

Diabetes treatment



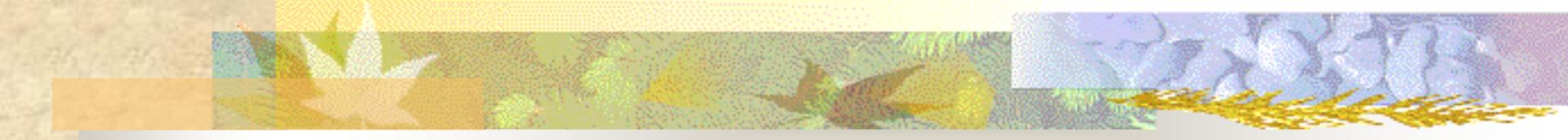
Prof.MUDr.Kateřina Štechová, Ph.D.

- Treatment ≠ Drugs only
- Treatment goals
- DM2 treatment
- Insulinotherapy



Different DM types – different approaches

- Always 3 main pillars
 - Diet
 - Medication
 - Lifestyle (exercise)



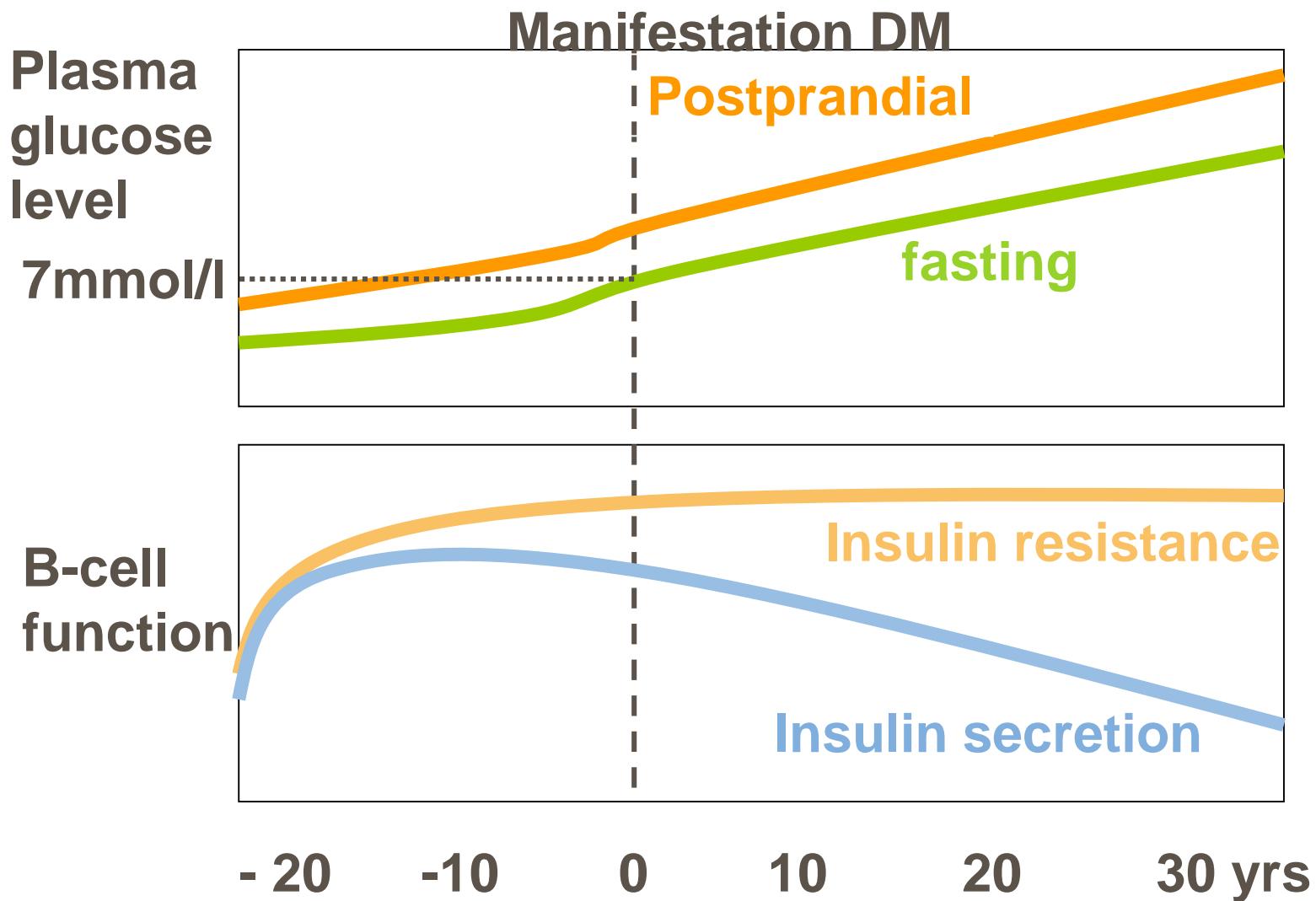
Treatment goals

- Glycaemia
 - HbA1c
 - Glycaemic variability
- Other metabolic parameters
- Life quality



DM2 PHARMACOTHERAPY

Natural course of DM2



Typ 2 diabetes treatment

Insulin resistance

- Diet
- Exercise
- Metformin
- Glitazons
- α -glukosidase inhibitors

↓ insulin requirements

SGLT2 inhibitors

GLP-1R agonists
DPPIV inhibitors

↑ plasma insulin level
-secretagogues of insulin
-Exogenous insulin

Insulin secretion



Metformin contra-indication

Risk of lactate acidosis

- Limited liver function
- **Limited kidney function**
- Respiratory and heart failure
- Alcohol abusus



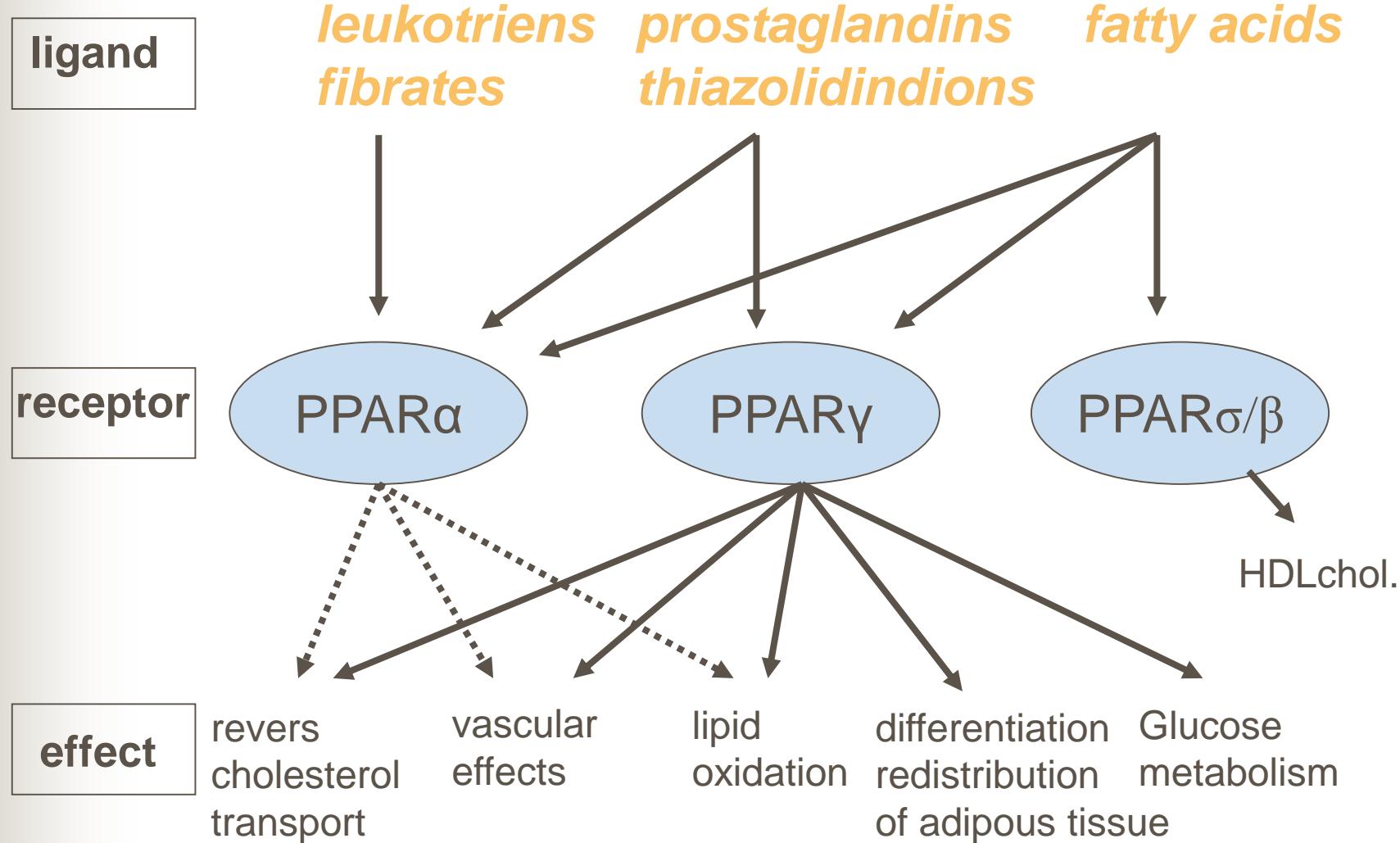
Metformin – drugs and dosage

- 500 – 850– 1000mg 3x daily
- GLUCOPHAGE (tbl, XR tbl, eff)
- SIOFOR
- METFIREX
- STADAMET
- Metformin GAL, AL, TEVA...

Thiazolidindions - glitazones

1. ciglitazon 1982 –
2. troglitazon (Rezulin®) – PAD introduced in 1996 U.S.A. and 1997 in GB
3. rosiglitazon and pioglitazon – 2000
4. netoglitazon

Pleiotropic effects of PPAR receptors family



Benefits x risk of glitazons treatment

Benefits:

- Better metabolic control
- ↓insulin rezistance
- ↓visceral adipose tissue (redistribution)
- ↓blood pressure
- improving β-cell function
- Improving endotelial function
- ↓fat deposits in liver (NASH)

Risk:

- Hepatotoxicity
- Weight gain/ ↑ body adipose tissue/
↑subcutaneous adipose tissue
- Fluid retention/oedema
- Pulmonary oedema
- Risk of heart failure
- Risk of ischemic vascular attacks????

Pioglitazon (ACTOS), 15 – 45mg 1x daily

Contra-indications:

- **Hypersensitivity**
- **Heart failure** present or in history (NYHA III – IV)
- Restricted liver function
- Pregnancy and breast feeding
- Glitazons **are not to use in combination** therapy with insulin
- Be careful in patients with vascular problems

Acarbose

- pseudotetrasacharide, doesn't absorb
- **inhibits alfa-glukosidase**
- → glucose absorption is limited and delayed; ↓ PPG
1,5-3 mmol/l
- ↓ FGP
- ↓ TG (↓ synthesis VLDL in hepatocytes) and ↓ chol
- ↓**risk of cardiovascular complication**

- GLUCOBAY – 100mg tbl – 1 - 2 tbl 3x daily



Sulfonylurea - insulin secretagogues

- Stimulates insulin secretion
- B-cell function must be present

Sulfonylurea – insulin secretagogues

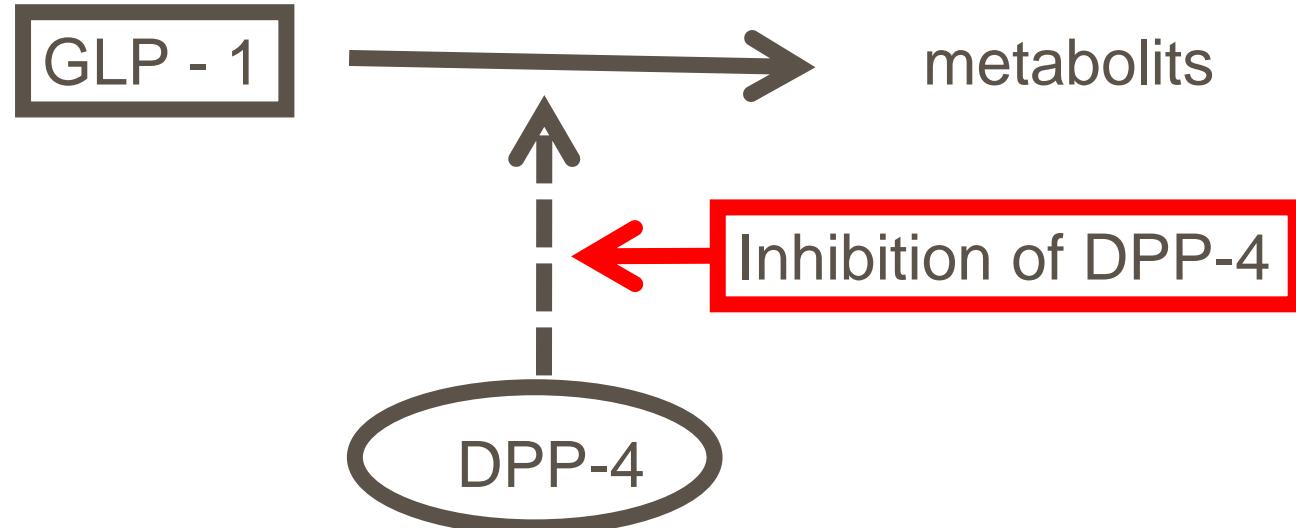
- Glibenclamid – MANINIL, GLUCOBENE (3,5 – 5mg 3x daily), risk of hypoglycaemia!!!
- Gliclazid – DIAPREL MR 1 – 4tbl 1 – 2x daily
- Glipizid - MINIDIAB
- Glimepirid – 1 – 4mg 1x(2x) daily – AMARYL, GLYMEXAN
- Gliquidon – GLURENORM 1tbl 3x daily – allowed in patients with restricted kidney function



Incretin mimetics and incretin „enhancers“

- mimic the normal effect of incretin hormones
- Glucagon like peptid 1

GLP-1 Receptor agonists



Incretins

- GLP-1 receptor agonists
 - exenatid (Byetta – 2x daily 5 – **10**ug)
 - liraglutid (Victoza – 1x daily 0,6 – **1,2** – 1,8mg)
- Inhibitors of dipeptidyl-peptidase IV
 - Sitagliptin (JANUVIA – 100mg 1x daily),
combination with metformin JANUMET 50/850,
50/1000mg 2x daily
 - Vildagliptin (GALVUS), with metformin EUCREAS
 - Saxagliptin (ONGLYZA)



Glucuretics

—
glucosuria
as diabetes
treatment?

dapagliflozin
canagliflozin

Other possibilities

Bariatric (metabolic)
surgery

Tx

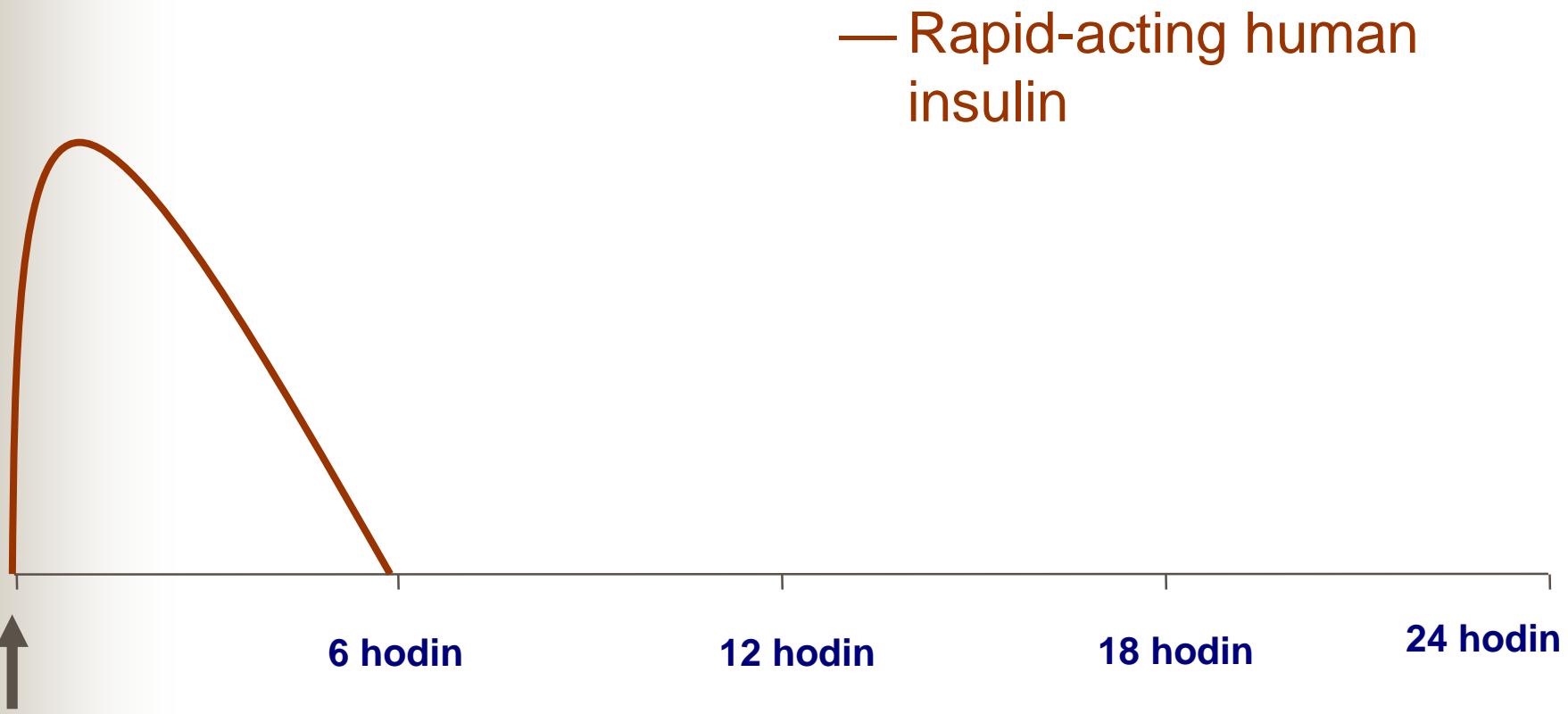
- Pancreas (+kidney)
- Islets

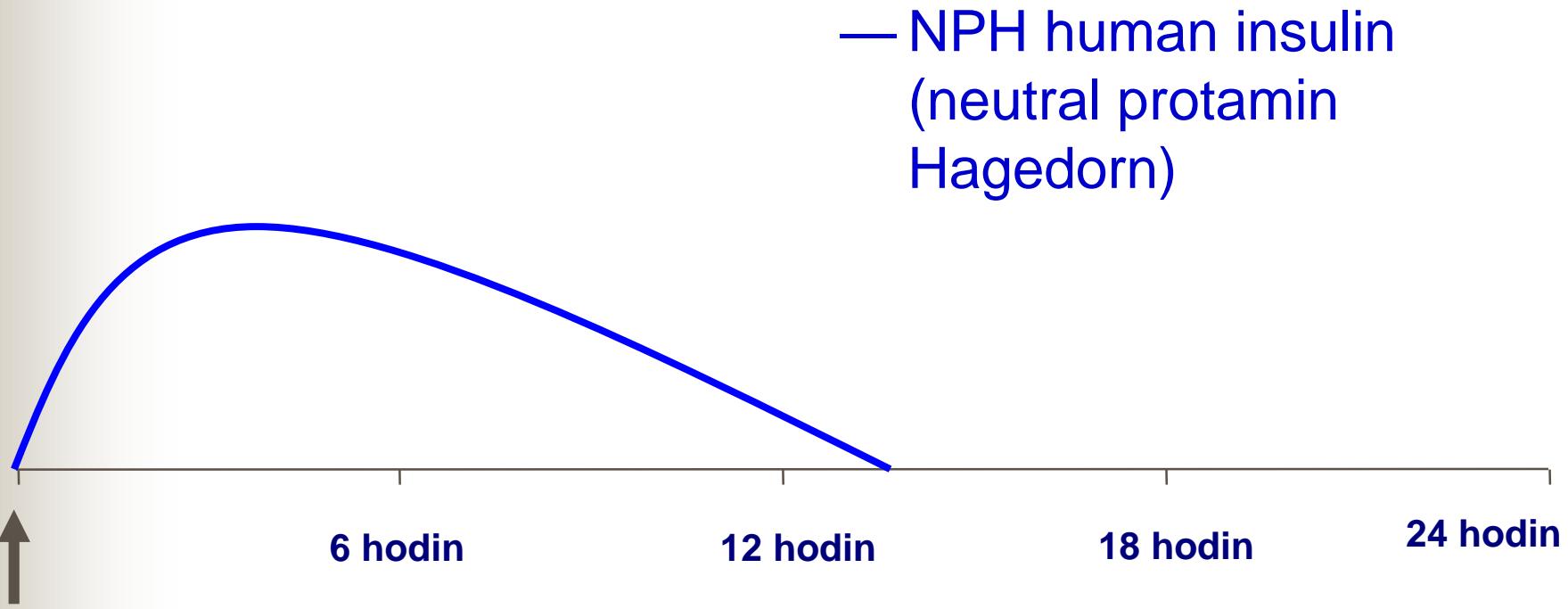
- ?Stem cells? (research)

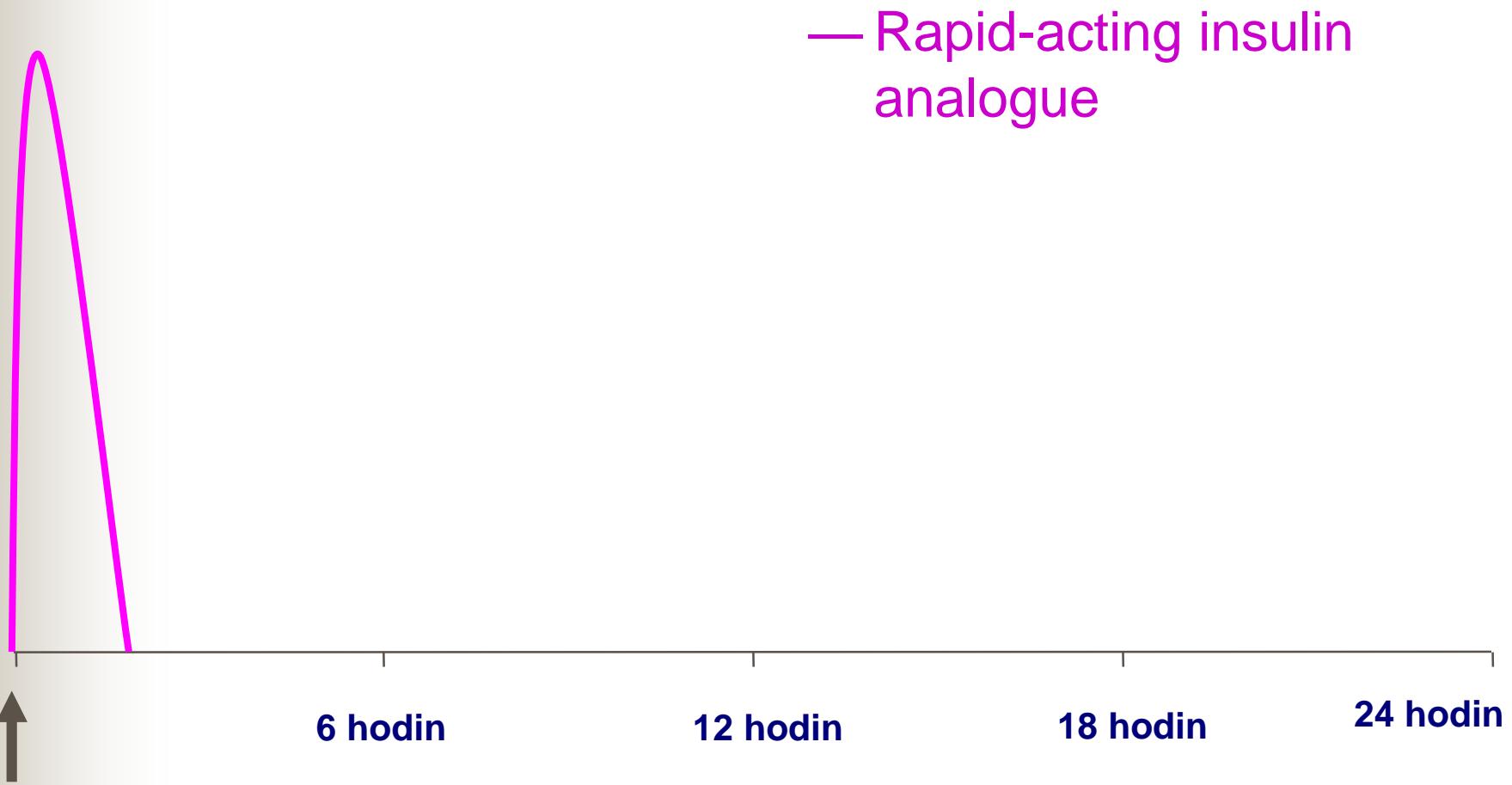


Insulin

- Proteohormon
- Contains 51 aminoacids in two chains.
- Produced in pancreatic islets
- $\approx 40\text{U/day}$ - $\frac{1}{2}$ „basal secretion“ – $\frac{1}{2}$ „stimulated secretion“ – after meals

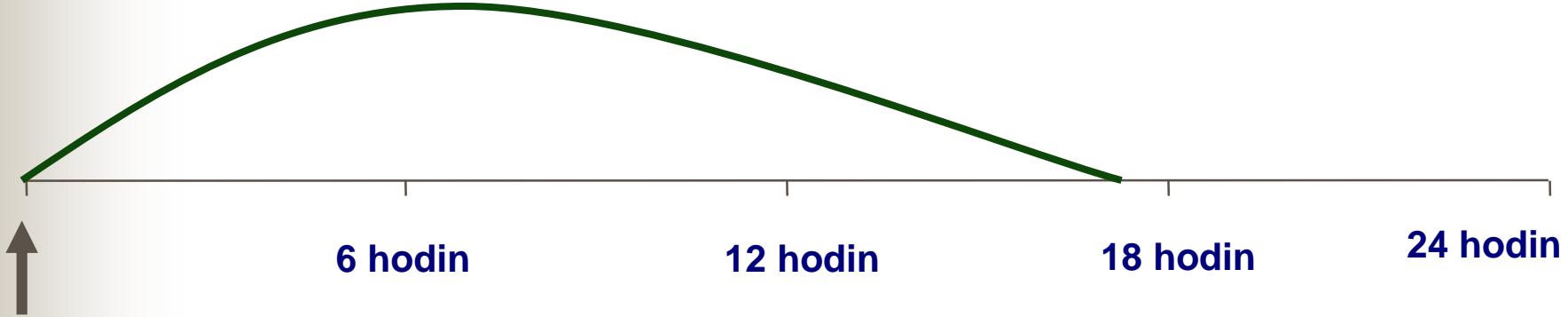


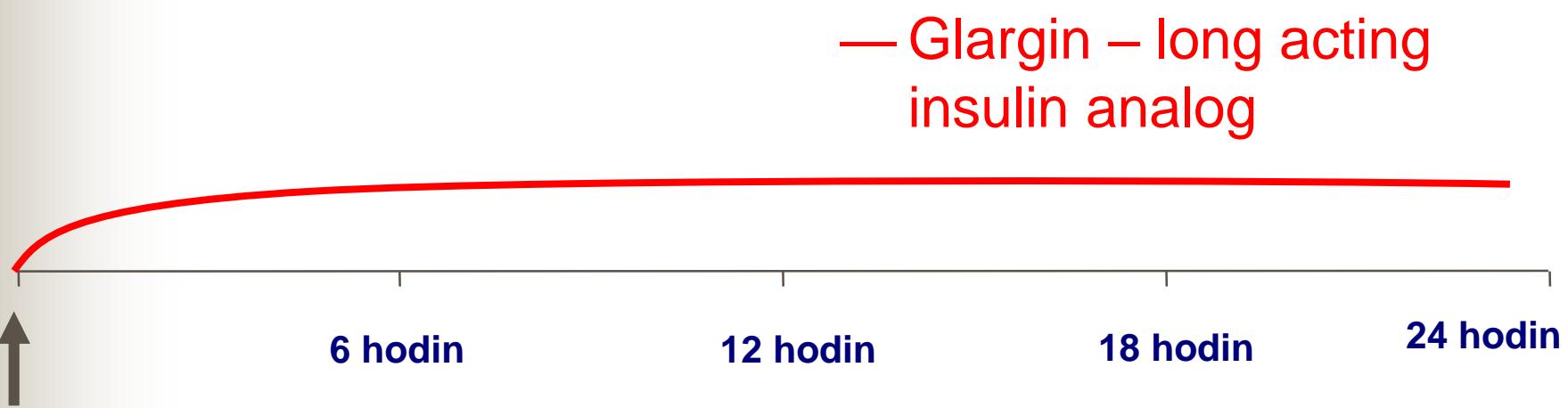




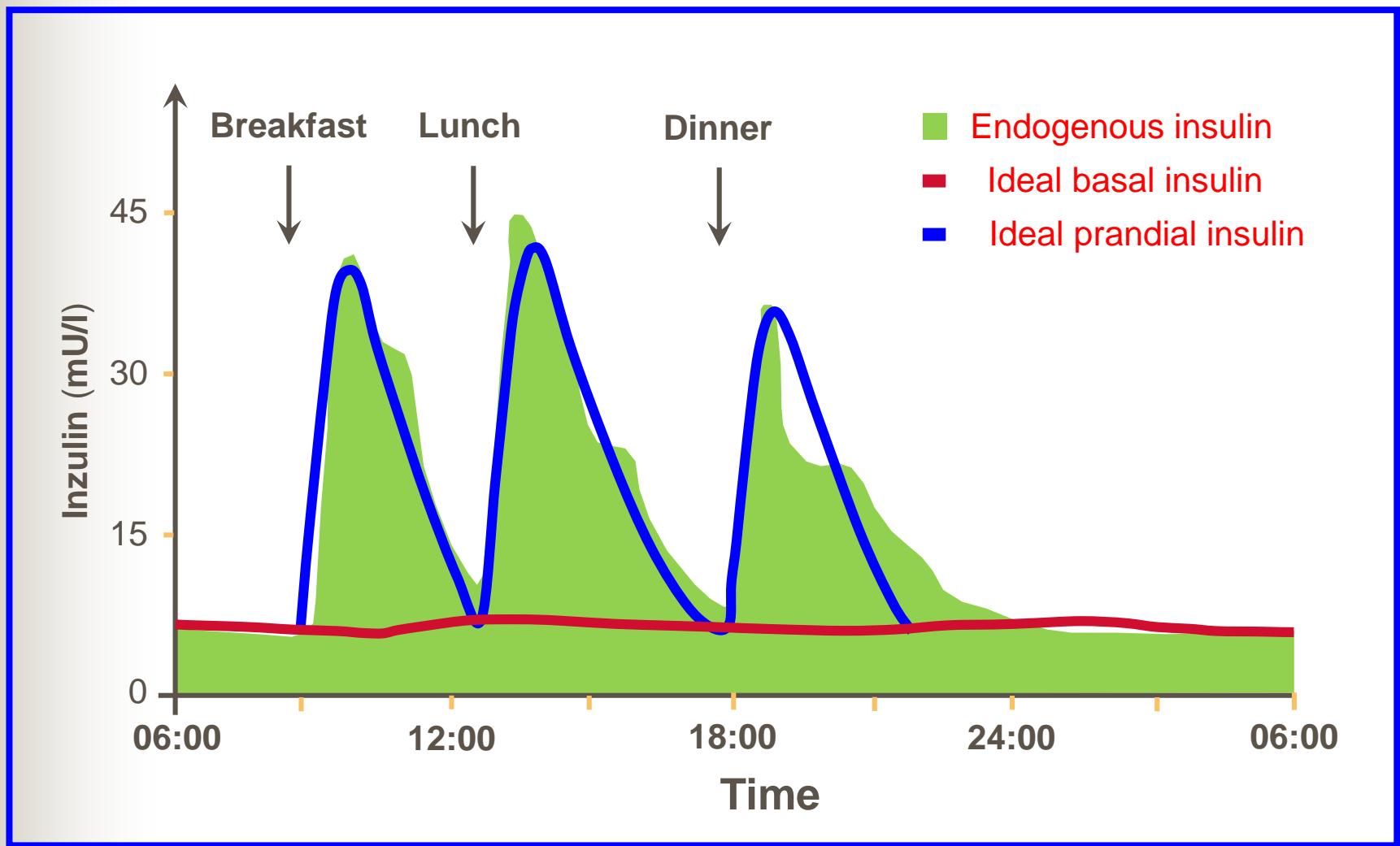


— Detemir = (middle)long
acting insulin analogue

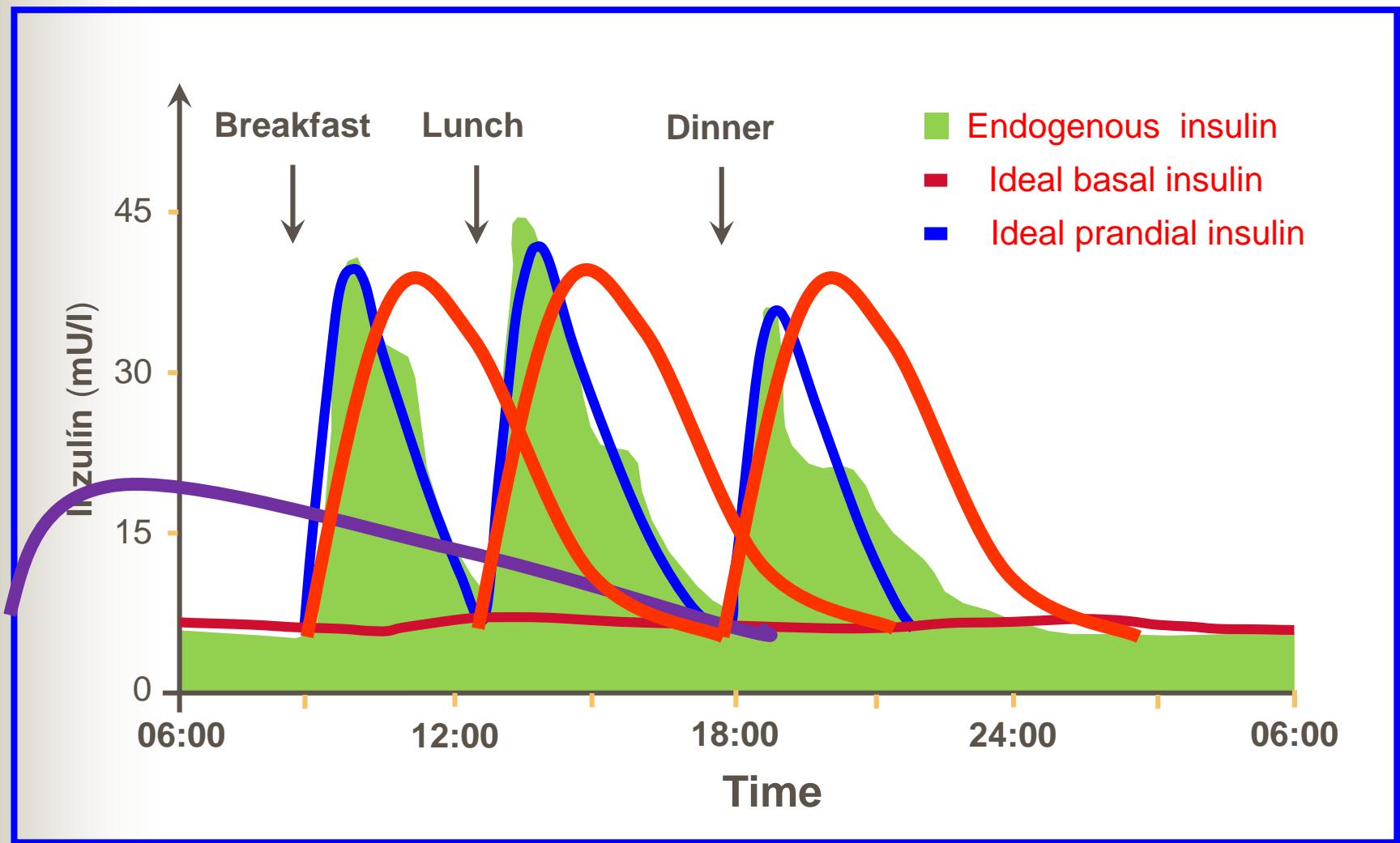




Mimic the natural insulin secretion...



...HM does not imitate the natural insulin secretion....

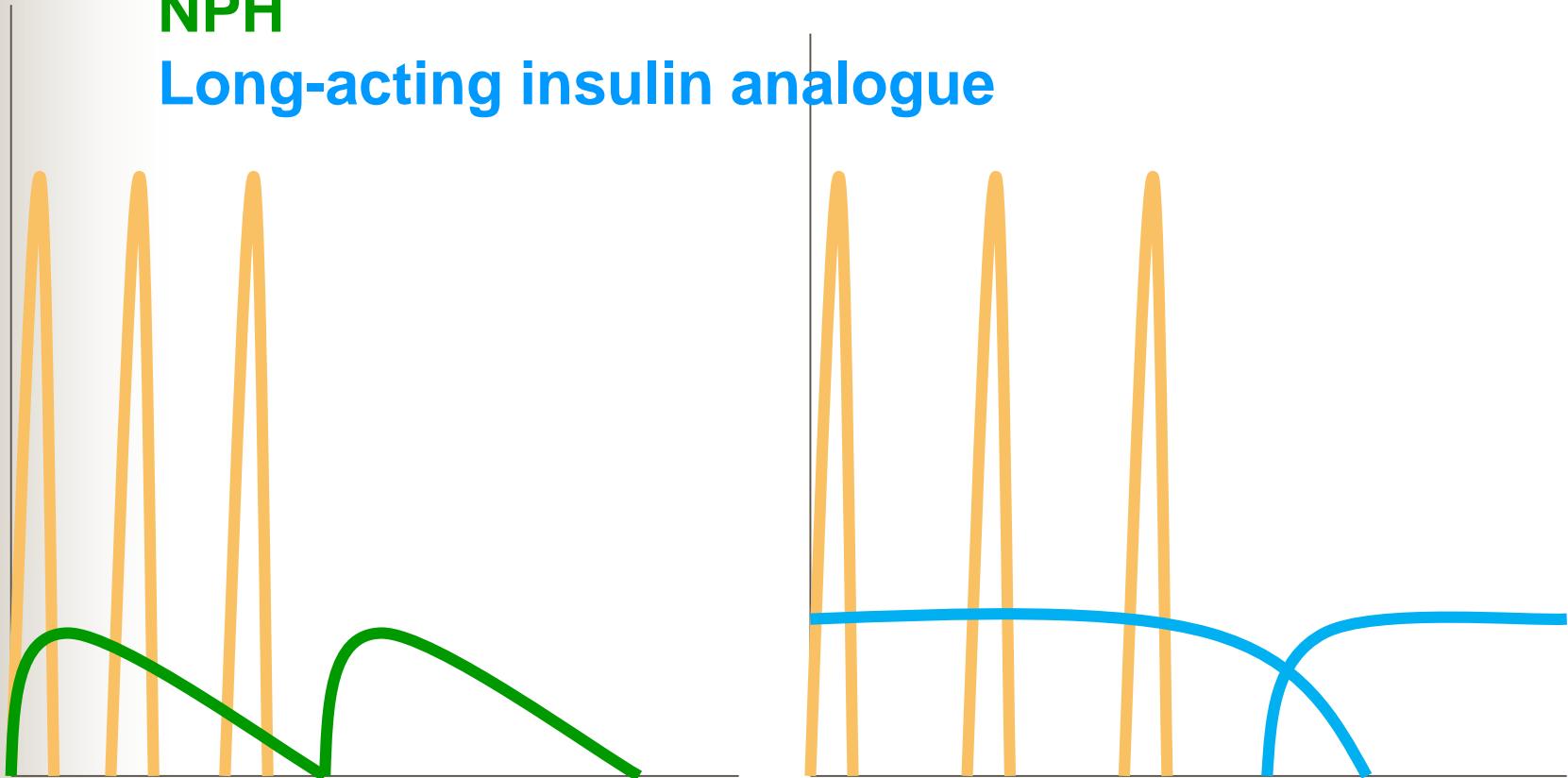


Intensified insulin regimen - DCCT

Rapid-acting insulin analogue

NPH

Long-acting insulin analogue



Insulins

Human insulins

Short acting	Actrapid HM, Humulin R, Insuman Rapid
Middle-long acting	Insulatard HM, Humulin N, Insuman Basal
	x
Mixtures	Humulin M3, Mixtard 30

Rapid acting insulin analoges

aspart	Novorapid
lispro	Humalog
glulisin	Apidra
biAsp 30, protrah.lispro	NovoMix 30, Humalog mix 25/75 nebo 50/50

Long acting insulin analoges

glargin	Lantus, Toujeo, Abasaglar
detemir	Levemir



CSII (Continuous Subcutaneous Insulin Infusion)

Rapid analogue only
„Basal-bolus regime“

Linked to CGM

Type 2 diabetes mellitus



Basal insulin??

