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C-Reactive Protein and Erythrocyte Sedimentation Rate Testing

Effective Date: December 5, 2018

Scope

This guideline applies to the clinical use of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as investigative tests in adults aged ≥ 19 years.

Key Recommendations

- CRP is the preferred first test to support a diagnosis of inflammatory or infectious conditions, rather than ESR. There is no indication for ordering ESR when CRP is elevated.
- According to the British Columbia Laboratory Services Outpatient Payment Schedule, ESR will be performed only if a written indication is provided on the requisition. If CRP and ESR are ordered together, most outpatient laboratories will only perform CRP because only CRP is payable.[1]
- Clinical features that together **may** prompt a requisition for CRP are:
  a) **unexplained symptoms** or a deterioration of health status; **and**
  b) an inflammatory or infectious disease is suspected; **and**
  c) a specific diagnosis is not made effectively by other means.
- **Repeat testing for CRP depends on the clinical status of the patient.** It may be used in routine monitoring of patients with inflammatory arthritis and other rheumatic conditions. For most infections, repeat CRP is not indicated and assessment should be made on clinical grounds (e.g., when following treatment of cellulitis,[2] pneumonia or urinary tract infections).
- The only indication for CRP assessment in **asymptomatic** individuals is in the stratification of cardiovascular risk. High sensitivity (hs) CRP is one of several tools which may be used in patients at intermediate cardiovascular risk to help decide whether a statin should be started. If hsCRP is desired, it should be specifically requested on the laboratory requisition.
- **In the appropriate clinical context, and if CRP is normal**, then ESR may provide useful information when:
  a) Used in combination with other biomarkers in patients who are known to have systemic lupus erythematosus (SLE) or other rheumatic conditions and who are known not to mount a CRP response.[3–5]
  b) Used in combination with other clinical tests when considering the possibility of low-grade bone and joint infections (e.g., osteomyelitis[6] and early prosthetic joint infections[5]

Background

CRP is produced in the liver as part of the acute phase response. It is directly measurable and responsive to changes in the inflammatory process. CRP concentration peaks rapidly, approximately 48 hours after the inflammatory stimulus.[7] When the stimulus for production stops, CRP decreases quickly.[7]

ESR is an indirect measure of inflammation. ESR levels increase at a slow rate in response to inflammation and can take weeks to return to normal levels.[5] A variety of factors influence the sedimentation rate such as physiological factors (e.g., older age, female gender and pregnancy[5, 8]), pathological factors (e.g., plasma immunoglobulin and fibrinogen concentrations[5]) and technical issues.[9] Hence, CRP is the preferred test when considering investigating an inflammatory clinical state.

Compared to CRP, false negative and false positive test results can occur when measuring ESR due to the slow response rate and lack of specificity respectively.[5] However, both tests have limited diagnostic ability and their appropriate uses are outlined in the Tests section below. **If the clinical history and physical exam findings are suggestive of specific disease processes, other investigations are usually more appropriate.**

Tests

According to the British Columbia Laboratory Services Outpatient Payment Schedule, ESR will be performed only if a written indication is provided on the requisition. If CRP and ESR are ordered together, most outpatient laboratories will only perform CRP because only CRP is payable.[1]

CRP and ESR in British Columbia

MSP Cost of Tests[1]		
ESR	**(fee item 90515)**	**$10.61**
CRP/hsCRP	**(fee item 91300)**	**$10.31**

Current to January 1st, 2018

C-Reactive Protein

CRP may be ordered:

a) during the diagnosis of inflammatory and infectious disease;
b) during monitoring of inflammatory and infectious disease; or
c) to review a therapeutic approach in primary prevention of cardiovascular disease in patients assessed at intermediate risk. This is the only indication for CRP assessment in **asymptomatic** individuals.

All CRP assays measure the same protein though laboratories differ in their measurement methods. High sensitivity (hs) CRP is a designation given to laboratory assays that measure CRP levels below 3 mg/L. Laboratories reporting CRP values less than 3 mg/L are using an hsCRP assay. CRP and hsCRP perform equally well for the diagnosis and monitoring of infectious and other inflammatory conditions. CRP assays measuring below 3 mg/L (hsCRP) can be used to stratify patients for cardiovascular disease risk (see Table 1 below). **If hsCRP is desired for cardiovascular risk stratification, hsCRP should be specified on the laboratory requisition as it may need to be forwarded to a laboratory that performs this test.**

Table 1. Utility of hsCRP and CRP Assays for Cardiovascular Risk Stratification and in the Diagnosis and Monitoring of Inflammatory or Infectious Disease

Assay	Cardiovascular Risk Stratification	Inflammation/ Infection	Lower Limit of Detection
hsCRP	YES	YES	0.1 – 0.3 mg/L (note: this value varies between laboratories)
CRP (non hsCRP)	NO	YES	3 – 5 mg/L (note: this value varies between laboratories)

Inflammation and Infection

Within the appropriate clinical context, CRP levels above 10 mg/L can help support the diagnosis of an inflammatory or infectious process. However, CRP levels less than 10 mg/L do not rule out an inflammatory or infectious process.

Clinical features that together **may** prompt a requisition for CRP are:

a) **unexplained symptoms** or a deterioration of health status; **and**
b) an inflammatory or infectious disease is suspected; **and**
c) a specific diagnosis is not made effectively by other means.

CRP may be used to monitor the activity of:

a) rheumatic conditions such as vasculitis (e.g., temporal (giant cell) arteritis[10–12] and polymyalgia rheumatica[13, 14)] and inflammatory arthritis (e.g., rheumatoid arthritis[15, 16] and SLE[3, 4]);
b) inflammatory bowel disease (e.g., ulcerative colitis and Crohn's disease);[17] or
c) infections which require long term antibiotics and which are difficult to monitor clinically (e.g., osteomyelitis[18] or prosthetic joint infections).

Repeat testing for CRP depends on the clinical status of the patient. It may be used in routine monitoring of patients with inflammatory arthritis and other rheumatic conditions. For most infections, repeat CRP is not indicated and assessment should be made on clinical grounds (e.g., when following treatment of cellulitis,[2] pneumonia or urinary tract infections).

hsCRP and Cardiovascular Disease (CVD)

When a patient without clinical cardiovascular disease is found to be at intermediate risk for CVD based on their Framingham Risk Score, hsCRP is one of several tools which can be used to raise or lower their estimated cardiovascular risk (see the associated BC Guideline *Cardiovascular Disease – Primary Prevention* for further information on cardiovascular disease risk stratification). Patients at moderate cardiovascular risk who have an hsCRP > 2mg/L (and typically < 10 mg/L) may benefit from statin therapy.[19, 20]

Erythrocyte Sedimentation Rate

CRP is the preferred first test to support a diagnosis of inflammatory or infectious conditions, rather than ESR. There is no indication for ordering ESR when CRP is elevated.

In the appropriate clinical context, and if CRP is normal, then ESR may provide useful information when:

a) Used in combination with other biomarkers in patients who are known to have systemic lupus erythematosus (SLE) or other rheumatic conditions and who are known not to mount a CRP response.[3–5]
b) Used in combination with other clinical tests when considering the possibility of low-grade bone and joint infections (e.g., osteomyelitis[6] and early prosthetic joint infections[5]).

Resources

Patient and Caregiver Resources

- HealthLinkBC.ca: C-reactive protein and high sensitivity C-reactive protein

References

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Abbreviations

CRP C-Reactive Protein
ESR Erythrocyte Sedimentation Rate
hsCRP High sensitivity C-Reactive Protein
SLE Systemic lupus erythematosus

This guideline is based on scientific evidence current as of the effective date.

The guideline was developed by the Guidelines and Protocols Advisory Committee in collaboration with BC's Agency for Pathology and Laboratory Medicine and adopted by the Medical Services Commission.

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