Appendix

Tests of Endocrine Function and Normal Values

INTRODUCTORY NOTES

These protocols are included for general guidance only. They were designed for use in a specialist children's endocrine unit and may not always be applicable elsewhere. It is the responsibility of clinicians performing the tests to ensure that correct local procedures are followed, particularly in relation to the administration of drugs, patient safety and comfort.

Further information on dynamic testing can be obtained from one of the texts cited in the Foreword.

COMBINED ANTERIOR PITUITARY FUNCTION TEST

PRINCIPLE

A combined provocation test is used to test for adequate excretion of GH, TSH, LH and FSH. Basal levels of GH are of no value because of the pulsatile nature of secretion. Likewise, exercise and sleep are both very poor stimuli for GH secretion and should not be used. IGF-1 and IGFBP-3 levels, if interpreted together, may give some information about GH status, but have an unacceptably high false-positive and false-negative value (especially post-irradiation), and so stimulated secretion, as described below, is required in most cases to confirm or refute GH deficiency and before treatment is commenced. It may be necessary and advisable to perform two tests of GH secretion in cases of isolated GHD.

The 'gold standard' test is still the insulin tolerance test + TRH + GnRH test, which has the advantage of allowing the assessment of ACTH secretion in response to hypoglycemia in a more predictable manner than with clonidine. However, this test has led to death in some circumstances and it should remain confined to experienced units, which will already have an established protocol; it is therefore not described here.

MATERIALS REQUIRED

Pharmaceutical

- Clonidine, TRH and LHRH (separately or combined in a single ampoule).
- Depot testosterone (for boys of TW2 bone age greater than 10 years).

Other

- Lithium heparin containers.

APPROXIMATE LENGTH OF TEST

Three hours, excluding any overnight preparation.

PATIENT PREPARATION

The exact procedure employed in males depends upon the age of the patient. If older than 10 years but with no signs of endogenous sexual development, consideration should be given to prior priming with sex steroids as there is good evidence that false-positive results will result in the relatively hypogonadotropic milieu of delayed puberty. Sex steroid priming is achieved by giving 100-mg depot testosterone esters i.m. 3–5 days before the test. There is no evidence that priming of females is required, but in some countries priming is still performed, for example with 25 µg ethinylestradiol twice a day for 5 days.

The patient is fasted overnight before the test. Venous access is secured and fixed into position along with a three-way stopcock for the duration of the test. The line is kept patent with heparinized saline.

Clonidine may make the subject nauseated, dizzy and hypotensive; young children may become very sleepy. TRH and GnRH can produce flushing and a metallic taste in the mouth. The subject must be fully recovered and have taken a meal before discharge home.

Other tests of GH release

A safe alternative to clonidine is to use arginine monohydrochloride, 12.5% solution, 0.5 g/kg infused over 30 min with blood taken at –30 min in addition to the samples described above.

Glucagon, GHRH, L-dopa and metaclopramide have all at some time been used as GH secretagogues.

PROCEDURE

Oral clonidine (150 μg/m^2) is given at time 0.

The standard dose of TRH is 5–7 μg/kg (up to 200 μg) and that of GnRH is 2.5 μg/kg (up to100 μg) injected over 2 min at time 0, immediately after the clonidine has been taken.

SAMPLES REQUIRED

Blood is collected at each timepoint according to the schedule in **Table A.1**. The volume required will vary according to local laboratory needs. The time of collection of the samples should be carefully recorded.

INTERPRETATION OF RESULTS

Growth hormone

Adequate secretion = more than 7 μg/L (using the 1 mg = 3 IU conversion).

As discussed in Chapter 2, this level is arbitrary and has tended to increase over time. Certainly, levels of 3.5 μg/L or less are indicative of more severe deficiency than intermediate levels.

TSH

Hypopituitary = all levels usually within normal basal range
and an increase to peak level of less than 5 mU/L (when basal level < 2 mU/L)
or an increase to peak level of less than 3-fold basal (when basal level > 2 mU/L).

Hypothalamic = level at 20 min greater than five times the upper limit of the normal basal range
or level at 20 min less than level at 60 min (when both levels are above the normal basal range), with a slow fall from this peak if a 120-min sample is analyzed.

Normal = results that are neither hypopituitary nor hypothalamic.

FSH and LH

Normal pubertal response = peak levels more than 3-fold greater than basal, LH peak > FSH. Must be interpreted in relation to bone age (see below) and physical maturation.

Prolactin

Prolactin is released in response to TRH. A similar rising 'hypothalamic pattern' may be seen. Basal levels should be interpreted in relation to the reference range. Inappropriate increases may be seen secondary to compression of the pituitary stalk or with prolactinomas.

Testosterone, estradiol

Normal = basal levels within the age-appropriate reference ranges (see below).

Cortisol

Cortisol may rise in response to clonidine administration, reflecting an intact hypothalamopituitary axis. If started after an overnight fast, the basal level

Time	GH	TSH	FSH & LH	Cortisol	Prolactin
0	+	+ Give clonidine, TRH & LHRH	+	+	+
20	+	+	+	+	+
60	+	+	+	+	+
90	+	—	—	+	—
120	+	+	—	+	—
150	+	—	—	+	—

Basal samples should be taken at 0900 hours for FT_4, ACTH, IGF-1 and IGFBP-3.

Table A.1 Schedule of sample collection for combined anterior pituitary function test

should be <120 nmol/L and the ACTH detectable, usually <40 pmol/L. However, the combined test described above is not an adequate test of cortisol secretion and if there is a reason to suspect adrenal insufficiency it is the authors' practice to combine it with a short, low-dose Synacthen test.

SHORT, LOW-DOSE SYNACTHEN TEST

PRINCIPLE

A synthetic form of ACTH is given to test the responsiveness of the adrenal cortex by production of cortisol. Older protocols relied on huge doses (250 μg/m^2) of Synacthen. The high-dose test can still be used in cases where primary adrenal failure is likely and estimation of intermediary adrenal hormones is important. Estimation of intermediary compounds (17α-hydroxyprogesterone) can give information about biosynthetic defects, such as atypical 21-hydroxylase deficiency (see below).

The low-dose test has been shown to generate more physiologic levels of ACTH and can detect subtle adrenal underactivity, for instance secondary to steroid medication. The protocol for the low-dose test is given but differs from the original only in the size of the Synacthen bolus and the need for more frequent, early, timed sampling.

MATERIALS REQUIRED

Pharmaceutical

- Synacthen – tetracosactrin acetate, 5% dextrose.

Other

- Lithium heparin tubes for blood.

APPROXIMATE LENGTH OF TEST

Ideally, a midnight sample should be collected at some point prior to the test; otherwise 1 h (or 150 min if combined with pituitary function tests).

PATIENT PREPARATION

In atopic individuals anaphylaxis can occur rarely in response to Synacthen, even at low dose; consequently a supply of emergency drugs should be available and the patient supervised carefully.

SAMPLES REQUIRED

Lithium heparin blood at each timepoint for cortisol, EDTA tube for ACTH (must be spun and frozen within 15 min).

PROCEDURE

Dissolve 125 μg in 500 mL 5% dextrose to give a solution of 250 ng/mL. Mix thoroughly. Give Synacthen i.v. at a dose of 500 ng/m^2. Collect blood 10, 20, 30, 60 and 120 min after dose.

INTERPRETATION OF RESULTS

Primary or secondary hypocortisolemia

The midnight and pre-dose cortisols should show a normal diurnal variation (midnight usually undetectable but up to 280 nmol/L (10 μg/dL); 0800 hours pre-dose 120–660 nmol/L (4.3–23.5 μg/dL) with ACTH detectable but <40 pmol/L; a raised ACTH level at baseline indicates adrenal pathology.

The normal response to Synacthen is a rise of cortisol of at least 280 nmol/L (10 μg/dL) to a peak of at least 550 nmol/L (20 μg/dL). Inadequate response indicates impaired adrenal cortical function.

Suspected adrenal enzyme disorders

Use standard 250-μg dose. A rise in 17α-hydroxyprogesterone to levels >10 nmol/L (5 μg/L) is seen in atypical 21-hydroxylase deficiency. The test can be used to promote secretion of any other adrenal steroid if blocks in the synthesis pathway are suspected, either alone or in combination with a 24-h urinary steroid profile.

CORTICOTROPIN RELEASING FACTOR (CRF) TEST

PRINCIPLE

Human or ovine CRF is given to test the responsiveness of the pituitary in producing ACTH and then cortisol. Ovine CRF has a longer duration of action for the stimulation test. This test is sometimes useful as a means of discriminating pituitary from ectopic ACTH-dependent Cushing's syndrome. It can be used to test pituitary recovery after surgery, irradiation or suppression.

MATERIALS REQUIRED

Pharmaceutical

- CRF, human or ovine preparations are available.

Other

- EDTA and lithium–heparin tubes for blood.

APPROXIMATE LENGTH OF TEST

Four hours

PATIENT PREPARATION

The test should commence at 0900 hours.

SAMPLES REQUIRED

Lithium–heparin blood at each timepoint for cortisol, EDTA tube for ACTH (must be spun and frozen within 15 min).

PROCEDURE

Give CRF 100 μg i.v. over 60 s. Collect blood at −15, 5, 15, 30 and 60 min after dose.

INTERPRETATION OF RESULTS

With pituitary adenoma, the mean ACTH and cortisol rise from baseline at 15 and 30 min should be >20% (up to 1000%). There is little response in ectopic ACTH production. In pituitary recovery after operation, etc. the cortisol level should exceed 500 nmol/L at one timepoint.

GROWTH HORMONE SUPPRESSION TEST

PRINCIPLE

Glucose, given as in an oral glucose tolerance test (GTT), will suppress GH production except in situations of pituitary overproduction. With the availability of IGF-1 and IGFBP-3 (which will be raised in pituitary gigantism), this test is rarely necessary.

MATERIALS REQUIRED

Pharmaceutical

- Oral glucose solution.

Other

- Fluoride oxalate and heparinized containers.

APPROXIMATE LENGTH OF TEST

Two hours, excluding overnight fast.

PATIENT PREPARATION

The patient should be admitted after an overnight fast. Venous access should be secured.

PROCEDURE

Samples for glucose and GH are collected at time 0, and then glucose, 1.75 g/kg, is administered orally (maximum dose 75 g). Blood is drawn at 30, 60, 90 and 120 min. Test any urine passed for the presence of glucose.

INTERPRETATION OF RESULTS

Basal GH concentration should be less than 3 μg/L. GH should fall to an undetectable level through the test. Failure to suppress GH levels and an abnormal glucose response (true blood sugar level >10 mmol/L (182 mg/dL) = frank diabetes; >6.7 mmol/L (122 mg/dL) = impaired glucose tolerance) are indicative of a pituitary adenoma.

GH may fail to suppress in chronic severe anemia, hepatic cirrhosis, porphyria and malnutrition.

IGF-1 GENERATION TEST

PRINCIPLE

If GH resistance is suspected, the ability of exogenous GH to stimulate IGF-1 can be measured.

MATERIALS REQUIRED

Pharmaceutical

- Growth hormone.

Other

- Heparinized containers.

APPROXIMATE LENGTH OF TEST

Four days.

PATIENT PREPARATION

Administer GH 0.03 mg/kg daily, for 4 days.

PROCEDURE

Samples for GH, IGF-1 and IGFBP-3 estimation are collected on day 0, and those for IGF-1 and IGFBP-3 on day 5.

INTERPRETATION OF RESULTS

In GH resistant states the basal GH concentration should be more than 3 μg/L. IGF-1 level should be low and not show a rise after 4 days of GH treatment. IGFBP-1 concentration will be low throughout.

ORAL GLUCOSE TOLERANCE TEST

Glucose tolerance tests are required much less commonly in children than in adults. The diagnosis of

diabetes can almost always be made by a random fasting plasma glucose level. A 2-h level is all that is required to confirm the diagnosis in rare borderline cases of diabetes. However, delineation of some of the rarer forms of diabetes can be made by simultaneous measurements of insulin and glucose. The procedure is the same as outlined above for a GH suppression test above (omitting the measurement of GH, but including the simultaneous assay of insulin at time 0 and intermediate timepoints to 2 h). Other basal or stimulated testing of C peptide and lactate may be useful in some circumstances.

INTRAVENOUS GLUCOSE TOLERANCE TEST

PRINCIPLE

An intravenous glucose tolerance test eliminates gastrointestinal factors that can affect the oral test. It allows calculation of a disappearance rate for circulating glucose that is related to insulin status. The test is performed only rarely.

MATERIALS REQUIRED

Pharmaceutical

- D-Glucose as a 50% solution w/v in water.

Other

- Fluoride oxalate bottles for blood.

APPROXIMATE LENGTH OF TEST

1.5 h plus overnight fast.

PATIENT PREPARATION

Fast patient overnight.

SAMPLES REQUIRED

Blood in fluoride oxalate tubes at each timepoint.

PROCEDURE

Glucose is given i.v. as a 25% solution at a dose of 0.5 g/kg body weight over 5 min. A stopwatch is started when half the dose has been given. Blood samples are collected at exactly 5, 10, 20, 30 and 60 min. All urine passed over 2 h is tested for glucose.

INTERPRETATION OF RESULTS

Blood glucose results versus time are plotted on semi-logarithmic graph paper to calculate the half-life. The disappearance constant, k, is calculated:

$$k\ (\%\ \text{per min}) = \frac{(0.693 \times 100)}{\text{half-life}}$$

Disappearance rates are normally 1–3%. They are reduced in diabetes and increased in hyperinsulinism.

WATER DEPRIVATION (URINE CONCENTRATION) AND DDAVP STIMULATION TESTS

PRINCIPLE

Fluid intake is restricted and urine osmolality measured to assess renal concentrating ability. DDAVP may be administered to distinguish renal tubular from posterior pituitary dysfunction. ADH measurement is useful to distinguish nephrogenic (usually raised) from central (low) diabetes insipidus.

MATERIALS REQUIRED

Pharmaceutical

- DDAVP (1-deamino-8-D-arginine vasopressin).

Other

- Universal containers for urine.
- Lithium–heparin tubes for blood.

APPROXIMATE LENGTH OF TEST

1–2 days.

PATIENT PREPARATION

The patient is weighed before and periodically during the test. The frequency of weighing depends on the age of the child and suspected disorder. It should not be less frequent than every 4 h and may have to be hourly or even half-hourly in suspected nephrogenic DI. Calculate 5% of the body weight, subtract it from the starting weight, and discontinue the test if the patient's weight falls below this level. Terminate the test at any time if there are clinical signs of serious dehydration.

SAMPLES REQUIRED

Lithium–heparin blood samples for sodium and serum osmolality. Urine container for osmolality. Note time of collection on tubes. Direct measurement of basal ADH level may be useful in some circumstances.

PROCEDURES

Fluid deprivation

Day 1

Normal diet and fluid intake. Send each specimen of urine passed for measurement of volume and osmolality – at least every 4 h. Note the collection time on the container. If the osmolality of any urine is greater than 700 mmol/L (mOsmol/L), no further testing is required.

Day 2

At 0830 hours give a normal feed. Weigh the patient. Allow no more food or fluid. Collect blood samples for osmolality and sodium. Collect all urine passed and send immediately to the laboratory for the measurement of volume and osmolality as before.

Collect blood for osmolality and sodium at least 4 hourly. Terminate the test as soon as any urine osmolality is greater than 700 mmol/L or if there are clinical signs of significant dehydration.

The length of the test depends on the age of the child and clinical response to dehydration. Careful observation of the child is required throughout the test.

INTERPRETATION OF RESULTS

If any urine sample has an osmolality greater than 700 mmol/L (mOsmol/L), concentrating ability is adequate and the test should be terminated.

If there has been inadequate urinary concentration, proceed to a DDAVP test.

DDAVP test

The patient is allowed to eat normally, but restrict infants to half-normal fluid intake and limit older children to 0.5 L fluids to prevent excessive drinking in the 8 h after DDAVP has been administered to prevent overhydration and hyponatremia. DDAVP is given i.m. at a dose of 0.125 µg for children and one-tenth of this for infants (who may be extremely sensitive to DDAVP in the presence of congenital DI).

INTERPRETATION OF RESULTS

If adequate concentration is achieved after DDAVP, this suggests satisfactory renal concentrating ability but an inadequate secretion of posterior pituitary AVP (central DI). If there is inadequate concentrating ability after DDAVP, renal unresponsiveness to AVP (nephrogenic DI) is demonstrated and the basal ADH level may be raised. In habit polydipsia, if prolonged, there may be dilute urine passed even after a prolonged period of water deprivation, making differentiation from partial central DI difficult. In these cases a hypertonic saline test performed on a specialist unit may help the diagnosis by creating a mild hyperosmolar state and promoting ADH release in the habit drinker.

DEXAMETHASONE SUPPRESSION TESTS

PRINCIPLE

Dexamethasone is a potent steroid that will suppress ACTH secretion, and hence cortisol, in the normal situation but not in Cushing's syndrome.

MATERIALS REQUIRED

Pharmaceutical

- Dexamethasone.

Other

- Lithium–heparin tubes for blood.

APPROXIMATE LENGTH OF TEST

One day for overnight test, 5 days for the high-dose test.

SAMPLES REQUIRED

Lithium–heparin blood at each timepoint for cortisol and ACTH; urine containers for free cortisol estimation and urinary steroid profile.

PROCEDURE AND INTERPRETATION OF RESULTS

Measure basal cortisol and ACTH levels:

- If both are raised, administer oral dexamethasone, 1.0 mg per 1.7 m^2 at 2300 hours. Determine serum cortisol concentration at 0800–0900 hours the following morning. The morning cortisol level should be less than 50 nmol/L (1.8 µg/dL) or at least 50% of the pre-test morning cortisol concentration.
- If ACTH is undetectable and there is hypercortisolemia, an adrenal cause is proven and no further tests are required.
- If ACTH is detectable or raised, and there is failure of suppression of cortisol in response to the overnight test, dexamethasone should be administered in a dosage of 0.5 mg/m^2 four times a day for 2 days, and blood estimations repeated. Then continue with dexamethasone 2.0 mg/m^2 four times daily for a further 2 days.

Collect 24-h urine samples each day for free urinary cortisol and steroid profile.

If cortisol excretion is not suppressed by the low dose of dexamethasone, some form of Cushing syndrome is virtually certain. If there is some suppression on the higher dosage, pituitary Cushing disease is most likely, while a lack of any suppression indicates an adrenal tumor.

INVESTIGATION OF HYPOGLYCEMIA IN CHILDREN

PRINCIPLE

Hypoglycemia has a wide variety of causes in children (see Ch. 11). These include various metabolic problems in which hypoglycemic episodes occur intermittently. To overcome this difficulty in investigation, a suitable approach is the measurement of the intermediary metabolites directly involved in glucose homeostasis after a prolonged, supervised fast (6, 12 or 24 h depending on age) or during an actual hypoglycemic attack.

MATERIALS REQUIRED

Lithium–heparin and fluoride oxalate containers for blood; urine containers.

APPROXIMATE LENGTH OF TEST

Up to 24 h.

PATIENT PREPARATION

For a prolonged fast in older children, start the test between 1600 and 2100 hours and take samples at 0900 and 0012 hours or 1600 hours the following day. In young children, or when hyperinsulinism is strongly suspected, do not begin the fast until 0900 hours.

The patient can be given water to drink during this time. It is advisable to check the plasma glucose level regularly and, if symptoms of hypoglycemia occur, either by laboratory assay or on the ward by means of a reliable bedside method, then terminate the test and treat with oral glucose or 2 mL/kg 10% dextrose voer 3 min followed by an infusion of 0.1 mL/kg per min to keep the blood sugar between 5 and 8 mmol/L (90–144 mg/dL). If hypopituitarism is suspected, also give 100 mg hydrocortisone i.v.

SAMPLES REQUIRED

- Fluoride tube: glucose, lactate, alanine, free fatty acids, β-hydroxybutyrate and carnitine.
- Heparinized blood: cortisol, GH and insulin (plasma should be separated from cells promptly and stored at –20°C). (In cases of possible factitious hypoglycemia due to insulin administration, measure C peptide along with insulin.) A chilled tube sent straight to the laboratory is required to measure ammonia levels in hyperinsulinism.
- Urine: sample as soon as possible after hypoglycemia for organic acids and acylcarnitines. (In cases of possible factitious hypoglycemia due to oral hypoglycemic agents, send urine for toxicology.)

INTERPRETATION

See Chapter 11.

PHOSPHATE EXCRETION INDICES

PRINCIPLE

There is a maximal rate (transport maximum, Tm) for the active reabsorption of some solutes by the renal tubule. Abnormalities in the Tm for phosphate (TmP) may have primary causes as in familial hypophosphatemic rickets or be secondary due to the effect of parathyroid hormone. Direct assay of PTH in combination with a calcium level may obviate the need for this procedure in many cases.

MATERIALS REQUIRED

Lithium–heparin containers for phosphate and creatinine estimation, and urine container.

APPROXIMATE LENGTH OF TEST

One to 2 h, excluding overnight fast.

PATIENT PREPARATION

Overnight fast.

SAMPLES REQUIRED

After an overnight fast, collect a urine sample over 1–2 h and a single blood sample. Assay phosphate and creatinine on each sample.

RESULTS

Calculate:

a) The phosphate : creatinine clearance ratio:

$$\frac{C_p}{C_{cr}} = \frac{(P_{cr} \times U_p)}{(P_p \times U_{cr})}$$

where P_{cr} is plasma creatinine, P_p is plasma phosphate, U_{cr} is urine creatinine and U_p is urine phosphate (all in mmol/L).

b) The tubular reabsorption of phosphate:

$$TRP = (1 - C_p/C_{cr}) \times 100$$

c) The phosphate excretion index:

$$PEI = (C_p/C_{cr}) - ([0.155 \times P_p] - 0.05)$$

INTERPRETATION

In familial hypophosphatemic rickets, the TRP and TmP/GFR (which can be estimated directly or is roughly equivalent to TRP × P_p) and the plasma phosphate concentration are low. The C_p/C_{cr} and PEI may be high.

Raised PTH concentration in hyperparathyroidism decreases TRP and TmP/GFR, and increases C_p/C_{cr} and PEI, causing phosphaturia.

In hypoparathyroidism TRP and TmP/GFR are increased, and C_p/C_{cr} and PEI are reduced.

hCG TESTS

PRINCIPLE

hCG is an LH-like compound that will stimulate testosterone production from the testes in the normal state. Testosterone is converted to DHT in the presence of normal 5α-reductase activity.

MATERIALS REQUIRED

Pharmaceutical

- hCG (or recombinant LH if available).

Other

- Lithium–heparin containers for blood estimations of testosterone and DHT.

APPROXIMATE LENGTH OF TEST

From 5 days to 3 weeks (see below).

SAMPLES REQUIRED

Blood for testosterone, DHT, androstenedione and DHEAS.

PROCEDURE

Give hCG 1500 units i.m. for an infant and 2000 units i.m. for an older child on days 0, 1 and 2. Take blood samples on days 0 and 3.

In situations of prolonged cryptorchidism, or where testicular damage is highly likely, give hCG 1000 units twice weekly for 3 weeks and take blood on day 0 and 48 h after the last injection.

INTERPRETATION

A rise in testosterone concentration from the baseline demonstrates intact testicular Leydig cell function. If a prolonged test produces a rise in testosterone, spontaneous puberty is possible (assuming normal gonadotropin function), although surveillance will still be required and long-term ability to virilize plus fertility may still be in doubt.

Failure of a rise in DHT level (testosterone: DHT ratio > 25 or absolute DHT level < 1 nmol/L) implies 5α-reductase deficiency. The differential rise of testosterone to DHEAS and androstenedione can be used to explore defects in testosterone biosynthesis (see Ch. 8).

GENETIC TESTS IN PEDIATRIC ENDOCRINOLOGY

Table A.2 gives only a few of the most important locations, or specific gene abnormalities, of relevance to pediatric endocrinology, and indicates where analysis may help in management.

NORMAL VALUES

The cautions given in Chapter 11 regarding interassay variation, inappropriate age-related values and heterophilic antibodies in immunoassays should be heeded. Ideally all values given in **Table A.3** should be interpreted against a validated local range. Drugs and diet can interfere with some assays. Acute ill health, stress during the sampling procedure and prematurity can also cause variation.

Levels of steroid precursors and urinary steroid profiles, IGF-1 and IGFBP-3 levels, are highly specific to the assay system used, the local population and age/pubertal status; thus normal values will not be quoted for these compounds.

Some peptide hormone levels are given as units per liter. Standardization of biologic equivalence of recombinant products to weight in milligrams is currently in progress, but older human and less pure preparations are still in use to validate assays, which makes exact conversion difficult.

Condition	Defect	Chromosome
Adrenal		
Adrenoleukodystrophy	*ADLP* (*VLCFA*)	Xq28 + other?
CAH (common form)	21-Hydroxylase	p21.3
Adrenal hypoplasia	*DAX1* (deletion)	Xp21
Cellular receptors/signaling		
Laron syndrome	GH receptor	5p
Testotoxicosis	LH receptor (activation)	2p21
Male pseudohermaphroditism	LH receptor (deletion)	
See Chs 4 & 10	Insulin receptor	19p13.3-2
McCune—Albright	G protein	20q13.2
Thyroid hormone resistance	Thyroid hormone receptor β	3p
Nephrogenic DI (dominant)	Aquaporin 2	12q
Nephrogenic DI (X-linked)	Vasopressin receptor	Xq28
Kallmann	*KAL1*	Xp
GH resistance	IGF-1	12q22-24.1
Intracellular receptors		
Androgen insensitivity	Androgen receptor	Xq12
Ovary/testis		
Male pseudo-hermaphroditism	*DAX1* (duplication)	Xp21
Hypogonadotropic hypogonadism	*DAX1* (deletion)	Xp21
Gonadal dysgenesis (some)	*SRY*	Yp11.3
Camptomelic dysplasia	*SOX9*	17q
AMH deficiency	*AMH*	19p13.3
Pancreas		
MODY1	HNF-4α	20q12-13.1
MODY2	Glucokinase	7p15-13
MODY3	HNF-1α	12q24.2
MODY4	Insulin promoter factor	13q12.1
MODY5	HNF-1β	17cen-q21.2
PHHI (some)	*SUR1*	11p15
PHHI + hyperammonemia	*GLUD1*	10q23.3
DIDMOAD	Wolframin	4p & 4q
Pituitary		
Septo-optic dysplasia (some)	HESX-1	3p21
TSH deficiency	TSHβ	1p13
LH deficiency	LH	19q
FSH deficiency	FSH	11p
Combined GH—TSH	*PIT1*	3q
Diabetes insipidus (some)	ADH	20p13

Table A.2 Some genetic test in pediatric endocrinology

Condition	Defect	Chromosome
Syndromes		
Prader—Willi	Imprinting (SNRPN)	15q11
Noonan	Unknown (linkage analysis)	12q24
Beckwith—Wiedemann	Imprinting (IGF2 gene)	11p15.5
Marfan	Fibrillin	15q, 17q
Williams	Elastin	7q11.23
NF1	Neurofibromin	17
Leri—Weill	*SHOX*	Pseudoautosomal region of Xp
Thyroid/parathyroid		
MEN II	*ret* proto-oncogene	10q11.2 (1p)
MEN I	Menin (suppressor protein)	11q13

Table A.2 *Cont'd*

Hormone	SI units	Conversion factor (if relevant)
ACTH (early a.m.)	2–20 pmol/L	0.22 = pg/mL
ADH	1–5 pmol/L	0.992 = pg/mL
Epinephrine (adrenaline)		
Infant	<30 pmol/L	5.46 = ng/L
Child	<80 pmol/L	
Adult	<200 pmol/L	
Androstenedione		
Prepuberty	<3.5 nmol/L	0.0349 = ng/dL
Male	4.5—10.5 nmol/L	
Female	4—10 nmol/L	
C peptide	20—50 nmol/L	33.3 = mg/dL
Calcitonin	<30 pmol/L	0.29 = ng/L
Cortisol		
Early morning	120—660 nmol/L	28 = µg/dL
Midnight	Up to 280 nmol/L	
FSH		
Prepubertal	<3.5 U/L	
Pubertal, follicular	2–7 U/L	
Glucose	3.0—6.5 mmol/L	0.057 = mg/dL
GH		
Stimulated	>7 µg/L	(1 mg = 3 IU standard)
Suppressed	<0.3 µg/L	
HbA1c (assays vary)	<6%	
hCG	<5 IU/L	
17α-Hydroxyprogesterone		
Males	<12 nmol/L	3.0 = µg/L
Females	<10 nmol/L	
(increased in sick and premature neonates)		
Insulin	<10 mU/L	
(interpret w.r.t. glucose in hypoglycemia)		
Lactate	<2.5 mmol/L	0.1 = mg/dL
LH		
Prepubertal	<2 U/L	
Pubertal, follicular	<12 U/L	
Pubertal, mid-cycle	<70 U/L	
Norepinephrine (noradrenaline)		
Infant	<100 pmol/L	5.91 = ng/L
Older	<900 pmol/L	
Estrogen (E_2)		
Prepubertal	<60 pmol/L	3.67 = pg/mL
Adult male	<250 pmol/L	
Adult female, mid-cycle	Up to 1500 pmol/L	
Osmolality (plasma)	275—295 mmol/L	= mOsmol/L
Prolactin (unstressed)	<800 pmol/L	44.4 = µg/L

Table A.3 Normal values

Hormone	SI units	Conversion factor (if relevant)
Progesterone		
Prepubertal	<1.5 nmol/L	3.18 = μg/L
Pubertal, follicular	<5 nmol/L	
Pubertal, luteal	15—90 nmol/L	
PTH (intact)	2—8 pmol/L	10 = ng/mL
SHBG		
Male	20—45 nmol/L	2.0 = μg/L
Female	50—80 nmol/L	
Testosterone		
Prepubertal and female	<1.0 nmol/L	0.035 = ng/dL
Pubertal male, post hCG	10—25 nmol/L	
TBG	N/A	7—17 mg/L
TSH (high sensitivity)	0.3—5.0 mU/L	
Thyroxine		
Free	9—23 pmol/L	12.9 = ng/dL
T_3 (free)	4.5—8.0 pmol/L	0.015 = ng/dL
Urinary free cortisol	<250 nmol/day	2.8 = μg/day
VMA (24 h urine)	<40 μmol/day	5 = mg/day

Table A.3 *Cont'd*