Pathology of ENDOCRINE SYSTEM

Endocrine glands are collection of specialized cells that synthesize, store and release their secretion directly into the blood stream. They are capable of responding to internal & external environments for coordinating a multiplicity of activities that maintain homeostasis.

Endocrine cells that produce **Polypeptide hormones**, have (i) well developed Endoplasmic reticulum with attached Ribosomes that assemble hormone and (ii) a prominent Golgi apparatus for packaging hormone into granules for intracellular storage & transport.

Steroid hormone-secreting cells have large Lipid Bodies in the cytoplasm that contain Cholesterol and other precursor molecules. The lipid bodies are in close proximity to extensive tubular network of smooth endoplasmic reticulum (ER) & Large Mitochondira that contain the Hydroxylase & Dehydrogenase Enzyme System.

Steroid-producing cells lack secretary granules & do not store significant amount of Preformed hormones.

- Hormones derived from TYROSINE amino acid : Catecholamines (Polypeptides – like Epinephrine and Norepinephrine) & Iodothyronine Hormones (are Steroids – like T3 & T4/Thyroxine)

MECHANISM of Endocrine Diseases / Pathophysiology of Endocrine Disease

Diseases of Endocrine system result in variety of pathogenic mechanisms. These diseases may eventually lead to ABNORMALITIES / DISTURBANCES in:

I. In Biosynthesis / Secretion of Hormones
II. In Hormones interaction with specific Receptors on Target cells
III. Or in Post-receptor signals and responses

The sequel of any such disturbances include either underproduction / overproduction of hormones and the diseases result from “too little or too much” hormones.

Briefly, various Pathogenic mechanisms of endocrine diseases have been classified broadly as below:

1. **PRIMARY HYPO-FUNCTION of Endocrine Glands:**

   Here hormone secretion becomes Sub-normal (below normal) due to (a) destruction of secretory cells by disease, (b) failure of Endocrine glands to develop properly or , (c) biochemical defect in synthetic pathway of a hormone.

Eg.: Immune-mediated Injury causes Hypofunction of glands like Adrenal Cortex, Thyroid Glands etc.

Eg.2: Failure of gland development also results in Primary Hypofunction. Example-failure of 'Oro-Pharyngeal Ectoderm' to differentiate into the hormone-secreting cells of Anterior Pituitary (Adenohypophysis) in Dogs, resulting in **PITUITARY DWARFISM**.

2. **SECONDARY HYPO-FUNCTION of Endocrine Gland:**

Destructive Lesion in one Endocrine Gland, interferes with secretion of Tropic Hormones. Reduced expression of Hormone from the gland, result in Hypofunction of target Organs. So, the Hypofunction of target endocrine gland is SECONDARY to the effect on Organ releasing tropic Hormones.

Eg: Neoplasm of Pituitary – interference secretion of various Pituitary Tropic Hormone – leading to Hypofunction of Adrenal Cortex, Thyroid, Gonads etc.

3. **PRIMARY HYPER-FUNCTION of Endocrine Gland**

   Here, any lesion like Neoplasms in Endocrine Gland, synthesize and secrete a hormone at an Autonomous Rate. Thus, Hormones are secreted in excess of body's ability to utilize & degrade, so resulting in syndrome of 'Hormone Excess'.

   Eg: Hyperfunction of Parathyroid Chief Cell OR Thyroid-C cells OR Secretory cells of Adrenal Medulla.

4. **SECONDARY HYPERFUNCTION of Endocrine Gland:**

Here, a Lesion in one Endocrine Gland (eg. Anterior Pituitary), which secretes tropic hormone - leads to excess secretion of tropic hormones – which eventually turns on leading to long-term stimulation and hyper-secretion of hormone by Target Endocrine Organ.

Classical Eg.: ACTH-secreting Neoplasms derived from Pituitary corticotrophs in Dogs - result in hypertrophy and hyperplasia of secretory cells of Adrenal Cortex and leads excess secretion & activity of Cortisol

5. HYPERSECREATION of Hormones or Hormone-like factors from Non-Endocrine Neoplasms:

Most of such released substances are Polypeptides - & Steroid substances are not secreted by Non-Endocrine Neoplasms.

Classical Eg.: Adenocarcinomas of Apocrine gland at Anal sac of Dog – leads to produce Parathyroid hormone related Protein (PTHrP) – it stimulates Ca+ metabolism from Bones – development of persistent Hypercalcemia; although Parathyroid Glands are smaller than normal.

6. ENDOCRINE DYSFUNCTION Due to Failure of Target Cells:

Steroid & Iodothyronine Hormones penetrate cell membranes , bind to cytosolic receptors & are transported to nucleus – where they interact with genetic information in cells to increase new protein synthesis.

Polypeptides / Catecholamines - bind to receptors on Cell Surface of target cells - activates membrane bound Adenylate Cyclase Enzyme – that generate intracellular messenger – cAMP – which elicit a Physiological response.

Failure of Target Cells to respond to a hormone, can therefore be due to a lack of Adenylate cyclase in cell membrane or Down-regulation/ destruction of cytosolic / cell surface receptors.

7. ENDOCRINE HYPERACTIVITY – Secondary to Disease in other Organs:

Eg.: Hyperparathyroidism – that develop secondary to Chronic renal failures or Nutritional imbalances – leads retention of 'Phosphorus' and the subsequent destruction of PCT cells then interfere metabolic activation of Vitamin-D - By enzymes Alpha-1-hydroxylase in Kidneys – resulting in deficiency of Vit-D.

It further cause impaired Intestine Absorption of calcium – resulting in progressive **Hypocalcemia** – It in turn lead a long-term Parathyroid Stimulation – and Generalized Demineralization of Skeletal Bones..

8. FAILURE of FOETAL Endocrine Function:

Subnormal foetal endocrine function interfere foetal development, resulting Prolonged Gestation.

Eg.: in few breeds, there is failure of Adenohypophysis development (Ant. Pituitary) due to Genetic Defects (through normal Neurophypophysis) – leading to lack of Foetal tropic hormones in last trimester – and resulting HYPOPLASIA of target Endocrine Organ like Adrenal Cortex, Gonads and Thyroid Follicular Cells.

9. ENDOCRINE DYSFUNCTION resulting from Abnormal Degradation of Hormone (HYPER):

Here hormone secretion is Normal, but due to decreased Degradation / utilization rate – the **Blood levels are Raised**

Classical Eg**:** is Syndrome of Feminization (in Humans) due to Hypersecretion of estrogens associated with CIRRHOSIS & decreased Hepatic Degradation of estrogens.

Eg: Parathyroid hormones is normally degraded in Kidneys - and in Chronic Renal Diseases – due to reduced renal degradation of parathyroid hormones – leads Decrease urinary excretion of calcium - it leads to Systemic State of **Hypercalcemia**.

10. IATROGENIC (Physician-induced) SYNDROMES of Hormone Excess:

Administration of hormones, influence the activity of Target cells & result in Clinical disturbance.

Eg 1: Prolonged daily administration of high doses of Adrenal Corticosteroids (for treatment) leads to functional disturbances associated with **Cortisol excess**, like muscle weakness, Hair-loss etc., and marked atrophy of Adrenal Cortex.

Eg 2: Injection of Synthetic Progesterone for preventing Estrus in Dogs, stimulate Increased Secretion of Growth Hormone by Pituitary (somatotrophs) resulting in ACROMEGALY.

Pathology of PITUITARY GLAND (Hypophysis)

Pituitary Gland is considered the "Conductor or Master" of Endocrine Orchestra".

It has two important parts:

1. **Anterior Pituitary (AdenoHypophysis)** – Composed of Epithelial cells arranged as Cords / Nests and is basically mixture of Secretory cells & is derived from Rathke's Pouch (Primitive Foregut)
2. **Posterior Pituitary (NeuroHypophysis)** – it represents Extension of Brain originating from Diencephalon and is composed of Tangled / Twisted Nerve Fibres.

1. ADENOHYPOPHYSIS is divided into 3 parts:
   - A. pars distalis (largest portion)
   - B. pars tuberalis
   - C. pars intermedia

SECRETORY Cells of AdenoHypophysis (named upon its staining characteristics):

S. No.	Class of Cells	Cells Types	Hormones Released
1.	**ACIDOPHILS**	**Somatotrophs**	Growth Hormone (GH)
		Luteotrophs	Luteotropic Hormone (LTH or Prolactin)
2.	**BASOPHILS**	**Gonadotrophs**	Leutinizing Hormone (LH)
			Follicle Stimulating Hormone (FSH)
		Thyrotrophs	Thyrotropic Hormones like Thyroid Stimulating Hormone (TSH)
3.	**CHROMOPHOBES**	Do not reveal any Cytoplasmic Granules (**Corticotrophs**)	Adreno-Cortocitropic Hormone (ACTH)
			Melanocyte Stimulating Hormone (MSH)

2. NEURONOHYPOPHYSIS secretes :

A. Anti-Diuretic Hormone (ADH) also k.a. Vasopressin
B. Oxytocin

PITUITARY DWARFISM in Dogs:

Due to failure of ORO-PHARYNGEAL ECTODERM of RATHKE'S POUCH to differentiate into (tropic hormones secreting) Secretory Cells of ***pars distalis*** (adenohypophyseal hormone).

It results in formation of Enlarged, Multi-lobulated Cyst in ***Sella turcica*** (concavity of sphenoid bone that house Pituitary Gland) and an **Absence of Adenohypophysis**.

JUVENILE PANHYPOPITUITARISM:

Diminished secretion of all Pituitary Hormones in young animals (Inherited disease by Autosomal recessive gene).

- Dwarf pups appear normal from Birth – 2 months. Then gradual slow growth – retention of Puppy Haircoat – absence of Puppy Guard Hairs (Protective Haircoat).
- Alopecia develops gradually
- Progressive Hyperpigmentation of Skin

HYPERPITUITARISM – It is manifested with Overgrowth and Proliferation of Bones. (Eg. Acidophilic Cell Adenoma – leads High Somatotropin - High GH)

GIGANTISM : is due to increased secretion of SOMATOTROPIN and is seen in **YOUNG** growing individuals. Individual grows Tall and skin/sub-cut tissue shows fibrous hyperplasia

ACROMEGALY- Its seen in **ADULTS** & since no growth in bone occurs, so Bones becomes Thicker and Broader. Enlargement of EXTREMITIES and KYPHOSIS i.e. excessive outward curvature of the spine, causing hunching of the back, is also seen.

HYPOPITUITARISM

- Pituitary Dwarfism or **Infantilism**
- Symmond's Disease (**Pituitary Cachexia**) [Dogs- post partum necrosis of Pituitary due to hemorrhage led thrombosis]
- Diabetes insipidus

DIABETES INSIPIDUS: is a bio-metabolic disorder that results when ADH production or secretion is reduced (due to failure of hypothalamic-hypophyseal system) OR when target cells in kidney lack Biochemical Pathways necessary to respond to Circulating hormones. Its then that resorption of water from glomerular filtrate do not take place, so large quantities of urine with Low Specific Gravity is passed. This condition is called "Diabetes insipidus" and it is a form of POLYURIA caused by an inability to concentrate urine.

It called 'insipidus' because Urine is insipid (w/o colour taste). It is in TWO FORMS:-

1. **Pituitary Form / Hypophyseal / Central Form**: due to Pituitary neoplasms - DI results from Compression & Destruction of pars nervosa (of Neurohypophysis) or SupraOptic Nucleus of Hypothalamus.

   Disturbance of ADH Synthesis /Secretion – due to large pituitary neoplasms – or dorsally expanding Cyst – or Inflammatory Granuloma.

   Compression interrupts Axons that Transport ADH from its site of production (Supraoptic Nucleus of Hypothalamus) – to the site of release in Cappilary network of pars nervosa.

   Clinical Signs: Ploydipsia (Excess Thirst) ; Polyuria (Excess Urine); and Low Specific Gravity of Urine (less than 1.01)

2. **Nephrogenic Form**: is result of the result of the failure of renal tubular epithelial cells to respond to ADH and can occur due to Chronic Renal Diseases

In either form, HYPOTONIC URINE (with osmolality equivalent to or less than that of plasma) is produced, even in the face of water deprivation

Pituitary pars intermedia dysfunction (PPID) is the most commonly diagnosed endocrine disorder of horses. Although it has been called **Equine Cushing's disease**, its pathogenesis is distinct from that of human or Canine Cushing's disease.

PATHOLOGY of THYROID GLAND

Thyroid is LARGEST Endocrine Organ and Histologically, Thyroid Gland consists of FOLLICLES of varying sizes that contain COLLOID.

Follicles are lined by Cuboidal-Columnar FOLLICULAR CELLS that have numerous long Microvilli and they produce COLLOID. Their Secretory Pole is directed towards "Lumen of Follicle" and Cells have large rER and Golgi apparatus for synthesis and packaging of Protein THYROGLOBULIN.

The second Endocrine Cell population is k.a. "**C-cells**" or **Parafollicular Cells** that secrete hormone '**Calcitonin**'. These are located either in the wall between follicular cells or as small groups between follicles. Secretory Pole is directed towards "Inter-follicular Capillaries"

Thyroxine (T4) and T3 are Steroid-like Iodothyronine Hormones

Calcitonin is Polypeptide Hormone

Synthesis of THYROID HORMONE:

Active circulating Thyroid hormones are (i) Thyroxine / Tetra-IodoThyronine (T4) and (ii) Tri-IodoThyro**nine** (T3)

Synthesis of Thyroid Hormone is unique, as its final assembly takes places EXTRACELLULARLY in Follicle lumen.-

1. Follicular cells take up IOD**IDE** from Plasma - this IODIDE is oxidized to IO**DINE** (by Enz. IODIDE PEROXIDASE) inside the **microvilli** of Follicular cells.
2. Thyroglobulin, is a glycoprotein is also synthesized on ribosomes of rER inside Follicular Cells utilizing 'TYROSINE' amino acid along with others. Thyroglobulin is packed into vesicles and release in lumen.
3. In Follicular Lumen, Iodine is bound to Tyrosine residues (Iodination), to form the mono-iodotyrosine (MIT) & di-iootyrosine residues.
4. The MIT and DIt undergo coupling in presence of Enzyme PEROXIDASE to from T3 (1 MIT+2 DIT) and T4 (1 DIT+ 1 DIT).

5. Secretion of Thyroid hormone in blood stream from Follicular Colloid (in lumen) is initiated by elongation of microvilli - pseudopodia formation in the Follicular Cells -- Phagocytize Colloid as droplets --- fuse with lysosomes - finally diffuse from cells into neighboring capillaries

DEGENERATIVE AND INFLAMMATORY LESIONS of Thyroid

1. **Follicular Atrophy**:

   Its seen in Dogs - Progressive Loss of Follicular Epithelium & its replacement with Adipose connective tissue, with minimal inflammatory response. Clinical Signs of Hypothyroidism are seen and Thyroid Gland is markedly reduced in size

2. **Lymphocytic Thyroiditis** (Immune Mediated):-

   Seen mostly in Dogs - as an Inherited auto-immune disease linked to Production of 'auto-antibodies' directed against Thyroglobulin, and other Colloid antigens.

   Thyroid show Multifocal to Diffuse infiltration of Lymphocytes, Plasma Cells & Macrophages; Colloid is Vacuolated & many contain cellular debris with inflammatory cells

3. GOITRE

GOITRE

It is defined as the "Non-Inflammatory" and "Non-Neoplastic" Enlargement of Thyroid Glands resulting from "inadequate Thyroxine synthesis & Decreased Blood Levels of T3 & T4" - which commonly results from IODINE Deficiency – occurs in all Domestic Animals & Birds.

The Enlargement can be due to (i) Increase in Thyroid tissue (Hypertrophy or Hyperplasia) OR (ii) Increased amount of Colloid, distending the Lumen.

In Hyperplasia, Follicular cell become Tall & Columnar - and Formation of Papillary Folds in the Epithelial Linings.

The GOITRE is generally classified into 5 different types:

1. DIFFUSE / HYPERPLASTIC / PARENCHYMATOUS GOITRE
2. COLLOID GOITRE / SIMPLE Goitre
3. NODULAR / ADENOMATOUS GOITRE
4. EXOPTHALMIC GOITRE
5. CONGENITAL (Dys-hormonogenetic) GOITRE

DIFFUSE / HYPERPLASTIC / PARENCHYMATOUS GOITRE:

Its characterized by marked Hyperplasia of Follicular Cells and depletion of Colloid

Etiology:

a. Iodine Deficiency / Iodine Deficient Diets

b. Goitrogenic Substances in Feed - [**Goitrogenic substances** are naturally occurring substances that disrupt production of thyroid hormone by interfering / disrupting with Iodine uptake in Thyroid Glands. Eg: ThioUracil, Isoflavones (in Soybean); ThioUrea, Sulphonamides in Drugs; Plants of family Brassicaceae (Soybean & Cabbage)].

c. Genetic Defects – in enzyme responsible for biosynthesis of Thyroid Hormone, *Eg*. Iodide-peroxidase

d. In certain cases – Iodine Excess too can lead.

Pathogenesis:

TSH stimulates the production of Thyroxine while increased Thyroxine blood levels REDUCES TSH release in balancing fashion.

- ✓ In Idoine Defficinecy - inadequate Thyroxine Synthesis -- Reduced T4 & T3 levels -- Pituitayr so stimulate more of TSH -- result in CONTINUED and GREATER stimulation of Thyroid -- Thyroid undergo Hyperplasia/hypertrophy of Follicular cells -- THUS Enlarge to cause HYPERPLASTIC GOITRE
- ✓ Goitrogens leads to interference in Iodine Uptake & Inadequate Thyroxine syntheisis – leads to decreased concentration of T4 & T3 -- this stimulates Pituitary and Increase TSH
- ✓ In Excess of Iodine - High Level of Blood IoDIDE -- leads to Saturation of enzyme 'Iodide-peroxidase' and further down-regulation of enzyme -- leads to interference in synthesis of T3 & T4. It seen commonly in FOALS

Lesions: Thyroid Enlarged, Follicles are irregular in size with varying amount of colloid that is scanty / absent. Lining epithelium are Tall & Columnar with many having Papilary projections into the lumen

COLLOID GOITRE: (also k.a SIMPLE GOITRE)-

Its characterized by Enlargement & Distention of Follicles, which are filled with Colloid. This Goitre type is more common in Animals.

Etiology: Periodic Iodine Deficiency; Ingestion of Goitrogenic substances, Excess Physiological Demands in adolescents; Involution of Hyperplastic Goitre.. etc

Pathogenesis: Colloidal Goitre represents "Involutionary Phase" of Hyperplastic Goitre in Animals – that results when Iodine is 'Returned in Diet' or when "Iodine Defficiency is Periodic" or when requirement of Thyroxine have 'diminished in Older Animals'.

The Hyperplastic follicular cells continue to produce Colloids, BUT Endocytosis / Phagocytosis of Colloid by Follicular Cells is Decreased. Because in response to return of normal T3 & T4 Blood Levels, then the Pituitary TSH levels are diminished.

So, diminished TSH, induces Endocytosis of Colloid – while the Hyperplastic cells continue to produce the Colloid. This situation leads to progressive distention of Follicle and hence to Colloid Goitre.

Lesions: Both Thyroid Lobules are diffusely enlarged and increased in size BUT are more Translucent and Lighter in Colour. Microscopically, walls of follicles are stretched & columnar epithelium is become flattened.

NODULAR / ADENOMATOUS GOITRE:

Is characterized by MULTIPLE, SPHERICAL, White-to-Tan colored **NODULES** of varying sizes and is seen in OLD Horses, Cats and Dogs.

Etiology: The Nodules may be the outcome of alternating Hyperplasia, Hypertrophy and Involution processes affecting the Glands.

Lesions: Such nodules may Histologically be either 'Noduler Hyperplasia' OR 'Thyroid Adenoma'.

The Multifocal Nodular Hyperplasia in Most Animals (except Cats) are Endocrinologically INACTIVE and Histologically they are Not Encapsulated & result in minimal compression of adjacent parenchyma. Nodules are translucent, and contains Cysts or vesicles filled with Colloids.

Adenomas on other hand tend to be Solitary, Well Encapsulated and Fairly Uniform in histological structure and They cause COMPRESSION of Surrounding Parenchyma owing to progressive Growth. They are Endocrinologically ACTIVE.

EXOPTHALMIN GOITRE:-

Seen in Humans and not usually seen in animals. In Humans, its also known as GRAVE'S Disease / TOXIC Goitre / OR GOITRE of HYPERTHYROIDISM and its considered of Auto-Immune Origin.

CONGENITAL (Dys-hormonogenetic) GOITRE:-

It is an "Inherited Form of Goitre" seen in Sheep-Goats-& Cattle. It is GOITRE of HYPOTHYROIDISM and signs include Poor Growth Rate, Absence of normal Wool, Weakness, Subcutaneous Myxodematous Swellings.

Basis cause is Inherited defect in Thyroglobulin Biosynthesis.

Define Cretinism: Growth Retardation or Physical Deformity / Dwarfism / Mental Retardation most often due to Congenital Iodine Deficiency Syndrome / Congenital Hypothyroidism

PATHOLOGY associated with ADRENAL GLANDS

<table>
<tr><th colspan="3">ADRENALS</th></tr>
<tr><td colspan="2">**CORTEX** (Outer)</td><td>**MEDULLA** (Inner)</td></tr>
<tr><td colspan="2">Mesoderm Origin</td><td>Ectoderm Origin (of Neural Crest)</td></tr>
<tr><td colspan="2">STEROID Secreting</td><td>CATECHOLAMINE Secreting</td></tr>
<tr><td>***Zona glomerulosa*** (Sigmoid 'S')</td><td>MINERALOCORTICOIDS (Aldosterone)</td><td rowspan="3">*Epinephrine (Adrenaline)

** NorEpinephrine (NorAdrenaline)</td></tr>
<tr><td>**Zona fasciculata** (long anastomosing Cords)</td><td>GLUCOCORTICOIDS (Cortisol ; CorticoSterone)</td></tr>
<tr><td>**Zona reticularis** (small grps; surrounded by cappilaries)</td><td>SEX STEROIDS (Progesterone; Estrogen or Androgens)</td></tr>
</table>

MINERALOCORTICOIDS:

The important one is **Aldosterone hormone** --- which regulates "Potassium Metabolism" and act on Distal Nephron to:

- ✓ Increase Tubular Excretion of Potassium (K+)
- ✓ Increase Uptake / Resorption of Na+ and Cl- from Glomerular filtrate

GLUCOCORTICOIDS: **Cortisol (Cortisone)** AND lesser Corticosterone

- ✓ Action on carbohydrate, Protein and Fat metabolism with (i) Tendency to Hyperglycemia & Increased Glucose production, (ii) Decreased Lipogenesis & Increased Lipolysis in Adipose Tissue
- ✓ Supress Inflammatory & Immunologic responses

- ✓ Negative effect on Wound Healing

SEX STEROIDS: Progesterone, Estrogen & Androgens

(VIRILISM : appearance of Secondary Male characters in Females)

HYPER-CORTISOLISM / HYPER-ADRENOCORTICISM

(commonly k.a. **CUSHING'S DISEASE**)

Relatively common in Older DOGS & sign/symptoms results mainly due to Chronic Overproduction and Prolonged Exposure to CORTISOLS by the Hyperactive Adrenal Cortex (middle layer; **Zona fasciculate).** Wide range of disturbances and lesions occurs from combined Glyconeogenic, Lipolytic, Protein Catabolic & Anti-inflammatory effects of Glucocorticoids.

Etiology:

i. Most common cause is **Functional Corticotroph Adenoma** (ACTH-secreting) of the Pituitary Glands. – It leads to Bilateral Adrenal Cortical Hypertrophy & Hyperplasia.
ii. Rarely, functional Adrenal Neoplasms

Signs & Lesions:

- ➢ Polyphagia - Appetite and Food intake in Increased
- ➢ Muscles of Abdomen / Extremities are weakened & atrophied
- ➢ Gradual Pendulous Abdomen / Enlargement
- ➢ LORDOSIS – abnormal curvature of spine; Muscle Trembling
- ➢ Hepatomegaly
- ➢ Skin Lesions over point of Wear – (i) Atrophy of Epidermis & Pilosebaceous apparatus AND (ii) Dystrophic Mineralization - Cutaneous calcification is characteristic lesion in Dogs. Numerous Calcium crystals deposited along collagen & Elastin in dermis, despite normal blood Ca+ & P concentrations

IATROGENIC HYPERADRENOCORTICISM is the result of glucocorticoid therapy, which results in decreased ACTH secretion and adrenocortical atrophy. Spontaneous Canine Cushing's Disease / Syndrome, in contrast, is usually the result of ACTH secretion by hyperplastic or neoplastic adenohypophyseal (anterior pituitary gland) corticotrophs, which causes bilateral, diffuse or multifocal adrenocortical hyperplasia, especially in the zona fasciculata.

Equine Cushing's Disease is different AND it is **Pituitary pars intermedia dysfunction (PPID)**

HYPO-ADRENOCORTICISM

(commonly k.a. **ADDISON'S DISEASE**)

(its NOT just **HYPO-Cortisolism but of HORMONES OF ALL Layers)**

Primarily its CHRONIC ADRENO-CORTICAL Insufficiency of mineralocorticoid and glucocorticoid hormones. It is usually attributed to autoimmune destruction of the adrenal cortex and is seen in Dogs AND They have BILATERAL Adreno-Cortical Atrophy involving ALL LAYERS of Adrenal Cortex.

Precise Pathogenesis is Not Known, however it could be Immune-Mediated.

Pituitary Lesions have not been found associated.

A. It occurs in Young Adults to Middle Aged Dogs AND result in marked alterations in Serum Levels of K+, Na+ and Cl- concentration. Less Potassium is excreted by Kidneys in Urine (**Hypokaluria**) resulting in marked excess in the Blood Potassium Levels (**Hyperkalemia**). Similarly there's Increased Na+ and Cl- levels in Urine and corresponding decline in Blood levels. Blood Hyponatremia & Hyperkalemia (electrolyte imbalance) are HALLMARK of Addison's Disease.

   Severe Hyperkalemia, leads to Cardiovascular Disturbances including pronounces **BRADYCARDIA** (Slow Heart Beat)

B. Decreased Production of Glucocorticoids leads to **HYPOGLYCEMIA** and **HYPERPIGMENTATION of SKIN** in Dogs (may be lack of Pituitary feedback OR Increase Levels of ACTH /MSH etc)

C. The Production of all the 3 classes of Corticosteroids is DEFICIENT.

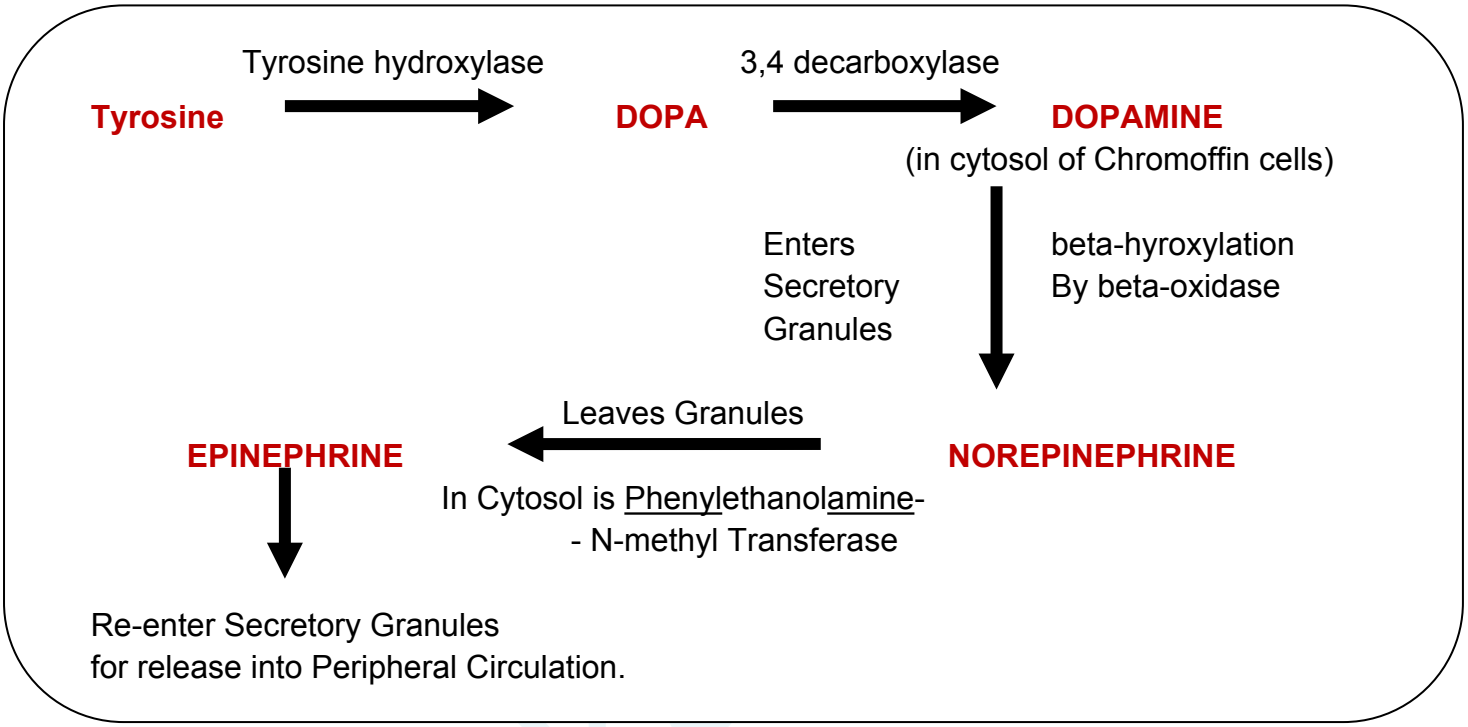
   Adrenal Cortex is reduced to almost 1/10th of its normal Thickness; Capsule is thickened and Fibroblastic Proliferation is noticed.

HYPERALDOSTERONISM

Primary hyperaldosteronism, known in human beings as Conn's disease, is increasingly recognized in **CATS** as the result of adrenocortical carcinoma, adenoma, or hyperplasia.

ADRENAL MEDULLA

Secretory cells of Adrenal medulla are called **CHROMAFFIN CELLS / Pheochromocytes** and few Ganglion Cells too.



The Action of "Phenylethanolamine - N-methyl Transferase" Enzyme is that it CONVERTS the Nor-Epinephrine to Epinephrine AND "It is Corticosteroid Hormone Dependent (Cortex)"

PHEOCHROMOCYTOMAS:

Pheochromocytomas are neoplasms of the **Chromaffin Cells** of the adrenal medulla, which may be Unilateral or Bilateral &usually occur in Cattle and Dogs.

Although **epinephrine** is the predominant catecholamine of the normal adult adrenal medulla, functional pheochromocytomas tend to produce mainly **norepinephrine**. Excessive catecholamine production by a pheochromocytoma can cause systemic hypertension.

NEUROBLASTOMAS are primitive neuroectodermal tumors that can develop in the central or peripheral nervous systems.

GANGLIONEUROMAS are frequently located in the adrenal medulla or within sympathetic ganglia. In ganglioneuroma, which develop in the adrenal medulla or in ganglia, the neoplastic cells differentiate into multipolar ganglionic neurons. Thus, the neoplastic tissue consists of neuronal cell bodies and bundles of axons.

Adrenal and para-adrenal neuroblastomas and ganglioneuromas resemble their counterparts elsewhere in the nervous system

DISORDERS OF THE CHEMORECEPTOR ORGANS

Chemoreceptor organs, especially the **Carotid Body** (near the bifurcation of the carotid arteries) and **Aortic Body** (near the ascending aorta at the base of the heart), can give rise to neoplasms called **CHEMODECTOMAS** or **PARAGANGLIOMAS**.

Aortic Body Chemodectomas are diagnosed more commonly than those of the carotid body in domestic animals, and they are observed mainly in dogs, especially in the brachycephalic breeds.