PASSION ACADEMIC TEAM

YU - MEDICINE

MUSCULOSKELETAL SYSTEM

Sheet#2 - Pharmacology

Lec. Title : Rheumatoid Arthritis (Part 1)

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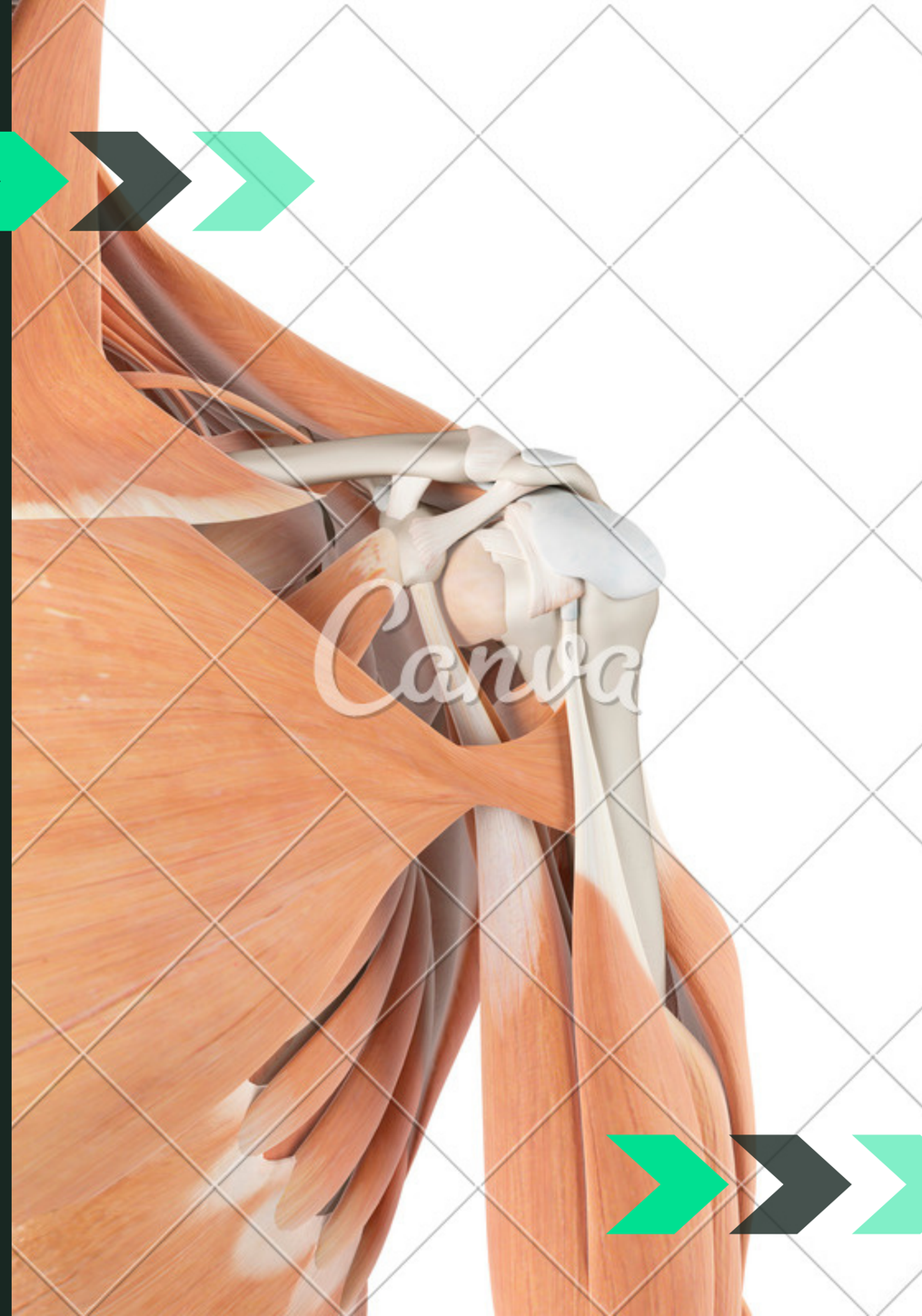

Rheumatoid arthritis

- ***definition*** : Rheumatoid arthritis (RA) is a complex systemic inflammatory condition manifesting initially as symmetric swollen and tender joints of the hands and/or feet.

- general infos :

- RA is an autoimmune disease and associated with high rate of disability and poor quality of life.
- RA usually starts and Mainly dominant in small joints.
- Some patients may experience low disease activity, where is others may present with high disease activity and/or extraarticular manifestations and this this is duo to the immunity of the individual.
- The systemic inflammation of RA leads to joint destruction, disability, and Because RA is a systemic disease it will affect all systems in our body and will cause premature death, mainly related to cardiovascular diseases.

- In children👶 RA is called **juvenile idiopathic arteritis (JIA)**

-pathophysiology :

- the **synovium** tissue which lines the spaces of joints is the most type of tissues which is affected by RA and when it happen it shows some changes :
  1. A thickened, inflamed membrane lining called **pannus**.
  2. Development of new blood vessels (**angiogenesis**).
  3. Influx of inflammatory cells in the Synovial fluid, predominantly T lymphocytes.
- The most significant immune components involved in the pathophysiology of RA are :
  1. **T lymphocytes.**
  2. **B lymphocytes.**
  3. **Kinases.**
  4. **Cytokines.**

- Because RA is a systemic disease it will have complications associated with it such as :

1. **Cardiovascular disease**
2. **Infections**
3. **Malignancy**
4. **Osteoporosis**

And as long as the disease is in good control and the activity of the disease is less, the development of these complications will be less.

-The diagnosis of RA :

- The diagnosis of RA is done by a scoring system where u add points for each criteria if The total of points is 6 or greater it indicates the patient have RA.

- There are 4 criteria for scoring :

1. joint involvement
2. Serology
3. Acute-phase reactant
4. Duration of symptoms

- In RA we have two main antibodies to keep an eye on which are :

1. Rhematoid factor (RF).
2. anticitrullinated protein antibodies (ACPA) .

- The most clinically important features associated with poor long-term outcomes include:

1. high disease activity
2. positive autoantibodies (RF or ACPA)
3. early presence of bony erosions by radiography.

ACR/EULAR 2010 Classification Criteria for Rheumatoid Arthritis[1]

Criteria	Score
Joint involvement	
1 large joint (hips, knees, ankles, elbows, shoulders)	0
2–10 large joints	1
1–3 small joints (MCPs, PIPs, MTPs, wrists)	2
4–10 small joints	3
More than 10 joints (at least one small joint)	5
Serology (need at least one result for classification)	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
Acute-phase reactants (need at least one result for classification)	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
Duration of symptoms	
Less than 6 weeks	0
More than 6 weeks	1
TOTAL:	6 or greater indicates definite RA

- There is a website used to score the disease activity of the RA, was firstly used for researches and because how important and efficient these grading website are they are now used clinically

https://www.msdmanuals.com/medical-calculators/RheumatoidArthritisDAS28-ja.htm.

هذا الرابط فقط للفائدة واذا حاب تعرف اكثر عن كيفية توزيع النقاط

- goals of treatment of RA :

1. The fist goal we always want to accomplish is reducing or eliminating pain.
2. Reduce disease activity to the lowest possible level, ideally remission, as soon as possible.
3. Protect articular structures and function.
4. Control systemic complications.
5. Improve/maintain quality of life.

لازم يكون العلاج للRA بشكل مباشر وشديد عشان ما يبدا يسبب مشاكل مثل الالتهابات وامراض القلب

- We always need to put in consideration how painful the RA for the patient, sometimes it's not that significant when we just use data so we always need to ask the patient how painful it really is.

المختصر انو دائما لازم نسأل المريض اذا كان بتألم حتى ولو ما كان ببين على الفحص

- treatment of RA :

- Any patient that have RA should be treated with at least one or more disease-modifying antirheumatic drugs (DMARDs) to reduce disease activity.
- DMARDs are the mainstay of RA treatment because modifying the disease process can prevent or reduce joint damage rather than merely providing symptomatic relief.
    - Types of **DMARDs** :
        1. Traditional nonbiologic DMARDs.
        2. Biologic DMARDs.
        3. Janus-jinase inhibitors.

- The difference between traditional nonbiological and biological DMARDs is nonbiological are normal chemical drugs were the biological one are Synthesized from living cells or living tissue.
- The choice of initial DMARDs depends on:

1. Safety and efficacy data
2. Disease severity
3. Patient's characetistics (comorbidities, likelihood of adherence)
4. Cost
5. Clinician experience with the medication.

كل ما زادت خبرة الطبيب زادة سهولة العلاج يعني الدكتور المتمرس ايده بتكون ماخذة على الادوية

• **Methotrexate** alone or in combination therapy is the initial treatment of choice.

DMARD Monotherapy means the usage of only one drug.

• Depending on disease severity, combination therapy may be initiated at the time of diagnosis or after an adequate trial of DMARD monotherapy.

If the disease severity is low monotherapy is enough

• If a patient has evidence of rapid disease progression (eg, worsening radiographic erosions), a more aggressive treatment plan may be warranted with more frequent follow-up to achieve the goal of remission or low disease activity.

• Nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids also have specific roles in the treatment of RA

• Agents such as azathioprine, cyclosporine, minocycline, gold salts, and anakinra are used rarely today .

- treatment of RA :

Before (6) months :

- We wil use a nonbiologic DMARD monotherapy if the disease activity is either low or high, like Methotrexate (preferred), hydroxychloroquine, leflunomide, or sulfasalazine
- Or if the disease activity is high we can immediately use the combination of nonbiologic DMARD therapy like: Methotrexate/sulfasalazine, methotrexate/hydroxychlo-roquine, or methotrexate/ sulfasalazine/ hydroxychloroquine.

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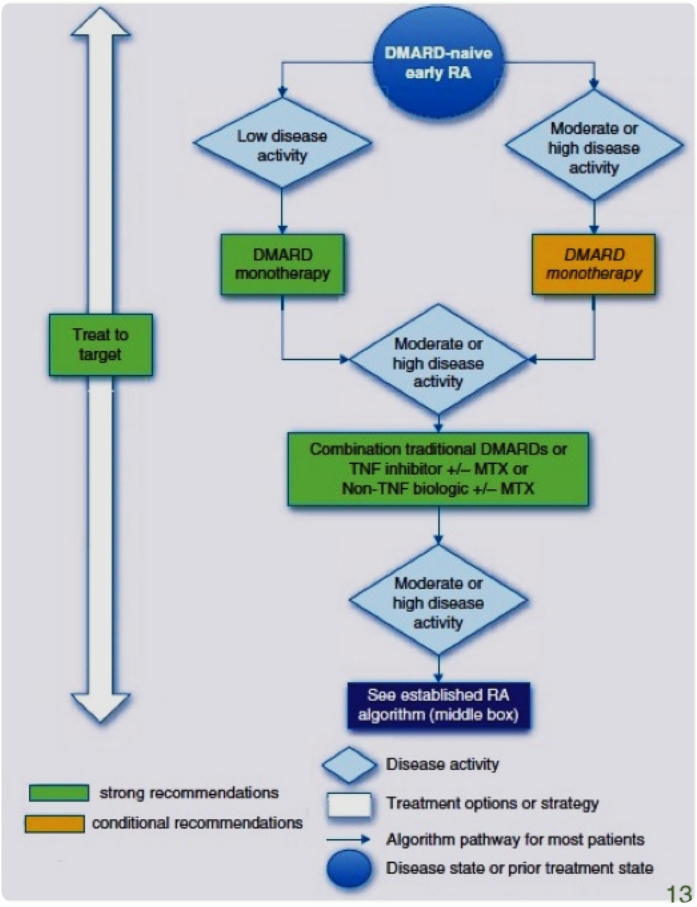
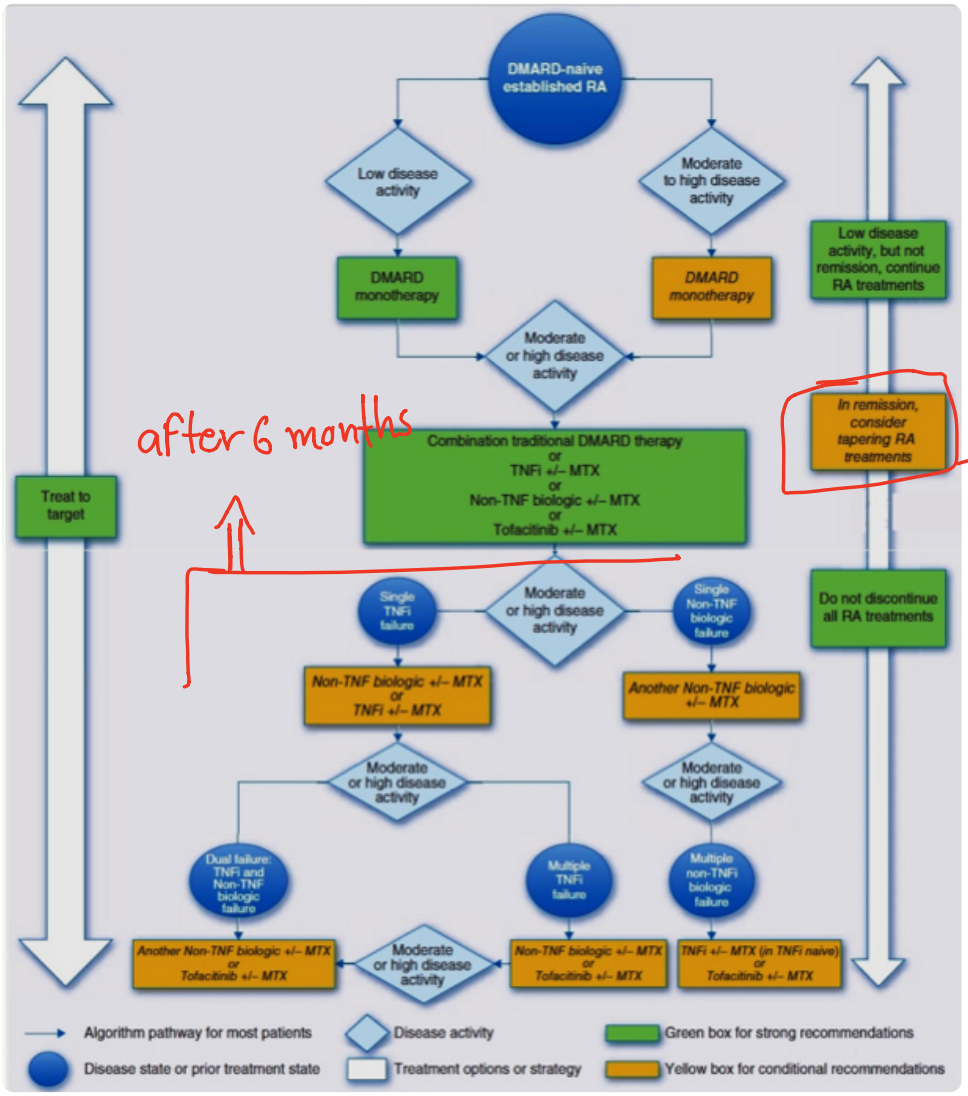


After (6) months :



- If we give TNF inhibitor + methotrexate and the patient is after 1 year, remission can start tapering for the RA medication, but it needs to stay under control and slow tapering.
- We can go up or down on this Algorithm to have the best result with the least complicated rigid.

-***Things we need to know for treatment :***

- The usage of biologic DMARD + biologic DMARD is avoided because of the increased risk of infection due to excessive immmunosuppression.
- There is no evidence that the benefits of combination biologic DMARD therapy outweigh the potential risks, especially the increased risk of infections.

-***Nonpharmacologic therapy :***

قراءة سريعة كافية هون 👏

- All patients should receive education about the nonpharmacologic and pharmacologic measures to help manage RA.
- Occupational and physical therapy may help patients preserve joint function, extend joint range of motion,and strengthen joints and muscles through strengthening exercises.
- Surgery to replace or reconstruct the joint may be necessary for extensive joint erosions.

-***Pharmacologic therapy***

- Bridge therapy/ Symptomatic relief

The current standard of care for RA treatment is to initiate disease-modifying therapy immediately, But it may take weeks to months for the patient toexperience relief so we initiate “bridge therapy” or short-term use of certain medications to provide symptomatic relief until the disease modifying drug reaches its therapeutic effect.

يعني ان الDMARD بياخذو وقت طويل حتى يبدأو يخففوا الالم لهيك بنحتاج مساعدات عشان تخفف الالم لحتى يبلش مفعول الDMARD يشتغل وهاي العملية اسمها bridge therapy

من هاي المساعدات

1. NSAIDs
2. Glucocorticoids

-*NSAIDs :*

• NSAIDs are just Symptomatic relief

These agents provide analgesic and anti-inflammatory benefits for joint pain and swelling.

However, they do not prevent joint damage or change the underlying disease.

• Choice of an agent depends on:

cardiovascular risk

potential for GI-related adverse events

adherence to medication regimen

insurance coverage.

-*Glucocorticoids :*

• In contrast to NSAIDs, low-dose glucocorticoid treatment effectively reduces inflammation through inhibition of cytokines and inflammatory mediators and prevents disease progression.

• However, due to the adverse effect profile, the goal of glucocorticoid use is to keep doses low and use the drugs as infrequently as possible.

• For bridge therapy: ≤ 3months.

• Intraarticular administration of glucocorticoids may be considered in RA for rapid control of inflammation if a limited number of joints are affected

The main difference between NSAIDs and glucocorticoids is that the glucocorticoids prevents the progression of the disease but only with low doses