Test Definition: IL6DX

Interleukin-6, Serum

Overview

Useful For

Evaluating patients with suspected chronic inflammatory disorders, such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, or inflammatory bowel disease

Evaluating patients with Castleman disease

Evaluating patients with suspected systemic infection

Evaluating patients with suspected localized infection, specifically prosthetic joint infection

Assisting in identifying severe inflammatory response in patients with confirmed COVID-19 illness to aid in determining the risk of intubation with mechanical ventilation, in conjunction with clinical findings and the results of other laboratory testing

Highlights

Fact sheets for this emergency use authorization (EUA) assay can be found at the following links:
-For healthcare providers: www.fda.gov/media/142598/download
-For patients: www.fda.gov/media/142599/download

Method Name

Immunoenzymatic

NY State Available

No

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into plastic vial

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Ambient	24 hours	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Interleukin 6 (IL-6) has important roles in both innate and adaptive immunity.(1) IL-6 can be produced by a variety of different cell types, including macrophages, endothelial cells, and T cells. This production can be initiated in response to microbial invasion or other cytokines, such as tumor necrosis factor. As part of the innate immune system, IL-6 acts on hepatocytes to induce expression of C-reactive protein (CRP), fibrinogen, and serum amyloid A, also known as the acute phase response. Within the adaptive immune response, IL-6 plays a key role in activating antibody-producing B cells to proliferate, leading to an enhanced antibody response.

Concentrations of IL-6 are elevated in patients with infection, sepsis, and septicemia. During inflammatory conditions, the concentration of IL-6 can increase severalfold, highlighting its clinical relevance as a major alarm signal in response to infections (sepsis/septicemia), inflammation, autoimmunity, and cancer, including Castleman disease. In addition, IL-6 concentrations appear to correlate with the severity of sepsis, as defined by clinical and laboratory parameters.(2) Elevations in IL-6 also appear to be associated with more localized infections, such as prosthetic joint infections (PJI).(3) A recent meta-analysis demonstrated that IL-6 had improved diagnostic accuracy for PJI compared to CRP, erythrocyte sedimentation rate, and white blood cell counts. IL-6 is also elevated in numerous chronic inflammatory disorders, including rheumatoid arthritis (RA), systemic lupus erythematosus, ankylosing spondylitis, and inflammatory bowel disease.(4)

There is evidence that IL-6 is involved in the pathogenesis of certain chronic inflammatory disorders. Tocilizumab, an antibody that blocks IL-6 function by binding to the IL-6 receptor, has been approved for the treatment of RA. In a randomized trial, 50% to 60% of patients receiving tocilizumab and methotrexate showed improvement in clinical signs and symptoms of RA, compared to only 25% of patients receiving methotrexate alone.(5) Siltuximab, a monoclonal antibody against IL-6, is also sometimes used to treat Castleman disease. However, the presence of Siltuximab may interfere with some IL-6 assays, leading to the proposed use of CRP as a surrogate marker to monitor Siltuximab efficacy.(6-8)

IL-6 has also been shown to be elevated in COVID-19 patients. There is some indication that patients with more severe disease may develop elevated circulating IL-6. The significance of this finding is still being elucidated, including whether monitoring of circulating IL-6 levels can help with patient management, prognosis, or response to treatment.(9,10)

Reference Values

< 6.4 pg/mL

Interpretation

Elevated concentrations of interleukin 6 may indicate an ongoing inflammatory response and could be consistent with a systemic infection, localized infection, or chronic inflammatory disease.

Cautions

Interleukin 6 (IL-6) is a nonspecific marker associated with an inflammatory response and is not diagnostic for any specific disease or disease process. Elevated concentrations of IL-6 must be interpreted within the clinical context of the patient.

Normal concentrations of IL-6 do not exclude the possibility of an ongoing inflammatory process.

Interleukin-6 concentrations may be elevated in patients receiving IL-6 receptor inhibitors, such as tocilizumab, due to receptor blockade and reduced clearance of IL-6. As a result, IL-6 concentrations are not reflective of adequate tocilizumab response. Additionally, patients receiving anti-IL-6 monoclonal antibodies such as siltuximab may also exhibit interference in IL-6 measurements. For both patient cohorts, a more reliable assessment of IL-6-mediated inflammation can be obtained by measuring downstream acute-phase reactants, such as C-reactive protein.

Clinical Reference

1. Scheller J, Chalaris A, Schmidt-Arras D, Rose-John S. The pro- and anti-inflammatory properties of the cytokine interleukin-6. Biochim Biophys Acta. 2011;1813(5):878-888
2. Tsalik E, Jaggers B, Glickman SW, et al. Discriminative value of inflammatory biomarkers for suspected sepsis. J Emerg Med. 2012;43(1):97-106
3. Berbari E, Mabry T, Tsaras G, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2010;92(11):2102-2109
4. Gabay C: Interleukin-6 and chronic inflammation. Arthritis Res Ther. 2006;8 Suppl 2:S3
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6. Yoshizaki K, Murayama S, Ito H, Koga T. The Role of interleukin-6 in Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):23-36. doi:10.1016/j.hoc.2017.09.003
7. Sarosiek S, Shah R, Munshi NC. Review of siltuximab in the treatment of multicentric Castleman's disease. Ther Adv Hematol. 2016;7(6):360-366. doi:10.1177/2040620716653745
8. Chen F, Teachey DT, Pequignot E, et al. Measuring IL-6 and sIL-6R in serum from patients treated with tocilizumab and/or siltuximab following CAR T cell therapy. J Immunol Methods. 2016;434:1-8. doi: 10.1016/j.jim.2016.03.005
9. Gubernatororova EO, Gorshkova EA, Polinova AI, Drutskava MS. IL-6: Relevance for immunopathology of SARS-CoV-2. Cytokine Growth Factor Rev. 2020;53:13-24
10. Ashrafzadeh-Kian S, Campbell MR, Jara Aguirre JC, et al. Role of immune mediators in predicting hospitalization of SARS-CoV-2 positive patients. Cytokine. 2022;150:155790. doi:10.1016/j.cyto.2021.155790

Performance

Method Description

This assay is a simultaneous 1-step immunoenzymatic (sandwich) assay. A sample is added to a reaction vessel along with the paramagnetic particles coated with mouse monoclonal anti-human interleukin-6 (IL-6), blocking reagent, and the alkaline phosphatase conjugate. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of IL-6 in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.(Instruction manual: Access IL-6 Interleukin-6 Instructions for Use. Beckman Coulter, Inc; A83733J, 10/2020)

PDF Report

No

Day(s) Performed

Monday through Friday, Sunday

Report Available

1 to 3 days

Specimen Retention Time

7 days

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has received Emergency Use Authorization (EUA) by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

83529

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value

IL6DX	Interleukin-6, S	26881-3

Result ID	Test Result Name	Result LOINC® Value
IL6DX	Interleukin-6, S	26881-3