Appendix

Definitions

ACTH: see adrenocorticotrophic hormone.

Addison's Disease: any of a group of life-threatening disorders caused by severe hypofunction of the adrenal cortex.

Adenylyl cyclase: the enzyme that converts ATP to cAMP. Adenylyl cyclase activity is regulated by G proteins (which are in turn regulated by cell surface receptors). Adenylyl cyclase production of cAMP is a key event in the cAMP second messenger pathway.

Adrenarche: the developmental change that occurs in the adrenal during the early part of puberty, consisting primarily of the organization of the zona reticularis and an increase in the production of adrenal androgens.

Adrenocorticotrophic hormone (ACTH): a 39 amino acid peptide hormone produced as a larger precursor called proopiomelanocortin (POMC). ACTH is released from the anterior pituitary in response to CRH. Acutely, ACTH stimulates adrenal steroid hormone biosynthesis; chronically, it stimulates adrenal hypertrophy and hyperplasia.

Agonist: a molecule that elicits a biological effect upon binding to a receptor (*cf*. antagonist).

Ambiguous genitalia: a condition in which excessive (in females) or insufficient (in males) androgen action (or rarely, action of other hormones) results in aberrant development of the genitals such that visual gender identification at the time of birth is difficult or impossible. The most common cause of ambiguous genitalia in females is congenital adrenal hyperplasia; in males ambiguous genitalia can be due to an enzyme deficiency in androgen biosynthesis or to partial androgen resistance.

Androgen: any androgen receptor agonist. The major physiological androgens are testosterone and dihydrotestosterone (DHT). Androstenedione and dehydro-epiandrosterone (DHEA) are referred to as adrenal androgens because they are synthesized in the adrenal and have some androgenic activity; however, this activity is almost certainly a result of conversion to testosterone in peripheral tissues, because DHEA and androstenedione have little direct stimulatory effect on the androgen receptor.

Angiotensin converting enzyme: a dipeptidyl carboxypeptidase responsible for catalyzing the removal of the last two amino acids from angiotensin I to form angiotensin II.

Angiotensin II: an eight amino acid peptide hormone which stimulates the zona glomerulosa to produce aldosterone, and which possesses potent vasoconstrictor

activity. Angiotensin II is produced from angiotensin I by angiotensin converting enzyme.

Angiotensinogen: an inactive ~55 kDa glycoprotein produced in the liver and other tissues, cleaved by the specific protease renin to yield angiotensin I. The circulating levels of angiotensinogen are primarily dependent on liver-derived protein; the angiotensinogen produced in peripheral tissues is probably involved in paracrine effects in those tissues. Although constitutively produced, the amount of angiotensinogen released by the liver may change as a result of hormonal stimulation.

Antagonist: a molecule that binds a receptor with little or no direct biological effect; note, however, that antagonists *do* have biological effects in that they compete with agonists for receptor binding, and thereby reduce or eliminate the biological response that results from agonist binding to the receptor (*cf.* agonist). Alternatively, an antagonist is a molecule that has the opposite biological effect to that of a given hormone due to an agonist effect on a separate biological pathway (*e.g.*, epinephrine antagonizes the effect of insulin on hepatic gluconeogenesis).

Atrial natriuretic peptide (ANP): a member of a family of peptide hormones released from the heart and several other organs which reduce blood pressure due to actions in the kidney, adrenal, and vascular system.

Apoptosis: programmed cell death. Apoptosis is required for proper development, and for a variety of normal functions in adults, especially deletion of auto-reacting immune cells and of cells exhibiting abnormal functioning. Carcinogenesis usually requires inactivation of the apoptotic pathways.

Autocrine: a system in which a signaling molecule is produced and responded to by the same cell. An autocrine factor may also have paracrine and endocrine functions.

Binding protein: a molecule that binds a ligand but is incapable of eliciting a direct biological effect as a result (*cf.* receptor). The apparent functions of binding proteins are to act as buffers to ameliorate rapid changes in hormone concentrations, to lengthen the plasma half-life of the hormone, and to act as transport proteins for relatively insoluble molecules. Binding proteins vary in specificity and in affinity for their ligands; in general they have lower (albeit still respectable) affinity for their ligands than do the receptors for those ligands. Examples of binding proteins include *serum albumin*, which binds essentially any hydrophobic molecule with moderate to low affinity compensated for by the fact that serum albumin is present in large quantities, and *corticosteroid binding globulin (CBG)* which binds cortisol, but relatively little of the structurally related aldosterone.

CAH: see congenital adrenal hyperplasia.

Calcitriol (1α,25-dihydroxy-Vitamin D): the hormonally active metabolite of Vitamin D.

cAMP (cyclic adenosine monophosphate): the first second messenger to be discovered. cAMP is produced by the action of adenylyl cyclase on ATP.

cAMP-dependent protein kinase (Protein Kinase A): a serine and threonine specific protein kinase activated by, and part of the signal transduction pathway for, cAMP.

Catechol-O-methyl transferase (COMT): a liver enzyme that catalyzes a major catecholamine inactivation reaction, the methylation of the catecholamine 3-hydroxyl group.

CBG: see corticosteroid binding globulin.

CNS: central nervous system.

cGMP (cyclic guanosine monophosphate): a second messenger molecule. cGMP is produced by the action of guanylyl cyclase on GTP.

Cholecalciferol: vitamin D_3, the form of vitamin D synthesized in the skin.

COMT: see catechol-O-methyl transferase.

Conformational change: a change in structure that results in a change in function (*e.g.*, steroid receptors are thought to undergo a conformational change upon ligand binding; this change is structure is thought to allow interaction with other transcription factors and result in modulation of gene transcription).

Congenital adrenal hyperplasia (CAH): a life-threatening disorder in which part of the cortisol synthetic machinery is defective. The most common cause is decreased or absent 21-hydroxylase activity; CAH may also be the result of deficiencies in other proteins in the pathway (the enzymes 3β-hydroxysteroid dehydrogenase/Δ5-Δ4-isomerase, 11β-hydroxylase, or much more rarely, in 17α-hydroxylase/17-20-lyase, in cholesterol side-chain cleavage enzyme, or in cholesterol transport into the mitochondria). The effects of defective aldosterone production are most acutely lethal, but defective aldosterone synthesis alone does not result in CAH. In the common forms of CAH, female infants usually exhibit ambiguous genitalia due to overproduction of adrenal androgens.

Constitutive: synthesized and/or released in significant quantities in the absence of stimulation (*e.g.*, the release of angiotensinogen from the liver is constitutive, occurring at normal levels without requiring activation of any control mechanism, although release can be increased by several hormones).

Corticosteroid binding globulin (CBG): a serum protein that binds glucocorticoids with fairly high affinity. In some literature, CBG is referred to as transcortin.

Corticotropin releasing hormone (CRH): a hypothalamic 41 amino acid peptide hormone that stimulates the anterior pituitary to produce ACTH.

CRE (cAMP-response element): an enhancer element regulated by the transcription factor CREB in response to increased cAMP levels.

CREB (cAMP-response element binding protein): a transcription factor, which, when phosphorylated by Protein Kinase A, binds to a CRE and regulates gene expression.

Cytochrome P450: a heme-containing enzyme capable of inserting oxygen atoms into carbon-hydrogen bonds of unsubstituted carbons. The cytochromes P450 comprise a large evolutionarily-related superfamily. In humans, these enzymes are involved in a number of synthetic reactions (especially in steroid hormone biosynthesis) and are responsible for metabolism of hormones and xenobiotic compounds.

CRH: see corticotropin releasing hormone.

Cushing's Syndrome: any of a group of disorders of differing underlying cause, characterized by excessive glucocorticoid action.

DCCT (Diabetes Control and Complications Trial): a large scale clinical trial which found that tight control of plasma glucose reduced long-term diabetic complications in Type I diabetic patients.

Desensitization: decreased responsiveness of a cell to stimulation. Desensitization most commonly refers to lowered response to a given amount of ligand observed after prolonged exposure to the ligand. Desensitization is usually the result of altered post-receptor effects. Both desensitization and down-regulation are mechanisms by which cells avoid over-stimulation.

Dexamethasone (9α-fluoro-16α-methyl-1,4-pregnadiene-11β,17α,21-triol-3,20-dione): a long acting synthetic glucocorticoid. Dexamethasone has a relatively low affinity for CBG, and is specific for glucocorticoid type II receptors. Due to its high degree of specificity, dexamethasone is the primary glucocorticoid used in experiments examining glucocorticoid action; in some literature discussions, the term dexamethasone is synonymous with glucocorticoid.

DHEA (dehydroepiandrosterone; abbreviated as DHA in some literature): an adrenal androgen. DHEA is produced by the zona reticularis of the adult adrenal cortex in significant amounts; it can serve as a precursor for peripheral androgen and estrogen synthesis and may have direct hormonal actions. During fetal life, fetal adrenal DHEA and DHEAS are the main substrates for placental estrogen synthesis.

DHEAS (dehydroepiandrosterone sulfate: abbreviated as DHAS in some literature): the major circulating adrenal androgen. DHEAS is produced by the zona reticularis of the adult adrenal cortex in significant amounts; it can serve as a precursor for peripheral androgen and estrogen synthesis and may have direct hormonal actions. During fetal life, fetal adrenal DHEA and DHEAS are the main substrates for placental estrogen synthesis.

Diabetic ketoacidosis (DKA): a life-threatening phenomenon of untreated or undertreated Type I diabetes mellitus characterized by markedly elevated plasma glucose and ketone body levels, lowered plasma pH, dehydration, and, in severe cases, coma.

Diacylglycerol (DAG): a compound consisting of a glycerol backbone with two of the three hydroxyls forming ester links to fatty acids. One example is the cleavage product of phosphatidyl inositol-bis-phosphate; this form of DAG is the second messenger which (in conjunction with elevated calcium levels induced by inositol trisphosphate) activates Protein Kinase C.

DKA: see diabetic ketoacidosis.

DOC (deoxycorticosterone): a weak mineralocorticoid and intermediate in aldosterone biosynthesis.

DOPA (dihydroxyphenylalanine): an intermediate in synthesis of dopamine, norepinephrine, and epinephrine; the product of the rate limiting tyrosine hydroxylase reaction.

Down-regulation: decreased number of receptors. Down-regulation usually occurs following prolonged exposure to a stimulating ligand. Both desensitization and down-regulation are mechanisms by which cells avoid over-stimulation.

Endocrine: a system in which a signaling molecule is produced in one organ (usually an endocrine gland), is transported by the blood stream, and is responded to by a distant target. An endocrine factor may also have paracrine and autocrine functions. The endocrine system is usually taught separately from the nervous and immune systems. However, the functions of all three systems overlap and interactions among them are critically important in both normal and pathological states.

Ergocalciferol: Vitamin D_2, the form of Vitamin D produced by irradiation of the plant compound ergosterol.

Estrogen: any compound that acts as an estrogen receptor agonist. The major physiological estrogen is estradiol; in humans, estrone and estriol are also produced (estriol levels are especially high during pregnancy), but have about 10-fold lower affinity for the estrogen receptor.

Euthyroid: exhibiting the symptoms of normal levels of thyroid hormone. Note that this status may be unrelated to the measured serum levels of thyroid hormone, although it is usually (but not always) associated with normal levels of TSH.

Evolutionarily-related: exhibiting a degree of similarity in protein and/or DNA sequence considered to be too great to be a result of chance. In some cases the sequence conservation extends over the entire protein (*e.g.*, the cytochrome P450 enzyme superfamily, in which members exhibit similarity ranging from about 15% to >95% throughout the protein sequence); in other cases the similarity is observed only in relatively short segments (*e.g.*, the steroid hormone receptor

superfamily, in which the DNA-binding domain is highly conserved (40% to 95% identical), while other domains of the protein appear less conserved, or completely divergent.

Glucocorticoid: any compound that acts as a glucocorticoid receptor Type II agonist. Note that there is a functional component to this definition, and therefore aldosterone, which has high affinity for the Type II receptor, is not normally considered to be a glucocorticoid, because it is not present in quantities sufficient to have a physiologically relevant glucocorticoid effect. The major physiological glucocorticoid in humans is cortisol (in rats, corticosterone is the main glucocorticoid); several synthetic glucocorticoids are used pharmacologically (*e.g.*, dexamethasone and prednisone).

Graves' Disease: a hyperthyroid condition due to TSH receptor-stimulating antibodies. Graves' disease is often associated with other autoimmune attacks, most notably on the tissues behind the eye (which results in exophthalmos).

Guanylyl cyclase: an enzyme that converts GTP to cGMP. All forms of guanylyl cyclase that have been described are receptor proteins; some are transmembrane receptors for peptide hormones (*e.g.,* the receptor for ANP), while others are soluble cytoplasmic proteins (*e.g.*, the receptor for nitric oxide). Guanylyl cyclase production of cGMP is a key event in the cGMP second messenger pathway.

G protein: a member of a family of multimeric proteins involved in signal transduction; G proteins are activated by binding GTP, and become inactive following the hydrolysis of the bound GTP to GDP.

G protein-linked receptor: a member of a large superfamily of transmembrane receptor proteins, including the receptors for epinephrine, ACTH, CRH, TSH, PTH, and calcitonin, and the parathyroid calcium sensor.

GRTH (generalized resistance to thyroid hormone): a genetic hypothyroid disorder caused by either absence (in recessive disorder) or point mutation (in dominant form) of thyroid hormone receptor-β gene product.

Half-life ($t_{1/2}$): the time required for 50% of a given material to disappear. Clearance of a hormone or other biochemical molecule is similar to radioactive decay in that the amount of material usually disappears exponentially rather than linearly (fitting the equation $N = N_0 e^{-\lambda t}$, where $t_{1/2} = \frac{\ln(2)}{\lambda}$). Therefore, after 1 half-life, 50% of a starting amount is cleared; after 2 half-lives, 75%; after 3, 87.5% . . . . The half-life of a given biochemical molecule is dependent on the rate of excretion and on the rate of metabolism to inactive compounds, and may vary significantly depending on the presence or absence of other hormones and carrier proteins.

Hashimoto's Syndrome: an autoimmune attack on the thyroid resulting in destruction of the thyroid and consequent hypothyroidism.

hCG (human chorionic gonadotropin): a placental glycoprotein hormone related to LH, FSH, and TSH. While hCG is primarily considered to have LH-like activity, at high concentrations it also exhibits some TSH-like activity.

Heat shock protein (hsp): originally a protein produced by a cell in response to "heat shock" (*i.e.* temperature above the preferred temperature of the cell; usually 42-44°C for cells that prefer 37°C). It has since been shown that heat shock proteins are present in cells under normal conditions; most, but not all, are expressed in larger amounts following a stress stimulus, of which heat is only one example. Heat shock proteins play roles in folding newly produced and denatured proteins, and in transporting proteins across membranes within the cell. The heat shock proteins are divided into several families based on similarities of sequence and function: hsp60, hsp70, and hsp90 are the most well characterized families, although others also exist. The number refers to the approximate size (in kilodaltons) of the original member of the class; this can sometimes be misleading: *e.g.*, the *E. coli* hsp90 analog is about 72 kDa.

Homeostasis: maintenance of a physiological component within a narrow range. Homeostasis should not be confused with equilibrium; physiological levels of the component under homeostatic control must be maintained by active processes in order to support life, and in general, these levels are far from equilibrium values.

HONK (Hyperglycemic hyperOsmotic Non-Ketotic coma): a life-threatening phenomenon of untreated or undertreated Type II diabetes mellitus characterized by markedly elevated plasma glucose, dehydration, and coma.

Hormone: a molecule whose role is to carry a signal from one cell to another. In classical endocrinology, a hormone is a molecule that travels through the bloodstream to its target in another organ. While this definition is still correct, it has been broadened somewhat due to the discovery that some compounds act in autocrine and paracrine fashion. For example, estradiol has actions in the ovarian cells that synthesize it, as well as in target tissues throughout the body.

Hormone resistance: a condition in which markedly elevated levels of a hormone are required to elicit an effect. Resistance may be due to receptors with decreased or abolished affinity for the hormone, to reduced levels or absence of the receptor, or to inhibition of post-receptor responses. Examples include glucocorticoid resistance, in which the GR Type II has decreased affinity for glucocorticoids, recessive GRTH, in which the TRβ is either absent or completely inactive, and glucocorticoid-induced insulin resistance and most forms of Type II diabetes mellitus, in which the cellular response to the insulin receptor is reduced, although the receptor is apparently normal.

Hormone response element (HRE): a DNA sequence that is recognized by a hormone receptor or other hormonally responsive transcription factor and acts as an enhancer element. Note that the HRE sequence usually is specific for the relevant binding protein (*e.g.*, an ERE [= estrogen response element] has a different sequence from that of a GRE [= glucocorticoid response element])

Hormone-sensitive lipase: an enzyme that hydrolyzes triacylglycerol from lipid stores to release free fatty acids and glycerol to the circulation. Hormone-sensitive lipase activity is stimulated by epinephrine and inhibited by insulin; hormone-sensitive lipase gene expression is stimulated by glucocorticoids.

HRE: see hormone response element.

HSD (hydroxysteroid dehydrogenase): an enzyme that oxidizes steroid hydroxyl groups to ketones, or reduces steroid ketone groups to hydroxyls. Members of this class include 11β-HSD, which inactivates cortisol in mineralocorticoid target tissues, and 3β-HSD/Δ5-Δ4-isomerase, part of the steroid hormone biosynthesis pathway.

hsp: see heat shock protein.

Hyperkalemia: elevated plasma potassium levels (beyond normal physiologic range).

Hypernatremia: elevated plasma sodium levels (beyond normal physiologic range).

Hyperplasia: an increase in size of an organ (or subset of cells within an organ) due to controlled cell division, often as the result of chronic hormonal stimulation.

Hyperthyroid: exhibiting the symptoms of excessively high levels of thyroid hormone. Note that this status may be unrelated to the measured serum levels of thyroid hormone.

Hypertrophy: an increase in size of an organ (or subset of cells within an organ) due to increase in size of the individual cells, often as the result of prolonged hormonal stimulation.

Hypokalemia: low plasma potassium levels (below normal physiologic range).

Hyponatremia: low plasma sodium levels (below normal physiologic range).

Hypothyroid: exhibiting the symptoms of excessively low levels of thyroid hormone. Note that this status may be unrelated to the measured serum levels of thyroid hormone.

IDDM (insulin-dependent diabetes mellitus): Type I diabetes mellitus; a disorder caused by destructive autoimmune attack on the β-cells of the pancreas, characterized by metabolic abnormalities, especially, but not limited to, severe hyperglycemia.

Inositol trisphosphate (IP_3): a second messenger, produced by hydrolysis of phosphatidyl inositol-bis-phosphate by phospholipase C, that stimulates a release of calcium from intracellular stores.

IRS (insulin receptor substrate): a second messenger protein activated by phosphorylation on tyrosine (usually by the insulin receptor kinase) and

inhibited by phosphorylation on serine. At least four IRS proteins are known to exist.

Knockout mutation: a technique of molecular biology in which a given gene can be selectively inactivated (usually, for technical reasons, in mice or the fruit fly *Drosophila melanogaster*) in order to examine the effects of lack of the gene on development and normal functioning.

Ligand: a molecule that binds to another molecule. In physiology, the term ligand is used primarily for hormones and hormone antagonists, and refers to their ability to interact with receptors and/or binding proteins.

Lipoprotein lipase: an enzyme responsible for removal of fatty acids from lipoproteins for transport into cells. Lipoprotein lipase is stimulated by insulin, and inhibited by epinephrine.

mCi (milliCurie): a unit of radioactivity. A Curie is defined to be 2.22×10^{12} disintegrations per minute; thus, one mCi = 2.22×10^{9} dpm.

Mineralocorticoid: any compound that acts as a mineralocorticoid (glucocorticoid receptor Type I) agonist. Note that there is a functional component to this definition, and therefore cortisol, which has high affinity for the Type I receptor *in vitro*, is not considered to be a mineralocorticoid, because in mineralocorticoid target tissues cortisol is inactivated prior to binding to the mineralocorticoid receptor. Aldosterone is the main physiological mineralocorticoid.

Mitogen: a compound that stimulates cell division.

Morphogen: a compound that stimulates cellular differentiation.

Neoplasia: cancer; an increase in size of an organ due to uncontrolled cell division of a subset of cells within that organ.

NIDDM (non-insulin dependent diabetes mellitus): Type II diabetes mellitus; a heterogeneous group of metabolic disorders of largely genetic origin, characterized by markedly reduced sensitivity to insulin. The name NIDDM is not really appropriate, because many patients require insulin treatment to restore metabolic control.

Osteoblast: a specialized cell responsible for bone deposition and remodeling. Osteoblasts respond to PTH by decreasing anabolic activity, and by inducing osteoclast differentiation and function.

Osteoclast: a specialized polynuclear cell derived from hematopoietic precursors that enzymatically degrades and resorbs bone. Osteoclasts are target cells for calcitonin which specifically inhibits their recruitment, number, and function.

P450scc: cholesterol side chain cleavage enzyme; also called cytochrome P450scc (also, in older literature, desmolase). P450scc catalyzes the conversion of

cholesterol to pregnenolone, the rate limiting step for all steroid hormone biosynthesis.

Paracrine: a system in which a signaling molecule is produced in one cell and is responded to by nearby cells. A paracrine factor may also have autocrine and endocrine functions.

Parathyroid hormone (PTH): an 84 amino acid peptide produced by the parathyroid responsible for raising serum calcium concentration.

Peripheral tissues: in endocrinology, essentially any tissue not a part of an endocrine organ, especially if serving an endocrine function. For example, in post-menopausal women, all endogenous estrogen production occurs in peripheral tissues using adrenal androgens (ovarian estrogen synthesis has ceased, and the adrenals lack the enzymes required to synthesize estrogens). The estrogen produced exhibits hormonal effects, but is not produced in an endocrine tissue.

Peroxisome proliferator-activated receptor (PPAR): an orphan steroid receptor superfamily member protein. At least three genes code for PPAR proteins. While the physiological ligand(s) for the PPAR gene products have not been identified, these proteins are implicated in the responses to DHEA, DHEAS, and some xenobiotic compounds, including troglitazone (the Type II diabetes drug).

Phenylethanolamine-N-methyl transferase (PNMT): the enzyme that catalyzes the conversion of norepinephrine to epinephrine. The enzyme is only present in the adrenal medulla, because only the medulla is exposed to sufficiently high levels of cortisol to induce PNMT expression. Note: although this enzyme is required for epinephrine synthesis, it is *not* the rate limiting step in the production of any of the catecholamines.

Phosphatase: an enzyme that catalyzes the removal of a phosphate from a compound.

Phosphatidyl inositol (PI): a membrane phospholipid which can serve as a precursor for phosphatidyl inositol-bis-phosphate or diacylglycerol.

Phosphatidyl inositol-bis-phosphate (PIP_2): a membrane phospholipid derived from phosphatidyl inositol that is a substrate for phospholipase C hydrolysis to diacylglycerol and inositol trisphosphate.

Plasma: the supernatant material from blood that has been removed from the body in the presence of anticoagulants and centrifuged. Often used in discussion as meaning the non-cellular fraction of blood, in which case it is essentially interchangeable with the term serum.

PNMT: see phenylethanolamine-N-methyl transferase.

POMC (proopiomelanocortin): a protein that acts as a precursor for several biologically active peptides, including ACTH, melanocyte-stimulating hormone, and β-endorphin.

PPAR: see peroxisome proliferator-activated receptor.

Progestin: any compound that acts as a progesterone receptor agonist. Progesterone is the only physiological progestin; synthetic progestins are major components of hormonal contraceptives.

Protein kinase: an enzyme that phosphorylates other proteins.

Protein kinase A: see cAMP-dependent protein kinase.

Protein kinase C: a serine and threonine specific protein kinase activated by, and part of the signal transduction pathway for, calcium and diacylglycerol.

Pseudogene: a sequence of DNA that appears similar to a normal gene, but is either not expressed, or produces an inactive protein. Pseudogenes are thought to arise from duplications of functional genes followed by one or more mutations. Pseudogenes may be examples of evolution in action: steps on a pathway to a potential new function (superfamilies are thought to be the result of this pathway). Pseudogenes are also the source of some genetic disorders, because the presence of two highly related sequences in close proximity results in occasional mistakes during crossing-over; for example, the prevalence of 21-hydroxylase deficiency is probably a consequence of this phenomenon.

PTH: see parathyroid hormone.

PTHrP (parathyroid hormone-related peptide): any of three proteins produced from a single gene that have PTH-like activity. PTHrP is secreted by a number of tumors, resulting in hypercalcemia of malignancy; its normal physiological role is incompletely understood, but it is probably a paracrine factor involved in local regulation of calcium levels, and probably plays a role in maintaining fetal serum calcium levels.

PTU (propylthiouracil): an antithyroid drug that inhibits both thyroid hormone synthesis and peripheral conversion of T4 to T3.

Receptor: a protein associated with a cell that allows a response to an agonist. Receptors have four characteristic properties: 1) **high affinity** for the ligand, 2) **low capacity** for the ligand (usually 1 ligand/receptor), 3) **high specificity** for the ligand (*i.e.* the receptor will bind one ligand, but has much lower affinity for closely related molecules), and 4) a direct **biological response** as a result of ligand binding. The last property, the biological effect, is complex, and depends on the receptor type; it is also the reason for the distinction between receptors and binding proteins. Receptors fall into two major categories: cell surface and intracellular. There are many types of cell surface receptors in several families of evolutionarily unrelated proteins; these have the common feature that their actions are mediated by one of the second messenger pathways. In contrast, most

of the currently described intracellular receptors are members of a single superfamily of evolutionarily-related proteins, which appear to act directly as modulators of gene transcription. (*Examples*: the receptors for epinephrine, ACTH, acetylcholine, and TSH are cell surface receptors; the receptors for estradiol, cortisol, retinoic acid, and triiodothyronine are intracellular receptors.)

Renin: a specific protease produced by the juxtaglomerular apparatus of the kidney that cleaves angiotensinogen to form angiotensin I. Renin catalyzes the rate limiting step in angiotensin II synthesis.

RIA (radioimmunoassay): a technique for using antiserum obtained from experimental animals to measure small quantities of biological molecules.

rT3 (reverse-T3; 3,3´,5´-triiodothyronine): an inactive metabolite of T4, produced by the action of 5-deiodinase, which removes iodine from the inner ring of T4.

Secosteroid: a modified steroid backbone with an open B ring (*e.g.*, vitamin D).

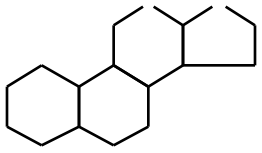
Second messenger: a small molecule (*e.g.*, cAMP or inositol trisphosphate), protein (*e.g.*, IRS), or ion (*e.g.*, calcium) involved in signal transduction; the levels or activity of a second messenger change in direct response to hormone binding to its receptor, and result in alterations in the status of the cell.

Serum: the supernatant material from blood that has been removed from the body, allowed to coagulate, and then centrifuged. Often used in discussion as meaning the non-cellular fraction of blood, in which case it is essentially interchangeable with the term plasma.

Serum albumin: a ~67 kDa protein that is a major component of serum and binds any hydrophobic molecule with moderate to low affinity. It therefore functions as an auxiliary carrier protein for most steroid hormones and for thyroid hormone. (May be called BSA [= bovine serum albumin], or HSA [= human serum albumin], or simply albumin).

Sex hormone binding globulin (SHBG): a serum protein that binds the steroid hormones testosterone and estradiol with fairly high affinity. Also called TEBG (testosterone estradiol binding globulin).

Steroid: any compound containing the cyclopentanoperhydrophenanthrene fused ring system. The term steroid applies both to hormonally active compounds, such as cortisol and estradiol, and to their hormonally inactive precursors and metabolites, such as pregnenolone and cortisone.



cyclopentanoperhydrophenanthrene

$t_{1/2}$: see half-life.

T3 (3,5,3´-triiodothyronine): the active form of thyroid hormone. Most T3 is produced by the action of 5´-deiodinase, which removes iodine from the outer ring of T4; some T3 is released by the thyroid.

T4 (3,5,3′,5′-tetraiodothyronine, thyroxine): the major form of thyroid hormone secreted by the thyroid and in circulation. T4 is converted to T3 in peripheral tissues.

TBG: see thyroxine binding globulin.

TG: see thyroglobulin.

Thyroglobulin (TG): a very large (~660 kDa) homodimeric glycoprotein that functions as the site of thyroid hormone synthesis.

Thyroid peroxidase (TPO): the key enzyme in thyroid hormone biosynthesis. In the presence of hydrogen peroxide, TPO catalyzes the two step reaction involved in the incorporation of iodide into tyrosine residues in TG, as well as the coupling reaction that produces the TG-bound T3 and T4.

Thyroid stimulating hormone (TSH): a heterodimeric glycoprotein hormone related to LH, FSH, and hCG (TSH has an α-subunit identical to those of the other hormones in the family, but a different β-subunit). TSH is released from the pituitary, and stimulates the thyroid to produce thyroid hormone; chronically high levels of TSH result in hypertrophy and hyperplasia of the thyroid.

Thyrotropin: another name for TSH.

Thyrotropin releasing hormone (TRH): a hypothalamic post-translationally modified tripeptide hormone that stimulates TSH release from the pituitary.

Thyroxine binding globulin (TBG): the serum glycoprotein, synthesized in the liver, that acts as the major carrier for the thyroid hormones, with a higher affinity for T4 than for T3. Although constitutively produced, the amount of TBG released may change as a result of hormonal stimulation.

Thyroxine: another name for 3,5,3′,5′-tetraiodothyronine (see T4).

TPO: see thyroid peroxidase.

Transcription factor: any molecule that assists in the synthesis of RNA. The term transcription factor usually refers to any of a number of proteins that form a complex with DNA and/or with other proteins, and act to stabilize the binding of the RNA polymerase during initiation of transcription. The term therefore includes proteins that bind to enhancer elements (*e.g.*, proteins from the steroid hormone receptor family), and proteins that bind to promoter elements (*e.g.*, TF II D, the TATA box binding protein complex).

Transthyretin: one of two serum carrier proteins for the thyroid hormones; also present in cerebral spinal fluid. Older literature refers to transthyretin as thyroxine binding pre-albumin (TBPA).

TRH: see thyrotropin releasing hormone.

TSH: see thyroid stimulating hormone.

Tyrosine hydroxylase: the rate limiting step in catecholamine synthesis. Tyrosine hydroxylase catalyzes the conversion of the amino acid tyrosine (which can be used for protein synthesis and as a substrate for the production of other hormones) to DOPA, which can only be converted to other catecholamines.

Vitamin D: one of two secosteroid compounds (one is derived from cholesterol; the other from the plant compound ergosterol) that act as the precursor for the production of 1α,25-dihydroxy-Vitamin D, the major stimulator of intestinal calcium uptake.

Xenobiotic: any compound not produced in the body (especially derived from the diet) that exhibits biological activity.

Zona fasciculata: the central, and largest zone of the adult adrenal cortex, and the primary site of cortisol synthesis. The zona fasciculata also produces DHEA and DHEAS.

Zona glomerulosa: the outermost zone of the adult adrenal cortex and the site of aldosterone production.

Zona reticularis: the innermost zone of the adult adrenal cortex; produces cortisol, DHEA, and DHEAS. It is not known why two zonæ produce the same steroids, although some studies suggest that the zona reticularis is more responsible for adrenal androgen production than the zona fasciculata. The zona reticularis is poorly organized until adrenarche.