Insulin therapy

Lek. Marta Siomkajło
Dr n. med. Justyna Kuliczkowska-Płaksej
Dr n. med. Marcin Kałużny

Department of **Endocrinology**, **Diabetes and Isotope Therapy**

Physiology

The glucose methabolism is precisely adjustable both after a meal and under fasting conditions

Between meals: every minute 130 mg of glucose appears and is removed from the blood.

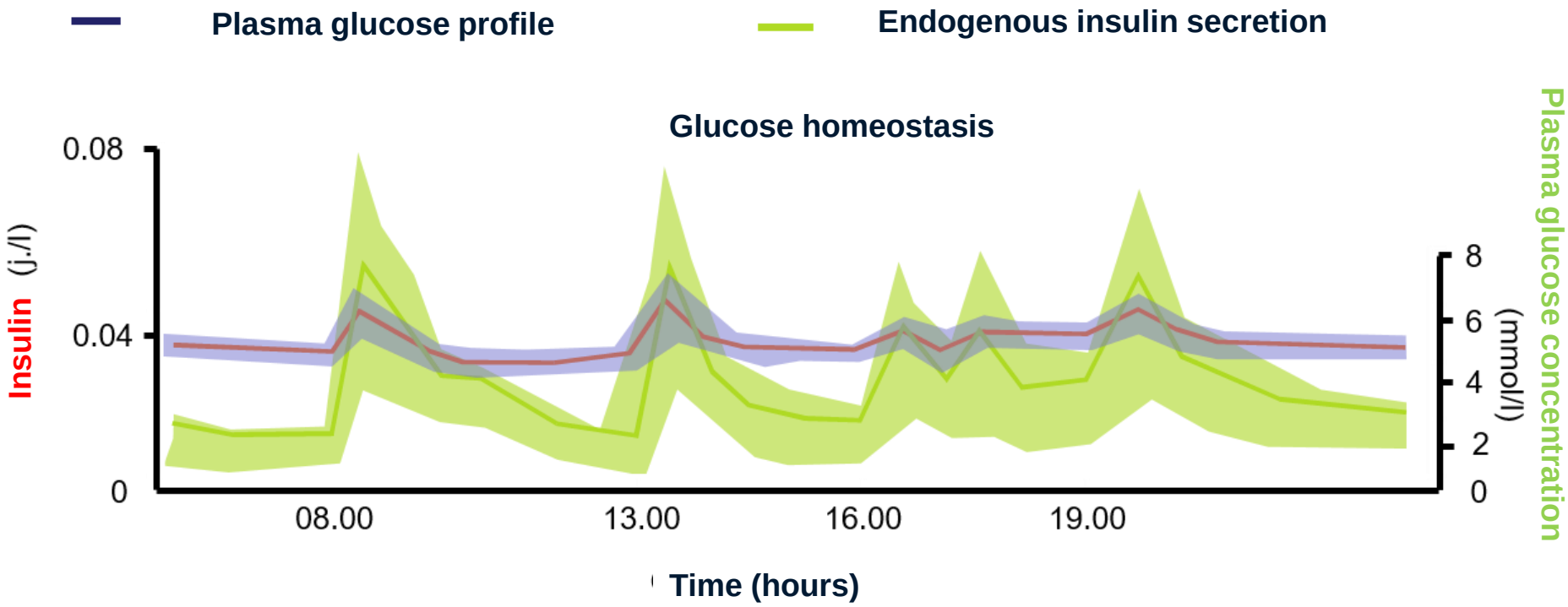
Rate and direction <–> ratio of insulin and counter-regulatory hormones

After a meal: glycemia increases after approx. 15 minutes; maximum glucose concentration appears after approx. 30-60 min. During this time, there is about 5-fold increase in insulin concentration observed

The end of meal absorption – after 5 hours

The pancreas of a healthy person produces 28-36 units of insulin / day

Physiology


Plasma glucose profile
Endogenous insulin secretion
Glucose homeostasis
Insulin (j./l)
0.08
0.04
0
08.00
13.00
16.00
19.00
Time (hours)
8
6
4
2
0
(mmol/l)
Plasma glucose concentration

Physiology

SIGNIFICANT ASYMMETRY IN THE HORMONAL REGULATION OF GLUCOSE CONCENTRATION

INSULIN

GLUCAGON
ADRENALIN
GLYCOCORTICOSTEROIDS
THYROID HORMONES
GROWTH HORMONE

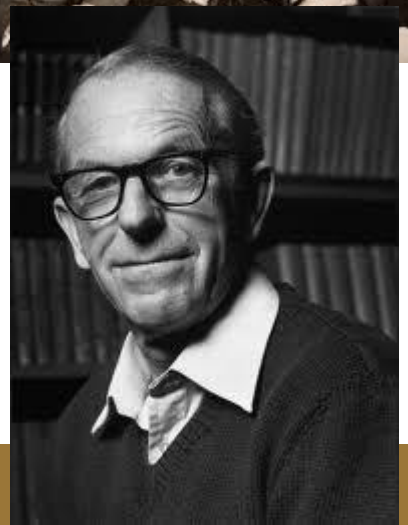
History

Discovery of insulin - 1922 Frederick Banting (Nobel) and Charles Best

1958 - establishing the amino acid sequence of insulin (Frederick Sanger, Nobel)

1969 - spatial structure (Dorothy Hodgkin, Nobel)

1963 - chemical synthesis of insulin



Until the discovery of insulin, diabetes was a deadly disease and most common treatment was a starvation diet.

<u>Recent modifications</u>

- extension of action by using a suspension
- production by genetically modified bacteria (E. coli) and yeasts
- synthetic analogs of human insulin

Types of insulin

- **Bolus** - control of postprandial glycemia; all situations requiring rapid blood glucose lowering:
- Fast-acting regular human insulin
- Rapid-acting human insulin analogues
- **Basal** - basal insulin secretion:
- Intermediate acting human insulin; isophane (NPH)
- Long-acting human insulin analogues
- **Mix** of human and analog insulins **(pre-mixed insulin)**

Bolus insulins

BOLUS INSULINS

(Rapid-acting human insulin)

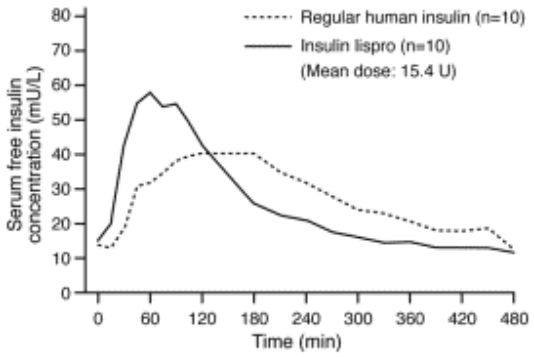
- administration: subcutaneously, intravenously, intramuscularly (intramuscular administration is not recommended)
- all types of diabetes; situations requiring rapid ↓ glycemia, postprandial glycemia correction
- supply 30 min. before meals
- peak of action after 2-3 hours
- time of action 6-8 h
- **Actrapid, Gensulin R, Humulin R, Insuman Rapid, Polhumin R**

BOLUS INSULINS

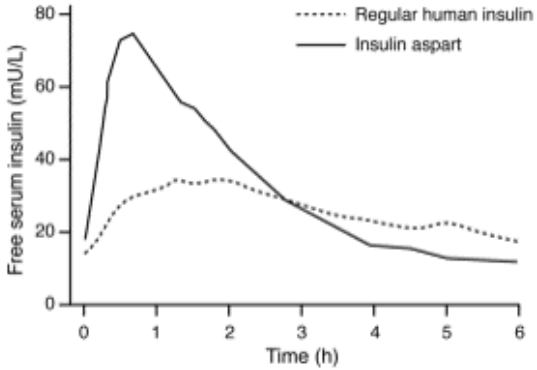
(fast acting human insulin analogues)

Types of analogues human insulin:

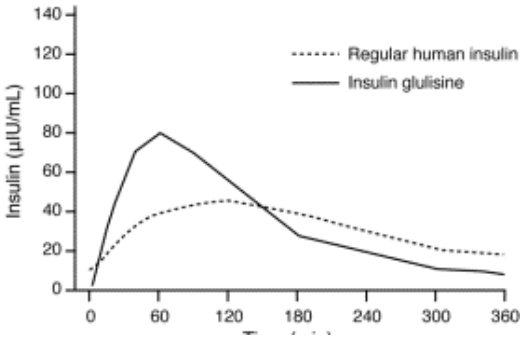
- **Insulin lyspro (Humalog),**
- **Insulin aspart (NovoRapid)**
- **Insulin glulisine (Apidra)**
- **Insulin faster aspart (Fiasp)**



lyspro



aspart



glulisine

BOLUS INSULINS

(fast-acting human insulin analogues)

- fast absorption
- faster onset and shorter time of action

- subcutaneous administration just before a meal

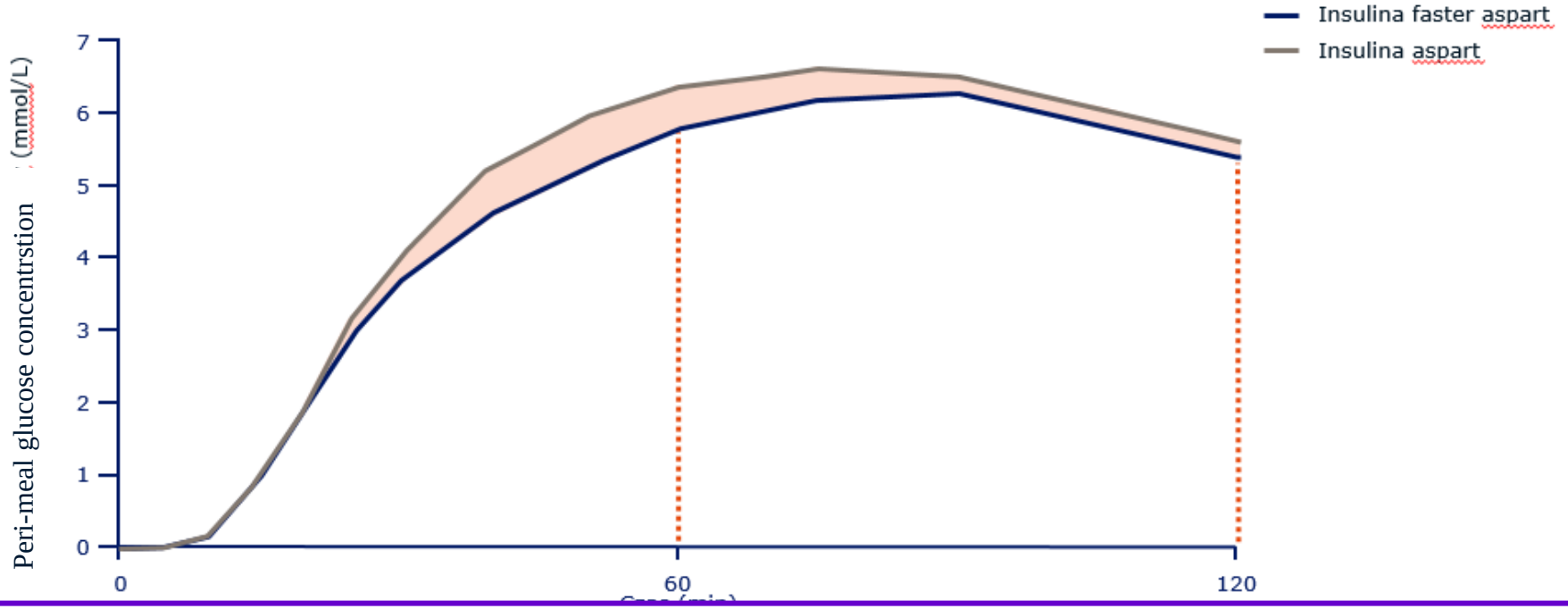
(≤ 15 minutes before a meal; exceptionally during or after a meal)

- onset of action 15 min. after subcutaneous administration
- peak of action after 30-60 min. (aspart after 1-3 h)
- duration 3-4(5) hours

BOLUS INSULINS

faster aspart

Impact for postprandial glycemia



More effective reduction of glucose concentration within **the first** hour of administration by insulin faster through more effective inhibition of liver glucose production (gluconeogenese and glycogenolysis). Difference in glucose concentration after 2 hours in comparison of aspart and faster aspart

Comparison of fast-acting analogues with rapid-acting regular insulin

Faster absorption of analogues and higher concentrations:

- better control of postprandial glycaemia
- lower frequency of hypoglycaemia (also at night)

Possibility of injection just before, during and after a meal

- greater flexibility and comfort of life

No statistically significant difference was demonstrated in reducing the risk of cardiovascular events or preventing diabetes complications

Disadvantages

- higher price of analogues
- too short action of analogues with protein-fat meals

BASAL INSULINS

BASAL INSULIN

The intermediate-acting NPH insulin

- isophane suspension of human insulin **(NPH)** **(ang. Neutral Protamine Hagedorn)**

  Gensulin N, Humulin N, Insulatard, Insuman N, Polhumin N

- **administered only subcutaneously in 1 or 2 doses (morning and evening)**

- **delayed onset of action - after 90 min.**
- **peak of action after 4-6 hours**
- **duration of action 20 h**

BASAL INSULINS
Long-acting insulin analogues

Flat time-action profile - "Peakless"

- **insulin glargine U-100 (Lantus)**
- **Insulin glargine U-300 (Toujeo)**
- **insulin detemir (Levemir)**
- **insulin degludec (Tresiba)**

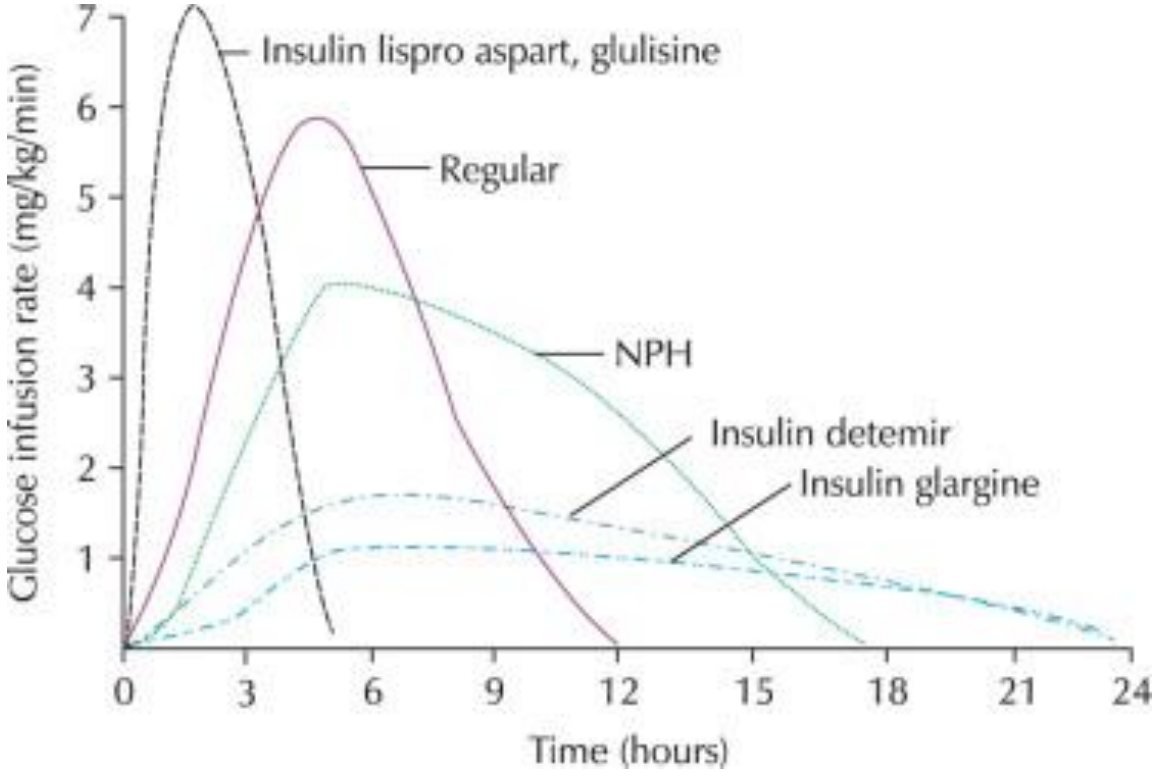
Longer duration of action - 16-22 h (detemir), up to 24 h (glargine U-100); > 40 h (degludec) = **can be administered once daily**

Potential for flexible dosing - „window" for administration, eg. glargine U-100 +/- 1 hour, glargine U-300 +/- 3 hours, degludec +/- 8 hours.

Must not be administered intravenously !!!

BASAL INSULINS
Long-acting insulin analogues vs NPH

- **NPH**
  - relatively short duration of action (more frequent injections),
  - high intra-individual variability of action (with subsequent administrations in the same person, the peak of insulin action occurs at different times) (more hypoglycaemia),
  - high inter-individual variability of effect (when administered in two different people, the peak of insulin effect occurs at different times) (more hypoglycaemia)
- **long-acting analogues**
  - comparable ↓ HbA1c with lower frequency of nocturnal hypoglycaemia,
  - better quality of life (lower risk of hypoglycaemia, fewer injections).



Total time

(3-4(5) h)

(6-8 h)

(18-20 h)

(16-24 h)

Dose-dependent pharmacokinetics! Particularly important in the case of fast-acting insulins. The higher the dose, the longer the rising arm, the later the peak, and the longer the total duration of insulin action.

PREMIXED INSULINS

(two-phase mixed human insulins)

= fast-acting regular insulin+NPH

- **subcoutaneus administration**
- **administration 30 min. before a meal**
- **mainly for type 2 diabetes melitus ,1-2 injections (breakfast, dinner)**

Available premixed NPH insulin

Brand name	Short acting component (%)	Longer lasting component (%)
Gensulin M30	**30**	**70**
Gensulin M40	**40**	**60**
Gensulin M50	**50**	**50**
Humulin M3	**30**	**70**
Insuman Comb 25	**25**	**75**
Mixtard 30	**30**	**70**
Mixtard 40	**40**	**60**
Mixtard 50	**50**	**50**
Polhumin Mix-2	**20**	**80**
Polhumin Mix-3	**30**	**70**
Polhumin Mix-4	**40**	**60**
Polhumin Mix-5	**50**	**50**

Newer pre-mixed insulins

= **rapid acting human insulin analogues + protamine suspension of this analogue**

Pre-mixed insulin with lyspro component: Humalog Mix 25, 50

Pre-mixed insulin with aspart component: Novomix 30, 50

- **mainly for type 2 diabetes melitus ,1-2 injections (breakfast, dinner)**

Pre-mixed insulins

Brand name	Composition	onset of action (min.)	peak (h)	duration of action (h)
Humalog Mix 25	**25% lispro in neutral solution /75% lispro in protamin suspention**	**15**	**1-2/4-8**	**10-16**
Humalog Mix 50	**50% lispro in neutral solution /50% lispro in protamin suspention**	**15**	**1-2/4-8**	**10-16**
NovoMix 30	**30% aspart in neutral solution /70% aspart in protamin suspention**	**15**	**1-2/4-8**	**10-16**
NovoMix 50	**50% aspart in neutral solution /50% aspart in protamin suspention**	**15**	**1-2/4-8**	**10-16**
Novomix 70 (unavailable in Poland)	**70% aspart in neutral solution /30% aspart in protamin suspention**	**15**	**1-2/4-8**	**10-16**

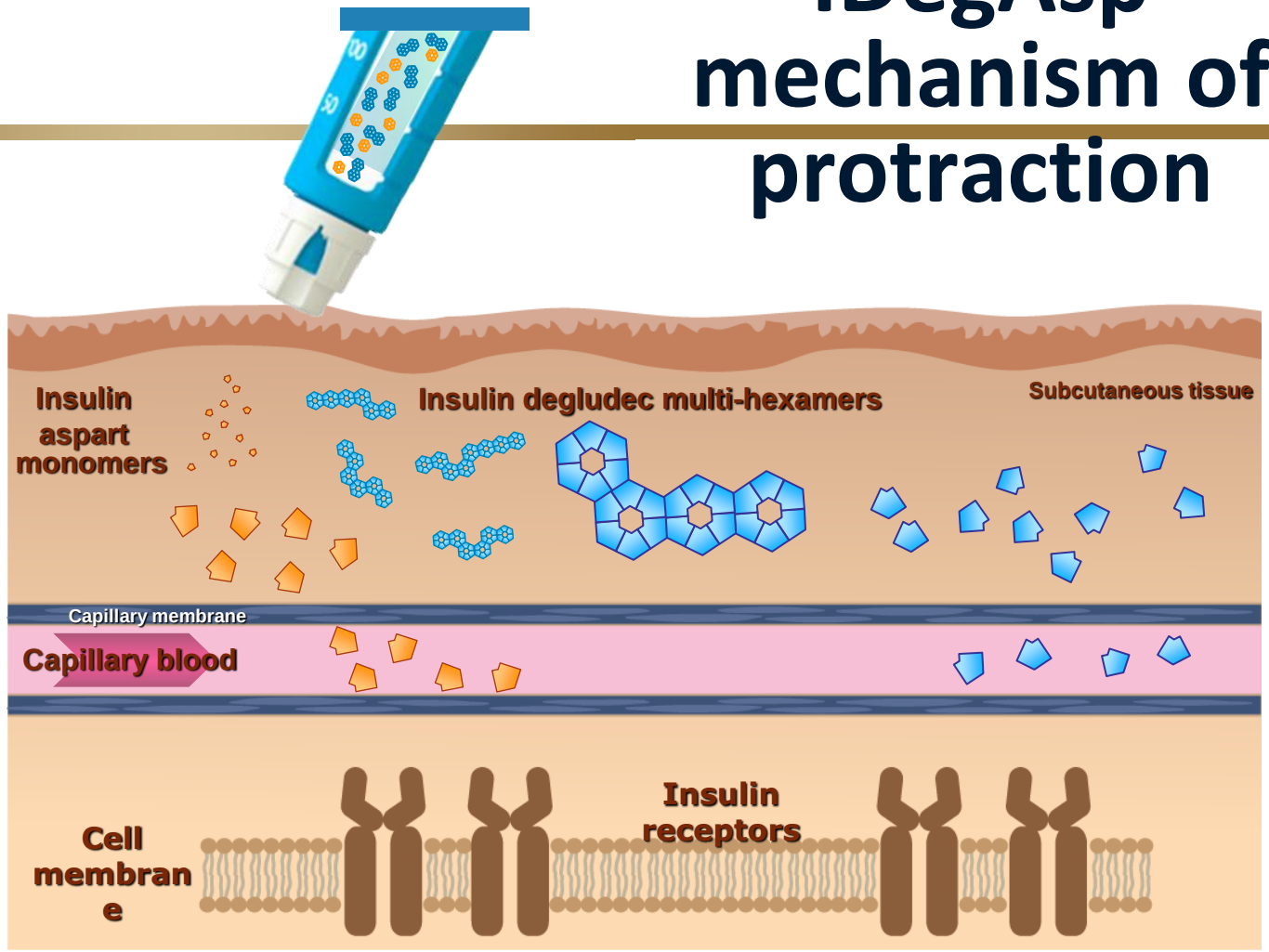
Pre-mixed insulin Ryzodeg® (IDegAsp)

IDegAsp – soluble formula degludec insulin and aspart

= **degludec insulin (IDeg) (70%) + aspart insulin (IAsp) (30%) in one solution - two independent formulas**

IDeg – dihexamers (subcutaneously forming multi-hexamers)
and
Aspart – heksamers (rapidly dissociating subcutaneously into monomers)

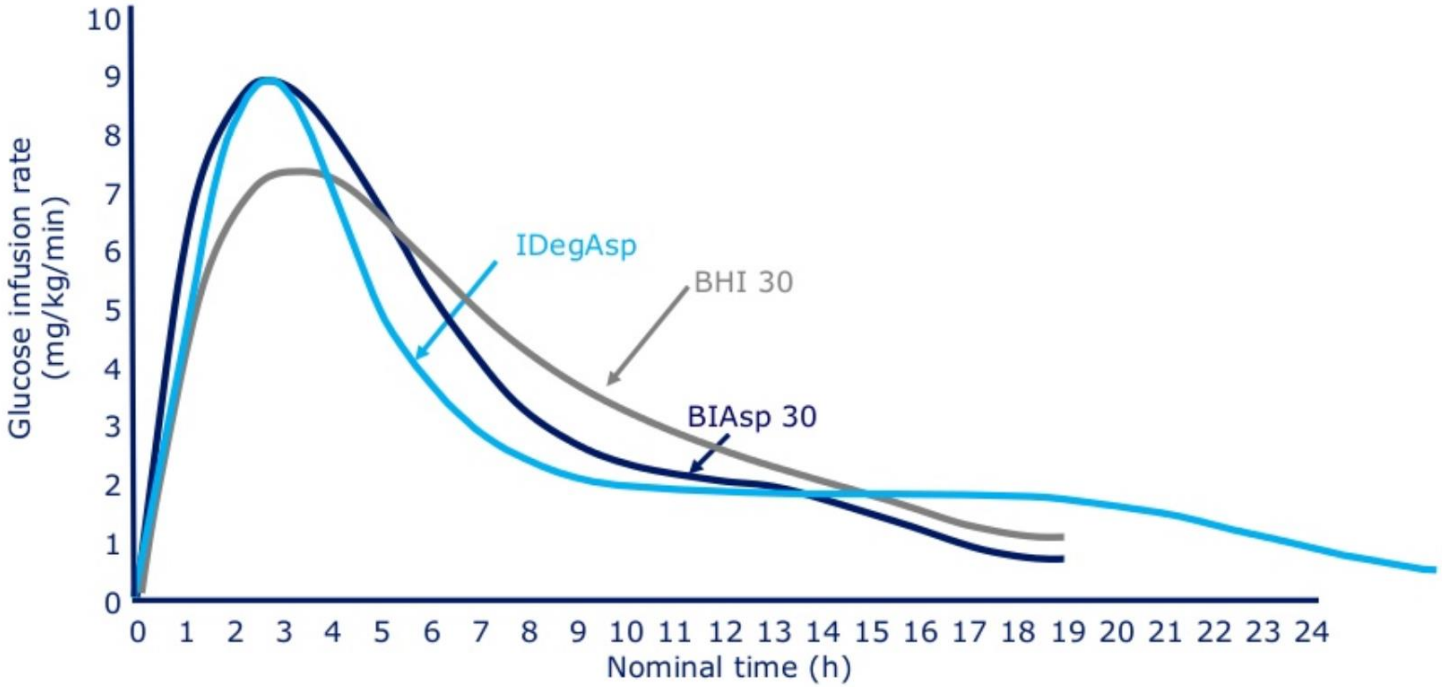
IDegAsp mechanism of protraction



Jonassen *et al. J Pept Sci* 2010;16(Suppl. 1):32

Action profiles of premixed insulin 30/70

Profile: IDegAsp vs BIAsp 30 & BHI30



IDegAsp = degludec 70% + aspart 30%

BHI 30 = regular insulin 30% + NPH insulin 70%

BIAsp 30 = insulin aspart 30% + insulin aspart with protamine suspention70%

Insulin administration

- **<u>subcutaneously</u> –** insulin pen, continuous subcutaneous insulin infusion (CSII) devices (also known as insulin pumps)
- **Intravenously (emergency, hospital)**

- Rarely, insulin may be injected **into a muscle (not used actually)**

Subcutaneous administration

- **Rapid acting/fast acting insulin analogues/premixed insulin – abdomen**
- **Long acting insulin – outer surface of the thighs, shoulders, buttocks**
- **prevention of post-insulin lipohypertrophy - rotational change of injection sites**
- **prevention of accelerated absorption under the influence of physical exertion - avoiding administration to areas that will be subjected to exercise / training**
- **injection depth - the length of the needle depending on the thickness of the subcutaneous tissue**

Intravenous administration

- fast acting and rapid acting insulin
- rapid dose adjustment to glycemia
- mainly in acute diabetes complications associated with hyperglycaemia
- do not administer intravenously: insulin suspension (NPH, premixed insulin - human and analogue insulin), long-acting analogues !!!!

Intramuscular administration

- This should happen only under a medical supervision in a hospital or medical care setting if cannot administer i.v. in a keto / hypermolar coma

- more effective in these cases than the administration of s.c. (less blood perfusion through the subcutaneous tissue)

Continuous subcutaneous insulin infusion (CSII) devices - personal insulin pump

the most common indications

1. „The dawn effect”.
2. Frequent hypoglycemia in patients with type 1 diabetes
   - severe,
   - < 70 mg/dl ≥ 4 weekly,
   - unable to achieve target HbA1c without frequent hypoglycaemia,
   - hypoglycemia unawareness.
3. Persisting HbA1c values 6,5-9,0%
   - despite intensification of treatment in a well-educated patient in the principles of intensive functional insulin therapy,
   - cooperating with the diabetes team,
   - adhering to the principles of self-control (≥ 6 blood glucose measurements / day).
4. Shift work people whose school / professional activity is irregular or travel frequently with a change of time zone with HbA1c <9.0%.
5. People engaged in competitive sports or regularl high-intensity physical activity with HbA1c <9.0%.
6. Children up to 10 years of age with type 1 diabetes.

Continuous subcutaneous insulin infusion (CSII) devices

the most common contraindications

1. **HbA1c ≥ 9,0%** (average from last year)
2. **Mental diseases** (psychoses, severe depression, also in parents of children up to 10 years of age).
3. **Intellectual disorders** (also in parents of children up to 10 years of age), making it impossible to understand the principles of intensive insulin therapy and pump operation.
4. **Eating disorders**.
5. **Addictions** (also in parents of children up to 10 years of age).
6. **Unexcused absences from doctor's appointments at the diabetes clinic.**
7. **Failure to follow or understand the principles of intensive functional insulin therapy** (e.g., lack of adequate blood glucose self-control, lack of ketone control in situations of prolonged hyperglycemia, imprecise estimation of mealtime insulin dose).
8. **More than 1 episode of ketoacidosis in a year**.
9. **Severe, rapidly progressing proliferative retinopathy** before or during laser therapy.
10. **Lack of acceptance of the disease despite full diabetes care and psychological help**

Insulin pumps disadvantages

- wearing the device, subcutaneous puncture (replaced every 3 days)
- the price of the pump and fittings
- more frequent skin infections
- failure → development of acidosis / coma

Insulin pump

- **insulin pump with continuous blood glucose measurement -** cooperation with a device for continuous blood glucose measurement

Indications for insulin therapy

independent of blood glucose levels

- **type 1 diabetes**
- **LADA (Latent Autoimmune Diabetes in Adults)**
- **diabetes in cystic fibrosis**
- **pregnancy**
- **justified wish of the patient**

- LADA + obesity / overweight - a favorable combination of insulin and metformin

Indications for insulin therapy

In type 2 diabetes

<u>Temporary</u> (with the possibility of returning to the typical algorithm):

- recently diagnosed diabetes with glycemia ≥ 300 mg/dl + symptoms of hyperglycemia,
- decompensation of diabetes due to temporary causes (infection, trauma, corticotherapy, etc.),
- surgical procedures - perioperative period,
- acute coronary syndrome / coronary artery angioplasty,
- stroke,
- other acute medical conditions requiring hospitalization in the intensive care unit,
- pregnancy and breastfeeding.

Indications for insulin therapy

In type 2 diabetes

The natural course of the disease

- initiation of permanent insulin therapy in type 2 diabetes as part of intensified treatment
- part of combination therapy
- secondary ineffectiveness of oral medications (HbA1C> 7% despite intensification of pharmacological and behavioral therapy)
- intolerance of oral antidiabetic drugs

Insulin Therapy:

- basal insulin,
- mealtime insulin
- pre-mixed insulins 1-2 injections,
- base-plus-base + bolus model for the biggest meal,
- multiple injections in the base-bolus-base model + mealtime boluses,
- intensive functional insulin therapy.

Principles of insulin therapy

Diabetes mellitus t. 1 - absolute insulin deficiency and the need for insulin treatment

Insulin therapy = substitution

Diabetes mellitus t. 2 - insulin resistance and progressive β-cell dysfunction. Therapy intensification. On average, 5-6 years after diagnosis, it is necessary to start insulin therapy.

Insulin therapy = deficiency supplement

Simple -> complex: pre-mixed, basal-plus, multiple injections, intensive functional insulin therapy

Intensive functional insulin therapy (FIT)

- **Individual adjustment of insulin doses** to the size of meals, blood glucose levels and physical activity
- **Basic treatment for type 1 diabetes**
- total insulin requirement:
  - initial dose: 0.5-0.8 units/kg/d
  - honey-moon phase: 0.2-0.5 units/kg/d
- basal insulin (intermediate-acting / long-acting analog) - 30-50% of the daily dose
  - 1x / day at bedtime or 2 times / day - in the morning and at bedtime
- mealtime insulin (rapid-acting / fast-acting analog) - 50-70% of the daily dose
  - before meals or between meals a correction dose
  - the dose depends on the meal, exercise, blood glucose and time of day

Intensive functional insulin therapy (FIT)

The mealtime insulin dose is calculated using:

- number of carbohydrate exchangers (1 WW - corresponds to 10 g of carbohydrates)
- sometimes the number of protein and fat exchangers (WBT - the amount of protein and fat with an energy value of 100 kcal) - typically in some patients using a personal insulin pump
- a conversion factor determining the amount of insulin administered per 1 WW - insulin / WW ratio
- an average of 1 unit of insulin per 1 WW / 1WBT (0.7-1.5 units)
- on average, 1 unit of insulin reduces glycemia by 30-60 mg / dl - an indicator of insulin sensitivity

Estimating insulin doses

- **Insulin / WW indicator:**
- **Rule 500:** How many grams of carbohydrate does balanced a 1 unit insulin supply?

500 / day insulin dose, e.g. 500/50 = 10

→ 1 unit of insulin balances the consumption of 10g of carbohydrates (1WW)

- **Insulin sensitivity index :**

Rule 1500: How much, on average, 1 IU of insulin lowers glycemia?

1500 / daily dose of insulin, e.g. 1500/50 = 30 → the administration of 1 unit lowers glycemia by an average of 30 mg - correction doses

Alternative: rule 400 and rule 1700

Intensive functional insulin therapy

personal insulin pump

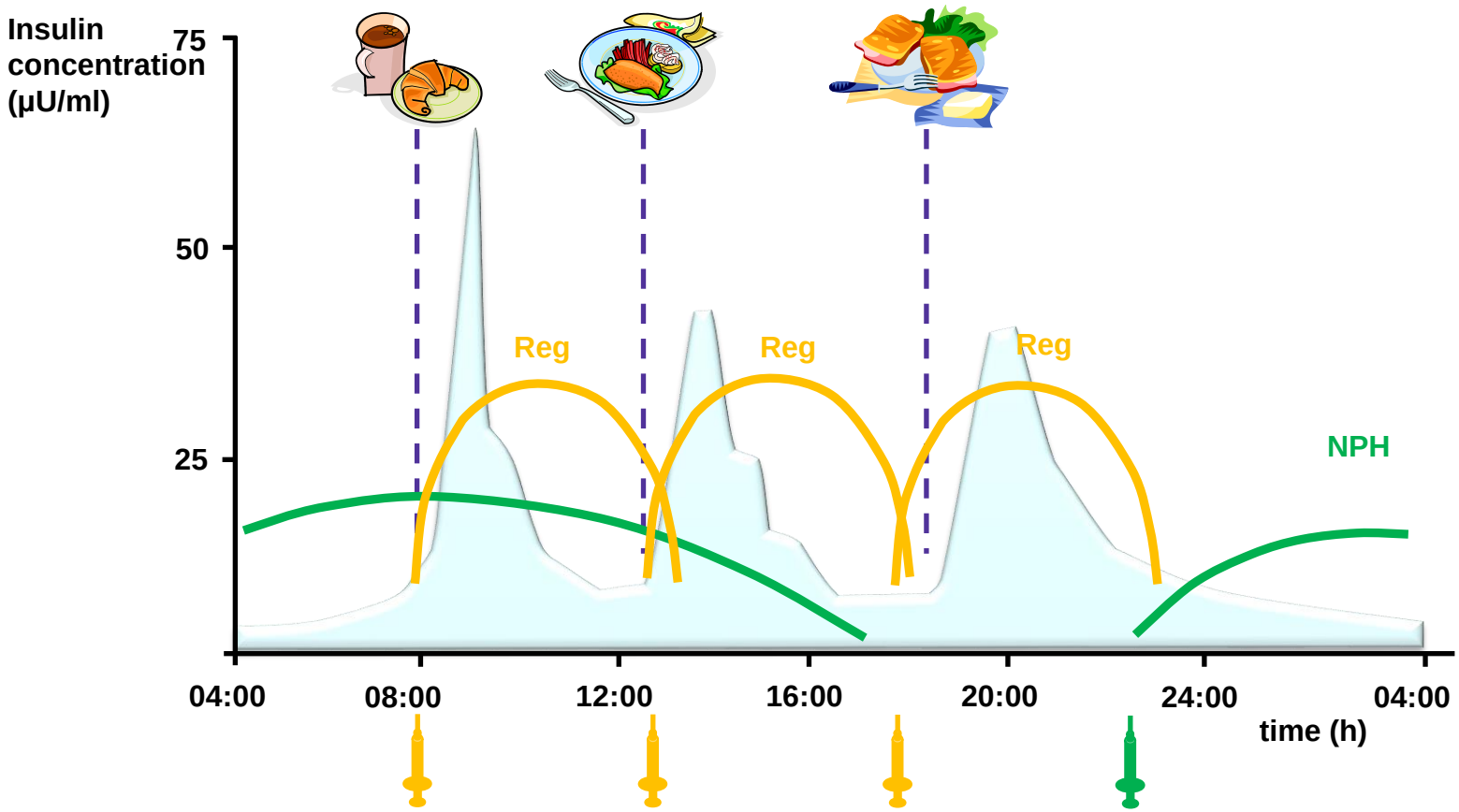
- continuous subcutaneous infusion (30-40% of the day) + preprandial boluses (simple, extended, complex)
- fast-acting analogs (or rapid-acting regular insulin,
- more flexible and precise insulin delivery,
- better glycemic control,
- lower frequency of hypoglycaemia,
- lower insulin consumption (70% of the dose used in pen therapy).

Intensive insulin therapy

in all types diabetes

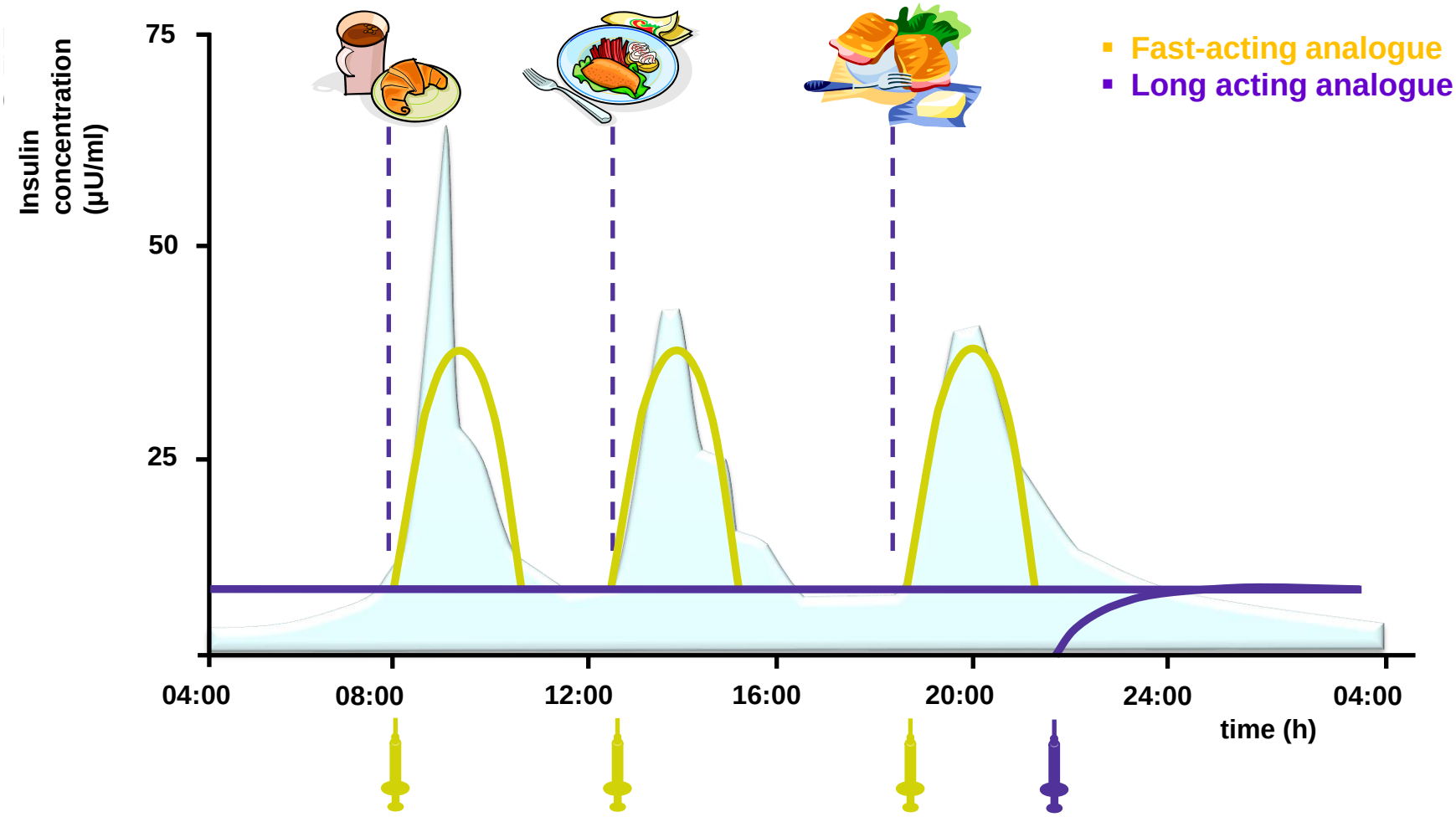
- intermediate-acting insulin / long-acting analogue 1-2 times / day (at bedtime, in the morning)
- short-acting insulin / rapid-acting analogue to meals in fixed doses
- regular lifestyle necessary
- meals similar to the amount of WW
- worse control of diabetes and a greater risk of hypoglycaemia compared to functional intensive insulin therapy

The model of intensive insulin therapy
based on NPH and short-acting insulin (R, Regular)

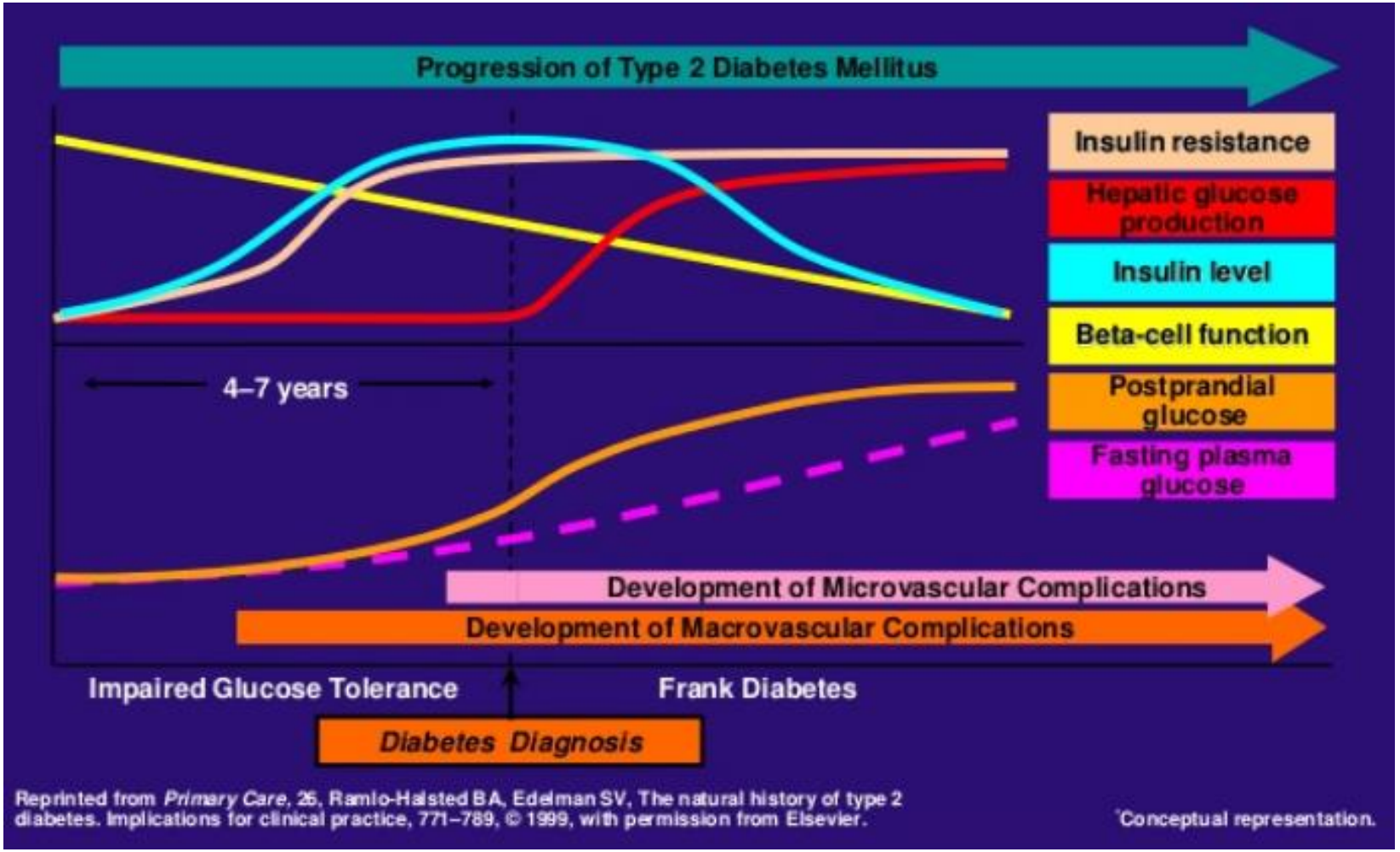


zmodyfikowano wg: Mayfield JA i wsp. Am Fam Physician 2004; 70:E489-E500,E511-2

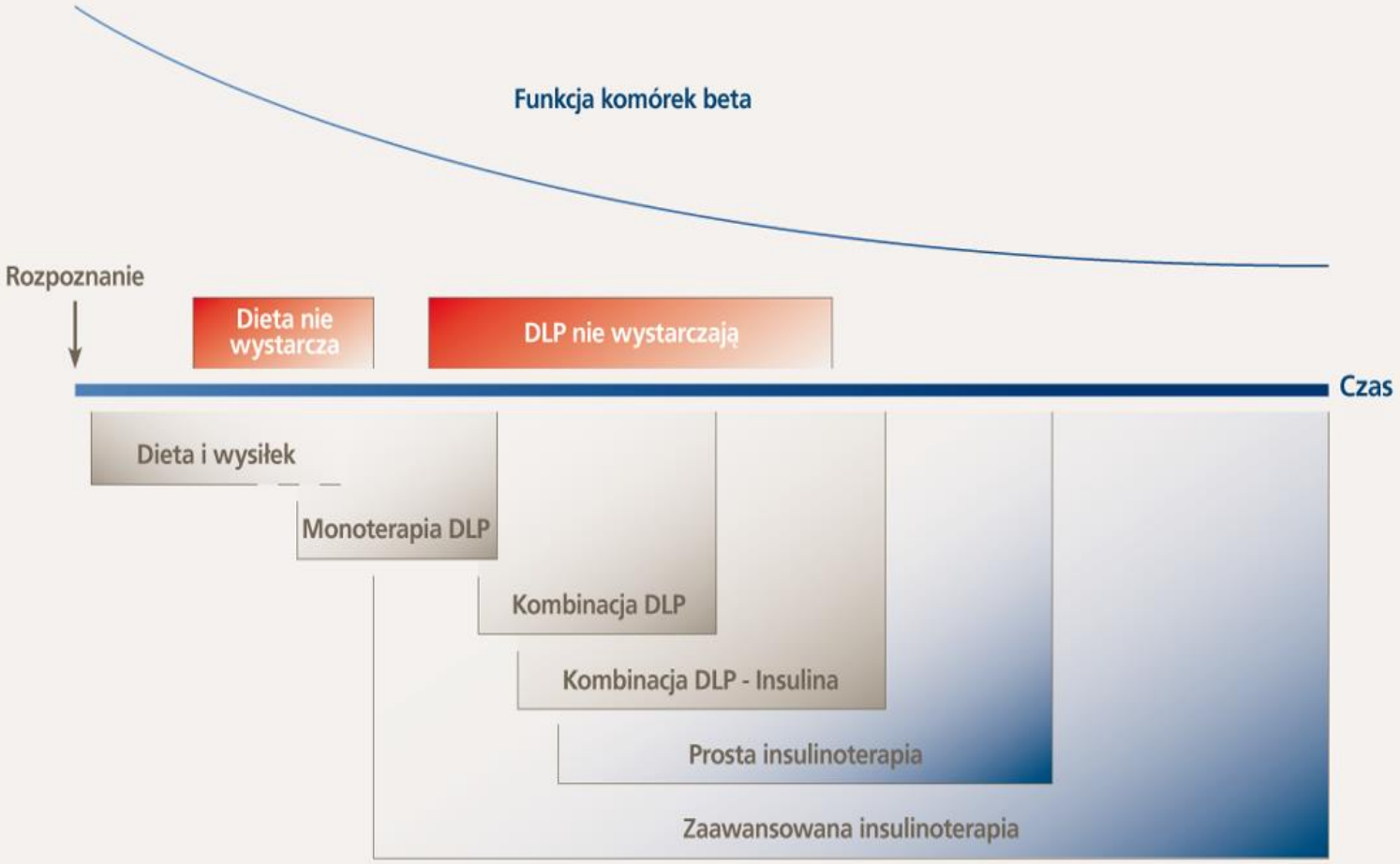
Model of intensive insulin therapy
based on analogue insulins



Etiopathogenesis of diabetes



Insulin therapy in type 2 diabetes



Type 2 diabetes – insulin therapy

- a temporary model of intensified treatment of type 2 diabetes
- combination therapy - basal insulin + oral medications
- long-acting insulin / analogue - one injection:
- morning hyperglycemia (the most common situation) - insulin given in the evening
- Fasting normoglycemia and daytime hyperglycemia - morning insulin

- initially 10 units or 0.1-0.2 units / kg bw. + 2-4j. every 4-5 days to achieve target fasting blood glucose (watch out for nocturnal hypoglycaemia especially when using NPH insulin)

Intensified insulin therapy in type 2 diabetes

Increased hyperglycemia, high HbA1c - possibility of introducing:

- pre-mixed insulin,
- base model,
- the base-plus model,
- base-bolus model,
- intensive functional insulin therapy.

Intensified insulin therapy in type 2 diabetes

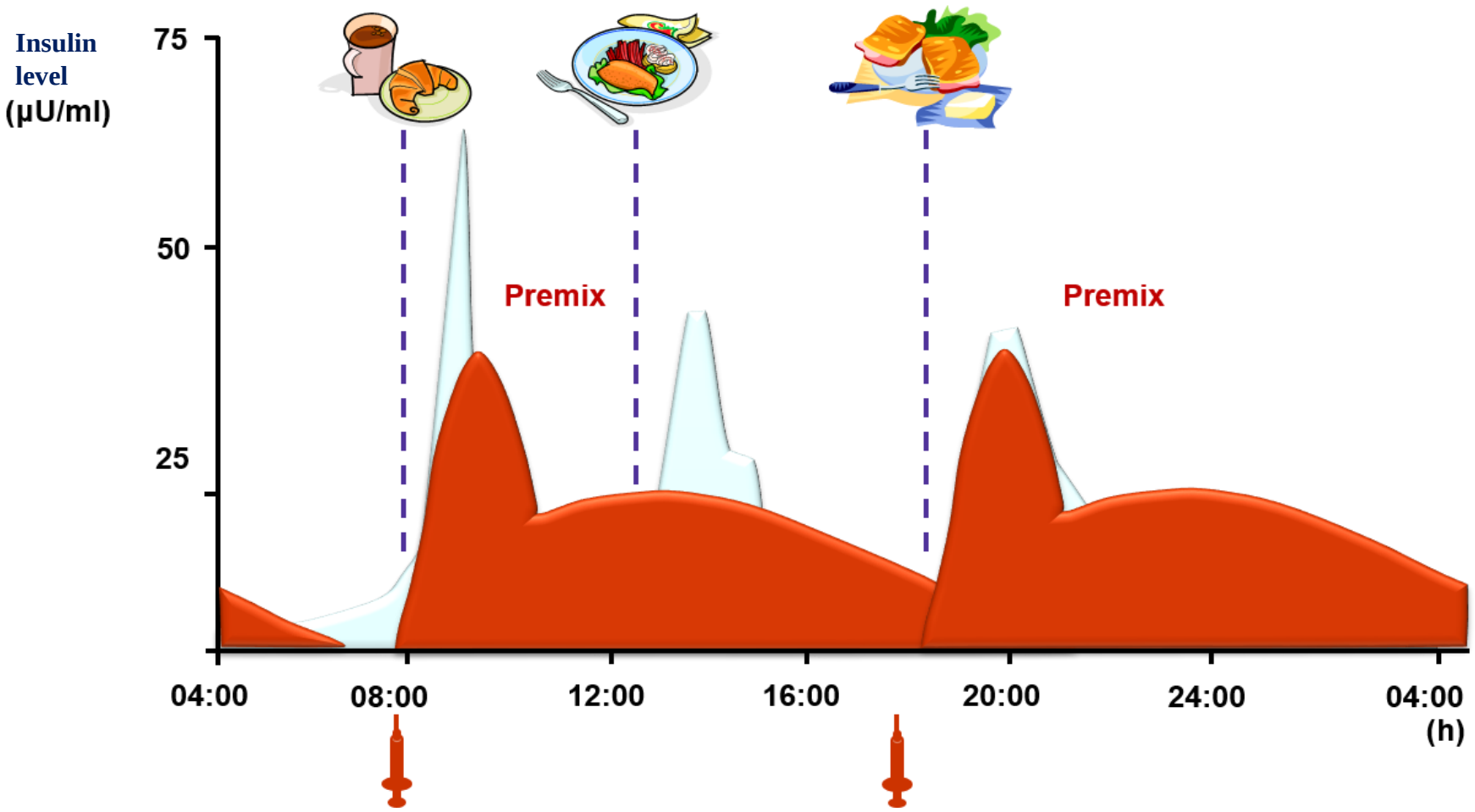
- insulin requirement > 40 units / day - 2 doses of intermediate-acting insulin / mixture, possibly discontinuation of insulin secretagogues
- insulin requirement > 80 units / day - third injection of regular insulin / rapid-acting analogue at lunchtime, possibly multiple injection algorithm
- insulin requirement> 100 units / day (insulin resistance) - cause / adverse effects to be considered
- attempting ↓ insulin resistance → 72-96 h continuous IV insulin infusion

Conventional insulin therapy
Pre-mixed human / analog insulin

- 2 times a day (breakfast and dinner)
- 2 x a day (breakfast and dinner) + short-acting insulin / fast-acting analog (lunch)

- is not recommended in type 1 diabetes !!!
- older age (> 70 years) and long-term diabetes (> 20 years), previous stroke / infarction (with target HbA1c <8.0%)
- short projected survival time, dependence on the care of others
- memory impairment, reduced manual dexterity, reluctance to repeated injections, lack of care and help
- regular lifestyle, frequent snacks

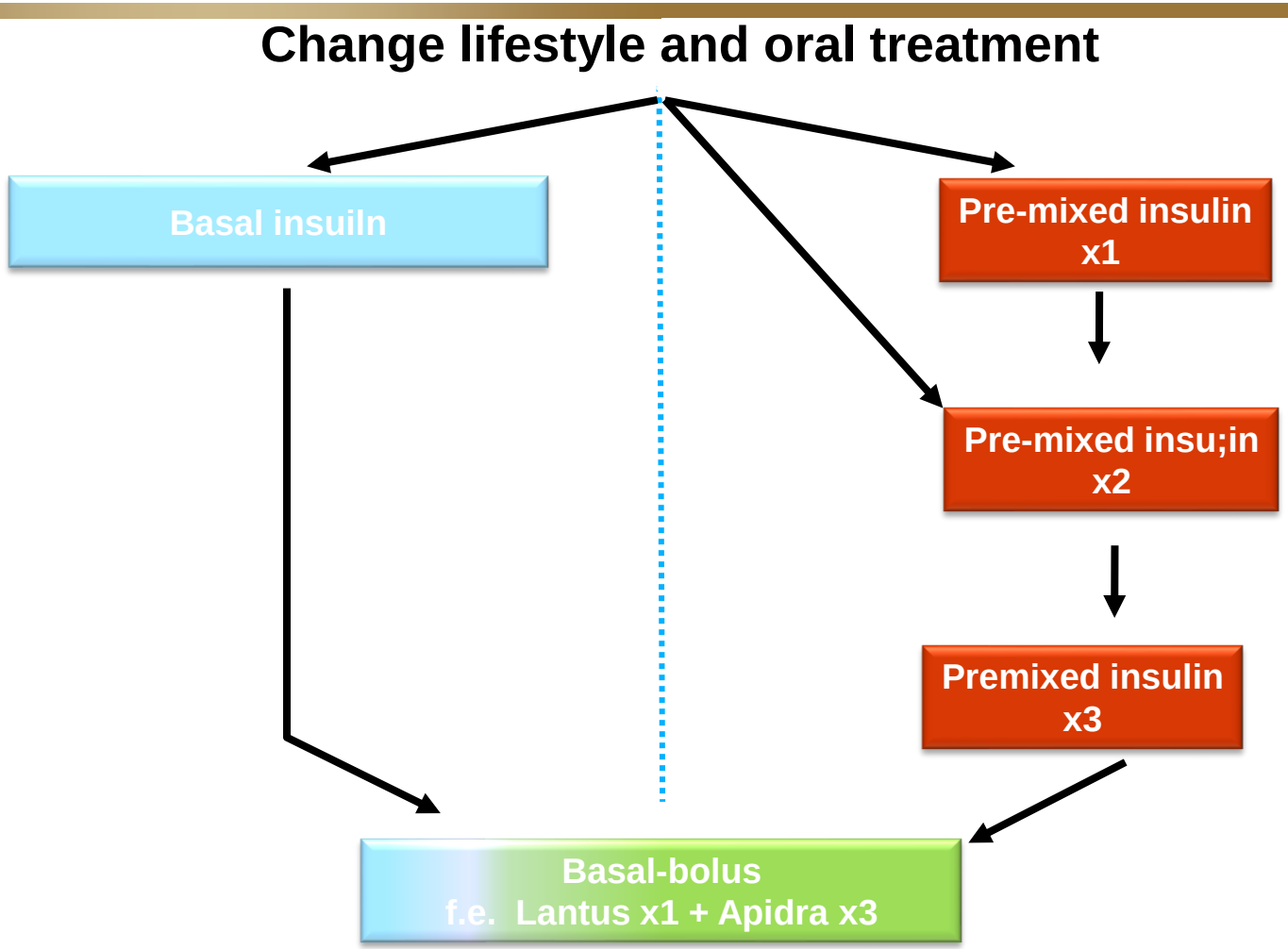
Conventional insulin-therapy



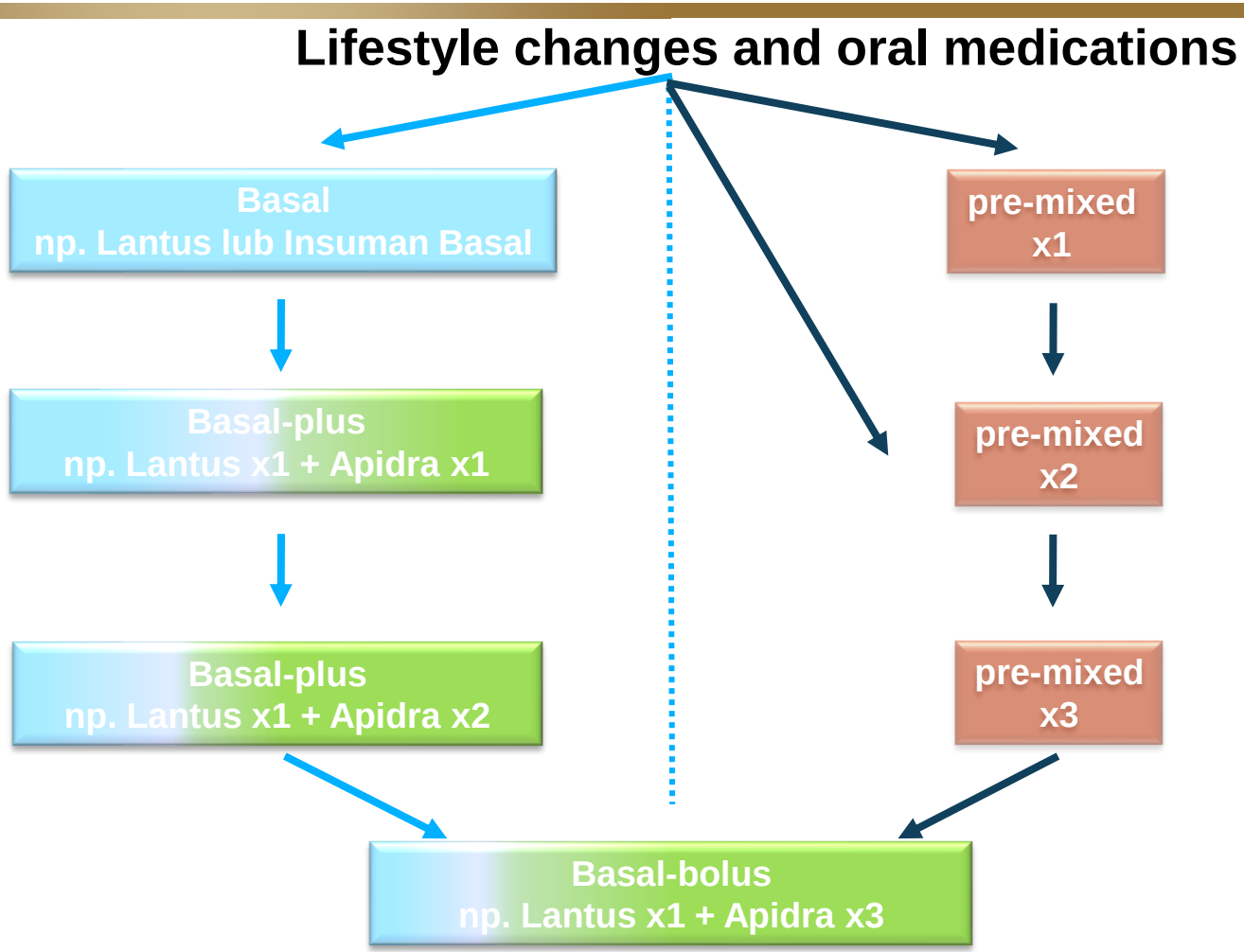
Pre-mixtures are not the ideal solution in the treatment of type 2 diabetes

- Little flexibility.
- Concentration peak between 2 and 6 hours after injection.
- Variable absorption due to formulation (suspension).
- Increased risk of hypoglycaemia in the early morning hours and at night.
- Fear of hypoglycaemia may lead to increased food consumption and, consequently, to unwanted weight gain and patient dissatisfaction with the therapy.

Traditional approach to insulin therapy in type diabetes2



An alternative approach to initiation and intensification of insulin therapy inT2D



Insulin therapy in T2D

In some cases of type 2 diabetes, with normal fasting glycemia, it is sufficient to use only short-acting insulin / fast-acting analogues per meal.

Select the type of per meal insulin which determines?

➢ the patient's lifestyle

- fast-acting analogues - greater freedom in terms of eating times, can be administered just before a meal

➢ number and composition of meals

- fast-acting analogues - protection of each meal containing digestible carbohydrates (most meals)
- 1 injection of short-acting human insulin is sufficient for the consumption of 2 meals with an interval of 2-3 hours (consumption of one meal will cause hyper- or hypoglycaemia)

➢ type of diet

- a diet richer in carbohydrates (favoring postprandial hyperglycemia) a fast-acting insulin analogue
- a diet with a lower percentage of calories from carbohydrates, more proteins and fats better short-acting insulins

Glyceamia monitoring

Assessment of the correctness of insulin dose selection

insulin dose	time for measuring glycemia
meal	1,5-2,0 h postprandial
basal insulin	fasting measurements and possibly at night

Monitorowanie glikemii

Complete glycemic profile:

- in the morning on an empty stomach
- before each main meal
- 90-120 minutes after each main meal

bedtime

- at night 2:00-3:00

Abbreviated glycemic profile:

in the morning on an empty stomach

90-120 minutes after each main meal

Blood glucose monitoring

Sposób leczenia cukrzycy	Częstość pomiarów glikemii przy prowadzeniu samo-kontroli
Wielokrotne (tj. co najmniej 3 × dziennie) wstrzyknięcia insuliny Intensywna funkcjonalna insulinoterapia, niezależnie od typu cukrzycy	Wielokrotne (tj. co najmniej 4 × dziennie) pomiary w ciągu doby według ustalonych zasad leczenia oraz potrzeb pacjenta
Chorzy leczeni wyłącznie dietą	Raz w miesiącu skrócony profil glikemii (na czczo i 2 godz. po głównych posiłkach) oraz raz w tygodniu o różnych porach dnia
Chorzy stosujący doustne leki przeciwcukrzycowe i/lub analogi GLP	Raz w tygodniu skrócony profil glikemii (na czczo i po głównych posiłkach), codziennie 1 badanie o różnych porach dnia
Chorzy na cukrzycę typu 2 leczeni stałymi dawkami insuliny	Codziennie 1–2 pomiary glikemii, dodatkowo raz w tygodniu skrócony profil glikemii (na czczo i po głównych posiłkach) oraz raz w miesiącu dobowy profil glikemii

With multiple injections of 4 times a day is a minimum, but for good glycemic control most patients should take 7-8 measurements a day.

Physical activity

- glycemic control before, during (every 30 minutes) and after exercise
- safe glycemia before exercise: 140 - 180 mg / dl
- optimal during exercise: 100 - 180 mg / dl
- when glycemia before exercise:
- > 250 mg / dL in type 1 diabetes
- > 300 mg / dL in type 2 diabetes
- + ketones in urine → avoid exercise
- The effect of aerobic (aerobic) and resistance exercise on glycaemia is different
- 4-6 hours after exercise, a predisposition to hypoglycaemia may occur
- In diabetes, regular exercise is more important (every day or every 2nd day than its intensity)

Physical activity

- ↓ 30-50% of short-acting / rapid-acting insulin dose peaking during exercise or post-exercise
- personal insulin pumps - reduction of basal insulin flow by 20-80% depending on the duration / intensity of exercise (preferably 2 hours before its start)
- against unplanned effort - additional 20-30 g (2-3 WW) of simple sugars for every 30 minutes. effort
- avoid insulin supply to the limbs burdened with exercise!

Insulin adverse events

- **Frequent**
- hypoglycemia
- weight gain
- Insulin related lipohypertrophy

- **Rare**
- Insulin related swelling
- post-insulin neuropathy (post-insulin neuritis)
- allergic reactions (to stabilizing substances in solution containing insulin)
- Insulin-related lipodystrophy

Hypoglycemia

The most common and severe complication of insulin therapy

Definition: Serum glucose <70 mg / dL regardless of the presence of symptoms.

Hypoglycemia unawareness - not feeling pathologically low blood glucose values - a complication of recurrent hypoglycemia and / or the consequence of autonomic neuropathy.

Hypoglycemia

Severe hypoglycaemia: an episode that requires the assistance of another person to administer glucose, glucagon, or take other measures.

Recurrent severe hypoglycaemia: ≥ 2 episodes of severe hypoglycaemia within the last 12 month

Hypoglicemia

- **Risks factors**

➢ **insulin therapy (monotherapy, combination therapy)**

- **lower risk in patients**:
  - treated with fast and long-acting analogues
  - using personal insulin pumps

➢ **sulfonylureas (monotherapy / combination therapy)**

➢ **incorrect doses** of the above-mentioned drugs in the situation of: ↑ physical exertion, ↓ caloric intake, alcohol consumption

➢ **aspiration to normalize HbA1c too quickly**

- in the elderly, with ischemic heart disease - can be a direct threat to life !!!

Causes of hypoglycemia

- alcohol
- skipping a meal despite administering insulin / too much insulin dose
- physical exercise without modifying insulin therapy
- too quick absorption of insulin (hot bath, being in the sun)

- diabetic gastroparesis - delayed absorption of meals
- deficiency of hormones counteracting insulin - hypothyroidism, adrenal insufficiency

Symptoms of hypoglycemia

- neurovegetative - excessive stimulation of the adrenergic system
  - hand tremor, ↑ sweating, paleness, palpitations,
  - pupil dilation,
  - anxiety, fear, hunger for wolves.
- neuroglycopenia
  - with further ↓ glycemia,
  - drowsiness, memory difficulties, disorientation, headache, blurred vision, double vision
  - irritability, anxiety, aggression,
  - slurred speech,
  - balance disorders.

Symptoms of hypoglycemia

- long-term diabetic patients with frequent hypoglycemia - vegetative symptoms poorly expressed or absent, only symptoms of neuroglycopenia present

- recurrent hypoglycemia - symptoms of neuroglycopenia present only when blood glucose <30-40 mg / dl

Hypoglycaemia
Hypoglycaemic coma

- the most severe form of hypoglycaemia
- unconsciousness, sometimes without any preceding symptoms
- sometimes Babinski's symptom, clonic-tonic convulsions

Hypoglycemia
Prognosis

Severe hypoglycaemia:

→ death,

→ irreversible changes in the brain,

→ neuroglycopenic encephalopathy (↓ intellectual performance, memory impairment, mood swings, character changes).

Hypoglycemia - management

- temporary - conscious patient:

- 10-20 g glucose (1-2 WW) p.o. (tablets, gel) or a sweetened drink (↑ glycemia after about 10-20 minutes) + complex carbohydrates - blood glucose measurement after 60 minutes
- blood glucose monitoring
- consider glucagon (s.c., i.m.)
- treated with intensive insulin therapy - 15 g of p.o. glucose → glycemia after 15 minutes → in case of persistent hypoglycaemia → glucose 15 g → glycemic control after another 15 minutes (15/15 rule)

Hypoglycemia - management

Unconscious/ impaired consciousness

- safe side position
- 20% i.v. glucose (0.2 g glucose / kg b.w.), then infusion of 10% glucose i.v
- difficulties with i.v. access - glucagon i.m. or s.c. (1 mg) (ineffective after strenuous exercise and alcohol, beware in type 2 diabetes!)
- after regaining consciousness - p.o. carbohydrates
- long-term follow-up after waking (risk of recurrence of hypoglycaemia)
- if it is necessary to administer glucagon to patients with type 2 diabetes or after drinking alcohol - hospitalization is necessary!

Hypoglycemia - management

- patients treated with insulin and sulfonylureas - risk of long-term hypoglycaemia - prolonged glucose infusion
- treated with long-acting insulin - possible delayed recurrence of hypoglycaemia
- evere hypoglycaemia - need for hospitalization

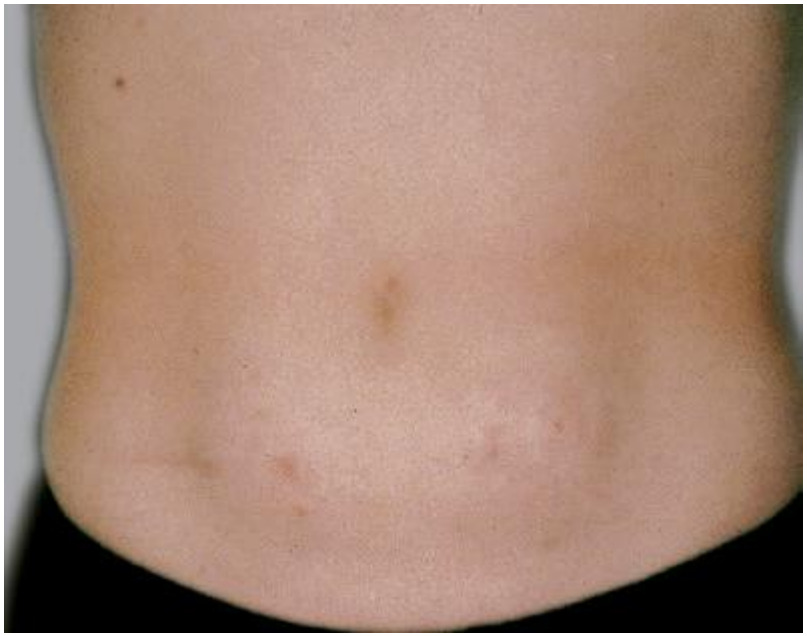
Management of unawareness of hypoglycaemia

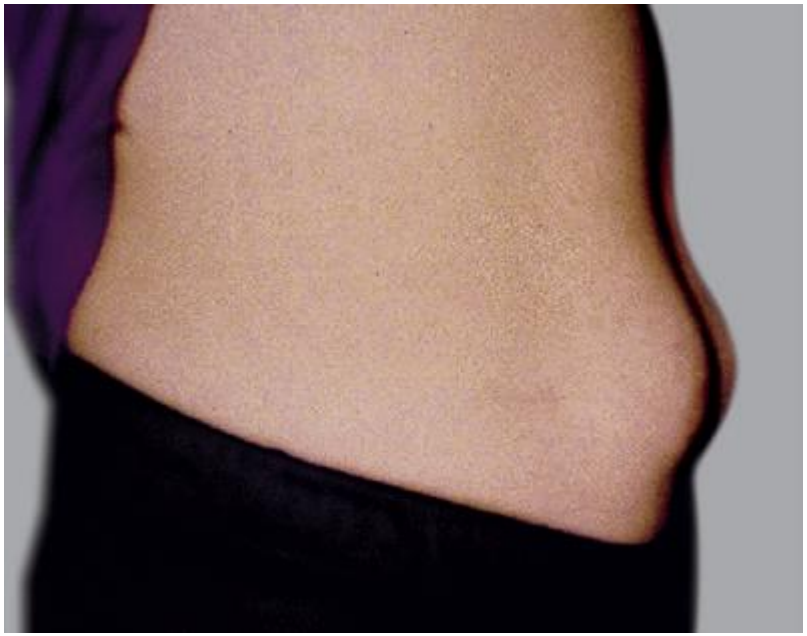
- education,
- taking this situation into account in the professional activity (drivers!),
- modification of the therapy should be considered,
- frequent self-monitoring, consideration of the use of continuous glucose monitoring (CGMS for drivers required).

CGMS (ang. Continous Glucose Monitoring System)

Insulin-related lipohypertrophy

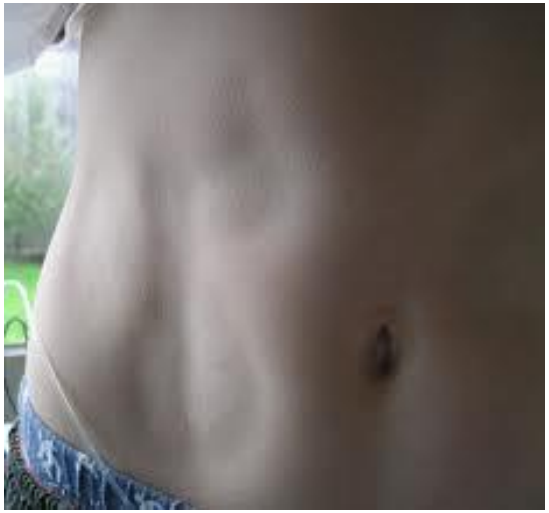
- adipose tissue overgrowth at the site of insulin administration - anabolic effect on lipid metabolism
- treatment - rotation (change) of the place of insulin administration, massage



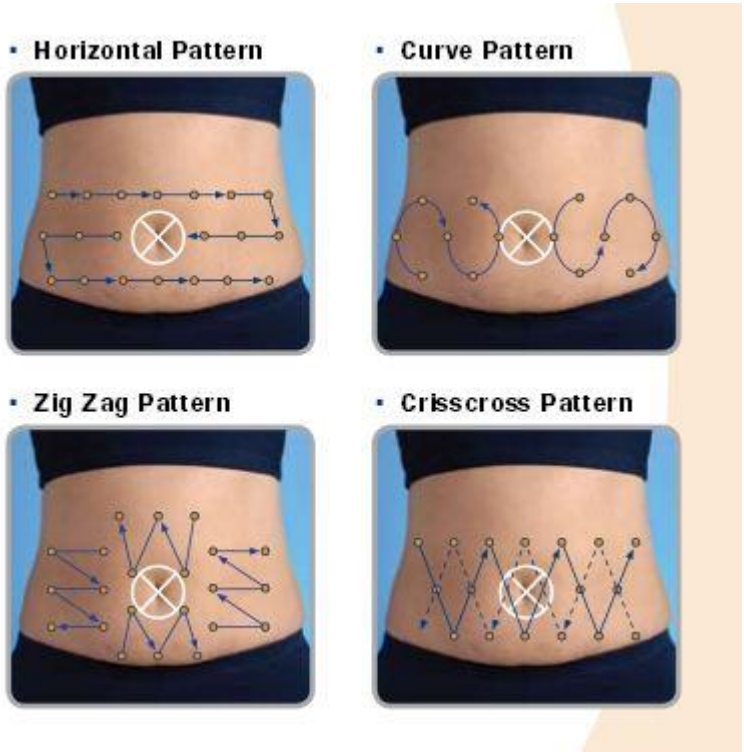


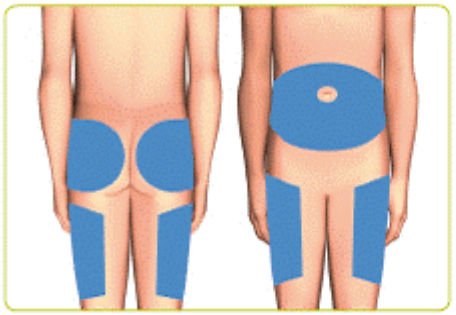
Insulin lipodystrophy

- complication of the use of animal insulins
- loss of adipose tissue at the sites of insulin administration - local immune reaction
- rotation of injection sites

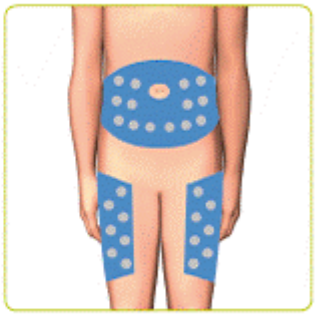


Rotational change of places of insulin injections





Suitable sites for insulin injections



Rotation scheme for injection sites

AccuCheck infusion set