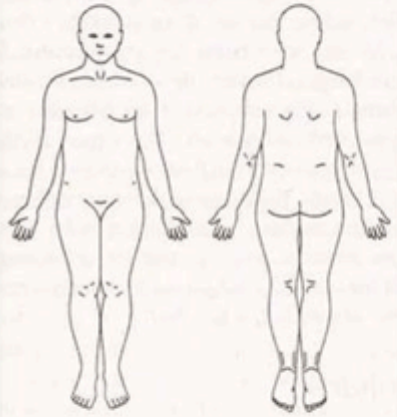
Pain. Methodology of Investigation: *Characteristics*

Short Form McGill Pain Questionnaire

FIGURE 10-2 | The McGill Pain Questionnaire

Part 1 Where Is Your Pain?

Please mark on the drawing below, the areas where you feel pain. Put E if external, or I if internal, near the areas which you mark. Put EI if both external and internal.



Part 2 What Does Your Pain Feel Like?

1 Flickering, Quivering, Pulsing, Throbbing, Beating, Pounding	2 Jumping, Flashing, Shooting	3 Pricking, Boring, Drilling, Stabbing, Lancinating	4 Sharp, Cutting, Lacerating
5 Pinching, Pressing, Gnawing, Cramping, Crushing	6 Tugging, Pulling, Wrenching	7 Hot, Burning, Scalding, Searing	8 Tingling, Itchy, Smarting, Stinging
9 Dull, Sore, Hurting, Aching, Heavy	10 Tender, Taut, Rasping, Splitting	11 Tiring, Exhausting	12 Sickening, Suffocating
13 Fearful, Frightful, Terrifying	14 Punishing, Grueling, Cruel, Vicious, Killing	15 Wretched, Blinding	16 Annoying, Troublesome, Miserable, Intense, Unbearable
17 Spreading, Radiating, Penetrating, Piercing	18 Tight, Numb, Drawing, Squeezing, Tearing	19 Cool, Cold, Freezing	20 Nagging, Nauseating, Agonizing, Dreadful, Torturing

Part 3 How Does Your Pain Change With Time?

1. Which word or words would you use to describe the pattern of your pain?

1	2	3
Continuous, Steady, Constant	Rhythmic, Periodic, Intermittent	Brief, Momentary, Transient

2. What kind of things relieve your pain?

3. What kind of things increase your pain?

Part 4 How Strong Is Your Pain?

People agree that the following 5 words represent pain of increasing intensity. They are:

1	2	3	4	5
Mild	Discomforting	Distressing	Horrible	Excruciating

To answer each question below, write the number of the most appropriate word in the space beside the question.

1. Which word describes your pain right now? ____
2. Which word describes it at its worst? ____
3. Which word describes it when it is least? ____
4. Which word describes the worst toothache you ever had? ____
5. Which word describes the worst headache you ever had? ____
6. Which word describes the worst stomach-ache you ever had? ____

Source: Reprinted from *McGill Pain Questionnaire from PAIN, VI:* 277-299, © 1975 with permission from International Association for the Study of Pain.

SHORT-FORM McGILL PAIN QUESTIONNAIRE

RONALD MELZACK

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0)	1)	2)	3)
SHOOTING	0)	1)	2)	3)
STABBING	0)	1)	2)	3)
SHARP	0)	1)	2)	3)
CRAMPING	0)	1)	2)	3)
GNAWING	0)	1)	2)	3)
HOT-BURNING	0)	1)	2)	3)
ACHING	0)	1)	2)	3)
HEAVY	0)	1)	2)	3)
TENDER	0)	1)	2)	3)
SPLITTING	0)	1)	2)	3)
TIRING-EXHAUSTING	0)	1)	2)	3)
SICKENING	0)	1)	2)	3)
FEARFUL	0)	1)	2)	3)
PUNISHING-CRUEL	0)	1)	2)	3)

NO PAIN ——— WORST POSSIBLE PAIN

PPI

0 NO PAIN ____
1 MILD ____
2 DISCOMFORTING ____
3 DISTRESSING ____
4 HORRIBLE ____
5 EXCRUCIATING ____

© R. Melzack, 1984

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Pain. Methodology of Investigation: *Associated Symptoms*

- Cardiovascular
- Pulmonary
- Abdominal
- Urinary
- Migraine
- Mood
- Depression
- Self-esteem

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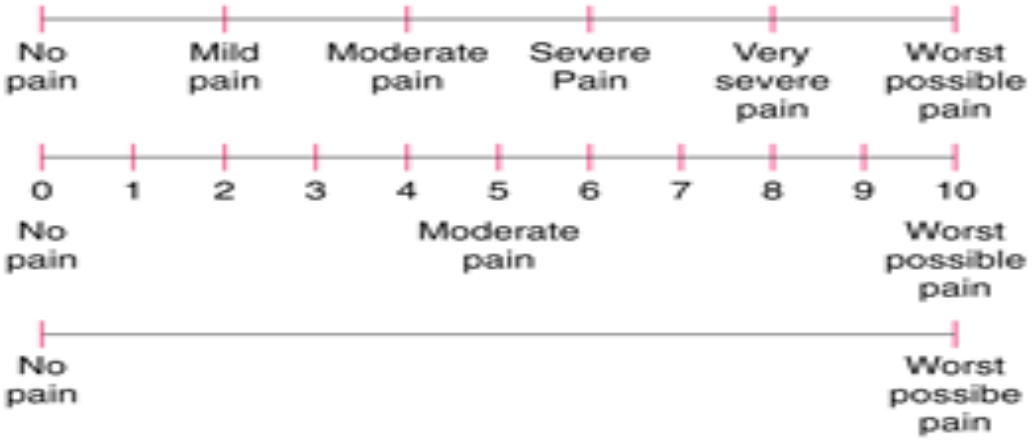
Pain. Methodology of Investigation: *Evaluation*

Visual Analog Scale



Word Descriptor Scale

0 = No pain
1 = Mild pain
2 = Distressing pain
3 = Severe pain
4 = Horrible pain
5 = Excruciating pain

Graphic Scale

Verbal Scale

"On a scale of 0 to 10, with 0 meaning no pain and 10 meaning the worst pain you can imagine, how much pain are you having now?"

Functional Pain Scale

0 = No pain
1 = Tolerable and pain does not prevent any activities
2 = Tolerable and pain prevents some activities
3 = Intolerable and pain does not prevent use of telephone, TV viewing, or reading.
4 = Intolerable and pain prevents use of telephone, TV viewing, or reading.
5 = Intolerable and pain prevents verbal communication

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Pain. Methodology of Investigation: *Evaluation*

P-Q-R-S-T FORMAT

- ✓ PROVOCATION: how the injury occurred & what activities increase or decrease the pain
- ✓ QUALITY: characteristics of pain
- ✓ REFERRAL/ RADIATION
  - Referred: site distant to damaged tissue that does not follow course of peripheral nerve
  - Radiating: follows peripheral nerve, diffuse pain

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Pain. Methodology of Investigation: *Articular Pain*

Etiology of Joint Pain

Mono-articular Pain

- **Trauma** : (overuse – fractures – hemarthrosis).
- **Internal derangement or intra-articular trauma** (Meniscus injury – ligament tear)
- **Infectious or Septic arthritis** (eg, bacterial, fungal, viral, mycobacterial, spirochetal, parasitic).
- **Reactive arthritis** (Aseptic inflammatory arthritis).
- **Crystal-induced disease** (gout or pseudogout)
- **Periarticular syndromes** (eg, bursitis, epicondylitis, fasciitis, tendinitis, tenosynovitis)

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Pain. Methodology of Investigation: *Articular Pain*

I. Articular or Nonarticular ?

- Articular pain is localized to a specific joint, both passive and active Range Of Motion (ROM) are restricted in all planes.
- Nonarticular pain originates from periarticular structures (tendon or bursa), only active ROM is restricted in the plane of involved structure.
- Diffuse nonarticular conditions: generalized hypermobility and fibromyalgia (diffuse aches and pain)

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Pain. Methodology of Investigation: *Articular Pain*

Patterns of pain

Degenerative joint pain: pain on joint use, stiffness after inactivity, pain at end of day after Use (osteoarthritis)

Inflammatory joint pain: pain and prolonged stiffness in the morning, at rest, and with use (Inflammatory arthritis)

Mechanical joint pain: pain related to joint use only (unstable joint)

Bone pain: pain at rest and at night (Tumor, Paget's, fracture)

Neuropathic :diffuse pain and paresthesia in dermatome, worsened by specific activity (root or peripheral nerve compression)

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Pain. Methodology of Investigation: *Articular Pain*

Patterns of Diagnostic Importance

Pattern of joint involvement

- **Simmetrical MCF and PIF joints**
  - *Rheumatoid Arthritis*
- **Asymmetrical DIP joints**
  - *Seronegative Arthritides*
- **Spine involvement**
  - *Seronegative Arthritides*
- **Involvement of DIP, as well as big joints and spine**
  - *Osteoarthritis*
- **History of acute inflammation (mono-oligo-articular)**
  - *Acute Gout*
  - *Chondrocalcinosis (Pseudogout)*

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Pain. Methodology of Investigation: *QoL*

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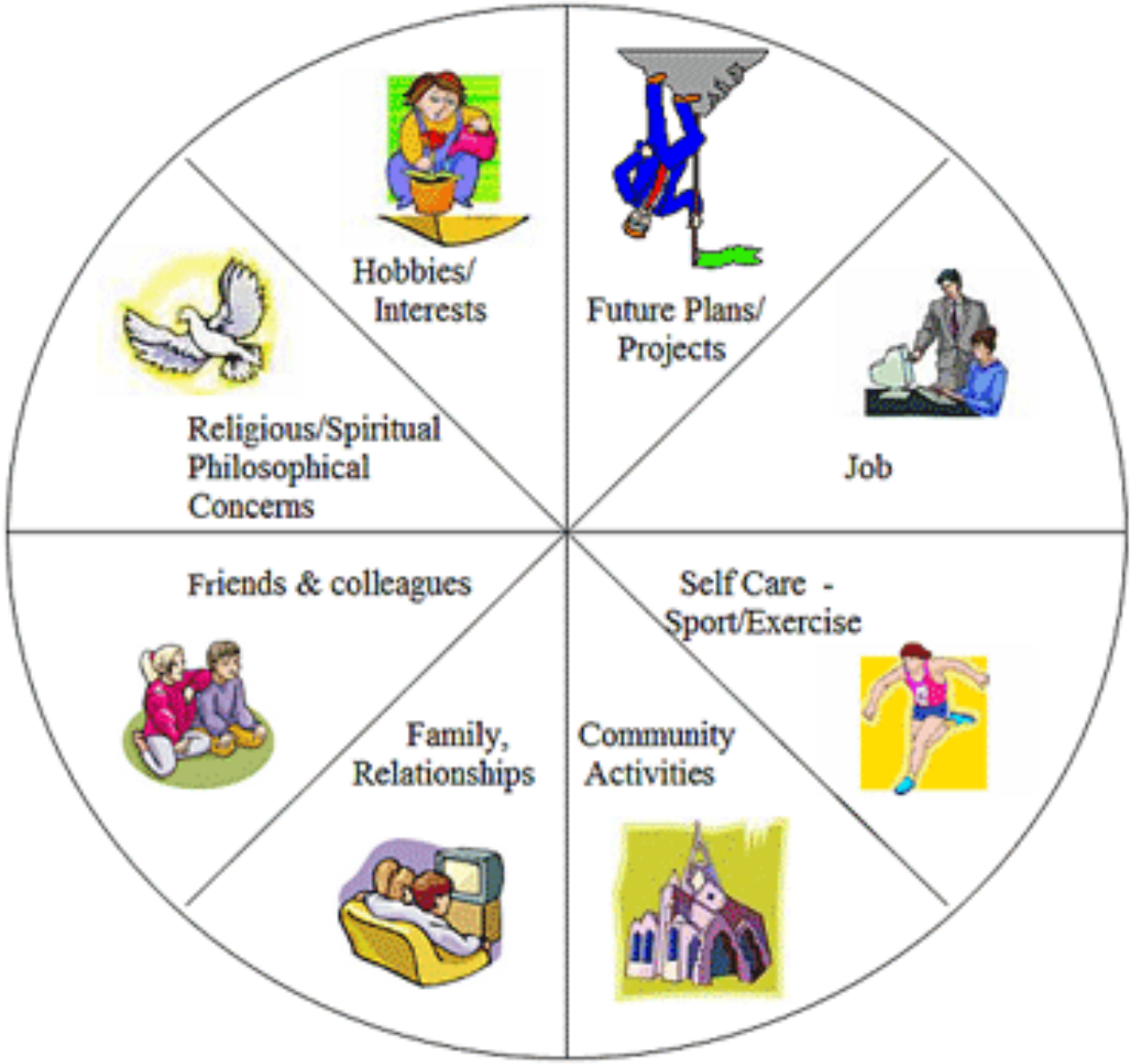
Pain. Methodology of Investigation: *ADL*



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Pain. Methodology of Investigation: *Red Flags*

- Systemic signs and / or symptoms
- Fever
- Loss of body weight
- Loss of appetite
- Aspecific laboratory data: ESR, CRP, total iron, anemia of chronic disorders *et al*.

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Contents

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Anamnesis of Pain: *Take-Home Messages*

- **Personal History**
  - **Associated Diseases and Associated Therapies**
- **Carefully Anamnesis of Pain**
- **Evaluation of Pain and Characteristics of Pain**
- **Evaluation of Systemic Signs and Symptoms**
- **Consider *Red Flags***

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ARTHRITIDES of PERIPHERAL JOINTS

Contents

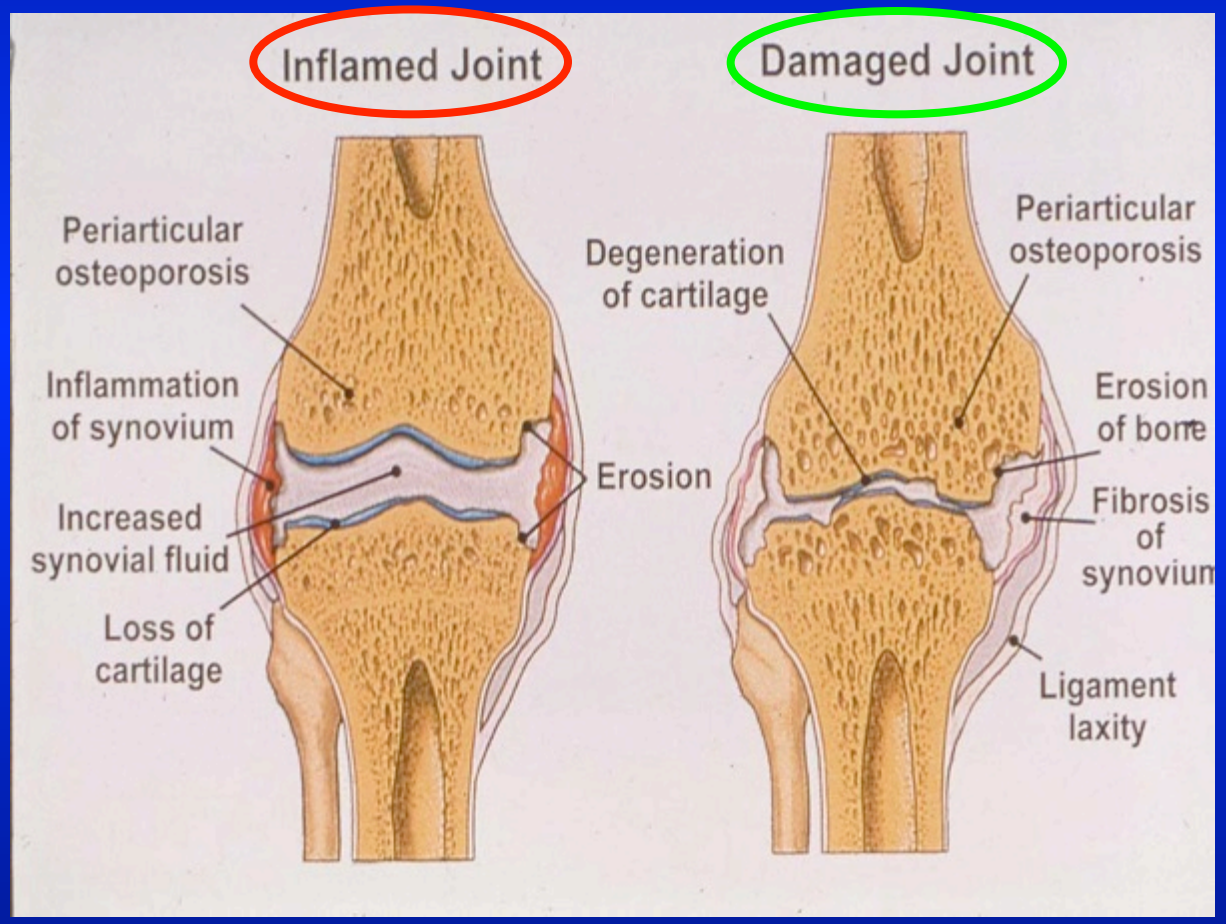
Osteoarthritis

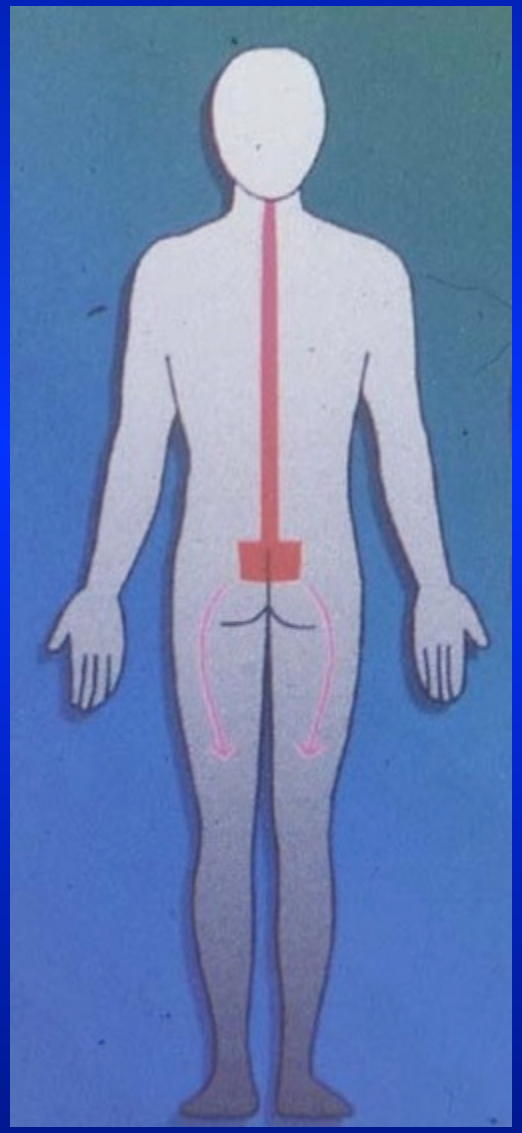
Rheumatoid Arthritis

Spondiloarthritides

Microcrystal Arthritis

Rheumatic Diseases:
degeneratives and inflammatories





DD: inflammatory *vs* degenerative symptoms

Inflammatory disease is

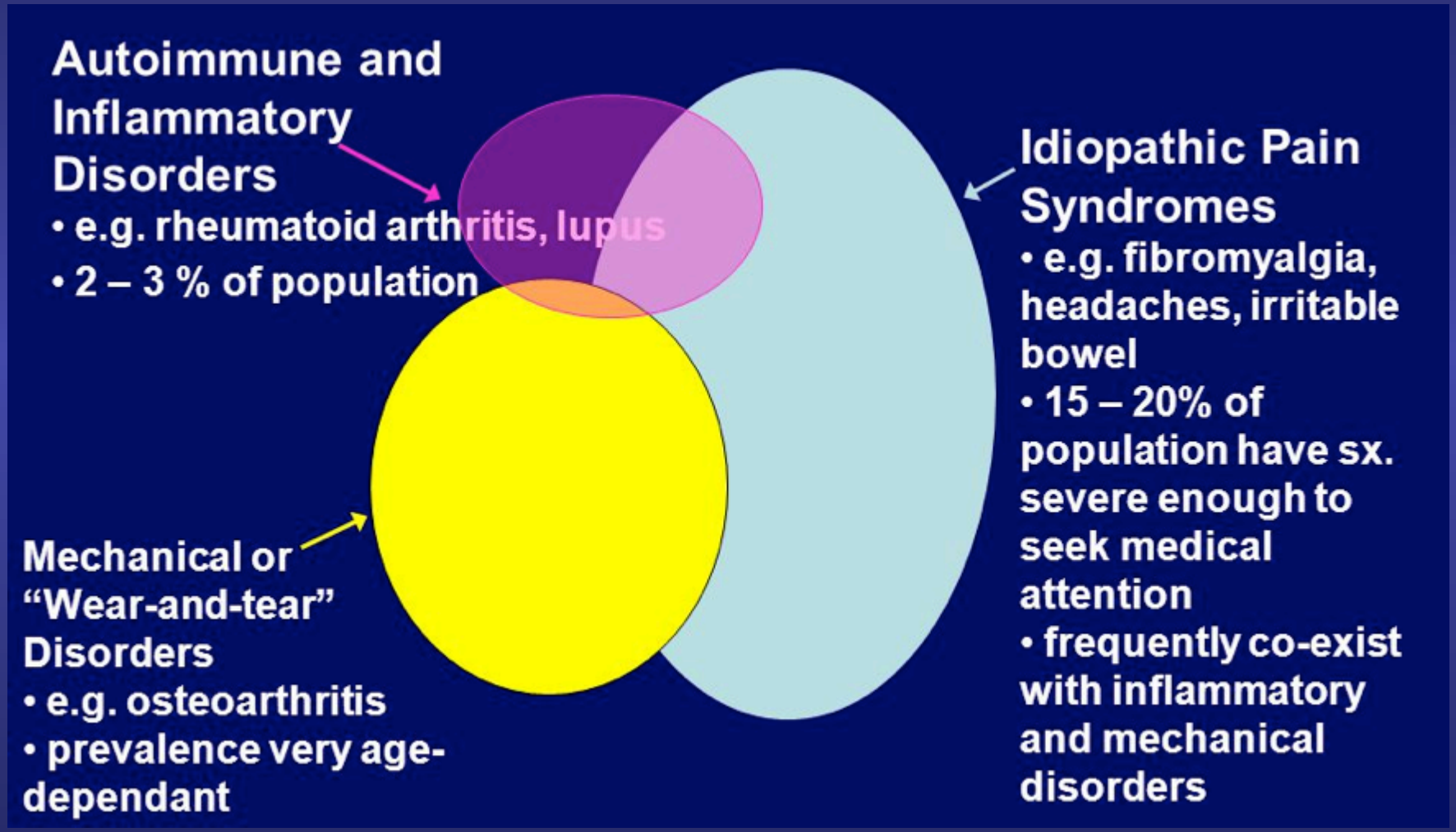
Less likely	More likely
Pain after use/at end of day	Pain worse after rest/in morning
Morning stiffness for <30 minutes	Morning stiffness for >30 minutes
No night-time pain	Night-time pain troublesome*
No systemic symptoms	Systemic symptoms present*
Chronic symptoms	Acute/subacute presentation

* Bear in mind that night pain and systemic symptoms can be indicative of other serious pathology including cancer, infections etc.

Osteo_Myo_Articular Pain

Symptoms and Signs	***mechanic***	*inflammatory*
Pain at rest	No	Yes
Pain at wake up	No	Yes
Pain on movement	Increases	Reduces
Morning stiffness	No	Yes
Stiffness after inactivity	Variable	Yes
Signs of inflammation	No	Yes
Variability due to environmental change	yes	No

What Causing Chronic Pain ?



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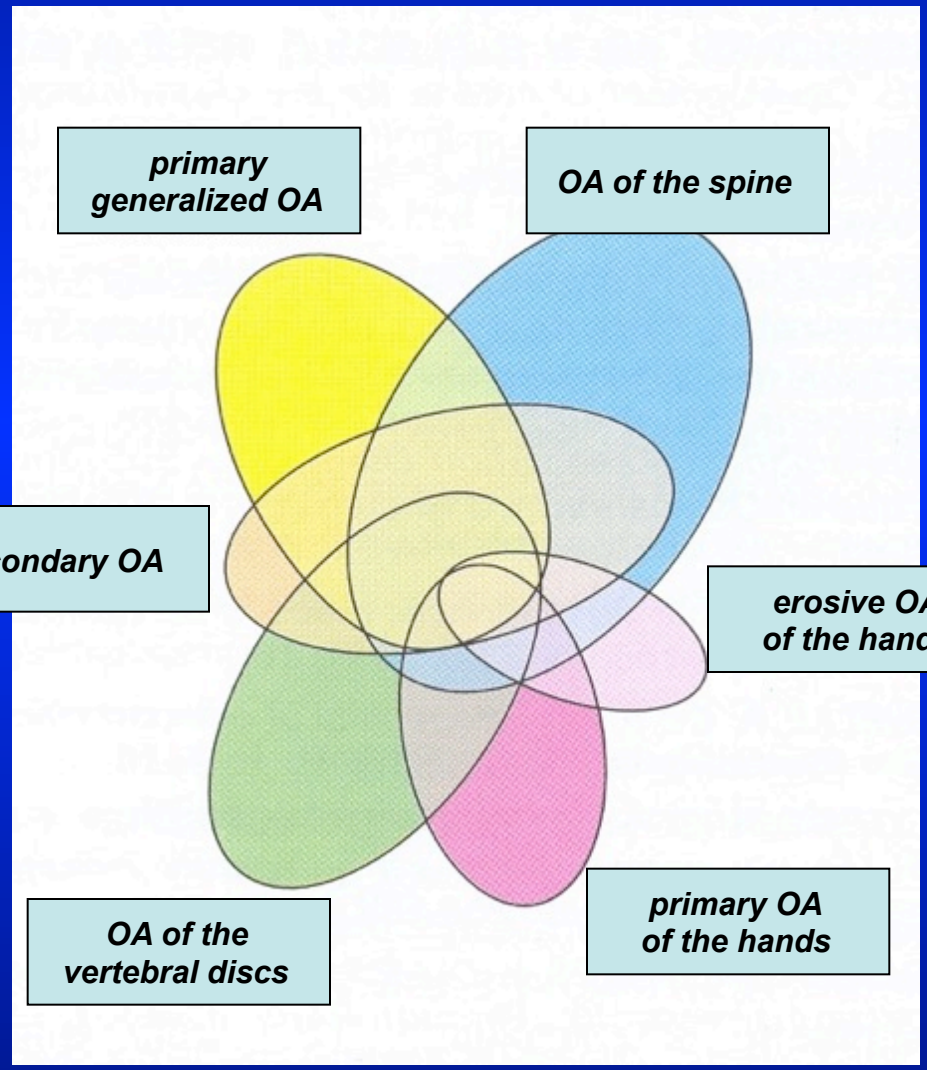
Osteoarthritis

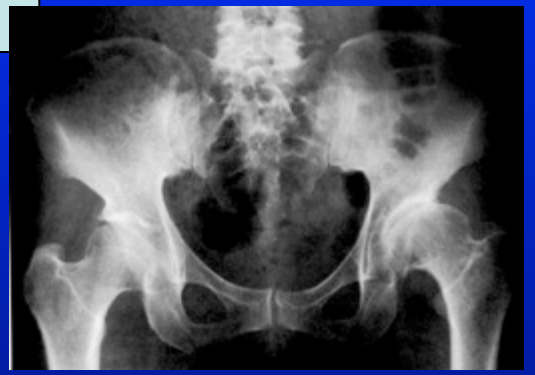
Rheumatoid Arthritis

Spondiloarthritides

Microcrystal Arthritis

The Osteoarthritis Syndrome





The Osteoarthritis Syndrome

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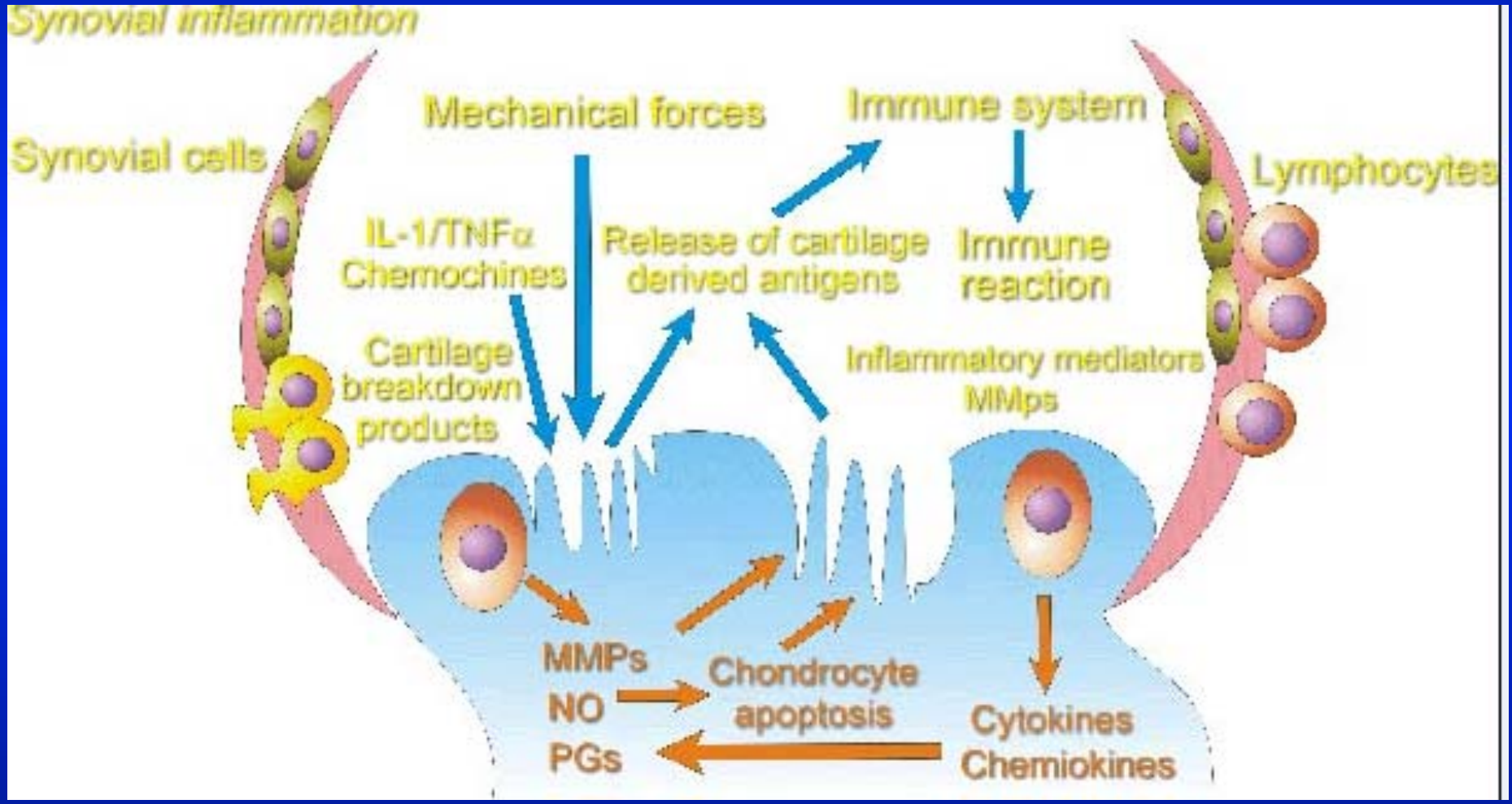
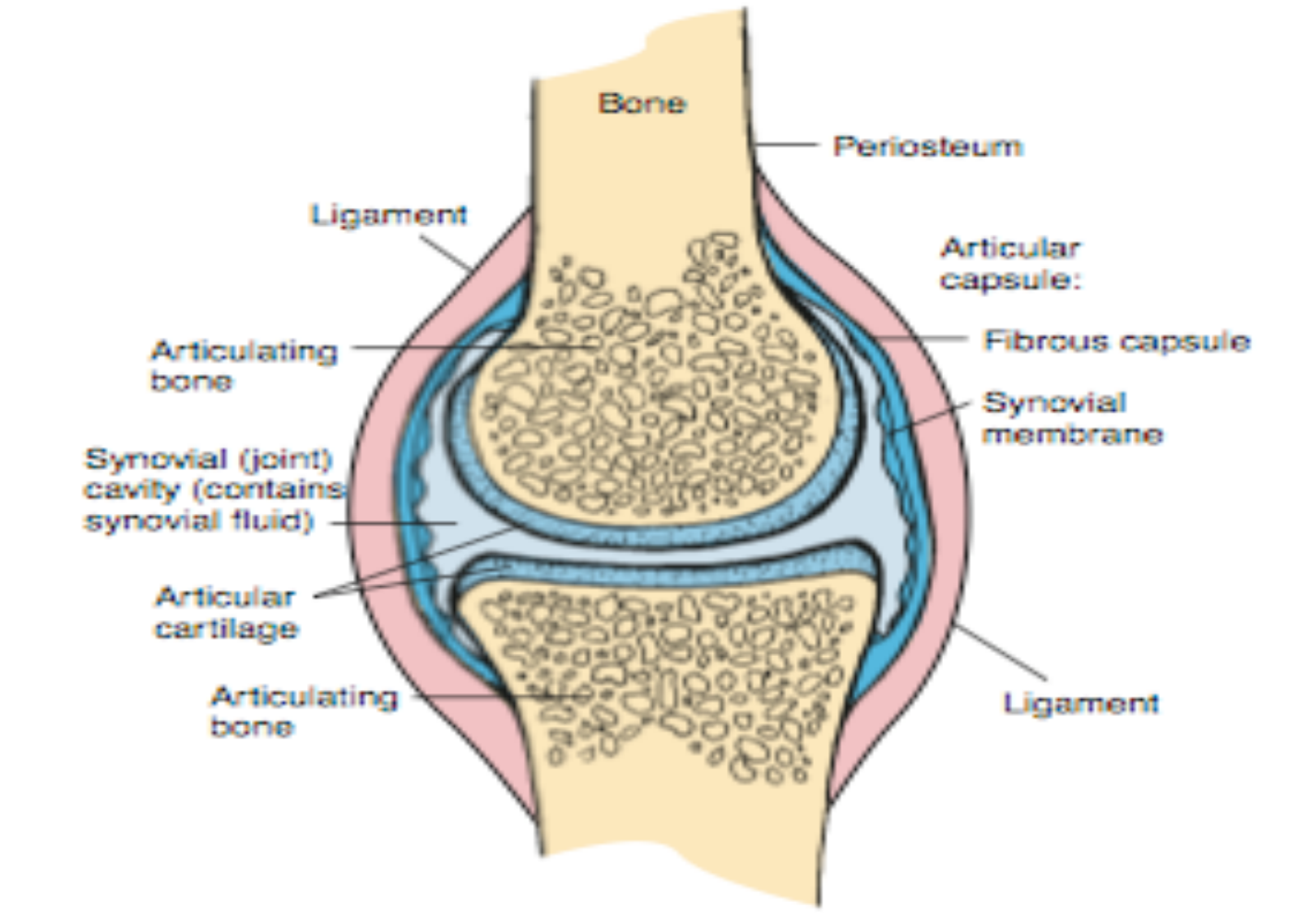
OA: *pathogenesis*



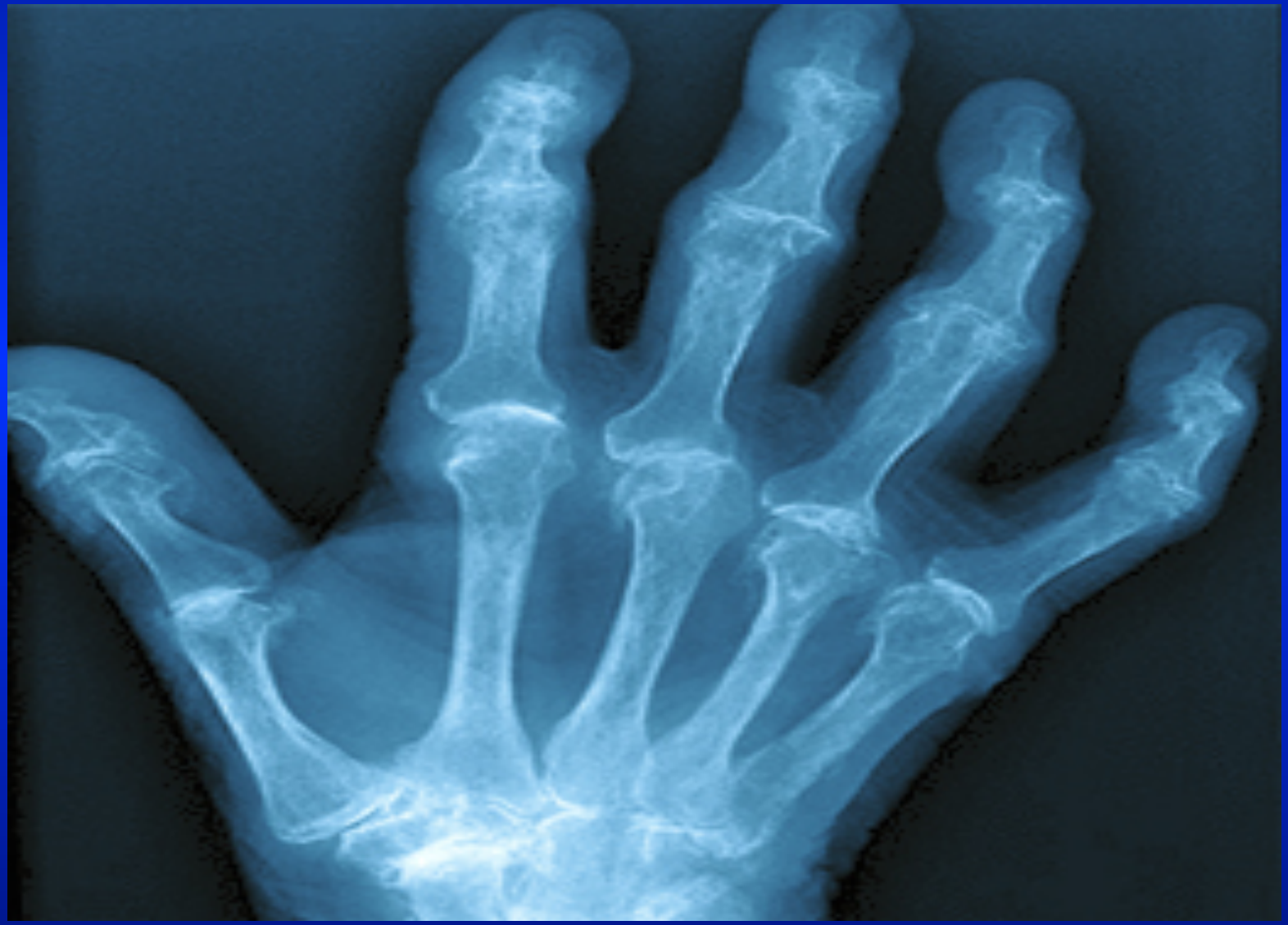
OA: *pathogenesis*



OA of the knee

OA of the hands

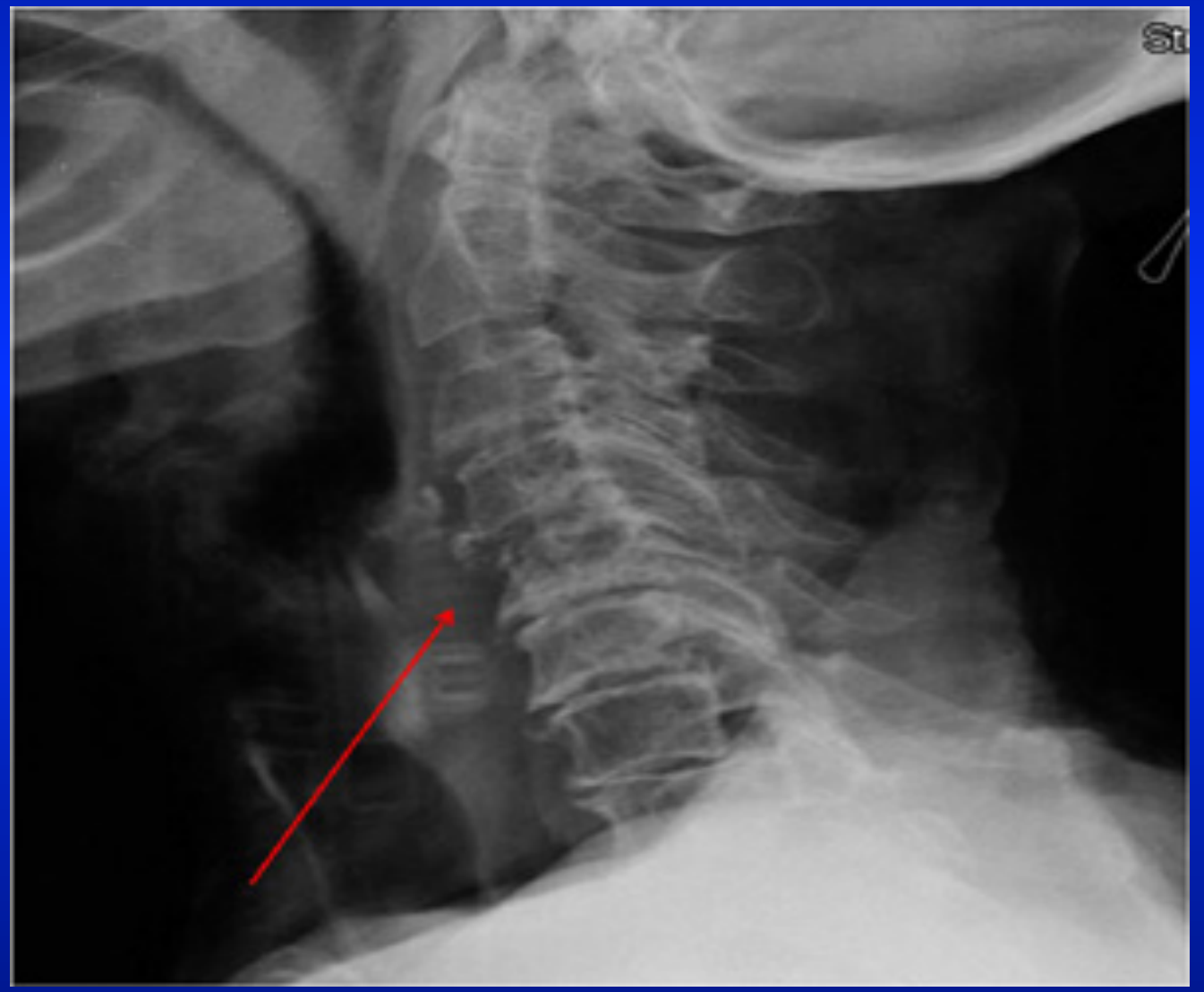
OA of the hands



OA of the coxofemural joints

OA of the spine (lumbar)

OA of the spine (cervical)



Osteoarthritis: *treatment*

• **PCM**	***pain***
• NSAIDs	*flares of inflammation*
• **WEAK OPIOIDS**	***pain***
• **STRONG OPIOIDS**	***pain***
• **ADJUVANTS**	***pain***
• CHONDROPROTECTIVE AGENTS	*DMARDs (?)*


It`s coffee
TIME

Contents

Osteoarthritis

Rheumatoid Arthritis

Spondiloarthritides

Microcrystal Arthritis

Rheumatoid Arthritis

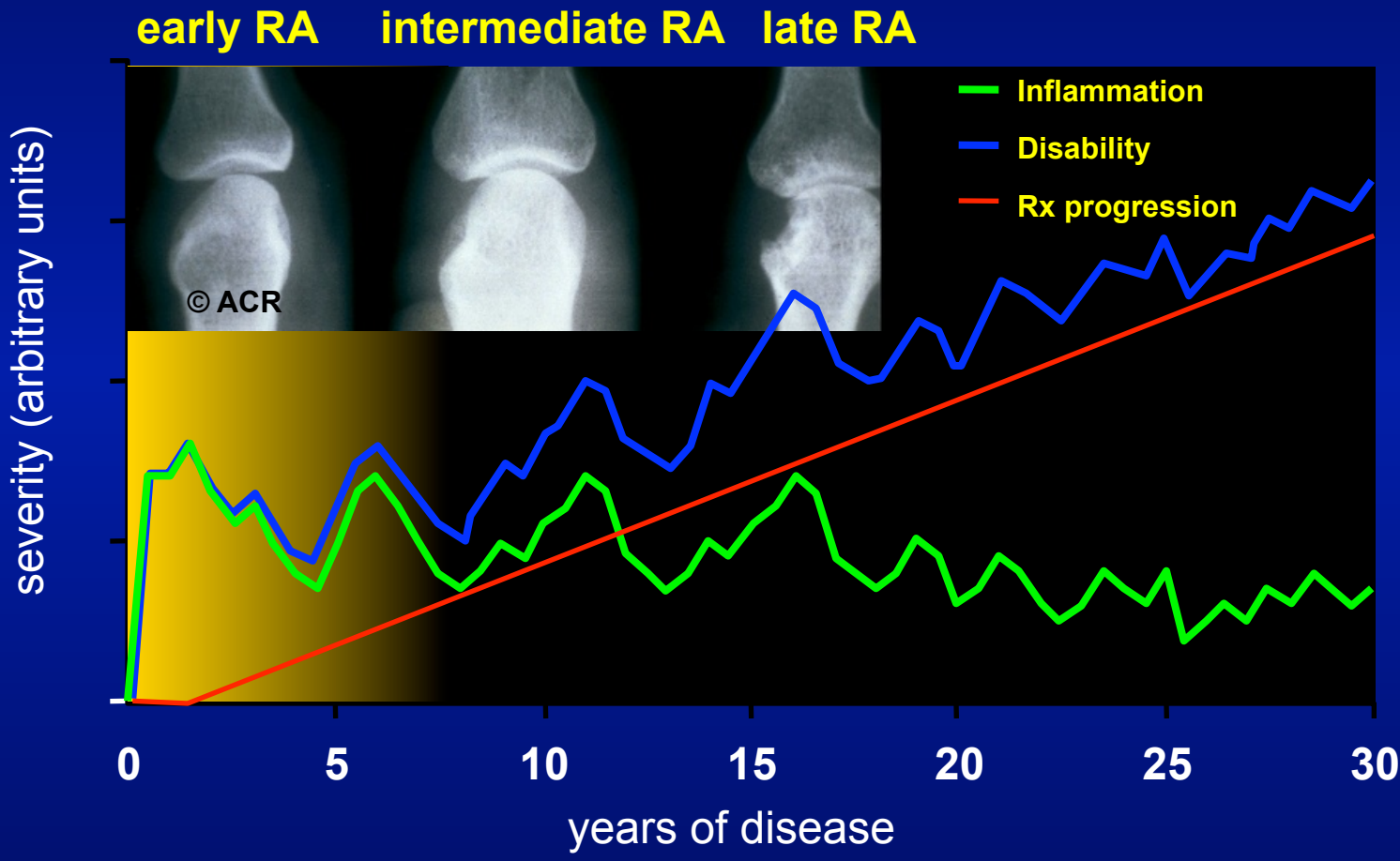
Progressive changes in joints

- Stage I:
  - Inflammation of the synovial membrane spreads to articular cartilage & other soft tissues.
  - Limitation of joint movt with pain & muscle spasm

Osteo_Myo_Articular Pain

Symptoms and Signs	*mechanic*	*inflammatory*
Pain at rest	No	**Yes**
Pain at wake up	No	**Yes**
Pain on movement	Increases	**Reduces**
Morning stiffness	No	**Yes**
Stiffness after inactivity	Variable	**Yes**
Signs of inflammation	No	**Yes**
Variability due to environmental change	yes	**No**

Natural history – the disease in the years

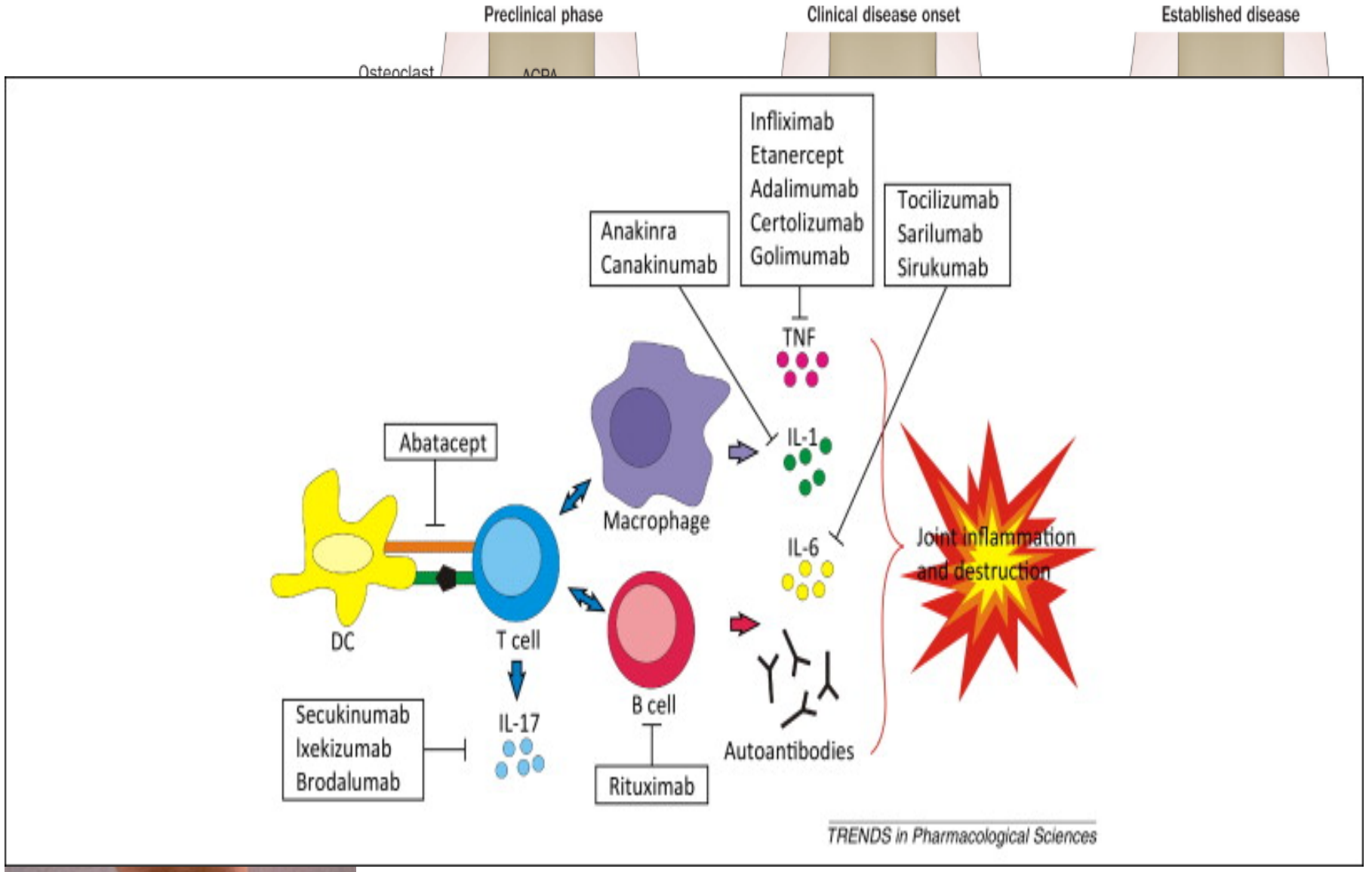


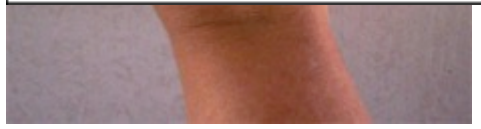
Graph: Adapted from Kirwan JR. J Rheumatol. 2001;28:881-886.
Photo: Copyright © American College of Rheumatology.

early

late

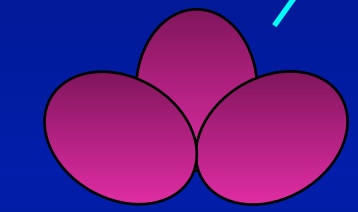
intermediate





Nat Rev Rheumatol. 2012 November ; 8(11): 656–664.

The Role of TNF.α in the Pathogenesis of Rheumatoid Arthritis



TNF.α

Macrophages	↑ Pro-inflammatory cytokines ↑ Chemokines	Increased inflammation
Endothelium	↑ Adhesion molecules	Increased cell infiltration
	↑ Vascular endothelial growth factor (VEGF)	Increased angiogenesis
Hepatocytes	↑ Acute phase response	Increased CRP in serum
Synoviocytes	↑ Metalloproteinase synthesis	Articular cartilage degradation
Osteoclast Progenitors	↑ RANKL expression	Bone erosions

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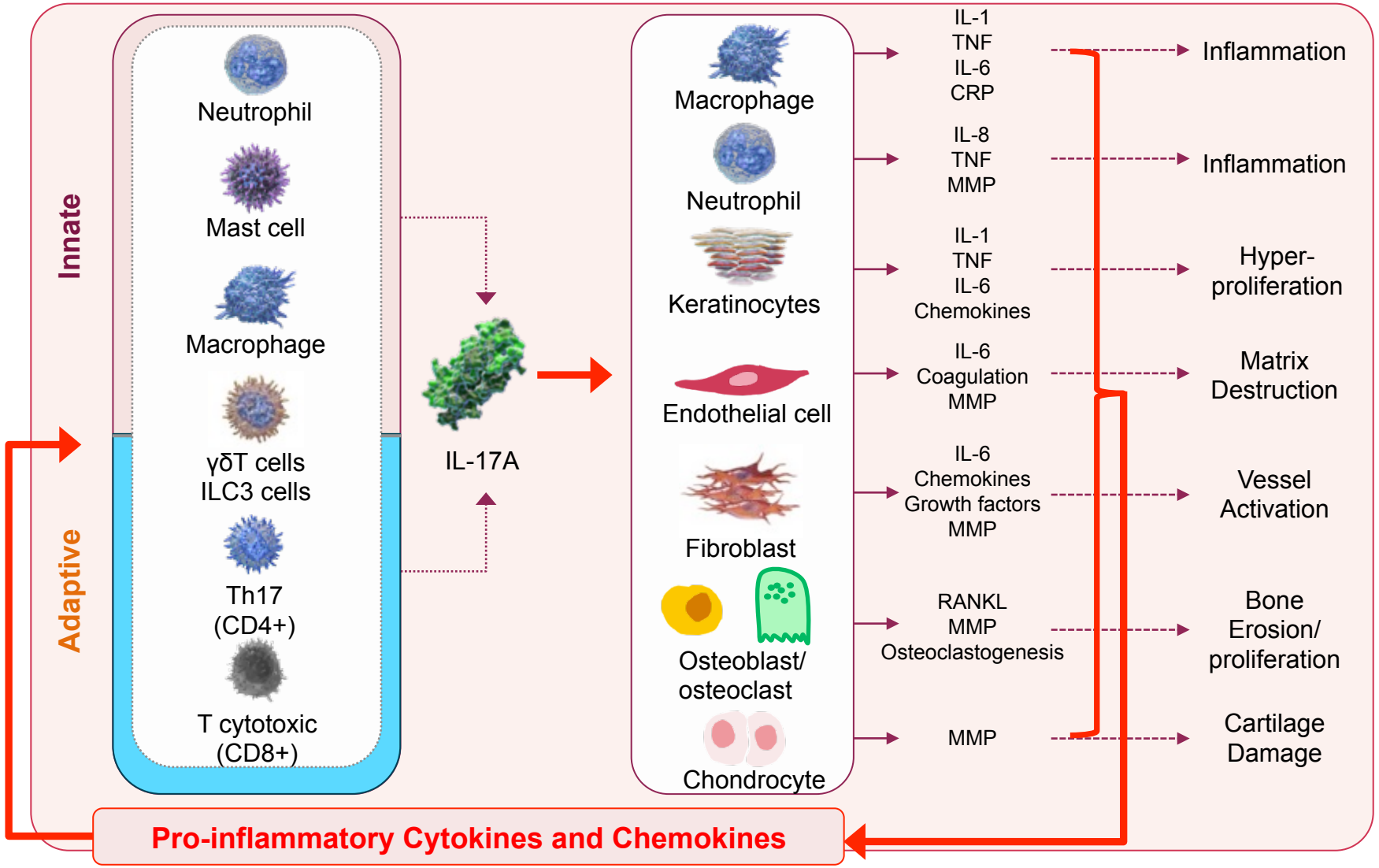
IL-17A is the Main Effector Cytokine in the IL-17 Family and Drives Chronic Inflammation in RA and in SpA



1. Lin A, et al. *J Immunol*. 2011;187:490–500; 2. Nestle F, et al. *N Engl J Med*. 2009;361:496–509; 3. Res P, et al. *PLoS One*. 2010;5:e14108; 4. Cai Y, et al. *Immunity*. 2011;35:1–15; 5. Miossec P, et al. *N Engl J Med* 2009;361:888–98

Rheumatoid Arthritis: *treatment*

• PCM	*pain*
• **NSAIDs**	***pain and inflammation***
• **STEROIDS**	***inflammation and DMARD***
• **DMARDs**	***pathogenesis (weak activity)***
• WEAK OPIOIDS	*pain*
• STRONG OPIOIDS	*pain*
• ADJUVANTS	*pain*
• **ANTI-TNFalfa molecules**	***pathogenesis (strong activity)***
• **ANTI-CKs molecules**	***pathogenesis (strong activity)***

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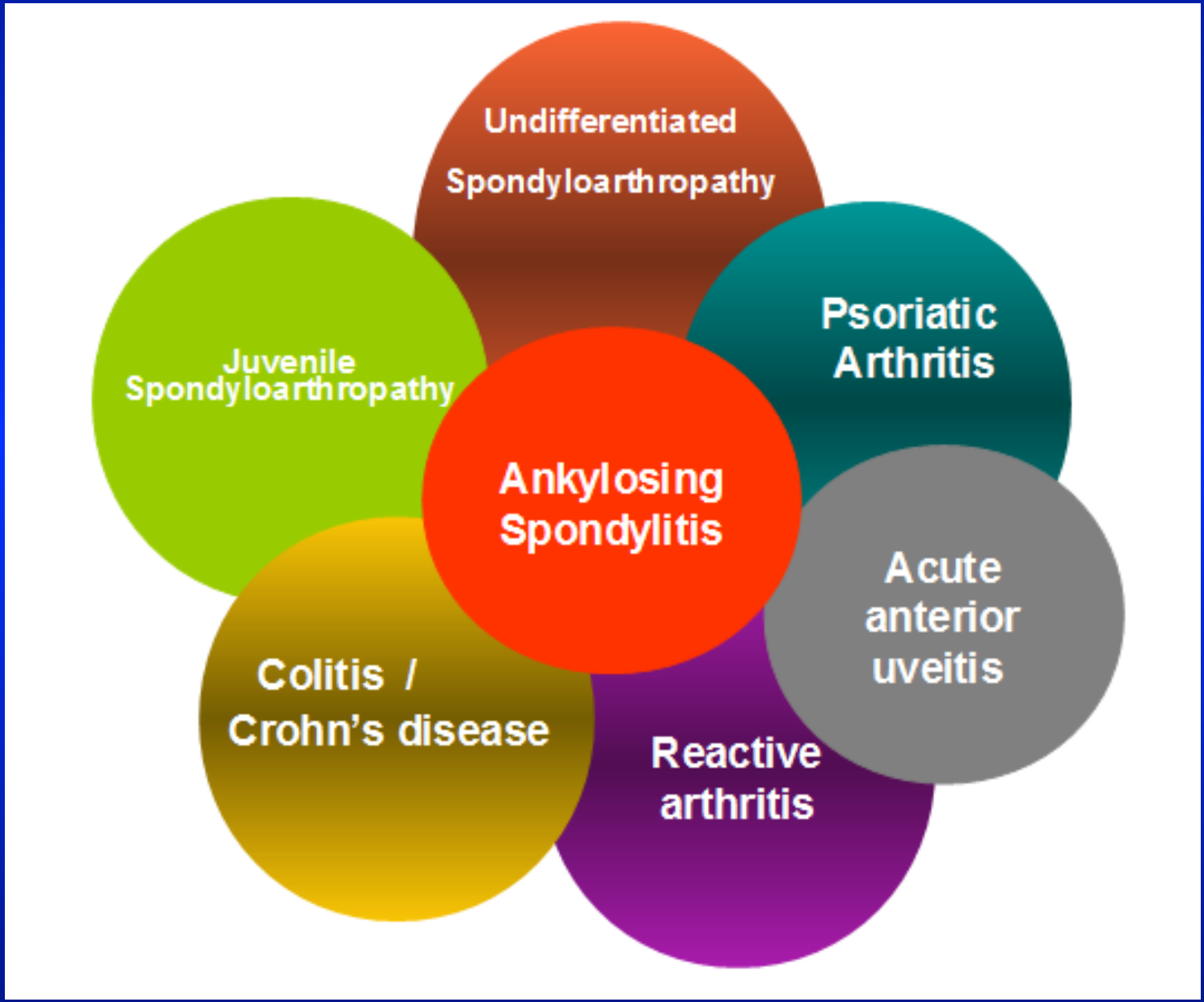
Osteoarthritis

Rheumatoid Arthritis

Spondiloarthritides

Microcrystal Arthritis

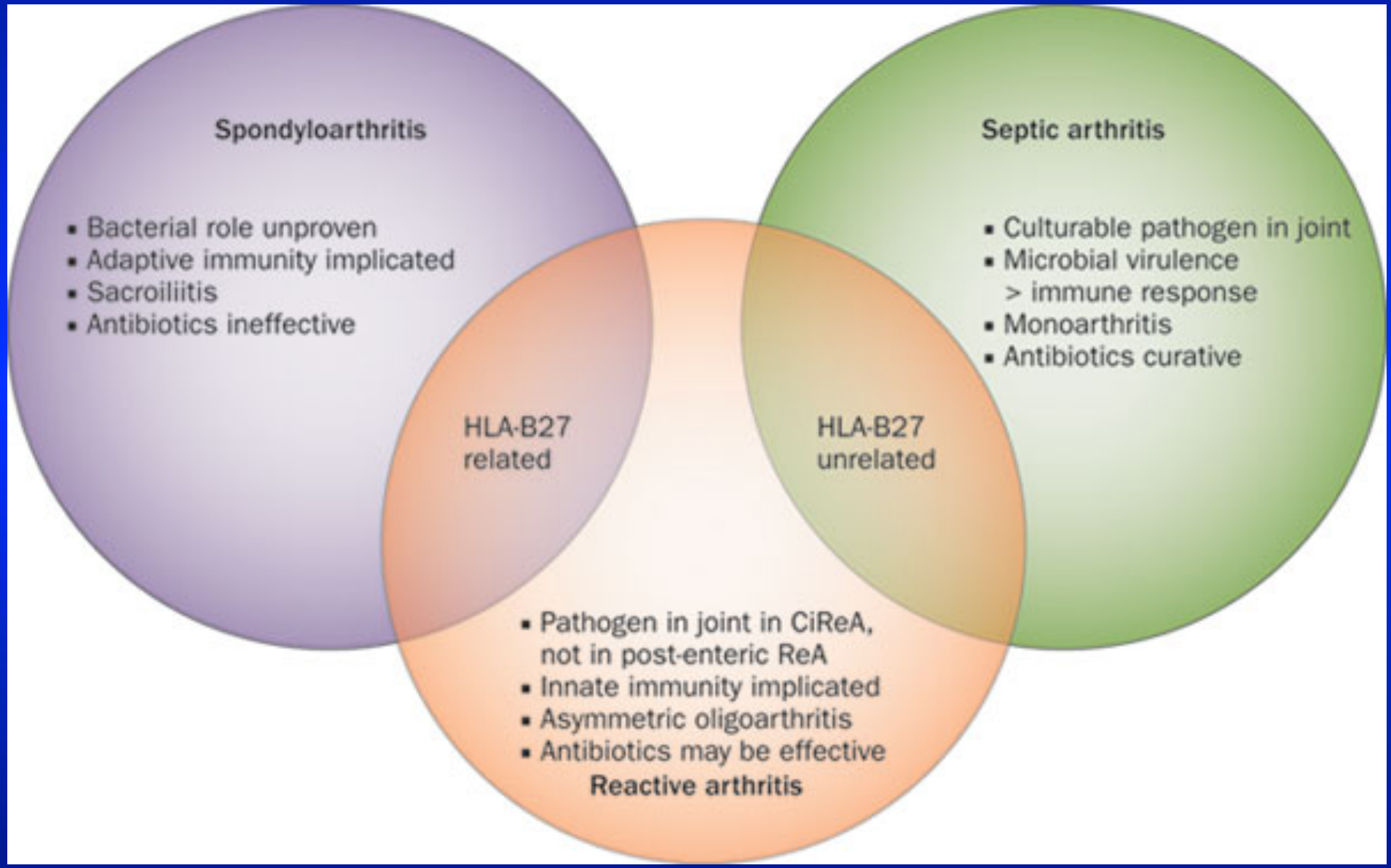
Spondiloarthropathies



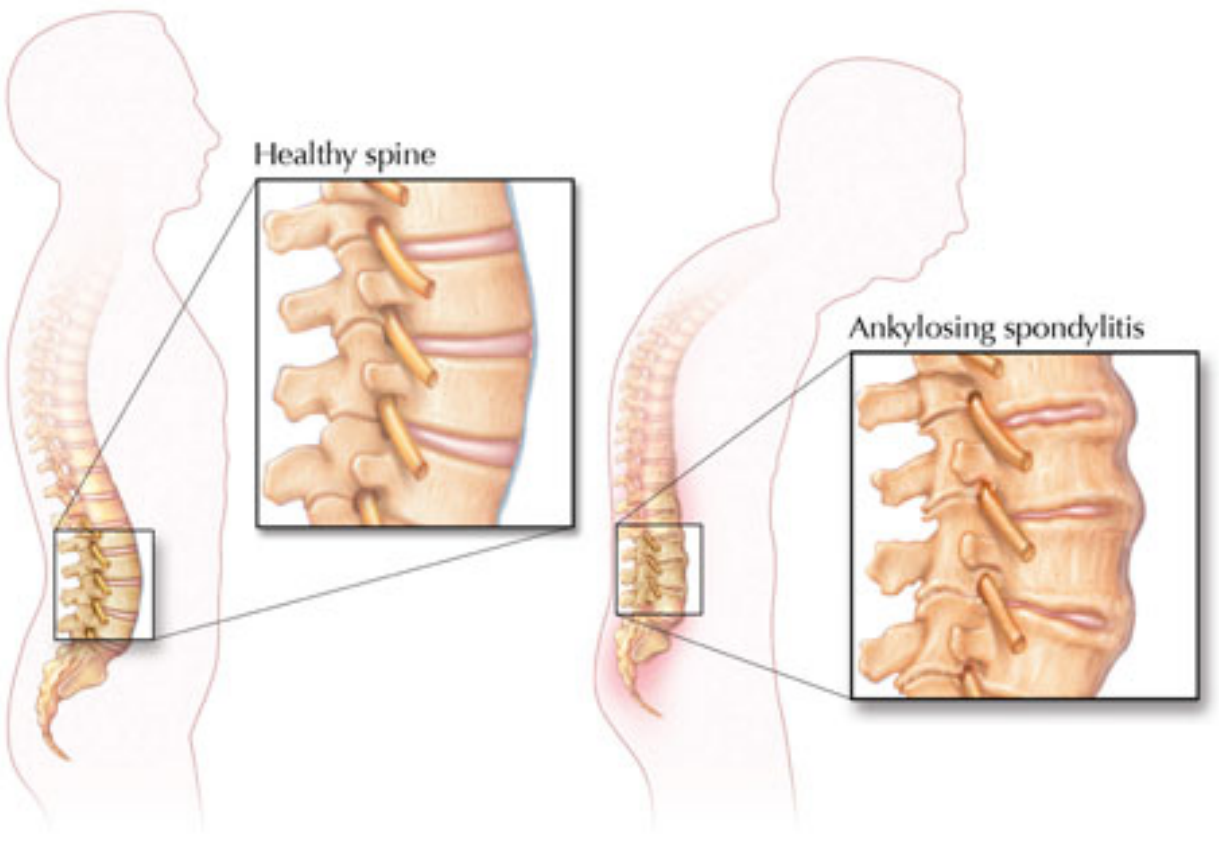
Spondiloarthropathies

Features	Ankylosing spondylitis	Reactive arthritis	Psoriatic arthritis	Enteropathic arthritis
Age of onset	20-30 years	20-30 years	35-45 years	Any age
Male:female ratio	3:1	5:1	1:1	1:1
Peripheral arthritis	Asymmetrical lower extremities	Asymmetrical lower extremities	Any joints	Asymmetrical lower extremities
Spine involvement	Symmetrical sacroiliitis (100%), delicate marginal syndesmophytes: lumbar spine and lower thoracic spine involved initially	Asymmetrical sacroiliitis, bulky marginal syndesmophytes	Asymmetrical sacroiliitis, bulky marginal syndesmophytes: cervical spine involvement most commonly	Symmetrical sacroiliitis, delicate marginal syndesmophytes
Enthesitis	Uncommon	Common	Common	Less common
Dactylitis	Uncommon	Common	Common	Uncommon
Dermatological manifestations	Non-specific	Keratoderma blennorrhagica, circinate balanitis	Psoriasis	Erythema nodosum, pyoderma gangrenosum
Uveitis	Occasional	Common	Occasional	Occasional
Other extra-articular manifestations	Aortic regurgitation, conduction defects, upper lobe pulmonary fibrosis, IgA nephropathy	Aortic regurgitation	Aortic regurgitation	Aortic regurgitation
Familial aggregation	Common	Common	Common	Common
HLA B27	90%	80%	40%	30%

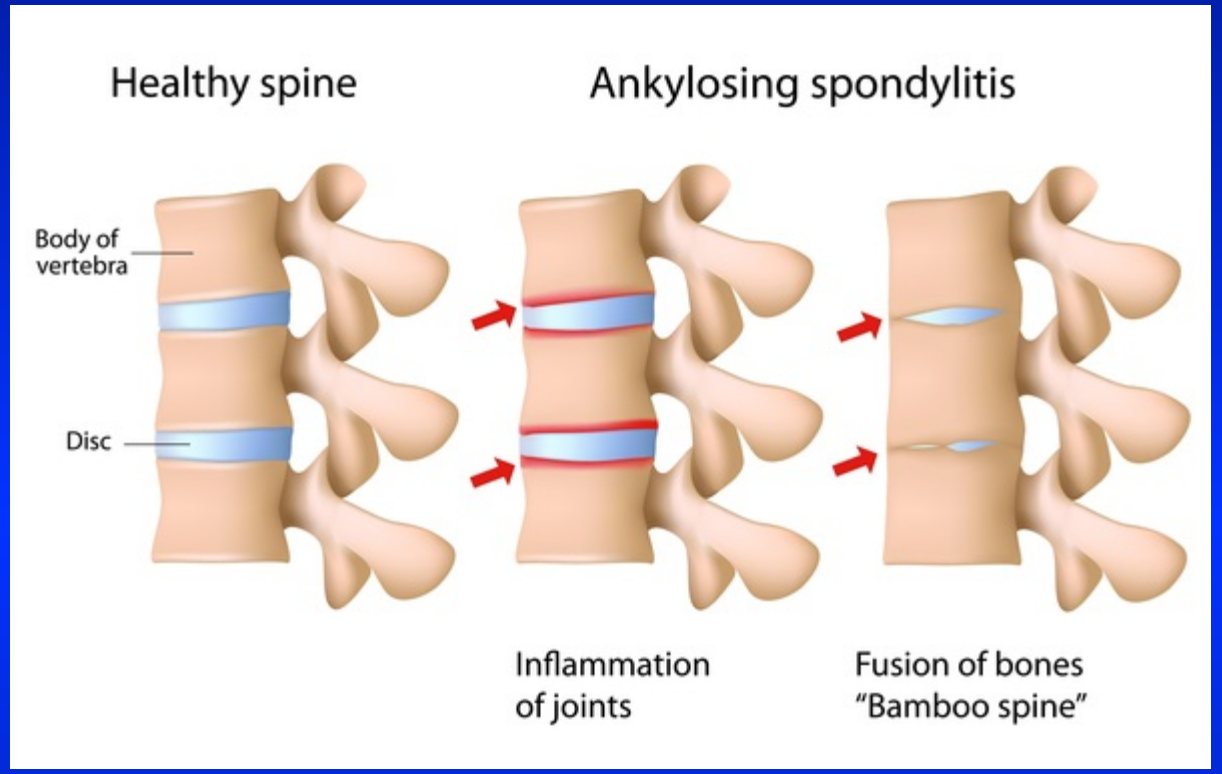
Spondiloarthropathies



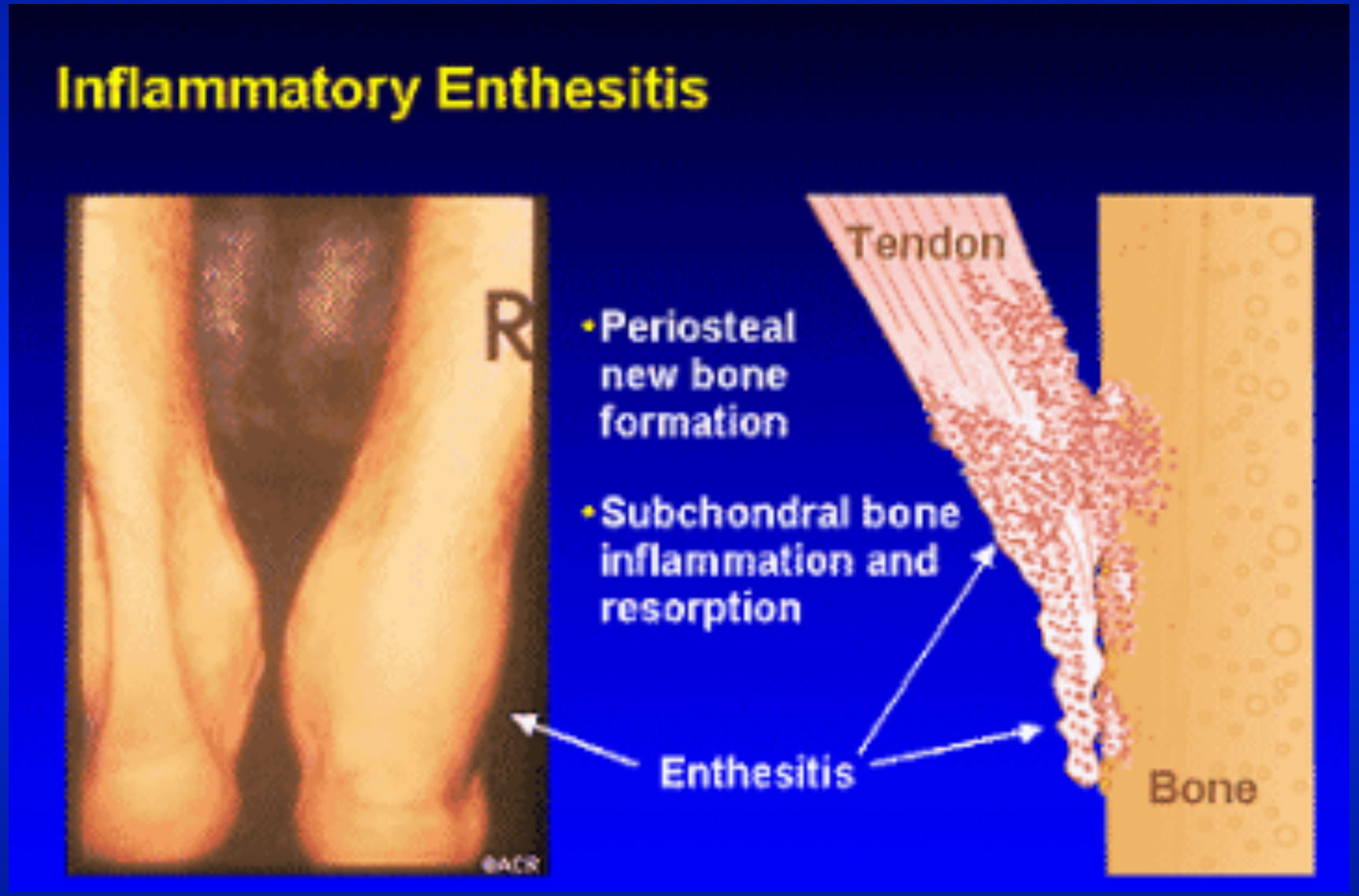
Spondiloarthropathies



Ankylosing spondylitis is the most common of inflammatory disorders called spondylo-arthropathies. Ankylosing spondylitis may lead to fusion between the spinal vertebrae and the sacroiliac joints connecting the spine and pelvis. Left untreated or in advanced stages, the result can be a hunched-forward posture and restricted chest expansion.



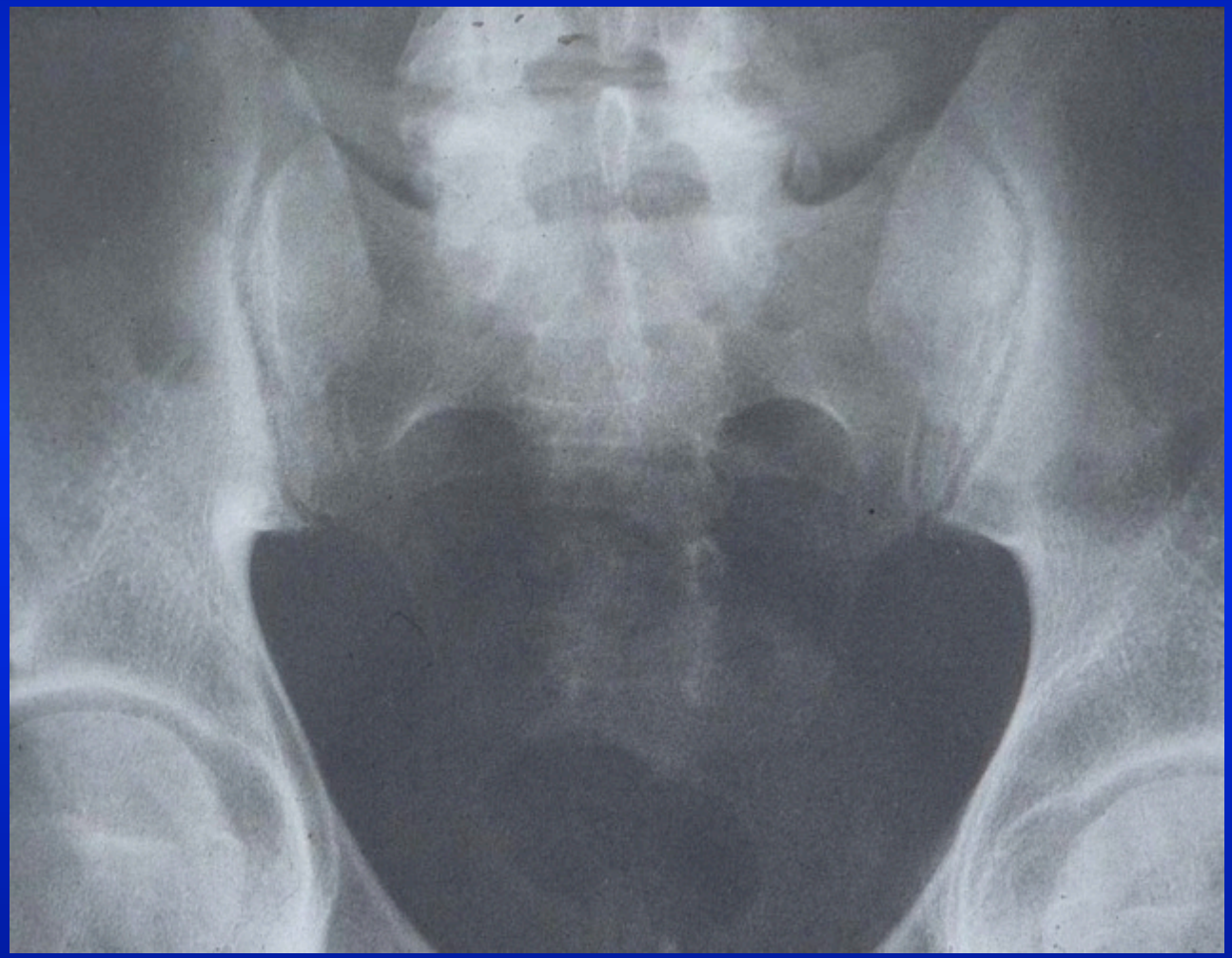
Spondiloarthropathies



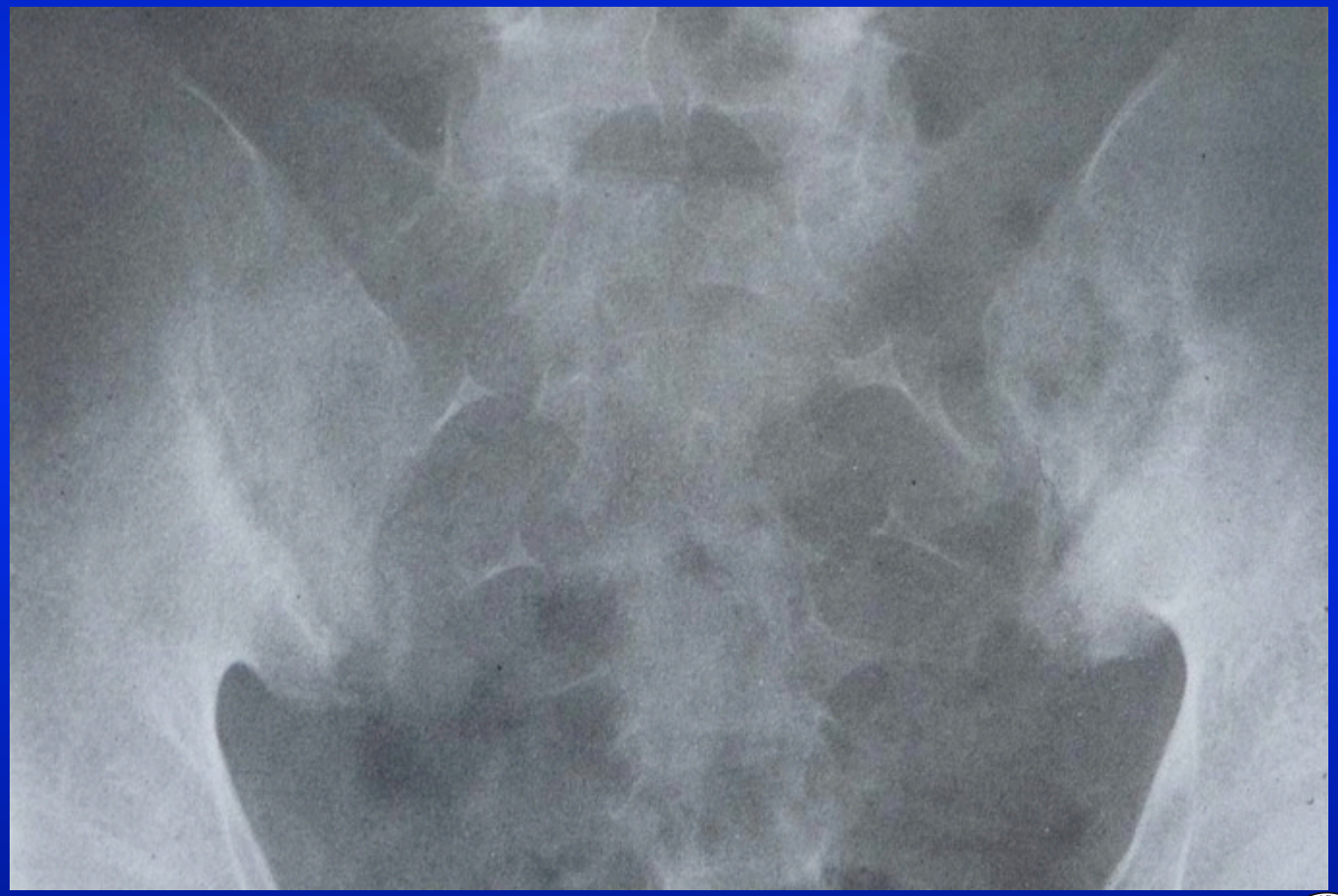
Sacroiliitis

asymmetric localization
of radioactive tracer

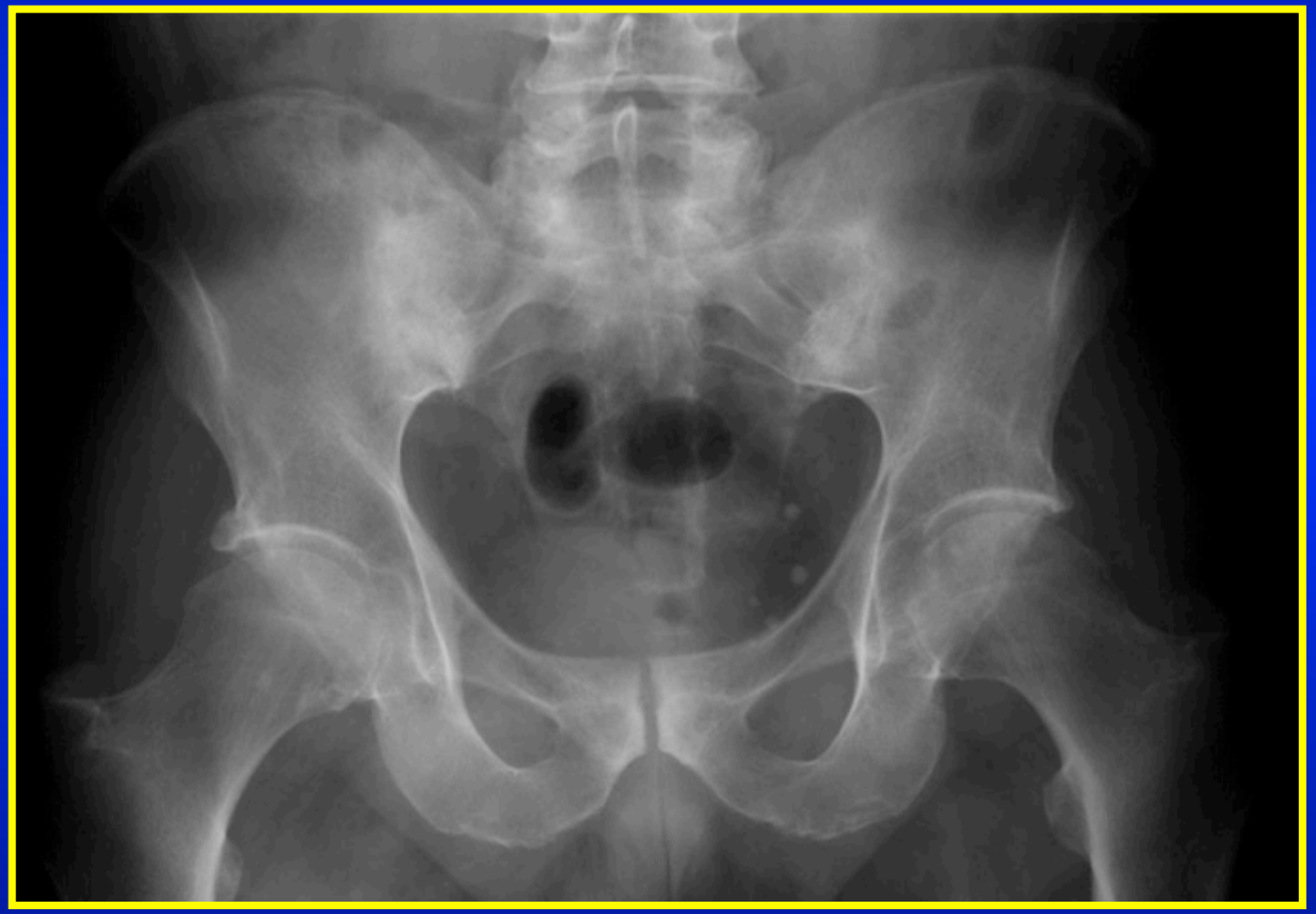
Stage 1



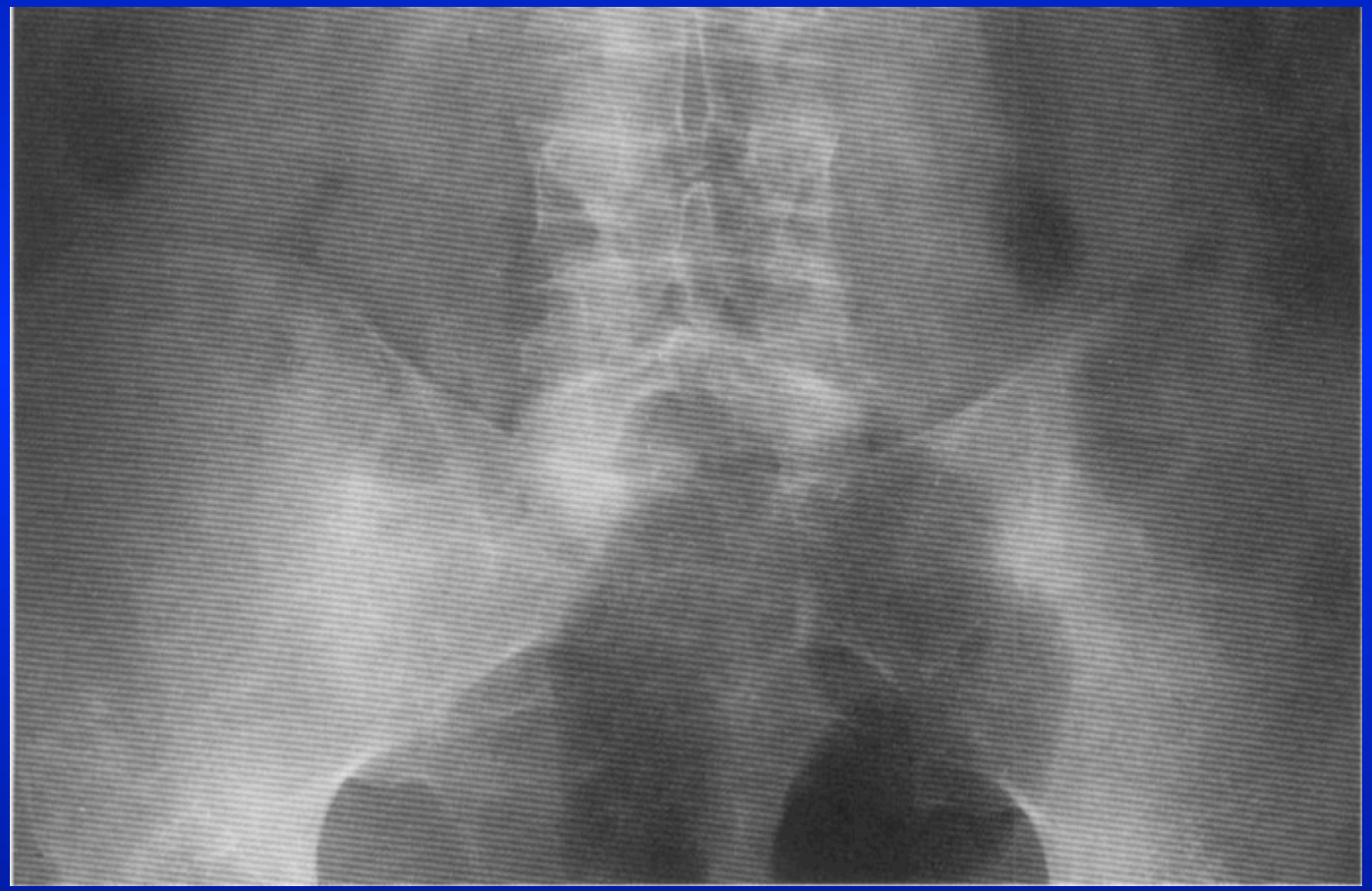
Stage 2



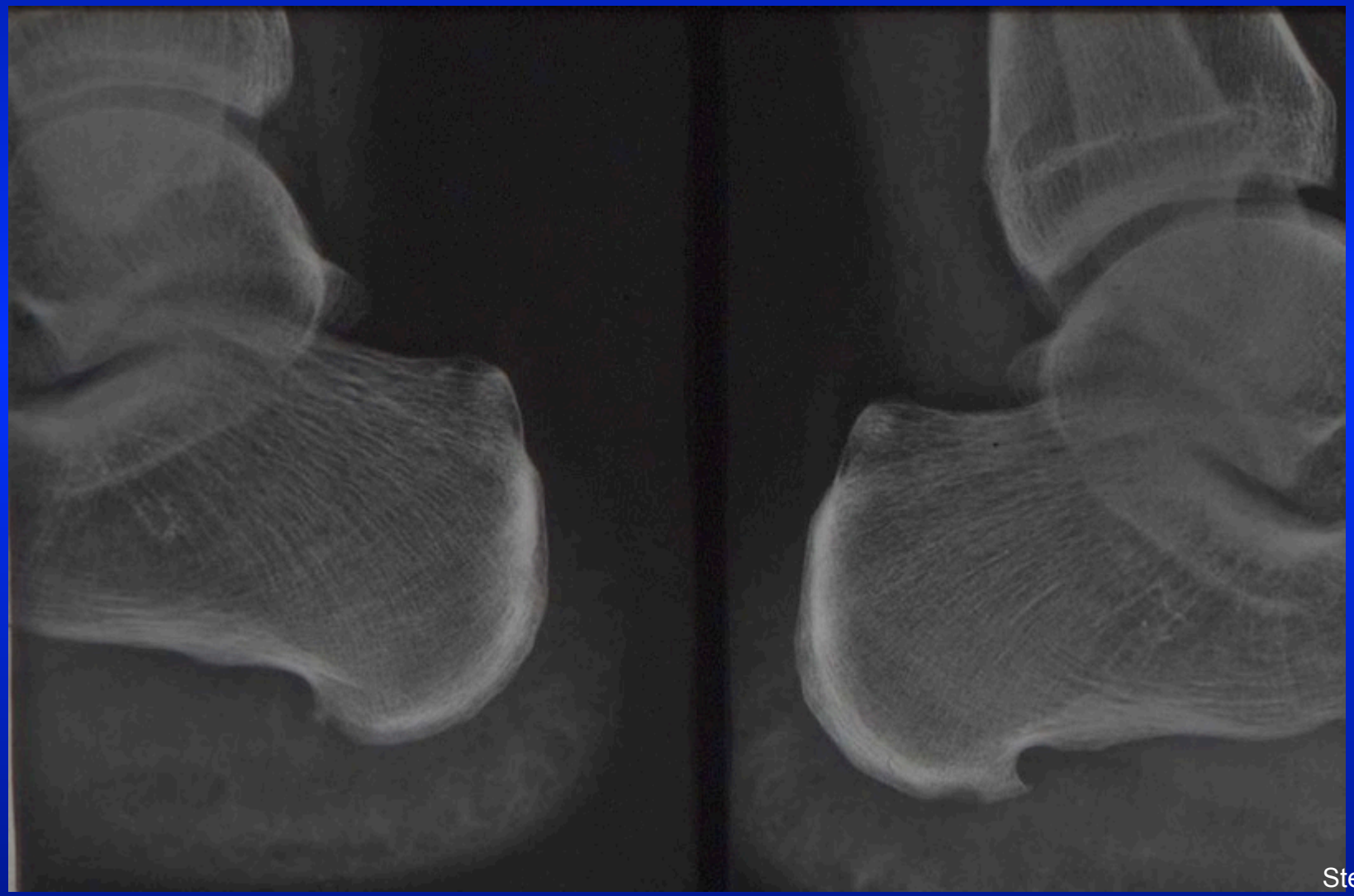
Stage 3



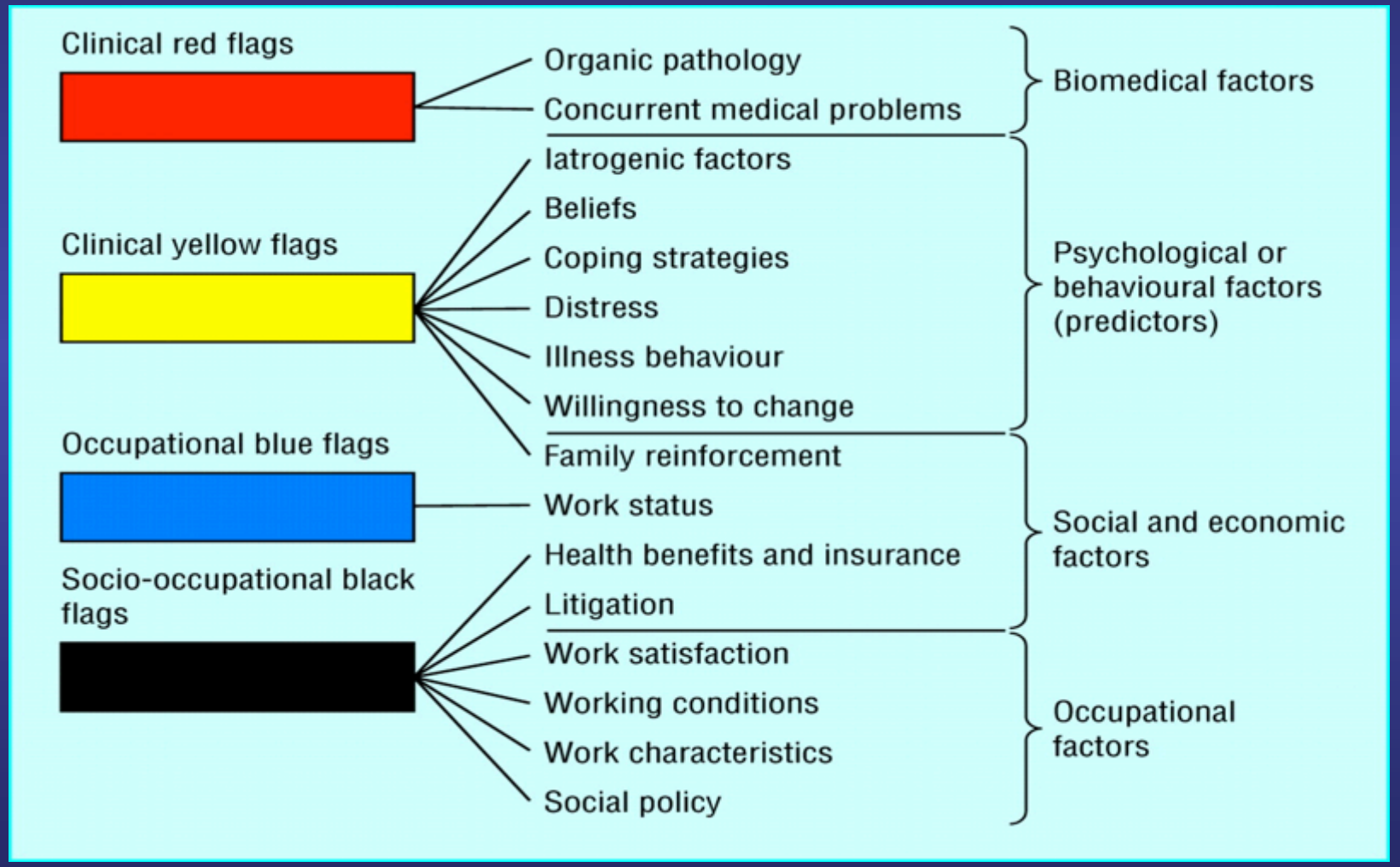
Stage 4



Calcaneous spine



Low Back Pain: *Red Flags*



Spondiloarthropathies: *treatment*

- NSAIDS/COX2
  - symptomatic relief but do not halt disease
- DMARDs – (eg **methotrexate**)
  - some disease modifying effect but not against spinal progression
- **Anti TNF agents**
  - great promise

Contents

Osteoarthritis

Rheumatoid Arthritis

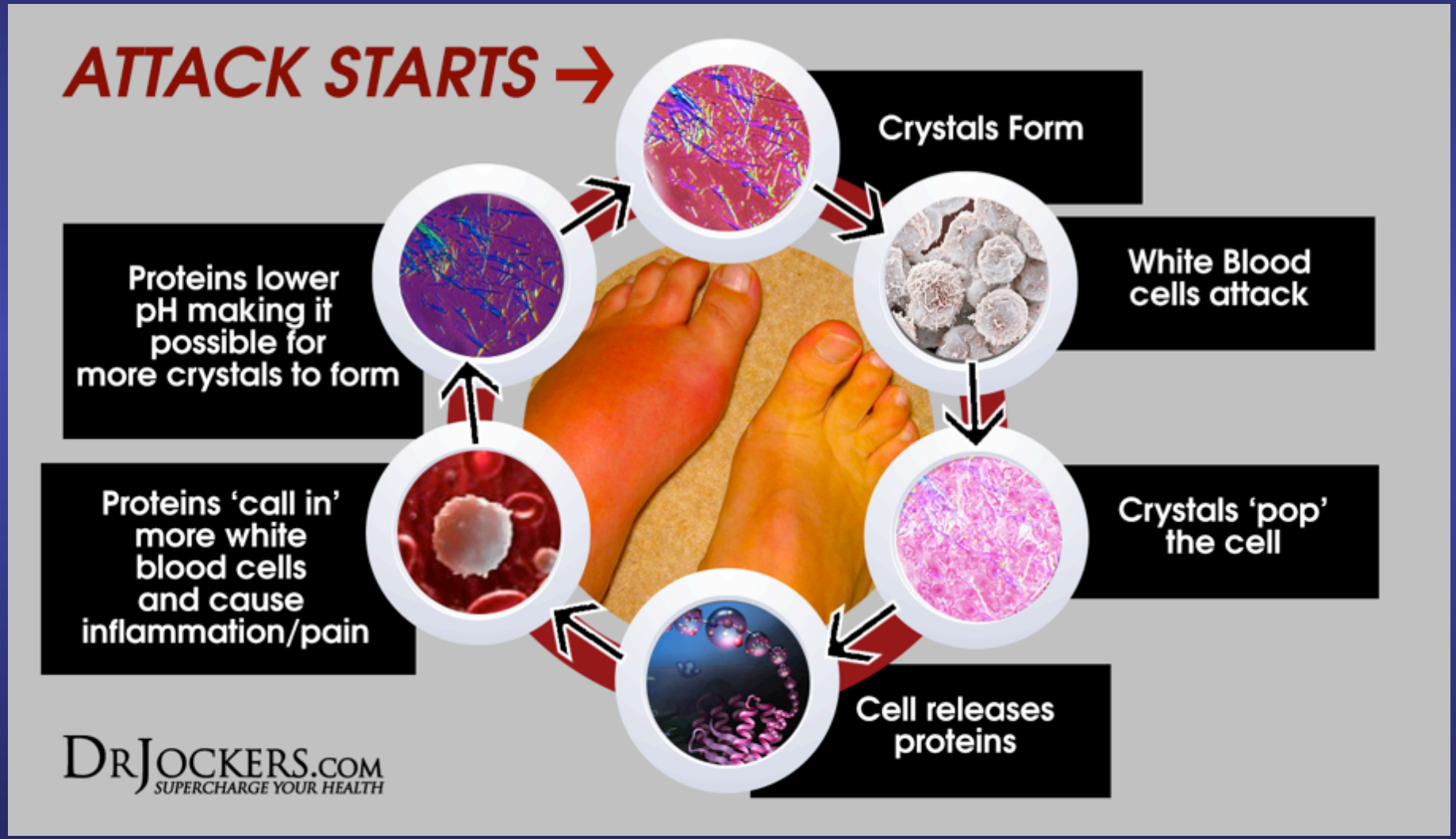
Spondiloarthritides

Microcrystal Arthritis

Microcrystal Arthritis: Acute Gout

- Acute gout is a painful condition that typically affects only one or a few joints.
- The big toe, knee, or ankle joints are most often affected.
- Throbbing, crushing, or excruciating pain
- Joint appears warm and red. Fever may be there.

Acute Gout: *pathogenesis*



Acute Gout (podagra)

Acute Gout (chiragra)

Tophaceous Gout

Gout: *dietetic remedies*

FOOD THAT SHOULD BE AVOIDED DURING GOUT

1

Limit the intake of foods that stimulate the production of uric acid such as fatty fish, shell fish, meat, eggs and caffeine. It increases the production of uric acid.

2

During acute attack white flour, yeast products like bread should be avoided.

3

Do not consume leafy vegetables like spinach, cabbage, brocoli etc.

4

Avoid alcohol- It increases the production of uric acid.

5

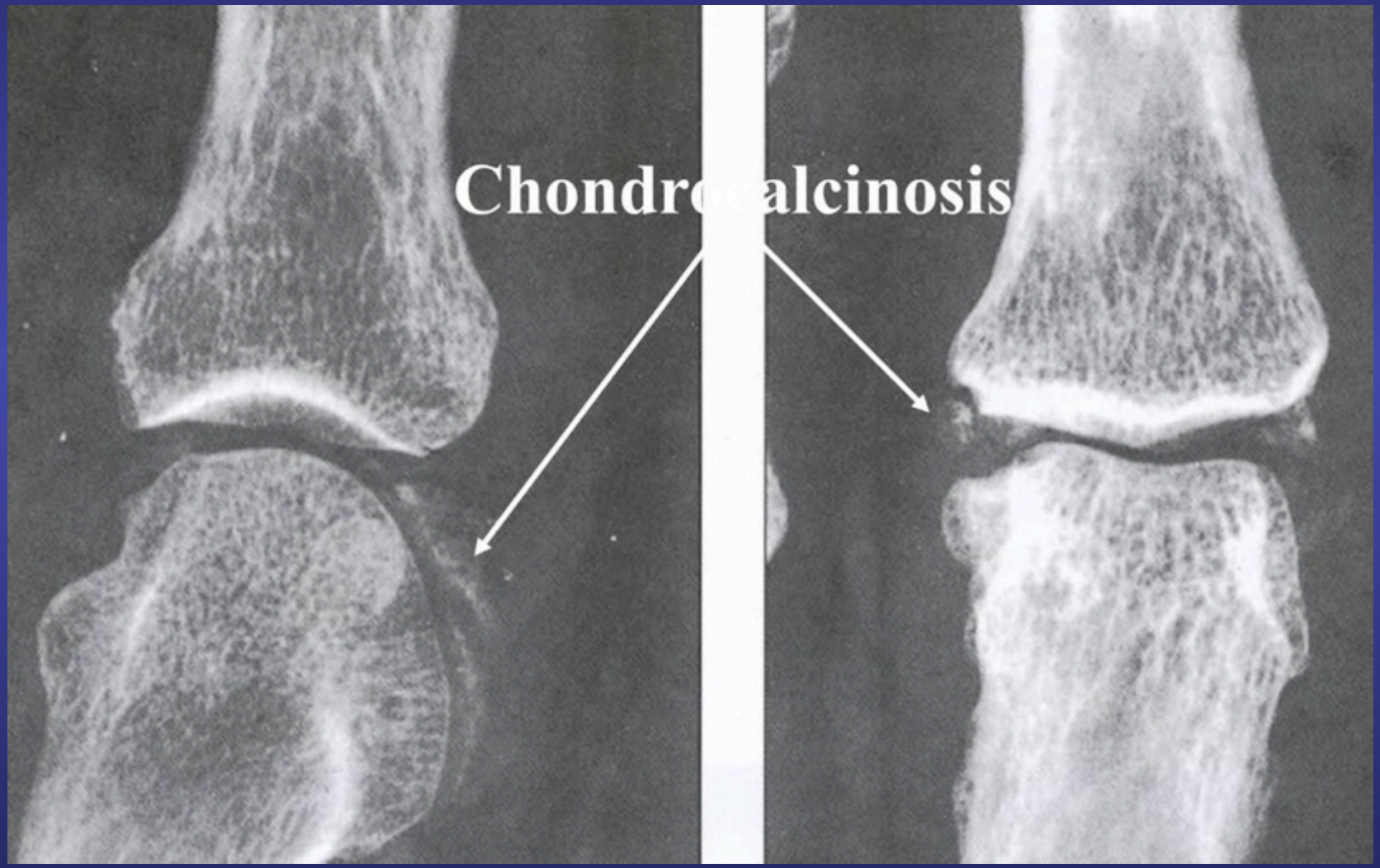
Keep away yourself from cakes, pastries, sugar etc.

Gout: *therapy*

- NSAIDs — inflammation and pain
- COLCHICINE — pathogenesis
- ALLOPURINOL — prevention and pathogenesis
- FEBUXOSTAT — prevention and pathogenesis
- LESINURAD — uricosuric effect
- (avoid steroids !)

Microcrystal Arthritis*: Chondrocalcinosis*

Microcrystal Arthritis*: Chondrocalcinosis*



Chondrocalcinosis*: therapy*

- NSAIDs
- COLCHICINE
- STEROIDS

LOW BACK PAIN

Low Back Pain: *Key Concepts*

LBP is an uncomfortable and painful sensation in the lumbar and buttock regions originating from neurons near or around the spine that are injured or irritated by one or more pathologic spine processes or attributed as lumbar/ buttock pain but provoked by extra-spinal disorders.

LBP represents the most frequent clinical situation in the developed countries, second only to common cold syndrome. In the USA, LBP is responsible for more than 5% of all physician office visits, and it is one of the most common causes of pain and impairment in adults.

Low Back Pain: *Key Concepts*

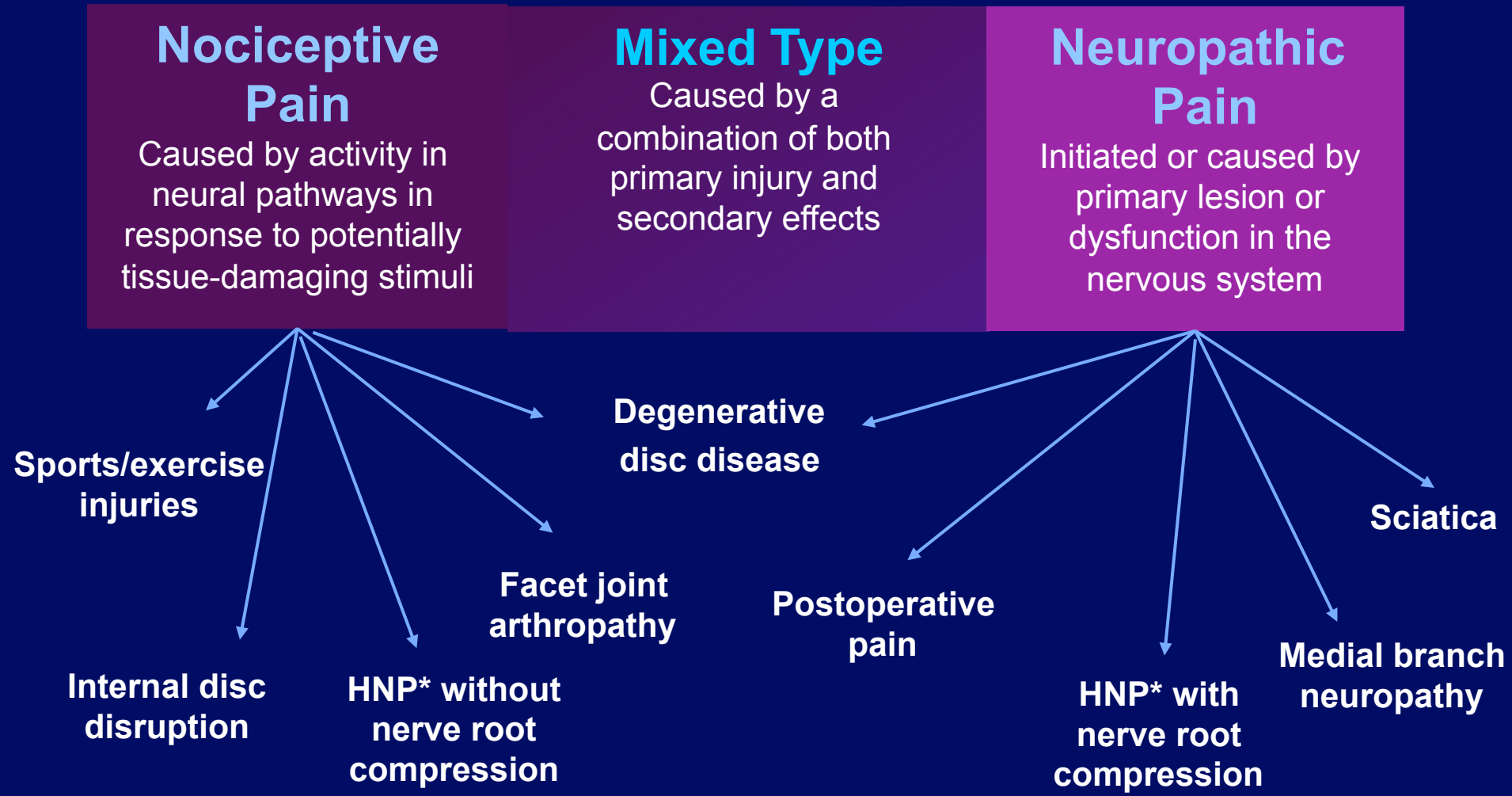
LBP often presents itself as an acute attack (**acute LBP**, aLBP), and it is most common in the age range from 30 to 50 years. The natural history of an aLBP concludes with complete recovery in almost 90% of cases after 8 weeks, but a smaller percentage have repeated attacks as well as develop **chronic LBP** (cLBP). In this case, cLBP leads to a huge economic burden in terms of workday loss and medical resource usage.

The majority of patients shows a **mechanical LBP** (mLBP) that does not require any investigation and/or specific therapy. By the way, the responsibilities of physicians are to identify the minority of patients affected by **systemic LBP** (sLBP): in other words, is mandatory to reveal and to study the more serious and severe or potentially dangerous sLBP, not only for *quoad valetudinem* (in terms of quality of life) but even also for *quoad vitam*.

Natural History of LBP

- **Acute LBP**
  - inflammatory or neuropathic injury
  - resolves spontaneously with minimal treatment
- **Intermittent, relapsing LBP**
  - more challenging diagnostic and treatment dilemma
  - precipitates symptomatic care and more aggressive interventions aimed at specific underlying pathology
- **Unremitting, recurring chronic LBP**
  - structural, neurophysiological, and biopsychosocial pathology
  - requires management at all these levels
  - major public health problem

Nociceptive *vs* Neuropathic LBP



*Herniated nucleus pulposus.

History

- **Any evidence of systemic disease?**
  - Age (especially >50), hx of cancer, unexplained weight loss, chronic infection
  - Duration
  - Presence of nocturnal pain
  - Response to therapy
  - Many patients with infection or malignancy will not have relief when lying down
    - note for arthritis patients – young age, nocturnal pain and worsening with rest are common in AS

Therapy

- **Chronic low back pain**
  - **intensive exercise** improves function and reduces pain, but is difficult to adhere to
  - **anti-depressants**: many with chronic LBP are also depressed
    - ? maybe for those without depression (TCA)
  - **opioids**
    - small RCT showed better effect on pain and mood than NSAIDs
    - no improvement in activity
    - side effects: drowsiness, constipation, nausea

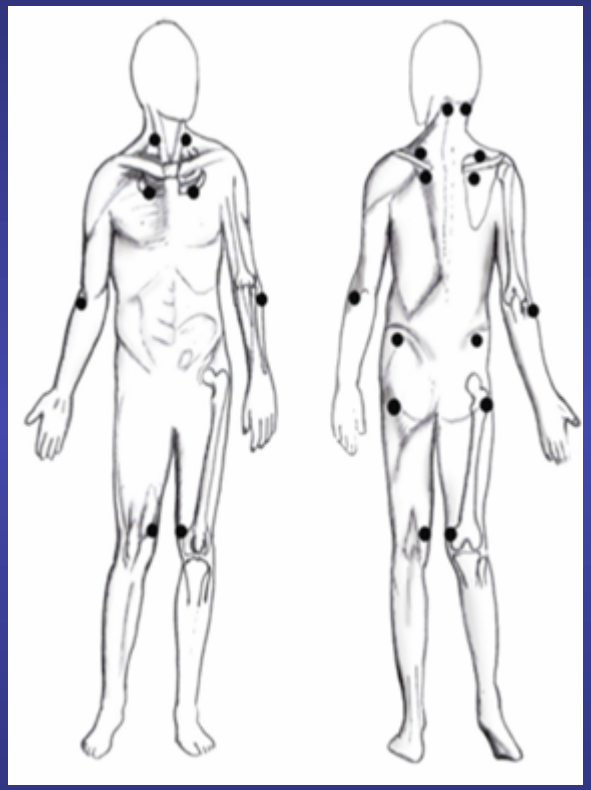
FIBROMYALGIA

Fibromyalgia

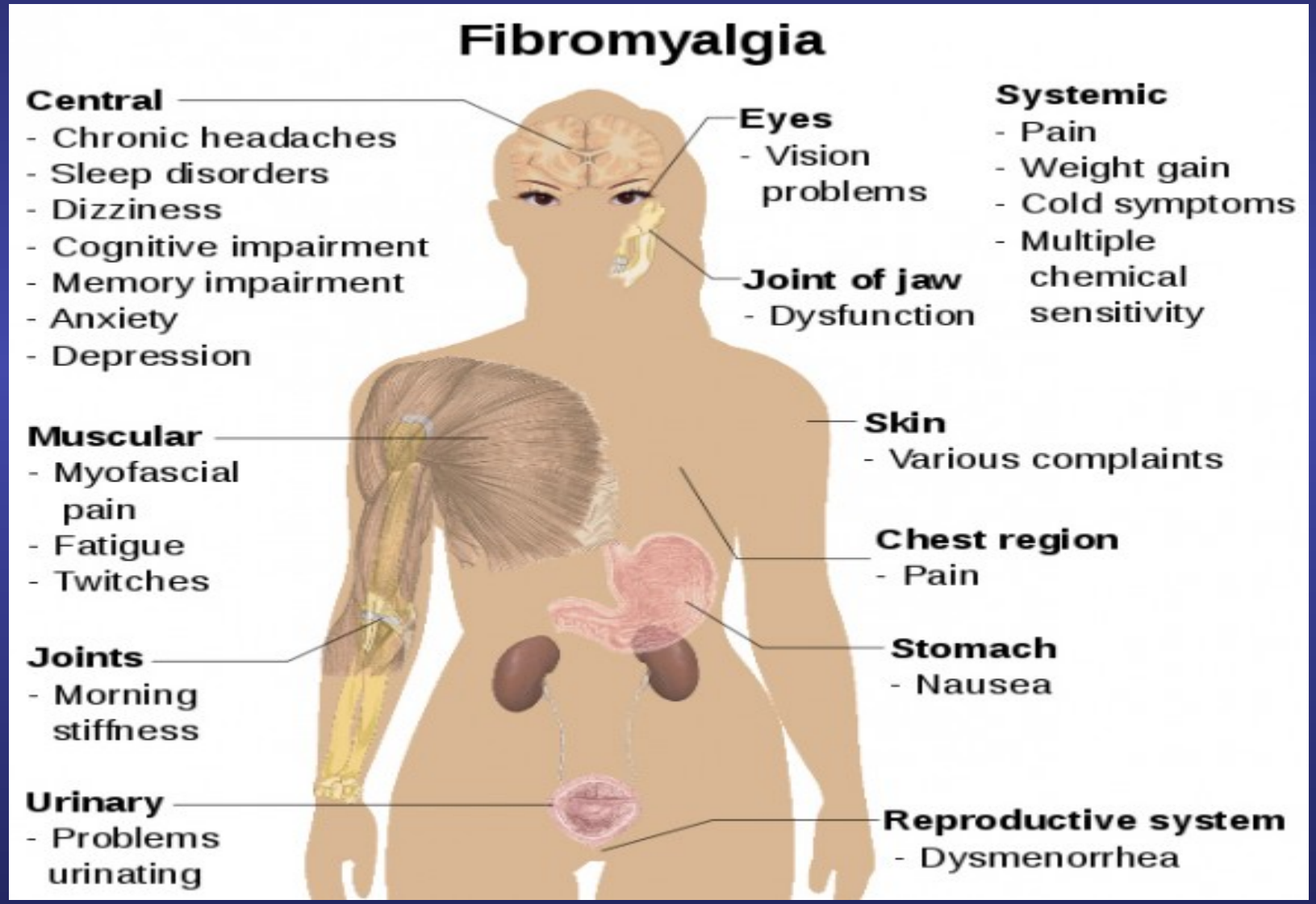
What Is Fibromyalgia?

- Fibromyalgia (FM) is a condition of chronic widespread pain
  - Primary components are widespread pain, body aches, and tenderness
    - Fibromyalgia patients often have heightened sensitivity to pain (hyperalgesia); in addition, nonnoxious stimuli may result in pain (allodynia)
  - Other core symptoms include sleep disturbance and fatigue

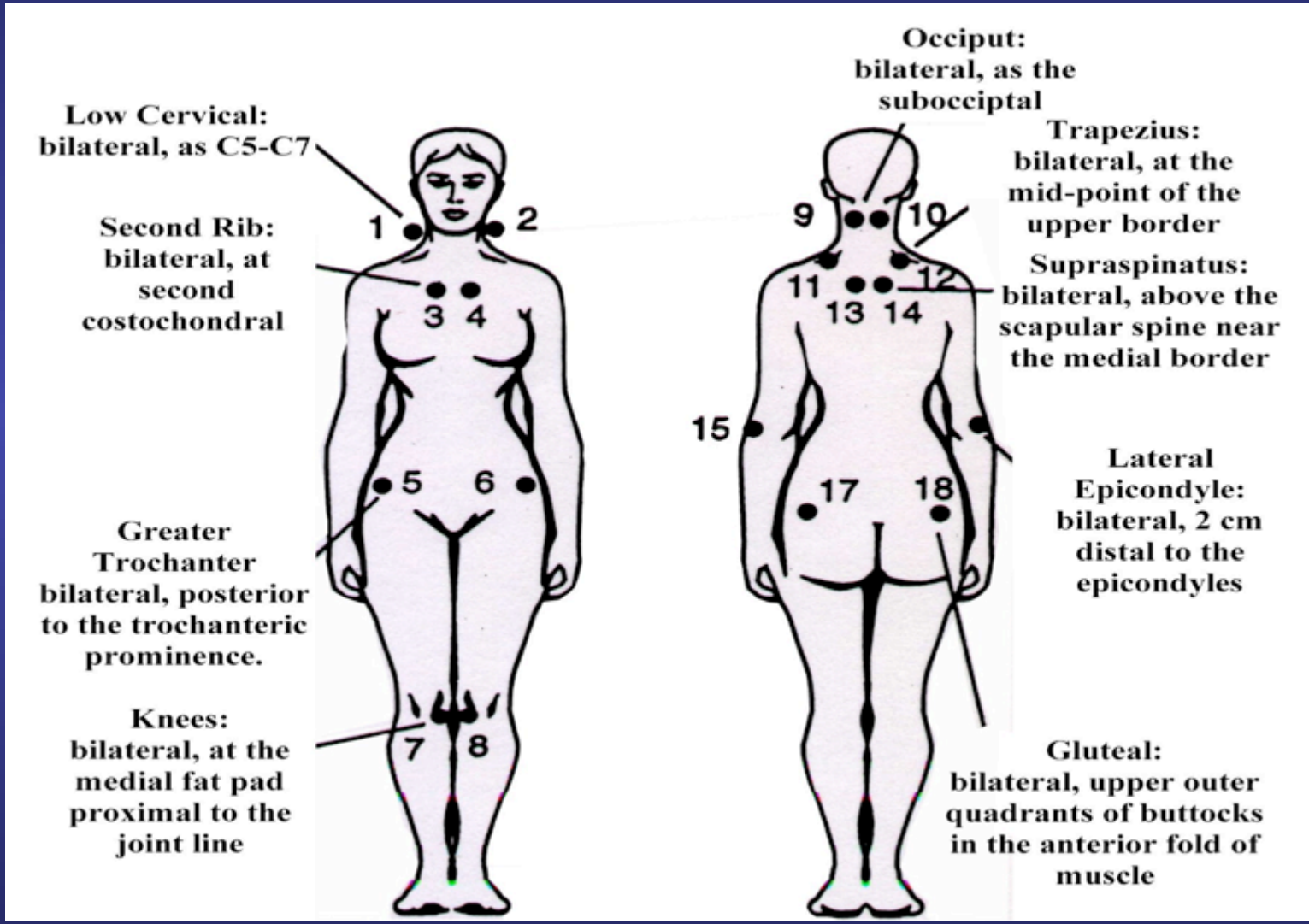
Burckhardt CS, et al. APS Clinical Practice Guideline Series, No.4. Glenview, IL; 2005. Henriksson KG. *J Rehabil Med.* 2003;(Suppl 41):89-94. Staud R, et al. *Nat Clin Pract Rheumatol.* 2006;2:90-98. Wolfe F, et al. *Arthritis Rheum.* 1990;33:160-172. Gracely RH, et al. *Arthritis Rheum.* 2002;46:1333-1343.



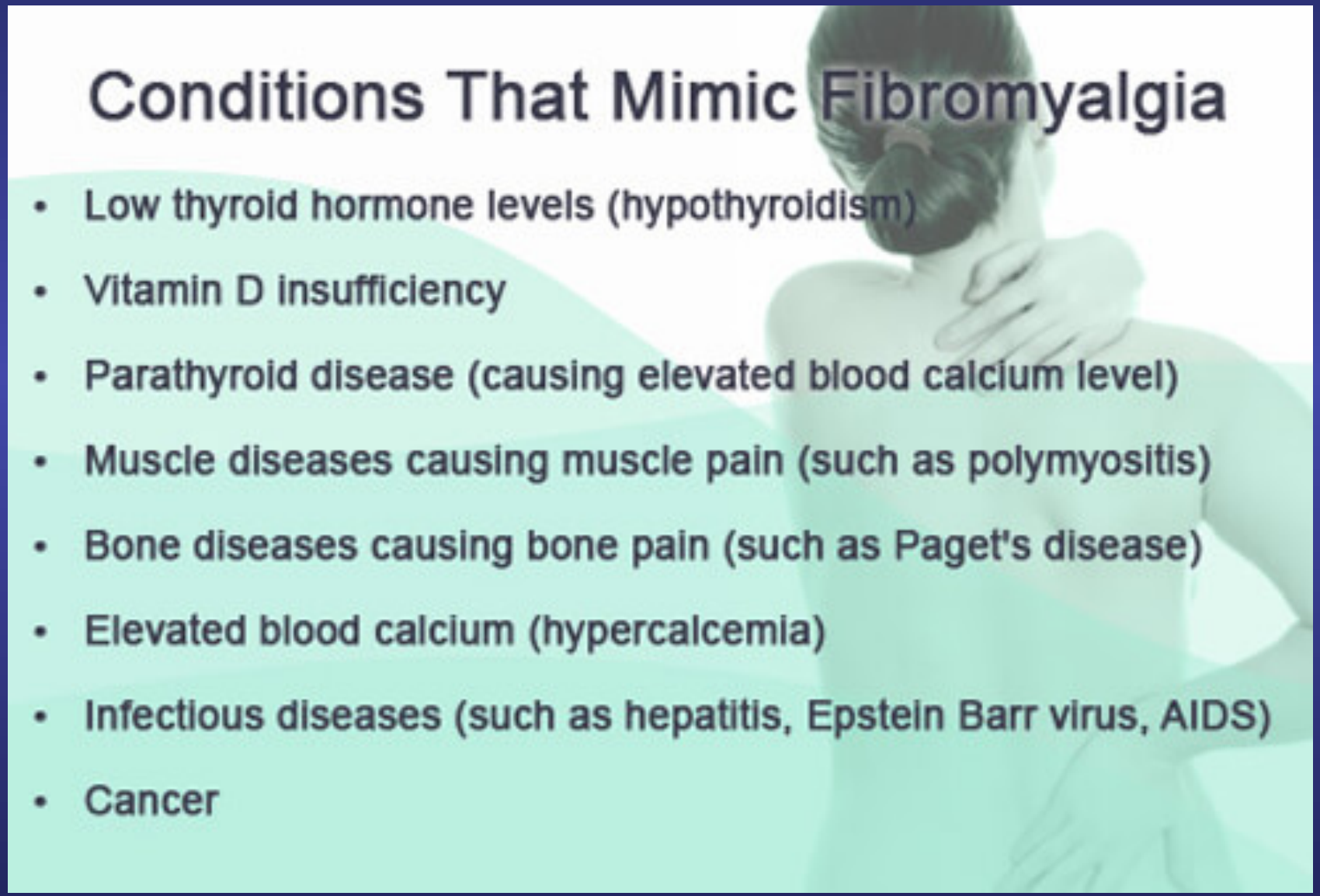
Fibromyalgia: *symptoms*



Fibromyalgia: *tender points*



Fibromyalgia: *differential diagnosis*

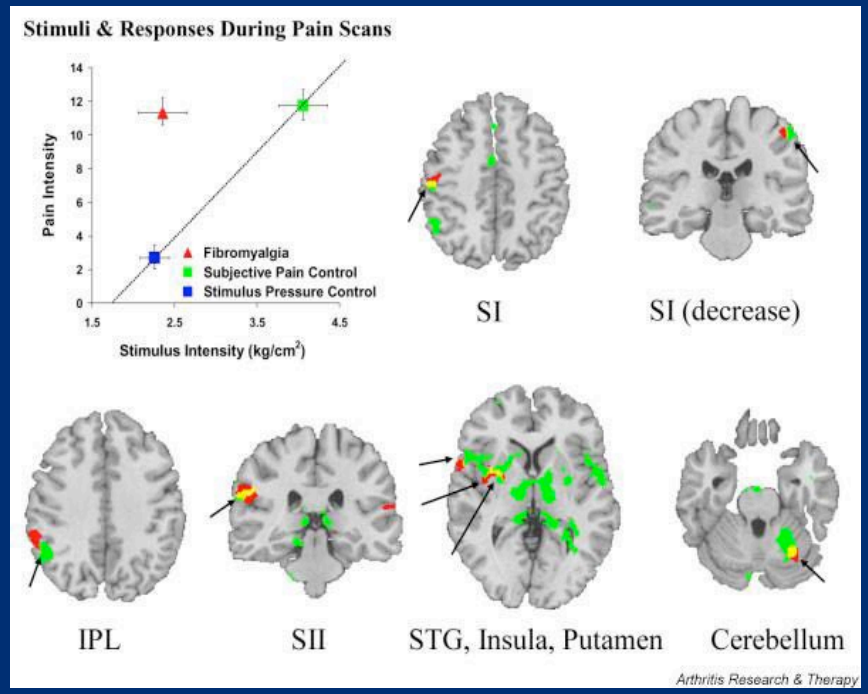


PATHOGENESIS OF FIBROMYALGIA

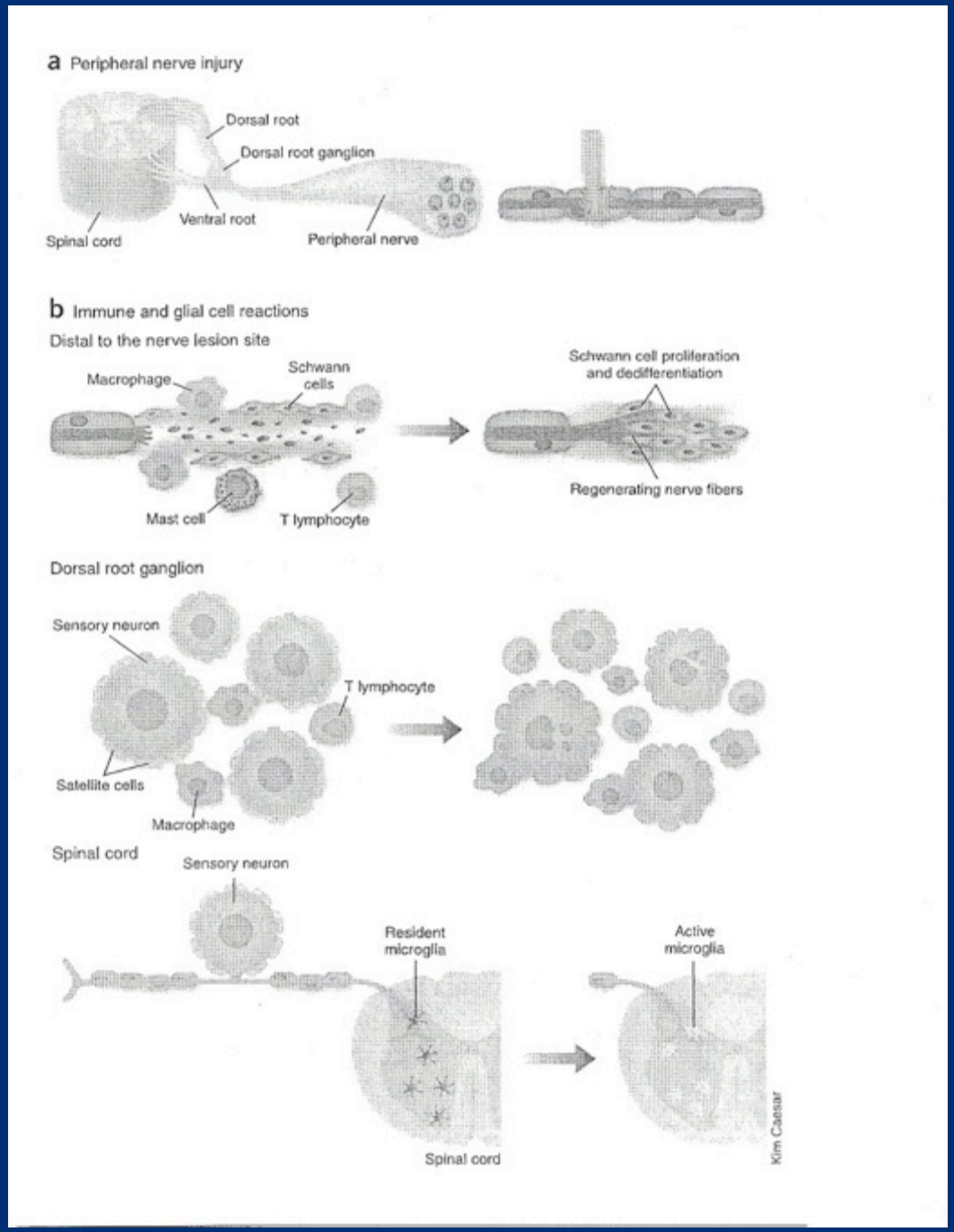
disfunctional sdr due to modified central sensitization

pro-algogenic CKs (IL-1β, IL-6, TNF-α)
neurotrasmitters with nociceptive input
(substance-P, NGF, BDF)

neurotrasmitters of inhibitory way
discending pain control systems
(serotonin, norepinephrine, dopamine)



Gracely, 2002

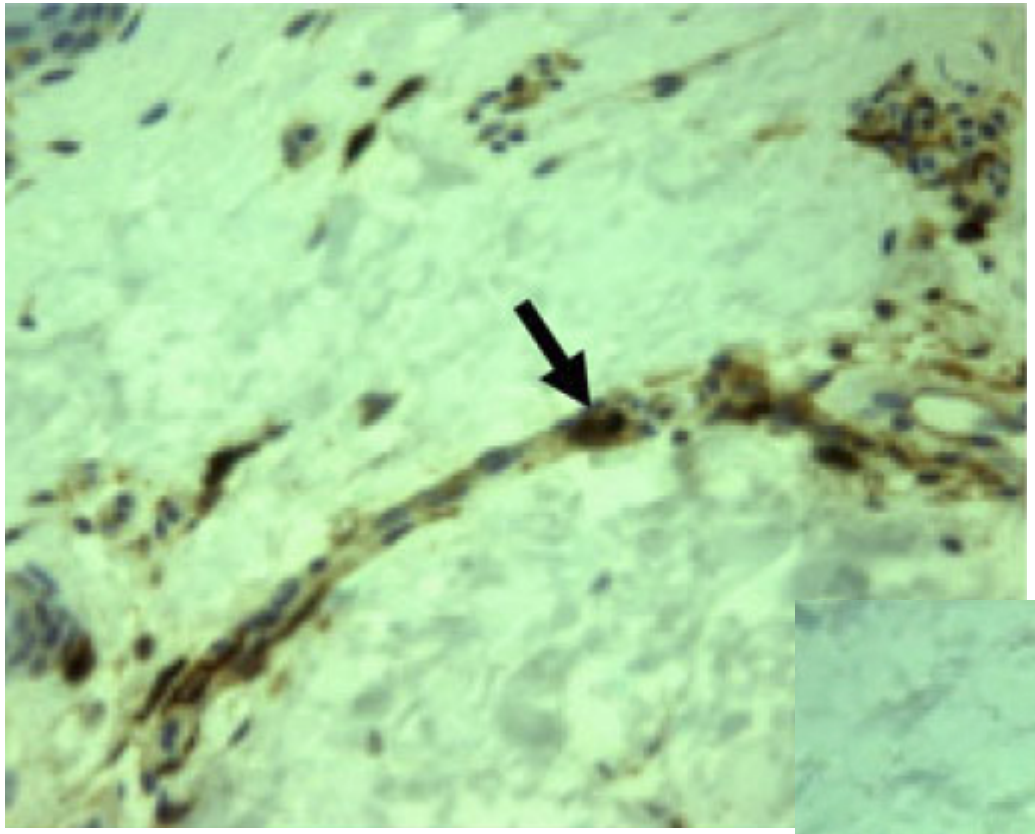


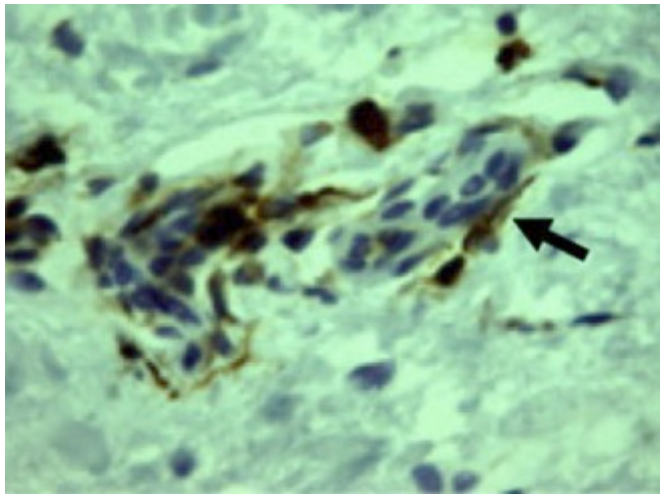
Immune and glial cell responses to peripheral nerve injury

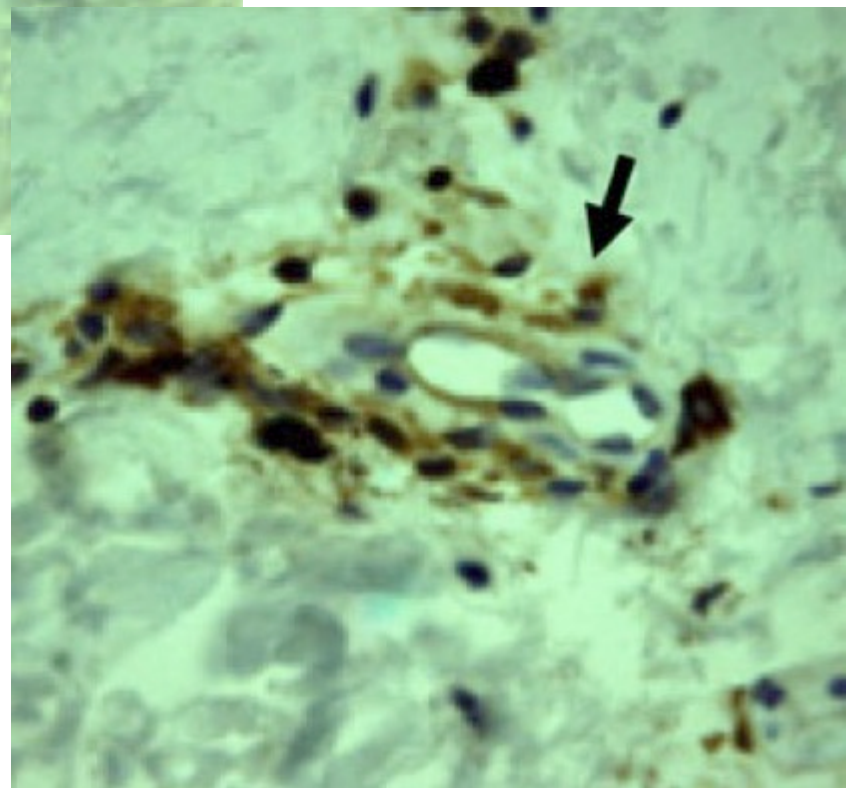
a) recruitment and activation of immune cells

b) glial cell reactions

- *distal to the lesion*
- *dorsal root ganglion*
- *spinal cord*







In FM the mastocytes are associated with blood vessels close by tender points

Stefano Coaccioli, unipg

Fibromialgia: *red flags*