



Congenital Adrenal Hyperplasia: Laboratory Diagnosis

The diagnostic algorithms presented herein are intended to help the clinician select appropriate laboratory tests when congenital adrenal hyperplasia (CAH) is suspected. The work-up is complex owing to the various enzymatic defects (Figure 1) and clinical presentations and must include the patient's family history as well as clinical

and laboratory findings. Protocols for the work-up vary with treatment centers. The testing options presented in this test guide are based on accepted diagnostic standards¹⁻¹⁰ and have been reviewed by Medical Directors at Quest Diagnostics Nichols Institute.

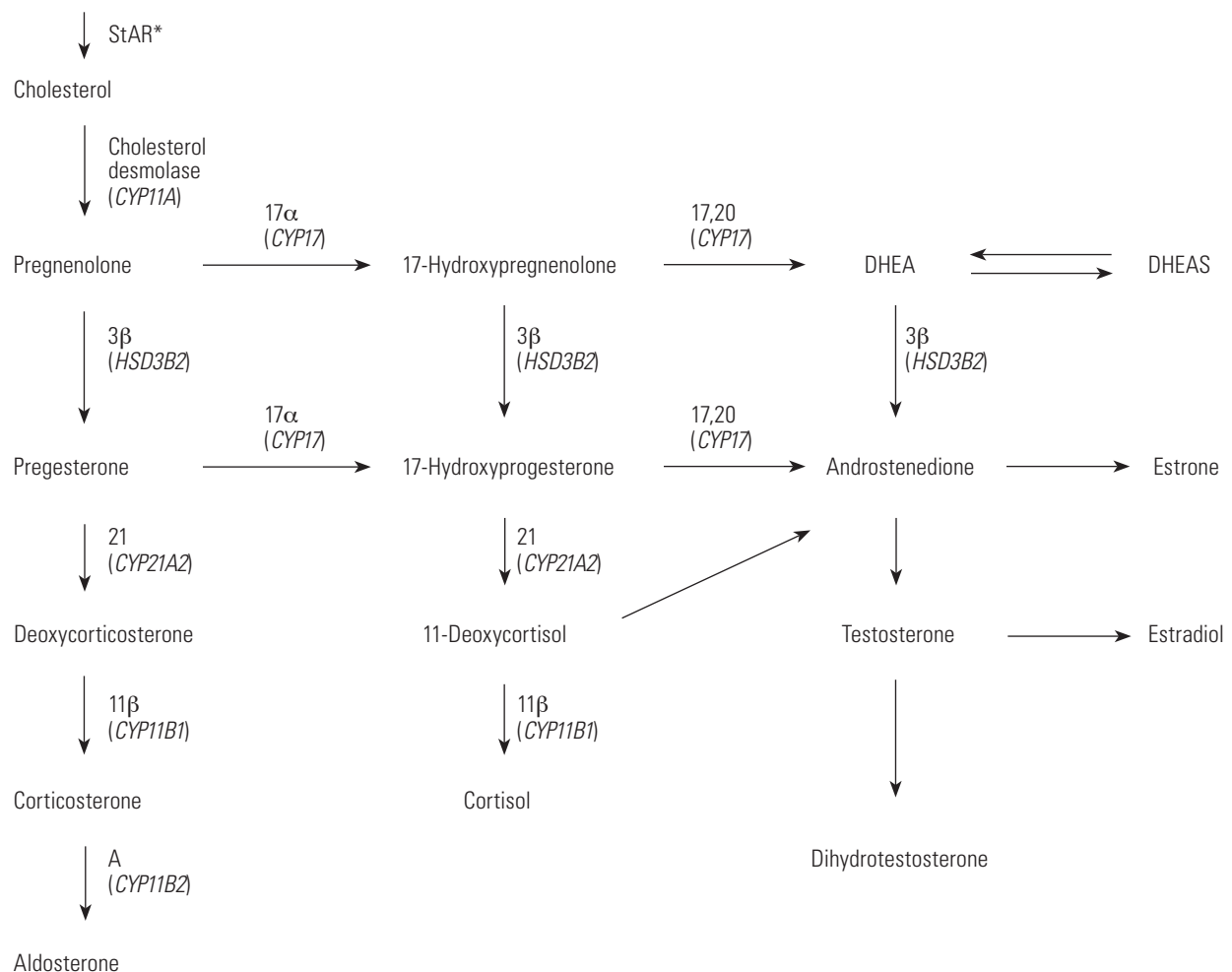


Figure 1. Synthetic pathways of adrenal steroid synthesis. Enzymes and encoding genes are indicated at arrows. When an enzymatic defect occurs, steroids proximal to the defect increase and are frequently shunted into other products, and steroids distal to the defect decrease (eg, a deficiency of 11 β -hydroxylase will cause increased levels of deoxycorticosterone, progesterone, 11-deoxycortisol, and 17-hydroxyprogesterone and decreased levels of corticosterone, aldosterone, and cortisol). 17 α , 17 α -hydroxylase; 17,20, 17,20-lyase; 3 β , 3 β -hydroxysteroid dehydrogenase; 21, 21-hydroxylase; 11 β , 11 β -hydroxylase; A, two-step process of aldosterone synthesis: 1) hydroxylation of corticosterone to form 18-hydroxycorticosterone, 2) oxidation of 18-hydroxycorticosterone to form aldosterone; DHEA, dihydroepiandrosterone; DHEAS, dihydroepiandrosterone sulfate.

*StAR, steroid acute regulatory protein: transports cholesterol from the outer to inner mitochondrial membrane.

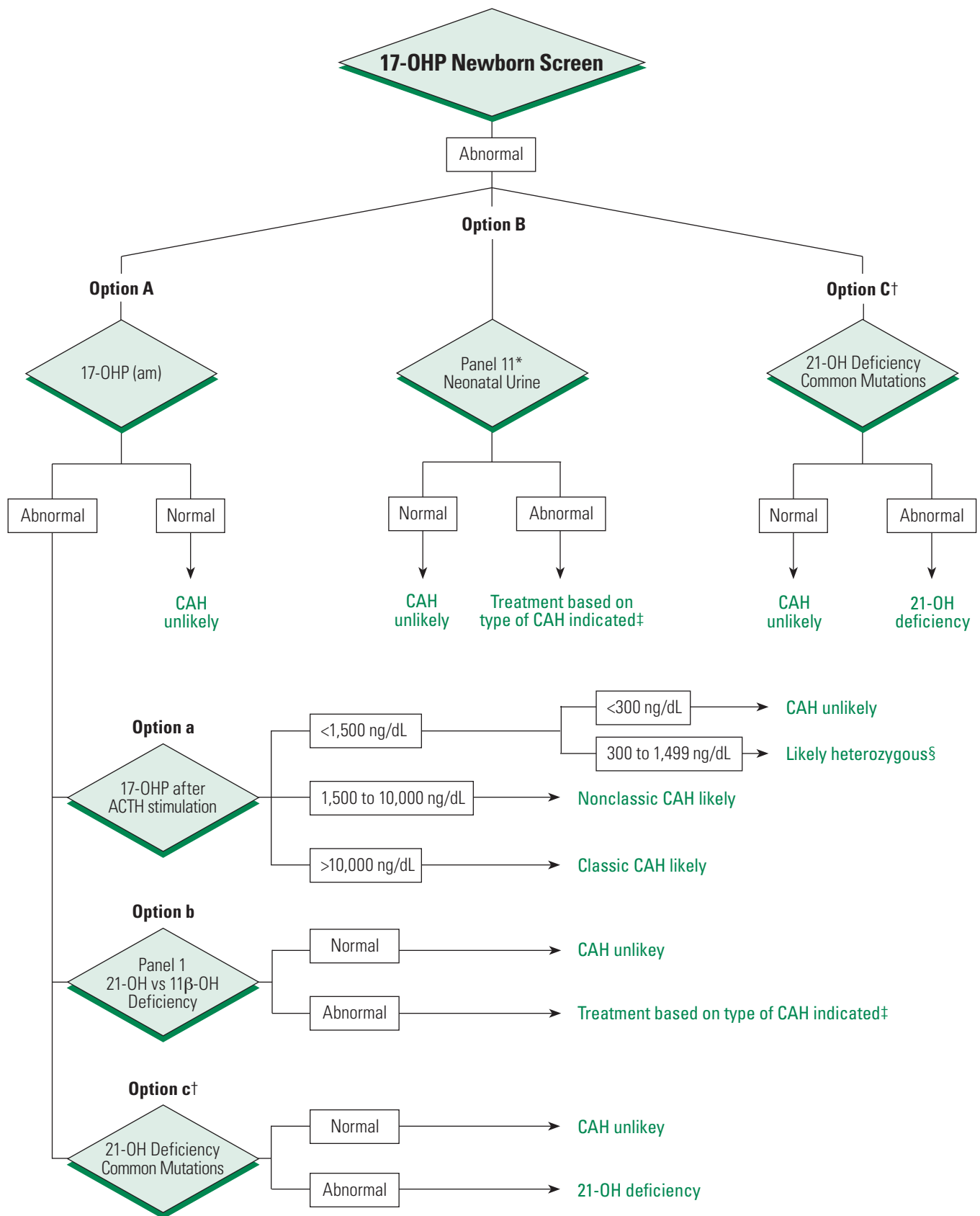


Figure 2. Testing options that can be used when the newborn screen is abnormal and there are no signs or symptoms of CAH. 17-OHP, 17-hydroxyprogesterone; 21-OH, 21-hydroxylase; 11β-OH, 11β-hydroxylase.

*Neonates up to 28 days old.

†Deoxycorticosterone and/or 11-deoxycorticosterone may be indicated to rule out 11β-hydroxylase deficiency.

‡DNA testing (21-OHD Common Mutations) may be indicated to confirm a diagnosis of 21-hydroxylase deficiency, to assess fetal risk during pregnancy, or for family studies.

§One allele contains a functional copy of *CYP21A2* and the second allele contains a non-functional copy of *CYP21A2*.

Individual with Suspected CAH

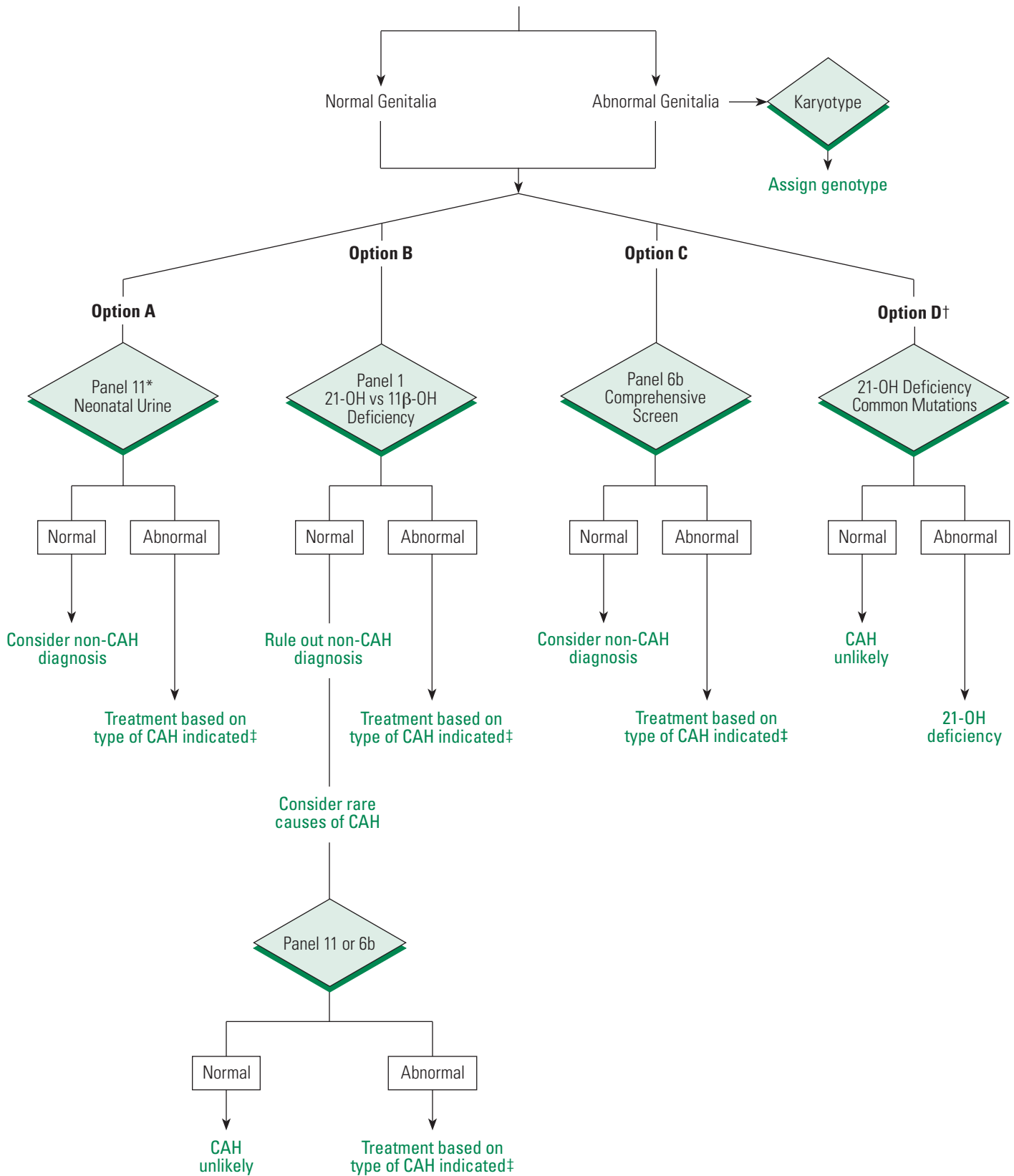


Figure 3. Testing options that can be used when CAH is suspected. 21-OH, 21-hydroxylase; 11β-OH, 11β-hydroxylase.

*Neonates up to 28 days old.

†Deoxycorticosterone and/or 11-deoxycorticosterone may be indicated to rule out 11β-hydroxylase deficiency.

‡DNA testing (21-OHD Common Mutations) may be indicated to confirm a diagnosis of 21-hydroxylase deficiency, to assess fetal risk during pregnancy, or for family studies.

Table. CAH Panels* and Genetic Assays

Test Code	Test Name
15269X	Panel 1 (21-OH vs 11 β -OH deficiency) <i>Includes 17-OHP, androstenedione, 11-deoxycortisol, testosterone, cortisol, 11-deoxycortisol/cortisol ratio, 17-OHP/11-deoxycortisol ratio</i>
15272X	Panel 2 (salt-wasting 21-OH deficiency) <i>Includes 17-OHP, 11-deoxycortisol, cortisol, aldosterone</i>
15273X	Panel 3 (aldosterone synthase deficiency) <i>Includes 17-OHP, 11-deoxycortisol, 18-OH corticosterone, aldosterone, 18-OH corticosterone/aldosterone ratio, 17-OHP/11-deoxycortisol ratio</i>
15274X	Panel 4 (female 17 α -OH deficiency) <i>Includes progesterone, 17-OHP, estradiol, corticosterone, cortisol, aldosterone, progesterone/17-OHP ratio</i>
15276X	Panel 6 (StAR deficiency) <i>Includes pregnenolone, DHEA, cortisol, aldosterone</i>
10299N	Panel 6b (comprehensive screen) <i>Includes 17-hydroxypregnenolone, DHEA, progesterone, 17-OHP, androstenedione, deoxycorticosterone, 11-deoxycortisol, testosterone, cortisol</i>
15277X	Panel 7 (monitor 21-OH deficiency) <i>Includes 17-OHP, androstenedione, testosterone</i>
15279X	Panel 8 (male 17 α -OH deficiency) <i>Includes progesterone, 17-OHP, testosterone, corticosterone, cortisol, aldosterone, progesterone/17-OHP ratio</i>
15280X	Panel 9 (3 β -HSD deficiency) <i>Includes 17-hydroxypregnenolone, DHEA, 17-OHP, androstenedione, cortisol, DHEA/androstenedione ratio, 17-hydroxypregnenolone/17-OHP ratio</i>
10046N	Panel 11 (neonatal urine: diagnose 21-OH, 11-OH, 17 α -OH, and 3 β -HSD deficiencies) <i>Includes 15 steroid analytes and 11 ratios</i>
14755X†	21-OH Deficiency Common Mutations <i>Includes P30L, In2G, G110del8, I172N, exon 6 cluster mutation (I235N, V236E, M238K), V281L, F306+1nt, Q318X, R356W, and P453S mutations, and 30-kb deletion</i>
16072X†	21-OH Deficiency Rare Mutations <i>Includes complete sequencing of CYP21A2</i>

21-OH, 21-hydroxylase; 11 β -OH, 11 β -hydroxylase; 17 α -OH, 17 α -hydroxylase; StAR, steroid acute regulatory protein; 3 β -HSD, 3 β -hydroxysteroid dehydrogenase; DOC, deoxycorticosterone; DHEA, dihydroepiandrosterone; 17-OHP, 17-hydroxyprogesterone; 18-OH corticosterone, 18-hydroxycorticosterone.

*Panel components may be ordered individually; also available: Plasma Renin Activity (10537N) and Direct Renin (787X).

†This test was developed and its performance characteristics determined by Quest Diagnostics Nichols Institute. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Performance characteristics refer to the analytical performance of the test.

References

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