

'C' for CRP and 'E' for ESR

Introduction

From a time when “CRP” meant “Infection”, to “ESR” being branded and dismissed as a nonspecific test of “Inflammation,” we have come a long way towards understanding their clinical significance. Since the last few years, a renewed interest in simple and known to all tests like the C reactive protein (CRP), Erythrocyte sedimentation rate (ESR) amongst other acute phase markers has been evoked non more than during the recent COVID pandemic and more recently the adenoviral onslaught. The idea behind this month’s “WORD” is to sensitise and re sensitise the pediatrician to the already known aspects and try to share some practical clues on how to interpret the two most used tests in day-to-day practice. *(Specially with regards inflammation /infection)*.

What is CRP and ESR?

- C-reactive protein (CRP) first identified in the serum of patients with acute inflammation, is a substance that reacted with the "C" carbohydrate antigen of the capsule of pneumococcus and is a pentameric protein synthesized by the liver, whose level rises in response to inflammation.
- CRP is an acute-phase reactant protein that is primarily induced by the IL-6 action on the gene responsible for the transcription of CRP.
- ***Hence it reflects the IL-6 levels in the blood.***
- The erythrocyte sedimentation rate (ESR) measures the rate at which the red blood cells (RBCs), or erythrocytes, in a sample of whole blood, sediment to the bottom of the Westergren tube.
- ESR is an acute phase reactant protein that primarily reflects the blood levels of fibrinogen which usually increase in inflammation.
- ***Hence it reflects fibrinogen levels in the blood.***

When to send CRP and ESR in rheumatological practice?

When there is a clinical context for secondary infection /infection causing an inflammatory complication /auto inflammatory condition/ autoimmune diseases, the most common situations being,

- Pyrexias of unknown origin (PUO) with
- ✓ Nonspecific /constitutional symptoms (fatigue or chronic tiredness, muscle weakness, joint symptoms dizziness, weight loss)
- ✓ Mucocutaneous manifestations (Hard palate ulcers, Rashes, skin tightness, Raynaud's phenomenon, brittle hair or hair loss, alopecia)
- ✓ Dry eyes and/or mouth, salivary gland enlargement
- ✓ Unexplained proteinuria / neuropsychiatric features (specially girls)
- ✓ Evanescent rash, lymphadenopathy, polyserositis ,HS megaly
- ✓ Signs consistent with vasculitis

Other indications

- High suspicion of macrophage activation syndrome
- To rule out bacterial infections

“Both CRP and ESR are suggestive markers of inflammation and /or infection.”

What are the things to know as a practising pediatrician for day-to-day practice ?

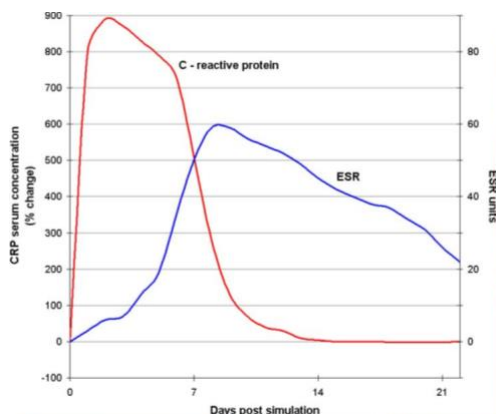


Fig 1. The CRP /ESR timeline – Crp is quick to rise and fall, while ESR rises slowly and comes down slowly

CRP	ESR
Produced by hepatocytes in response to inflammation	Rate at which the red blood cells (RBCs), or erythrocytes, in a sample of whole blood, fall to the bottom
Half-life 5-7 hrs ; rises within 12-24 hrs ,peaks in 2-3 days returns to normal by 5-7 days (<i>Fig 1 vide supra</i>)	Half-life fibrinogen 100hrs hrs, hence slow to rise and slow to fall (over weeks)
More sensitive to infection Can go up in severe inflammation too.	Less sensitive and specific for inflammation/infection
False positive/high – Age, Obesity , diabetes	False positive/high- Females Anemia ,tilt*/ temperature errors (Lab), Low albumin, Hyperthyroidism DM , Pregnancy , IVIG
False negative/low – NSAIDS, Steroids ,Hepatic failure	False Negative/low – MAS/HLH, Sickle cell anemias

*- A 3-degree angle/tilt from vertical while recording in the tube deviates the ESR by 30 !!

“In rheumatology ,ideal to send both CRP and ESR together for better interpretation in conjunction with the clinical scenarios”

How to interpret ESR and CRP Reports ? Whats the merit of sending both ESR and CRP together ?

As mentioned above, neither are specific enough to suggest the underlying pathology (infection /inflammation) eg.: CRP goes high in an inflammatory condition like MAS, MIS-C , Kawasaki disease while ESR can be high in infections or low in infection associated complications like HLH.

Hence when sent together , with the support of a good clinical history and examination , the pretest predictive value of the two could help sort out the diagnostic dilemma .

When sent together simultaneously ,the following four situations are most likely

CRP	ESR	Interpretation
High	High	Infection/Serositis/Synovitis*
High	Low	MAS/HLH
Low	High	SLE/Rheumatological***
Low	Low	Complete recovery

****Classic example of CRP going high in rheumatology is systemic arthritis (cytokine mediated- IL6).***

***** Sick child with a CRP/ESR discrepancy often suggests a brewing MAS/HLH like situation***

******SLE is a disease where CRP is usually normal as it is Interferon mediated (inhibiting CRP); only exception being lupus serositis /arthritis/synovitis .***

Take home messages

- **Clinical settings decide when to send CRP and ESR since the pretest probability determines interpretation .**
- **CRP , while is extremely sensitive in infections , it can be high in severe inflammatory conditions**
- **ESR should be done on a fasting sample ; careful interpretation warranted since it is affected by lots of physiological factors**
- **Doing both together oftens helps analysing the pathology improving the possibility of a correct diagnosis**

“NEXT COMING F- Ferritin and Fibrinogen”



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