

# THYROID HORMONE EFFECT

A thick, horizontal yellow brushstroke with a textured, painterly appearance, extending across the width of the slide below the main title.

PHYSIOLOGY OF HORMONE  
APRIL 2007

# THE THYROID GLAND



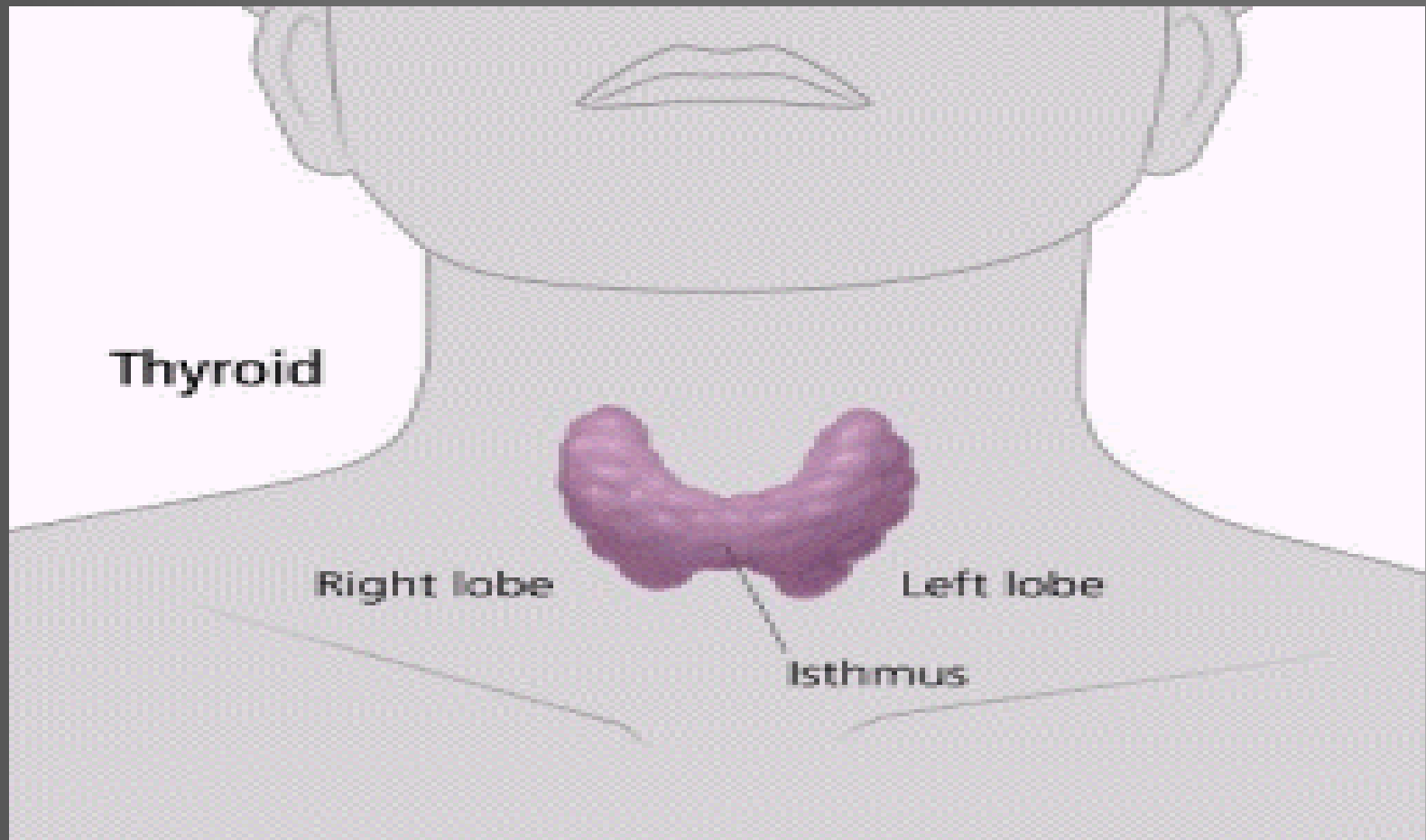
⌘ OVER TRACHEA

⌘ TWO LARGE LATERAL LOBES  
CONNECTED BY AN ISTHMUS

⌘ 15 to 20 g

⌘ FUNCTIONAL UNIT IS THE FOLLICLE:  
EPITHELIAL CELLS AROUND A HOLLOW  
VESSICLE FILLED WITH THYROGLOBULIN

The thyroid, situated in the neck  
close to the larynx



# THE THYROID HORMONES



⌘ THYROGLOBULIN: STORAGE FORM  
BINDS HORMONES

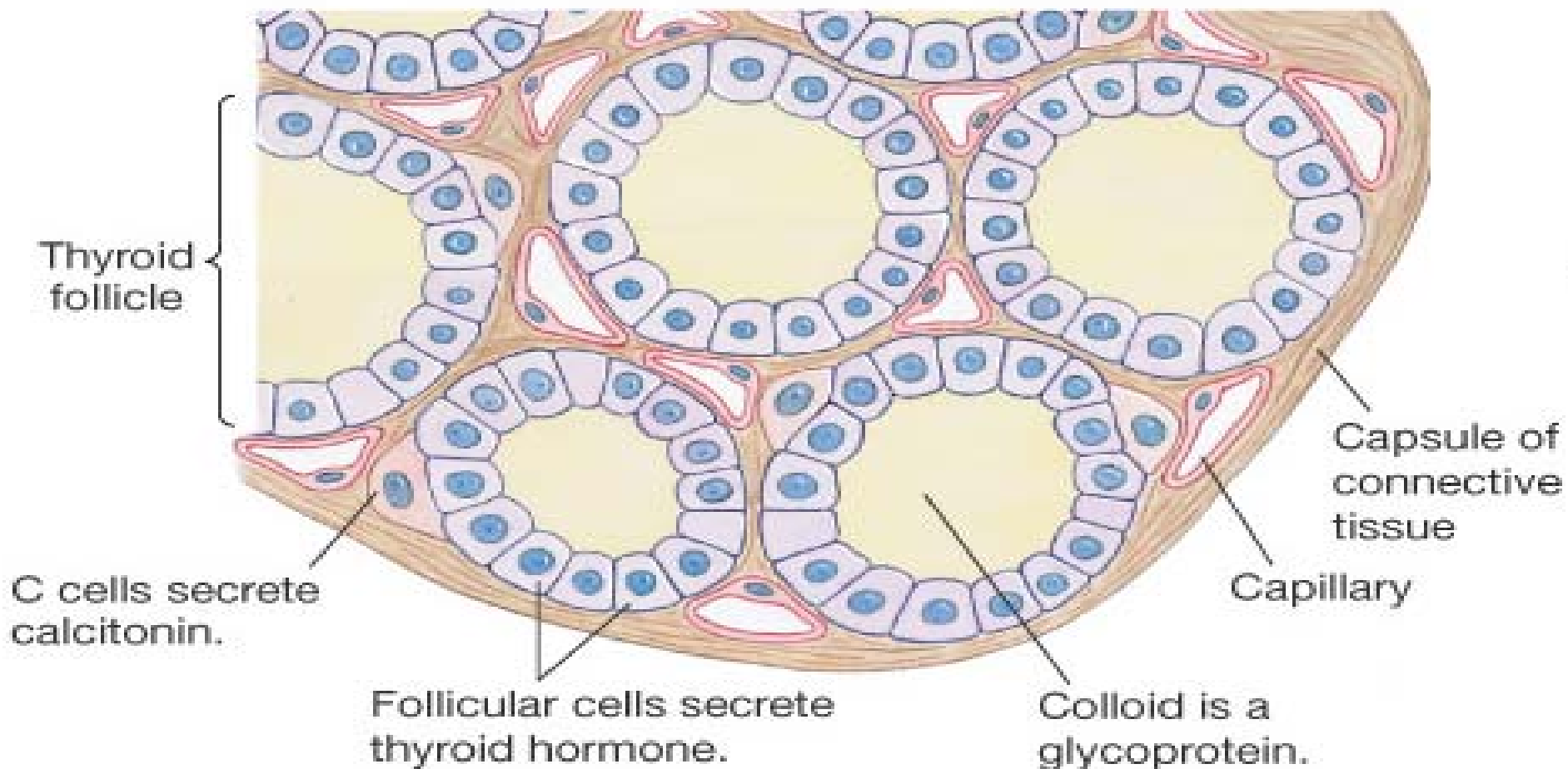
⌘ TETRAIODOTHYRONINE

⌘ TRIIODOTHYRONINE

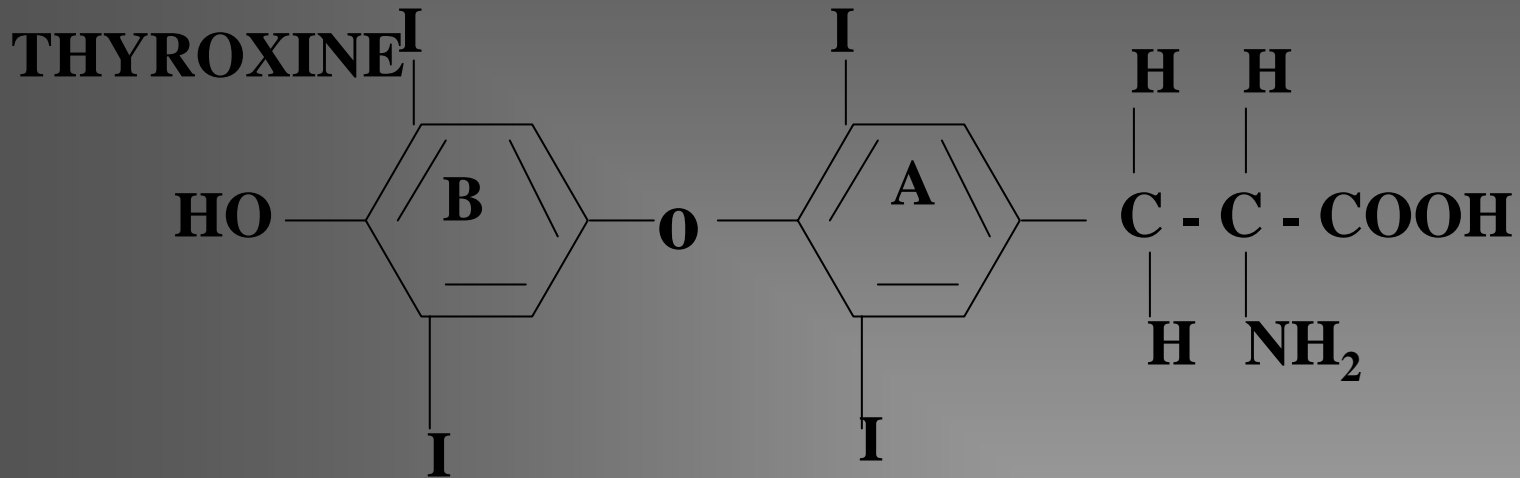
⌘ IODINE REQUIRED FROM DIETARY  
INTAKE

# Thyroid follicles

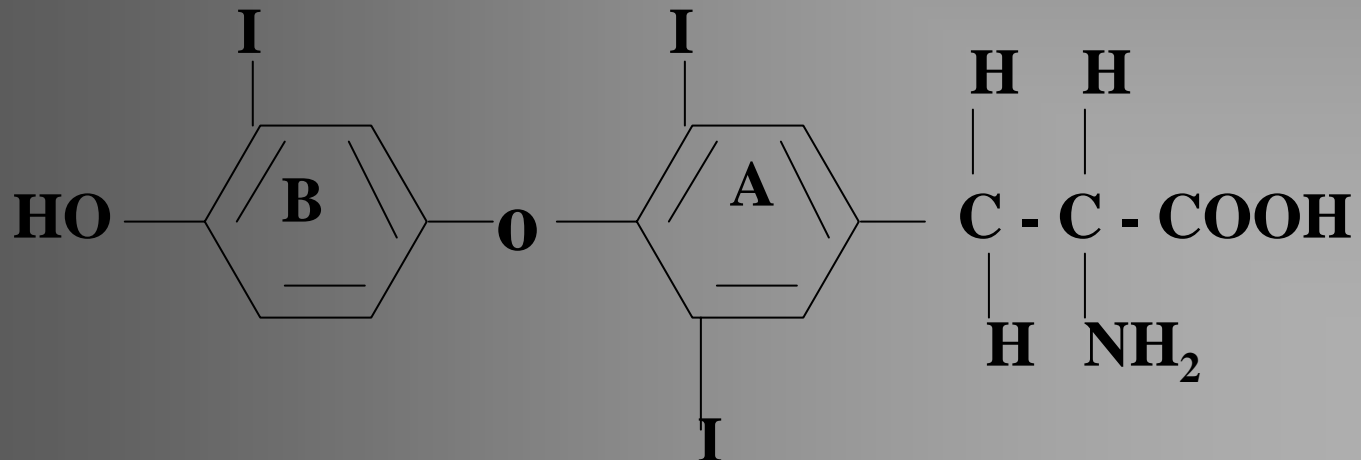
(b) Section of thyroid gland



# THYROID HORMONES



**TRIIODOTHYRONINE**

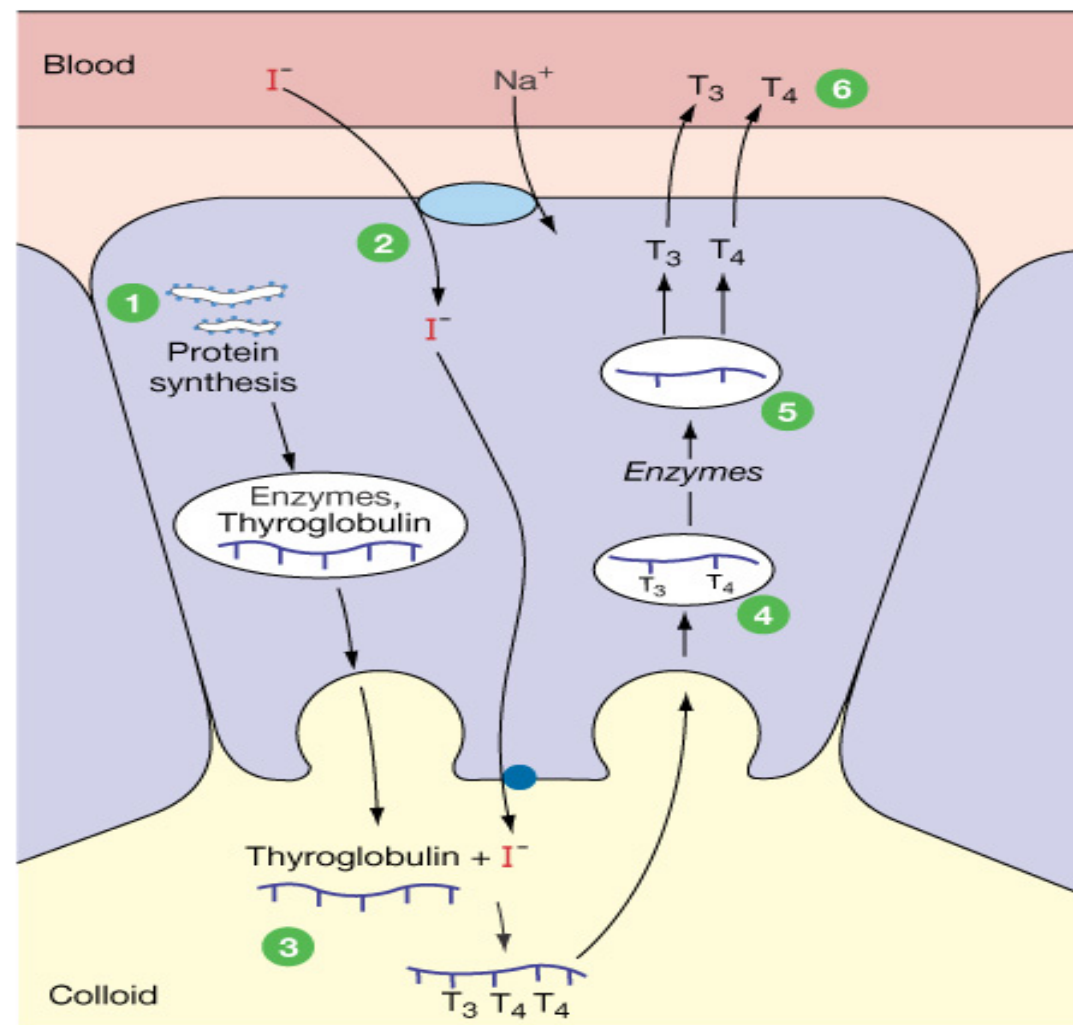


# THYROID HORMONE SYNTHESIS



- ⌘ **DEPENDENT ON IODINE (IODINE PUMP CONCENTRATES IODINE IN CELLS)**
- ⌘ **DEPENDENT ON TYROSINE**
- ⌘ **PARTIALLY SYNTHESIZED (THYROGLOBULIN) EXTRACELLULARLY AT LUMINAL SURFACE OF FOLLICULAR CELLS AND STORED IN FOLLICULAR LUMEN**

# Thyroxine and its precursors: Structure & Synthesis



- 1** Follicular cell synthesizes enzymes and thyroglobulin for colloid.
- 2** I<sup>-</sup> is co-transported into the cell with Na<sup>+</sup> and transported into colloid.
- 3** Enzymes add iodine to thyroglobulin to make T<sub>3</sub> and T<sub>4</sub>.
- 4** Thyroglobulin is taken back into the cell.
- 5** Intracellular enzymes separate T<sub>3</sub> and T<sub>4</sub> from the protein.
- 6** Free T<sub>3</sub> and T<sub>4</sub> enter the circulation.



# EFFECTS OF IODINE



- ⌘ DURING IODINE DEFICIENCY, HORMONE SYNTHESIS IS IMPAIRED
- ⌘ EXCESS IODINE ALSO INHIBITS SYNTHESIS

# THYROID HORMONE SECRETION



- ⌘ WITH TSH STIMULATION, ENDOCYTOSIS BRINGS THE THYROGLOBIN BACK INTO FOLLICULAR CELLS
- ⌘ THYROGLOBULIN IS DEGRADED TO  $T_3$  AND  $T_4$

# 99% OF THYROID HORMONE IN THE BLOOD IS BOUND



- ⌘ **THYROXINE-BINDING GLOBULIN (TBG)**
- ⌘ **THYROXINE-BINDING PREALBUMIN (TBPA) [TRANSTHYRETIN]**
- ⌘ **ALBUMIN**
- ⌘ **ABOUT THREE TIMES AS MUCH AS IS SECRETED AND DEGRADED IN A SINGLE DAY (BUFFER)**
- ⌘ **T<sub>4</sub> BINDS BETTER THAN T<sub>3</sub>**

# THYROID HORMONE'S EFFECTS



- ⌘ **METABOLIC RATE: INCREASED BMR**
- ⌘ **CALOROGENIC: INCREASED HEAT PRODUCTION(OXIDATIVE METABOLISM)**
- ⌘ **SYMPATHOMIMETIC: FLIGHT OR FIGHT**
- ⌘ **CARDIOVASCULAR:INCREASES RESPONSIVENESS OF HEART**
- ⌘ **GROWTH: ESSENTIAL FOR NORMAL GROWTH OF SKELETAL SYSTEM (PERMISSIVE OR SYNERGYSTIC WITH GH, INSULIN-LIKE GROWTH FACTOR), CNS, ANS**
- ⌘ **NERVOUS SYSTEM:DEVELOPMENT AND ADULT ACTIVITY**

# METABOLIC EFFECTS OF THYROID HORMONE



- ⌘ CALOROGENIC EFFECT: INFLUENCES TOLERANCE TO COLD, AVAILABILITY OF ATP
- ⌘ CARBOHYDRATE METABOLISM: INCREASED GLUCOSE ABSORPTION FROM GUT, GLYCOGENOLYSIS, GLUCONEOGENESIS, GLUCOSE OXIDATION.
- ⌘ LIPID METABOLISM: LIPOGENESIS IN ADIPOCYTES, IN COORDINATION WITH BLOOD GLUCOSE LEVELS

# CONTROL OF FUEL METABOLISM



⌘ GLYCOGENESIS

⌘ GLYCOGENOLYSIS

⌘ GLUCONEOGENESIS

⌘ PROTEIN SYNTHESIS

⌘ PROTEIN DEGRADATION

⌘ FAT SYNTHESIS

⌘ FAT BREAKDOWN

# GLYCOGENESIS



- ⌘ **GLYCOGEN IS A BRANCHED POLYMER OF GLUCOSE STORED IN THE LIVER AND MUSCLE CELLS**
- ⌘ **SYNTHESIS IS BY SEPARATE PATHWAY FROM BREAKDOWN**
- ⌘ **HIGHLY REGULATED BY INSULIN**

# GLYCOGENOLYSIS

# GLYCOGENOLYSIS



- ⌘ **BREAKDOWN OF GLYCOGEN STORES INTO GLUCOSE**
- ⌘ **REGULATES BLOOD GLUCOSE BETWEEN MEALS**
- ⌘ **HOMONALLY CONTROLLED (GLUCAGON, EPINEHRINE, NOREPINEPHRINE AND CLUCOCORTICIDS) AMPLIFIED BY THYROID HORMONE**



# GLUCONEOGENESIS



- ⌘ **PRECURSORS ARE 3 AND 4 CARBON COMPOUNDS**
- ⌘ **VIA FRUCTOSE PHOSPHATE**
- ⌘ **GLUCAGON CONTROLLED AIDED BY THYROID HORMONE**
- ⌘ **MAIN PRECURSOR ALANINE AND OTHER AA**

# PROTEIN DEGRADATION



- ⌘ **USUALLY BALANCED BY SYNTHESIS**
- ⌘ **NO ENERGY STORES IN FORM OF PROTEIN**
- ⌘ **CAN BE ENHANCED BY GLUCAGON AND THYROID HORMONES LEADING TO GLUCONEOGENESIS**

# THYROID HORMONE EFFECTS ON NITROGEN METABOLISM



⌘ **ENHANCES BOTH SYNTHESIS AND  
DEGRADATION OF PROTEINS**

⌘ **EXCESS HORMONE PROMOTES  
DEGRADATION**

# FAT SYNTHESIS

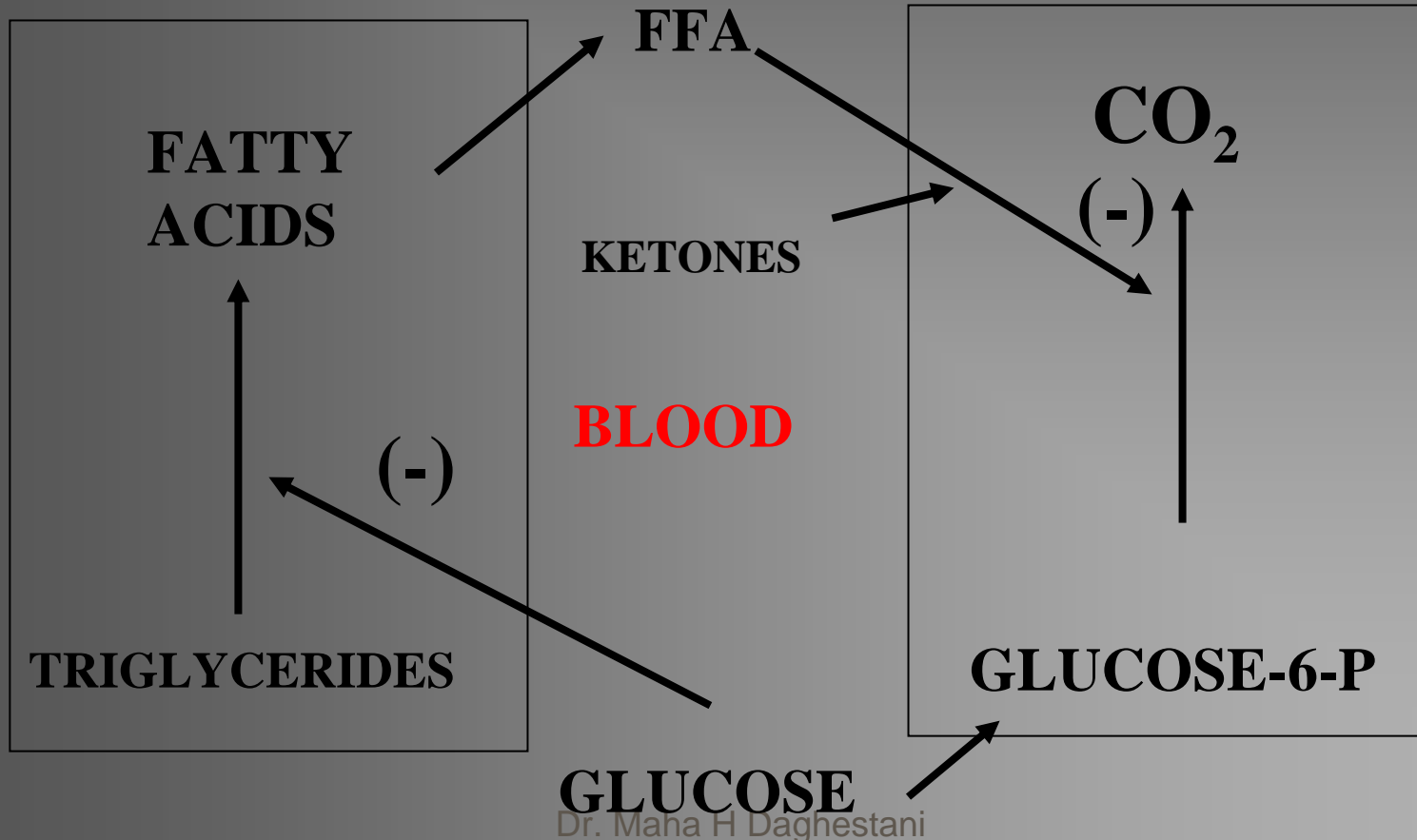


- ⌘ **GLUCOSE - FATTY ACID CYCLE**
- ⌘ **FATTY ACIDS PRODUCED CONSTANTLY IN ADIPOSE TISSUE.**
- ⌘ **BECOME FFA OR BECOME TRIGLYCERIDES DEPENDING ON  $\alpha$ -GLYCEROL PHOSPHATE FROM GLUCOSE OXIDATION**
- ⌘ **NEED OPTIMAL AMOUNTS OF THYROID HORMONE**

# GLUCOSE - FATTY ACID CYCLE

**ADIPOCYTE**

**MYOCYTE**

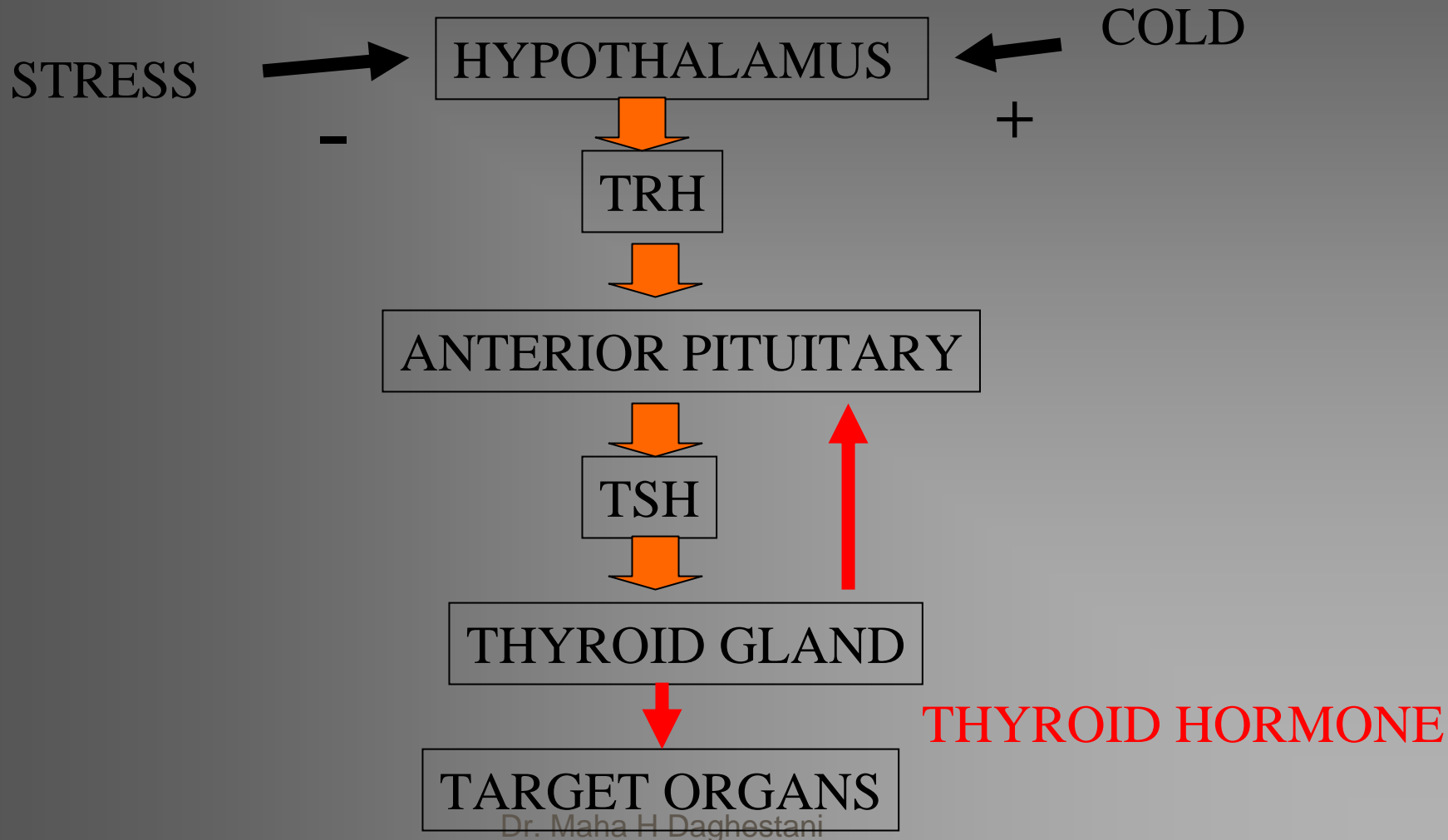


# THYROID AND TEMPERATURE REGULATION

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- ⌘  $T_3$  IS THE DOMINANT FORM INVOLVED
- ⌘ EXPOSURE TO COLD CAUSES  $T_4$  CONVERSION TO  $T_3$  .
- ⌘ PROMOTES CALOROGENIC EFFECT (LONG TERM COLD ADAPTATION)
- ⌘ SHORT TERM EFFECTS DUE TO SYMPATHETIC MIMETIC EFFECTS AND THE SHIVERING RESPONSE OF MUSCLES

# REGULATION OF THYROID SECRETION



# EFFECTS OF TSH



⌘ GREATLY INCREASES ENDOGENOUS SYNTHESIS AND SECRETION OF HORMONE

⌘ INCREASES BLOOD FLOW

⌘ PLEIOTROPIC EFFECT ON GLANDULAR TISSUE, RNA AND DNA SYNTHESIS (HYPERPLASIA), PHOSPHOLIPID METABOLISM, ETC.



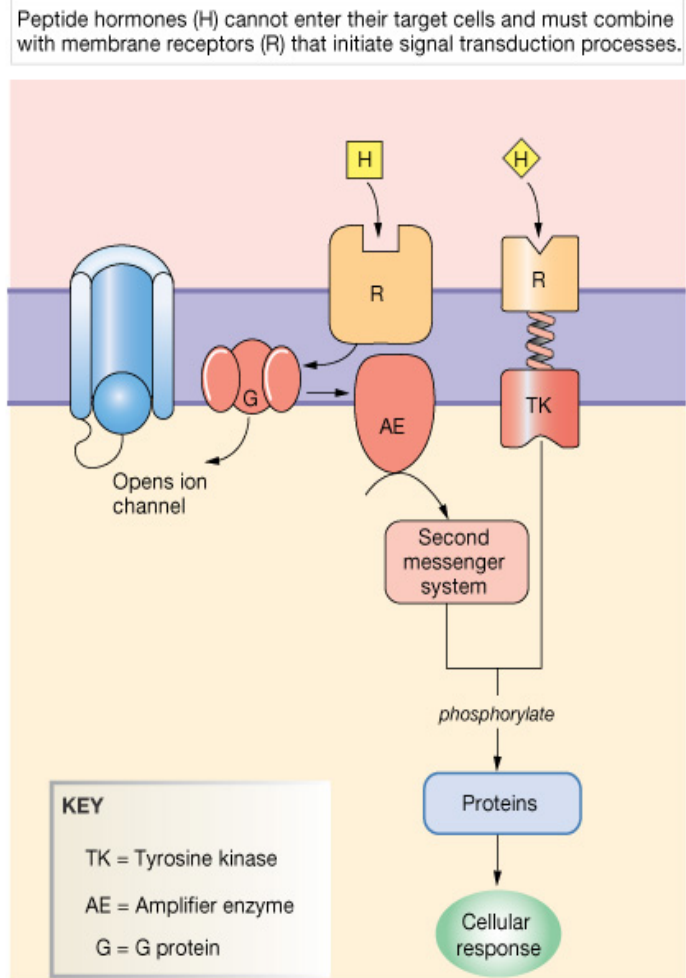
# TSH MODE OF ACTION



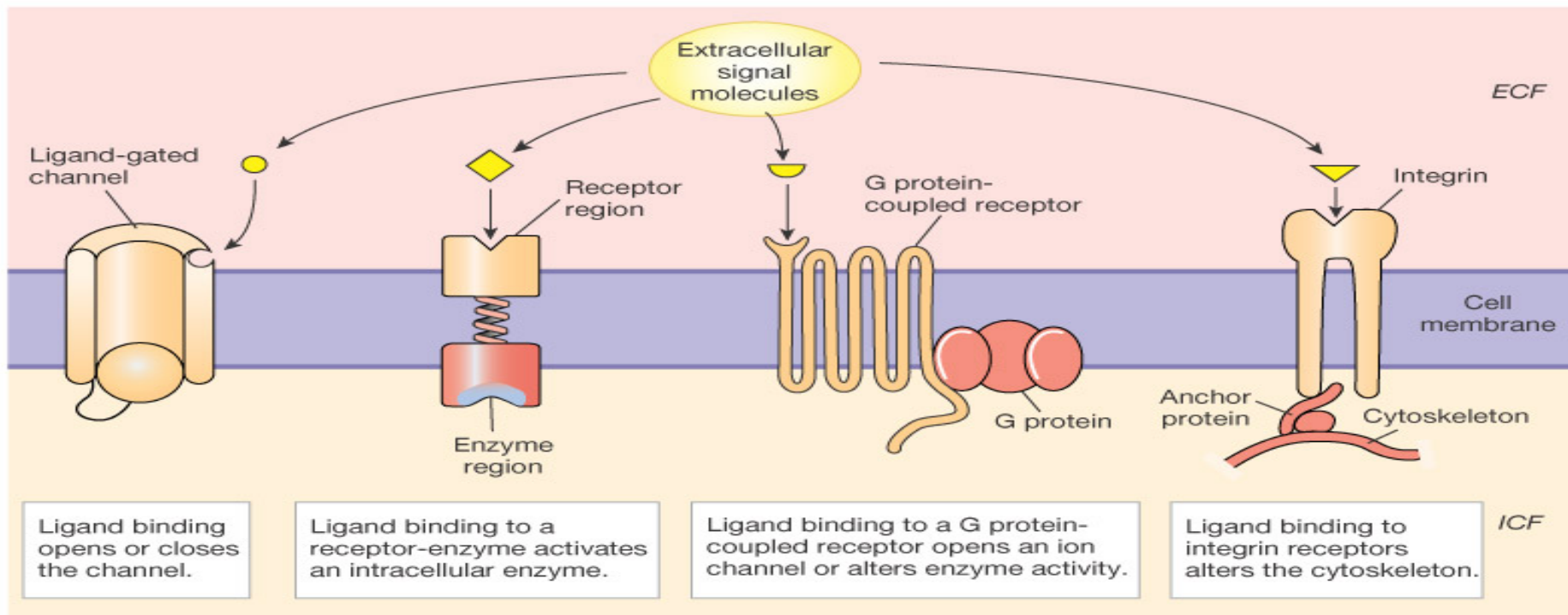
- ⌘ RECEPTOR SPANS MEMBRANE
- ⌘ G-PROTEIN SUPERFAMILY
- ⌘ cAMP SECOND MESSENGER
- ⌘ INFLUENCES EVERY STEP OF THE HORMONE SYNTHESIS, STORAGE, AND SECRETION.

# TSH MODE OF ACTION

Peptide hormones (H) cannot pass directly through the lipid bilayer and must combine with membrane receptors (R) that initiate signal transduction processes in the target cell



# Four general types of receptors for fast-acting hormones



Ligand binding opens or closes the channel.

Ligand binding to a receptor-enzyme activates an intracellular enzyme.

Ligand binding to a G protein-coupled receptor opens an ion channel or alters enzyme activity.

Ligand binding to integrin receptors alters the cytoskeleton.

# ABNORMALITIES OF THYROID FUNCTION



## ⌘ HYPO

- ⌘ REDUCED BMR
- ⌘ POOR TOLERANCE OF COLD
- ⌘ GAIN OF WEIGHT
- ⌘ FATIGUE
- ⌘ SLOW, WEAK PULSE
- ⌘ SLOW REFLEXES AND MENTATION
- ⌘ MYXEDEMA
- ⌘ GOITER
- ⌘ CRETINISM

## ⌘ HYPER

- ⌘ GRAVE'S DISEASE: TSI (THYROID STIMULATING IMMUNOGLOBULIN-MIMICS TSH)
- ⌘ EXOPHTALMOS
- ⌘ GOITER

Any Question?

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