Endocrine function tests are used as an aid in assessing the function of specific target organs to exogenous agents and monitoring the response over specified time intervals. A list of common tests and recommended draw times are given below. Tests available are:

- Rapid ACTH Stimulation Test
- Prolonged ACTH Stimulation Test
- Thyrotropin-Releasing Hormone (TRH) Stimulation Test
- Overnight Low-Dose Dexamethasone Suppression Test
- Overnight High-Dose Dexamethasone Suppression Test
- Metyrapone Stimulation Test
- GnRH Stimulation Test

**Rapid ACTH Stimulation Test**

*Rationale*—The administration of adrenocorticotropic hormone (ACTH) to normal subjects results in a rapid rise in serum cortisol level. Patients with adrenal destruction (Addison’s disease) show no change in serum cortisol levels after ACTH administration. Patients with atrophy of the adrenal cortex due to exogenous glucocorticoid treatment or dysfunction of the pituitary gland or hypothalamus may show a slight rise in serum cortisol levels, but not one of normal magnitude.

*Procedure*—A baseline blood specimen is drawn for determination of a serum cortisol level; then 250 µg cosyntropin (1-24 ACTH) is given intramuscularly or intravenously. Further specimens for serum cortisol determination are drawn 30 and 60 minutes after injection.

*Interpretation*—A normal peak serum cortisol level is >20 µg/dL. The peak value is more important than the incremental change. The incremental change may not be seen in patients who are tested at times of stress when their adrenal output of cortisol is already maximally stimulated by endogenous ACTH.

**Prolonged ACTH Stimulation Test**

*Rationale*—Multiple-day ACTH stimulation testing for assessment of adrenal cortex function is required occasionally to evaluate adrenal cortisol responsiveness. A common situation is the diagnosis of adrenal insufficiency, which is treated with glucocorticosteroids before establishment of an etiology. Prolonged ACTH stimulation is also used to distinguish primary from secondary or tertiary causes of adrenal insufficiency.

*Procedure*—ACTH gel (80 U/d) is injected for 3 days. This is followed by a standard 8-hour infusion of ACTH (250 µg cosyntropin over 8 hours). Urinary free cortisol and serum cortisol are measured daily.

*Interpretation*—Serum cortisol values that are >20 µg/dL exclude primary adrenal insufficiency. Glucocorticoid withdrawal would be required before assessing secondary or tertiary adrenal insufficiency in such cases. Little or no increase in cortisol secretion is seen in primary adrenal failure even over successive days. A progressive staircase rise is seen over 2 to 3 days in adrenal insufficiency caused by pituitary or hypothalamic disease or steroid level suppression. Little or no response is also seen in congenital adrenal hyperplasia due to 21- and 17-hydroxylase deficiencies.

**TRH Test: Thyrotropin-Releasing Hormone Stimulation of Thyrotropin Release**

*Rationale*—The pituitary cells that produce thyroid-stimulating hormone (TSH) are exquisitely sensitive to changes in thyroid hormone concentrations. When thyroid hormone levels rise above normal, TSH release from the pituitary gland is reduced or blocked; when thyroid hormone levels fall below normal, TSH release in response to TRH is exaggerated.

*Procedure*—No patient preparation is necessary. A baseline specimen is drawn for TSH determination. Five hundred µg of TRH is given intravenously, and repeat specimens are drawn for TSH determination at 30 and 60 minutes after injection.

*Interpretation*—A typical response is a 5- to 10-fold increase of TSH level above baseline, with the peak value occurring at 30 minutes. Flat or blunted responses are seen in hyperthyroidism (usually with a high T4 or T3 concentration) and in hypothyroidism secondary to hypopituitarism (usually with a low T4 concentration). An exaggerated response (peak TSH level >35 mU/mL) is seen in early primary hypothyroidism. Patients with hypothyroidism secondary to hypothalamic disorders may show a response of normal magnitude but also a delayed peak.

**Overnight Low-Dose Dexamethasone Suppression Test**

*Rationale*—Dexamethasone, a cortisol analogue, suppresses ACTH and cortisol production in normal subjects but not in patients with Cushing’s syndrome. Used as a screening test for Cushing’s syndrome and endogenous depression.
Procedure—Administer Dexamethasone (Decadron) in a single 1 mg dose orally at 11 p.m. (exact dose should be determined by physician). Specimens for plasma cortisol should be drawn the next day at 8 a.m., 4 p.m., and 11 p.m. Some physicians may direct less specimens be drawn.

Interpretation—Normal individuals will show suppression of cortisol (<4 µg/dL) for at least 24 hours after the dexamethasone dose. Patients suffering from Cushing’s syndrome or adrenocortical tumors will show no suppression in the cortisol levels. Patients suffering from endogenous depression will show normal cortisol suppression in the early morning (8 a.m.) specimen, but escape from suppression later in the day (4 p.m. or 11 p.m.). The recommended screening test for Cushing’s syndrome prior to a suppression test is a 24-hour urinary free cortisol level, which is a good discriminator of Cushing’s patients versus the normal population.

Overnight High-Dose Dexamethasone Suppression Test

Rationale—Patients with Cushing’s syndrome due to an ACTH-producing pituitary adenoma usually show suppression of cortisol with high-dose dexamethasone. Patients with Cushing’s syndrome due to other causes (adrenal cortical adenoma, adrenal cortical carcinoma, ectopic production of ACTH) usually do not demonstrate any change in cortisol level.

Procedure—Dexamethasone (4 mg) is given orally at 11 p.m. or 12 a.m. Blood is drawn for determination of plasma cortisol at 7 a.m. or 8 a.m. the next morning, or 8 to 9 hours after dexamethasone is given.

Interpretation—Most patients with Cushing’s syndrome show a suppression of baseline cortisol level of at least 50%. If suppression is <50%, the test should be repeated with 8 mg to 24 mg of dexamethasone.

Overnight Metyrapone (Metopirone) Test

Rationale—Metyrapone inhibits 11β-hydroxylase, the enzyme that catalyzes the step immediately preceding cortisol synthesis. As the blood level of cortisol falls, the negative feedback effect is diminished, causing release of ACTH from the pituitary gland. The stimulatory effect of ACTH on the adrenal cortex leads to a rise in 11-deoxycortisol, the compound immediately preceding cortisol in the biosynthetic pathway.

Procedure—Baseline specimens for cortisol, 11-deoxycortisol, and ACTH may be drawn at 8 a.m. the day before testing.

Metyrapone (30 mg/kg body weight) is given orally at midnight with milk or a snack (to delay absorption). At 8 a.m. the following morning, blood is drawn for determination of 11-deoxycortisol, cortisol, and ACTH levels.

Interpretation—In normal subjects, 11-deoxycortisol increases from <1 µg/dL after metyrapone stimulation, and ACTH values exceed 150 pg/mL. No response or impaired response may be seen in pituitary or hypothalamic disease combined with inadequate enzyme blockade (plasma cortisol >3 µg/dL) or with Cushing’s syndrome caused by adrenal tumors or nonendocrine ACTH-secreting tumors. Exaggerated responses may be seen in pituitary Cushing’s syndrome.

Gonadotropin-Releasing Hormone (GnRH) Stimulation Test in Children

Rationale—The hypothalamic releasing hormone GnRH stimulates release of both luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in normal individuals. Subnormal responses are seen in some patients with pituitary or hypothalamic disorders. However, the magnitude of LH and FSH response to GnRH is usually predictable from the basal LH and FSH levels. This test may be useful in patients in whom the clinical picture and basal gonadotropin measurements are inconclusive.

Procedure—The test may be performed without regard for previous feeding or time of day. After baseline specimens are obtained for LH or FSH determination, or both, a dose of 2.5 µg/kg (maximum 100 µg) of GnRH is given intravenously. Specimens for LH or FSH determination, or both, should be drawn every 15 to 30 minutes for 1 to 2 hours.

Interpretation—LH response should increase by 3- to 10-fold. The FSH response is of lesser magnitude (usually a 1.5- to 3-fold increase). The peak responses for both LH and FSH occur between 15 and 30 minutes. Patients with pituitary disorders may have normal, diminished, or absent responses. In patients with hypothalamic disorders, the response may be exaggerated, normal, diminished, or absent.

Reference