Test Definition: DHES1

Dehydroepiandrosterone Sulfate, Serum

Overview

Useful For

Diagnosis and differential diagnosis of hyperandrogenism (in conjunction with measurements of other sex steroids)

An adjunct in the diagnosis of congenital adrenal hyperplasia

Diagnosis and differential diagnosis of premature adrenarche

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.6 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a General Request (T239) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Ambient	7 days	
	Frozen	30 days	

Clinical & Interpretive

Clinical Information

Dehydroepiandrosterone (DHEA) is the principal human C-19 steroid. DHEA has very low androgenic potency but serves as the major direct or indirect precursor for most sex steroids. DHEA is secreted by the adrenal gland and production is at least partly controlled by adrenocorticotropic hormone. The bulk of DHEA is secreted as a 3-sulfoconjugate (DHEA-S). Both hormones are albumin bound, but binding of DHEA-S is much tighter. In gonads and several other tissues, most notably skin, steroid sulfatases can convert DHEA-S back to DHEA, which can then be metabolized to stronger androgens and to estrogens.

During pregnancy, DHEA-S and its 16-hydroxylated metabolites are secreted by the fetal adrenal gland in large quantities. They serve as precursors for placental production of the dominant pregnancy-related estrogen, estriol. Within weeks after birth, DHEA-S levels fall by 80% or more and remain low until the onset of adrenarche. Adrenarche is a poorly understood phenomenon peculiar to higher primates, which is characterized by a gradual rise in adrenal androgen production. It precedes puberty but is not causally linked to it. Early adrenarche is not associated with early puberty or with any reduction in final height or overt androgenization and is generally regarded as a benign condition, not needing intervention. However, girls with early adrenarche may be at increased risk of polycystic ovarian syndrome as adults, and some boys may develop early penile enlargement.

Following adrenarche, DHEA-S levels increase until the age of 20, up to maximum levels roughly comparable to that observed at birth. Levels then decline over the next 40 to 60 years to around 20% of peak levels. The clinical significance of this age-related drop is unknown and trials of DHEA-S replacement in the elderly have not produced convincing benefits. However, in young and old patients with primary adrenal failure, the addition of DHEA-S to corticosteroid replacement has been shown in some studies to improve mood, energy, and sex drive.

Elevated DHEA-S levels can cause symptoms or signs of hyperandrogenism in women. Men are usually asymptomatic, but through peripheral conversion of androgens to estrogens can occasionally experience mild estrogen excess. Most mild to moderate elevations in DHEA-S levels are idiopathic. However, pronounced elevations of DHEA-S may be indicative of androgen-producing adrenal tumors. In small children, congenital adrenal hyperplasia (CAH) due to 3 beta-hydroxysteroid deficiency is associated with excessive DHEA-S production. Lesser elevations may be observed in 21-hydroxylase deficiency (the most common form of CAH) and 11 beta-hydroxylase deficiency. By contrast, steroidogenic acute regulatory protein or 17 alpha-hydroxylase deficiencies are characterized by low DHEA-S levels.

An initial workup in adults might also include total and bioavailable testosterone (TTBS / Testosterone, Total and Bioavailable, Serum) measurements. Depending on results, this may be supplemented with measurements of sex hormone-binding globulin (SHBG1 / Sex Hormone-Binding Globulin, Serum) and occasionally other androgenic steroids (eg, 17-hydroxyprogesterone).

Reference Values

MALES

1-14 days: DHEA-S levels in newborns are very elevated at birth but will fall to prepubertal levels within a few days.

Tanner Stages*

Mean	Age	Reference Range (mcg/dL)
Stage I	>14 days	11-120
Stage II	11.5 years	14-323
Stage III	13.6 years	5.5-312
Stage IV	15.1 years	29-412
Stage V	18.0 years	104-468

*Puberty onset (transition from Tanner stage I to Tanner stage II) occurs for boys at a median age of 11.5 (+/-) 2 years. For boys, there is no proven relationship between puberty onset and body weight or ethnic origin. Progression through Tanner stages is variable. Tanner stage V (adult) is usually reached by age 18.

18-30 years: 105-728 mcg/dL

31-40 years: 57-522 mcg/dL

41-50 years: 34-395 mcg/dL

51-60 years: 20-299mcg/dL

61-70 years: 12-227 mcg/dL

> or =71 years: 6.6-162 mcg/dL

FEMALES

1-14 days: DHEA-S levels in newborns are very elevated at birth but fall to prepubertal levels within a few days.

Tanner Stages*

Mean	Age	Reference Range (mcg/dL)
Stage I	>14 days	16-96
Stage II	10.5 years	22-184
Stage III	11.6 years	11-296
Stage IV	12.3 years	17-343
Stage V	14.5 years	57-395

*Puberty onset (transition from Tanner stage I to Tanner stage II) occurs for girls at a median age of 10.5 (+/-) 2 years. There is evidence that it may occur up to 1 year earlier in obese girls and in African American girls. Progression through Tanner stages is variable. Tanner stage V (adult) is usually reached by age 18.

18-30 years: 83-377 mcg/dL

31-40 years: 45-295 mcg/dL

41-50 years: 27-240 mcg/dL

51-60 years: 16-195 mcg/dL

61-70 years: 9.7-159

> or =71 years: 5.3-124 mcg/dL

Interpretation

Elevated dehydroepiandrosterone sulfate (DHEA-S) levels indicate increased adrenal androgen production. Mild elevations in adults are usually idiopathic, but levels of 600 mcg/dL or more can suggest the presence of an androgen-secreting adrenal tumor. DHEA-S levels are elevated in more than 90% of patients with such tumors, usually well above 600 mcg/dL. This is particularly true for androgen-secreting adrenal carcinomas, as they have typically lost the ability to produce down-stream androgens, such as testosterone. By contrast, androgen-secreting adrenal adenomas

may also produce excess testosterone and secrete lesser amounts of DHEA-S.

Patients with congenital adrenal hyperplasia (CAH) may show very high levels of DHEA-S, often 5- to 10-fold elevations. However, with the possible exception of 3 beta-hydroxysteroid dehydrogenase deficiency, other steroid analytes offer better diagnostic accuracy than DHEA-S measurements. Consequently, DHEA-S testing should not be used as the primary tool for CAH diagnosis. Similarly, discovering a high DHEA-S level in an infant or child with symptoms or signs of possible CAH should prompt additional testing, as should the discovery of very high DHEA-S levels in an adult. In the latter case, adrenal tumors need to be excluded and additional adrenal steroid profile testing may assist in diagnosing nonclassical CAH.

Girls below the age of 7 to 8 and boys below the age of 8 to 9 who present with early development of pubic hair or, in boys, penile enlargement, may be suffering from either premature adrenarche or premature puberty or both. Measurement of DHEA-S (DHES1 / Dehydroepiandrosterone Sulfate, Serum), dehydroepiandrosterone (DHEA_ / Dehydroepiandrosterone [DHEA], Serum), and androstenedione (ANST / Androstenedione, Serum), alongside determination of sensitive estradiol (EEST / Estradiol, Serum), testosterone and bioavailable (TTBS / Testosterone, Total and Bioavailable, Serum), or free testosterone (TGRP / Testosterone, Total and Free, Serum), sex hormone-binding globulin (SHBG1 / Sex Hormone-Binding Globulin, Serum), and luteinizing hormone (LH / Luteinizing Hormone [LH], Serum), follicle-stimulating hormone (FSH / Follicle-Stimulating Hormone [FSH], Serum) levels will allow correct diagnosis in most cases. In premature adrenarche, only the adrenal androgens, chiefly DHEA-S, will be above prepubertal levels, whereas early puberty will also show a fall in SHBG levels and variable elevations of gonadotropins and gonadal sex-steroids above the prepuberty reference range.

Levels of DHEA-S do not show significant diurnal variation.

Many drugs and hormones can result in changes in DHEA-S levels. Whether any of these secondary changes in DHEA-S levels are of clinical significance and how they should be related to the established normal reference ranges is unknown. In most cases, the drug-induced changes are not large enough to cause diagnostic confusion, but when interpreting mild abnormalities in DHEA-S levels, drug and hormone interactions should be taken into account.

Examples of drugs and hormones that can reduce DHEA-S levels include: insulin, oral contraceptive drugs, corticosteroids, central nervous system agents that induce hepatic enzymes (eg, carbamazepine, clomipramine, imipramine, phenytoin), many antilipemic drugs (eg, statins, cholestyramine), dopaminergic drugs (eg, levodopa/dopamine, bromocriptine), fish oil, and vitamin E.

Drugs that may increase DHEA-S levels include metformin, troglitazone, prolactin, many neuroleptic drugs (by indirect implication)), danazol, calcium channel blockers (eg, diltiazem, amlodipine), and nicotine.

Cautions

There are currently no established guidelines for dehydroepiandrosterone sulfate (DHEA-S) replacement or supplementation therapy or its biochemical monitoring. In most settings, the value of DHEA-S therapy is doubtful. However, if DHEA-S therapy is used, then it seems prudent to avoid overtreatment, with its associated hyperandrogenic effects. These are particularly likely to occur in postmenopausal females if DHEA-S levels approach or exceed the upper reference range. Most supplements contain dehydroepiandrosterone (DHEA), but the in vivo conversion to DHEA-S allows monitoring of either DHEA or DHEA-S.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies or heterophile antibodies) which may cause interference in some immunoassays. 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. Sciarra F, Tosti-Croce C, Toscano V. Androgen-secreting adrenal tumors. Minerva Endocrinol. 1995;20:63-68
2. Young WF Jr. Management approaches to adrenal incidentalomas. A view from Rochester, Minnesota. Endocrinol Metab Clin North Am. 2000;29(1):159-185
3. Ibanez L, DiMartino-Nardi J, Potau N, Saenger P. Premature adrenarche-normal variant or forerunner of adult disease? Endocr Rev. 2000;21(6):671-696
4. Collett-Solberg P. Congenital adrenal hyperplasia: from genetics and biochemistry to clinical practice, part I. Clin Pediatr (Phila). 2001;40(1):1-16
5. Allolio B, Arlt W. DHEA treatment: myth or reality? Trends Endocrinol Metab. 2002;13(7):288-294
6. Salek FS, Bigos KL, Kroboth PD. The influence of hormones and pharmaceutical agents on DHEA and DHEA-S concentrations: a review of clinical studies. J Clin Pharmacol 2002;42(3):247-266
7. Elmlinger MW, Kuhnel W, Ranke MB: Reference ranges for serum concentrations of lutropin (LH), follitropin (FSH), estradiol (E2), prolactin, progesterone, sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEA-S), cortisol and ferritin in neonates, children, and young adults. Clin Chem Lab Med. 2002;40(11):1151-1160
8. Charoensri S, Chailurkit L, Muntham D, Bunnag P. Serum dehydroepiandrosterone sulfate in assessing the integrity of the hypothalamic-pituitary-adrenal axis. J Clin Transl Endocrinol. 2017;7:42-46. doi:10.1016/j.jcte.2017.01.001
9. Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical diagnosis of adrenal insufficiency: the added value of dehydroepiandrosterone sulfate measurements. Endocr Pract. 2011;17(2):261-270
10. Bancos I, Hahner S, Tomlinson J, Arlt W. Diagnosis and management of adrenal insufficiency. Lancet Diabetes Endocrinol. 2015;3(3):216-226

Performance

Method Description

The Access dehydroepiandrosterone sulfate (DHEA-S) assay is a competitive binding immunoenzymatic assay. A sample is added to a reaction vessel with paramagnetic particles coated with goat anti-rabbit:rabbit anti-DHEA-S and DHEA-S alkaline phosphatase conjugate in TRIS-buffered protein solution. 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 inversely proportional to the concentration of DHEA-S in the sample. The amount of analyte in the sample is determined from a stored, multipoint calibration curve.(Package insert: Access DHEA-S. Beckman Coulter Inc; 04/2023)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
1 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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
82627

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DHES1	Dehydroepiandrosterone Sulfate, S	2191-5

Result ID	Test Result Name	Result LOINC® Value
DHES1	Dehydroepiandrosterone Sulfate, S	2191-5