**Inflammatory Markers**

The *acute phase response* (APR) is the body’s reaction to *tissue injury*, which may be for a variety of reasons:
- trauma
- myocardial infarction
- acute infections
- chronic inflammation (e.g. rheumatoid arthritis)
- burns

The APR is mediated by cytokines (e.g. IL-1, IL-6 and TNF), which stimulate the liver to synthesise a number of proteins, including:
- C-reactive protein (CRP)
- Alpha-1 anti-chymotrypsin
- Alpha-1 anti-trypsin
- Haptoglobins
- Caeruloplasmin
- Amyloid A
- Fibrinogen
- Ferritin
- Complement C3, C4
- Hepatoglobin

There may be a corresponding decrease in:
- Pre-albumin and albumin
- Transferrin

**Erythrocyte Sedimentation Rate (ESR)**

The ESR measures the distance (mm) that red cells have fallen after one hour in a vertical column under the influence of gravity. Simply speaking, APR-related proteins coat red cells, causing them to ‘stick’ together in columns (*rouleaux*). This results in them falling faster, hence a higher rate.

ESR is a *non-specific* indicator and may be influenced by all the different acute phase response proteins (above). Although it may suggest that a disease is present, it is *not* diagnostic of any one particular disease. A rise of ESR with a normal CRP may help to limit the potential diagnoses (see below). It is also worth remembering that ESR rises with *age* and *anaemia*, as well as in *oral contraceptive pill users* and in *pregnancy*.

The rise with age can be adjusted for, using the *Westergren method*, which will produce the upper limit of normal for an individual:

Men – Age (in years) divided by 2.
Women – Age (in years) add 10, then divide by 2.

Generally speaking, however, an ESR of over 40 mm/h is likely to be abnormal and one exceeding 50 mm/h raises real concern. An ESR above 100 mm/h *is* associated with serious infection, malignancy, autoimmune etc.

The possible causes of a raised ESR is extensive and so difficult to commit to memory. In practice, it is more likely to be raised together with clinical signs, so shortening the list of possibilities. However, it is possible that the ESR may be the only abnormality evident in that patient. If it is mildly elevated, it is
reasonable to re-check in a month. However, if elevated above 100mm/h, it is definitely advisable to investigate further.

Low ESR is can be found in:
- Heart failure
- Polycythaemia rubra vera (PRV)
- Sickle-cell anaemia
- Treatment with steroids
- Cryoglobinaemia

Clearly, it should only require a relatively modest rise in ESR here to stimulate further investigation.

When associated with infection, ESR rises after about 2 days and declines after about 10 days.

A list worth committing to memory is one comprising conditions in which a high ESR may exist with a normal CRP:
- SLE
- Giant cell arthritis/polymyalgia rheumatica.
- Myeloma
- Leukaemia
- Ulcerative colitis

C-reactive Protein
CRP is just one part of the acute phase response. It is particularly good for monitoring inflammation/infection. As with ESR, it rises with inflammation, but does so more rapidly and more intensely – after 4-6 hours, doubling in concentration every 6 hours. Levels can be increased several hundred times. It then reduces quickly – after 2-3 days of recovery. Simply put, this might be considered in terms of the fact that ESR rises as an indirect response to the APR. In comparison, the CRP is produced as part of the APR (its role being to activate the classical complement pathway).

It may therefore be used to follow the response to treatment (e.g. antibiotics) or monitor disease activity (e.g. Crohn’s disease). Of note, CRP is normal or mildly raised due to viral infection (e.g. 10-50mg/L) and raised more markedly with bacterial infection (e.g. 50-200mg/L). Again here, CRP can be used to monitor disease activity. Also of note, CRP is unaffected by the presence of anaemia. For this reason it can be argued to be a more accurate inflammatory marker.

In summary
- There are many causes of raised CRP and/or ESR. Consider it as part of the ‘bigger clinical picture’.
- ESR is susceptible to change by anaemia.
- ESR takes more time to rise and stays high for longer.
- ESR may be high when CRP is not (always remember SLE).
- CRP can be useful in monitoring disease and following the response to treatment.

Note
The original notes on these topics were written in 2006 by medical student Tom Worrall. They are presented in good faith and every effort has been taken to ensure their accuracy. Nevertheless, medical practice changes over time and it is always important to check the information with your clinical teachers and with other reliable sources. Disclaimer: no responsibility can be taken by either the author or publisher for any loss, damage or injury occasioned to any person acting or refraining from action as a result of this information.