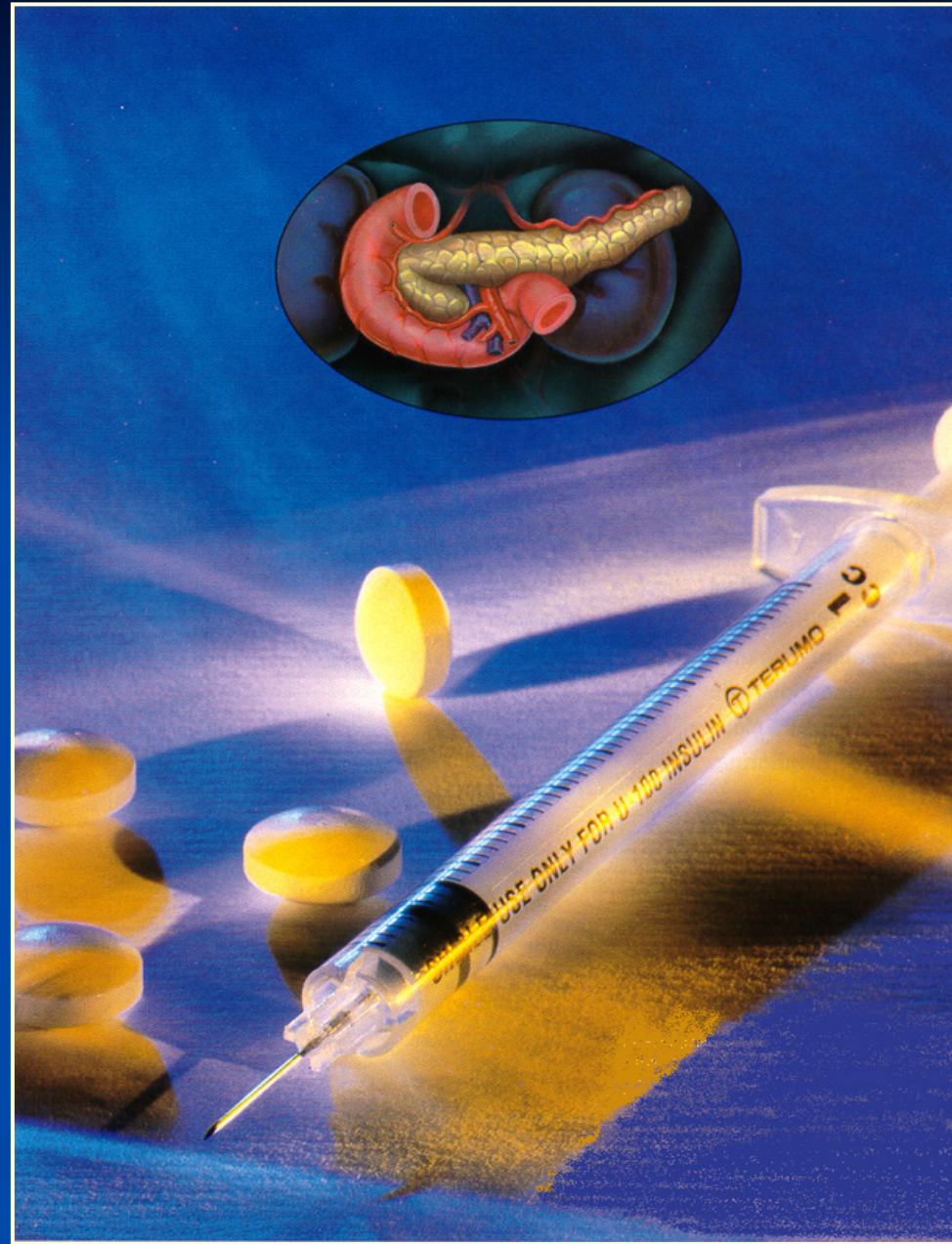
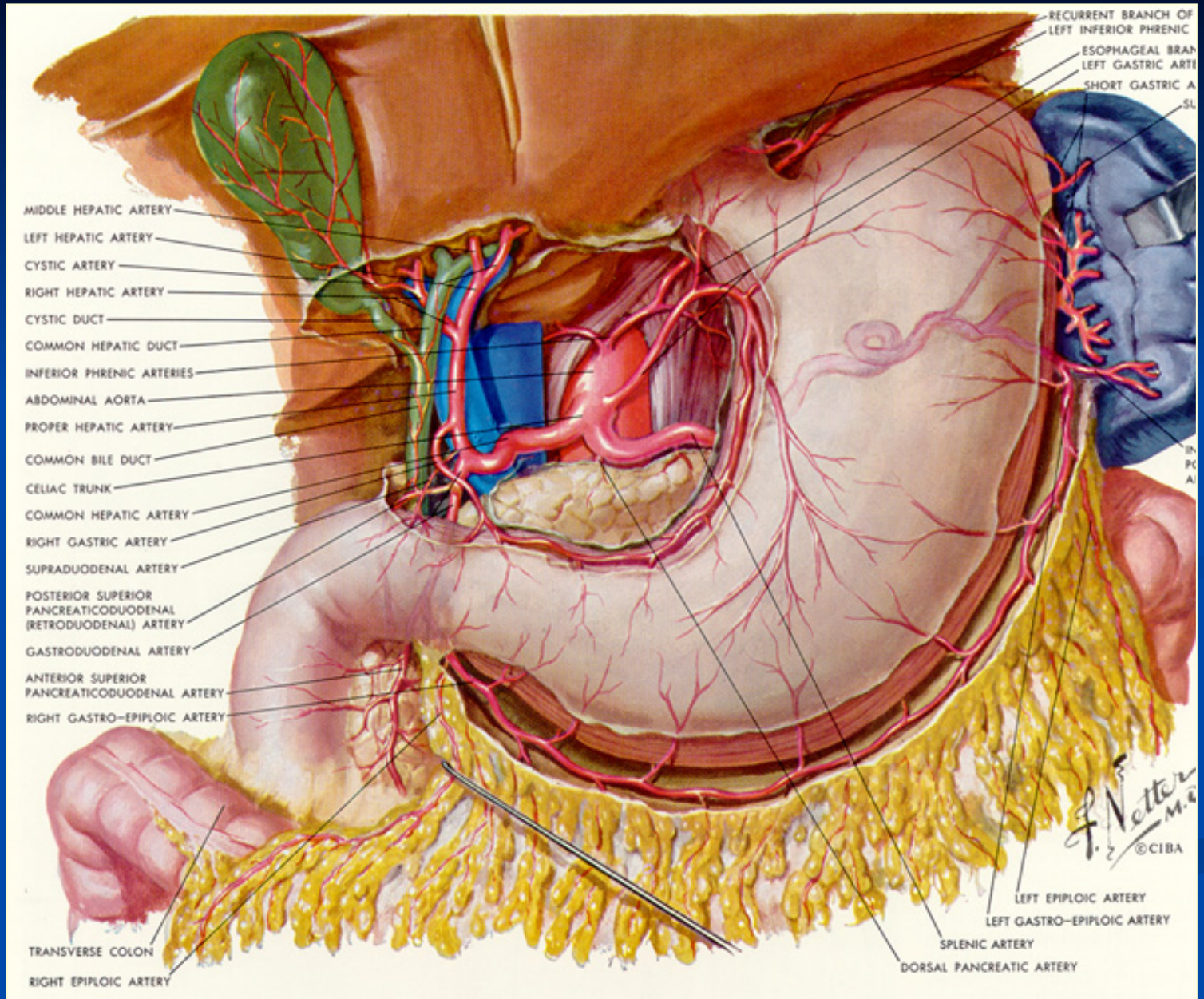


Management & Treatment of Diabetes Mellitus

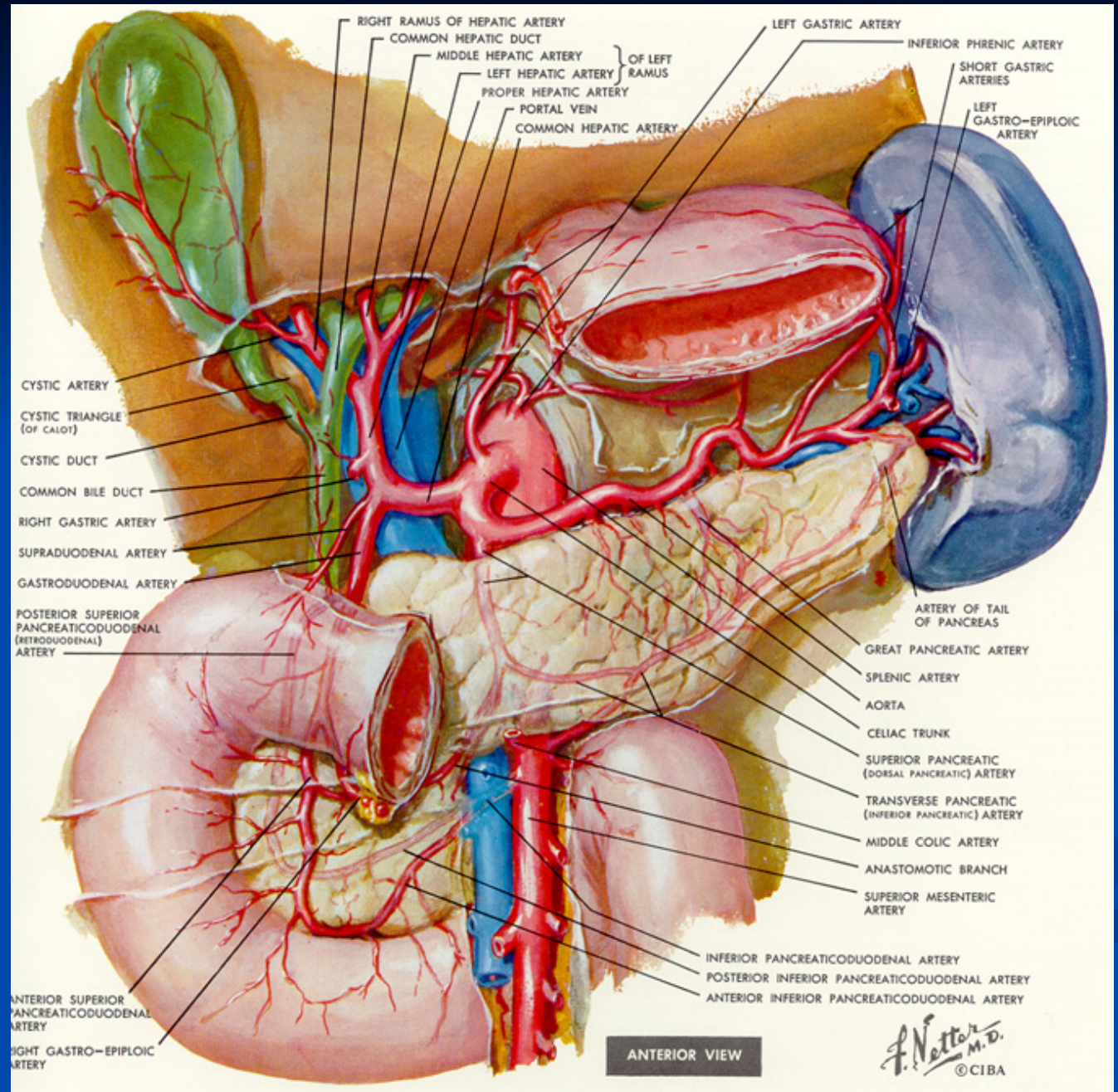
Southern California University
of Health Sciences



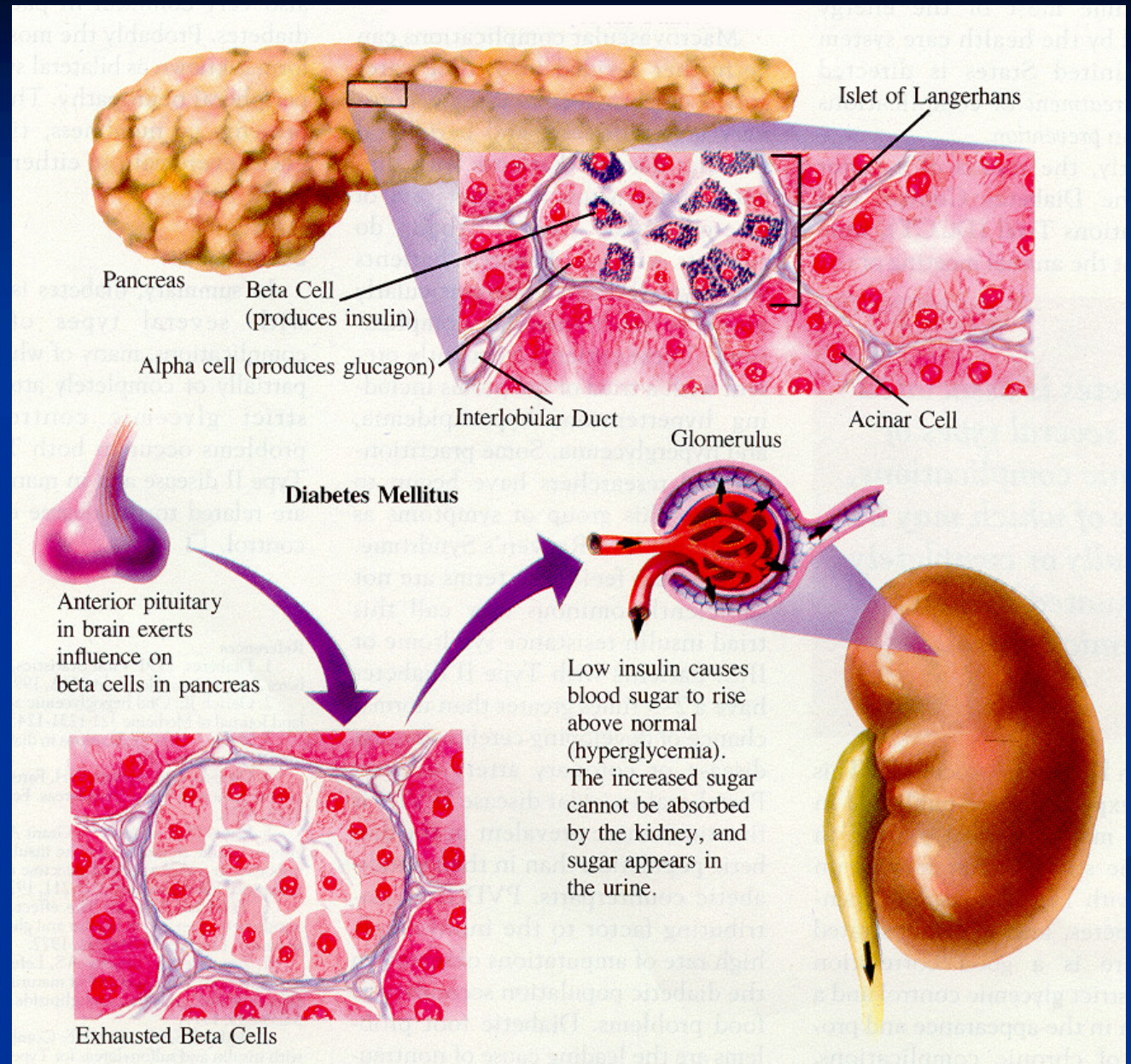
ANATOMY



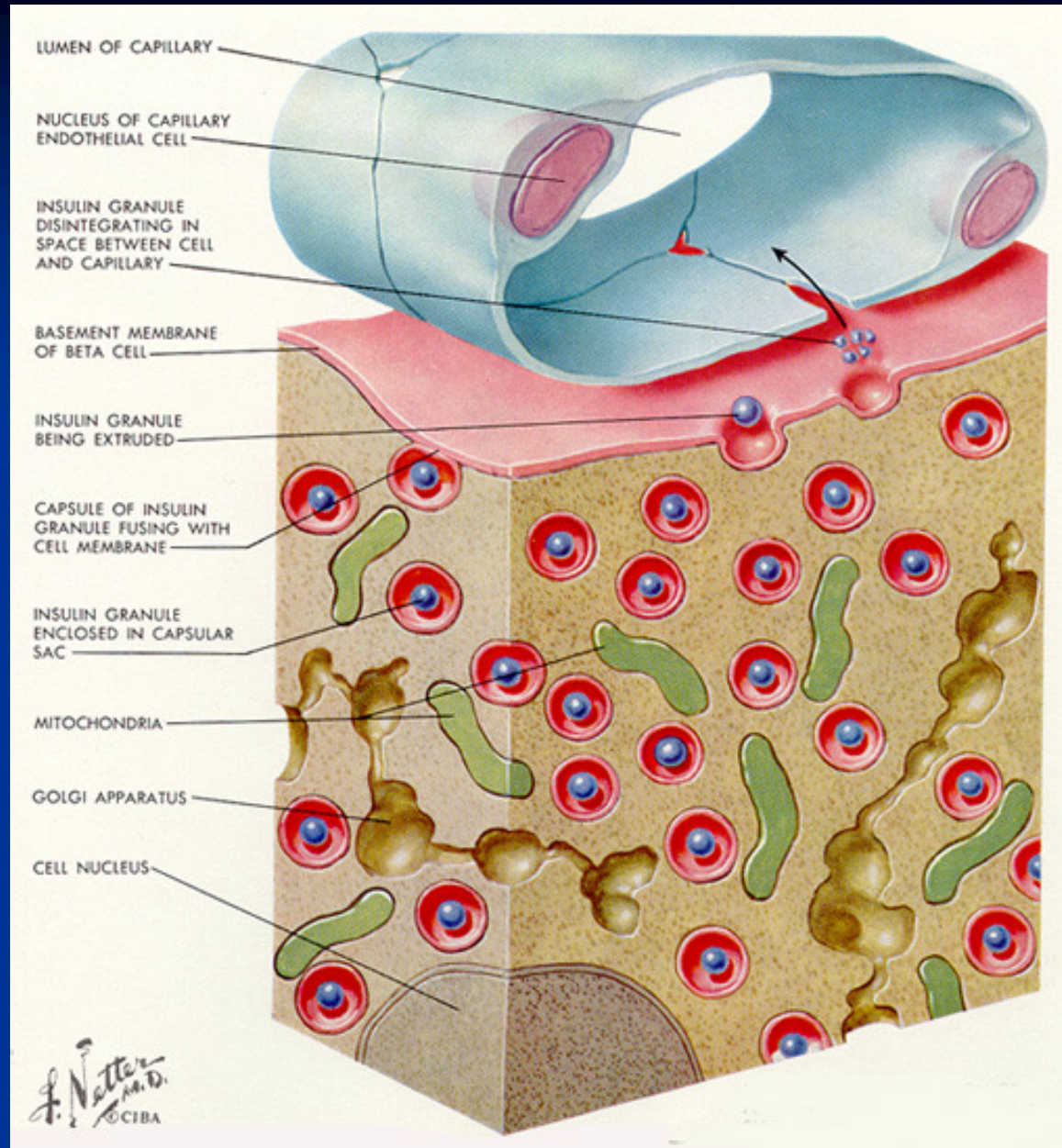
ANATOMY



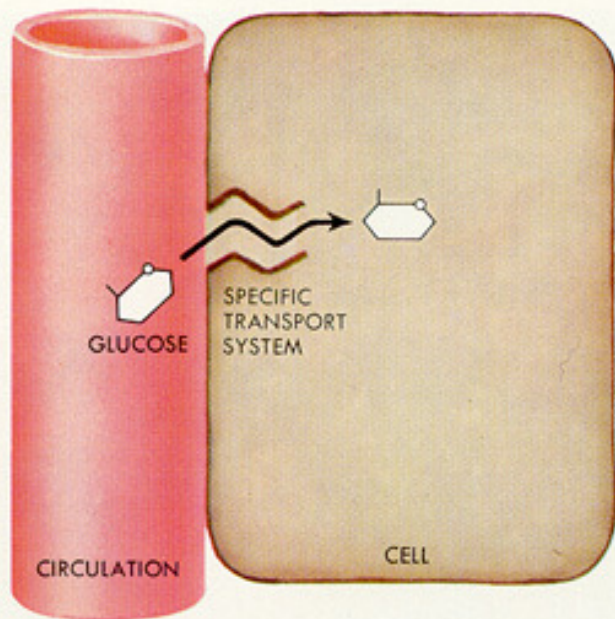
PHYSIOLOGY



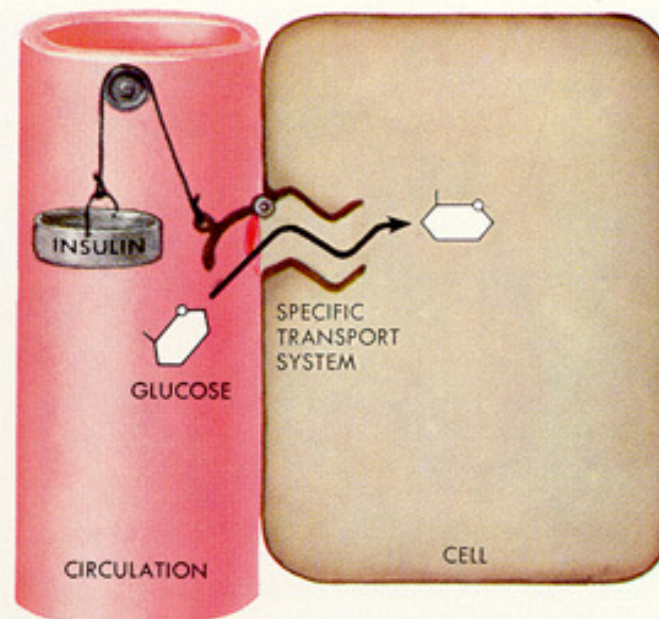
PHYSIOLOGY



FUNCTION OF INSULIN



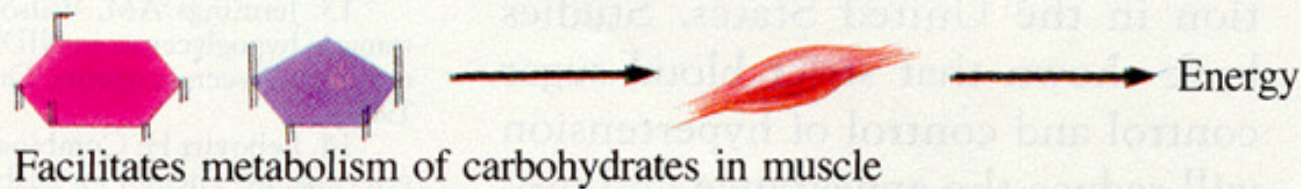
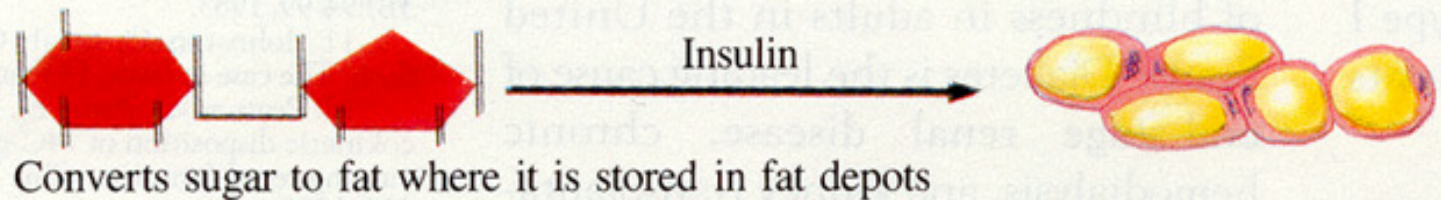
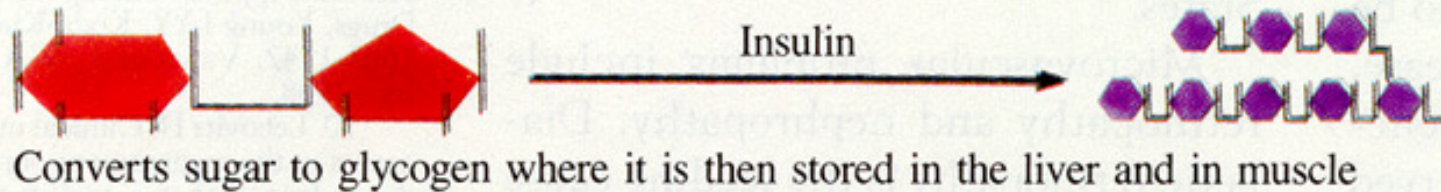
RED BLOOD CELLS; NEURONS
TRANSPORT (ENTRY) SYSTEM SPECIFIC
FOR CERTAIN SUGARS:
INSULIN HAS NO EFFECT ON RATE OF UPTAKE



FAT CELLS; MUSCLE CELLS
SPECIFIC TRANSPORT SYSTEM KEPT
INHIBITED OR COVERED:
INSULIN REMOVES COVER AND THUS
PROMOTES UPTAKE

FUNCTION OF INSULIN

Functions of Insulin



Lowers
Blood
Sugar
Level

I. General Considerations

A. Type I (“Juvenile Onset” or IDDM)

- IDDM results from autoimmune destruction of beta cells
- inability to secrete insulin
 - > ketone formation --> DKA

- ✓ Fatty acids are converted to glucose by the liver, releasing ketones into the bloodstream → DKA
- DKA is a life-threatening medical emergency

Diabetic Ketoacidosis (DKA)

Diagnostic criteria for DKA

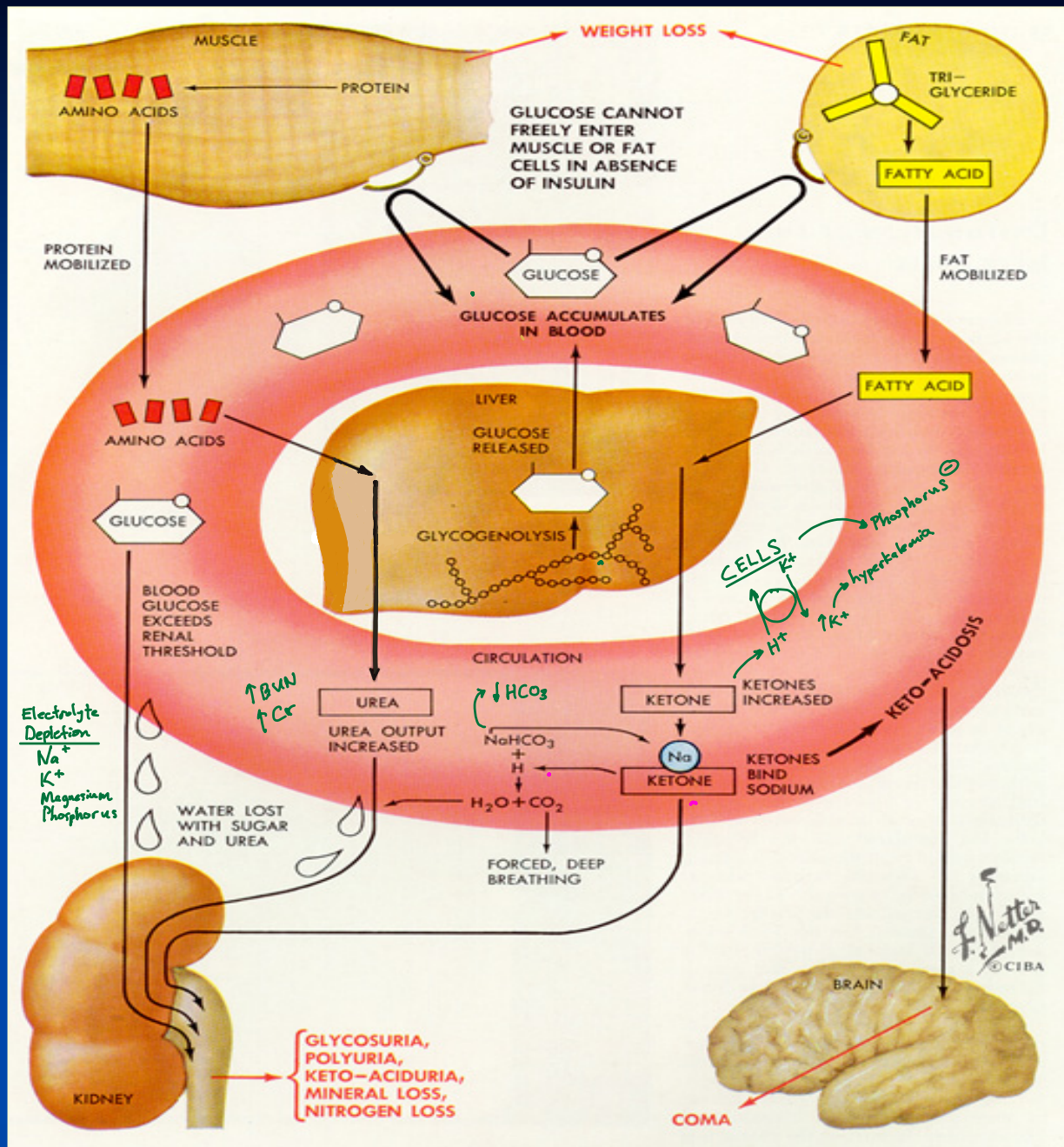
	DKA		
	Mild	Moderate	Severe
Plasma glucose(mg/dl)	More than 250	More than 250	More than 250
Arterial PH	7.25 - 7.30	7.00 - 7.24	Less than 7.00
Serum bicarbonate(mEq/L)	15 - 18	10 - 14	Less than 10
Urine ketones	+ve	+ve	+ve
Serum ketones	+ve	+ve	+ve
Effective serum osmolality(mOsm/kg)	Variable	Variable	Variable
Anion gap	More than 10	More than 12	More than 12
Alteration in sensoria	Alert	Alert / drowsy	Stupor / coma

Normal Values

BG: 90-110

pH: 7.35-7.45

HCO₃: 21-28



Columnar Dosing Protocol

DIRECTIONS:

Start infusion using the drip rate (ml/hr) in **COLUMN No.2** for the current Blood Glucose Range

To determine the new drip rate, compare the current BG Range to the previous BG Range.

If current BG Range is lower than the previous BG Range,
STAY IN THE SAME COLUMN

If current BG Range has not dropped
MOVE 1 COLUMN TO THE RIGHT

*If more than 16 columns are needed:
See back of page.*

When hourly **BG** is 90-140, stay in the same column to determine the new drip rate.
DO NOT CHANGE COLUMNS

When new BG is less than **90**, **MOVE 1 COLUMN TO THE LEFT** and refer to Figure No. 2 for D50 treatment.

(FIGURE No. 1)

TARGET BG 90-140 (1)

Blood Glucose Ranges (mg/dl)	column 1	column 2	column 3	column 4	column 5	column 6	column 7	column 8
Over 450	4.4	8.8	13.2	17.6	22	26.4	30.8	35.2
385-450	3.6	7.2	10.8	14.4	18	21.6	25.2	28.8
334-384	3	6	9	12	15	18	21	24
290-333	2.5	5	7.5	10	12.5	15	17.5	20
251-289	2.1	4.2	6.3	8.4	10.5	12.6	14.7	16.8
217-250	1.7	3.4	5.1	6.8	8.5	10.2	11.9	13.6
188-216	1.4	2.8	4.2	5.6	7	8.4	9.8	11.2
163-187	1.2	2.4	3.6	4.8	6	7.2	8.4	9.6
151-162	1	2	3	4	5	6	7	8
141-150	0.9	1.8	2.7	3.6	4.5	5.4	6.3	7.2
131-140	0.8	1.6	2.4	3.2	4	4.8	5.6	6.4
121-130	0.7	1.4	2.1	2.8	3.5	4.2	4.9	5.6
111-120	0.6	1.2	1.8	2.4	3	3.6	4.2	4.8
106-110	0.5	1	1.5	2	2.5	3	3.5	4
101-105	0.4	0.9	1.3	1.8	2.2	2.7	3.1	3.6
96-100	0.4	0.8	1.2	1.6	2	2.4	2.8	3.2
90-95	0.3	0.7	1	1.4	1.7	2.1	2.4	2.8
80-89	0.3	0.6	0.9	1.2	1.5	1.8	2.1	2.4
70-79	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6
60-69	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Under 60	0	0	0	0	0	0	0	0

BC	D50W	ACTION (Figure No.2)
80-89	Do Not Give	- If you have not moved 1 column to the left as directed above, do so now and give D50 per BG
70-79	10 ml IV Push	

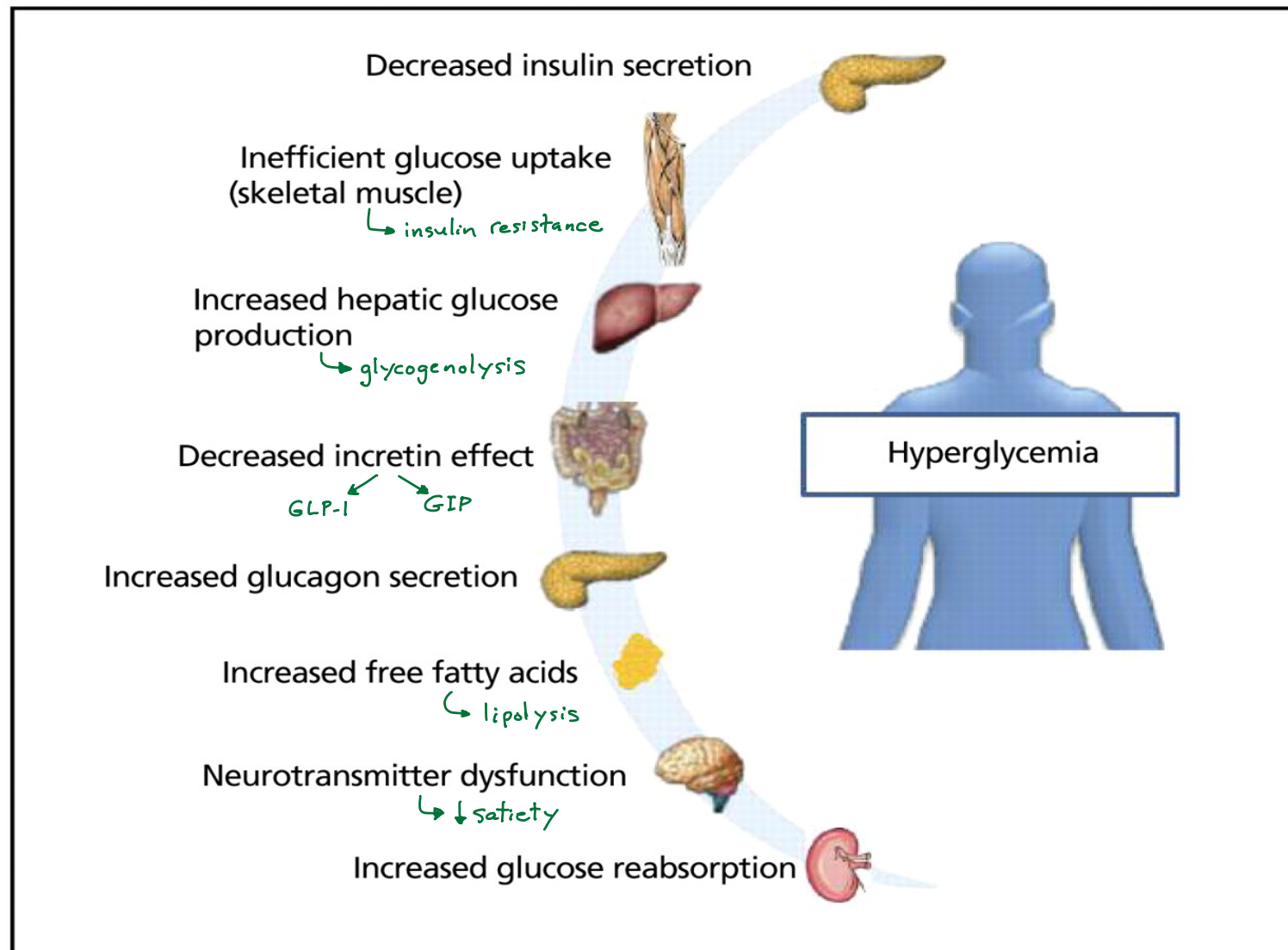
KEYPOINTS FOR NURSING (Figure No.3)
Hourly BG required until target range achieved for 4 consecutive hours, then B
If tube feeding or TPN paused, stop insulin infusion. Resume when nutrition re

Glucose Level (mg/dL)	Low Dose Regimen	Medium Dose Regimen	High Dose Regimen
Humalog Sliding Scale	(0-6 UNITS) AC & HS	(0-12 UNITS) AC & HS	(0-18 UNITS) AC & HS
Serum FBS < 60	Dextrose 12.5 GM	Dextrose 12.5 GM	Dextrose 12.5 GM
60-150	0	0	0
150-200	1	2	3
201-250	2	4	6
251-300	3	6	9
301-350	4	8	12
351-400	5	10	15
> 400	6	12	18

B. Type II (“Adult Onset” or NIDDM)

- NIDDM results from resistance to insulin and impaired response of beta cell to glucose ---> hyperglycemia
- ✓ • sufficient endogenous insulin is usually present to prevent ketoacidosis

B. Type II DM (cont.)



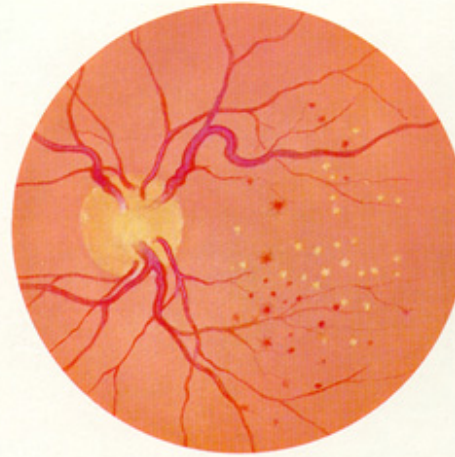
C. Complications of Diabetes

- polydipsia, polyuria, polyphagia, nocturia, hypoglycemia, fatigue, and blurred vision
- DKA --> Type I Diabetes
- Non-Ketotic coma --> Type II Diabetes

(2) Chronic Complications

(a) Microvascular

- diabetic
retinopathy



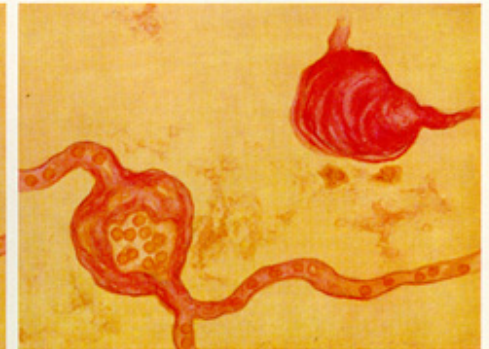
VENOUS DILATATION, MICRO-ANEURYSMS, MINUTE HEMORRHAGES AND YELLOWISH SPOTS IN OCULAR FUNDUS



RETINITIS PROLIFERANS AND MASSIVE HEMORRHAGE



THIN-WALLED MICRO-ANEURYSMS AND CAPILLARY KINKING IN FLAT PREPARATION OF RETINA (X 500)
H=HEMORRHAGE; D=DISSECTING ANEURYSM;
E=EXUDATE



PARTIALLY HYALINIZED AND COMPLETELY HYALINIZED (THROMBOSED) MICRO-ANEURYSMS (X 500)



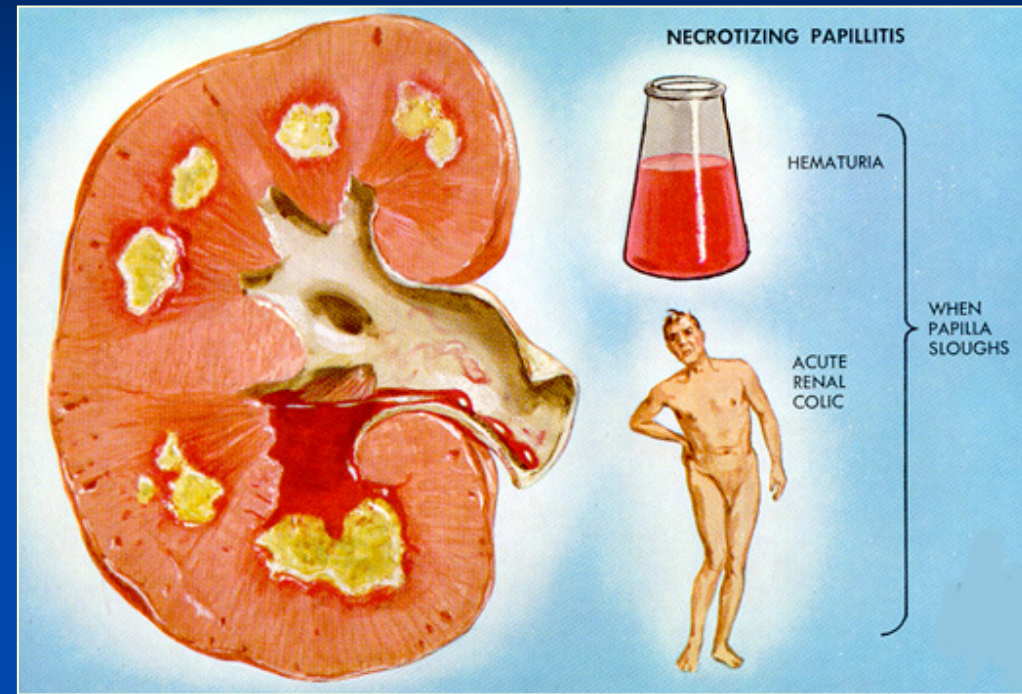
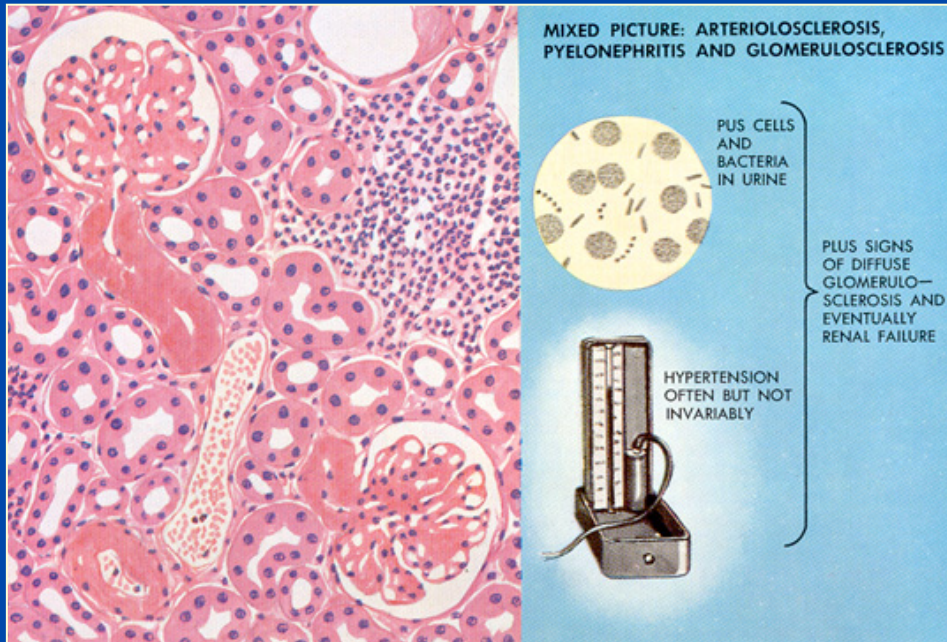
CATARACT

F. Netter M.D.
© CIBA

(2) Chronic Complications

b. kidney disease

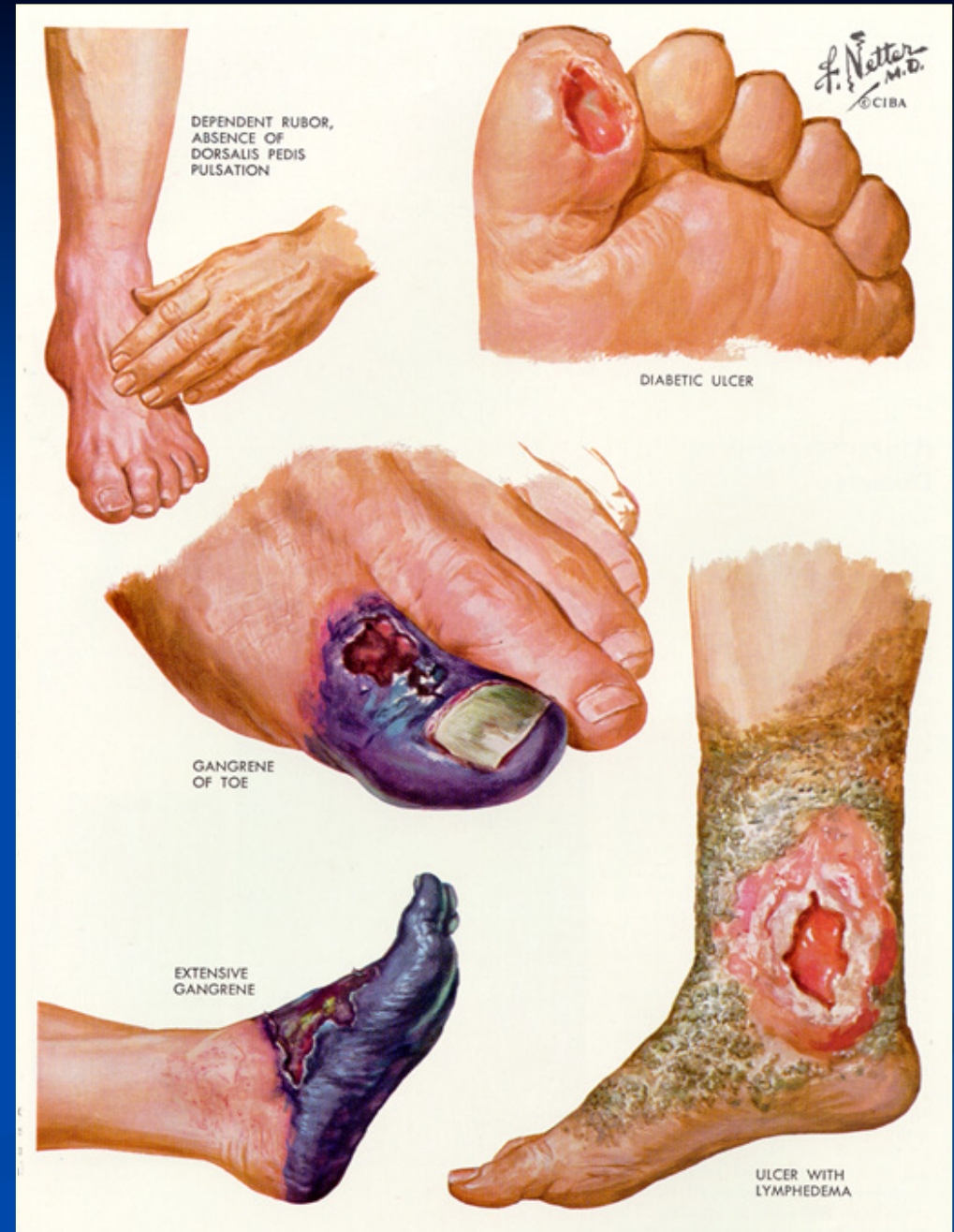
- glomerulosclerosis
- pyelonephritis → CKD
DKD



- necrotizing papillitis

(b) Macrovascular

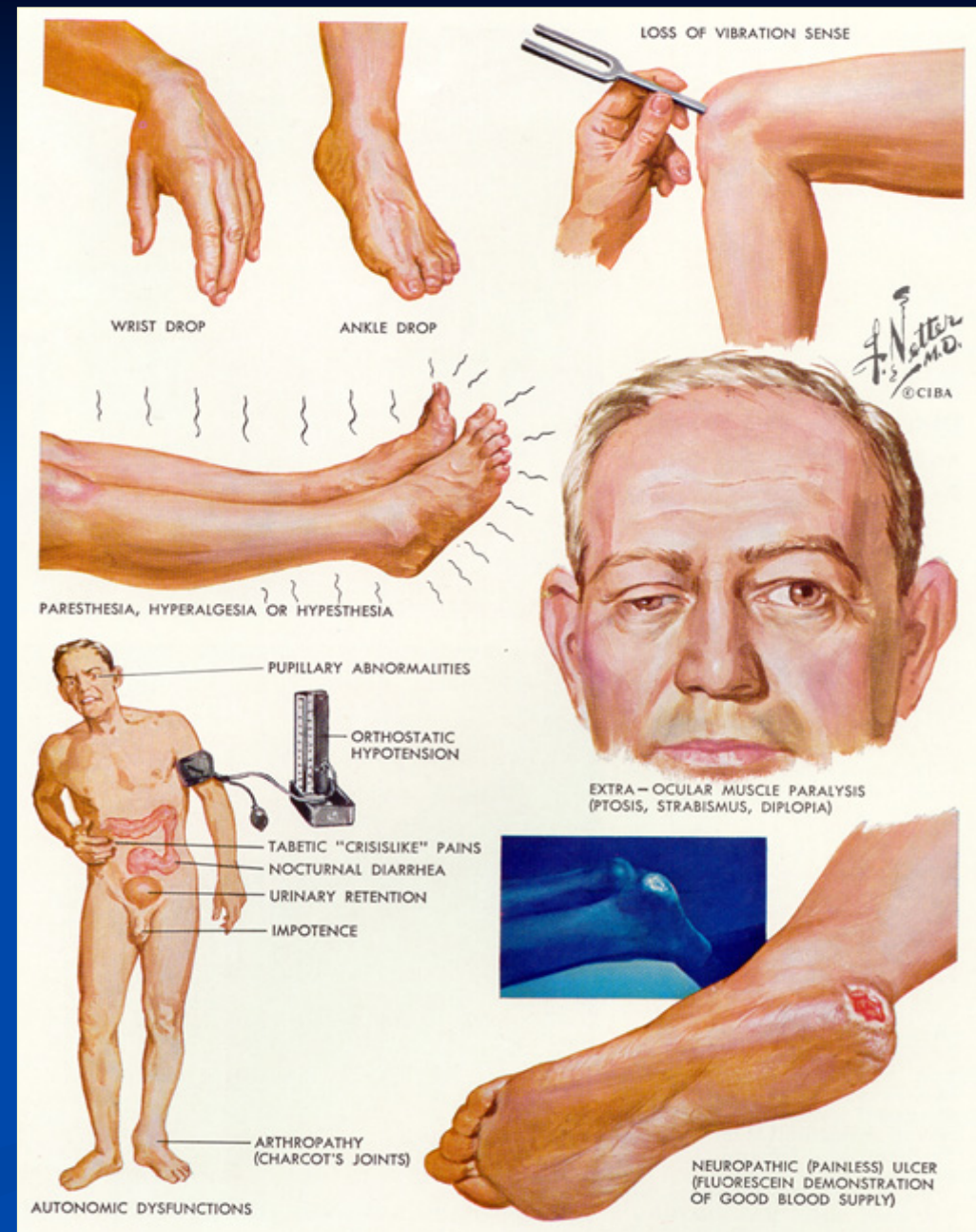
- cerebrovascular disease → ↑ stroke
- cardiovascular disease → ↑ MI
- peripheral vascular disease
 - ↳ diabetic foot infections



(c) Neuropathy

- orthostatic hypotension
- numbness and/or pain in extremities
- gastroparesis
- diabetic foot disease/ulcers

diabetic neuropathies



III. Criteria for diagnosis of PREDIABETES & DIABETES

Criteria for the Diagnosis of PREDIABETES

A1C $\geq 5.7\%$, but $< 6.5\%$

OR

Fasting plasma glucose ≥ 100 mg/dL (fasting is no food for at least 8 hours), but < 126 mg/dL

OR

Two-hour plasma glucose ≥ 140 mg/dL during an oral glucose tolerance test, but < 200 mg/dL

Criteria for the Diagnosis of DIABETES

A1C $\geq 6.5\%$

OR

Fasting plasma glucose ≥ 126 mg/dL (fasting is no food for at least 8 hours)

OR

Two-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test

OR

Symptomatic patients with a random plasma glucose ≥ 200 mg/dL

IV. Treatment of Diabetes

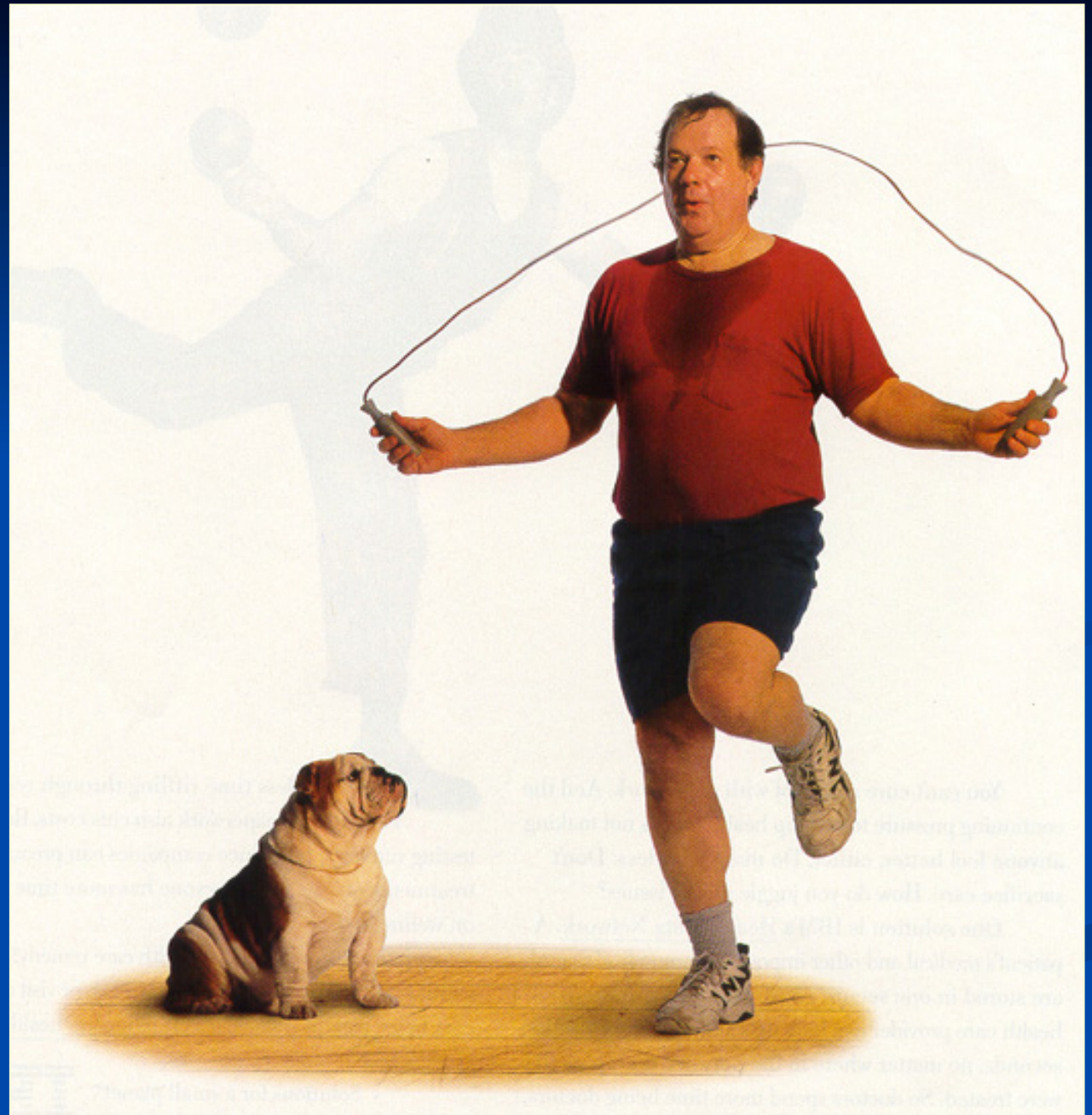
A. Lifestyle Modifications

(2) Nutrition

- timing of meals
- nutritional content of meals
- body weight

(2) Exercise

- increases utilization of glucose
- improves insulin utilization
- improves lipid profile



Sample Caloric Requirement (BEE) Calculation for Stressed Patients

Female: $655 + (9.6 \times \text{wt. in kg}) + (1.85 \times \text{ht. in cm}) - (4.7 \times \text{age})$

Male: $66 + (13.7 \times \text{wt. in kg}) + (5.00 \times \text{ht. in cm}) - (6.8 \times \text{age})$

Sample Calculation (based on patient-specific parameters: ht, wt, age, and disease state)

S.Y. is a 64 year-old female patient with major sepsis. Calculate her caloric requirement based on her pathologic condition. Her height is 5'4" and body weight is 140 pounds.

Conversion Factors:

- body weight from pounds to kg. : $140 \text{ lbs} / 2.2 = 63.64 \text{ kg}$
- height from inches to cm. : $5'4" = 64 \text{ inches} \times 2.54 = 162.56 \text{ cm}$

$$\begin{aligned} \text{BEE} &= 655 + (9.6 \times \mathbf{63.64}) + (1.85 \times \mathbf{162.56}) - (4.7 \times \mathbf{64}) \\ &= (655 + 610.94 + 300.74) - (300.8) \\ &= 1265.88 \text{ kcal / day} \end{aligned}$$

Multiply the BEE value by the appropriate "**disease stress factor**", which provides additional calories to account for the degree of physiologic stress (based on increased metabolic requirement during pathologic condition – i.e., **major sepsis**).

$$\text{BEE for major sepsis} = \mathbf{1.5} \times 1265.88$$

Answer → 1898.82 kcal / day

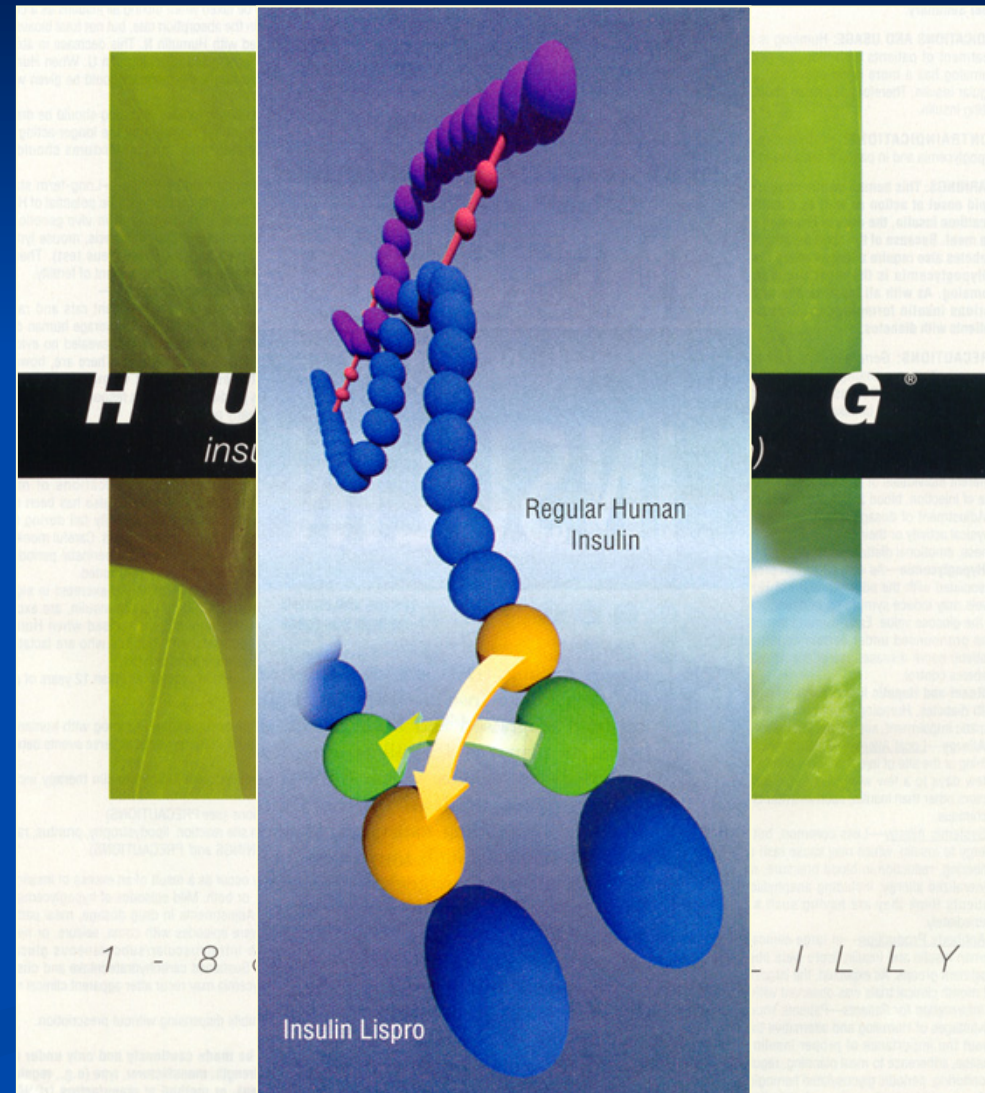
III. Pharmacologic Management of IDDM

A. Insulin Products

(1) Rapid-Acting Insulin

(a) Humalog (Lispro)

- onset: 10 - 15 min
- peak: 45 min - 1 hr
- duration: 2 - 4 hrs



(1) Short-Acting Insulin

Regular Insulin (Humulin R)

- onset: 30 - 60 min --> peak: 2 - 4 hrs
- duration: 5 - 7 hrs

(2) Intermediate-Acting Insulin

NPH (Isophane)

- onset: 1 - 2 hrs --> peak: 6 - 14 hrs
- duration: 24+ hrs

Insulin Comparison Chart

Insulin Name	When does it start working? (onset)	When will the effect be the greatest? (peak)	How long will it lower blood glucose? (duration)	Notes for Use	Cost estimate
Rapid Acting					
Lispro (Humalog™)	<15 minutes	0.5-3 hours*	3-5 hours AC:HS	If mixing with NPH, rapid acting insulin should be drawn into syringe first. Mixture should be given immediately to avoid effects on peak action.	\$96 (10 ml vial) \$183 (5x3 ml pen cartridges)
Aspart (Novolog™)	<15 minutes	0.5-3 hours*	3-5 hours		\$102 (10 ml vial) \$205 (5x3 ml pen cartridges)
Glulisine (Apidra™)	<15 minutes	0.5-3 hour*	3-5 hours		\$96 (10 ml vial) \$184 (5x3 ml pen cartridges)
Short Acting					
Regular (Novolin R™ or Humulin R™)	0.5-1 hour	2-4 hours	4-8 hours AC:HS	May be mixed with NPH in same syringe. Mixing order should be the clear regular drawn up first, then the cloudy NPH (ie "clear to cloudy").	\$53 (10 ml vial Humulin or Novolin) \$121 (5x3 ml Novolin pen cartridges) \$89 (5x3 ml Innolet cartridges)
Intermediate Acting					
NPH (Novolin N™ or Humulin N™)	2-4 hours	4-10 hours	10-18 hours Q12H	Available as pen or in vial to be used with syringe.	\$52 (10 ml vial Humulin or Novolin) \$121 (5x3 ml pen cartridges) \$91 (5x3 ml Innolet cartridges)
Long Acting					
Glargine (Lantus™)	4-6 hours	Same action throughout the day	24 hours	Do not mix with other insulins. Available as pen or in vial. Duration (clinical trial data): 6 hrs (0.1 U/kg), 12 hrs (0.2 U/kg), 20 hrs (0.4 U/kg), 23 hrs (0.8 U/kg and 1.6 U/kg)	\$97 (10 ml vial) \$177 (5x3 ml Solostar pen cartridges)
Detemir (Levemir™)	2-3 hours	6-8 hours	Dose-dependent 5.7-23.2 hours Q12H		\$95 (10 ml vial) \$182 (5x3 ml pen cartridges)
Combinations					
Humulin or Novolin 70/30	0.5-1 hour	2-10 hours	10-18 hours	70% NPH +30% regular insulin. Insulin action includes 2 peaks (1 from each formulation).	\$54 (10 ml vial) \$135 (5x3 ml pen cartridges) \$94 (5x3 ml Innolet cartridges)
Novolog Mix 70/30 Humalog Mix 75/25 or 50/50	<15 minutes	1-2 hours	10-18 hours	Novolog Mix: aspart protamine 70% + aspart 30% Humalog mix: 75/25=75% lispro protamine + 25% lispro 50/50=50% lispro protamine + 50% lispro Insulin action includes 2 peaks (1 from each formulation).	Humalog Mix 75/25: \$102 (10 ml vial), \$174 (5x3 ml pen cartridges)

C. Biochemical Indices of Metabolic Control

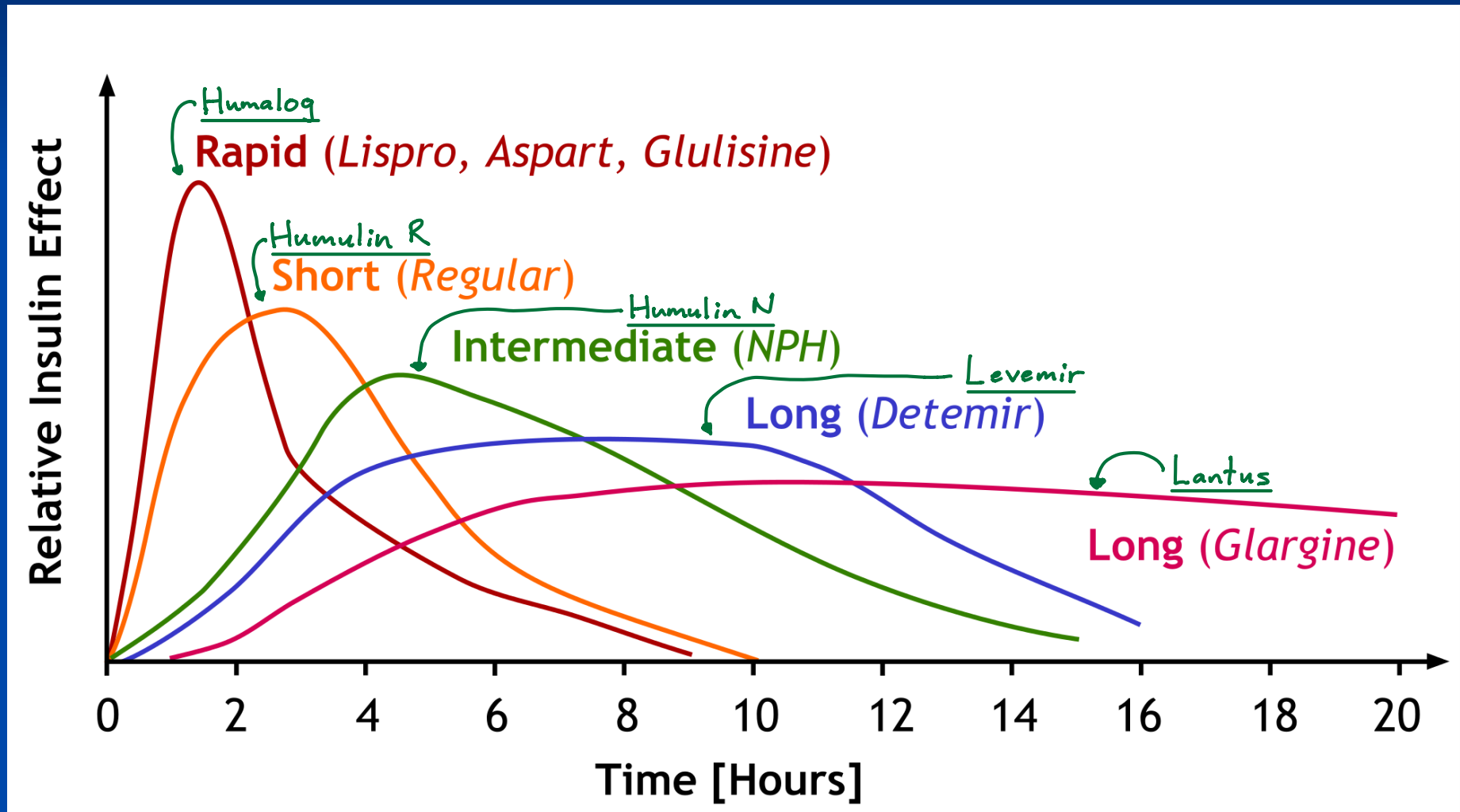
<u>Indice</u>	<u>Normal</u>	<u>Intensive</u>	<u>Acceptable</u>	<u>Poor</u>
Fasting	< 115	70-120	<140	>200
2 hrs pp	< 140	< 180	< 200	> 235
<u>HgbA1c</u>	<u>4 - 6 %</u>	<u>6 - 7 %</u>	^{7.5} <u>7.5 - 8.0</u>	<u>> 9.0</u>
<u>Urine Gluc</u>	neg	<u>rare</u>	<u>intermit</u>	<u>constant</u>
<u>Urine Keto</u>	neg	<u>rare</u>	<u>rare</u>	<u>intermit</u>

D. Insulin Regimens

- daily insulin requirements:
 - 0.5 - 1.0 units insulin / kg bd wt / day
- general rule:
 - 1 - 2 units insulin --> ↓ 30-50 mg/dl BG

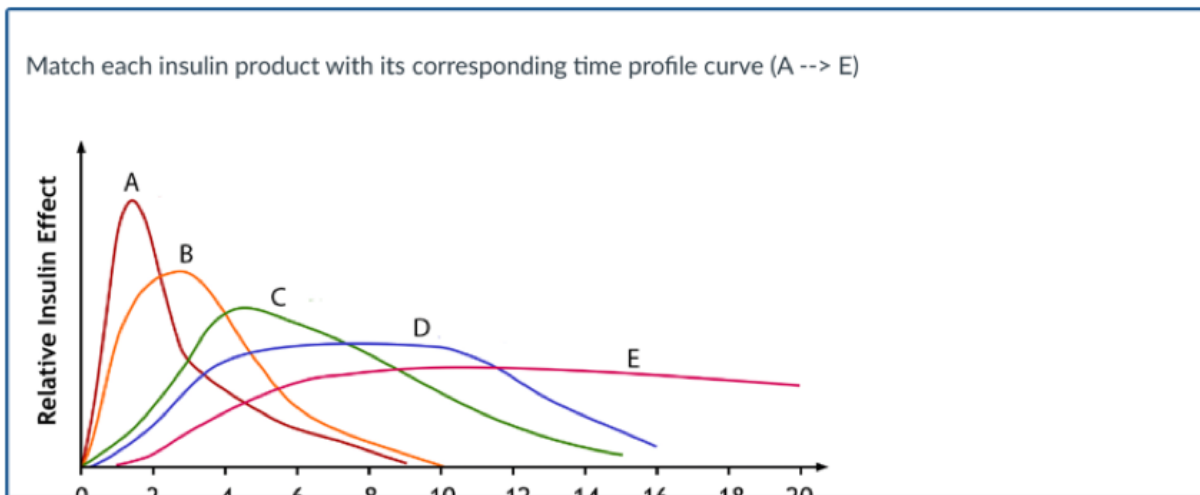
E. Time Profile Curves of Current Insulin Products

Lispro (Humalog), Aspart (Novolog), Glulisine (Apidra), Regular (Humulin R), NPH (Humulin N), Detemir (Levemir), and Glargine (Lantus)





Match each insulin product with its corresponding time profile curve (A --> E).

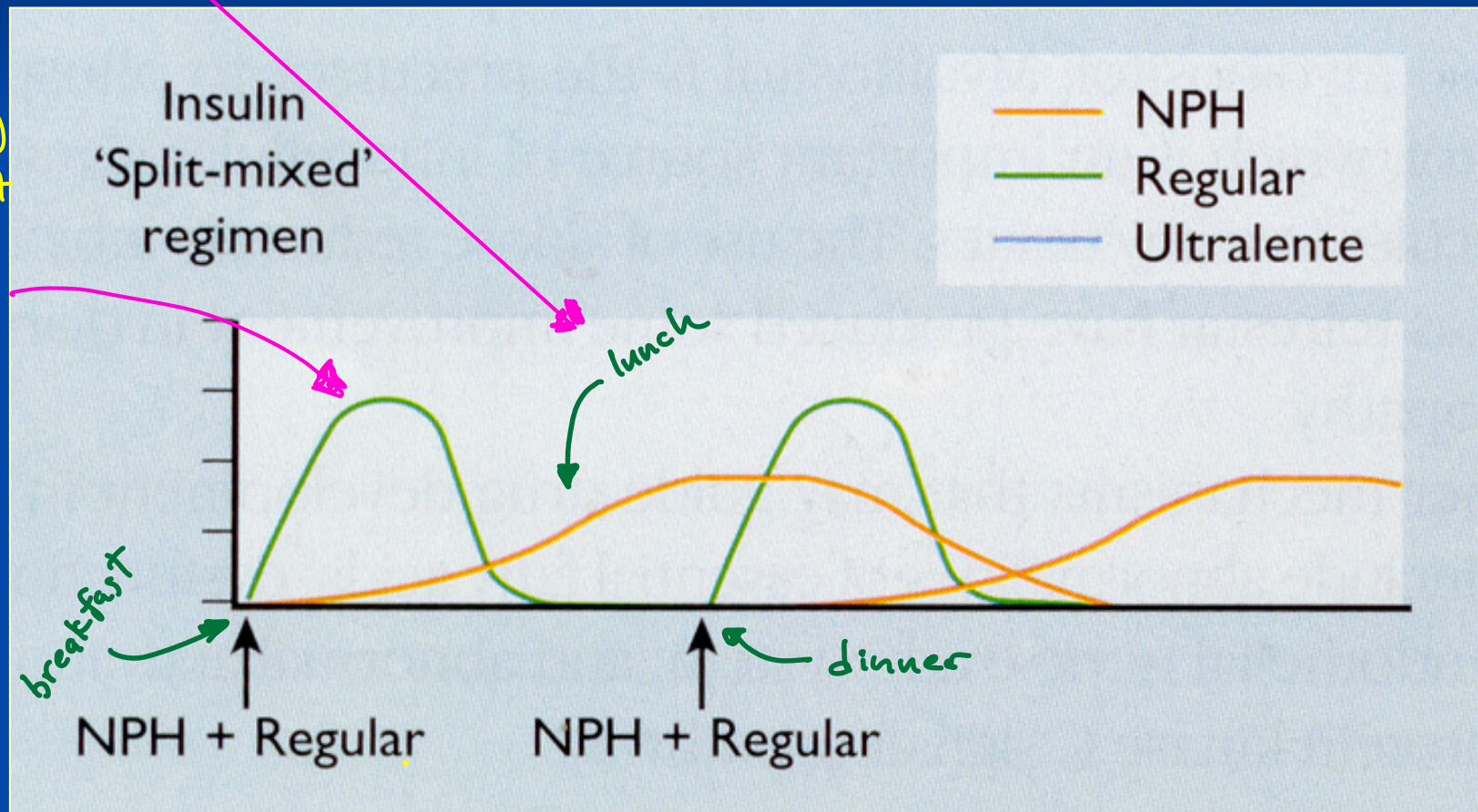


(1) Method 1: 7AM --> NPH:Reg (2/3 of daily dose)

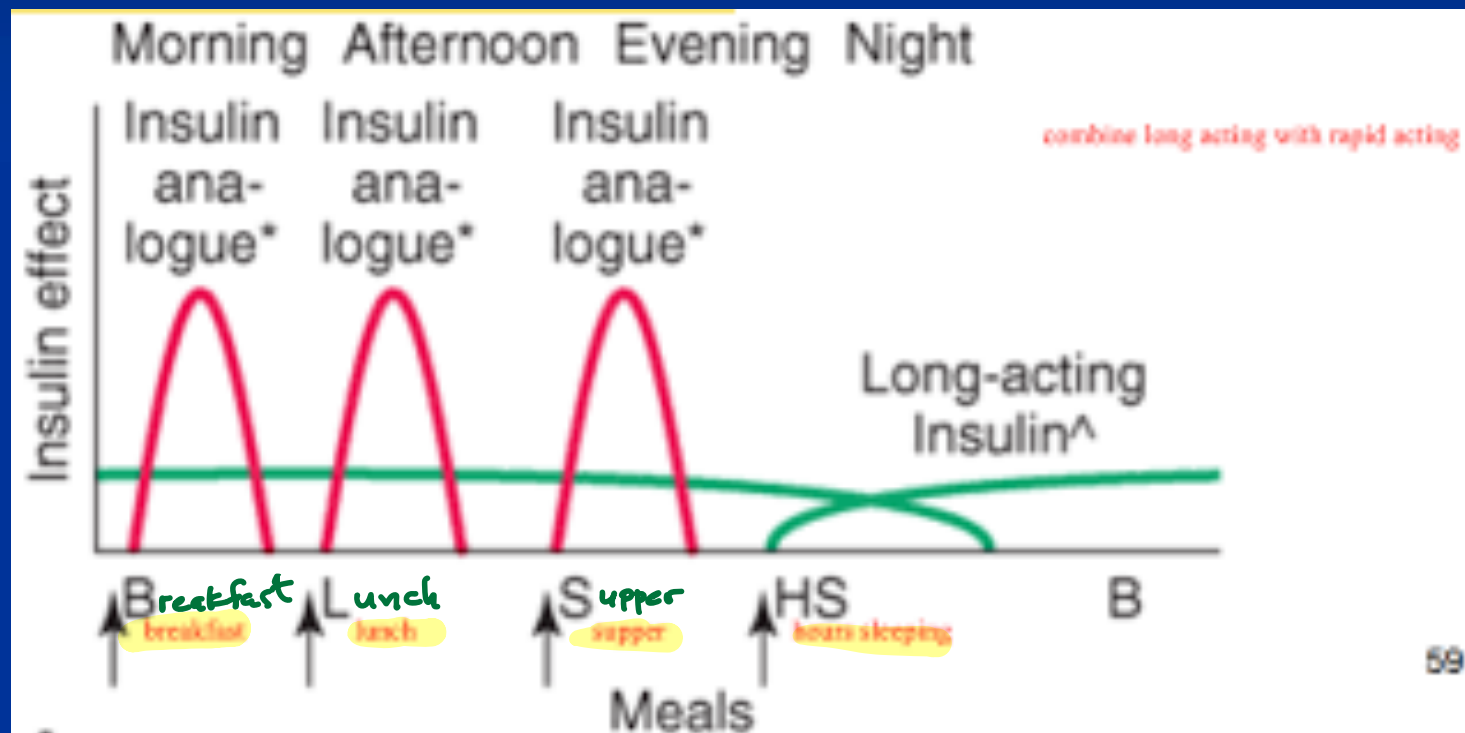
6 PM --> NPH:Reg (1/3 of daily dose)

✓ NPH at breakfast
to cover lunch

✓ Regular
Insulin
(Humulin R)
at breakfast
to cover
breakfast



(2) Method 2: Lispro (Humalog) + Insulin Glargine (Lantus)

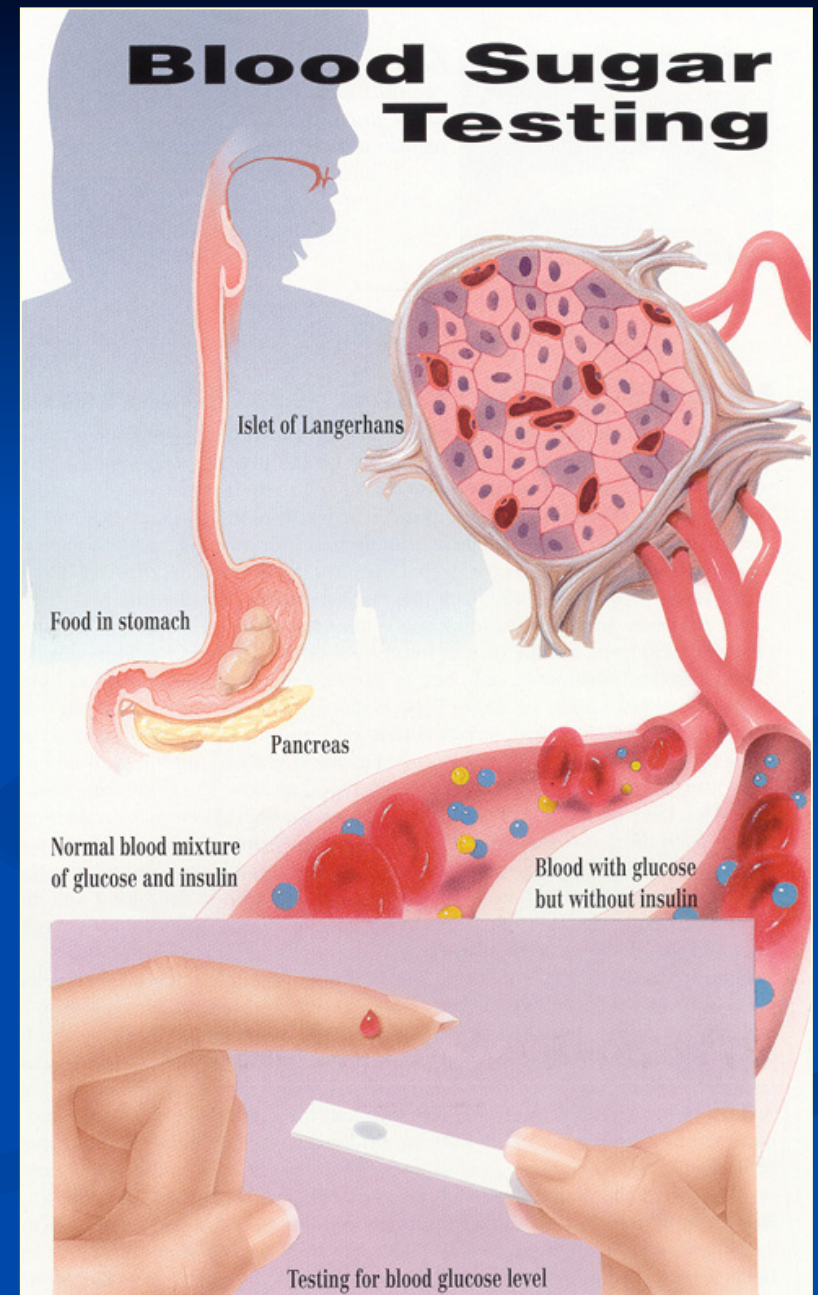


E. Monitoring Patients on Insulin Therapy

(a) ac & hs

(b) occasionally at 0300 during periods of insulin dose adjustments

(c) whenever hypoglycemia is suspected



F. Hypoglycemia

(1) Signs & Symptoms

- palpitations, tachycardia, blurred vision,
sweaty palms, generalized sweating,
tremors, hunger, confusion, anxiety,
irritability, headache, tingling and
numbness, and seizures
- nocturnal hypoglycemia --> nightmares,
restless sleep, profuse sweating, and
morning "hangover"

F. Hypoglycemia (cont.)

(2) Treatment --> 10-20 gm rapidly absorbed carbohydrate (MR x 1 in 15-20 min if BG < 60 or still symptomatic)

- examples: OJ (1/2 cup), apple juice (1/3 cup), grape juice (1/4 cup), sugar (2 tsp or 2 cubes), Lifesavers (5-6 pieces), B/D glucose tabs (2 tabs)
- if patient is unconscious
 - > glucagon 1 mg SQ, IM, or IV or
 - > glucose 25 gm IV (Dextrose 50% 50 ml)

(3) Drugs Associated with Hypoglycemia

<u>Drug</u>	Effect	Mechanism
<u>ethanol</u>	+++	(-) glycogenolysis (-) gluconeogenesis
<u>beta-blockers</u>	++	(-) <u>glycogenolysis</u> <i>β₂ blockade (liver)</i> <u>masks sx's hypoglycemia</u>
<u>salicylates</u>	++	↑ <u>insulin secretion/sensitivity</u> ↑ <u>serum sulfonylurea levels</u> <i>plasma protein binding displacement</i>

NSAIDs

G. Hyperglycemia

(1) Signs & Symptoms

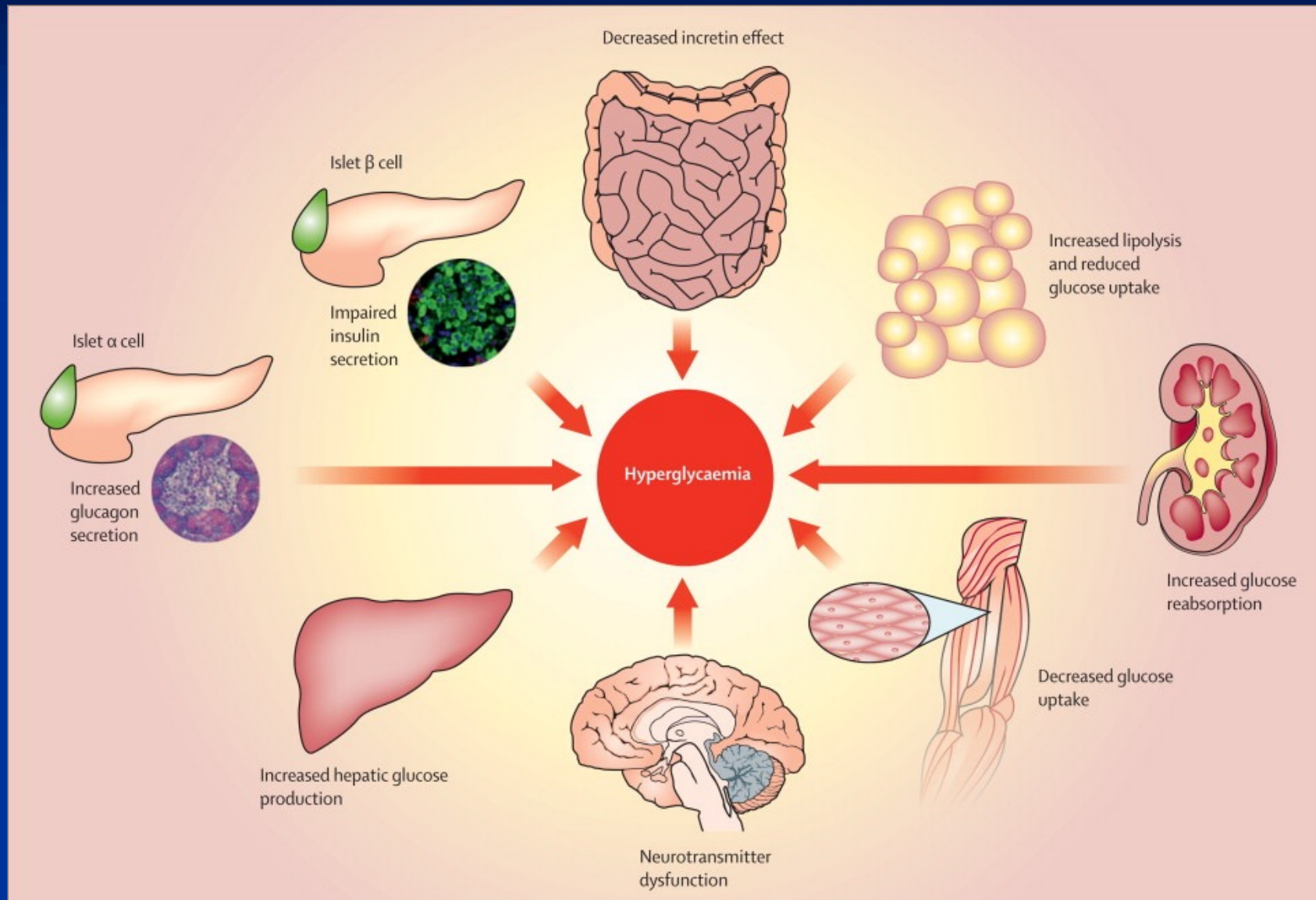
- ✓ • polydipsia, polyuria, polyphagia, fatigue, etc...

(2) Somogyi Effect --> "post-hypoglycemic hyperglycemia" or "rebound hyperglycemia"

- tx: → reduction of evening regular insulin dose
 - increase calories at evening meal
 - increase evening NPH dose

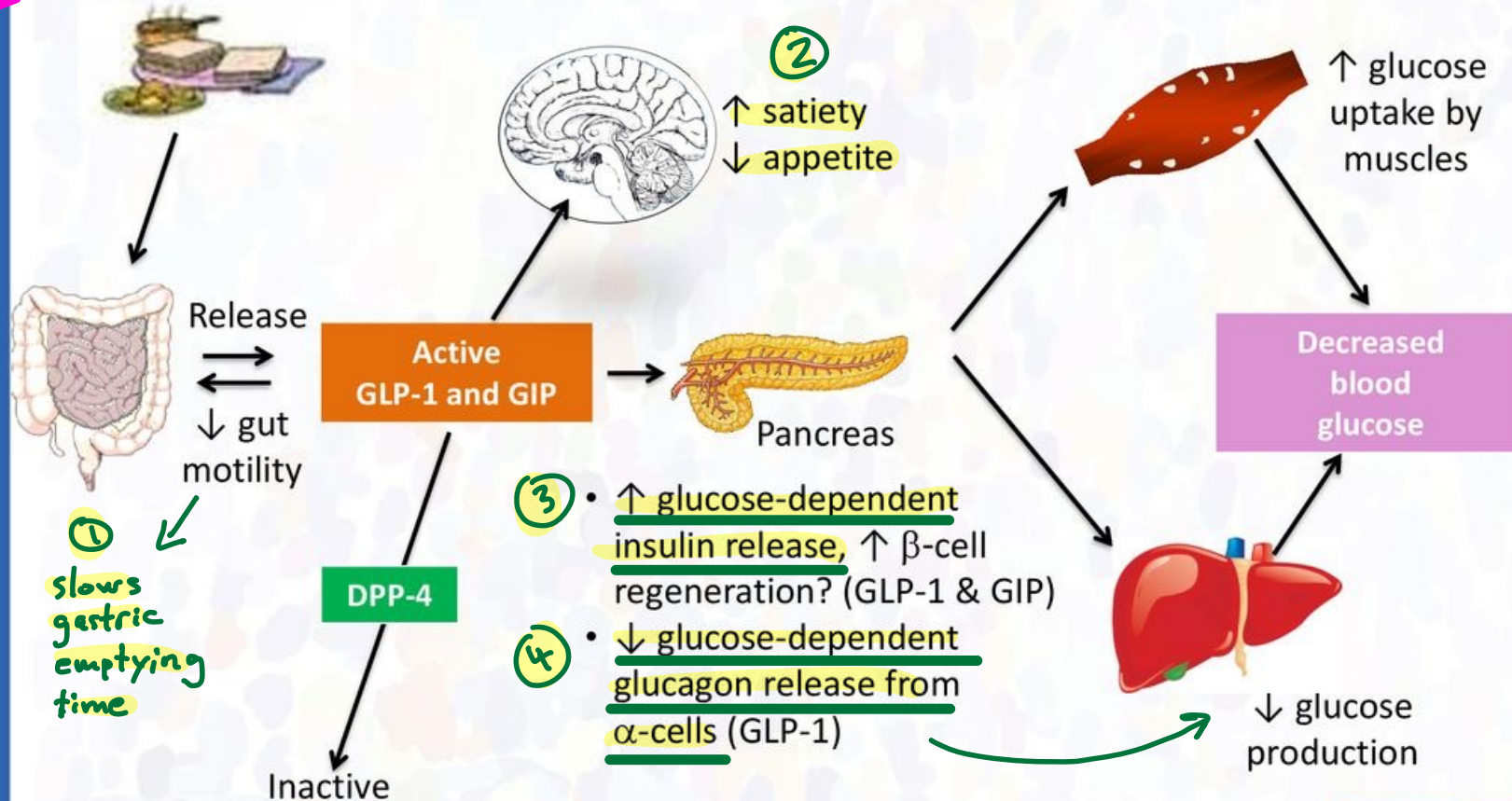
caused by
glycogenolysis
at 3-4 AM

IV. Pharmacologic Management of Type II DM



Role of Incretins in Glucose Homeostasis

Mechanisms of Action of Incretins (1→4)



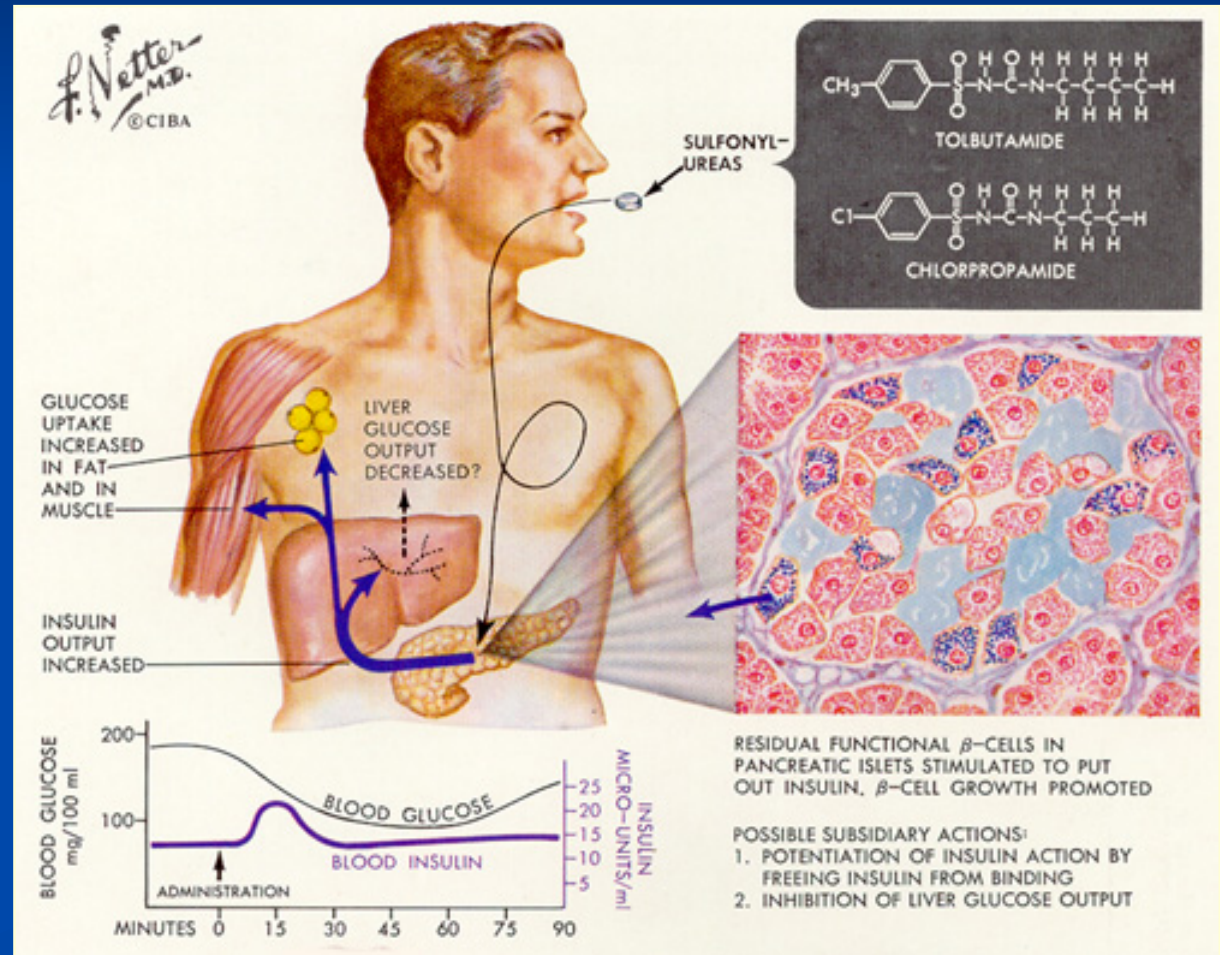
Adapted from Drucker DJ. *Cell Metab.* 2006;3(3):153-165.
Nauck MA. *Am J Med.* 2011;124(1 Suppl):S3-18.



A. Sulfonylurea Drugs (cont.)

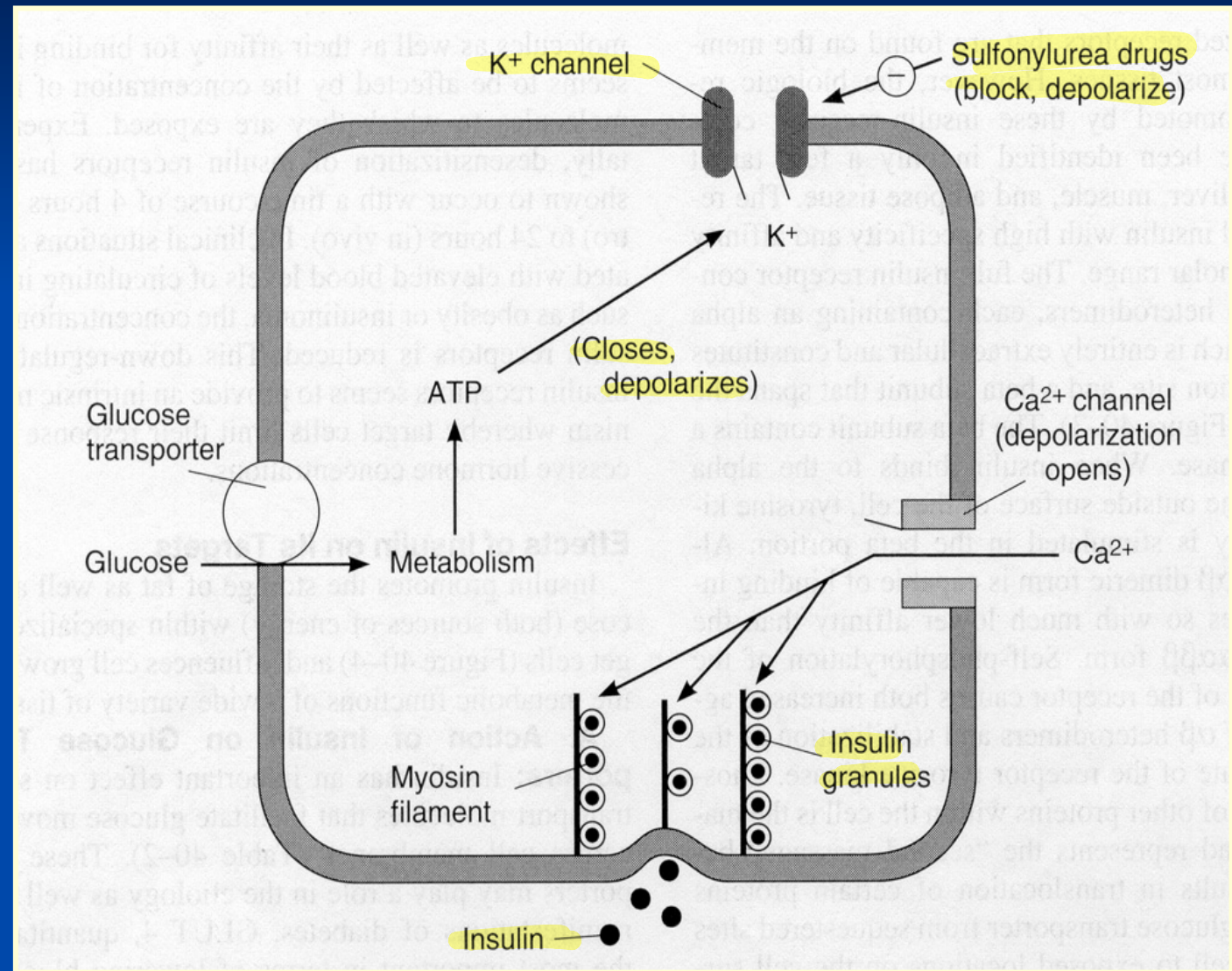
(1) Mechanism of Action

→ increase production
and release of
insulin by the
pancreas



A. Sulfonylurea Drugs (Mechanism of Action)

block K
channels
↓
depolarizes
beta cells
↓
insulin release



A. Sulfonylurea Drugs (cont.)

(1) Mechanisms of Action (cont.)

(b) reduction of serum glucagon levels

(c) increased affinity of insulin for receptor sites

A. Sulfonylurea Drugs (cont.)

First Generation Sulfonylureas

- (1) Tolbutamide (Orinase)
- (2) Tolazamide (Tolinase)
- (3) Chlorpropamide (Diabinese)

A. Sulfonylurea Drugs (cont.)

Second Generation Sulfonylureas

(1) Glyburide (Diabeta, Micronase)

(2) Glipizide (Glucotrol)

(3) Glimepiride (Amaryl)



M



SE



longest half-life → once daily QAM dosing

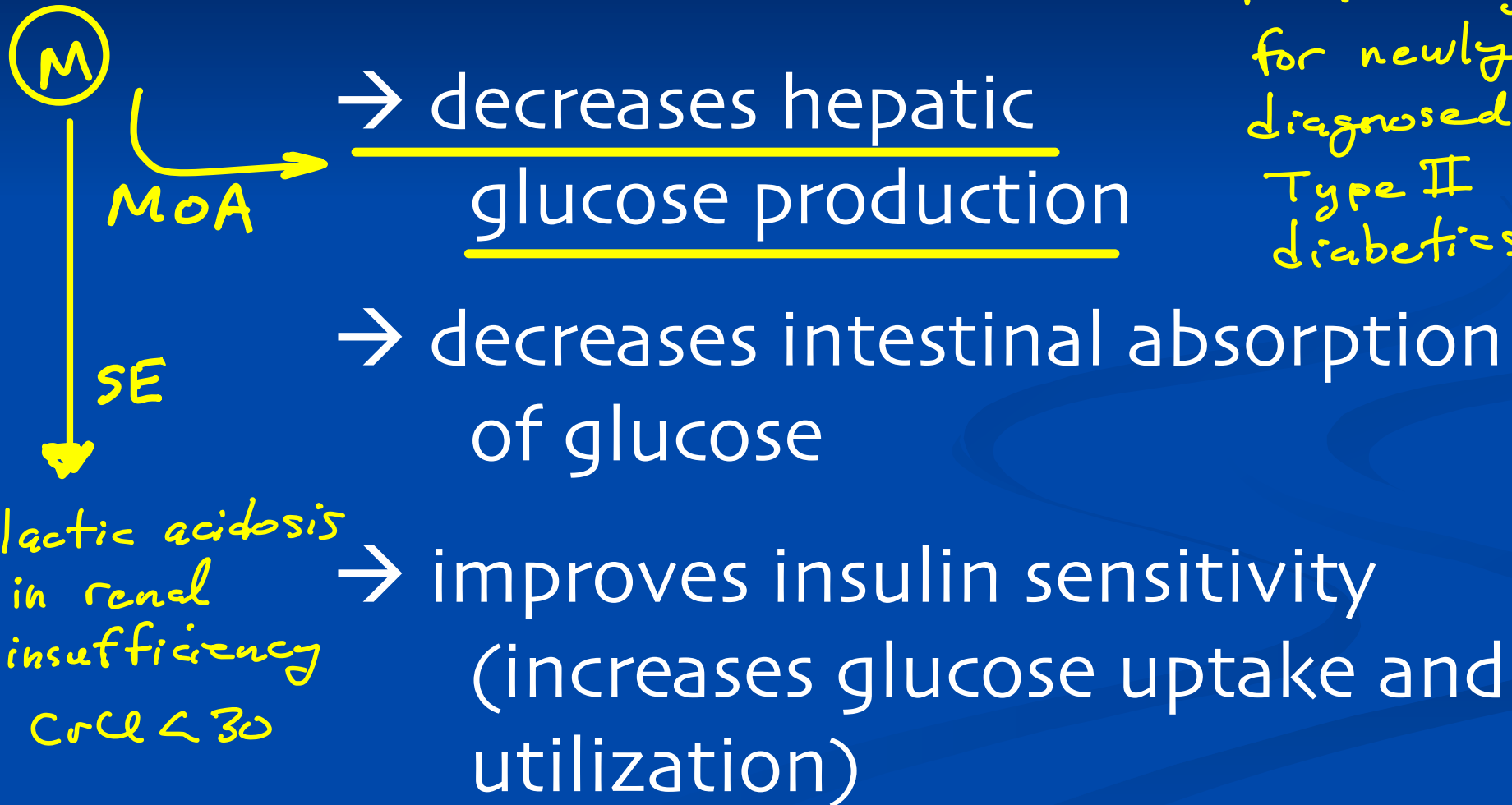
Side Effect: Potential of hypoglycemia

→ MOA: increases pancreatic insulin secretion

B. Metformin (Glucophage)

Mechanisms of Action

✓ Metformin is 1st-line agent for newly diagnosed Type II diabetics



Metformin (cont.)

(b) side effects (most common): diarrhea, nausea, vomiting, bloating, flatulence

(c) dose: 500 mg to 2500 mg / day in divided doses with meals (BID)

(d) GFR < 30 ml/min → contraindicated
GFR < 45 ml/min → caution: risk vs benefit

high metformin levels → lactic acidosis

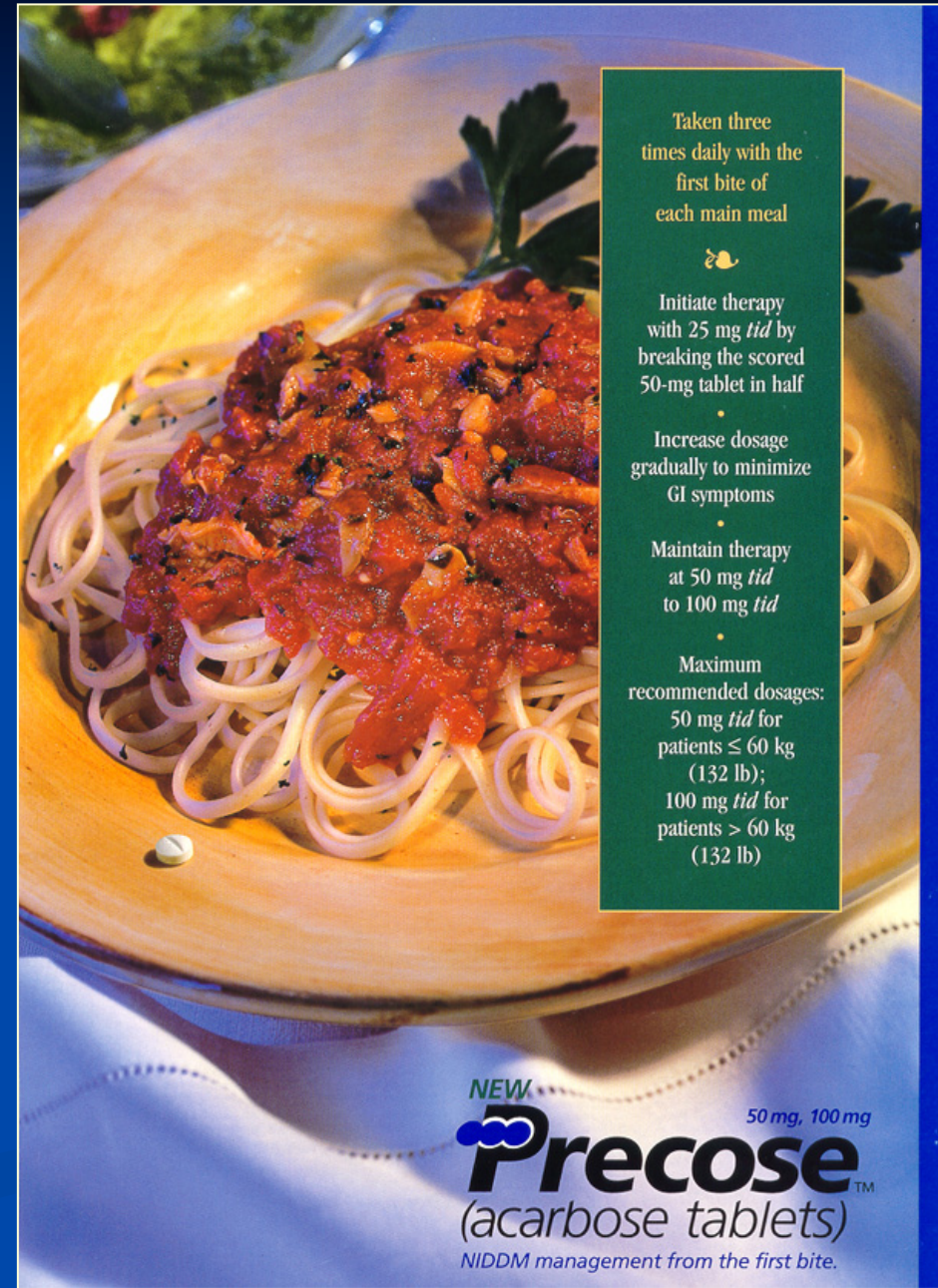
C. Acarbose (Precose)

Mechanism of Action

→ inhibits breakdown
of carbohydrates
by inhibiting alpha-
glucosidase
(secreted by small intestine)

MOA

M^{SE} → diarrhea, abdominal pain, flatulence



Taken three times daily with the first bite of each main meal

Initiate therapy with 25 mg *tid* by breaking the scored 50-mg tablet in half

Increase dosage gradually to minimize GI symptoms

Maintain therapy at 50 mg *tid* to 100 mg *tid*

Maximum recommended dosages:
50 mg *tid* for patients ≤ 60 kg (132 lb);
100 mg *tid* for patients > 60 kg (132 lb)

NEW Precose™ (acarbose tablets)
50 mg, 100 mg
NIDDM management from the first bite.

Acarbose (Precose)

(b) side effects (most common)

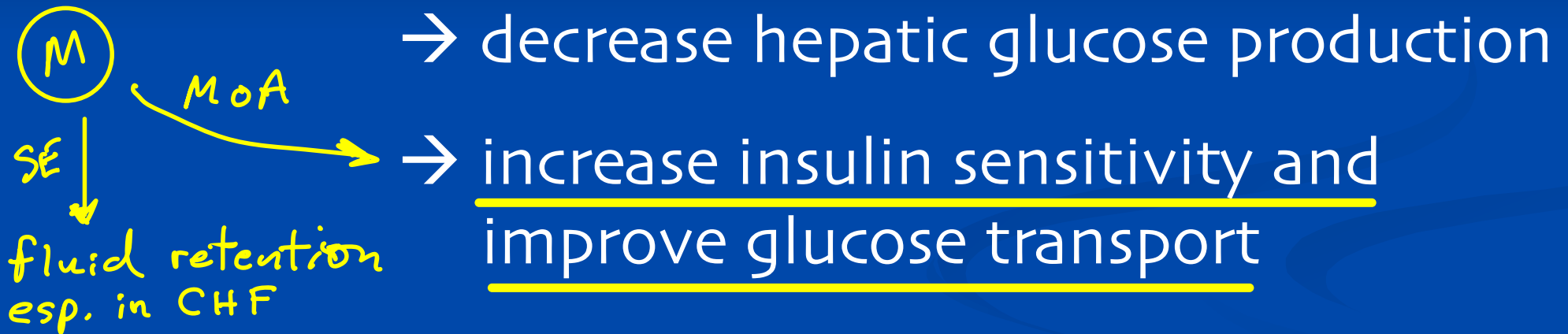
- abdominal pain, diarrhea, and flatulence (d/t undigested carbohydrates in lower GI tract)

(c) dose --> 50-100 mg TID with first bite of each meal



D. Thiazolidinediones: Rosiglitazone (Avandia) & Pioglitazone (Actos)
(TZD's = Glitazones)

Mechanism of Action of TZD's:



(i.e., improving insulin sensitivity in muscle and adipose tissue and inhibiting hepatic gluconeogenesis)

TZD's (cont.): Rosiglitazone (Avandia) & Pioglitazone (Actos)

Side Effects: Weight gain, fluid retention, osteopenia, increase in CHF in those at risk

E. DPP-4 ("Gliptins") Inhibitors

Sitagliptin (Januvia)

Linagliptin (Tradjenta)

MOA: slows the inactivation of incretin

incretin → increase insulin secretion

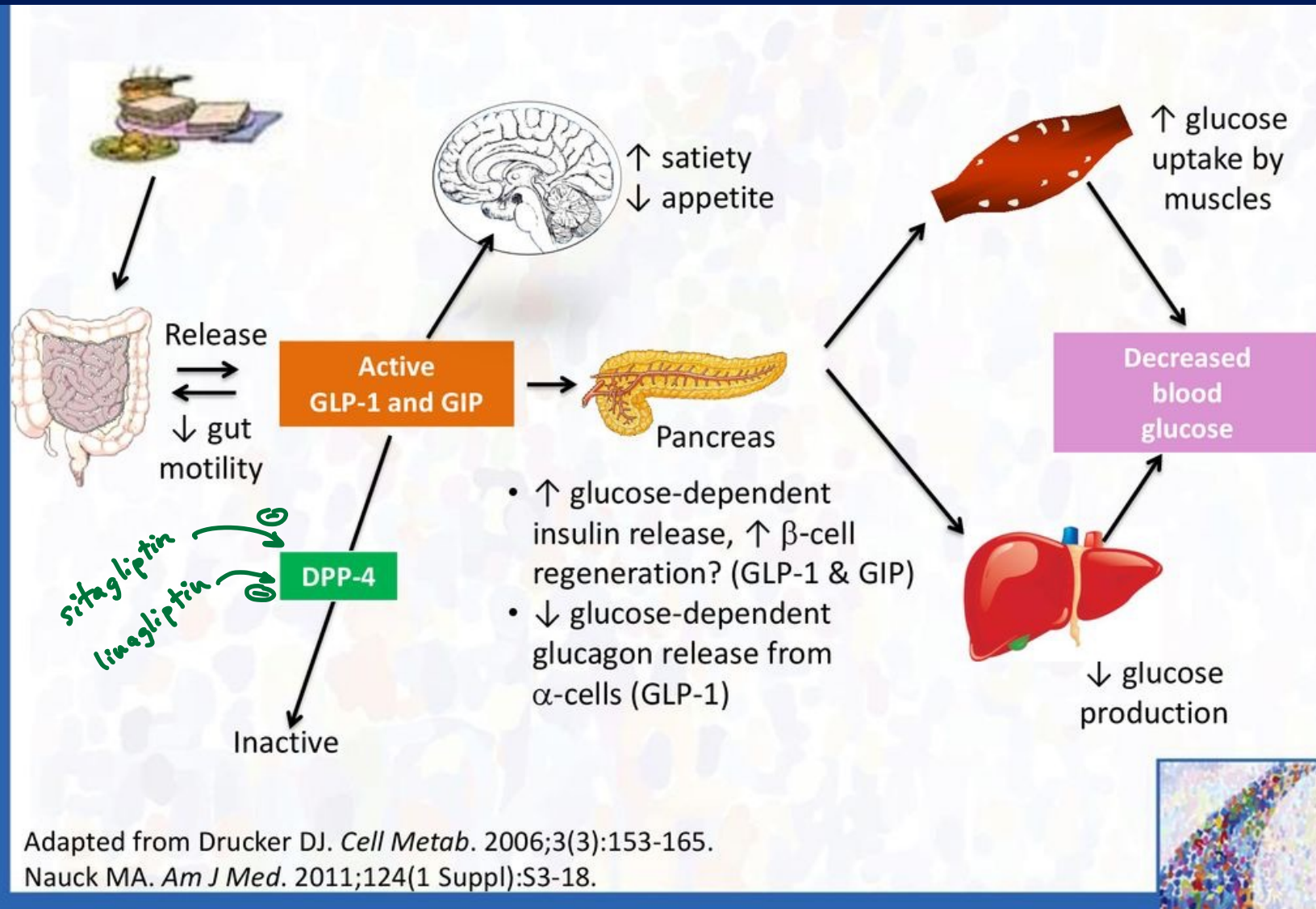
(GLP-1) → decrease glucagon secretion

→ decrease gastric emptying time

→ increase satiety (neuronal signals)

Side Effects: URI, Stuffy nose, sore throat, diarrhea
and stomach discomfort

Role of Incretins in Glucose Homeostasis



F. GLP-1 Receptor Agonists

(M)

MOA

SE

nausea
vomiting

✓ Increase Insulin Release
PLUS

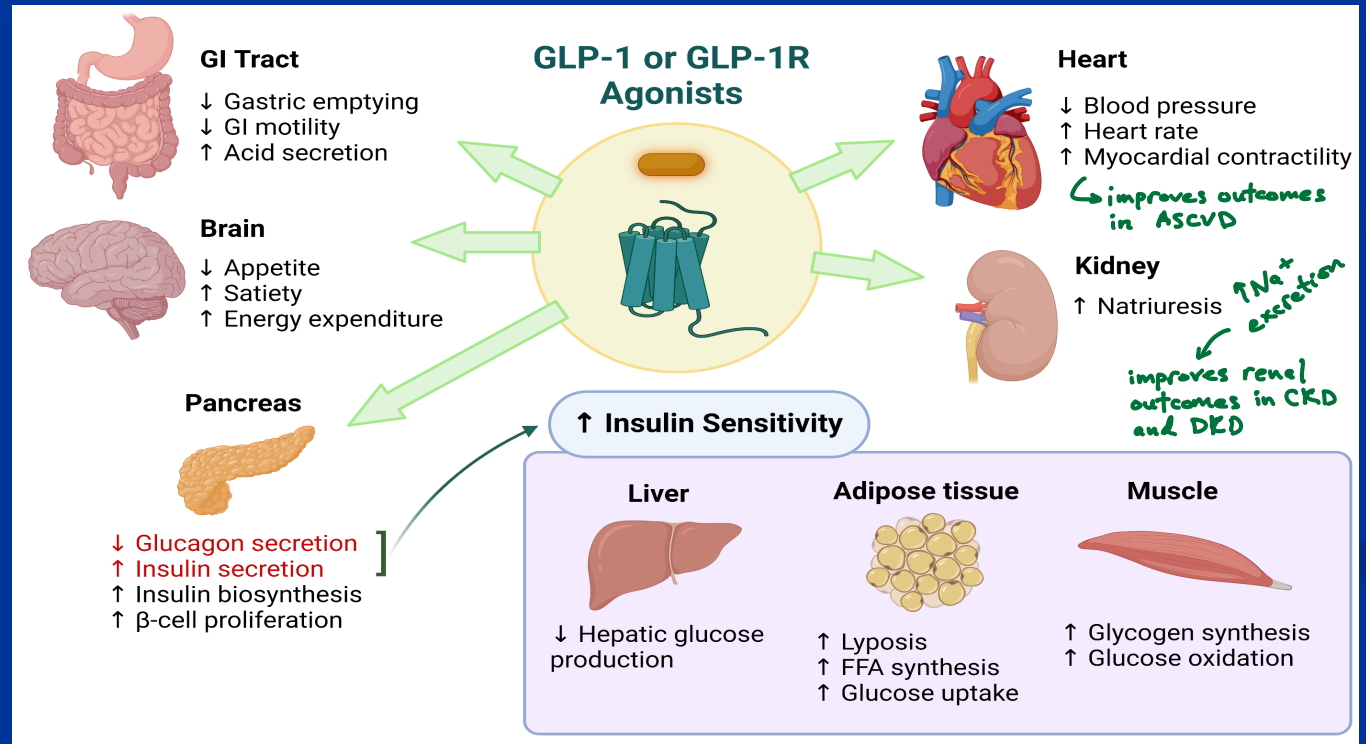
✓ Decrease Glucagon Release
PLUS

✓ Increases Satiety
PLUS

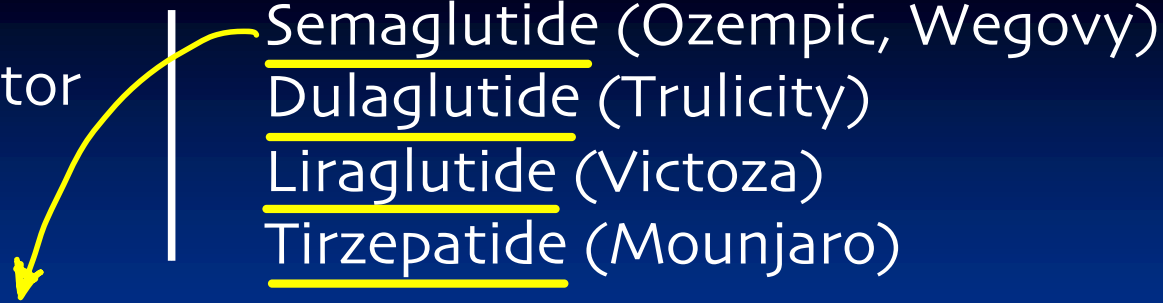
✓ Slows Gastric Emptying Time

Semaglutide (Ozempic, Wegovy)
Dulaglutide (Trulicity)
Liraglutide (Victoza)
Tirzepatide (Mounjaro)

injectable
(SC)
products



GLP-1 Receptor
Agonists



Semaglutide (Ozempic, Wegovy)
Dulaglutide (Trulicity)
Liraglutide (Victoza)
Tirzepatide (Mounjaro)

Adverse Effects (Gastrointestinal)

- Nausea (26-50%) and Vomiting; Diarrhea.
- Nausea: (1) reduced with gradual dose titrations and (2) wanes with continued use.

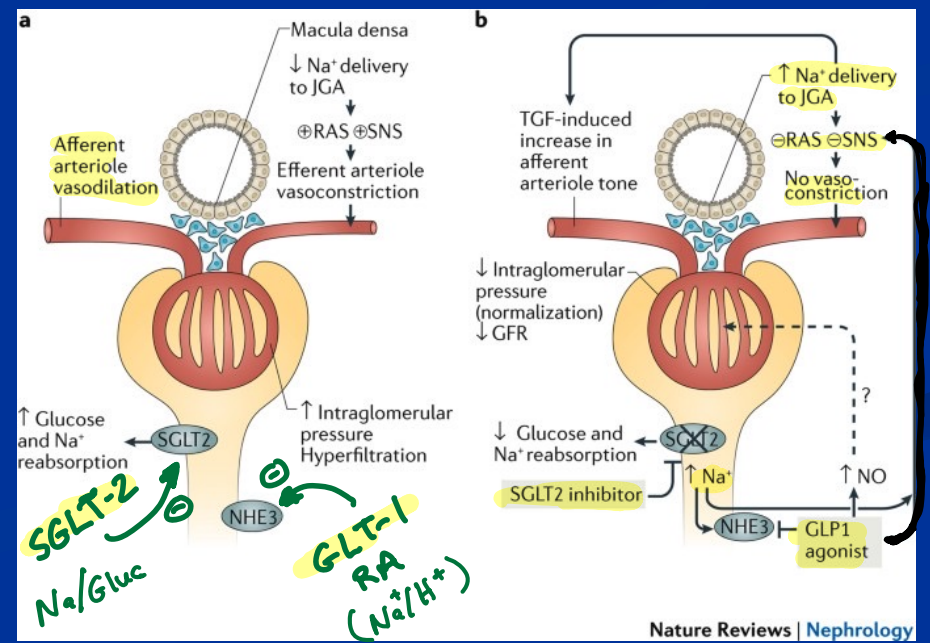
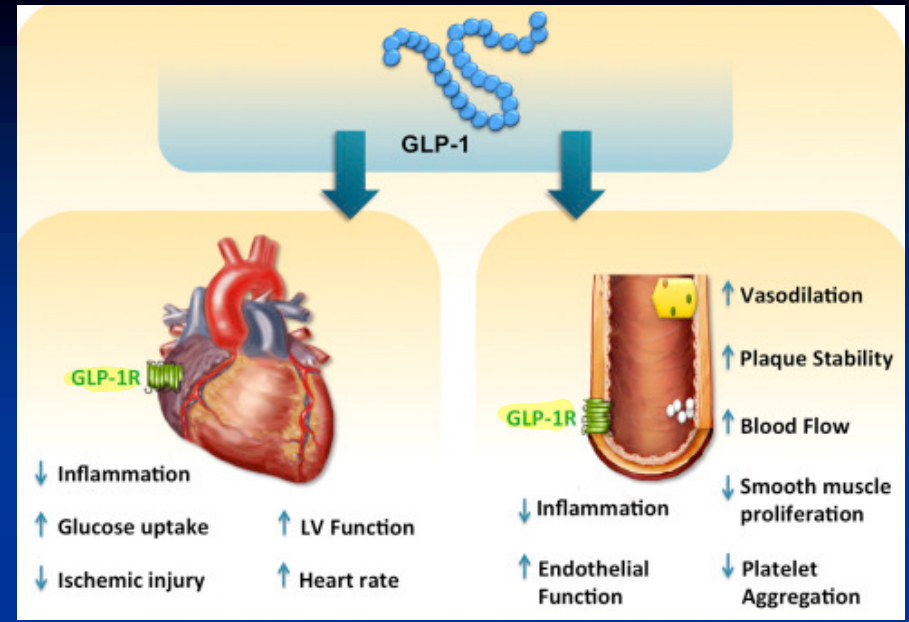
General Considerations

- GLP-1 receptor agonists are indicated for use in combination with metformin for patients with existing ASCVD when weight loss is a primary consideration and cost or injectables formulations of GLP-1 agonists are not limiting factors.
- GLP-1 receptor agonists may also be used in combination with basal insulin with or without metformin when HgbA1C levels remain persistently high.
- Tirzepatide (Monjaro) is a dual-acting GLP-1 and GIP receptor agonist for Type II diabetic patients without ASCVD who may benefit from weight loss, since there is insufficient evidence that tirzepatide provides protection against ASCVD.

GLP-1 Receptor Agonist Benefits in ASCVD (Atherosclerotic Cardiovascular Disease) and CKD

CKD

- In CKD, GLP-1 RA induces natriuresis and diuresis by inhibiting the sodium-hydrogen exchanger 3 (NHE3) located in the renal proximal tubular → increases tubular sodium transport to the macula densa → reduces intraglomerular pressure and hyperfiltration → restores tubular glomerular feedback and improves kidney outcomes in CKD.
- In CKD, GLP-1 RA decreases circulating concentrations of angiotensin II → decreases BP and Na/H₂O retention.



G. SGLT-2 Inhibitors (Sodium-Glucose Co-Transport Inhibitors)

(M)

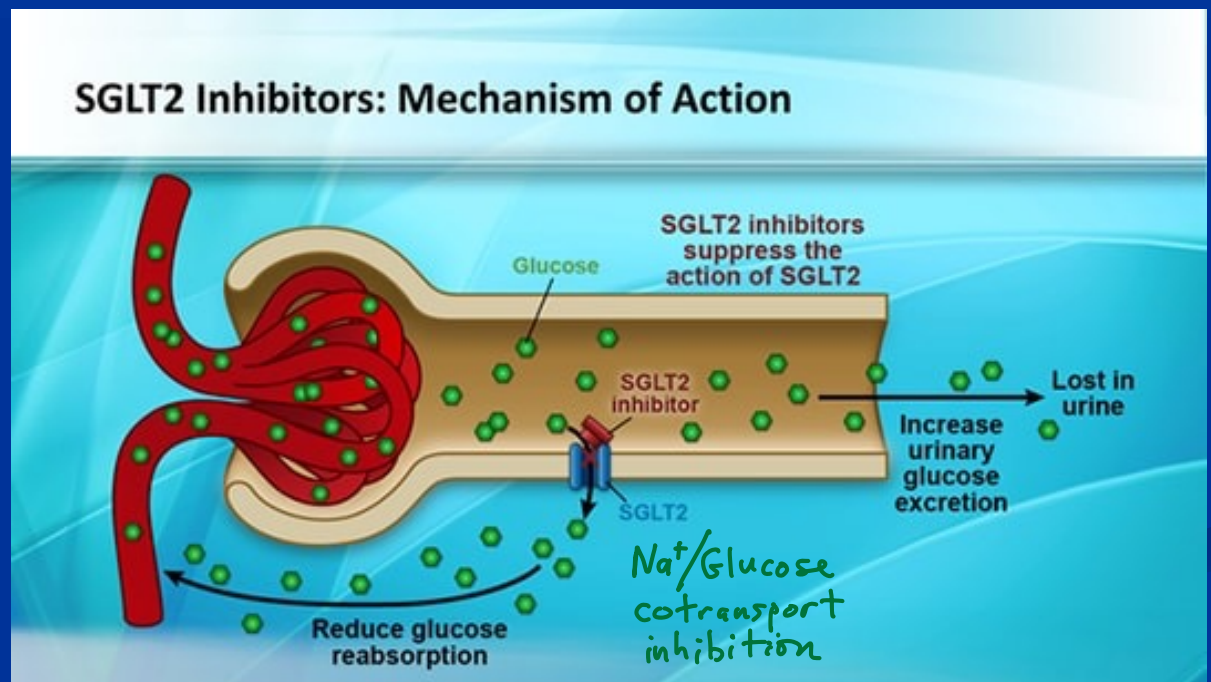
MOA

SE

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)

dehydration, yeast infections,
UTI's

MOA: Lower blood glucose levels by increasing kidney excretion of glucose into the urine



SGLT-2 Inhibitors
(Sodium-Glucose Co-
Transport Inhibitors)

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)

Adverse Effects: Yeast infections (vaginal candidal infections), UTIs, dehydration → hypotension, DKA, and bone fractures

Note: SGLT-2 Inhibitors are contraindicated in patients with CrCl \leq 30 ml/min.

Match each of the following agents with its corresponding mechanism of action (MOA).

Metformin (Glucophage) Decreases hepatic glucose production

Semaglutide (Ozempic, Wegovy) Increases effects of incretins
(GLP-1 Receptor Agonist)

SGLT-2 Inhibitor: Canagliflozin (Invokana) Increases kidney excretion of glucose

Sulfonylurea: Glimepiride (Amaryl) Increases pancreatic insulin secretion

Alpha-Glucosidase Inhibitor: Acarbose (Precose) Inhibits carbohydrate breakdown in small intestine

Match each of the following agents with its corresponding side effect(s).

Metformin (Glucophage) Lactic acidosis in renal insufficiency (CrCl<30)

TZD's: Pioglitazone (Actos) Fluid retention, especially in CHF patients

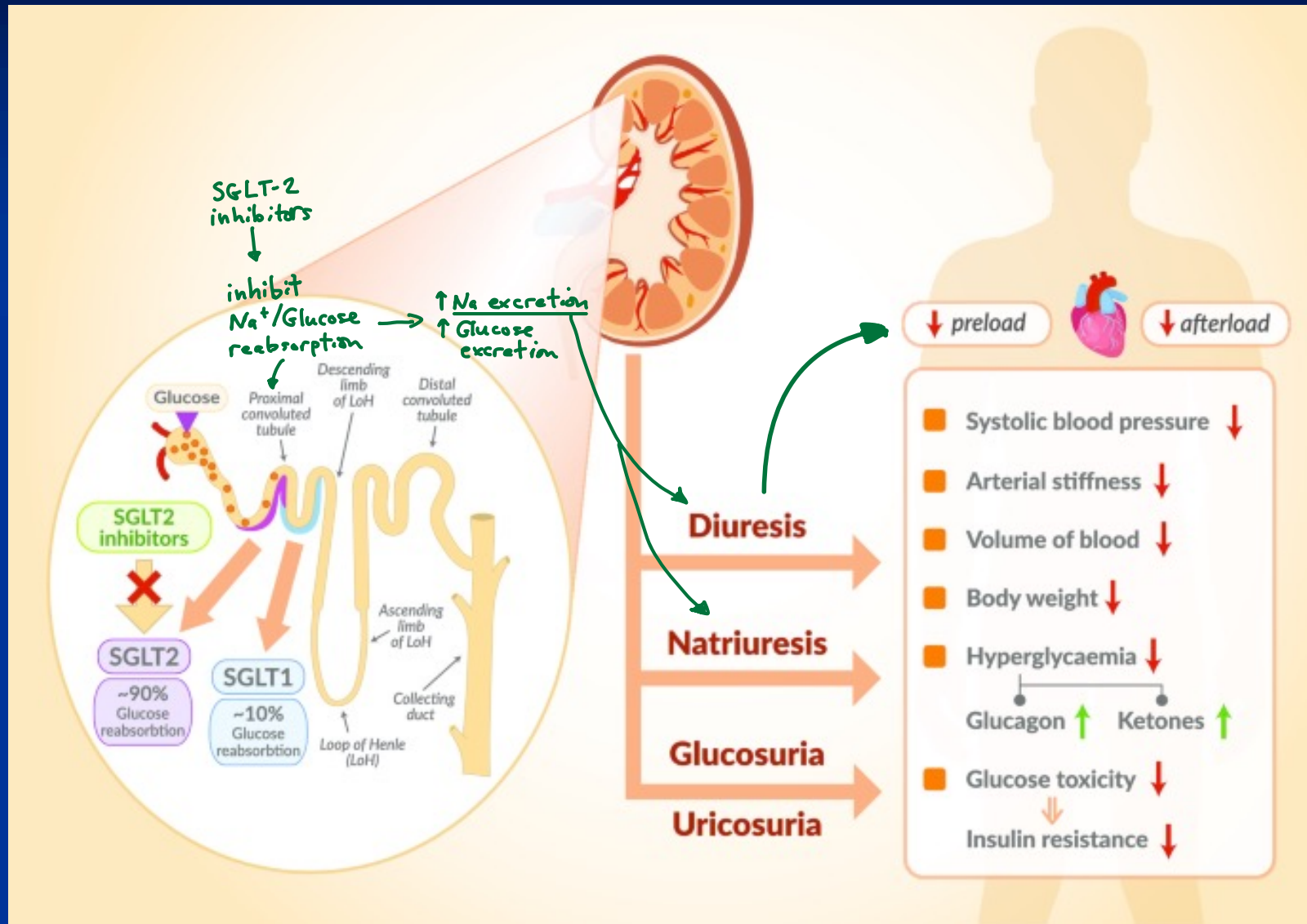
SGLT-2 Inhibitors: Canagliflozin (Invokana) Dehydration, UTIs, yeast infections

Sulfonylurea: Glimepiride (Amaryl) Risk of hypoglycemia

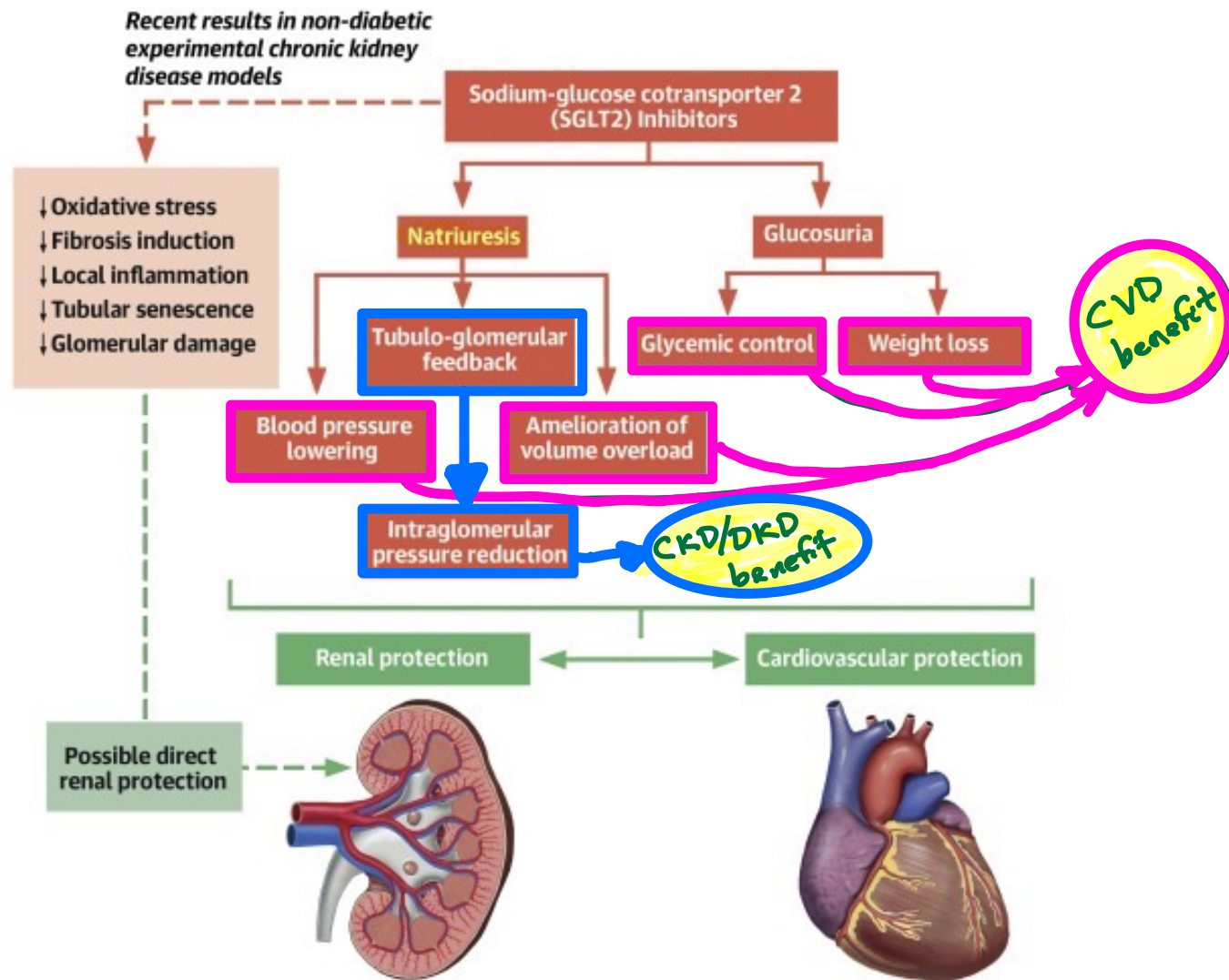
Alpha-Glucosidase Inhibitor (Precose) Diarrhea, abdominal pain, flatulence

Semaglutide (Ozempic, Wegovy) nausea, vomiting
(GLP-1 Receptor Agonist)

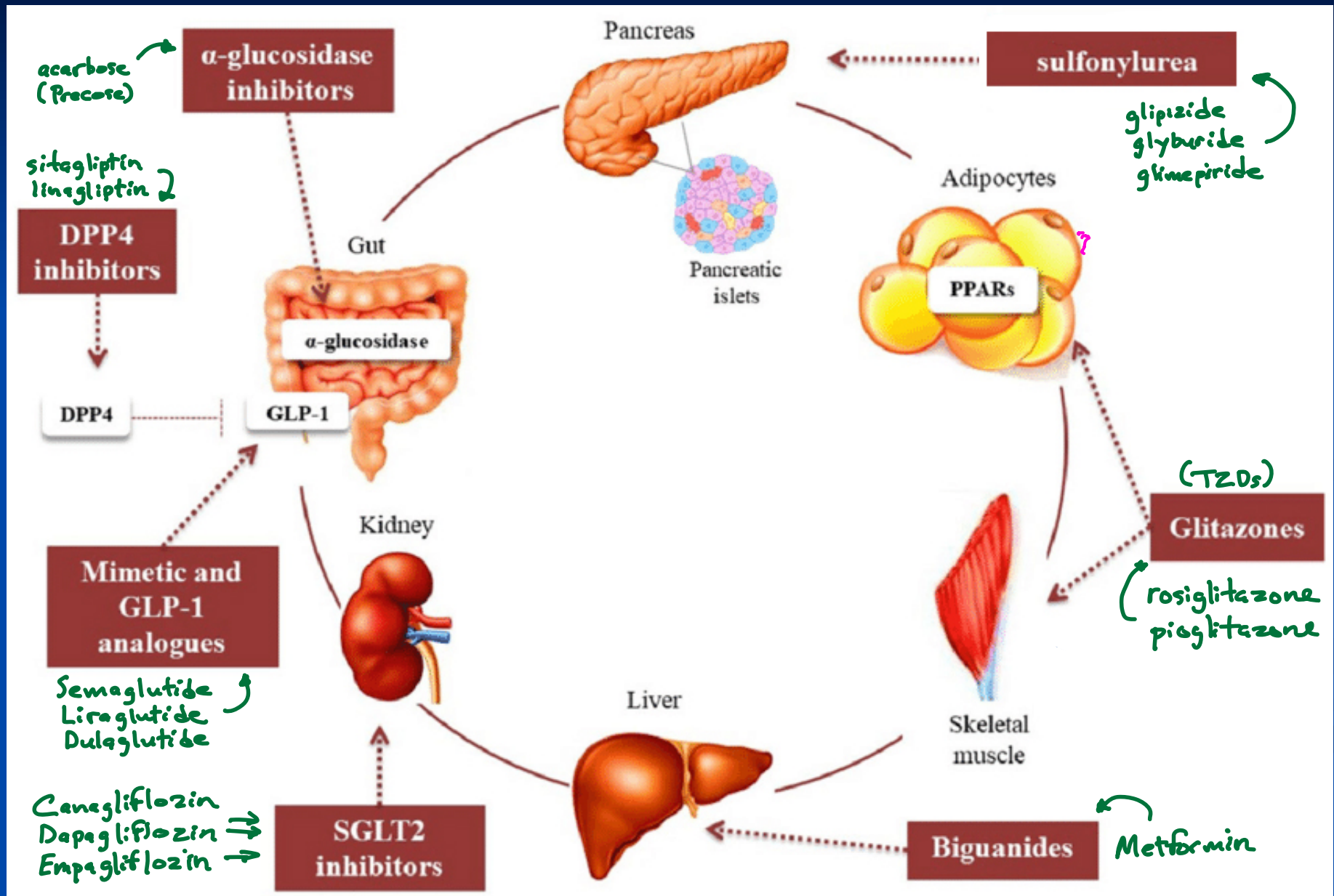
SGLT-2 Inhibitors: Cardiovascular Protection



SGLT-2 Inhibitor Cardiorenal Protection Summary

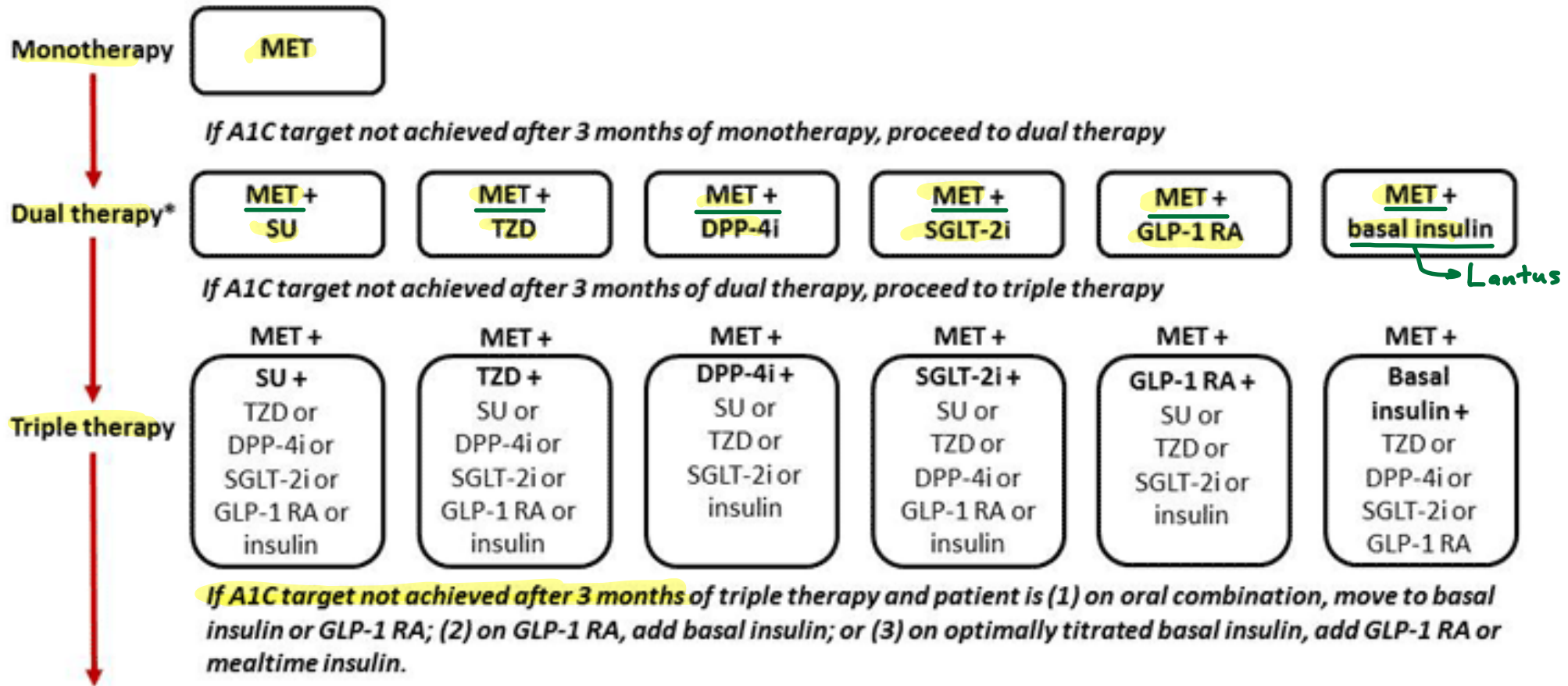


OVERVIEW: Pharmacologic Agents in the Treatment of Type II DM



V. Antihyperglycemia Tx in Adults w/ Type II DM

Lifestyle changes: **healthful eating, weight management, increased physical activity, diabetes education**



Combination injectable therapy

* Consider initial **dual therapy** if A1C $\geq 9.0\%$; † Consider starting at this stage if blood glucose ≥ 300 mg/dL, A1C $\geq 10\%$, or patient is markedly symptomatic.

Summary of Glucose-Lowering Pharmacologic Agents in Type II DM

Intervention	Expected decrease in A1C with monotherapy (%)	Advantages	Disadvantages
Initial therapy			
Lifestyle change to decrease weight and increase activity <i>Diet + Exercise</i>	1.0 to 2.0	Broad benefits	Insufficient for most within first year owing to inadequate weight loss and weight regain
Metformin	1.0 to 2.0	Weight neutral	GI side effects, contraindicated with renal insufficiency (eGFR <30 mL/min/1.73 m ²)*
Additional therapy[¶]			
Insulin (usually with a single daily injection of intermediate- or long-acting insulin initially) <i>Lantus</i>	1.5 to 3.5	No dose limit, rapidly effective, improved lipid profile	1 to 4 injections daily, monitoring, weight gain, hypoglycemia, analogs are expensive
Sulfonylurea (shorter-acting agents preferred) glipizide, glyburide, glimepiride	1.0 to 2.0	Rapidly effective	Weight gain, hypoglycemia (especially with glibenclamide or chlorpropamide)
GLP-1 receptor agonist (daily to weekly injections) semaglutide, dulaglutide, liraglutide	0.5 to 1.5	Weight loss, reduction in major adverse cardiovascular events (MACE) (liraglutide, semaglutide, dulaglutide) in patients with established CVD and potentially for those at high risk for CVD	Requires injection, frequent GI side effects, expensive <i>injectable</i> N/V → cost
Thiazolidinedione (TZD's) pioglitazone, rosiglitazone	0.5 to 1.4	Improved lipid profile (pioglitazone), potential decrease in MI (pioglitazone)	Fluid retention, HF, weight gain, bone fractures, potential increase in MI (rosiglitazone) and bladder cancer (pioglitazone)
SGLT2 inhibitor canagliflozin, dapagliflozin, empagliflozin, tirzepatide	0.5 to 0.7	Weight loss, reduction in systolic blood pressure, reduced cardiovascular mortality in patients with established CVD, improved renal outcomes in patients with nephropathy	Vulvovaginal candidiasis, urinary tract infections, bone fractures, lower limb amputations, DKA
DPP-4 inhibitor (gliptins) sitagliptin, linagliptin	0.5 to 0.8	Weight neutral	Possible increased risk of HF with saxagliptin, expensive
Alpha-glucosidase inhibitor acarbose	0.5 to 0.8	Weight neutral	Frequent GI side effects, 3 times/day dosing

HgbA1c most effective

HgbA1c moderately effective

HgbA1c minimally effective

Wt loss
↓ MACE
(ASCVD)

Wt loss
ASCVD
CKD

