Functional Medicine University's Functional Diagnostic Medicine Training Program

Module 7 * FDMT561A

Introduction to Functional Endocrinology

By Wayne L. Sodano, D.C., D.A.B.C.I., & Ron Grisanti, D.C., D.A.B.C.O., M.S.
http://www.FunctionalMedicineUniversity.com

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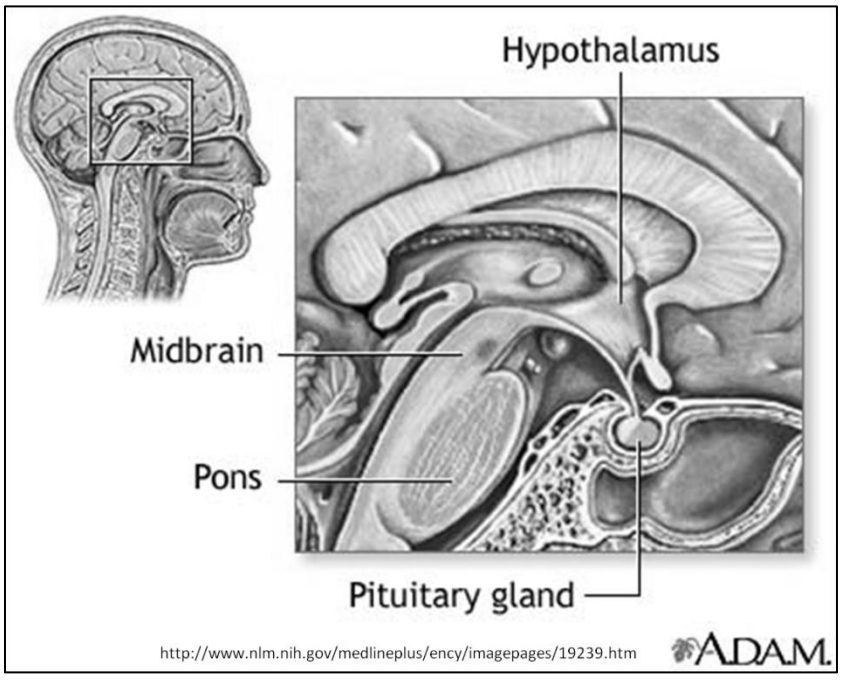
Perhaps a more appropriate title of this lesson would be the "Introduction to Functional Neuroimmunoendocrinology" based on the fact that chemical messengers are used in all three of these systems and the interconnections that exist among them. To effectively address a dysfunctional endocrine system, the nervous system and the immune system must be assessed in addition to other body systems.

Both the endocrine and nervous systems integrate stimuli and response(s) to changes in the external and internal environment. They are both crucial to coordinate the functions of highly differentiated cells, tissues and organs. The principle functions of the endocrine system are: to maintain the internal environment of the body, integrate and regulate growth and development and control and maintenance of sexual reproduction, and fetal growth and development.

Before discussing the endocrine system in detail, a brief discussion of the limbic system is in order. The limbic system has direct input to the hypothalamus, and therefore the endocrine system . The limbic system regulates the autonomic and endocrine functions, particularly in response to emotional stimuli. The limbic system has been conceptualized as the "feeling and reacting brain". Therefore, stress has a major influence on the functions of the limbic system, and therefore, the endocrine and autonomic systems. The limbic system has its input and processing side, as well as an output side. The input side includes the *limbic cortex*, *amygdale* and the *hippocampus.* The output side includes the *septal nuclei* and the *hypothalamus.*



The hypothalamus receives input from various sources, and is the primary output node of the limbic system, as well as other sources including the olfactory, viscera, and retina. It has sensors for temperature, osmolarity, glucose concentration and sodium concentration, and also contains receptors for hormonal control, signaling the pituitary gland.

Hypothalamic functions and influences:

- Homeostasis – temperature, glucose concentration, sodium concentration, osmolarity. The liver plays a pivotal role in the regulation of glucose metabolism because it is the key organ that maintains glucose levels during fasting. An emerging body of literature has demonstrated the important role of the hypothalamus in controlling hepatic glucose production. *The hypothalamus senses circulating nutrients and hormones, conveying the energy status to the central nervous system, which, in turn controls hepatic glucose production in part way by the autonomic nervous system. Overfeeding results in the failure of the hypothalamus to sense circulating nutrient and hormones, and a loss of central control of hepatic glucose production*.[2]

- Hunger, thirst, response to pain, level of pleasure, sexual satisfaction, anger, aggressive behavior

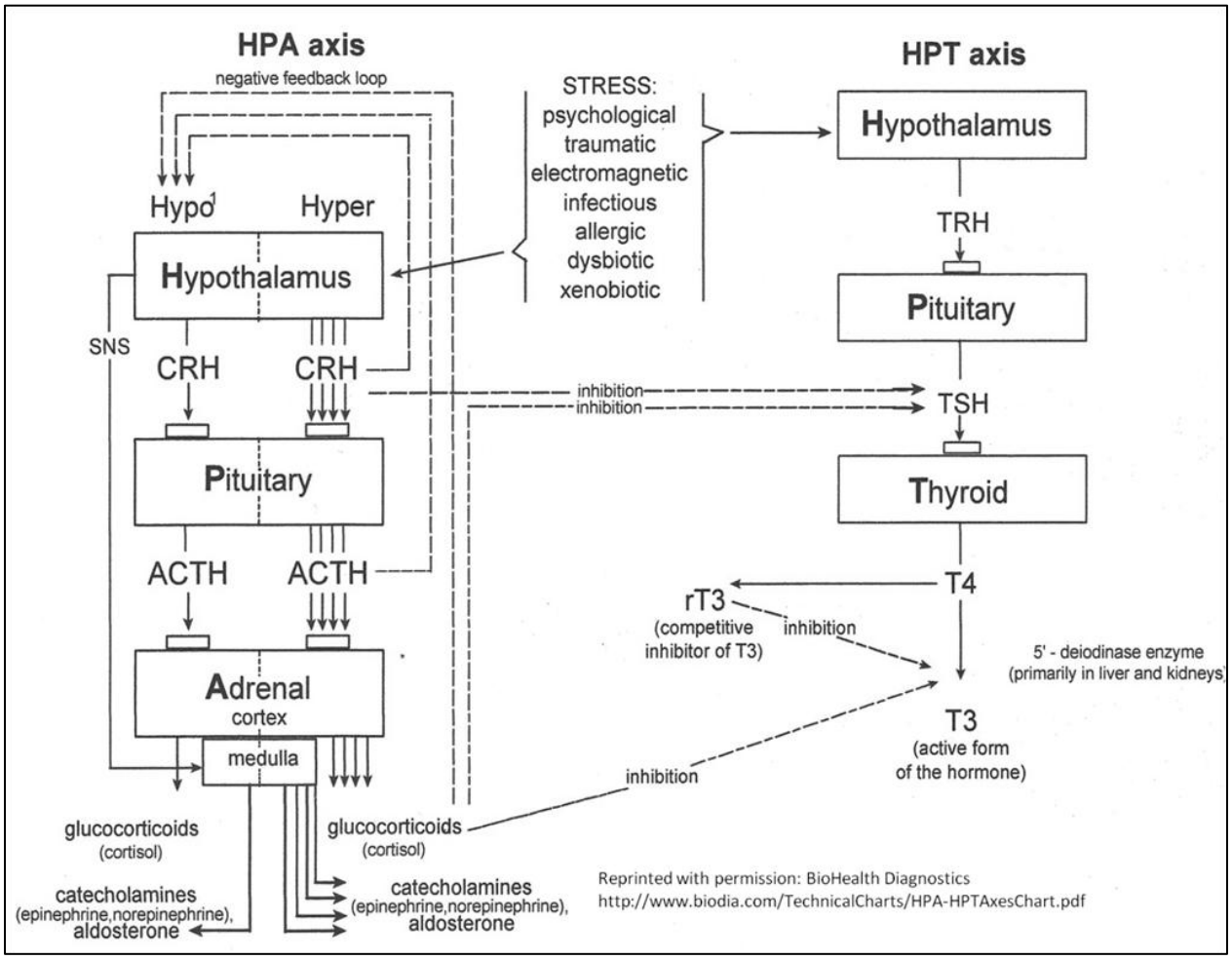
- Control over the pituitary (the master gland) - the hypothalamus controls hormone production in the pituitary gland through several releasing hormones. (*The major hormones and systems can be viewed as a "Top down Organization".)*

- Control of the autonomic nervous system

- Circadian rhythms

- Appetite – The adipocytes produce a protein called leptin that is released when we over eat. The hypothalamus senses the level of leptin and subsequently decreases the appetite.

Let's take a brief look at what are known as the **HPA and HPT Axes**. (The HPA stands for the Hypothalamus-Pituitary – Adrenal Axis and the HPT stands for the Hypothalamus-Pituitary-Thyroid Axis.)



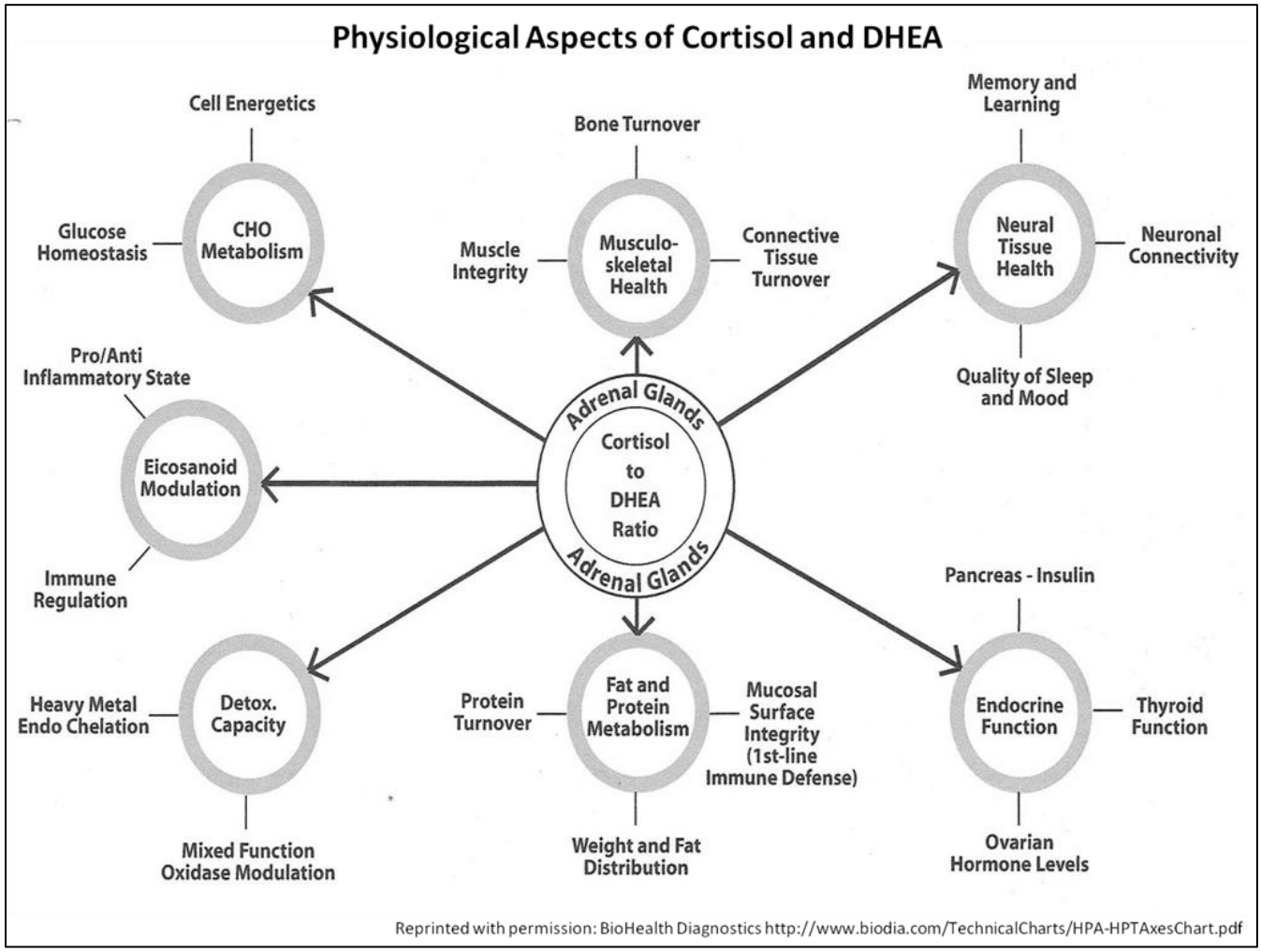
Given the direct influence of the HPA axis on the HPT axis, adrenal function should always be evaluated when assessing thyroid function.

Major points:

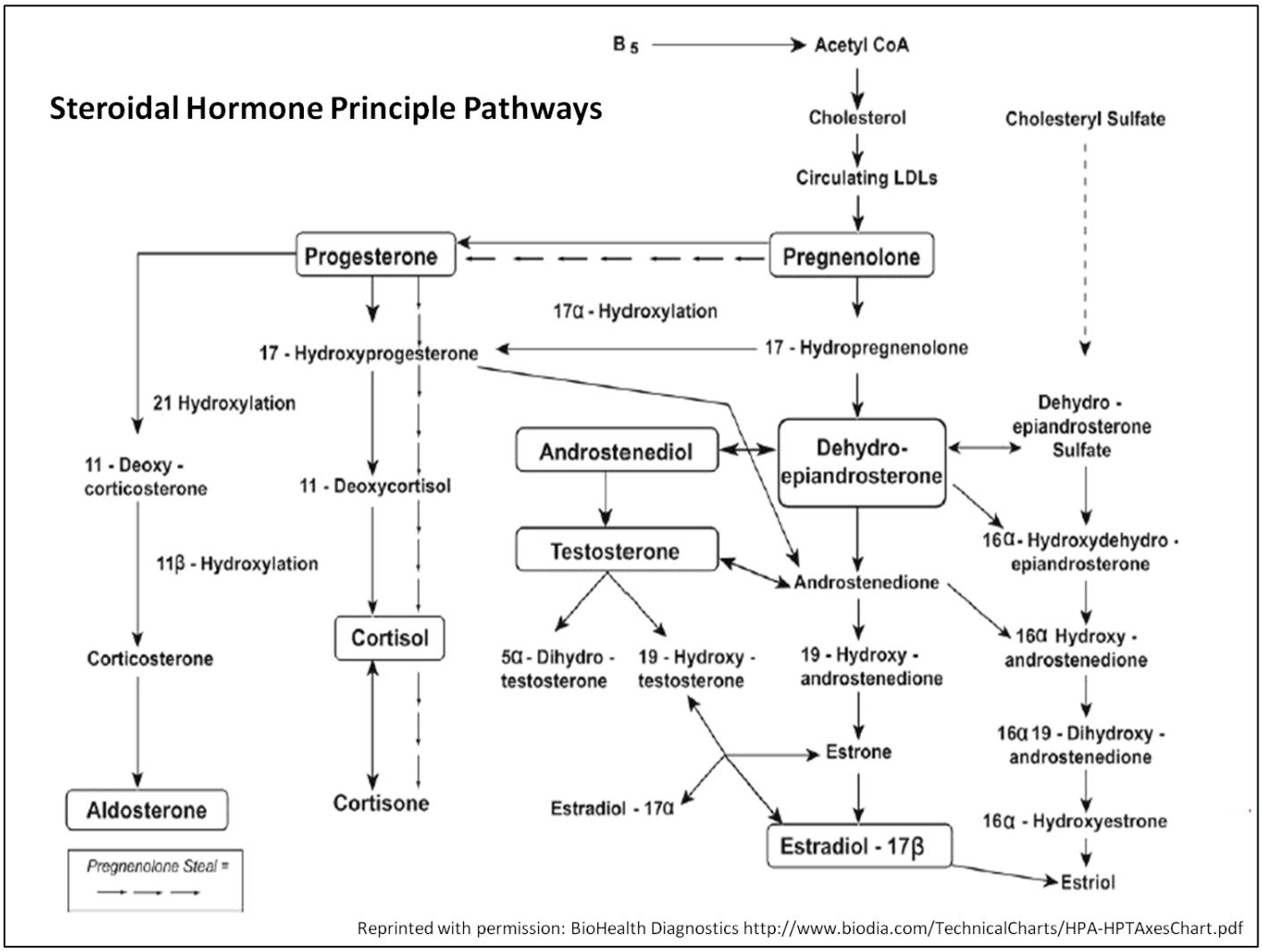
- Excess CRH inhibits TSH.
- Excess glucocorticoids (e.g. cortisol) inhibit conversion of the less active T4 to the more active T3.
- Excess high cortisol can result in high output of rT3 which inhibits T3.

Common Acronyms:

- HPA Axis = Hypothalamic Pituitary Adrenal Axis HPT Axis: Hypothalamic Pituitary Thyroid Axis
- CRH = Corticotrophic Releasing Hormone ACTH = Adrenocorticotrophic Hormone
- TRH = Thyroid Releasing Hormone TSH = Thyroid Stimulating Hormone rT3 = Reverse T3



Cortisol is the primary hormone that directs immune function and is involved in virtually all aspects of body function. Both cortisol and DHEA have genetic influences. When cortisol and DHEA work together in harmony (maintaining a normal ratio between cortisol and DHEA), the body is then said to be in a normal state of adaptation to stress.
When unable to maintain this normal state of adaptation the body can now enter into a state of maladaptation to stress. This is now referred to as a chronic stress response, i.e. pregnenolone steal/cortisol escape/elevated cortisol to DHEA ratio. The longer one stays in a state of chronic stress the more compromised all aspects of body function become. This can ultimately result in hormone, immune and metabolic systems breakdown.



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The body's preferential pathway under chronic stress is called Pregnenolone Steal or Cortisol Escape. When the body is in a "chronic stress response", pregnenolone, the precursor to all the rest of the steroidal hormones, is diverted (see arrows) to cortisol – cortisone. This is at the detriment of all the other steroidal hormones; i.e. progesterone, aldosterone (mineral/cortical pathway/sodium-potassium pump), DHEA and its metabolites: the sex hormones, estrogens and testosterone. As pregnenolone is diverted to cortisol-cortisone, DHEA depletion begins. The result is an elevated cortisol to DHEA ratio. This is measurable with the Functional Adrenal Stress Profile. Simply divide the cortisol sum by the DHEA(s) average to get the ratio. A normal ratio is approximately 5:1 to 6:1.

Case History

Before entering into the functional neuroanatomy and physiology, I want to present a case history from one of my old files. (The treatment protocols I used for this patient will be addressed in a future lesson.)

Case Study: 02/08/2006

Patient: Female 48 years-old
Occupation: School bus driver
Previous Occupation: Worked with/around motor vehicles; family business. Pumped own fuel daily.
Chief complaint: *"All joints hurt" (Patient questions possibility of MS? RA? Autoimmune Disease?)*

- Started Synthroid .05 mg: 2/7/2006
- Cancerous colon polyp removed 7/23/2004
- Herpes simplex (chronic breakouts)
- Carpal Tunnel Syndrome
- Positive TPO (Thyroid Antibody)

Review of Systems & Past History

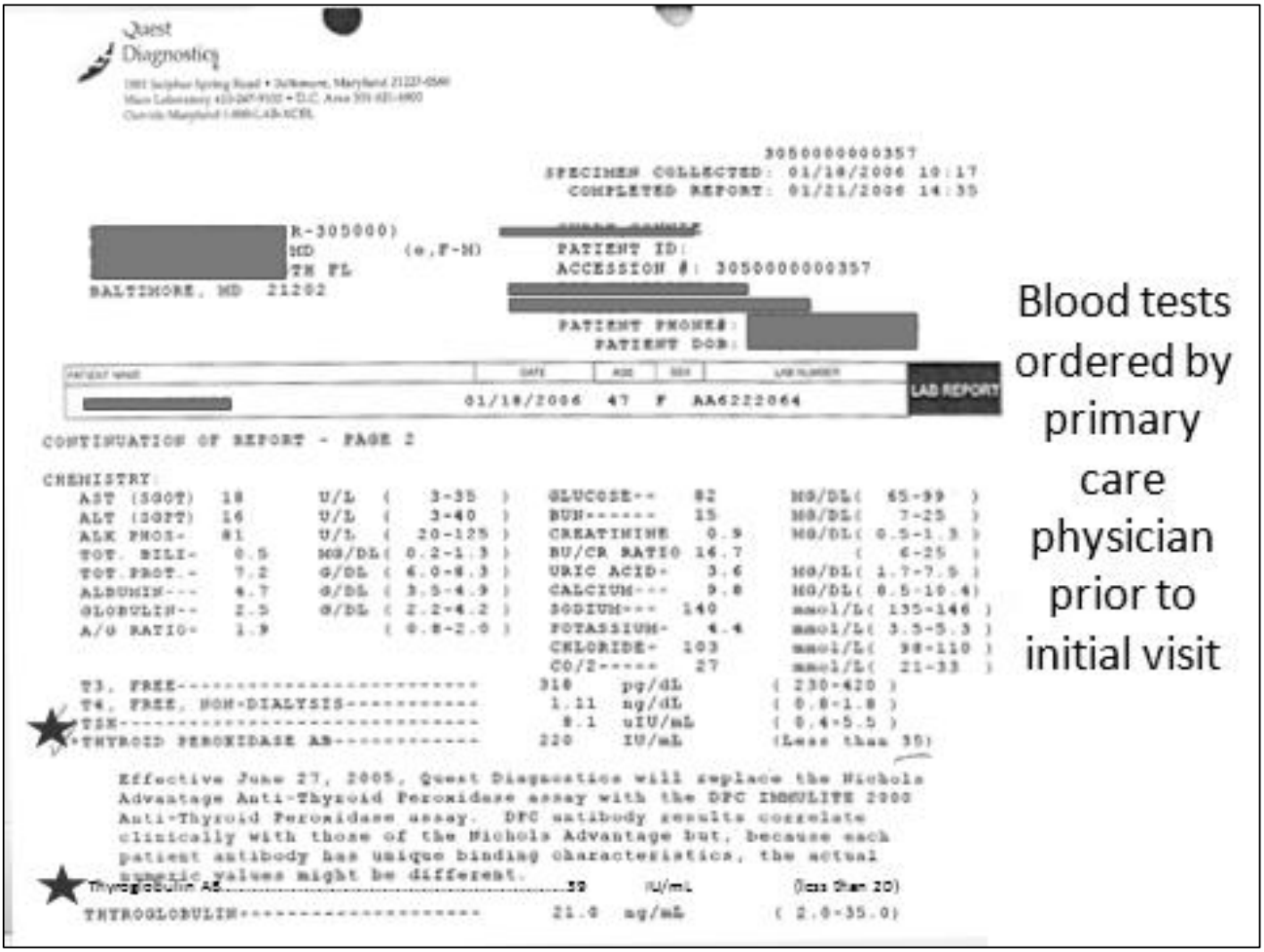
- Enlarged thyroid
- Bruising easily and dry skin
- Weight gain, weakness, sleeping disturbances, hot flashes, low sex drive, low blood pressure, MVP, depression/mood swings
- Endometriosis/uterine fibroids
- Hysterectomy 12/26/2000; left ovary, adhesions and appendix 12/7/2001

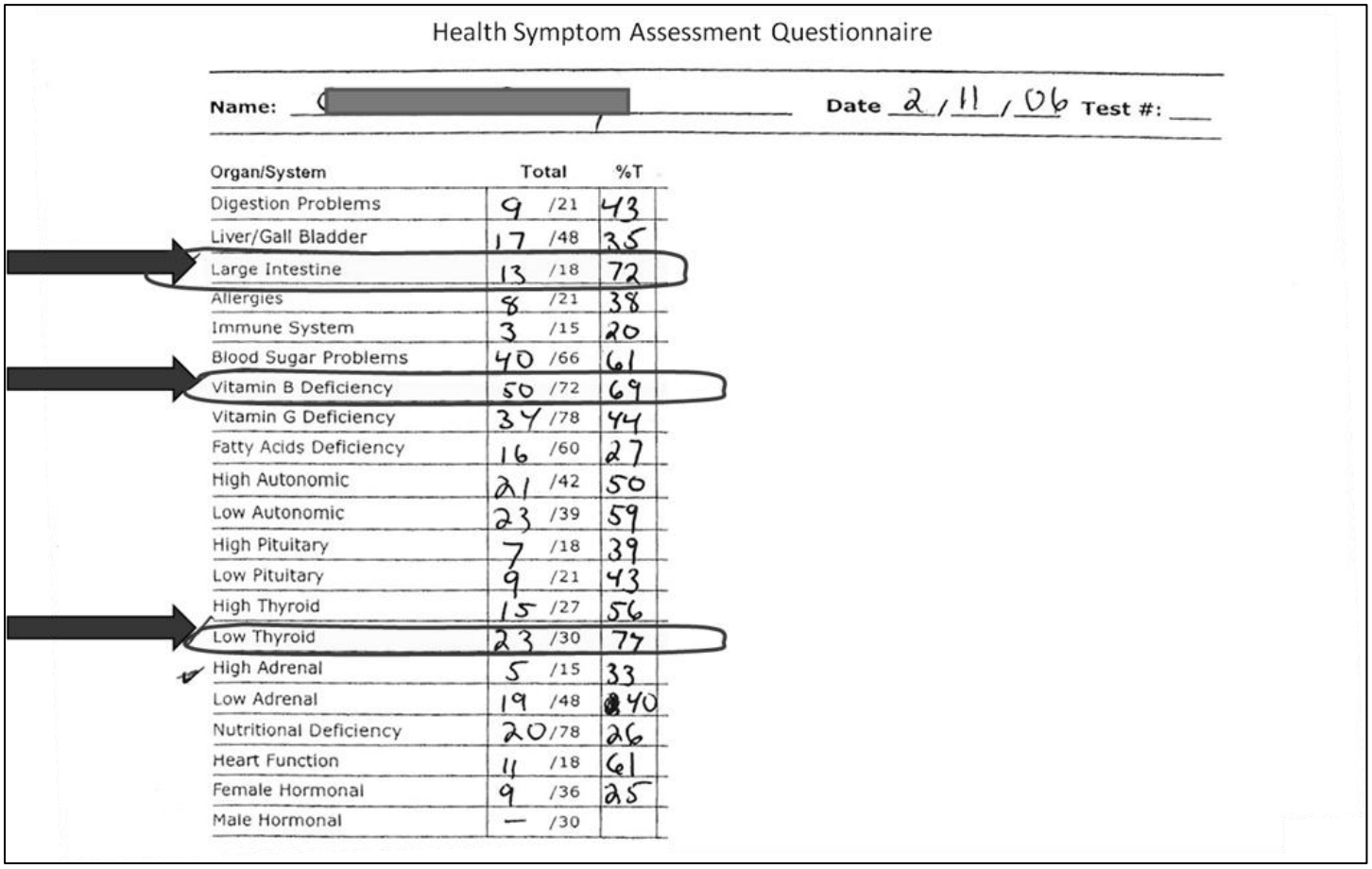
Menstrual History

- Age 14: Menarche; irregular cycles 26-48 days
- Age 17: Began BCP; regular periods for 8 years; no health problems
- 1984: First yeast infection
- 1984: Married; stopped BCP – irregular periods began with heavy bleeding and clotting
- Age 33: Bleeding on/off during first pregnancy-delivered 2 weeks early-breast fed 3 months-stopped due to bleeding nipples
- Age 36: 2nd pregnancy no bleeding – breast fed 19 months –no problems
- Ages 38-39: Menstrual cycles better
- Age 40: Began with heavy bleeding/clotting
- Age 43: Fibrocystic breast disease
- Age 46: Began treatment with medical doctor.

Physical Exam

- Ht: 5' 4"
- Wt: 140 lbs
- Pulse: 68 b/m
- Resp: 16
- Temp: 98.2
- BP: 110/64 R 116/70 L
- Neuro/Ortho: WNL
- Abd: left lower quadrant: significant tenderness
- Hair: Thin: pulls out easily
- Skin: Dry scalp
- Tongue: White coating, scalloped





Health Symptom Assessment Questionnaire

Name: [redacted] Date 2/11/06 Test #: ___

Organ/System	Total	%T
Digestion Problems	9 /21	43
Liver/Gall Bladder	17 /48	35
Large Intestine	13 /18	72
Allergies	8 /21	38
Immune System	3 /15	20
Blood Sugar Problems	40 /66	61
Vitamin B Deficiency	50 /72	69
Vitamin G Deficiency	34 /78	44
Fatty Acids Deficiency	16 /60	27
High Autonomic	21 /42	50
Low Autonomic	23 /39	59
High Pituitary	7 /18	39
Low Pituitary	9 /21	43
High Thyroid	15 /27	56
Low Thyroid	23 /30	77
High Adrenal	5 /15	33
Low Adrenal	19 /48	40
Nutritional Deficiency	20/78	26
Heart Function	11 /18	61
Female Hormonal	9 /36	25
Male Hormonal	— /30	

There are three general classes of hormones:

1. *Steroids* (e.g. estrogens) These hormones are synthesized from cholesterol and are not stored.

2. *Amino acid derivatives* (e.g. epinephrine, thyroid hormones)

3. *Peptide hormones* (e.g. insulin) - Amino acid and peptide hormones are stored in secretory vessels until they are needed.

(The eicosanoids are also considered hormones and are derived from fatty acids)

The Endocrine Glands

Gland/Tissue/Organ	Hormone(s)	Major function(s)	Basic Chemical Structure
Hypothalamus	1. Corticotropin-releasing hormone 2. Gonadotropin-releasing hormone 3. Growth hormone-releasing hormone 4. Growth hormone inhibitory hormone (aka- somatostatin) 5. Thyrotropin-releasing hormone	1. Release of ACTH 2. Release of LH and FSH 3. Release of growth hormone 4. Inhibits release of growth hormone 5. Stimulates secretion of TSH and prolactin	All from peptides
Pineal	Melatonin	1. Maintains circadian rhythm 2. Helps control the timing and release of female reproductive hormones 3. Antioxidant effects 4. May help strengthen immune system	Amine (tryptophan)
Anterior Pituitary	1. Growth hormone 2. Thyroid stimulating hormone (TSH) 3. Adrenocorticotropic hormone (ACTH) 4. Prolactin 5. Follicle-stimulating hormone (FSH) 6. Luteinizing hormone (LH)	1. Protein synthesis and growth 2. Stimulates synthesis and secretion of thyroid hormones 3. Stimulates synthesis and secretion of cortisol, androgens and aldosterone 4. Promote development of breast tissue and secretion of milk 5. Causes growth of follicles in the ovaries and sperm maturation in the testes 6. Stimulates testosterone synthesis in the testes; stimulates ovulation and the formation of the corpus luteum; stimulates estrogen and progesterone synthesis in the ovaries	All from peptides

Posterior Pituitary	1. Antidiuretic hormone (ADH) 2. Oxytocin	1. Increases water reabsorption by the kidneys and causes vasoconstriction 2. Stimulates uterine contraction and milk ejection from the breasts	Both from peptides
Thyroid	1. Thyroxine (T4) 2. Triiodothyronine (T3) 3. Calcitonin	1. Increases metabolism 2. Increases metabolism 3. Promotes deposition of calcium in the bones and decrease calcium ion concentration in the extracellular fluid	1. Tyrosine 2. Tyrosine 3. Peptide
Parathyroid	Parathyroid hormone (PTH)	Controls serum calcium ion concentration by increasing calcium absorption by the GI tract and kidneys and releases calcium from the bones	Peptide
Adrenal Cortex	1. Cortisol 2. Aldosterone	1. Multiple metabolic functions and anti-inflammatory effects 2. Increases renal sodium resorption, potassium secretion and hydrogen ion secretion	Both from steroids
Adrenal Medulla	1. Epinephrine 2. Norepinephrine	Sympathetic stimulation	Both from Tyrosine
Pancreas	1. Glucagon 2. Insulin	1. Increase synthesis and release of glucose from the liver 2. Promotes glucose entry into the cells	Both from peptides
Testes	Testosterone	Promotes development of male reproductive system and secondary sexual characteristics	Steroid

Ovaries	1. Estrogens (estriol, estradiol, estrone) 2. Progesterone	1. Promotes development of female reproductive system and secondary sexual characteristics 2. Stimulates the uterine glands to secrete uterine milk; promotes development of breast lobules and alveoli; vital role in pregnancy	Both from steroids
Placenta	1. Human chorionic gonadotropin (HCG) 2. Human somatomammotropin 3. Estrogens 4. progesterone	1. promotes growth of corpus luteum (CL) and secretion of estrogens and progesterone by CL 2. may promote development of fetal tissue and mother's breasts 3. (as above) 4. (as above)	1. Peptide 2. Peptide 3. Steroid 4. Steroid
Kidney *(skin and liver are also part of the metabolism of vitamin D)*	1. 1,25Dihydroxycholecalciferol 2. Erythropoietin	1. Increases intestinal absorption of calcium and promotes bone mineralization 2. Increases erythrocyte production	Steroid
Heart	Atrial natriuretic peptide (ANP)	Increases sodium excretion by the kidneys and reduces blood pressure	Peptide
Stomach	Gastrin	Stimulates HCl production	Peptide
Small intestines	1. Secretin 2. Cholecystokinin (Other gastrointestinal hormones include: Motilin, Gherlin, Gastric inhibitory polypeptide, serotonin, somatostatin, incretins)	1. Stimulates pancreas to release bicarbonate and water 2. Stimulates gall bladder contraction and release of pancreatic enzymes	1. Peptide 2. Peptide

Adipocytes	Leptin	Inhibits appetite and stimulates thermogenesis	Peptide
Thymus	1. Thymopoietin 2. Thymulin 3. Thymosin alpha 1	1. Depresses neuromuscular transmission, induces T-cell markers, and has a role in the generation of cytotoxic T cells and prevention of autoimmunity 2. Stimulates most T-cell functions.	All from peptides
Eicosanoids "local hormones"	1. Prostaglandins 2. Protacyclins 3. Leukotrienes 4. thromboxanes	Various roles in inflammation, fever, regulation of blood pressure, blood clotting, and immune system modulation	Fatty Acid Derivatives
Liver	1. Insulin-like growth factors 2. Angiotensinogen (aka- renin substrate)	1. Growth hormone released from the pituitary stimulates the liver to produce IGF 2. Precursor for angiotensin	Peptide

Chemical Messengers

Chemical messengers coordinate a significant amount of body functions. The chemical messenger systems of the body include:

- Neurotransmitters
- Endocrine hormones
- Neuroendocrine hormones
- Paracrines
- Autocrines
- Cytokines

1. *Neurotransmitters* – these chemicals allow the transmission of signals from one neuron to another. Neurotransmitters are also found at the axon endings of the motor neurons, where they stimulate muscle contraction.

Table of Neurotransmitters[1]

Transmitter Molecule	Derived From	Site of Synthesis
Acetylcholine	Choline	CNS, parasympathetic nerves
Serotonin 5-Hydroxytryptamine (5-HT)	Tryptophan	CNS, chromaffin cells of the gut, enteric cells
GABA	Glutamate	CNS
Glutamate		CNS
Aspartate		CNS
Glycine		spinal cord
Histamine	Histidine	hypothalamus
Epinephrine synthesis pathway	Tyrosine	adrenal medulla, some CNS cells
Norepinephine synthesis pathway	Tyrosine	CNS, sympathetic nerves
Dopamine synthesis pathway	Tyrosine	CNS
Adenosine	ATP	CNS, peripheral nerves
ATP		sympathetic, sensory and enteric nerves
Nitric oxide	Arginine	CNS, gastrointestinal tract

"Many other neurotransmitters are derived from precursor proteins, the so-called *peptide neurotransmitters*. As many as 50 different peptides have been shown to exert their effects on neural cell function. Neuropeptides are responsible for mediating sensory and emotional responses including hunger, thirst, sex drive, pleasure and pain."[1]

2. *Endocrine Hormones* – these chemicals are released by the glands or specialized cells into the blood stream.

3. *Neuroendocrine hormones* – these hormones are secreted by neurons into the blood stream. Neuroendocrine hormones are secreted by the hypothalamus, the pituitary gland, the pineal gland and the adrenal medulla.

4. *Cytokines* – cytokines are peptides secreted by the cells into the extracellular fluid. Examples of cytokines include; interleukins, lymphokines and leptin. (You should recall that interleukins and lymphokines are involved with the immune system.)

5. *Paracrines* are messengers secreted by cells into the extracellular fluid. These hormones interact with receptors on neighboring cells. Some examples of paracrine hormones (messengers) include cytokines and neurotransmitters. (serotonin, melatonin, dopamine, epinephrine and norepinephrine)

6. *Autocrines* are messengers secreted by cells that affect the function of the same cell it was secreted from. Autocrine signaling can occur within the cytoplasm or by interacting on the cell receptors. An example of autocrine hormones are the eicosanoids.

An example of a functional medicine approach to neurotransmitter dysregulation is illustrated below.

One of the active forms of folic acid is called 5-methyltetrahydrofolate (aka L-methylfolate). This form of folic acid is used in the formation of three neurotransmitters; serotonin, dopamine and norepinephrine (collectively known as the tri-monoamines). Anti-depressants are prescribed in an attempt to restoring monoamine function. In order for an anti-depressant to act, the monoamine must be present in adequate amounts. The active form of folic acid plays a role in the synthesis of the monoamines. L-methylfolate can pass through the blood brain barrier where it modulates the product of the tri-monamines in a three step process.

- *Step 1* : L-methylfolate assists in the production of a nutrient called tetrahydrobiopterin (BH4), which is a critical cofactor for the production of monoamines.

- *Step 2* : BH4 activates the rate limiting enzymes for the synthesis of monoamines. (tyrosine hydroxylase and tryptophan hydroxylase)

- *Step 3:* Tyrosine + (BH4 + *tyrosine hydroxylase*)→ Dopamine and Norepinephrine

  Tryptophan + (BH4 + *tryptophan hydroxylase*) → Serotonin

Hormone Concentration in Circulating Blood

Hormones are normally present in the plasma and interstitial tissue at concentrations in the range from as little as 1 picogram in each milliliter of blood to at most a few micrograms per milliliter of blood. Because of these very low physiological concentrations, sensitive protein receptors have evolved in target tissues to sense the presence of very weak signals. In addition, systemic feedback mechanisms have evolved to regulate the production of endocrine hormones.[1]

Feedback Control of Hormone Secretion (Regulation)

1. *Negative feedback* – Prevents over activity of the hormones systems. After the release of hormone, the actions caused by the hormone suppress further release of the hormone. An example of negative feedback is seen when the hypothalamus releases TRH which causes the pituitary to release TSH; which in turn causes the thyroid to secrete T4. When the T4 level is adequate, it feeds back to the hypothalamus and pituitary, causing a decrease in secretion of both TRH and TSH. It's important to keep in mind that only when the target tissue activity rises to the appropriate level will the feedback signals to the endocrine gland become powerful enough to decrease hormone secretion.

Feedback regulation can occur at the following area:

- Gene transcription and translation involving hormone synthesis
- Hormone processing by the cells
- Releasing stored hormones

2. *Positive feedback* – Some hormones cause a positive feedback; that is, a hormone causes the secretion of a hormone. Estrogen can cause the pituitary to secrete luteinizing hormone (LH) before ovulation. LH can then cause the ovaries to secrete more estrogen.

3. *Cyclical Variations of Hormone Release*

   Some hormonal secretions can vary due to season changes, stage of development, diurnal cycle and sleep.

Hormone Carriers in the Blood

Once a hormone is secreted by an endocrine tissue, it generally binds to a specific plasma protein carrier, with the complex being disseminated to distant tissues. Plasma carrier proteins exist for all classes of endocrine hormones. Carrier proteins for peptide hormones prevent hormone destruction by plasma proteases. Carriers for steroid and thyroid hormones allow these very hydrophobic substances to be present in the plasma at concentrations several hundred-fold greater than their solubility in water would permit. Carriers for small, hydrophilic amino acid-derived hormones prevent their filtration through the renal glomerulus, greatly prolonging their circulating half-life.[1]

Clearance of Hormones from the Blood

The concentration of hormones in the blood is governed by two factors:

1. Rate of secretion into the blood
2. Rate of clearance from the blood- "metabolic clearance rate" (protein-bound hormones are cleared at much slower rate.)

The clearance rate for hormones from the blood occurs in several ways:

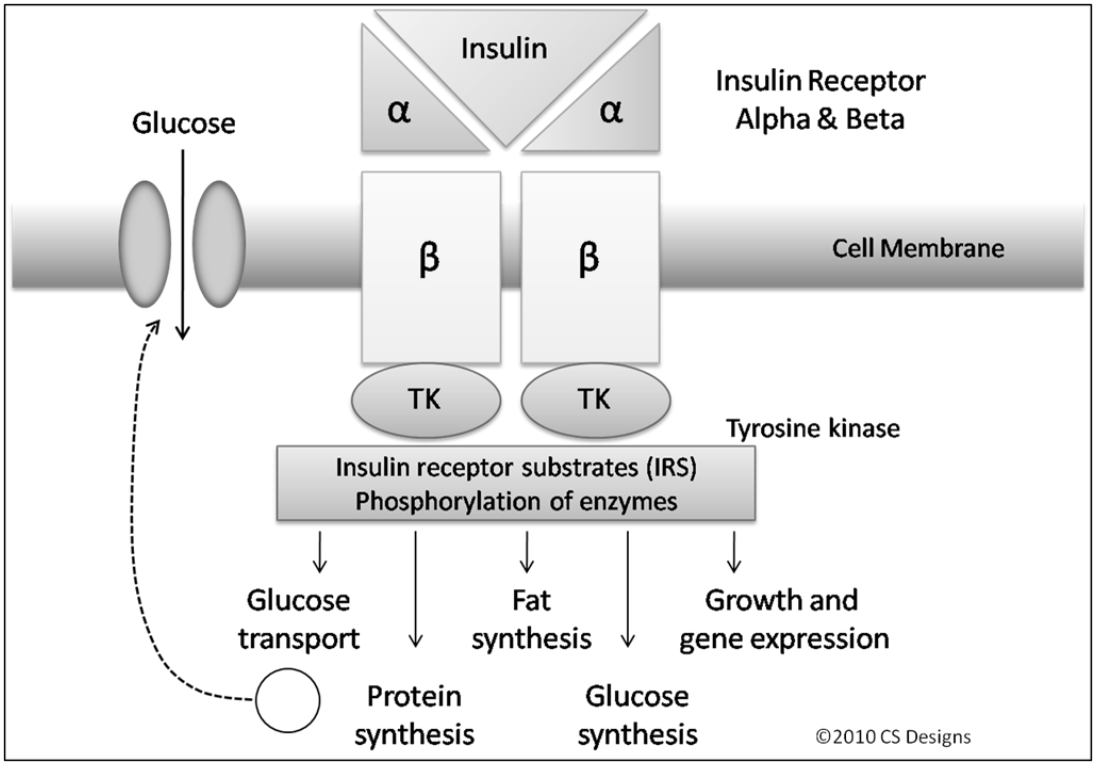
1. Metabolic destruction by the tissues (degraded by enzymes at their target site)
2. Binding with the tissues
3. Excretion by the liver into the bile (Phase I and Phase II detoxification)
4. Excretion by the kidneys into the urine

Target Cells, Hormone Receptors and Principle Mechanism of Hormone Action

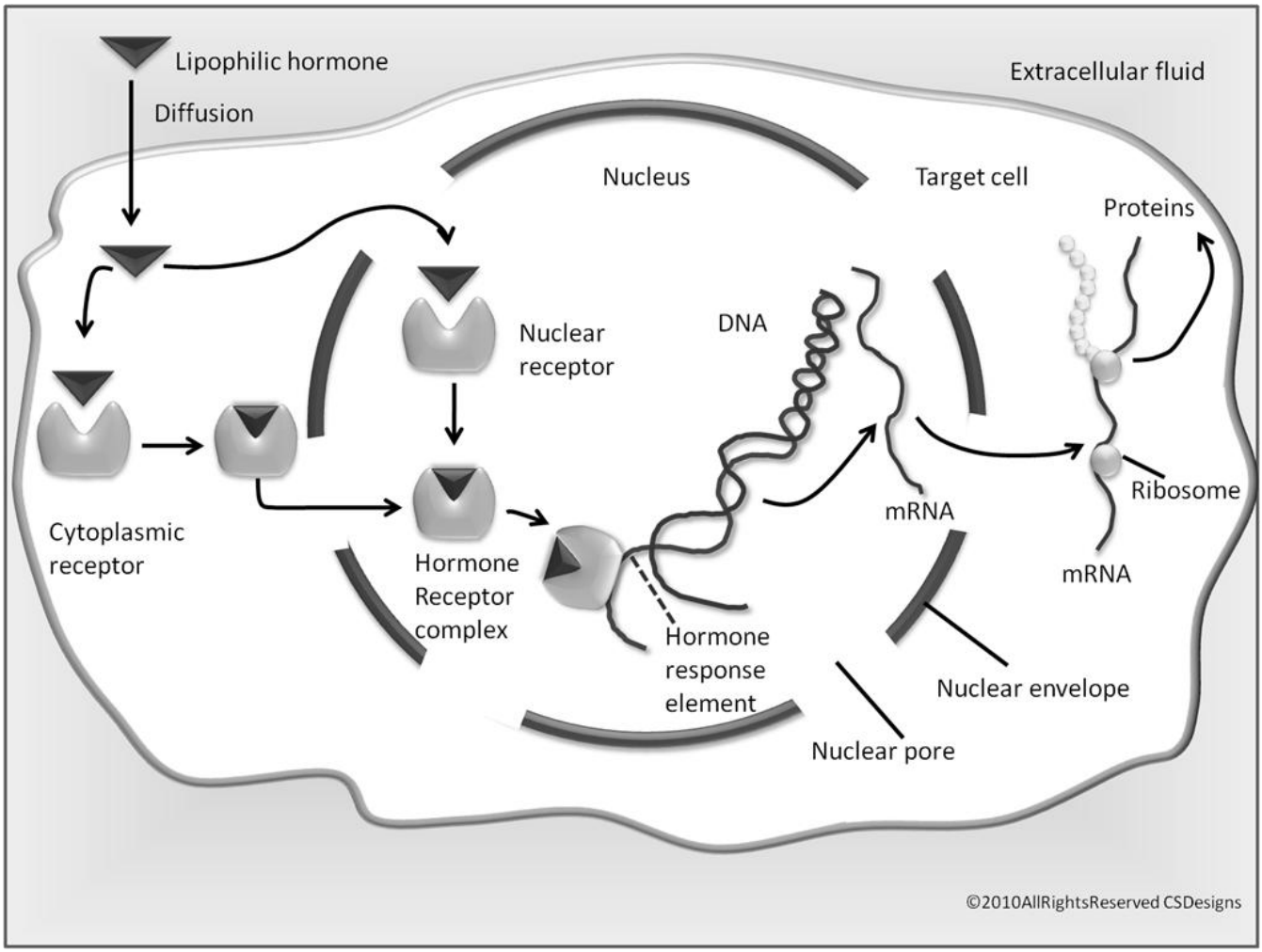
Tissues capable of responding to endocrines have two properties in common: one: they possess a receptor having very high affinity for hormone, and two: the receptor is coupled to a process that regulates metabolism of the target cells.

1. *Cell Surface Receptors (in or on the surface)* - Receptors for most amino acid-derived hormones and all peptide hormones are located on *the plasma membrane*. Activation of these receptors by hormones (the first messenger) leads to the intracellular production of a second messenger, such as cAMP, which is responsible for initiating the intracellular biological response.

   - Protein, peptides, and catecholamine – example (catecholamines –epinephrine, norepinephrine and dopamine)
   - Mechanism of Action – generation of second messengers which alter the activity of molecules in the cell, usually enzymes



2. *Intracellular Receptors (in the cytoplasm or in the nucleus)* - Steroid and thyroid hormones are hydrophobic and diffuse from their binding proteins in the plasma, across the plasma membrane to *intracellularly localized **receptors***. Thyroid hormone enters the cell by facilitated diffusion and steroid hormones enter the cell by simple diffusion. The resultant complex of steroid and receptor *bind to response elements of nuclear DNA*, regulating the production of mRNA for specific proteins.[1]

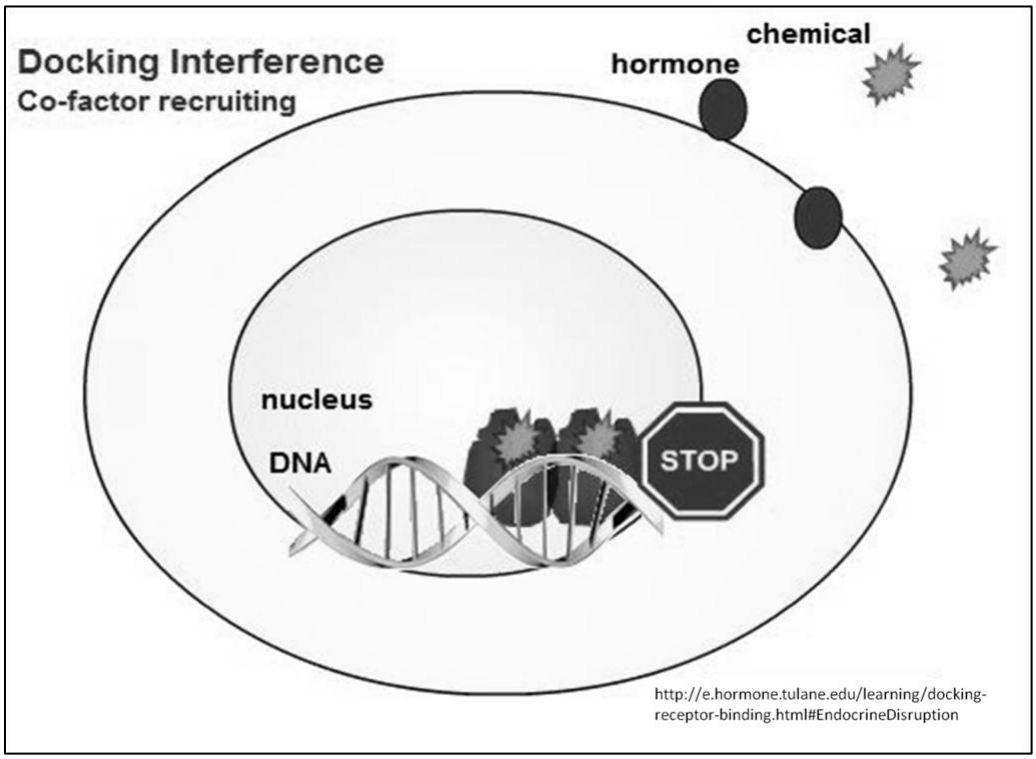


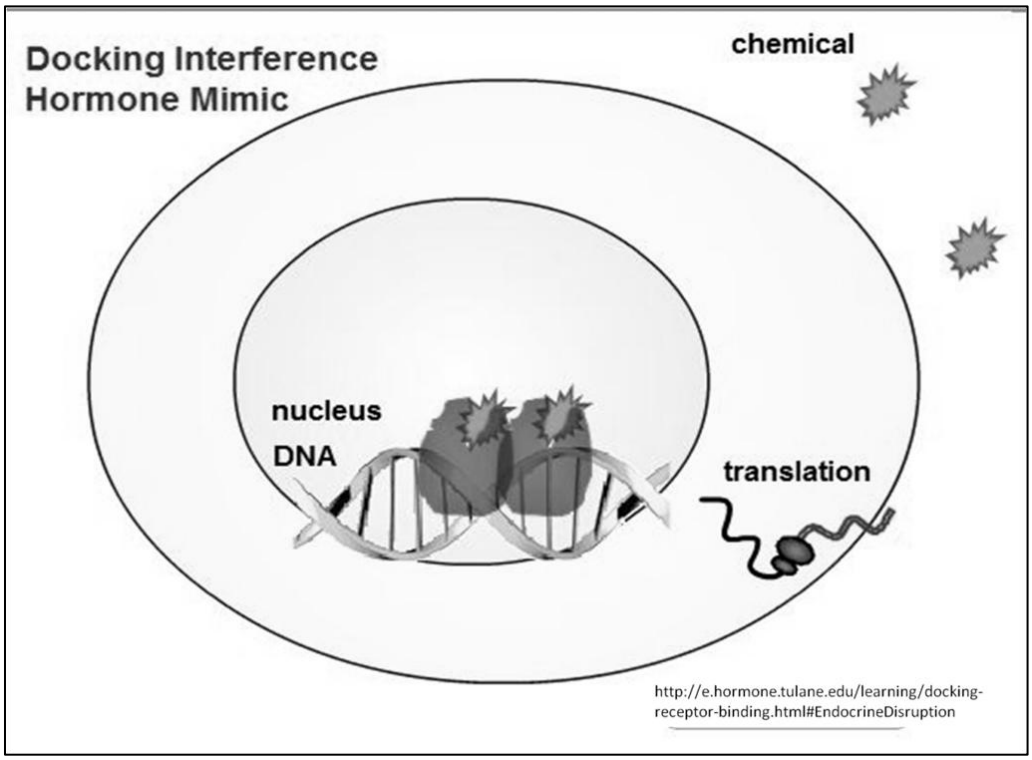
Endocrine Disrupting Chemical (Hormone Disruptors)

The EPA (Environmental Protection Agency) has defined endocrine disruptors as the following:

- Chemicals with potential to interfere with the function of the endocrine system
- Chemicals (endocrine disrupting chemicals) are exogenous agents that interfere with the production, release, transport, metabolism, binding, action, or elimination of the natural hormones in the body responsible for the maintenance of homeostasis and the regulation of developmental processes.
- EDC's can include man-made chemicals such as pesticides and plasticizers, natural chemicals found in plants (phytoestrogens), pharmaceuticals, or hormones that are excreted in animal or human waste.

"Endocrine-disrupting chemicals were originally thought to exert actions primarily through nuclear hormone receptors, including estrogen receptors (ERs), androgen receptors (ARs), progesterone receptors, thyroid receptors (TRs), and retinoid receptors, among others. Today, basic scientific research shows that the mechanism is much broader than originally recognized. Thus, endocrine disruptors act via nuclear receptors, non-steroid receptors (e.g. neurotransmitter receptors such as serotonin receptor, dopamine receptor, and norepinephrine receptor), and orphan receptors, enzymatic pathways involved in steroid biosynthesis and/or metabolism, and numerous other mechanisms that converge upon the endocrine and reproductive systems. Thus, from a physiological perspective, an endocrine-disrupting substance is a compound, either natural or synthetic, which, through environmental or inappropriate developmental exposure, alters the hormonal and homeostatic systems that enable the organism to communicate with and respond to its environment."[3]

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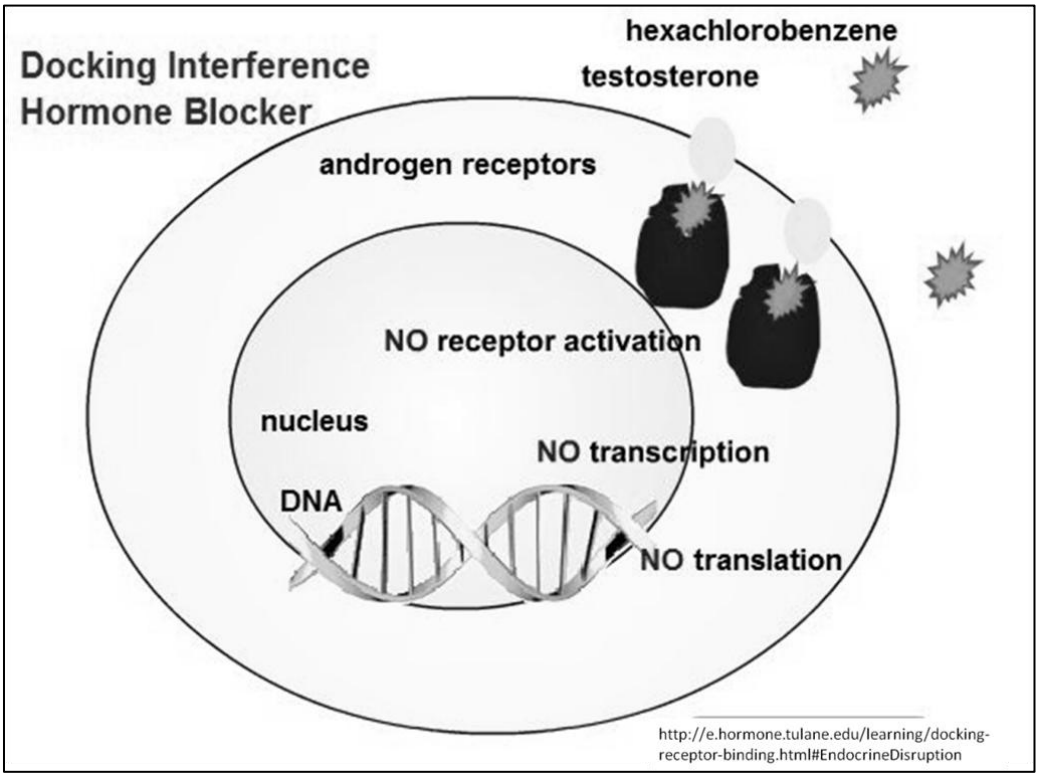
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DNA
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Widespread Pollutants with Endocrine-Disrupting Effects

Persistent organohalogens

Compounds	Hormone system affected
Benzenehexachloride (BHC)	Thyroid
1,2-dibromoethane	Reproductive
Chloroform	Reproductive
Dioxins and furans	Estrogen
Octachlorostyrene	Thyroid
PBBs	Estrogens/Thyroid
PCBs	Estrogen/Androgen/Thyroid
PCB, hydroxylated	Thyroid
PBDEs	Thyroid
Pentachlorophenol	Thyroid

Food Antioxidant

Compound	Hormone System Affected
Butylated Hydroxyanisole (BHA)	Estrogen

Pesticide

Compound	Hormone System Affected
Acetochlor	Thyroid (decrease of thyroid hormone levels, increase in TSH)
Alachlor	Thyroid
Aldrin	Estrogen
Allethrin, d-trans	Estrogen
Amitrol	Thyroid
Atrazine	Neuroendocrine-pituitary (depression of LH surge), testosterone metabolism
Carbaryl	Estrogen and Progesterone
Chlofentezine	Thyroid
Chlordane	Testosterone and Progesterone
Cypermethrin	Disruption of reproductive system
DDT	Estrogen
DDT Metabolite, p,p'-DDE	Androgen
Dicofol (Kelthane)	Estrogen
Dieldrin	Estrogen
Endosulfan	Estrogen
Ethylene thiourea	Thyroid
Fenarimol	Estrogen
Fenbuconazole	Thyroid
Fenitrothion	Antiandrogen
Fenvalerate	Estrogen

Pesticide (con't)

Fipronil	Thyroid
Heptachlor	Thyroid
Heptachlor-epoxide	Thyroid/reproductive
Iprodione	Inhibition of testosterone synthesis
Karate/cyhalothrin	Thyroid
Kepone (Chlordecone)	Estrogen
Ketoconazole	Effects on reproductive systems
Lindane (Hexachlorocyclohexane)	Estrogen/Androgen
Linuron	Androgen
Malathion	Thyroid
Mancozeb	Thyroid
Maneb	Thyroid
Methomyl	Thyroid
Methoxychlor	Estrogen
Metribuzin	Thyroid
Mirex	Antiandrogenic activity; inhibits production of LH. Potentially thyroid
Nitrofen	Thyroid
Nonachlor, trans-	Estrogen
Oxychlordane	Reproductive
Pendimethalin	Thyroid
Pentachloronitrobenzene	Thyroid
Permethrin	Estrogenic
Procymidone	Androgen
Prodiamine	Thyroid
Pyrimethanil	Thyroid
Sumithrin	Androgen
Tarstar	Thyroid
Thiazopyr	Thyroid
Thiram	Aneuroendocrine-pituitary (depression of LH surge), thyroid (decrease of T4, increase of TSH)
Toxaphene	Estrogen/Thyroid
Triadimefon	Estrogen
Triadimenol	Estrogen
Tributyltin	Reproductive
Trifluralin	Reproductive/Metabolic
Vinclozolin	Androgen
Zineb	Thyroid
Ziram	Thyroid

Phthalate

Compound	Hormone System Affected
Butyl benzyl phthalate	Estrogen
Di-n-butyl phthalate (DBP)	Estrogen, Androgen
Di-ethylhexyl phthalate (DEHP)	Estrogen, Androgen
Diethyl Phthalate (DEP)	Estrogen

Other Compounds

Compound	Hormone System Affected
Benzophenone	Estrogen
Bisphenol A	Estrogen
Bisphenol F	Estrogen
Benzo(a)pyrene	Androgen
Carbendazim	Reproductive
Ethane Dimethane Sulphonate	Reproductive
Perfluorooctane sulfonate (PFOS)	Thyroid, Reproductive
Nonylphenol, octylphenol	Estrogen
Resorcinol	Thyroid
Styrene dimmers and trimers	Estrogen

Metals

Compound	Hormone System Affected
Arsenic	Glucocorticoids
Cadmium	Estrogenic
Lead	Reproductive
Mercury	Reproductive/Thyroid

Summary

As stated earlier in this lesson, chemical messengers are part of the endocrine system, nervous system and immune system, as well as other systems in the body. When measuring any of these messengers in biological fluids, clinicians often consider replacing the low level substance or substances without giving consideration to numerous factors involved in hormone (and chemical messenger) regulation. For example, a low amount of a substance may be due to several conditions that effect or disrupt the feedback mechanism such as tissue sensitivity, the presences of endocrine disruptors, nutrient depletion and metabolism dysfunction. An excess of a substance may be caused by a reduced sensitivity, as in insulin and thyroid resistance.

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