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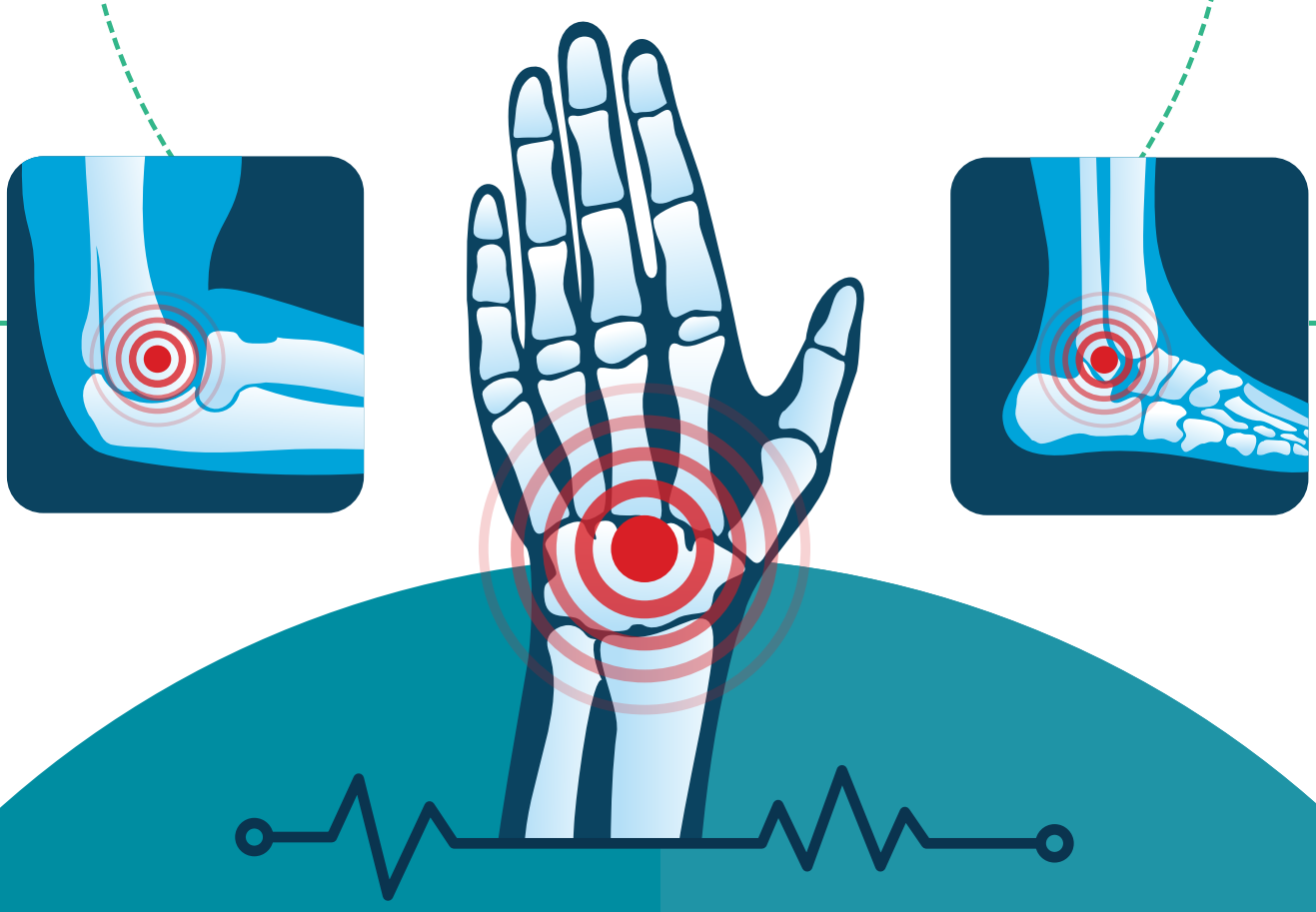

Pathway for Diagnosis and Pharmacological Management of Rheumatoid Arthritis

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SAUDI SOCIETY FOR RHEUMATOLOGY

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Disclaimer

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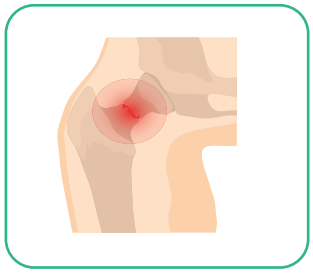
ABBREVIATIONS

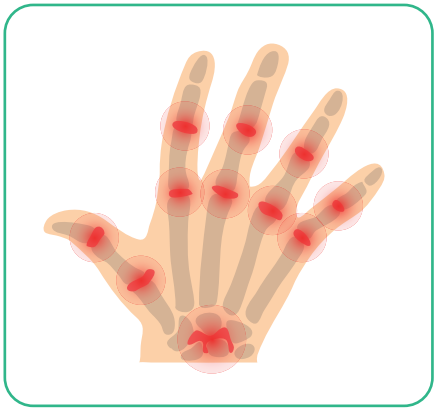
Sl. no	Abbrevation	Full form
01	CBC	Complete blood count
02	CRP	C-reactive protein
03	HAQ	Health Assessment Questionnaire
04	RA	Rheumatoid arthritis
05	RF	Rheumatoid factor
06	TB	Tuberculosis
07	DMARDs	Disease-modifying anti-rheumatic drugs

INTRODUCTION

This pathway covers the pathway for managing rheumatoid arthritis (RA).



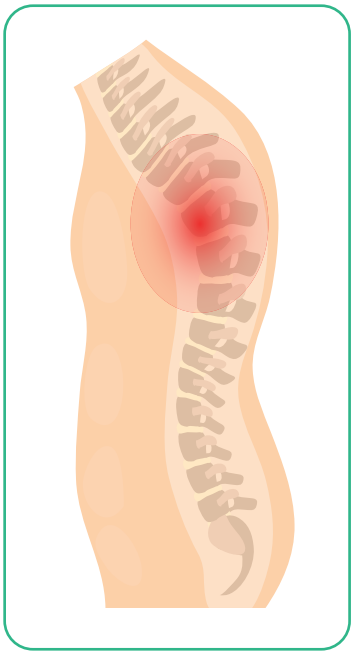
It aims to improve quality of life by ensuring that people with RA have the right treatment to slow the progression of their condition and control their symptoms. People should also have rapid access to rheumatology specialist care for early diagnosis within three months of their symptoms and if their condition suddenly worsens.



RA is the most common autoimmune inflammatory arthritis in adults. RA has a significant negative impact on the ability to perform daily activities, including work and household tasks, and health-related quality of life, and it increases mortality.

RA is characterized by inflammation and swelling of the synovium of the joint, with subsequent destruction of articular structures. Patients with active RA also experience systemic inflammation that is associated with a variety of comorbidities, most importantly cardiovascular disease, which contribute to the increased morbidity and mortality noted in this group than in the general population.

The pain, fatigue, and disability associated with RA significantly reduce the health-related quality of life. Moreover, RA imposes a substantial economic burden upon patients, due to the increased cost of medical care as well as the loss or reduction of employment, frequently during peak working years.



The recommendations in this pathway represent the views of the members of the Saudi Society for Rheumatology.
These recommendations have been arrived at after due consideration of the available evidence. When exercising their judgment, professionals and practitioners are expected to take this guideline completely into account, along with the individual needs, preferences, and values of their patients or those availing their services.
It is not mandatory to apply the recommendations, and the pathway does not override the responsibility to make decisions appropriate to the circumstances of the individual, after consultation with them and their families.

This RA pathway will be used by:	• Health care professionals, rheumatologists, internists, family physicians • Commercial and providers

The ADAPTE process was used, modified to Five Steps as developed by Kristiansen et al, which include:

1. Planning

2. Initial assessment of the recommendations

3. Modification

4. Publication

5. Evaluation

Multiple workshops were conducted over a one-year duration (2019-2020). The Five Steps adaptation process was selected because of its simple and practical approach. The final document was peer-reviewed and edited accordingly.

OBJECTIVES

The objective of this project is to develop a pathway for the medical management of patients with RA.

Table I: Objectives	
01	Early RA diagnosis and referral
02	For the use of disease-modifying anti-rheumatic drugs (DMARDs), including conventional synthetic DMARDs (cDMARDs), targeted biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs), and glucocorticoids
03	Treat-to-target (T2T) strategy in RA management
04	Clarify differences in recommendations for patients who are DMARDs-naïve versus those in patients who have already been treated with one or more DMARDs
05	Clarify differences in recommendations for patients with low versus moderate-to-high disease activity
06	Include recommendations for pharmacologic therapies in the management of RA patients with comorbid conditions (e.g. congestive heart failure, hepatitis B or C, cancer, history of serious infections)
07	Include recommendations for vaccine administration

EARLY RA DIAGNOSIS AND REFERRAL

Arthritis is characterized by the presence of joint swelling, associated with pain or stiffness.

- Joint swelling not due to trauma or bony swelling suggests early inflammatory arthritis, especially if associated with pain and morning stiffness >30 min.
- Patients presenting with arthritis (any joint swelling associated with pain and stiffness) should be referred to, and seen by, a rheumatologist, ideally within 6 weeks after the onset of symptoms.
- Clinical examination is the method of choice for detecting synovitis. In doubtful cases, ultrasound with power Doppler, and MRI might be helpful to detect synovitis.
- Clinical examination: 4-finger test, scissor technique, or 2-thumb technique by a primary care physician trained by a rheumatologist.
- Patients with arthralgia without clinical arthritis and without other diagnosis or other explanation for the arthralgia.
- History taking:
  - Joint symptoms of recent onset (duration <1 year)
  - Symptoms located in MCP joints
  - Duration of morning stiffness ≥60 min
  - Most severe symptoms present in the early morning
  - Presence of a first-degree relative with RA
- Physical examination:
  - Difficulty making a fist
  - Positive squeeze test of MCP joints
- Septic arthritis should be considered in adults presenting with acute monoarthritis, particularly in the presence of joint pain, erythema, warmth, and immobility. The most important risk factors for septic arthritis are prosthetic joint, skin infection, joint surgery, RA, age older than 80 years, diabetes mellitus, and renal disease.
- Excluding diseases (infections, reactive arthritis, connective tissue diseases, polymyalgia rheumatica and crystal-induced arthritis) other than RA requires careful history taking and clinical examination, including the following laboratory tests: complete blood cell count (CBC), ESR, C-reactive protein (CRP), urinary analysis, transaminases, antinuclear antibodies, rheumatoid factor (RF), anti-citrullinated peptide (anti-CCP), hepatitis B and C screening.
- In every patient presenting with early arthritis to the rheumatologist, the following factors predicting persistent and erosive disease should be measured: number of swollen and tender joints, ESR or CRP, levels of RF and anti-CCP antibodies, and radiographic erosions. Patients at risk of developing persistent or erosive arthritis should be started with DMARDs as early as possible, even if they do not yet fulfill established classification criteria for inflammatory rheumatological diseases.
- Patient information concerning the disease and its treatment and outcome is important. Education programs aimed at coping with pain, disability, and maintenance of work ability may be employed as adjunct interventions.
- NSAIDs should be considered in symptomatic patients after evaluation of gastrointestinal, renal, and cardiovascular status.
- Referral to the hospital where a rheumatologist is available to establish a definite diagnosis and start management.

EARLY RA DIAGNOSIS AND REFERRAL

Pathway I: Early RA Diagnosis

Target population: Patients aged >16 years presenting with joint swelling associated with pain or stiffness

The aim in treating RA is to induce complete remission, minimize joint damage and functional loss, alleviate pain, and maximize quality of life

6 WEEKS

	Diagnosis of RA	Prognostic indicator monitoring	Differential diagnosis
History	• Joint pain and swelling • Small joint swelling • Previous episodes • Morning stiffness >30 min • Family history of RA	• Activity limitations • Comorbidities • Risk factors for cardiovascular disease (e.g. smoking)	• Infective arthritis (e.g. fever, rash) • Reactive arthritis (e.g. post-infective throat, gut, sexually acquired) • Other inflammatory arthritis (e.g. Psoriatic rash, nail pits, asymmetrical joint pattern, decreased spinal ROM, diarrhea) • Crystal arthritis (e.g. Tophi) • Connective tissue diseases (e.g. Raynaud, butterfly rash, photosensitivity) • Metabolic
Clinical Examination	• Three or more tender and swollen joint areas • Symmetrical joint involvement in hands and/or feet • Positive squeeze at MCP or MTP joints **Grade B**	• Number of tender and swollen joints • Extra- articular manifestations (eg. nodules, vasculitis, lymphadenopathy) • Cardiovascular comorbidity (e.g. blood pressure and cholesterol)	
Management	• Raised ESR and/or CRP • Level of RF and anti-cyclic citrullinated peptide antibody (ACPA) **Grade A**	**Extra testing as clinically indicated:** • Full blood count • Renal function • Fasting lipids, glucose • Liver function test • X-ray chest, hands and feet • Urinalysis	• ANA • Urate • Synovial fluid analysis

Absence of any of these key symptoms, signs or test results does not necessarily rule out RA

Initial	• Simple analgesics • NSAIDs/COX-2 inhibitors (after evaluation of cardiovascular, gastrointestinal and renal status, check for internal consistency) • If failed, low dose corticosteroids afterconsulting a rheumatologist • DMARDs as prognosis		
Rheumatology Referral	Referral to hospital or centre (where rheumatologist is available)	• When access available Immediately when multiple swollen joints, particularly if positive RF and/or anti-CCP antibody • Within 6 weeks after persistent swelling in more than one joint even if RF is negative • If NSAIDs or steroids are required beyond 6 weeks after initial treatment	NO immediate access contact rheumatologist to initiate DMARDS through the SSR or higher tertiary care center

Go to early RA management

INVESTIGATIONS FOLLOWING DIAGNOSIS

- Immediately after establishing a diagnosis of RA: measure RF ± anti-CCP antibodies, unless already measured to confirm diagnosis.
- Baseline CBC with differential count, urea and electrolytes, liver function test, Hepatitis B and C screening
- X-rays of the hands and feet, unless X-rays were performed to inform diagnosis
- Measure functional ability using, for example, the Health Assessment Questionnaire (HAQ), to provide a baseline for assessing the functional response to treatment.
- If anti-CCP antibodies are present or there are erosions on X-ray: Advise the person that they have an increased risk of radiological progression but not necessarily an increased risk of poor function, and emphasize the importance of monitoring their condition, and seeking rapid access to specialist care if disease worsens or they have a flare.

T2T Strategy

- Aim to achieve remission of active RA in early disease or at least low disease activity in established RA (T2T).
- Consider achieving remission as a target rather than low disease activity in patients with increased risk of radiological progression (presence of anti-CCP antibodies or erosions on X-ray at baseline assessment).
- In adults with active RA, measure CRP and disease activity (using a composite score such as DAS28 or CDAI) monthly or every 3 months in specialist care until the target of remission or low disease activity is achieved.

Initial Pharmacological Management

cDMARDs

- For adults with newly diagnosed active RA: Offer first-line treatment with cDMARD monotherapy using oral methotrexate (MTX) with folic acid supplement, leflunomide or if there is contraindication to MTX give sulfasalazine as soon as possible and ideally within 3 months of onset of persistent symptoms.
- Consider hydroxychloroquine for first-line treatment as an alternative to oral MTX, leflunomide, or sulfasalazine for mild or palindromic disease. Escalate dose as tolerated.
- Consider short-term bridging treatment with glucocorticoids (oral, intramuscular, or intra-articular) when starting a new cDMARD.

ESTABLISHING A DIAGNOSIS OF RA BASED ON ACR CRITERIA

Pathway II: Establishing a Diagnosis of RA Based on ACR Criteria

Measure RF and anti-CCP antibodies and obtain X-rays of the hands and feet to establish whether erosions are present

CBC, differential, urea and electrolytes, hepatic profile, hepatitis B and C, tuberculin test, chest X-ray, flu and pneumococcal vaccine	Measure ESR and CRP and disease activity (using a composite score such as DAS28 or CDAI)	Measure functional ability using, forexample, the HAQ, to provide a baseline for assessing the functional response to treatment

Active RA

Early RA (3-6 months from first symptoms)	Established RA (symptoms for more than 6 months)

Treat active RA in adults with the aim of achieving a target of remission or low disease activity if remission cannot be achieved (treat-to-target)

Start cDMARD MTX as monotherapy. Escalate dose to 20 mg/week within 3 months as tolerated. If there is contraindication to MTX, give leflunomide or sulfasalazine

Consider hydroxychloroquine for first-line treatment as an alternative to oral methotrexate, leflunomide or sulfasalazine for mild or palindromic disease

Consider short-term bridging treatment with glucocorticoids (oral, intramuscular, or intra-articular) when starting a new cDMARD

Use a composite score such as DAS28 or CDAI monthly or every 3 months in specialist care until the target of remission or low disease activity is achieved. Upon failure to achieve target after 3 months, consider adding biologics or JAK inhibitors

CLINICAL DIAGNOSIS OF RA

Pathway III: Clinical Diagnosis of RA

Contraindication to MTX

No

Tapering dose of CS Oral/IM

Inject highly inflamed joints**

Yes

Assess comorbidities and family planning

Initiate MTX monotherapy or MTX based combination

MTX Oral or SQ
Target dose 15–25 mg with folic acid supplement

LEF | SSZ | HC

Initiate other csDMARD monotherapy or combination

LEF | SSZ | HC

- RA: Rheumatoid arthritis
- MTX: Methotrexate
- CS: Corticosteroids
- IM: Intramuscular
- SQ: Subcutaneous
- LEF: Leflunomide
- SSZ: Sulfasalazine
- HCQ: Hydroxychloroquine
- DAS28: Disease activity index
- in 28 joints
  SDAI: Simplified disease activity index
- CDAI: Clinical disease activity index

**Aim at discontinuation at 24 weeks*
***Inject with either methylprednisolone or triamcinolone*

Evaluate at 12 weeks

Clinical improvement based on patient and physician perspective + Assess target disease activity by composite outcome measures (DAS28 or SDAI or CDAI)

Yes

Assess target disease activity at 12–24 weeks by composite outcome measures (DAS28 or SDAI or CDAI) achieved (remission/low disease activity)

No

Go to Phase 2
(RA pathway with biologics or JAK inhibitors)

Yes

- Maintain target for 52 weeks
- Consider down titration of therapy

No

Inject highly inflamed joints**

Perform one or more of the following:
1. Optimize MTX dose
2. Switch from oral to SQ MTX
3. Switch from MTX monotherapy to MTX based combination
4. Switch to Phase 2

Pathway IV: Phase 2 of RA Diagnosis

RA pathway for patients who are non-responsive or not reaching target on cDMARDs after 3-6 months.

Choose most appropriate agent. If no clear indication is available for a specific agent, use the least expensive biologic, with the most preferable or other mode of action (listed in alphabetical order):
- Abatacept + MTX
- Adalimumab + MTX
- Certolizumab pegol + MTX
- Etanercept + MTX
- Golimumab + MTX
- Infliximab + MTX
- Tocilizumab + MTX

Or JAK inhibitors (listed in alphabetical order):
- Baracitinib
- Tofacitinib

If patient planning to get pregnant, consider monotherapy with the safest anti-TNF, preferably certolizumab

Patient with contraindication or adverse event to MTX

Consider monotherapy biologics (tocilizumab/abatacept, etanercept, certolizumab, adalimumab, or JAK inhibitors)

NO
Primary non-response OR not reaching target (on csDMARD) after 3–6 months

Seropositive**

(Listed in alphabetical order)
- Abatacept + MTX
- Adalimumab + MTX
- Certolizumab + MTX
- Golimumab + MTX
- Infliximab + MTX
- Tocilizumab + MTX
- Rituximab + MTX

OR

JAK inhibitor:
- Baracitinib
- Tofacitinib
- Upadacitinib

Seronegative

Consider biologic
- Any anti-TNF + MTX
- Tocilizumab + MTX

OR

JAK inhibitor:
- Baracitinib
- Tofacitinib
- Upadacitinib

Primary non-response: Lack of improvement of clinical signs and symptoms to induction therapy (i.e., when the patient has never responded to the drug)

**New evidence suggests seropositive patients (anti-CCP or RF) are more likely to have a greater response with abatacept than patients who are seronegative. May be considered as an additional option instead of rituximab

*S/C & IV versions available (IV can be used if clinician feels it is most appropriate) after evaluation of patient factors

Pathway V: Phase 3 of RA Diagnosis

Pathway for primary non-responders to biologic agents in combination with MTX.

Choose most appropriate agent. If no clear indication is available for a specific agent, use the least expensive biologic (listed in alphabetical order):

- Abatacept + MTX
- Adalimumab + MTX
- Certolizumab pegol + MTX
- Etanercept + MTX
- Golimumab + MTX
- Infliximab + MTX
- Tocilizumab + MTX

Or JAK inhibitors (listed in alphabetical order): • Baracitinib • Tofacitinib • Upacitinib

If yes: Consider a second anti-TNF (if first biologic is anti-TNF), a biologic with a different mechanism of action, or a JAK inhibitor (patients can be switched to another anti –TNF agent if they experience an adverse event within 6 months)

Has the biologic agent been withdrawn because of an adverse event within 6 months of treatment?

Consider certolizumab/ tocilizumab/any biosimilar JAK Inhibitor

NO

Primary non-response to first biologic (on MTX)

- Non-response to certolizumab after 3 months
- Non-response to any other biologic agent after 6 months

Seropositive**

Seronegative

Does the patient have a contraindication to rituximab?

NO

Rituximab + MTX

Continue rituximab + MTX only if adequate response (improvement of DAS28 of 1.2 points or more.) Should be given no more frequently than 6 months.

Has the patient:
Developed a CI to rituximab?
Withdrawn due to an adverse event?
Non-response to rituximab?

YES

Abatacept + MTX
Adalimumab + MTX
Certolizumab + MTX

Consider biologic
- Any anti-TNF + MTX
- Tocilizumab + MTX

OR

JAK inhibitor:
- Baracitinib
- Tofacitinib
- Upadacitinib

YES

Primary non-response: Lack of improvement of clinical signs and symptoms to induction therapy (i.e. when the patient has not ever responded to the drug)

**New evidence suggests seropositive patients (anti-CCP or RF) are more likely to have a greater response with abatacept than patients who are seronegative. May be considered as an additional option instead of rituximab

*S/C & IV versions available (IV can be used if clinician feels it is most appropriate) after evaluation of patient factors

RA Pathway for Patients who are Non-Responsive or Not Reaching Target On cDMARDs After 3-6 Months

Adalimumab, etanercept, infliximab, certolizumab pegol, tocilizumab, abatacept and JAKi all in combination with MTX, are recommended as options for treating RA, only if: Disease is moderate-to-severe and has not responded to intensive therapy with a combination of conventional DMARDs (cDMARDs).

Adalimumab, etanercept, certolizumab pegol, tocilizumab or abatacept, and JAKi can be used as monotherapy for people who cannot take MTX because it is contraindicated or because of intolerance, when the above criteria are met.

The biologic used should be chosen in the first instance on the basis of clinical judgment (as informed by factors suggested in this pathway) along with national or local guidance, and the overall value proposition offered by the individual medicines. The rationale for the choice should be documented.

- If more than one drug treatment is suitable, the least expensive option should be chosen (after considering administration costs, dosage and price per dose, and patient preference).
- Where NICE has already recommended the originator biological medicine, the same guidance will apply to the biosimilar medicine.
- Pharmacovigilance is essential for any new biological medicine, including biosimilars.
- Additional monitoring is indicated with a black triangle. Patients being prescribed a biologic should be enrolled on relevant registries that collect data on the safety and effectiveness of the biologic in clinical practice.

Changing from originator to a biosimilar

- There is growing evidence that patients in a stable clinical response or remission may be switched to the biosimilar at the same dose and dose interval. This should only be done after discussion and agreement with individual patients with an explanation for the reason for changing.
- Changing a patient on a biologic originator medicine to a biosimilar should be done at the point of prescribing the medicine.
- No automatic substitution of a biologic with a biosimilar should occur at the point of dispensing the medicine.

SCREENING QUESTIONS ASKED IN THE CLINIC

- **Y/N Initial Details Previous TB/TB contact** *(Details)*
- **Recent travel abroad** *(i.e., TB high risk countries) (Which Country/Dates)*
- **History of heart failure** *(NYHA class III or IV) (Details)*
- **History of recurrent infection** *(Details)*
- **History of interstitial lung disease** *(ILD) (Details such as extent of ILD 21)*
- **History of cancer** *(Type/Date when occurred/Date of all clear)*
- **Date of last mammogram (50 years +)** *(Encourage patient to visit GP if > 3 years)*
- **Date of last pap smear (25 years +)** *(Encourage patient to visit GP if > 3 years)*
- **History of infusion reaction to any agent** *(To what/type of reaction)*
- **Allergy** *(Details)*
- **Tocilizumab**
- **Diverticulitis** *(Caution advised due to perforation risk, especially if also on NSAIDs or oral steroids)*

RA and Tuberculosis (TB)

Definition:

Latent TB is defined as a persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB disease.

Association between TB and TNF alpha inhibitors:

All TNF alpha inhibitors carry a risk for reactivation of latent TB. The time of onset (activation of latent TB) varies, with a median of onset in infliximab of (5.5 months) compared to adalimumab (18.5 months).

Clinical presentation of reactivated TB due to TNF alpha inhibitors can be challenging as the incidence of extrapulmonary TB is higher and the patient may lack any respiratory symptoms. Therefore, it is crucial to screen all patients for latent TB before starting biological therapies.

HOW TO SCREEN?

There is no investigation that can completely exclude the presence of latent TB. For that, history and physical examination are crucial. Look for contact with a TB patient, previous TB diagnosis, or treatment and any previous TB screening tests.

Any patient with a strong history of contact with a pulmonary TB patient should be referred to an ID or pulmonology clinic regardless of screening test results.

Two investigations are now available for screening of latent TB:

1. Tuberculin skin test (TST)
2. Interferon gamma release assay (IGRA)

Both are acceptable investigations with conflicting studies preferring one over the other test.

Table II: Interpretation of TST

TST reaction (induration)	Situation in which reaction is considered positive
<5 mm	Test is considered negative (but close contacts should still be referred for further evaluation).
≥5 mm	• HIV infected patient • Close contact • Abnormal chest radiograph with fibrotic changes consist with TB • Immunosuppressed patients (e.g. those on prednisolone 15 mg ≥ for 1 month)
≥10 mm	• IV drug users • Chronic renal failure on dialysis • Malignancies like lymphoma, leukemia, and lung cancer • Health care workers • Residents and employees in jail
≥15 mm	Positive for all patients

TREATMENT OF LATENT TB

Before starting treatment, chest X ray and careful history and examination should be done to roll out active TB

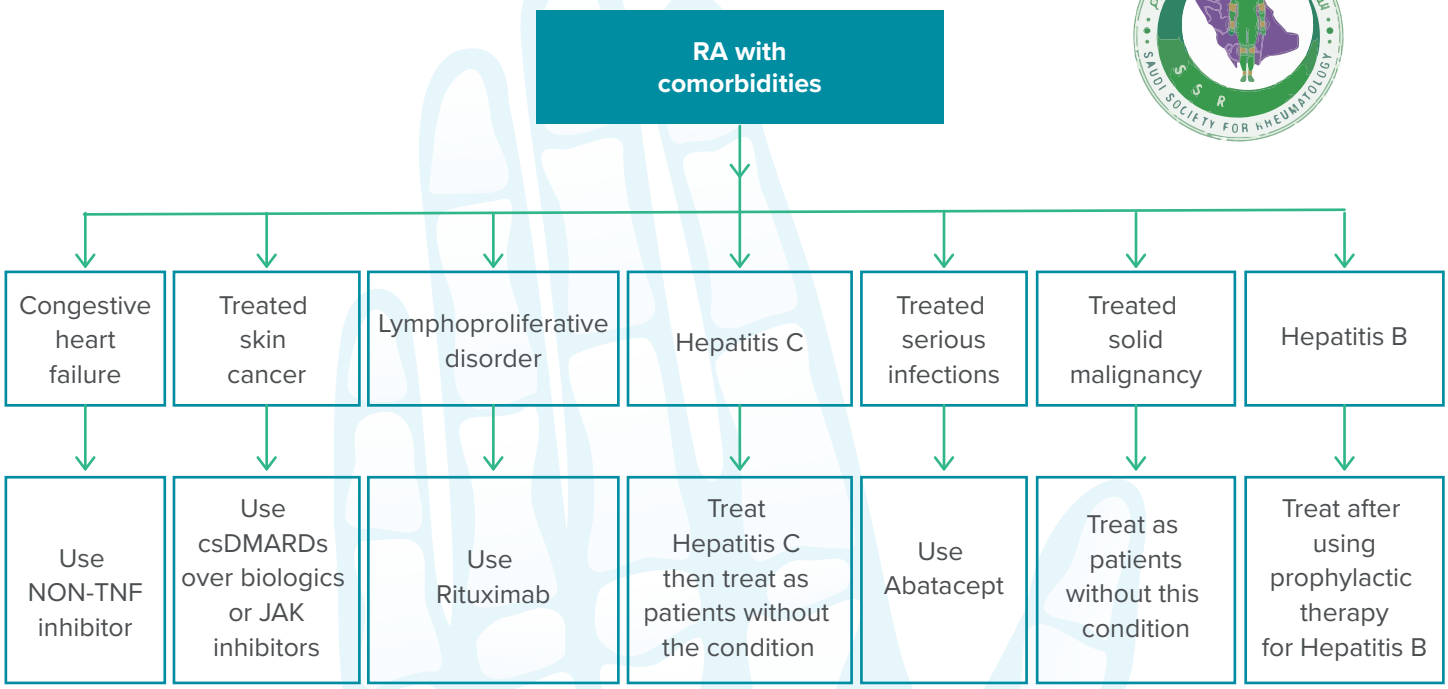
If no evidence of active TB, treatment options are:

1. **Isoniazid** (5 mg/kg) max 300 mg PO daily for 9 months (most widely used regimen)
2. **Rifampin** (10 mg/kg) max 600 mg PO daily for 4 months
3. **Isoniazid** 900 mg + **Rifapentine** 900 mg both once weekly for 12 weeks

When to start TNF alpha inhibitor after starting anti-TB medication?

Recent studies showed safety of starting anti-TB within 3 weeks, but this is still subject to debate.

Pathway VI: Treatment of RA with Comorbidities



Consider the following in treatment of patients with RA with a comorbid condition:

1.Congestive heart failure:
Non-TNF inhibitors are preferred over TNF inhibitors in patients with heart failure.
Use of TNF inhibitors should be avoided because of the risk of worsening heart failure.

2.Hepatitis B:
Patients infected with hepatitis B virus can receive immunosuppression after receiving prophylactic therapy for hepatitis B.

3.Hepatitis C:
Patients receiving treatment for hepatitis C virus infection can receive the same treatment as in patients without this condition. In patients with hepatitis C infection that are not receiving antiviral therapy, use of csDMARDs is preferred over TNF inhibitors.

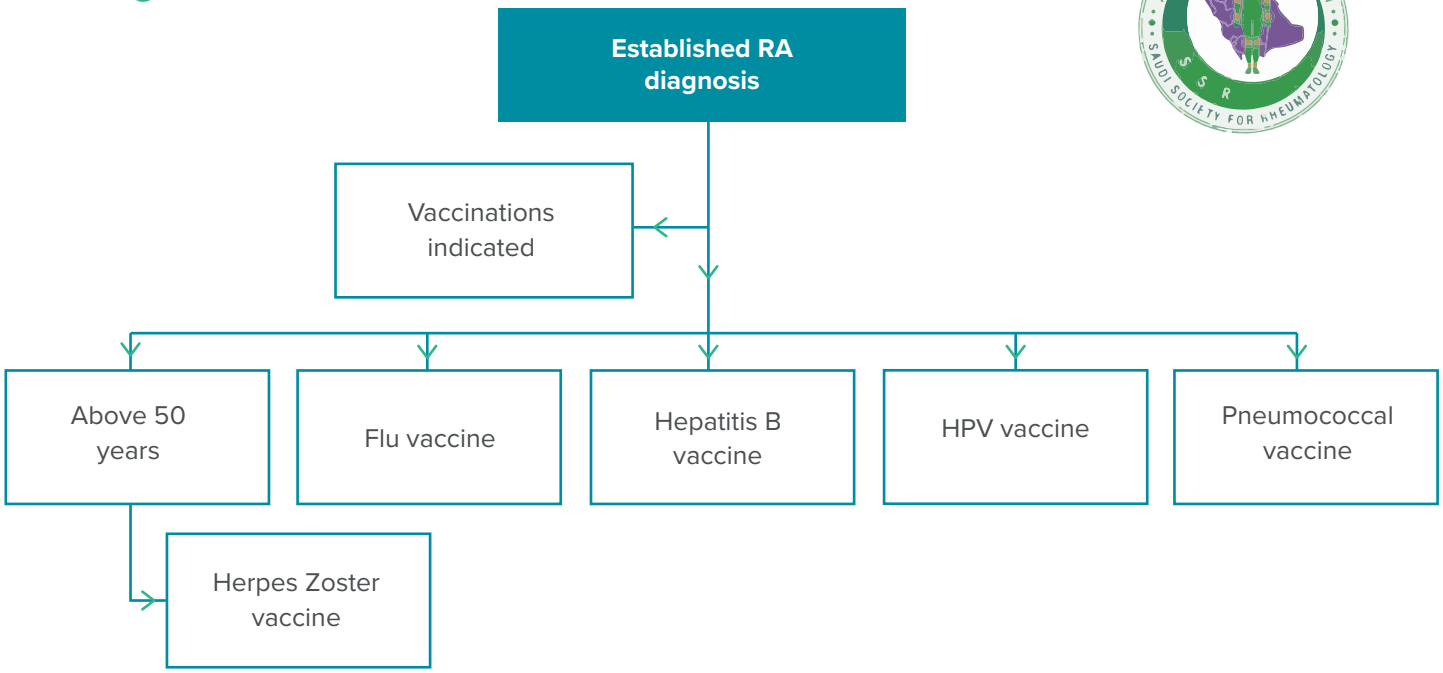
4.Previously treated skin cancer: csDMARDs are preferred over biologics and tofacitinib

5.Previously treated lymphoproliferative disorder: Rituximab is the preferred biologic in these patients

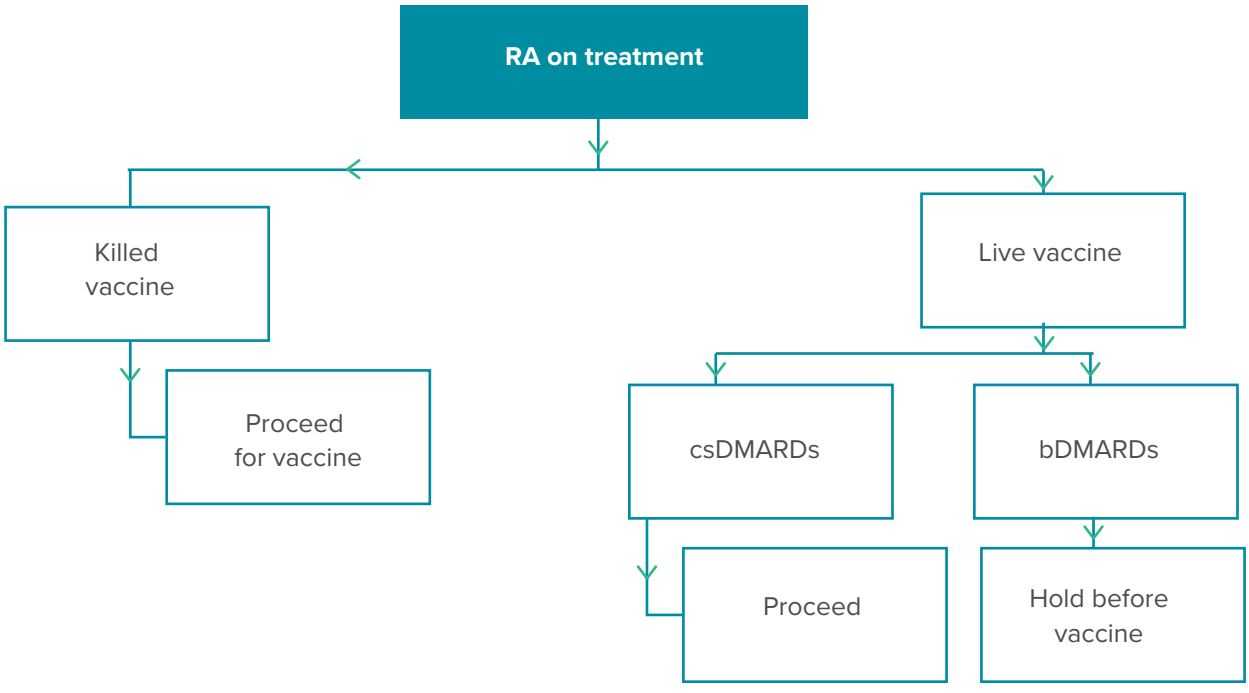
6.Previously treated solid organ malignancy:
Same recommendation as in patients without this condition.

7.Past serious infections: Abatacept is the preferred biologic for these patients.

Pathway VII: Vaccinations for Patients with an Established RA Diagnosis



Pathway VIII: Vaccinations for Patients with RA Already on Treatment



LIVE VACCINE TABLE

Table III: Live Vaccine Table

Live Vaccine	Brand Name
BCG Influenza	Bacillus Calmette-Guerin Vaccine Fluenz Tetra®
Measles, Mumps and Rubella combined vaccine (MMR)	MMRvaxPRO®, Priorix®
Poliomyelitis (oral)	Poliomyelitis Vaccine, live (oral) GSK OPV
Rotavirus (oral)	Rotarix®
Typhoid (oral)	Vivotif®
Varicella-Zoster	Varilrix®, Varivax®, Zostavax®
Yellow fever	Stamaril®

Table III: Live Vaccine Table

Biologic	Time to Elapse Before Giving a Live Vaccine
Adalimumab	3 months
Infliximab	2 months
Golimumab	3 months
Etanercept	1 month
Certolizumab pegol	3 months
Rituximab	6 months
Tocilizumab	3 months
Abatacept	3 months

NON-LIVE VACCINES

- Non-live vaccines are considered to be safe to administer to patients on immunosuppressants and biologic therapies.
- Pneumococcal vaccine should be administered 2-4 weeks before starting a biologic as response after starting treatment can be poor.
- Patients treated with rituximab may receive non-live vaccinations.
- Vaccinations should ideally be completed at least 4 weeks prior to first administration of rituximab (due to a risk of reduced response).
- Vaccinations for influenza and pneumococcal infection are still advisable for patients on rituximab.

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Considerations for vaccination

- Immunosuppressive therapy is generally defined as:
  - Prednisolone 20 mg daily, or equivalent, for 2 or more weeks.
  - MTX 0.4 mg/kg/week
  - Azathioprine 3 mg/kg/day or more
- Live vaccines are generally avoided while on immune suppressive therapy.
- Vaccines are ideally given 2–4 weeks prior to immune suppression.
- Flu vaccine should be given annually.
- Holding MTX for 2 doses after flu vaccine can improve the response to the vaccine.
- 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PCV23) are recommended.
- In a previously unvaccinated patient:
  - Give PCV13 as soon as possible
  - Give PCV23 after 8 weeks then a second dose after 5 years
- Previously received 2 doses of PCV23:
  - Give one dose of PCV13
- In a previously unvaccinated patient:
  - Give PCV13 at least 1 year after PCV23
  - Give the second PCV23 after 8 weeks from the PCV13 and 5 years from the first PCV23

Case 1:

A 45-year-old lady with RA who is still active despite treatment with MTX 20 mg weekly and hydroxychloroquine 400 mg daily. Clinic assessment revealed a DAS 28 score of 5.9 which is consistent with severe activity. She also has history of heart failure on bisoprolol, lisinopril, and furosemide. She also has history of previously treated breast cancer 2 years ago. She was prepared to start on biologic therapy because of persistent disease activity.

ANSWER:

Based on the recommendations written above, this patient should be on biologics other than TNF inhibitors because of the history of heart failure. Patients with history of previously treated solid organ malignancy would be treated like patients without such condition, so the treating rheumatologist would have options to choose from with the exclusion of anti-TNF biologics.

Case 2:

A 60-year-old man with diabetes and hypertension was evaluated for RA activity. He was still complaining of pain and stiffness despite being treated with MTX 20 mg weekly, hydroxychloroquine 200 mg daily and prednisolone 5 mg daily. He also had history of multiple admissions for pneumonia and urinary tract infections secondary to benign prostatic hyperplasia. The assessment in the clinic showed a DAS 28 score of 6.0, which was consistent with severe activity.

ANSWER:

Based on the recommendations written above, this patient should be started on abatacept. The patient has a clear history of recurrent serious infections. In such a scenario, abatacept would be the preferred biologic to start because it carries the lowest risk for further increasing the risk of infections.

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