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Position Statement

Subject:	**Appropriate Use of the Erythrocyte Sedimentation Rate Test**
Approval Date:	July 2016, February 2019
Review Date:	February 2022
Reviewed by:	BPPQ
Number:	5/2016

The Royal College of Pathologists of Australasia is committed to the appropriate and responsible use of pathology testing to guide medical decision-making by health care professionals and patients using high quality cost effective evidence-based care wherever possible.

This Position Statement is a guide for medical practitioners on the appropriate use of the Erythrocyte Sedimentation Rate Test (ESR) in clinical care. The ESR is often requested in inappropriate clinical circumstances.[1,2]

Background

The ESR is a non-specific indicator of the acute phase response to a wide spectrum of clinical diseases including infection, acute and chronic inflammation, tissue injury, malignancy, hyperglobulinaemia/paraproteinaemia and systemic autoimmune disorders. The extent, pattern and time course of change in the various proteins involved in the acute phase response can differ in varying inflammatory conditions.

Another commonly used measure of the acute phase response is the C-reactive protein (CRP) derived from hepatocytes. The CRP is a sensitive assay and the level rises rapidly in response to inflammation with very high levels being highly associated with infection; CRP has a much shorter half-life than that of fibrinogen and immunoglobulins. Therefore CRP generally falls more rapidly than the ESR in response to successful therapy and/or inflammatory disease recovery.[3] Because CRP rises and falls more rapidly than the ESR, CRP is more useful in serial monitoring in individual patients.

Neither the ESR nor CRP is disease-specific nor can these tests differentiate the underlying pathological process leading to elevated results e.g. distinguishing sepsis from non-infective inflammation. Results of ESR and CRP analysed simultaneously in an individual patient can be concordant or discrepant, significantly so on occasion. High CRP/low ESR discordances have been reported most often in infections, myocardial infarction and venous thromboembolism and high ESR/low CRP discordances in connective tissue disease and ischaemic cerebrovascular disease.[4]

Marked increases in ESR and CRP are often associated with significant illness e.g. elevations of the ESR to 100 millimetres [mm] per hour or greater can be seen in infection, malignancy and autoimmunity while a CRP of 200mg/L is typically seen in bacterial infection/sepsis.[3,5]

The Test

The ESR is the measured rate of fall of red cells suspended in plasma [expressed as mm per hour] and interpreted as the general degree of elevation of the ESR above the quoted normal reference range rather than the absolute number reported. An elevated ESR can

result from clinical disease as well as technical and other factors which can also produce lower or higher than expected results. Female gender, pregnancy, increasing age, anaemia, certain renal conditions and obesity can result in an elevated or higher than expected ESR. Red cell poikilocytsis, polycythaemia, cachexia, low fibrinogen, marked leucocytosis, cardiac failure and high levels of bile salts can be associated with a very low ESR or lower than expected ESR in patients with inflammation.[6]

Several pre-analytical and analytical technical factors can result in spuriously high or low ESR results.[7]

Clinical Utility of ESR Testing

As with any medical investigation the ESR should be used in an appropriate clinical context with an appreciation of the correct interpretation of the result and the limitations of the test.

ESR measurement in patients with non-specific illness is not warranted due to its low sensitivity and specificity; neither in general should extensive investigations be instituted in healthy subjects with mild elevations of the ESR as a sole abnormality.

Numerous studies of varying quality in children and adults and systematic reviews have evaluated the ESR as a marker of infection, inflammation, vascular disease or malignancy, alone or in comparison to or together with the CRP, including their use as markers of disease activity or therapeutic response. In some conditions ESR and/or CRP have been reported to have utility in at least aiding diagnosis (often in conjunction with other clinical and investigation findings) and/or in monitoring change in disease activity. The CRP in some reports appears to outperform the ESR and the CRP is likely to be a more sensitive marker for many particularly infective conditions and especially for monitoring therapeutic response and disease activity.

Clinical practice guidelines that include available evidence and expert consensus opinion continue to include ESR and/or CRP in diagnostic or disease monitoring advice/algorithms in a variety of rheumatic, inflammatory, infective, malignant, neurological, vascular, gastroenterological and miscellaneous disorders. Some authors and expert groups claim that use of both the ESR and CRP in combination maximises sensitivity and specificity in certain limited clinical circumstances as listed below.

Recommendations

- The ESR should not be used as a non-specific screening test in individuals with non-specific symptoms.

- ESR testing should be restricted to certain clinical contexts including:

    - aiding diagnosis and therapeutic monitoring of giant cell [temporal] arthritis and polymyalgia rheumatic +/- in association with CRP[8,9,10]
    - systemic lupus erythematosus (SLE); the use of ESR and CRP may be useful especially in the context of infection versus disease flare in this patient group[11]
    - a marker of disease activity in osteomyelitis[12,13]
    - a marker of disease activity in prosthetic joint infection[14,15]
    - risk assessment in Hodgkin lymphoma and monitoring for disease relapse[16]

- ESR testing may also be of value in:

- aiding diagnosis and disease monitoring in rheumatoid arthritis +/- in association with CRP[17]
- paediatric inflammatory bowel disease[18]
- evaluation of acute back pain in adults where infection or malignancy is suspected[19]

- Measurement of CRP may be superior to ESR in the clinical assessment and monitoring of some clinical, especially infective, conditions.

- An isolated modestly raised ESR in an asymptomatic individual should not in general trigger extensive non-directed investigation.

- If an ESR is found to be significantly elevated, subsequent investigations should be performed as guided by the individual clinical features and the results of other more specific investigations e.g. serum protein electrophoresis, targeted imaging etc.

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