Test Definition: HE4

Human Epididymis Protein 4, Serum

Overview

Useful For

Aiding in monitoring patients with treated epithelial ovarian cancer for recurrence or progression

This test should **not be used** as a screening test for ovarian cancer.

Method Name

Electrochemiluminescence Immunoassay (ECLIA)

NY State Available

No

Specimen

Specimen Type

Serum

Specimen Required

Patient Preparation: For 12 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	84 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

Human epididymis (HE) protein 4 belongs to the family of whey acidic four-disulfide core (WFDC) proteins. Currently, the biologic function of HE4 is unknown.

Human epididymis protein 4 has been shown to be overexpressed in 93% of serous, 100% of endometrioid, and 50% of clear cell ovarian carcinomas. In a study of 233 patients with a pelvic mass, including 67 with epithelial ovarian cancer, HE4 had a higher sensitivity for ovarian cancer detection than cancer antigen (CA) 125, 72.9% versus 43.3%, respectively, at a specificity of 95%. Researchers also found HE4 to be elevated in more than half of the ovarian cancer patients who did not have elevated CA 125 levels; therefore, the combination of markers provided slightly improved cancer diagnostic sensitivity for the detection of ovarian cancer.

The main established application of HE4 is in post-therapy monitoring of ovarian cancer patients, who had elevated pretreatment levels. In this setting, it complements CA 125 measurement and facilitates follow-up of patients with little or no CA 125 pretreatment elevations.

Certain histological types of ovarian cancer (mucinous or germ cell tumors) rarely express HE4, therefore the use of HE4 is not recommended for monitoring of patients with these types of ovarian cancer.

Reference Values

Females: < or =140 pmol/L
Males: Not applicable

Interpretation

Increase in human epididymis protein 4 (HE4) suggests recurrence or disease progression, while a decrease suggests therapeutic response. A change in serum HE4 concentration of greater than or equal to 20% is considered significant.

Cautions

Results cannot be interpreted as absolute evidence of the presence or absence of malignant ovarian disease, because mild elevations of human epididymis protein 4 (HE4) might also be present in individuals with benign gynecologic conditions (ovarian cysts, cystadenomas, leiomyomas, myomas, fibromas, and endometriosis), hypertension, congestive heart failure, and kidney or liver disease.

Serial testing for patient HE4 results should be used in conjunction with other clinical methods for monitoring ovarian cancer.

The use of this test in disease states other than ovarian cancer has not been clinically validated.

Serum markers are not specific for malignancy and values may vary by method. Values obtained with different assay methods cannot be used interchangeably. Correlation studies between this method and the previous enzyme-linked immunosorbent assay method show good correlation (correlation coefficient =0.92). However, this method will, on average, give 28% higher HE4 concentrations and individual patient results may vary more than would be calculated from the correlation equation.

Ideally, when changing methods, parallel testing using the old and new method allows for establishing the patient's HE4 baseline levels with the new method (rebaseline).

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. The presence of antibodies to streptavidin or ruthenium can rarely occur and may also interfere in this assay. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

1. Moore RG, Brown AK, Miller MC, et al. The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass. Gynecol Oncol. 2008;108(2):402-408
2. Ferraro S, Braga F, Lanzoni M, Boracchi P, Biganzoli EM, Panteghini M. Serum human epididymis protein 4 vs carbohydrate antigen 125 for ovarian cancer diagnosis: a systematic review. J Clin Pathol. 2013;66(4):273-281
3. Dochez V, Caillon H, Vaucel E, Dimet J, Winer N, Ducarme G. Biomarkers and algorithms for diagnosis of ovarian cancer: CA125, HE4, RMI and ROMA, a review. J Ovarian Res. 2019;12(1):28. Published 2019 Mar 27. doi:10.1186/s13048-019-0503-7

Performance

Method Description

Testing is performed on the Roche cobas e801. The Roche Elecsys HE4 (human epididymal protein 4) assay is a sandwich electrochemiluminescence immunoassay that employs a biotinylated monoclonal HE4-specific antibody and a monoclonal HE4-specific antibody labeled with ruthenium complex. HE4 in the specimen reacts with both the biotinylated monoclonal HE4-specific antibody (mouse) and the monoclonal HE4-specific antibody (mouse) labeled with ruthenium, forming a sandwich complex. Streptavidin-coated microparticles are added, and the mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed. Application of voltage to the electrode induces the chemiluminescent emission, which is then measured against a calibration curve to determine the amount of HE4 in the patient specimen.(Package insert: Roche Elecsys HE4. Roche Diagnostics; V 3.0, 06/2024)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

1 to 3 days

Specimen Retention Time

14 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 been cleared, approved, or is exempt 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

86305

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HE4	HE4, S	55180-4

Result ID	Test Result Name	Result LOINC® Value
HE4	HE4, S	55180-4