week 1

Blood

☆ Total body water can be determined by using of "deuteriumoxide (D_2O)" 2017. mid

* ^3H_2O , Antipyrin (phenazon)

Date Sep 7 Thu.

(ポイント) intracellular の方が多い!!

☆ Body fluid — 70 kg man だったら、

42L が water

(60% is water)

- intracellular fluid 2/3 (28L)
- extracellular fluid 1/3 (14L)
  - intravessel (blood Plasma) 3 - 3.5L
  - interstitial 11L 80%

(※ transcellular fluid ... eye ball , Joint)

by inulin , mannit

by ^{131}I- albumin , Evans blue

☆ Cellular elements

- RBC (erythrocyte) ♂ 4.5 - 6 M / μL
  ♀ 3.9 - 5.3 M / μL ← ∵ mensttruational bleeding

- WBC (leukocyte) 4K - 10K / μL

  - Neutrophil granulocyte 50 - 70 % — against bacterial infection の時 ↑
    - Phagocytosis ~~(→ can be Mφ)~~
  - Lymphocyte 20 - 40 %
    - T cell ... cellular immune responce → T cell can kill other cell (NK cell)
    - B cell ... can produce different immunoglobulin molecules

      IgA , IgD , IgG , IgE , IgM ... humoral immune response (liquid)

      Plasma protein (circulating in blood stream)
  - Monocyte 2 - 8 % , φ : 20 μm (biggest WBC !)

    leave the vessel → Mφ
    - Phagocytosis
  - Eosinophil granulocyte 1 - 4 %
    - allergic rxn の時 ↑
    - parasitic infection の時 ↑ → GI tract にいると...
  - Basophil granulocyte 0.5 %
    - produce "Histamin" ("Heparin") (→ Mast cell)

    昔はこう書かれていた

Never Let Monky Eat Banana

60 30 6 3 1

Date

- Platelet (Thrombocyte) 150k - 400k / μL

☆ Blood plasma

- water
- plasma protein … 60-80 g/L → 5 functions
  - albumin 1/3
  - globulin 1/3
  - fibrinogen 2-4 g/L
- glc
- ions

organic elements: plasma protein, glc
inorganic elements: ions

5 functions:
- hemostasis (blood clotting) ← coagulation ∵ clotting factor is plasma protein
- transport e.g. iron is transported by "transferrin" ∽ hormone や ion も 例 albumin によって よく運ばれる
- immune function ∽ immunoglobulin, interleukin, cytokine
- pH regulation ∽ act as buffer
- maintain colloid osmotic pressure
  - acidosis の時は $[H^+]$↑ なので だから、plasma protein should bind H^+ to normalize.
  - alkalosis の時は、逆に plasma protein が release H^+!

☆ filtration … water molecule leave the capillary

plasma protein … against filtration

→ water

edema … filtration is increased すること

forces

① hydrostatic pressure of capillary (outward) ∽ blood pressure と思って ok!

② colloid osmotic pressure of plasma (inward)
= oncotic pressure

③ hydrostatic pressure of interstitium (inward)

② ③ against filtration!

∽ edema の時に massage すると 良いのは この為.

④ colloid osmotic pressure of interstitium (outward)

Net filtration pressure = ① - ② - ③ + ④

Date

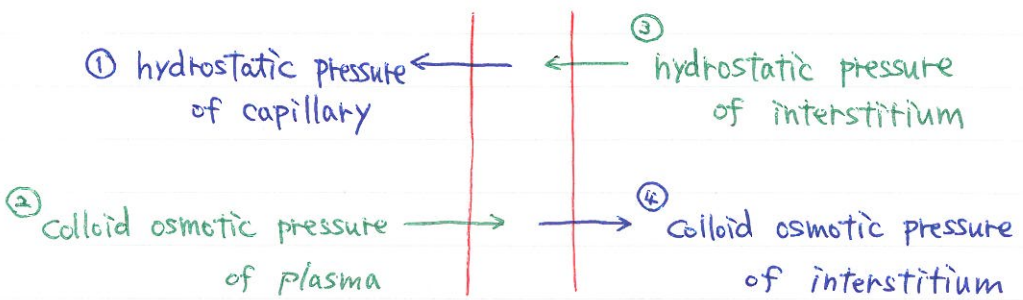
食事 protein 不足すると、Liver can NOT produce plasma proteins

Q1. Protein malnutrition の時、filtration は？ ⇒ ② ↓ ⇒ filtration ↑

Q2. How would filtration change if sb has Liver failure / alcoholism ? ⇒ 同上

Q3. How would filtration change when Thrombosis ? ⇒ more blood in vessel ⇒ blood pressure ↑ ⇒ ① ↑ ⇒ filtration ↑
(blood clot in vein) ∵ 心に帰れない.

Q4. How would filtration change when there are more glycoprotein outside vessel ? ⇒ colloid osmotic pressure of interstitium ↑ ⇒ filtration ↑



☆ glucose 3.5 - 8.5 mmol / L (after meal) ※ 5.5 mmol / L = 100 mg / dL (ヨーロッパ / イラン・日本)
$\bar{X}$ = 4 - 6 mmol / L (before meal)

☆ ions in blood plasma

④ - K^+ = 4 - 5 mmol / L (very important !!) (内) 150 mmol / L (30倍)
∽ if hyperkalemia ($[K^+]$↑) ⇒ die (∵ K^+ can stop heart in dyastole) heart surgery では心を止める為にあえてやる！
if hypokalemia ⇒ arrythmia (不整脈)

① - Na^+ = 135 - 150 mmol / L (内) 15 mmol / L (1/10) ⟩ maintained by "Na^+, K^+ - ATPase" $3\,Na^+ \rightleftarrows 2\,K^+$

② - Cl^- = 96 - 106 mmol / L

③ - HCO_3^- ≈ 24 mmol / L

⑥ - Mg^{2+} ≈ 1 mmol / L
- PO_4^{3-} ≈ 1 mmol / L

⑤ - Ca^{2+} ≈ 2.5 mmol / L ⟩ 50% … free form
50% … bound to plasma protein

week 2

Date Sep 14 · Thu.

☆ ion conc. 高い順に並べると、

K^+_{in} (>150 mmol/L), Na^+_{out} (135-150), Cl^-_{out} (96-106), Na^+_{in} (15), K^+_{out} (4-5), Ca^{2+}_{out} (2.5), Mg^{2+}_{out}

☆ filtration questions !

Q1: protein malnutrition ⇒ Liver can NOT produce plasma protein ⇒ ② colloid osmotic pressure of plasma ↓ ⇒ filtration ↑ (② = inward force)

Q2: dehydration ⇒ blood volume ↓ ⇒ blood pressure ↓ ⇒ ① hydrostatic pressure of capillary (outward) ↓ ⇒ filtration ↓

Q3. Glycoprotein @ interstitial space ↑ ⇒ ④ Colloid osmotic pressure of interstitium (outward) ↑ (dilution のイメージ) ⇒ filtration ↑

Q4. Histamin ⇒ Permeability of the vessel ↑ ⇒ more water is filtered ⇒ filtration ↑

Q5. Right ventricle failure の時 periphery の filtration はどうなる？

⇒ Lung への Stroke Volume ↓ ⇒ blood stack in periphery ↑ (Peripheral venous stasis) ⇒ edema (filtration ↑)

Q6. Acute Left ventricular failure ⇒ blood volume in Lung ↑ ⇒ pulmonary edema (periphery f ↓)

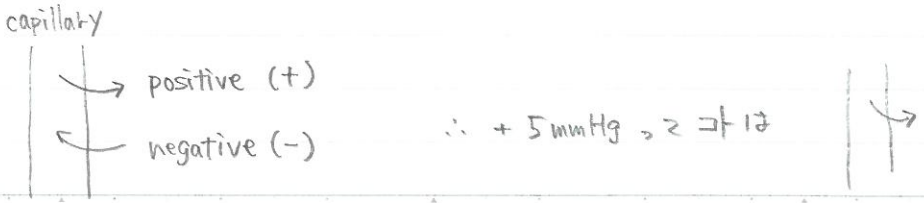
Q7. Liver failure ⇒ Liver can NOT produce plasma protein ↓ ⇒ ② Colloid osmotic pressure of plasma ↓ ⇒ inward force ↓ ⇒ filtration ↑

Q8. hydrostatic pressure of interstitial fluid ↑ ⇒ inward force ↑ ⇒ filtration ↓

Q9.

hydrostatic pressure of capillary	: 35 mmHg	← outward force
colloid osmotic pressure of plasma	: 30 mmHg	} inward force
hydrostatic pressure of interstitium	: 5 mmHg	} inward force
colloid osmotic pressure of interstitium	: 5 mmHg	← outward force

Net filtration pressure = ① - ② - ③ + ④ = + 5 mmHg



Q10. Which value is NOT Physiological range ?

♀ RBC 4.1 M / μL
Thrombocyte 250K / μL
WBC 12K / μL
- Neutrophil : 75%
- Lymphocyte : 20%
- M·B·E : 2%

⇒ Leukocyte cout 4K-10K / μL
neutrophil granulocyte distribution : 50~70%
⇒ WBC is high & neutrophil ↑
⇒ bacterial infection

Q11. 70mg / L plasma protein is normal ? ⇒ too low (∵ Plasma protein 60-80 g/L)

☆ Q12. 4.1 M / μL RBC for adult man ? ⇒ Low (∵ ♂ RBC 4.5-6 M / μL)

Q13. 200k thrombocyte for small kid ? ⇒ normal (∵ Thrombocyte 150k-400k /μ

✧☆ Q14. 8% eosinophil granulocyte ? ⇒ High (∵ eosinophil 1-4%)

☆ Q15. 125 mmol / L extracellular Na^+ ⇒ Low (∵ $[Na^+]_{out}$ = 135-150 mmol/L

Q16. which leukocyte is involved in parasitic rxn ? ⇒ Eosinophil granulocyte

Q17. which leukocyte is biggest in size ? ⇒ Monocyte (ϕ: 20 μm)

Q18. which leukocyte is involved in humoral immune response ? ⇒ B cell

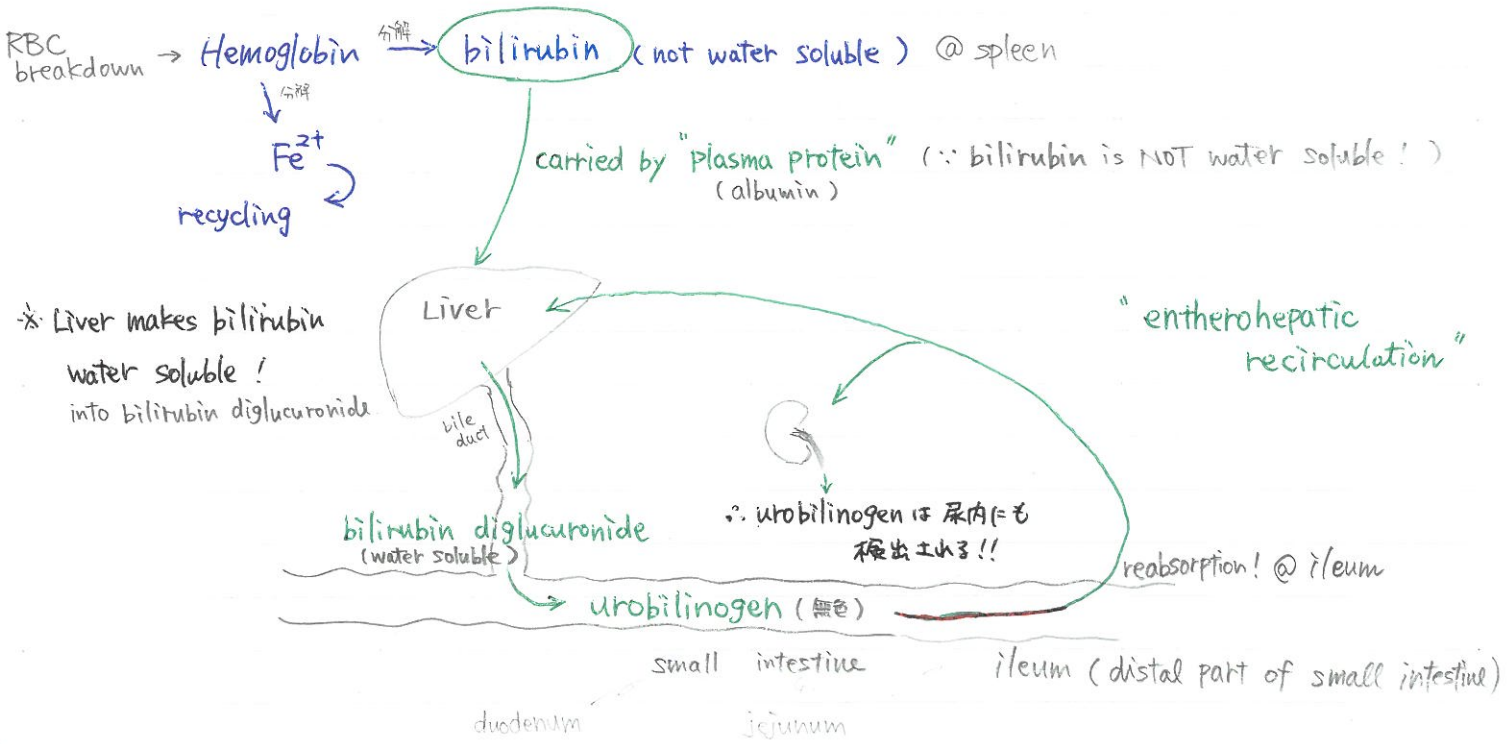
Q19. , cellular immune response ? ⇒ T cell

Date

☆ RBC detail

life span : 120 days ⇒ degraded in spleen
- Reticuloendothelial system

✧ Reticuloendothelial system



Q1. How would you call high cc. of bilirubin in blood plasma ? ⇒ jaundice

☆ Q2. C.C. of urobilinogen in urine is Zero ⇒ bile stone (行き場を失ったbilirubin は blood stream へ!)
but there are a lot of bilirubin in blood plasma

Q3. life span of RBC 40 days の時、bilirubin c.c. in plasma は ... ⇒ increase
urobilinogen c.c. in urine は ... ⇒ increase
∵ more & more RBC are degraded, more & more bilirubin produced!

ϕ diameter of RBC = 7 - 7.5 μm

Microcytosis < 7 ~ 7.5 μm < Macrocytosis

microcytic anemia
- iron deficiency

∵ surface of RBC is covered by Hemoglobin
if iron ↓ ⇒ Hb ↓ ⇒ smaller

もし RBC count low ⇒ macrocytic anemia

コレらが不足すると、cell division があまり起こらず、RBCの数が減り、sizeが大きくなる!

※ VB_{12} can NOT be absorbed alone

3 Reasons
- VB_{12} deficiency
- follate deficiency
- intrinsic factor deficiency

⇒ DNA synthesis に使われる!

VB_{12} & intrinsic factor make complex which is absorbed from ileum.

↑ produced by parietal cells of stomach

Date

= mean volume of one RBC

☆ MCV (Mean Corpuscular Volume) --- Volume of average RBC

$$= \frac{Ht}{RBC\ count}$$

adult **82 - 92 10^{-15} fL**

infant 100 - 120 fL

ヘマトクリット
Ht = $\frac{\text{formed element (= cells)}}{\text{whole blood (cells + plasma)}}$ → 99% formed element is RBC !

(♂ 0.42 - 0.52
♀ 0.37 - 0.47)

- anemia
- after bleeding
- pregnancy
- 多飲

< Hematocrit <

- dehydration (eg. vomiting . diarrhea . burning)
- erythrocytosis (RBC↑)
- polycythemia vella (Red Bone Marrow Tumor)
  ↓
  Too many RBC are produced

pregnant lady has more plasma.

出血時は同じ量の cells と plasma が失われるが、plasma の方は interstitial fluid の流入により補われる.
⇒ blood volume は正常になるが ヘマトクリットは lower

Q1. calculate blood volume.

blood plasma : 3L
Ht : 0.4

$$Ht = \frac{cells}{cells + plasma}$$

Ht = 0.4, cells = x, plasma = 3L

$\rightleftarrows 0.4x - x = -1.2$

$\rightleftarrows x = 2$

∴ blood volume = 5L //

microcytosis < MCV < macrocytosis

82 - 92 fL

(∵ MCV っていうのは、RBC 1コあたりの volume をイミする)

1 cause
- iron deficiency

3 causes
- VB12 deficiency
- follic acid deficiency
- intrinsic factor deficiency

(MDS : Myelodysplastic Syndrome) (group of cancer..)
(alcoholism)

(貧) Hb c.c. は常に上!! (分子)
(貧) RBC count は常に下!! (分母)

☆ MCH (Mean Corpuscular Hemoglobin) … average Hb content in 1 RBC

$= \frac{\text{Hb c.c.}}{\text{RBC count}}$

28 - 36 pico gram

microcytosis < MCH < macrocytosis

iron deficiency　28 - 36 pg　VB12 deficiency / folate 〃 / intrinsic factor 〃

Hemoglobin concentration ♂ 140 - 180 g/L / ♀ 120 - 160 g/L

☆ MCHC (Mean Corpuscular Hemoglobin Concentration) … Hb content in 1L of RBC

$= \frac{\text{Hb}}{\text{Ht}}$ (= $\frac{\text{MCH}}{\text{MCV}}$)

310 ~ 360 g/L　→ 1Lの RBC を集めてきたら その中には 310~360g のヘモグロビンがあるよ〜ってコト.

✧ Function of Hemoglobin

① O_2 transport
② CO_2 transport
③ most important buffer system (pH regulation)

Q: what makes it perfect buffer ? 2 reasons !
⇒ 1. High concentration makes it good buffer
2. Hemoglobin has a lot of "Histidine" molecule
contains "imidazole" group
↳ can easily bind & release H^+ (or OH^-)

Histidine
R = - CH_2 - (imidazole ring: NH, N)

imidazole
(N, N, H)

✧ CO_2 transport in blood

normal 比は less than 5%

① CO_2-Hb (= Carbamino-Hemoglobin) } very important !
② HCO_3^- (bicarbonate) }
③ Physically dissolved form ⇒ just 7% of CO_2 ← ∴ not so important !

※ be careful !

"Carboxy hemoglobin" は "CO-Hb" のコト! 超キケンな奴.
∵ carbonmonoxide can bind Hb 300× stronger than O_2

1% CO in air can kill us.

Date

Q1. $[HCO_3^-]$ が高いのは femoral vein or femoral artery ? ⇒ vein $pCO_2 = 46mmHg$ in Vein

∵ Deoxygenated blood is full of CO_2 which is coming from the tissue.

And CO_2 is transported by 3 ways ... ⇒ HCO_3^- 濃度が高い = CO_2 濃度高いと置換えるよ

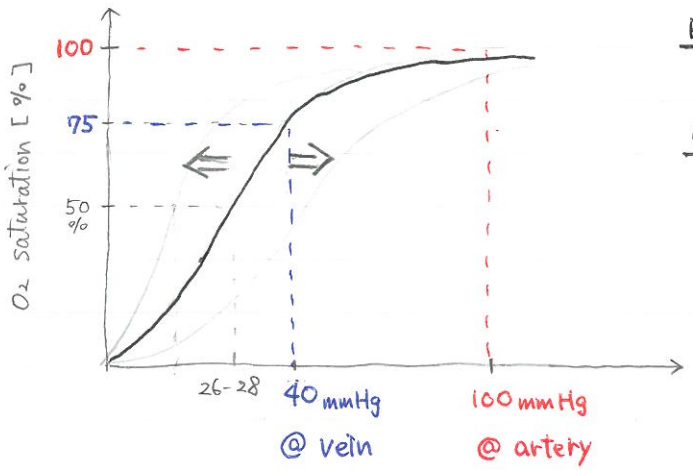
Q2. Artery だけど carry unoxygenated blood なのは ? ⇒ Pulmonary artery

心から出るモノ

Q3. Vein だけど carry oxygenated blood は ? ⇒ Pulmonary vein

O_2 transport in blood

☆ O_2-Hb Saturation curve



- affinity of O_2 to Hb decrease
- Hb can release O_2 easily

low affinity

Right shift ... weaker connection b/w O_2 & Hb

Left shift ... strong interaction b/w O_2 & Hb

PO_2 [mmHg] ⇒ O_2 partial pressure

venous blood では 75% のヘモグロビンが O_2 を運んでいる！ (75% of Hb is saturated)

Right Shift 5 Reasons

CADET, face Right ! 陸軍士官学校生！右向け右！

① Hyper Capunia ... High CO_2 partial pressure → need O_2 → O_2 を手放してほしい (Hb) (CO_2↑)

② Acidosis ... $[H^+]$ ↑ ⇒ too intensive exercise ⇒ too much glycolysis ⇒ lactate↑

③ 2,3-BPG ↑ (D)

④ Exercise ⇒ 単純に運動したら組織では O_2 必要とするっしょ。 skeletal muscle tissue

⑤ Hyper Thermia ... Body Temperature ↑ ⇒ 代謝亢進 ⇒ more O_2 needed !

Q: Leukocytosis (WBC↑) では O_2 saturation どうなる ? ⇒ No change

Sep 21 Thu

femto : 10^{-15} Pico : 10^{-12}

Q1. Plasma volume : 3L
RBC count : 5M/μL
Hct : 0.5
Hb c.c. : 150 g/L
WBC count : 8000/μL
Thrombocyte : 200k/μL

MCV, MCH, MCHC 求めよ.

$MCV = \frac{Htc}{RBC} = \frac{0.5}{5 \cdot 10^6} = 1.0 \times 10^{-7}$ μL be careful
$= 1.0 \times 10^{-13}$ L
$= 100 \times 10^{-15}$ L
$= 100$ fL ← ちょい高い.

$MCH = \frac{Hb}{RBC} = \frac{150\ g/L}{5 \cdot 10^{12}/L} = 30 \times 10^{-12}$ g $= 30$ pg
↑ normal

$MCHC = \frac{Hb}{Htc} = \frac{150\ g/L}{0.5} = 300$ g/L ← ちょい低い.

Q2. MCV. MCH. MCHC の normal value は? ⇒ MCV 82-92 fL
MCH 28-36 pg
MCHC 310~360 g/L

Q3. Thrombocytopenia の時 O_2-Hb saturation curve は? ⇒ No change

Q4. Lymphocytosis (WBC↑) 〃 ⇒ No change

Q5. Low PH 〃 ⇒ Right shift (Acidosis)

Q6. Hypothermia 〃 ⇒ Left shift

Q7. increase 2,3-BPG level 〃 ⇒ Right shift

Q8. Hypocapunia 〃 ⇒ Left shift

Q9. Macrocytic anemia の 3つの原因は? ⇒ Vitamin B_{12} / follate / intrinsic factor deficiency

Q10. Microcytic anemia の原因は? ⇒ iron deficiency

Q11. RBC と Thrombocyte 大きいのは? ⇒ RBC. φ RBC : 7.2 μm, φ platelet : 2~4 μm
Lecture 1~3 μm

Q12. RBC と Thrombocyte 寿命長いのは? ⇒ RBC RBC : 120 days, Thrombocyte : 2 weeks

Q13. nucleus と mitochondria を持つのはどっち? ⇒ ~~Thrombocyte~~ none of them

RBC vs Thrombocyte の続き

Q14. which one can transport O_2 ? ⇒ RBC

Q15. which one can stop bleeding ? ⇒ Thrombocyte

✦ Q16. which one can form blood clot ? ⇒ None of them

∵ Thrombocyte は "Thrombocyte plaque" 作るが、blood clot は作らない！

Q17. Cellular immune response に重要なのは？ ⇒ T lymphocyte

✡ Hemostasis 止血

what if you cut your hand with knife and bleeding,
what is the very first mechanism which can decrease the blood loss ?

① Vasoconstriction

1st step は 血管収縮！

Vasoconstricter strong order

1. Endothelin → most powerful vasoconstrictor !!
   is released from "injured endothel cells"

2. Adrenaline , NorAdrenaline (epinephrine, norepinephrine)
   ↳ Catecholamine family に属する
   ↳ α_1 Receptor に反応すると vasoconstriction 起こる

✦ 3. Thromboxane A II

4. ATP

✦ 5. PGF2 (Prostaglandin F2)

6. Serotonin

7. Vasopressin (ADH) → produced by "Hypothalamus" (視床下部)
   ↳ V_1 Receptor
   ↓
   stored & released from "posterior pituitary gland" (下垂体後葉)

8. Angiotensin II

Hemostasis の 2nd step は 血小板の活性化と凝集！

② Thrombocyte activation / aggregation
"
Platelet

Thrombocyte の additional info

- ~~Nucleus~~ (無核!!!) と mitochondria を持つ
- life span : 2 weeks
- 中に different vesicles がある。 CAST
  - contains
    - Serotonin
    - ADP
    - Thromboxane A II
    - Clotting factor XIII (13)
- φ 2 μm
- produced in Bone marrow

Which hormone can increase the Thrombocyte formation ?
⇒ Thrombopoietin (← secreted by kidney)

What is the ancient cell for Thrombocyte ? ⇒ Megakaryocyte

Activator	Inactivator
- Serotonin	- NO (Vasodilator)
- Thromboxane A II	- PGI2 (Prostacyclin) (Vasodilator)
- Adrenaline / Noradrenaline with α-Receptor	(- Bradykinin)
- ADP	
- Coagulation factor IIa (Thrombin)	

if Thrombocyte is activated,
Vesicles are released while exocytosis
⇒ Vesicle 内の Serotonin, ADP, TXA II が
さらに他の Thrombocyte を activate する!!

Why thrombocyte activation so important?
⇒ when Thrombocyte active, it can attach to other Thrombocyte by glycoprotein bridge ⇒ "Thrombocyte plaque"

"
positive effect

Q: Ca^{2+} を必要とする反応は？

くなると

① IXa が行う反応 → X → Xa
② VIIa 〃 → X → Xa
③ Xa 〃 → II → IIa

Bleeding time : 2-3 min < 5 min

↳ inform us about Thrombocyte function & Thrombocyte count & Von Willebrand factor

if Von Willebrand factor deficiency
or Thrombocytopenia ⇒ Bleeding time
or Thrombocyte function new jó Longer than 5 min.

③ Blood Clotting

most of clotting factors are produced by "Liver"!

Exthinsic Pathway

Why is it called "exthinsic"?
⇒ 血管内には無い外部(injured tissue)からの Tissue Factor が血管内に入り込むコトによって始まるから.

Tissue Factor, Phospholipid, Ca^{2+} (Thromboplastin reagent)

VII → VIIa

= Exthinsic Tenase Complex

※ VIIa だけでは、X を activate できない!

Inthinsic Pathway

Why "inthinsic"?
⇒ blood itself can be clotted without any exogenous compound (eg. tissue factor)

High Molecular Weight Kininogen

HMWK

factor XII → XIIa

Prekallikrein → kallikrein (activated to)

XI → XIa

IX → IXa + VIIIa, Ca^{2+}, PL

= Inthinsic Tenase Complex

実験では、blood を watch glass に乗せたが、これは HMWK が glass に attach して、反応が始まる.

X → Xa + Va, Ca^{2+}, PL

= Prothrombinase Complex

How to activate?
※ それぞれの clotting factor は "protease" activity を持つ!
⇒ 例えば、VIIa は X 末端のアミノ酸を cleave するコトによって Xa に変える! (activation すき!)

Prothrombin (clotting factor II) → Thrombin (IIa)

fibrinogen (factor I) → fibrin monomer (Ia)

XIIIa (fibrin stabilizing molecule)

fibrin polymer

※ XIIIa は protease activity は持たない!
が、fibrin monomer を集めて、fibrin net (fibrin polymer) を形成する!

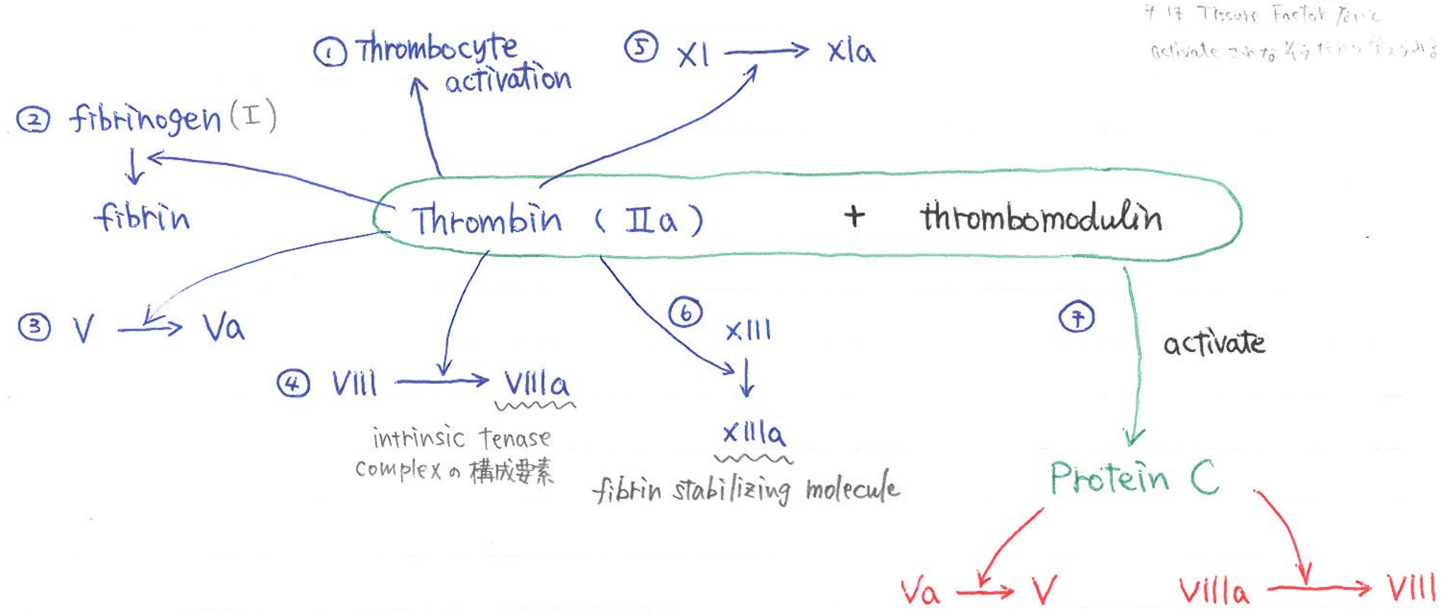
"Blood Clot"

Thrombin is key molecule for blood clotting system

1 5 8 11 13

☆ Thrombin の 7 important function !

覚え方 - 5/8 誕生日 × 2
- あとは 7 以外の素数 + 1
↑ (Ⅲ)
7 は Tissue Factor ないと activate されない 気がするから覚えられる



ここからは、clotting factor formation

Vitamin K dependent clotting factors

下の4つの clotting factor を作るのに VK が必須！
⇒ VK は clotting factor formation に必須.

納豆！
- factor II (prothrombin), VII, IX, X ← produced in Liver
- 上記4つの Protein は、act in Liver … γ-carboxilation を行う

II, VII, IX, X の γ position を カルボキシル化(活性化) するのに Vitamin K が必要！
⇒ without γ-carboxylation, II, VII, IX, X (Vitamin K dependent clotting factor) is useless

- Vitamin K antagonist e.g. Cumarin (warfarin)
  ↳ Clotting time ↑ ⇒ slows down the clotting
  (∵ 納豆の γ-carboxylation は vit K dependent)

in vivo でのみ 働く！！

Anticoagulant 2種類！

Vitamin K dependent anticoagulants
- Protein C
- Protein S

Vitamin K dependent Clotting factor is produced in Liver & it can make γ-carboxylation also in Liver.
& Vitamin K act ONLY in Liver.
(∵ VK is active in Liver!)

Q1. Test tube に blood 入れて 大量の VK を入れた. Clotting time はどうなる？ ⇒ No change

Q2. Vitamin K の pill を 大量服用すると、 〃 ？ ⇒ faster.

Date

☆ Clotting time　5-10 min.　37°C ← we need Thermostate.

↳ inform us about "intrinsic Pathway" IC

↓

if XII, XI, IX problem ⇒ Clotting time ↑

※ problem w/ vasoconstriction, thrombocyte, extrinsic pathway は Clotting time には無関係

☆ Prothrombin time　13-22 s

測定には

- anticoagulated plasma が必要 → どうやって作る? How to prevent blood clotting?
  - Remove Ca^{2+}

Ca^{2+} を取り除くには (キレートする) 4つの方法がある.

↓

右記の4つは free Ca^{2+} と結合して Complex を形成することで血中から Ca^{2+} を取り除く.

- EDTA
- Citrate (No-Citrate)
- Oxalate
- Acetate

} in vitro のみ可能

- Thromboplastin reagent
  - contains Tissue Factor, Ca^{2+}, Phospholipid → ※ ここに VIIa を足せば Exthinsic Tenase Complex となる

↳ inform us about "Exthinsic Pathway" EP

↓

if factor VII, X, II, I に問題あると、Prothrombin time ↑

Date

genes on X chromosome

clotting time ↑

☆ Hemophilia A ... factor VIII deficiency
〃 B IX deficiency
} inherited disease ⇒ prothrombin time ↑

How would you treat these inherited disease ?
⇒ just give factor VIII & IX

☆☆ Function of Heparin — ×1000 faster (+) → antithrombin III → thrombin (IIa), IXa, Xa

※ Heparin は basophil によって分泌される！

※ antithrombin III is very slow lazy molecule
→ Heparin can make it faster ×1000.
(more active)

☆ ABO system

※ antigen make themselves unique. eg. transplant で kidney もらった時 immune system realize that has different Ag what I have. My immune produce Antibody against kidney

surface of RBC

antigen = hemaglutinogen = agglutininogen

antibody = hemaglutinin = agglutinin

A — H — A antigen
anti-B antibody
IgM family → big molecule ∴ can NOT Pass through placenta

B — H — B antigen
anti-A

Q：A型の♀が B型の♂と結婚して子供が B型の場合でも子供が immune problem 起こさないのは？
⇒ A♀の anti-B は Placenta を通過しないから、子供への影響なし!!

O — H — H antigen
φ A antigen
φ B antigen
anti-A
anti-B

Q：なんで A型・B型どちらも輸血したことないのに anti A/B antibody 持ってるの？
⇒ A & B antigen is ubiquitas, everywhere in environment you can take them via microorganism, food, drink. Your immune system is exposed to A & B antigens. That's why our immune system produce Antibodies against these antigens.

AB — H — A antigen, H — B antigen
φ anti-A antibody
φ anti-B antibody

Bonbay Type blood group ... φ H antigen, φ A antigen, φ B antigen
Antibody は anti A, anti B, anti H 持つ

Q: when do you think my immune system start to produce anti A & anti B Antibody ?
⇒ Immune system is strong enough to produce Antibody in half year old. So if you are newborn blood Type O. What kind of Antibody are there ? ⇒ Non ! .. immune system start to produce Antibody around half year old.

Heparin works both in vivo / in vitro

Date Sep 28 Thu

Q1. Tell me the chronological order of the intrinsic Pathway activation.

① HMWK activate "Prekallikrein" to "kallikrein".
② "kallikrein" activate "factor XII" to "activation factor XII"
③ "XIIa" activate "XI"
④ "XIa" activate "IX"
⑤ "Inthinsic Tenase Complex (IXa, VIIIa, Ca^{2+}, PL)" activate "X"
⑥ "Prothrombinase Complex (Xa, Va, Ca^{2+}, PL) activate "Prothrombin" to "Thrombin"
= II = IIa
⑦ "Thrombin (IIa)" activate "fibrinogen (I)" to "fibrin monomer (Ia)"
⑧ "XIIIa" makes "fibrin monomer (Ia)" polymer = "fibrin polymer"
‖
fibrin stobilizing complex

Q2. Tell me clotting factor which do NOT have Protease activity ⇒ ① XIIIa
④ Va ② Ca^{2+} (IV)
cofactor — ⑤ VIIIa ③ fibrin (Ia)

Q3. which factor can you find in vesicular Thrombocyte can produce? ⇒ XIII

Q4. which factors are Vitamin K dependent factor? ⇒ II, VII, IX, X

✧✧ Q5. which anticoagulant factors are Vitamin K dependent? ⇒ Protein C, Protein S

Q6. Tell me the 7 functions of the Thrombin? ⇒ ① Thrombocyte activation
② activate "fibrinogen" to "fibri
③ activate "V"
④ activate "VIII"
⑤ activate "XI"
⑥ activate "XIII"
⑦ + thrombomodulin activate "Protein C"
Protein C inactivate "Va" & "VIIIa"

✧✧ Q7. Hypercalcemia 患者では clotting time はどうなる? ⇒ No change (speed は不変)

Q8. factor XI deficiency 患者で Prothrombin time どうなる? ⇒ No change 13s. 22s
∵ Prothrombin time shows up "Extrinsic Pathway" but "XI" is involved in "intrinsic pathway".

Date

Q9. what does "cumarin" do ? ⇒ Antagonist of Vitamin K

Q10. cumarin pill を飲むと clotting time ⇒ both slower
prothrombin time はどうなる？

Q11.

hemaglutination

O	A	B	C		
				⇒	invalid (Control should'nt react)
−	−	−	−	⇒	O (∵ 他の antigen もない)
			−	⇒	AB
		−	−	⇒	B

↑ anti A Antibody を入れる！

Q12. What is Bonbey type blood group ? ⇒ They don't have "H antigen".

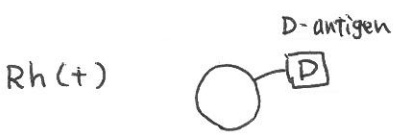
Q13. When I was young, what kind of hemaglutinin (Antibody) are there in my blood plasma ?
I'm O. Rh(-) 1 week old ⇒ There are NO Antibodies.

Q14. If patient has anti A & anti D antibody, 患者の blood type は？ ⇒ B, Rh(-)
もし、Rh(+)の人が anti D antibody 持ってたら、Those antibody kill the fetus.

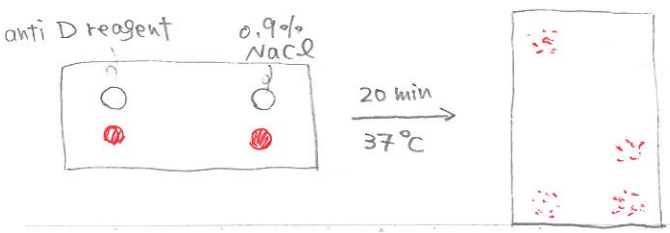
Q15. B型♀と A♂の子供が A型 or AB型だった場合、anti A antibody kill fetus ?
⇒ NO. ∵ IgM doesn't pass through the placenta
(but IgG can pass through the placenta)

Rh (Rhesus monkey) Rh(+)っていうのは RBC表面に D-antigen があることを意味する

antibody (hemaglutinin)



may have anti-D Antibody
IgG



※ Rh incompatibility
(Erythroblastosis fetalis)
⇒ ⊖母に対して2人目の⊕子は危険!!

子の anti-D が子の D-antigen と攻撃しあう

Q16. RBC counting, WBC 〃, Thrombocyte 〃, Rh blood type determination, ABO 〃 のどれが dilution 必要としない？ ⇒ Rh blood Typing
(∵ ABO では 1 drop of NaCl が全てに加えられる)

Q17. blood sample, burker's chamber, cover glass, microscope ⇒ Nothing
Hayem's solution Turk's solution
↑ RBC counting

Q18. 上記 + mixing pipette (1:10) ⇒ WBC counting
(RBC counting は 1:100 dilution

Q19. How long is normal bleeding time? ⇒ 2-3 min (less than 5 min)

Cardio Vascular System

Q: what is the normal Blood Pressure in your brachial artery? ⇒ 120/80 mmHg

- Pulse Pressure = Systolic pressure − diastolic Pressure
  40 mmHg 120 80

- Mean Arterial Pressure (MAP) → average pressure of all our arteries

  $= \frac{\text{systolic Pressure} + 2\,\text{diastolic Pressure}}{3}$

  Q: why 2 times of diastolic pressure?
  ⇒ ∵ diastole is 2 times longer than systole

  = diastolic pressure + 1/3 Pulse pressure
  = CO × TPR

amplitude 最大!!
6 ∵ gravitation force

Q: Standing position で 血圧高いのは brachial a. or femoral a.? ⇒ femoral artery

Q: lying position では? ⇒ same.

Q: Pulmonary artery (trunk) の normal blood pressure は? ⇒ 24/9 mmHg (24/15 mmHg is acceptable)

- Pulse Pressure : 15 mmHg
- MAP (Mean Arterial Pressure) : ≈ 15 mmHg

※ systemic circulation の blood pressure の方が Pulmonary circulation よりも 高い!

Date

diastolic pressure !!
less than 5 !!

✨ ☆ Q : Blood Pressure in Left ventricle ⇒ 120/5 mmHg

☆ Q : 〃 Right ventricle ⇒ 24/1~2 mmHg

☆ Q : dead man の blood pressure in everywhere ⇒ 7 mmHg (∵ Blood is still there. to capillary と vein と artery と the blood press the wall)

Normal Heart Rate : 60 - 100 beats / min
> 100 ⇒ Tachycardia
< 60 ⇒ Bradycardia

Stroke Volume : 70 - 80 mL in Rest ··· Volume of blood which is pumped from left Ventricle to Aorta
= EDV(150) - ESV(70)

Cardiac Output : 5 - 6 L / min. in Rest ··· How much blood is pumped to the circulation in one minute
(20-30L/min in exercise)
= HR × SV
= MAP / TPR*

* TPR is inversly proportional to "diameter" of the vessels !
$R = \frac{8\eta l}{\pi r^4}$

Ejection Fraction = SV / EDV = (EDV - ESV) / EDV 50 - 70 % in rest

↑ How many percent of blood is pumped to the Aorta in one systole

✨ Q : TPR = ? EF = ?
BP = 110/80 mmHg
HR = 60 /min
EDV = 150
ESV = 50

$CO = \frac{MAP}{TPR} \rightleftarrows TPR = \frac{MAP}{CO} = \frac{80 + 1/3 \times 30}{60 \times 100 = 6\,L}$
$= \underline{15}$ [mmHg · L/min]

$EF = \frac{SV}{EDV} = \frac{100}{150} = \underline{66\%}$

MAP = CO × TPR 忘れがちw

Cardiac cycle is depend on Heart Rate.

Cardiac Cycle

Duration of Cardiac cycle = $\frac{60s}{HR}$
(= R-R interval)

Lecture

eg. HR = 75/min. ⇒ $\frac{60}{75}$ = 0.8s (= 800 mS

- 1/3 systole = 270 mS 0.3s
- 2/3 diastole = 530 mS 0.5s

※ 1/3 of cardiac cycle is "systole", 2/3 of cardiac cycle is "diastole".

Q: When do you think Coronary circulation in diastole or systole? ⇒ diastole のみ

∵ When there is systole, ventricle wall contract, Pressure is higher than 120 mmHg
⇒ Small vessels on the wall of ventricle are compressed ⇒ There is NO blood flo
in the Coronary during systole.

✧ Q: When HR↑, How would the duration of systole or diastole change?

(∵ 分母が大きくなれば、全体は小さくなる.
⇒ diastole は2倍長いから significant difference!)

⇒ diastole ↓↓
(systole ↓)

✧ Q: How do you think that Heart can survive? ⇒ Coronary dilation

(HR↑ような運動してると duration of diastole ↓↓
それも coronary circulation は diastole でしか起きない)

duration of diastole は短くなるが、
coronary vessels are wider
⇒ in diastole, more blood can go through
the coronary circulation

What is the compensation mechanism?

HR↑ ⇒ Sympathetic Nervous System is activated
⇒ β_2 Receptor (in coronary) cause vasodilation (Coronary dilation

Date

Systole　3 phase

beginning of systole

① isovolumetric contraction … All valves are closed.

- Ventricular volume does NOT change.
- Ventricular Pressure ↑ (eg. Left Ventricle … 5 mmHg → 80 mmHg)
  diastolic Pressure of Aorta

★ At the beggining of Systole (= isovolumetric contraction),
AV valves are closed which generate 1st Heart Sound
→ Ventricular pressure が atrial pressure よりも 高くなった から 起こる.

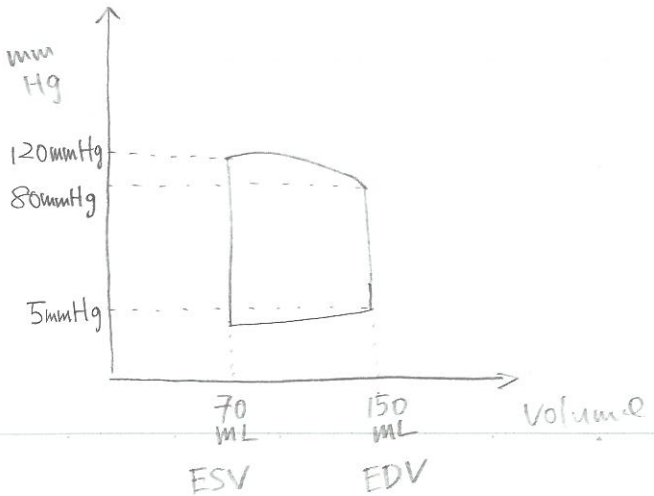
② Rapid ejection phase ~ 75% of Stroke Volume is ejected!

- Semilunar valves are opened (aortic valve & Pulmonary valve)
- AV valves are closed
- Ventricular volume ↓
- Ventricular Pressure ↑ → 120 mmHg

③ Slow ejection Phase

- Semilunar valves are opened
- AV valves are closed
- Ventricular volume ↓

} Same as Rapid ejection



Date

diastole 5 phase

⓪ protodiastole 40ms

~ b/w systole & diastole, there is a short period.

☆ At the beginning of the diastole, semilunar valves close which generates 2nd Heart Sound

→ arterial pressure が ventricular pressure よりも 高くなると 起きる.

(※ 1st Heart Sound は At the beginning of systole の closure of the AV valves!)

Q: Which heart sound is longer 1st or 2nd ? ⇒ 1st Heart Sound

ルードゥップ
1st 2nd
longer

① isovolumetric Relaxation

- All valves are closed (Both Semilunar valves & AV valves are closed)
- Ventricular volume does NOT change
- Ventricular pressure ↓

② Rapid filling Phase ~ 80% filling

- AV valves are opened, Semilunar valves are ~~opene~~ closed.
- Ventricular volume ↑
- Ventricular Pressure ↑ ~ very very slight increase. (∵ 血はいっぱい入ってくるけど relax してる)

Blood rushes into the Ventricle

☆ Ventricular wall vibration generates 3rd Heart Sound

⇒ Normal in children, abnormal in adult

③ Slow filling Phase ~ 15% filling

- 上に同じ (ゆっくり血が流入するコト以外は 全く同じ!)

✧ ④ Atrial systole

- AV valves are opened
- Semilunar valves are closed
- Ventricular Volume ↑
  - Atrial systole の blood filling は 全体の ~~20~~ 5% を 占める. (∴ Rapid / slow filling phase ~ Lecture!
    but if HR↑ ⇒ more than ~~20~~ 5% (∵ diastole is shorter) 合わせて ~~20~~ 95% !)
- Ventricular Pressure ↑ slightly increase

☆ 4th Heart Sound = Pathological, Problem of Atrial systole.

week 5

1

Date Oct 5th Thu

Q1. What do we use for WBC counting ? ⇒ Türk-solution , Bürker's chamber , microscope coverglass , 1-10 mixing pipett

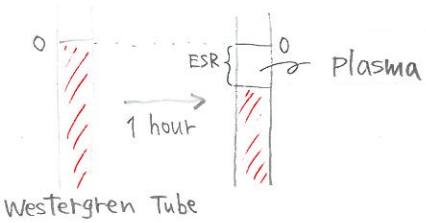
Q2. What is your diagnosis ? Patient is ♀.
RBC : 3.3 M/μL , Reticulocyte ratio : 0.5%
WBC : 9500/μL , TCT : 212K/μL
♀ RBC : 5.9 μm , MCV = 76 fL , MCH = 22pg

⇒ microcytosis (iron deficiency)

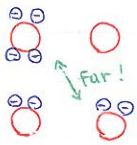
♀ RBC	3.9 - 5.3 M / μL
♂ RBC	4.5 - 6 M / μL
WBC	4K - 10K / μL
TCT	150k - 400k / μL
MCV	82 - 92 fL
MCH	28 - 36 pg

✧ Q3. Erythrocyte Sedimentation Rate is increased by ESR ↓
↑ Settle down faster

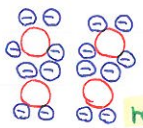
ESRの測り方
1.6 mL blood
0.4 mL citrate
to remove Ca^{2+}



① Anemia 分かんなくなったら逆を考える! →



① Erythrocytosis (RBC ↑)



② globulin ↑
fibrinogen ↑
= glue

② dehydration
∵ loose blood plasma = less plasma
→ RBC closer each other
= Repel each other !

③ infection (inflammation)
= more Ig (globulin ↑)

④ Tumor

⑤ Pregnant
(∵ has more plasma
→ RBC far away each other)

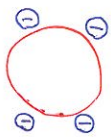
ESR
♂ 2 - 6 mm / hour
♀ 3 - 10 mm / hour

③ microcytosis

relatively more negative !

④ albumin / globulin ↑

⑥ macrocytosis



charge is relatively less negative.

最初は cell も plasma も同じだけ流出するが、plasma は interstitial fluid の流入により元に戻る!

bleeding も同じ

⑧ Menstruation
(≒ anemia)

⑦ albumin / globulin (+ fibrinogen) ↓
(∵ globulin ↑)

Q4. CO = ? EF = ?

HR = 80/min
EDV = 160 mL
ESV = 80 mL

CO = SV × HR
SV = EDV - ESV

CO = 80mL × 80/min
= 6.4 L/min 5-6L/min

EF = SV / EDV (EDV - ESV / EDV)

EF = 80/160 = 50% 50-70% 正常値

✧ Q5. MAP↑, CO→ の時 TPR 変化は？ ⇒ ↑ (∵ MAP = CO × TPR)

Q6. EDV→, HR→, ESV↑ の時、CO 変化は？ ⇒ ↓ (∵ CO = SV (EDV - ESV) × HR)

✧ Q7. diastolic pressure →, Pulse Pressure ↑
[redacted] の時. MAP は？ ⇒ ↑ (∵ MAP = diastolic pressure + 1/3 pulse pressure)

Q8. TPR を上昇させる molecule を List せい. ⇒ vasoconstricter を答えれば良い.

E × 3
① Endothelin ← strongest vasoconstrictor
② Epinephrine } via α1 Receptor
③ Norepinephrine } ※ β2 R は vasodilator (VS)

A × 4
④ ADH
⑤ Angiotensin II
⑥ Thromboxane A II
⑦ ATP
⑧ PGF2 (Prostaglandin F2)
⑨ serotonin
(⑩ CO)

✧☆ Q9. if HR↑, atrial systole would pump more or less? ⇒ more blood
(atrial contraction increase or decrease?)
∵ there is NO time for ventricular filling
(Rapid filling phase
slow filling phase)

That's why atrial systole is more important!

Q10. HR = 60 beats/min の時の duration of cardiac cycle 求めい. ⇒ 1s ∵ 60s/HR

Q11. HR = 120 beats/min 〃 ⇒ 500ms

Date

Q12. HR = 75 beats/min の時、duration of systole は？ ⇒ 270 ms ∵ $\frac{60}{75} \times \frac{1}{3} \times 1000$

cf. duration of diastole は 530 ms

Q13. Tell me the chronological order of the cardiac cycle.

(started from isovolumetric relaxation)

⇒ isovolumethic relaxation → Rapid filling phase → slow filling phase → atrial systole (contraction)

→ isovolumethic contraction → Rapid ejection phase → slow ejection phase → 戻る.

Q14. ventricular volume ↑, ventricular pressure ↓

All the valves are opened なるは どの phase？ ⇒ non of them or dead man

(※ isovolumethic relaxation だとしたら、all valves are closed！)

Q15. 3rd Heart Sound が 聞こえるのは どの phase？ ⇒ Rapid filling phase

✧ ✶ Q16. 2 atria, 2 ventricles が relax する phase は？ ⇒ Rapid filling と Slow filling phase.

non of them かと 思ったあ.

Q17. which Heart Sound is longer, 1st or 2nd？ ⇒ 1st Heart Sound

✶ Q18. Split が normal なのは 1st or 2nd？ ⇒ 2nd Heart Sound

※ split とは... aortic valve と pulmonary valve が do NOT close at the same time

mittal valve と thicuspid valve 〃

★ it is normal that aortic valve & pulmonary valve do NOT close at the very same time

※ mittal valve と thicuspid valve は 同時に 閉じなきゃ ダメ !!

Q19. In which phase of the cardiac cycle can you hear the 4th Heart Sound？

⇒ atrial systole

Q20. How can you calculate the TPR？ ⇒ $TPR = \frac{MAP}{CO}$

Q21. what is the formula to calculate cardiac output？ ⇒ $CO = SV \times HR$

$CO = \frac{MAP}{TPR}$

Q22. if HR↑, How would the duration of coronary circulation change？

shorter or longer？ ⇒ shorter ∵ coronary circulation takes place in dyastole

duration of cardiac cycle = $\frac{60s}{HR}$ だから HR↑ ⇒ duration ↓

Date

Normal value

Q 23. Resting Heart Rate = 120 beats/min 는 ? ⇒ Tachycardia 60 - 100 beats / min

Q 24. CO in Left ventricle = 6 L
Right " = 5 L 는 ? ⇒ abnormal ∵ it must be the same
∵ Frank-Starling

Q 25. normal mean arterial pressure in pulmonary artery 는 ? ⇒ ≈ 15 mmHg ∵ 24/9 mmHg

Q 26. " in systemic circulation ? ⇒ 93.3 mmHg ∵ 120/80 mmHg

Sequence of Heart activation

Q : What is the normotopic place generating the heart rhythm? ⇒ SA node

SA node ① 0.01 m/s ⇐ slowest
action potential ↓ travel
atrial muscle ④ 1 - 1.2 m/s
internodal pathway
↓
AV node ② 0.02 - 0.05 m/s
↓
His bundle
↓ } ⑤ 2-3 m/s
Tawara bundles
(Right / Left bundle branches)
↓
Purkinje fiber ⑥ 4 m/s ⇐ fastest
↓
Ventricular muscle ③ 0.2 - 1 m/s
finally ventricular m. is activated!

Conduction velocity (increasing order)
= speed of action potential

Q : なんで AV node は遅いの?
AV delay の physiological purpose は?
⇒ gives time for ventricular filling
AV node の conduction velocity が
充分速かったら、atrium と ventricle が
contract at the very same time なちゃう
↓
atrium contract → some blood pump
into the ventricle → その後 ventricle
should contract!! 時間稼ぎ!

Q : Way of the activation について.
myocardium is activated from endocardium (inside) toward pericardium (outside) !!

activation is from Apex to the Base!
∵ purkinje fibers are coming backward!

Q : Physiological location of Pacemaker cell ~ rhythm generator

- SA node (normotopic) — 60~100 … physiological HR — 70 action potentials / min. (60)
  - もし、SA node doesn't work ⇒ AV node が boss!
- AV node — 40 - 50 beats / min. (40)
- His bundle — 15 - 20 beats / min ← can NOT survive (20)

↓ generate Action Potential!

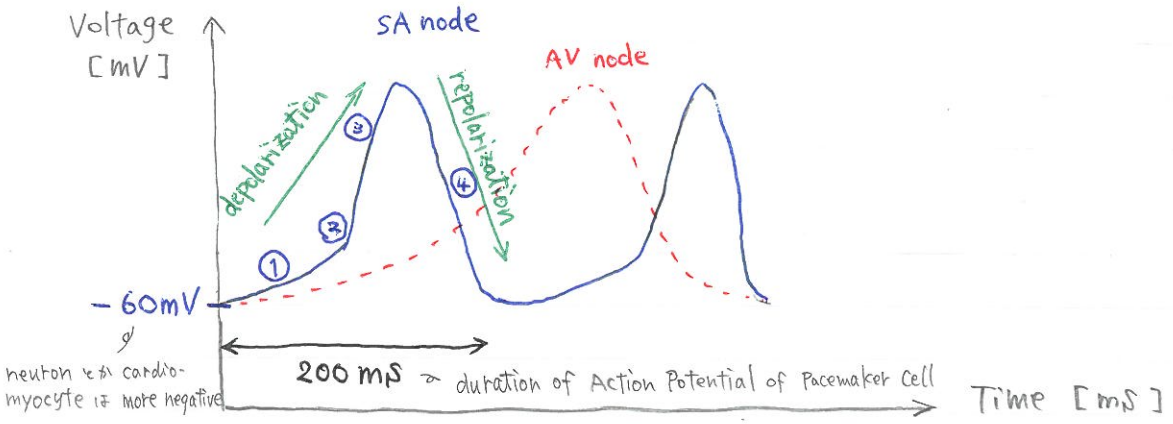
Koru Yei ↓

※ exercise したら、SA node は generate more action potential!!

※ SA node も AV node も 働かなくなっちゃったら 死んじゃう.

SA node , AV node

Action Potential of Pacemaker Cell



① Non - Selective Cation channel (Na^+ channel) mainly permeable Na^+

↳ important for "slow diastolic depolarization"
responsible

↳ funny current ≈ この Na^+ inward の ヨト

$[Na^+]_{out} \overset{10X}{>} [Na^+]_{in}$

② T - type Ca^{2+} channel ← important for "early depolarization"

Transient (一時的に、一瞬 的に)

共通 ③ L - type Ca^{2+} channel ← This time Action Potential is evoked !

Long lasting

共通 ④ Voltage dependent K^+ channel ≈ K^+ outflow → repolarization.

Q: SA node と AV node の 違いは ?

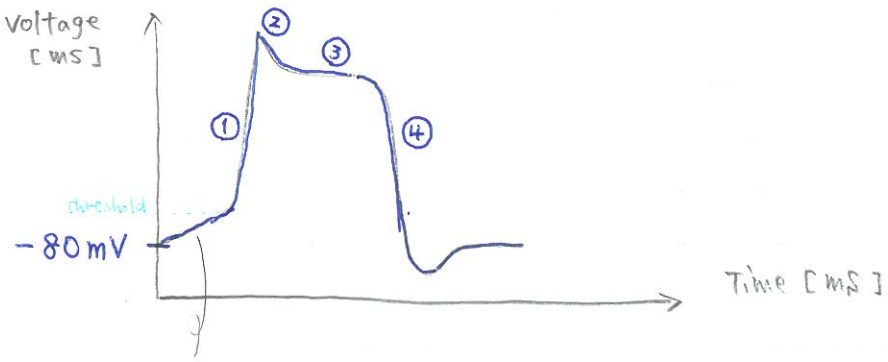
⇒ AV node generate less action potential

→ slow diastolic depolarization would be slower. takes more time to get an action potential

⇒ Bundle of His は even more slower !

atrial muscle , ventricular m.
His bundle , Purkinje fiber

Action Potential of Cardiomyocyte



Action Potential coming from Pacemaker Cell

voltage-gated inactivating channel

① Fast Voltage dependent Na^+ channel ⊢ TTX , Lidocaine

↳ Na^+ influx → Action Potential is evoked.

② Early K^+ channel

↳ K^+ outflow → " early repolarization "

共通 ③ L-type Ca^{2+} channel

↳ Ca^{2+} influx → important for " plateau phase "

K^+ outflow vs Ca^{2+} influx → balance each other

④ Late K^+ channel (= voltage dependent K^+ channel)

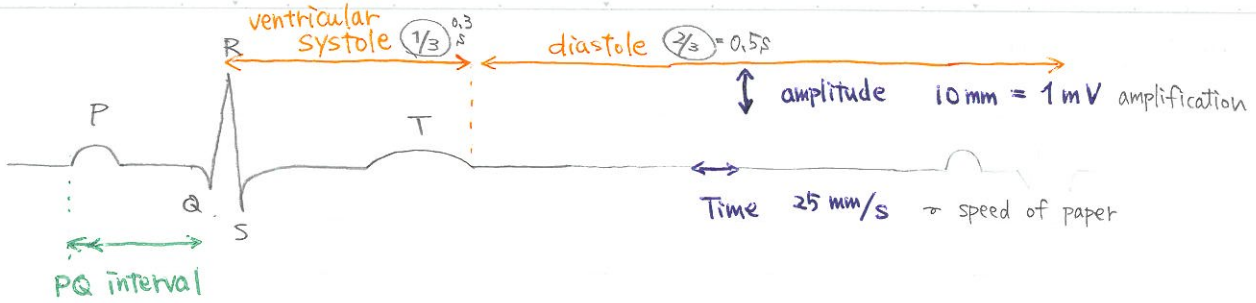
↳ K^+ outflow → " repolarization "

electrical activity

ECG

- can record the "electroactivity" of the heart

※ can NOT see any "mechanical" movement



can record the

P wave ... atrial depolarization 60 - 110 ms

※ atrial contraction を測定しているわけではない!! 確かに. atrial depolarization will be followed by atrial contraction. but it's just an electrical signal.

atrial depolarization → atrial contraction
(P wave) (atrial systole)

QRS complex ... ventricular depolarization 80 ms (40 - 100 ms)

T wave ... ventricular repolarization duration is depend on HR.

※ atrial repolarization is hidden by QRS ∴ atrial repolarization は見えない!!

PQ (PR) interval ... atrial - ventricular conduction time 120 - 200 ms

if > 200 ms ... 1st degree of AV block ☆

※ Action Potential is generated by SA node and it takes time to get ventricle.

☆ 1st degree of AV block とは... Conduction time b/w the atrium & ventricle is longer than 200 ms のコトをいう.

Q: High acclimatization の時、 pulmonary artery resistance ↑

Q: environment temperature = 35°C の時、 Basal Metabolic Rate ↑
= 15°C 〃 ↑

Q: streching of Right atrium leads to ADH production ↑
∵ Bainbridge reflex → sympathetic activation → β_1 Receptor @ juxaglomerular apparatus
produce Renin → RAAS が働き、Angiotensin II が ADH を分泌する.

Q: extrasystole の始まりは supraventricular で起きる.
(compensatory phase の後に) QRS complex は physiological である.

Q: hypoxia では、vasodilation in periphery が起こるから、blood flow to peripheral tissure increase.

Date Oct 13 Fri

Q1 : In which phases of the cardiac cycle the AV valves are open ? ⇒ Rapid filling , Slow filling pha , atrial systole

Q2. all valves are close ? ⇒ isovolumetric contraction / relaxation

Q3. Ventricular volume が biggest なのは ? ⇒ isovolumetric contraction (at the end of atrial systole)

Q4. ventricular volume が smallest は ? ⇒ isovolumetric relaxation

Q5. semilunar valves are closed は ? ⇒ isovolumetric relaxation , Rapid filling phase , slow filling phase , atrial systole , isov- contraction

Q6. EF = ? CO = ? HR = 80 beats/min EDV = 160mL ESV = 80mL

CO = HR × SV , SV = EDV - ESV ∴ CO = 80 × 80mL = 6.4L/min

Ejection Fraction = $\frac{EDV - ESV}{EDV}$ ∴ EF = $\frac{80}{160}$ = 50%

EF の normal value = 50 - 70%

CO = 5 - 6 L/min

Q7. Normal Heart Rate は ? ⇒ 60 - 100 beats / min. ↑ ⇒ Tachycardia , ↓ = Bradycardia

* Q8. chronological order of the heart activation . ⇒ ① SA node ② atrial muscle , internodal bundles ③ AV node ④ His bundle ⑤ Tawara bundle ⑥ Purkinje fiber ⑦ ventricular muscle

Q9. which part of the heart , conduction velocity is the fastest ? ⇒ Purkinje fiber 4m/s

Q10. why do we have AV delay ? ⇒ it gives time for ventricular filling

Q11. Which part of Heart Sound is longer 1st or 2nd ? ⇒ 1st

Q12. split が normal なのは ? ⇒ 2nd

Q13. ventricular pressure が ↓ する phase は ? ⇒ isovolumetric relaxation

Date

Q14. How long is the normal PR interval ? ⇒ 120 - 200 ms

if > 200 ms ⇒ 1st degree of AV block

✧ Q15. How long QRS ? ⇒ 40 - 100 ms

✧ Q16. How long normal P wave ? ⇒ 60 - 110 ms

P wave ↓ atrial systole

Q17. which wave represent the atrial systole ? ⇒ none of them.

※ atrial depolarization !!

Q18. which wave represent the atrial repolarization ? ⇒ none ∵ it's hidden by QRS

Q19. if R-R interval = 1s , HR would be ? ⇒ 60 beats/min.

★ speed of the ECG = 25 mm/s

★ Amplitude of ECG ● 10 mm = 1 mV ← Amplitude is proportional to the voltage

Q20. if the distance b/w 2 R waves = 25mm , HR は ? ⇒ 60 beats/min. ∵ 25mm = 1s ⇒ 1s に 1回 beat

※ duration of cardiac cycle = $\frac{60s}{HR}$ ⇒ 60 (1s)

Q21. R-R = 12.5 mm の時 . HR は ? ⇒ 120 beats/min. 12.5mm = 0.5 s

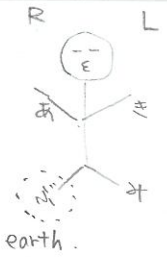
☆ Q22. QRS の長さは ECG では 何 mm ? ⇒ 2 mm (∵ 25 mm/s × 0.08 s) QRS = 80ms

(1mm ~ 2.5 mm) ← QRS = 40~100 ms

Q23. Normal P-R interval in ms ⇒ 120 - 200 ms

☆ Q24. Normal P-Q interval in mm ⇒ 3 - 5 mm (∵ 120-200 ms × 25mm/1000ms)

☆ Limb electrode (3+1)



① Right hand ··· Red electrode

② Left hand ··· yellow "

③ Left foot ··· green "

Earth : Right foot ··· black "

☆ Chest electrode (6)

V1 ··· 4th intercostal space , right side of the sternum

V2 ··· 4th intercostal space , left side of the sternum

V3 ··· b/w V2 and V4

V4 ··· 5th intercostal space , left side of the sternum , midclavicular line

V5 ··· 5th intercostal space , left side of the sternum , anterior axillary line

V6 ··· 5th intercostal space , left side of the sternum , mid axillary line

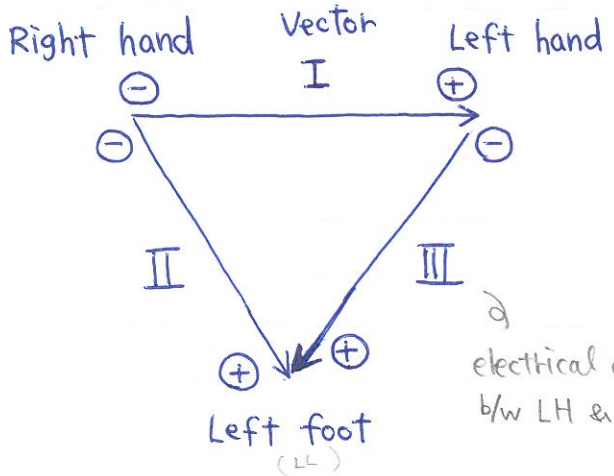
Now Let's discuss different leads unit . you need to know We have 3 bipolar limb leads , 3 unipolar limb leads , 6 unipolar chest leads !

Date

☆ Bipolar limb leads (3)

↳ Einthoven triangle

negative pole



Q. why this is important ?

⇒ They can see the Heart from different angle.

⇒ when we see the heart from different angles, there are more likely to we can figure out abnormality.

Einthoven law ··· II = I + III

if I = 5mm, II = 7mm ⇒ III = 2mm

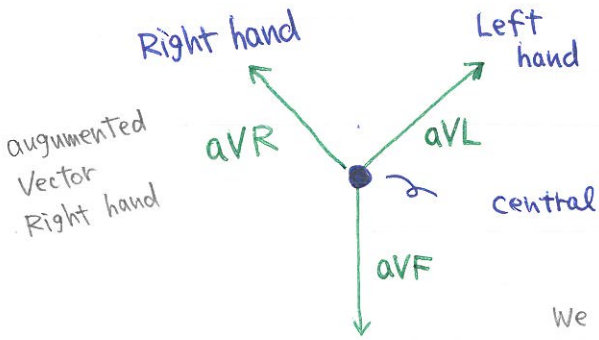
Q. Why it is called "bipolar" ? ⇒ ∵ There are always 2 active electrodes so we can measure the electrical difference b/w these 2 electrodes.

☆ Unipolar limb leads (3)

↳ Goldberger augmented

※ augmented 라고 amplify, magnify

∵ eletrical signals are very small so we need to amplify.

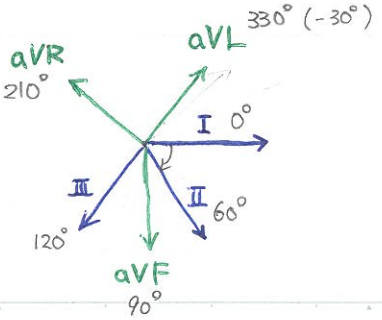


central terminal = 500 Ω resistance

He built huge resistance at the ECG machine it's called "central terminal"

We can measure the electrical difference b/w central terminal and Right hand. this vector is called "aVR"

if I draw the all electrodes in one cardinate → Zero angle is Vector I.

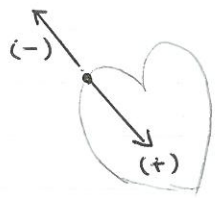


Date

unipolar limb leads 続き

Sometimes we can see postive P wave, positive QRS complex and ⊕ T wave, it's norm but what if you can get negative P wave, ⊖ QRS, ⊖ T wave

Q. what makes the wave positive & negative ?



⇒ positive wave ··· Action Potential is approaching towards the given electrode

⇒ Negative wave ··· Action Potential goes to the opposit way as the electrode is placed

That's why aVR, we can see negative waves. (∵ opposit way)

⇓

aVR is normal if we can see negative P, QRS, T wave.

(+) towards the electrode

(−) ← aVR opposit to the electrode.

☆ unipolar chest leads (6)

if R = 1 mm, S = 5 mm ⇒ Amplitude = −4 mm

V1, V2 } Right Ventricle ※ aVR

negative (∵ R-S = negative)
QRS 波が normal !

V3, V4 } Septum of the ventricle

QRS ≈ 0 (zero) (∵ R-S = 0)
turning point

V5, V6 } Left ventricle

positive QRS (∵ R-S = ⊕)

✦ Q. which unipolar chest leads can we see negative QRS ? ⇒ V1 and V2 (aVR ↑ limb lead 下記)

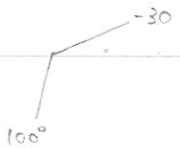
∵ R < S

次ページは Normal electrical axis of the heart, there are 3 ways to calculate but for physio one of those is enough ! just memorize easiest one !

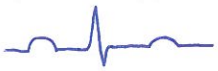
電気(action Potential)の流れの向きのハナシ

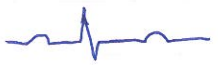
☆ electrical axis of the heart

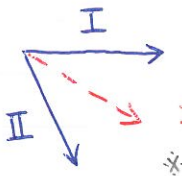
Normal electrical axis = −30 ~ 100°



ポイント lead Ⅰ & Ⅱ のみに注目！

Ⅰ  QRS = (+)

Ⅱ  QRS = (+)

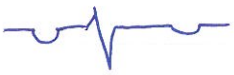


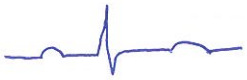
コレが electrical axis of the heart!

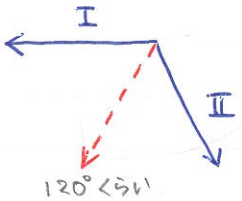
※ ちょうど真ん中ではない！

amplitude によって変わる!! Normal!

(∵ −30°~100°)

Ⅰ  QRS = (−)

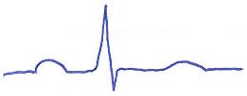
Ⅱ  QRS = (+)

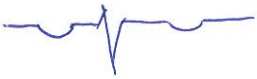


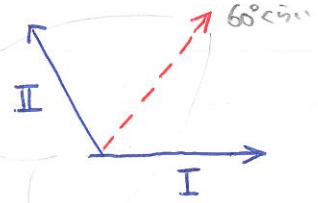
Right deviation

action Potential の流れが右側に寄っちゃってる状態

(心が右に傾いてるだけのこともある)

Ⅰ  QRS = (+)

Ⅱ  QRS = (−)



Left deviation

※単に心が傾く case と心の向きは OK だけど AP の流れが異常な case がある.

↑ この♡はやりすぎw

まとめ

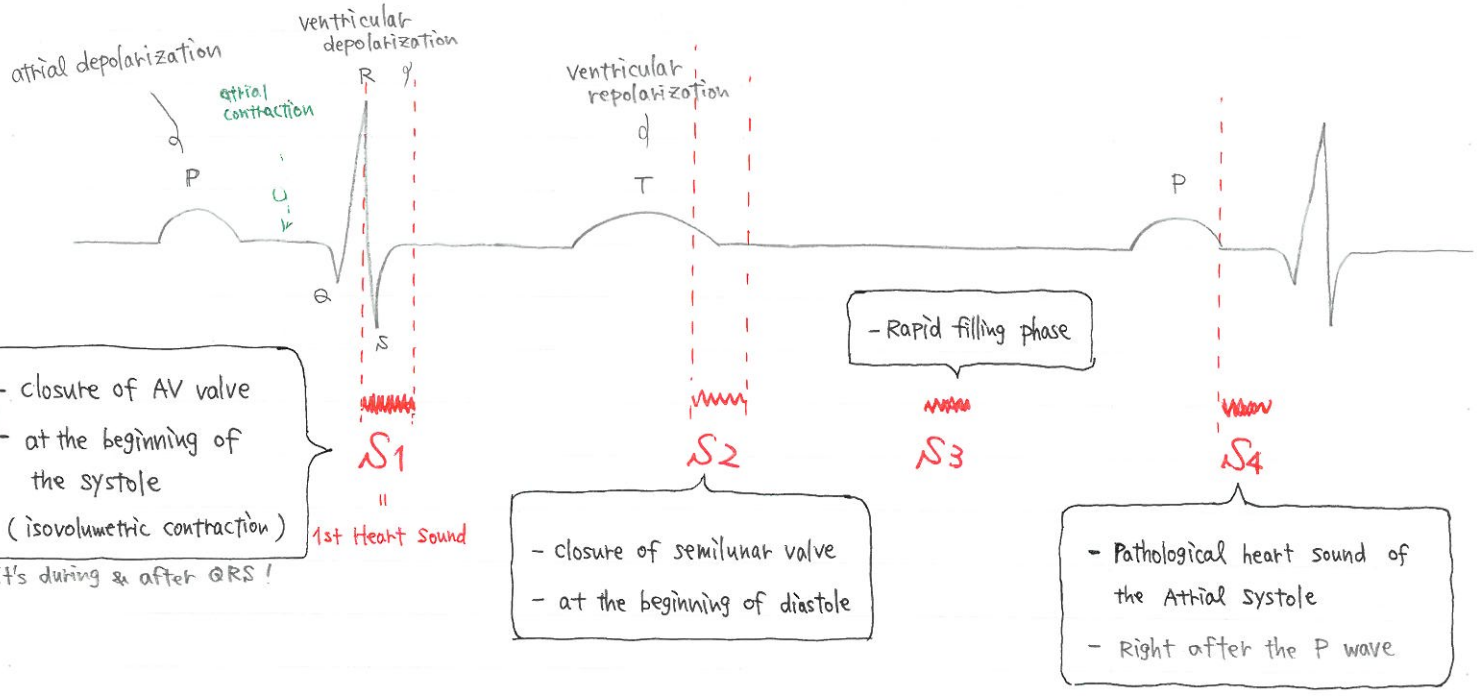
when Ⅰ(+), Ⅱ(+) ⇒ electrical axis is Normal!

Ⅰ(−), Ⅱ(+) ⇒ Right deviation

Ⅰ(+), Ⅱ(−) ⇒ Left deviation

✡ PCG (Phonocardiography)

- We can visualize the Heart Sound
- We need - ECG - microphone which can record the heart sound



You guys need to know where to place the microphone (membrane of microphone)
it depends on which valve would you like to hear the best

auscultation Point

- mitral valve ··· 5th intercostal space , left side of the sternum , 9cm from sternum (bicuspid)
- Tricuspid valve ··· 4th / or 5th intercostal space , left side of the sternum , parasternally
- Aortic valve ··· 2nd intercostal space , Right side of the sternum , parasternally

blood flow goes from left to Right (∵ aorta is cross ↗)
(∵ sound is transmitted with the blood flow)

- Pulmonary valve ··· 2nd intercostal space , Left side of the sternum , parasternally

Heart は止めin innervation を失っても しばらくは 大丈夫!
but Para/sympathetic Nervous system influence the heart rate.

Q. If we cut the all nerves = there is no innervation of the heart, heart would stop or NOT ?

⇒ Still beating! ∵ Heart has automacy as the SA node (Pacemaker cells) generate the rhythm ∴ Heart transplantation is possible!

innervation of the Heart

☆ Parasympathetic activation

↳ can reach the Heart via Vagus nerve (CN X) ※ Neurotransmitter of Vagus n. is Ach.

↓

Ach ※ Ach is released from Vagus n.

↓

Muscarinic Ach Receptor @ Heart

↑

Atropine

✧ Parasympathetic nervous system が亢進すると
以下 5つ (メイン) の Heart effect が起きる! CD Bit

★ ① negative chronotropic effect = HR ↓ ← Most important function of Vagus nerve.
time (frequency)
↳ diastole: longer ∵ duration = 60s/HR
⇒ circulation of coronary is longer!

② negative Dromotropic effect = Conduction Velocity ↓ (speed of AP ↓)
(cowel → transport)
⇒ つまり、SA node → AV node への移動に もっと時間かかる!

Q. How what can you see from ECG the negative dromotropic effect ?
⇒ conduction velocity ↓, ということは、atrial ventricular conduction time ↑
つまり、PQ interval ↑ ⇒ 1st degree of AV block (if PR interval > 200ms)

③ negative Bathmotropic effect = Excitability of the heart ↓
オクロど発狂にさるんイ・ジ

④ negative inotropic effect = Contraction force of the heart ↓
※ Vagus n. は 主に SA node, AV node atrial muscle を innervate する。
= SV ↓ (∵ less blood pumped out)

⑤ negative tonotropic effect = tone of Heart ↓

⑥ negative Lucitropic effect = capability of Heart Relaxation ↓
Santa Lucia サ〜ンタルチ〜ア〜

~~* β blocker と言った場合、~~
~~β_1 blocker を意味する！~~

Date

☆ Sympathetic activation

Heart receive sympathetic fibers from Thoracolumbar segment from T_1 - T_4.

- T_1 - T_4 Thoraco-Lumbar segment
- NA, Adrenaline (6) → β_1 Receptor @ Heart ← β blocker* e.g. プロプラノロール

sympathetic nervous system の neurotransmitter は NA, Adrenaline !

CD Bit

Heart Effect

① positive Chronotropic effect = HR ↑

② positive Dromotropic effect = Conduction velocity ↑

③ Positive Bathmotropic effect = Excitability of cardiac muscle ↑

④ positive inotropic effect = contraction force of the Heart ↑

⑤ positive tonotropic effect = tone of the cardiac muscle ↑

⑥ positive lucitropic effect = capability of the Heart to Relax ↑

cf. - adrenal gland は innervated by Preganglionic fiber of the Sympathetic nervous system !
- adrenal gland (= 放出する) NT は Ach
- adrenal gland は Catecholamine を blood stream (= 分泌する.

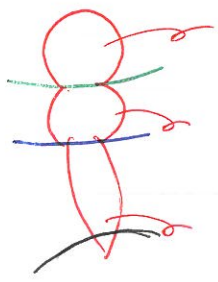
cf. α blocker も β blocker も 高血圧の薬 !

Tyrosine → L-DOPA → dopamine → Noradrenaline → Adrenalin

W7

1

Date Oct 23 mon



① 1st ligature

② 2nd ligature

③ 3rd ligature
(remove apex of the ventricle)

sinus venosus ≒ SA node in Human

2 atria ≒ AV node 〃

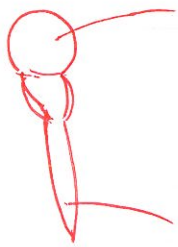
1 ventricle ≒ His bundle 〃

→ can generate the rhythm

① Heart stops —10 min.→ Heart starts to beat again but HR↓ (∵ atria (AV node))

② Heart stops → Heart starts to beat again but HR↓↓↓ (∵ His bundle generate

③ Heart stops. No heart beats. ▽ Apex does NOT have pacemaker cells.



ventricleの temp だけを上げ下げ!

Sinus venosus (≒ SA node)

↳ Temp ↑ ⇒ HR↑, contractility → ~ fever の時 HR上がるのは この為

↳ only for sinus venosus (SA node) ↓ ⇒ HR↓, contractility →

ventricle (≒ His bundle)

↳ Temp ↑ ⇒ HR →, contractility ↑ = amplitude ↑

↳ Temp ↓ ⇒ HR →, contractility ↓

Date

正確には正しくない！

Q1. How would your HR change if I give you "atropine"? ⇒ HR↑ (∵ atropin ↷ Ach para)

Q2. How the atropin block the vagus nerve? ⇒ Atropine blocks the Muscarinic acetylcholine receptor

Q3. How would the HR change you had "sympathetectomy"? ⇒ HR↓ (∵ Sympathetic nerv system ↑ HR parasympathetic is more dominant ↵)

Q4. How would the HR change if you give "β-blocker"? ⇒ HR↓ (∵ β-blocker block the β_1 Receptor)

※ β-blocker は Tachycardia の 患者に使わせる！

Q5. Where would you place the 6th chest lead (electrode)? ⇒ 5th intercostal space + mid axillary line

Q6. 2nd chest electrode? ⇒ 4th intercostal space + left side of the sternum

Q7. How many ~~chest~~ electrode should be placed on the limbs? ⇒ RA RL LA LL あぶくみ

Q8. If you stimulate the left vagus nerve, How the PQ interval change? ⇒ PR interval ↑ (∵ Left vagus n. mainly innervate "AV node".)

if the AV node is stimulated by vagus nerve, Negative Dromothopic effect occur

⇓

Conduction Velocity ↓ (in AV node)

Q9. What is the normal PR interval? ⇒ 120 ms ~ 200 ms

(もし、200ms 以上だと、1st Degree of AV block

Q10. If you stimulate right vagus nerve, ECG は? ⇒ RR interval ↑ (∵ HR↓)

(∵ Right vagus nerve innervate "SA node", ここは、HR↓, ということは ECG全部↑ Longer)

Q11. RR interval = 12.5 mm の時、HR は? ⇒ 120 beats/min.

① paper speed = 25 mm/s ⇒ 12.5 mm = 0.5 s, Duration of cardiac cycle $\overset{0.5s}{=} \frac{60s}{HR}$ ∴ HR = 120

2 methods!! ② HR = 1500 / RR interval in mm

HR = 60 / RR interval in second

Date

Q 12. If RR interval = 25 mm, HR would be? ⇒ 60 beats/min

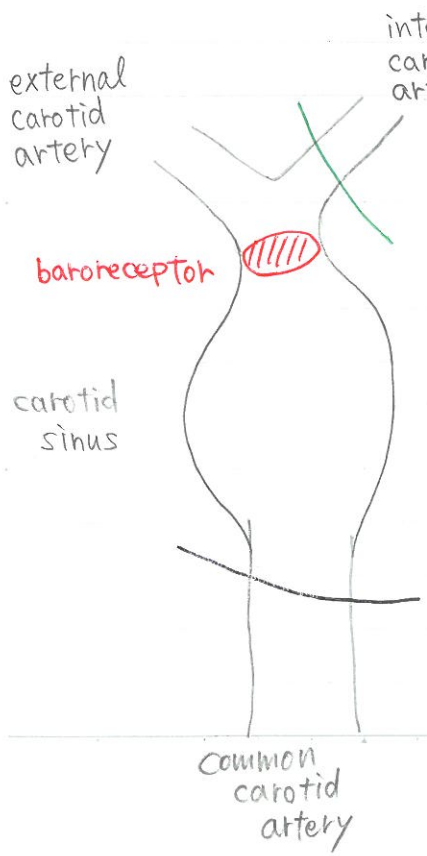
☆ Cardiovascular reflex

are present only if the Heart is innervated

if you remove the Heart (Heart transplantation), There is NO cardiovascular reflex

⇒ Cardiovascular reflex needs normal innervation of the Heart

Name	Adequate stimulus	Receptor	Afferent fiber	Efferent fiber	NT	Effect
	BP↑ を baroreceptor 感知すると、activity of baroreceptor ↑			Brain		
① carotid sinus reflex	BP↑ in carotid sinus	high pressure baroreceptor (mechanoreceptor) (= BP detector.)	IX (= glossopharyngeal n.)	X	Ach	HR↓ BP↓
	どちらも depressor reflex family			muscarinic Ach receptor in Heart is activated		
② depressor reflex	BP↑ in aortic arch	high pressure baroreceptor (mechanoreceptor)	X	X	Ach	HR↓ BP↓
③ Pressor reflex	BP↓	baroreceptor activity↓	IX X	sympathetic activation (Thoracolumbar n.)	NA A	HR↑ BP↑



※ baroreceptor is sitting at the bifurcation of the carotid sinus.

ligature ⇒ BP↓ HR↓ (∵ depressor reflex)

more blood in carotid sinus

→ baroreceptor detect High BP

→ depressor reflex により BP↓ HR↓

普通の狭め方はコレ!

(carotid sinus reflex)

or decrease diameter

ligature ⇒ BP↑ HR↑ (∵ Pressor reflex)

baroreceptor detected BP↓

⇒ glossopharyngeal n が BP 下がってるゾ〜!って脳に伝える ⟹ Pressor reflex により HR↑ BP↑

コレらは nerve (IX, X) が切れてたら機能しない!!

	Name	stimulus	Receptor	Afferent	Efferent	NT	Effect
④	Loven reflex	Pain	Pain Receptor	Pain fiber	sympathetic nervous system	NA A	HR↑ BP↑ TPR↑

Efferent: sympathetic nervous system → (α1 receptor) → vasoconstriction in periphery
↑ ∵ Pain is stress!

※ old ppl can die in dentistry because of Loven reflex.
too much pain ⇒ Loven reflex ⇒ BP↑↑ ⇒ Heart failure / brain hemorrhage

※ local vasodilation (∵ つねったらそこは赤くなる)

↱ for 内臓

※ under operation に anastatic drug & muscle relaxant を 2つ投与しなければいけない所を、muscle relaxant のみ投与された場合、手術中の痛みを全て感じつつも、筋が動かせないので医師に伝えることもできない、という悲劇が起きる。
⇒ 但し、患者が pain を感じた時に生じる Loven reflex によって、BP↑↑ となるので doctor はここで気づかなければならない！ HR↑↑
⇒ イケてない doctor はここで気づかずに β1-blocker で BP, HR 下げようとする。

	Name	stimulus	Receptor	Afferent	Efferent	NT	Effect
⑤	chemo reflex	Hypoxia (O2↓)	carotid body aortic body	IX X	sympathetic activation	NA A	HR↑ BP↑

carotid body / aortic body → peripheral chemoreceptor is sensitive for Hypoxia
sympathetic activation ↑ ∵ Hypoxia is stress!

※ arterial blood pressure : 90~100 mmHg (正常値)

	Name	stimulus	Receptor	Afferent	Efferent	NT	Effect
⑥	Goltz reflex	Hit abdomen	mechano receptor	Splanchnic nerve → Vagus nerve	vagus n.	Ach	HR↓ - may stop the Heart

※ お腹を強打されると死ぬ、という アレ。

	Name	stimulus	Receptor	Afferent	Efferent	NT	Effect
⑦	Bainbridge reflex	venous Return↑	low pressure baroreceptor (mechanoreceptor)	X	sympathetic activation	NA A	HR↑ BP↑

venous Return↑ = from Central Vein to Right Atrium

venous return↑ ってコトは、もっとガンガン駆出しないと！

low pressure baroreceptor の例：central vein, right atrium

2017 12/13 stretching of Right Atrium ⇒ ADH↑

Name	stimulus	Receptor	Afferent	Efferent	NT	Effect
⑧ Bezold-Jarish reflex	oversttetch of venttricular wall (overload the venttricle) ↓ when Hypoxia, Pain	many	X	X	Ach	HR ↓ BP ↓

※ 大量の血液が ventricle に流入することによって、ventricle が overstretch されるのが stimulus.
⇒ 大量の血液を ventricle に流入させるためには、diastole を長くする必要がある.
(∵ ventricular filling は diastole に起こる)
⇒ diastole を長くするためには、parasympathetic nerve を stimulate すればよい.

※ discount in Lidl, old lady buy a lot of water, she bring them to 4th floor
4階まで重いモノを運ぶと おばあちゃんの ventricle は overload なってる.
つまり HR↑↑ ってこと! ってことは、diastole = short ってコト (∵ ventricular filling の為の充分な時間がない!) ってコトは Heart does NOT receive much blood
⇒ old lady が部屋の前で止まると、ハァーハァーって てすりにつかまって呼吸整える.
meanwhile Heart Rate decreases. (Bezold-Jarish reflex) → 良い奴!
HR ↓ ⇒ diastole is more longer ⇒ more blood to the ventricle

※ 但し、我々が テクテク歩いたりしても Bezold-Jarish reflex は働かない!
∵ vessels are NOT fragile ⇒ We can have coronary dilation ∵ β2 receptor
⇒ SO ventricle can receive enough blood.
↳ おばあちゃんの vessels は fragile だから、神は Bezold-Jarish reflex を作った そうな

⑨ Cushing reflex	inttracranial pressure ↑	mechano receptor	vegetative fiber	vagus n.	→	HR ↓ ★★★
				sympathetic activation	→	BP ↑

MAP = CO × TPR (∵ vasoconsttriction in Periphery)

※ vagus n. と sympathetic nervous system are activated at the same time!

Date

Bradycardia

※ intracranial pressure ↑ ⇒ Cushing reflex ⇒ HR ↓ , BP ↑

☆ intracranial pressure ↑ は危険！

∵ There are 3 tissues in the skull ① brain tissue ② blood ③ cerebrospinal fluid
one of those volume is larger ⇒ intracranial pressure ↑
e.g. brain hemorrhage ⇒ intracranial pressure ↑
hit the head ⇒ brain becomes swollen ⇒ intracranial pressure ↑
brain tumor ⇒ intracranial pressure ↑

∵ brain stem is compressed！
⇒ medulla oblongata には cadiovascular center と respiratory center がある！

∴ intracranial pressure ↑ には注意！

※ neurologist が cerebrospinal fluid を採取する時、we need to be sure intracranial pressure is NOT high.
∵ if patient has high intracranial pressure & we put the needle here, huge amount of cerebrocranial fluid is left.
⇒ brain would go to the foramen magnum
⇒ medulla oblongata is compressed by tonsil of cerebellum
⇒ cardiovascular center & respiratory center would be killed.

※ One of the sign of the increased intracranial pressure is HR ↓ but BP ↑ ∴ Cushing reflex は neurologist にとって超重要！

⑩ Oculo cardial reflex — push eye ball — baroreceptor — vegetative fiber — vagus n. — HR ↓
- may stop the heart
- retina damage

※ 海でシャークに攻撃されそうになったら、目ん玉やっつける！ only chance to survive w

week 8

1

Date Oct 26 Thu

Q1. How would HR change, in depressor reflex ? ⇒ HR↓

Q2. 〃 Cushing reflex ? ⇒ HR↓ (★ BP↑)

Q3. 〃 Bezold-Jarish reflex ? ⇒ HR↓

Q4. 〃 Bainbridge reflex ? ⇒ HR↑

Q5. 〃 Pressor reflex ? ⇒ HR↑

Q6. 〃 Loven reflex ? ⇒ HR↑ (✦ TPR↑)

Q7. 〃 , when you cut the Vagus n. ? ⇒ HR↑

Q8. 〃 , when you give Atropine ? ⇒ HR↑

Q9. 〃 , when you give β-blocker ? ⇒ HR↓

Q10. 〃 , when you cut the Sympathetic fiber ? ⇒ HR↓

Q11. 〃 , if you make the Vagotomy ? ⇒ HR↑

Q12. 〃 , in oculocardial reflex ? ⇒ HR↓

★Q13. 〃 , when you ligate common carotid artery ? ⇒ HR↑

Q14. , when you stimulate torture the sciatic nerve ? ⇒ HR↑ (∵ Loven reflex) pain !

Q15. 〃 , when you make ligature around external carotid artery ? ⇒ HR↓

Q16. 〃 , when you increase the temp. of sinus venosus ? ⇒ HR↑, contractility→

Q17. 〃 , when you decrease the temp. of ventricle ? ⇒ HR→, Amplitude↓ (= contraction force)

Date

Q18. 〃 , if you make the Stanius I ligature ? ⇒ Heart stop , and then start again slowe

Q19. Where do you need to put the thread for Stanius I ? ⇒ b/w sinus venosus & atrium

Q20. Which one is HR↓ in Q18 atrium or ventricle ? ⇒ both ↓ (HR is same each other

Q21. How would you make 2nd Stanius ligature ? ⇒ b/w atrium & ventricle

Q22. what do you expect after 2nd Stanius ligature ? ⇒ Heart stop and then start again Even slower

Q23. which one is faster atrium ~~or~~ oh ventricle ? ⇒ atrium

Q24. How would you make 3rd Stanius ligature ? ⇒ cut the Apex of the ~~Heart~~ ventricle

Q25. what do you expect after 3rd Satnius ligature ? ⇒ Stop forever ...

Q26. what is the Physiological solution for the fish or frog ? ⇒ Ringer solution

Q27. what does the Ringer Solution Contain ? ⇒ 0.65 % NaCl , 0.05 % $NaHCO_3$ pH = 7.2
(0.7% NaCl in Workbook)
0.02% KCl , 0.02 % $CaCl_2$

Q28. You stimulate the Heart during systole intensively above threshold. ⇒ No
Can you make the extra systole ? ∵ absolute refractory period
* Heart can NOT be tetanized (skeletal m. & Smooth m. can be tetanized but Heart NOT,
⇒ if Cardiac m. has tetany contraction, the pump function would be Zero
so patient would be dead in a minute. (∵ No Cardiac Output !)

Q29. What is the "korotkoff sound" ? ⇒ Sound of Turbulent blood flow

Q30. When can you hear the korotkoff sound ? ⇒ b/w diastolic & Systolic

Q31. Why ? ⇒ - when the pressure in the cuff is higher than the systolic Pressure, there is No blood flow (= No sound)
- when the pressure in the cuff is b/w Systolic pressure & Diastolic during Systole the artery opens, during diastole close, so open close open close that's why the Turbulent flow we can hear
- when the pressure in the cuff lower than diastolic pressure the blood flow would be continuous → There is No korotkoff sound

Date

Q32. In the fish heart, how many sinus venosus, atrium, ventricle ? ⇒ 1, 1, 1
(cf. frog 1, 2, 1)

Q33. When you record the ECG from the fish heart, where do you need to place the electrodes ? ⇒ One of the ⊕ electrode in ventricle
Two other electrodes are Anywhere on the fish though...

Q34. in human, Sinus Venous would be the ? ⇒ SA node

Q35. if you decrease the Temp. of the Sinus Venosus, How would the R-R interval change in ECG ? ⇒ longer (∵ HR↓)
∵ RR interval = $\frac{60s}{HR}$ $\frac{1500mm}{HR}$

Q36. How would the amplitude of the contraction change if you decrease the Temp. in the Sinus venosus ? ⇒ doesn't change

Q37. Where do you listen the Aortic Valve ? ⇒ 2nd intercostal space to the Right parasternally

Vessels

↳ innervated by Sympathetic nervous system

↳ NA, A } α_1 … vasoconstriction
β_2 … vasodilation

- Vessels of the GI tract
- Vessels of the Urogenital system
- Vessels of the Skin

※ in which Receptor is responsible for the positive Heart effect ?
⇒ β_1 Receptor in the Heart

- Coronaries
- Vessels of the skeletal m

✧ Q : Which vessels have innervation ? ⇒ All except capillary

✧ capillary do NOT have innervation !
(∵ There is NO smooth muscle !!)

Vascular Resistance

★ Resistance of the vessel $= \frac{l}{r^4}$

$R = \frac{8\eta l}{\pi r^4}$

← Resistance of the vessels are directoly proportional to the length and indirectly proportional to the radius on the power of 4 !

A

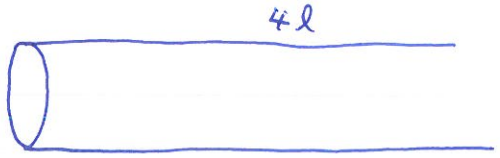
B

Q : Which one would have higher resistance ? ⇒ B

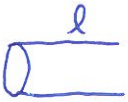
Q : How many times higher ? ⇒ 8 times

Resistance of A $= \frac{2}{2^4} = \frac{1}{8}$

C



D



Q : which one higher resistance ? ⇒ D

Q : How many ? ⇒ 4 x

Resistance of C $= \frac{4}{2^4} = \frac{1}{4}$

※ Resistance is also proportional with the viscosity !

viscosity of PLASMA is independent of tube ϕ !! ⇐ (Plasma & water is normal Newtonian fluid) 2017 mid

5

blood is NOT Newtonian fluid

☆ Viscosity of the blood

$R = \frac{8\eta l}{\pi r^4}$ と全て対応 可

Temp ↑ ⇒ Viscosity ↓
Temp ↓ ⇒ η ↑
} indirectly proportional ← Think about Honey !

Htc ↑ ⇒ η ↑
Htc ↓ ⇒ η ↓
} directly proportional

Velocity ↑ ⇒ η ↓
V ↓ ⇒ η ↑
} indirectly proportional

ϕ ↓ ⇒ η ↓
ϕ ↑ ⇒ η ↑
} diameter is directly proportional

※ Capillary の Viscosity は lower !

☆ Velocity of the blood

Fast slow

artery > vein > capillary

∵ Total cross section area of all the artery is the Smallest !
⇒ Blood velocity is faster !

※ Total cross sectional area of the capillaries = 4800 cm^2
Kristof
2600 cm^2 Lecture
3500 cm^2 Kornyei

artery > arteriole

vein > venule

☆ Blood Pressure

Just follow the blood flow !!

Left Ventricle > Artery > Capillary > Vein > Right atrium

Left atrium > Right atrium 1~5 mmHg

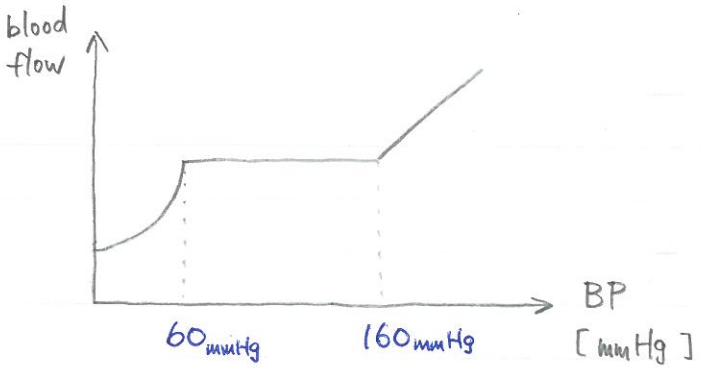
Lowest !!

☆ Auto Regulation

w/o any innervation (or reflex)
⇒ they can change the Resistance to maintain the constant blood flow.

MAP : 60 - 160 mmHg

⇒ Blood flow is Constant



Q : which organ has the Auto regulation ?

1. Heart
2. Brain ← important organs !
3. kidney

※ Lung receives enough blood ...

∵ (systolic - diastolic)

Q : How to Calculate the MAP ? ⇒ 1. diastolic pressure + 1/3 Pulse pressure
2. (systolic Pressure + 2 diastolic pressure) / 3

∵ diastole is 2 times longer than Systole

※ When you're upset , your BP increase ⇒ Your brain should NOT receive more blood
When you're tired , your BP decrease ⇒ Your brain receives same amount of blood or for the Heart ...

⇒ Blood flow should be the same !

Q : What is the mechanism of the Auto Regulation ?

mural = on the wall
⇒ through the wall the BP is High

壁内外圧差

BP ↑ ⇒ Transmural Pressure ↑

∵ in the smooth m , There is mechanosensitive Ca^{2+} channel

↓

mechanosensitive Ca^{2+} channel Open ! (∵ mechanical stretch)
@ Smooth m.

↓

Ca^{2+} influx

↓

smooth m. contraction

↓

Vasoconstriction

⇓

Constant blood flow ! (this is the Purpose !)

Q : BP 90/60 → 160/100 なったら,
How would the Resistance of vessel change ?
e.g. artery of the Heart or Brain or kidney

⇒ Resistance ↑ to get the same blood

∵ if the BP↑ , Artery is totally opened ⇒ more & more blood goes into the Heart, kidney, Brain
But, if there is vasoconstriction the more more blood is restricted.

Bayliss Effect

BPが上がった時に
血流を一定に保つ仕組み

Date

Quick Review

Q: List 9 vasoconstrictors. ⇒ ① Endothelin ② Epinephrine ③ Norepinephrin 3E
④ ADH ⑤ Angiotensin II ⑥ Thromboxane A II ⑦ ATP 4A
⑧ PGF_2 ⑨ Serotonin

☆☆ Hypoxia → Vasoconstrictor in Pulmonary Circulation
→ Vasodilator in Periphery

☆☆ Epinephrine → α_1 Receptor : Vasoconstrictor
Norepinephrine β_2 " : Vasodilator

Q: When you inject the very low dose of Epinephrine ⇒ decrease
How would the Blood Pressure change ? ∵ low dose bind to β_2 Receptor 1st !

※ Affinity of the Epinephrine is Higher to the β_2 Receptor

☆ Low dose of Epinephrine → vasodilator → BP ↓
Norepinephrine

☆ High does of Epinephrine → vasoconstrictor → BP ↑ (∵ bind to α_1 Receptor)

Q: Why high does increase BP ? Give 3 Reasons.

① vasoconstriction — if you give high dose, Epinephrine can get to the Heart
② HR ↑ (∵ ⊕ chronotropic) and bind β_1 Receptor ⇒ HR↑
③ SV ↑ (∵ ⊕ inotropic effect) ⇓
positive inotropic effect ⇒ Contractility ↑ ⇒ SV ↑
CO ↑

☆☆ Epinephrine → Low dose : Vasodilator (∵ β_2 Receptor)
Norepinephrine High dose : Vasoconstrictor (∵ α_1 Receptor)

Date

Vasodilators

① NO (EDRF) Endothelin Derived Relaxing Factor

② Prostaglandin I_2 = Prostacyclin

③ Histamin

④ Bradykinin + VIP + Substance P + CGRP

Local vasodilator

1. Adenosin
2. Acidosis ($[H^+]\uparrow$)
3. $[K^+]\uparrow$ (hyperkalemia)
4. Temp. ↑
5. $CO_2\uparrow$ (Hypercapnia)
6. $O_2\downarrow$ (Hypoxia)*
7. Lactate

when anearobic glycolysis, Glc → Lactate ↑
⇒ run out of O_2 ⇒ Hypoxia
⇒ muscle produce a lot of CO_2 ⇒ Hypercapnia
⇒ muscle Temp. ↑
⇒ local acidosis (∵ Lactate, CO_2)
⇒ muscle are working during depolarization
⇒ K^+ outflow (∵ Voltage dependent K^+ channel)
⇒ Hyperkalemia

why we need local vasodilator ?

Muscle need more O_2, need fresh blood w/ O_2, Glc, nutrients
⇒ when vasodilation, more blood can flow to that area

* Hypoxia is local vasodilator in periphery
But ! Vasoconstrictor in Pulmonary Circulation

Respiratory System

☆ Minute Ventilation = (Breathing Rate) × (Tidal Volume)

one respiratory cycle

7 - 9 L / min. | 14 - 18 times / min | 0.5 L

☆ Alveolar Minute Ventilation = (Breathing Rate) × (TV - dead space)

the volume of air which can get to the alveoli in one minute

0.15 L

the space which is NOT involved in gas exchange

※ The Purpose of Ventilation is Gas Exchange.

Normal Gas Tension

decreasing order

☆ pO_2 (oxygen partial Pressure)

Atmospheric pO_2 > Exhaled air pO_2 > Alveoli pO_2 > Arterial blood pO_2

115 mmHg | 100 mmHg | 95 mmHg

21 % = 159 mmHg

∵ alveoli O_2 + dead space same as atmospheric O_2

100 - 115 mmHg

90 - 100 mmHg

※ if Hypoxia ⇒ should be lower

※ atmospheric pressure at sea level = 760 mmHg

> Capillary blood pO_2 > Venous blood pO_2

40 mmHg

lowest O_2 pressure

☆ pCO_2

※ CO_2 is transported by 3 different ways ⇒ ① CO_2-Hb (Carbamino-Hb)
② HCO_3^-
③ Physically dissolved form

Venous blood pCO_2 > Capillary blood pCO_2 > Arterial blood pCO_2 > ··· > Atmospheric air pCO_2

46 mmHg | 40 mmHg | lowest CO_2 pressure

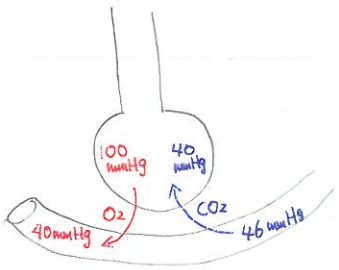
(11/9) kind of opposit of pO_2

Q: Which artery carry the 46 mmHg pCO_2 ? ⇒ Pulmonary artery

Q: Which vein carry the 100 mmHg O_2 ? ⇒ Pulmonary vein

Q: What do you think O_2 or CO_2 diffusion better b/w the alveoli & the capillary ? ⇒ CO_2

10 times better !



$\Delta pO_2 = 60\ mmHg$
$\Delta pCO_2 = 6\ mmHg$

✧ CO_2 can diffuse 10× easily !

Different Pattern of Breathing

☆ Apnoea … No breathing ≒ Cessation of breathing 無呼吸

☆ Apneusis … Prolonged inhalation , short expiration
it refer "brain damage" or "dying people"

息詰の逆

☆ Tachypnoea … fast breathing rate 犬のハァハァって感じ

☆ Hyperventilation … breath more than you need 恋人に泣きじゃくりながら懇願する時の呼吸

- pCO_2 in blood ↓ (Hypocapnia) ∵ CO_2 washed out ! To the breath.

by carbonic anhydrase in RBC

$$CO_2\downarrow + H_2O \rightleftharpoons H^+\downarrow + HCO_3^-$$

→ Respiratory Alkalosis

→ free $[Ca^{2+}]$ ↓

(∵ during Alkalosis , Plasma protein bind Ca^{2+} instead of H^+)

分かりにくい時は逆を考える… Acidosis の時 H^+ が いっぱいだから Plasma protein は H^+ を たくさん 結合する. ⇒ free $[Ca^{2+}]$ ↑ この逆 !

- pO_2 in blood → ∵ during the Normal respiration , Hb is saturated with O_2 98 %

doesn't change significantly (maybe slightly ↑)

98 % of Hb can bind O_2 ⇒ There is No more place for O_2 transport

week 9

Nov 2nd

☆ Hypoventilation … breath less than we need

- CO_2 ↑ (Hypercapnia) $CO_2\uparrow + H_2O \rightleftarrows H^+\uparrow + HCO_3^-$

Respiratory acidosis

↳ free $[Ca^{2+}]$ ↑

- pO_2 ↓ (Hypoxia)

※ normal arterial pO_2 は？ ⇒ 90 - 100 mmHg

venous ⇒ 40 mmHg

☆ Cheyne - Stokes breathing … irregular breathing pattern

⇒ Hypoventilation - pCO_2 ↑ - pO_2 ↓ - Respiratory acidosis - free Ca^{2+} ↑

※ cheyne - Stokes breathing が出たら、Hypoventilation の時に現れる肢を選べばよい。

☆ Kussmaul - breathing (kissing mouth)

… compensation of metabolic acidosis

↳ H^+ ↑

要な Respiration に関係ない奴ら全部！

- diabetes mellitus
- after severe diarrhea
  ∵ intestinal fluid is alkaline
  ⇒ when you have diarrhea, you can loose large amount of intestinal fluid
- drink acid eg. coke
- kidney failure

なぁぞ Lung should decrease the $[H^+]$ somehow

They can decrease $[H^+]$ if **minute ventilation** ↑ (Hyperventilation の状態を作る)

minute ventilation ↑ ⇒ CO_2 ↓ + $H_2O \rightleftarrows H^+$ ↓ + HCO_3^-

Respiratory alkalosis ぞ metabolic acidosis を相殺する！

(hyperventilation)

⇒ Hyperventilation

※ metabolic acidosis の時は、kussmaul - breathing をすれば $[H^+]$ を相殺できる。

(Hyperventilation)

Date

☆ Alveolar Pressure = pulmonary pressure

760 mmHg at Sea level

during inhalation … alveolar pressure < atmospheric pressure ∵ air go from High P to low

exhalation alveolar pressure > atmospheric pressure

at the end of inhalation
expiration = ∴ NO air movement
during Apnoea ∵ No breathing

☆ intrapleural Pressure = intrathoracic Pressure

during inhalation … more Negative 24th
exhalation … less Negative May

always Negative !!
during normal respiratory cycle

※ intrapleural pressure が Negative じゃない時とは？
Pneumothorax (PTX) ⇒ Cut the pleura ⇒ intrapleural P. (+) ⇒ Lung Collapsed.

✧ ☆ Transpulmonary Pressure = alveolar pressure − intrapleural pressure

(+) normally (−)
if (−) ⇒ exhalation force expiration (+)

2017. mid

Kussmaul - breathing の Cause

- Hypercaphia
- diabetes mellitus
- diarrhea
- drink acid
- kidney failure

} metabolic acidosis !

※ つまり、Kussmaul - breathing は metabolic acidosis の compensation として pH を元に戻すために行われる Hyperventilation のことである！

Date

☆ Valsalva maneuver

TLC

- maximal expiratory pressure → toilet, deliver
- exhale against the closed glottis

+ 60 mmHg in Lab

⇒ intrathoracic (intrapleural) pressure is Positive ∵ exhale

↳ Venous Return ↓ (or Zero) ∵ Central Vein ≈ 1 mmHg

∵ if intrathoracic pressure > 1 mmHg ⇒ Central veins are compressed

Blood stack in Periphery !

SV ↑ at the very 1st moment ∵ There is still blood circulating in the pulmonary circulation

SV ↓↓↓ after 1 ~ 2 second

CO ↓↓

Pulse is weak. (may disappear)

BP ↓↓ (∵ MAP = CO × TPR)

baroreflex により sympathetic activation 起こって HR↑, TPR↑

(Pressor reflex)

✕ Valsalva maneuver causes : ① increased Peripheral Resistance (∵ TPR↑)

② elevated jugular venous pressure (∵ Venous Return is almost Zero)

③ decrease in arterial blood pressure (∵ SV is almost zero → BP ↓↓)

④ tachycardia (∵ BP↓↓ ⇒ Pressor reflex = HR↑, TPR↑)

⑤ increased blood volume in systemic circulation (∵ Blood stack in periphery)

(ポ) Valsalva も Müller も 結論は同じで、SV ↓, BP ↓, HR ↑, TPR ↑, weak pulse

違いは Venous Return !

☆ Müller maneuver

RV

- maximal inspiratory Pressure を測るやつ
- inhale against the closed glottis → in lab, 1st exhale as much as you can and then try to inhale w/o buccal m. (∵ buccal 使ったら intrabuccal P. になっちゃう)

⇒ intrathoracic pressure is Negative

↳ Venous Return ↑↑↑

Frank Starling Law

⇓

⇓

⇓

Stroke Volume ↓

⇓

Cardiac output ↓

⇓

Blood Pressure ↓

↳ Sympathetic discharge ↑ (@carotid sinus (pressor reflex など))

⇓

HR↑ , TPR↑

∵ Venous Return increase that much

⇒ Overstretch in Ventricular wall

⇒ actin - myosin far away each other

⇒ ineffective pump function

Q: When increase Müller maneuver, blood stack where? ⇒ in the chest (heart, Lung)

Q: How about Pulse? ⇒ weak (may disappear)

(1) Valsalva と Müller で pulse weak! (may disappear)

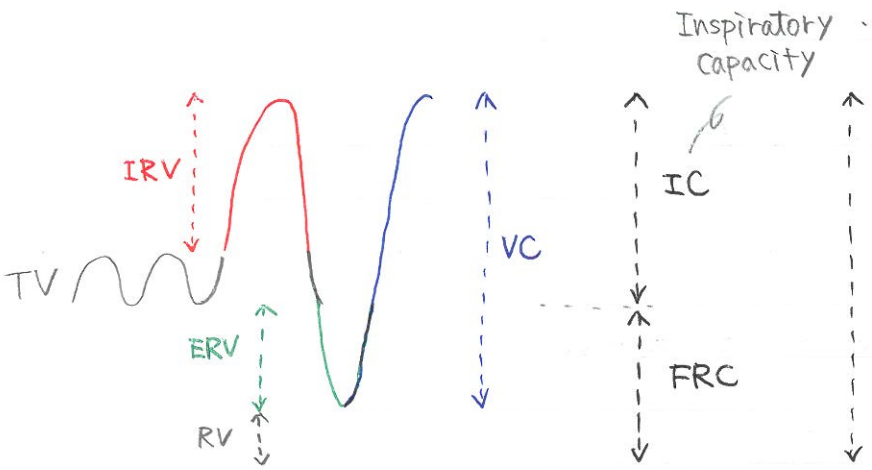
※ Blocking forced inspiration after full expiration leads to:

①

Date

☆ Static Lung Volume / parameter

capacity は



Inspiratory Capacity … You need to ask patient exhale normally and then inhale deeply. (IRV + TV)

Functional Reserve Capacity (ERV + RV)
… the Volume of Lung after normal exhalation

Tidal Volume … Normal inspiration, expiration

IRV (Inspiratory Reserve Volume) … after normal inhalation, still inspire

ERV (Expiratory Reserve Volume) … after normal expiration, exhalale

RV (Residual Volume) … at the end of the deepest exhalation に残ってる Volume

⇒ RV can NOT be exhaled !!

※ Even if you die, RV is still there !

※ We can just remove the Residual Volume, if there is Pneumothorax.
If you cut open the chest, ERV and RV will be leave !
⇒ in case of Pneumothorax, there is only minimal air (<100mL) on the Lung !

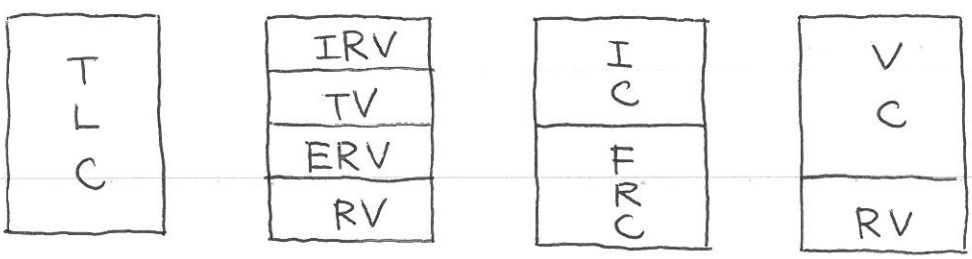
VC (vital Capacity) … after deepest exhalation → deepest inhalation
〃 inspiration → 〃 exhalation

VC = IRV + TV + ERV

TLC (Total Lung Capacity) … at the end of the deepest inhalation
The Lung Volume

※ RV, FRC, TLC can NOT be measured by Spirometer ! RVいってたら測れない !
∵ You can measure only that which can be exhaled !! ← RV can NOT be exhaled.

→ How can we measure them ? ⇒ Helium dilution method



Q : VC = ?
IC = 4L, TV = 1L
FRC = 2L, RV = 1L

5L

speed counts

we could measure all of them ①~⑤

☆ dynamic Lung Parameter

① FEV1 (Forced Expiratory Volume in 1st Second)

… You need to ask the patient inhale as much as you can (air) and exhale as fast as you can

The Volume which is exhaled 1st Second would be the FEV1 !!

Q: How many % of VC can be exhaled in the 1st Second ? ⇒ 80 %

$$\text{Tiffeneu index} = \frac{FEV_1}{FVC} = 80\%$$

if Tiffeneu index < 70 % ⇒ Obstructive Pulmonary disease

(e.g. asthma , COPD) Chronic Obstructive Pulmonary Disease

Tape !

⇓

FEV1 ↓

(∵ expiration longer)

⇒ Tiffeneu index ↓

expiratory problem ! ∵ There is airway constriction (eg. broncho constriction)

→ there is some fluid inside the bronchi → expiration is longer & harder.

※ Restrictive Pulmonary disease ⇒ Compliance of the Lung ↓ ($\frac{\Delta V}{\Delta P}$)

capability of the Lung to Expand

Belt !

⇓

Problem w/ inhalation

Tiffneu index ≧ 80 %

※ Normally, Compliance should be high

つまり、small pressure difference should create the high volume difference 通時

→ High Pressure differences are created ⇒ less Volume difference

② PEF (Peak Expiratory Flow) 10L/s in Mgnus

… Top speed of exhaled air

③ PIF (Peak Inspiratory Flow) … Top speed of inhaled air

④ $MEF_{75\%}$ (Maximal Expiratory Flow 75%) … 75% of VC is still in the Lung

⑤ $MEF_{50\%}$ … 50% of the VC is still in your lung

⑥ $MEF_{25\%}$ … only 25% of the VC is in your lung

slowest !

At the beginning of the exhalation , speed is faster. ⇒ $MEF_{75\%} > MEF_{50\%} > MEF_{25\%}$

At that time , exhaled air which is coming from small bronchioli or alveoli or the stuff

✡ innervation of the Lung

Fight or Fright 時には more O2 要.

→ by Sympathetic Nervous System → NA, A → β2 Receptor in the Lung

⇒ bronchodilation ⇒ Air way Resistance ↓

∵ $R = \frac{8\eta L}{\pi r^4}$

→ by ParaSympathetic Nervous System → Vagus n. → Ach

↓

Muscarinic Ach Receptor

3 functions of ParaSympathetic activation

✧ ① broncho Constriction … Para - が亢進するのは rest 時 ∴ bronchoconstriction 起きても呼吸に問題は無い

② Surfactant Production by Type II Pneumocyte

→ Surface Tension ↓ … if surface Tension ↑ ⇒ alveoli would collapse.
So Surfactant prevent the alveoli from collapsion.

→ keeps the alveoli open

Q: where do you think the surfactant is more important in the small alveoli or large?

⇒ small alveoli (∵ small alveoli has higher tendency to collapse

because of Laprace Law : $P = T \cdot \frac{2d}{r}$ (r↓ 分を T↓ で取り戻す.

⇒ small alveoli Collapse easily.

⇒ surfactant is more important in small alveoli.

Q: when does the Surfactant start to produce? ⇒ 6~7 months (3rd Trimester)

※ sufficient after 32nd week by Anatomy lecture

(28th-32nd week by Horvath is enough)

glucocorticoid Surfactant Production is also increased by glucocorticoid

eg. Cortisol … stress hormone

⇒ That's why it's better if you would like the baby by a natural way, shouldn't choose the C section (if w/o indication). During baby coming out, baby's head is compressed that is huge stress for the baby ⇒ glucocorticoid are produced

⇒ glucocorticoid increase the Production of the Surfactant. → more likely baby will survive

In Hungry,
if There is Premature delivery
glucocorticoid is injected
to the baby's skeletal m.
through the uterus
(28)
(特に 32 week 前の premature baby には有効)

Date

③ Hering - Breuer reflex (ヘーリング ブロイウェル)

... when we inhale, Pulmonary tissues are stretched and mechanoreceptor detect

during inhalation ... Pulmonary Stretch
↓
mechanoreceptor が感知
↓
exhalation start.

→ via Vagus n. → info is transmitted which "inhalation is good"
→ At the end of inhalation, reflex ON
→ brain order "exhale NOW!!"

⇒ Protect the Lung from Over filling

※ Respiratory arrythmia
totally Normal !!

- inhalation ⇒ HR↑
- expiration ⇒ HR↓

∵ Sympathetic activation

Normal Respiratory Pattern

Vagotomy

deep inhalation
deep exhalation

amplitude↑ of breathing deeper!

∵ No Hering - Breuer reflex
(overfilling しない為の機構が止まったら overfilling しちゃう!)

stimulate Vagus n.

Vagus apnoea 無呼吸

∵ Hering-Breuer reflex が働きまくって、filling できる容量を減らしちゃう.

Date

carotid sinus can be depressor & or pressor reflex !

atropine → HR↑

β receptor agonist → HR↑

" antagonist → HR↓ ← β Receptor blocker

α Receptor blocker → BP↓

α R agonist ⇒ BP↑

α Receptor antagonist → BP↓

Ach → HR↓
BP↓

Ach Esterase blocker → HR↓ (∵ more Ach !)
BP↓

Q: if HR↑ ⇒ amplitude doesn't change.

Q: when airway resistance↑ ⇒ RV↑
⇒ Peak flow↑
⇒ FEV_1↓

PEF↑ PIF↑

Obstructive pulmonary disease

GI

★ sympathetic activation / innervation

↳ digestive motility of GI tract ↓

↳ but contract shincter m.

↳ decrease GI juice production ↓ { less saliva, less gastric juice, less pancreatic juice

★ Parasympa activation → good for digestion

↳ digestive motility ↑

↳ GI juice production ↑

★ Saliva … produced by salivary gland

↳ 1~1.5L / day → ガムや噛めば more saliva

↳ hypo osmotic … lower than blood plasma
< 280 mOsm (blood plasma: 280 - 300 mOsm)

↳ slightly acidic (around 7.0) (blood pH 7.35 - 7.45)
↑ primary saliva は alkaline

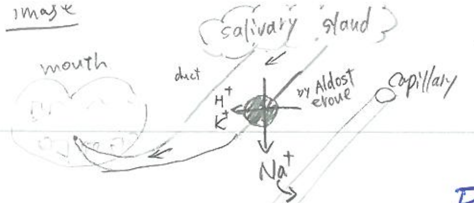
Contains

- H_2O
- IgA → mucosal defence
- lysozyme … immuno molecule, antibacterial effect (kill the bacteria)
- mucin … can lubricate bolus (bolus slippery function)
- amylase … carbohydrate digestion → saliva amylase は口の中に何分も食べ物クチャクチャしてれば monosaccharide まで digest できるけど、普通は数秒で(飲)すぎるから。mono- までは分解されない

↳ stomach の pH = 2 で inactive に!

食後に デザート食べるのは良い w
胃でも消化できる ∵ pH higher

image



← Collecting duct と同じ

Saliva vs Plasma

㊀小 less — Na^+ — < — ㊀大 ∵ reabsorbed !

↑ ∵ aldosterone (mineral corticoid)

Na+ reabsorption 与える影響

Secondary saliva

from in salivary duct the Na^+ be reabsorbed ! → to blood stream

primary saliva isoosmotic =

That's why saliva is Hypo Osmotic !!

[NaCl] ↓ less — Cl^- — < — ㊀大 more

Na^+Cl^- always follow

at the end of the day

㊀大 > K^+, HCO_3^-, H^+, CN^- — less

∵ They're secreted to the Saliva !

→ Rate of salivation ↑ → less time for reabsorption

Q: Gum かんだら → Na^+ ↑, Cl ↑ → plasmaまでは いかないけど 上昇

Q: when do we use glossopharyngeal n? (CN IX) ⇒ Pharyngeal phase

Not oral phase
Not esophageal phase

Q: Other function of " CN IX ⇒ Carotid sinus reflex

(1. Pressor reflex
2. chemo reflex)

saliva 量 増えると… osmolarity ↑ , pH ↑

absorb できない!!

transport time of esophagus ... less than 10 second

main function of esophagus
- upper 1/3 skeletal m.
- lower 2/3 smooth m.

solid food

gastroesophageal sphincter ... open when food arrive there

↳ insufficiency の時は、open → acidic gastric juice may get to the esophagus = reflux

= Heart Burn

gastric juice 1 L / day

pH ≈ 1~2 (1~3)

☆ Stomach

↳ chief cell ... produce Pepsinogen (inactive)

HCl → Pepsin (active) ... protein digestion

positive feedback.

↳ Parietal Cell - produce HCl & intrinsic factor

↳ bind VB12

IF+VB12 Complex can be absorbed at distal part of small intestine (ileum)

(3) direct
- gastrin (+)
- Histamin (+)
- (Ach) GRP (+)

(2) indirect
- Vagus n. (parasympathetic activation)
- Amino Acid (+)
- Stretch of stomach GRP (+)

gastrin 分泌を促進することで間接的に HCl production ↑

(3) direct

HCl ↓

⊣ Secretin

⊣ CCK

⊣ GIP (gastric Inhibitory Polypeptide)

(1) indirect

⊣ Somatostatin (inhibit gastrin [produce])

1

★ Gastrin … produced by G cell → located in 90% Stomach, 10% duodenum

→ digestive motility of Stomach ↑

(+) ↑ GRP (gastrin releasing peptide)

(+) ← Amino Acid

(+) ← stretch of stomach

⊣ Smatostatin, Acidic gastric juice (low pH) — Negative feedback

∵ gastrin can produce HCl, if enough HCl ⇒ We don't need more gastrin.

2

★ CCK → ⑤ digestive motility of small intestine ↑

① ↳ inhibit gastric emptying → 胃に止める. duodenumでゆっくりdigestするため

② ↳ Contract gall bladder

③ ↳ relax the sphincter of Oddi

④ ↳ Pancreatic enzyme Secretion ↑ (all of them) Trypsinogen, chymotrypsinogen, amylase, lipase

⑥ ↳ Promote function of secretin

⑦ ↳ Satiety (satisfactory) acting to the brain — feel full, okay [illegible]

HCO_3^- ↑ から HCl ↓ の流れ!

[3]

☆ Secretin

↳ Pancreatic juice production ↑

↳ HCO_3^- content of pancreatic juice ↑

↳ HCO_3^- 〃 bile ↑

((neutralize HCl

secreted / reabsorbed

Pancreatic juice の $[Cl^-]$ ↓ ∵ HCO_3^-/Cl^- antiporter

cf. kidney の PCT では Cl^-/anion exchanger として登場

↳ inhibit HCl production of parietal cell of Stomach

[4]

☆ GIP (gastric inhibitory peptide)

↳ HCl production in Stomach ↓

↳ digestive motility of stomach ↓

[5]

☆ motilin

↳ digestive motility of stomach, ↑
small intestine ↑
proximal part of large intestine ↑

※ it doesn't increase the motility of the distal colon !!

⇒ But, Gastrocolic Reflex increase distal colon digestive motility.

phases of gastric juice production

1. Cephalic phase ← smell. taste. sight. think about food
   (brain)
   40-45% ↳ vagus n. is activated ← reflex
   ↳ gastric juice production ↑

2. Gastric phase ← food arrives at the stomach
   50-55%
   stretching wall of the stomach
   ↓
   HCl ↑ ← gastrin ↑ production @ G cell
   more than 50% of HCl* in this phase (*produced)

3. intestinal phase — chyme (half digested food w/ gastric juice) arrive at the duodenum

✦ Entero Gastric inhibitory Reflex
(one of the feedback mechanism)
↳ large amount of acidic, high osmolarity chyme arrives at duodenum
↓
CCK (key hormone) is produced
↓
inhibit gastric emptying

Q: Why we need this reflex?
⇒ it gives some time to digest, neutralize the HCl.

Normally when stomach is empty, the volume is about 50 mL
when eat a lot ⇒ as big as 1.5 L
⇒ duodenum can NOT expand that much than the stomach

intestinal phase 続き

◇ Gastro Colic Reflex

∵ it can give some room for the food ⇒ distal colon should empty

food arrives at stomach
stretch stomach

⇓

motility of distal colon ↑

ポンポンが 食べたらすぐ defecation するのは このため！

☆ Pancreatic Juice

alkaline, PH 8 ~ 8.9 (6)
(∵ HCO_3^-)
⊕ ← Secretin

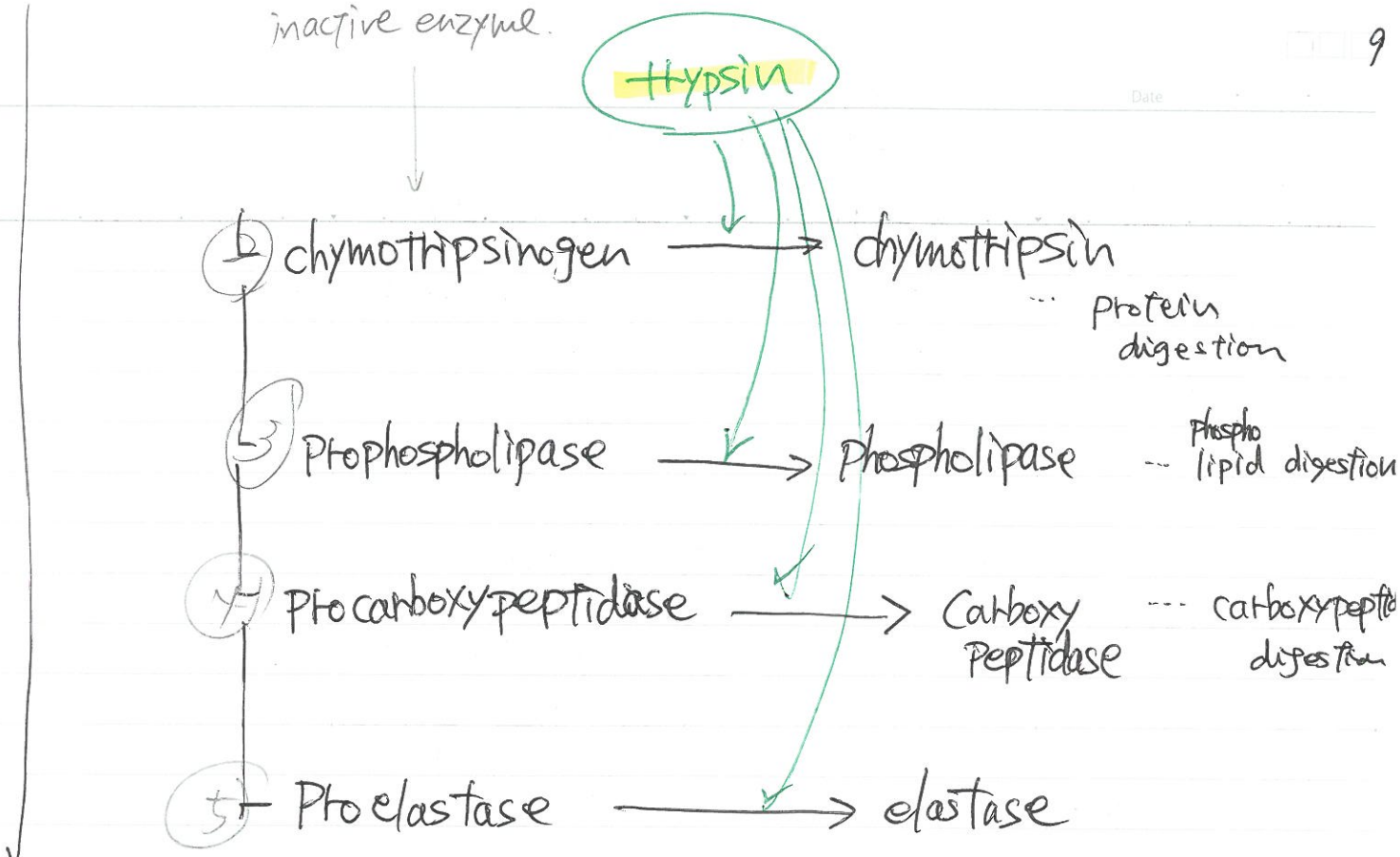
※ salivaの時は分泌亢進で Na^+ Cl^- ↑ だったが、Pancreatic Juice 分泌亢進では HCO_3^- / Cl^- antiporter が亢進する為、HCO_3^- ↑ , Cl^- ↓ となる.

- ↳ ion Cl^- ↓ HCO_3^- ↑
- ↳ H_2O
- ↳ inactive enzymes (5) → is activated in duodenum
  - └ (1) Trypsinogen → Trypsin → protein digestion

enteropeptidase (produced in small intestine) → Trypsinogen → Trypsin
(protease activity N terminal のAAを切る!)
act in duodenum

Trypsin → Trypsinogen (positive feedback)

kind of same as Clotting factor ~



Active enzymes (4) (produced in Active form)

1. amylase → Carbohydrate digestion
2. lipase +2 → lipid digestion
   - need bile for cofactor
3. DNase ... DNA digestion
4. RNase ... RNA "

pancreatic juice = all nutrients digest

☆ Bile ... produced by Liver
stored in gall bladder

0.5 L/day いっぱい lipid Protein 含めば もっと

PH ≈ 7.5~8 ∵ HCO_3^- ⊕ Secretin

Bile function

- Ions
- water
- cholesterol
- elastin
- bile pigment (bilirubin ... biliverdin ... bilistanrdin)
- bile salts

emulsification of the Lipid

↳ lipase can digest the lipid
(& produced by pancrease)

produced by "Hepatocyte" only !!

Small intestinal juice

2L / day pH 7.5-8

- brush border enzyme located on the surface the microvilli
  - ↳ finish the digestion

(only monosaccharid / Amino Acid. can be absored) (monomer form ~~ɛ obs ifs~~)

Proximal (duodenum)	middle (Jejunum)	distal (ileum)
- Ca^{2+}	- fat	- VB_{12}
- ~~Fe~~ $^{2+}$ - apoferitin we need (ferrous form)	- fat soluble vitamins ↓ VA.D.E.k	- Bile pigment
- follate		- Bile Salts.
- carbohydrate		
- Amino Acid		

major.

~~R~~absorption

12 # Large intestinal juice

0.2L/day
pH: 7.5~8

function: (+) store the feses / undigestible particles.

(2+) ion absorption
H2O absorption
but NO nutrients absorption!

(2-) bacteria produce Vitamin (VK)

water content of daily feses ··· 100~150 mL/day

GI juice production
(8L/day が 空腸で secrete されるが 7.9L が 再吸収される)

if severe diarrhea → metabolic acidosis.
(lose a lot of amount of alkalum)

Vomit → metabolic alkalosis
∵ loose a lot gastric juice.

Compensated by kussmaul - breathing
to increase Minute Ventilation

kidney

Date: Nov 9th Thu

RBF (Renal Blood flow)

= 1250 mL/min 20-25% of Cardiac Output.

$$RBF = \frac{RPF}{1 - Htc}$$

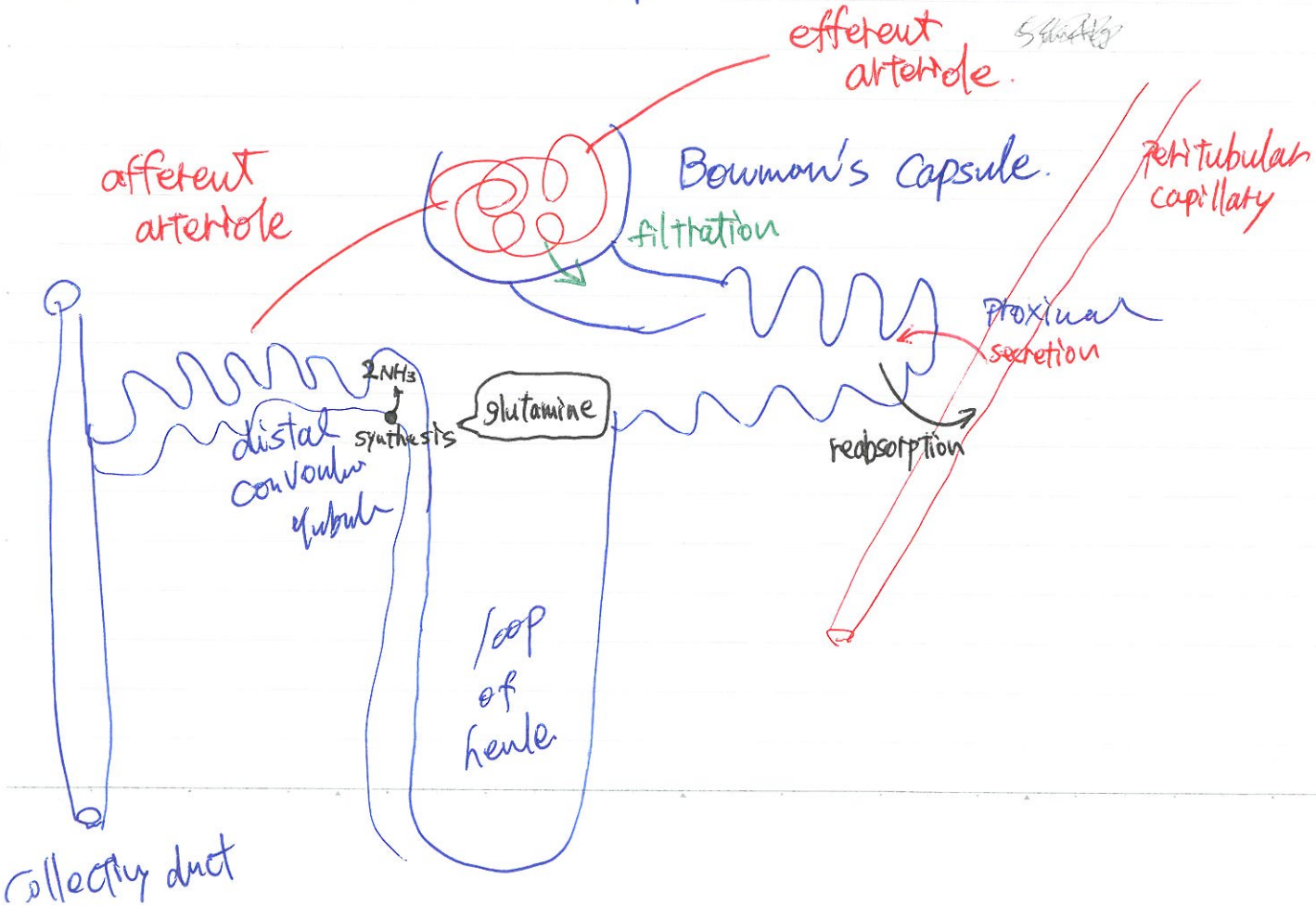
RPF = 650 - 670 mL/min.

GFR = 180 L/day = 120-125 mL/min.

Urine Volume = 1 - 1.5 L/day

Urine Flow Rate = 1 mL/min.
(Minute Diresis) ave.

Functional unit = nephrone 1 million



Date

Net Urine Production = filtration − reabsorption + secretion + synthesis

☆ filtration

3 layers
① fenestrated endothel (small window (small molecule can pass through) eg water, ions)
② negatively charged basement membrane → Proteinurea では ここが ダメになる
③ Podocyte layer

☆ filtration Pressure

Net filtration Pressure = hydrostatic Pressure of glomerulus (BP of glomerus) 60 mmHg
− Colloid osmotic pressure of Plasma 30-35 mmHg (28 mmHg)
− hydrostatic pressure of Bowman's capsule 18 mmHg (in Proximal Convoluted tubule)
↓
intra renal pressure と同じ

= 5 ~ 15 mmHg

effective Net filtration Pressure of efferent arteriole
afferent arteriole の effective filtration Pressure

dilate afferent arteriole ⇒ increase
Constrict efferent ⇒ 〃
⇒ decrease

inulin は reabsorb と secrete どちらもされないから使われる！

Liver failure ⇒ filter ↑

$$GFR = C_{inulin} = \frac{U \times V}{P}$$

U: inulin cc. in urine
V: urin flow rate (Minute Diuresis) 1mL/min
P: inulin cc in plasma

$C_{endogenous\ creatinine} > C_{inulin}$

$C_{endogenous\ creatinine}$: 140 - 150 mL/min (17% larger)

C_{inulin}: 120 - 125 mL/min

(∵ small amount secretion)

Glucose Clearance $= \frac{U \times V}{P}$ → 1mL/min

U: glucose cc. in urine = 0

P: 4-6 mmol/L

= Zero !

Tmax = [redacted] mmol/L → untreated diabetes mellitus

RPF = RBF × (1 − Htc)

$E_{PAH} = 0.9$

☆ $RPF \approx C_{PAH} = \frac{U \times V}{P} = 600\ mL/min.$

660 mL/min.

↑ freely filtered
also secreted !

renal vein cc. 10% (almost 0)

☆ Urea Clearance = 50 mL/min.

☆ endocrine functions of the kidney

↳ EPO ← Hypoxia 時 → RBC formation

↳ Thrombopoietin. → tct formation.

↳ calcitriol = vitamin D_3 = 1,25 dihydroxy cholecalciferol

↳ imp for Ca^{2+} reabsorption = $[Ca^{2+}]$ ↑ in plasma

↳ Renin → angiotensinogen → angiotensin I

☆ free water clearance.

(+) diluted urine — osmolarity less than plasma. C.C.

(−) osmolarity ↑

Cortex much 90% of RBF

outer medulla 8%

inner medulla 2%

innervation of the kidney

☆ sympathetic innervation

α1 Receptor.

↳ vasoconstriction

↳ less blood

RBF ↓

β1 Receptor @ juxtaglomerular apparatus

↓

Renin ↑

☆ NO !!

parasympathetic

120

★ $FF = \frac{GFR}{RPF} = 20\%$

660

glucose $E = 0$ — 全く排泄されない!!

~~PAH~~

inulin

~~E = 1~~

E

PAH $E = 0.9$

$E = 0.2$

- freely filtered
- No reabsorption
- No secretion

★ Autoregulation

60 - 160 mmHg

↳ RBF is Constant!!

Bayliss ~~Effect~~

BP↑ ⇒ smooth m ↑ ⇒

Rh incompatibility

Rh (-) 2nd Rh (+) baby is dangerous

fibrinogen

~~fibrinogen~~ 2-4 g/L

⅔ albumin

⅓ globulin

vagus n. cut → HR ↑ sympathetic dominant

minimal air < 100mL

vagus n → GRP

Date

と略します...

Date Nov 23 Thu

☆ Proximal Convoluted Tubule (PCT)

- 2/3 of ions are reabsorbed actively
- 2/3 of water (120 L/day) → AQP 1, 3, 4 ※ ADH can regulate only AQP 2 !! @ collecting duct
  ∵ GFR = 180 L/day
  ※ ADH doesn't influence water reabsorption @ proximal convoluted tubule

- at the end of PCT, isoosmotic (∵ same amount of ions & water reabsorbed)

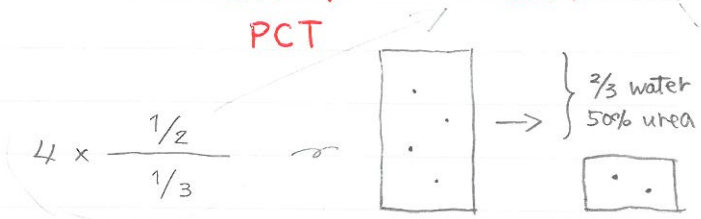
- 50% of urea is reabsorbed
  - freely filtered
  - passively reabsorbed
  - passively secreted
  - ※ No active transport !

more water is reabsorbed than urea !

[urea]plasma = 4 mmol/L

✧ at the end of PCT 6 mmol/L

$4 \times \frac{1/2}{1/3}$



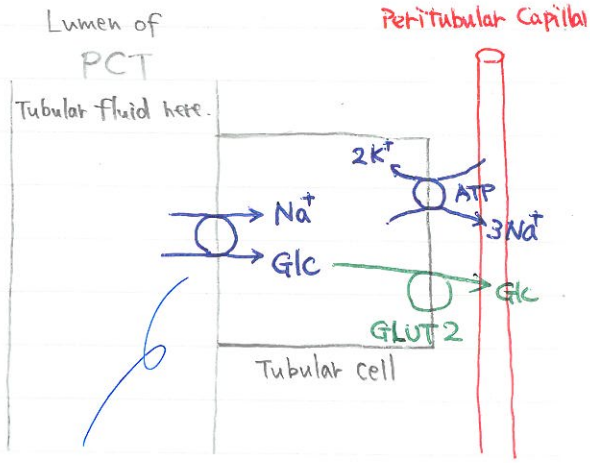
(primary filtrate)

Q: Total concentration of Ca^{2+} in PCT is ? ⇒ 1.25 mmol/L

∵ Ca^{2+} is freely filtered, but 50% of Ca^{2+} is bound to plasma protein not filtered !

- Secondary active co-transporter
  - located at luminal surface
    - ① Na^+ - Glc co-transporter
    - ② Na^+ - AA "
    - ③ Na^+ - HPO_4^{2-} " (phosphate)

PTH (Parathyroid Hormone)



Transport Max = 9 mmol/L

diabetes mellitus

When Glc cc in plasma exceed 9 mmol/L ⇒ Glc show up in urine = Glucosuria

Q: Is it physiological to show Glc in urine ? ⇒ Yes ∵ drink too much coke temporarily

Glucosuria ⇒ Osmotic diuresis ∵ Glc is osmotically active & it takes water, ions with it

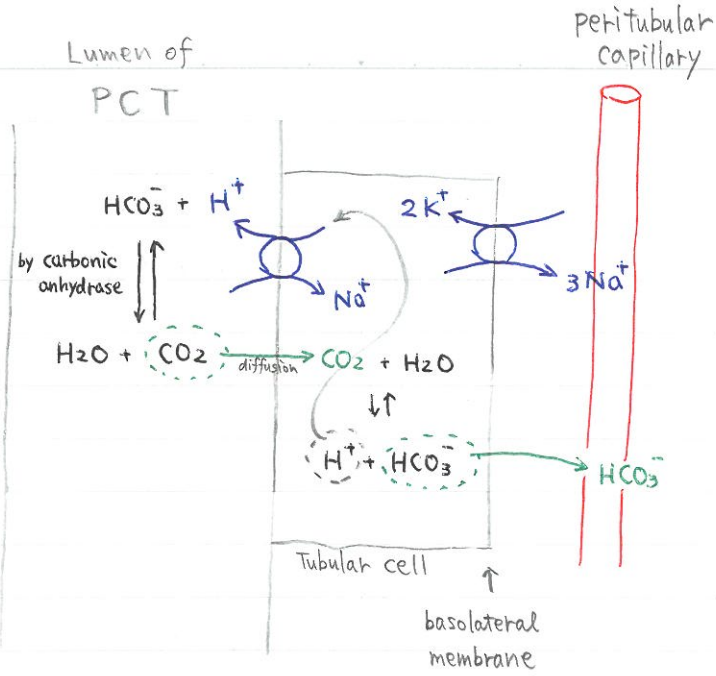
Q: If you inject PTH, How would blood plasma phosphate c.c. change ? ⇒ decrease
urine " ⇒ increase

HCO_3^- reabsorption is indirect process.

Date

(中) Na^+ / H^+ exchanger is involved in "HCO_3^- reabsorption"

- Secondary active antiporter
  - ① Na^+ / H^+ exchanger
    - ↑ Angiotensin II
    - ※ if Angiotensin II ↑
      - ⇒ Na^+ reabsorption ↑
  - ② $Cl^- /$ anion exchanger



補足
saliva のトコで Cl^-/HCO_3^- antiporter 出てきた.

- Channel
  - ① Ca^{2+} channel
  - ② Mg^{2+} 〃
  - ③ Cl^- 〃

Q: PCT にある protein で正しくないのはどれか.

⇒ Na^+ / Glc antiporter is NOT correct

AQP 1, 3, 4, Na^+-phosphate cotransporter, Cl^-/anion exchanger
Na^+-AA cotransporter, Ca^{2+} channel, Na^+ / Glc antiporter,
Mg^{2+} channel, Cl^- channel

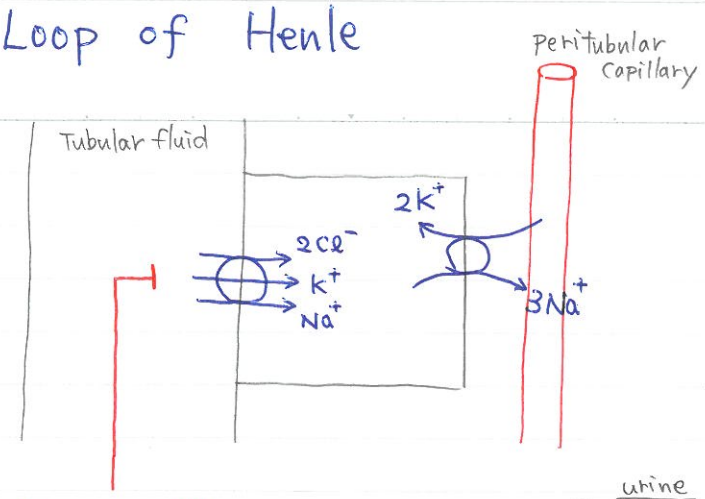
☆ Thin descending part of Loop of Henle — by Japanese Tutor

- ONLY passive transport
- permeable to H_2O (by AQP1)

a 800 mg Calcium daily intake is required in men to reach the Calcium balance (2018 mid)

☆ Thick ascending part of Loop of Henle

- impermeable to H_2O always !
- active ion reabsorption
  - ✧ ① $Na^+ - K^+ - 2Cl^-$ cottransporter
    (primary active transport)
  - ② Ca^{2+} channel



diluting segment — ion cc. ↓

(∵ ions が再吸収されるけど H_2O はされないから !)

Furosemide … Loop diuretic drug

urine 4-6L/day

strongest diuretic drug !! 利尿薬

- urine ↑
- Blood Volume ↓
- BP ↓

☆ Distal Convoluted Tubule

- iso / hypo - osmotic (∵ right after "diluting segment")
- $Na^+ - Cl^-$ cottransporter … 5% of $NaCl$ is reabsorbed in DCT

Thiazide diuretic drug

- Ca^{2+} channel
- Ca^{2+} ATPase
- Na^+ / Ca^{2+} exchanger
- Na^+ / K^+ ATPase

} These are involved in Ca^{2+} reabsorption ! (10%)

(※ 2/3 of Ca^{2+} are reabsorbed in PCT

PTH (+)

※ PTH は DCT での Ca^{2+} 再吸収を促進 !

※ PTH increase the # of these proteins !

※ PTH inhibits $Na^+ - HPO_4^{2-}$ cottransporter in Proximal Convoluted Tubule.

Q : Patient w/ hyperparathyroidism , blood Ca^{2+} cc. ⇒ ↑
urine Ca^{2+} cc. ⇒ ↓
plasma PO_4^{3-} cc. ⇒ ↓
urine PO_4^{3-} cc. ⇒ ↑

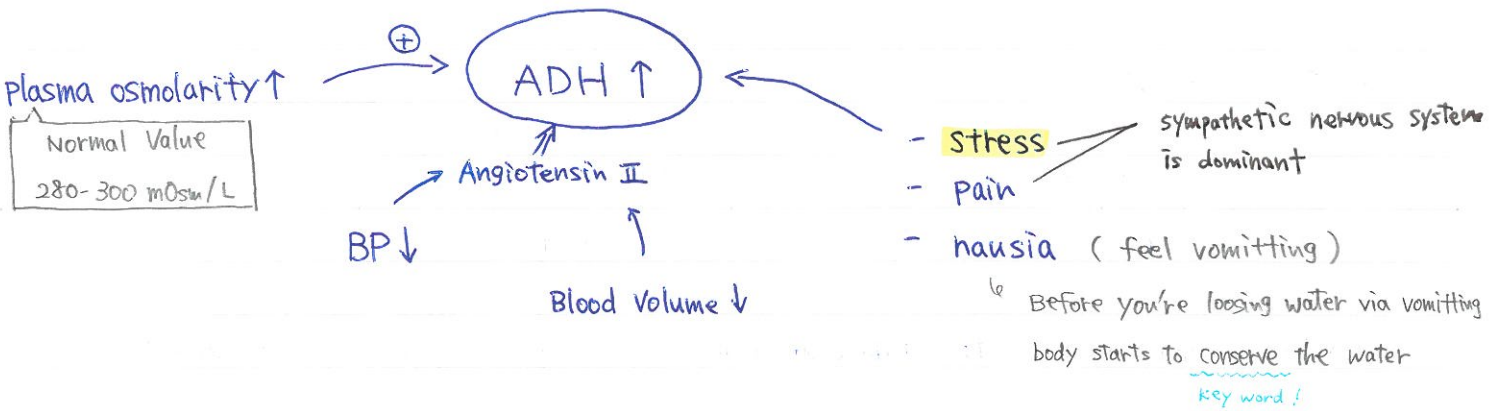
✡ Collecting duct

① ADH (vasopressin , arginine vasopressin) 9AA

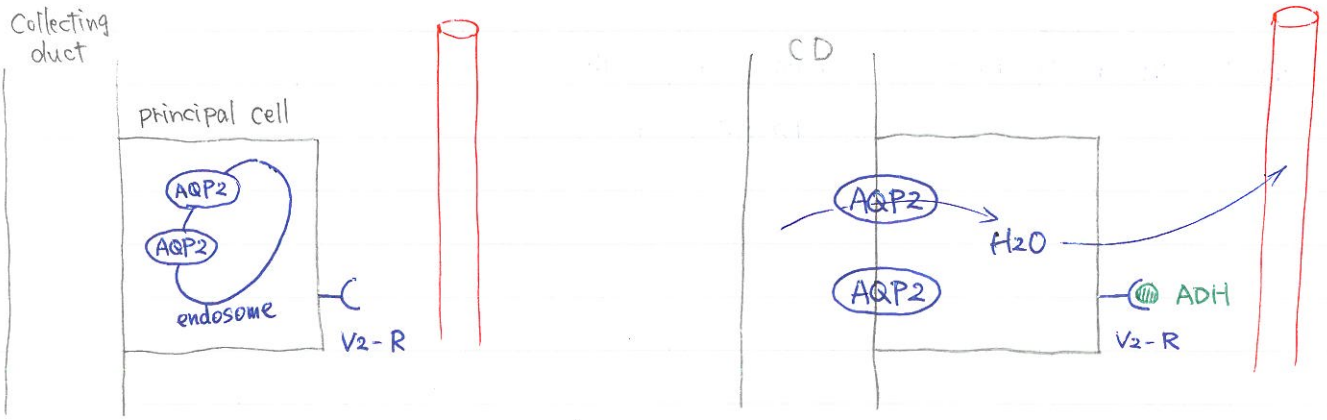
- Produced by " Hypothalamus " → axonal transport
- stored / released by " Posterior Pituitary gland "

Transport Maximum

※ Anterior Pituitary gland に向かうのは、" portal circulation "



- 2 Receptors
  - ① V_1-R … @ vessels ⇒ Vasoconstriction
  - ② V_2-R … @ Collecting duct



w/o ADH — AQP2 molecule move to Luminal Surface — w/ ADH

⇓

Collecting duct is impermeable to H_2O.

✧ Central diabetes insipidus
→ No ADH production @ Hypothalamus
↳ urine volume ↑
↳ water diuresis (low osmolarity)
10 - 15 L / day

w/o ADH Large amount of diuretic urine is produced

✧ Nephrogenic diabetes insipidus
↳ there is ADH can NOT act
↳ problem w/ V_2-R or AQP2 or 2nd messanger

more serious

治療
鼻からコカインの吸うみたいに吸入

Date

∵ No need to conserve water

How would the ADH c.c. change?

Q: if you drank 1 L of tea ⇒ ADH ↓

Q: if you run 42.195 km w/o drinking water ⇒ ADH ↑

Q: if you are in the desert ⇒ ADH ↑

Q: if you drink alcohol ⇒ ADH ↓ ∵ 2 reasons

1) Volume of alcohol

アルコール飲むと おしっこ行きたくなるのは この為 ↳ 2) Alcohol ⊣ ADH producti

Q: if you lost 1 L of blood ⇒ ADH ↑

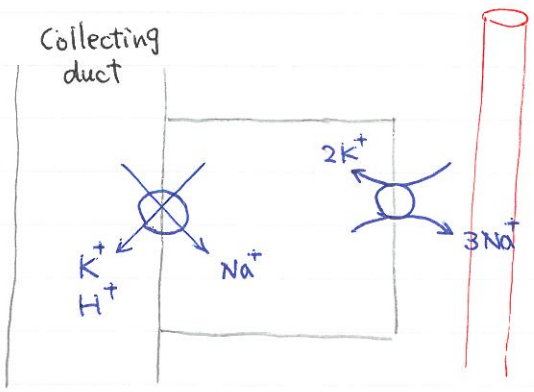
② Aldosterone (mineralocorticoid) … produced by glomerular zone of adrenal cortex

= outer layer

↑ K^+ (Hyperkalemia)

↑ Angiotensin II

- Na^+ reabsorption ↑
- K^+, H^+ secretion ↑ (excretion ↑)



✧ Conn Syndrome (Hyperaldosteronism) … adrenal cortex produce too much Aldosterone.

↳ BP ↑ (∵ Na^+ reabsorption is followed by water reabsorption sooner or later)

↳ Plasma K^+ ↓ … Hypokalemia

↳ pH ↑ … metabolic alkalosis ⇒ free Ca^{2+} ↓ (∵ when alkalosis, less $[H^+]$ ⇒ Plasma protein release H^+ and bind Ca^{2+})
($[H^+]$ ↓)

☆ Renin - Angiotensin - Aldosterone System (RAAS)

Angiotensinogen → (Renin) → Angiotensin I → (ACE) → Angiotensin II

- Angiotensinogen: produced by Liver
- Renin: produced by kidney
- ACE (Angiotensin Converting Enzyme): produced by endothel cell of Lungs

※ Renin is Enzyme !! NOT Hormone !!!

※ ACE is secreted to blood stream so target tissue is NOT ONLY Lungs.

✦ 6 different ways of BP↑ by Angiotensin II

① Vasoconstrictor ⇒ TPR↑ ⇒ BP↑

② Thirst ↑ ⇒ drink water ⇒ Blood Volume ↑ ⇒ BP↑

③ Salt hunger ↑

④ directly increases Na^+ reabsorption @ Proximal Convoluted Tubule
↳ Na^+ / H^+ exchanger の転写促進
⇒ Blood Volume ↑ ⇒ BP↑

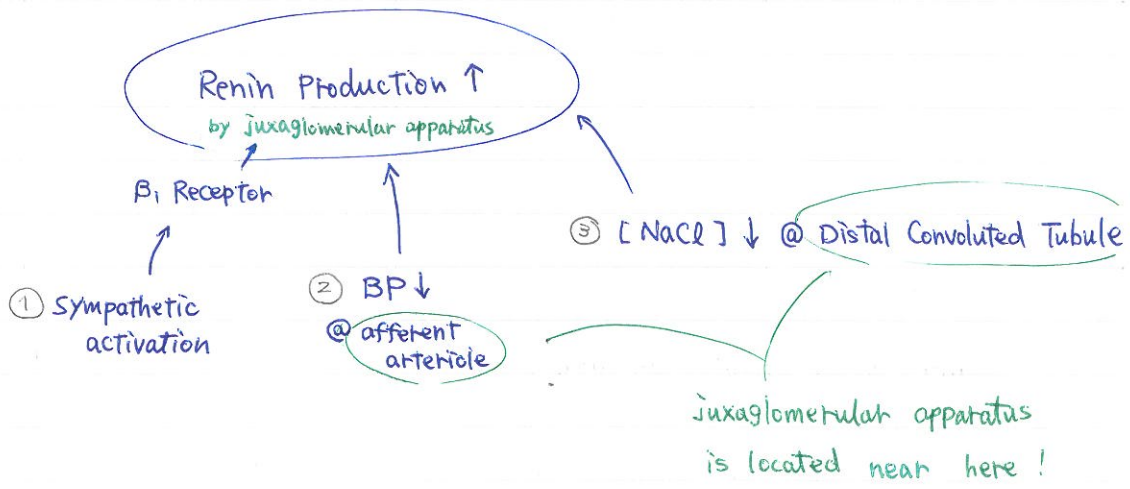
indirectly ! →

⑤ Aldosterone ↑ ⇒ Na^+ reabsorption ↑ @ Collecting duct

⑥ ADH production ↑
⇒ vasoconstrictor
⇒ water retension ↑ @ Collecting duct
(∵ ADH makes Collecting duct water permeable via AQP2)

retension : 保有量

Q: What is the adequate stimulus for Renin Production ? (3つ !)



Date

✦ Q: if you intake ACE inhibitor, ⇒ K^+↑ (Hyperkalemia)
which ion c.c. change in the plasma which is dangerous ?
∵ ACE inhibitor ⇒ No Angiotensin Ⅱ ⇒ No Aldosterone
⇓
K^+ remains in the body ⇐ No K^+ secretion @ Collecting duct

※ When you give Angiotensin Ⅱ blocker or Aldosteron blocker or ACE blocker
you need to think about [K^+] ! (∵ it may lead to Hyperkalemia)

Q: Why do you think the Hyperkalemia can be dangerous ? ⇒ can stop the Heart in diastole

cf. Hypercalcaemia may stop the Heart in systole (∵ too much contraction)

③ ANP (ANH , Athio Peptin) ... Atrial Natriuretic Peptide 心房性ナトリウム利尿ペプチド

Na^+ を尿中に排泄すること

↳ produced by Atrium of the Heart when stretching
(= when Blood Volume is large)

↳ urine Volume ↑ 利尿する方向!!
Blood Volume ↓
BP ↓

- 28 AA
- 心臓の負荷を下げる方向!
(body fluid 下げる) 降圧剤

4 way to increase urine Volume

ANP
1) GFR↑ ∵ more filtered, more urine
2) directly inhibits Na^+ reabsorption @ Collecting duct (∵ ナトリウム利尿)
3) attenuate the function of Aldosterone (= inhibit)
4) inhibits ADH production

(+) Angiotensin Ⅱ の逆を考えれば良い。

Q: What is the endocrine functions of the kidney ? ⇒ To produce ① EPO when Hypoxia
② Thrombopoietin ③ Calcitriol (= Vitamin D_3 = 1,25 dihydroxy Cholecalciferol) ④ Renin

☆ PTH の働き まとめ

① ⊣ Na^+ - HPO_4^{2-} cotransporter @ PCT

② → Ca^{2+} 再吸収 @ DCT

Q1: How does the calcitriole c.c. change when kidney failure ? ⇒ decrease

VD3 or 1,25-dihydroxy Calciferol

Q2: How does the blood plasma K^+ c.c. change when kidney failure ? ⇒ increase

∵ kidney can NOT secrete the K^+ in Collecting duct. (by aldosterone)

Q3: How would the Creatinine level change ? ⇒ increase

same reason above

Q4: which hormone is connecting the Collecting duct ? ⇒ ADH, Aldosterone, ANP

↓

Na^+ reabsorption

- hCG と LH は かなり似てる. (hCG と FSH / TSH も まあまあ似てる)
- ADH と oxytocin メッチャ 似てる
- GH と prolactin メッチャ 似てる

Endocrinology

posterior hypophysis
RH系 + oxytocin + ADH

Date Nov 30 Thu

☆ 5 Hormones produced in Hypothalamus in Anterior Pituitary

Hypothalamus		Anterior Pituitary
① oxytocin	* Neuroendocrine reflex	① Prolactin
② GnRH (LHRH)	- afferent part	② LH, FSH
③ GHRH	thinking about baby	③ GH
④ TRH	touching	④ TSH
⑤ CRH	- efferent part	⑤ ACTH
	Hormone* production	

① oxytocin*

… very similar to ADH ! (structure (9AA), function, produced place, stored / released place,) (Receptor)

- Produced in Hypothalamus (2nd semester: Supraoptic nuclei, Paraventricular nuclei)
  - ↓ axonal transport ← transport mechanism
- stored & released in Posterior pituitary gland

✧ function

1) uterus contraction ← increase the contractility of the uterus
2) milk ejection … myoepithelial cell contraction of the breast (both are contraction of smooth m.)
   - ※ Not milk production (Prolactinの仕事)
3) maternal behavior ← 赤ちゃんの面倒みるようになること (look after the kids)
4) pair bonding = oxytocinが love hormone とも由来 (living together, touching each other)
5) trust ↑, empathy ↑ ⇒ oxytocin is produced

✧ Receptor

1) OT-R (oxytocin-Receptor)
2) V_1-R
3) V_2-R

} ∵ very similar to ADH (vasopressinのVだよ) ← vasoconstrictionの方のReceptor

V_2-R ← water retension (reabsorption) conservation ∵ AQP2が luminal surface of collecting duct に移動

- 9 Amino Acids and similar structure !

Q: which hormone levels are larger in portal circulation than peripheral circulation? ⇒ d) TRH

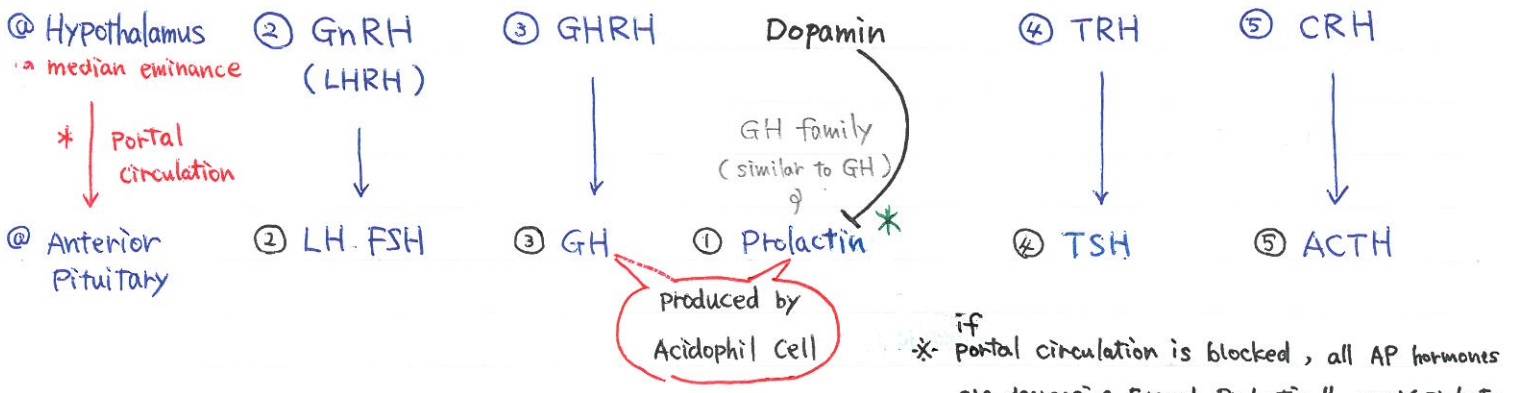
a) oxytocin b) GH c) TSH d) TRH e) Tyroxin

RH系は全部ね

2

* Blood are capilarized 2 times. - It takes up Releasing Hormone in the Hypothalamus
- It releases the Releasing Hormone in the Anterior Pituitary gland

Releasing Hormones are produced in the different parts of the Hypothalamus and transported by median eminance.



if
※ portal circulation is blocked, all AP hormones are decreasing Except Prolactin !! ONLY Prolactin increase !!

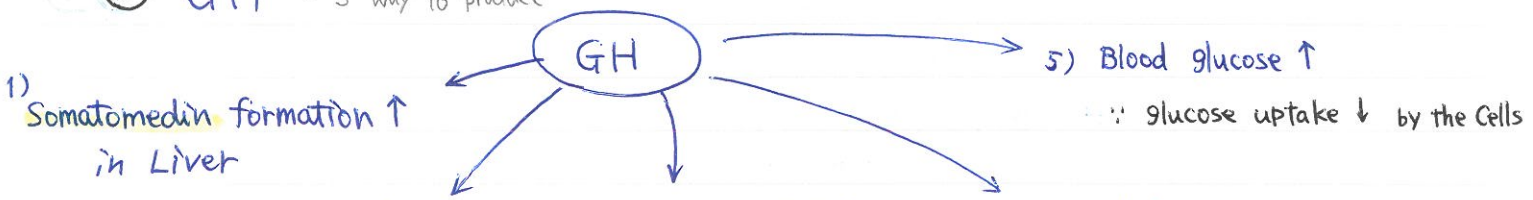
※ Dopamin inhibits "Prolactin" production by tuberoinfundibular dopaminergic system

⇒ if there is NO dopamin in tuberoinfundibular dopaminergic system,
Prolactin is produced and results in milk production

⇒ if there is NO damine even in men, men are able to produce milk

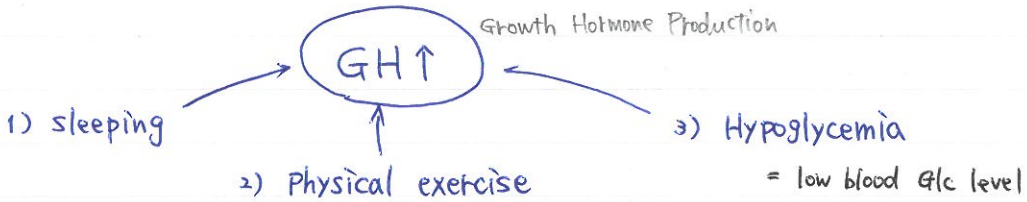
③ GH

- 5 functions.
- 3 way to produce



※ body builder inject the GH and increase the muscle size. ∵ Anabolic effect
But!
fat contents are low ∵ Lipolysis

※ あと Anabolic effect ↑ と言えば、
Testosterone, insulin



if GH ↓ ⇒ Pituitary dwarfism
↳ body size is proportionally smaller → Not only the legs and arms are smaller But also Trunk, neck
※ There is NO mental Problems. → other dwarfism are mentally challenged

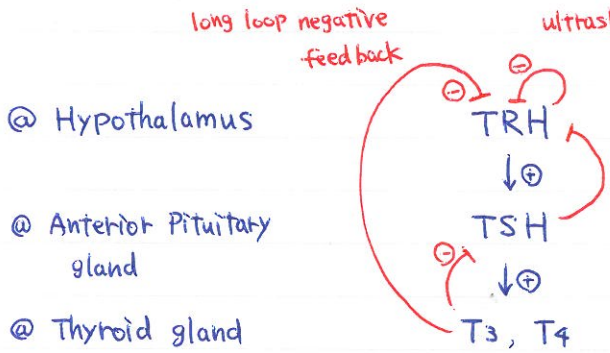
if GH ↑ before puberty ⇒ Giantism over 2m !

if GH ↑ after puberty ⇒ Acromegaly

… body size is NOT so bigger
But actal parts are bigger
eg. nose, ears, hands, feet

※ during pregnancy → fact size ↑ も同じ理由

✡ Thyroid Hormone (T_3 , T_4)



∵ 1st T_4 is produced → 1 iodine cut

more active!

T_3 : Tri - iodo Thyronine … contains 3 iodine ions.

T_4 : Tetra - iodo Thyronine = Thyroxine

consists of 2 Tyrosine AA which is covalently bounded

※ if iodine deficiency ⇒ both T_3 and T_4 are decreasing

✧ functions of T_3, T_4 (Thyroid Hormone)

- development of CNS
  maturation brain
- growth process
- BMR ↑ (Basal Metabolic Rate)
- HR ↑ (∵ β_1 Receptor sensitivity ↑)
- BP ↑ (systolic pressure ↑ → pulse pressure ↑)
- Cholesterol level ↓ of plasma

(Thyroid Hormone deficiency)

lack of T_3, T_4

- mentaly challenged (cretinism)
- Hypothyroidism → dwarfism

Body size is NOT proportional

Legs & arms are short

But, Trunk, Neck, Head are Normal

Q: How can you know somebody has Hyperthyroidism but you didn't examine yet ?

⇒ BMR ↑ so these guys are very nervous and open the all windows because they are hot

They can NOT tolerate the hot so they prefer the cold. They are sweating.

⇒ after examination, There are high HR, BP and cholesterol level is low

Q: Hypothyroidism patient cholesterol level ?

⇒ High

☆ TSH

4 functions

↳ T_3, T_4 ↑
↳ size of Thyroid gland ↑
↳ iodine uptake ↑ to the thyroid gland
↳ Thyroglobulin production ↑
- it is in the Thyroid gland
- it contains a lot of Tyrosine AA

1 Thyroid Hormone production

we need
- 2 Tyrosine AA covalently bound together
- 3 or 4 iodine place on

※ Speaking of the TSH, You need to know increasing anything related to the Thyroid Hormone production!

if TSH ↑ ⇒ goiter (enlargement of the Thyroid gland)

Q: When do you think that can be goiter?
Hyper or Hypo or Euthyroidism

Goiter の cause NO-1 は?

iodine deficiency (endemic goiter)

↳ T_3, T_4 ↓ → No less negative feedback → TSH ↑↑

※ euthyroidism で goiter になり得る理由

軽い iodine deficiency → T_3, T_4 ↓ → less negative feedback → TSH ↑
→ TSH が T_3, T_4 の産生を促すため T_3, T_4 level 戻に戻る

it depends on "TSH"

☆ GnRH

♂

Hypothalamus — GnRH
↓
Anterior Pituitary gland — LH, FSH

Testicle
- Leydig cell ⇒ Testosterone Production
- Sertoli cell ⇒ spermatogenesis

4 functions — intracellular receptor

☆ Testosterone ∵ steroid hormone
- → metabolic rate ↑ 10%
- → anabolic function
  - → Protein synthesis ↑ ⇒ muscle mass ↑
- → larynx size ↑ ⇒ deeper voice
- → hair production ↑

(LH stimulates testicle & testicular weight ↑)
∴ testosterone 注射すると ⇒ Testicular weight ↓

Q: Do you think there is testosterone in ladies? ⇒ Yes (but lower cc.)

Q: Can you tell me the steroid Hormone that we discussed last time? ⇒ Aldosterone

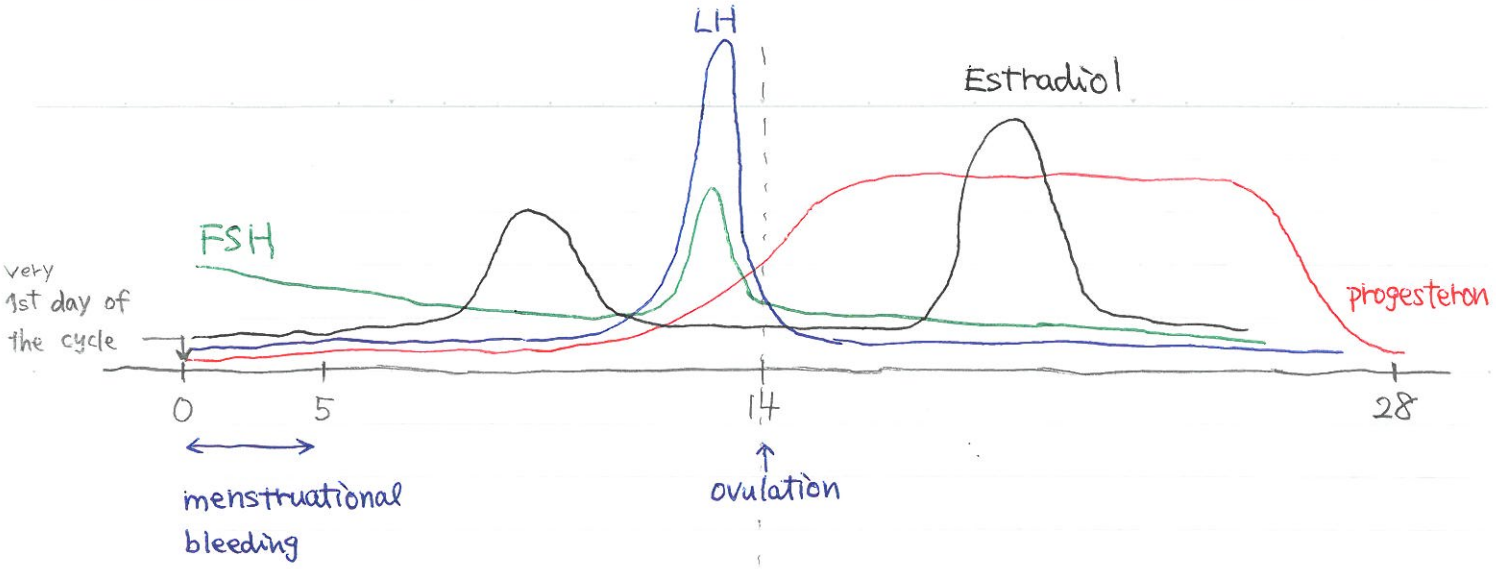
♀

Hypothalamus — GnRH
↓
Anterior Pituitary gland — LH, FSH (⊕)
Ovary — E_2 (estradiole*), P (progesterone)

* estradiole level is constantly high in the late follicular phase (24-48 hours long)
⇒ There is a positive feedback mainly on the LH production but FSH as well

✧ estradiole production
- requires LH & FSH
- requires Theca interna cell & granulosa cell

6 ✡ Hormonal change during the menstrual cycle



ovary :	follicular phase	luteal phase
uterus :	proliferative phase	secretory phase

Q: what would happen if the progesteron & estradiol levels drop suddenly? ⇒ end of the cycle
⇒ menstruational bleeding
(next cycle would start)

fertilization

- 12 ~ 15 days
- @ ampulla of uterine tube
- egg is passive → after the fertilization = active (∵ pellucida rxn)

↓ move toward the uterus

implantation

- 1st week after the fertilization (day 6)

Q: which is the pregnancy hormone ? ⇒ hCG (human Cholionic Gonadtropin)

Date Dec 4th mon

☆ hCG … glycoprotein hormone

- hCG
- TSH
- LH
- FSH

They have α and β subunits

(α subunit … identical
β subunit … different)

→ Produced by "trophoblast cells"

→ Produced 2 weeks after the fertilization

→ you can show it in urine by immunological / biological pregnancy test (Lab)

→ reaches Maximum at the end of the 1st trimester (week 10 ~ 12)

→ stop producing only after the delivery period (∵ Placenta is also delivered)
= becomes Zero

※ 出産後は placenta が無いから hCG = 0 となる.

※ Placenta & trophoblast cells produce hCG !

→ similar to (LH) closest ! ⇒ hCG can act on LH Receptor
TSH LH can act on hCG Receptor
FSH

☆ hPL (human Placenta Lactogen = human somatomammotropin hormone)

☆ Prostaglandins → uterus contraction

↗

oxytocin

main はコッチ !

※ during delivery Period, oxytocin & Prostaglandins are released

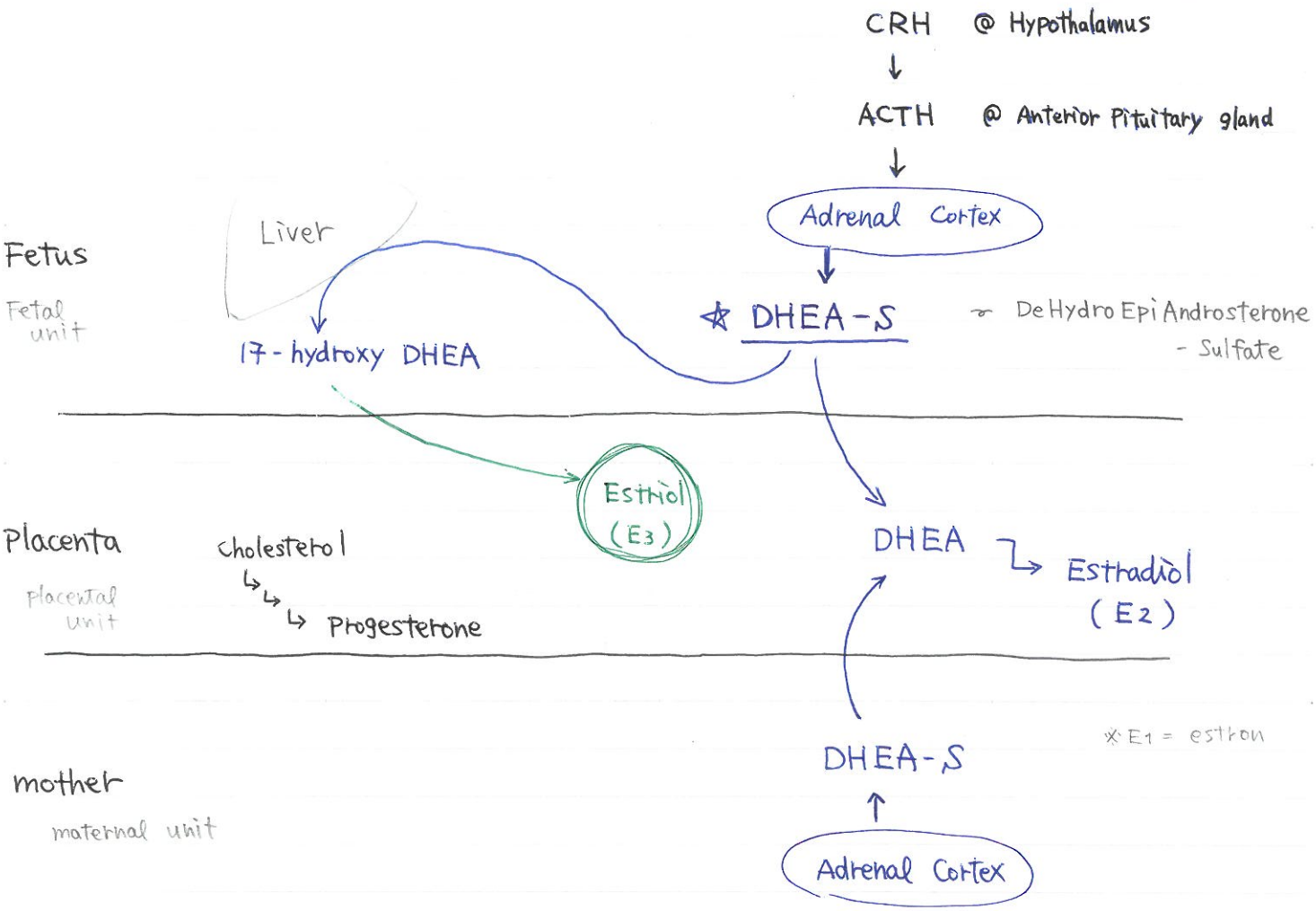
☆ Relaxin … peptide hormone → membrane receptor

→ relaxing the Joint during delivery

intracellular receptor
- Estradiol - Progesterone
- testosterone
- Thyroid hormone (T3, T4)

Date

✡ Feto placental unit



✧ Estriol is very informative medical indication !!

∵ Estriol level gives information about placenta, adrenal cortex of the fetus, , Anterior pituitary gland, Hypothalamus and also Liver.

⇒ if Estriol level is okay, it means Fetus & Placenta should be healthy.

key molecule in Feto Placental unit is "Estriol".

※ Placenta itself produces "Progesterone" onLY. ... hCGは??

Fetoplacental unit

※ ~~Placenta~~ produces 1) Progesterone 2) Estradiol (E2) 3) Estriol (E3)

※ E2, E3 っていうのは、hydroxy group の数が 2つが 3つが

☆ metabolism

- Actual Metabolic Rate
- Basic Metabolic Rate

$$= \frac{\text{consumed } O_2/h \times \text{oxygen heat equivalent}}{\text{body surface area}}$$

20 kJ/L O_2

AMR

Metabolic Rate ↑

- Thyroid Hormone (T_3, T_4)
- ambient temperature ↑
- ambient temperature ↓ (∵ shivering)
- specific dynamic effect
  - ↳ digest the food
- male (10% high)
- pregnancy
- lactation
- Hyperthermia (fever)
- Stress
- Physical exercise (increase 200-300%)
- mental activity (increase 3-4%)

Metabolic Rate ↓

- sleeping
- age
- female
- Hypothermia

Q: What is "Thermo neutral temperature" ?

⇒ 1) 27 - 28 °C if you're naked

2) room temperature with normal clothes

Q: Sumo Wrestler の方が baby よりも MR 高い理由は ? ⇒ Body surface ← ホント これ ??

Sumo : $3m^2$

BMR

- 12 h after last meal
- No stress . laying position but not sleeping
- No medication
- No physical activity
- normal body temperature
- Thermoneutral ambient temperature

Q: What is the main nutrients ⇒ 1) Carbohydrate 2) protein 3) fat

	Biological value		Calorimetry (physical value)	
1 g Glc	17 ~ 19 kJ/g	⟶	17 ~ 19 kJ/g	··· Complete oxydation

$C_6H_{12}O_6 + 6\,O_2 = 6\,CO_2 + 6\,H_2O + 2800\,kJ$

1 g Protein	17 kJ / g	⟶	21 kJ/g	··· oxidation is NOT complete

Biologically ··· large energy content of Nitrogen molecule are produced
(carbamid / urea)

Calorimeter ··· Complete oxidation 1= ₹1..
Protein → CO_2 + H_2O + NO_2

※ Human body couldn't complete oxidation so do NOT produce NO_2.

1 g fat	37 - 40 kJ / g	⟶	37 - 40 kJ / g	··· complete oxidation

※ we have to intake all of them ∵ There are essential AA and lipid

Q: In which case do you think that the metabolic rate would increase more while you are digesting carbohydrate or protein or fat? ⇒ protein (∵ it's hard to digest protein)

$$RQ = \frac{\text{produced } CO_2}{\text{consumed } O_2}$$

RQ: Respiratory Quotient

$RQ_{CHO} = 1$ ← $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O \Rightarrow \frac{6}{6} = 1$

$RQ_{protein} = 0.8$

$RQ_{lipid} = 0.7$

☆ mechanism of loosing heat / gaining heat

1) Conduction (touching window) ⇔ loose heat / gain heat (touching heating system)

2) Convection (cold outside wind) ⇔ loose heat / gain heat (go to Sahara)

3) Radiation ⇔ loose heat ··· we radiate the heat to the cold environment / gain heat ··· sun, heating system radiating the heat

4) Evapolation → ONLY loosing heat

Q: Which mechanism is good for both loosing & gaining heat when you go to Dubai in Summer? ⇒ none (at the same time)

Hot climate で loosing heat できるのは Evapolation のみ!

☆ pH regulation

Q : List the 4 main buffer system

- Plasma protein 60 - 80 g / L
- HCO_3^- 24 mmol / L
- HPO_4^{2-} 1 mmol / L
- Hemoglobin ♂ 140 - 180 g/L ♀ 120 - 160 g/L

Q : which one is the best buffer ?

⇒ Hemoglobin

Q : what makes it perfect buffer ?

⇒ 1) High concentration

2) contains a lot of "Histidine" molecule

contains "imidazole" group

→ can easily bind & release H^+

✧ Hypoventilation

↓

$CO_2 \uparrow + H_2O \rightleftarrows H^+ \uparrow + HCO_3^-$

→ Respiratory Acidosis

※ blood pH = 7.35 ~ 7.45

⇒ Respiratory Acidosis の状態と判断したら … $CO_2 \uparrow \wedge H^+$ (pH < 7.35)

✧ Hyperventilation

↓

$CO_2 \downarrow + H_2O \rightleftarrows H^+ \downarrow + HCO_3^-$

→ Respiratory Alkalosis

Q1 pH = 7.28 pCO_2 = 52 mmHg ⇒ Respiratory acidosis

(Normal value Arterial pCO_2 = 40 mmHg
Venous pCO_2 = 46 mmHg)

Q2. pH = 7.55 pCO_2 = 41 mmHg ⇒ metabolic alkalosis

Q3. pH = 7.4 pCO_2 = 45 mmHg ⇒ Normal

Q4. pH = 7.25 pCO_2 = 35 mmHg ⇒ metabolic acidosis

Q5. pH = 7.52 pCO_2 = 25 mmHg ⇒ Respiratory alkalosis

HCO_3^- が main (24 ± 2 mmol/L)

☆ Base Excess ⇒ ± 2 mmol / L

… amount of base in your body (it can be positive or & negative)

… acidosis や alkalosis になった時に、compensation として pH を 7.0 に戻すのに必要な base の量

- Chronic metabolic acidosis (compensated) ⇒ Negative

∵ HCO_3^- がバシバシ H^+ と合体しちゃうから

- Chronic metabolic alkalosis (compensated) ⇒ Positive

∵ H_2CO_3 が足りない分の H^+ を放出！

その時に 同量の HCO_3^- も放出される.

- Acute metabolic acidosis
- Acute metabolic alkalosis

} Base Excess is Normal

BE = ± 2 mmol/L の範囲内

Q : BE = + 4 mmol/L , pH = 7.44 , pCO_2 = 44 mmHg ⇒ chronic metabolic alkalosis

Q : BE = + 1 mmol/L , pH = 7.49 , pCO_2 = 42 mmHg ⇒ acute metabolic alkalosis

(∵ pH is NOT compensated yet)

Q : which organ is very important for pH regulation ? ⇒ 1) kidney
2) Lung

Q : when there is acidosis, How is urine pH ? ⇒ should be acidic to get rid of H^+

※ more H^+ is excreted but more HCO_3^- is reabsorbed

Q : if there is a patient w/ untreated diabetes mellitus & metabolic acidosis
What kind of compensation occur ?

⇒ 1) kidney would excrete more H^+
2) Kussmaul Breathing (increasing minute ventilation)

if metabolic alkalosis ⇒ 2) lower minute ventilation (Cheyne-Stokes Breathing)

2015 mid-term Oct 31 Tue

1. HR = ?

A. fever ⇒ HR↑

B. Threshold potential becomes less Negative ⇒ HR↓
= positive

C. Vagus n are cut bilaterally ⇒ HR↑

D. inhalation in rest ⇒ HR↑

E. max. diastolic potential becomes more positive. ⇒ HR↑

2. Calculation of Lymphocyte (WBC counting)

4 leukocytes (given) × 5 × 5 (large square) × 10 (dilution) × 10 (height) × 0.25 (% of lymphocyte given) = 2500 /μl

large square : 1/5 × 1/5
small 〃 : 1/20 × 1/20

計算間違いポント有をつける…

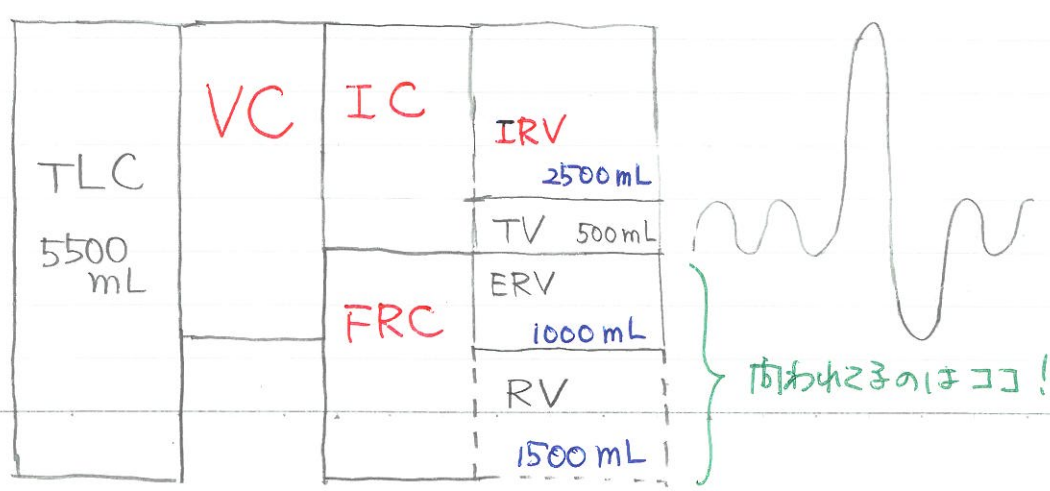
3. RBC a istonic ? Hypo ? Hyper ? isotonic solution = 0.9% NaCl
= 3.8% Na-citrate

☆ Acetic Acid treatment (1%) ⇒ for Hemolyse only RBC → Türk's solution に含まれる.

cf. Leukocyte counting で Nucleus を染めるのは, Gentian Violet

4. When the Respiratory muscles are completely relaxed, the volume of air in the lungs is …

⇒ RV + ERV
= FRC
= TLC − IC



Date

5. ○ The total cross sectional area along the circulatory system is the largest at the capillaries

○ The blood Pressure in the superior vena Cava is affected by the respiration

○ The velocity of the blood flow along the circulatory system is the largest at the Artery , slowest at the Capillary

○ Arterioles are resistance vessels ∵ a lot of smooth m. ⇒ good BP regulation !!

veins are capacitance vessels

○ sympathetic innervation has an effect on all vessels except capillaries !

6. Blood Cell Counting について

A : RBC counting , diluted by a factor of 100

B : Drabkin reagent 使うのは、 determination of Hb .

C : Reticulocytes do NOT have a nucleus !!

Reticulocyte can be stained by brilliant cresyl blue solution !

D : Türk's solution stains the nucleus of WBC . ← 1% acetic acid break RBC gentian violet が核染める.

E : Bürker's chamber is NOT needed for differential leukocyte count.

7. ○ : Hypocaphia is caused by Hyperventilation

○ : Vital Capacity is always higher than FEV

※ FEV1 と言えば、最初の1秒でどれだけ息を口に出せるか!? の値.

○ : VC = IRV + TV + ERV

○ : Lab で belt を使ったのは、 Restrictive Pulmonary disease ⇒ FVC ↓

例：

セロテープ

Obstructive pulmonary disease ⇒ FEV1/FVC ↓

例 : Asthma , COPD

⇒ airway resistance ↑ (FEV_1 ↓) , RV ↑

70%未満

○ TLC = IC + FRC

= VC + RV

8. The acute effect of Angiotensin II （BP↑方向に考えれば良い）
   - increased Aldosteron synthesis & secretion
   - thirst
   - decreased Na^+ excretion of the kidney （= reabsorption↑ってイミ）
   - vasoconstriction in the Arterioles （Arteriole は resistance vessel ！）
     ↳ BP上げ下げする時は arteriole に働きかけるのが一番早い.
   - increased Na^+ reabsorption

9. Correct temporal sequence of the events of the cardiac cycle
   ① closure of AV valve （1st Heart Sound）
   ② isovolumetric contraction
   ③ opening of the semilunar valve
   ④ ejection
   ⑤ closure of the Semilunar valve （2nd Heart Sound）
   ⑥ isovolumetric relaxation
   ⑦ opening of AV valve
   ⑧ ventricular filling

10. FEV_1 = ?　frequency : 14/min , TV = 0.5L , FVC = 6L
    Tiffeneau index = 70%
    FEV_1 = FVC × Tiffeneau index　　FEV_1 = 6L × 0.7 = 4.2L

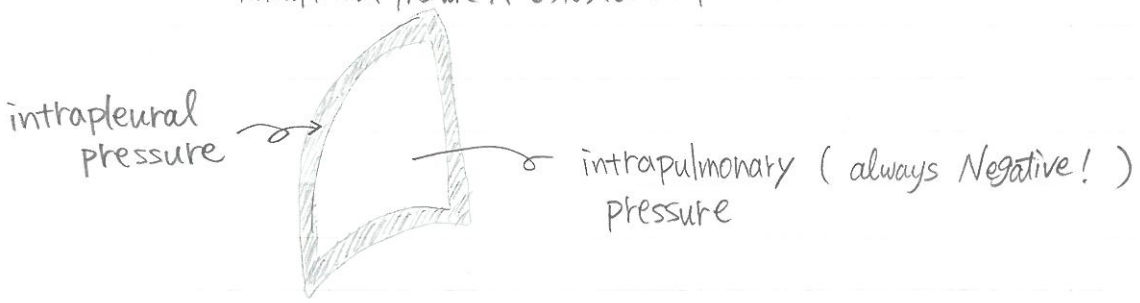
11. ○ Secretin stimulates bicarbonate secretion of the Pancreas
    ○ Gastrin stimulates gastric acid secretion
    ○ Motilin stimulates emptying of the stomach

※ CCK stimulates Pancreatic juice (HCO_3^-, enzymes) secretion
CCK stimulates Contraction of gallbladder
CCK inhibits Oddi's sphincter muscle. （⇒ CCK は oddi sphincter の relaxation に働く）
7 functions !!

12. ○ Müller maneuver is performed by forceful attempted inhalation against the closed glottis

○ during forced inspiratory state, the intrapleural pressure becomes more Negative (intrapulmonary も！同じ.)

↳ コレは、inspirationの時に intrapleural pressure が どうなってるかってコト.



※ inspiration … alveolar pressure が negative になることで 起こる. そ正しいけど

(rib が水平に)

↳ ① contraction of external intercostal m. & diaphragm (∵ diaphram下へ)
② Thoracic cavity ↑ (注) 肺に変化なし)
③ intrapleural pressure ↓ (∵ thoracic cavity だけ 拡がったから space 大)
④ 肺が受動的に拡張 (∵ 周りから肺を押す力 が 減ったから 拡がれるようになた)
= intrapleural Pressure
⑤ 肺に空気が入る！

∴ inspiration 時、intrapleural pressure ↓ で ok.

✦ ○ Müller maneuver leads to Pulmonary Stasis 肺うっ血

cf. Müller maneuver leads to HR ↑ (∵ inspiration 時. intrapleural pressure ↓ すると Periphery から blood が 戻ってきやすくなる為 Venous Return ↑ ⇒ CO ↑ ⇒ HR ↑ (∵ CO = SV × HR)

stop, accumulation

※ Pulmonary Stasis とは、Pulmonary circulation ↑ を イミする.

∴ Müller maneuver = inspiration = intrapleural pressure ↓ ⇒ Venous Return ↑

⇓

Pulmonary circulation ↑ ⇐ CO of Right Ventricle ↑

Pulmonary circulation に 血が 貯まる 状態

13. Renal function 正常値

Filtration Fraction = 0.2 (20%)

Free water Clearance = ⊕だったら dilution ⊖だったら Concentration 起きる

Urine Flow Rate = 1 mL/min

GFR = 120 mL/min. = C_{inulin}

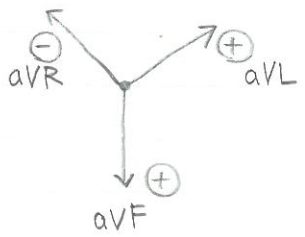
RPF = 660 mL/min ≈ C_{PAH} = 600 mL/min ∵ E_{PAH} = 0.9

Endogenous Creatinine Clearance = 1.17 × GFR

RBF = 1250 mL/min (1/4 of CO) 140mL/min

E_{PAH} = 0.9 の意味は
1 入ったら 0.9 排泄されるってコト
(1 入ったら 0.1 は再吸収される)
⇒ ホントは 1 入ったら 1 排泄される
イヌリンのクリアランスが best for GFR

14. The T wave of the Physiological ECG is Negative in the aVR, V_1, V_2



15. Rate of Ventricular contraction を isolated heart において下げるのはどれか？ つまり HR 下げるってコト. ⇒ Ach

※ Atropine ⊣ muscarinic Ach Receptor ∴ Atropine ⇒ HR↑
α_1 agonist ⇒ vasoconstraction
β_1 〃 ⇒ positive Heart Effect ∴ β_1 agonist ⇒ HR↑
epinephrine ⇒ bind to β_1 Receptor ∴ epinephrine ⇒ HR↑

呼吸性 不整脈

16. ○ Respiratory Arrhythmia is Physiologic.
⇒ inspiration 時に HR↑, expiration 時に HR↓ 現象のコト ⇒ 正常

○ Due to the Vascular elasticity, the Blood flow is continuous in the Veins!

○ The propagation velocity of the pulse wave is 4 - 16 m/s

Date

17. Effects of thermal stimulations on frog's heart
A: Cooling of the ventricle ⇒ contractility ↓ (HR doesn't change)
B: Warming of the sinus venosus ⇒ HR↑ (contractility doesn't change)

18. ○ ADH regulates mainly the expression of aquaporin-2 channel.

○ more than 50% (= 67%) of the water absorption takes place in the proximal convoluted tubule (Na^+ K^+)

○ water reabsorption takes place in the proximal convoluted tubule also in case of ADH deficiency !! (∵ ADH がなくても Aquaporin-1 があるから)
↳ AQP 2

○ more than 50% of Ca^{2+} reabsorption takes place in the Proximal Convoluted Tubules

19. Strong electric stimulation of the sciatic nerve in the cat will lead to BP↑ HR↑ TPR↑ by Loven reflex.

※ Heart effect は... 起こらない!! (∵ sciatic n. は Heart に innervate しない!)
⇒ もし、innervate してるなら、stimulate すれば Positive Heart Effect 起こるが...

20. Breakdown of erythrocytes in the body e.g. albumin
○ yields bilirubin which is carried by Plasma protein (60-80g/L) to the liver

○ takes place in the reticulo-endothelial system

○ yields iron release, most of which is retained for further use.

○ is NOT required for the synthesis of bile salts

21. In case of acute increase of the **Airway Resistance** :

↳ diameter of airway が影響 !!

○ FEV_1 decreases

※ Airway Resistance と Blood Vessel Resistance と同じように考えれば…

$R = \frac{l}{r^4}$ ($R = \frac{8\eta l}{\pi r^4}$ … poiseuille equation)

Resistance ↑ ⇒ r ↓ ⇒ Similar To COPD asthma ⇒ FEV_1 ↓

Obstructive Pulmonary disease (セロテープの吹く)

☆ Airway Resistance ↑ = φ ↓ = asthma (OPD) ⇒ FEV_1 ↓ (RV↑)

cf. セロテープ Lab = Obstructive Pulmonary disease ⇒ Airway Resistance ↑ , FEV_1 ↓

cf. belt lab = Restrictive Pulmonary disease ⇒ FVC ↓

22. At which air volume in the lungs can we exert the max. voluntary expiratory positive pressure ?

↳ Valsalva maneuver

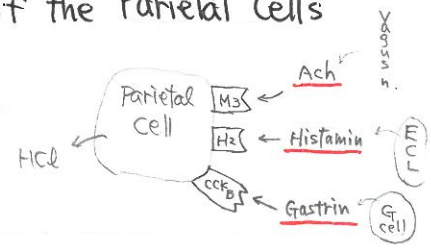
(intrapleural pressure = positive !)

なぜか TLC

23. Direct stimulatory action on the acid secretion of the Parietal Cells

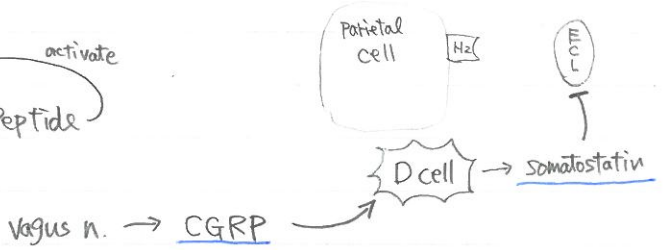
☆ Parietal Cell からの HCl 分泌を促進する奴ら

① Gastrin from G Cell
② Ach from Vagus n.
③ Histamin from H Cell (ECL) … Entero Chromaffin Like Cell 古い呼称。



☆ Parietal Cell からの HCl 分泌を inhibit する factor

① GIP
② Somatostatin from D cell ← activate
③ CGRP → Calcitonin Gene Related Peptide
④ Secretin
⑤ CCK



24. What results in development of edema ? ⇒ filtration ↑

① Hydrostatic Pressure of capillary (outward) ↑ = Venous Pressure ↑
② Colloid osmotic Pressure of plasma (inward) ↓
③ Hydrostatic Pressure of interstitium (inward) ↓
④ Colloid osmotic Pressure of interstitium (outward) ↑

w 1

Date Jan 29 mon

mid term test

20th Apr

30 Q . 45 min

15 Q Lab

15 Q theory

2nd semester material ONLY !!

week 1 ~ 10

* Last year, a lot of Questions from week 1, 2 !!

19 points = 1 bonus !

Final test

80 Q . 110 min

40 Q 1st sem.

40 Q 2nd semester

半分は 1st Semester から出るって！

> 43 ⇒ 2

> 66 ⇒ 5

2nd Semester material

① endocrinology … 2 weeks
- adrenal cortex
- endocrine pancreas

② skeletal / smooth muscle … 2 weeks

③ Neurophysiology … 10 weeks

endochinology

※ adrenal cortex is very important !
without adrenal cortex, we can survive only for 1 week.

Date

adrenal cortex

☆ No innervation !!

※ innervation があるのは adrenal medulla の方 !
↑
sympathetic

☆ 3 layers !

1. glomerular zone (outer layer)
2. fasciculate zone (middle layer)
3. reticular zone (inner layer)

※ CRH increase the ACTH production in Anterior Pituitary gland

General info

CRH → ACTH → glucocorticoid axis

@ Hypothalamus → CRH
↓ portal vessel
@ Anterior Pituitary gland → ACTH

ADH ⊕
Catecholamin ⊕
stress (indirectly) ⊕

ACTH ⊕ → @ adrenal cortex
ACTH ⊕ → mineralocorticoid - aldosterone
ACTH ⊕ → glucocorticoid - cortisol (mainly !)
ACTH ⊕ → sexual steroid - androgen

※ ACTH mainly regulate "glucocorticoid" !

1. glomerular zone —produce→ mineralocorticoid - aldosterone

Function ① Na^+ reabsorption in Collecting duct, in salivary gland, in sweat gland

② K^+, H^+ secretion

mineralocorticoid - aldosterone

ACTH ⊕ → mineralocorticoid - aldosterone
Angiotensin II ⊕ → mineralocorticoid - aldosterone
$[K^+]\uparrow$ ⊕ → mineralocorticoid - aldosterone
Hyperkalemia *

Most important Hormone to regulate the aldosterone !

* Hyperkalemia can stop the Heart in diastole. ⇒ Aldosterone can get rid of K^+. (aldosterone secrete K^+ to the urine)

☆ Hyperaldosteronism (Conn Syndrome)

- BP ↑ (∵ Na^+ reabsorption is followed by water reabsorption sooner or later) retension
- plasma K^+ ↓ (Hypokalemia)
- pH ↑ (metabolic alkalosis) ⇒ free Ca^{2+} ↓

☆ "18 - aldehyde oxygenase" can be found ONLY in glomerular zone.
which is needed for aldosterone production

※ if too much "18 - aldehyde oxygenase" ⇒ conn syndrome

※ 18 - aldehyde oxygenase が glomerular zone にしかないため、aldosterone はその zone でしか作られない !!

CRH → ACTH → glucocorticoid (stress axis と呼ぶ)

Date

2nd layer of adrenal cortex

2. fasciculate zone —produce→ glucocorticoid … stress hormone

- cortisol in human (cortisol)
- (in rodent : corticosteron)

☆ Function of glucocorticoid

① Blood glucose level ↑

- gluconeogenesis ↑ (formation of Glc)
- glucose uptake by the cell ↓
- glycogenesis in Liver ↑ (formation of glycogen) ← it's kinda strange …

Q: How can increase the Glc level if increase the glycogenesis?

A: At the end of the day, despite the increasing the glycogenesis. Blood Glc level increase because "gluconeogenesis ↑" & "glucose uptake ↓" will increase more than "glycogenesis ↑".
⇒ Sum at the end. increase the Blood Glc level.

why do we need storage of glycogen?

Q: Why do you think that nature forms that glycogenesis increase in stress situation?

A: In stress, we need Glc to fight. Because "stress axis" (CRH → ACTH → glucocorticoid axis) is about the "Long Term Stress". For example, exam period, 2 months long stress.
That's why glucocorticoid (cortisol) stores the glycogen & you can use this glycogen as a Glucose storage. That's why glycogenesis ↑.
During the War, you can't eat that much so you need to store your Glc in your Liver as glycogen & when you need it (when acute stress situation ← when you need fight or flight) you can mobilize this Glc from your glycogen.

Q: Which hormone can mobilize the Glc from glycogen in the Liver?
because as you can see glucocorticoid (cortisol) store it.
What is the acute stress situation? Your HR ↑, BP ↑ Which is the Hormone here? or neurotransmitter released in acute stress situation?

A: Epinephrine! Norepinephrine!

② Catabolic effect

Q: What does "catabolic effect" say?

A: Breakdown complicated compound to simple compounds

→ Proteolysis (breakdown protein)
→ muscle mass ↓

so, Stress is NOT good for your muscle!

∴ Body builder はケンカしちゃダメ! (∵ stress!) → glucocorticoid (cortisol) Level ↑
→ Proteolysis ↑ … このボディビルダーはストレスのせいで筋肉が付かないコトに気づき、catabolic effect のせいで破局しましたとさ

Date

glucocorticoid (cortisol) function 続き

③ surfactant production ↑

※ Respiratory system の所で、できた！
Vagus n. can increase the surfactant production by Type II pneumocyte & also glucocorticoid (cortisol) increase the surfactant production.

④ lipolysis ↑ (mainly) in limbs (breakdown of Lipids)
↳ central shift of adipose tissue

※ abdomen can be fat belly those patient who has the high glucocorticoid but exttemity is very very skinny.

つまり、Neck , head , trunk には fat あるけど、Limbs には fat 無し！

kinda side effect! ⑤ Bone weight ↓ (→ osteoporosis) ← breakdown of the Bones
→ So mineral contents of Bone will be less.

∴ glucocorticoid (cortisol) は breakdown of protein , Lipid , Bone を引き起こす！

⑥ Supress the immune system
→ anti - inflammatory effect
→ anti - allergic effect

※ if sb has very serious allergy rxn, You can give glucocorticoid to her / him to supress the allergy.

但し、拒絶反応を防ぐためとは言え、cortisolの長期副用は side effect 有り.
⇒ atrophy of adrenal cortex ⇒ ACTH ↓

つまり、cortisol 投与を止める際、急にゼロにしちゃうと ACTH ↓ の影響で ⇒ BP ↓ , BS ↓ になっちゃう.

∴ cortisol を止める時は 徐々に ゆっくり 止めるコト！
(※ 副腎 adrenal cortex の機能復活！)

※ if patient got other kidney , the patient's immune system would reject new kidney would attack the new kidney because the patient's immune system can NOT recognize the new kidney . That's why You need to give some glucocorticoid (cortisol) to inhibit the immune system & that's why there are a lot of side effects if you give glucocorticoid therapy
⇒ diabetes mellitus , Osteoporosis , cataract

34m 女の子

→ WBC count ↓ (∵ glucocorticoid inhibit Lymphocyte proliferation)

⑦ side effect in CNS → sleepy

※ glucocorticoid (cortisol) Level が高いと眠くなる！

★ High dose of glucocorticoid ⇒ mineralocorticoid effect ← aldosterone の効果と同じ効果が現れる！
- BP ↑
- K^+ ↓ ⇒ hypokalemia
- H^+ ↓ ⇒ alkalosis

if these 3 enzymes are NOT working, all the Hormones would be androgens
⇒ virilism / androgenital syndrome

Date

Q: 必要な molecule と enzyme は？

☆ glucocorticoid production

first molecule is ... **Cholesterol** - そして、steroid hormone synthesis には Vitamin C が必要！

+ 必要な enzyme は 3つ！

① 21 β hydroxylase → if deficiency ⇒ salt loosing androgenital syndrome
② 17 α 〃 ... can be found ONLY in fasciculate Zone & reticular zone
③ 11 β 〃 Not in glomerular Zone !!
↳ if deficiency ⇒ non salt loosing androgenital syndrome

cf. ココにあるのは 18-aldehydrogenase which is needed for aldosterone production

☆ 2 diseases about glucocorticoid (cortisol)

① Cushing Syndrome ... glucocorticoid level is too High !!

4 Reasons

1) CRH ↑ → ACTH ↑ → glucocorticoid ↑
@Hypothalamus (CRH producing tumor)

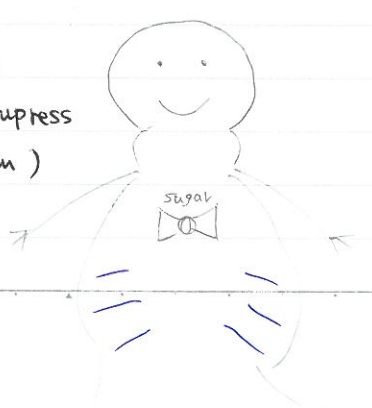
2) ACTH ↑ → glucocorticoid ↑
· Problem of anterior pituitary gland / Lung Cancer can produce ACTH
(ACTH producing tumor)

Primary Cushing →

3) glucocorticoid ↑
glucocorticoid Producing Tumor in adrenal cortex @ fasciculate zone

4) iatrogenic Cushing ... too much glucocorticoid therapy
(autoimmune disease の1つ)
※ Kristof の友達で昔 Rheumatoid arthritis の子がいた。彼女は痛みを control する為に大量の glucocorticoid を処方されてた為、卒業する頃には Cushing Syndrome になっていた。

Cushing patient look like



- infection 起こしやすい (∵ glucocorticoid supress the immune system)
- moon face
- obese neck (buffalo hump) — adipose tissue in neck
- obese thunk
- skinny extremity
- blood Glc level → Diabetes mellitus — side effect of Cushing Syndrome
- Strias (∵ catabolic effect) → parmanent
- Blood Pressure ↑
(∵ glucocorticoid has mineralocorticoid effect)

Date

※

② addison disease (Bronze disease) … glucocorticoid level is too Low

→ BP ↓

→ BS ↓ (Hypoglycemia) → low blood Glc level

ACTH ↑
↓
glucocorticoid ⊖ ↓

※ ACTH should increase glucocorticoid level.
glucocorticoid has negative feedback on the ACTH
⇒ If glucocorticoid level is low, ACTH level would be high.
(∵ negative feedback doesn't work)

☆ POMC (Pro-opio melanocortin) → ACTH is produced from POMC gene

can produce ↙ ↓ ↓ ↘

ACTH　MSH　β-LPH　β-endorphin

MSH: Melanocyte Stimulating Hormone

β-endorphin → makes us feels good → Positive reinforcing effect (reward)

⇓

※ addison disease (Broze disease) 患者の肌が darker なのは、glucocorticoid level が低下したことで POMC gene の転写が促進され、MSH ↑ ⇒ Melanin in skin ↑ による！
(ACTH ↑ と MSH ↑ は同時に起こる！)

⇒ There are 2 Types of addison disease, "white addison" & "Brown addison"

3 Reasons

1) CRH ↓ → ACTH ↓ → glucocorticoid ↓ ⇒ "white addison"
∵ ACTH ↓ ってことは MSH also low!

2) ACTH ↓ → glucocorticoid ↓ ⇒ "white addison"

Primary addison →

3) adrenal cortex failure → glucocorticoid ↓
adrenal cortex can NOT produce glucocorticoid. ⇓ ∵ No Negative feedback
ACTH ↑, MSH ↑ ⇒ "Brown addison"

Q: How can you Tell whether "Brown addison" or "Tanning" in Hawaii?

A: mouth の中や palm, sole など日焼けしない下コが Brown だったら、"Brown addison"

※ addison disease では ACTH は高いのも低いのもあり得る!!

Date

3. reticular zone —Produce→ androgen hormone
(sexual steroids)

disease

virilism / androgenital syndrome (男性化) → ♀: hair production in face ↑, muscle ↑, deeper voice
→ ♂: 同上 but Not obvious

Q1: Where is the CRH produced ? ⇒ Hypothalamus

Q2: How would the CRH get to the Anterior Pituitary gland ? ⇒ portal circulation

✧ Q3: What does CRH stand for ? ⇒ Corticottopin Releasing Hormone.

✧ Q4: What does ACTH stand for ? ⇒ AdrenoCorticoTropic Hormone

✧ Q5: What is ACTH regulated by ? ⇒ ⊕ 1) ADH 2) catecholamin 3) Sttess (indirectly)

Q6: what is the most important hormone to regulate the "aldosterone" ? ⇒ Angiotensin II

Date

True or False Q

Q1: glucocorticoid increase glycogenolysis ? ⇒ False, increase glycogenesis

Q2: glucocorticoid is anabolic ? ⇒ False, catabolic

Q3: Crucial vitamin of steroid hormone production is ? ⇒ vitamin C

Q4. we produce steroid hormone ONLY from cholesterol diet ? ⇒ False. Liver produce cholesterol
source of cholesterol

Q5. How would the glucocorticoid change the WBC count ? ⇒ decrease

Q6. How can they (glucocorticoid) change the Ca^{2+} content of the bone ? ⇒ ↓
the muscle mass ? ⇒ ↓
the adipose tissue in limb ? ⇒ ↓
the BP ? ⇒ ↑

Q7. what kind of situation / mechanism can increase CRH production ? ⇒ any kind of stress
Hypovolemia, Hypoglycemia, Physical stress (malathon), psychological stress (exam)

※ Normally Glc is the only source for brain. (in case long lasting starvation, keton body can be used though)

Q8. what increase ACTH production ? ⇒ 1) ADH 2) catecholamine 3) stress

Q9. 4 reasons for Cushing disease ? ⇒ 1) CRH ↑ 2) ACTH ↑ 3) glucocorticoid ↑ 4) iatrogenic Cushing

Q10. 3 Reasons for androgenital syndrome ? (virilism) ⇒ 1) androgen ↑ 2) 21β, 11β hydroxylase deficiency 3) androgen producing tumor (@ reticular zone of adrenal cortex)

Q11. 3 Reasons for addison's disease ? ⇒ 1) CRH ↓ 2) ACTH ↓ 3) adrenal cortex failure

Q12. BP ↑ in conn syndrome ? or Cushing ? or addison ? ⇒ conn syndrome & Cushing syndrome

Q13. Hypoglycemia in conn ? cushing ? or addison ? ⇒ addison syndrome

Q14. POMC products ? ⇒ 1) ACTH 2) MSH 3) β-LPH 4) β-endorphin

Parasympathetic activation of the Heart (= おけき)
Receptor は ... Muscarinic Ach R !!

W2

Date Feb 5 mon

adrenal medulla

∵ adrenal medulla is modified sympathetic ganglion

↑

innervated by sympathetic preganglionic fiber

(in case of the autonomic nervous system, preganglionic neurons are located in CNS and they can reach the ggl & in the ggl, postganglionic neurons are sitting & they are innervated by here)

↳ cholinergic fiber — NT - Ach

innervates

Nicotinic - Ach R in adrenal medulla
(also in sympathetic / parasympathetic ganglion)

preganglionic fiber can increase catecholamin production !

chromaffin cells
- produce catecholamin
  - Adr (main !)
  - NA
  - dopamin

catecolamin degradation → we need 3 enzyme

① MAO A — MonoAmino Oxydase
② MAO B
③ COMT — Catecholamine Ortho-Methyl Transferase

※センメルヴァイス uni のエラい先生が 右の3つの enzyme が responsible for aging と言って MAO A inhibitor を推奨している

Pheochromocytoma ... adrenalin producing Tumor (benigh tumor)

↳ BP ↑ , cardiac output ↑ , TPR ↑
↳ BS ↑
↳ Airway Resistance ↓ ∵ β_2 Receptor in bronchi / bronchioli ⇒ bronchodilation
↳ tachycardia (HR ↑)

★ Alarm reaction - acute stress reaction

Cannon ... fight or flight reaction
(the guy who describe it first)

Adrenalin ↓

↳ BS ↑ ← glycogenolysis in Liver ↑ @ β_2 Receptor (break down of glycogen)
↳ HR ↑
↳ Metabolic ↑
↳ BP ↑
↳ Free fatty acid ↑ ← β_3 Receptor (= より) lipolysis ↑ ∵ adrenalin can mobilize FA from fat tissue via β_3 Receptor
(Free FA can be used by skeletal m.)
↳ Respiration rate ↑
minute ventilation ↑
↳ Airway resistance ↓ ∵ β_2 Receptor in bronchi ⇒ bronchodilation
↳ Coronary circulation ↑ ∵ coronary dilation by β_2 R
↳ digestive motility ↓
↳ GI sphincter constriction ↑ urogenital sphincter constriction ↑

余った blood は 筋肉へ!!

These vessels contain mainly α_1 Receptor !

↳ Blood flow in, GI ↓
urogenital system ↓
skin ↓
} vasoconstriction via α_1 Receptor

↳ Blood flow in skeletal m ↑ ... vasodilation via β_2 Receptor

☆ endocrine Pancreas

Langerhans islet cells

α cell (produce) → glucagon
β cell → insulin
δ cell → somatostatin

Normal Glc (blood) ... 4 - 5.5 mmol/L ... fasting Glc (before meal)

5.6 - 6.9 mmol/L ... IFG (impaired fasting Glc) before meal

7 mmol/L ... diabetes mellitus (before meal)

Blood Glc Level ↑
by which hormone ?
- glucagon
- epinephrine
- NE
- glucocorticoid
- T_3, T_4 (indirectly) ∵ Glc uptake from small intestine (diet) — Thyroid Hormone increase
- GH
- somatostatin (indirectly) ∵ Insulin ↓ ⇒ BS ↑

Blood Glc level ↓
- insulin のみ

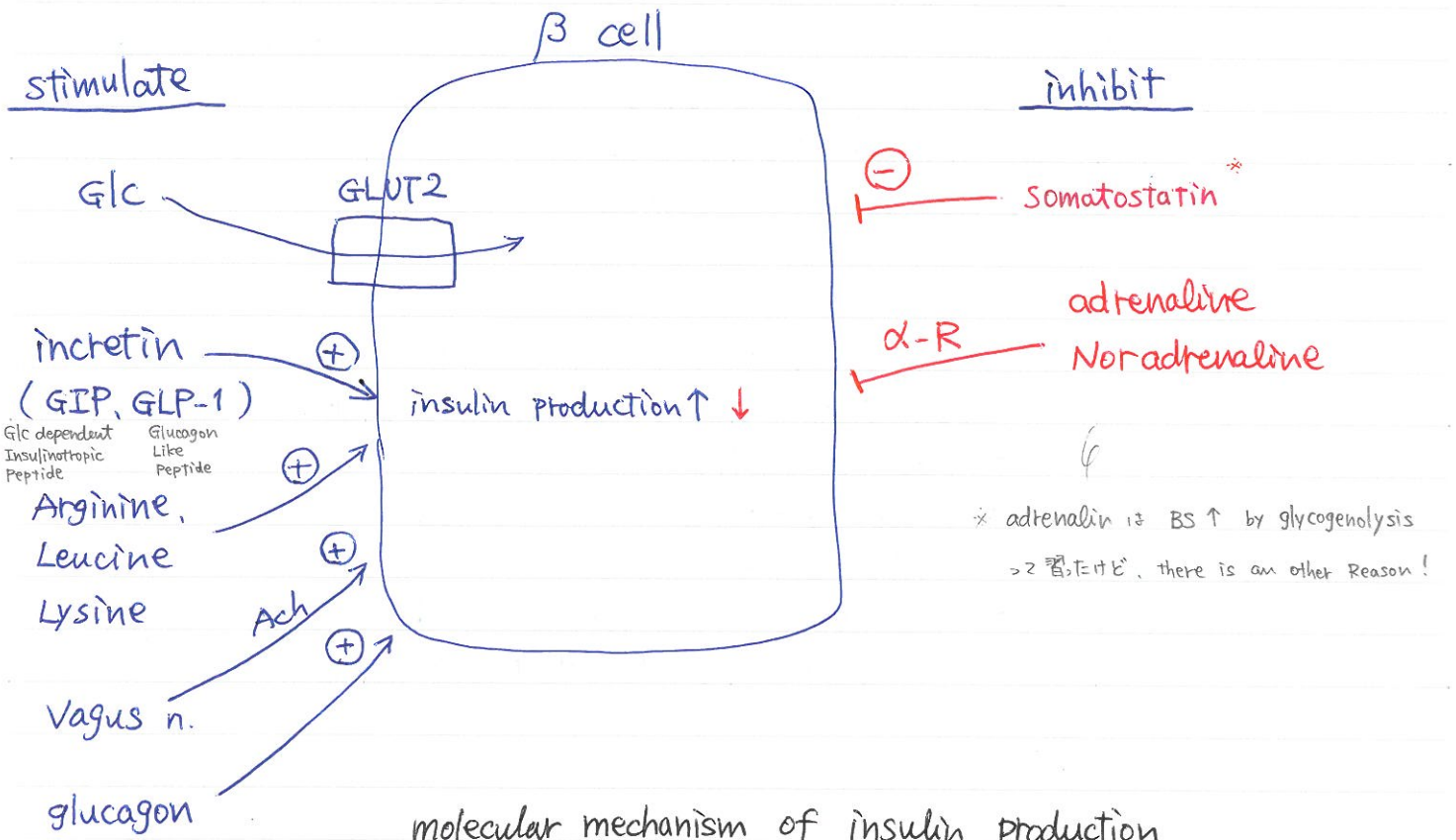
Let's focus on insulin !

Date

- membrane receptor (Tyr kinase)
- water soluble
- peptide hormone

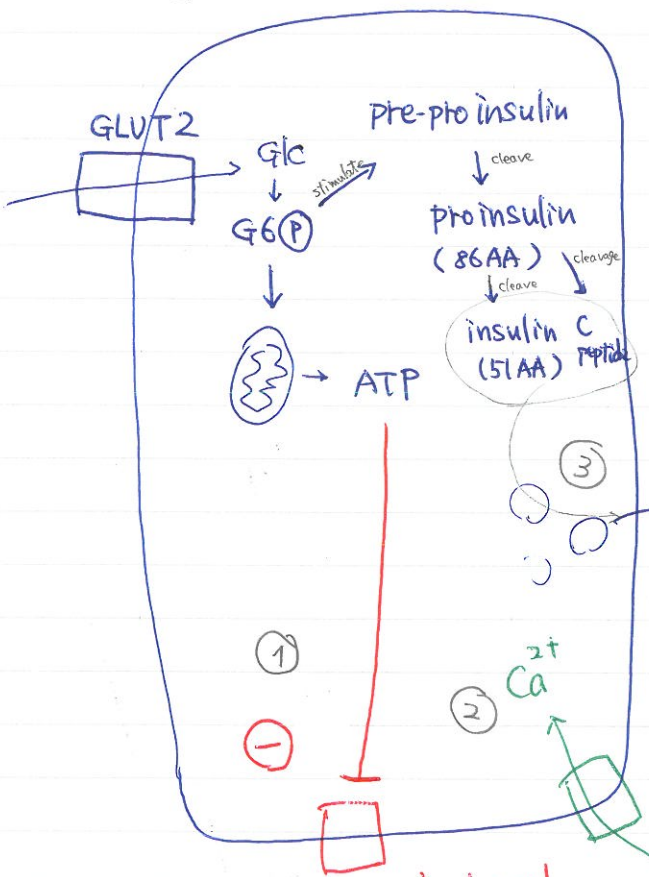
insulin ... -51 AA , produced by β cell

※ "somatostatin" is always inhibitory !



※ adrenalin は BS ↑ by glycogenolysis
>2 習ったけど, there is an other Reason !

molecular mechanism of insulin production



C peptide ... weak insulin like effect

cf. Protein C inactivate Va & VIIIa
(Don't mix !)

※ insulin が vesicle の中 に入っている !

- insuline is released !!
- C peptide も !

↳ if close ⇒ more positive ⇒ depolarization !!

4 insulin というホルモン. Anabolic !

Date

3 main organs エネルギー蓄える系の方向！

functions of insulin

1) Liver ... - gluconeogenesis ↓ (formation of new Glc ↓)
- glycogenesis ↑ (glycogen synthesis ↑) → ※ also by Glucocorticoid
- glycogenolysis ↓ (glycogen breakdown ↓)
- glucose release from Liver ↓
- Fatty acid production from Glc ↑

2) Skeletal m. ... - glucose uptake ↑ via GLUT4
- glycogenesis ↑ (formation of glycogen from Glc ↑)
- AA uptake ↑ to the skeletal m.
- protein synthesis ↑ = Anabolic function
- Proteolysis ↓
- AA release from skeletal m. ↓
- K^+ uptake ↑ to the skeletal m. cells = insulin stores K^+ in skeletal muscle cell

Q: The patient has 31 mmol/L BS level, what will you give to him?

A: insulin shot ⇒ You will kill him! why ?? Because, if you give only insulin, insulin increase K^+ uptake in skeletal m ⇒ so extracellular space K^+ level is extremely low ⇒ Hypokalemia may cause "Arrhythmia". (cf. Hyperkalemia may stop the heart in diastole)

So. Correct answer is that you need to give "infusion" (water + insulin + $\underline{K^+}$)

Q: The patient's Blood K^+ level is 7.5 mmol/L, what would you give ? (Normal $[K^+]$ = 4-5 mM)

A: Just insulin ⇒ You will kill him ! why ?? insulin decrease BS level ⇒ hypoglycemic coma

So. You need to give infusion (water + insulin + $\underline{Glc}$)

Q: The patient has diabetes mellitus. Dr. inject 20 UI insuline and her BS in the morning is High. What can be the reason ?

A: 1) Probably the amount of insulin is too less.

2) probably the amount of insulin is too much ⇒ during the night, there was very low BS level. ⇒ anti-insulin hormone such as glucagon, adrenalin, GH will increase ⇒ BS ↑

Q: How can you tell (1) or (2) ?

A: You need to measure the BS level during the night.

if there was high BS level during whole night ⇒ (1)

Date

3. Adipose tissue ··· - Glc uptake ↑ via GLUT4
- FA production ↑ from Glc
- lipolysis ↓
- lipid synthesis ↑ → lipid storage ↑
- lipoprotein lipase activity ↑
(VLDL / chyromicron release lipid & stored in adipose tissue)
- hormone sensitive lipase activity ↓
(∵ insulin stores lipid ⇒ it doesn't mobilize the storage)

2) adipose tissue に Lipid が蓄えられる →
1) VLDL等から Lipid を取り出す →
3) Lipid の mobilize が抑えられ、adipose tissue に無事 Lipid が蓄えられる。 →

function

① GLUT 1 ··· @ RBC - Glc uptake
✧ in the CSF, Glc c.c. is lower than blood plasma ∵ Glc is used by neuron
@ Blood Brain Barrier - Glc uptake through BBB

② GLUT 2 ··· @ β cell of Pancreas - regulation of insulin production & release
Low affinity / High capacity
a Blood Glc level should be higher than normal
a a lot of Glc molecules can be uptaken by GLUT2
@ Liver - Glc uptake & release
@ kidney - Glc reabsorption @ vasolateral membrane
@ small intestine - Glc absorption @ vasolateral membrane

③ GLUT 3 ··· @ neuron

④ GLUT 4 ··· @ skeletal m.
@ adipose tissue
} Just GLUT4 is insulin dependent
✧ w/o insulin, GLUT4 is NOT active at all !

⑤ GLUT 5 ··· @ small intestine - Fructose uptake

next week glucagon

6

Q15. You eat sth. when you're in absorptive phase, which hormone is the most important ? ⇒ insulin

Q16. How about post absorptive phase ? ⇒ glucagon
(already digested, No absorption in small intestine)

endogenous vs exogenous insulin

☆ for some reason, you hate kristof, you give him insulin shot ⇒ He would have hypoglycemic coma

Q: How doctor figure this case is crime or he had insulin producing tumor ?

A: if you give him insulin shot, his BS level is low & his C peptide level is low despite of high insulin level ! ∵ 1 insulin - 1 C peptide (equimolar 等モル)
same amount of insulin & C peptide are released

So if you want to kill him, you should give him C peptide as well ! ☺

Tell me insulin stimulate or inhibit following chemical mechanism

Q1 : Lipolysis インスリンの効果でどうなるの ? ⇒ inhibited by insulin ↓
(∵ insulinは血中Glcを下げる方向に働く!)

Q2 : gluconeogenesis ⇒ inhibited ↓

Q3 : glycogenesis ⇒ stimulated ↑

Q4. glycogenolysis ⇒ ↓

Q5. extracellular K^+ level ∵ insulin ⇒ K^+ uptake↑ to the skeletal m. ⇒ ↓
⇒ つまりは細胞外のK^+(血中のK^+)は下がる

Q6. insulin is catabolic or anabolic ? ⇒ anabolic

Q7. proteolysis ⇒ ↓

Q8. is it true insulin release glc to the blood stream ? ⇒ No 逆!

Q9. is it true that free fatty acid level↑ in the blood stream ? ⇒ No!
(∵ insulin inhibit lipolysis !)

✧ Q10. Tell me 2 enzymes which are affected by insulin & How ? ⇒ 1) Lipoprotein lipase … stimulated
2) hormone sensitive lipase … inhibited

insulin + α

✧ Q11. Tell me more anabolic hormones ⇒ 1) GH 2) testosterone Thyroid Hormoneは?

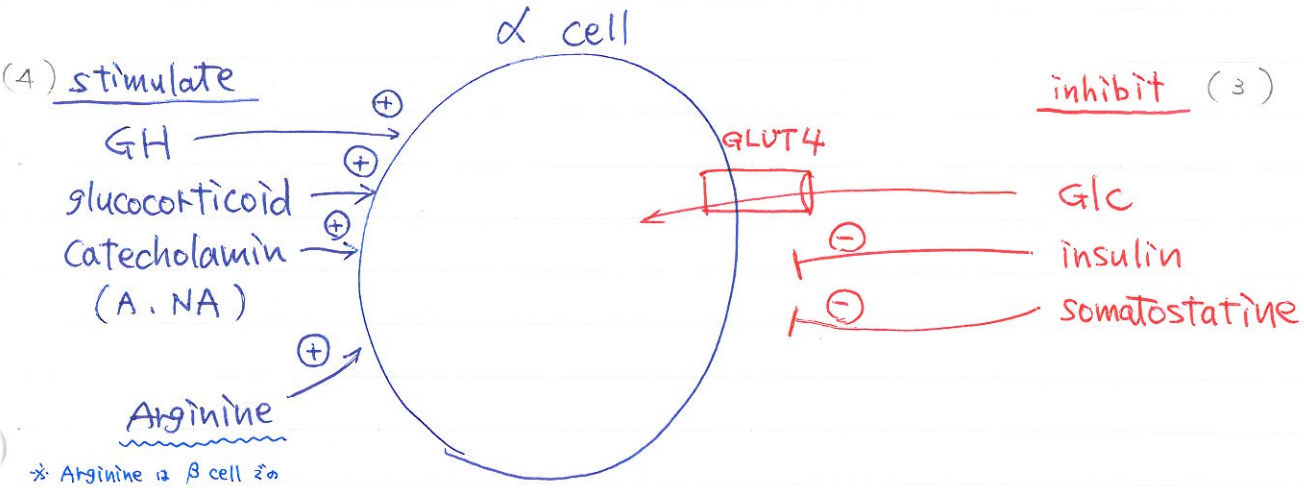
Q12. Tell me what δ cell doing ? ⇒ produce somatostatin

Q13. Which transporter & channels are important for insulin production & release ? ⇒ 1) GLUT 2 2) ATP sensitive K^+ channel
3) voltage dependent Ca^{2+} channel

Q14. which Glc transporter is insulin dependent ? and locate where ? ⇒ GLUT 4
@ skeletal m, adipose tissue

α cell

↳ produce **glucagon** - peptide hormone



※ Arginine ㅋ β cell 에 insulin production 을 stimulate!

How these hormones increase BS level ?

glucagon → glycogenolysis ↑
→ gluconeogenesis ↑

T_3, T_4 → glc absorption from small intestine ↑

GH → glc level ↑ ← Glc uptake by the Cells ↓

Adrenalin, NA → glycogenolysis in Liver ↑
via β_2-Receptor
adrenergic receptor

~ A / NA can stimulate β_2 receptor
⇒ glycogenolysis ↑

glucocorticoid → gluconeogenesis ↑
→ Glc uptake ↓

Date

diabetes mellitus

Type I
= IDDM
∵ insulin deficiency
∵ more than 90 % of β cell die

Type II
= NIDDM
Non Insulin Dependent Diabetes Mellitus
∵ insulin resistance
→ insulin Receptor loose their sensitivity

typical onset : 14 - 24 years old (Type I) / : after 40 years old (Type II)

- viral infection → certain virus destroy the β cell
- autoimmune disease
  - ↳ anti-β cell Antibody 血中をグルグル回る
    → destroy β cell

Body shape

Type I
- skinny (∵ insulin is important for storage of protein, glycogen, adipose tissue)
  No insulin ⇒ less storage, lipolysis ↑

Type II
- usually obese
  (∵ BS ↑ but cells are starving!)
  (∵ eating a lot, drinking too much coke ⇒ insulin ↑↑↑
  ⇒ insulin Receptor less & less sensitive!)

1st Symptoms of diabetes mellitus
(Type I, Type II 共通)

- polyuria --- daily urine volume ↑ (∵ There is osmotic diuresis. Glc = osmotically active!)
- polydypsia ··· thirst ↑
- polyphasia ··· eat a lot
  Type I Q: How can they loose energy?
  ⇒ energy loose to urine (Glc)
- itchy skin
- glycosuria

How can you figure ppl have low Glc level?

Symptoms of Hypoglycemia

- Hungry — if you want ask questions to Dr. Kornyei, you should go after lunch! 
- agression (∵ anti-insulin hormone ↑ = stress hormone) Terrorist usually hypoglycemia (??)
- tachycardia - palpation ∵ A, NA
- pale skin ∵ A, NA via α_1 R → vasoconsthriction in vessels of skin
- sweating ↑ ∵ sympathetic activation to compensate low BS level
  (cold sweat)

What kind of endocrine diseases can increase BS level ?

endocrine reasons for diabetes mellitus

- Cushing syndrome → glucocorticoid ↑
- giantism / Acromegaly → GH ↑
  (befor puberty) (after puberty)
- Pheochromocytoma (∵ adrenalin level ↑ ⇒ BS ↑)
- glucagonoma (glucagon producing tumor)
- Somatostatinoma (somatostatin producing tumor)

+α (gestational diabetes mellitus
↳ during pregnancy → GH like hormone is produced
↓
BS ↑)

⇒ after delivery, you have to be careful because normally it's automatically cured but, sometimes that can be diabetes mellitus

- Hyperthyroidism 忘れてT=！

• Q17. which hormone can increase BS level ?

⇒ 1) Adrenalin, NA 2) glucagon 3) GH
4) glucocorticoid 5) Thyroid hormone (T_3, T_4)
6) Somatostatin (← indirectly !)
↳ insulin ↓ ⇒ BS ↑

during the day, hormone level would change.

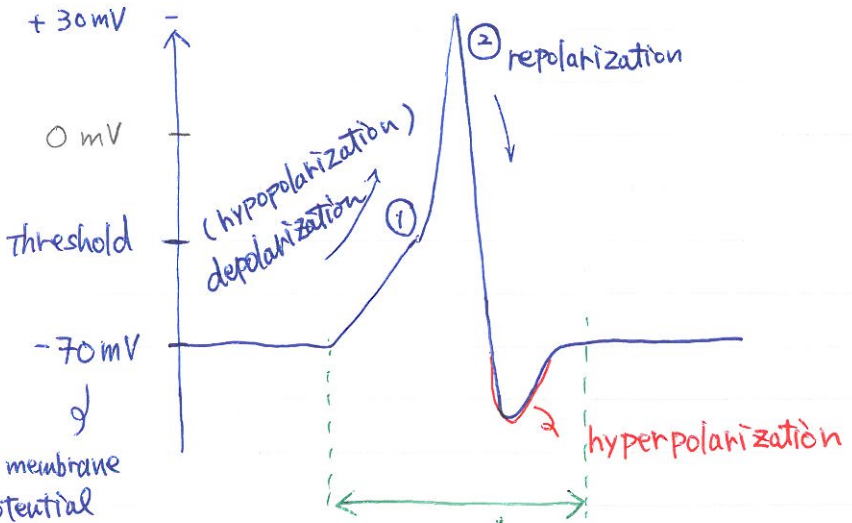
Q18. which hormone has diurnal rhythm which reaches maximum early in the morning ?

⇒ Cortisol

※ some man has heart attack early in the morning because stress hormon increases. But ladies are safe because estradiole has protective function.
⇒ woman doesn't have this cardiovascular disease

Neurophysiology

Action Potential



* Pacemaker cell では、200mS ですこ.

① fast voltage dependent Na^+ channel ⊖— TTX (Tetrodotoxin)

↳ Na^+ influx ∵ c.c. gradient ∵ electrical gradient

below 0 mV の時しか働かない!

② voltage dependent K^+ channel ⊖— TEA (Tetra Ethyl Ammonium)

↳ K^+ outflow ∵ electrochemical gradient

above 0 mV の時のみ働く. 常に働く (below 0mV では cc gradient のみ働く)

Q: Which AP is (duration of) longest or shortest ?

shortest	:	neuron	< 4 mS
		skeletal m.	4-6 mS
		heart	200 - 300 mS ← 1st Sem. athial cell, ventricular cell, Pacemaker cell
longest	:	smooth m.	can be > 300 mS

Q: At the top of AP (action potential), which is higher c.c. extracellular $[Na^+]$ or intracellular ? ⇒ extracellular

Q: During hyperpolarization, which is higher $[K^+]_{out}$ or $[K^+]_{in}$? ⇒ $[K^+]_{in}$

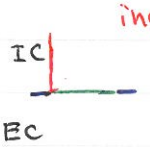
Date

① fast voltage dependent Na^+ channel

activation gate

- 70 mV ··· is closed

below threshold



inactivation gate

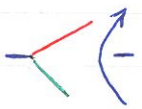
activation gate

- 40 mV ··· activation gate open

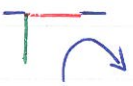
above threshold

- 20 mV ··· activation gate is more & more open

But! at the same time, inactivation gate start to close.



+ 30 mV



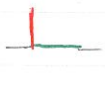
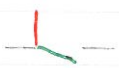
refractory period

··· 1 ~ 2 ms

In case of the neuron,

refractory period is very very short!

cf. in case of the Heart, it was hundreds ms.

	activation gate	inactivation gate	
- 70 mV	close	open	
- 40 mV	open	open	
- 20 mV	open	open	
+ 30 mV	open	close	

During Anatomy 1. You can see ulnar n, median n, which are axon!
cell body is located in spinal cord or in the brain (CNS). So we use peripheral nerve, those are axon.

Erlanger - Gasser classification of axon

classification of neuron according to size & conduction velocity (axon)

Name	diameter	conduction velocity	function
Aα	15 μm	70 - 120 m/s	- motor neuron → innervate skeletal muscle - primary endings of muscle spindle
Aβ	8 μm	30 - 70 m/s	- sensory eg. touch - secondary endings of muscle spindle
Aγ	5 μm	15 - 30 m/s	- motor fibers of muscle spindle
Aδ	3 μm	12 - 30 m/s	- sensory eg. touch, pain, temperature (cold) (sharp sudden pain)
B ↑ thin myelinated	3 μm	3 - 15 m/s	- autonomic preganglionic fiber ↳ sympathetic → paravertebral ggl / prevertebral ggl — located @ CNS → innervate ggl ↳ parasympathetic ... ggl is located in the wall of innervated organ ↳ Ach --- cholinergic fiber → both sympathetic & parasympathetic preganglionic neuron
C ↑ unmyelinated (No myelin sheath)	1 μm	1 m/s	- pain fiber (dull pain) (warm) - autonomic postganglionic fiber Sympathetic post ganglionic fiber: mostly! ↳ NA ... Noradrenergic; 5% ↳ Ach ... cholinergic fiber → innervate sweat gland Parasympathetic ↳ Ach

review
- adrenal medulla is innervated by "sympathetic preganglionic fibers"

※ in case of autonomic nervous system, there are Preganglionic & Postganglionic neurons

high dose of nicotin → Nicotinic Ach Receptor
located @ ganglion of Postganglionic neuron

Q: Which fiber is longer, sympathetic or parasympathetic preganglionic axon? ⇒ Parasympathetic preganglionic fiber is longer

∵ in case of the parasympathetic nerve, ggl is located in the wall of the innervated organs. e.g. vagus n is coming from the brain. in anatomy when you dissect the neck region, you can see the vagus n, those fibers are Parasympathetic preganglionic fiber and the ggl is located in the Heart, GI tract, Lung. So Parasympathetic preganglionic fiber is pretty long!

But, sympathetic fiber is originated from "spinal cord" & ggl is located close to the spinal cord so called "paravertebrally" & "prevertebrally"

So, sympathetic preganglionic fiber is usually shorter than parasympathetic.

Q: which is longer, sympathetic or Para- postganglionic fiber?

A: Parasympathetic postganglionic fiber is shorter!

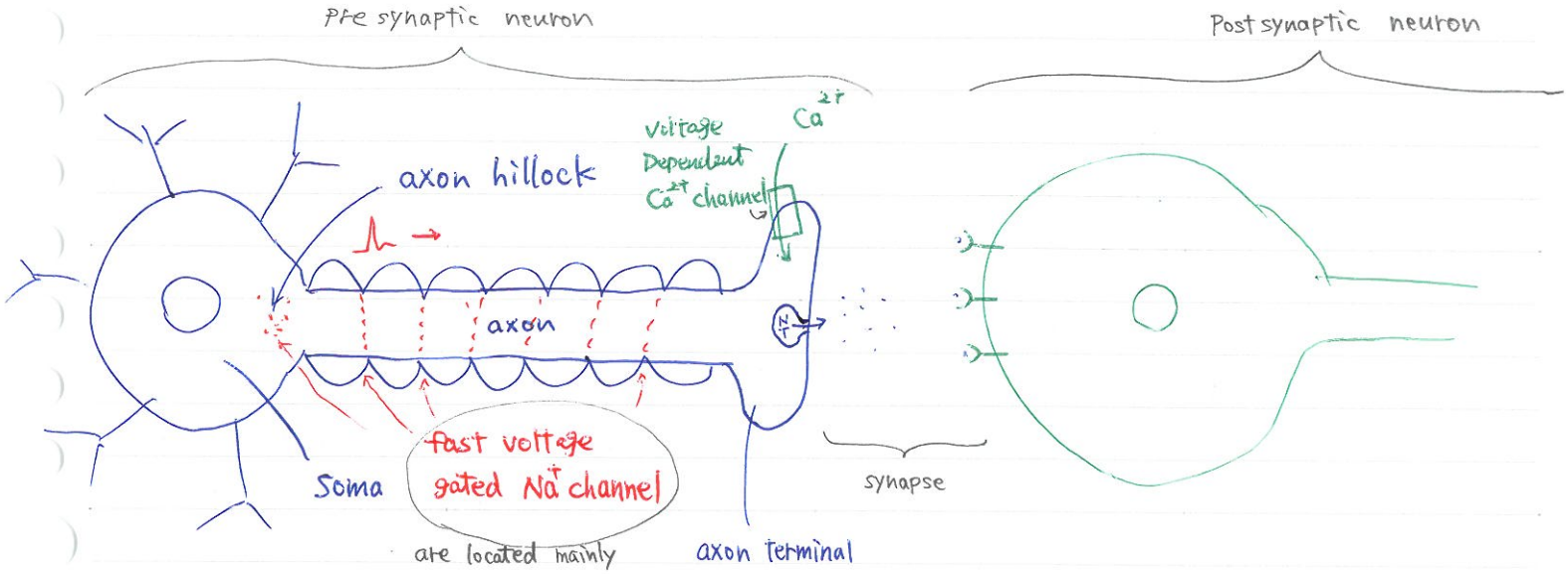
∵ ggl is located in the wall of the innervated organ → So postgglionic axon should travel only a couple of mm.

↗ next page!

But for example, Sympathetic ggl is located somewhere close to the spinal cord & they can innervate the vessels (except capillary!)
→ arteriole in your toe is 1 m from the ggl So sympathetic Postgglionic fiber can be as long as 1 m!

w4 ⇒ Sympathetic fiber is longer, Parasympathetic axon is shorter in autonomic postganglionic fiber. Date Feb 19 mon

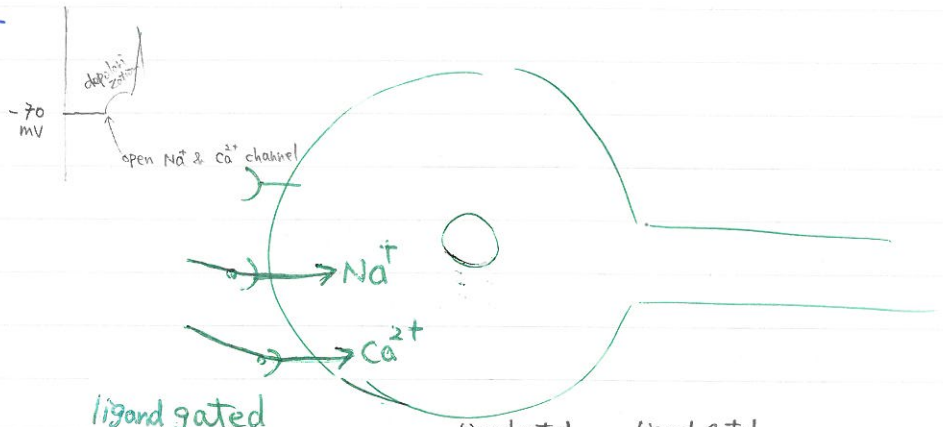
Synapse - chemical - electrical ... very few



※ if there is NO voltage dependent Ca^{2+} channel activation
⇒ NT can NOT be released to the synapse.
(∵ Ca^{2+} signal is important for NT releasing)

Neurotransmitter

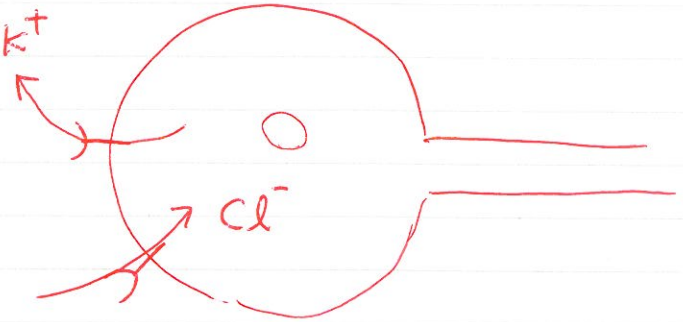
→ excitatory NT
- ↳ glutamate
- ↳ aspartate

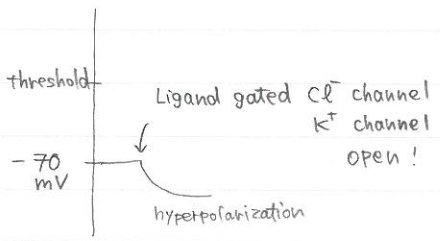


ligand gated ion channel (can be Na^+ channel & Ca^{2+} channel)

Ligand gated Ligand gated

→ inhibitory NT
- ↳ GABA
- ↳ glycin



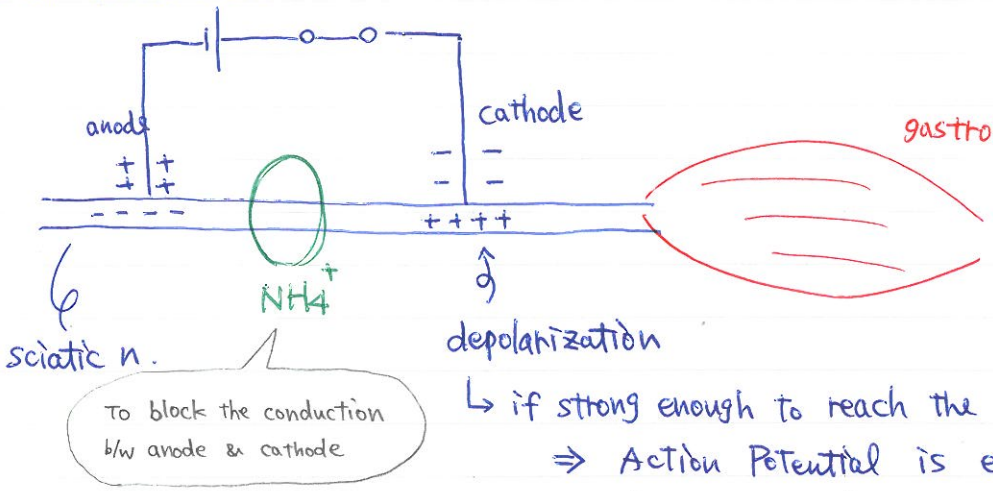


Date

※ cathode は cation ⊕ を引きつけるから (−) !!

Polar excitment

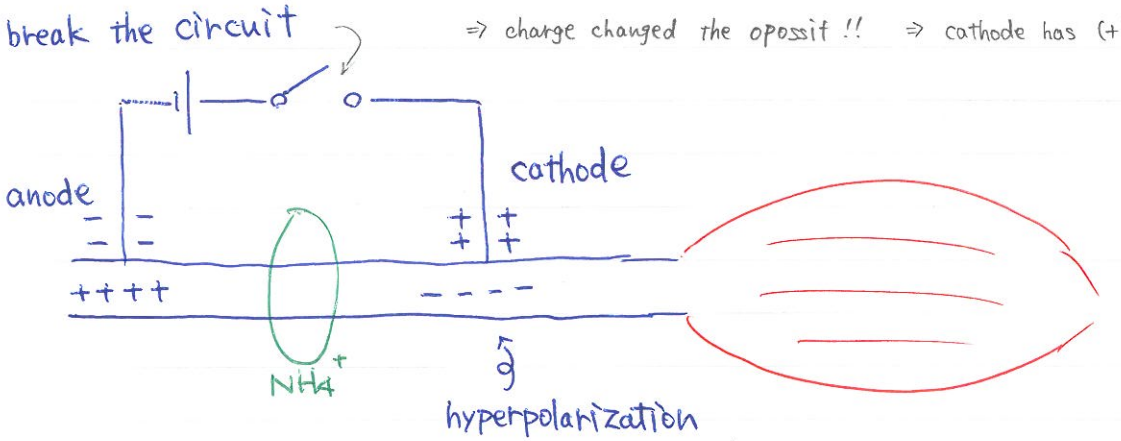
1) cathode is closer to the muscle



↳ if strong enough to reach the threshold
⇒ Action Potential is evoked
↳ AP travel through the axon & excite the muscle

	start stimulation	Break (stop the stimulation)
cathode is closer	+	−

✧ when break the circuit ⇒ charge changed the opossit !! ⇒ cathode has (+) environment



around cathode ⇒ so in this case (when break the circuit)
cathod behave as anode !

when break the circuit

Q1. How does the glucocorticoid change the Blood Glc level ? ⇒ ↑

✧ Q2 : what is the mechanism ? ⇒ 1) gluconeogenesis from AA ↑ 2) Glc uptake by skeletal m. ↓ adipose tissure

Q3 : How do you think that the skeletal m cell & adipocyte can uptake Glc ? ⇒ GLUT 4

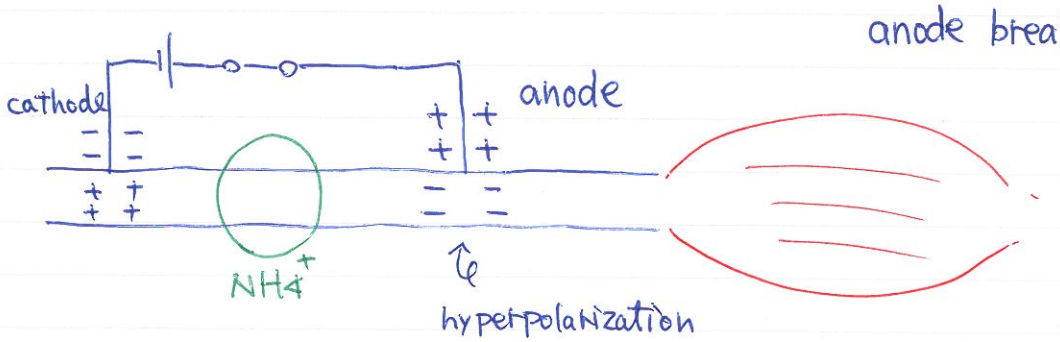
⇒ what cortisol does , it places GLUT 4 from the membrane into the intracellular space (into endosome)
That's why Glc transporter can NOT take up the Glc .

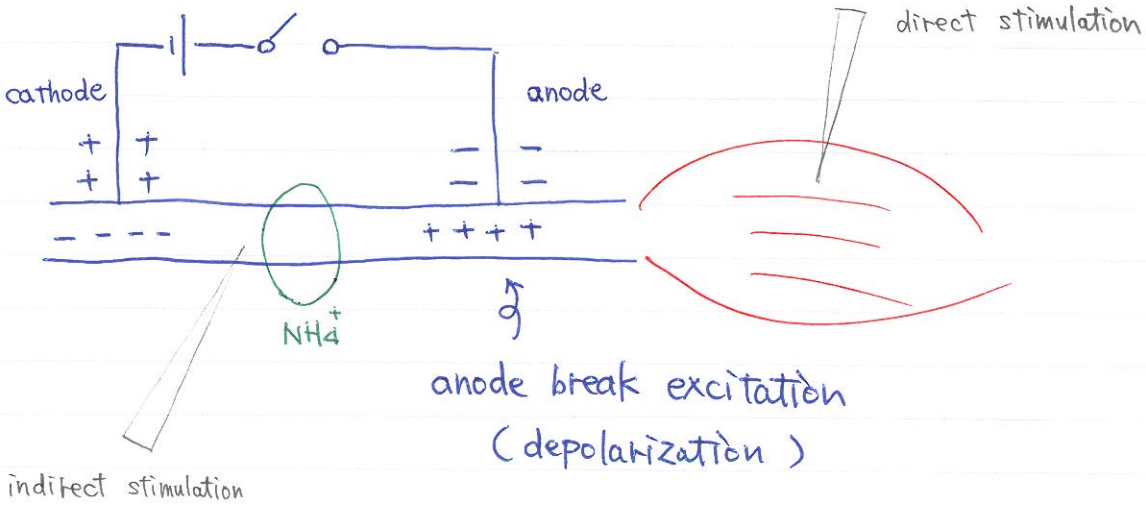
Date

2) anode is closer to muscle

Start	Break
−	+

anode break excitation





Q4 : Tell me anabolic hormones. ⇒ 1) insulin 2) Growth Hormone 3) Testosterone

Q5. what are the main reasons of diabetes mellitus ? ⇒ Type I (IDDM) … insulin deficiency

Type II (NIDDM) … insulin resistance

Q6. Tell me endocrine reasons of diabetes mellitus ? ⇒ 1) Cushing syndrome

2) giantism / acromegaly
GH↑ before puberty GH↑ after puberty

3) Pheochromocytoma

4) glucagonoma

5) Somatostatinoma

6) gestational diabetes mellitus

7) Hyperthyroidism

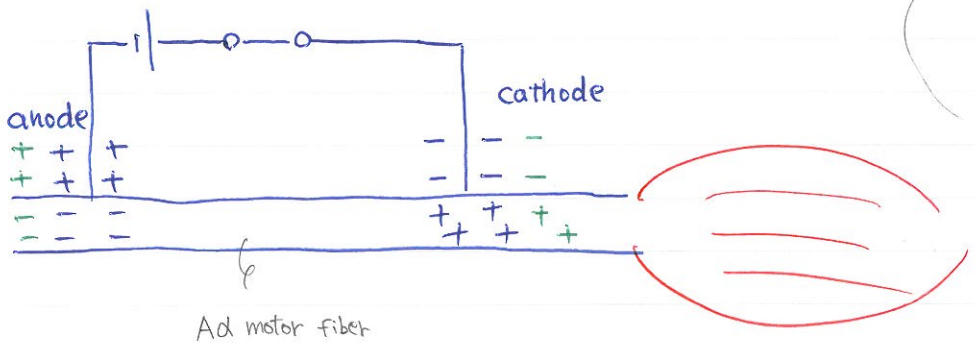
Date

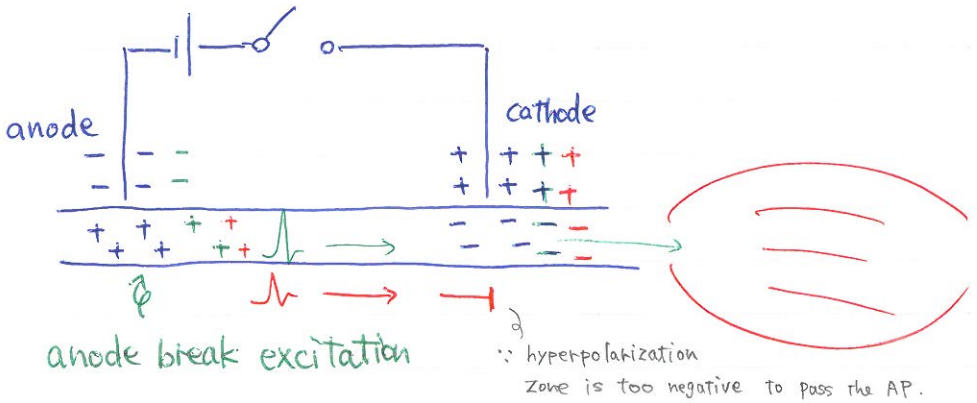
cathode make excitation is stronger than anode break excitation

Pflüger's law

	Start	Break
- low (weak) stimulus intensity (just above the threshold)	⊕	⊖
- middle (medium) "	⊕ ⊕	⊕ → anode break excitation (∵ There is NO NH_4^+ block)
- strong "	⊕ ⊕ (⊕)	⊖

✧ cathode is closer to the muscle



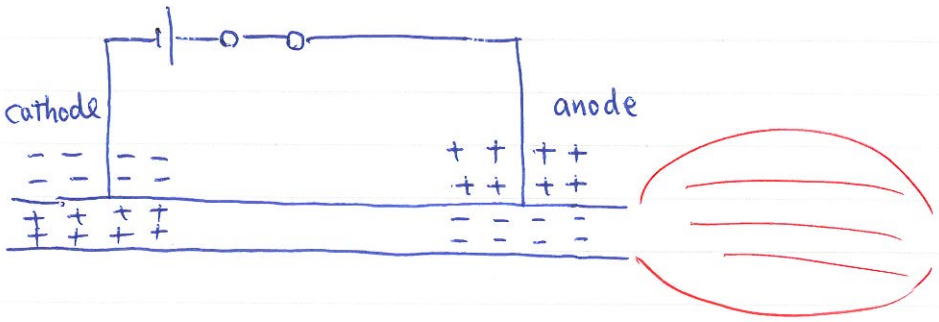


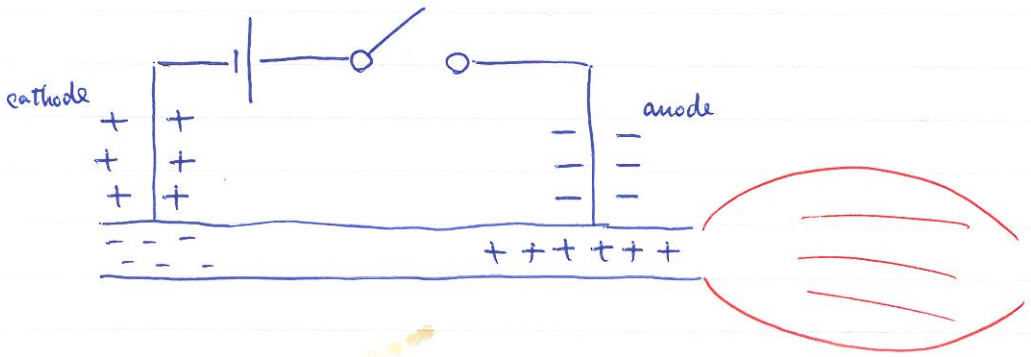
✧ anode is closer

	Start	Break
- strong	⊖	⊕ ⊕

Date

✧ anode is closer





Q7 : How can you block the fast voltage dependent Na^+ channel ? ⇒ TTX (Tetrodotoxin)

Q8 : How " voltage dependent K^+ channel ? ⇒ TEA (Tetra Ethyl Ammonium

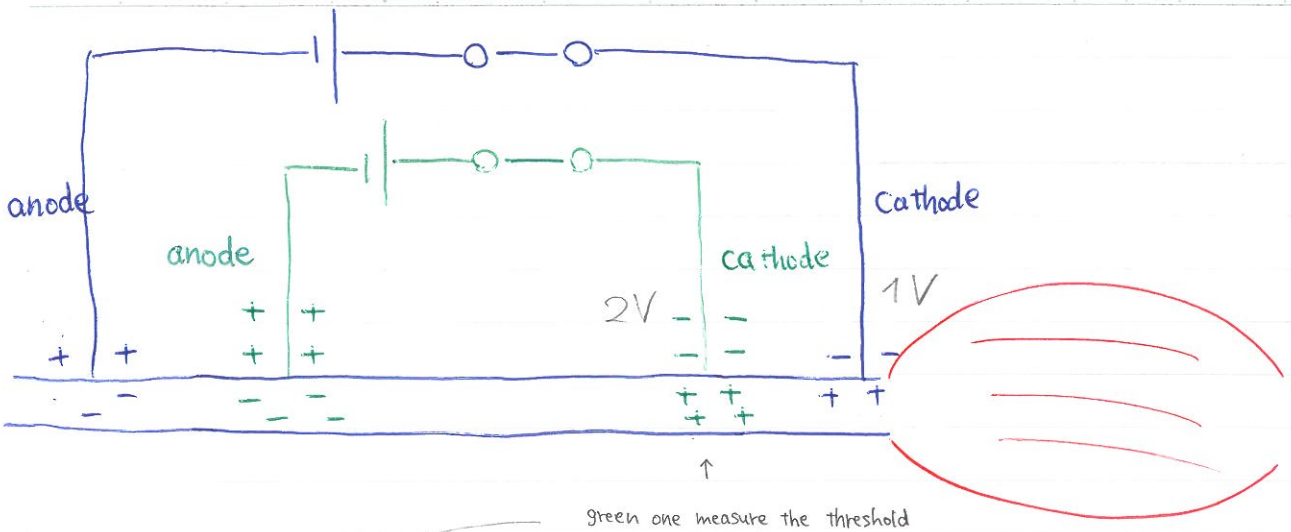
Q9 : What is the connection b/w the diameter & conduction velocity ? ⇒ The wider is the fasteh.
Aα is the widest = fastest

Q10 : Tell me which axon is myelinated ? ⇒ Aα , Aβ , Aγ , Aδ , B fibers
(ONLY C fiber is unmyelinated)

around the cathode excitability ↑

Catelectrotonus

2 stimulators !



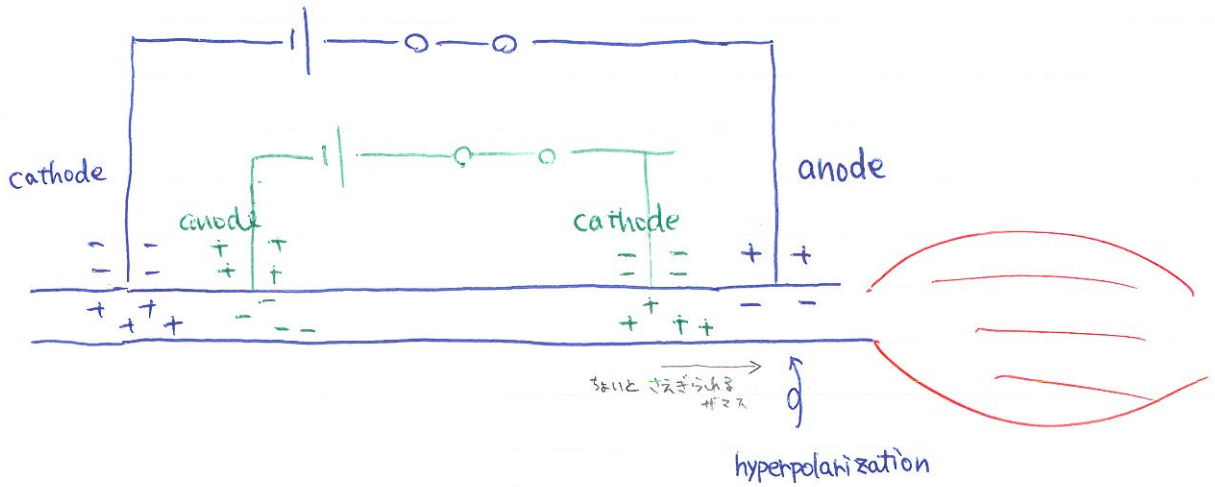
green one measure the threshold and it was 2V.

eg. threshold is 2V. Switch on green = 1.5V ⇒ ⊖ (∵ 1.5V is below threshold)
+ switch on blue = 1V as well ⇒ ⊕ (∵ 2.5V is above ∘) ⇒ depolarization

(excitability is increased !)

anelectrotonus

↳ around the anode excitability ↓



eg. threshold = 2V, Switch on green = 2V ⇒ ⊕ (∵ 2V is above threshold)
+ Switch on blue = 1V ⇒ ⊖ (∵ 2-1 = 1V is below threshold)

⇓

so if we want to have AP, we should use more than 3V of green cathode ! (∵ 3-1 = 2V is enough to evoke AP)

w5

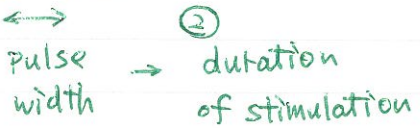
Date Feb 26 mon

Q 9 (중)... when you stimulate the nerve or muscle, there are 2 main characteristics of the stimulus.

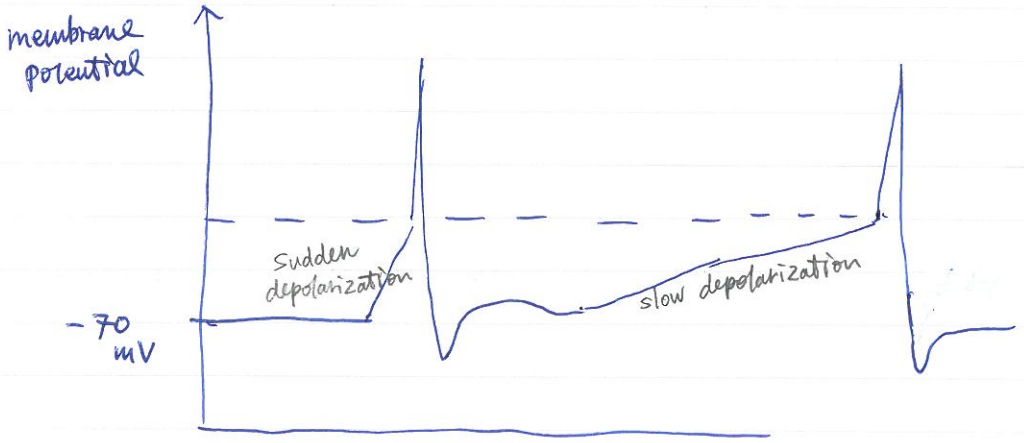
1) amplitude ↕
2) duration ↔

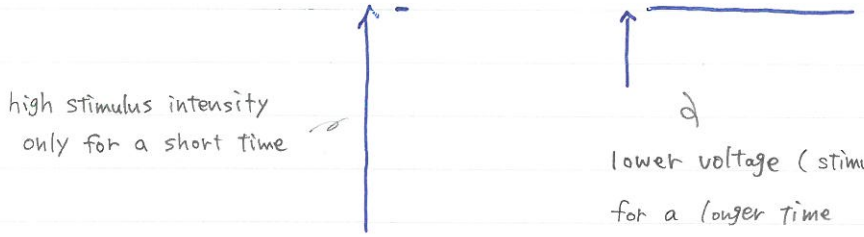
① amplitude of the stimulus, given by Volt(V).

both of them shows same result.



pulse width → ② duration of stimulation





high stimulus intensity only for a short time

lower voltage (stimulus intensity) for a longer time

Q1. when you stand the stimulation, excitability is increased around anode or cathode? ⇒ cathode

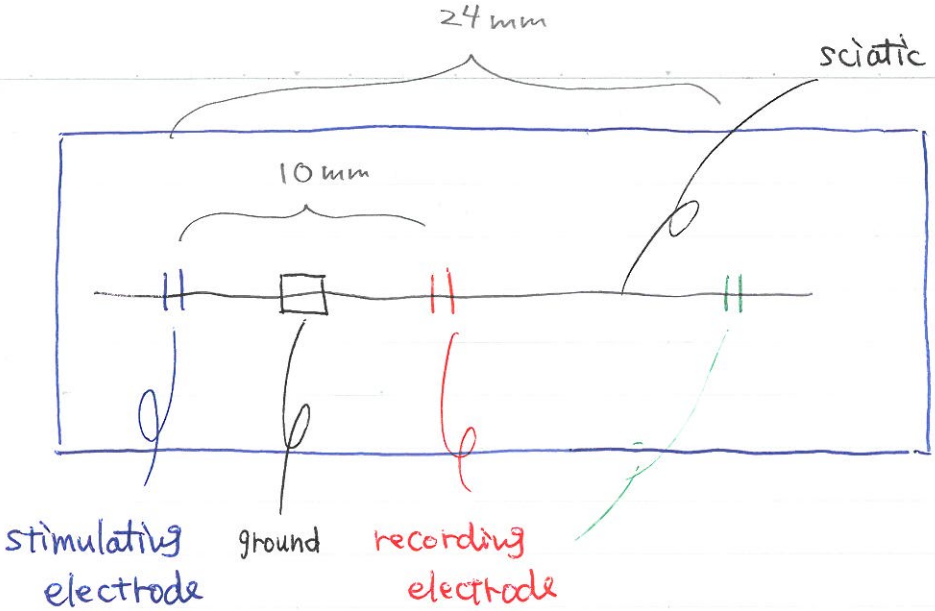
Q2. Is it true that anode always make hyperpolarization? ⇒ No. (∵ anode break excitation)

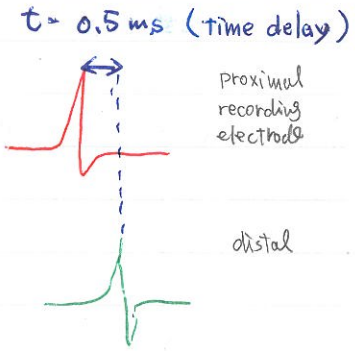
Q3. which is negative pole? ⇒ cathode

Q4. what is the function of NH_3 in b/w anode & cathode? ⇒ to prevent AP propagate

Q5. How can you check the nerve preparation is intact? ⇒ to use

Date

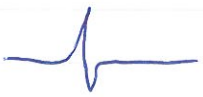




$$v = \frac{\text{distance}}{\text{time}} = \frac{s}{t} = \frac{14\ \text{mm}}{0.5\ \text{ms}} = 28\ \text{m/s}$$

2V → minimum threshold

Q Stimulus intensity is below (threshold) (1.5V) ⇒ ——— No AP! (Action Potential) — isoelectrical line!

Q above (2.5V) ⇒ 

Q increase stimulus intensity 5V ⇒ amplitude is increased

∵ more & more axon are activated

⇒ So more & more AP are given to "Compound AP" (so called) ↑ millions of AP are summated!

∵ sciatic nerve is millions of axon. & each axon has different threshold!

Q. above maximum threshold ⇒ no change in shape

∵ all nerve fibers are activated

↓ ∵ All or Nothing law

※ Compound AP is different from individual AP. (∵ in case of individual AP, amplitude is the same!)

Q6. What does direct stimulation mean? ⇒ stimulation on the muscle

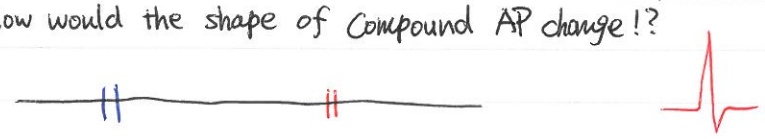
Q7. How does threshold change in case of Catelectrotonus? ⇒ lower

Q8. What is the chronaxie? ⇒ minimum time required to excite the nerve or muscle when double of the rheobase is applied.

Date

Q: When you set 2nd recording electrode far away from stimulating electrode (つまり, increase distance. How would the shape of Compound AP change!?

①



②

Answer.

Aα . Aβ . Aγ , Aδ , B , C fibers ⇒ becomes wider!

∵ in the sciatic nerve, there are different axons

1m distance → C fiber (1m/s) → 1 s

Aα (70-120 m/s) → 0.01 s

Q: Cool down the nerve. How conduction velocity change? ⇒ ↓

In the football match, when there is an injured guy, Dr cold suprey the injured area. why? Because that cools down the area & conduction velocity slow down and probably pain information via the C fiber can NOT get to the brain

Q9. What is the rheobase ? ⇒ minimum electrical current which is required to excite the nerve or muscle when the duration of the stimulation is indefinitely long.

Q10. What is minimum threshold & maximum threshold ?

⇒ minimum threshold ... at least 1 axon is activated ← axon which has a lowest threshold is activated

⇒ maximum threshold ... all of the axons are activated ← axon which has a highest threshold is activated too.

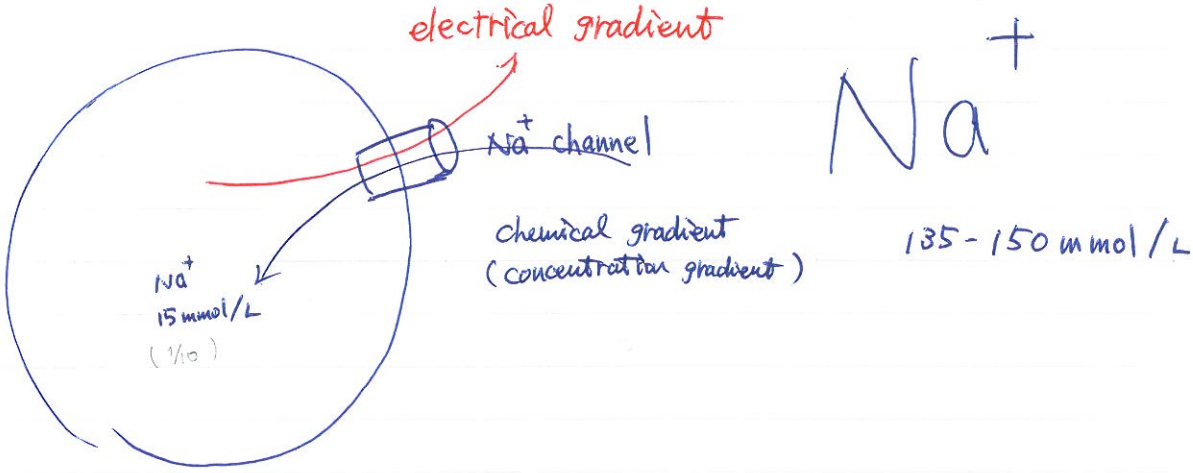
Q11. How can you block the fast voltage dependent Na^+ channel ? ⇒ TTX (Tetrodotoxin)

Q12. 〃 Voltage dependent K^+ channel ? ⇒ TEA (Tetra Ethyl Ammonium)

balance

when Na^+ channel open, the Net Na^+ movement is Zero.

Equilibrium membrane potential of Na^+



↳ + 60 mV

Q + 70 mV membrane potential ⇒ Na^+ outflow ∵ Cell try to reach equilibrium potential so positive Na ion should leave.

Q + 60 mV ⇒ Net Na^+ movement is Zero.

Q + 20 mV ⇒ Na^+ influx

Q 0 mV ⇒ Na^+ inflow ↝ electrical gradient 없어 direction!

- 60 mV ⇒ influx

- 90 mV ⇒ influx

Q13. Where is the fast voltage dependent Na^+ channel located ? ⇒ 1) axon hillock 2) Ranvier Node

✧ Q14. Is there any ion channel underneath the myelin sheath ? ⇒ voltage dependent K^+ channel

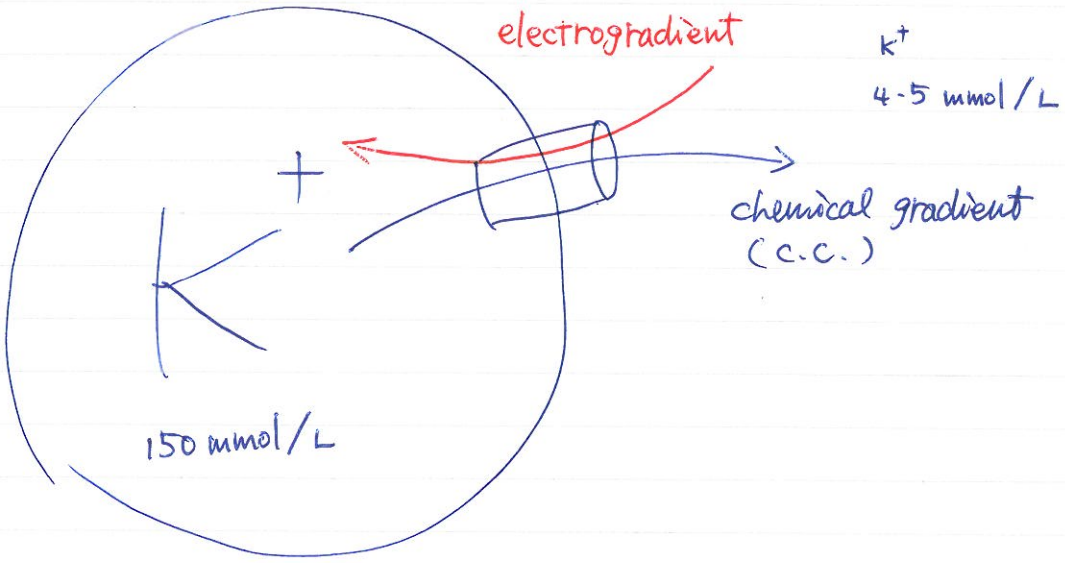
✧ Q15. Where is the ligand gated ion channel located ? ⇒ 1) dendrite 2) Soma (Perikaryon)

Q16. Can you tell me excitatory NT ? ⇒ 1) aspartate 2) glutamate

Q17. 〃 inhibitory NT ? ⇒ 1) GABA 2) glycin

Date

Equilibrium membrane Potential of K^+



↳ - 90 mV

Q
- 110 mV membrane potential ⇒ K^+ inflow
- 100 mV ⇒ inflow
- 90 mV ⇒ Zero
- 70 mV ⇒ K^+ outflow
0 mV ⇒ outflow

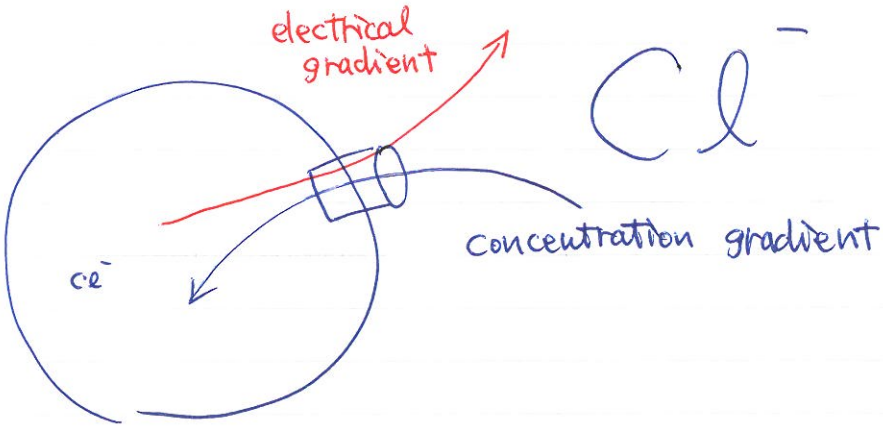
Q18. Do you think neuron has refractory period or NOT ? ⇒ yes

1st Semester. heart has long refractory period, that's why the Heart can NOT be tetanized.

Q19. When refractory period is as long as 2 ms, you stimulate the nerve like crazy
What is the maximum frequency (firing rate) ? ⇒ 500 times/s

Date

Equilibrium membrane Potential of Cl^-



↳ - 60 mV

Q: Cl^-

- 110 mV ⇒ outflow
- 85 mV ⇒ outflow
- 60 mV ⇒ Net Cl^- change is Zero
- 30 mV ⇒ inflow
- 0 mV ⇒ inflow
+ 30 mV ⇒ inflow

Q: Na^+ influx & K^+ outflow ⇒ - 90 mV → + 60 mV
(+60) (-90)

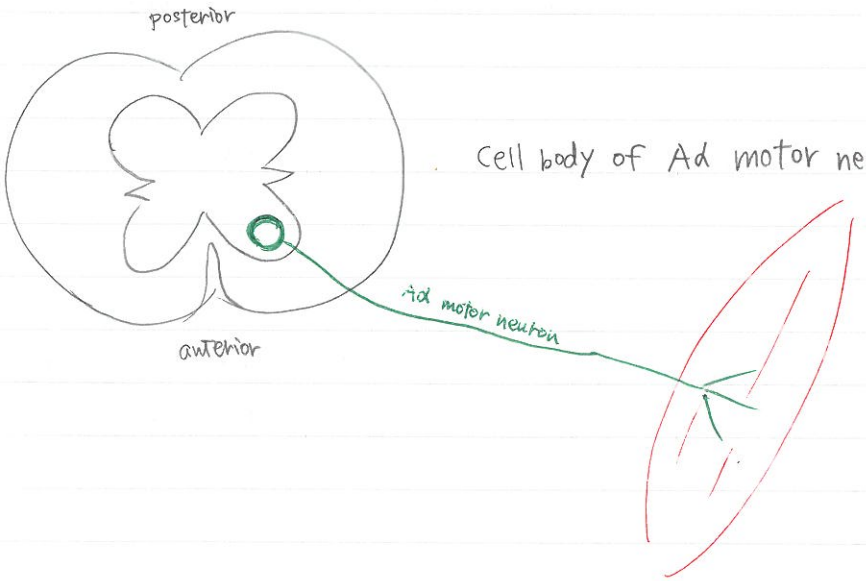
Q: Na^+ outflow & K^+ influx ⇒ No way !

Q: Na^+, Cl^- influx at the same time ⇒ - 60 mV → + 60 mV

Date

Neuromuscular Junction

consists of Aα motor neuron



Cell body of Aα motor neuron is located in anterior horn of the spinal cord.

Aα motor neuron innervate muscle fibers.

1 muscle fiber is activated by 1 axon / Aα motor neuron

1 motor neuron can innervate hundreds of muscle fiber

Motor Unit = 1 motor neuron & muscle fibers that it innervates

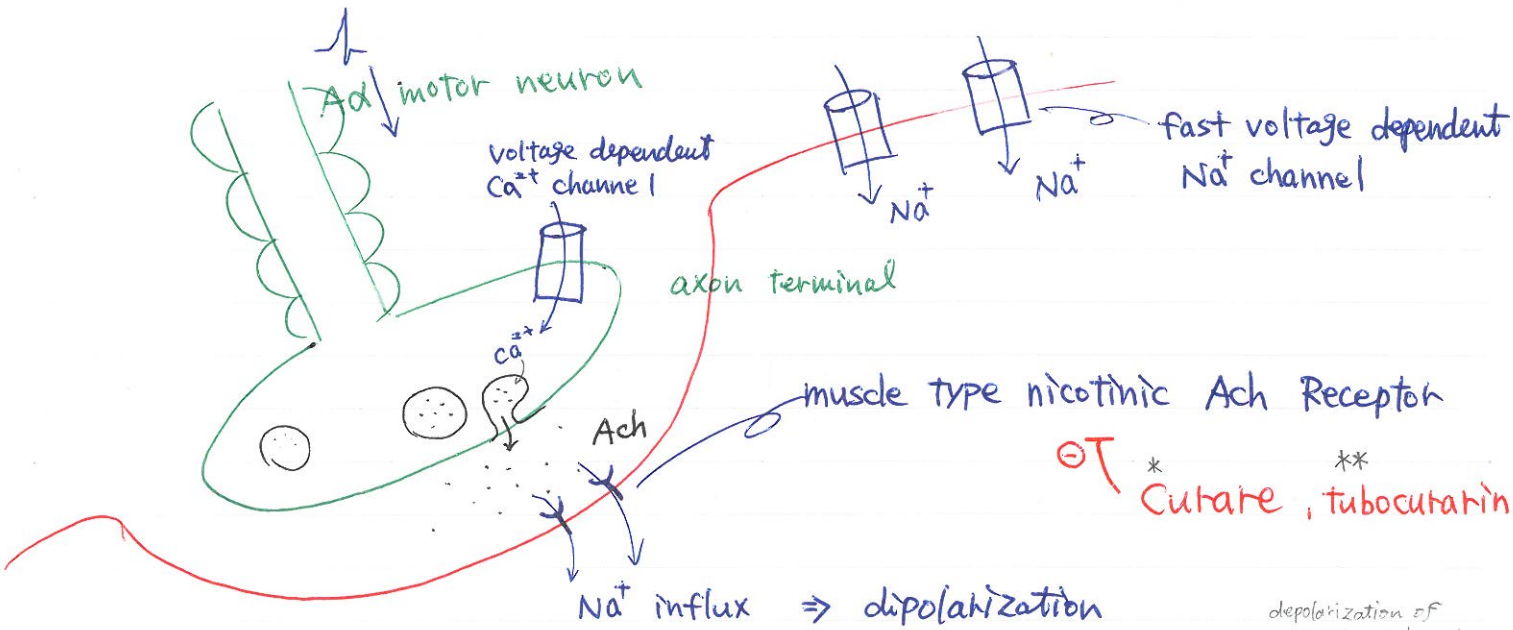
Date .

big muscle ⇒ less motor neuron is enough

rude muscle

gluteus maximus
latisimus dorsi ⇒ 1 motor neuron innervate about 500 muscle fibers

extraocular muscle ⇒ 1 motor neuron innervates less than 10 muscle fiber
↳ pricise muscle
That's why we can do eye contact.



depolarization of skeletal muscle 의 가

‖

end plate potential

⇓

fast voltage dependent Na^+ channel

⇓

AP !

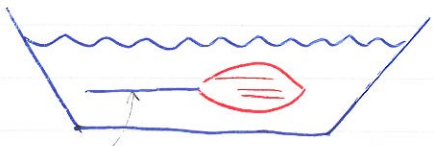
※ Ach opens the muscle type nicotinic Ach Receptor

* Curare is the arrow poison for naitive American from frog and shoot the animal
Curare block the nicotinic Ach Receptor ⇒ Poor animal could NOT move any more
(The animal can feel the pain this time , can feel fear ... just can NOT move.

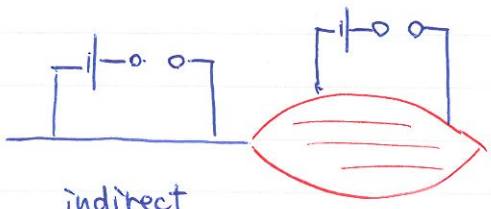
** During the Surgery , you are going to use "muscle relaxant" = "tubocurarin" (d-tubocurarin)

Q36 a 補足

1% Curare, 10 min. incubation



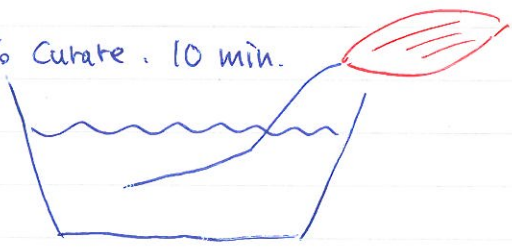
sciatic n. gastrocnemius m.



indirect → No muscle contraction (∵ Ach can NOT bind to Receptor because block by Curare)

direct → muscle contraction ∵ directly above threshd

1% Curare, 10 min.



indirect → ↓ ⊕ ∵ musde type

direct → ↓ ⊕

Q1. How do you think that conduction velocity change if you cool down the nerve ? ⇒ ↓

Q2. How would the conduction velocity change if you give "Lidocaine" ? ⇒ ↓ (∵ Lidocaine is one of the most famous local anesthesia !)

Q3. How would it change if you give "ether narcosis (anesthesia)" ? ⇒ ↓

※ It's Lab part. Sciantic nerve in pipe shape tube is anesthetized by ether → conduction decreases. and you need to apply the higher voltage to excite the nerve & muscle.

Q4. You set the membrane potential to + 10 mV. ⇒ influx, outflow, inflow

Na^+, K^+, Cl^- influx or outflow respectively.

∵ Equilibrium membrane potential of Na^+, K^+, Cl^- is + 60mV, -90mV, - 60mV.

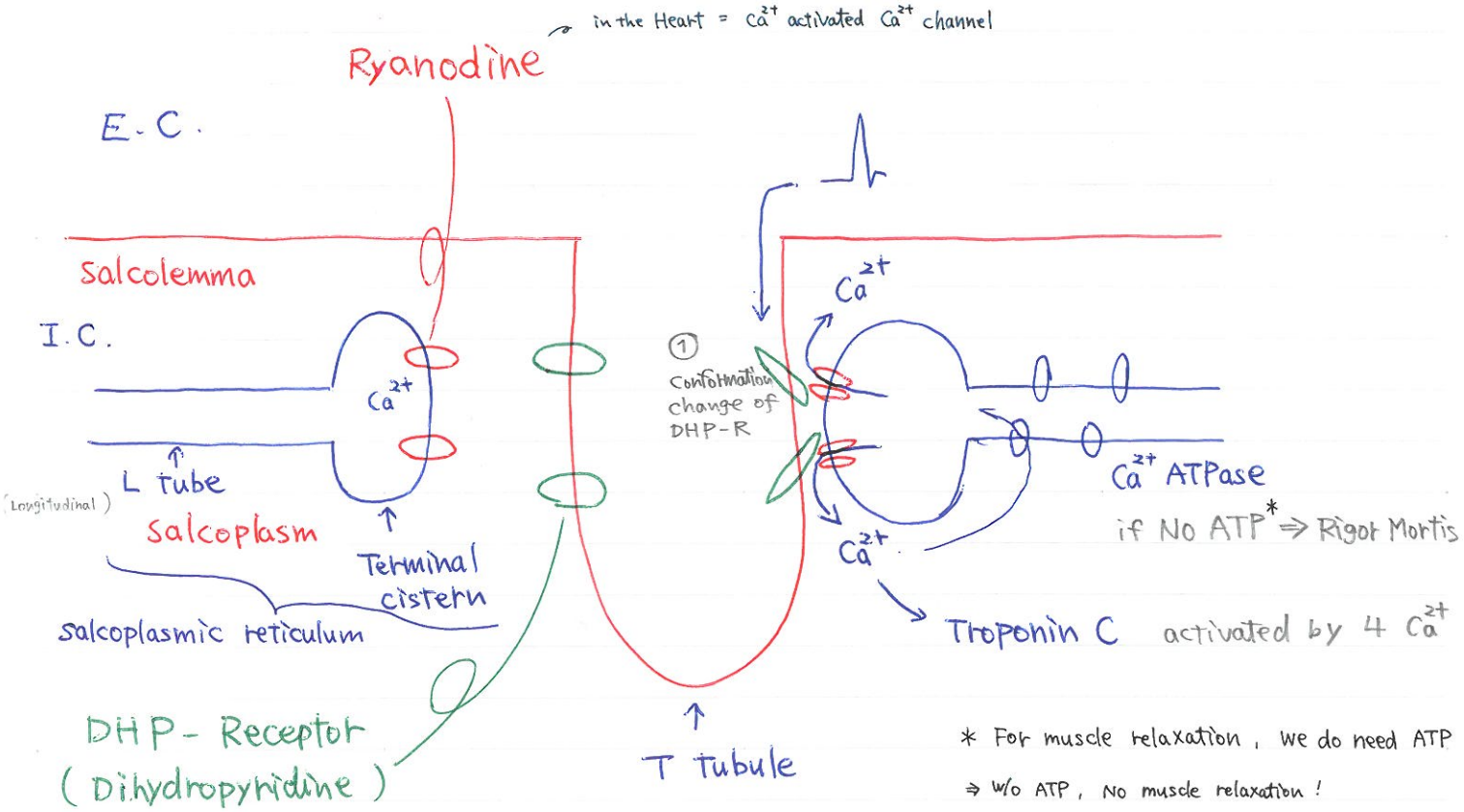
Q: why Cl^- influx ? ⇒ Because of 2 reasons. ① chemical gradient … $[Cl^-]_{out} > [Cl^-]_{in}$

② electrical gradient … which make the Cl^- to enter the cell to try to reach the Equilibrium potential (-60mV)

Date

※ Triate means 3 of sth

Triate : 1 T-tuble + 2 Terminal cistern



if No ATP* ⇒ Rigor Mortis

* For muscle relaxation, we do need ATP

⇒ w/o ATP, No muscle relaxation !

1) AP coming to the T tubule 2) DHP-Receptor detect the voltage → conformation change

3) Conformation change of DHP-R activate the Ryanodine receptor → Ca^{2+} is released from terminal cistern into salcoplasm

4) Ca^{2+} bind to troponin C. (1 troponin C can bind 4 Ca^{2+}
= 1 troponin C is activated by 4 Ca^{2+} ions)

Na^+, K^+, Cl^- influx or outflux ?

		Na^+	K^+	Cl^-
Q5.	You set the membrane potential to -125 mV	⇒ influx	influx	outflux
Q6.	〃 -60 mV	⇒ influx	outflux	No flow

↑ Cl^- Net movement is Zero

Q7. 〃 b/w -90mV & -60mV ⇒ influx, outflow, outflow

Q8. Where is the Cell body of Aα neuron located ? ⇒ anterior horn of spinal cord

Q9. which fiber has the lowest threshold ? ⇒ Aα

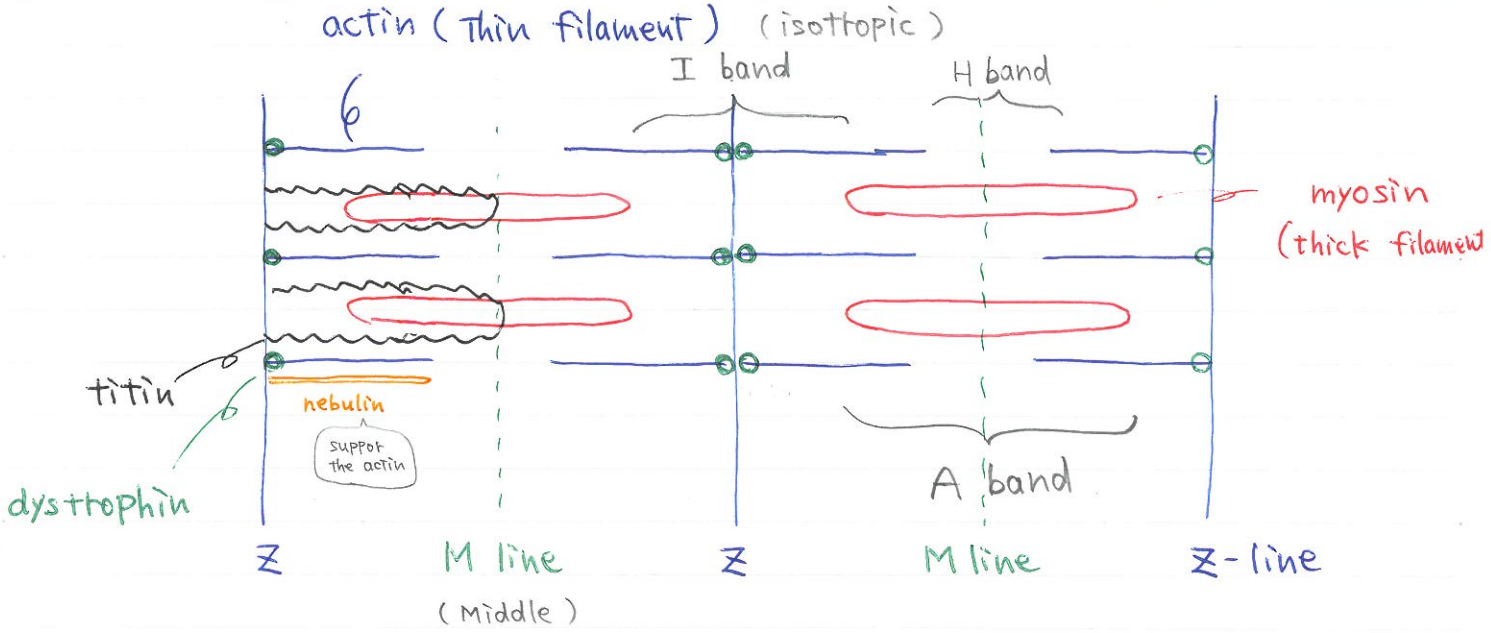
∵ lowest threshold = highest excitability = highest velocity

skeletal muscle のハナシ (smooth m. には sarcomere 無し!!

Sarcomere is b/w Z-lines.

Date

Sarcomere ... optimal size of sarcomere to exert maximum power = 2 ~ 2.5 μm



※ nebulin is the thin filament in the skeletal m. as long as actin

A band contains both

I band 〃 only thin filament (I ... Isotropic)

H band 〃 only thick 〃

muscle shortening → Z-Z is shorter
H band 〃
I band 〃
} Hi "Band"!

※ dystrophin anchors the actin to the Z line.

※ titin touches the actin to the Z line ... titin coming from the Z line, going to the M line & there is loop & then coming back to the Z line.

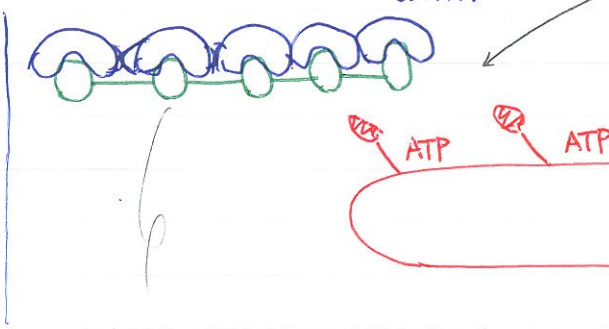
Q10. Which axons are unmyelinated ? ⇒ C fibers

Q11. Where do you think that the fast voltage dependent Na^+ channels are located ? ⇒ axon hillock & Node of Ranvier

Q12. where is the fast voltage dependent Na^+ channel in C fiber ? ⇒ axon hillock & whole axon

Resting State ... No Ca^{2+}, ATP is there

Relaxation (No AP, No contraction)



There is No actin-myosin interaction.
Why!? Because myosin binding site on actin are occupied by the "tropomyosin-troponin complex"

~ There is ATP on myosin head

tropomyosin-troponin complex

↳ contains - 1 tropomyosin
- 1 troponin C → Ca^{2+} binding
- 1 troponin I → inhibit interaction b/w actin & myosin
- 1 troponin T → connects Tropomyosin to other troponin molecule

Q13. If you increase the distance b/w the stimulating electrode & recording electrode
How would the shape of compound action potential change? ⇒ becomes wider

Q14. If you increase the stimulus (intensity) below the minimum threshold
How would the shape of the compound AP change? ⇒ there is NO AP

Q15. If you increase above Max. threshold ? ⇒ doesn't change any more

Q16. If b/w minimum & maximum threshold ? ⇒ amplitude increases

Q17. What is the min. threshold ? ⇒ The stimulus intensity when at least 1 axon is activated which has the lowest threshold.

Q18. What is the max. threshold ? ⇒ The stimulus intensity when all axons are activated

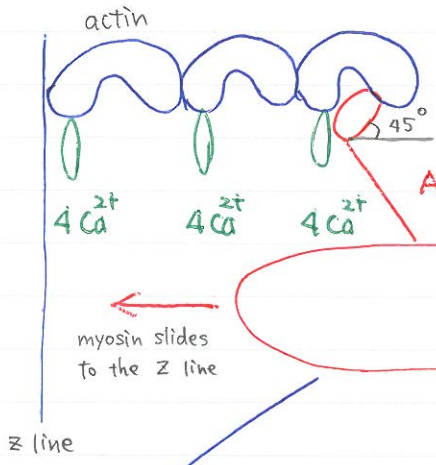
Q19. Why do you need increase the stimulus intensity to reach the Maximum threshold ?
⇒ 1) location (∵ some of them locate farther to electrode)
2) different types of axon → has different threshold

Date

Activation → Action Potential is coming

↳ Ca^{2+} is there, ATP is there

intracellular Ca^{2+} is enough in skeletal m
(released from terminal cistern)



Troponin C binds Ca^{2+} → Conformation of Tropomyosin-Troponin Complex would change
→ myosin binding site on the actin would be free
→ That's why myosin head can bind to the myosin binding site on the actin → Tilting the head (45°)

Further activation
we need
- Ca^{2+}
- ATP

Relaxation
we need
- ATP
- ↓ Ca^{2+}

Rigor
we need
- Ca^{2+} (∵ can NOT pump back)
- ↓ ATP

single AP or Compound AP ?

Q20. which one is inhibited by TTX ? ⇒ both

Q21. which one can be inhibited by TEA ? ⇒ both

Q22. which one has only one threshold ? ⇒ single

Q23. which is true for All or None law ? ⇒ single

Q24. which of them has refractory period ? ⇒ both

Q25. Tell me the step of muscle contraction. ⇒ ① Ad motor neuron are activated
② AP coming toward the muscle ③ voltage dependent Ca^{2+} channel @ axon terminal open
④ Ca^{2+} influx ⑤ Neurotransmitter (Ach) is released to synaptic cleft ⑥ Ach bind to skeletal muscle type nicotinic Ach R ⑦ Na^+ influx by ligand gated Na^+ channel ⑧ voltage gated Na^+ channel open when reach threshd

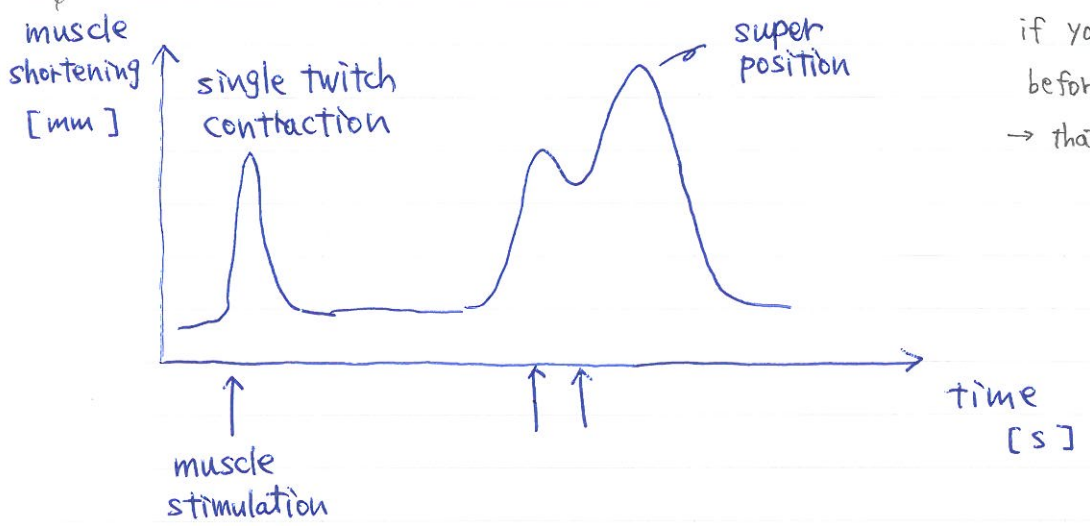
motor unit = 1 motor neuron & muscle fibers that it innervates eg. extraocular m.

in case of pricise muscle, 1 motor neuron innervates only a few muscle fibers.

(IR) 1 muscle fiber is innervated by 1 motor neuron !!

muscle contraction

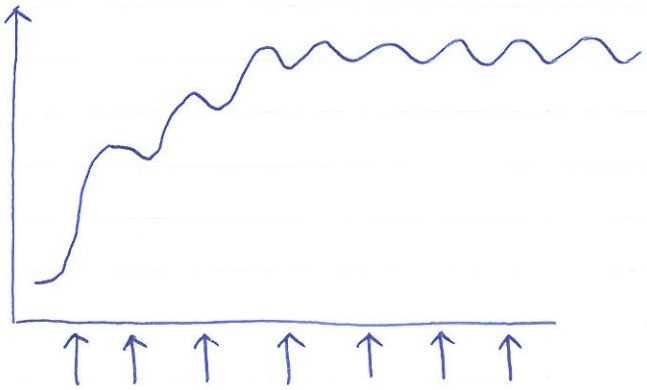
6



if you stimulate the muscle before the complete relaxation

→ that would be the super position

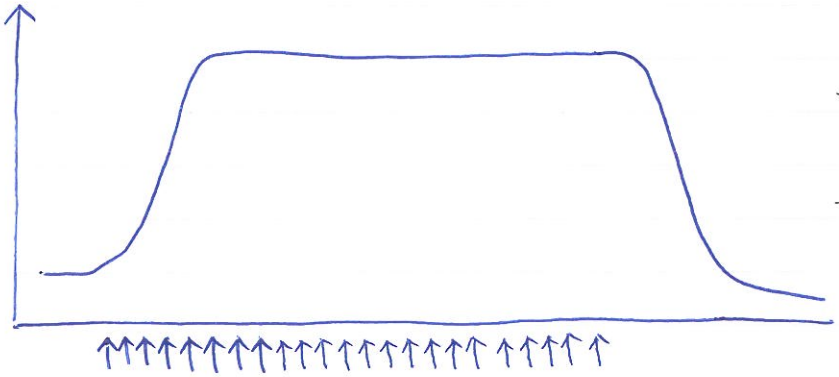
incomplete tetanus



if you stimulate muscle several times but interstimulus interval is NOT so long & NOT too short

→ That would be "incomplete tetanus"

Complete tetanus



When you stimulate the muscle even more, higher rates, fregently.

→ There is No Time for the muscle to relax

→ That would be "complete tetanus"

Q26. How would you call the depolarization in case of skeletal m? ⇒ end plate potential

Q27. How can you block the nicotinic Ach Receptor? ⇒ Curare

Date

If you inject Curare to Kristof. what can he do or NOT

Q28. Can he hear you ? ⇒ yes

Q29. If his eye open, Can he see you ? ⇒ yes

Q30. Can he feel pain ? ⇒ yes

Q31. Can he move his muscle ? ⇒ No

Q32. Can he just make eye blink ? (まばたき) ⇒ No (∵ skeletal m)

Q33. How his HR & BP change when you inject Curare and cause him pain ? ⇒ increase

Q34. Why HR & BP increase above ? ⇒ Loven reflex ∵ pain

Q35. How do you call the Curare in clinical practice ? ⇒ (d-) tubocurarine

Q36. If you put frog muscle-nerve preparation to the 1% Curare solution and incubate 10 min (both sciatic n. & gastrocnemius m.) and then you remove it from Curare solution and stimulate directly & indirectly. what happen !? ⇒ direct … muscle contraction
indirect … No muscle contraction

Q37. Why we call "indirectly" ? ⇒ Because you stimulate the nerve and then nerve stimulate the muscle.

Q38. When you place only sciatic n to the Curare solution. muscle is outside … do same thing. what happen ? ⇒ direct … muscle contraction
indirect … 〃
∵ nicotinic Ach-R is located in muscle. so Curare doesn't affect it.

Q39. You stimulate the nerve-muscle preparation indirectly. and you can NOT get the muscle contraction at all. what can be the problems ? (There is NO Curare Now) ⇒ 1) nerve is NOT intact
double checked by
2) stimulator is just a piece of shit
3) muscle is 〃
4) stimulus intensity is below threshold

Date

Q40. Can you imagine the situation when the excitability increases around anode ? ⇒ Yes Anode break excitation (when switch off)

Q41. which is stronger cathode make excitation or anode break excitation ? ⇒ Cathod make excita

Q42. When you start stimulation , which is negative ? ⇒ Cathode

Q43. How could you memorize it ? ⇒ I'm a dog person. I don't like cat . = ⊖

Q44. When you apply medium stimulus intensity when would you get the muscle contraction ? Both ⇒ When I switch on & off

Q45. 〃 weak stimulus below threshold ? ⇒ never

Q46. 〃 weak but threshold stimulus ? ⇒ when I switch on

Q47. strong ⇒ when I switch on

Q48. How would you call the cell membrane of skeletal m. ? ⇒ Sarcolemma

Q49. 〃 cytoplasm 〃 ⇒ Sarcoplasm

Q50. If there is NO Ca^{2+} ATPase on the L tube. what happen ? ⇒ Rigor (mortis) = increase muscle tone & small movement as well

Q51. Tell me the location of Ryanodine Receptor ? ⇒ wall of terminal cistern

Q52. inside the T tubule, there is IC or EC space? ⇒ Extracellular

Q53. which one is the Ca^{2+} channel in case of the skeletal m ? ⇒ Ryanodine Receptor

Q54. which one has the voltage sensor ? ⇒ DHP-R

Q55. How long is the titin molecule ? ⇒ as long as sarcomere

Q56. What does A band contain ? ⇒ both thin & thick filament

Date

Q57. What does I band contain ? ⇒ only thin filament

Q58. H ⇒ only thick filament

Q59. If there is muscle shortening
which band will be shorter ? ⇒ H band & I band (Hi band :))
(A band would be the same)

Q60. What does tropomyosin-troponin complex contain ? ⇒ 1) 1 tropomyosin
2) 1 troponin C
3) 1 troponin I
4) 1 troponin T

Date

skeletal m.

I	IIa	IIb
- red muscle	in b/w.	- white muscle
- myoglobin ↳ O2 storage		- glycogen rich
		- Anaerobic → Lactate glycolysis
- rich in capillary		
- Aerobic glycolysis takes place		- fast muscle twitch is faster!
		- stronger
- slow		
		- fatigue early
- antigravitation muscle ↳ do NOT get tired early		

you can sit (stand) for a long time because of Type I antigravitation skeletal m.

Q1. What is the optimal size of the sarcomere to exert max. power ? ⇒ 2 ~ 2.5 μm

Q2. What does the A band contain ? ⇒ both thin & thick filament

Q3 Where is the ryhodine receptor located ? ⇒ wall of terminal cistern

Q4. 〃 DHP receptor 〃 ? ⇒ wall of T tubule

Q5. Which of them has voltage sensor ? ⇒ dihydropyridine Receptor

Q6. How can you evoke the (complete) tetanic muscle contraction ? ⇒ 30 - 40 Hz stimulation

Q7. 〃 incomplete tetanic m. contraction ? ⇒ around 5 Hz stimulation

Q8. What is the superposition ? ⇒ You need to apply twin stimulus.
2nd contraction is more significant.
(muscle is more shorter)

Date

* single unit means that whole smooth m. contract at the same time.

Smooth m.

** multi unit means that each smooth m contract independently.

* single unit

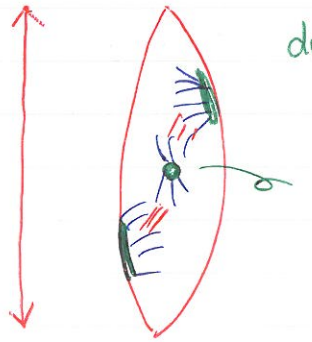
- uterus
- respiratory m.
  - bronchi
  - bronchioli

multi-unit **

- pupillary m.
  - pupillary sphincter
  - pupillary dilator
- arrector pili @ hair

structure of the smooth m.

* in smooth m, There is NO salcomere
No Z line, No tropomyosin-troponin complex



length : max. 500 um

dense plague ... supporting structure for smooth m. actin
it is on the wall of smooth m.

smooth m. actin

dense body ... in myoplasm

instead of Z line, smooth m has dense plague & dense body

smooth m. myosin ... in b/w smooth m. actin

ϕ : 2-10 um cf. skeletal m. ϕ : 50-100 um

ratio b/w $\frac{\text{actin}}{\text{myosin}} = \frac{13}{1}$ cf. in case of skeletal m. $= \frac{2}{1}$

Q9. How do you block the muscle type nicotinic Ach-R ? ⇒ Curare, tudocurarine (clinical)

Q10. How can you evoke the muscle contraction under the curare solution ? ⇒ to stimulate directly to the muscle

Q11. How long is the titin molecule ? ⇒ length of a whole salcomere

Q12. what is the function of Troponin I ? ⇒ to inhibit the actin-myosin interaction

How the muscle contraction going on !?

Date

steps of smooth muscle contraction

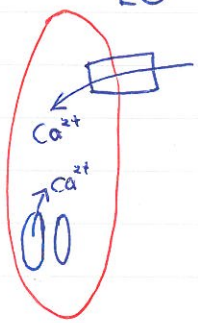
↳ 4 Ca^{2+} - calmodulin

if there is Ca^{2+}, Ca^{2+} can bind to Carmodulin. Carmodulin is a regulatory protein. Ca^{2+} - carmodulin complex activate MLC kinase.

activation

EC

myosin - light chain kinase



sarcoplasmic Reticulum

relaxation

actin - myosin

ATP ADP

Contraction

actomyosin phosphate complex

Phosphate group connect actin & myosin

myosin light chain Phosphatase

Ca^{2+} source ... half from extracellular
the other half from sarcoplasmic reticulum.

Q13. what is the angle of the myosine head & neck in case of the relaxation ? angle b/w myosine head & neck. ⇒ 90°

Q14. " in case of contraction ? ⇒ 45°

Q15. Which muscle is faster Type I or Type IIb ? ⇒ Type IIb

Q16. what makes Type I skeletal muscle red ? ⇒ myoglobin & rich in capillary

Q17. what is the function of myoglobin ? ⇒ O_2 storage

Q18. Type I muscle does Aerobic or Anaerobic glycolysis ? ⇒ Aerobic

Q19. Why Type IIb muscle is white ? ⇒ glycogen rich, less myoglobin less capillary

Q20. Which muscle is dominant in marathon runner ? ⇒ Type I skeletal m.

Q21. What is the Ca^{2+} source in skeletal m ? ⇒ intracellular only

Q22. in smooth m ? ⇒ both intra / extracellular

Q23. in cardiac m ? ⇒ "

Date

Smooth m. vs skeletal m.

Smooth m.		skeletal m.
- autonomic (involuntary)	innervation	- somatomotor (voluntary) nervous system (main innervation!)
		- autonomic → can modify the function e.g. vasodilation in skeletal m. ($\because \beta_2$-R)
only vessels are innervated by autonomic nervous system - sympathetic innervation - vasodilation		
minus - 40 ~ - 70 mV (unstable)	resting membrane potential	minus - 90 mV (stable)
longer than 100 ms	duration of AP	4 ~ 6 ms
- ligand gated Ca^{2+} channel - Voltage gated Ca^{2+} channel - K^+ channel	channels	- ligand gated Na^+ channel → muscle type nicotinic Ach R in the NMJ - Voltage gated Na^+ channel - K^+ channel (important for repolarization)
AP ← generated by Ca^{2+} influx		AP ← caused by Na^+ influx
- dens plague - dens body	Supporting structure of actin	- z lines
- IC + EC	Ca^{2+} source	- IC.

Q 24. What is the phosphate source in smooth m ? ⇒ ATP

Q 25. Which muscle is longer ? skeletal or smooth m ? ⇒ skeletal m.

Q 26. " wider ? ⇒ skeletal m.

Date

different types of smooth m.

Name	innervation	NT	Receptor	function
Pupillary dilator m.	sympathetic	NA, A	α_1 - R	mydriasis (pupil dilation)
Pupillary sphincter muscle	parasympathetic	Ach	muscarinic Ach - R	myosis (pupil constriction)
erector pili m.	sympathetic	NA, A	α_1 - R	pilo erection - animal looks bigger
smooth m. in vessels	sympathetic	NA, A	β_2 - R α_1 - R	vasodilation vasoconstriction
bronchi bronchioli	sympathetic	NA, A	β_2 - R	bronchodilation ∵ need more O_2
	parasympathetic	Ach	muscarinic Ach - R	bronchoconstriction
sphincters	sympathetic	NA, A	α_1 - R (α_2 - R)	sphincter constriction
smooth m. in GI tract	sympathetic	NA, A	α_1, α_2, β_2	digestive motility ↓ GI juice production ↓
	parasympathetic	Ach substance P neurotensin	muscarinic	digestive motility ↑ GI juice production ↑

Q27. Where can you find β_3 - Receptor ? ⇒ in adipose tissue

Q28. What is the function of the β_3 - R ? ⇒ lipolysis (break down of the lipid)

Date

Lab Questions

Q: How can you see that there is a proestrus ? ⇒ There are nucleated epithelial cells

Q: " estrus ? ⇒ There are anucleated epithelial cells

Q: what is the dominant cell type in the metaestrus ? ⇒ leukocytes

Q: " diestrus / anestrus ? ⇒ only few cells are present those are mainly leukocyte

Q: in human, the proestrus is what? which phase ? identical to what ? ⇒ proliferative phase / follicular phase
uterus ovary

Q: " metaestrus & anestrus ? ⇒ secretory phase / luteal phase

Q. How long is the phase ? ⇒ about 1 day each phase whole period : 4-5 days

Q. what kind of rat do you need here ? ⇒ adult female rat
to vagina
+ Physiological saline solution + eye dropper
→ place on the slide → dry

Q. what is the dye solution ? ⇒ methylene blue incubation time : 10-15 min

pregnancy test

Date

We use immunological method (we didn't use biological method this year)

= male frog test カリーマイニーテスト ?

… we inject the urine (♀) under the skin of the frog (♂)

if there are hCG in the urine (♀), hCG stimulate the sperm in the frog (♂)

(increase the motility of sperm

1) Pregnancy stick test

invalid　positive　negative　invalid

Q: Which Antibody do we use in immunological method ? ⇒ anti β hCG Antibody

Q: hCG is belonged to which hormone family ? ⇒ glycoprotein

LH . FSH . TSH as well

Q: Can you recall the subunits ? ⇒ α & β

Q: which is identical ? ⇒ α is identical

β is different

Q: Tell me the reason why the test can be false positive . ⇒ if ♂ … Testicular cancer

♀ - after menopause*

- Choliocarcinoma

↳ hCG producing tumor

- mola hydatidosa

(hydatidiform mole)

- Wilms Tumor → kidney tumor

* Normally , Estradiol & Progesteron have negative feedback on FSH & LH production

⇒ after menopause , Estradiol level is low → So No negative feedback

↓

FSH ↑

LH ↑

← FSH & LH are similar to hCG ← false positive !

Q: 〃 false negative . ⇒ - if hCG level is NOT high enough

↳ Test again 1 week later .

Q: When do you think that the pregnancy test is positive ?

How many days after the fertilization ? ⇒ about 2 weeks

Date

w 8

Date Mar 23 · Fri

Fetus is inside uterus, after the delivery period uterus becomes very small.

Q1. Muscle shortening is more significant in case of Smooth m or skeletal m ?
⇒ Smooth m.

Q2. duration of AP is longer in smooth m. or skeletal m. ?
⇒ Smooth m ... > 100 ms
cf. skeletal m ... 4-6 ms

Are their structures in smooth m. or skeletal m. ?

Q3. troponin C
⇒ only in skeletal m

Q4. Calmodulin
⇒ only in smooth m.

Q5. what's the function of calmodulin ?
⇒ Ca^{2+}- calmodulin complex activate MLC kinase
Myosin Light chain

Q6. Z line
⇒ only in skeletal m.

Q7. actin
⇒ both

Q8. myosin
⇒ both

Q9. nebulin
⇒ only in skeletal m.

Q10. List thin filament in skeletal m.
⇒ 1) actin 2) nebulin 3) troponin I
4) troponin C 5) troponin T 6) tropomyosin

Q11. what's the function of Ryanodine Receptor in skeletal m. & in cardiomyocyte ?
⇒ Skeletal m ... activated by DHP Receptor & release Ca^{2+} from terminal cistern
⇒ Cardiomyocyte ... Ryanodine R is Ca^{2+} activated Ca^{2+} cha

Q12. what does DHP-R do ?
⇒ skeletal m ... 1) conformation change by detecting voltage
2) open Ryanodine R
⇒ Heart m ... DHPR = Ca^{2+} channel ⇒ Takes extracellular Ca^{2+}

Q13. Tell me connection b/w cardiomyocyte ?
⇒ gap junction

Q14. Tell me innervation of Pupillary dilator m.
& NT, Receptor, function
⇒ sympathetic
NA, A
α_1-R
mydriasis
(dilation of Pupil)

Date

Q15. Tell me the innervation of vessels ?
& Receptors ? functions ?
⇒ only sympathetic
α_1-R ··· vasoconstriction
β_2-R ··· vasodilation

Q16. which one has spontaneous activity (contraction)
antrum or aorta ?
⇒ antrum

Q17. antrum is part of what ?
⇒ GI tract (stomach)

Q18. Tell me the pacemaker cell of GI tract .
⇒ Cajal cell (Name of spanish guy.)

Q19. When you apply A. NA to the aorta preparation
what would be the effect ?
⇒ Vasoconstriction
(∵ There're α_1-R in aorta)

Q20. How can you block α_1-R ?
⇒ Phentolamine

Q21. " β-R ?
⇒ Propranolol

Q22. What is atropine?
⇒ Muscarinic Ach R blocker

Q23. what is the verapamil ?
⇒ Ca^{2+} channel inhibitor
(L type)

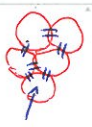
Q24. which one would inject to prevent both
smooth m. constriction of antrum & aorta ?
⇒ verapamil

Q25. Speaking of the mechanism of the AP
in the skeletal m. which ion influx is needed ?
⇒ Na^+ influx

Q26. in the smooth m. ?
⇒ Ca^{2+} influx

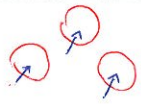
Q27. Tell me the example of single unit smooth m.
⇒ 1) uterus 2) bronchi 3) bronchioli

Q28. what does " single unit " mean ?
⇒ whole smooth m works as 1 unit
∵ cells are connected via gap junction



Date

→ pupillary sphincter
→ pupillary dilator



Q 29. Tell me example of multi unit smooth m. ⇒ 1) Pupillary m. 2) arrector pili

Q 30. Tell me the EMG signal if you relax the muscle completely. ⇒ isoelectric line (flat line)

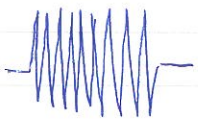
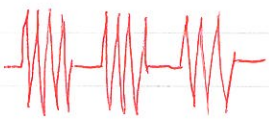
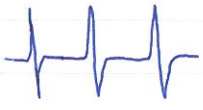
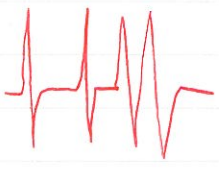
EMG (Electro Myo Graphy)

with a EMG, we can record the electrical activity of a skeletal m

2 Types

surface electrode (we did in Lab)
- it's NOT dangerous, painful but
- w/ surface electrode, you would see all the electrical activity of whole muscle
- (you can NOT distinguish motor unit potential)

deep electrode (needle electrode) → put the needle into the muscle
- ↳ we can record motor unit potential ... precise detection
- ∵ it can see one motor neuron w/ the innervated muscle fibers
- ↓
  - Painful
  - may cause infection

	Normal muscle	Neurogenic lesion	myogenic lesion
		could be car accident ... problem w/ motor neuron (motor fibers are injured)	problem w/ muscle itself
spontaneous activity		 Small muscle contractions are present	
you need to ask your patient to relax the muscle		fibrilation	there is No problem w/ motor neuron ⇒ There is No spontaneous activity
		why!? ⇒ normally Ach bind to muscle type nicotinic Ach R but in Neurogenic lesion There are less motor neuron → less Ach released	
		That's why the Receptors become extremely sensitive (Hypersensitive)	
		⇒ And w/ diffusion of some Ach molecule can get there & activate its Receptor which is so sensitive	
Maximum contraction	 complete interference	 No complete interference	 complete interference w/ low amplitude
	∵ at the same time, thousands of motor fibers & thousands of motor units are activated ⇒ You can NOT distinguish b/w different motor units ∵ They're happening at the same time.	less motor neuron ↓ less motor unit potentials	There is motor unit potential ↑ There is NO problem w/ motor neuron but there is problem w/ muscles ⇒ muscles give smaller electric signals
motor unit potential	 biphasic & triphasic waves	 giant potential	 normal biphasic / triphasic waves but low amplitude
		∵ Receptors are extremely sensitive → There is more Na^+ influx ⇒ Amplitude of Potential is bigger than normal	

※ this is kinda opposit as Type II diabetes mellitus
∵ large amount of insulin would decrease the sensitivity of the insulin Receptor so there is a disensitization

Date

Somato Sensory System

Dorsal Column Medial Lemniscus System (DCML)

In this system. You can feel the ...

- Proprioception
  ... you can tell the position of Joint, muscle
- vibration
- fine touch
  - ↳ graphesthesia (背中に書いた数字が分かるアレ)
  - ↳ 2 point discrimination

} epicritic sensation

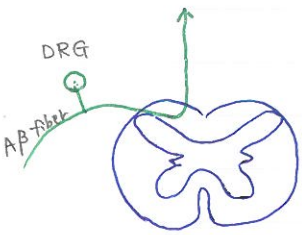
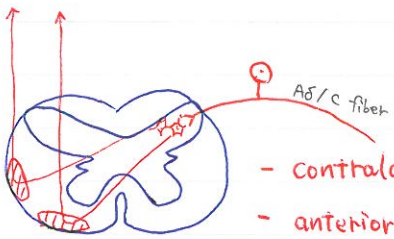
Q: which part of the body is the best for 2 point discrimination? ⇒ Lip

Q: If you touch your finger on ice OR I touch 2 pens on your finger, which information would get earlier to your brain ?
⇒ 2 point discrimination DCML

spinothalamic system = anterolateral system

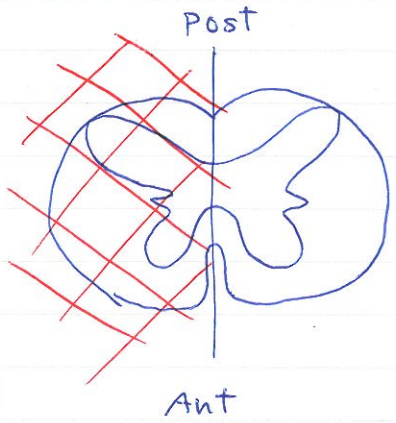
- pain
- Temperature
- Crude touch

} protopathic sensation

	Aβ fiber	Aδ, C fiber
termination	post central gyrus @ Parietal lobe Br. 3, 1, 2	Same as DCML
location of Pathway	 w/o synapse w/o decussation goes up to the brain ∴ - ipsilateral - dorsal column	 - contralateral - anterior / lateral
site of decussation	- medial lemniscus system @ brain stem	- spinal cord at the level where somatosensory neurons enter
1st synapse	- cuneate nucleus / gracilis nucleus	- spinal cord a dorsal horn

Date

Brown Sequard Syndrome



e.g.
Thoracic Level
T5. T6

when half of the spinal cord is destroyed.

Right leg

↳ can feel
pain, Temp, crude touch
(∵ spinothalamic tract = contralateral)

↳ can NOT feel
- proprioception
- vibration
- fine touch
  - graphesthesia
  - 2 point discrimination

(∵ DCML = ipsilateral)

Left leg

↳ protopathic sensation is lost
(can NOT feel
pain, Temp, Crude touch)

Q: What kind of sensory quality is lost below the injury?		Protopathic	Proprioception / epicritic
	⇒ injured side	○	× (Not fee
	the other side	×	○

Q. If I can NOT feel 2 point discrimination in my left hand & I can NOT feel Temp with my Right hand, Where is my problem?

⇒ Left half of spinal cord at the level upper than C5 - T1 (brachial plexus)

Q. What can be survive if you have a lesion at the T7, T1, C6, C4? which is lethal?

⇒ C4 (∵ Phrenic n. innervates diaphragm)

Date

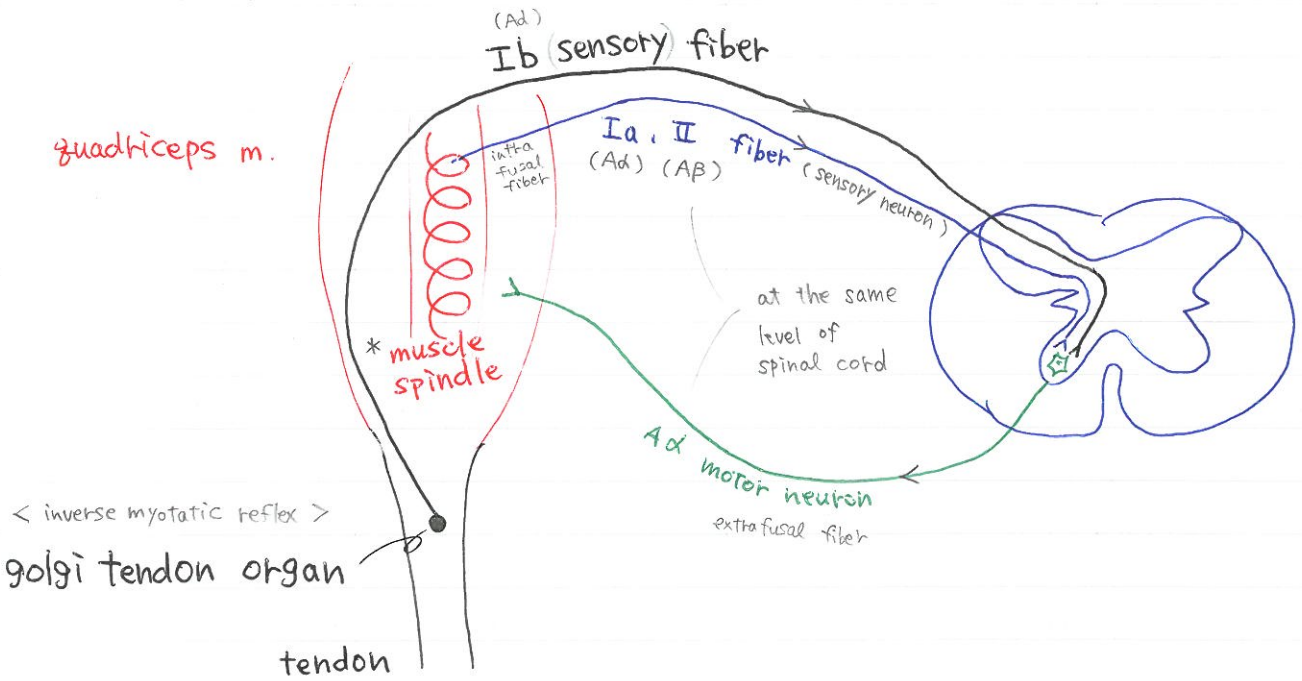
reflex

2 main types !

① Proprioceptive reflex / monosynaptic reflex / myotatic reflex / deep reflex

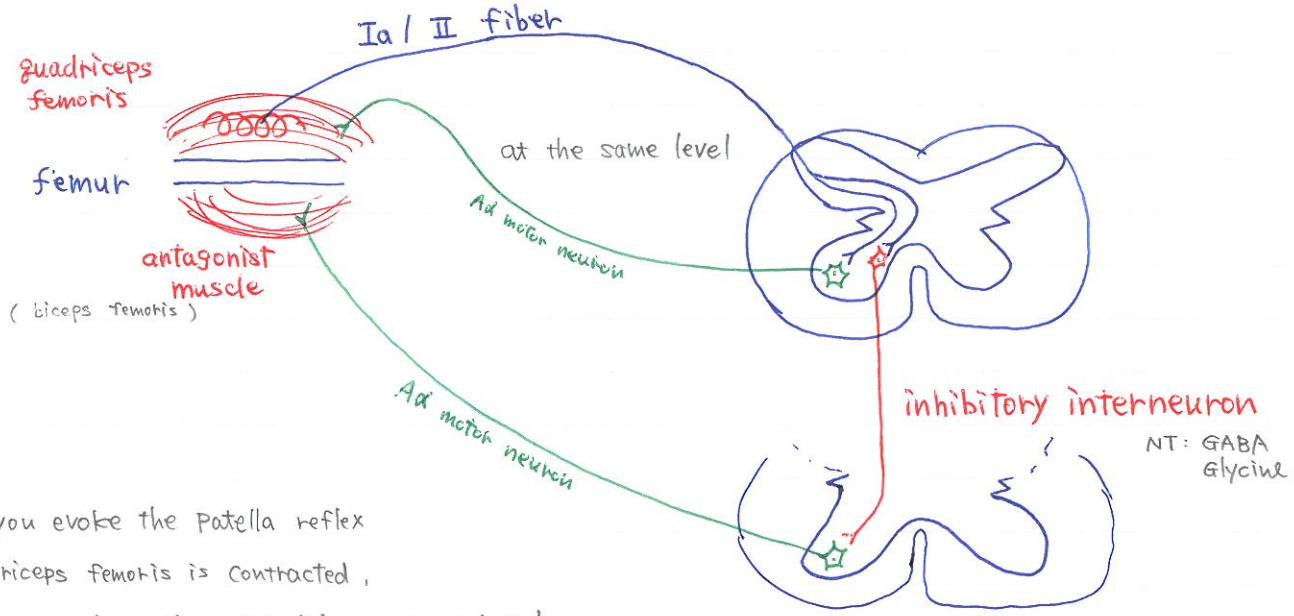
reflex arch

< anterior view >



* muscle spindle can detect both dynamic & static stretch !

< lateral view > when a muscle is contracted, the antagonist m. is relaxed at the same time



※ When you evoke the patella reflex

→ quadriceps femoris is contracted,

at the same time, the antagonist m. are relaxed.

(biceps femoris
semitendinosus
semimembranosus)

You can examine this part is intact or NOT ↓

Receptor が muscle にある！

Date

Proprioceptive reflex (続)

	reflex center	instruction
1) masseter reflex	Pons	open the mouth & just relax it → you put your finger on the chin & hit your finger by reflex hammer ⇒ close the mouth by masseter m. contraction
2) biceps reflex	C5 - C6 segments	you just put your finger over the biceps tendc & hit you finger by reflex hammer ⇒ Flexion & Supination of biceps brachii
3) Triceps reflex	C6 - C8 segments	you need to hit Tendon of Triceps brachii ⇒ reflex response is Extension
4) brachioradial reflex	C5 - C6 segments	you need to put your finger over the distal radius & hit your finger ⇒ reflex response is Flexion & Supination
5) brachioulnar reflex	C7 - C8 segments	you need to put your finger over the distal ulna & hit your finger ⇒ response is Extension at the elbow
6) abdominal muscle reflex	Th8 - Th12 segments	The patient is lay in the back & below the Ribs You need to hit the muscle / tendon ⇒ response is Contraction of abdominal m.
7) Patellar reflex	L2 - L4 segments	you need to hit the tendon of quadriceps femoris ⇒ reflex response is Extension at knee joint
8) ankle jerk reflex / achilles tendon reflex	S1 segment	you need to hit the achilles tendon w/ reflex hammer ⇒ reflex response is Plantar flexion.

Date

② Exteroceptive reflex / polysynaptic reflex / skin reflex / surface reflex

1) Corneal reflex
- sensory n ... ophthalmic n. (V/1)
- motor n. ... facial n.

You need to touch Cornea w/ clear cotton wool from lateral view (out of visual field)
⇒ reflex response is Eye blink

2) Pharyngeal reflex
- IX (glossopharyngeal)
- X (vagus)

You need to touch the posterior wall of pharynx
⇒ response is gargling ? Vomitting Coughing

3) mamillary reflex — Th4 segment

You need to touch nipple w/ cold object
⇒ response is nipple erection

4) superficial abdominal reflex — Th7 - L1 segments

You need to scratch the surface of abdominal skin
⇒ response is ipsilateral muscle contraction

5) Cremaster reflex — L1 - L2 segments

You need to scratch the medial part of the Thigh
⇒ response is ipsilateral testicle is elevated

6) Plantar reflex — S_1 - S_2 segments

You need to scratch the lateral part of the sole
⇒ Physiological response : Plantar flexion

★ Pathological response : dorsal flexion

Babinski reflex / sign ... pyramidal tract lesion

7) anal reflex — S4 - S5 segments

You need To touch anus w/ cold object
⇒ response is anal sphincter constriction

※ You need to know ① How to evoke the reflex ?
② what is the reflex response ?
③ what is the reflex center ?
④ proprioceptive or exteroceptive ?

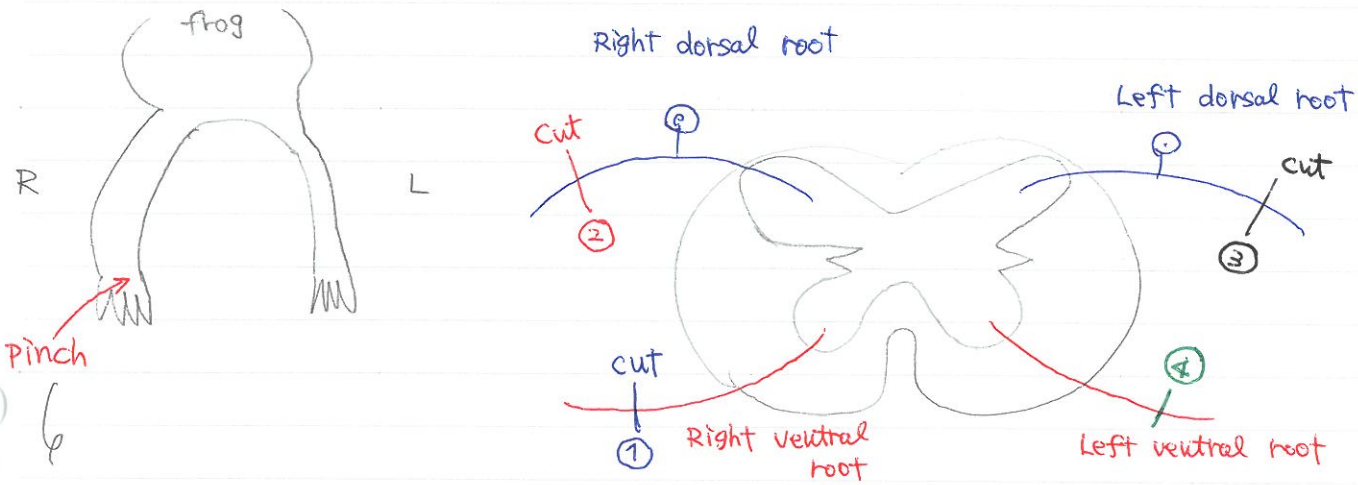
Q. If patient has Babinski reflex, What's the problem ? ⇒ pyramidal tract lesion

↱ ipsilateral flexion
contralateral extension

Date Mar 26 mon.

Flexor caused extensor reflex ... can be evoked in human as well

For example, when you stuck the sharp object (needle, glass) on the floor ⇒ You make the flexion on the same side (ipsilateral flexion) & extension contralaterally



You cause the pain on the Right side

⇒ ⓪ ipsilateral flexion & contralateral extension (intact)

① ONLY contralateral extension

(∵ sensory information can get into the spinal cord
but ipsilateral motor fibers are cut so there is NO ipsilateral flexion
but contralateral motor fibers are intact !)

② No Response (∵ sensory info couldn't come to the spinal cord)

③ Both ipsilateral flexion & contralateral extension

④ only ipsilateral flexion

Bell - Magendie law

- anterior fiber is motor fiber
- posterior fiber is sensory fiber

Date

No head off , whole nervous system is still working

intact frog

	what is examined	instruction
1) corneal reflex	(aff) V/1 (eff) VII	touch the cornea ⇒ eye blink
2) Turning reflex	vestibular system	you need to place the frog on its back ⇒ frog turn back to the original position
3) Compass reflex	vestibular system (※ Not visual system !!) ∵ frog can NOT see out of the chamber.	you need to place the frog in a chamber & rotate the chamber clockwise ⇒ frog turns anticlockwise (against the rotation)
4) inmobility reflex / motionless reflex (freezing reflex)	a lot ...	You need to place the frog on its back & you need to press the sternum for a few sec & release slowly w/o touching legs ⇒ frog is NOT moving (playing dead) ↳ プレデターに食べられない為のreflex.

spinal frog (only spinal cord is intact) ⇝ head is removed.

grasping reflex can NOT be evoked on spinal animals (2018. mid)

when you decapitate the frog, there is a spinal shock.
spinal shock is shorter in frog (mins) than human (weeks).

1) wiping reflex — you need to put acetic acid paper on the skin of the frog ⇒ w/o head, frog can still feel that the acid is dangerous to the skin ⇒ frog wipe it away.

2) reflex time — you can measure, you need to place one of the leg into the acetic acid solution & measure the time
↳ higher c.c. ⇒ reflex time is shorter.

3) embrassing reflex (hugging reflex) — you need to put your finger on the chest ⇒ frog will hug your finger (mainly in male frog) ∵ spring is meeting period & poor frog think it female frog.

4) Brondgest phenomenon — You need to put the decapitated frog on the hook ⇒ hind leg is NOT hanging passively But there is flexion. (flexor tone)
↳ proprioceptive reflex ← ∵ gravity force stretch the muscle spindle & this info is taken to the spinal cord ⇒ agonist muscle is contracted)
↳ flexor tone

※ For proprioceptive reflex, intact sensory & motor fibers are needed.

Q: if you cut the Left anterior fiber, which leg can be flexed ? ⇒ Right leg

Date

Basal ganglion

① ⇒ cortex → striatum ⊣ substantia nigra ⊣ Thalamus

NT: glutamate

① The motor information is coming from the cortex. From the cortex, Striatum receive some fibers (excitatory fiber) And Striatum can innervate the substantia nigra, substantia nigra receives inhibitory fibers from Striatum (NT: GABA) From the substantia nigra to the striatum, there are dopaminergic pathways which is called "nigrostriatal dopaminergic system". From the substantia nigra, there are inhibitory fibers which innervate the Thalamus. (NT: GABA)

⇒ If this loop is active, Thalamus is activated (∵ inhibition of the inhibition = disinhibition = activation)

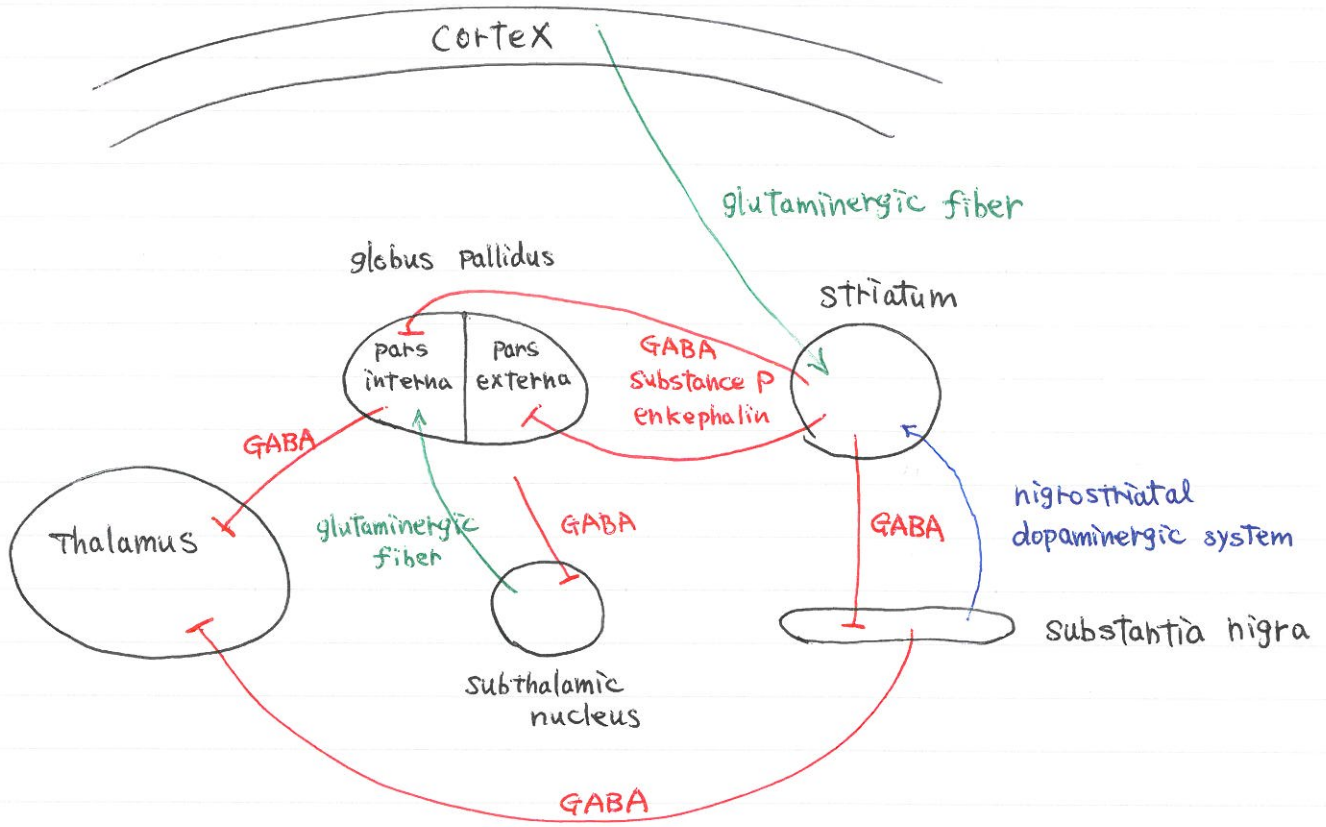
② There is an other main structure which is "globus pallidus = Pallidum" and it has "pars externa" & "pars interna". And both of them receive GABAergic pathway (inhibitory) from the striatum (NT: GABA. substance P. enkephalin) From Pars interna of globus pallidus, inhibitory fibers are going to the thalamus.

⇒ cortex → striatum ⊣ Pars interna ⊣ Thalamus (disinhibition! = activation)

③ Subthalamic nucleus receives GABAergic fibers from the Pallidum & From Subthalamic nucleus there are glutaminergic pathway to the Pars interna of the pallidum (indirect pathway)

Thalamus is inhibited

⇒ cortex → striatum ⊣ Pars externa ⊣ subthalamic nucleus → internal pallidum ⊣ Thalamus ⇒ inhibition



Q: if ③ indirect pathway (inhibition) is NOT working, what would be the symptom?

⇒ Hemiballism .. involuntary big movement in one side

contralateral

↳ caused by : injury of Subthalamic nucleus
injury of pathway b/w pallidum & subthalamic nucleus

if Left subthalamic nucleus is injured, ⇒ you can observe Hemiballism on the Right side.

Date

Q: What is the name of the disease which is present in the nigrostriatal dopaminergic system is NOT working properly ?

Parkinson's disease ... extracellular dopamine level is very low

Treatment

- deep brain stimulator which is implanted to the basal ganglion (striatum). There is battery under the skin
  - final option (∵ invasive, dangerous treatment ∵ brain infection) in Pécs 6-8 operation / week
- L-DOPA ... can pass through BBB (Blood Brain Barrier) * Dopamine can NOT.

symptoms

- Resting themor *
- rigidity (increased muscle tone)
- bradykinesia (slow movement)
  hypokinesia (small ")
  akinesia (NO ") ... can NOT move at all
- micrography (extremely small letter)
- postural instability
  - Q: How do you examine ? => You grab the patient's shoulder & pull toward you
    => Parkinson's patient can NOT hold their balance.
- increased salivation ... cholinergic system > dopaminergic system is dominant
  ∵ salivary gland is innervated by cholinergic fiber !
- poor facial expression ∵ bradykinesia, hypokinesia, akinesia for facial muscles

* There is another themor which is "intension themor" or action themor.
  - refers to cerebellar disease.

e.g. You would like to take my pen and there is shaking movement

Date

Q1. How can you examine the C5 - C6 segments ?
⇒ 1) biceps reflex 2) brachioradial refle

Q2. L4
⇒ Patellar reflex L2 - L4

Q3. S1
⇒ ankle jerk reflex / achilles tendon reflex

Q4. C8
⇒ 1) Triceps reflex 2) brachioulnar refle
C6 - C8 C7 - C8

Q5. Pons
⇒ masseter reflex

Q6. Th 10
⇒ abdominal muscle reflex Th8 - 12

Q7. List 4 reflexes that you need to put your finger over the tendon & hit your finger by reflex hammer.
⇒ 1) masseter reflex
2) biceps reflex
3) brachioradial
4) brachioulnar
} more important !

Q8. If there is NO pain sensation in the Right leg, & there is NO 2 point discrimination in the Left leg, where is the injury ?
→ spinothalamic pathway (contralateral)
→ DCML (ipsilateral)
⇒ left

Q9. How would you call the disease that the half of the spinal cord is injured ?
⇒ Brown Sequard syndrome

Q10. Speaking of the muscle spindle, it can detect dynamic or static stretch ?
⇒ Both

Q11. What is the type of the sensory neuron which is arise from the golgi tendon organ ?
⇒ Ib

Q12. 〃 muscle spindle ?
⇒ Ia & II

Q13. Can we evoke myotatic reflex if we cut the dorsal root ?
※ myotatic reflex = proprioceptive reflex
⇒ NO
∵ dorsal root is part of the reflex arch.
Both sensory neuron & motor neuron are needed

Date

Q14. Speaking of the inhibition of Q13, which muscles are inhibited ?
⇒ antagonist m.

Q15. Tell me the type of the sensory neuron in case of the vibration feeling.
⇒ Aβ

Q16. 〃 pain, Temp, Crude touch.
⇒ Aδ, C fiber

Q17. Tell me the site of the decussation in case of the dorsal column system ?
⇒ medial lemniscus system

Q18. 〃 spinothalamic system.
⇒ spinal cord at the same level where the somatosensory n. enter

Q19. Tell me the site of first synapse in case of the DCML & spinothalamic tract.
(upper body) (lower body)
⇒ DCML : cuneate nucleus / gracilis nucleus
spinothalamic tract : dorsal horn

Q20. in which system do you think that there is a relay in the Thalamus ?
⇒ Both DCML & spinothalamic tract
∵ Thalamus is the biggest sensory relay !

Q21. Tell me the termination of these pathway.
⇒ post central gyrus @ parietal lobe Br. 3, 1, 2

Q22. where the pathways are located in grey matter or white matter ? in the spinal cord
⇒ white matter

Q23. when there is Brown Sequard Syndrome, is there any motor problem / disability ?
⇒ yes, ipsilaterally !
∵ descending tract (pyramidal tract)
80% : lateral corticospinal tract ··· pyramidal decussation

Q24. if there is brain haemorrhage in the left post central gyrus, which sensory qualities are lost ?
⇒ All sensory quality on Right side
All sensory fibers are contralateral after decussation !

Date

Q 25. if there is a problem in the pre central gyrus, on the Left side
What would be the symptom ? ⇒ can NOT move the Right side.
∵ pyramidal decussation

Lab Questions

Q 26. When you record the EMG, what you can see
in case of spontaneous activity, there is NO electrical activity
// maximum contraction, // complete interference
w/ low amplitude
and when you measure the motor unit potential,
there is biphasic & triphasic waves but small amplitude
What would be the problem ? ⇒ myogenic lesion

✦ Q 27. What is the problem w/ the myasthenia gravis ? ⇒ Autoimmune disease
↳ Antibody is produced against muscle type nicotinic Ach R
That's why muscle is weak & muscle shows fatigue quickly.
because muscle type nicotinic Ach R are blocked by Antibodies

Q 28. What is the muscle type nicotinic Ach R blocker ? ⇒ Curare, tubocurarin

I will give you different reflexes and Just tell me Proprioceptive (P) or Exteroceptive reflex (E)

Q 29. Plantar reflex ⇒ E
Q 30. achilles tendon ⇒ P
Q 31. masseter reflex ⇒ P
Q 32. Cremaster reflex ⇒ E
Q 33. Pharyngeal reflex ⇒ E
Q 34. Corneal reflex ⇒ E

Q 35. Tell me which reflexes can be evoked ONLY in intact frog, w/o decapitation
⇒ 1) Corneal reflex 2) Turning reflex 3) Compass reflex 4) immobility

Q 36. How can you measure the reflex time in frog ?
⇒ you need to put the acetic acid solution to the leg of spinal frog

Q 37. What does summation mean in case of frog reflexes ?
⇒ You need to stimulate the frog's leg w/ electrode, stimulus intensity should below the threshold but when you do it several times at some point it moves the leg

Date Apr 2nd mon. W10

Q1. what does Brondgest phenomenon mean ? ⇒ You need to hang the decapitated frog Then hind leg is flexed.

Q2. And which reflex is this ? ⇒ Proprioceptive reflex

✧ Q3. When you decapitate the frog & you just put it on the hook, you can see flexion immediately after the decapitation or you need to wait ? ⇒ we have to wait ∵ spinal shock (in spinal shock, we can NOT see any of those reflexes)

✧ Q4. How long is the spinal shock in frog & in human ? ⇒ frog : 5-10 minutes human : weeks

✧ Q5. When you pinch the left leg of the frog & you cut the Right Posterior fiber ⇒ ipsilateral flexion & Contralateral extension

Q6. what if you cut Left Posterior fiber ⇒ No Response

Q7. Left anterior fiber ⇒ contralateral extension

Q8. Right anterior fiber ⇒ ipsilateral flexion

Q9. Tell me the symptom if subthalamic nucleus is injured. ⇒ Hemiballism

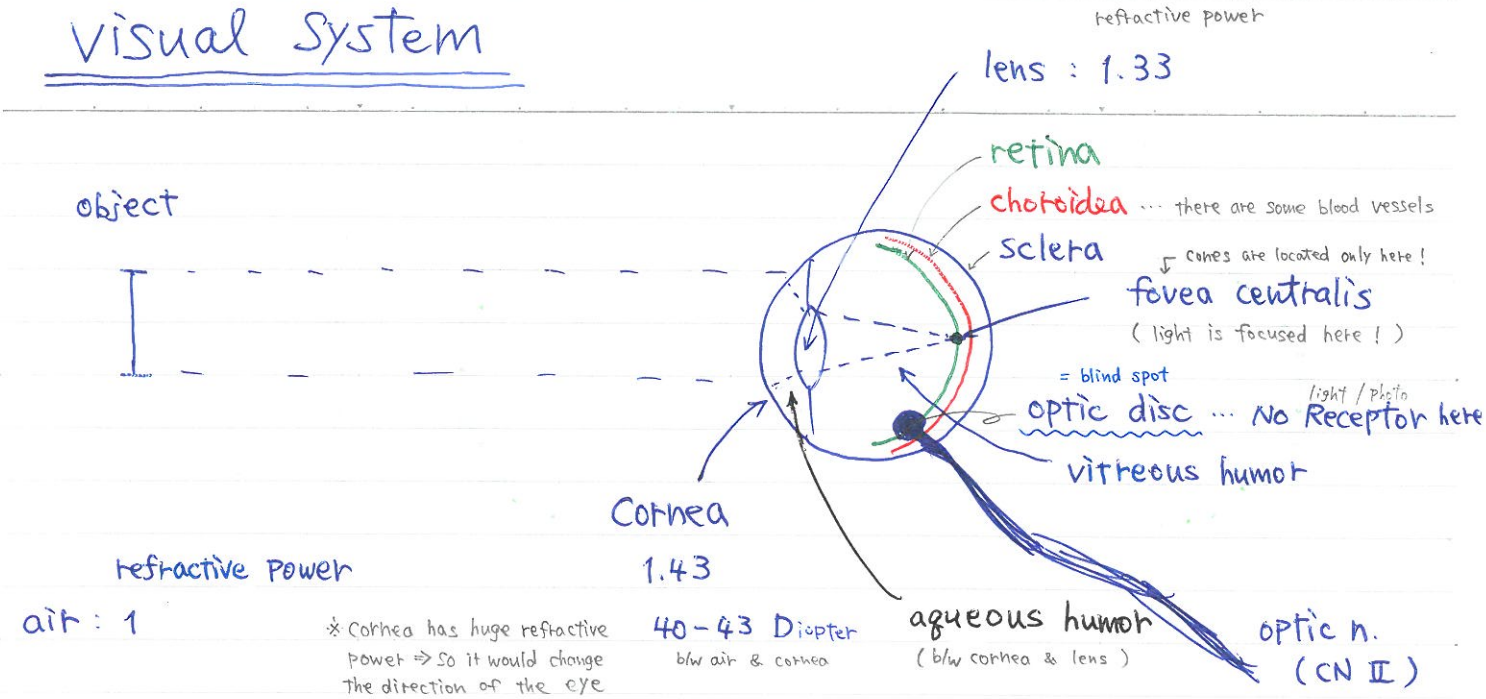
in case of Parkinson's disease

Q10. Tell me the treatment. ⇒ 1) deep brain stimulator, 2) L-DOPA

Q11. Tell me the symptoms ⇒ 1) Resting tremor 2) rigidity (m. tone ↑)
3) bradykinesia / hypokinesia / akinesia
4) micrography 5) postural instability.
6) increased salivation
7) poor facial expression

Date

Visual System



Visual Pathway

Q: which cell can detect the light stimulus in the retina? ⇒ photoreceptor

Q: which is important for color vision ? ⇒ Cones

Light

↓

- Photoreceptor
  - rods ... important in dim light →→ You can NOT see the color but You can see the different shade of grey
  - cones
    - blue cones ... can detect blue light
    - green "
    - red "

↓

- bipolar cell

↓

- ganglion cell

↓ axon of the ganglion cell

- optic nerve

↓

- optic chiasm

↓

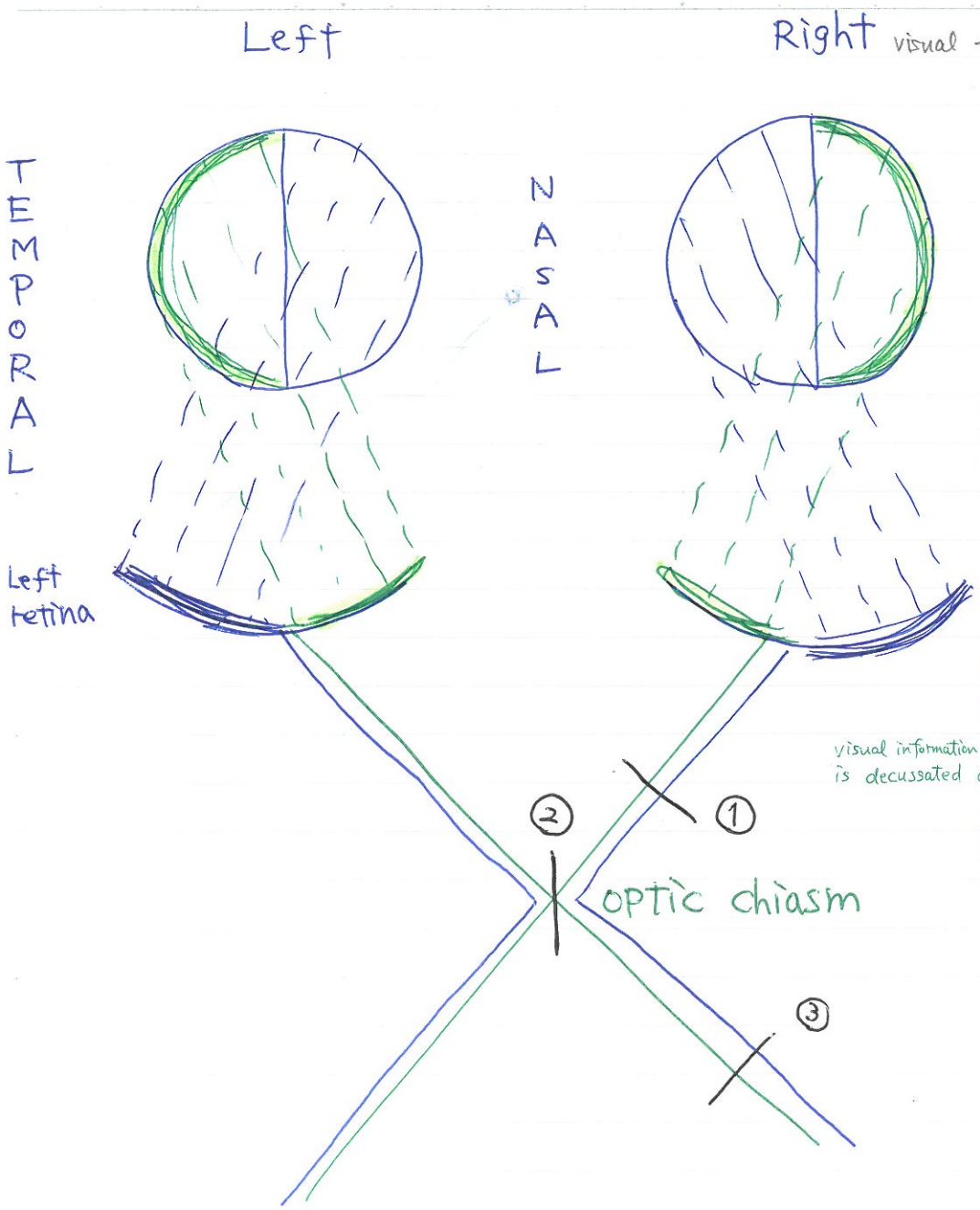
- optic tract
  - → Superior colliculus
  - → Pretectal region
  - → lateral geniculate body ✧ most imp pathway from optic tract
    - ↳ optic radiation

↓

primary visual cortex @ occipital lobe Br. 17 ← process visual info.

Date

Let's see the visual pathway from the other way



From the (temporal) lateral visual field, visual information goes to the medial part of the retina

From the medial part of the visual field, Light enters to the temporal part of retina

visual information which is collected from nasal part of retina is decussated at optic chiasm

meanwhile, visual info which is coming from temporal part of the retina would stay on the same side (No decussation)

Cut		symptom	L	R
①	Right optic n.	→ Right eye anopia		
②	optic chiasm (just cut green fiber)	→ bitemporal hemianopia* ... caused by pituitary gland tumor		Tube vision
③	Right optic tract	→ homonymous hemianopia		

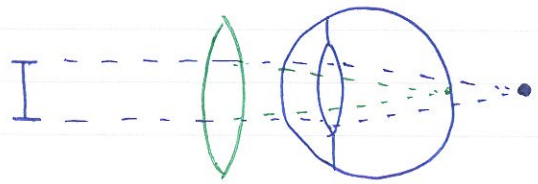
* The patient w/ bitemporal hemianopia should be careful against car accident because of Tube vision (Temporal visual field is lost)

Normally, laser of light are focused on fovea centralis but ... Date

ametropic eye

Hypermetropia (far sighted) 遠視 kristof

... laser of light are broked on focus behind the retina
∵ refractive power is NOT strong enough



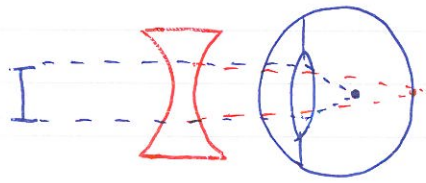
Q: what kind of lens should be given to the patient w/ Hypermetropia ? ⇒ convex lens / positive lens

convex lens
(positive lens)

⟷ longitudinal axis of eyeball ... is usually shorter than normal

Myopia (" short sighted ")

... lase of light are broked on focus in front of the retina
∵ refractory power is stronger than it should be (屈折力)



C.f. Q: By the way, what is "myosis" ? ⇒ pupillary sphincter muscle constriction

Q: what is the pupillary dilation ? ⇒ mydriasis ミドライアシス

Concave lens
(negative lens)

when you are older than 40 years old, every 10 years, refraction power would decrease w/ 1 diopter ∵ lens is more & more rigid

Presbyopia プレスビエピア 老眼 ... with age lens become more rigid / less flexible

↳ There is problems w/ accomodation

⇒ Convex lens

※ when you are focused on the object which is close to the eye, ⇒ lens should be more convex.
But patient w/ Presbyopia can NOT focus on the object which is close to the eye (∵ lens is rigid) ⇒ can NOT accomodate

Astigmatism 乱視 ... cornea is NOT spherical (※ Normal cornea is spherical)

in different angle, refraction is different

⇒ cylindrical lens

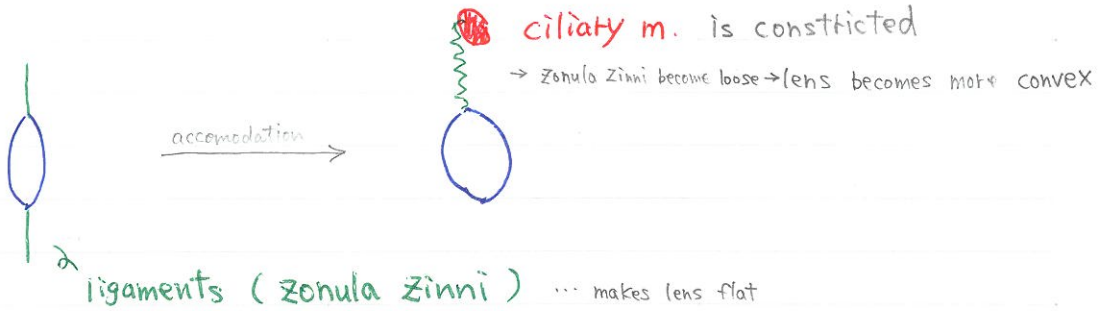
※ speaking of the retina, picture is upside down & smaller than real life

Date

accomodation triad

より近くを見る時

↳ convergence (寄) of eyeball
↳ pupil constriction (∵ accomodation is under parasympathetic control)
↳ lens becomes more convex



↳ ligaments (zonula zinni) ... makes lens flat

Q: when do you use ciliary m. ?
When you focus on the object which is far away or close to the eye ? ⇒ close to the eye

※ when you focus on object which is far away ⇒ ciliary m can be relaxed ⇒ lens would be more flat

Date

Pupil reflex / light reflex

Photoreceptors @ Retina
↓
bipolar cells
↓
ganglion cells
↓
optic nerve
↓
optic chiasm
↓
optic tract
↓
pretectal region
↓
Edinger-Westphal nucleus ~ parasympathetic nucleus ← cell body
↓
parasympathetic preganglionic fiber ← axon
↓ oculomotor n. (CN III)
Ciliary ganglion
↓
parasympathetic postganglionic fiber → Ach
↓
Pupillary sphincter m. ← muscarinic Ach-R ← atropin
↓
miosis (pupillary constriction)

Pupil reflex

When you illuminate one of my eye, There is Pupil constriction in both eye, the opposit eye as well !!

Q: How can you block the pupil reflex ? ⇒ atropin

Q: How would the pupil reflex change if you give me "eserine" or physostigmine ?
it is NOT affected ? or significant or less significant ?

⇒ "eserine" = Acetylcholine esterase inhibitor
= parasympathomimetic agent
⇒ Ach c.c. ↑↑ ⇒ parasympathetic reaction ↑↑
⇒ pupil constriction is even more significant

Date

※ Cones are located only in fovea centralis

Human is trichromate — Brain can mix any kinds of color.

- blue cones
- green cones
- red cones

Problems with red cones

- reduced pigment in red cone ⇒ protanomaly … Red color vision is affected
- red cones are absent or NOT working ⇒ protanopia … Red color blindness

reduced pigment of green cones ⇒ deuter anomaly

green cones are NOT working or missing ⇒ deuter anopia

most frequent problems

(reduced pigment of blue cones)

problem w/ blue cones ⇒ Tritanomaly

blue cones are NOT working at all ⇒ Tritanopia

- it's more freguent in male (∵ color vision is linked to X chromosome)

w 11 Date Apr 9 mon

Q1. What does Presbyopia mean ? ⇒ 1) with age, lens become more rigid
2) There is problems w/ accomodation

Q2. How can you colligate ? ⇒ 3) Convex lens (positive lens)

Q3. What is " Amblyopia " ? ⇒ Problem w/ a visual cortex (弱視)
if you have Hyperwettropia (遠視) or Strabism (斜視),
that would be the double vision in your brain about the given object → Brain shut down one of the eye
∴ Practically, literally, one of the eye become blind.

in early age, what you need to do
You need to cover the good eye & brain should use the other eye which is neglected.

Q4. What is " Astigmatism " ? ⇒ 1) The shape of Cornea is NOT spherical but elipsoid, longitudinal
2) Refraction is different in different angle

Q5. How can you colligate it ? ⇒ 3) Cylindrical lens

Tell me which is NOT part of the visual system

Q6. Thalamus ⇒ yes (∵ lateral geniculate body is part of Thalamus)
Q7. occipital lobe ⇒ yes
Q8. medial geniculate body ⇒ No (∵ This is part of the Auditory Pathway)
Q9. Superior olive ⇒ No (∵ 〃)
Q10. Edinger westphal nucleus ⇒ yes
Q11. ciliary ganglion ⇒ yes (∵ This is part of pupil / light reflex)
Q12. optic radiation ⇒ yes
Q13. Superior colliculus ⇒ yes

✧Q14. When the photon is absorbed, photoreceptor is Hyperpolarized or Hypo / depolarized ? ⇒ Hyperpolarization is the signal for the brain
↳ photoreceptor also hyperpolarize the bipolar cell
(Bipolar cell is also hyperpolarized !)

Q15. Which of the visual field is lost in chiasma lesion ? ⇒ bitemporal hemianopia 

Q16. What if you cut the left optic tract ⇒ homonymous hemianopia 

Date :

Q17. How can you colligate the far sightedness ? ⇒ convex lens (positive lens)

Q18. what is the name of far sightedness ? ⇒ Hypermetropia / Hyperopia 遠視

Q19. How can you colligate the near sighted ? ⇒ concave lens (negative lens)

Q20. in case of near sightedness , longitudinal axis of the eye ball is usually longer or shorter ? ⇒ longer

Q21. what is deuter anopia ? ⇒ There is NO green color vision
∵ green cones are NOT working at all or missing

Q22. What is the problems of Blue ? ⇒ Tritanomaly , Tritanopia

Q23. if there is a problem w/ red cones ? ⇒ protanomaly , protanopia

✧Q24. which pigment can absorb the light ? ⇒ ① rhodopsin @rods ② iodopsin @cones

rhodopsin consists of 2 parts
- opsin
- retinal

11-cis-retinal —light→ trans-retinal
(cis conformation)

(This is the molecular mechanism which is going on in your photoreceptors)

Q25. which vitamin is important for the Photoreceptor ? ⇒ Vitamin A

Q26. what is the main problem w/ vitamin A deficiency ? ⇒ problem w/ dim light

Q27. which receptors are affected first w/ V.A. def. ? ⇒ rods ∴ after sunset we can NOT see that much

Q28. which receptor is ONLY active during day time ? ⇒ only the Cones
when illumination is good

Q29. List the chronological order of visual pathway ? ⇒ ① photoreceptor, ② bipolar cell, ③ ganglion cell, ④ optic nerve
⑤ optic chiasm, ⑥ optic tract, ⑦ superior colliculus
⑧ pretectal region, ⑨ lateral geniculate body
⑩ optic radiation, ⑪ primary visual cortex
@ occipital lobe Br. 17

Date

✡ Pain transmission

Pain

Pain ↑

- Hyperalgesia 痛覺過敏
  (increased pain sensation)
- Allodynia 異痛症
  if you touch the skin very gently
  but patient feels painful !
  (it shouldn't be painful !)

cause

- sensitivity of Nociceptors ↑
- inflammation would cause increased pain sensation
  - → local acidosis
  - ← inflammatory mediators
    - IL
    - cytokines
    - TNF

Pain ↓

- Hypoalgesia (Hypalgesia)
- Anesthesia during surgery
- Analgesia by pain killer

- sensitivity of Nociceptors ↓
- adaptation of Nociceptors

✡ Neurotransmitters involved in Pain Pathway

- Substance P
- enkephalin
- endorphin

} can decrease the pain

4 ultraviolet radiation can NOT be stimulus for nociceptors (2018. mid)

There is problem w/ neuron, somatosensory system

Date

Nociceptive Pain

- strong mechanical stimulus
- injury of skin
- Sunburn
- break bone
- free nerve endings are stimulated
  - ← hot
  - ← cold
  - ← local acidosis

  } by Temp.

free nerve endings contain

- TRVP-1 Receptors

can be stimulated by

← spicy food (capsaicin)

(myocardial infarction)

→ ischemia of Heart → chest pain (Nociceptive pain)

→ ischemia of skeletal m. ··· when you work out so hard, you feel pain in the muscle

literally painful !

※ if you stimulate the TRVP-1 Receptors, there is a Nociceptive Pain !

Neuropathic Pain

- Compression of sensory neuron
- " spinal cord
- Spontaneous excitation activity of primary / secondary Nociceptors

(without any trigger stimulus , fake pain)

- eg. diabetes mellitus ··· fake pain in the limbs

speaking of the fake pain, that can be the problem w/ the biggest relay system in the brain = " Thalamus "

- Spontaneous activity of Thalamus which is involved in Pain transmission

↳ Thalamic pain → You can NOT give painkiller ∵ There is NO harmful stimulus

very painful → commit Suicide ···

∴ final option ··· Cut the fiber b/w Thalamus & cortex

- Spontaneous activity of Cortex which part is involved in Pain transmission
- malfunction of Periaqueductal gray matter

↓ increase Neuropathic pain

can inhibit the pain transmission

Q : what is the name of molecule which is in the spicy food & that would be the TRVP-1 Receptor agonist ?

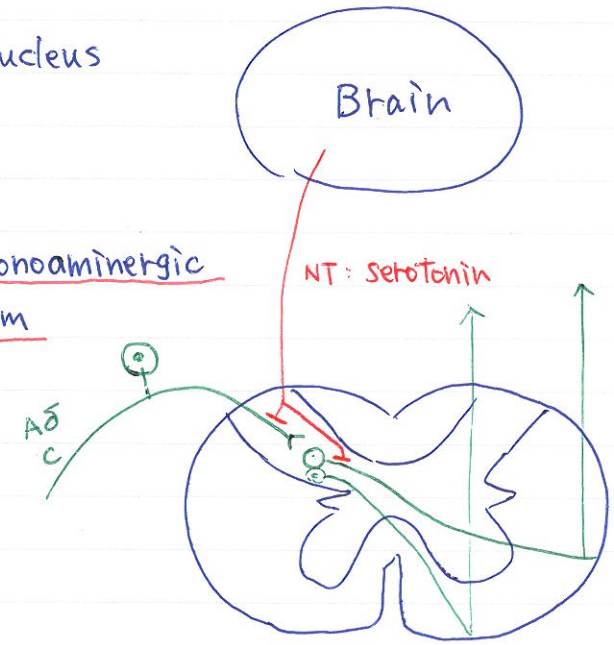
⇒ Capsaicin

Date

✡ descending monoaminergic system

- coming from Raphe nucleus in the brain

Raphe Nucleus



descending monoaminergic system

cf. monoamine ... A / NA . dopamine

※ descending monoaminergic system inhibits the pain transmission at the level of spinal cord.

- presynaptic membrane w/ Serotonin.
- post "

※ if there is a problem w/ descending monoaminergic system, that would also be a neuropathic pain

Date

✡ Auditory System

2 main characteristics of sound that we can hear

frequency

20 - 20,000 Hz

- > 20,000 Hz ⇒ ultrasound
  - bats
  - rodents
  - dorphins

human can NOT hear !

- < 20 Hz ⇒ infrasound
  - elephant can communicate w/ infraSound !

dB = 1/10 Bell

0 dB = 20 μPa (micro Pascal)

- we can hear 0 dB ! (healthy person)
- Normally the threshold is 0 dB ! (for the human ear)
- if the threshold is >30 dB
  ⇒ it refers to the Hearing Defect !
- if you can NOT hear the 90 dB sound
  ⇒ it means you are practically "deaf".
- if your auditory system is very good,
  you can even hear the -10 dB Sound ! (minus)

How can it be negative !?

$$\text{Sound Pressure level [dB]} = 20 \times \log \frac{Px}{Po}$$

(Po = 20 μPa)

Px : given sound pressure

Po : standard sound pressure
↳ always 0 dB = 20 μPa

Q : what's the difference b/w 20 dB & 40 dB ?
How many times difference ?

⇒ 100 times

$\because \frac{40}{20} = \log 10^2$

$Px_1 \ll Px_2$ (100 times)

50 - 60 dB ··· when I am talking to you
80 dB ··· very noisy street
100 dB ··· gun shot next to your head → can destroy your auditory system

Q: why do we have ear ? => to collect the Sound. + increase. amplify the Sound via dB.

Elephant Collect more Sounds !

Date

✡ Auditory Pathway

External Auditory meatus

↓ Sound wave activate mechanically Tympanic membrane

Tympanic membrane

↓

malleus
incus
stapes
} @ middle ear

Q: what's the most important functions of ossicles ?

↳ 1) Transmit the sound
2) amplify the Sound

↓

oval window

↓

Cochlear

↓

Organ of Corti

↓

Spiral ganglion ... cell bodies are located here !

↓

Cochlear nerve

↓

Cochlear nucleus

↓

Superior olive

↓

Lateral lemniscus

↓

inferior colliculus

↓

medial geniculate body @ Thalamus

↓

Auditory radiation

↓ if destroyed ⇒ Auditory Agnosia ... you can hear the Sound But you can NOT recognize (just Sound

Primary auditory cortex @ Temporal lobe Br. 41. 42

↓

Wernicke area ... to understand language

if destroyed ⇒ sensory aphasia ... you can hear somebody talking to you But you can NOT understand

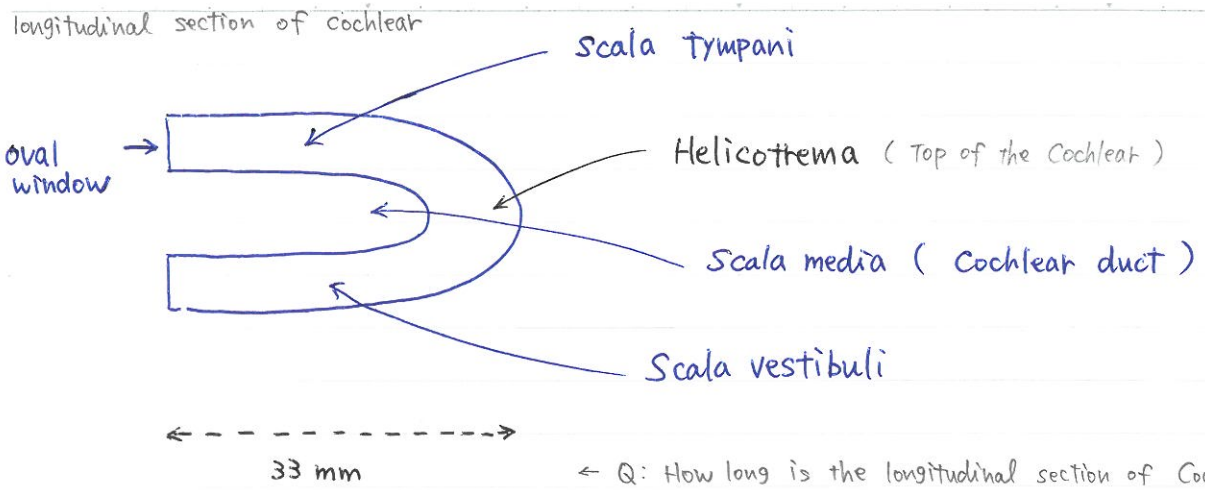
cf. visual Agnosia ... problem w/ visual cortex => you can see But can NOT recognize

Tactile Agnosia ... when you touch the key, you can NOT tell. w/o vision

Date

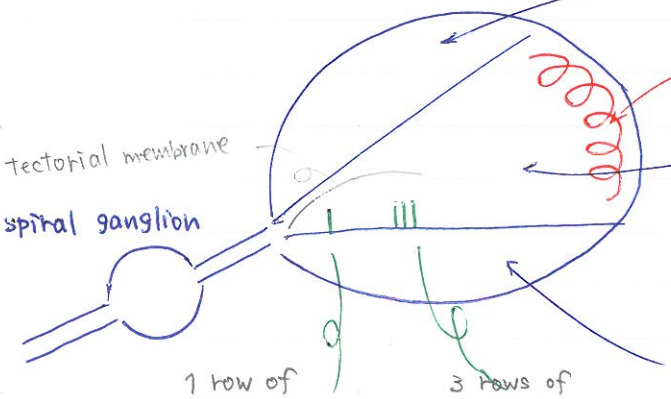
✡ Cochlear

longitudinal section of cochlear



← Q: How long is the longitudinal section of Cochlear ?

Transverse section of Cochlear



Scala tympani ··· filled w/ Perilymph

Similar to ExtraCellular fluid

··· High c.c. of Na^+

Stria vascularis — can make endolymph

Scala media ··· filled w/ endolymph

(Cochlear duct)

Similar to IntraCellular fluid

··· rich in K^+

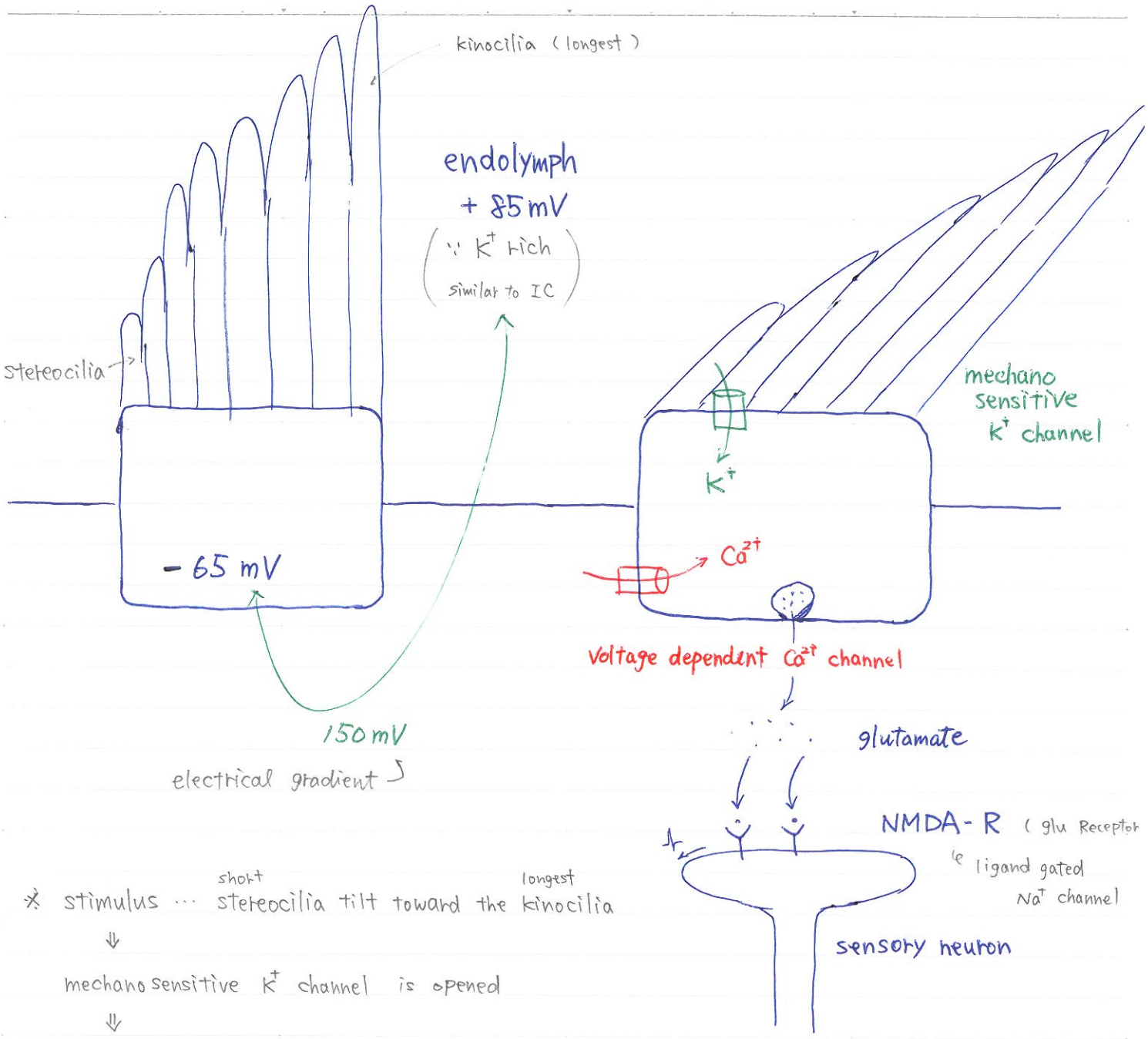
Scala vestibuli ··· filled w/ Perilymph ≈ rich in Na^+

1 row of inner hair cell
- detect the Sound

3 rows of outer hair cell
- amplify the sound
- modify "

Date

☆ inner hair cell



* stimulus ··· short stereocilia tilt toward the longest kinocilia

⇓

mechano sensitive K^+ channel is opened

⇓

K^+ influx ⇒ depolarization

⇓

Voltage dependent Ca^{2+} channel is opened

⇓

Ca^{2+} influx

⇓

NT released from the vesicle (NT : glutamate → excitatory NT)

⇓

NT (glu) bind to NMDA-R

⇓

Na^+ influx ⇒ depolarization *

Visual system ⇒ Hyperpolarization !

* cf. Photoreceptor, bipolar cell } are hyperpolarized

Should be depolarized though ! ㅠㅠ

Date 58 07

☆ Vestibular System

main function ... to maintain the balance

⇒ with vestibular system, we can recognize the accelelation.

- Angular accelelation ... when you're rotated, at the beginning / end of the rotation, There is a signal
  - ↳ semicircular canal can detect (is important to detect it)

- Linear accelelation
  - → uthicle ... can detect horizontal acceleration (ユートリクル)
  - → saccule ... vertical (elevator)

Vestibular system can regulate the eye movement which is

- Nystagmus

There are 2 components

- fast component ... Nystagmus is named after fast component.
- slow 〃 ↓

So when the slow component is leftword, but fast is rightword

⇒ That would be the right Nystagmus.

Speaking of the direction of the hystagmus. There are 3 main directions

- horizontal nystagmus
- vertical 〃
- rotational 〃

Date

Physiological Nystagmus

1) Thermal Nystagmus

... Pour the hot water in one of the ears

⇒ hot water will increase the temperature in the vestibular system

⇒ that would be the perilymph movement in the vestibular system

⇒ hot water causes **ipsilateral nystagmus**

- fast component is toward the stimulus

→ So you look toward the stimulus

※ if hot water enters both ears

⇒ NO nystagmus !

⇒ cold water cause **contralateral nystagmus**

2) Optokinetic Nystagmus

... you're sitting in the train & your friend is infront of you

→ your friend is looking out of the window & she focus on the tree

But because of the train is moving ... her eye move fast

3) Postrotational Nystagmus

... your friend sit the rotational chair & you rotate it

→ At the moment you stop the rotation, her eye ball is still moving

⇒ So fast component is Contralateral ! (oposit direction!)

(if you rotate left word, Nystagmus is right word)

w13

Date May 1st Tue

✡ EEG (Electroencephalography)

↳ record electrical activity of the brain ← if Heart ⇒ ECG. if skeletal muscle ⇒ EMG

↳ can see PSP (Post Synaptic Potential) :-) can NOT see AP !!

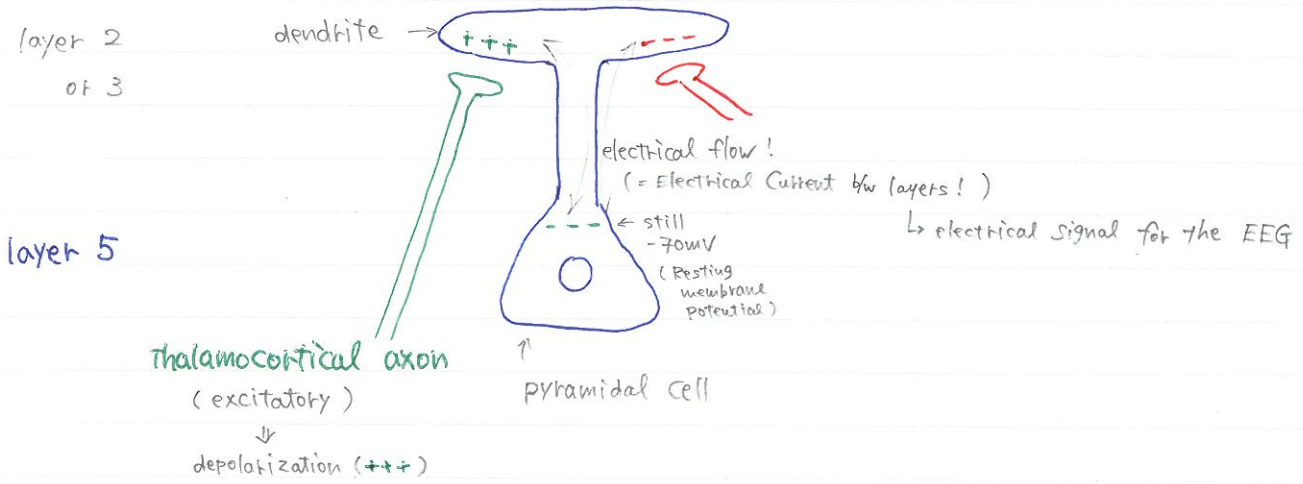
↳ ancient ppl believed so ...

↳ EPSP
↳ IPSP
} main generator is Pyramidal Cells

Q: where is the Pyramidal Cells located in brain ? ⇒ mainly 5th layer of Cortex

⇒ if there is depolarization or hyperpolarization in Pyramidal cell → That would be the electrical difference b/w different layers → That would be the Electrical Current → This electrical Current can be detected by EEG

Let me show you what I mean !



Speaking of the EEG, it can NOT record 1 single PSP → at the same time abount 1 million PSP should happen (EPSP or IPSP) → That would give you EEG wave.

Before discussing about different types of EEG waves, let's talk about the Electrodes.

✦ Electrodes

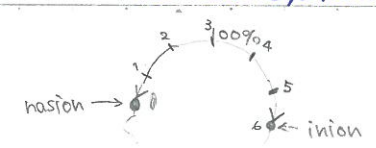
Q: What kind of electrodes should be placed on the skull ?

- ground electrode @ ear (in lab)
- active / different electrode
- passive / indifferent

} at least 3 electrodes ! ← minimum !

8 / 16 electrodes in lab → can be 32 / 64 / 128 electrodes (# of electrodes)

↳ 10-20 system ... 10% - 20% - 20% - 20% - 20% - 10% ← place of electrodes



Date

✧ Types of EEG waves

30-100 waves in 1 second

frequency

1) γ wave — 30-100 Hz
- frequency is high (so many signals in 1 second)
- amplitude of signal is small
- when you focus on sth like 3.14 x 3.14 = ?
  - eg. maths

γ wave can NOT be too long , you can NOT keep this focus for long time

∴ γ wave is only for few seconds

2) β wave — 13-30 Hz
- when awake adult (open eyes)
- when REM phase of sleeping (paradox sleep)
- desynchronization

During physio test , β wave is dominant (sometime γ wave but mainly β wave)

∵ γ wave can NOT maintain 110 min.

Q: Why REM Phase of sleeping is called "paradox" ?

⇒ Because you're sleeping so not consicous but EEG signal is kinda same as when you're awake

3) α wave — 8-13 Hz
- when closed eye & relax (Not sleep) meditation
- synchronization

it means (frequency is lower & amplitude is larger)

Q: When you close your eyes, where do you think that the α wave shows 1st ? ⇒ occipital lobe

4) θ wave (Theta) — 4-8 Hz
- in sleeping adult } normal
- in children anytime }

↳ in awake adult = brain disturbance
↖ abnormal !

※ if you put electrode on the kid , that can be γ / β / α / θ even δ wave

it's totally kinda random . But,

if you put electrode on Kristof's skull & you can record mainly θ waves

→ That means that He has a brain disturbance .

Date

(frequency is low
(amplitude is large

5) δ wave 0 - 4 Hz - normal in sleeping adult during deep sleep
- 〃 in infant / small children, anytime

- pathological in awake adult
= brain disturbance
(brain injury)

What is the medical relevance of the EEG examination ? when do we use EEG exam ?

indication

1) sleeping disorder diagnosis

2) epilepsy

Speaking of the epilepsy , EEG is very important tool
Why !? Because . there are some epileptic seizure that can NOT be treated w/ drug . ⇒ And final solution is To remove that area from the brain = "focus point"

2 main types of epilepsy

grand mal seizure
(big seizure)
- unvoluntary movement
- Not conscious
- shaking , break bone sometimes

Petit mal seizure
(small seizure)
- absence problem (talking ○ stop moving . thinking for a while)
- Not conscious (They can NOT recall the seizure)

if patient has temporal lobe epilepsy, you can see the epileptic seizure earlier in the electrode that is near the temporal lobe than other electrodes

Q: How can you recognize Petit mal seizure w/ EEG ?
A: There is a " 3 Hz spike wave "
↳ 3 waves in 1 second

(☲) it's NOT AP !!
∵ EEG can just record PSP
(EPSP & IPSP)

Q: How can you evoke the epileptic seizure ? How can you trigger it ?
⇒ To evoke epileptic seizure , you can use after
1) flashing light (stroboscope)
2) Hyperventilation for a long time
3) Sleeplessness (lack of sleeping)

3) brain death diagnosis

← isoelectric line
⇓
it means that brain does NOT work at all
⇓
brain death

Date

☆ Sleep

if you wake up suddenly in REM phase
sometimes, you can NOT move your limbs
because you're still in atonia = sleep paralysis 金縛り

1.5h in 1 cycle

contains

1 slow wave sleep

Parasympathetic Tone
- HR↓, BP↓
- Metabolic Rate↓
- Respiration↓
- Muscle Tone↓

in this phase, you can conserve the energy

1 REM phase (paradox sleep)

10 min

↳ easy to wake up & good mood & You can talk about dreams

- dreams
- Atonia (zero No muscle tone) except eye muscle & respiratory m.
- lack of Thermoregulation
- irregular autonomic function
  - ↳ HR↑↓, Respiration is irregular

Q: How can you desynchronize?
A: ask patient to open the eye

4 stages of slow wave sleep

if you fall a sleep that is

1) First stage ··· α waves disappear (∵ α waves are present when you're relax closed eye)
   → θ waves show (Light sleep)
2) Second stage ··· There are Sleep spindle & K-complex
3) Third stage ··· δ wave (deep sleep) ··· frequency = 2-4 Hz
   low freq, high amplitude
   ↕ synchronization
4) Fourth stage ··· δ wave (deepest sleep) ··· freq. < 2 Hz
   lowest freq. largest amplitude
   ↳ difficult to wake up

REM phase in utero ··· 80% of whole sleeping ∵ REM phase is imp for brain development

in newborn ··· 50-60% ∵ REM phase is imp. for converting shortterm memory to long term memory
⇒ So you can process your info during REM phase

in adult ··· 20%

Date

☆ Hypothalamus

- Thermoregulation ... set point = 36 - 37 °C

< 36°C ⇒ produce heat

> 37°C ⇒ loose more heat

Q: How is the hypothalamus informed about Temp.?

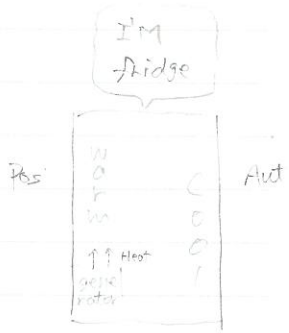
input - Peripheral Thermoreceptors ... @ skin, Liver, skeletal m.

↓

Q: which pathway take the Temp. info?

spinothalamic pathway ... Aδ, C fiber

- Local Thermoreceptor @ Hypothalamus
- immune molecule ... interleukin, cytokine → fever
  can change the Temp.
- anterior Hypothalamus ... Cooling center
  - ↳ vasodilation in periphery → warm skin (loose more energy)
  - ↳ sweating
  - ↳ change in behavior (taking of clothes)



< mnemonic >

- Posterior Hypothalamus ... warming center
  - ↳ vasoconstriction
  - ↳ sweating ↓
  - ↳ shivering
  - ↳ change in behavior

Date

- Regulation of food intake

Lateral Hypothalamus	VentroMedial Hypothalamus
- Hunger Center	- Satiety Center
if destroy ⇒ Aphasia / anorexia	⇒ Obese
- They don't eat	
- Skinny	
- Glc sensitive neuron	- Glc Receptor neuron

- Anorexigenic molecule ... - Leptin (produced by adipose tissue)
  - cck *
  ↳ food intake ↓

- Orexigenic molecule ...
  - Orexin
  - Ghrelin (GH releasing hormone)
  - insulin → BS ↓ → more hungry
  ↳ food intake ↑

- Glucose monitoring system

Glc

Glc Receptor cell ↑	Glc sensitive Cell ↓
∮	∮
Glc increase the activity of Glc Receptor Cell	Glc decrease the activity of Glc sensitive cell

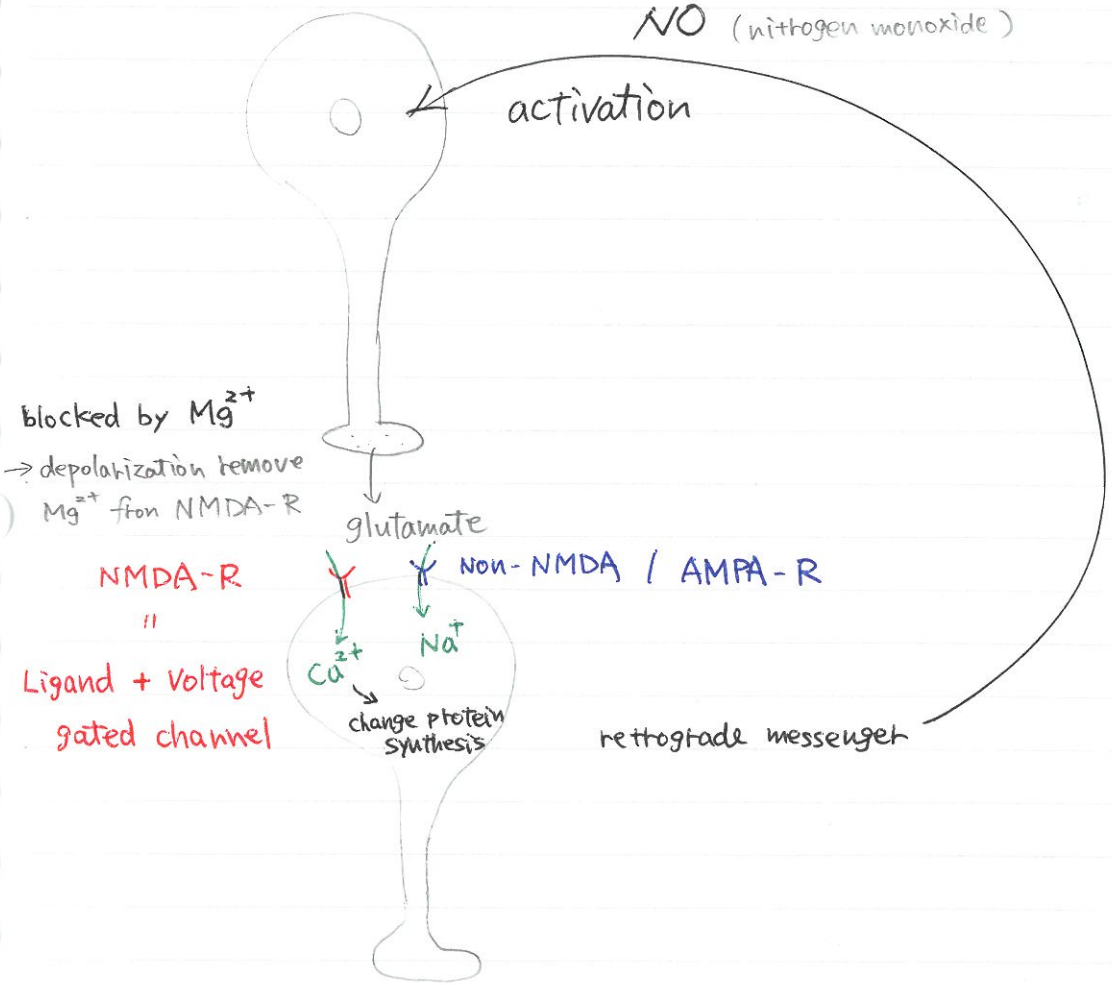
Q: Where is the Glc Receptor neuron located ? ⇒ VMH (ventroMedial Hypothalamus)

Q: 〃 Glc Sensitive neuron located ? ⇒ LH (Lateral Hypothalamus)

∵ if you eat ⇒ BS ↑ ⇒ Glc sensitive neuron dicrease the activity

⇒ LH activity is decreased.

☆ LTP (Long Term Potentiation)



Q: what's the most important characteristic of NMDA-R ? ⇒ Mg^{2+} block it

London cab-drivers have larger hippocampus ∵ they study a lot & has mental map in their brain.
Spacial learning

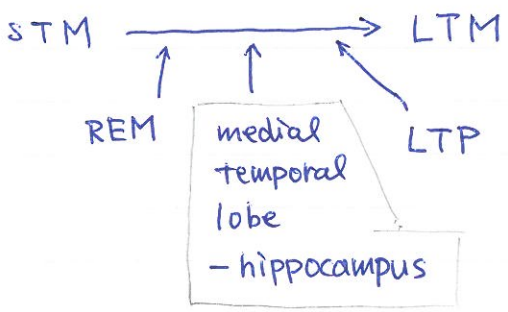
Date

☆ memory

1) Sensory memory
   - capacity is High
   - duration: < 1 ~~●~~s
   - iconic - visual memory
   - echoic - acoustic "
   - taste, smell, somatosensory

2) Short term memory / working memory
   - seconds - minutes
   - low capacity ... 7 ± 2 items
   - ↑ prefrontal center

3) long term memory
   - capacity : ∞
   - duration : years - decades



To forget sth ⇒ LTD is important

Date

LTM

declarative memory (explicit ")

episodic
- breakfast
- 1st day in Pécs

semantic
- facts
- reciting a poem

↑

med student

non-declarative memory (implicit ")

procedual
- skills / habit
- how to ride bicycle

↑

surgeon

- basal ggl
- cerebellum
- motor cortex

priming
- many cortical region
- Rose
- P_Y__O

red

What is the flower which initial is "R"?

classical conditioning / Pavlonian "
- uncondition stimulus → food in mouth
- uncondition respons → salivation
- condition stimulus → hing a bell

→ associative learning

- expemimenter controls it
- works in human
- Time delay is importan b/w condition stimulus & uncondition "
- extinction
  - condition response is gone if NO Reward

* other associative learning
- instrumental
- operant learning
  - ↳ behavior is changes because of its consequences

→ reward — positive reinforcement
→ Punishment - Negative reinforcement

- can be developed in human
- repetition is important
- animal acts

Date

Non-associative learning

habituation

- motor response ↓
- repetitive stimulation
- Not related to muscle fatigue
  - No muscle fatigue
  - No sensory adaptation

sensitization

- painful / harmful / annoying stimulus

※ Kandel
- serotonin
- cAMP → PKA ↑
- K^+ channel ↓ → depolarization
- Voltage gated Ca^{2+} channel
  ↳ Ca^{2+} influx → Ca^{2+} act as 2nd messanger → NT release

special types of Conditioning

1) imprinting
2) autoshaping
3) conditioned taste aversion
4) latent learning
5) curiosity