Renal & Endocrine System

Kidney Function & Structure

① Humans Cannot turn N from Protein into a gas, therefore we make two compounds.

(Nitrogen) → Urea ($\frac{15\ mg}{dL}$) & Creatinine ($\frac{1\ mg}{dL}$) ← (Nitrogen)

Nitrogenous waste through Urine

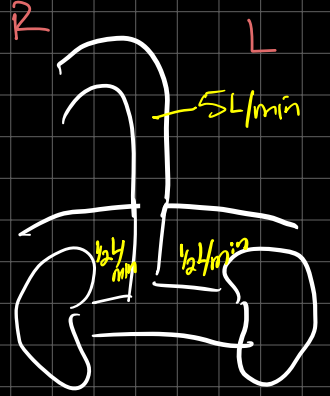
- Uria: Suffix for "in the urine"
- Produce Urea in the liver & Creatin in Skeletal Muscle
- Still Making both Compounds When in Renal Failure

→ Kidney failure: High Concentrations of Urea & Creatin

⇒ Uremia: Death in 10 days w/out Dialysis: Run Persons blood through a Chamber & Excrete Cr & Urea

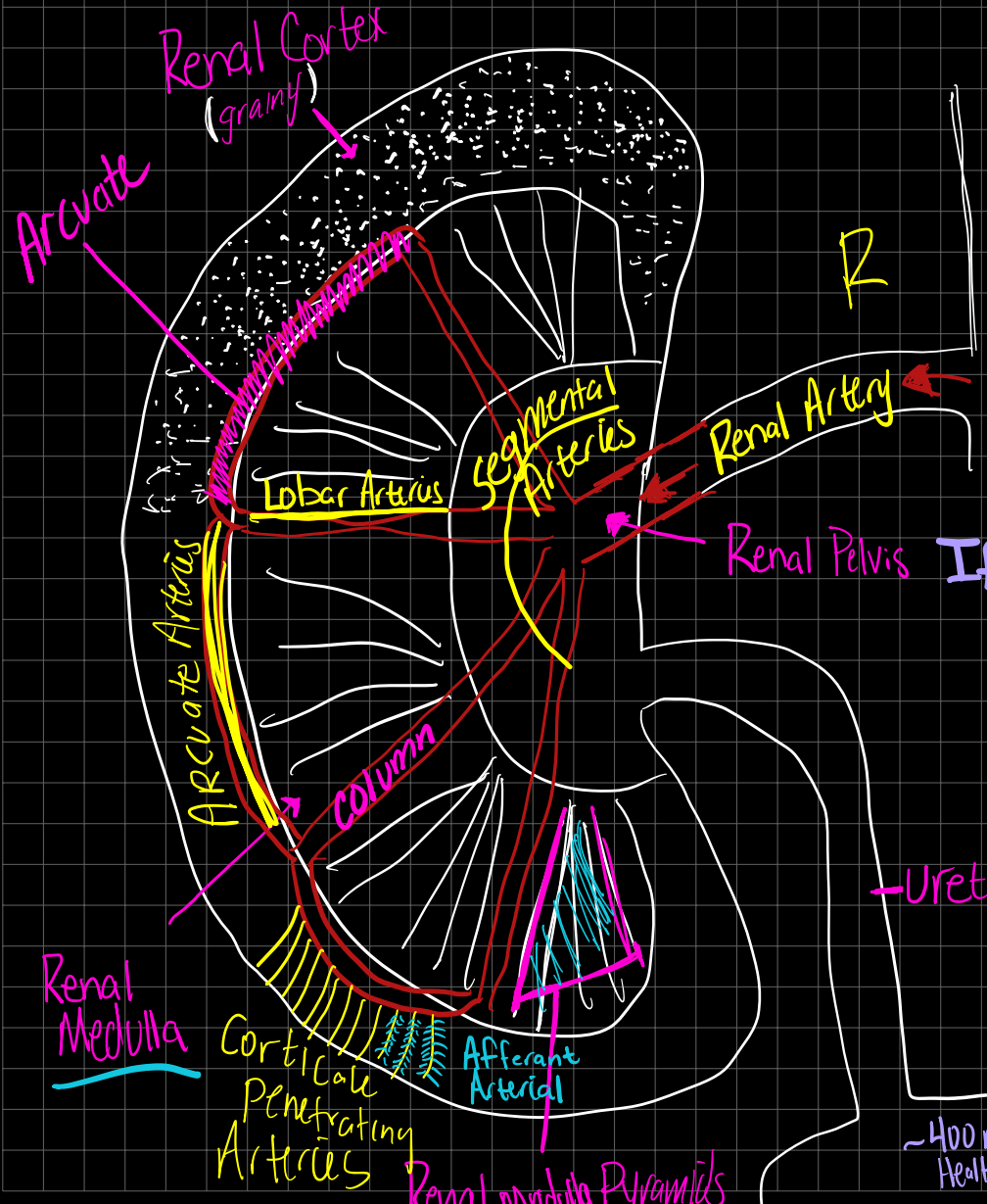
- Blood Sample: Measurement of: Blood glucose, Na^+, K^+, blood Urea Nitrogen (BUN)

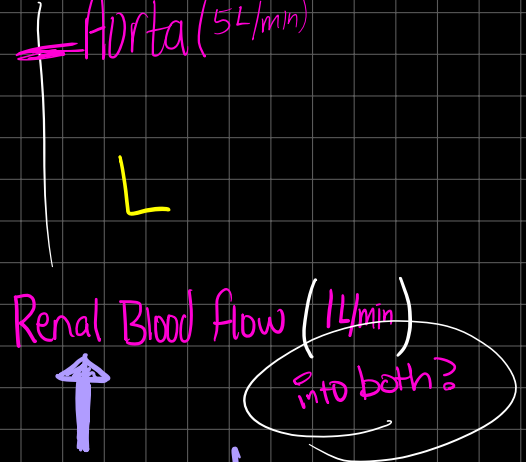
② Maintain Water balance in body to keep Na^+ levels in Check



* 20% Blood flow ?!?! Thats a lot!

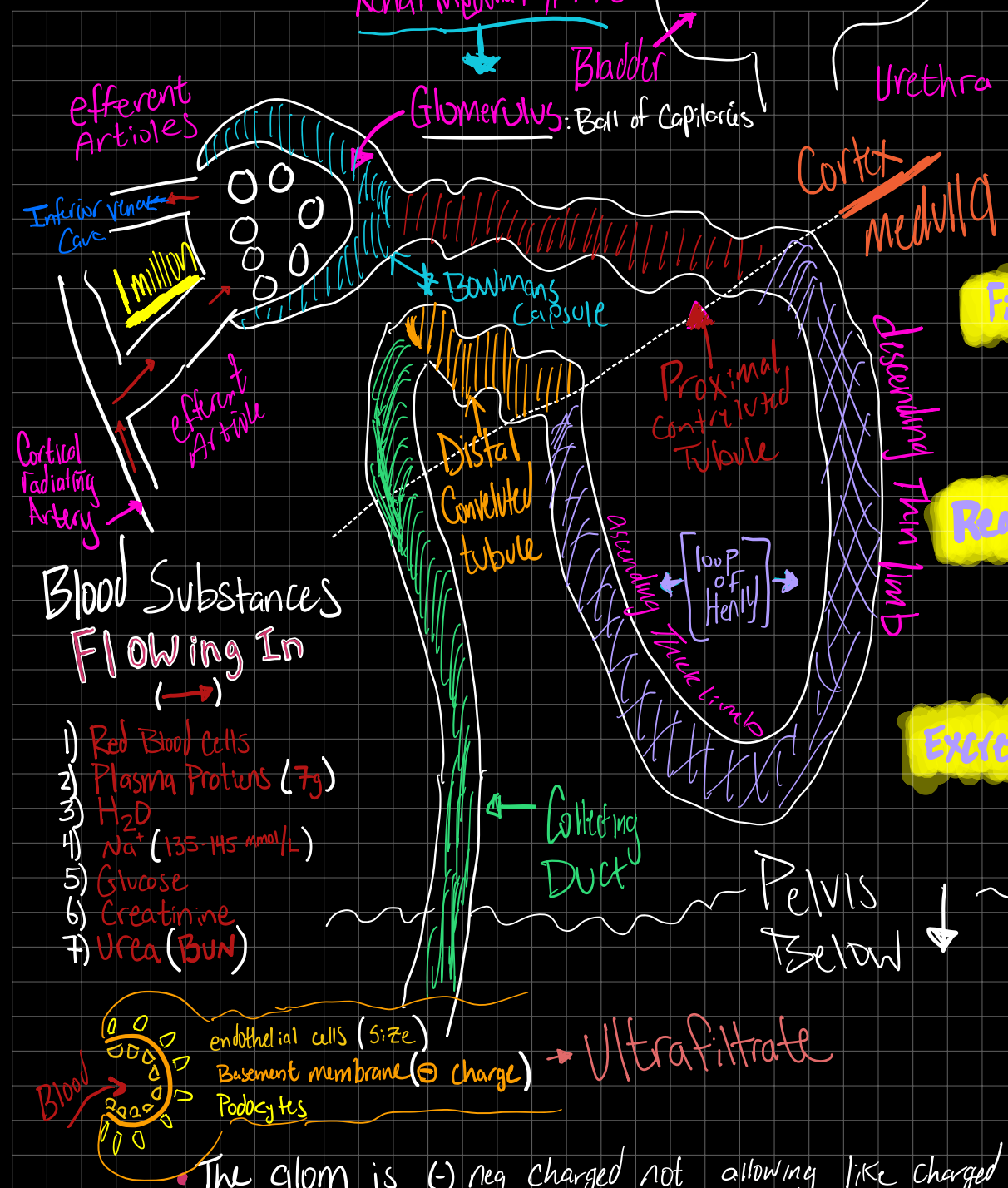
- Normal Urine production = 1 mL/min
- Diuresis: Higher than 1 mL/min production of Urine
- Diuretics: Decrease blood Volume → Less Venous return → Lower Bp / Decrease [Na+]
  - ★ Too much; Urinate To Death
- Diguria: .3 ml/min or lower, from Renal failure





- Renal artery enters Kidney & Branches to the renal Columns
  - Segmental arteries -
- Segmentals go through to the Cortex
  - Interlobar Arteries -
- Interlobar arteries Connect @ border - Arcuate Arteries -
- Branching of the arcuate are The - Cortical radiating Arteries
- Stemming from the Cortical radiating Arteries are
  - afferent arteioles -
  (1 million / Kidney)

- Hydronephrosis: Enlarged pelvis due to stone Stuck in Ureter; Urine Can't move out
  - Soln. → Surgery / diuretic / morphine
- Kidney stone: Formed from Dehydration
  - Oliguria → Static urine in Pelvis
  - Stones form of stuff / Hematuria



- The loop of Henle form Pyramids
- Blood Substances 1&2 get filtered (Seperated under pressure)
  3-7 pass through glomerus

Filtration

- **Hematuria**: Heme/RBC in Urine
  → Glomerus Damaged, Endothelial layer
  Soln:
- **Proteinuria**: Plasma Protiens in Urine
  → Glomerus Damaged, Basment Membrane
  Soln:
  - (Possible to have both)

Reabsorption

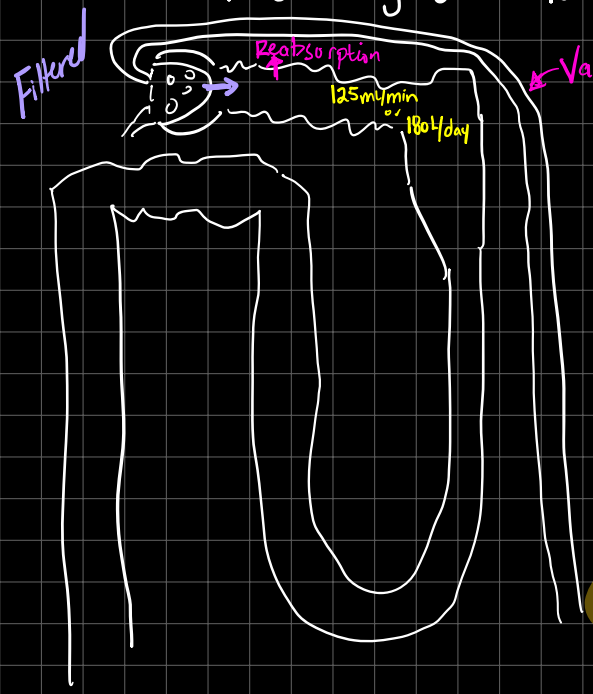
- 6&7 are excreted
- Blood Substances 3-5 are reabsorbed back into blood Stream

Excretion

- The glom is (-) neg charged not allowing like charged plasma proteins through [Also too Big]
- The more Na^+ reabsorbed → The more H_2O gets reabsorbed [Amount based on loop of Henle]
  → More Na^+ → Higher [urine] → less H_2O lost

Soln: Morphine or Diuretics

- A Collecting duct longer than the loop of henle → Powder Urine / No H_2O loss



- Glomerular Filtration Rate (GFR): [Healthy: 125 ml/min or 180 L/day]: The rate at which fluid is filtered out the glomeruli (12.5% or 1L)
- 875mL goes out the efferent arteriole
- If GFR decreases; Urea & Creatin increase in bloodstream
- 99.5% of H_2O reabsorbed, 99.5% Na^+, 100% Glucose
- 50% of Urea reabsorbed, 0% Cr reabsorbed

$\left(\frac{Bun}{Cr} - \frac{5}{1}\right)$

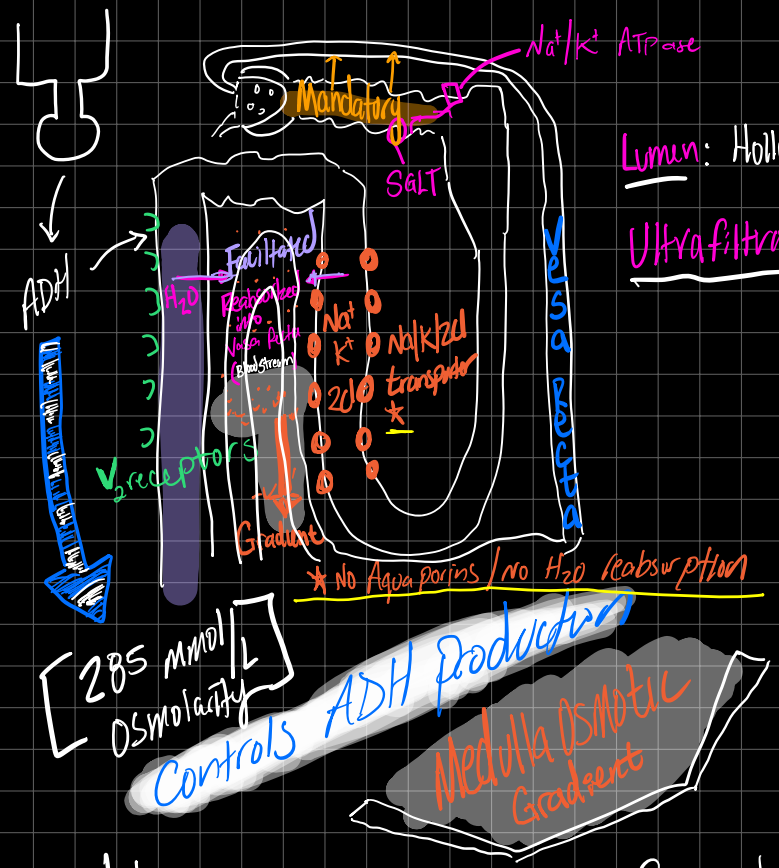
- Diabetes Mellitus: Glucose in Urine / Glycosuria
- 3-5 reabsorbed into the Vasa Recta which is used to filter Urea & Cr
- Renal Failure: GFR below 30 ml/min

Soln: Dialysis / Kidney Transplant / death

Renal Failure → AKA → Kidney Failure

- Glomerular Hematura: RBC in loop of Henle → Urine / Entered from Glom / Diabetes or Hypertension — Dismorphic Shape RBC
- non-Glom Hematura: RBC in Urine / UTI or Bladder Cancer / Entered in After Pelvis — RBC shape is preserved

Reabsorption

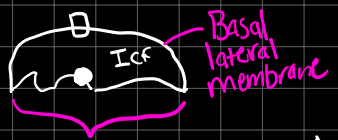


Lumen: Hollow tube where fluid/Air flows

Ultrafiltrate: fluid flowing through PCT to Pelvis

- 65% Na^+ reabsorbed in Proximal Convel Tubule
  - ⇒ Mandatory H_2O reabsorbtion 65%
- H_2O reabsorbed in the Collecting Duct
  - → Facilitated H_2O reabsorption
  - Facilitated by Pituitary gland (Connected to) which produces ADH (Anti diuretic Hormone)
    - A hormone is produced here but helps over there -
- ADH increases H_2O reabsorbtion in Collecting duct
  - → Small amounts of urine
  - ADH ⇒ Vasopressin
- **Diabetes insipidus**: Disease of the pituitary gland which Decreases ADH production; less H_2O reabsorbed
  - GFR Same
  - → Soln. DD AVP, recombinant engineered ADH for Humans (nasal spray)
  - DDAVP is given to bedwetters to increase ADH, Increase H_2O reabsorbtion → Smaller urine output

- Na^+ is reabsorbed first, then followed by H_2O due to osmosis
- 67% Na^+ reabsorbed in PCT/DCT/Mandatory ascending (M F)
- Along PCT are Cells



- Black circle in apical membrane
  - ⇒ Sodium Glucose Transport (SGLT)
    - → Causes Na^+ & Glucose into PCT & then Na^+ transported out by the Sodium Potassium - ATpase & the Basal lateral membrane into the vasa recta

→ 200 mg/dl
(Transport max)

Diuretic increase Urine

Drugs

1) Hypertension
2) Pulmonary Edema
3)

① "Flozen": Antagonizes SGLT / (diuretic)
- less Na^+ reabsorption ↓
increases urination Ex.

② "Anti ADH": Antagonize Pituitary gland / diuretic
- Decrease ADH production Slows down facilitated reabsorption
Example: Ethanol, alcohol, Coffeine

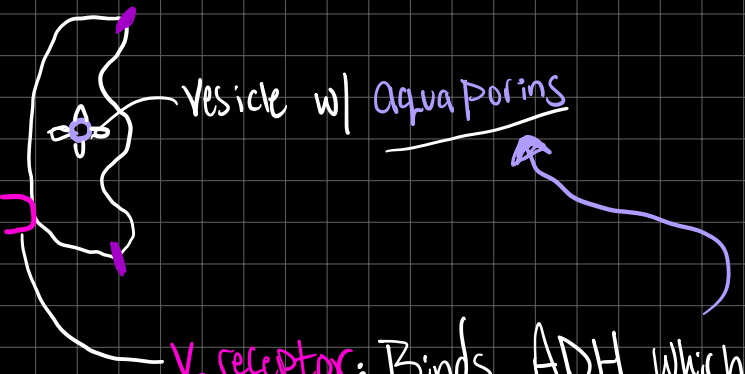
③ "Tan": V_2 antagonists, Aqua Porins in ICF
- Decrease H_2O absorption, but Na^+ must be first
Example: tolvaptan / Flozatan

④ "Iasix": loop diuretic / slows Na^+ absorption by antagonizing the $Na^+/K^+/2Cl$ transporter which slows H_2O absorption
Where? Ascending limb of loop of Henle
Example: Given for Pulmonary Edema

→ Most diuretic reabsorb less Na^+

Amount Reabsorbed depends on [Glucose] relative to T_{max} $[Gl] <$ Absorb more
$[Gl] >$ Absorb less, Glucosuria, Polyuria,

- A Foley Catheter is used when one is under general Anesthesia to track urine output



V_2 receptor: Binds ADH which then Signals to embed themselves in the apical membrane which Allows H_2O out of the Collecting Duct (Makes permeable)

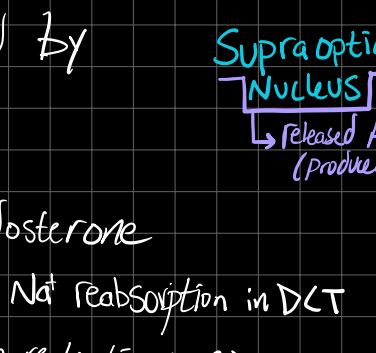
- In the ascending limb of apical membrane
→ $Na/K/2Cl$ transporter
- Na^+ is reabsorbed but ascending limb is not permeable to H_2O b/c there are no Aqua Porins

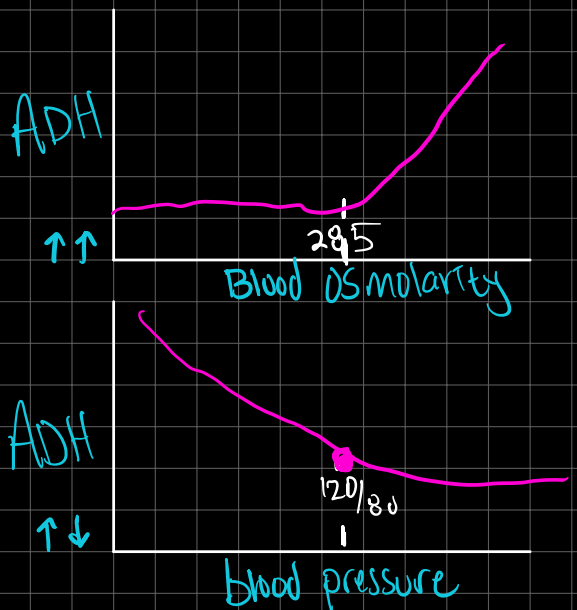
- Na^+ is reabsorbed but Regulated by Aldosterone in the DCT

- **Conn's Disease**: too much Aldosterone
  - ↳ Tumor in Adrenal Gland → Increases Na^+ reabsorption in DCT
  - → Increases H_2O reabsorption in CD
  - → Hypertension / ↑BV & BP

- **Addison's Disease**: Too low Aldosterone
  - ↳ Cancer → Opposite of Conn's
  - → Edema / hyponatremia / Syncopy

- Gland sitting on top the kidney is Where Aldosterone Comes from
  - Adrenal Gland





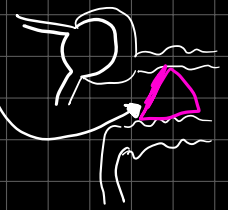
Cells respond to:

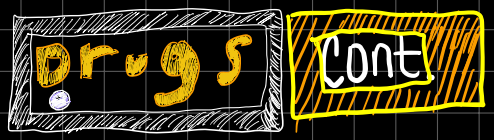
① Blood osmolarity:
- → [Conc] of Solutes dissolved → 285 mol/L
- ocean 750 ⟷ water 0
- Hyperosmotic / Hypoosmotic
- → When dehydrated
  - Increased osmolarity
  - Neurons ↑ Ap → ↑ ADH
  - low urine / ↑ H_2O reabsp.
- → Directly related
  - ADH ↑ & BP

② Blood Pressure:
- → If low BP, ↑ ADH, Collecting duct perm, H_2O ↑ in vasa recta → BP ↑
- → If High Bp, ↓ ADH

- DCT has aldosterone receptors to pump more Na^+ to vasa recta

- Juxtaglomerular Apparatus
  - → Renin Angiotensin Aldosterone System
  - → Bp ↓, Bv ↓ ⇨ Produce renin
  - → Renin breaks angiotensinogen & breaks it down to Angiotensin I
  - → ACE enzyme (Angiotensin Converting Enzyme)





Mantril - osmotic diuretic
Thiazide

⑤ Pril Drugs (in lungs): ACE inhibitors, stops Ace from turning Angiotensin I to II which decreases amount of aldosterone produced from the adrenal gland
- ↓ Na^+, ↓ H_2O, ↓ Bv

ex. Lisinopril

in lungs which converts Angiotensin I to II

→ Angiotension II goes to stimulate adrenal gland

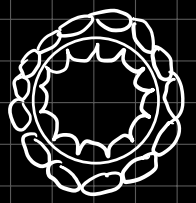
→ more aldosterone produced, ↑ Na^+ reabsorbed, Bp ↑

Blood Glucose Regulation

- Glucose in Human: 70-100 mg/100 mL
  (Normal) Euglycemia
  - Hyper: Above 100 → Endothelium dysfunction
  - Hypo: Below 70 → CNS Dysfunction
    Below 40 → Coma

- Blood Brain Barrier (BBB)
  → Stops most things from getting in
  → Glucose/O_2 allowed in
  → Brain is glucose dependent

⑥ Spironolactone: In the DCT, Blocks aldosterone receptors, decrease Na^+ reabsorpt.

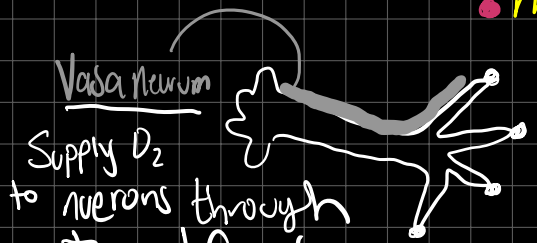


- Hyper: Endothelial Disfunction
  → ↓NOS, ↓NO

- Nephropathy: Endothelial Disfunction In Kidneys

- Retinopathy: In eyes

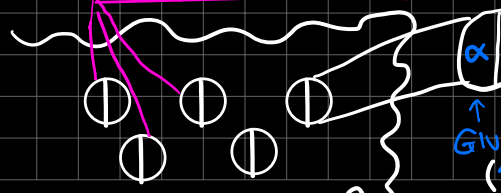
- Neuropathy: Nerve Death
  - Most likely to Sensory nerves (smaller neurons)



Peripheral Neuropathy - damaged Vasa Nervum → Endothelial Disfunction

IN OUR Pancreas: Antagonistic Control of blood Glucose

Islets of Langerhans



Counter regulatory Pancreatic Hormones

Glucagon Receptors

Phosphorylase which breaks 1,4 Bonds

Activates

Liver

Stores Glucose/liver glycogen

3 Days

α(1,6) Bonds Sep's 1,4 Bonds "Highly Branched"

α(1,4) Bonds: Production by

Hers Disease

- Don't make phosphoralase
  - No breaking α 1,4 bonds
  - Nocturnal Hypoglycemia
  - BG ↓ / Hepatomegalia (large liver)

→ Drink or Eat

- Asleep
  → Glucagon binds to receptors on liver
  → phosphoralase is signaled & Breaks ACH Bonds
  → Glucose leaves liver
- Eating food
  → Insulin Secreted & binds to insulin receptor on Skeletal muscle
  → Signal GLUT 4 to translocate to membrane
  → Glucose into skeletal muscle

Brings GL to normal levels

Tyrosine Kinase
Insulin receptor
Glycogen Synthase
Tetramer
↳ Insulin Receptor Substrate 1
↳ get phosphate
Ca^{2+}
GLUT 4 Transporters

Insulin Signal Transduction Pathway

Intercellular to Sarcolemma

- Glucose that needs to be turned into glycogen by a synthase
- Glycogen in Skeletal muscle
  → Phosphoralase can break Alpha 1,4 bonds & use the glucose to make ATP

Insulin does What?

1) Inhibits phosphoralase
2) Inhibits Gluconeogenesis
3) increase Glucose output at skeletal muscle; less intake

Starvation: Once 3 days worth of liver glycogen is gone; Muscle proteins will be Converted into glucose: Gluconeogenesis

- Body mass ↓, lost muscle,
- Get edema → loss of protein → Fg PP↓ Protein Malnutrition

Diabetes Mellitus: (Honey Urine)

Blood glucose of 200+ glucose/Where Some is Urinated out
→ Dilted urine / polyuria / Thirsty / lose weight
↳ ALOT ↑ (polydipsia)

Cause

① Type I / J.O. / IDDM (Juvenile Diabetes)
- Bcells Destroyed, ↑ BG
- Honey Urine
- Insulin injections
  ↳ Too Much Death

② Type II / AO / NIDDM (Adult onset)
- Insulin Resistant Receptor
- No Signaling GLUT 4

Oral Hypoglycemics
1) Fats
2) TNFα
→ affect Tyrosine kynase of Insulin receptor preventing Phosphoralation
① lipotoxicity
① Fat in Muscle Cells

Glipozide → Bcell → increase Insulin secretion

Gloplast
Met Formin → Liver shuts off liver

Mannitol: Fast acting loop diuretic / Osmotic diuretic like Glucose (Causes)

Helfonica: Slows liver Glucose output b/c Liver is insulin resistant / GLUT4 to Sarcolemma ← tells B Cells to increase insulin output ←

Reproductive Systems

Gestational Diabetes:
Insulin resistant during Pregnancy

Macrosomia
Fat baby
C section

Pituitary
Ant
Post

LH = Lutenizing Hormone
FSH = Folicle Stimulating Hormone
(produced by Granulosa cells)

E = Estradiol
P = Progesterone

Ovary
LH
FSH
Hormonal cells
Hormones make other ones
28 Day
(Almond shaped)

Uterus
28 Day
Endometrium - E, P Target
Myometrium - Smooth muscle

Hormone replacement therapy

Rabbit test
Produced when fertilized ovum is present

oviduct
Fimbria
ovum surrounded by Granulosa cells
Corpus luteum
primary follicle:

Uterus
HCG: rescue of corpus luteum
ensures cycle is one Direction

ovarian ligaments

7 mon.	2 mil
Born	1 mil
13 yr	½ mil
21 yr	200,000
51 yr	0

or

oviduct
16
17
18
19
5 Days to Wait for glycogen & Blood flow
of Day 15

Broad ligament
Hold Uterus, Ovaries, & Ducts in place in abdominal cavity

Oral Contraceptives
Work on Pituitary
(-) Feedback by E & P (↑ 3x)
→ Low LH & FSH / NO (+) FB or LH Spike

RU-486
Progesterone Receptor Antagonist
Pantagonist
Blood flow & Glucose ↓, menstrate
↓ VEGF GS
(first 3 months)

Ovarian Cycle
E
FSH
LH
P
Estradiol
5 14 15 21 28

[+/-] Cycle
E shuts off pituitary & makes negative feedback to only have 1 cycle @ a time

Uterine Cycle
E
FSH
LH
P
5 14 15 21 28

Follicular Phase

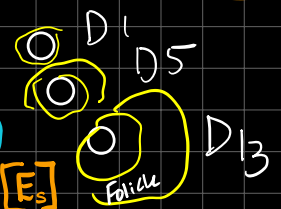
Days

(+) Feedback from Pituitary lets LH out
- midcycle spike

3 Phases (non pregnant)

① Follicular Phase (1-13)

- FSH causes primary follicles to grow (10x E prod) (uses E)
- Day 5: Graffian follicle (only granulosa cells ↑)
  - ↳ High [E_2]



② Ovulation (14)

- LH spike makes G follicle fuse to the ovary
  - → ovum is released / g cells make Corpus luteum (Produces E & P) (Day 15)

③ Luteal Phase (15-28) (P-driven)

- Vatenized Corpus luteum grow for 7 days (Day 21)
- If not pregnant (Day 28), Corpus luteum shrinks (Corpus albicans; 100)

- First cycle ever for a woman → Menarche
- Last cycle ever for a woman → Menopause
- Ovum contains DNA to make fetus is fertilized

Days

3 Phases

① Menstral Phase of UC (1-5)

- Enlarged endometrium (10x)
- E dependent / ↓ Blood flow & ↓ glycogen

② Proliferation Phase of UC (6-14)

- P activates Vascular Endo Growth Factor ✓
  - Veg + Glycogen Synthase → glycogen ↑ & Spiral Capillaries Form of endometrium
- Progest, Acid

③ Secretory Phase of UC (15-28)

- By Day 21 if not Preg. P Falls
- 9mm of endometrium shedding including

- Follicular Phase Defect: Doesn't ↑ (10x) (give E or Supplements)
- Luteal Phase Defect: Making Corpus luteum problems or inability for it to grow ovariary (give LH or P)
- Amenorrhea: lack of uterine cycle (low body fat)

Pregnancy

Ectopic pregnacy: egg stuck in oviduct

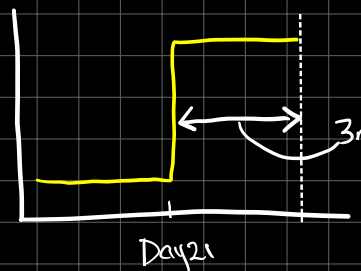
Placenta Previa: Os covered by Placenta

① On Day 20 as the ovum gets to the uterus, it will implant itself in

② Intercourse allows Spermatozoa to

the Wall & produce Human Chorionic Gonadotropin Which will act on the ovary & rescue the Corpus luteum before it shrinks
→ P&E will continue to rise

Fertilize the Ovum in the Oviduct & then implant in the wall of the Uterus (Now Zygote)

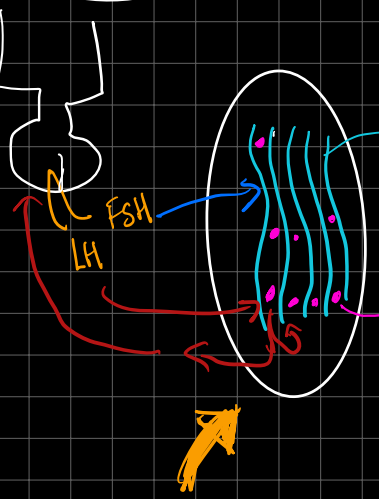


③ Last 6 months has Placenta to provide E&P / First 3 months E&P come from Corpus luteum thanks to HCG

④ Birth; Placenta Comes Out; E&P ↓ a lot!
- Post Partum Depression - Rapid drop in Progesterone

Precursor: PMS

Soln slowly ↓ E&P by Medication



Male Teste

Seminiferous tubules: produced Spermatazoa (800 per testis)
→ By FSH

Interstitial cells: produce testosterone
→ By LH

In Bloodstream
1) ↑ Muscle mass
2) ↑ Bone mass
3) ↑ RBC / EPO

Surgical Castration: removal of testes
→ decrease testosterone

LuPron: FSH & LH antagonist on the pituitary
→ used for Chemical Castration

FSH + LH Working on seminiferous tubules together produce spermozoa

gelding - neutered horse
stallion - not neutered

Oral contraception

Progesterone shut off pituitary

Testosterone stabilize testosterone

- Placenta Previa: low uterine implantation of ovum
- Endometriosis: retrograde of endometrium into oviducts & more
  - → Can cause infertility
    - Soln. ↓ E, stop proliferation & leakage into abdomen

Fertilization of ovum in Ampula first 1/3

Clomid Estradiol Antagonist lowers E_2 to reduce endometrium production

↑ FSH + LH
Works on pituitary

* Slow Estradiol production → Follicular Phase defects