M.Sc. 4th Semester

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Paper: PHY-401

Unit:33

Module: 03 (Part 2)

Topics: Synthesis and secretion of thyroid hormone & Thyroid function in pregnancy

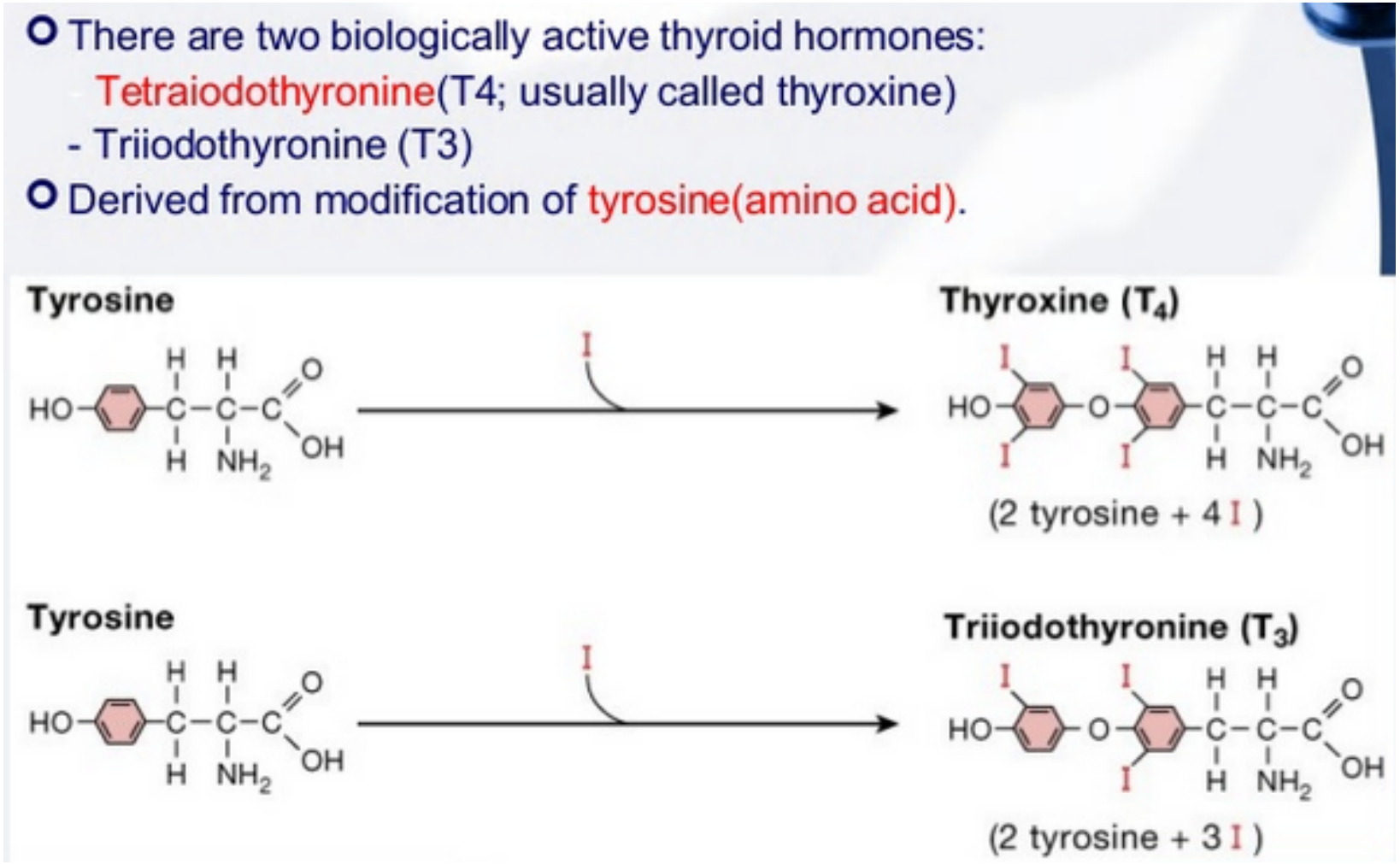
Name of the Teacher: Dr. Ankita Das

SYNTHESIS AND SECRETION OF THYROID HORMONES

Dr. Ankita Das

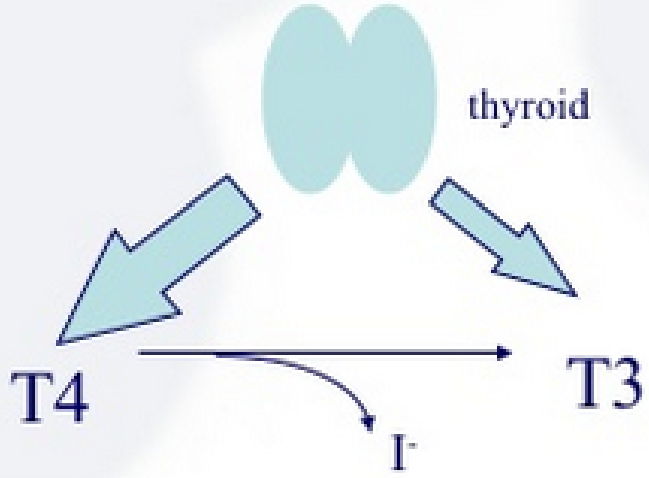
Thyroid Hormones:

- There are two biologically active thyroid hormones:
  - Tetraiodothyronine(T4; usually called thyroxine)
  - Triiodothyronine (T3)
- Derived from modification of tyrosine(amino acid).



Differences between T3 and T4

- The thyroid secretes about 80mg of T4, but only 5mg of T3 per day.
- However, T3 has a much greater biological activity about 10 folds than T4.
- An additional 25mg/day of T3 is produced by peripheral monodeiodination of T4 by enzyme called 5' Monodeiodenase.



- Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- Thus, adequate iodine intake either through diet or water is required for normal thyroid hormone production.
- Major sources of iodine are:
  - iodized salt
  - iodated bread
  - dairy products
  - shellfish
- Minimum requirement(RDA): 75 micrograms/day
- US intake: 200 - 500 micrograms/day

Iodine Metabolism

- Dietary iodine is absorbed in the GI tract, then taken up by the thyroid gland (or removed from the body by the kidneys).
- About 80% of the iodine is lost in urine where as only 20 % is taken up by the Thyroid follicular cells.
- The transport of iodide into follicular cells is dependent upon a Na^+/I^- co-transport system.
- Iodide taken up by the thyroid gland is oxidized by peroxide in the lumen of the follicle:

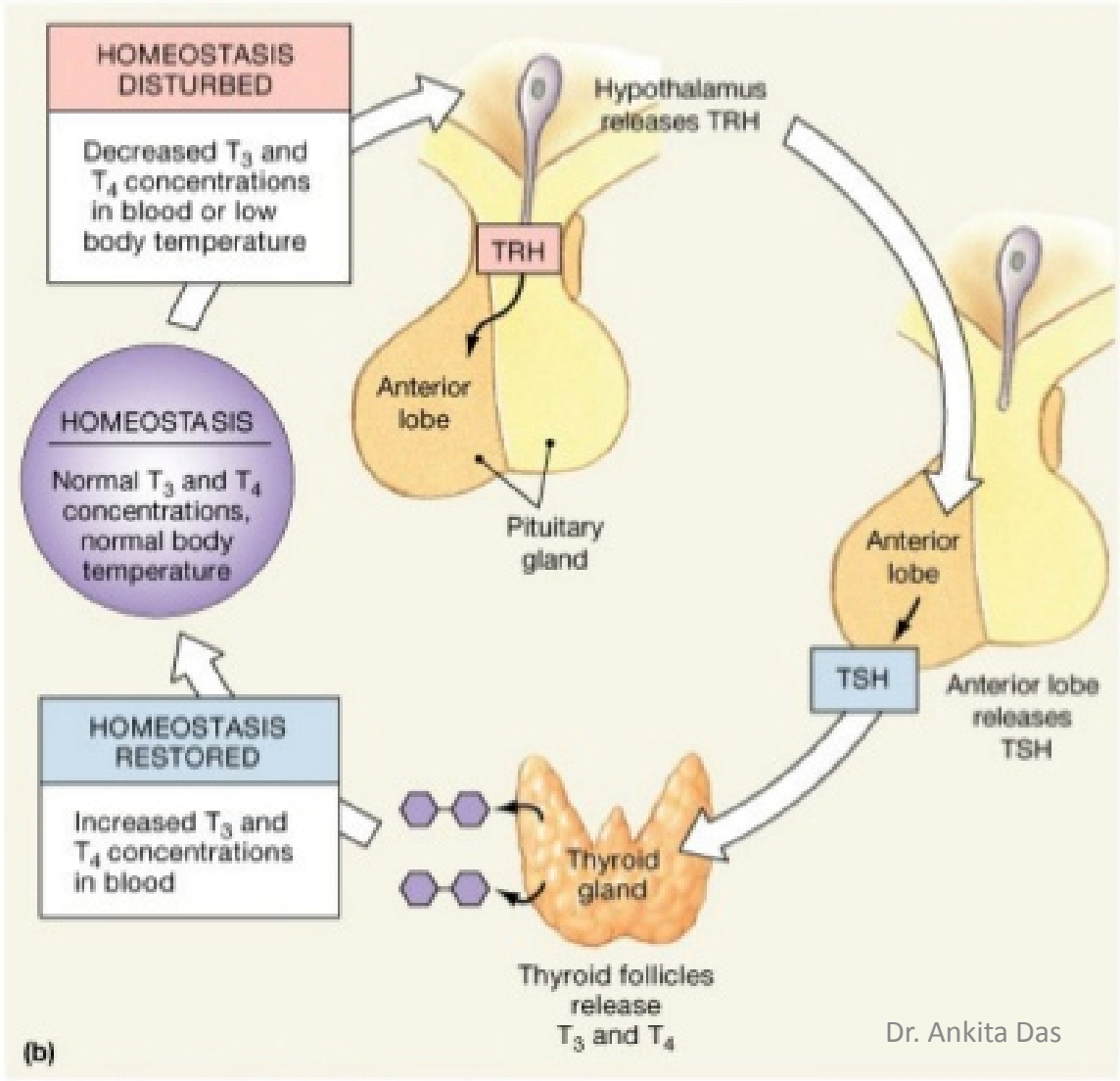
$$I^- \xrightarrow{\text{Peroxidase}} I^+$$

- Oxidized iodine can then be used in production of thyroid hormones.

Production of thyroglobulin

- Pituitary produces TSH, which binds to follicle cell receptors.
- The follicle cells of the thyroid produce thyroglobulin.
- Thyroglobulin is a very large glycoprotein.
- Thyroglobulin is released into the colloid space, where it's tyrosine residues are iodinated by I^+.
- This results in formation of monoiodotyrosine or diiodotyrosine.

REGULATION:


HOMEOSTASIS DISTURBED
Decreased T_3 and T_4 concentrations in blood or low body temperature
Hypothalamus releases TRH
TRH
Anterior lobe
Pituitary gland
HOMEOSTASIS
Normal T_3 and T_4 concentrations, normal body temperature
Anterior lobe
TSH
Anterior lobe releases TSH
HOMEOSTASIS RESTORED
Increased T_3 and T_4 concentrations in blood
Thyroid gland
Thyroid follicles release T_3 and T_4
(b)

Tyrosine -derived thyroid hormones

1- Tetraiodothyronine (thyroxine; T4).

2- Triiodothyronine (T3).

Synthesis of thyroid hormone

✓Thyroid hormone synthesis occurs in the follicular space of thyroid gland.

✓These hormones require:

1) **Thyroglobulin** (large protein molecule **TG**)
2) **Iodine** About 70% of the iodide in **TG** exists in the inactive precursors, **monoiodotyrosine (MIT)** and **diiodotyrosine (DIT),** while 30% is in the **iodothyronyl residues,** T4 and T3
3) **The amino acid tyrosine** is the starting point in the synthesis

Synthesis of thyroid hormone based the following steps:

Step 1: Uptake and concentrate of I^-

✓The thyroid is able to concentrate I− in luminal surface of the follicular cell.

✓This energitic process is linked to the (Na+-K+ ATPase pump).

✓Uptake of thyroidal I− is stimulated by TSH and inhibited by excess of iodine.

Step 2: Oxidation of iodine (organification)

✓Iodide is converted to iodine based **hyroperoxidase** (tetrameric protein) that requires hydrogen peroxide as an oxidizing agent.

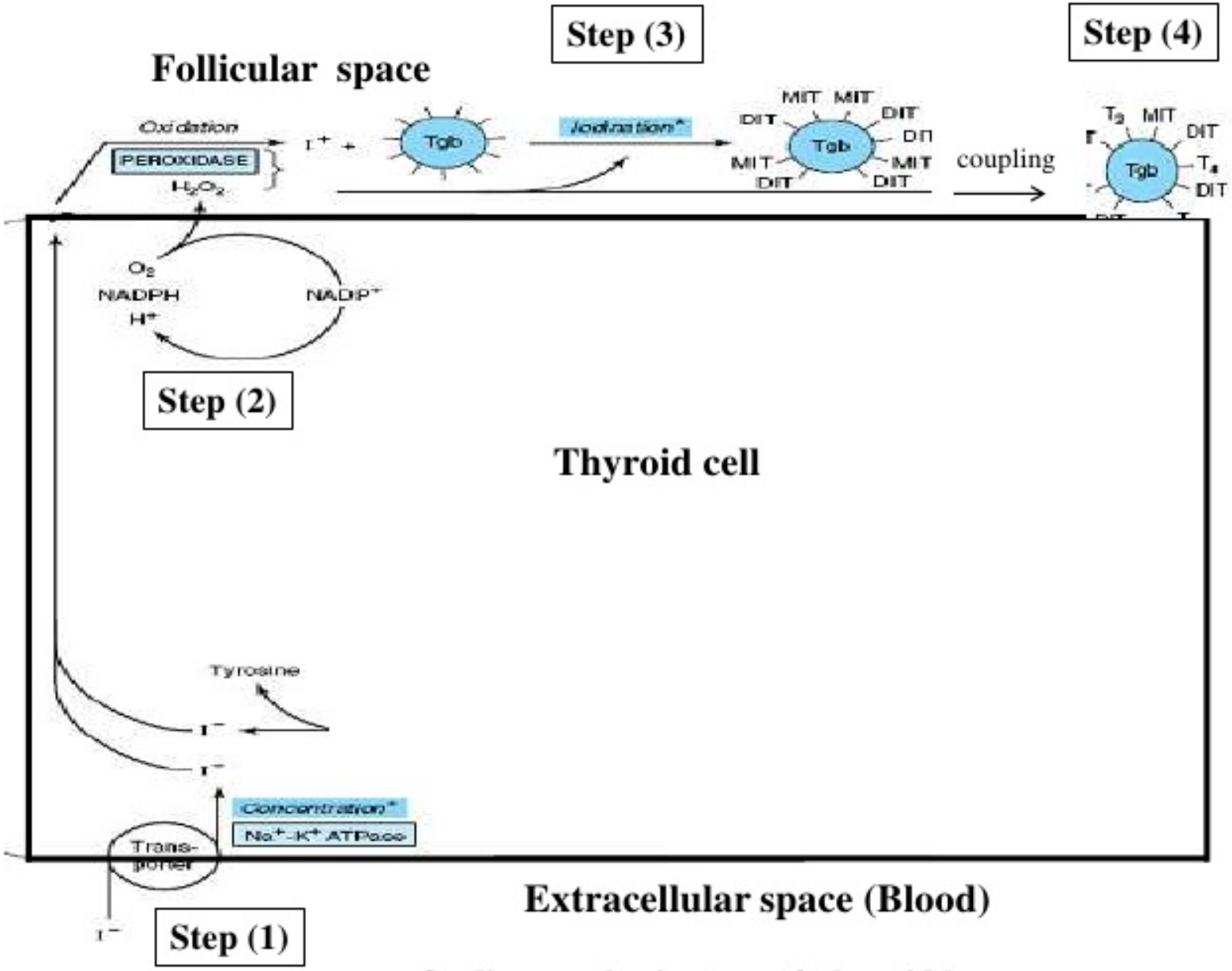
✓The H_2O_2 is produced by an NADPH-dependent enzyme resembling cytochrome *c* reductase.

Step (3): Iodination

Iodide is condensed onto tyrosine residues which reside along thyroglobulin resulting in either a mono-iodinated tyrosine (MIT) or di-iodinated tyrosine (DIT) being incorporated into thyroglobulin.

Step (4): coupling reaction

- ✓Iodotyrosine molecules are coupled together within the thyroglobulin.
- ✓Coupling two di-iodotyrosine molecules results thyroxin (T4).
- ✓Coupling a di-iodotyrosine and a mono-iodotyrosine results tri-iodothyronine (T3).



Outline synthesis steps of thyroid hormnes

Mechanism of Storage & secretion

✓Thyroid hormones are stored in an intracellular reservoir (colloid) in the follicular space

✓Thyroid cell is stimulated by TSH, then colloid re-enters the cell by of phagolysosome activity (pinocytosis).

✓Lysosomes produced various acid proteases to hydrolyze the thyroglobulins to release T4 and T3 into blood stream.

✓Excess of **mono and diiodothyronine** molecules in the thyroid are deionated by to removes I^- from the inactive

✓The I^- is reused again in T3 and T4 biosynthesis by thyroid cell.

Mechanism of Transport

➢Thyroid hormones are lipophilic with intracellular receptors and transported in blood by noncovalently binding proteins carriers like:

1) **Thyroxine binding globulin(TBG)**
2) **Thyroid binding pre-albumin(TBPA)**
3) **Albumin**.

➢Most of this circulates in bound form (inactive) with (TBG) and (TBPA).

➢Unbound (free) fraction is responsible for the biologic activity. therefore, measuring total thyroxine in the blood can be misleading.

Table 42–7. Comparison of T_4 and T_3 in plasma.

Total Hormone (µg/dL)		Free Hormone			$t^1/_2$ in Blood (days)
		Percent of Total	ng/dL	Molarity	
T_4	8	0.03	~2.24	3.0×10^{-11}	6.5
T_3	0.15	0.3	~0.4	$\sim 0.6 \times 10^{-11}$	1.5

Mechanism of degradation and excretion

Thyroid hormones (T_3&T_4) are degraded in peripheral tissues by total deiodination and inactivation based following steps:

Step (1): Deiodinated and decarboxylated

Step (2): Glucuronidation and sulfation in the liver to produce hydrophilics

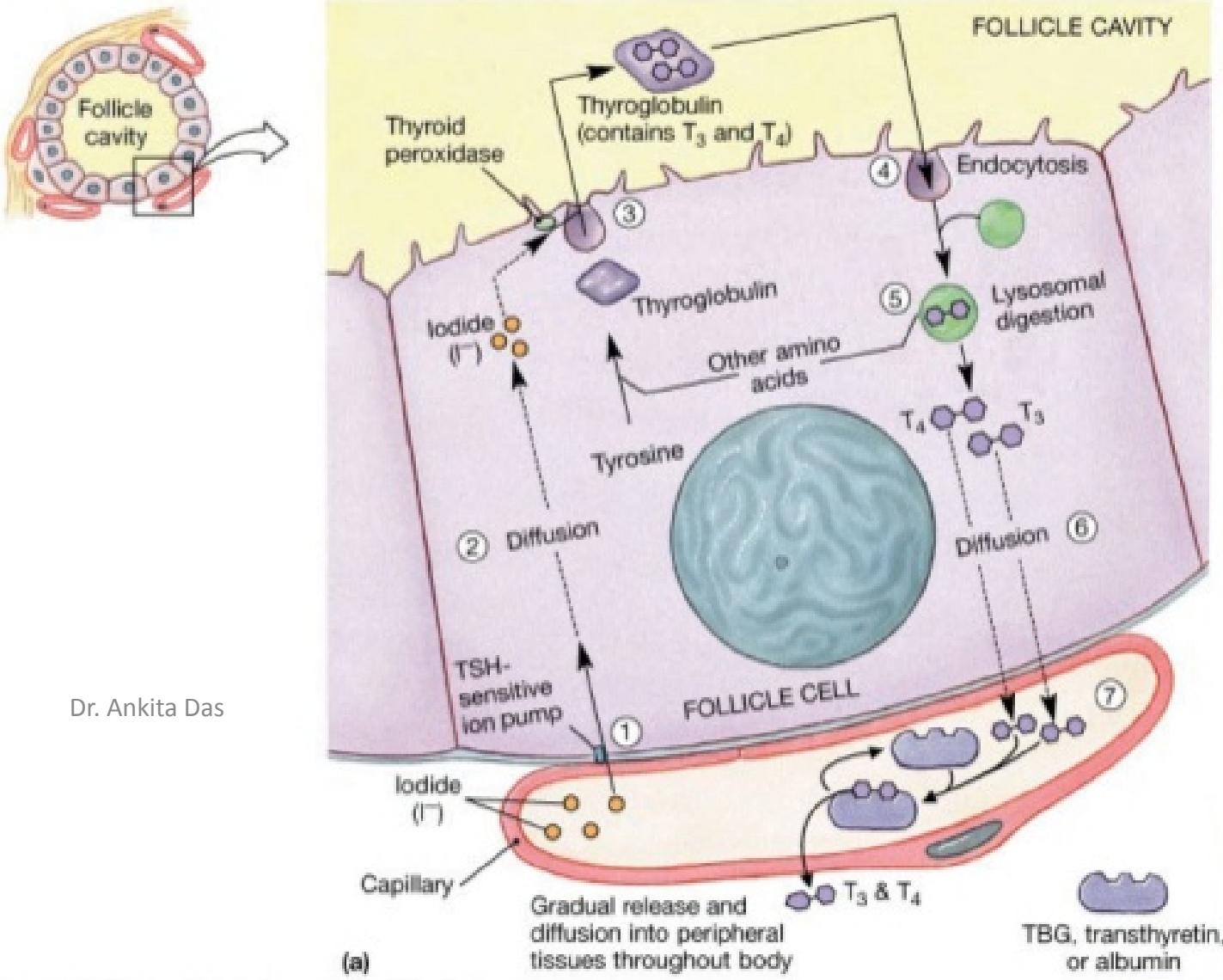
Step (3): Excretion in bile duct secretions into gut.

Step (4): Excretion of glucuronide conjugate in urine through kidney.

Metabolic effects of thyroid hormones: (Functions of T3 & T4)

1) Increasing oxygen consumption in most of the body tissues.
2) It promote protein synthesis by enhancing transcriptional level.
3) It promotes intestinal absorption and utilizationof glucose.
4) Increasing blood glucose level by activation of glycogenolysis & gluconeogenesis.
5) Stimulation of lipid turn over and utilization are stimulated by. Hence hypothyroidism is associated with elevated cholesterol level.
6) Regulation of water and electrolyte metabolism.

THYROID FOLLICLES WITH ACTIVITIES:



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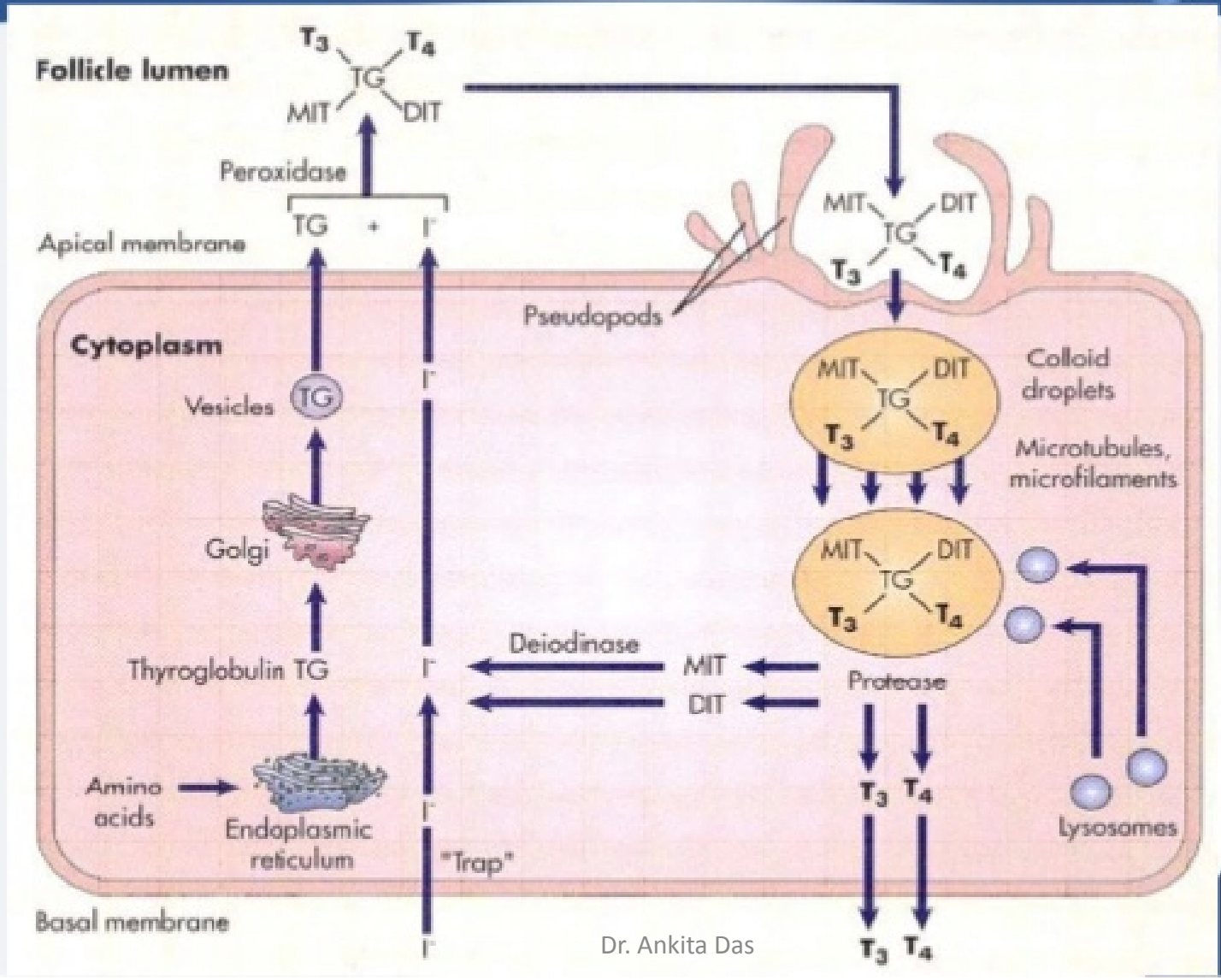
THYROID HORMONE SYNTHESIS



SUMMARY

The process of THs synthesis, storage and secretion requires a series of highly regulated steps:

- Uptake of iodide: iodide from plasma is actively transported by a sodium-iodine symporter on basal membrane of thyrocytes.
- Oxidation of iodide to iodine: this occurs on the luminal side of the apical membrane and requires thyroid peroxidase (TPO) and hydrogen peroxide, which is generated by a calcium-dependent flavoprotein enzyme system situated at the apical membrane.
- Organification: incorporation of iodine into tyrosyl residues on thyroglobulin. MIT and DIT are formed through action of TPO.

- Coupling of MIT and DIT: If two DIT molecules couple together, the result is the formation of T4; If a MIT and a DIT are coupled together, the result is the formation either T3 or rT3. T4, T3 and rT3 remain linked to thyroglobulin.

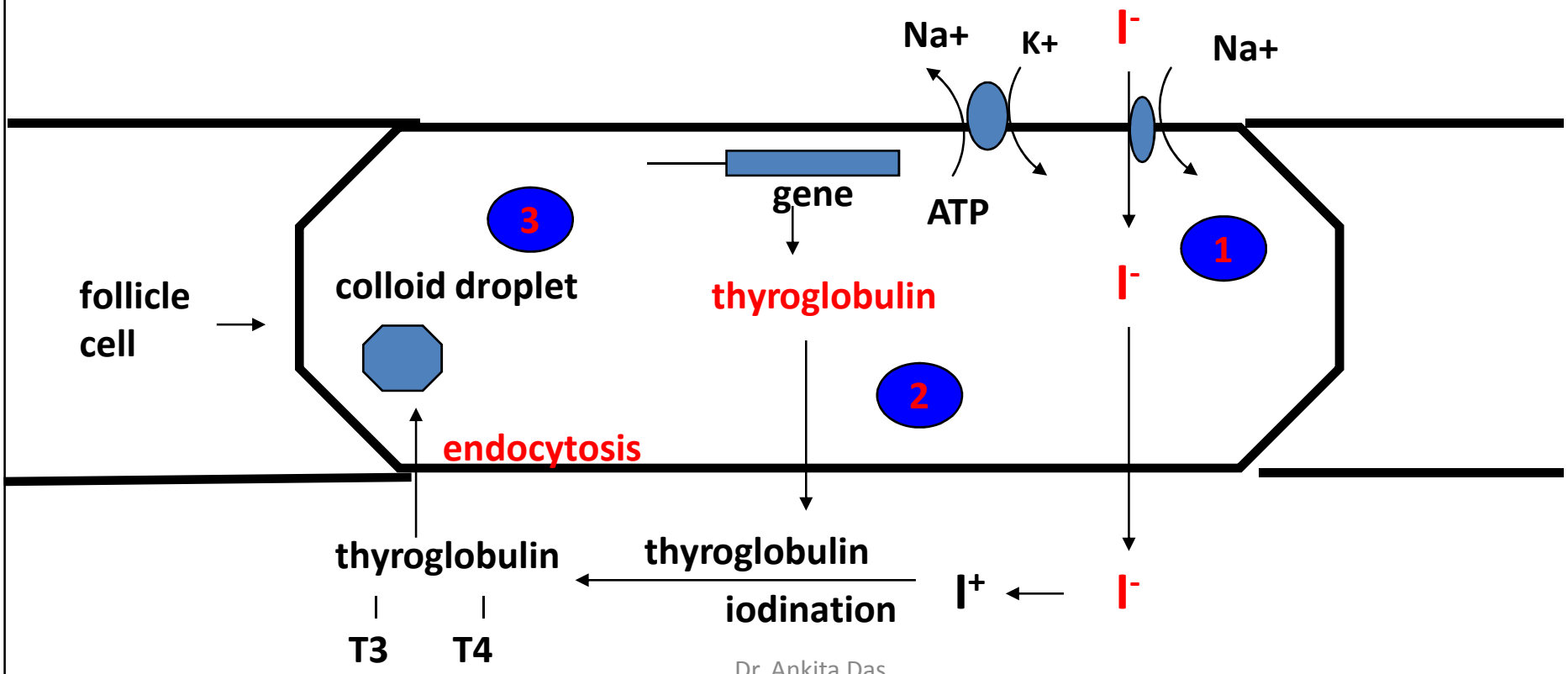
- Internalization: when there is demand for THs, Tg is internalized by pinocytosis and appears as colloid droplets that fuse with lysosomes and undergo proteolytic degradation to release: T4, T3, MIT and DIT; any MIT and DIT is deiodinated and the iodine conserved.

- Delivery of T4 and T3 into the circulation.

- TSH appears to stimulate each of the above processes.

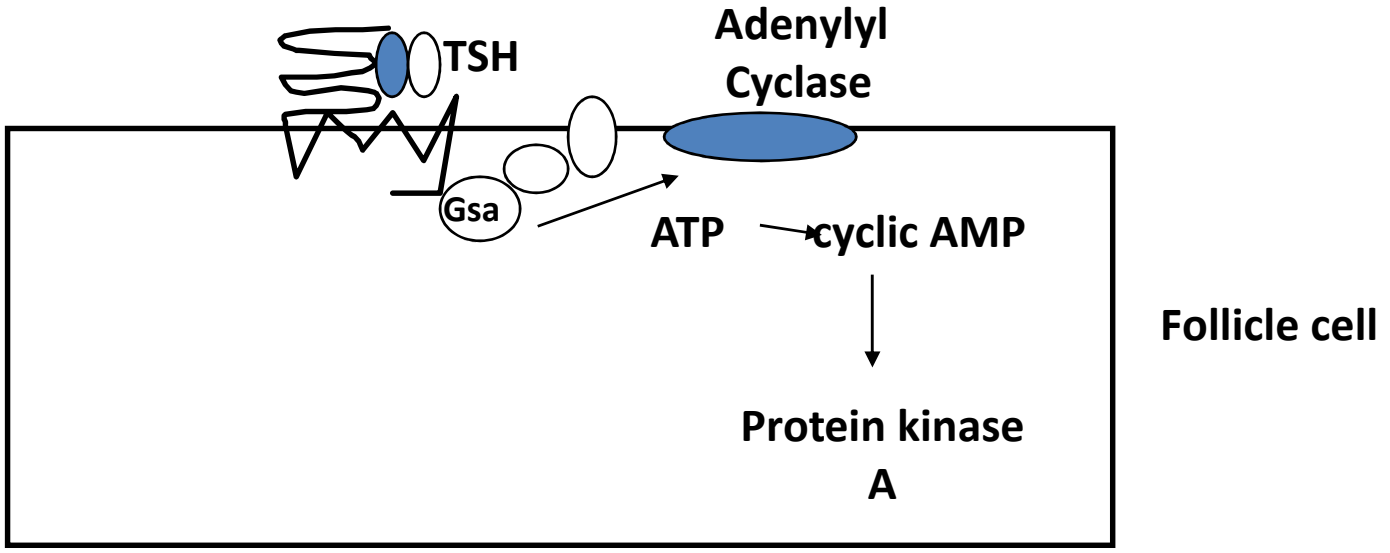
Action of TSH on the Thyroid

- TSH acts on follicular cells of the thyroid.
  - increases iodide transport into follicular cells
  - increases production and iodination of thyroglobulin
  - increases endocytosis of colloid from lumen into follicular cells



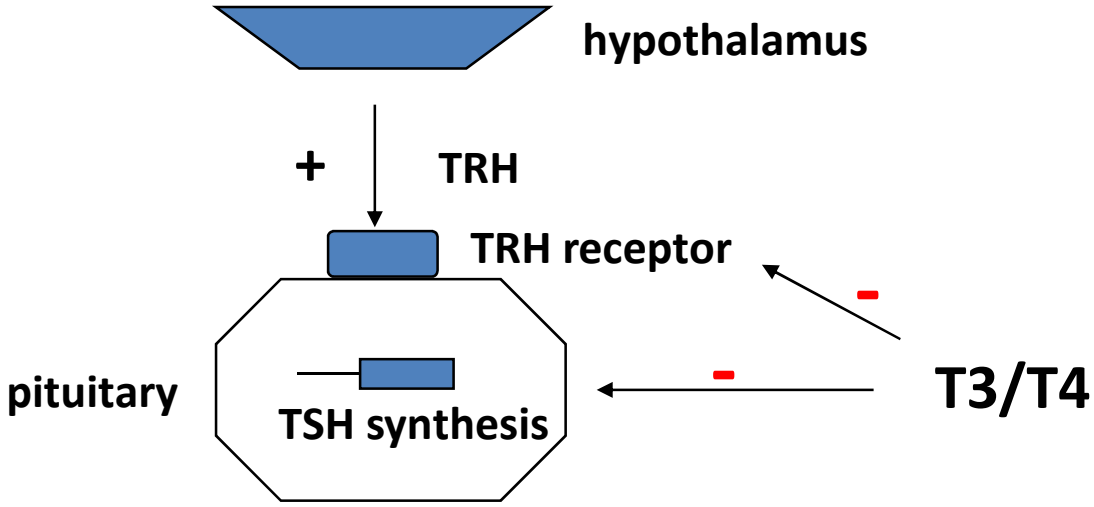
Mechanism of Action of TSH

- TSH binds to a plasma membrane-bound, G protein-coupled receptor on thyroid follicle cells.
- Specifically, it activates a Gs-coupled receptor, resulting in increased cyclic AMP production and PKA activation.



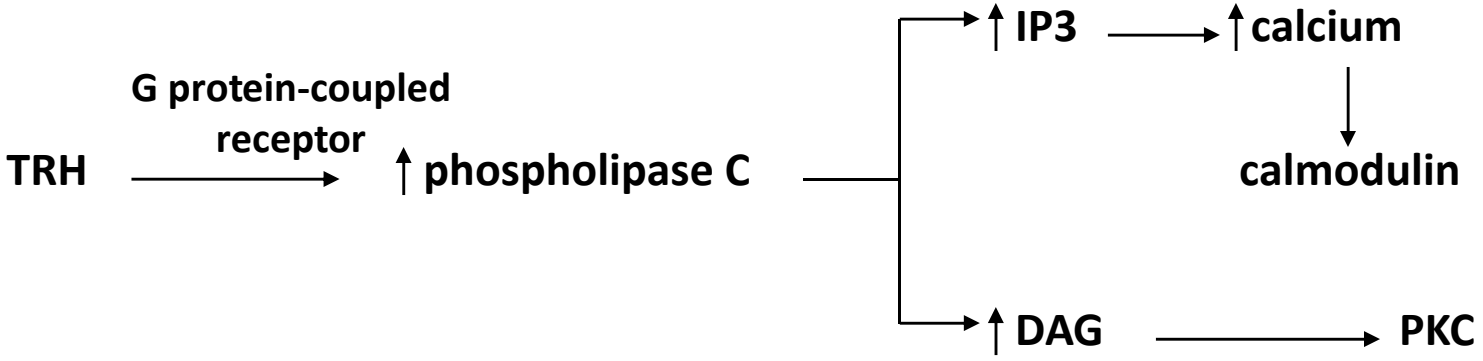
Regulation of TSH Release from the Anterior Pituitary

- TSH release is influenced by hypothalamic TRH, and by thyroid hormones themselves.
- Thyroid hormones exert negative feedback on TSH release at the level of the anterior pituitary.
  - inhibition of TSH synthesis
  - decrease in pituitary receptors for TRH



Regulation of TSH Release from the Anterior Pituitary

- Thyrotropin-releasing hormone (TRH) is a hypothalamic releasing factor which travels through the pituitary portal system to act on anterior pituitary thyrotroph cells.
- TRH acts through G protein-coupled receptors, activating the IP3 (calcium) and DAG (PKC) pathways to cause increased production and release of TSH.



- Thyroid hormones also inhibit TRH synthesis.

Actions of Thyroid Hormones

- Required for GH and prolactin production & secretion
- Required for GH action
- Increases intestinal glucose reabsorption (glucose transporter)
- Increases mitochondrial oxidative phosphorylation (ATP production)
- Increases activity of adrenal medulla (sympathetic; glucose production)
- Induces enzyme synthesis
- Result: stimulation of growth of tissues and increased metabolic rate.

Actions of Thyroid Hormones

- Thyroid hormones are essential for normal growth of tissues, including the nervous system.
- Lack of thyroid hormone during development results in short stature and mental deficits (cretinism).
- Thyroid hormone stimulates basal metabolic rate.
- What are the specific actions of thyroid hormone on body systems?

Cardiovascular system: Thyroid hormones increases heart rate, cardiac contractility and cardiac output. They also promote vasodilation, which leads to enhanced blood flow to many organs.

Central nervous system: Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state. Too little thyroid hormone, and the individual tends to feel mentally sluggish, while too much induces anxiety and nervousness.

Reproductive system: Normal reproductive behavior and physiology is dependent on having essentially normal levels of thyroid hormone. Hypothyroidism in particular is commonly associated with infertility.

Specific actions of thyroid hormone: development

- TH is critical for normal development of the skeletal system and musculature.
- TH is also essential for normal brain development and regulates synaptogenesis, neuronal integration, myelination and cell migration.
- **Cretinism** is a condition of severely stunted physical and mental growth due to untreated congenital deficiency of thyroid hormones (congenital hypothyroidism) due to maternal nutritional deficiency of iodine.

Effects of Thyroid Hormone on Nutrient Sources

Effects on protein synthesis and degradation:

-increased protein synthesis at low thyroid hormone levels (low metabolic rate; growth)

-increased protein degradation at high thyroid hormone levels (high metabolic rate; energy)

Effects on carbohydrates:

-low doses of thyroid hormone increase glycogen synthesis (low metabolic rate; storage of energy)

- high doses increase glycogen breakdown (high metabolic rate; glucose production)

Effects on Lipids: Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma. They also enhance oxidation of fatty acids in many tissues. Finally, **plasma concentrations of cholesterol and triglycerides are inversely correlated with TH levels.**

Thyroid Function in Pregnancy

Dr. Ankita Das

Introduction

- Most common endocrine disorder in pregnancy.
- 1-2% pregnant women.
- Pregnancy may modify course of thyroid disease.
- Pregnancy outcome can depend on optimal management of thyroid disorders.
- The Himalayan goiter belt - word's largest belt from Kashmir to Naga Hills.

CLINICAL IMPORTANCE OF PHYSIOLOGIC CHANGES IN PREGNANCY

PHYSIOLOGIC CHANGE	CLINICAL IMPORTANCE
Increased TBG	Need for ↑ T_4 production ↑ TT_3 & TT_4 levels Interference with FT_4 assay accuracy
Placental de-iodination of T_4	↑ T_3 & T_4 metabolism Need for ↑ T_4 production
Increased iodine clearance (renal clearance and fetal transfer)	↑ iodine requirement Risk of maternal and fetal hypothyroidism and goiter
B HCG elevation 1st TM	↑ FT_4 & ↓ TSH Transient mild thyrotoxicosis
Reduction in TSHRAb during pregnancy	Graves' disease improvement
Postpartum increase in thyroid antibodies	Exacerbation of Graves' disease Precipitation of postpartum thyroiditis

Events in fetus

Maternal thyroxine in coelomic fluid	→	6 weeks
THR gene expression in human brain	→	8 weeks
Fetal iodine uptake	→	10-14 weeks
Fetal thyroxine secretion	→	18 weeks

Normal values in pregnancy

Serum	Units	1st trimester	2nd	3rd
TSH	mU/L	0.03-2.3	0.03-3.7	0.13-3.4
FT_4	ng/dl	0.86-1.77	0.63-1.29	0.66-1.12
FT_3	pmol/L	3-5.7	2.8-4.2	2.4-4.1
ratio FT_4:FT_3 :: 4:1				

HYPOTHYROIDISM

- Incidence: 1 - 3 per 1000 pregnancies.
- Types:

✓ *Primary* - inadequate thyroid hormone production despite pituitary gland stimulation(including iodine deficiency).

✓ *Central* - insufficient stimulation of the thyroid by the pituitary or hypothalamus.

✓ *Subclinical* – Elevated TSH levels normal FT_4 in absence of clinical symptoms.

✓ *Overt* – increased TSH with low thyroxine levels with clinical symptoms.

Effect of hypothyroidism

ON PREGNANCY

- early pregnancy failure,
- pre-eclampsia(5-10%),
- placental abruption(1%),
- Preterm delivery(10-15%)
- Malpresentation,
- low birthweight,
- Stillbirth,
- PPH.

ON FETUS

- neurodevelopmental delay,
- deafness,
- stunted growth ,
- Peripartum hypoxia and
- increased risk of neonatal mortality

Preconceptional counseling

- Euthyroidism at the time of conception.
- If on treatment- delay pregnancy until TSH is normal.
- do not take levothyroxine and multivitamins at the same time (interference with absorption of thyroxine)
- adequate iodine intake (250mcg/d).
- Dietary goitrogens : cabbage, cauliflower, broccoli and even water purifying agents should be avoided. Boiled water is recommended.

NEONATAL HYPOTHYROIDISM

Causes:

- ✓ Thyroid dysgenesis
- ✓ Thyroid apasia
- ✓ Thyroid hypoplasia
- ✓ Thyroid ectopy
- ✓ Drug induced (thioamides ,amiodarone , lithium , potassium iodide)
- ✓ Dyshormogenesis
- ✓ TSH receptor mutations
- ✓ Thyorid hormone resistance
- ✓ Pendred's syndrome: defect in iodine organification and sensorineural deafness.

Management of fetal hypothyroidism

In utero therapy:

Fetus effectively absorbs T_4 from amniotic fluid.

3^{rd} trimester fetal T_4 requirement : 6 ug / kg /day.

Intraamniotic administration of 250 – 500 ug of thyroxine done at 7 – 10 days interval.

In term infants :

Requirement : 10 – 15 ug /kg /day.

TSH levels kept below 5 mU /l and T_4 levels at 10-16 ug /dl.

Tab thyroxine crushed and fed directly to the infant.

AUTOIMMUNE THYROID DISEASE

Thyroid antibodies:

- *directed towards cytoplasmic antigens-*
  - ✓ thyroid peroxidase (TPOAb) and
  - ✓ thyroglobulin (TgAb) antibodies.

- *directed to the TSH receptor-*
  - ✓ TSH receptor antibody (TSHRAb).

- TPOAB ⟶ present in 10-15% normal population.

- Thyroid autoimmunity ⟶ increased miscarriage rates.
- Causes :

✓ subtle maternal thyroid dysfunction

✓ autoimmune imbalance; rejection of the fetus

✓ thyroid antibodies affecting fetal thyroid gland ; fetal loss

✓ Associated increased maternal age

Trophoblast secrete immunosuppressant factors

↓

↓ antibody titers

↓

graves disease improvement

↓

↑ antibody titer post partum

↓

postpartum flare up

↓

postpartum thyroiditis.

Thyrotoxicosis (thyroid storm)

- a generic term referring to a clinical and biochemical state resulting in over-production of and exposure to thyroid hormone
- Overt hyperthyroidism complicates approximately 2 in 1,000 pregnancies.

Causes of thyrotoxicosis in pregnancy

Intrinsic thyroid disease

- ✓ Graves' disease (most common)
- ✓ Toxic nodule – single or multiple
- ✓ Subacute or silent thyroiditis

Excessive, exogenous thyroid hormone

- ✓ Factitious
- ✓ Therapeutic(amiodarone)

Gestational thyrotoxicosis

- ✓ Hyperemesis
- ✓ Gestational trophoblastic disease
- ✓ Hydatidiform mole
- ✓ Multiple gestations
- ✓ Hydrops

Rare

- ✓ TSH producing pituitary tumour
- ✓ Iodine induced
- ✓ Struma ovaii.

Gestational transient thyrotoxicosis

- Cause: cross reactivity between hcg and TSH at thyroid receptor
- Nausea and vomiting leading to dehydration, electrolyte imbalance and weight loss.
- Spontaneous resolution by 18 weeks.
- Antithyroid medications avoided.

gestational transient thyrotoxicosis

- associated with hyperemesis gravidarum
- can be due to high levels of human chorionic gonadotropin (hCG) resulting from molar pregnancy
- high hCG levels → TSH receptor stimulation and temporary hypothyroidism
- rarely symptomatic
- treatment with antithyroxine drugs- not beneficial
- expectant management
- not associated with poor pregnancy outcomes

- Pregnant women with hyperthyroidism are at increased risk for:
  - spontaneous pregnancy loss
  - congestive heart failure
  - thyroid storm
  - preterm birth
  - Preeclampsia
  - fetal growth restriction, and
  - increased perinatal morbidity and mortality

Grave's disease

- **the most common cause of thyrotoxicosis in pregnancy**
- **An autoimmune condition** characterized by **production of thyroid-stimulating immunoglobulin (TSI) and thyroid-stimulating hormone binding inhibitory immunoglobulin (TBII)**

→facilitate the thyroid-stimulating hormone (TSH) receptor in the mediation of thyroid stimulation and inhibition

- **Hyperthyroidism- thyrotoxicosis** resulting from an **abnormally functioning thyroid gland.**

- **Thyroid storm- acute, severe exacerbation of hyperthyroidism**

Impact of Pregnancy on Thyroid:

- **Thyroxine (T4),** the major secretory product of the thyroid gland, is **converted in peripheral tissues to triiodothyronine (T3)**
- **T3-** biologically active form
- T4- secretion is under the direct control of pituitary TSH
- T4 and T3 are transported in the peripheral circulation bound to thyroxine-binding globulin (TBG), transthyretin (formerly called "prealbumin") and albumin.
- Less than 0.05% of plasma T4, and less than 0.5% of plasma T3, are **unbound and able to interact with target tissues**

- **20 weeks' gestation**
  - reduced hepatic clearance
  - estrogen-induced change in the structure of TBG that prolongs serum half-life

→ plasma TBG increases 2.5 folds → → 25% to 45% increase in serum total T4 (TT4) from a pregravid level of 5 to 12 mg to 9 to 16 mg

** Total T3 (TT3) increases by about 30% in the first trimester and by 50% to 65% later

- Pregnancy → increase in available protein →transient change in free T4 (FT4) and free thyroxine index (FTI) in the first trimester (possibly related to an increase in hCG)

- Increased concentrations of TSH → stimulate restoration of the free serum T4 level, such that FT4 and FTI levels are generally maintained within the normal non-pregnant range

Ultrasound evaluation of the thyroid gland during pregnancy

- Increase in volume
- Echo structure remains unchanged (Plasma iodide levels decrease in pregnancy due to fetal use of iodide and increased maternal renal clearance)
- 15% to 18% increase in size of the thyroid gland
  - enlargement usually resolves after delivery
  - not associated with abnormal thyroid function tests

Diagnostic Approach:

- Mild hyperthyroidism:
  - Fatigue
  - increased appetite
  - Vomiting
  - Palpitations
  - Tachycardia
  - heat intolerance,
  - Increased urinary frequency
  - Insomnia
  - Emotional instability

- The suspicion increases if patient has
  - Tremor
  - Nervousness
  - frequent stools
  - excessive sweating
  - brisk reflexes
  - muscle weakness
  - goiter
  - Hypertension
  - weight loss.
  - Grave's ophthalmopathy (stare, lid lag and retraction, exophthalmos)
  - dermopathy (localized or pretibial myxedema)

- Untreated hyperthyroidism poses considerable maternal and fetal risks, including preterm delivery, severe preeclampsia, heart failure, and thyroid storm

Characteristics of Thyroid Storm:

- - a hypermetabolic complication of hyperthyroidism:
  - hyperpyrexia (temperature >41ºC)
  - cardiovascular compromise (tachycardia out of proportion to the fever, dysrhythmia, cardiac failure)
  - gastrointestinal upset (diarrhea)
  - central nervous system changes (restlessness, nervousness, changed mental status, confusion, and seizures).

- Thyroid storm is usually seen in patients with poorly controlled hyperthyroidism complicated by additional physiologic stressors, such as **infection, surgery, thromboembolism, preeclampsia, and parturition**

Management of thyroid Storm

- Thyroid storm is a clinical diagnosis based on severe signs of thyrotoxicosis:
  - significant hyperpyrexia (>103ºF or >41ºC) neuropsychiatric symptoms
  - Tachycardia with a pulse rate exceeding 140 beats/min
  - congestive heart failure
  - Gastrointestinal symptoms (nausea and vomiting) accompanied by liver compromise

Management of Thyroid Storm:

- Obstetric intensive care unit (ICU)/ ICU that has continuous fetal monitoring and can handle an emergent delivery
- Therapy is designed to:
  - Reduce the synthesis and release of thyroid hormone
  - Remove thyroid hormone from the circulation and increase the concentration of TBG
  - Block the peripheral conversion of T4 to T3
  - Block the peripheral actions of thyroid hormone
  - Treat the complications of thyroid storm and provide support
  - Identify and treat potential precipitating conditions

Management of Thyroid Storm

- Supportive adjunctive care for the patient in thyroid storm are:
  - IV fluids and electrolytes
  - Cardiac monitoring
  - Consideration of pulmonary artery catheterization (central hemodynamic monitoring to guide beta-blocker therapy during hyperdynamic cardiac failure)
  - Cooling measures: blanket, sponge bath, acetaminophen, avoid salicylates (risk of increased T4). Acetaminophen is the drug of choice
  - Oxygen therapy (consider arterial line to follow serial blood gases)
  - Nasogastric tube

Medications:

- Reduce synthesis of thyroid hormones:
  - Thionamides : propylthiouracil (PTU)
  - Methimazole)

→ inhibit iodination of tyrosine -- leading to reduce synthesis of thyroid hormones and block peripheral conversion of T4 to T3

  - can reduce the T3 concentration by 75%

Postpartum Care:

- Most asymptomatic women should have a TSH and free T4 performed approximately 6 weeks postpartum

- PTU and methimazole are excreted in breast milk
  - PTU is largely protein bound and does not seem to pose a significant risk to the breastfed infant
  - Methimazole has been found in breastfed infants of treated women in amounts sufficient to cause thyroid dysfunction
    - at low doses (10-20 mg/d) it does not seem to pose a major risk to the nursing infant

Summary

- Thyroid storm
  - a life-threatening condition, requiring early recognition and aggressive therapy in an intensive care unit setting.
  - During gestation, women with hyperthyroidism should have their thyroid function checked every 3-4 weeks.
  - Grave's disease represents the most common cause of maternal hyperthyroidism during pregnancy
  - Only 0.2% of gestations are complicated by thyroid storm and more than 90% of cases are caused by Grave's disease
  - Increased production of thyroid hormone occurs when autoantibodies (thyroid-stimulating antibody [TSAb] -- formerly known as LATS [long-acting thyroid stimulator]) against TSH receptors -- acts as TSH agonists.

Books to refer:

1.Medical Physiology, Guyton and Hall
2.Medical Physiology, Ganong
3.General Physiology, A.K. Jain
4. Human Physiology, Dr. C. C. Chatterjee

Practice Questions:

1. What do you mean by MIT and DIT?
2. Describe the steps involved in synthesis of thyroid hormone.
3. How thyroid hormone is degraded and excreted from the body?
4. Briefly explain the functions of thyroid hormones.
5. How the release of TSH from the anterior pituitary is regulated?
6. Mention the clinical importance of the physiological changes of TH in pregnancy.
7. Mention the effects of hypothyroidism on fetus.
8. Briefly describe the causes of neonatal hypothyroidism and its management.
9. What is thyrotoxicosis? Mention its cause during pregnancy.