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This Week in Rheumatology

Ankylosing Spondylitis

Recent research highlights key advances in understanding and managing ankylosing spondylitis (AS) and axial spondyloarthritis (axSpA). A study by Cuesta-Lopez et al. (RMD Open) reveals that sustained CRP elevation in axSpA is strongly linked to endothelial dysfunction and increased cardiovascular (CV) risk, driven by IL-6, CDCP-1, and PON-3. Anti-TNF therapy improved metabolic and inflammatory profiles, underscoring its role in mitigating CV risk. Meanwhile, Yang et al. (Arthritis Research & Therapy) compared TNF and IL-17 inhibitors in AS patients with prior biologic exposure, finding TNF inhibitors had higher retention rates, though lower BASDAI and fewer prior biologics were stronger predictors of drug survival than class choice. On the safety front, Kim et al. (Scientific Reports) demonstrated that while NSAIDs were associated with short-term eGFR decline, long-term cumulative renal impairment was minimal, supporting cautious but not prohibitive use. Finally, Ferrandiz-Espadin and Liew (Current Rheumatology Reports) emphasized diagnostic delays in axSpA, advocating for MRI and AI tools to improve early detection, while updated Canadian guidelines endorsed JAK inhibitors and biologic tapering in stable disease. Together, these studies underscore the importance of personalized treatment strategies, balancing efficacy, safety, and early intervention.

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Gout

Recent research highlights the significant role of lifestyle and dietary factors in managing gout and reducing flares. A systematic review by Mustafa et al. (2024) analyzed eight studies (n=47,879) and found that polyunsaturated fatty acid-rich fish, regular physical activity, and higher vegetable intake may lower gout activity, while high purine intake (particularly from animal sources), alcohol, and obesity exacerbate flares. Dietary changes showed mixed effects on serum uric acid levels, underscoring variability in individual responses. Despite limitations like recall bias, the findings reinforce the potential of non-pharmacological interventions in gout management. Further research is needed to refine clinical recommendations.

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Immunology

Recent research highlights the interplay between immune dysregulation and disease, with probiotics emerging as a potential modulator of inflammation and oxidative stress in non-communicable diseases (NCDs). A meta-analysis of 18 RCTs (Yu et al., BMC Pharmacol Toxicol) demonstrated that probiotic supplementation significantly reduced CRP, TNF-alpha, and MDA levels (high certainty for CRP/MDA), while boosting GSH—though effects on IL-6, NO, and TAC were inconclusive. This suggests probiotics may mitigate key biomarkers in NCDs, though variability in study designs warrants cautious optimism. Meanwhile, maternal immune activation during pregnancy appears linked to neurodevelopmental outcomes, as evidenced by a Norwegian cohort study (Walle et al., BMC Med). Maternal immune-mediated conditions (e.g., asthma, T1D, Crohn’s) were associated with a 20-50% increased ADHD risk in offspring, with stronger effects than paternal conditions—hinting at fetal immune programming via the maternal-fetal interface. Notably, paternal asthma also showed a significant association, suggesting genetic or shared environmental factors may contribute. Together, these studies underscore the immune system’s dual role as both a therapeutic target (via probiotics) and a potential driver of developmental disorders, with implications for clinical management across specialties.

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Osteoarthritis

Recent research highlights diverse approaches to managing osteoarthritis (OA), from pharmacological interventions to innovative diagnostic tools. A meta-analysis by Hsueh et al. (2025) demonstrated that curcumin significantly reduces serum CRP and TNF-alpha levels in knee OA patients, though its impact on other inflammatory markers like IL-6 or ESR was inconclusive, suggesting a need for further synovial fluid studies. Meanwhile, Yang et al. (2024) leveraged machine learning and gait analysis to classify hip OA severity with 98% accuracy, offering a non-radiographic tool for early detection and grading. On the surgical front, Zhang et al. (2024) found that hyperbaric oxygen therapy post-TKA accelerated muscle recovery and reduced inflammation, while Pedersen et al. (2024) emphasized shared decision-making using a patient decision aid (PtDA) to improve decisional quality in severe OA cases. Romosozumab outperformed denosumab in increasing lumbar spine BMD in elderly women with OA and osteoporosis, though cardiovascular risks warrant monitoring (Sobue et al., 2024). Finally, Chae & Kim (2024) identified fractures, comorbidities, and socioeconomic factors as key drivers of rising medical costs in OA patients, underscoring the need for targeted management strategies.

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Other Rheumatic Diseases

Recent studies highlight key advances in understanding and managing rheumatic diseases, particularly dermatomyositis (DM), interstitial lung disease (ILD), and fibromyalgia. In anti-MDA5-positive DM, anti-interferon-alpha antibodies were found in 17.6% of patients and correlated with higher disease activity, rapid progressive ILD (RP-ILD), pulmonary infections (especially fungal), and mortality, suggesting their utility as biomarkers (Sun et al.). For autoimmune-associated ILD progressing to pulmonary fibrosis (PPF), antifibrotics like nintedanib and pirfenidone significantly reduced functional respiratory impairment risk (HR 0.58 and 0.68, respectively), though emphysema and smoking worsened outcomes (Nieto et al.). Meanwhile, a retrospective study of idiopathic inflammatory myopathies (IIM) identified ILD as a major mortality driver (15.9% vs. 6.2% in non-ILD), with age, respiratory failure, tumors, and anti-MDA5 antibodies as key predictors. The novel "AIRMT" score effectively stratified mortality risk (Yu et al.). In fibromyalgia, neuroanatomical subtypes emerged: one with widespread gray matter volume (GMV) increases linked to poorer treatment response, and another with normal GMV and better outcomes, underscoring the need for personalized approaches (Wu et al.). Protocolized tacrolimus-based triple therapy (glucocorticoids, IV cyclophosphamide) outperformed ciclosporin-based regimens in anti-MDA5-DM-ILD, achieving zero composite mortality/LTOT events vs. 40% ($p = 0.020$) and lower cytomegalovirus reactivation (Yamada et.). Collectively, these findings emphasize biomarker-driven stratification, targeted antifibrotics, and tailored immunosuppression to improve outcomes in complex rheumatic diseases.

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Psoriatic Arthritis

Recent research highlights the reliability of patient-reported outcome measures (PROMs) for monitoring non-musculoskeletal manifestations (NMMs) in psoriatic arthritis (PsA). A study by Nielung et al. (RMD Open, PMID: 40617585) validated PROMs for dactylitis, skin/nail psoriasis, and uveitis in 300 Danish PsA patients from the DANBIO registry. Patients self-reported symptoms, which were compared to physician assessments (gold standard). Results showed high sensitivity/specificity for psoriasis (1.0/0.94) and uveitis (1.0/0.99), and moderate agreement for dactylitis (κ=0.57) and nail psoriasis (κ=0.66). Adding a dactylitis photo improved accuracy, reducing patient-reported digit counts by 0.3 units. Notably, blinding physicians to PROMs did not affect outcomes, reinforcing PROMs' utility in routine care. These findings support integrating patient-reported data to streamline NMM monitoring, particularly for skin and joint involvement, though dactylitis may require visual aids for optimal accuracy.

References

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Rheumatoid Arthritis

Recent research on rheumatoid arthritis (RA) highlights innovative therapeutic strategies and predictive tools to optimize treatment. CAR-T cell therapy, traditionally used in hematological cancers, is now being explored for RA, with promising approaches like CD19-targeted B-cell depletion and chimeric autoantibody receptors (CAARs) showing potential to restore immune tolerance (Blagov et al.). Meanwhile, machine learning models, particularly AdaBoost, are proving robust in predicting remission to biologic DMARDs (bDMARDs) using baseline clinical data, with DAS28 and swollen joint count as key predictors (Salehi et al.). Synovial tissue RNA-sequencing from the STRAP trial identified gene signatures predictive of response to etanercept, tocilizumab, and rituximab, offering a precision-medicine approach (Lewis et al.). In real-world settings, methotrexate (MTX) enhances effectiveness of certain biologics like golimumab and tocilizumab, while glucocorticoids (>5 mg/day) increase safety risks with JAK inhibitors (Ebina et al.). Additionally, the weight-adjusted waist index (WWI) emerged as a superior prognostic marker for cardiovascular and all-cause mortality in RA compared to BMI (Liu et al.). Finally, adaptive immune responses to SARS-CoV-2 remain largely intact in RA patients on immunomodulators, though rituximab notably impairs humoral and CD8+ T-cell responses (Beretta et al.). Together, these advances underscore a shift toward personalized therapy and improved risk stratification in RA management.

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Scleroderma

Recent advances in systemic sclerosis (SSc) treatment highlight a shift toward precision medicine and novel therapeutic strategies. Traditional immunosuppressants like mycophenolate mofetil, cyclophosphamide, and rituximab remain cornerstone therapies for skin and lung involvement, while autologous hematopoietic stem cell transplantation offers a disease-modifying option for high-risk patients. Tocilizumab and nintedanib are now established for preserving lung function in SSc-associated interstitial lung disease (SSc-ILD). For pulmonary arterial hypertension (PAH), early combination therapy with endothelin receptor antagonists and phosphodiesterase-5 inhibitors—augmented by newer agents like selexipag and riociguat—has improved survival and quality of life. Emerging approaches, including CD19-targeted CAR-T cells, bispecific antibodies, and therapies targeting interferon pathways, BAFF, melanocortin, FcRn, and PDE4B, reflect a growing emphasis on biomarker-driven, personalized care. These innovations aim to alter disease trajectories and enable early, targeted interventions across organ systems, from gastrointestinal to musculoskeletal

involvement. The field is rapidly evolving, with a focus on integrating current organ-based strategies with cutting-edge disease-modifying therapies.

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Sjogren's Disease

A recent retrospective cohort study (Tsai et al., *Annals of Medicine*) compared COVID-19 outcomes in primary Sjogren’s syndrome (pSS) patients treated with hydroxychloroquine (HCQ) versus methotrexate (MTX). Analyzing real-world data from TriNetX (2020–2023), the study found that HCQ-treated patients had a 25.9% lower risk of contracting COVID-19 than MTX-treated patients after propensity score matching (n=1045 per cohort). This protective effect was particularly pronounced in younger (18–64 years) and unvaccinated patients. While HCQ was also associated with reduced adverse outcomes in patients with comorbidities like chronic kidney disease or neoplasms, no significant differences in severe COVID-19 outcomes (e.g., hospitalization, mortality) were observed between the cohorts. The study highlights HCQ’s potential role in mitigating COVID-19 risk in pSS, though further research is needed to clarify its impact on disease severity.

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Systemic Lupus Erythematosus

Recent research on Systemic Lupus Erythematosus (SLE) highlights advances in risk stratification, biomarkers, and novel therapies. A meta-analysis by Xuan et al. (Immunologic Research) identified key infection risk factors in SLE, including older age, male gender, active disease, kidney injury, high-dose glucocorticoids, and low C3 levels, underscoring the need for tailored infection prevention strategies. Meanwhile, Aybey et al. (Journal of Translational Medicine) developed refined IFN-I and IFN-II gene signatures, demonstrating their utility in distinguishing disease severity in SLE and predicting immune checkpoint inhibitor response in cancer, offering a nuanced tool for monitoring interferon-driven pathology. On the diagnostic front, Wang et al. (Advances in Rheumatology) linked cerebral small vessel disease (CSVD) burden scores to cognitive impairment in SLE, suggesting MRI-based CSVD scoring as a predictive tool. In therapeutics, Wobma et al. (Nature Reviews Rheumatology) advocate for CAR T-cell therapy in pediatric SLE, emphasizing multidisciplinary collaboration to address unique challenges in this population. Alemayehu et al. (Scientific Reports) identified circulating miRNAs (e.g., miR-181a, miR-223) as promising noninvasive biomarkers for lupus nephritis (LN), with panels showing superior diagnostic performance. Finally, Pireddu et al.

(Journal of Autoimmunity) revealed that TNFSF13B variant carriers had higher flare and renal flare risks but derived greater benefit from belimumab, positioning genetic stratification as a potential guide for personalized therapy. Together, these studies underscore progress in precision medicine, from risk prediction to biomarker-driven treatment optimization in SLE.

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Vasculitis

Recent research on vasculitis highlights key epidemiological and clinical insights. A Norwegian population-based study (Kilian et al., *RMD Open*) analyzed antineutrophil cytoplasmic antibody-associated vasculitides (AAV) incidence and prevalence from 2000–2016, revealing an annual AAV incidence of 12.2 per million adults, with granulomatosis with polyangiitis (GPA) being the most common subtype (60%). The study found an 11% discordance in AAV classification between the 2022 ACR/EULAR criteria and the EMA algorithm, with the former shifting cases from GPA to microscopic polyangiitis (MPA). Notably, AAV incidence and prevalence increased over time, peaking at 143.7 cases/million in 2016. Meanwhile, a retrospective cohort study (Papachristodoulou et al., *Clinical Rheumatology*) demonstrated that early glucocorticoid initiation (within 7 days of symptom onset) in giant cell arteritis (GCA) significantly reduced relapse risk (OR = 0.214) and prolonged relapse-free survival (17 vs. 11.6 months), while also

lowering glucocorticoid doses during tapering. Together, these studies underscore evolving diagnostic criteria's impact on AAV epidemiology and reinforce the importance of prompt treatment in GCA to improve outcomes and reduce steroid burden.

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