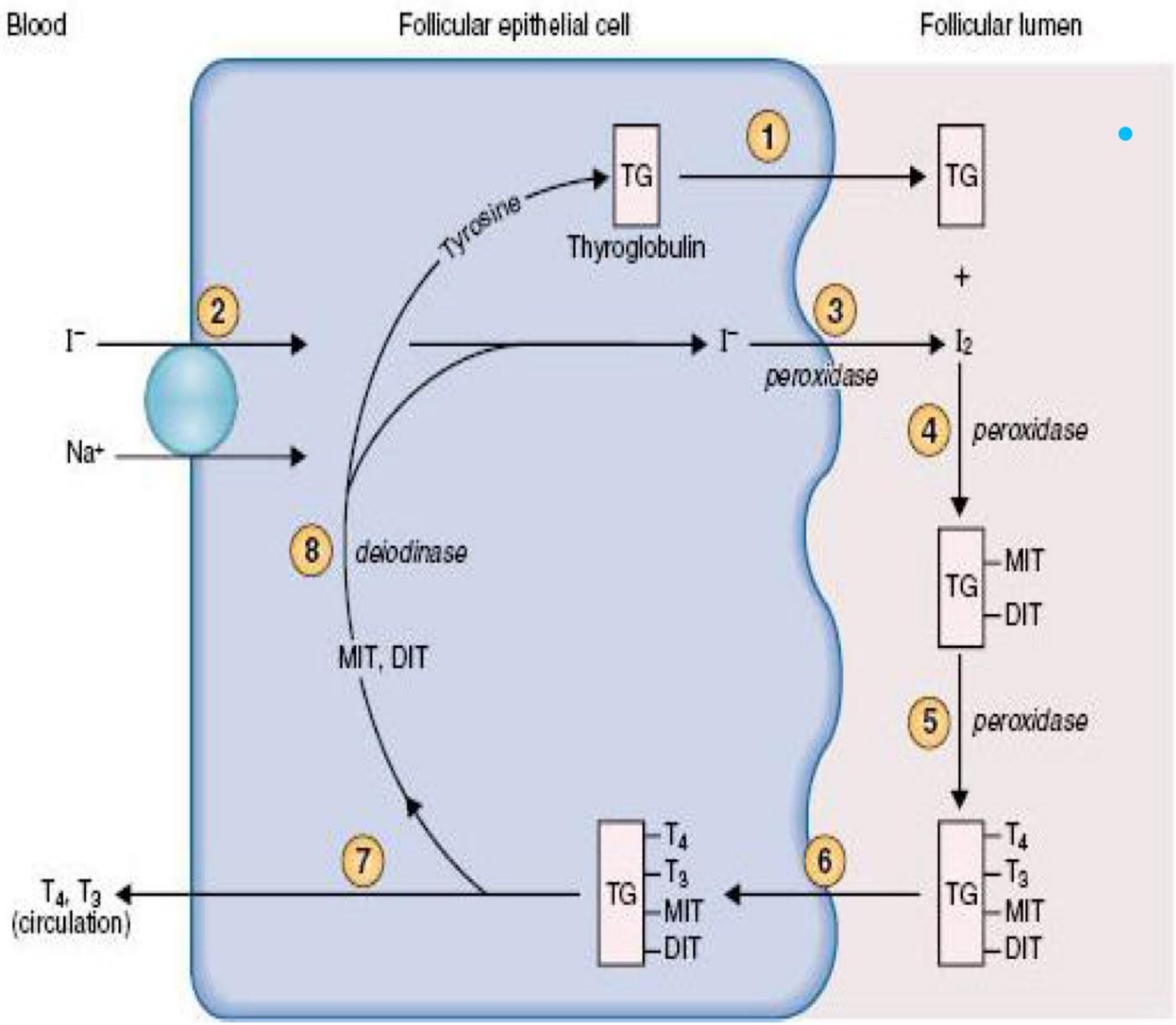
thyroid gland	
Anat	-two lobes and a junc between them -on either side of larynx & A. to trachea
Hormones	-T3 -T4 -reversed T3(inactive T3) -Calcitonin
Synthesis site	-follicular cells: T3 & T4 -Parafollicular cells: Calcitonin (there are follicles within the gland, the cells lining it are follicular cells, the ones adjacent to them are parafollicular cells)
Features	-T3 is most active but least abundant -contain a huge amount of iodine, supplied in diet -its hormones are synthesized both IC & EC -total body iodine intake must equal its output -thyroid have 250x more conc iodine than blood

Synthetic steps of its hormones	**1**- combining 140 molecules of tyrosine (which is glycopr) inside RER. and send it to Golgi, to form thyroglobulin then send it to follicular lumen **2**- intake of blood iodine via active pumps "iodine-Na cotransporter" (cuz the iodine conc in thyroid is higher than circulation) (stimulated by TSH) -wolff chaikoff effect: the higher conc of iodine in blood, the less active the pumps. Meaning when you have high iodine in circulation, the iodine active pumps will stop working and you'll have less thyroid hormones released **3**- the iodine taken from plasma is in form of iodide, so thyroid sends it to lumen as it is, and there peroxidase enz is used to convert it to iodine, which is usable **4**- binding of iodine to thyroglobulin inside the lumen by peroxidase enz, to form MIT & DIT (mono/di iod tyrosin). The iodine remains att to thyroglobulin forming MIT/DIT-thyroglobulin complex , until the gland is stimulated **5**- on the surface of thyroglobulin, DIT binds to DIT, & MIT binds to DIT, forming T4 & T3 "on the surface of thyroglobulin, so thyroglobulin has on its surface: T4, T3 and some DIT & MIT that didn't bind together and remained like that" (DIT binds to DIT faster than DIT binds to MIT, hence the amount of T4 is much larger). Then stores the entire thyroglobulin molecule with its surface subs in the follicle/lumen. (the amount stored is suff for 3 months) **6**- once thyroid is stimulated, follicular cells endocytose one thyroglobulin molecule, then fuses it with a lysosome to hydrolysis it, and the products are: T3, T4, DIT, MIT & thyroglobulin. T3 & T4 are released into circulation, while DIT, MIT & thyroglobulin are recycled by deiodinase.

Steps summary

(very important to understand it well - its really easy)



nice Steps summary of imp info			
Event	**Site**	**Enz**	**Inhibitor drug**
TG synthesis and send to lumen	RER, Golgi, lumen		
Na-I cotransport	Basal mem, junc with circulation		perchlorate & thiocyanate
Iodide to iodine	Lumen	Peroxidase	Propylthiouracil
I-TG bind forming MIT/DIT-TG-comlx	Apical mem surface-lumen	Peroxidase	Propylthiouracil
Forming T3&T4-MIT&DIT-TG-cmlx	Apical mem surface-lumen	Peroxidase	Propylthiouracil
Stimulus: TG endocytosis	Apical mem		
Hydrolysis & releasing T3,T3, MIT,DIT & TG	Lysosome	Protease	
MIT&DIT recycle	IC	Deiodinase	

* Propylthiouracil: is used to treat hyperthyroidism

Back to thyroid gland	
Hormones in blood	**Bound** -inactive -80% -binds to <u>thyroxin-boundable-globulin</u> (made my liver) -small portion binds to albumen **Free** -active! -small amount: T3 (more, cuz it's the needed form) -smaller amount: T4 -it's the only type that triggers negative FB
Blood hormones in	**Liver failure** -causes hypopremia (specially TBG) → more free hormones in circulation → trigger negative FB → less hormones secretion **Pregnancy** (a mother must have enough for her and her child) Liver makes more TBG → more bound and less free → negative FB stimulates more secretion (so it pregnancy, liver produces more TBG to indirectly get more thyroids T3 &T4)
T3 & T4 (thyroids) uptake	1- unbound from Pr (its very slow, cuz it has very high affinity to bind) (half of body's T4 takes 6 days to unbound & 1 day for T3) (T4 is much less toxic. That's why we secrete it as T4 then convert it to T3 once we need it, by deiodinase enz. "90% of all T4 is converted to T3 before use") 2-thyroids easily diffuse through cells and goes to N (can stay there stored for weeks) 3- in the N, T3 binds to Thyroid Hormone Receptor on the DNA and exerts an effect (forming specific Pr - mRNA)
Thyroids	**BMR**

effects	-is the energy required for u to exist doing nothing -anthyroidemia = 50% less BMR -hyperthyroidemia = 50-100% more BMR **Metabolics** -Carbs: more glucose GIT absorbtion & cells uptake glycogenolysis & gluconeogenesis -fat: lipolysis & free fatty acids oxidization. Loosing cholesterol in feces (hypocholestrolemia) -Pr: very high catabolism (muscles atrophy) *-all the effects are done by hyperstimulation of these enz:* Cytochrome oxidase NAPDH cytochrome C reductase malic enz protolytic enz Alpha glycerophosphate dehydrogenase **CVS** -inc HR & SV (thus inc CO) (thus more blood to tissues) -dec perephral resistance -induced by CAT-like effects of thyroids (acts on cardiac Beta-receptors, altering: SR, Ca-ATPase, myosins) (so beta blockers "propranolol" is used to treat hypertsm) **Bone** -bone formation, maturation, ossification & plates fusion -def in infants causes dwarfism & irreversible mental retardation **GIT** -inc appetite, GIT juices, motility -hyperthyroidism: dia. -hypothyrodism: constipation

	CNS -in infants, its <u>essential</u> for CNS maturation -adults hypertsm: hyperexcitability & irritability (disturbance) -adults hypotsm: less memory & mentality. Slow movement **Resp** -hyperventilation -inc RBCs <u>2,3-DPG</u> → faster O2 disassociation
Regulation MOA	by HT-PG axis **TRH** -Pr (tripeptide) -by HT (paravent. N) -acts on PG A. lobe (thyrotrophs) to release TSH **TSH** -glycopr -starts release at 12 gestational week of embryo -affects thyroid growth and its hormones release -inc effictivness of all steps of biosynthesis of thyroids
Regulation factors	Factors releasing thyroid hormones -thyroid-stimulating Ig (antibodies mimicking TSH “graves”) -inc TBG (in pregnancy) Factors inhibiting thyroid hormones release -deiodinase def -less TBG in blood -excessive iodine intake (wolff effect) -perchlorate, thiocyanate & Propylthiouracil (meds)