Rheumatoid Arthritis in 2022

Beyond the Biologic Era

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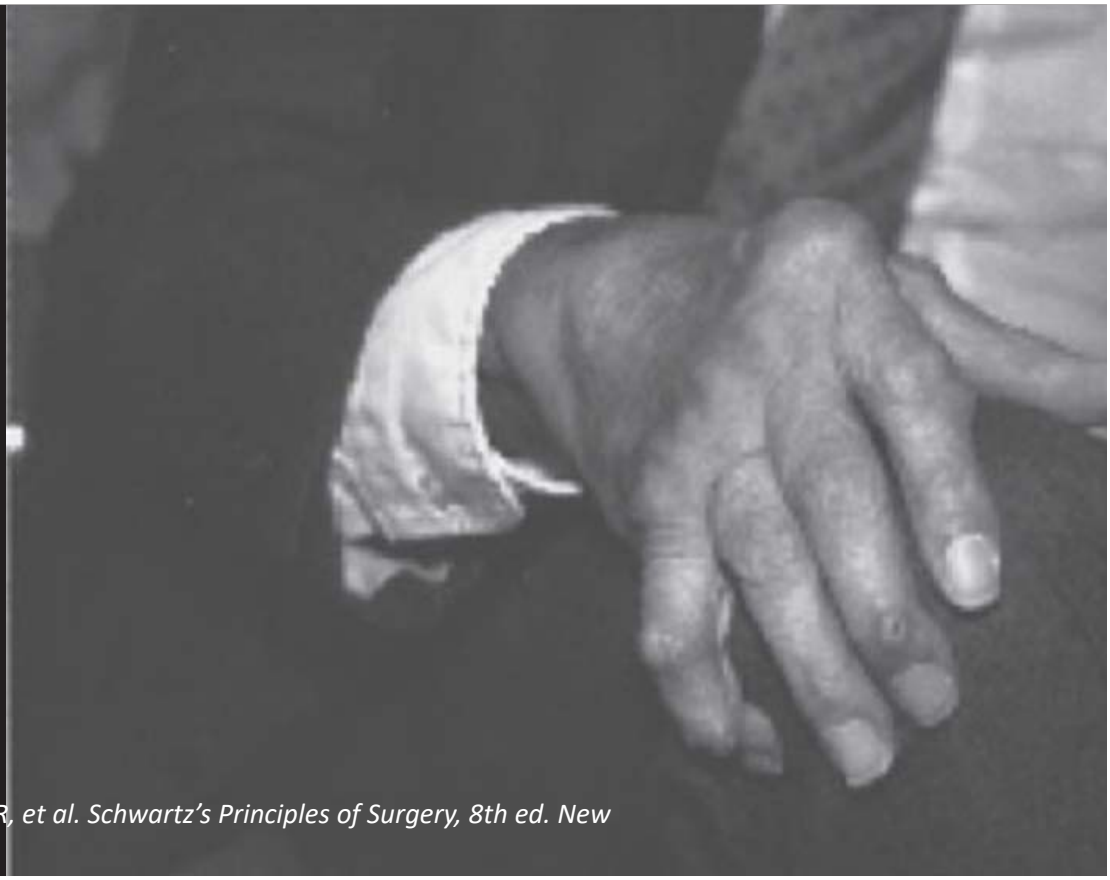
Objectives

- By the end of the presentations, participants should be able to:
- a) Apply a "Treat-to-target" methodology in the management of RA
- b) Understand newer RA medications
- c) Monitor RA patients on DMARDs and Biologic therapies

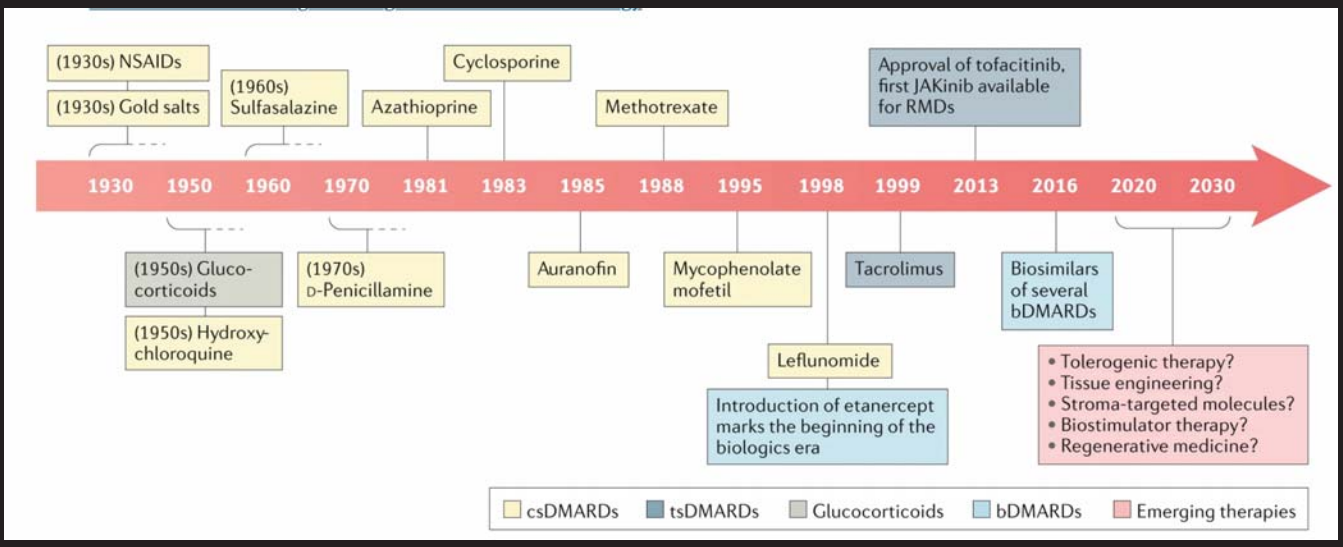
A little history…

- More than 2300 years ago, Hippocrates, was quoted saying "It is incredible how fast the mischief spreads."



Brunicardi FC, Anderson DK, Billiar TR, et al. Schwartz's Principles of Surgery, 8th ed. New York: McGraw-Hill, 2005.

Advances in the medical treatment of RA



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Advances in the medical treatment of RA

- Early Diagnosis
  - Change in classification criteria

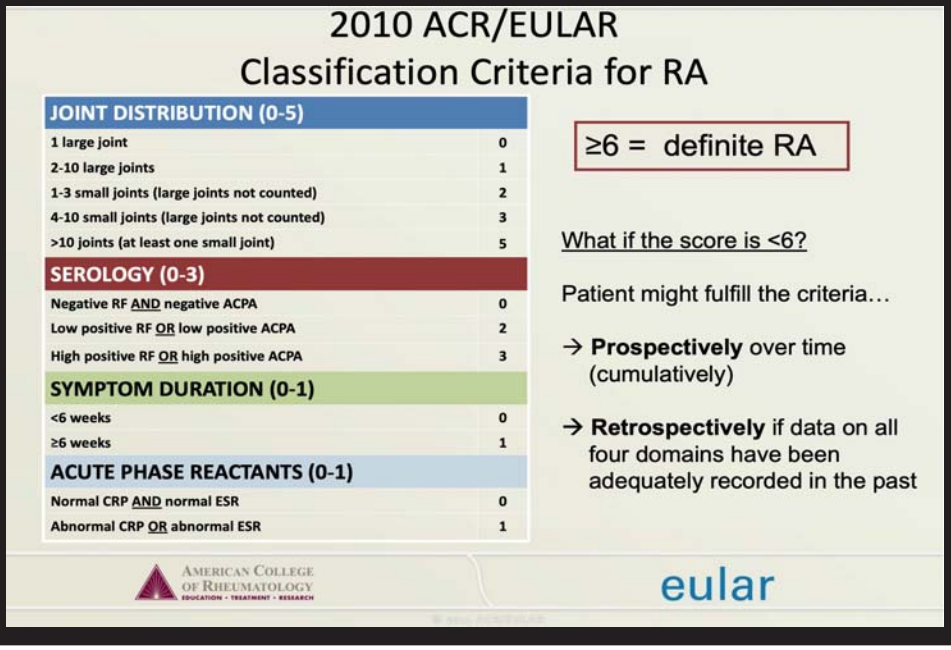
1987 American College of Rheumatology (formerly American Rheumatism Association) revised classification criteria for rheumatoid arthritis

Criterion	Description
Morning stiffness	Morning stiffness in and around the joints, lasting at least one hour before maximal improvement.
Arthritis of three or more joint areas	At least three joint areas (out of 14 possible areas; right or left PIP, MCP, wrist, elbow, knee, ankle, MTP joints) simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) as observed by a physician.
Arthritis of hand joints	At least one area swollen (as defined above) in a wrist, MCP, or PIP joint.
Symmetric arthritis	Simultaneous involvement of the same joint areas (as defined above) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs, without absolute symmetry is acceptable).
Rheumatoid nodules	Subcutaneous nodules over bony prominences or extensor surfaces, or in juxta-articular regions as observed by a physician.
Serum rheumatoid factor	Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in less than 5 percent of normal control subjects.
Radiographic changes	Radiographic changes typical of rheumatoid arthritis on posteroanterior hand or wrist radiographs, which must include erosions or unequivocal bony decalcification localised in, or most marked adjacent to, the involved joints (osteoarthritis changes alone do not qualify).

Note: For classification purposes, a patient has RA if at least four of these criteria are satisfied (the first four must have been present for at least six weeks).

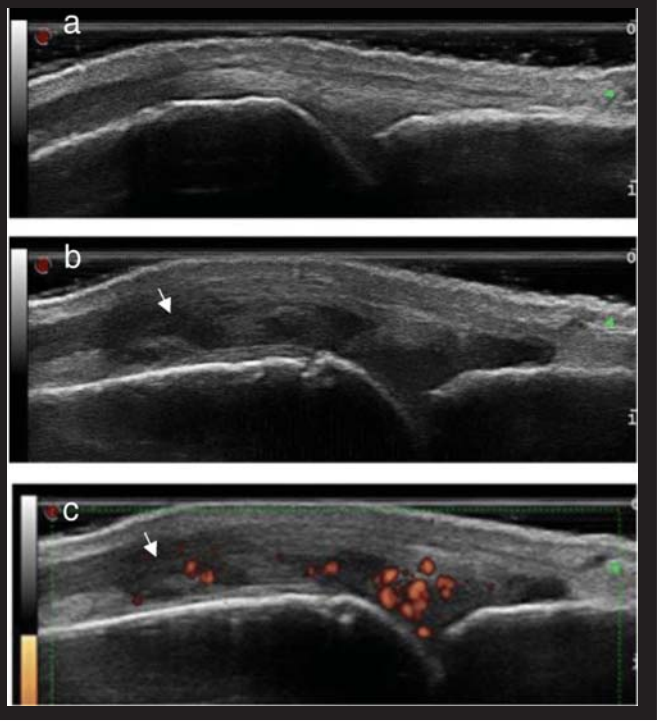
Advances in the medical treatment of RA

- Early Diagnosis
  - Change in classification criteria



Advances in the medical treatment of RA

- Early Diagnosis
  - MSK ultrasound



Advances in the medical treatment of RA

- Combination vs step wise therapy

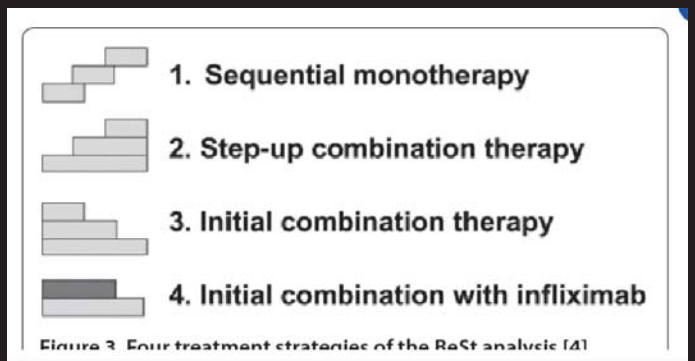


Figure 3. Four treatment strategies of the BeSt analysis [4].

Published in Arthritis research & therapy 2011

Understanding emerging treatment paradigms in rheumatoid arthritis

F. Breedveld, B. Combe

Advances in the medical treatment of RA

- Combination vs step wise therapy

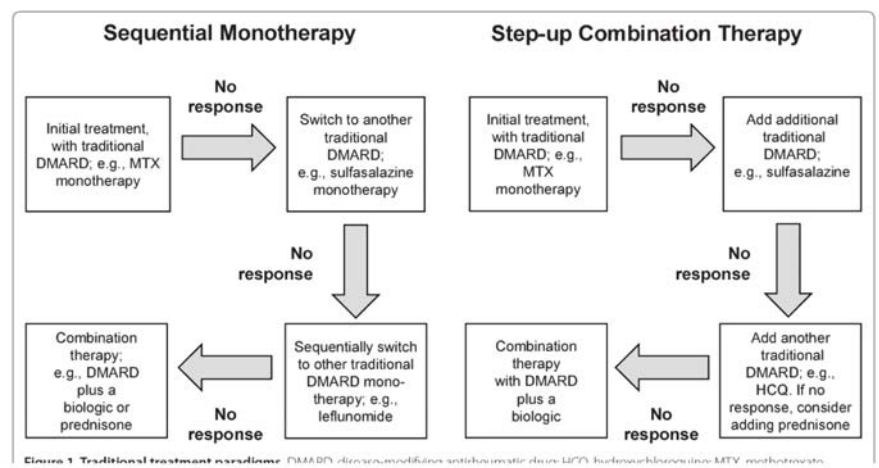


Figure 1. Traditional treatment paradigms. DMARD, disease-modifying antirheumatic drug; HCQ, hydroxychloroquine; MTX, methotrexate.

Published in Arthritis research & therapy 2011

Understanding emerging treatment paradigms in rheumatoid arthritis

F. Breedveld, B. Combe

Treat to target in RA

- What is the target?
- How do you measure it?
- What do you do if your patient doesn't meet the the target?

Treat to target in RA

- What is the target? Remission or Low disease Activity
- How do you measure it? DAS 28, CDAI etc
- What do you do if your patient doesn't meet the the target? ESCALATE

Treat to target in RA

- What is Remission or Low Disease Activity?

- **Boolean Based Definition**
  At any time point, a patient must satisfy all of the following:
  - Tender Joint Count ≤1
  - Swollen Joint Count ≤1
  - CRP ≤1 mg/dL
  - Patient Global Assessment ≤1 (on a 0-10 scale)
- **Index Based Definition**
  At any time point, a patient must have SDAI ≤3.3

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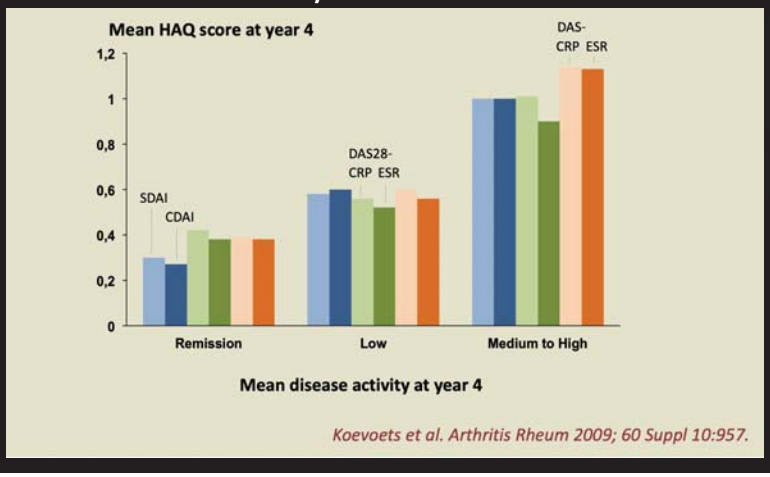
Treat to target in RA

- Why Remission or Low Disease Activity?



Koevoets et al. Arthritis Rheum 2009; 60 Suppl 10:957.

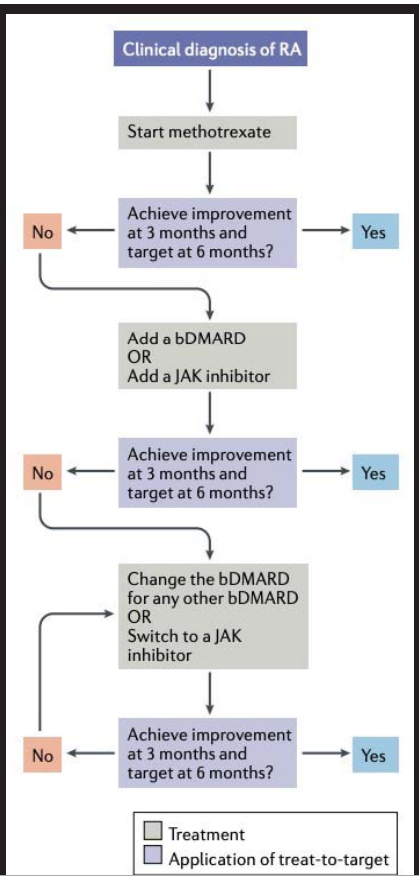


Fig. 2 | **Treat-to-target in the EULAR treatment recommendations for RA.** In this simplified treatment algorithm for rheumatoid arthritis (RA), the EULAR recommendations are followed[8,34]. Notably, the choice of therapy is not, strictly speaking, part of the treat-to-target strategy; however, it is clearly related to treat-to-target. The idea behind including treatment options is that when the treat-to-target strategy compels the rheumatologist to choose a different therapeutic agent, these recommendations might help in making that choice. bDMARD, biologic DMARD; JAK, Janus kinase.

Treat to target in RA

Don’t forget…

How to Choose Amongst Therapies?

- DMARDS
  - Methotrexate is anchor medication
    - GFR> 30
    - Liver monitoring Q2-3 months
    - Stop 3 months prior to conception
  - Leflunomide
    - Liver monitoring Q2-3 months
    - Arterial Hypertension
    - Needs wash out prior to conception
  - Sulfasalazine
    - CBC q2 weeks x 6 weeks, q monthly x 6 months then q3months
  - Hydroxychloroquine
    - Eye exam

How to Choose Amongst Therapies?

- Biologics:
  - Anti-TNFs (s/c or IV)
  - Abatacept (s/c or IV)
  - Tociluzimab (s/c or IV)
  - Rituximab (IV)
  - Kinase Inhibitors (po)

Monitoring for RA patients

- Cardiovascular disease risk
- Infection risk
  - Pre-biologic screening
  - Vaccines
- Malignancy risk
- Mental Health

Monitoring for RA patients

- Cardiovascular disease risk
  - 2x higher risk of developing atherosclerotic cardiovascular disease than the general population, similar to patients with diabetes.
  - The risk of ischaemic heart disease is increased early in the disease
  - The risk of cerebrovascular incidents is increased by about 50% whereas the risk of myocardial infarction is doubled
  - 2x the risk of developing congestive heart failure
    - both heart failure with preserved ejection fraction and heart failure with reduced ejection fraction.
  - Improved cardiovascular mortality in last 20 years attributed to better therapy
  - 50% of risk associated with traditional risk factors

Lancet Rheumatol 2021; 3: e58–70

Monitoring for RA patients

- Infection Risk
  - Screening Prior to initiating therapy
    - CBC, Creatinine/GFR, ALT, Albumen
    - TB (PPD or quantiferon plus chest x-ray)
    - Hepatitis B and C, HIV
    - Chest x-ray
  - B cell depleting therapy: baseline immunoglobulins
  - Anti-IL6 and kinase inhibitors: Baseline lipid profile

Rheumatology, Volume 58, Issue 2, February 2019, Pages 220–226

Monitoring for RA patients

- Infection Risk- Vaccines
  - May be an attenuated response
  - Should receive covid, influenza, pneumococcal (13 and 23 valent) and zoster
  - Live vaccines should be avoided

Malignancy Risk

- Biologic therapies should not be started in patients with active malignancy
- No conclusive evidence for an increased risk of solid tumours or lymphoproliferative disease linked with biologic therapy
- Possible risk of skin cancers with anti-TNF therapy
- Rituximab may be considered as a first-line biologic option in RA patients with previous malignancy

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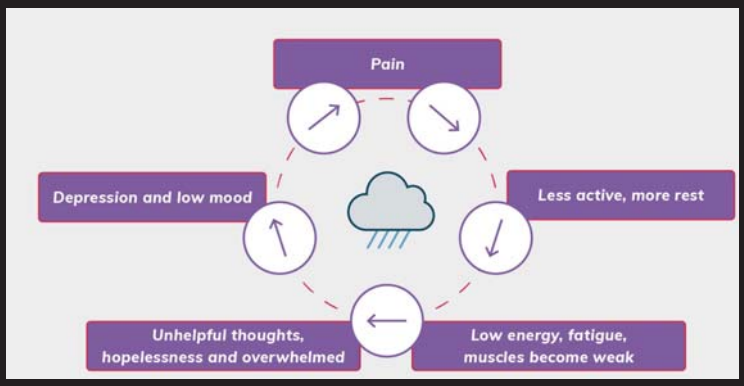
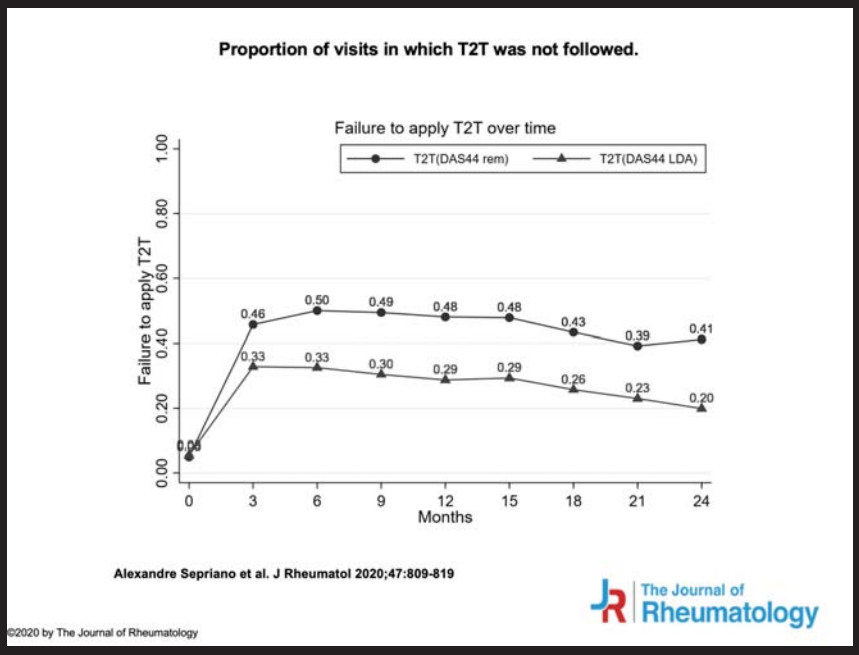
Monitoring for RA patients

- Mental Health
  - RA patients are more prone to have anxiety, depression and cognitive impairment compared to the general healthy population
  - Results in higher disease activity in RA mainly due to fatigue and bodily pain.



Rheumatol Ther. 2020 Sep;7(3):457-471

RA- Treating to Target is not easy



Conclusions

- A diagnosis of rheumatoid arthritis in 2022 is no longer devastating
  - Patients are diagnosed earlier in the disease
  - Treatment is started earlier
  - Treat to target strategy guides therapy
  - Disease remission is the goal
  - Monitoring for side effects remains important