HORMONES OF PHYSIOLOGICAL IMPORTANCE

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<td>Vasopressin (ADH)</td>
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<td>Dopamine</td>
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<th>THYROID</th>
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<tr>
<td>Vasopressin (ADH)</td>
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<tr>
<th>ADRENAL MEDULLA</th>
<th>ADRENAL CORTEX</th>
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<tr>
<td>Dopamine</td>
<td>Pregnenolone</td>
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<td>Noradrenalin</td>
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<td>17 β-Estradiol</td>
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<td>Estrone</td>
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<tr>
<th>OVARIeS</th>
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<tr>
<td>17 β-Estradiol</td>
<td>Progesterone</td>
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<tr>
<td>Estrone</td>
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<td>Dihydrotestosterone</td>
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<td>Estriol</td>
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<td>Estrone</td>
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PINEAL (EPIPHYSIS) GLAND
Therapy Localisation: GV1
Muscle Association: Teres Major

Secretes
- Serotonin
- Melatonin
- Epithalamin
- TRH
- Vasopressin (ADH)
- Prolactin (PRL)
- Somatostatin
- Noradrenalin
- Dopamine
- GnRH (LT-RH)

The pineal gland contains tissues that have relatively large interstitial spaces and have fenestrated capillaries, which are highly permeable and permit diffusion of large molecules from the general circulation. Elsewhere in the brain tight capillary endothelial junctions prevent such diffusion known as the blood – brain barrier.
The pineal gland was considered to be the “seat of the soul” by Rene Descartes. It is located at the roof of the posterior portion of the third ventricle and has no direct neural connection with the brain except for sympathetic innervation via the superior cervical ganglion.
The pineal gland releases its secretions into the general circulation and probably into the extracellular fluid of the brain and thus eventually entering the cerebral spinal fluid.

SEROTONIN
Produced from the essential amino acid Tryptophan. The chromophobe cells of the small intestine produce 90% of serotonin, 10% by the raphe nucleus of the brain stem. Acts as a neurotransmitter causing depression in some parts of the brain and stimulation in other parts.
Also acts as a mediator of the inflammatory process.
Precursor to melatonin.
Nutritional factors to stimulate: Tryptophan, P5P, NADPH, Folinic acid, (Biopterin), Iron, Thiamine, Vit C, Zn.
Phytoceuticals: Spices and culinary herbs

MELATONIN
Melatonin secretion is regulated by the sympathetic nervous system and is increased in response to hypoglycaemia and circadian rhythms such as light and dark. It is most abundant and active in total darkness. Production and secretion peaks at around 2AM. The conversion of serotonin to N-Acetyl serotonin is regulated by N-acetyl tranferase and requires Acetyl-CoA and zinc to cofactor. The Hydroxyindole-O-methyltransferase and S-Adenosylmethionine, which requires magnesium, then convert n-Acetyl Serotonin to Melatonin. Activation of the N-acetyl tranferase is
inhibited by broad spectrum light on the retina and other exposed parts of the skin possessing photoreceptors.

Melatonin production peaks around puberty, which is when children begin to grow out of having nightmares. (Melatonin ensures a good nights sleep with pleasant dreams.) High circulating levels of melatonin in infant children will inhibit gonadal growth. It progressively declines with age probably due to calcification of the pineal gland.

Melatonin is also secreted by the retina, the gastrointestinal tract, and the liver, lungs, skin and in certain lymphocytes.

Melatonin exerts a regulating effect on all the steroid (stress related) hormones when levels are at their highest. Main effect is on high levels of glucocorticoids. During the night it inhibits sexual function.

Melatonin induces a state of relaxation leading to sleep if there is no exposure to light. It does not act as a sleeping medicine – only as a relaxator so inducing sleep.

Melatonin helps to lift depression caused by excess serotonin and stimulates the mono oxidase enzymes to break down the catecholamine hormones.

Melatonin acts on the thymus gland to differentiate undifferentiated white cells into mature T, B, and NK cells. (Also helped by Blue/green algae)

It is a powerful antioxidant against the hydroxyl radical and can pass readily through the lipid cells membranes and enter the nucleus. Here it protects the DNA structures of the chromosomes from hydroxyl radicals. It also aids in excision repair of damaged DNA structures.

**Nutritional factors to stimulate Melatonin** are Tryptophan, P5P, Folinic acid, NADPH, Iron, Thiamine, Vit C, Panthethine and Zinc, Methionine, Mg, ATP.

**Phytoceuticals:** Spices and culinary herbs

**EPITHALAMIN**

Acts in a similar way to melatonin. It was isolated by Vladimir Dilman of St Petersburg. Epithalamin extends life span and slows down ageing in laboratory rats and mice. In animal studies, Epithalamin has been shown to shrink cancerous tumours, and to reduce injury caused by exposure to X-rays. Like melatonin it increases immune function and lowers blood lipids such as cholesterol and triglycerides. Epithalamin can restore fertility in aged rats and is being tested on human females nearing menopausal age.

Epithalamin and melatonin work synergistically

**Nutritional factors to stimulate:**

**Phytoceuticals:** Spices and culinary herbs

**THYROTROPHIN-RELEASING HORMONE (TRH)**

Is a tripeptide and is the major stimulant of the hypophysis to produce Thyroid Stimulating Hormone (TSH). It is secreted directly by the epiphysis into the general circulation and by the hypothalamus to stimulate the hypophysis.

**Nutritional factors to stimulate:**

**Phytoceuticals:** Spices and culinary herbs
SOMATOSTATIN (GROWTH HORMONE RELEASE INHIBITING HORMONE) (GRIH)
Inhibits the secretion of Growth Hormone (GH), TSH, insulin, Glucagon, gastrin, Secretin, and VIP. Also secreted by the pancreatic islets, the gastrointestinal mucosa and the C cells of the thyroid gland.

Nutritional factors to stimulate:
Phytoceuticals: Kelp, Spices and culinary herbs
HYPOTHALAMUS
Therapy Localisation: GV20
Muscle Association: None

Secretes
- Corticotropin – Releasing Hormone
  Acronym: CRH  Pituitary Target: ACTH, LPH, MSH, Endorphins
- Thyrotropin – Releasing Hormone
  Acronym: TRH  Pituitary Target: TSH, PRL
- Gonadotropin – Releasing Hormone
  Acronym: GnRH (LH-RH)  Pituitary Target: LH, FSH
- Growth Hormone – Releasing Hormone
  Acronym: GRH  Pituitary Target: GH
- Growth Hormone Release – Inhibiting Hormone (Somatostatin)
  Acronym: GRIH  Pituitary Target: GH, TSH, FSH, ACTH
- Prolactin Inhibiting Hormones
  Acronym: PIH  Pituitary Target: PRL

CORTICOTROPHIN-RELEASING HORMONE (CRH)
Is a 41 amino acid peptide, which stimulates the production of adrenocorticotropic hormone (ACTH), from the pituitary (hypophysis). It has a half-life of one hour. It is inhibited by Oxytocin. CRH is also secreted from human placenta. The levels of CRH increase significantly during late pregnancy and delivery.
Nutritional factors to stimulate:
Phytoceuticals: Spices and culinary herbs

THYROTROPHIN-RELEASING HORMONE (TRH)
Is a tripeptide and is the major stimulant of the hypophysis to produce Thyroid Stimulating Hormone (TSH). It is secreted directly by the epiphysis into the general circulation and by the hypothalamus to stimulate the hypophysis.
Nutritional factors to stimulate: Methylene tetrahydrofolate
Phytoceuticals: Spices and culinary herbs

GONADOTROPHIN-RELEASING HORMONE (GnRH)
Is a multi peptide that directly stimulates the production of Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) from the Hypophysis. It can inhibit Prolactin secretion.
Nutritional factors to stimulate: Methylene tetrahydrofolate
Phytoceuticals: Spices and culinary herbs

GROWTH HORMONE RELEASING HORMONE (GRH)
Stimulates growth hormone (GH) secretion by somatotrophs. It is similar to many gastrointestinal peptides including secretin, vasoactive intestinal polypeptide (VIP) and gastric inhibiting peptide.
Nutritional factors to stimulate: Methylene tetrahydrofolate
Phytoceuticals: Spices and culinary herbs

GROWTH HORMONE RELEASE INHIBITING HORMONE (GRIH) OR SOMATOSTATIN
Inhibits the secretion of Growth Hormone (GH), TSH, insulin, Glucagon, Gastrin, Secretin, and VIP. Also secreted by the pancreatic islets, the gastrointestinal mucosa and the C cells of the thyroid gland.
Nutritional factors to stimulate:
Phytoceuticals: Spices and culinary herbs
PROLACTIN INHIBITING HORMONES (PIH)
Main PIH is Dopamine, which binds to the dopamine receptors of the lactotrophs (stimulated by Vit B6). Disruption to the hypothalamic-hypophysis connection can inhibit release of dopamine leading to increased Prolactin (PRL) secretion. Other Prolactin Inhibiting Hormones are the neurotransmitters GABA and possibly Acetylcholine.

Nutritional factors to stimulate PIH: Tyrosine, Vit B6, Iron, Vit C, Cu, Folic acid, Vit B3, and GABA.
Phytoceuticals: Spices and culinary herbs

PROLACTIN RELEASING FACTORS
Prolactin release is increased during sleep, stress and nipple stimulation.
TRH
VIP which is increased by nipple stimulation or suckling.
Serotonin
Nutritional factors to stimulate: Essential fatty acids
Phytoceuticals: Fenugreek (Trigonella Foenum-Graecum) and other Spices and culinary herbs
ANTERIOR PITUITARY (HYPOPHYSIS)

Therapy Localisation: Glabella

Muscle Association: None

Weight change:
Underactive – pear shaped distribution
Overactive – general loss of body bulk

Secretes
- Growth hormone (GH)
- Prolactin (PRL)
- Thyroid Stimulating Hormone (TSH)
- Luteinizing Hormone (LH)
- Follicle Stimulating Hormone (FSH)
- Adreno Cortico Trophic Hormone (ACTH)
- β Lipotropin (β LPH)
- Melanocyte Stimulating Hormone (MSH)

GROWTH HORMONE (GH: SOMATOTROPHIN)

Is secreted by the somatotrophs of the anterior hypophysis. It promotes linear growth and is mediated by Insulin Like Growth factor (IGF-1). It increases protein synthesis by enhancing amino acid uptake and by accelerating mRNA transcription and translation. GH decreases protein catabolism by mobilising fat as the main source of fuel from adipose tissue and enhances the conversion of fatty acids to Acetyl Co. In excess it decreases carbohydrate utilisation and impairs glucose uptake into cells resulting in glucose intolerance and secondary hyperinsulinism.

Growth Hormone is modulated by Growth Hormone Releasing Hormone (GRH) and Somatostatin

Neural control (sleep, exercise and stress increase GH production)

Metabolic control. High protein especially Arginine and also low carbohydrate/protein intake stimulate GH production by inhibiting IGF-1 production. Fatty acids suppress GH production.

Nutritional factors to stimulate GH: Vit B12, folinic acid, zinc and arginine.

Phytoceuticals: leafy green vegetables, Spices and culinary herbs

PROLACTIN (PRL)

Secreted by the lactotrophs of the anterior hypophysis and stimulates lactation in the postpartum period and breast development during pregnancy. It is stimulated by breast suckling and in turn inhibits estrogens and progesterone thus reducing risk to further conception. However high estrogens and progesterone in turn inhibit PRL release.

Elevated PRL levels create a shortened luteal phase of the menstrual cycle and may lead to anovulation. In men high levels lead to decreased testosterone production.

Stimulated by TRH, VIP, Acetylcholine, Nipple stimulation, Exercise, Stress and sleep.

Inhibited by Dopamine

Nutritional factors to stimulate PRL: Essential fatty acids.

Phytoceuticals: Fenugreek (Trigonella Foenum-Graecum), Licorice (Glycrrhiza Glabra) other Spices and culinary herbs
THYROID STIMULATING HORMONE (TSH)
Attaches to the high affinity receptors in the thyroid and stimulating iodine uptake, hormonogenesis and release of T4 and T3. It is mediated by cAMP. TSH also causes thyroid hypertrophy and increased vascularity by promoting mRNA and protein synthesis.
It is stimulated by TRH, cold
It is inhibited by Somatostatin, Dopamine and by thyroid hormone feedback.
**Nutritional factors to stimulate:**
**Phytoceuticals:** Kelp, Spices and culinary herbs

LUTEINIZING HORMONE (LH) AND FOLLICLE STIMULATING HORMONE (FSH)
Both bind to receptors in the ovary and testes and regulate gonadal function by promoting sex steroid production and gametogenesis.
In men LH stimulates testosterone production from the interstitial cells of the testes (Leydig cells). FSH stimulates testicular growth and aids in sperm cell maturation. Both LH and FSH are required for full maturation of spermatozoa.
In women, LH stimulates estrogens and progesterone production from the ovary. A surge of LH production in the mid menstrual cycle induces ovulation and continued secretion stimulates the corpus luteum to produce progesterone. FSH controls the development of the ovarian follicle and the secretion of estrogens from this follicle is dependent on both FSH and LH.
They are stimulated by Gonadotrophin Releasing Hormone (GnRH) which maintains basal gonadotrophin secretion, generates phasic release of gonadotrophins for ovulation and determines the onset of puberty. Probably influenced by the epiphysis secretions to maintain the circadian rhythms.
They are also stimulated in the follicular stage by positive feedback of estrogens. Progesterone amplifies the duration of LH and FSH surge. Ovulation occurs 12hours after the LH peak and 36hours after the estrogens peak. The remaining follicular cells in the ovary are converted, under the influence of LH, to the progesterone secreting corpus luteum. After 12-14 days the corpus luteum involutes, resulting in decreased estrogens and progesterone levels and then uterine bleeding.
They are inhibited by Inhibin secreted by the Sertoli cells of the seminiferous tubules.
**Nutritional factors to stimulate:** 
**Phytoceuticals:** Chasteberry (Vitex agnus castus), Sage (Salvia Officinalis), Watercress. Other Spices and culinary herbs

ADRENOCORTICOTROPHIN HORMONE (ACTH)
Is produced by the anterior pituitary and stimulates the secretion of glucocorticoids, mineralocorticoids and androgenic steroids from the adrenal cortex. ACTH binds to receptors on the adrenal cortex and stimulates steroidogenesis through the mediation of cAMP. Excess production produces hyperpigmentation of the skin.
It is stimulated by corticotrophin releasing hormone (CRH) in a pulsatile manner with a peak before awakening and a decline as the day progresses and also elevates after feeding. All forms of stress, pain, trauma, hypoxia, hypoglycaemia, cold, surgery, depression and
A fast and a slow negative feedback system regulate ACTH production.
**Nutritional factors to stimulate:**
**Phytoceuticals:** Spices and culinary herbs
β LIPO TROPIN (β LPH)
And its family of peptide hormones, including β Endorphin has the same secretory mechanics to ACTH. They increase in response to stress, hypoglycaemia, and are suppressible with glucocorticoids. They are elevated in Cushing’s and Addison’s disease. β Endorphin acts as an endogenous opiate.
Nutritional factors to stimulate:
Phytoceuticals: Spices and culinary herbs

MELANOCYTE STIMULATING HORMONE (MSH)
Melanocyte Stimulating Hormone (MSH) is stimulated along with ACTH and is responsible for the skin hyperpigmentation in cases of ACTH excess. It stimulates the production of melanin from mast and other cells and is probably mediated by melatonin.
Nutritional factors to stimulate:
Phytoceuticals: Spices and culinary herbs
POSTERIOR PITUITARY (HYPOPHYSIS)

Weight change:
Underactive – spare tyre fat distribution
Overactive – general loss of body bulk

Secretes
Vasopressin – Anti Diuretic Hormone (ADH)
Oxytocin

VASOPRESSIN – ANTIDIURETIC HORMONE (ADH)
ADH acts through two receptors V1 and V2.
V1 receptors mediate vascular smooth muscle contraction and stimulate prostaglandin synthesis and liver glycogenolysis. Activation of these receptors increases phosphatidylinositol breakdown, thus causing cellular calcium mobilisation. ADH effects on V1 receptors in peripheral arterioles increase blood pressure, which leads to bradycardia and inhibition of sympathetic nerve action.
V2 receptors, which produce the renal actions of vasopressin, activate G proteins and stimulate the generation of cAMP. It increases the water permeability of the luminal membrane of the collecting duct epithelium. Low levels of ADH lead to polyuria.

Nutritional factors to stimulate:
Phytoceuticals: Kelp, Spices and culinary herbs

OXYTOCIN
Primarily affects uterine smooth muscle contraction. It increases both the frequency and the duration of action potentials during uterine contraction. Estrogens enhance the action of oxytocin by reducing the membrane potential of smooth muscle cells, thus lowering the threshold of excitation. Towards the end of pregnancy, as estrogen levels become higher, the membrane potential of uterine smooth muscle cells becomes less negative, rendering the uterus more sensitive to oxytocin. The number of oxytocin receptors in the uterus also increases at this time, and their activation causes cellular calcium to be mobilised through polyphosphatidylinositol hydrolysis.
Parturition. As the foetus enters the birth canal, the lower segments of the uterus, the cervix and then the vagina are dilated and this causes reflex release of oxytocin. Strong uterine contractions cause further descent of the foetus, further distension and further release of oxytocin.
Lactation. Oxytocin is secreted as a response to nipple stimulation leading to contraction of the myoepithelial cells of the mammary ducts and the ejection of milk.

Nutritional factors to stimulate:
(Dopamine)-Tyrosine, P5P, B3
(Insulin)- Zinc, Glucose
(PGE2)- Arachidonic acid, alcohol
Bioflavonoids
Phytoceuticals: Clove (Eugenia caryophyllata) and other Spices and culinary herbs
THYROID

Therapy Localisation: Over the gland
Muscle Association: Teres Minor left for T4 and T3
                 Teres Minor right for Calcitonin

Weight change:
Underactive - fat distribution on the trunk, face, upper arms and upper legs.
Overactive – general loss of body bulk

Secretes
  Mono Iodo Tyrosine (MIT)
  Di Iodo tyrosine (DIT)
  Triiodothyronine (T3)
  Tetraiodothyronine (T4)

Calcitonin (CT)
Thyroid hormones regulate gene expression, metabolic rate, tissue differentiation and general development. Thyroxin hormones require iodine for biological activation, which takes place in thyroglobulin. Thyroglobulin contains 115 tyrosine residues, each of which is a potential site of iodination. 70% of the iodine in thyroglobulin is in the inactive precursors monoiodotyrosine (MIT) and diiodotyrosine (DIT) while 30% is in the iodothyronyl residues T4 and T3. Normal ratio of T4 to T3 is 7 to 1. The production of T4 and T3 is TSH dependant and cAMP mediates the transcription of the thyroglobulin gene.

Production of Thyroxin

![Thyroxin structure](image)
Firstly iodine is concentrated in the thyroid by an energy dependent process. Iodine is then oxidised and taken up by the MIT and DIT globulins. Oxidised iodine then reacts with the tyrosyl residues in thyroglobulin, which requires thyroperoxidase enzymes. Two molecules of DIT couple to form T4 or one molecule of MIT and one of DIT couple to form T3. As this is an oxidative process free radicals are produced from iodothyrosine. Thyroglobulin hydrolysis is stimulated by TSH but is inhibited by oxidised iodine.

T4 and T3 is secreted via the lymph vessels and then circulates in the blood either bound to Thyroxine-Binding Globulin (TBG) or to Thyroxine-Binding Prealbumin (TBPA) or as the free hormones. TBG is formed in the liver and is stimulated by estrogens and inhibited by androgens. However, free T4 and T3 are inhibited by estrogens and stimulated by androgens.

80% of circulating T4 is deiodinised to T3 extrathyroidally as T3 binds to thyroid receptors sites 10x more readily than T4 and is the metabolically more active of the two hormones.

Thyroid hormones bind to specific high affinity receptors in the target cell nucleus. Their major function is to enhance general protein synthesis and cause positive nitrogen balance via increasing or decreasing gene transcription. T3 and glucocorticoids together enhance transcription of the GH gene so more GH is produced. Very high levels of T3 inhibit protein synthesis and cause negative nitrogen balance.

Thyroid hormones regulate all cells except the brain, retina, spleen, gonads, thymus and lungs.

Intrauterine or neonatal hypothyroidism results in cretinism. A goitre is an enlarged thyroid gland, which is an adaption to low levels of thyroid hormone production. There is always an elevated level of TSH.

**Hypothyroidism** - results in fatigue, sluggishness, lacking ambition, poor motivation, worse in the mornings, better for exercise, increased body weight, elevated blood lipids, increased tendency to coronary heart disease, lowered resistance to disease, worse with changes of season, cold hands and feet, skin problems, cracking and crevicing of the heels or hands, brittleness and softness of the fingernails, no nail half moons, premature loss of hair, low progesterone symptoms, constipation, poor memory, patients “go to pieces” easily under pressure, dislike being watched over, performing or being in crowds, poor concentration, sudden changes of personality, depression and crying for no known reason, costal cartilage hypersensitivity, generalised swelling, tendency to carpal and tarsal tunnel syndromes, puffiness under the eyelids, thick swollen tongue and loss of lateral third of the eyebrows.

**Nutritional factors to stimulate:** Phenylalanine, Vit B6, Iron, (occasionally Vit E and Vit B12), Tyrosine, Iodine, Selenium, Copper, Zinc, Melatonin and Manganese.

**Phytoceuticals:** Kelp, Spices and culinary herbs Watercress.
**Hyperthyroidism** – (Graves Disease) due to the production of Thyroid–Stimulating IgG (TSI) that activates the TSH receptor. TSI is not regulated by the feedback mechanism and so T$ and T3 levels continue to rise. Symptoms include tachycardia, widened pulse pressure, nervousness, insomnia, weight loss, weakness, excessive sweating, sensitivity to heat and a red moist skin.

**Nutritional factors to inhibit thyroxin release:** Vit A, High dose Iodine  
**Phytoceuticals:** Spices and culinary herbs  Watercress.

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**CALCITONIN (CT)**  
Is secreted by the parafollicular C cells of the thyroid gland and small amounts by the parathyroid and thymus glands. It basically decreases blood calcium levels but its mechanism is unknown.  
**Nutritional factors to stimulate:** Salmon fish  
**Phytoceuticals:** Spices and culinary herbs

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**PARATHYROID**  
**Therapy Localisation:** Just inferior to the angle of the jaw  
**Muscle Association:** Levator Scapulae

**Secretes**  
Parathyroid Hormone (PTH)

Parathyroid hormone is secreted by the parathyroid glands as a response to low levels of circulating Ca. Levels are regulated by the rate the degradation of the hormone rather than its production. Degradation occurs 20 minutes after proPTH is synthesized and is initially unaffected by Ca concentrations. Newly formed PTH can either be secreted immediately or be placed in storage vesicles for subsequent secretion. PTH secretion is inversely related to the concentrations of ionised calcium and magnesium. Phosphate levels have no effect on PTH secretion. PTH binds to a single membrane receptor protein found in bone and kidney tissues but absent in non-target cells. Hormone receptor interaction initiates activation of cAMP, which modulates gene expression for protein construction and mineralisation.  
**Nutritional factors to stimulate:**  
**Phytoceuticals:** Spices and culinary herbs
**ADRENAL MEDULLA**

**Therapy Localisation:** Locally over the gland or 2-5cm below the umbilicus  
**Muscle Association:** Sartorius, Gracilis, Tibialis Posterior, Soleus and Gastrocnemius  
**Secretes**  
- Dopamine  
- Noradrenalin  
- Adrenalin

The adrenal medulla is an extension to the sympathetic nervous system since preganglionic fibers from the splanchnic nerve terminate in the adrenal medulla where they innervate the chromaffin cells that produce the catecholamine hormones of dopamine, noradrenalin and adrenalin. The chromaffin cells synthesise, store and release hormones that act distally, thus functioning as an endocrine organ but regulated by the nervous system. The hormones aid adaptation to severe stress by integrated adjustment to the many complex processes in the organs vital to the response. They are aided by the glucocorticoids, growth hormone, vasopressin, angiotensin 11 and glucagon.

The major hormone produced is Adrenalin (80% of total catecholamine synthesis) which is not synthesised anywhere else in the body. Noradrenalin can be synthesised locally by the sympathetic nerves.

Catecholamines cannot cross the blood brain barrier and must be synthesised locally in the brain when required as neurotransmitters or as hormones.

All the catecholamine hormones are produced from tyrosine in 4 steps:

1. **ring hydroxylation**  
2. **decarboxylation**  
3. **side chain hydroxylation**  
4. **N-methylation**

Tyrosine is first converted to Dopa by the tyrosine hydroxylase enzyme and requires P5P, Vit B3, Iron, Cu, Vit C and folic acid as cofactors. Dopa is converted to Dopamine by the Dopa Decarboxylase enzyme and requires P5P and is inhibited by halogens (? chlorine and fluorine in water). Dopamine is converted to Noradrenalin by the Dopamine hydroxylase enzyme, which is Vit C, and Cu dependent.

Finally Noradrenalin is converted to Adrenalin by the N-Methyltransferase enzyme which requires a methyl donor such as Activated B12, Folinic acid, Betaine or Dimethylglycine.

Neural stimulation of the adrenal medulla results in the release of the hormones and is calcium dependent. It is stimulated by cholinergic and β-Adrenergic agents and inhibited by α-Adrenergic agents. They circulate bound to albumin and have a half-life of 10-30 seconds. They are metabolised by Catechol-O-methyltransferase and by the Monoamine Oxidase enzymes in the liver, stomach, kidney and intestine.
Catecholamines act through two classes of receptors –
\[ \alpha \]-Adrenergic
\[ \beta \]-Adrenergic

<table>
<thead>
<tr>
<th>Alpha 1</th>
<th>Alpha 2</th>
<th>Beta 1</th>
<th>Beta 2</th>
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<td>Stimulated by Adrenalin and Noradrenalin</td>
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<td>Stimulated by Adrenalin</td>
<td>Stimulated by Adrenalin</td>
</tr>
<tr>
<td>Stimulates Ca and PI intracellularly</td>
<td>Inhibits cAMP</td>
<td>Stimulated cAMP</td>
<td>Stimulates cAMP</td>
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Adrenalin binds to both Alpha and Beta-receptors whereas Noradrenalin binds only to Alpha 1 receptors. Hormones that bind to the Beta receptors stimulate adenylate cyclase whereas hormones that bind to the Alpha 2 receptors inhibit this enzyme thus inhibiting cAMP intracellularly. Alpha 1 receptors which are stimulated by noradrenalin, mediate calcium and phosphatidylinositol intracellularly.

**Nutritional factors to stimulate:** Tyrosine, P5P, NADPH, Folinic acid, Thiamine, Vit C, Cu, Iron, Zn

**Phytoceuticals:** Kelp, Rosemary (Rosemarinus officinalis), Thyme (Thymus vulgaris), Spices and other culinary herbs
ADRENAL CORTEX

Therapy Localisation: Locally over the gland or 2-5cm below the umbilicus

Muscle Association: Sartorius, Gracilis, Tibialis Posterior, Soleus and Gastrocnemius.

Weight change:
Underactive – rapid general weight loss, mostly fluid.
Overactive – general weight gain, mostly fluid.

Secretes
- Pregnenolone
- Progesterone
- Aldosterone
- Cortisol
- Dehydroepiandosterone (DHEA)
- Androstenedione
- Testosterone and Dihydrotestosterone (DHT)
- Estradiol
- Estrone
- Estriol
+ other biologically inactive hormones

All the above steroid hormones are produced in the adrenal cortex but the principal sex hormones after DHEA are mostly converted extra adrenally.

the Adrenal Cortex has three distinct regions of function
1. the zona glomerulosa which produces the mineralocorticoids
2. the Zona fasciculata which produces glucocorticoids and androgens
3. the Zona reticularis which also produces glucocorticoids and androgens.

Secretion of the steroid hormones within the adrenal and gonadal cells is directly into the circulation as there is very little storage capability.
MINERALOCORTICOIDs

Mineralocorticoids are regulated by the renin-angiotensin system and potassium levels. They regulate sodium retention. They also regulate gene expression directly through a specific receptor on DNA to affect the rate of transcription of specific genes. Mineralocorticoids weakly binds to albumin. Aldosterone is the main mineralocorticoid hormone.

The Renin-Angiotensin system is involved in the regulation of blood pressure and electrolytic metabolism. The primary hormone is Angiotensin 11, which is made from Angiotensinogen in the liver. It is the substrate for Renin, an enzyme produced in the renal afferent arterioles. Renin acts upon Angiotensinogen to produce Angiotensin 1. This is enhanced by both glucocorticoids and Estrogens. Angiotensin Converting Enzyme (ACE) converts Angiotensin 1, which increases blood pressure, to Angiotensin11, which also increases blood pressure and is the most powerful vasoconstrictor of arterioles and an Aldosterone stimulant. Angiotensin11 can be converted to Angiotensin 111, an equally potent vasoconstrictor and Aldosterone stimulant. In humans the plasma level of Angiotensin11 is 4x greater than Angiotensin 111. Angiotensin 111 is degraded by angiotensinase enzymes.

ANGIOTENSINOGEN (IN THE LIVER)

↓ ← RENIN (IN THE KIDNEYS)

ANGIOTENSIN 1

↓ ← ANGIOTENSIN CONVERTING ENZYME (ACE)

ANGIOTENSIN 11

↓ ← AMINOPEPTIDASE

ANGIOTENSIN 111

↓ ← ANGIOTENSINASE

DEGRADATION PRODUCTS

Nutritional factors to stimulate: Vit B3
Phytoceuticals: Licorice (Glycerrhiza glabra), Spices and culinary herbs

GLUCOCORTICOIDS

Cortisol is the most biologically active glucocorticoid hormone. Cortisol release is regulated by ACTH and in turn by CRH and regulated by a negative feedback. Cortisol regulates gluconeogenesis, suppresses host defence mechanisms and the response to stress. It regulates gene expression directly through a specific receptor on DNA to affect the rate of transcription of specific genes. Cortisol circulates both globulin bound form and in a free form which is the biologically active part.

Nutritional factors to stimulate: Vit B5, Vit C, Zinc
Phytoceuticals: Ginseng (Eleutherococcus), Spices and culinary herbs
SEX HORMONES

OVARIES

Therapy Localisation: Locally over the gland.
Muscle Association: Gluteus Maximus and Minimus, Piriformis and the Adductors

Weight change:
Underactive - fat distribution on the thighs and upper legs. Loss of secondary sexual characteristics.
Overactive – large breasts and increased general body fat deposition.

Secrete
17 β Estradiol
Estrone
Estriol
DHEA
Testosterone

CORPUS LUTEUM

Secretes
Progesterone

TESTES

Therapy Localisation: Locally over the gland.
Muscle Association: Gluteus Maximus and Minimus, Piriformis and the Adductors

Weight change:
Underactive – fat deposition on and around the abdomen (beer belly).
Overactive – general loss of body fat. Increase in body muscle bulk.

Secrete
Testosterone
Dihydrotestosterone (DHT)
DHEA
Estradiol
Estrone
Estriol

The gonads are bifunctional organs that produce germ cells and sex hormones. High local levels of the sex hormones are essential for germ cell development. The sex hormones act by nuclear mechanisms similar to the mineralocorticoids and the glucocorticoids.
The sex hormones are anabolic in function and are required for maintenance of skin, bone, muscle and fatty tissues.

DEHYDROEPIANDROSTERONE (DHEA)

Is produced in the adrenal cortex, ovaries, testes and the brain (?epiphysis) and is the most abundant androgen in the body. Females have 90% of the levels of males. Is the main daytime stress hormone regulating all steroid and other hormones. Peaks by age 20 years and declines with age and chronic stress. It stimulates sexual function, increases gonadal growth and maintains wakefulness. It lifts depression. It stimulates the thymus to differentiate and mature T, B and NK cells. It acts as an antioxidant and has oncostatic actions. It decreases high glucocorticoid and cholesterol levels, lowers blood pressure and stabilises body weight.
**FEMALES**

Estrogens are a family of hormones synthesised in a variety of organs. $17\beta$ Estradiol is the primary estrogen of ovarian origin. In pregnancy estriol is the primary estrogen and is largely produced in the placenta. Estrogens are formed by the aromatization of androgens that involves 3 hydroxylation steps, each of which requires O2 and NADPH.

There are 2 types of ovarian hormone producing cells
1. Granulosa cells that produce estradiol from androstenedione and testosterone.
2. The corpus luteum that produces progesterone and some estradiol (E2).

Significant amounts of estrogens are produced by the peripheral aromatization of androgens. The conversion of androstenedione to estrone (E1) is the major source of estrogens in the postmenopausal female. Aromatase activity is present in adipose cells and in the liver, skin and other tissues.

Estrogens are bound to sex hormone binding globulin (SHBG) and Progestins to Corticosteroid binding globulin (CBG). SHBG binds Estradiol 5x less avidly than it binds testosterone or DHT. Only the free unbound hormones have biological activity. Estradiol, Estrone and Estriol are all metabolised by the liver with glucuronate or by sulphation.

All estrogens are involved with the development of the female secondary sexual characteristics i.e. fat deposition in and around the breasts, trunk and hips. Estrogens stimulate the development of tissues involved in reproduction. These hormones stimulate the size and number of cells by increasing the rate of protein synthesis. There is proliferation of the vaginal epithelium, the uterine endometrium and the glands hypertrophy. The myometrium develops an intrinsic rhythmical motility and the breast ducts proliferate. Estrogens have some anabolic effects on bone and cartilage but largely function by inhibiting the breakdown of bone cells. They do not stimulate the development of new bone. This is under the influence of DHEA, progesterone and testosterone. They cause vasodilation and heat dissipation (primarily methoxyestradiol, methoxyestrone and estrone).

 Estradiol mainly targets the ovaries, fallopian tubes and the upper one third of the uterus.
Estrone mainly targets the mid portion of the uterus.
Estriol mainly targets the lower one third of the uterus and the vagina.

Progestins are actively metabolised in the liver to several compounds thus making them ineffective if given orally. Progestins reduce the proliferative activity of the estrogens on the vaginal epithelium and convert the uterine epithelium to to secretory, thus preparing the uterine epithelium for implantation of the fertilised ovum. Progestins enhance development of the acinar portions of the breast glands after estrogens have stimulated ductal development. Progestins decrease peripheral blood flow, thereby decreasing heat loss, so that body temperature tends to increase during the luteal phase of the menstrual cycle. Progestins require concurrent presence of estrogens to stimulate their receptor sites.

The number of oogonia in the female ovary declines with age probably due to increasing androgen production.

Estrogens and Progestins regulate gene expression directly by binding to receptors on the DNA to effect the rate of transcription of specific genes.
THE MENSTRUAL CYCLE

The human menstrual cycle results from the complex interactions between the hypothalamus, pituitary and ovary (and probably the epiphysis).

The Follicular Phase. A particular follicle begins to enlarge under the influence of FSH. E2 levels are low during the first week of the follicular phase, but rise progressively as the follicle enlarges. E2 levels reach maximum 24 hours before the LH and FSH peak and sensitisises the pituitary to GnRH. LH is released either in response to this high level in a positive feedback system or in response to sudden decline of E2 from its maximum level. High levels of estrogen, at this stage (e.g. contraceptive pill) suppresses LH and FSH release and inhibits the action of GnRH on the pituitary. Progesterone levels are low during the follicular phase. The LH peak precedes ovulation by 16-18hours.

The Luteal Phase. After ovulation, the granulosa cells of the ruptured follicle luteinise and form the corpus luteum which produces progesterone and some estradiol. Estradiol peaks about midway through the luteal phase and then declines to a low level. The major hormone of the luteal phase is progesterone which is required for preparation and maintenance of the secretory endometrium that provides nourishment for the implanted blastocyst. LH is required for the early maintenance of the corpus luteum and the pituitary supplies LH for about 10 days.
If implantation occurs (day 22-24 of the average cycle), this LH function is supplied by chorionic gonadotrophin (hCG), a placental hormone that is very similar to LH. hCG stimulates progesterone synthesis by the corpus luteum until the placenta begins synthesising larger amounts.

In the absence of implantation, (and hCG), the corpus luteum regresses and menstruation ensues. After the endometrium is shed, a new cycle commences. The luteal phase is always 14 ± 2 days in length. Variations in length are due to an altered follicular phase.

**Nutritional factors to stimulate Progesterone:** Essential fatty acids, Vit A  
**Phytoceuticals:** Spices and culinary herbs  
**Nutritional factors to stimulate Estrogens:** Vit A, Vit C, Vit E, Zinc, Vit B3, Boron, Magnesium, Chromium, Iodine.  
**Phytoceuticals:** Mumie, Anise star, Fenugreek, other Spices and culinary herbs
MALES
In males testosterone is produced in response to LH in the Leydig cells. Both LH and FSH are necessary for spermatogenesis which occurs firstly in the seminiferous tubules and later in the Sertoli cells.
Testosterone is synthesised from cholesterol to pregnenalone and then via the conversion using 5 enzyme pathways to testosterone. Dihydrotestosterone (DHT) is formed from testosterone by reduction of the A ring. Most DHT is derived from peripheral conversion.
DHT is the active form that targets the seminal vesicles, prostate, external genitalia, skin and hair.
Testosterone targets the Wolffian structures, spermatogonia, muscles, bones, kidney and brain. The plasma content of DHT should be only 10% of the circulating testosterone levels.
The testes also produce small amounts of Estradiol (E2) but most Estradiol in the male occurs peripherally by aromatization of testosterone and androstenedione to 80% of levels. Most testosterone enters the circulation bound to globulin. Only 1-3% is in the free form.
Testosterone and Dihydrotestosterone function to
1. sexual differentiation
2. spermatogenesis
3. development of secondary sexual characteristics
4. anabolic metabolism and gene regulation
5. male pattern behaviour
They affect gene regulation directly, similar to the adrenal steroids. They stimulate protein synthesis in male accessory organs and aids in the enlargement of the kidneys.

**Nutritional factors to stimulate**: Essential fatty acids, Vit B1, 2, 3, 5, Zinc, Vit E, Vit C, Vit A., Methylene tetrahydrofolate.
**Phytoceuticals**: Spices especially ginger and culinary herbs