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Research Article

VACCINATION TARGETS IN THE MANAGEMENT OF ANKYLOSING SPONDYLITIS

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ABSTRACT

Introduction: Ankylosing spondylitis (AS) and the closely related axial spondyloarthritis (axSpA) represents the chronic rheumatic diseases of the immune system hyperactive and including inflammation of the spine, inflammation of the sacroiliac joints, and diverse extraarticular phenomena like acute anterior uveitis, psoriasis, and inflammatory bowel disease. The multifactorial pathogenesis of AS includes a element of HLA-B27, immune system regulation, and the AS is the immune-mediated rheumatic disease patients suffer the most in the world from AS. Infections like influenza, pneumococcal pneumonia, herpes zoster, and hepatitis B virus (HBV) reactivation are major causes of illness and death that can be avoided in people with AS. Consequently, preventive measures, especially vaccination, have become essential elements of AS management. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have recently stressed the need for regular checks of immunization status, the use of inactivated vaccines first, the avoidance of live attenuated vaccines during immunosuppressive therapy, and the best timing of vaccines in relation to medication use.

Methods: This long abstract is derived from a systematic review of peer-reviewed literature with emphasis on infection risk, immunopathogenesis, and vaccination in AS. The inclusion criteria were clinical trials, observational studies, meta-analyses, and key international guidelines.

Findings: These patients are susceptible to infections because of a combination of factors. Immune dysregulation in AS, through changes in T-cell subsets and cytokine signaling, results in higher vulnerability to viral as well as bacterial pathogens. In addition, biologic agents—specifically, TNF-α inhibitors—have been associated with heightened risks of respiratory infection, reactivation of latent tuberculosis, and herpes zoster .

Discussion: Incorporation of vaccination into standard AS management is imperative to diminish infection burden. According to guideline recommendations, real-world research illustrates that vaccination coverage among AS patients is still suboptimal because of physician supervision, patient reluctance, and logistical challenges.

KEYWORDS: Ankylosing Spondylitis, Axial Spondyloarthritis, Vaccination, Biologics, Immunogenicity, and Prevention of Infections.

Introduction

Ankylosing spondylitis (AS) is a typical axial spondyloarthritis (axSpA) with early adult onset, male prevalence, and a disease course characterised by enthesitis, inflammation of the spine, and possible extra-articular features of uveitis, psoriasis, and inflammatory bowel disease[1]. Prevention of infection is at the core of total AS management. Two drivers of risk are: (i) a changed immune environment in spondyloarthritis; and (ii) the impact of immunomodulatory therapies, with greater complex effects under IL-17 blockade, particularly from TNF-α inhibitors and JAK inhibitors [1]. Vaccination has repeatedly lowered serious events due to respiratory pathogens and herpes zoster in immune-mediated rheumatic diseases (IMRDs) and is recommended by prominent societies with great emphasis[2].

The 2022 American College of Rheumatology (ACR) Guideline for Vaccines in Patients with Rheumatic and Musculoskeletal Diseases (RMDs) offers disease-agnostic recommendations transferable to AS[2], whereas the 2019 European Alliance of Associations for Rheumatology (EULAR) update offers AIIRD-wide, pragmatic suggestions (e.g., "strongly consider" influenza and pneumococcal vaccine, vaccinate in quiescence, and before immunosuppression if possible)[3]. The Advisory Committee on Immunization Practices (ACIP)/Centors for Disease Control and Prevention (CDC) schedules offer product-specific timing and intervals and are revised yearly[3].

Immunologic Background and Treatment Landscape in As

Immune Features with Implications for Vaccines

Ankylosing spondylitis (AS) and associated axial spondyloarthritis (axSpA) are defined by a unique immunologic profile in which innate and adaptive pathways coalesce on a Th17/IL-17–mediated axis. Increased IL-17 and IL-23 levels are found in most patients with axSpA, and tissue-resident innate lymphoid cells, γδ T cells (gdT17) and type-3 innate lymphoid cells (ILC3s) are capable of producing significant IL-17 regardless of traditional IL-23 signaling[4]. This IL-17-biased environment is relevant to vaccination at a biological level because IL-17 and concomitant cytokines play roles in mucosal barrier immunity, neutrophil recruitment, and production of antimicrobial peptides — pathways that are involved in both vaccine-induced immunity and innate pathogen clearance[5].

Aside from the IL-17/IL-23 pathway, AS reveals inputs from genetic predisposition (most notably HLA-B27), innate immune sensors, and disruptions of the function of the gut barrier and microbiome; these inputs collectively sculpt baseline host defences and can shape qualitative vaccine responses[6]. Yet, practically useful vaccine recommendations for AS are in large part based on evidence in wider immune-mediated rheumatic disease (IMRD) groups (rheumatoid arthritis [RA], psoriatic arthritis [PsA]) since there are numerous immunomodulatory medications and their consequent immunologic effects that are common to these conditions[7].

Therapies that Modulate Vaccine Response

Immunomodulating therapies applied in AS vary significantly in mechanism and in anticipated effects on risk of infection and vaccine immunogenicity. Here we outline major drug classes and evidence that should be considered by clinicians when preparing for immunization.

- NSAIDs. Non-steroidal anti-inflammatory drugs are commonly employed for symptomatic management in AS but do not significantly degrade vaccine immunogenicity and thus do not typically need adjustment in timing of vaccines[8].
- Traditional synthetic DMARDs (csDMARDs). Sulfasalazine occasionally is employed for peripheral spondyloarthritis manifestations; methotrexate (MTX) is less frequently utilized for isolated axial disease but can be utilized in peripheral arthritis. MTX routinely demonstrates the capacity to ablate humoral reactions to multiple vaccines, specifically influenza and pneumococcal vaccines, and serologic reactions to SARS-CoV-2 vaccines in various cohorts[9]. Pragmatic approaches like short-term holding of MTX at the time of vaccination (when disease control and patient risk allow) have been shown to enhance antibody responses in selected contexts and are addressed in guideline statements[10].
- Tumour necrosis factor-alpha (TNF-α) inhibitors. TNF inhibitors (adalimumab, infliximab, etanercept, golimumab, certolizumab) continue to be very effective for axial disease in biologic-naive patients who are in need of biologic therapy. In general, TNF blockade is linked to modestly elevated risk of serious and opportunistic infections (such as reactivation of latent ones like tuberculosis) and has been reported to be linked with hepatitis B virus (HBV) reactivation in HBsAg-positive patients who are not receiving prophylaxis[11]. In relation to vaccines, the majority of investigations demonstrate that responses to inactivated vaccines (pneumococcal, influenza) are usually maintained in TNF inhibitor-treated patients though titers can be modestly lowered from those of healthy controls[12]. Since TNF inhibition may allow reactivation of latent infections, baseline screening (for HBV, latent TB) and prophylactic vaccination (with indicated vaccines) prior to starting therapy are advisable[13].
- Interleukin-17 pathway inhibitors. IL-17 blockers (secukinumab, ixekizumab, bimekizumab) have efficacy in axSpA and are distinguished from TNF blockers by infection profile; e.g., IL-17 inhibition has a smaller

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signal for reactivation of tuberculosis but can slightly enhance rates of mucocutaneous candidiasis[14]. Notably for immunization, a number of controlled and observational reports describe intact humoral responses to inactivated influenza and other vaccines while on secukinumab therapy[15]. These findings justify the practical view that standard inactivated vaccines can be given during IL-17 inhibitor therapy without regular drug holding, though clinicians need to individualize decisions regarding new or live vaccines.

- Janus kinase (JAK) inhibitors. Oral JAK inhibitors (tofacitinib, baricitinib, upadacitinib and others) disrupt intracellular JAK–STAT signaling and thus modify several cytokine pathways important for antiviral and antibacterial immunity. Large reviews and aggregate clinical data suggest JAK inhibitors as a class are related to an increased risk of infection, and a consistent signal for herpes zoster reactivation (greater than with many biologics) has occurred across indications[16]. From a vaccine perspective, the additional risk of zoster makes the recombinant zoster vaccine (RZV; non-live) a priority in patients scheduled for or undergoing JAK inhibitor therapy. Data on vaccine immunogenicity during JAK inhibitor therapy are conflicting: some decreases in antibody responses to pneumococcal and other vaccines have been reported in pooled analyses[16], and considerations regarding timing (vaccinate prior to initiating JAKi when possible) are sensible.
- B-cell depleting agents and other targeted treatments. While not frequently first-line in axial disease, B-cell depletion (rituximab) and other drugs significantly compromise humoral immunity and dampen serologic response to virtually all protein-antigen vaccines[17]. Careful pre-treatment immunization (and, for certain vaccines, post-vaccination serologic screening) should be employed when these agents are utilized and timing windows in comparison to dosing (e.g., vaccinate before rituximab or when B-cell recovery is occurring) are crucial to optimize response[18].
- Glucocorticoids. Systemic corticosteroids are dose-dependently suppressive of vaccine responses; long-term or high-dose steroid use is linked with reduced vaccine immunogenicity and increased infection risk. All steroid bursts, even short ones, can impact some immune readouts; thus steroid minimization is a sensible addition to vaccine planning[18].

Practical Implications for Planning Vaccination

Together, the immunologic features of AS and drug-specific effects here create three clinician-friendly messages: (1) prioritize completion of non-live vaccines (influenza, pneumococcal, COVID-19, RZV, hepatitis B, HPV where appropriate) before starting potent immunosuppression when possible; (2) understand that MTX and B-cell depletion are the most reliable offenders for diminished humoral responses and schedule timing or temporary hold accordingly; and (3) obtain baseline screening for latent infections (HBV, TB) and provide antiviral prophylaxis or monitoring where appropriate to minimize risk of reactivation[19].

Vaccination Goals in As

Vaccination is still a pillar of infection prevention in ankylosing spondylitis (AS), especially due to the fact that patients are often being treated with biologic DMARDs (bDMARDs) and JAK inhibitors, which result in increased vulnerability to vaccine-preventable and opportunistic infections[20]. Recommendation bodies like EULAR (European Alliance of Associations for Rheumatology), ACR (American College of Rheumatology), and ACIP (Advisory Committee on Immunization Practices) suggest individualized immunization regimens in subjects with immune-mediated rheumatic diseases (IMRDs)[21].

Table 1: Overview of various vaccines

Immunologic Background	Impact on vaccination	Therapies
•IL-17/IL-23 Pathway (increase IL-17,ILC3) •Genetic Predisposition (HLA-B27,microbe) •Altered Mucosal Barrier (affects vaccine response)	•Mucosal Immunity •Neutrophils •Cytokines	•NSAIDS •csDMARDs •TNF inhibitors •IL-17 inhibitors •JAK inhibitors •B cell depletion •steroids

Targets can be classified into three categories:

- Universal (given to all adults, including AS patients),
- Risk-based (targeting IMRD/biologic use or comorbidities), and
- Catch-up (according to pre-existing immunity).

Universal and Strongly Recommended Targets

Influenza (Inactivated) — Yearly Vaccination

Reasoning: AS patients receiving immunomodulators (TNF inhibitors, IL-17 inhibitors, JAK inhibitors) are at higher risk of influenza complications such as pneumonia, hospitalisation, and death[22]. Yearly inactivated influenza vaccine lowers incidence and severity[22]. Immunogenicity &Safety: Research illustrates maintained antibody responses among AS patients on TNF inhibitors and IL-17 blockade[23]. JAK inhibitors can slightly dampen humoral responses, though T-cell immune responses are still sufficient[23]. GuidelinePosition:EULAR and ACR both stress yearly vaccination for all IMRD patients, preferably during the pre-flu season[24]. Timing:Vaccination may be administered before or concomitantly with biologic therapy but can be administered earlier seasonally[24].

Pneumococcal — PCV Then PPSV23

Rationale:Risk of pneumococcal disease is higher in AS patients on immunosuppressants. Meta-analyses attest decreased invasive pneumococcal disease (IPD) and pneumonia in IMRD groups following vaccination [24]. Immunization Options (ACIP 2025):•Single PCV20, or• PCV15 then PPSV23 after 8 weeks (intervals according to national guidelines)[24].Immunogenicity:TNF inhibitors can decrease antibody titers slightly but clinical protection is still substantial[25]. Timing:Ideally before biologic initiation, but vaccination is safe during treatment[25].

COVID-19 (mRNA and Other Platforms) Rationale

AS patients at increased risk for severe COVID-19 outcomes, especially on biologics or glucocorticoids[26]. Guideline Support: ACR wholeheartedly recommends primary immunization and boosters in all IMRD patients[26]. Timing Considerations: Give according to national guidelines. In the case of being on high-dose steroids or methotrexate, consider temporary deferment to maximize vaccine response[26].

Tetanus, Diphtheria, Pertussis (Td/Tdap)

Rationale: Routine adult vaccination is still applicable to AS patients. Tdap should be given once in adulthood, and then Td/Tdap every 10 years[27]. Special Note: Pregnant AS patients should be administered Tdap for every pregnancy to shield neonates[27]. Safety: Inactivated, safe in biologic therapy.

Hepatitis B (HBV)

Rationale: HBV reactivation has been described with TNF inhibitors and JAK inhibitors[28]. Therefore, screening (HBsAg, anti-HBs, anti-HBc) is required before immunosuppression. Vaccination Strategy: non-immune patients should be administered full HBV vaccination. High-dose or adjuvanted vaccines may enhance seroconversion in immunosuppressed patients[28].•post-vaccine antibody titers are to be test[28].

Herpes Zoster (Recombinant Zoster Vaccine, RZV) Rationale: Herpes zoster in IMRD patients is strongly increased, particularly on JAK inhibitors[29]. Vaccine Choice: The recombinant zoster vaccine[29] is safe and non-live. Two doses are administered (2–6 months apart, or 1–2 months if rapid schedule required). Guideline Position: ACIP does recommend RZV for immunocompromised adults ≥19 years[29]. EULAR also emphasizes shingles prevention in AS[29]. Immunogenicity: Excellent immune response even in biologic-treated IMRD patients[30].

Human Papillomavirus (HPV)

Rationale: Risk of HPV-associated malignancy may be enhanced in IMRD because of prolonged immunosuppression. Guideline: Adhere to usual age-related guidelines (usually through 26 years, some recommend up to 45 years). Immunogenic and safe in AS patients on biologics[30].

Hepatitis A

Rationale: Not always indicated, but should be used in AS patients with chronic liver disease, anticipated travel, or occupation-related risk.Vaccine Safety: Inactivated, safe during immunosuppressive therapy [30].

MMR and Varicella (Live Vaccines)

Rationale: AS patients should be tested for immunity to measles, mumps, rubella, and varicella. These live vaccines are contraindicated in patients on biologics or JAK inhibitors. Timing: 4 weeks before initiation of immunosuppression. Contraindicated during therapy[31].

Travel and Risk-Based Vaccines

Comprises Meningococcal (MenACWY, MenB), Haemophilus influenzae type b (Hib), Typhoid, Rabies, and Japanese Encephalitis. Rationale:Indicated by comorbidities, outbreaks, or travel.Inactivated forms are safe during biologic therapy[31].

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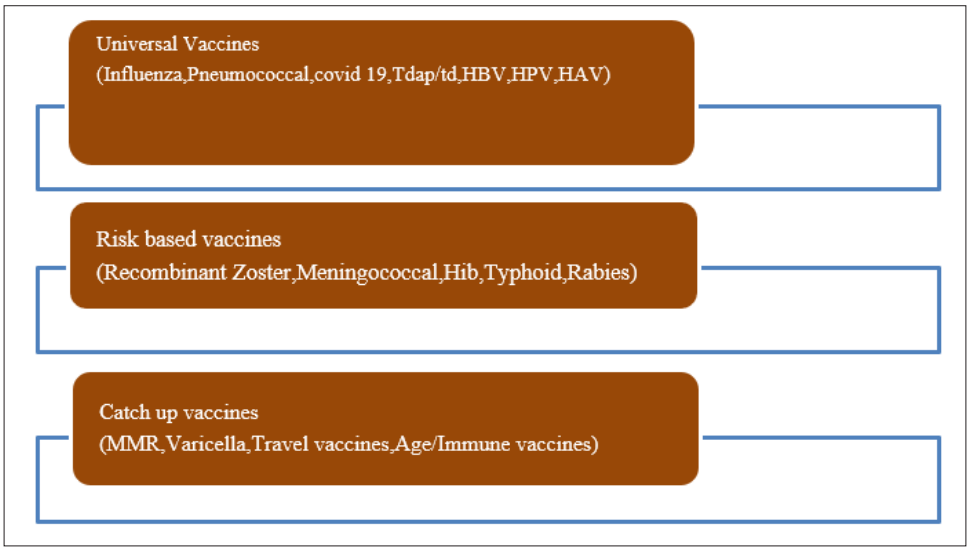

Flowchart 1: Type of vaccines

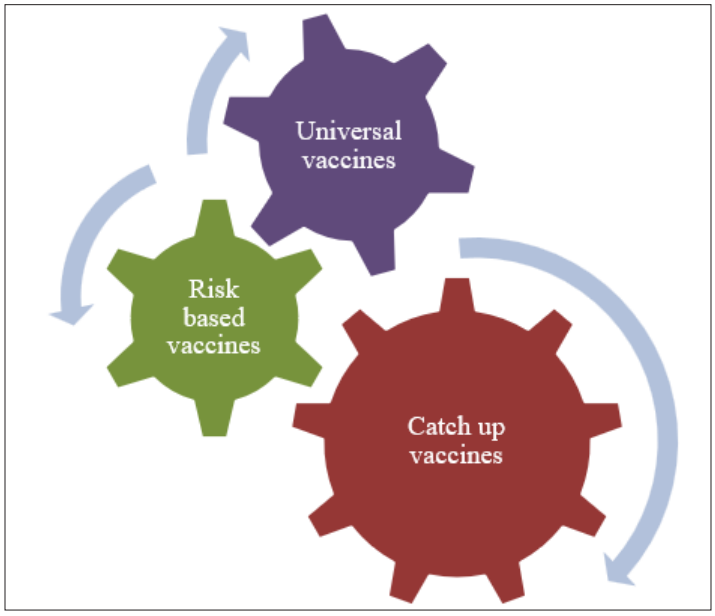

Figure 1: Interlocking functions of Vaccines

Drug-Aware Timing Strategies

Biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs), such as TNF inhibitors, IL-17/IL-23 inhibitors, and Janus kinase inhibitors (JAKi), have revolutionized the treatment of spondyloarthritis (SpA) and other immune-mediated rheumatic diseases. These treatments dampen host immunity and change susceptibility to infection. Therefore, vaccination and prevention strategies against infection need to be carefully coordinated with initiation, continuation, or interruption of drugs. Timing optimization of "drug-aware" vaccination is essential to achieve maximal protective efficacy, minimize infection load, and prevent safety hazards[31].

Before Initiation of Biologic/JAK Treatment

Screening for Infectious Diseases

Before initiating immunosuppression, baseline screening for silent infections and identification of vaccination requirements.

Hepatitis B Virus (HBV): The CDC (2025a) advises screening for HBsAg, anti-HBs, and anti-HBc in all patients initiating biologic/JAK therapy. HBsAg positivity is a marker of chronic infection necessitating antiviral prophylaxis; isolated anti-HBc implies previous exposure with risk of reactivation; and lack of markers indicates susceptibility and need for vaccination. TNFi, rituximab, and JAKi are most linked with HBV reactivation[32].

Tuberculosis (TB): Reactivation of latent TB is an old familiar complication of TNFi treatment. Screening with interferon-γ release assays (IGRAs) or tuberculin skin tests (TST), along with chest imaging in case of risk factors, is required[32]. Completion of prophylactic treatment for LTBI before starting TNFi significantly lowers the risk of reactivation[32]. With other biologics (e.g., IL-17

inhibitors), also baseline TB screening is recommended due to sporadic reactivation reports.

Other infections: HIV, HCV, and in certain contexts strongyloides screening is also indicated before intensive immunosuppression, particularly in endemic regions[32].

Principles of Vaccine Timing

Inactivated vaccines: Safe during immunosuppression, but immunogenicity is generally greater if administered before drug treatment. Research indicates better seroconversion rates for influenza and pneumococcal vaccines when they are given before TNFi or JAKi[33]. Thus, best practice is to administer recommended inactivated vaccines at least two weeks before initiating therapy.

Live attenuated vaccines: Since live vaccines depend on replication of weakened organisms, there is a high risk of disseminated infection once immunosuppression is initiated. To achieve sufficient replication and priming of immunity, they must be administered at least four weeks before therapy initiation[33]. For agents with deep or long-lasting effects (e.g., rituximab, alemtuzumab), still greater lead times are advised.

Priority Vaccines before Therapy

Influenza: Vaccination with inactivated influenza vaccine annually is highly recommended. Biologics do not abrogate but blunt immune responses[34].

Pneumococcal: New ACIP recommendations (2024–2025) favor a single dose of PCV20, or PCV15 with a follow-up dose of PPSV23 at least 8 weeks later. Pneumococcal vaccine is particularly crucial as pneumonia and invasive pneumococcal disease are exacerbated in immunosuppressed individuals[34].

COVID-19: Primary and booster doses should be given to all patients before immunosuppression. Antibody titers are greater when vaccinations are administered before initiating b/tsDMARDs[35].

Recombinant zoster vaccine (RZV, Shingrix): JAKi greatly enhance zoster risk [35]. Since RZV is not live, it may be administered preceding or concurrent with therapy, but initiating the two-dose series preceding therapy optimizes efficacy[35].

Hepatitis B: Non-immune individuals should be immunized, preferably with double-dose or high-dose regimens for immunocompromised patients[36]. Anti-HBs testing after vaccines can be used to confirm immunity.

Other vaccines: Tdap booster, HPV vaccine (through age 26 or 45 in some recommendations), and HAV in endemic regions should be boosted.

During Current Therapy

Inactivated Vaccines are Safe

Unlike previous concerns, several studies affirm that inactivated vaccines are safe on biologic and JAKi therapy and should not be withheld. Even though the rate of seroconversion can be lower, clinically relevant protection is obtained [37]. Influenza, pneumococcal, COVID-19, RZV, HBV, Tdap, HPV, and HAV vaccines are therefore all safe during continued therapy.

Methotrexate-specific Considerations

MTX is commonly used in peripheral SpA and RA. It has a definite immunosuppressive action on vaccine responses. Randomized controlled trials show that MTX hold for two weeks after influenza vaccination enhances antibody responses without significant flare risk [37]. More recent data imply that one week of hold is non-inferior to two weeks [38]. The ACR (2022) thus recommends a brief MTX hold following influenza vaccination in carefully selected patients, but this should be weighed against risk of flare and individualized by disease activity.

JAK inhibitor–specific Considerations

JAK inhibitors, including tofacitinib, baricitinib, and upadacitinib, are linked with increased risk of herpes zoster, usually presenting as multidermatomal or recurrent herpes zoster[39]. Thus, vaccination using RZV is highly recommended for all JAKi-treated individuals. There is limited information on vaccine immunogenicity with JAKi, but usual vaccine schedules are recommended with the caveat that responses may be dampened[39].

Monitoring Vaccine Responses

Where there are correlates of protection (e.g., anti-HBs against HBV), measurement of post-vaccination titers might be useful. Non-responders should be revaccinated or offered higher-dose preparations. For influenza and COVID-19, routine antibody testing is not advisable outside research contexts.

Live Vaccines

General Contraindication

Live vaccines (e.g., MMR, varicella, yellow fever, live attenuated influenza, oral typhoid) are typically contraindicated with therapy using TNFi, IL-17/23 inhibitors, and JAKi[39]. Immunosuppression predisposes to unchecked replication of attenuated organisms and subsequent potentially life-threatening infection.

Washout and Exceptional Cases

In exceptional circumstances where live vaccines are needed (e.g., yellow fever for unavoidable travel), drug washout and immune recovery times must be carefully carried out. The duration is based on the half-life and mechanism of the drug:

- TNFi: Typically need ≥2–3 half-lives before live vaccination.
- JAKi: Shorter washout (~1–2 weeks) might be adequate, but evidence is sparse.

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- B-cell depleting therapies (e.g., rituximab): Need much greater intervals (≥6–12 months).

Expert consultation is required, and options like chemoprophylaxis or delay in travel are usually more desirable.

Case Examples

- A patient on secukinumab who needs yellow fever vaccination for travel to Brazil should ideally delay travel or obtain non-live alternatives, as it is unsafe to vaccinate during IL-17 blockade.
- A young adult on tofacitinib who lacks prior varicella immunity should be vaccinated against varicella before initiating therapy, as live varicella vaccine is contraindicated once on JAKi.

Table 2: Therapeutic Overview

BEFORE THERAPY	DURING THERAPY	LIVE VACCINES	DRUG SP ADJUSTMENTS
➢ Screen for HBV, TB, HIV, HCV ➢ Inactivated vaccines ≥2 weeks before ➢ Live vaccines ≥4 weeks before	➢ Inactivated vaccines safe ➢ Monitor serology (HBV, others) ➢ Brief MTX hold after flu/COVID vaccines	➢ Contraindicated during therapy ➢ Only pre-treatment or after washout	➢ MTX → short hold improves response ➢ JAK inhibitors → prioritize recombinant zoster vaccine ➢ Rituximab → vaccinate before infusion / during B-cell recovery

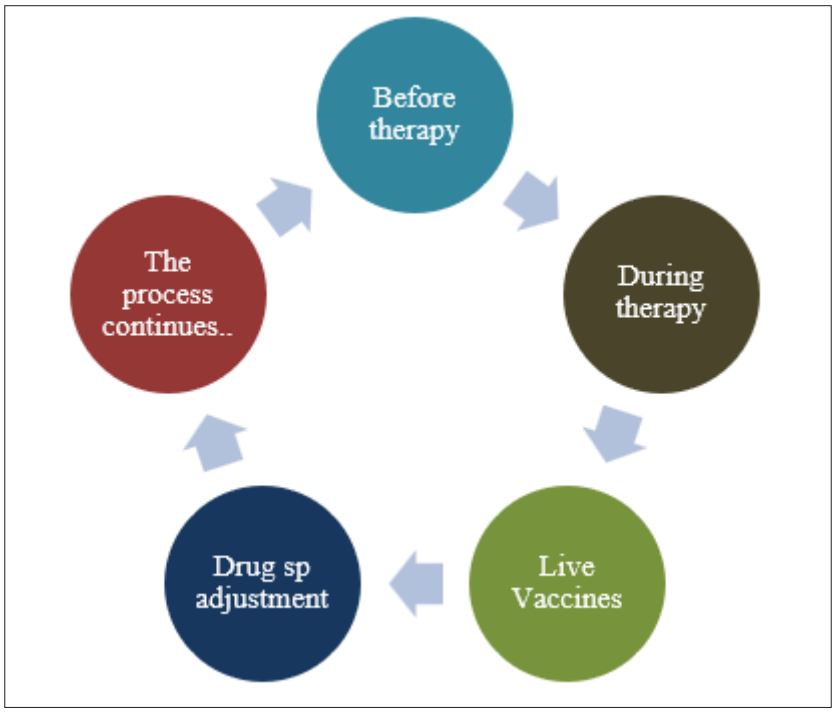

Figure 2: Cyclic relationships in the procedure of therapy

Evidence Snapshot by Vaccine in as/ Spondyloarthritis

Influenza

Yearly influenza vaccination is highly advised in inflammatory rheumatic and musculoskeletal disease (IMRD) patients, such as ankylosing spondylitis (AS), by the American College of Rheumatology (ACR) as well as the European Alliance of Associations for Rheumatology (EULAR) guidelines[39]. Vaccination is recommended based on evidence that influenza may cause severe respiratory illness and heightened hospitalization in immunosuppressed persons.

Under IL-17 blockade (e.g., secukinumab), a number of observational cohorts and small clinical trials have demonstrated intact seroconversion and titers similar to those of healthy controls[39]. This suggests that IL-17 inhibition has minimal adverse effects on humoral responses.

In patients receiving TNF inhibitors (TNFi), influenza response to vaccination is usually sufficient but sometimes slightly diminished compared to immunocompetent subjects. Although they have a little less seroprotection, the clinical response is still significant, and vaccinated patients have lower influenza-related morbidity than unvaccinated IMRD patients[40].

Pneumococcal

Pneumococcal vaccination is yet another pillar of preventive intervention for AS patients, considering their greater susceptibility to invasive pneumococcal disease (IPD) and pneumonia during biologic therapy. Real-world evidence and meta-analyses indicate that vaccination diminishes the risk of IPD and hospitalization in IMRDs, such as AS[41].

Vaccine immunogenicity is usually satisfactory in biologic-treated patients, although certain research indicates diminished antibody responses with methotrexate or corticosteroids at high doses. Of interest, TNFi and IL-17i treatments have not been linked to clinically important reductions in pneumococcal vaccine effectiveness[41].

Based on ACIP 2025 guidelines, adult vaccination should be conducted using either a single-dose regimen of PCV20 or a sequential regimen of PCV15 and PPSV23, with product-specific labeling and comorbidity-guided intervals [41]. Note that vaccination may occur before or concurrent with biologic therapy but preferably before immunosuppression to enhance immunogenicity[42]. For <65-year-old patients with IMRDs, earlier pneumococcal vaccination is recommended because of increased baseline risk[42].

Herpes Zoster (RZV, Recombinant Zoster Vaccine)

Risk of herpes zoster is enhanced in patients with IMRDs owing to both immunosuppressive therapy and disease-associated immune deficiency as well as the use of JAK inhibitors and chronic corticosteroid[43]. Thus, the non-live recombinant zoster vaccine (RZV) is recommended firmly for adults with immunocompromised states ≥19 years, given as a 2-dose regimen[44].

Data from DMARD-treated populations, such as rheumatoid arthritis and spondyloarthritis patients, demonstrate high immunogenicity and good tolerability with no excess of disease flares[45]. Observational study of effectiveness indicates 60–70% less shingles incidence in vaccinated autoimmune patients[46]. In contrast to the live zoster vaccine (Zostavax), RZV is safe during biologic therapy.

Hepatitis B

Hepatitis B virus (HBV) reactivation is a serious safety issue with TNF blockers and certain other biologics. HBsAg-positive or anti-HBc-positive patients can become reactivated with HBV when not treated prophylactically[47].

Therefore, screening for universal HBV serology (HBsAg, anti-HBs, anti-HBc) is necessary before the start of biologic or JAK inhibitor treatment[48]. Non-immune patients identified should be vaccinated against HBV before treatment is started whenever feasible. Vaccine immunogenicity can, however, be affected in immunosuppressed individuals, requiring post-vaccination anti-HBs titre testing and potential booster shots[49].

For high-risk patients of reactivation, antiviral prophylaxis using nucleostide analogues is recommended, advised by hepatology consultation[49].

COVID-19

The COVID-19 pandemic raised concerns about the vulnerability of IMRD patients. Present consensus advises that AS and other IMRD patients be given primary and booster doses of COVID-19 vaccines as per national immunization policies[49].

A number of studies indicate immunogenicity is maintained in biologic-treated patients like TNFi and IL-17i, with responses potentially mildly diminished relative to healthy controls. Methotrexate has been implicated to blunt humoral response, prompting the ACR to suggest short MTX holds (approximately 2 weeks) after vaccination in certain patients, weighing the threat of flare of disease against[50].

Most biologics may be safely maintained through vaccination, but clinicians ought to advise patients regarding temporary side effects (reactogenicity) and reemphasize the value of timely booster receipt[50].

HPV, HAV, and Tdap

- HPV vaccination can be given within the normal age group (through 26 years, with some catch-up to age 45), and has proven to be safe and effective in IMRD patients, including those who are on biologics[51].
- HAV is recommended for chronic liver disease patients, those who travel to endemic regions, or outbreak

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situations. Immunogenicity is usually preserved in IMRDs on biologics, although antibody responses are reduced somewhat[51].

- •Tdap/Td boosters need to be given according to routine adult immunization schedules (every 10 years) without biologic-specific dosing modifications[51].These vaccines are inactivated and can be given safely during biologic therapy, without needing to interrupt treatment.

Table 3: Evidence Snapshot by Vaccine in Ankylosing Spondylitis (AS)

Vaccine	Guideline Recommendation	Evidence In As / Imrds	Impact Of Therapies	Key Notes
INFLUENZA	Annual vaccination strongly advised [52].	Influenza causes severe respiratory illness & hospitalization in immunosuppressed patients	IL-17 inhibitors (e.g., secukinumab): intact seroconversion, similar to healthy controls. TNF inhibitors: response sufficient but slightly reduced	Vaccinated patients show lower influenza-related morbidity than unvaccinated
PNEUMOCOCCAL	Essential preventive strategy, esp. with biologics (ACIP 2025: PCV20 single dose or PCV15 + PPSV23 sequential)	Reduces invasive pneumococcal disease (IPD) and hospitalizations	Immunogenicity usually satisfactory; diminished with methotrexate or high-dose steroids. TNFi & IL-17i: no major reduction in effectiveness	Should be given before immunosuppression when possible; earlier vaccination recommended in <65 yrs with AS
COVID-19	Strongly recommended (primary + booster doses per ACIP & national protocols)	Reduces severe COVID outcomes in IMRD patients	Antibody titers higher if vaccinated before starting b/tsDMARDs	Safe with TNFi, IL-17i, JAKi; boosters important
HEPATITIS B (HBV)	Screening before biologics; vaccinate non-immune patients	Prevents HBV reactivation, esp. under TNFi therapy	Immunogenicity may be reduced; double-dose or high-dose regimens advised for immunocompromised	Post-vaccine serology (anti-HBs) recommended
HERPES ZOSTER (RZV – RECOMBINANT ZOSTER VACCINE)	Recommended for immunocompromised ≥19 yrs or ≥50 yrs [52]	Efficacy and safety confirmed even in patients on biologics/DMARDs	JAK inhibitors increase zoster risk, making RZV especially important	Not live → can be given during therapy
OTHER (MMR, VARICELLA, YELLOW FEVER, ETC.)	Live vaccines contraindicated during biologic/JAKi therapy	Safe only before therapy initiation	Require ≥4 weeks before biologics	Travel vaccines may need special planning

Safety: Disease Activity, Flares, and Adverse Events

Large-scale guideline syntheses all find that inactivated vaccines, including influenza, pneumococcal, and COVID-19 vaccines, do not raise the risk of disease flares among patients with immune-mediated rheumatic diseases (IMRDs) like ankylosing spondylitis (AS)[53]. Live vaccines, on the other hand, are contraindicated after a patient initiates biologic therapy or Janus kinase inhibitors (JAKi) due to the potential for viral replication in the absence of control[53].

The adjuvanted but non-live recombinant zoster vaccine is a valuable choice for immunocompromised individuals. Although it may be reactogenic with temporary side effects like fever, fatigue, and myalgias, evidence shows that its safety profile is tolerated, and rates of disease activity signals or flare induction are minimal[54]. For pneumococcal and influenza vaccines, adverse event rates are comparable to those in the general population with most events being self-limited and mild, for example, local pain or temporary fever [55]. Severe allergic reactions are still uncommon and are treated in accordance with general best practices[56].

India-Relevant Notes

While international guidelines like those from the American College of Rheumatology (ACR), European Alliance

of Associations for Rheumatology (EULAR), and the Advisory Committee on Immunization Practices (ACIP) have overarching direction, Indian clinicians increasingly depend on national consensus statements that accommodate vaccination practices to regional epidemiology and availability[57].

In the Indian scenario, pneumococcal vaccination is usually advised at an earlier stage in IMRD patients, irrespective of age, because of increased respiratory infections burden[57]. Also, as endemic hepatitis B virus (HBV) infection is prevalent in some areas, baseline HBV screening and catch-up vaccination are laid great emphasis on[58]. Priorities for other include inactivated typhoid vaccine (Vi-polysaccharide or conjugate) and hepatitis A vaccine in high-risk adults, especially in semi-urban and rural areas[58]. COVID-19 booster approaches follow national policies, with assurance of vaccine supply and product-specific efficacy considerations[58].

A Step-By-Step Drug-Informed Vaccination Plan for an Adult with As

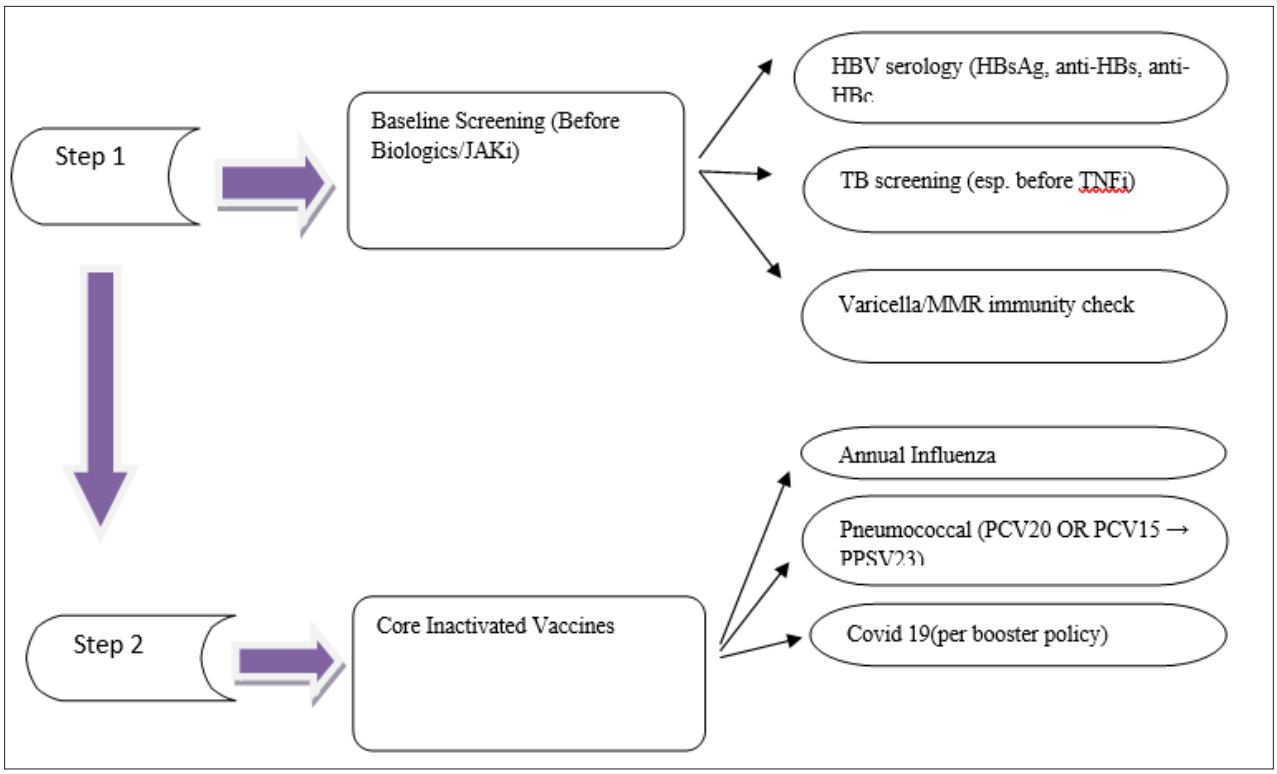
Step 1: Baseline screening. Serologic screening for HBV (HBsAg, anti-HBs, anti-HBc) prior to starting biologics or JAK inhibitors is required, along with evaluation of varicella and MMR immunity when vaccination status is unclear[59]. Screening for tuberculosis should also be performed according to biologic guidelines, which can determine the timing of initiating therapy[59].

Step 2: Core inactivated vaccines. These can be given even in the setting of immunosuppressive therapy. The annual influenza vaccine is necessary, together with pneumococcal vaccination according to ACIP 2025 recommendations (e.g., PCV20 single dose, or PCV15 followed by PPSV23) [60]. COVID-19 vaccination, including boosters, should be according to national protocols (MoHFW, 2023). RZV is recommended for immunosuppressed patients aged ≥19 years or otherwise ≥50 years[60]. Non-immune patients should receive HBV vaccination with post-vaccination serology if possible. Recommendations for Tdap/Td, HPV, and HAV are standard by age and risk[60].

Step 3: Live vaccines. Live-attenuated vaccines (such as MMR, varicella) are used only when given ≥4 weeks before beginning biologic or JAK inhibitor therapy[60].

Step 4: Medication timing adjustments. Methotrexate (MTX) can suppress vaccine responses; hence, short-term MTX withholding during influenza or COVID-19 vaccination is to be considered if flare risk is controllable[60]. For TNF inhibitors (TNFi) or IL-17 inhibitors, no inactivated vaccine dose adjustment is normally required. RZV usually doesn't need to interrupt therapy, although reactogenicity monitoring is sensible[60].

Step 5: Reminder and documentation. Documentation of vaccine information and inclusion of booster schedules during regular rheumatology follow-ups (e.g., biologic refills) minimizes immunization gaps[60].(Flowchart 1).



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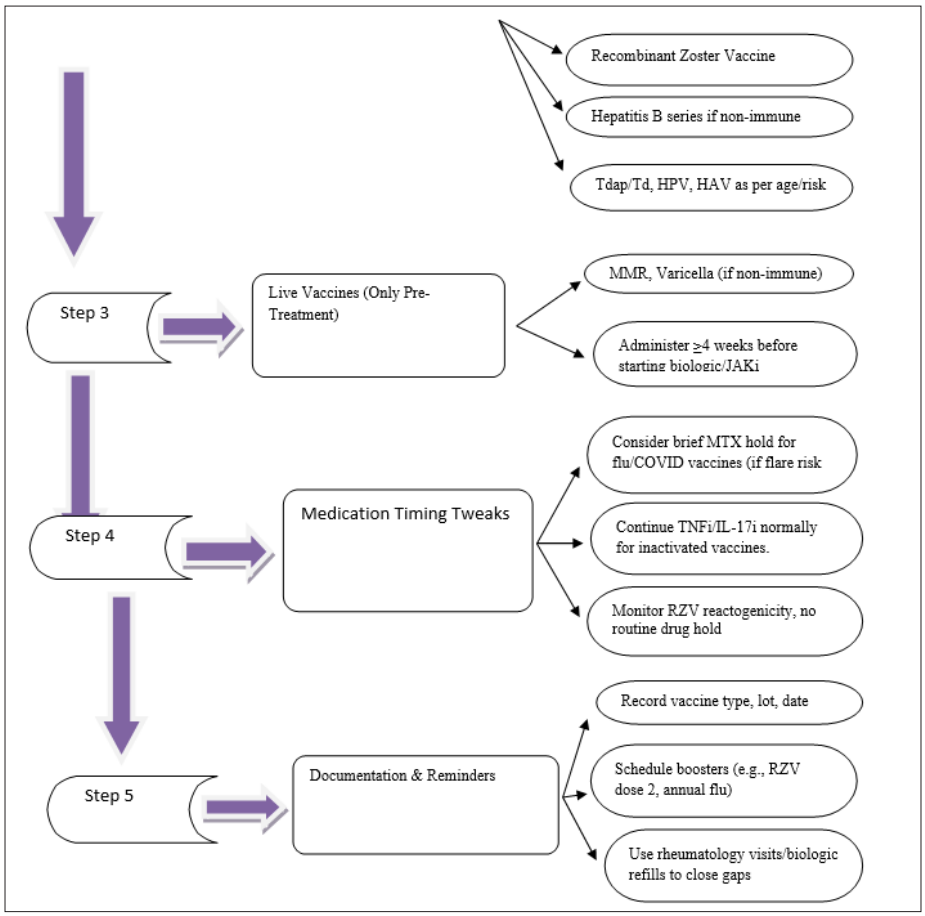

Flowchart 2: Stepwise Vaccination Plan in Ankylosing Spondylitis (AS)

Special Situations and Populations

Young adults on extended biologics. Immunocompromised recommendations must be adhered to by vaccination schedules, which is to say pneumococcal vaccines and RZV should never be postponed by chronological age alone[61].

Pregnancy planning. Live vaccines like MMR and varicella must be administered prior to conception alone, while Tdap is recommended in each pregnancy. The other inactivated vaccines like influenza and hepatitis B go by routine indications. Rheumatology and obstetrics staff must coordinate for safety[61].

Regular travelers. Patients might need inactivated vaccines for typhoid, hepatitis A, Japanese encephalitis, meningococcal disease, and rabies pre-exposure, depending on travel destination. All of these are safe in immunosuppression, if inactivated preparations are administered[61].

HBV-exposed or chronic carriers. Household contacts must be immunized if non-immune. Patients might need antiviral prophylaxis in addition to vaccination, coordinated by rheumatologists and hepatologist[62].

Post-vaccine surveillance. Although routine serologic follow-up is not needed for influenza or pneumococcal vaccination, anti-HBs titers must be measured after hepatitis B vaccination in immunocompromised individuals to ensure seroprotection[62].

Conclusion

Immunization is a pillar of prophylaxis in ankylosing spondylitis (AS), especially considering the universal practice of immunomodulatory and biologic medications that put patients at risk for infectious complications. Current guidelines favor an organized vaccination schedule that encompasses annual universal influenza vaccination, pneumococcal vaccine based on current Advisory Committee on Immunization Practices (ACIP) schedules, COVID-19 primary and booster doses, hepatitis B vaccine after universal screening protocols, and the recombinant zoster vaccine (RZV) in immunocompromised adults[63].

Significantly, inactivated vaccines are always proven to remain safe and immunogenic during treatment with tumor necrosis factor-alpha (TNF-α) inhibitors, interleukin-17 (IL-17) inhibitors, and Janus kinase (JAK) inhibitors. Vaccination can therefore continue without unwarranted discontinuation of effective treatment[63]. On the other hand, live-attenuated vaccines are still contraindicated after starting immunosuppressive treatment, leaving pre-treatment as a very important time period to use vaccines like MMR or varicella when appropriate[63].

IL-17 blockade-specific evidence (e.g., secukinumab) indicates maintained influenza vaccine responses in line with healthy controls, allaying fears of compromised immunity in such patients[63]. Likewise, observational studies as

well as trial data emphatically attest to the efficacy and good safety profile of RZV among patients with immune-mediated rheumatic conditions (IMRDs), even those on biologics or DMARDs[63].

Practically, planning for vaccination in AS should start with a baseline screening strategy: HBsAg, anti-HBc, and anti-HBs testing for HBV; tuberculosis testing; and confirmation of immunity to primary live vaccines before starting biologic therapy[64]. After therapy initiation, inactivated vaccines should be given as soon as possible, and treatment schedules should be modified in carefully selected instances (e.g., withholding methotrexate for a short interval during influenza vaccination to maximize response[64]. In the context of India, recent expert consensus focuses on the imperative need for prevention of HBV, given the high rate of HBV reactivation among patients who have been exposed to TNF inhibitors without prophylaxis[64]. Additionally, pneumococcal and COVID-19 vaccination strategies are also emphasized as region-specific, specifically based on the increased background burden of respiratory infections and uneven access to vaccines[64].

Finally, incorporating a systematic review of vaccines into each AS clinic encounter guarantees that patients are receiving proper and timely vaccinations, thus avoiding preventable infections, reducing drug interruptions, and maintaining long-term disease control[64]. A proactive evidence-based vaccination strategy thereby not only reflects international best practice but also promotes patient safety and quality of life across the AS treatment course.

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Conflict of Interest

None

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