ADRENAL STEROID RESPONSE TO ACTH: PEDIATRICS

Introduction

The data presented in this booklet summarize the normal studies done at Esoterix Endocrinology over the past several years on adrenal steroid response to ACTH in children. Through collaborative efforts with several pediatric institutions, we have been able to establish normal basal and response values for nearly all age groups. These comprehensive data now extend from premature infants through infancy, early childhood, pubertal ages, and adults. To our knowledge, they are the most extensive data currently reported on ACTH stimulation in children. Since the ACTH response of many adrenal steroids varies dramatically with age, the availability of these age related normal data has proven to be very useful in the interpretation of laboratory results and the evaluation of adrenal function in pediatrics.

Test Protocol And Conditions

Stimulation tests were performed on ambulatory subjects (when applicable) using a standard ACTH dose of 25 units (0.25 mg. Cortrosyn) given as an I.V. bolus. Blood samples were drawn at 0 and 60 minutes. No attempt was made to control posture in older subjects, or dietary intake of electrolytes. In some studies involving older children and adults, additional samples were drawn at 30 minutes after ACTH. These data have been omitted from the table because of space limitations, and also because our results do not support the need for additional post stimulation values. The amount of ACTH used for the short 60-minute test does not appear to be important, since all commonly used doses are pharmacological. Comparable response values have been observed with doses ranging from 0.05 - 0.5 units/kg.

Data Tables

Data are presented as the range and mean for baseline and 60-minute samples and for the increase above baseline or delta (—) value. Precursor/product ratios were determined separately for each subject and are not computed from the means and ranges of the respective steroids. The number of control subjects is given in the discussion section for each age group.

Assay Procedures

The steroids in these studies were determined with research quality procedures which have been used in the laboratory at Esoterix Endocrinology for many years. With the exception of cortisol and DHEA-S, which are assayed directly on aliquots of diluted serum, all of the methods involve some combination of solvent extraction and chromatographic purification. High pressure liquid, column, and paper chromatography systems are all used routinely for sample purification. Recovery is monitored on each sample with a 3H steroid tracer. Steroid-free samples (blanks), known standards, multiple level control pools, and randomly repeated samples are included in every assay run. An involved quality control system serves to prevent assay blanks by insuring that nitrogen drying systems are free of organic material, that solvents are redistilled, and that all glassware, chromatography media, and other materials used in the assays are solvent-washed to eliminate possible interference from non-volatile organic residues. This program is costly and time-consuming, but it is essential for reliable pediatric endocrine testing on a continuous daily basis.

Assays are performed in the laboratory by well-trained graduate-level biochemists and technologists who have demonstrated the ability to reliably handle this kind of methodology. The laboratory is supervised by Ph.D. level chemists who have been involved with the development of steroid assays and laboratory management for many years. Assays are reviewed by these section supervisors before any results are reported. All the antisera used in the assays were developed at Esoterix Endocrinology and were selected because their high sensitivity and low cross reactivity enable us to obtain specific results on small volumes of pediatric samples. Since our steroid laboratory uses more complex chromatography procedures, the specificity of our methods is not entirely dependent upon antibody crossreactivity as it is with many commonly used diagnostic kits and other "shortcut assays." Instead, specificity is achieved by using a high-quality antiserum in combination with a chromatography procedure which will provide specific assay results in a wide variety of abnormal and normal specimens.

The reliability of our routine steroid methods has been examined during development and in numerous studies over the years. These evaluation procedures have included combinations, or in some cases, all of the following verification checks

1. Cross-reaction of selected antisera with a large number of related steroids.
2. Comparison of assay results with those obtained using different antisera.
3. Evaluation of dose response linearity obtained with multiple volumes of sample extracts and/or chromatography eluates.
4. Comparison of the values obtained with alternate chromatography procedures.
5. Comparison of values after a second or additional chromatography procedure is added.
6. Evaluation of chromatogram peak homogeneity by determining the specific activity of the steroid in multiple sections of the steroid peak.
7. Evaluation of results in abnormal sera known to contain high-levels of precursor steroids.
8. Evaluation of the steroid response to physiological maneuvers, primarily stimulation and suppression tests.
9. Comparison of normal and abnormal values with those obtained using established assays.
10. Utilization of special chemical alterations or derivatives in situations where assay specificity requires additional confirmation.

Interpretation of Results

Some caution is indicated in the interpretation of ACTH response tests in children. In most cases, laboratory results are clear because they either fall within the normal reference range or stimulate well beyond the upper limit of normal in those patients with biosynthetic defects. In other situations, however, the interpretation of laboratory data is not apparent, and a number of variables, including those outlined below, should be considered.

1. Age-Related Changes—The ACTH response of many clinically relevant steroids changes substantially with age. Therefore, meaningful interpretation of results requires valid normal data for the age group in question.

2. Newborns and Premature Infants—It is recommended that newborn samples be taken on day two or three of life when steroid levels have become more stabilized and normal reference data are available. Values of many steroids in premature infants including 17-OH-progesterone are much higher than in full-term infants. Other steroids, in addition to 17-OH-progesterone, should be ordered to evaluate possible defects in these cases.

3. Methodology—The steroid values obtained in various laboratories are often not comparable because of methodological differences. Comparing results from one laboratory with either normal reference ranges or results from another laboratory may be misleading. In many situations, it is important to have normal data that are specific for the methods being used in the laboratory performing the test.

4. Variability of ACTH Response in Children—The results from large numbers of ACTH response tests processed in our laboratory over the past few years clearly demonstrate that a large variation exists in the response patterns of different steroids in children. Unusual response patterns are sometimes seen which are unlikely to be associated with any abnormality in steroid biosynthesis.

5. Utilization of Statistical Data—The clinical evaluation of test results based upon strict application of the statistical data published by Esoterix Endocrinology or other laboratories is questionable because of the number of factors which can influence test results. While the ACTH response test has been very useful for amplifying defects in steroid biosynthesis and identifying cases of late onset CAH, care should be taken to avoid interpreting data too narrowly. It should be recognized that defects capable of causing clinical problems are usually associated with dramatic elevations in precursor steroids and usually become obvious after stimulation with ACTH.

6. Variability of Steroid "Responsiveness" to ACTH—The ACTH responses of different adrenal steroids vary substantially and are frequently not well correlated. This situation results in wide variability in both the absolute levels and the ratios of different steroids. In addition, those steroids which are very sensitive to ACTH, such as 17-OH-pregnenolone and corticosterone, may have more pronounced fluctuations during the day. Unstimulated values may change substantially. This kind of variation must be considered when evaluating laboratory data.

7. Precursor/Product Ratios—Precursor/product ratios are useful, but should not be rigidly interpreted and must be evaluated relative to the actual stimulated levels of the steroids involved. In baseline samples, the use of precursor/product ratios is not meaningful unless the steroid levels are highly elevated.

8. Increases Above Baseline—Evaluating results by computing the response as a percentage or multiple increase above baseline is also useful, but again must be interpreted relative to the actual stimulated levels of the steroids in question. The serum levels in baseline samples can vary substantially as a result of diurnal variation, episodic secretion, stress or other conditions. Thus, the percentage increase can vary significantly depending upon the time of day and conditions under which the test was performed. For example, if response tests are done in the afternoon, some steroids which have a large diurnal variation may have an abnormal response when expressed as a multiple above baseline even though the stimulated serum levels never exceed the normal range.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Premature Infants 26-28 Weeks (N=21)			Premature Infants 34-36 Weeks (N=12)			Infants 1-6 Months (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Aldosterone (ng/dl)	192 5-635	320 13-1046	128 8-517	178 12-736	316 42-1365	148 28-629	27 2-71	77 4.8-166	50 2.7-123
Androstenendione (ng/dl)	239 63-935	607 121-1323	329 <10-745	323 61-875	731 162-1453	369 <10-1144	– <10-48	24 <10-87	– <10-45
Compound S (ng/dl)	539 110-1376	831 206-2504	292 15-1128	165 70-455	243 81-645	78 40-190	53 10-200	177 101-392	124 5-366
Corticosterone (ng/dl)	560 235-1108	4135 1667-8251	3574 1338-8016	1522 201-5030	7382 2240-11,900	5860 2039-10,141	581 78-2500	3720 2225-4974	3138 1149-4789
18-OH-Corticosterone (ng/dl)	218 10-670	453 35-1500	235 16-830	318 38-779	821 152-2183	530 114-2183	78 5-300	279 130-465	200 21-394
Cortisol (ug/dl)	6.0 1-11	19 6-52	13 4-41	14 3-34	35 16-76	21 6-44	12 3-22	38 27-50	26 19-41
DHEA (ng/dl)	*	*	*	*	*	*	*	*	*

* Note: DHEA values unavailable for HPLC/MS-MS for ACTH response

STEROID VALUES IN NORMAL SUBJECTS

PREMATURE INFANTS

ACTH response studies are summarized on 21 infants (12 males and 9 females) at 26-28 weeks gestation (4 days of life) and 12 infants (5 males and 7 females) at 34-36 weeks gestation (1 day of life). As previously reported,[1-4] the serum levels of most adrenal steroids in premature infants are strikingly elevated in relation to full-term and older infants. Some caution should be exercised in the interpretation of laboratory data in these patients to avoid confusion with congenital adrenal hyperplasia. The D-5 steroids, DHEA, pregnenolone and 17-OH pregnenolone, are especially elevated, reflecting decreased 3B-HSD activity and increased fetal adrenal synthesis of estriol precursors.

Serum levels of these steroids decrease progressively with age, so that values found in premature newborns at < 30 weeks, are considerably higher than those observed at 35 weeks and in full-term neonates. Serum levels then continue to decline in young infants and reach a plateau after one year. The finding of very high 17-OH pregnenolone levels in young infants has been evaluated further in our laboratory to determine whether the assay is measuring additional unknown steroids. Despite testing with a number of procedures commonly used to check method specificity, the values are unchanged, and we have not found any evidence that other steroids are contributing to these high results. The 17-OH pregnenolone values show a linear response when eluates of chromatograms are assayed at multiple doses.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Premature Infants 26-28 Weeks (N=21)			Premature Infants 34-36 Weeks (N=12)			Infants 1-6 Months (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
DHEA Sulfate (ug/dl)	392 123-882	*	*	406 248-660	*	*	25 5-111	*	*
DOC (ng/dl)	47 20-105	105 44-320	58 17-215	44 28-78	59 28-95	17 1-67	20 7-48	75 40-158	55 13-144
Pregnenolone (ng/dl)	793 260-2104	1879 962-3179	1086 70-2673	585 203-1024	1218 637-1888	686 162-1685	60 10-150	220 100-359	160 20-282
17-OH-Pregnenolone (ng/dl)	1402 375-3559	5176 2331-11,440	3775 1219-9799	1242 559-2906	3803 831-9760	2561 346-8911	320 52-828	1465 633-3286	1144 229-3104
17-OH-Progesterone (ng/dl)	471 124-841	774 285-1310	302 50-596	306 186-472	562 334-1725	256 18-1253	47 13-173	172 85-250	125 52-193
Testosterone (M) (ng/dl)	91 59-125	*	*	*	*	*	156 2-501	*	*
Testosterone (F) (ng/dl)	11 5-16	*	*	*	*	*	4.4 2-8	*	*

* DHEA-S AND TESTOSTERONE LEVELS ARE NOT SIGNIFICANTLY CHANGED BY LOW DOSE ACTH STIMULATION. BASELINE DATA ARE PRESENTED FOR REFERENCE PURPOSES ONLY.
**NOT DETERMINED BECAUSE OF HIGH VALUES DURING FIRST DAY OF LIFE.

PREMATURE INFANTS

Results obtained with different 17-OH-pregenolone antisera are also basically equivalent. Similarly, values obtained with methods using column, high pressure liquid, or paper chromatography are not different. Oxidation of samples with permanganate followed by chromatography also does not lower results. Finally, peaks from paper chromatograms are homogeneous and show a constant specific activity after elution and RIA of multiple fractions.

INFANTS 1-12 MONTHS

Stimulation studies were performed on 27 normal infants (16 males and 11 females) between the ages of 1 and 12 months. The results have been segregated into two groups, 1-6 months (N=15) and 6-12 months (N=12), in order to provide reference ranges for more restricted age groups and also because the levels of some steroids change significantly during this time period. The ACTH response values in this age group are significantly lower than those reported above for premature infants. The response of many r-4 adrenal steroids (progesterone, 17-OH-progesterone, cortisol, corticosterone, and 11-desoxycortisol) are similar to those observed in children and adults.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID PRECURSOR PRODUCT RATIOS Data Presented as Mean and Range	Premature Infants 26-28 Weeks (N=21)			Premature Infants 34-36 Weeks (N=12)			Infants 1-6 Months (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Pregnenolone / 17-OH-Pregnenolone	0.56 0.25-0.70	0.36 0.25-5.0	0.29	0.41 0.17-0.73	0.50 0.17-1.3	0.27	0.25 0.1-0.7	0.15 0.03-0.25	0.13
17-OH-Pregnenolone / 17-OH-Progesterone	2.9 1.1-5.2	6.7 3.6-11	3.8	3.9 1.8-6.5	6.7 3.6-12	7.0	6.1 2-22	8.5 3-20	9.1
17-OH-Progesterone / Compound S	0.95 0.35-2.4	1.17 0.25-2.1	1.03	2.1 0.9-4.8	2.8 0.8-4.2	4.5	1.2 0.4-3.1	1.1 0.5-2.0	1.0
17-OH-Progesterone (ng/dl) / Cortisol (ug/dl)	78 18-220	41 15-170	23	28 9.0-71	18 6.2-51	17	5.0 0.8-12	4.6 0.2-6.9	4.6
Compound S (ng/dl) / Cortisol (ug/dl)	89 25-300	44 10-189	22	22 2.9-115	7.5 3.1-26	3.8	4.4 0.8-10	4.7 2.4-10	4.8
DOC X 100 / Corticosterone	8.3 2.3-25	2.5 1.2-7.0	1.6	2.8 1.1-5.5	0.7 0.4-0.9	0.29	10 0.5-30	2.0 0.7-4.9	1.7
Corticosterone / 18-OH-Corticosterone	2.6 1.6-43	9.1 3.9-58	15	4.8 2.9-11	8.9 4.4-28	11.0	8.9 3-26	16 7-30	15
18-OH-Corticosterone / Aldosterone	1.2 1.0-4.5	1.4 0.8-2.6	1.8	1.8 1.1-10	2.6 1.2-11	3.8	2.7 1.3-5.0	4.9 2-13	4.0
Corticosterone (ng/dl) / Cortisol (ug/dl)	93 35-198	217 34-800	275	108 42-242	210 140-375	279	42 8-120	100 37-146	120

*NOT DETERMINED BECAUSE OF HIGH PROGESTERONE VALUES DURING FIRST DAY OF LIFE.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Infants 6-12 Months (N=12)			Infants 1-2 Years (N=11)			Children 2-6 Years (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Aldosterone (ng/dl)	16 2-39	54 5-94	38 3-55	18 5-43	44 28-85	21 7-53	11 2-22	29 13-50	18 6-41
Androstenendione (ng/dl)	– <10	– <10-47	– <10-28	– <10	– <10-37	– <10-31	– <10	– <10-35	– <10
Compound S (ng/dl)	40 10-156	194 135-262	154 20-252	56 10-129	229 170-318	173 60-261	53 7-210	211 95-323	160 53-279
Corticosterone (ng/dl)	559 78-3158	4003 2225-6529	3444 568-5115	695 135-2478	4002 2000-6315	3307 906-5134	454 159-2036	4418 1779-7554	3964 956-7301
18-OH-Corticosterone (ng/dl)	62 5-310	244 120-471	192 57-371	78 20-155	210 120-325	133 80-208	30 7-74	182 110-350	153 33-332
Cortisol (ug/dl)	13 6-23	40 25-60	27 17-41	13 6-25	33 23-40	20 7-28	11 6-19	27 20-33	16 5-24
DHEA (ng/dl)	*	*	*	*	*	*	*	*	*

* Note: DHEA values unavailable for HPLC/MS-MS for ACTH response

INFANTS 1-12 MONTHS (CONT.)

The D-5 steroids and the mineralcorticoids, however, are much higher and more variable. The stimulated levels of aldosterone, 18-OHB and DOC decrease during the first year and continue to decline in older infants. The response levels of the D-5 steroids (17-OH-pregnenolone, DHEA and pregnenolone) which are strikingly elevated in premature infants and newborns, decline progressively during the first 12 months of life. The exaggerated response of 17-OH-pregnenolone (2,000-4,000 ng/dl) frequently seen in young infants decreases during the first few months, so that stimulated values above 500 ng/dl are seldom seen beyond one year. Similarly, DHEA values which frequently stimulate above 1000 ng/dl in very young infants decline during this period and do not stimulate above 150 ng/dl after one year of age.

The finding of very high levels in premature infants followed by a long, slow decline in this age group suggests a progressive decrease in fetal adrenal activity.

CHILDREN 1-6 YEARS

Response test results are summarized on 26 normal controls (14 boys, 12 girls) between 1 and 6 years old. Data are reported separately for 1-2 years (N=11) and 2-6 years (N=15). In general, there is little change in steroid levels throughout this age group. The only notable exception being 17-OH pregnenolone, which continues to fall during the first year and is still somewhat higher in children at 1 to 1.5 years than in older age groups.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Infants 6-12 Months (N=12)			Infants 1-2 Years (N=11)			Children 2-6 Years (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
DHEA Sulfate (ug/dl)	11 5-38	*	*	15 7-32	*	*	10 5-20	*	*
DOC (ng/dl)	22 9-57	73 46-149	52 5-91	18 5-42	85 41-152	67 34-134	12 4-49	69 26-139	57 16-128
Pregnenolone (ng/dl)	43 12-137	159 75-294	116 43-282	33 10-93	89 44-135	55 4-113	35 17-50	69 34-99	35 15-75
17-OH-Pregnenolone (ng/dl)	124 14-647	937 257-2173	813 221-1981	42 14-207	299 55-732	257 35-712	41 10-103	172 45-347	131 16-276
17-OH-Progesterone (ng/dl)	25 11-106	170 102-267	145 48-247	30 4-105	179 65-353	154 40-341	34 7-114	135 50-269	110 16-176
Testosterone (M) (ng/dl)	4.5 2-8	*	*	4.0 2-8	*	*	4.0 2-8	*	*
Testosterone (F) (ng/dl)	3.1 2-8	*	*	*	*	*	*	*	*

* DHEA-S AND TESTOSTERONE LEVELS ARE NOT SIGNIFICANTLY CHANGED BY LOW DOSE ACTH STIMULATION. BASELINE DATA ARE PRESENTED FOR REFERENCE PURPOSES ONLY.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID PRECURSOR PRODUCT RATIOS Data Presented as Mean and Range	Infants 6-12 Months (N=12)			Infants 1-2 Years (N=11)			Children 2-6 Years (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Pregnenolone 17-OH-Pregnenolone	0.53 0.2-2.9	0.2 0.05-0.50	0.14	0.9 0.3-2.4	0.5 0.2-1.5	0.20	1.1 0.3-3.6	0.5 0.3-1.4	0.3
17-OH-Pregnenolone 17-OH-Progesterone	4.0 1.5-10	5.3 1.6-12	5.6	1.1 0.4-2.5	1.6 0.5-3.3	1.7	1.3 0.3-3.0	1.4 0.45-2.6	1.2
17-OH-Progesterone Compound S	0.8 0.5-1.9	0.9 0.5-2.0	1.1	0.7 0.4-1.5	0.8 0.5-1.6	0.9	1.1 0.3-2.1	0.7 0.5-1.4	0.7
17-OH-Progesterone (ng/dl) Cortisol (ug/dl)	1.7 1.2-4.6	4.0 2.0-6.0	5.3	1.9 1.0-6.5	5.5 1.8-10	7.7	3.1 1.2-8.0	5.2 3.1-10	6.9
Compound S (ng/dl) Cortisol (ug/dl)	2.3 1.0-5.3	4.6 3.5-8.0	5.7	4.0 1.0-6.8	7.2 5-10	8.6	4.6 1.8-6.0	7.9 3.8-11	10
DOC X 100 Corticosterone	7.5 3-18	1.7 1.2-2.6	1.5	3.5 2.0-7.0	2.3 1.2-4.5	1.8	3.2 1.2-5.6	1.6 0.9-3.3	1.4
Corticosterone 18-OH-Corticosterone	8.7 4-20	18 10-33	18	10 2-32	19 12-27	25	19 5-36	24 14-50	25
18-OH-Corticosterone Aldosterone	2.7 1.4-3.9	5.3 3-12	5.0	3.6 1.3-5.0	4.9 3.3-7.0	6.3	3.8 1.2-6.0	7.1 1.9-15	8.5
Corticosterone (ng/dl) Cortisol (ug/dl)	29 10-137	94 45-146	127	40 15-157	124 99-150	165	36 17-46	150 71-259	223

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N=18)			Early Puberty Males (N = 14)			Late Puberty Males (N = 15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Aldosterone (ng/dl)	9 4-21	25 14-42	16 5-35	7 2-14	23 10-33	16 7-22	7 3-14	22 13-32	15 7-25
Androstenendione (ng/dl)	– <10	19 <10-69	– <10-23	12 <10-52	30 <10-64	– <10	63 25-127	112 48-197	12 <10-95
Compound S (ng/dl)	53 14-136	188 95-254	135 34-182	53 11-151	180 115-284	127 35-241	49 14-115	169 87-218	120 44-168
Corticosterone (ng/dl)	483 155-1368	3911 2516-5648	3428 1958-5237	300 115-1219	3159 1472-4502	2859 998-4502	326 165-836	3022 1784-5060	2696 1074-4751
18-OH-Corticosterone (ng/dl)	35 16-72	183 95-289	140 79-240	25 5-73	152 68-196	127 63-186	30 14-62	120 73-206	93 21-198
Cortisol (ug/dl)	11 5-16	25 20-31	15 10-20	11 4-17	23 15-36	14 7-32	10 5-15	23 18-28	13 5-21
DHEA (ng/dl)	*	*	*	*	*	*	*	*	*

* Note: DHEA values unavailable for HPLC/MS-MS for ACTH response

PREPUBERTAL CHILDREN

Stimulation test data are reported for 18 normal controls (8 boys and 10 girls) between the ages of 6 and 11 years. The ACTH responsiveness of the D-5 steroids (17-OH-pregenolone and DHEA) increase significantly during this period and continue to change throughout puberty. This normal physiological process results in a significant increase in D5/D4 steroid precursor/product ratios and should not be misinterpreted as a mild 3-beta HSD deficiency.

PUBERTAL CHILDREN

Studies are reported on 56 normal pubertal controls between the ages of 12 and 17 years. The subjects were separated by sex and Tanner Stage into the following groups:

Early Pubertal Females	(Tanner Stage II-III N=12)
Late Pubertal Females	(Tanner Stage IV-V N=15)
Early Pubertal Males	(Tanner Stage II-III N=14)
Late Pubertal Males	(Tanner Stage IV-V N=15)

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N = 18)			Early Puberty Males (N = 14)			Late Puberty Males (N = 15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
DHEA Sulfate (ug/dl)	24 7-49	*	*	55 13-119	*	*	126 42-270	*	*
DOC (ng/dl)	10 4-17	48 22-120	38 16-70	9 2-15	38 12-74	29 7-44	8 5-13	30 19-46	23 7-36
Pregnenolone (ng/dl)	33 15-63	82 39-130	48 15-115	28 10-55	90 58-116	62 41-101	30 11-50	92 37-149	61 8-99
17-OH-Pregnenolone (ng/dl)	76 10-186	329 70-656	253 59-515	95 20-363	390 88-675	295 66-655	123 32-297	572 220-966	449 165-842
17-OH-Progesterone (ng/dl)	36 7-100	158 85-280	122 51-240	45 12-131	154 69-313	109 7-281	100 51-191	172 105-264	72 12-134
Testosterone (M) (ng/dl)	5 2-19	*	*	161 20-310	*	*	501 278-702	*	*
Testosterone (F) (ng/dl)	5 2-19	*	*						

* DHEA-S AND TESTOSTERONE LEVELS ARE NOT SIGNIFICANTLY CHANGED BY LOW DOSE ACTH STIMULATION. BASELINE DATA ARE PRESENTED FOR REFERENCE PURPOSES ONLY.

PUBERTAL CHILDREN (CONT.)

Pubertal stages were assigned on the basis of breast development and pubic hair in females and genitalia and pubic hair in males. Results on female controls in the luteal phase of their cycle (as indicated by serum progesterone levels) were excluded from the data summary. The response of D-4 steroids in pubertal age groups is similar to prepubertal children and adults. The D-5 steroids which begin changing at adrenarche continue to increase throughout puberty.

The ACTH response of DHEA and17-OH-pregnenolone in late puberty is considerably higher than the early pubertal ages. This increase is reflected in significant changes of the D5/D4 steroid ratios. The shift in D-5 steroid secretion is more pronounced in females. The stimulated levels of 17-OH pregnenolone and DHEA are significantly higher in late pubertal and adult females than in age equivalent male controls.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID PRECURSOR: PRODUCT RATIOS Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N=18)			Early Puberty Males (N=14)			Late Puberty Males (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Pregnenolone / 17-OH-Pregnenolone	1.0 0.2-2.8	0.3 0.16-0.85	0.2	0.5 0.1-1.7	0.3 0.15-1.0	0.2	0.4 0.1-1.1	0.2 0.1-0.3	0.13
17-OH-Pregnenolone / 17-OH-Progesterone	1.8 0.5-6.0	2.4 0.3-5.3	2.0	1.9 0.5-3.3	2.8 0.5-6.3	2.7	1.2 0.4-3.4	3.4 1.8-5.2	6.8
17-OH-Progesterone / Compound S	0.7 0.2-2.1	0.9 0.5-1.6	0.9	1.0 0.5-2.0	0.88 0.4-2.1	0.9	1.5 0.8-3.7	1.2 0.6-2.7	0.5
17-OH-Progesterone (ng/dl) / Cortisol (ug/dl)	2.8 0.8-5.0	5.4 2.8-9.0	8.1	5.7 2.0-13	7.7 3.6-16	9.1	9.5 5.0-19	7.4 4.0-11	5.0
Compound S (ng/dl) / Cortisol (ug/dl)	4.8 1.2-9.0	6.4 2.8-9.0	9.0	6.0 2-11	6.5 4.0-11	8.4	5.4 1.8-12	6.8 3.4-11	8.0
DOC / Corticosterone X 100	2.4 1.0-4.0	1.2 0.6-2.1	1.0	2.6 1.3-5.1	1.3 0.7-2.0	1.0	2.5 1.3-4.9	1.2 0.6-2.2	1.0
Corticosterone / 18-OH-Corticosterone	15 8-27	21 16-28	24	12 3-28	21 11-33	18	11 7-21	22 16-30	28
18-OH-Corticosterone / Aldosterone	3.8 2.6-7.1	6.9 5-12	8.7	3.6 2.0-5.7	7.2 3.4-13	7.9	4.2 3.0-5.6	5.6 3.9-9.6	6.2
Corticosterone (ng/dl) / Cortisol (ug/dl)	45 15-91	150 100-225	228	34 18-95	159 64-232	238	32 13-90	137 70-213	207

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N = 18)			Early Puberty Females (N = 12)			Late Puberty Females (N = 15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Aldosterone (ng/dl)	9 4-21	25 14-42	16 5-35	10 2-20	22 12-31	12 3-21	7 3-15	17 10-34	10 2-26
Androstenendione (ng/dl)	– <10	19 <10-69	– <10-23	39 10-154	71 26-183	– <10-23	93 39-182	130 62-311	– <10-91
Compound S (ng/dl)	53 14-136	188 95-254	135 34-182	52 15-130	171 90-251	120 34-233	53 15-115	154 78-237	101 38-182
Corticosterone (ng/dl)	483 155-1368	3911 2516-5648	3428 1958-5237	246 152-598	2928 2257-4725	2704 2079-4504	241 162-389	2953 1723-5102	2712 1372-4713
18-OH-Corticosterone (ng/dl)	35 16-72	183 95-289	140 79-240	39 10-82	150 69-196	110 58-173	23 9-68	131 82-242	108 61-204
Cortisol (ug/dl)	11 5-16	25 20-31	15 10-20	9 3-16	22 16-32	13 7-18	10 6-15	26 18-35	16 11-26
DHEA (ng/dl)	*	*	*	*	*	*	*	*	*

* Note: DHEA values unavailable for HPLC/MS-MS for ACTH response

PREPUBERTAL CHILDREN

Stimulation test data are reported for 18 normal controls (8 boys and 10 girls) between the ages of 6 and 11 years. The ACTH responsiveness of the Δ-5 steroids (17-OH-pregnenolone and DHEA) increase significantly during this period and continue to change throughout puberty. This normal physiological process results in a significant increase in Δ5/Δ4 steroid precursor/product ratios and should not be misinterpreted as a mild 3-beta HSD deficiency.

PUBERTAL CHILDREN

Studies are reported on 56 normal pubertal controls between the ages of 12 and 17 years. The subjects were separated by sex and Tanner Stage into the following groups:

Early Pubertal Females	(Tanner Stage II-III N=12)
Late Pubertal Females	(Tanner Stage IV-V N=15)
Early Pubertal Males	(Tanner Stage II-III N =14)
Late Pubertal Males	(Tanner Stage IV-V N=15)

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N = 18)			Early Puberty Females (N = 12)			Late Puberty Females (N = 15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
DHEA Sulfate (ug/dl)	24 7-49	*	*	47 10-136	*	*	143 24-421	*	*
DOC (ng/dl)	10 4-34	48 28-85	38 16-70	7 2-16	37 13-63	30 9-51	8 2-13	29 15-50	22 12-45
Pregnenolone (ng/dl)	33 15-63	82 39-170	48 15-115	39 15-84	89 33-139	50 5-95	41 19-87	146 76-218	105 38-191
17-OH-Pregnenolone (ng/dl)	76 10-186	329 70-656	253 59-515	132 33-451	527 251-756	395 108-683	208 44-542	1014 502-1402	806 438-1280
17-OH-Progesterone (ng/dl)	36 7-100	158 85-280	122 51-240	48 14-120	182 75-353	134 18-287	55 12-121	151 71-226	96 9-164
Testosterone (M) (ng/dl)	5 2-19	*	*	*	*	*	*	*	*
Testosterone (F) (ng/dl)	5 2-19	*	*	18 8-36	*	*	32 12-59	*	*

* DHEA-S AND TESTOSTERONE LEVELS ARE NOT SIGNIFICANTLY CHANGED BY LOW DOSE ACTH STIMULATION. BASELINE DATA ARE PRESENTED FOR REFERENCE PURPOSES ONLY.

PUBERTAL CHILDREN (CONT.)

Pubertal stages were assigned on the basis of breast development and pubic hair in females and genitalia and pubic hair in males. Results on female controls in the luteal phase of their cycle (as indicated by serum progesterone levels) were excluded from the data summary. The response of D-4 steroids in pubertal age groups is similar to prepubertal children and adults. The D-5 steroids which begin changing at adrenarche continue to increase throughout puberty.

The ACTH response of DHEA and 17-OH-pregnenolone in late puberty is considerably higher than the early pubertal ages. This increase is reflected in significant changes of the D5/D4 steroid ratios. The shift in D-5 steroid secretion is more pronounced in females. The stimulated levels of 17-OH pregnenolone and DHEA are significantly higher in late pubertal and adult females than in age equivalent male controls.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL PEDIATRIC SUBJECTS

STEROID PRECURSOR: PRODUCT RATIOS Data Presented as Mean and Range	Prepubertal Children 6-10 Years (N=18)			Early Puberty Females (N=12)			Late Puberty Females (N=15)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Pregnenolone 17-OH-Pregnenolone	1.0 0.2-2.8	0.3 0.16-0.85	0.2	0.43 0.2-0.9	0.2 0.1-0.3	0.12	0.3 0.1-1.1	0.15 0.08-0.27	0.13
17-OH-Pregnenolone 17-OH-Progesterone	1.8 0.5-6.0	2.4 0.3-5.3	2.0	2.9 0.7-8.0	3.5 1.5-7.0	3.0	4.3 0.8-10	7.7 3.0-17	10
17-OH-Progesterone Compound S	0.7 0.2-2.1	0.9 0.5-1.6	0.9	0.9 0.5-4.0	1.1 0.4-1.6	1.1	1.8 0.7-4.8	1.0 0.4-1.8	1.0
17-OH-Progesterone (ng/dl) Cortisol (ug/dl)	2.8 0.8-5.0	5.4 2.8-9.0	8.1	5.2 2.3-14	7.7 4.4-15	10	6.1 1.2-18	5.9 2.8-9.0	5.6
Compound S (ng/dl) Cortisol (ug/dl)	4.8 1.2-9.0	6.4 2.8-9.0	9.0	5.8 2.4-9.0	8.1 5.0-11.0	9.0	5.5 1.1-12	5.5 3.6-8.1	5.6
DOC X 100 Corticosterone	2.4 1.0-4.0	1.2 0.6-2.1	1.0	2.5 1.7-3.8	1.3 0.3-2.0	1.1	2.4 1.8-3.8	1.1 0.5-2.2	0.8
Corticosterone 18-OH-Corticosterone	15 8-27	21 16-28	24	11 3-26	22 12-35	25	11 4-29	20 11-40	25
18-OH-Corticosterone Aldosterone	3.8 2.6-7.1	6.9 5-12	8.7	3.9 1.9-5.3	7.2 5.7-12	9.1	3.7 1.7-8.0	7.8 5-13	10
Corticosterone (ng/dl) Cortisol (ug/dl)	45 15-91	150 100-225	228	33 15-65	142 77-236	208	28 12-43	114 70-145	169

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL ADULT SUBJECTS

STEROID Data Presented as Mean and Range	Adult Females Dex. Supp. (N=19)			Adult Females (N=19)			Adult Males (N=12)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Aldosterone (ng/dl)	6.6 1.2-21	20 7-33	13 3-22	8.4 2.4-25	20 6-28	12 2-19	7 3-11	17 7-26	10 0.3-18
Androstenendione (ng/dl)	81 37-148	207 79-289	88 <10-170	125 61-222	194 98-295	20 <10-137	86 50-210	159 78-285	32 <10-128
Compound S (ng/dl)	15 10-40	125 60-205	110 40-186	65 15-158	140 65-237	75 30-205	40 20-65	132 73-214	94 17-175
Corticosterone (ng/dl)	61 30-140	2743 1907-4268	2682 1704-4233	418 130-906	2890 1735-4752	2272 1280-4230	410 90-1204	3265 433-6590	2854 252-5386
18-OH-Corticosterone (ng/dl)	20 6-43	153 68-243	133 41-218	23 9-58	138 52-225	125 34-206	27 13-48	133 85-249	106 49-201
Cortisol (ug/dl)	1.5 <1-2.4	23 16-36	21 16-33	11 7-21	25 17-39	14 8-24	11 7-15	24 19-31	13 8-18
DHEA (ng/dl)	*	*	*	*	*	*	*	*	*

* Note: DHEA values unavailable for HPLC/MS-MS for ACTH response

ADULTS

Stimulation studies are reported on 31 normal adult controls (19 females and 12 males) between the ages of 20 and 45 years. Data from an additional study is also reported in which the ACTH stimulation tests were done on 19 females after overnight suppression with 1 mg of dexamethasone. Samples were collected on women only during the follicular phase of the menstrual cycle.

STEROID VALUES IN PATIENTS WITH ADRENAL HYPERPLASIA

Steroid data on a limited number of patients with different forms of CAH are summarized on pages 113-114. In most cases of CAH, the laboratory data are clearly abnormal and there is little confusion regarding interpretation. Precursor steroids in the pathway preceding the enzymatic block are usually very elevated. Those following the block may be low, normal or high. The precursor product ratios at the location of the biosynthetic defect, however, are usually well beyond the values found in unaffected individuals. It should be noted that unstimulated levels of some steroids in patients with CAH exhibit wide fluctuations throughout the day. This phenomenon which probably reflects changes in endogenous ACTH secretion must be taken into account when evaluating patients with late onset or mild forms of adrenal hyperplasia.

ADRENAL STEROID RESPONSE TO ACTH IN NORMAL ADULT SUBJECTS

STEROID Data Presented as Mean and Range	Adult Females Dex. Supp. (N = 19)			Adult Females (N = 19)			Adult Males (N = 12)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
DHEA Sulfate (ug/dl)	85 50-175	*	*	135 60-215	*	*	180 150-255	*	*
DOC (ng/dl)	4.6 2-15	33 9-87	28 6-78	7 3-19	29 12-90	22 5-70	6 3-13	26 14-38	20 2-32
Pregnenolone (ng/dl)	25 10-60	144 55-200	119 59-235	65 46-150	150 70-220	95 40-210	41 10-85	99 20-200	68 10-144
17-OH-Pregnenolone (ng/dl)	20 10-24	768 240-1255	748 230-1255	138 48-320	871 290-1382	733 175-1300	100 20-187	558 240-1000	461 160-850
17-OH-Progesterone (ng/dl)	45 17-135	124 59-247	79 42-202	58 22-140	140 65-250	82 31-190	66 35-150	168 45-258	102 24-139
Testosterone (ng/dl)	24 10-47	*	*	35 15-54	*	*	543 430-675	*	*

* DHEA-S AND TESTOSTERONE LEVELS ARE NOT SIGNIFICANTLY CHANGED BY LOW DOSE ACTH STIMULATION. BASELINE DATA ARE PRESENTED FOR REFERENCE PURPOSES ONLY.

STEROID VALUES IN PATIENTS WITH ADRENAL HYPERPLASIA (CONT.)

Because of these wide fluctuations, levels of key marker steroids may fall within the normal range when samples are drawn during the afternoon. Confusion with laboratory results or misdiagnosis in these cases can be avoided by using ACTH stimulation.

21-OH DEFICIENCY

Serum 17-OH progesterone (17-OHP) is the standard laboratory marker for this disorder. In classical 21-OH deficiency, the values of 17-OHP are strikingly elevated (up to 2000 times normal) and there is little need for stimulation tests. In mild or late onset cases, ACTH stimulation is recommended to amplify defects. If ACTH is not used, samples should be drawn during the morning hours, since late afternoon 17-OHP values may fall into the normal range.

11-OH DEFICIENCY

Serum 11-Desoxycortisol is highly elevated in patients with adrenal hyperplasia due to 11-OH deficiency and provides the most useful marker for this disorder. Stimulation tests are usually not required in young infants, but may be useful in evaluating older patients who have either a late onset or were not diagnosed until later in life. Nearly half of the cases summarized on page 113 were identified during evaluation for premature adrenarche.

STEROID PRECURSOR TO PRODUCT RATIOS IN NORMAL ADULT SUBJECTS

STEROID PRECURSOR: PRODUCT RATIOS Data Presented as Mean and Range	Adult Females Dex. Supp. (N=19)			Adult Females (N=19)			Adult Males (N=12)		
	0 Min	60 Min	Delta	0 Min	60 Min	Delta	0 Min	60 Min	Delta
Pregnenolone 17-OH-Pregnenolone	2.0 1.3-3.0	0.20 0.1-0.3	0.16	0.5 0.25-1.2	0.2 0.1-0.3	0.14	0.48 0.2-2.1	0.14 0.05-0.41	0.15
17-OH-Pregnenolone 17-OH-Progesterone	0.44 0.2-0.8	6.2 3.7-11	9.4	2.6 1.7-6.0	6.2 3.7-11	7.7	1.8 0.5-5.8	3.8 1.6-7.0	4.5
17-OH-Progesterone Compound S	2.5 2.0-14	1.0 0.8-2.4	0.8	0.9 0.7-5.0	1.0 0.9-2.4	1.3	1.9 0.8-4.9	1.2 0.6-1.7	1.1
17-OH-Progesterone (ng/dl) Cortisol (ug/dl)	23 10-60	5.4 2.8-9.1	3.8	4.2 1.9-9.3	5.4 2.8-9.1	6.8	6.1 2-13	6.6 2-9	8.0
Compound S (ng/dl) Cortisol (ug/dl)	9.5 2.5-34	5.4 2.3-70	5.1	5.0 0.7-6.2	5.4 2.3-7.0	5.3	3.5 1.4-5.1	5.5 3.4-7.4	7.2
DOC X 100 Corticosterone	8 4-20	1.2 0.5-1.7	1.0	1.0 1.2-3.6	1.2 0.5-1.7	1.0	1.6 0.5-3.2	1.2 0.5-5.8	1.0
Corticosterone 18-OH-Corticosterone	3.1 1.2-7.1	21 16-33	21	18 10-30	21 16-33	18	16 10-28	24 17-32	26
18-OH-Corticosterone Aldosterone	3.0 2.3-4.6	7.7 3.8-10	10	2.1 1.2-5.0	7.7 3.8-10	10	2.9 1.2-6.0	6.3 3-11	11
Corticosterone (ng/dl) Cortisol (ug/dl)	32 19-88	119 80-169	127	39 14-45	119 80-169	162	38 8-128	131 22-253	219

STEROID HORMONE LEVELS IN CONGENITAL ADRENAL HYPERPLASIA

STEROID		21-OH-Deficiency Classical (N=30)	21-OH-Deficiency Late Onset (N=20)	11-OH-Deficiency (N=20)
Aldosterone (ng/dl)	0 min	2-90	2-20	1-18
	60 min	*	8-41	1-40
Compound S (ng/dl)	0 min	10-520	15-45	570-26,000
	60 min	*	35-150	1200-50,000
Corticosterone (ng/dl)	0 min	45-1730	105-1110	70-1350
	60 min	*	1470-4800	101-5800
18-OH-Corticosterone (ng/dl)	0 min	2-145	25-70	2-45
	60 min	*	65-310	6-70
Cortisol (ug/dl)	0 min	1-18	3-12	1-26
	60 min	*	10-34	1-45
DHEA (ng/dl)	0 min	*	*	*
	60 min	*	*	*
DOC (ng/dl)	0 min	2-70	5-35	20-800
	60 min	*	20-75	225-2900
Pregnenolone (ng/dl)	0 min	190-3400	20-185	35-740
	60 min	*	75-760	180-970
17-OH-Pregnenolone (ng/dl)	0 min	600-22,000	20-510	125-1500
	60 min	*	500-2890	430-3650
17-OH-Progesterone (ng/dl)	0 min	3000-120,000	90-2078	30-1250
	60 min	*	1400-11,500	220-2360

*Not determined

17-OH DEFICIENCY

Corticosterone and to a lesser extent DOC are highly elevated in these patients, and provide useful laboratory markers. The data on the 5 patients summarized on page 114 are relatively consistent. Cortisol, other 17-hydroxylated steroids and androgens are consistently very low. Steroids not hydroxylated at the 17-position are elevated, but the most pronounced increase appears to be in corticosterone where values may be 100 times normal.

3-BETA-HSD DEFICIENCY

Unlike most forms of CAH, the interpretation of laboratory data in late onset or mild 3-Beta-HSD deficiency is not clear, and there is considerable disagreement regarding the incidence and diagnostic criteria for this disorder. The ACTH stimulated levels of 17-OH-pregnenolone and DHEA which are key marker steroids for this disorder are widely scattered. There is no readily apparent separation of 3-HSD deficient patients from those who have elevated levels of adrenal steroids for other reasons.

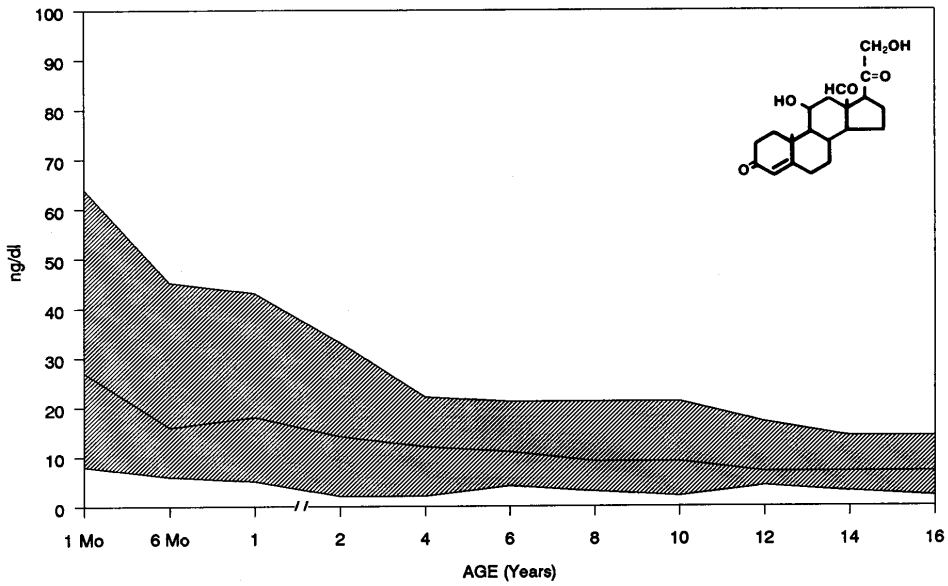
STEROID HORMONE LEVELS IN CONGENITAL ADRENAL HYPERPLASIA

STEROID		3-B-HSD Deficiency (N=6)	17-OH-Deficiency (N=5)	CMO-II Deficiency (N=5)
Aldosterone (ng/dl)	0 min	4-200	0.7-4.0	1-12
	60 min	*	2.3-5.0	1-18
Compound S (ng/dl)	0 min	260-1800	15-65	10-180
	60 min	*	25-94	145-360
Corticosterone (ng/dl)	0 min	80-5700	9000-40,000	700-9000
	60 min	*	20,000-57,000	3400-13,000
18-OH-Corticosterone (ng/dl)	0 min	16-380	100-300	85-2600
	60 min	*	300-550	130-4120
Cortisol (ug/dl)	0 min	1-15	0.5-3.0	3-16
	60 min	*	2.0-5.0	15-37
DHEA (ng/dl)	0 min	*	*	*
	60 min	*	*	*
DOC (ng/dl)	0 min	2-53	100-250	35-250
	60 min	*	200-480	60-550
Pregnenolone (ng/dl)	0 min	650-5900	300-800	*
	60 min	*	600-2400	*
17-OH-Pregnenolone (ng/dl)	0 min	2200-48,000	20-50	*
	60 min	*	20-50	*
17-OH-Progesterone (ng/dl)	0 min	335-4100	10-25	80-235
	60 min	*	25-50	140-490

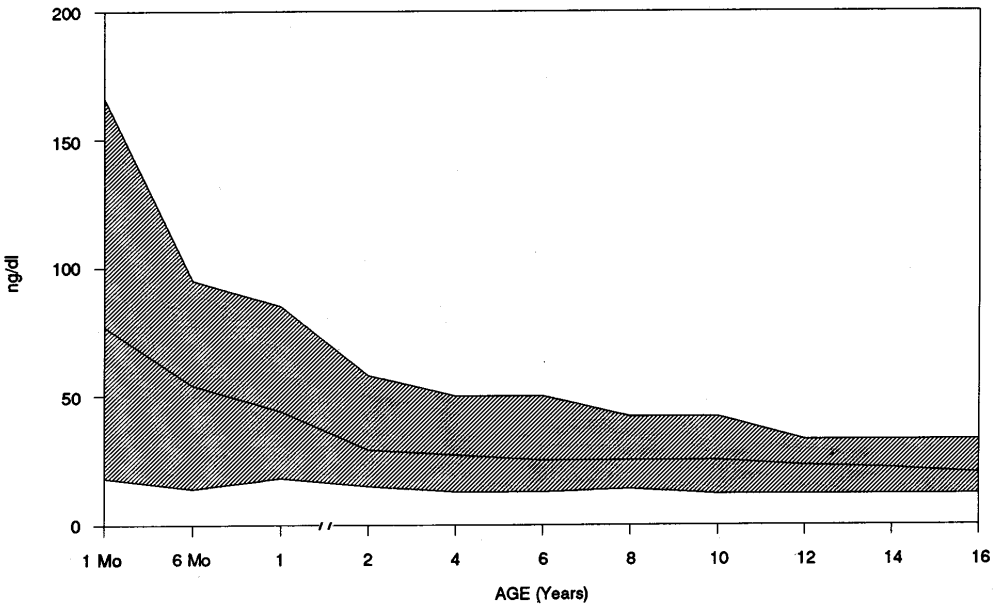
*Not determined

3-BETA-HSD DEFICIENCY (CONT.)
In children with premature adrenarche, the ACTH responses of 17-OH-pregnenolone and DHEA are elevated for age and are generally comparable with results seen in older pubertal children. It is not clear at the present time, however, whether this phenomenon results from a mild 3-Beta-HSD deficiency, or simply represents a premature expression of a normal physiological process. In adult women with hirsutism, the 17-OH-pregnenolone and DHEA responses are often considerably higher than normal. There is a wide variation in values, however, and with the exception of a small number of cases, there is no clear separation of the data. For this reason, there is a tendency to assign the diagnosis on a statistical basis and it is not clear whether all these patients have 3-Beta-HSD deficiency.

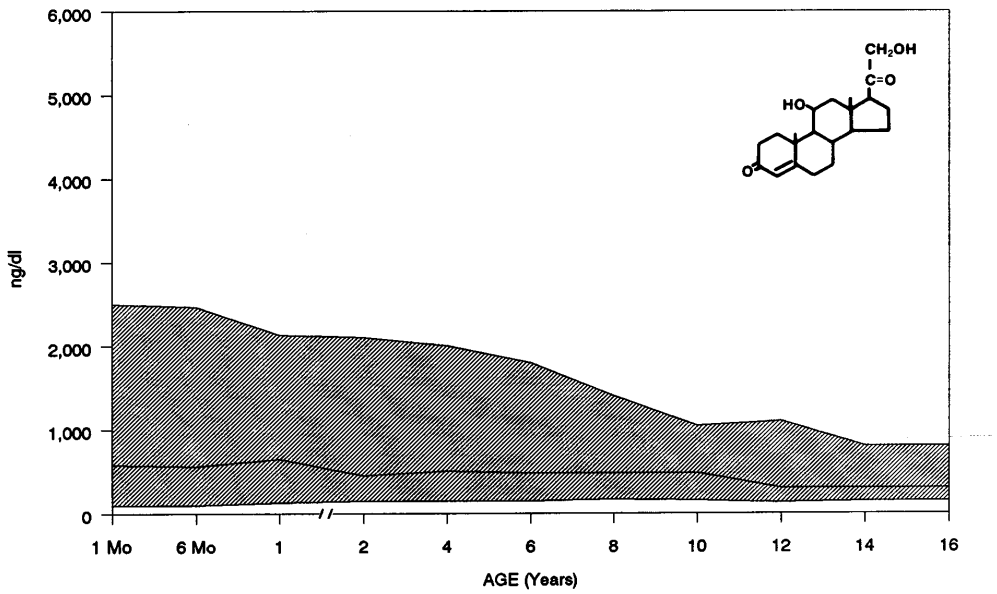
ALDOSTERONE
BASELINE/O MIN



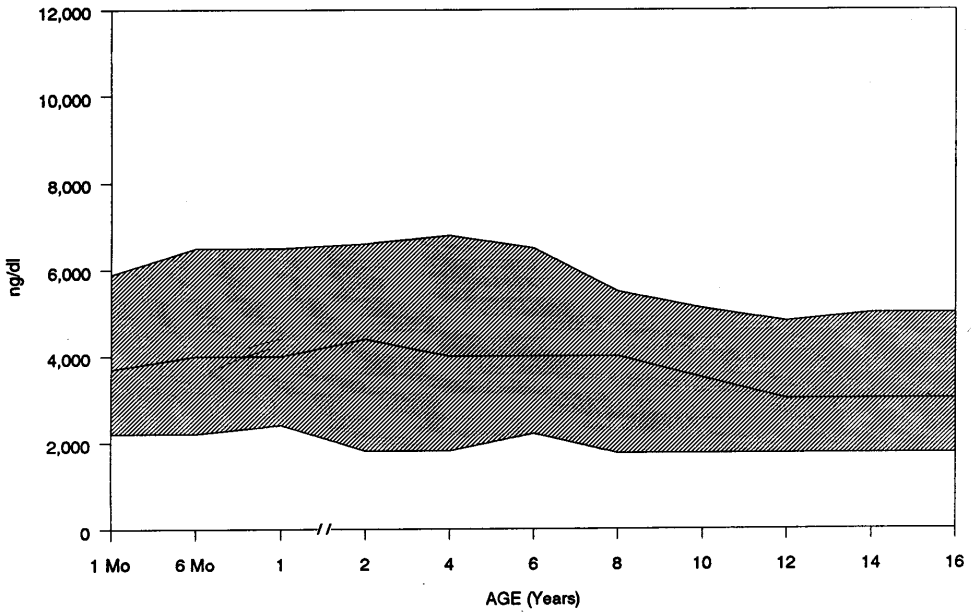
ALDOSTERONE
ACTH STIMULATION/6O MIN



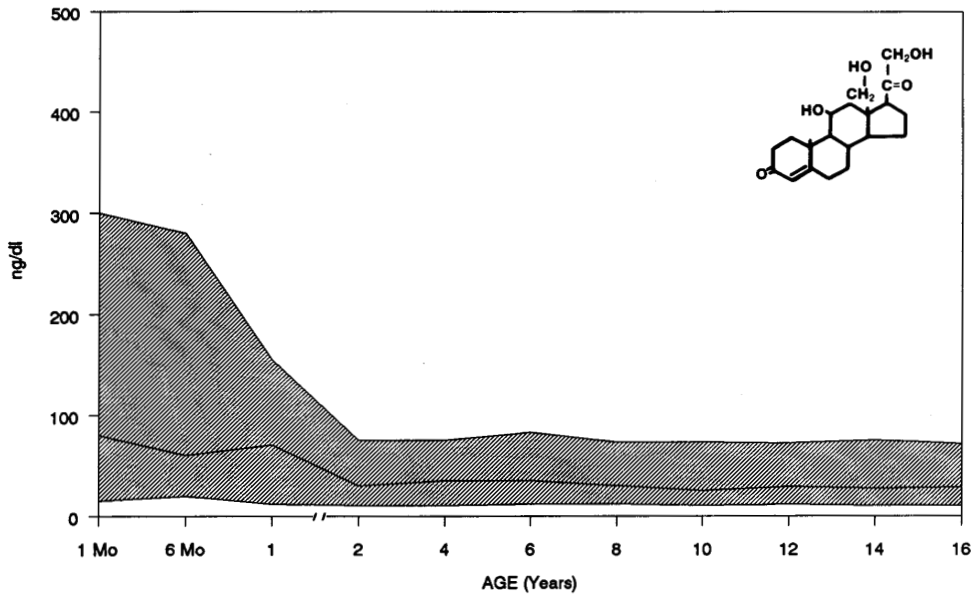
CORTICOSTERONE
BASELINE/O MIN



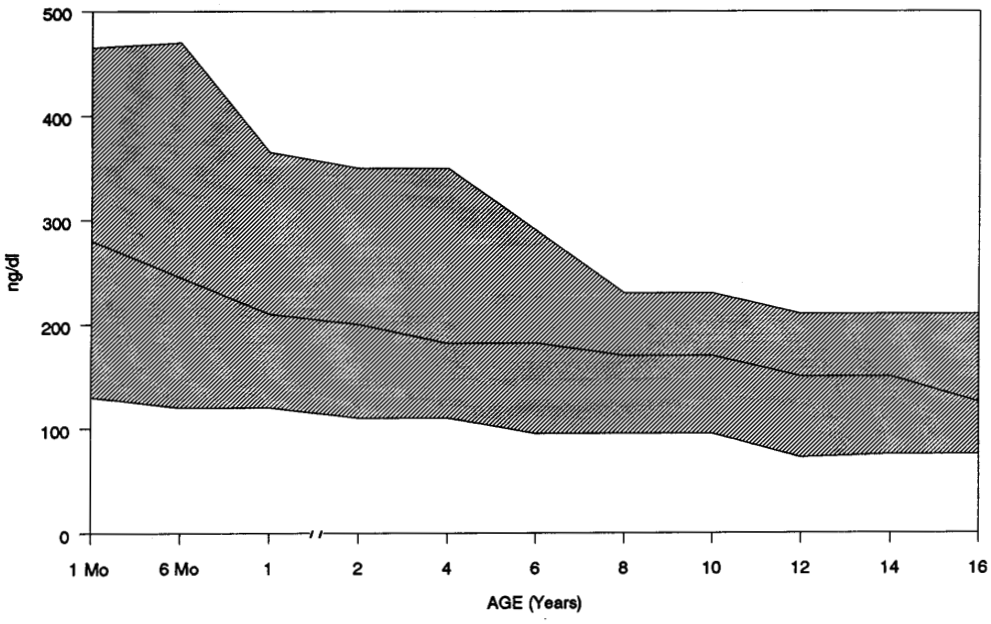
CORTICOSTERONE
ACTH STIMULATION/6O MIN



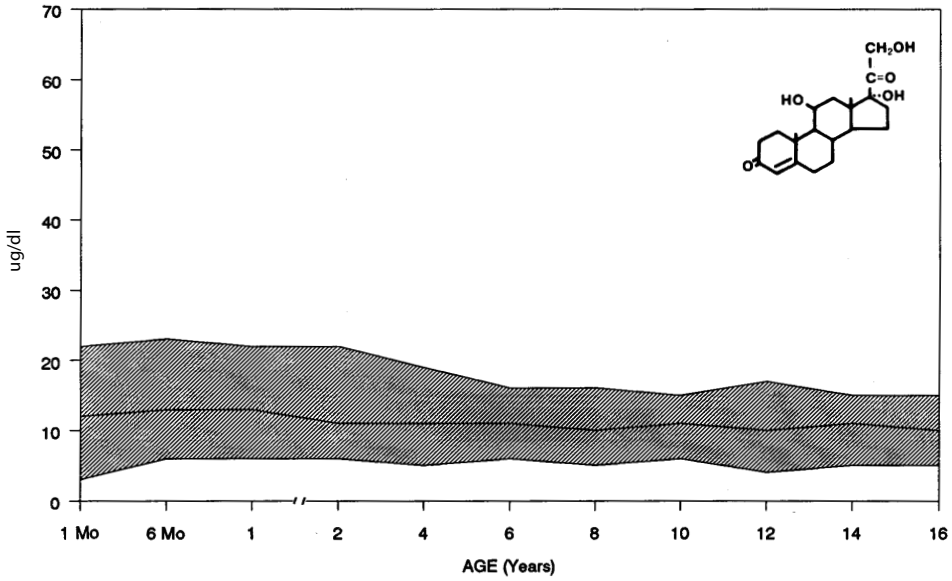
18-OH-CORTICOSTERONE
BASELINE/O MIN



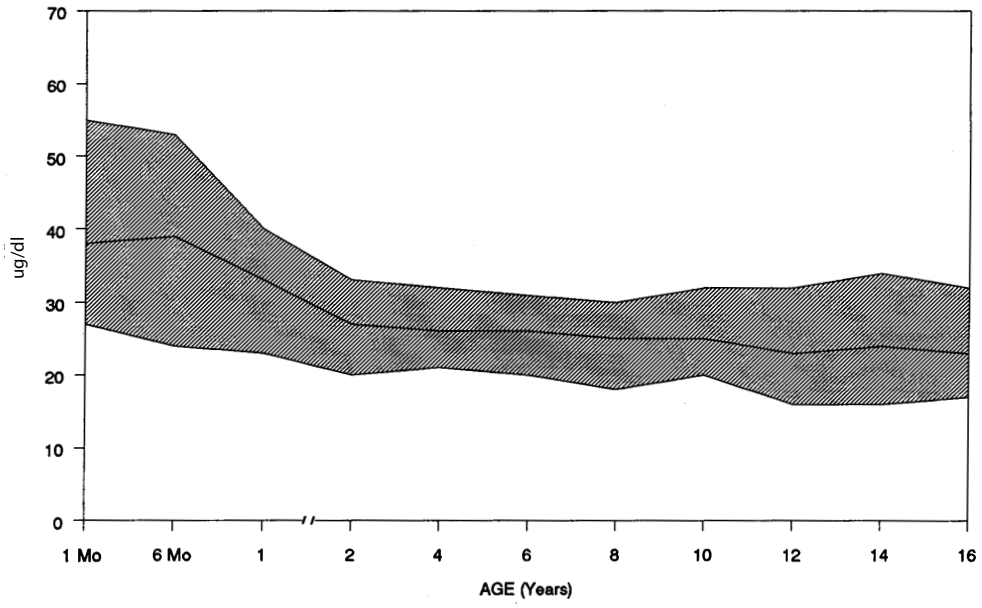
18-OH-CORTICOSTERONE
ACTH STIMULATION/6O MIN



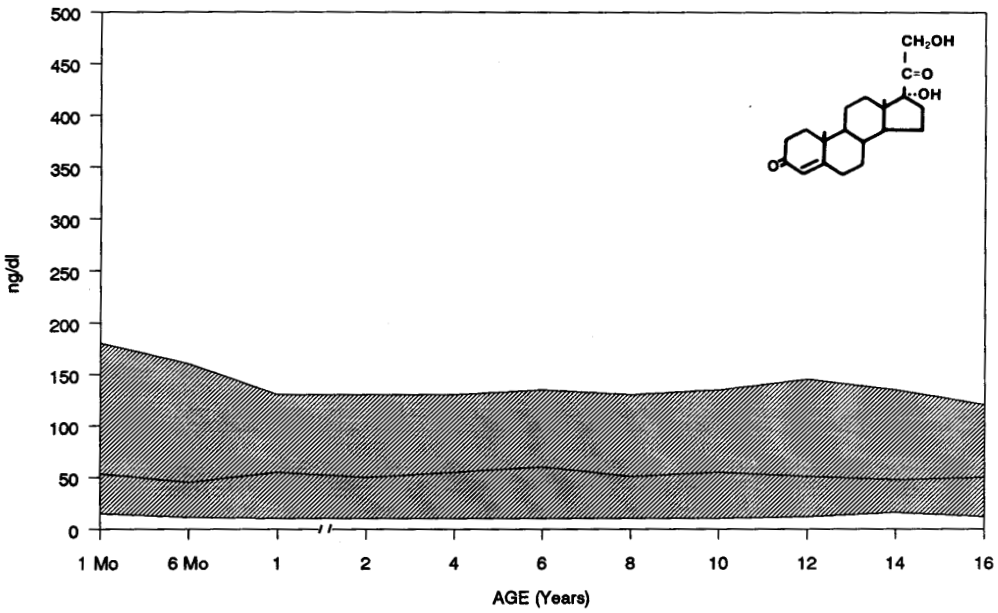
CORTISOL
BASELINE/O MIN



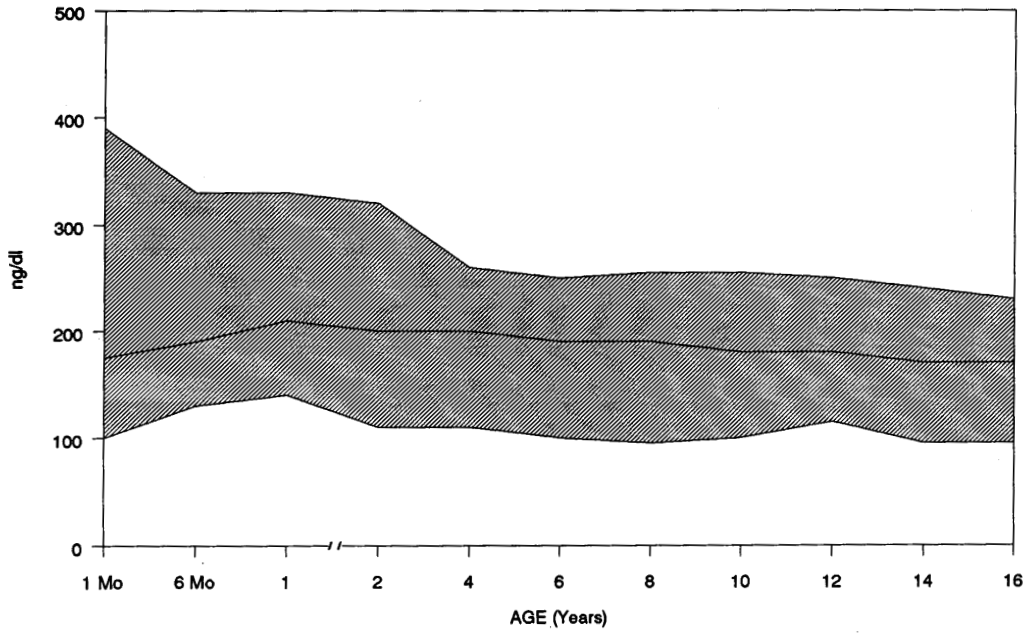
CORTISOL
ACTH STIMULATION/6O MIN



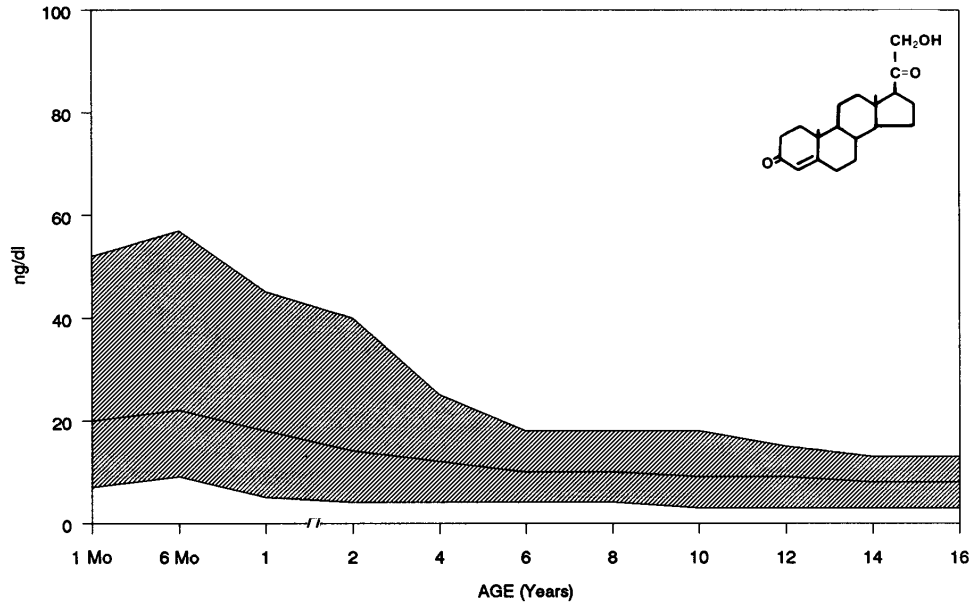
11-DESOXYCORTISOL
BASELINE/O MIN



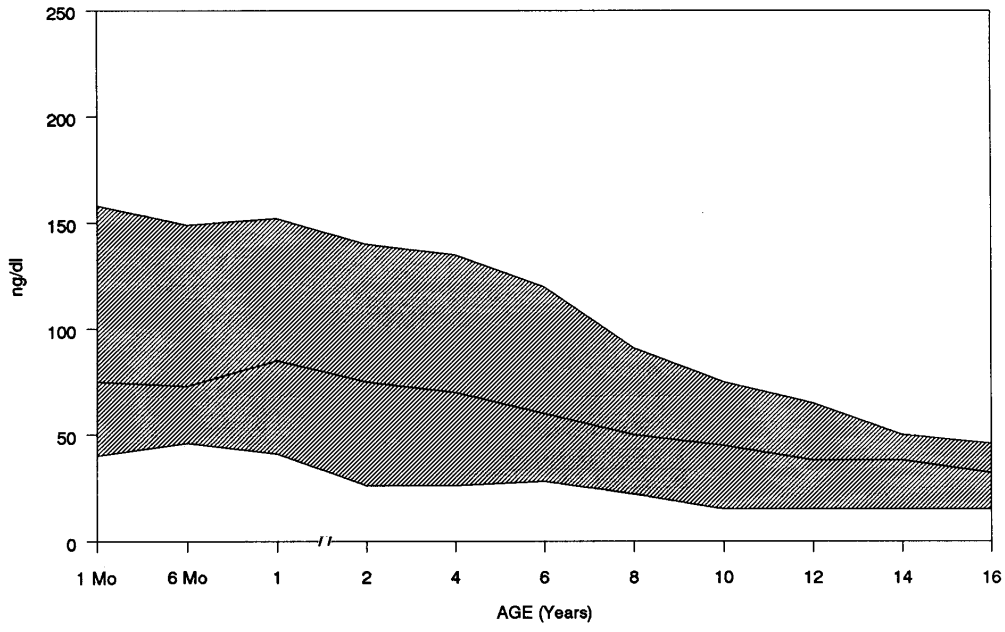
11-DESOXYCORTISOL
ACTH STIMULATION/6O MIN



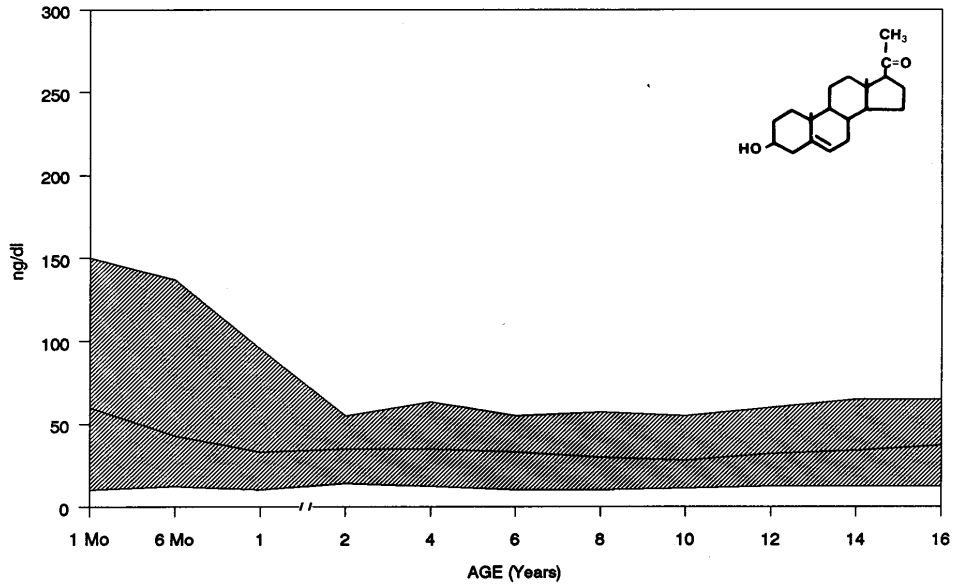
DEOXYCORTICOSTERONE
BASELINE/O MIN



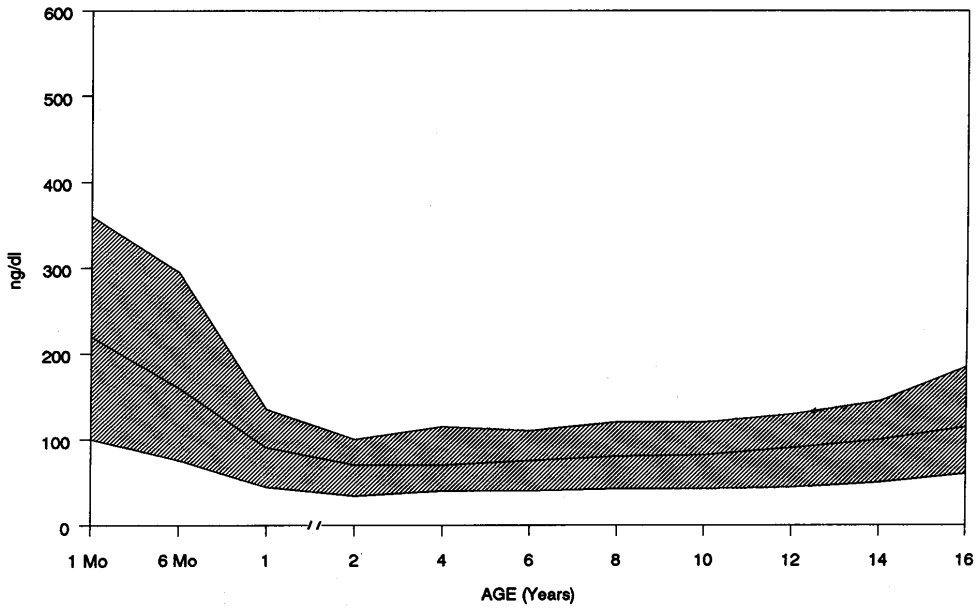
DEOXYCORTICOSTERONE
ACTH STIMULATION/6O MIN



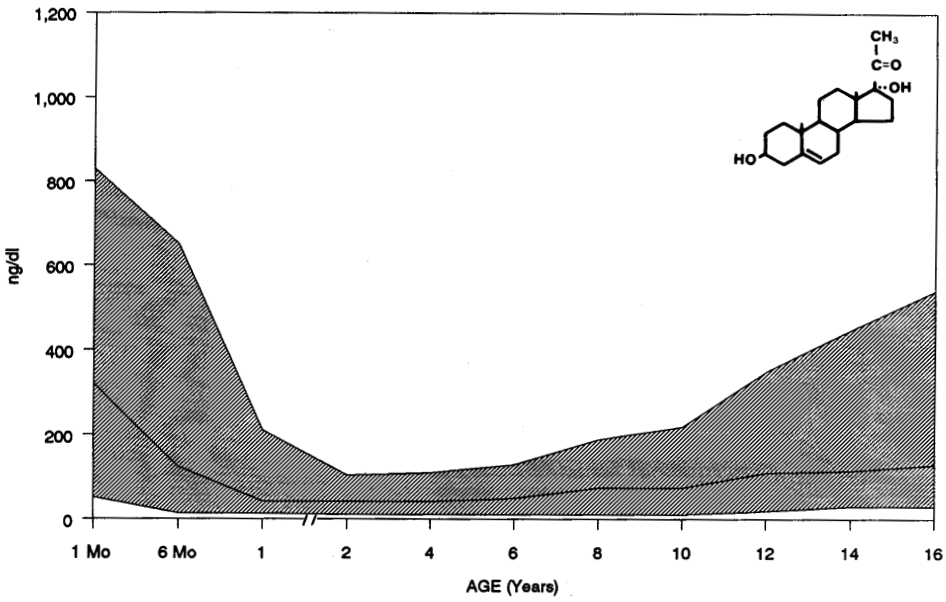
PREGNENOLONE
BASELINE/O MIN



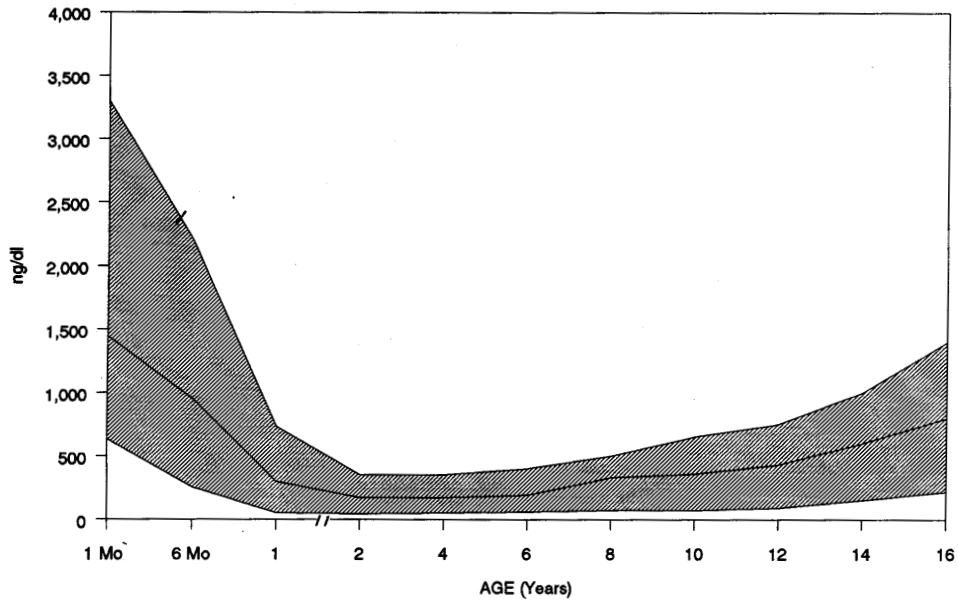
PREGNENOLONE
ACTH STIMULATION/6O MIN



17-OH-PREGNENOLONE
BASELINE/O MIN



17-OH-PREGNENOLONE
ACTH STIMULATION/6O MIN



17-OH-PROGESTERONE
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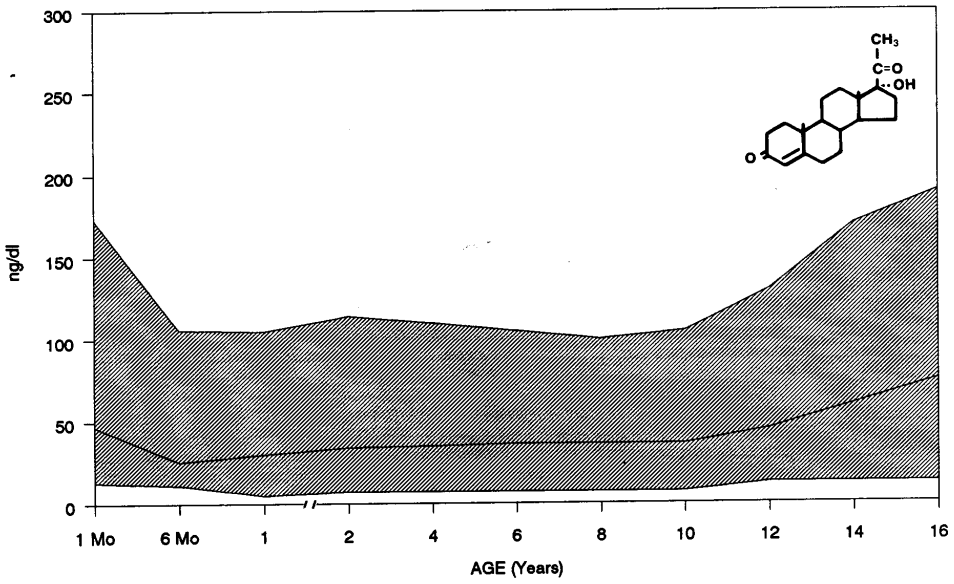

17-OH-PROGESTERONE
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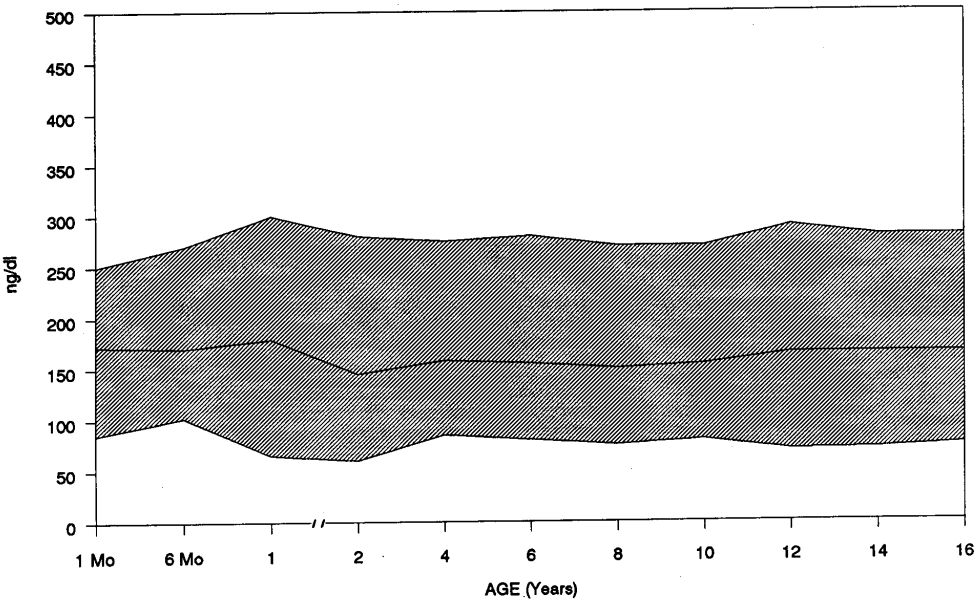

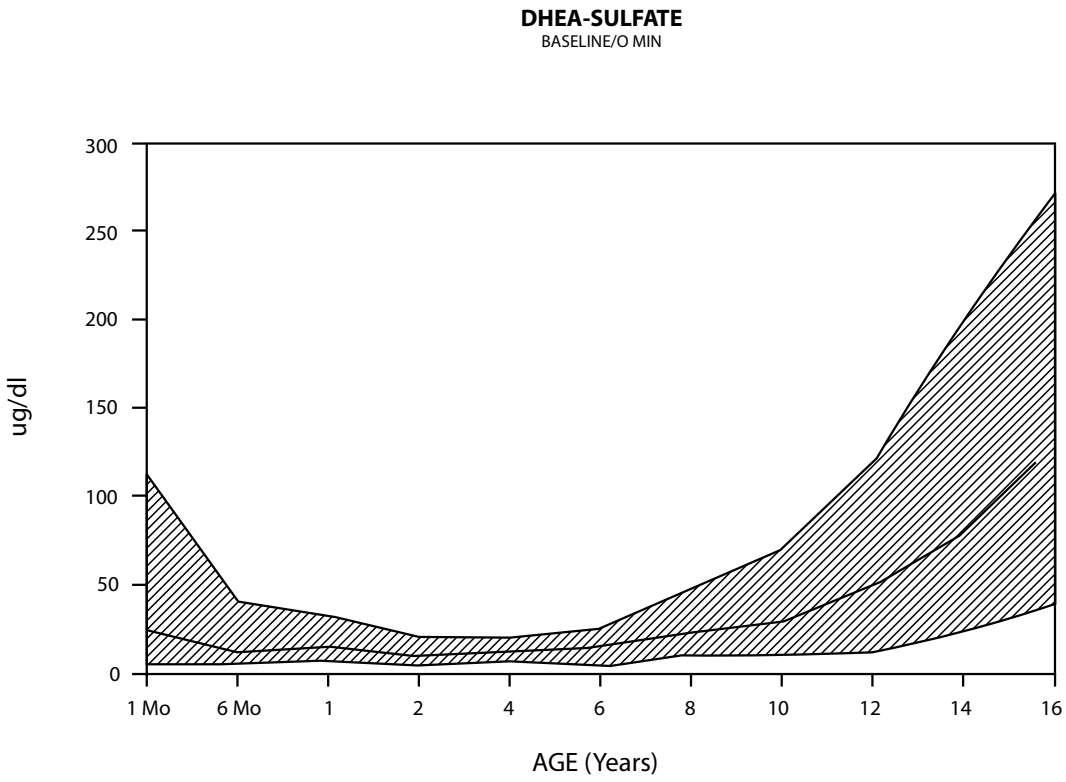

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