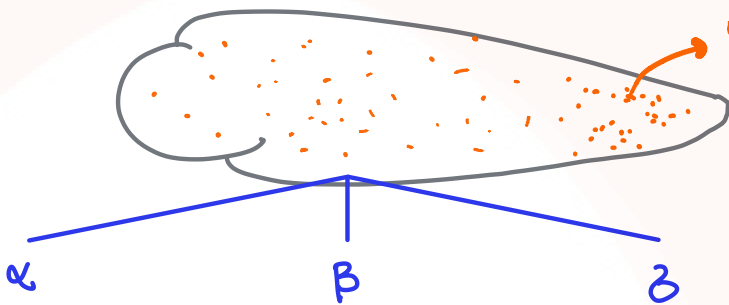


DIABETES MELLITUS

β -cell $\rightarrow$

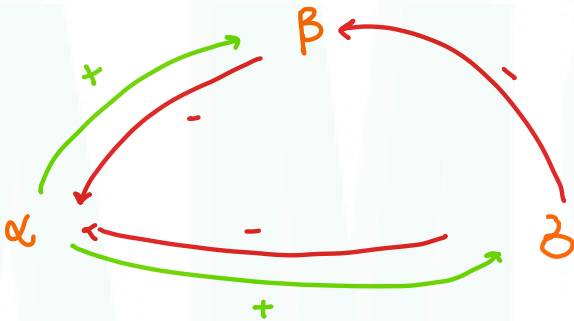
Islets of Langerhans

Pancreas

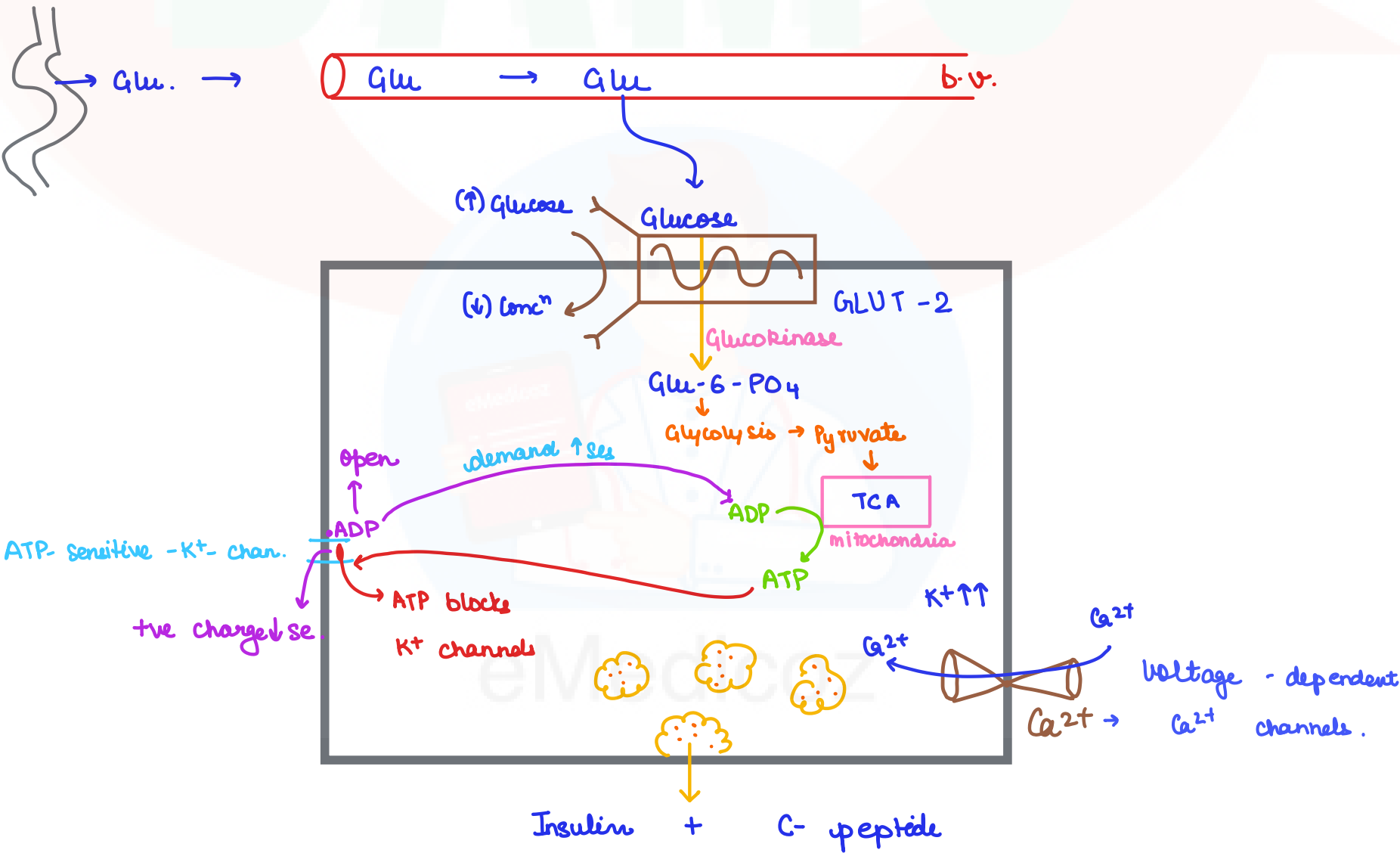


max^m @ tail

A- alpha - Aceha
D- don - 3



Mechanism of Insulin secretion $\rightarrow$



Clinical relevance of C-peptide: Exogenous Insulin vs. Endogenous Insulin

∴ Drugs →

(i) K^+ -channel-blockers → ↑ se Insulin secretion

- Sulfonylureas
- Meglitinide

(ii) K^+ -channel-opener → ↓ se Insulin secretion (insulinoma)

- Diazoxide

∴ Hyperglycemia + β -Cell defect →

MODY → maturity onset of Diabetes in young.

→ AD

→ age < 25 years.

R_x :

OHA

(sulfonylureas)

Diabetes Type	of MODY	defect
1		HNF-4- α (hepatocyte - nuclear - Transcription factor)
2		Glucokinase deficiency
3	(MPC)	HNF-1- α
4		Insulin - promoter - factor - 1
5		HNF-1- β
6		Neurogenic - differentiating - factor - 1

Type - I DM

Type -2 DM

→ auto - Immune destrⁿ of β -Cells.

→ ↑se to peripheral resistance Insulin

→ Islet - cell - antibodies

→ GAD - 65

→ Insulin

→ IA-2 / ICA 512

→ 2NT8

Before Insulin = 2U.

D-2 " = 10U.



↑se demand of Insulin



β -cells ⊕

↑se secrⁿ of Insulin



Hyperinsulinemia

workload on β -Cells ↑sing



destrucⁿ of β -Cell ↑se.

→ chromosome 6 assoc.

C/F →

Thin patient
age of onset < 30 yrs.

5 to 10% > 30 yrs.

→ high risk of DKA.

→ Rx: Insulin

C/F →

Obese
HTⁿ

generally age > 40 years.

∴ Dx - Criteria : (any 1 of following)

- 1.) symptoms of DM + RBS ≥ 200 mg/dl
- 2.) fasting blood sugar level ≥ 126 mg/dl
- 3.) HbA_{1c} $\geq 6.5\%$.
- 4.) 2 hr Plasma glucose ≥ 200 mg/dl during OGTT. (75gms.)

HbA_{1c}

→ glycated / glycosylated Hemoglobin

→

Blood

↑ Glucose

+

Hb

||

HbA_{1c}

→ standard method

→ Reflects glycemic history over past 2-3 m.

→ Conditions $\bar{c}$ Interfere with HbA_{1c} →

Hemo globinopathies

Wremia

Reticulocytosis

Transfusion of blood

Anemia

Fructosamine - assay

- Glycated albumin
- Glycemic status over the prior 2 weeks.

Glycation of major proteins such as

- collagen
- albumin
- fibrinogen
- globulins

∴ Management →

⇒ Treatment goals for Diabetes →

HbA _{1c}	< 7 %.
Pre-prandial glucose (FBS)	80 - 130 mg/dl
Post-prandial glucose	< 180 mg/dl
Blood pressure	< 140 / 90 mmHg
LDL	< 100 mg/dl
HDL	> 40 mg/dl In men > 50 mg/dl In women
Triglycerides	< 150 mg/dl

AFTER STARTING THE R_x :

FBS	< 130	> 130
PPBS	< 180	> 180
	↓	↓
	good glycemic control	poor glycemic control.

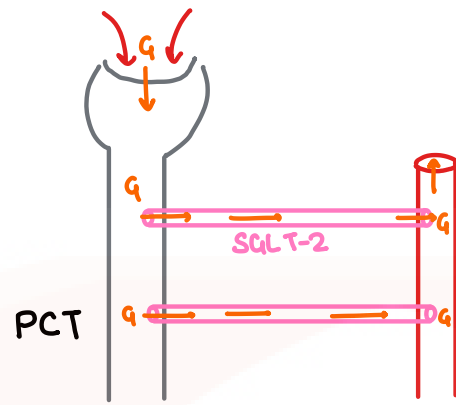
HbA_{1c}
Repeat : after 6 months after 3 months

Parenteral						
Amylin agonists ^{c,d***}	Slow gastric emptying, ↓ glucagon	Pramlintide	0.25–0.5	Reduce postprandial glycemia, weight loss	Injection, nausea, ↑ risk of hypoglycemia with insulin	Agents that also slow GI motility
GLP-1 receptor agonists ^{c***}	↑ Insulin, ↓ glucagon, slow gastric emptying, satiety	Exenatide, liraglutide, dulaglutide	0.5–1.0	Weight loss, do not cause hypoglycemia	Injection, nausea, ↑ risk of hypoglycemia with insulin secretagogues	Renal disease, agents that also slow GI motility; medullary carcinoma of thyroid
Insulin ^{c,d****}	↑ Glucose utilization, ↓ hepatic glucose production, and other anabolic actions	See text and Table 418-4	Not limited	Known safety profile	Injection, weight gain, hypoglycemia	
Medical nutrition therapy and physical activity ^{c*}	↓ Insulin resistance, ↑ insulin secretion	Low-calorie, low-fat diet, exercise	1–3	Other health benefits	Compliance difficult, long-term success low	

DAMS



eMedicoz



∴ Complications of DM →

Acute

chronic

1) Diabetic Keto acidosis (DKA)

2) Hyper-osmolar hyper-glycemic State

Micro-vascular

Macro-vascular

- retinopathy

- ?

- nephropathy

- CVA / stroke

- neuropathy

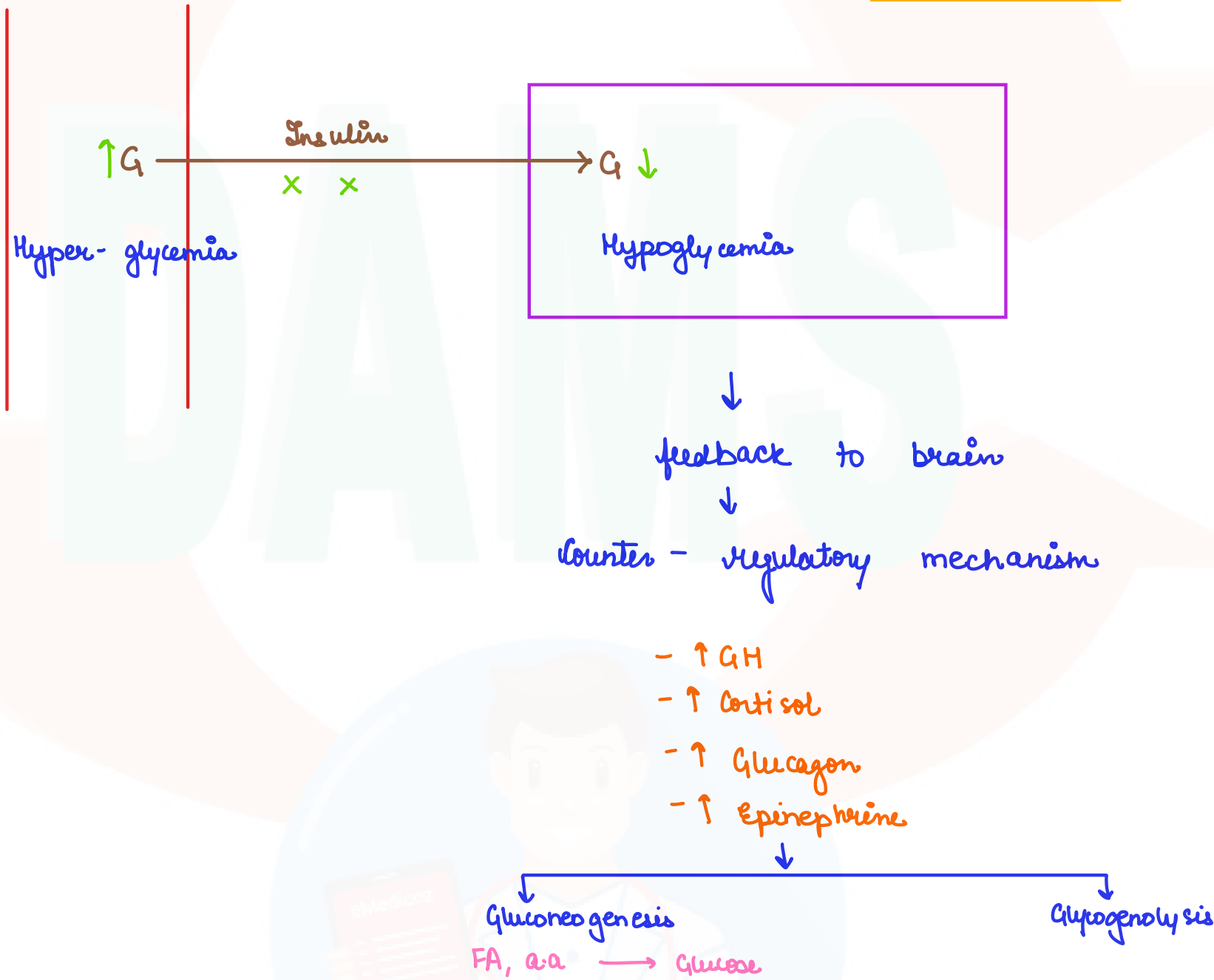
- Peripheral vasc. disease.

DKA

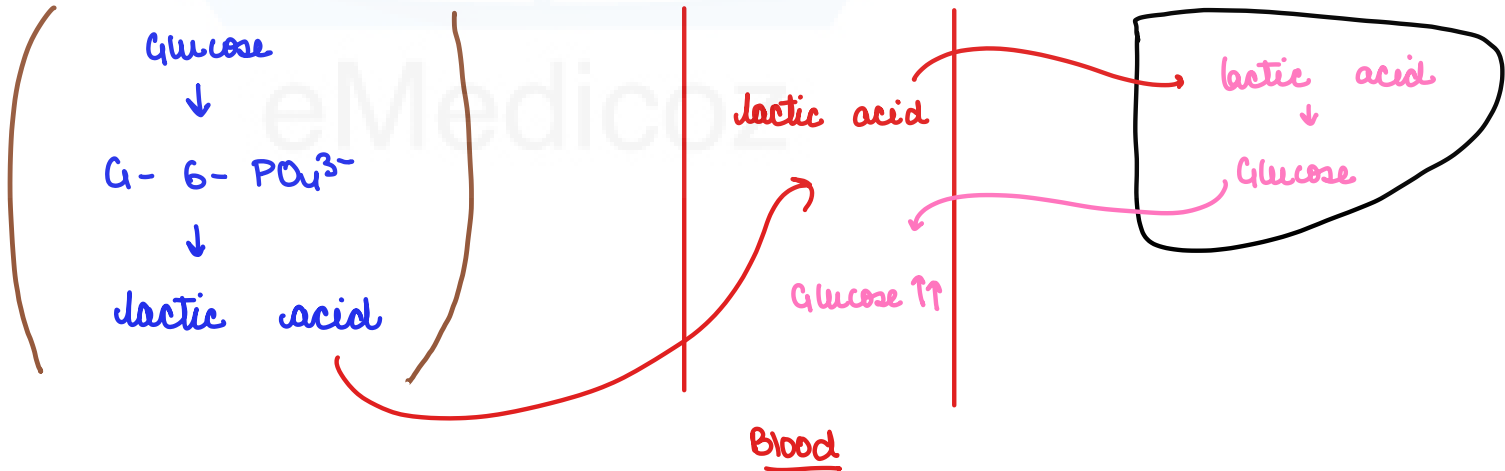
- more common in Type - 1 - DM.
- absolute def. of Insulin.

Trigger factors:

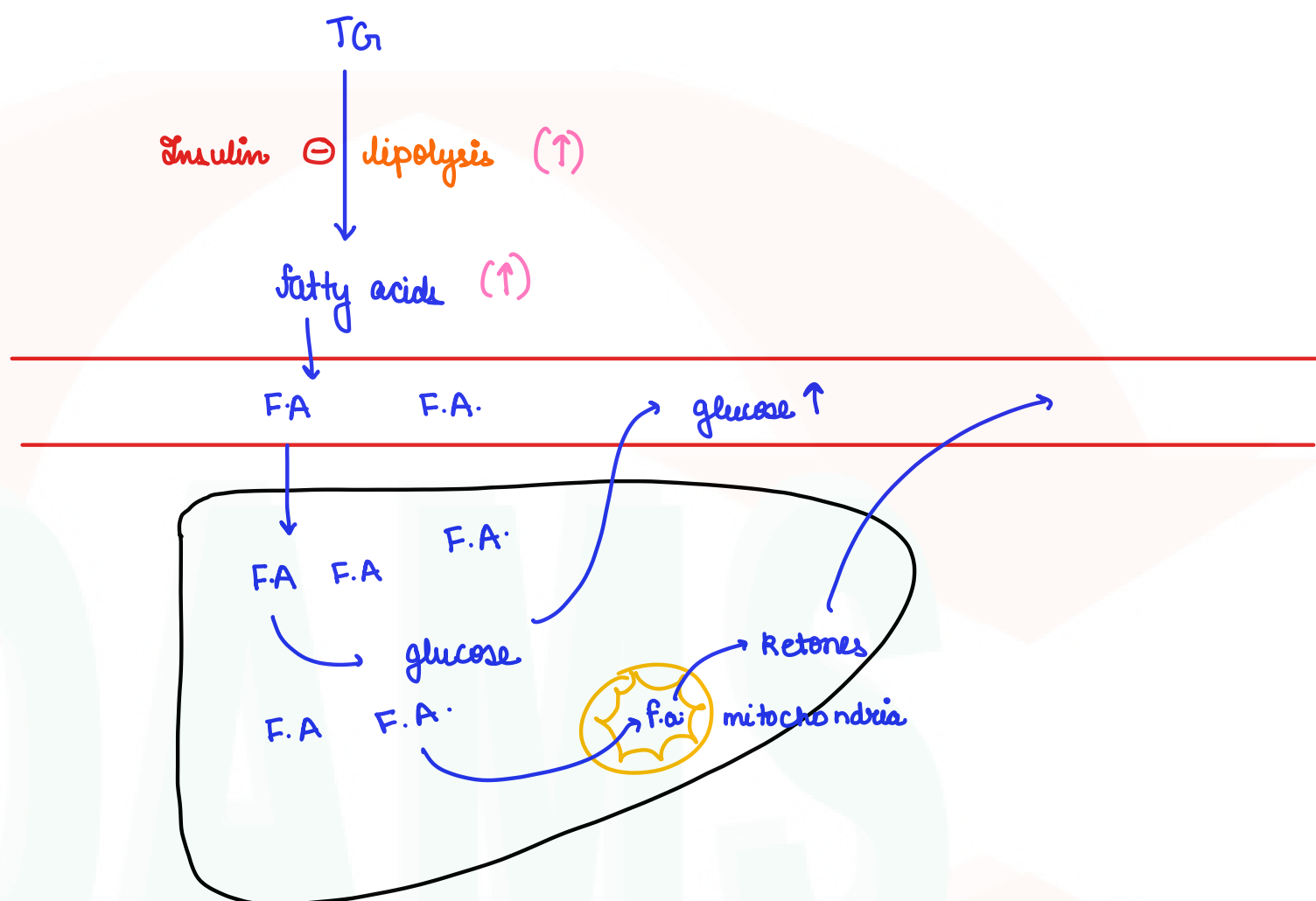
Infection
Stress
Surgery



I.) Muscle →



II.) Adipose tissue →



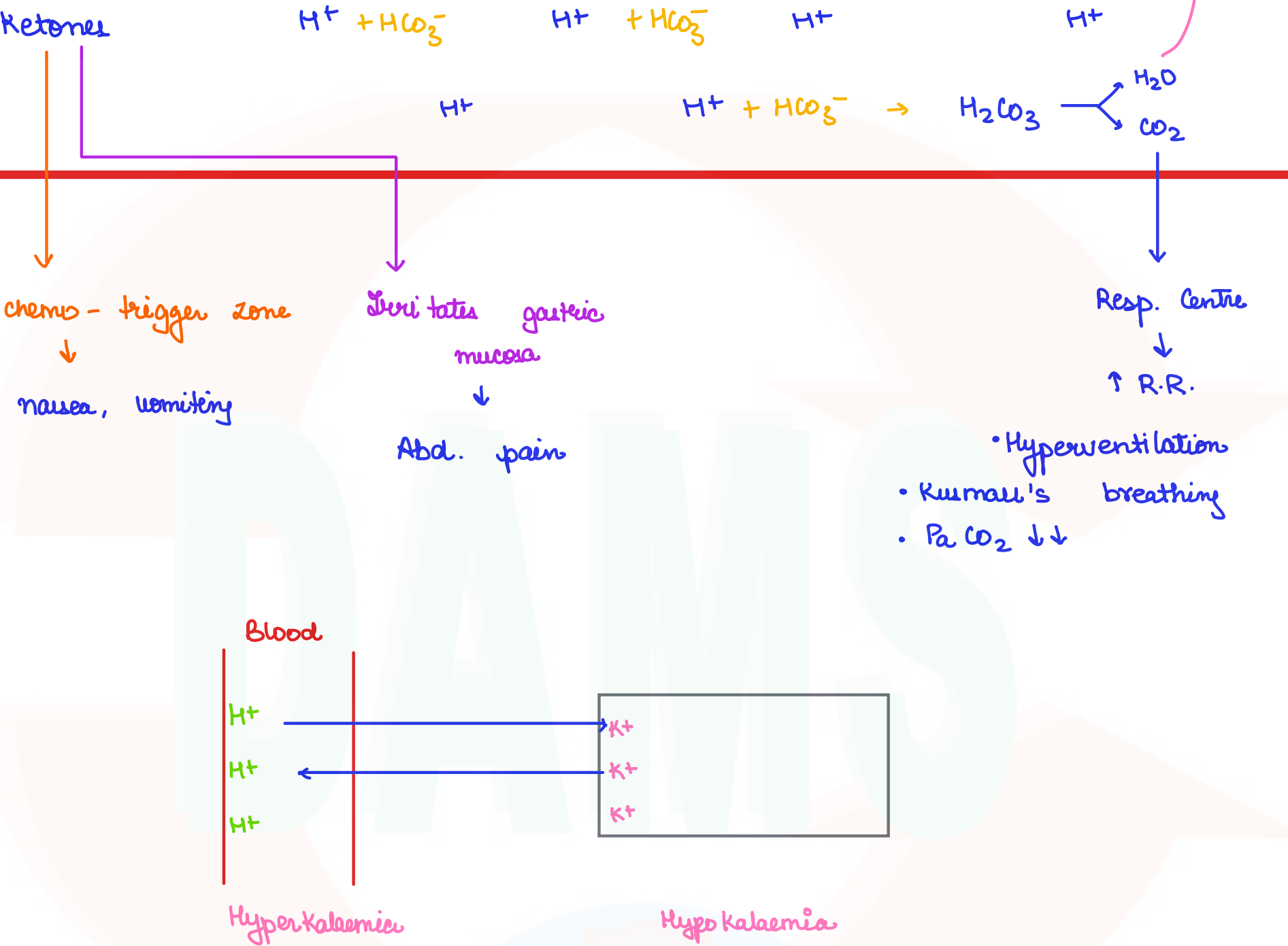
∴ Ketones →

1) Acetone - Gas Sweet → Lungs fruity → Expired. Smell to breath.

2) Acetoacetate

3) β -hydroxybutyrate

Ketones → Acids
↳ donate H^+



Anion - gap :

Normal $\Delta AG \rightarrow 8 \text{ to } 16 \text{ meq/L.}$

$$\left(\begin{matrix} \text{major +ve} \\ \text{charge} \end{matrix} \right) - \left(\begin{matrix} \text{major - ve} \\ \text{charge} \end{matrix} \right)$$

$$(\text{Na}^+) - (\text{HCO}_3^- + \text{Cl}^-)$$

$\Delta AG \rightarrow \uparrow$ ses in DKA ($\text{HCO}_3^- \downarrow\downarrow$)

C.S.

21 ♂ male R/c/o Type -1 DM
c/o - nausea
vomit
Abd. pain
Kussmaul's breathing

↑RR
sugar = 565 mg/dl.

Treatment

i/v fluids	Insulin	K ⁺ - Correction
0.9% N.S. 15 to 20 ml/kg/hr for 1 st 3 hours then , 250 to 300 ml/hr. 0.45% N.S. If Na ⁺ ↑sing monitor sugar 1 hourly sugar ≤ 200 mg/dl.	regular Insulin i.v. <u>dose</u> loading → 0.1 U/kg fb → 0.1 U/kg/hr Sugar → <200 <u>main action of Insulin</u> ↓ Inhibits lipolysis If K ⁺ < 3.3 meq/L ↓ C/I for Insulin	Correct K ⁺ ↓ then, Insulin.

Type - 1 D. M → ~~As~~ age advances → severe DKA chances↑.

K ⁺ - level	Insulin	KCl Sol.
<3.3 meq/L	X	40-80 meq / hr.
3.4 meq /L	✓	✓
3.5 to 5.0	✓	✓ (rate = 10 meq / hr) ↓sed.
>5.2	✓	X



HHS

- hyperosmolar - hyperglycemic state .
- common In type - 2- DM. (mild → moderate deficiency)
- Small amount of Insulin → to stop lipolysis
to start Ketolysis
- ketones are absent

∴ C/F →

C/F +nt In HHS	C/F absent In HHS
Polyuria Polyphagia Polydipsia dehydr ⁿ	Nausea Vomiting Abd. pain Kusumali's breathing

"Ketone synthesis starvation" can occur In HHS.

	HHS	DKA
Ketones	+	++++

Quantity Is so less that It can't give C/F.

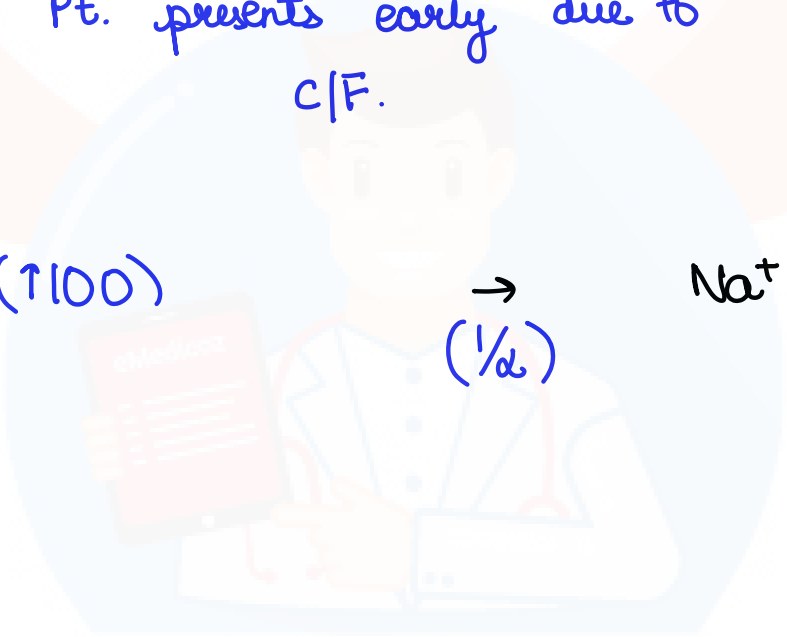
∴ Mx →

same as DKA
i/v fluids + Insulin + KCl

TABLE 418-6 LABORATORY VALUES IN DIABETIC KETOACIDOSIS (DKA) AND HYPERGLYCEMIC HYPEROSMOLAR STATE (HHS) (REPRESENTATIVE RANGES AT PRESENTATION)		
	DKA	HHS
Glucose, ^a mmol/L (mg/dL)	13.9–33.3 (250–600)	33.3–66.6 (600–1200)
Sodium, meq/L	125–135	135–145
Potassium ^{a,b}	Normal to ↑	Normal
Magnesium ^a	Normal	Normal
Chloride ^a	Normal	Normal
Phosphate ^{a,b}	Normal	Normal
Creatinine	Slightly ↑	Moderately ↑
Osmolality (mOsm/mL)	300–320	330–380
Plasma ketones ^a	++++	+/-
Serum bicarbonate, ^a meq/L	<15	Normal to slightly ↓
Arterial pH	6.8–7.3	>7.3
Arterial Pco ₂ , ^a mmHg	20–30	Normal
Anion gap ^a (Na – [Cl + HCO ₃])	↑	Normal to slightly ↑

Pt. presents early due to C/F. late presenⁿ.

Glucose (↑100) → Na⁺ (↓1.6)
(1/2)



CHRONIC

COMPLICATION

OF

DIABETES

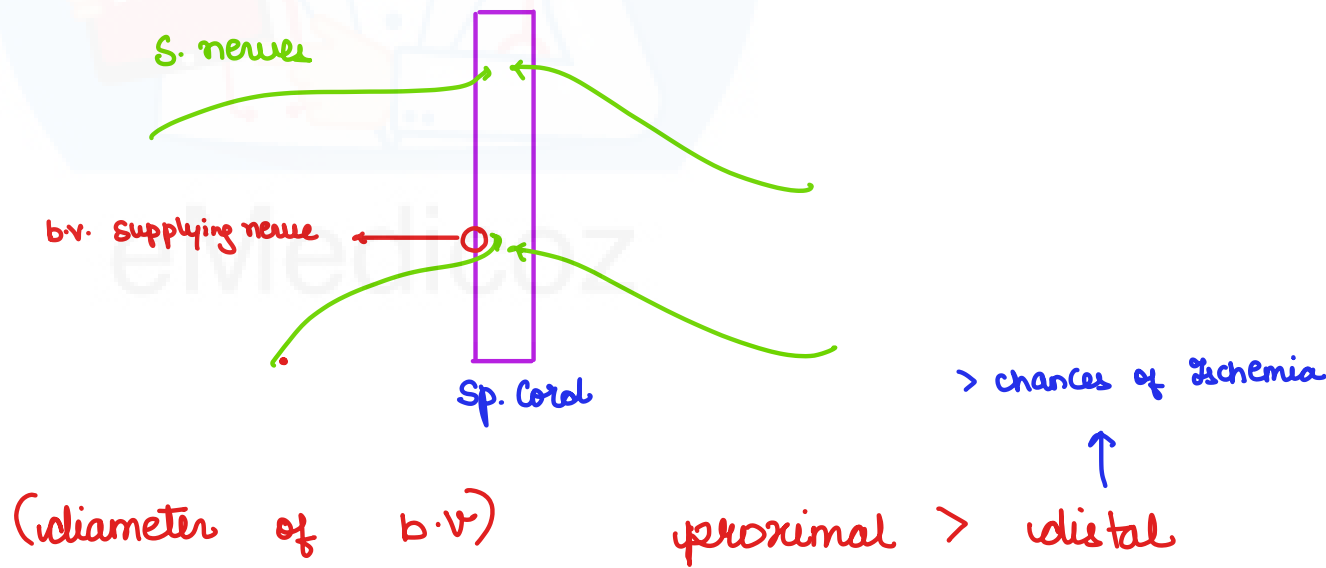


• Diabetic neuropathy →

Types →

I:) Distal symmetric Sensorimotor Polyneuropathy (DSPN)

→ m/c type .



→ b/d damage of sensory nerves progressing distal
↓
proximal.

→ neuropathy reaching mid - thigh
→ neuropathy " hand tips.
Gloves and Stocking Neuropathy.

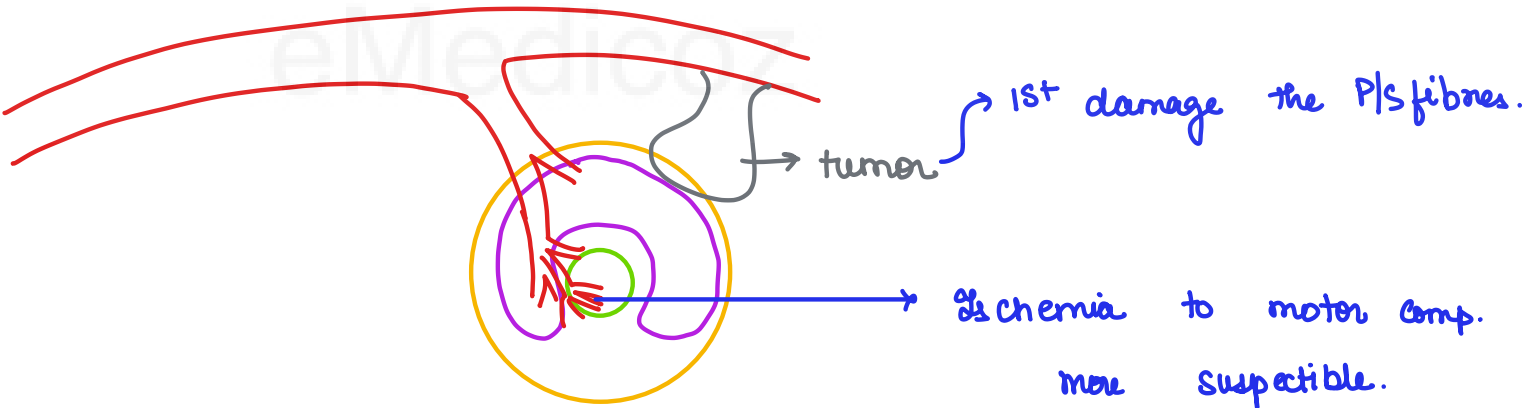
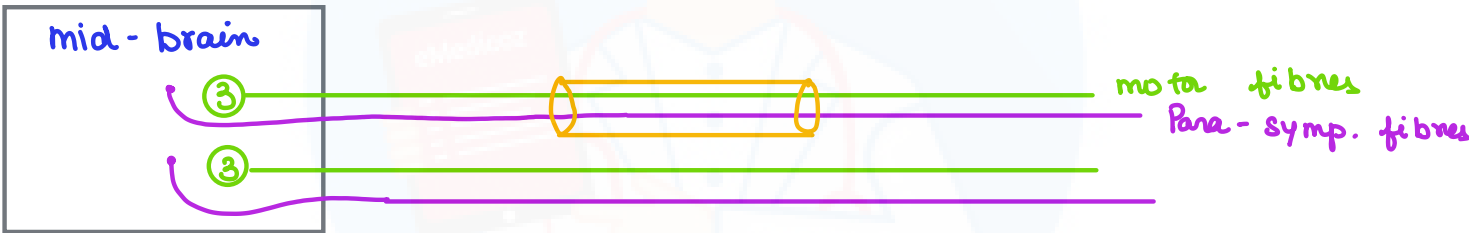
II.) Autonomic neuropathy →

Postural
Sexual
hypotension
dysfunction

III.) Mononeuropathy

Peripheral nerves → median nerve
ulnar nerve

Cranial nerve → m/c → 3rd nerve
↓
pupil sparing neuropathy.



IV.) Diabetic Amyotrophy / Radiculo - plexus - neuropathy /
 Bruns - Garland - Syndrome →

- plexopathy
- Back pain
- Atrophy of back muscle.

C.S.

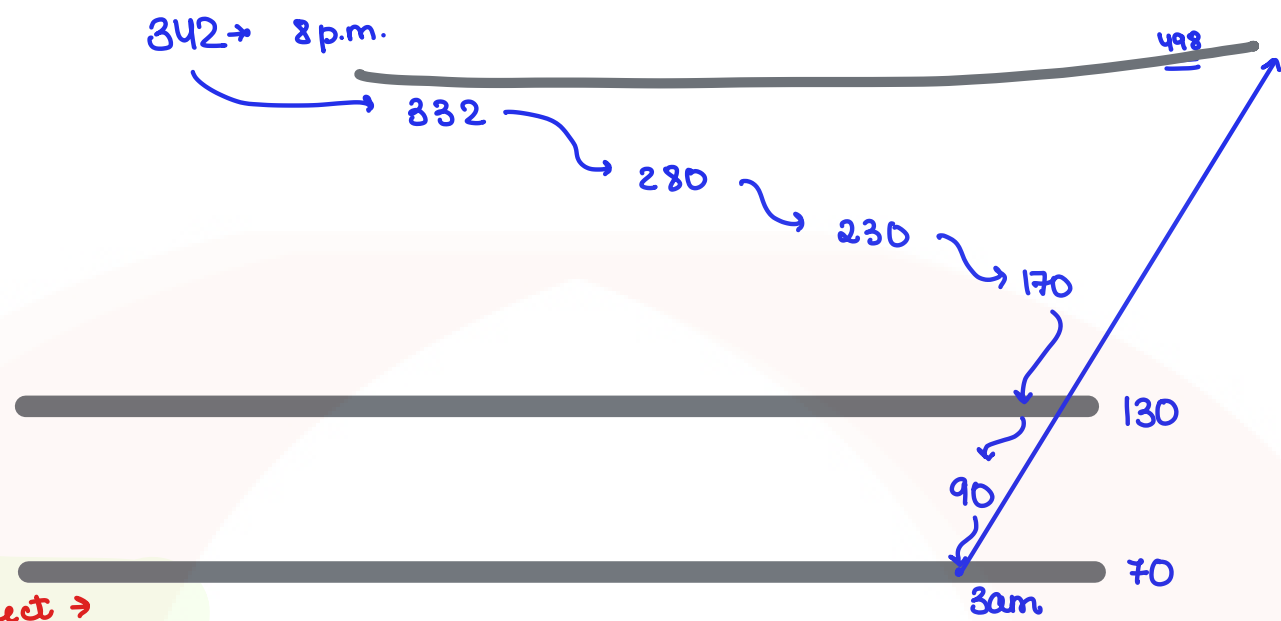
FBS = 386
 ↓ metformin
 380
 ↓ glimepiride
 372
 ↓ voglibose
 360
 ↓ niddagliptin
 342

Advise Insulin (0.1U/kg)
 wt. = 80kg
 8 unit s/c

8pm → 342 → 8U.

10a.m → 498
 (mon.)
 (next day)

→ don't change the dose.



Somogy's effect →

Peripheral res. to Insulin / sensitivity can't be calculated

some pts. develop Hypoglycemia
Hb
Hyperglycemia

Tlt: ↓ se the dose of Insulin.

Dawn Phenomenon →

Hyperglycemia throughout night.

Tlt: ↑ se the dose of Insulin.

SOMOGYI	EFFECT	DAWN	PHENOMENON
High dose of night Insulin		low dose of Insulin	
↓		or	
HYPOGLYCEMIA at night (3-5) am		↑ se resistance to Insulin	
↓		↓	
Counter-regulatory mechanism		HYPERGLYCEMIA (3-5 am)	
↓		↓	
HYPERGLYCEMIA at 8 am.		HYPER-GLYCEMIA (8am)	

Both are hyperglycemic condition that occurs in the morning but with different mechanism

Somogyi effect

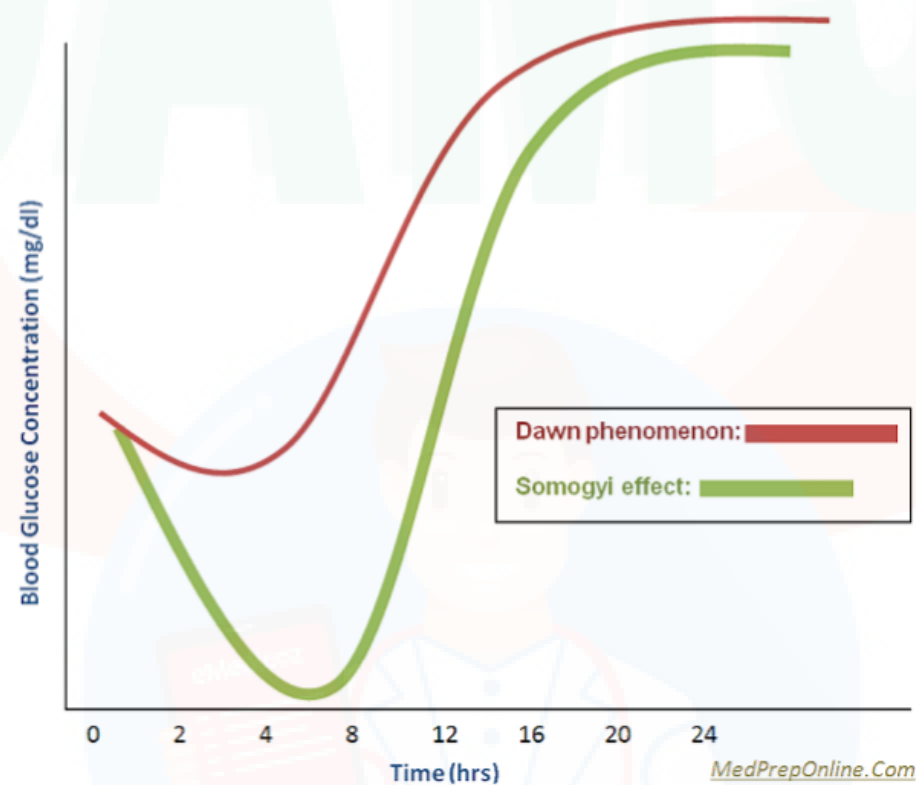
Man made. Due to poor diabetes management.

In the night, patient becomes hypoglycemic due to the action of the insulin and the drugs->glucagon is released->glycolysis->hyperglycemia

Dawn phenomenon

Physiological secretion of hormones(growth hormone, cortisol, catecholamines)

In the night, the insulin actions will eventually wear off and at the same time counter-regulatory hormones are secreted->hyperglycemia b'coz there is little amount of circulating insulin



HYPOGLYCEMIA

Whipple's triad -

Symptoms of Hypoglycemia
documented
reversal of symptoms on correcⁿ of Glucose.

Causes →

Treatment of DM → m/c cause.

Alcohol → stimulate Insulin Secⁿ

Hepatic failure / Hepatitis.
↳ Impaired gluconeogenesis and glycogenolysis.

Renal failure
Insulin excreted from kidney.

non-Islet cell tumors
Eg: Mesenchymal tumors
excrete IGF → ↑ Insulin sensitivity.

Insulinoma

C/F →

Palpitations

Tremors

anxiety

sweating

hunger

Pallor

↑ HR

↑ BP

eMedicoz

Investigations →

Serum Insulin

Serum C- peptide

Exogenous

Endogenous



Drug

- History
- Serum
- Urine

} drug level

Insulinoma

PET- Scan
CT- Scan

Insulinoma

T/E: Surgical resection

not possible

Diagonide

