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This Week in Rheumatology

Ankylosing Spondylitis

Recent research on ankylosing spondylitis (AS) highlights breakthroughs in immunopathology and treatment resistance. Wu et al. (2024) identified expanded CD8+ T cell subsets with unique TCR motifs (TRAV21/TRBV9) in HLA-B27-positive axial spondyloarthritis (axSpA) patients, supporting the arthritogenic peptide hypothesis. Monoclonal antibody targeting of these T cells shows promise in phase II trials. Neutrophils also play a dual role in inflammation and bone formation, with molecules like HIF-1α and NETs emerging as potential therapeutic targets. However, unanswered questions remain about HLA-B27-bound peptides and the efficacy of single-TCR therapies. Meanwhile, Bilici et al. (2024) link anti-TNF resistance to *Helicobacter pylori* infection, with resistant AS patients showing higher IgA seropositivity, elevated inflammatory markers (ESR, CRP), and worse functional scores (BASFI, ASDAS-CRP). Their findings suggest *H. pylori* eradication could improve anti-TNF response by mitigating gut-driven inflammation. Together, these studies underscore the complexity of AS pathogenesis—from HLA-B27-dependent T cell responses to microbiome-mediated treatment resistance—while pinpointing novel targets for precision therapy.

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Drugs and Pharmacology

Recent research highlights gabapentin's expanding clinical utility in pain and neurological disorders, tempered by significant risks. While its modulation of voltage-gated calcium channels makes it effective for conditions like diabetic neuropathy and fibromyalgia (off-label) and postherpetic neuralgia (approved), up to 25% of patients experience weight gain due to GI alterations and edema, complicating long-term adherence—particularly in metabolic disorders. More critically, gabapentin’s synergistic effects with opioids, though enabling dose reduction, amplify respiratory depression and overdose risks, especially in elderly or opioid-tolerant patients. Current evidence underscores the need for individualized dosing, patient education, and close monitoring to balance efficacy with safety. Further research is urged to refine prescribing practices and mitigate

adverse outcomes.

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Gout

Recent research highlights a rising global burden of early-onset gout (EOG) in individuals aged 15–39, driven significantly by high BMI. A 2024 study using GBD 2021 data (Chen et al., *Clinical Rheumatology*) found that EOG accounted for 1.3 million new cases and 5.1 million prevalent cases worldwide in 2021, with DALYs attributable to high BMI increasing markedly—54,909 of 170,599 total DALYs. Age-standardized incidence rates rose from 36.52 to 43.60 per 100,000 between 1990 and 2021, with the highest burden in high-income North America (115.02 per 100,000) and among males. Epidemiological shifts and population growth fueled this trend, while health inequalities persisted, disproportionately affecting higher SDI regions. The findings underscore the urgent need for targeted prevention strategies addressing obesity and gout in young populations, particularly in affluent areas where high BMI's contribution to DALYs is concentrated.

References

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Immunology

Recent research highlights the intricate interplay between immune function, sex hormones, and environmental factors in autoimmune diseases. Dai et al. (2024) underscore how sex hormones drive epigenetic modifications, shaping sex-biased immune responses in autoimmunity, with implications for biomarkers and targeted therapies. Meanwhile, Luo et al. (2024) demonstrate in a meta-analysis that vitamin D supplementation (≥3 months, daily dosing) reduces thyroid autoantibodies in AITD, particularly in vitamin D-deficient patients, suggesting a modifiable environmental influence on autoimmunity. On the infectious-immune interface, DiPalma et al. (2024) reveal bidirectional links between fungal infections and autoimmunity, where fungal pathogens exacerbate immune dysregulation, while immunosuppressive therapies heighten infection risk—calling for integrated management strategies. Separately, Deichmann et al. (2024) model post-vaccine antibody kinetics against SARS-CoV-2, identifying age, sex, and comorbidities (e.g., autoimmunity, diabetes) as predictors of waning immunity, offering a tool to

personalize protection estimates. Together, these studies emphasize the multifactorial nature of immune dysregulation, bridging hormonal, environmental, and infectious drivers to refine clinical approaches.

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Infectious Diseases

Recent research highlights the superior diagnostic performance of metagenomic next-generation sequencing (mNGS) in detecting co-infections among patients with connective tissue diseases (CTDs). A retrospective study of 304 CTD patients with suspected infections (Xiao et al., *Clinical Rheumatology*) found mNGS significantly outperformed conventional microbiological testing (CMT), with higher sensitivity (89.6% vs. 57.0%) and specificity (81.5%), particularly for bacterial and viral pathogens. Viral infections were the most prevalent, with shifting pathogen distributions post-COVID-19. mNGS-guided treatment adjustments improved clinical outcomes, including higher cure rates, reduced mortality, and shorter hospital stays. While mNGS alone excels, combining it with CMT optimizes pathogen identification and clinical management. This study underscores mNGS as a transformative tool for early infection detection and tailored antimicrobial therapy in CTD patients.

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Osteoarthritis

Recent research highlights the growing global burden of osteoarthritis (OA), particularly among postmenopausal women (PMW), with projections suggesting nearly 50% of PMW could be affected by 2045 (Tan et al.). OA and low back pain are primary drivers of disability-adjusted life years (DALYs) in this population, exacerbated by aging and demographic shifts, with regional disparities linked to

socioeconomic factors. Meanwhile, a randomized controlled trial protocol (Yap et al.) explores combining hydroxymethylbutyrate (HMB) and undenatured type-II collagen with exercise training to improve OA-related symptoms and biomarkers in knee OA patients, aiming to address functional decline in older adults. Surgical interventions for occupational rhizarthrosis (Mendes Ribeiro et al.) demonstrate significant pain reduction and improved work capacity, particularly in manual laborers, underscoring the value of early intervention. A network meta-analysis (Chen et al.) ranks knee braces, hydrotherapy, and exercise as top non-pharmacological therapies for knee OA, with braces showing consistent efficacy across pain, function, and stiffness metrics. Together, these studies emphasize the need for tailored, multimodal approaches—spanning prevention, nutritional and exercise interventions, and surgical options—to mitigate OA's escalating impact.

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Other Rheumatic Diseases

Recent research highlights diverse advancements in managing rheumatic diseases. A meta-analysis of low-dose naltrexone (LDN) for chronic pain found it superior to placebo in fibromyalgia (SMD -0.34, $p=0.0186$) but comparable to active controls, despite higher adverse events (IRR 1.4 vs. placebo). In juvenile idiopathic arthritis (JIA), a Norwegian study revealed similar bone mineral density (BMD) Z-scores between JIA patients and controls, emphasizing the role of physical activity in maintaining bone health (mean Z-score 0.2 in high-activity vs. -0.3 in low-activity groups). Meanwhile, hip denervation (HD) emerged as a promising intervention for JIA-related hip arthritis, showing sustained pain reduction (VAS 5.48→0.83, $p<0.0001$) and functional improvement (Harris Hip Score 59.6→83.3) over 16 weeks, outperforming intra-articular steroids. For adhesive capsulitis, posterior intra-articular hydro-dilatation provided the most durable pain relief and mobility gains, though suprascapular nerve block was preferred for severe pain. Lastly, a

review on IgG4-related disease underscored diagnostic challenges and the need for steroid-sparing therapies, with emerging interest in B-cell-targeted treatments amid ongoing pathogenesis debates.

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Psoriatic Arthritis

Recent research highlights advancements in both systemic and biologic therapies for psoriasis and psoriatic arthritis (PsA). A meta-analysis by Wang et al. (2024) demonstrated that calcipotriol-acitretin combination therapy significantly outperforms monotherapy in psoriasis, with higher efficacy (RR = 1.25–1.36), greater PASI score reductions (SMD = −2.26 to −3.79), and favorable modulation of inflammatory cytokines (e.g., reduced TNF-α, IL-17, IL-23). The combination also showed a safer profile, with lower perioral dermatitis risk than acitretin alone. Meanwhile, Godding et al. (2024) evaluated real-world cost-effectiveness of biologics, revealing adalimumab (with biosimilar discounts) as the most cost-efficient for achieving PASI75/90/100 or absolute PASI ≤3/≤1 responses. Among non-biosimilar biologics, brodalumab and guselkumab had the lowest cost per responder. The study underscores the impact of price transparency and the utility of absolute PASI thresholds in cost assessments. Together, these findings emphasize optimized therapeutic strategies: combination therapies for enhanced efficacy and safety in systemic treatment, and biosimilar-driven or IL-17/IL-23-targeted biologics for cost-effective biologic management.

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Rheumatoid Arthritis

Recent studies highlight advances in RA treatment efficacy, safety, and cardiovascular risks. Ozoralizumab (OZR) 30 mg showed rapid and sustained efficacy in MTX-inadequate responders (MTX-IR), with 12.8% achieving low disease activity (LDA) by day 3 and 70.9% by week 52 in the OHZORA trial. Growth mixture modeling identified a subgroup (55%) maintaining LDA long-term, linked to low baseline CRP and CDAI (Miyazaki et al., RMD Open). Meanwhile, the SUNSTAR trial protocol compares tocilizumab and abatacept in TNFi-IR patients, with CDAI improvement at 24 weeks as the primary endpoint, aiming to clarify optimal second-line biologic choices (Pascart et al., BMJ Open). On safety, a nationwide study found sulfasalazine and hydroxychloroquine reduced stroke risk (aOR 0.79 and 0.83, respectively), while glucocorticoids and tocilizumab increased it (aOR 1.71 and 3.47), though tocilizumab's association warrants cautious interpretation (Ahn et al., PLOS One). Additionally, JAK inhibitor withdrawal triggers a pro-inflammatory cascade via pJAK/pSTAT rebound, potentially explaining cardiovascular risks—a phenomenon less pronounced with Type II JAKinibs (Gurevic et al., PLOS One). Together, these findings underscore the importance of personalized treatment selection, balancing rapid efficacy, long-term control, and cardiovascular safety.

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Sjogren's Disease

Recent research on Sjögren's disease (SjD) highlights advances in outcome measures, therapeutic strategies, and long-term disease progression. The NECESSITY IHI Consortium review (Bowman et al., *Annals of the Rheumatic Diseases*) underscores unmet needs in primary SjD (pSjD), emphasizing the development of the *Sjögren's Tool for Assessing Response (STAR)*, a novel composite endpoint now undergoing validation in clinical trials. The study also explores B-cell hyperactivity, lymphoma risk, and the economic impact of pSjD, with input from regulatory agencies and patient advocates to optimize trial design and link clinical improvement to quality-of-life metrics. Meanwhile, the 9-year *SjögrenSER Prospective* study (Fernández-Castro et al., *Rheumatology International*) reveals dynamic disease evolution, with arthralgias and hematologic involvement declining over time, while pulmonary and renal manifestations persist. Key ESSDAI domains (articular, pulmonary, hematologic) showed the most variability, correlating with higher systemic treatment use. These findings underscore the need for phenotype-stratified follow-up protocols to address heterogeneous disease trajectories. Together, these studies highlight progress in outcome measurement and the importance of personalized management in SjD.

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Systemic Lupus Erythematosus

Recent research on Systemic Lupus Erythematosus (SLE) highlights novel insights

into disease mechanisms, prognostic tools, and targeted therapies. The FaMaLE study investigates maternal-fetal tolerance failure in pregnant SLE patients, hypothesizing its role in complications like pre-eclampsia and preterm birth. By analyzing immune cell composition in blood and placenta longitudinally, this prospective cohort aims to link dysregulation with adverse outcomes (Dankers et al., *Lupus Sci Med*). Meanwhile, Zhang et al. (*Lupus Sci Med*) identify the Total Tubulointerstitial Score (TTS) as a robust predictor of mortality and renal dysfunction in lupus nephritis, with TTS >2 independently associated with worse outcomes, underscoring the clinical relevance of tubulointerstitial lesions beyond glomerular pathology. On the therapeutic front, Chen et al. (*Arthritis Res Ther*) demonstrate that telitacicept—a dual BLyS/APRIL inhibitor—reshapes B cell subsets in active SLE, reducing naïve/transitional B cells and boosting regulatory B cells, correlating with improved clinical responses. Complementing this, Wu et al. (*Cell Mol Biol Lett*) review precision strategies targeting immune dysregulation (e.g., CAR-T for B cells, CD40L inhibitors for T-B cell crosstalk), emphasizing the need for biomarker-guided approaches to overcome patient heterogeneity. Together, these studies advance understanding of SLE pathogenesis while paving the way for mechanistically tailored interventions.

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