PEARLS AND PITFALLS OF RHEUMATOLOGIC LAB INVESITGATIONS

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TEST	PEARLS	PITFALLS
Rheumatoid Factor (RF)	The term 'rheumatoid factor' is a misnomer. RF positivity is seen in 5% of healthy individuals, and in a variety of non-rheumatologic conditions including Hepatitis C, HIV, subacute bacterial endocarditis, malignancy, and cirrhosis[1]. Most people with an elevated rheumatoid factor will not have rheumatoid arthritis (RA). Perhaps we should change the name of this test. RF testing is most useful in patients with a symmetric inflammatory polyarthritis, typically involving the MCP and PIP joints. Inflammatory features include prolonged morning stiffness (>1 hour), pain improving with activity, presence of joint swelling, and elevated CRP.	A negative RF does not rule out rheumatoid arthritis in patients with an inflammatory symmetric polyarthritis. 30 to 50% of RA patients can be RF negative.[2, 3] Therefore, RF negativity should not prevent referral of a patient with inflammatory arthritis.
Anti-CCP antibodies	Anti-CCP is highly specific for rheumatoid arthritis (96% specificity, 57% sensitivity),[4,5] and therefore when positive it is especially helpful in diagnosing RA. Anti-CCP is also a prognostic indicator. Anti-CCP positive RA patients are more likely to have joint destruction[6] and extra-articular manifestations such as interstitial lung disease[7].	Out of pocket expense: Anti-CCP testing through primary care currently costs the patient $75 in BC. If you will be referring the patient to rheumatology then anti-CCP testing can be deferred because it is covered by MSP if ordered by rheumatology. Moreover, many patients with rheumatoid arthritis will have a normal anti-CCP.
Anti-Nuclear Antibodies (ANA)	ANA testing is most useful in patients who have specific connective tissue disease (CTD) features such as inflammatory arthritis, pleurisy or pericarditis, Raynaud's phenomenon, interstitial lung disease, skin changes of scleroderma, rashes, and cytopenias. ANA testing is not indicated to evaluate fatigue or musculoskeletal pain in the absence of other features suggestive of a CTD. Lupis and other CTDs are primarily a clinical diagnosis.	Fatigue and arthralgias are common complaints, while ANA positivity is also common in the general population (30% at 1:40 titre).[8] Testing in patients with a low pre-test probability carries the risk of misdiagnosis, extraneous additional investigation, and referral expenses.[9]
HLA B27	Back pain is a very common complaint and 95% of HLA B27 positive people will NOT develop ankylosing spondylitis,[10] therefore testing HLA B27 in patients with back pain in general is not useful. HLA B27 testing is most useful when a patient has back pain with inflammatory features (age of onset < 40 years, pain improves with exercise, does not improve with rest). Suspicion for inflammatory back pain is increased in patients with a history of uveitis, inflammatory bowel disease, psoriasis or family history of ankylosing spondylitis.	HLA B27 negativity does not rule out spondyloarthritis. Up to 10% of Caucasian patients with ankylosing spondylitis are HLA B27 negative.[11] HLA-B27 negative spondyloarthritis is more common in non-Caucasian ethnic groups.

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Serum Uric Acid	Target 360: When you are treating gout, aim to achieve serum uric acid level of less than 360 mmol/L for patients in whom uric acid lowering therapy is indicated (≥2 gout attacks/year, presence of gouty tophi, renal calculi, or stage 2 CKD or worse).[12] Monthly serum uric acid testing is appropriate when initiating and titrating allopurinol dose. Once target is achieved, serum uric acid testing can be spaced out to every 6 months to ensure urate levels are within target.	In a patient with suspected gout, a normal serum uric acid does not rule out gout. Serum uric acid can transiently become normal during gout flares and for a few weeks later.[13] As well, an elevated serum uric acid in a patient with acute monoarthritis does not confirm a diagnosis of gout. Gout is best diagnosed by aspirating the joint and sending it for crystal analysis. The joint aspiration can also look for septic arthritis - a worrisome possibility in acute monoarthritis.
HLA B5801	Koreans, Han Chinese, Thai patients and patients of African background have higher than average frequency of HLA B5801 positivity, an HLA allele which confers a high risk of developing Allopurinol Hypersensitivity Syndrome (AHS). Therefore, consider testing for HLA B5801 in this group of patients prior to initiation of allopurinol, and if positive, allopurinol should be avoided.[12]	Adverse reactions to allopurinol can still occur in the absence of HLA B5801, and therefore allopurinol should be stopped if a patient experiences rashes, cytopenias, transaminitis or acute kidney injury.
Creatine Kinase (CK)	From a rheumatologic perspective, testing CK level is useful in patients with proximal muscle weakness to assess for the presence of an inflammatory myositis. Pre-test probability is increased with additional features such as exposure to statins, a new unexplained rash, or a confirmed/suspected malignancy. CK elevation in inflammatory myositis is usually not subtle, and typically it is elevated in the range of 5 to 50 times the upper limit of normal and does not normalize with rest.[14]	Elevated CK in an asymptomatic patient? If the patient has been exercising, repeat the CK after 3 or more days without exercise or strenuous activity. Further investigation is not recommended in an asymptomatic patient unless CK level exceeds the 97.5th percentile according to gender and race,[15, 16] i.e: • >1001 IU/L in Black males, >487 IU/L in Black females • >520 IU/L in Asian males, >194 IU/L in Asian females • >382 IU/L in White males, >295 IU/L in White females A very high CK can also be seen after trauma, IM injections, or very significant muscular exertion. It should improve within days without treatment.
ESR & CRP	It is rarely useful to order both ESR and CRP, and in British Columbia only CRP is payable when both ESR and CRP are ordered outside of the Emergency Department. CRP should be the preferred test because it is more specific for inflammatory conditions.	ESR is not very specific for inflammation and can be elevated in many non-inflammatory states, including elderly age, anemia, malignancy and chronic kidney disease.[17]

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