

Rheumatoid Arthritis: Time is of Essence

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Medicine Review Course
College of Physician, Singapore**

Case

A 56 year Malay woman (Malay speaking only, BMI 31 kg/m²) with history of OA knees presents with persistent B knee pain for 2 months. Stiffness throughout the day, pain is worse on walking. Her pain is temporarily better with NSAIDs.



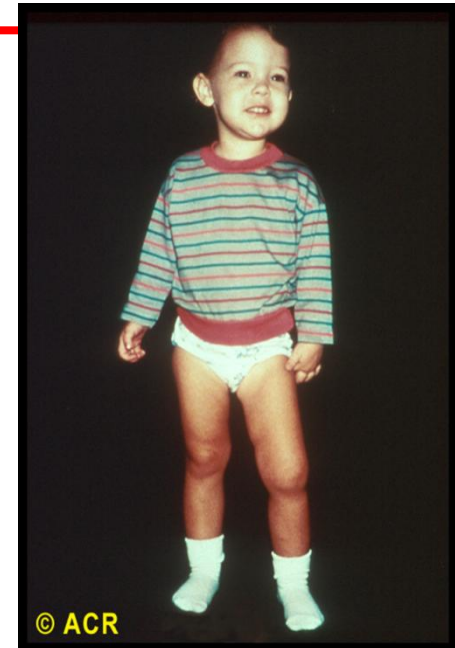
What are your thoughts?

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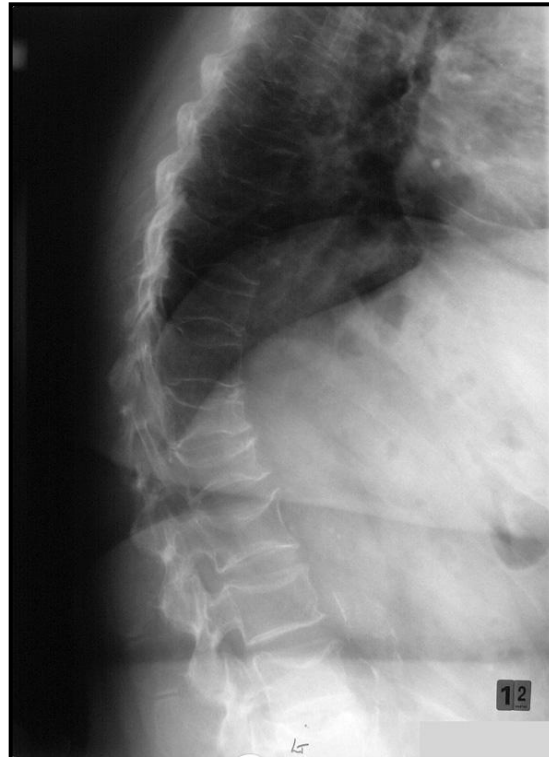
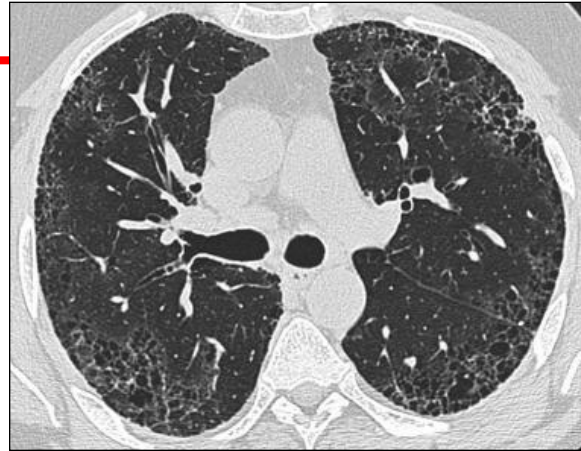
Objectives

- Why is early diagnosis and treatment of RA important
- How to diagnose RA early
- How to initiate treatment of RA
- What can you in comanaging patients with RA

RA is a painful and destructive arthritis



RA is a Systemic Disease



Effect of RA on Quality of Life, socioeconomic impact

Radiological evidence of joint damage¹

Within 0–2 years

- Approximately 1/3 stop work within 2 years of onset, increased prevalence thereafter

50% maximal radiological damage is observed²

Within 5 years

- High cost in the form of work-related disability, time off from work, need for joint replacement surgery

50% become disabled²

Within 10 years

19% became severely disabled³

Within 20 years

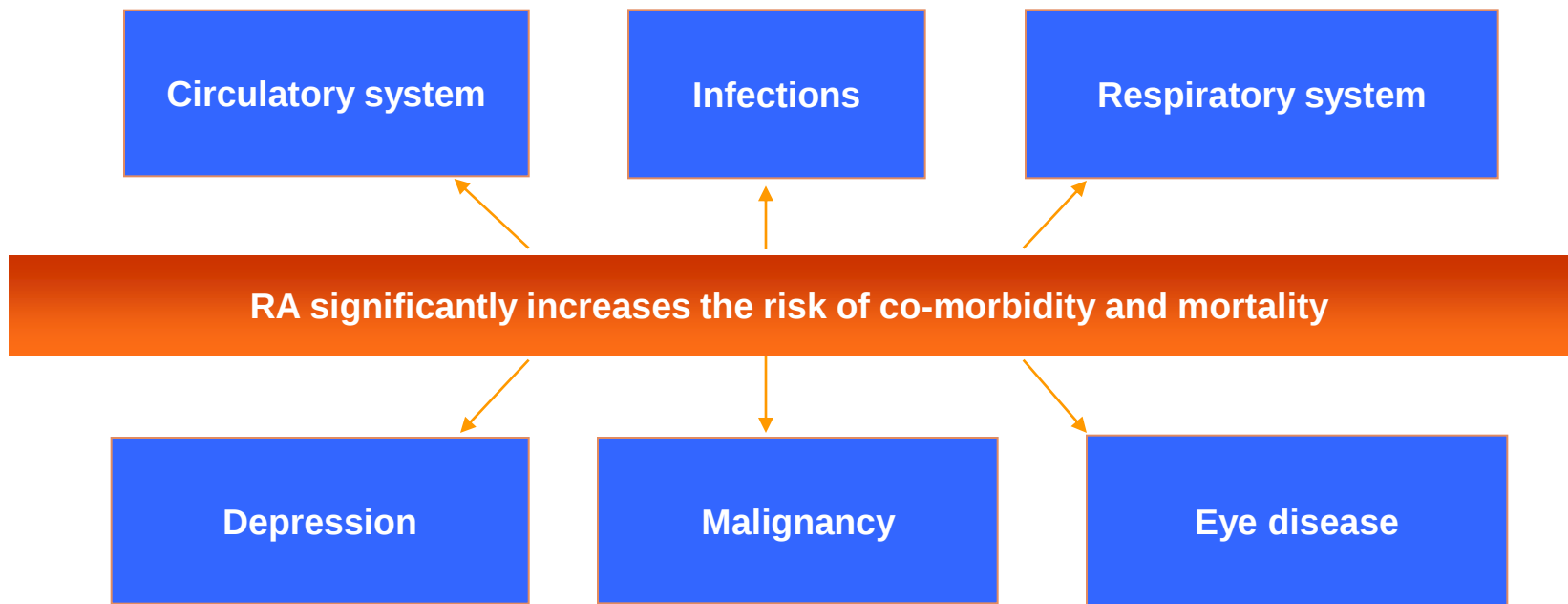
Ref 1. Dixey et al. Journal of Rheum. 2004. 31 sup69; 48-54

Ref 2. Pincus T. Rheumatic Disease Clinics of North America .1993. 21; 123-151

Ref 3. Scott et al. Lancet. 1987. 1108-1111

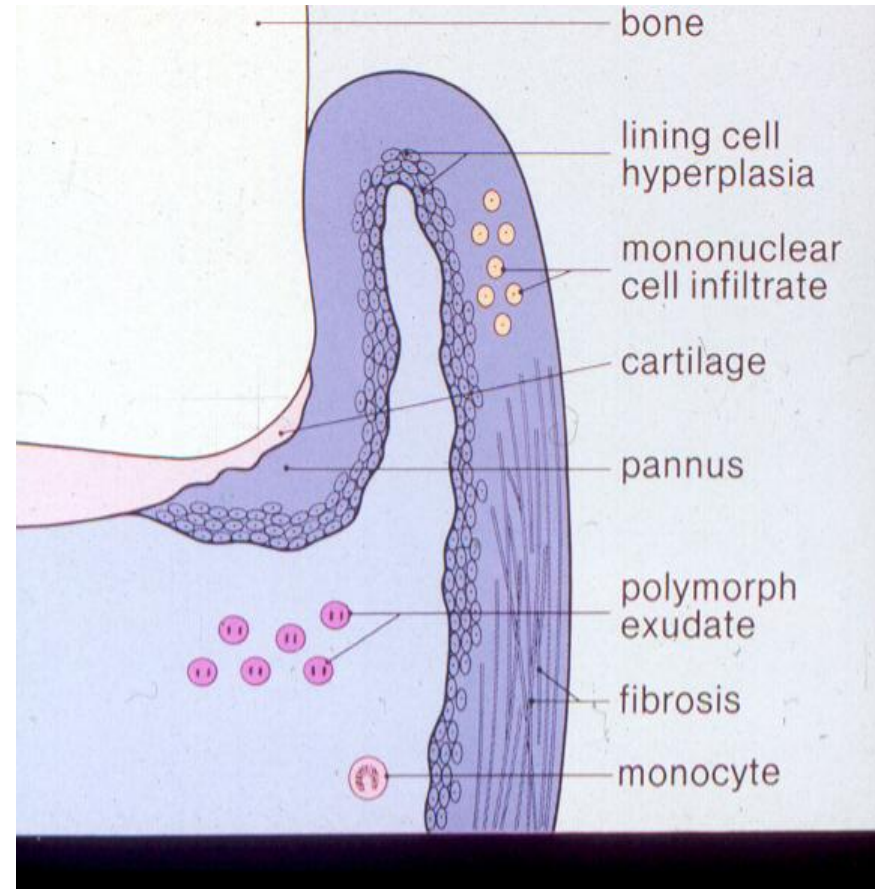
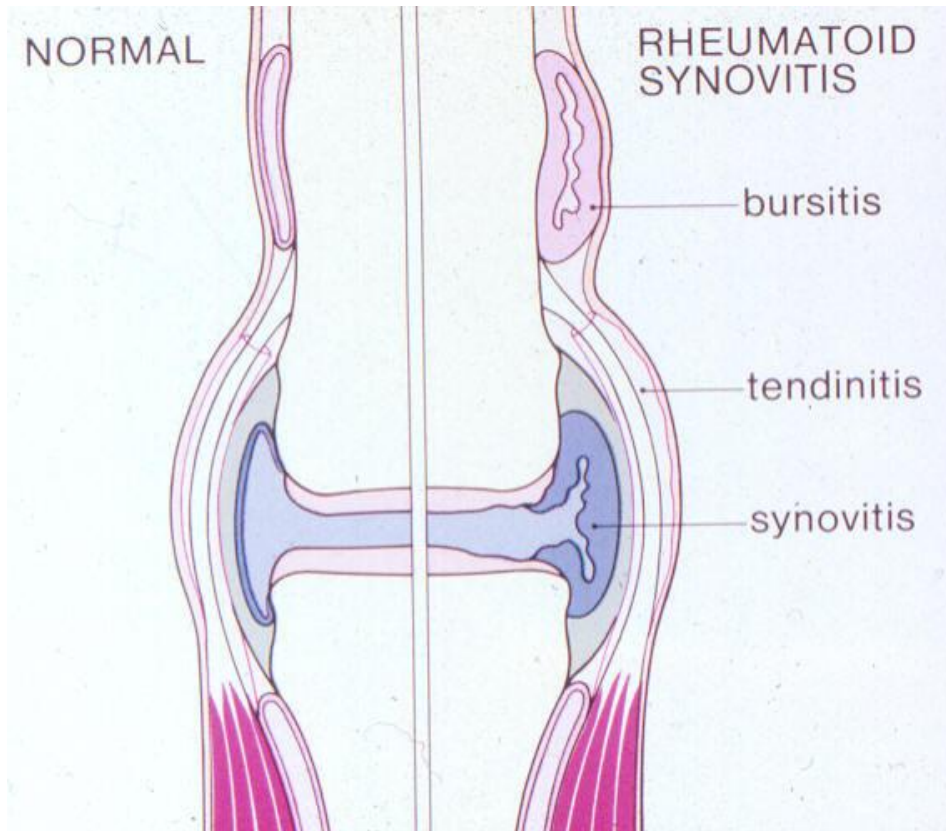
Co-morbidity and Mortality

- Patients with RA have a significantly increased risk of co-morbidity and mortality compared with the general population
- Life expectancy is reduced by 6 to 10 years¹



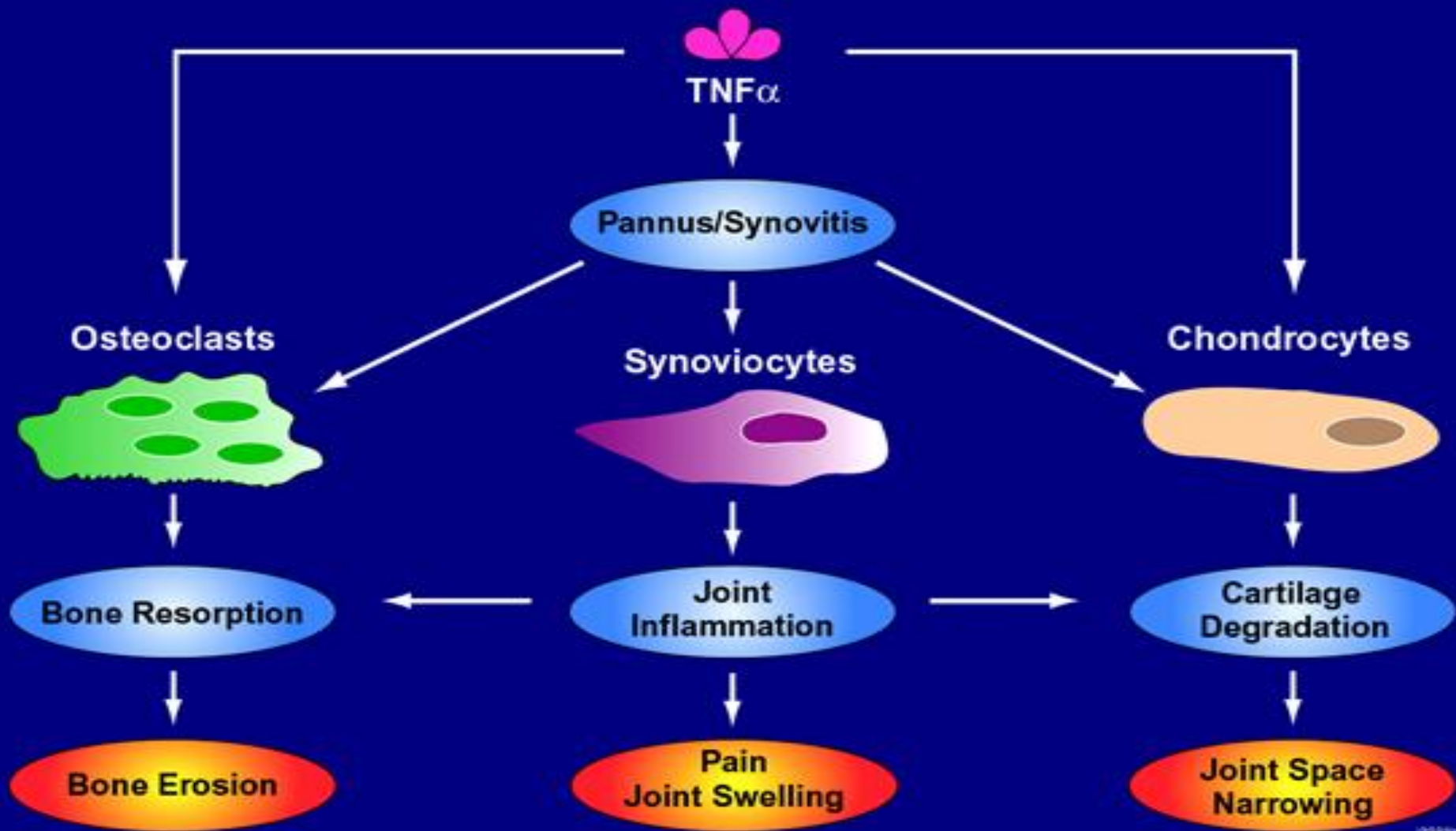
Synovitis is the hallmark

Inflammation (Synovitis) → Cartilage Damage → Joint Destruction → Disability

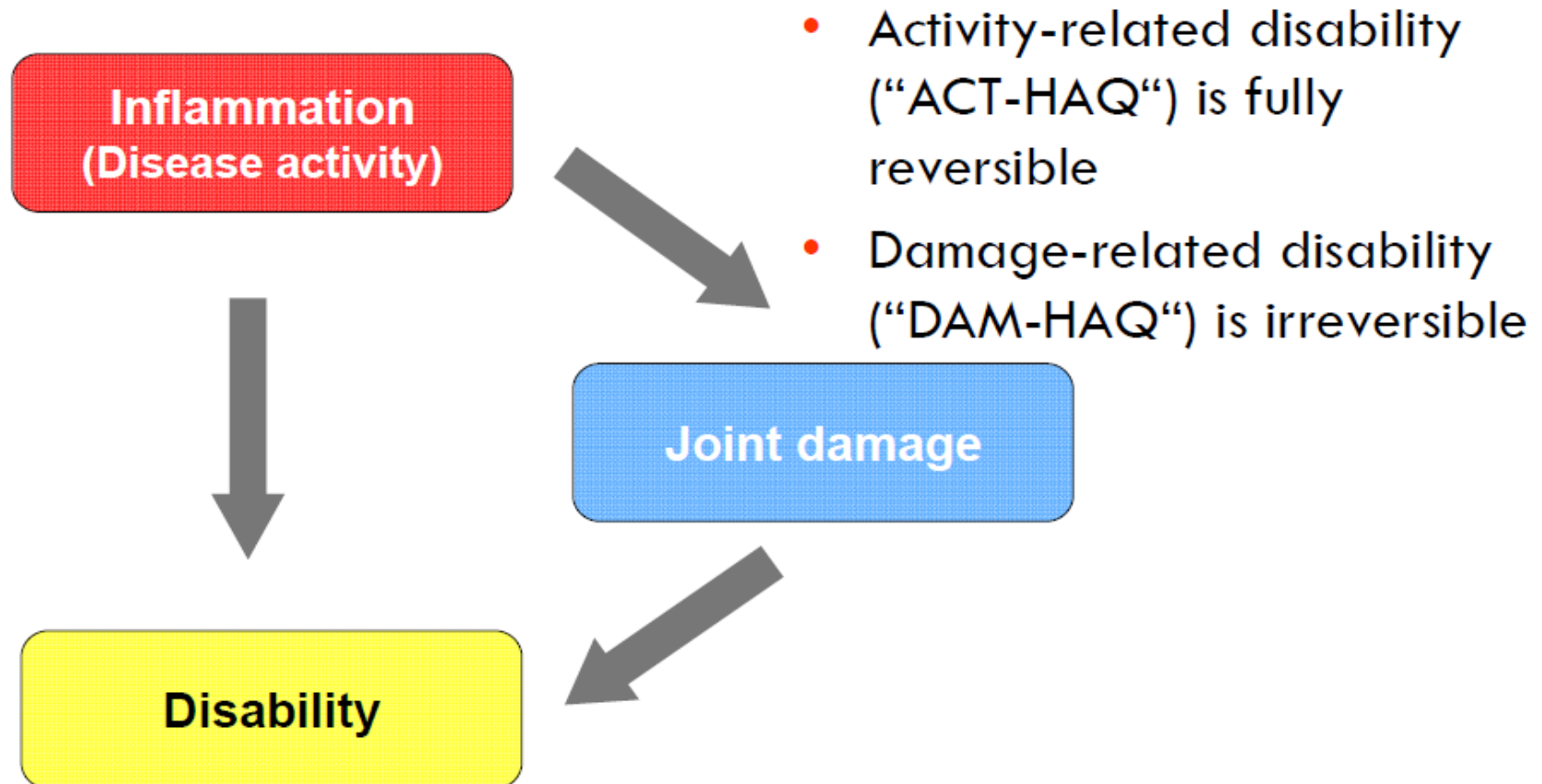


Tumor Necrosis Factor α

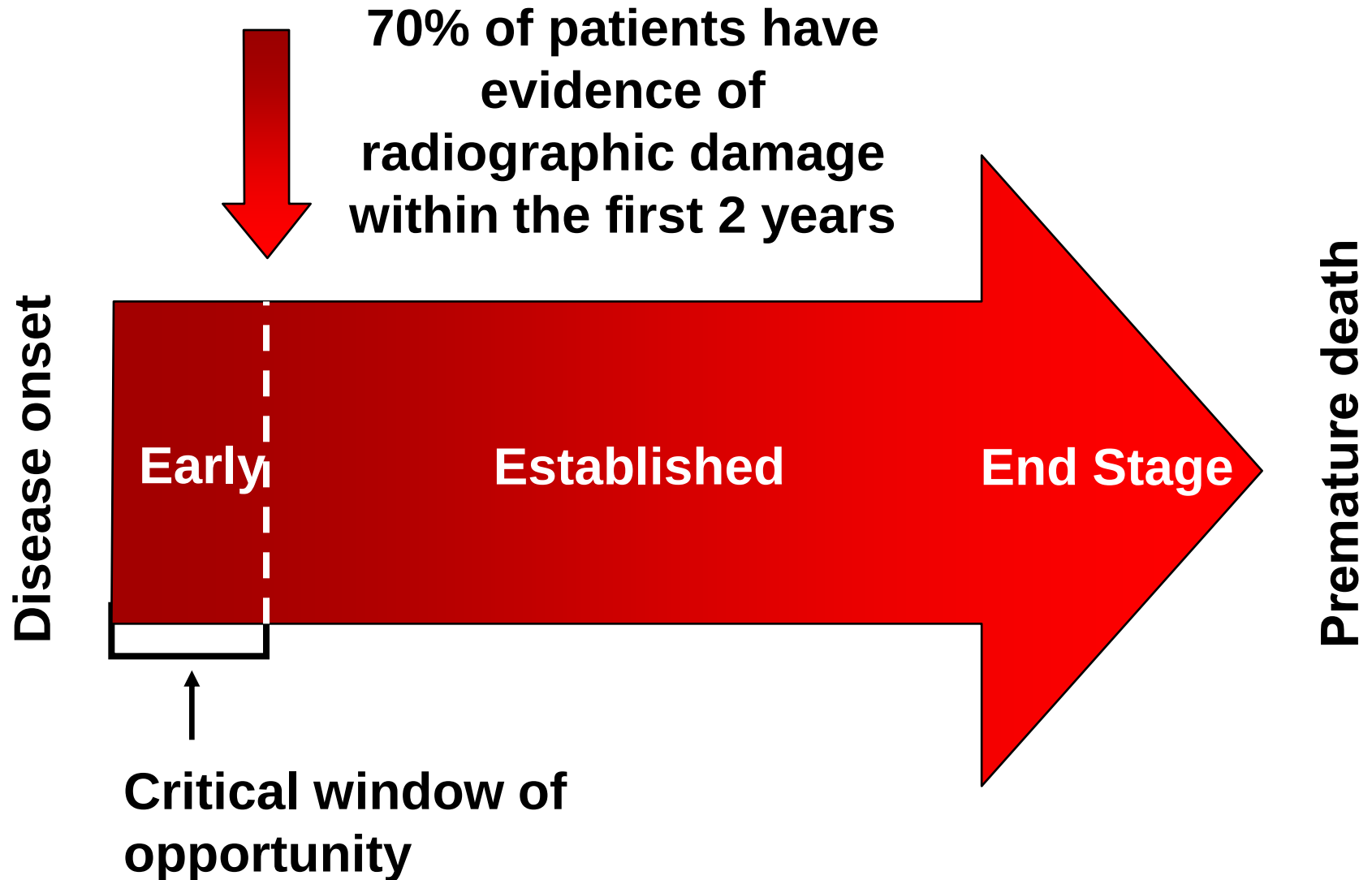
Key Player



Why do we care about Joint Damage?

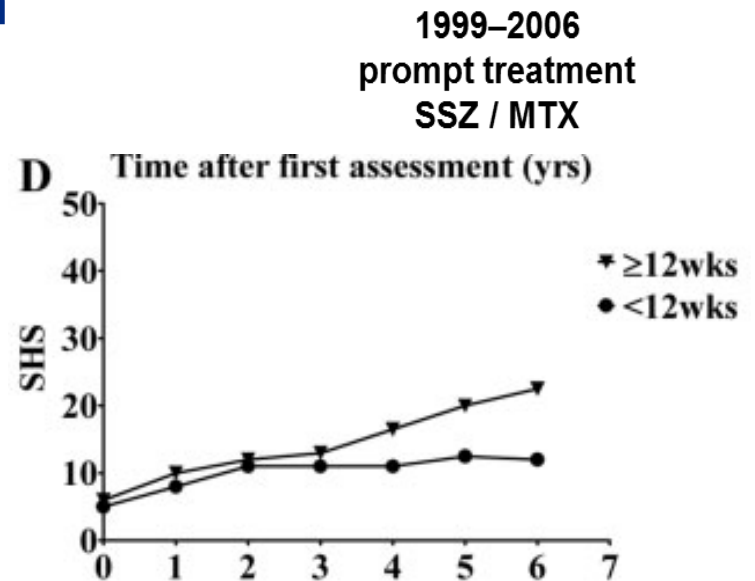
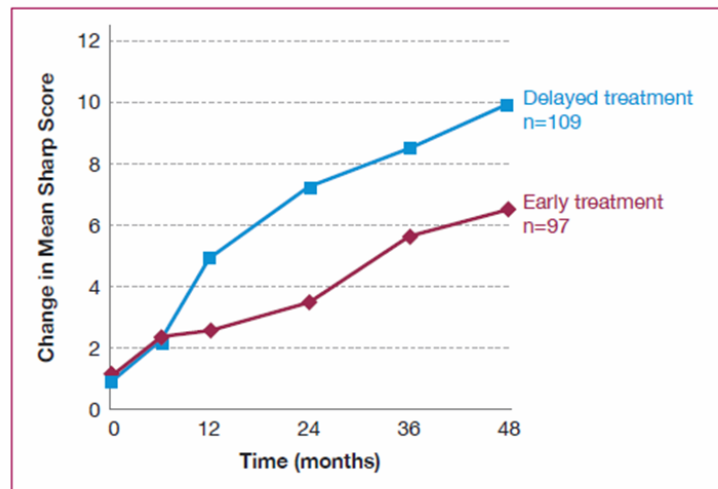


Importance of Early Aggressive Treatment of RA



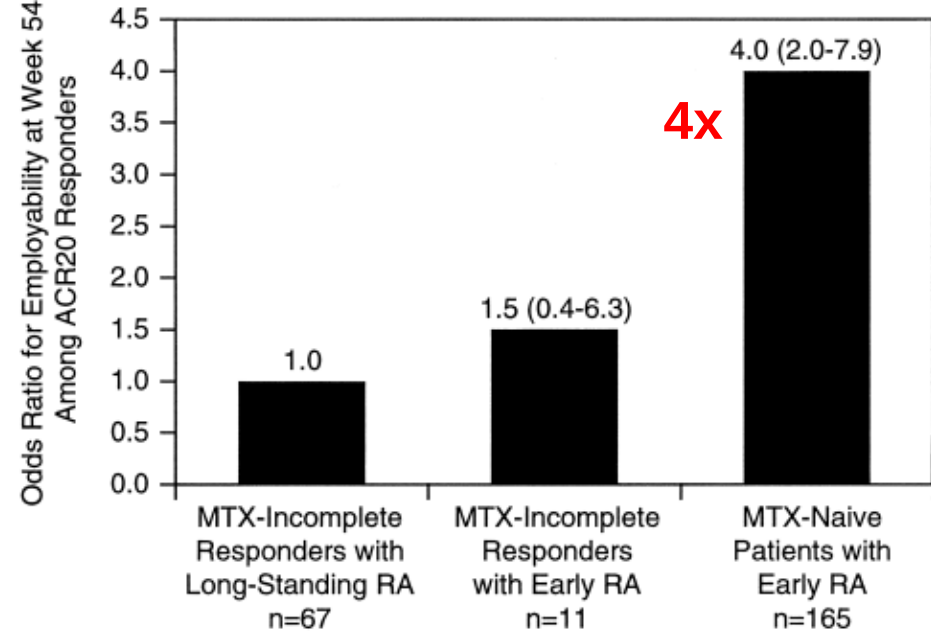
Window of Opportunity

- Delay of > 12 weeks between *symptom onset* and treatment = worse outcome
 - More Joint destruction $\rightarrow$ disability / HAQ
 - Rare DMARD free remission



Comparison of employability outcomes among patients with early or long-standing RA

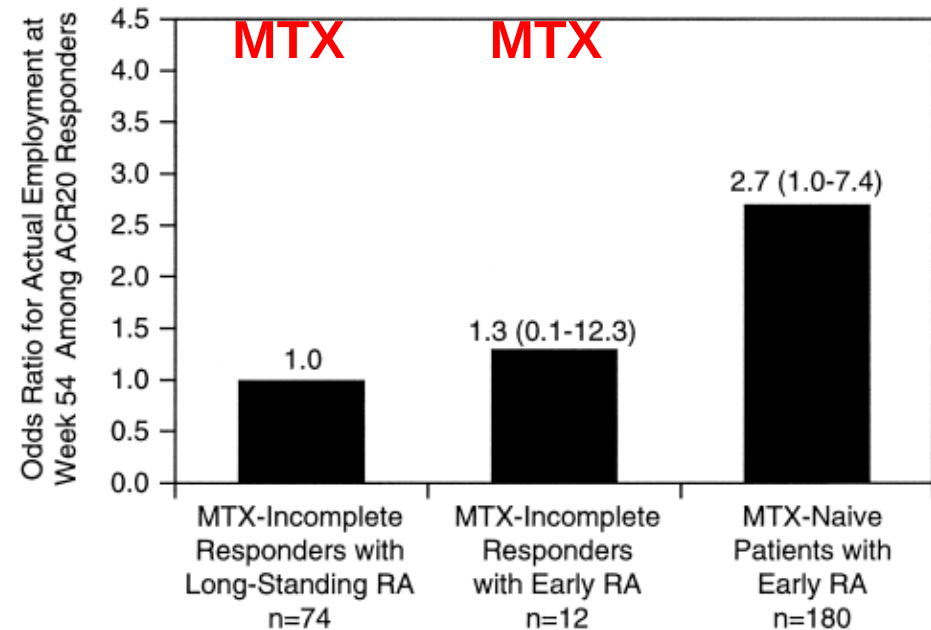
Intervention ASAP in the disease course maximizes an individual patient's employment potential



**LONG
Failed
MTX**

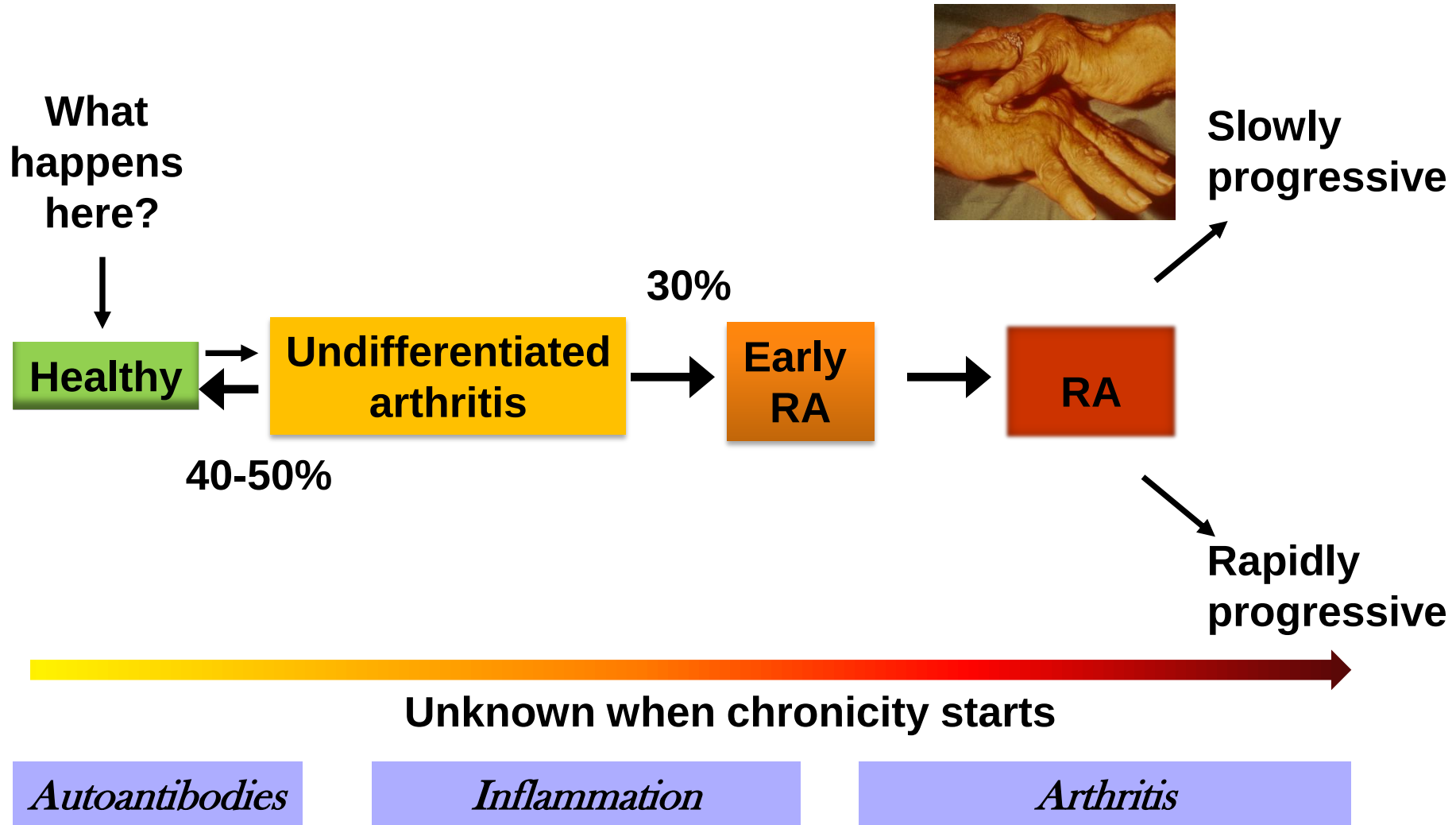
**EARLY
Failed
MTX**

**EARLY
Naive**



B

When does RA begin?



Difficulty in Identifying Early RA

- Vague symptoms
- **Patient** factors (“rheumatism”, TCM, “natural remedies”...)
- Health professionals **lack of time/ exposure/ experience**
- Falsely reassuring investigations
 - 50% negative for RF / CCP
 - 50% don’t mount ESR / CRP response
 - No abnormalities on initial XR
 - Most of the time only *late changes* on XR

Case – patients do not read the text book

A 56 year Malay woman (non-English speaking only, BMI 31 kg/m²) with history of OA knees presents with persistent B knee pain for 2 months. Stiffness throughout the day, pain is ?worse on walking. Her pain is temporarily better with NSAIDs.



What are your thoughts?

- A. Treat as for OA: PHx, most common, not classically “inflammatory”
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Tools for Disease Identification

Criterion	Definition
1. Morning stiffness	Morning stiffness in and around the joints, lasting at least 1 hour
2. Arthritis of ≥ 3 joints	The qualified areas are PIP, MCP, wrist, elbow, knee, ankle, and MTP joints
3. Arthritis of hand joints	At least 1 area swollen in a wrist, MCP, or PIP joint
4. Symmetric arthritis	Simultaneous involvement of the same joint areas on both sides of the body
5. Rheumatoid nodules	Subcutaneous nodules over bony prominences, extensor surfaces, or around joints
6. Rheumatoid factor	Positive rheumatoid factor
7. Radiographic changes	Including erosions or periarticular demineralization

1987 ACR Criteria: not useful for diagnosing early RA

Requires 4 out of 7, 1-4 for **> 6 weeks**

Tools for Early RA diagnosis : Quick screen

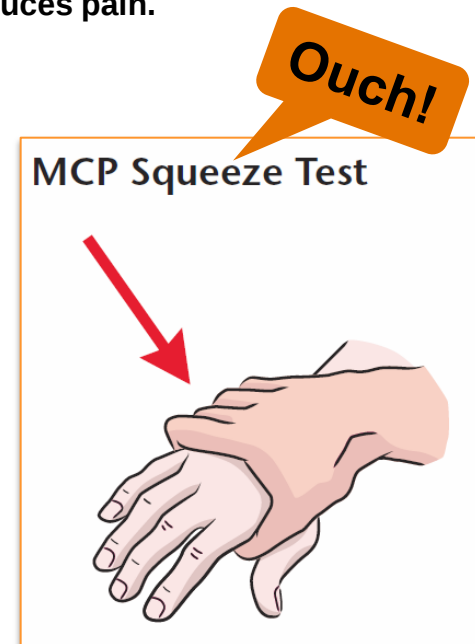
SSS (Swelling, Stiffness, Squeeze test) for Synovitis

- Swelling of ≥ 1 joints*¹
- Early morning stiffness ≥ 30 mins
- Positive MCP/MTP joint squeeze test

Placing one's thumb and index finger across the MCP joint line of the hand or the MTPs of the foot and squeezing across those joints: positive if it reproduces pain.

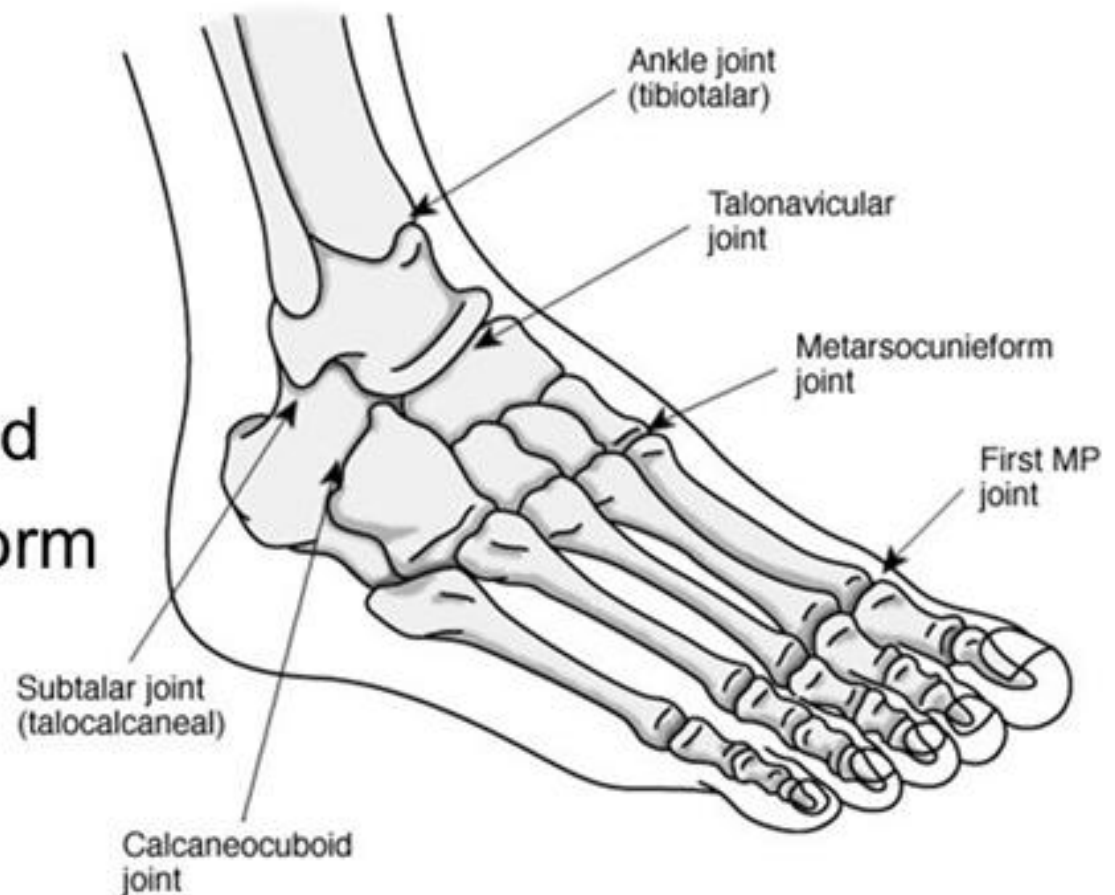
ATTN:

- **Small joints of the hands (wrists / MCPJ) or feet**
- >1 joint is affected
- Squishy, boggy, puffy, soft rather than bony hard



Joints of the Foot

- Tibiotalar
- Talocrural
- Subtalar
- Talonavicular
- Calcaneocuboid
- Metarsocunieform



How to detect synovitis of the feet



How do detect synovitis of the feet



Tools for Early RA diagnosis : Red Flags

- Progressive **loss of function**
- **Fatigue**
- History in **weeks / months**, rather than years



Tools for Early RA diagnosis : New RA 2010 criteria

Table 3. The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

	Score
Target population (Who should be tested?): Patients who	
1) have at least 1 joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of $\geq 6/10$ is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)#	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF <i>and</i> negative ACPA	0
Low-positive RF <i>or</i> low-positive ACPA	2
High-positive RF <i>or</i> high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP <i>and</i> normal ESR	0
Abnormal CRP <i>or</i> abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥ 6 weeks	1
Requires > 6 points for RA <i>or</i> typical erosions	

Rheumatoid Factor (RF)

- RF $\neq$ RA
- High titer RF correlates
 - with more destructive disease
 - extra-articular disease
 - subcutaneous nodules
 - increased mortality
- RF dose not reflect changes in RA disease activity

Other Laboratory Findings

- Anemia of inflammation
- Thrombocytosis
- Hypoalbuminemia
- High ESR, CRP
- Anti-cyclic citrullinated [anti-CCP] antibodies: highly specific for RA
 - Appearance may antedate clinical disease
 - Not uniformly present

Anti-cyclic citrullinated peptide (CCP)

In established RA :

Anti-CCP2:

- Sensitivity: 67% (- 85%)
- [50% in early RA]
- Specificity: 97%
- PPV 86%
- NPV: 81%

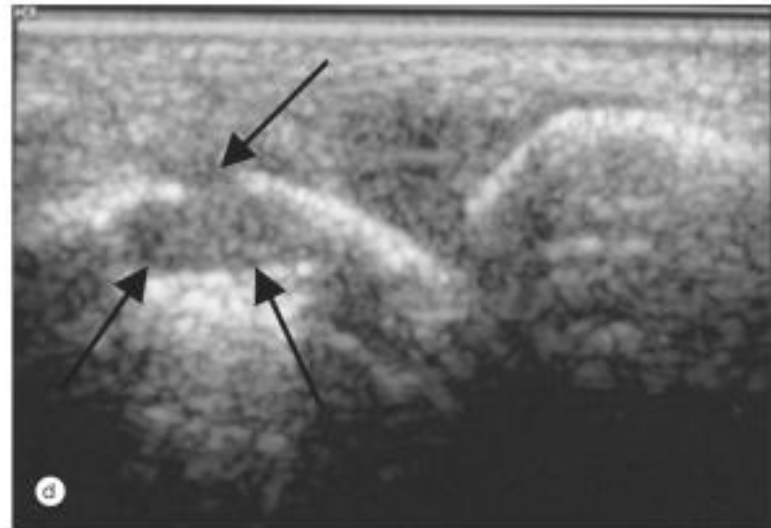
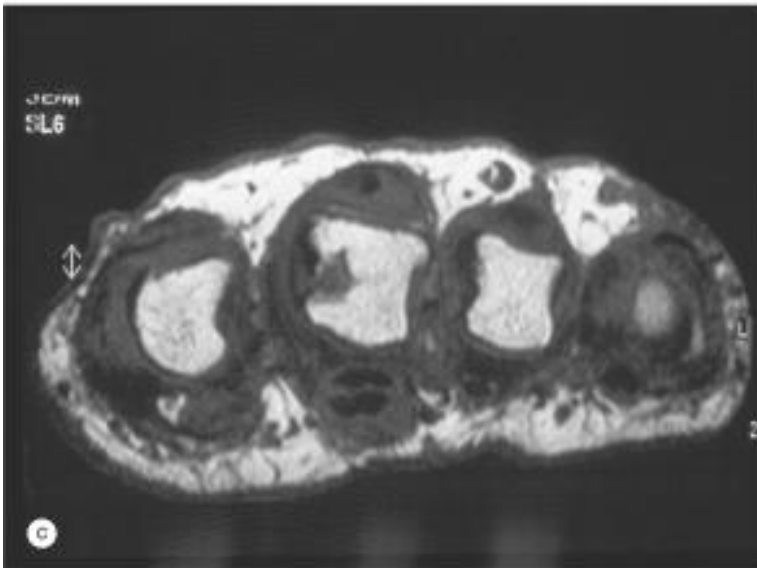
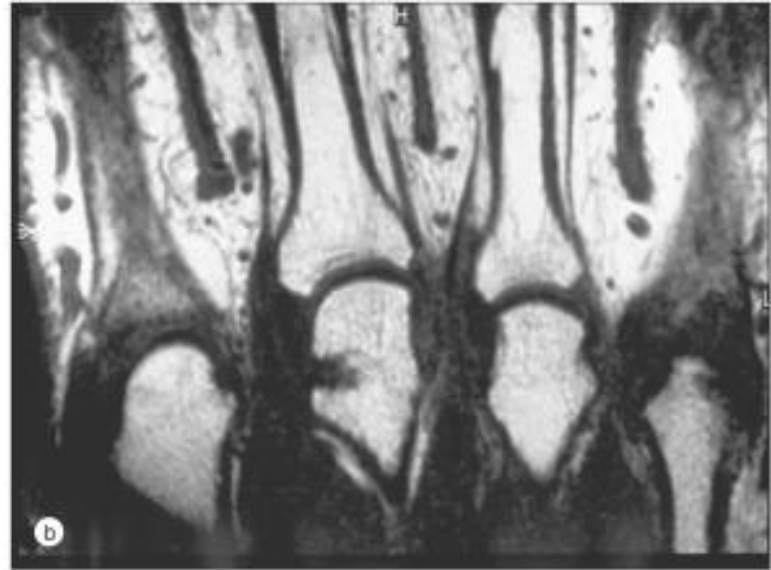
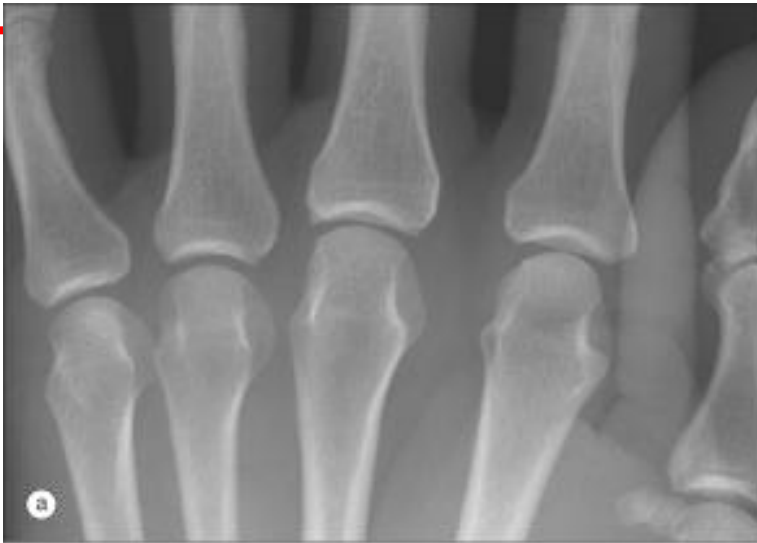
IgM rheumatoid factor:

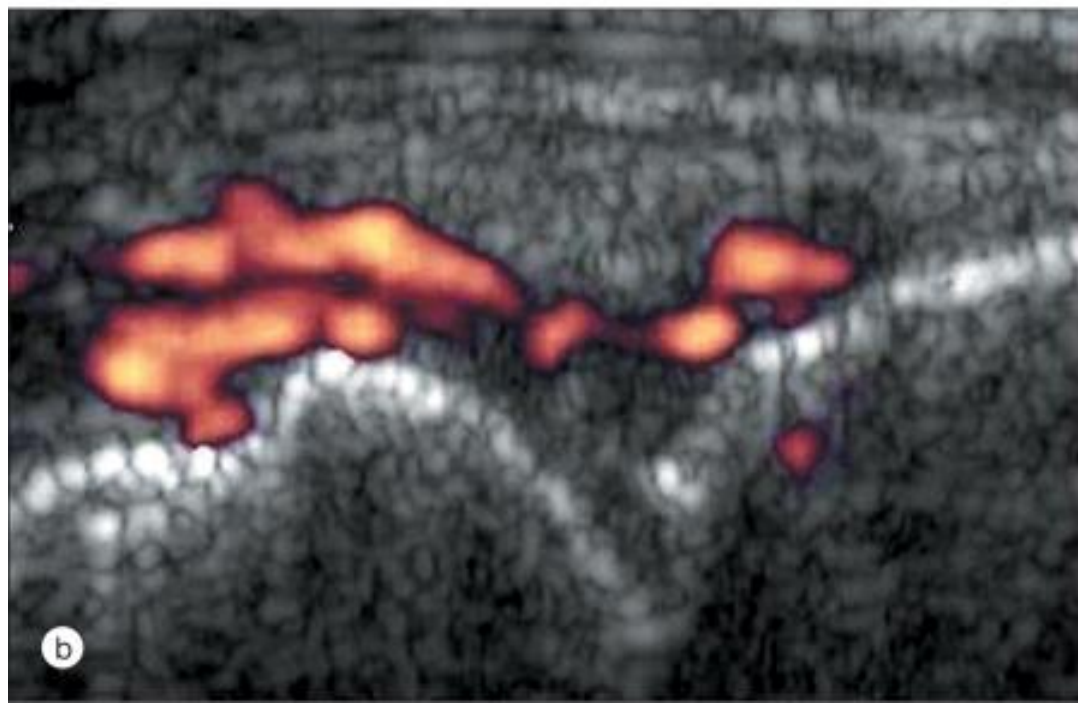
- Sensitivity: 69%
- Specificity: 85%

Anti-CCP

- Are predictive of radiographic damage
- Confirmatory but not always necessary
- Useful if RF negative
- Discriminate subacute/chronic infectious arthritides or other CTD-arthropathy

Tools for Early RA diagnosis : Imaging





Case

A 56 year Malay woman (non-English speaking only, BMI 31 kg/m²) with history of OA knees presents with persistent knee pain for 2 months. Stiffness throughout the day, pain is worse walking. Her pain is temporarily better with NSAIDs.



What are your thoughts?

- A. Be open minded, 2 pathologies,
- B. Review the history and physical exam (proper exposure, find synovitis)
- C. Order some blood tests
- D. Order Xrays knees (hands/feet)
- E. Treat first (Analgesia, NSAID, steroids) and see

Diagnose RA Early: Early Referral

Table 2. Recommendations for Early Referral

Physical Symptoms	• Joint symptoms > 6 weeks* • ≥ 3 swollen joints • Morning stiffness ≥ 30 minutes
Test Results	• Positive MCP or MTP squeeze test • Abnormal laboratory tests: CRP, ESR, RF, or anti-CCP

Changing expectations

A new dawn



**Therapeutic
window of
opportunity in
early RA**

High risk of rapid radiographic progression

- Those with poor prognostic factors
 - RF+, anti CCP +
 - high ESR/CRP
 - high joint counts
 - erosions at baseline

Treat to Target

- Primary goal = maximise long-term HrQOL through control of symptoms, prevention of structural damage, normalisation of physical & social function
- Aiming for clinical remission = absence of signs, symptoms and lab markers of significant inflammatory disease activity
- Measuring disease activity and adjusting therapy to reach the target



T2T: Measurement is key

SingTel 16:45 46%

HOME DAS28

CRP ESR

Tender Joints (mm/hr)

2 40

Swollen Joints VAS (0-100)

2 40

· RUN

DAS28ESR 4.34

activity Moderate

DAS28ESR disease activity

>5.1 high

3.2~5.1 moderate

<3.2 low

<2.6 remission

clear

PAST NOTE [RHEUMATOLOGY MULTI-DISCIPLINARY PROGRESS NOTES (FREE TEXT)]

Physical Examination

NOTE HISTORY

Tender Joints

Swollen Joints

Description	Value
Tender Joints(28)	7
Swollen Joints(28)	4
ESR (mm/hr)	125
CRP (mm/hr)	
Patient Global Assessment (mm)	80
Physician Global Assessment (mm)	
DAS 28 - ESR	6.54
DAS 28 - CRP	
SDAI	91.00

DAS28

2.6

3.2

5.1

Remission

Low

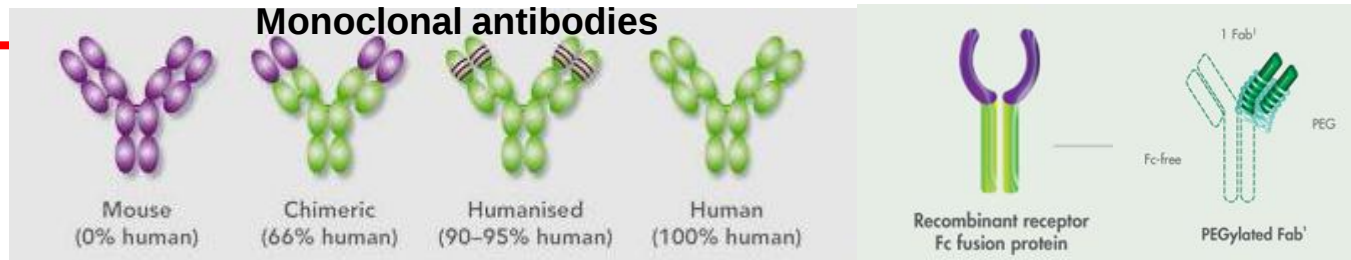
Moderate

High

RA Treatment Strategies

- Treat Inflammation (you can do this)
 - NSAIDs, COX II inhibitors
 - Low dose prednisolone (eg. 5-10mg om, not more than 2-3 weeks)
- Intra-articular steroids for large joint involvement
- **Methotrexate** is the corner stone
- Combination therapy especially for those with bad prognosis
- Other traditional DMARDs: Hydroxychloroquine, Sulfasalazine, Leflunomide
- PreDMARD tests: Baseline CXR, HBsAg, anti HCV, FBC, LFT, Creatinine

Biologics: targeted therapy



Anti-TNF α

INF

**ADA
GOL**

ETA

(CER)

Anti-IL6R

TOC

Anti-CD20

RTX

Anti-CTLA-4Ig

ABA

JAK inhibitor

TOF

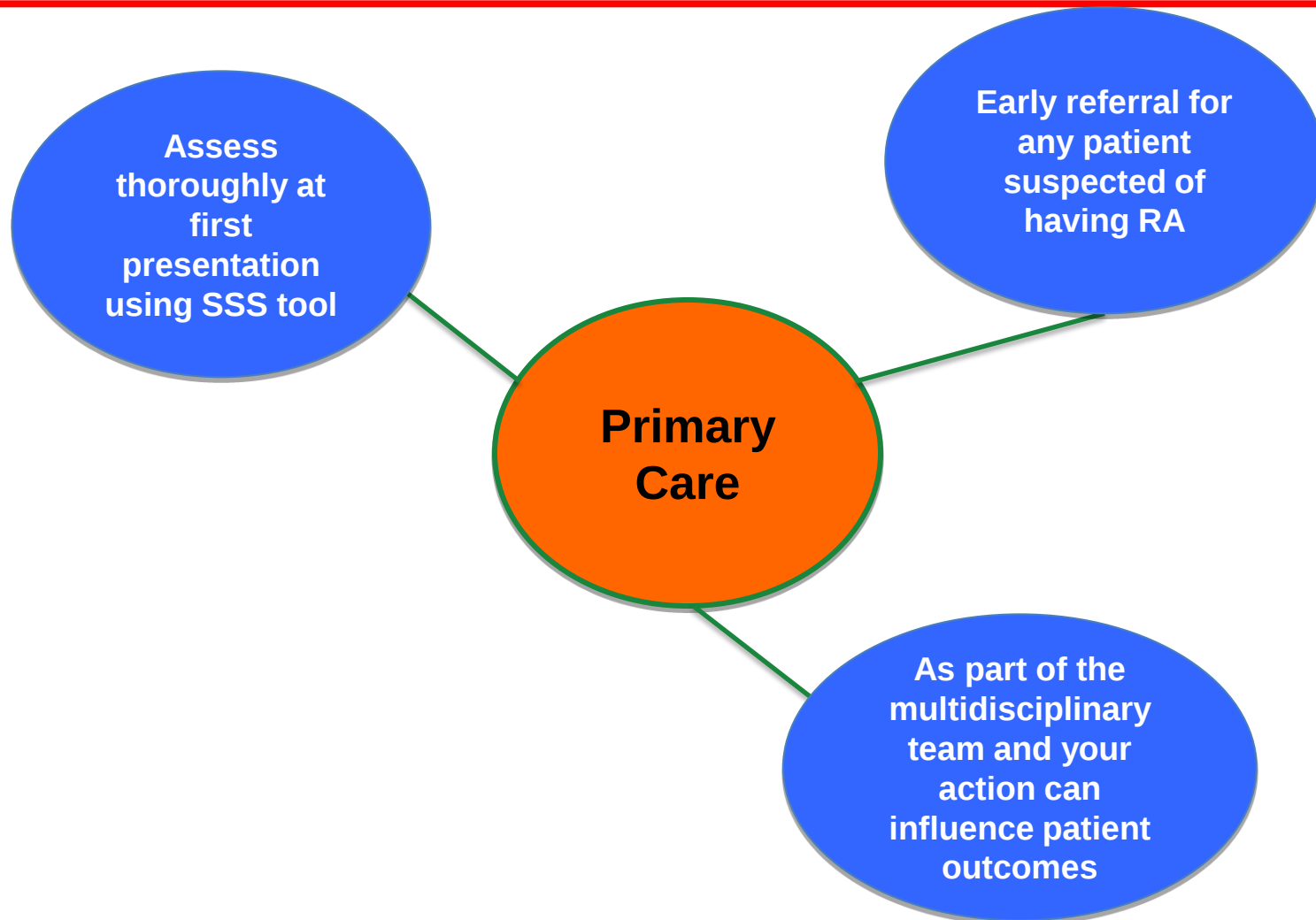
SYK inhibitor

Anti-IL17

Anti IL12 /23

INF: infliximab, ADA: Adalimumab, GOL: Golimumab, ETA: Etanercept
TOC: Tocilizumab, RTX: Rituximab, ABA: Abatacept, TOF: Tofacitinib

Key Actions for Primary Care/ Internist



Co-management of patients with RA

- Assess, monitor and optimise **cardiovascular risk**
- Keep up with **cancer screening** recommendations
- Keep up with age and comorbidity appropriate **vaccinations**
- Assess, monitor and optimise **bone health**
- Liaise with rheumatologist / nurse to manage any patient who has a flare, has **side-effects** from their medication
- Facilitate **blood work monitoring** for patients during dose titration

Be aware of

- Drug interactions, hepatotoxicity, nephrotoxicity
- Some live vaccines (e.g. Herpes zoster) may be contraindicated
- Risk of infection in patients on steroids, DMARDs and biologics – high index of suspicion, early referral and treatment – especially in the elderly and in those with other comorbidities.

Singapore Health Policies

- With effect from 1 Jun 2015, Rheumatoid Arthritis and osteoporosis have been added to the CDMP and Community Health Assist Scheme (CHAS) and Medisave use
- Needy patients are eligible for anti-TNF therapy by the Medication Assistance Fund (MAF) if fulfill set criteria* since April 2014

Case

A 56 year Malay woman

Saw OPS for 9 months before the first blood tests are done

Anemia, high ESR, CRP, RF negative,

Florid synovitis

Triple DMARD therapy and low dose prednisolone

Adalimumab

Thank you, Questions?
