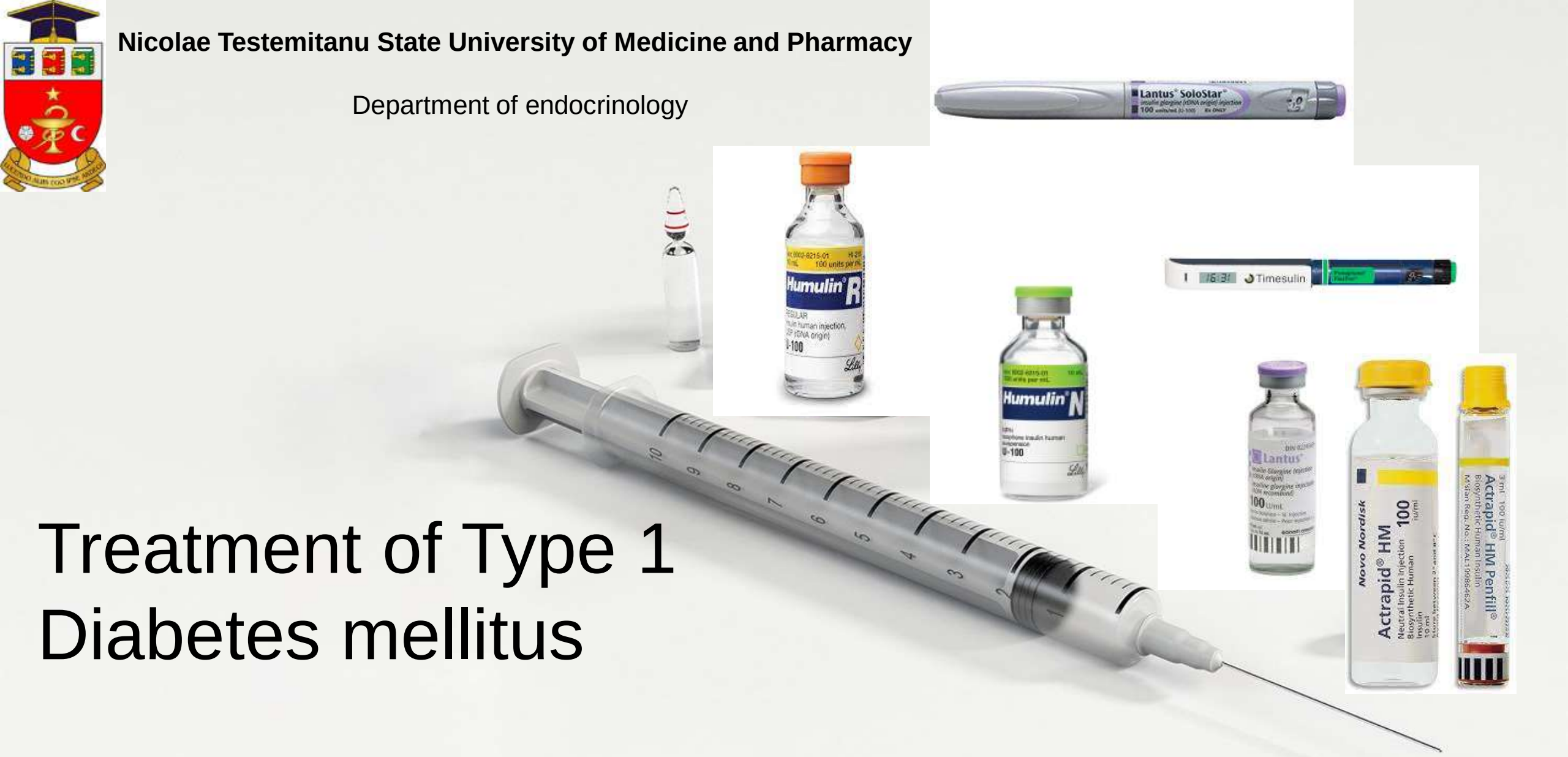
Nicolae Testemitanu State University of Medicine and Pharmacy

Department of endocrinology



Treatment of Type 1 Diabetes mellitus

Cristina Rizov,
Associate Professor, PhD

The purpose of therapy

01 **To suppress the negative effects of excessive hyperglycemia**

02 **To avoid and reduce long-term complications**

03 **Normal lifestyle**

04 **Normal physical growth & development**

Glycemic control - HbA1c level

- **HbA1c** - **is the major tool for assessing glycemic control** and has strong predictive value for diabetes complications.

- Reflects **average glycemia** over approximately **3 months**.

- Should be performed routinely in all patients:
  - at initial assessment and
  - as part of continuing care.

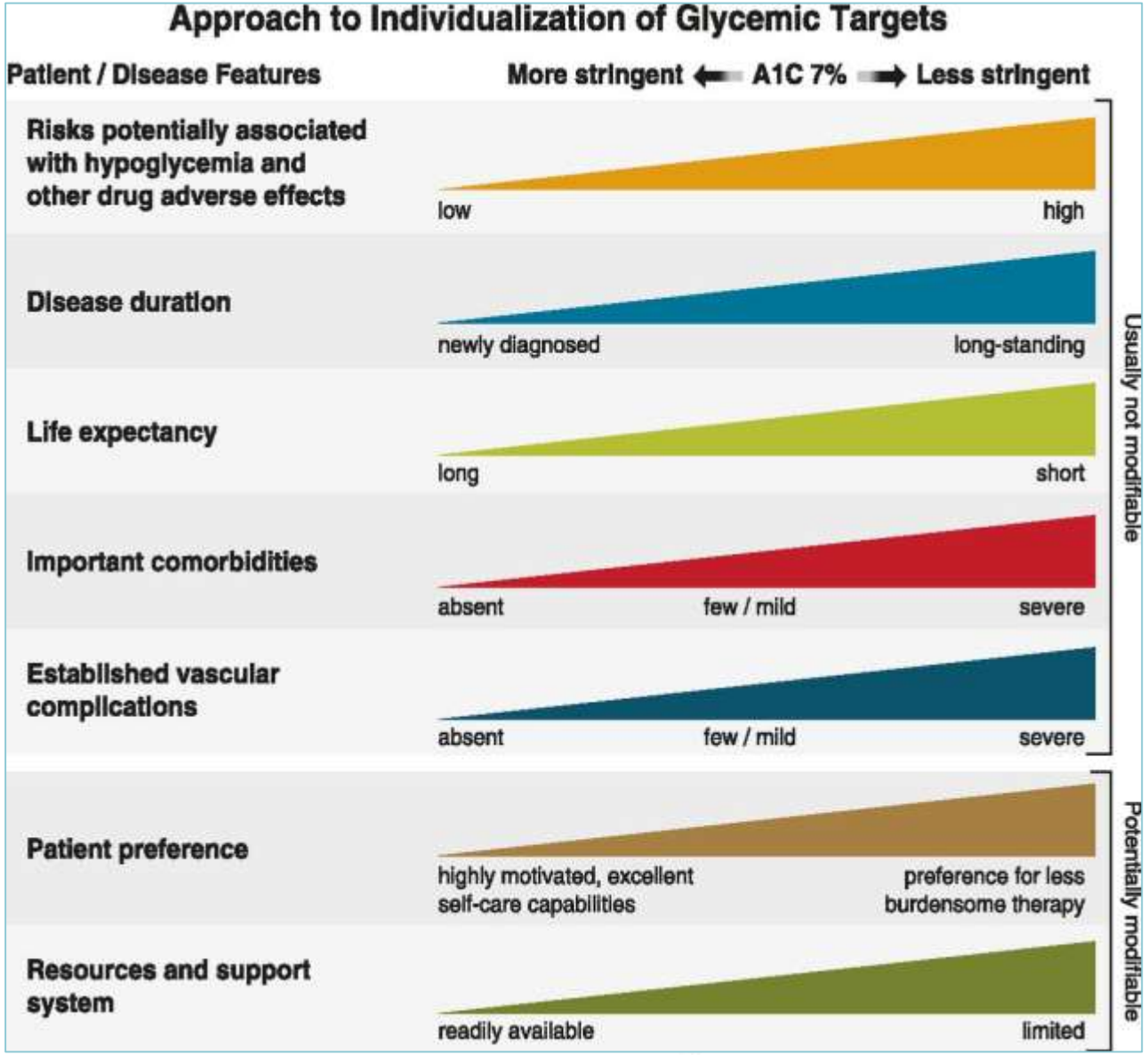
- Measurement approximately every 3 months determines whether patients' glycemic targets have been reached and maintained.

A1C goal for many nonpregnant adults of **<7%** (53
mmol/mol)

lower A1C levels (such as <6.5%) may be acceptable if this can be achieved safely without significant hypoglycemia or other adverse effects of treatment.

Less stringent A1C goals < 8% [64 mmol/mol]) may be appropriate for patients with:

- a history of severe hypoglycemia,
- limited life expectancy,
- advanced microvascular or macrovascular complications,
- extensive comorbid conditions,
- or long-standing diabetes,
- appropriate glucose monitoring, and
- effective doses of multiple glucose lowering agents including insulin.



Translating A1c to a blood sugar level

A1c	eAG (mg/dl)	eAG (mmol)
5%	97	5.4
6%	126	7.0
7%	154	8.6
8%	183	10.2
9%	212	11.8
10%	240	13.3
11%	269	14.9
12%	298	16.5
13%	326	18.1
14%	355	19.7

Glycemic recommendation for adults with diabetes

Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

↵* More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

↵† Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Lifestyle optimization

Nutrition

The National Academy of Medicine (formerly the Institute of Medicine) broadly defines nutrition therapy as the treatment of a disease or condition through the modification of nutrient or whole-food intake.

Exercises

Constant and adapted physical activity.

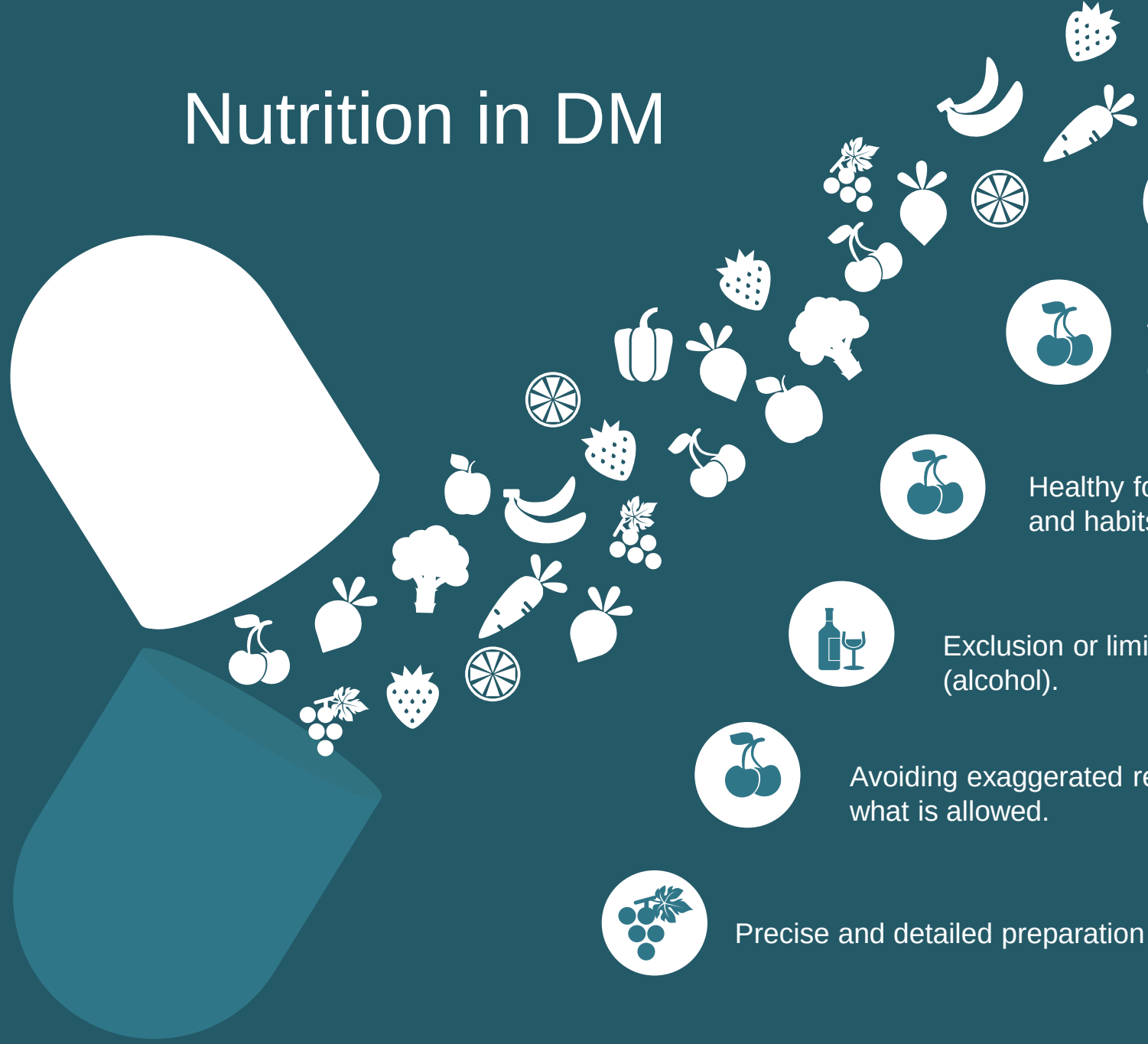
Non-smoking condition

Smoking aggravates micro- and macrovascular complications, especially nephropathy and neuropathy.

Stress prevention

The relationship between stress and diabetes is related to: increased risk of coronary heart disease and BP.

Nutrition in DM



Ensuring a balance between energy intake (through food) and the amount of energy costs imposed by life.

The composition is similar to that of non-diabetics, able to maintain good health.

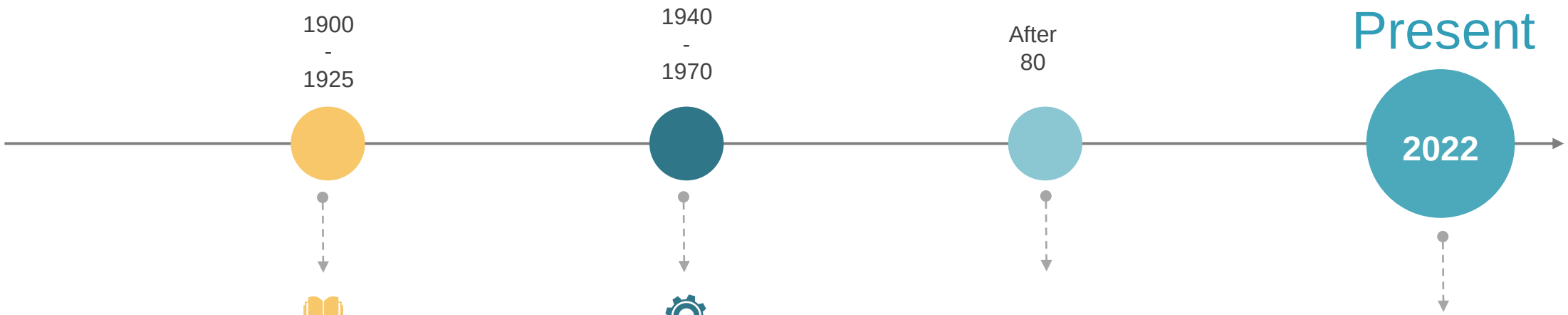
Healthy food preparation, respecting culinary tastes and habits.

Exclusion or limitation of harmful outcomes (alcohol).

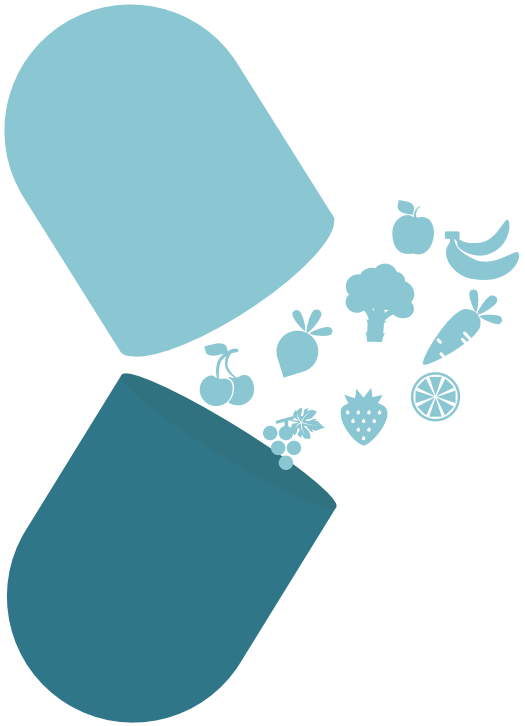
Avoiding exaggerated restrictions, insisting first on what is allowed.

Precise and detailed preparation of the diet.

Historical stages of the diet in DM



Principles of diet in T1DM



- **The composition of the diet,** in particular as regards carbohydrates;

- Establishing an optimal **relationship between insulin injections, and the timetable and constant carbohydrate content** of meals at the same time, from one day to the next.

Nutrition of the diabetic child and adolescent

Triad: Insulin therapy + Diet + Exercise

Objectives:

- Ensuring a normal growth and development;
- To avoide obesity (requires high doses of insulin);
- To avoide hyper and hypoglycemia;
- Good socio-professional integration;
- Degree of independence as high as possible.

General principles

To avoid large glycemic variations:

- Food should be the same in terms of schedule, quantity, quality (not "liberalization");
- Exclude foods with> 60% carbohydrates;
- To be divided into 3 main meals + 3 snacks

New !

- “Meal planning” meal planning in correlation with the practical insulin scheme;
- Dietary fiber ↑ = good glycemic control;
- Sweets in small quantities (sucrose) → at the end of complex lunches: they do not produce a higher increase in blood sugar.

Meal planning

- It is important to avoid hyperglycemia or hypoglycemia;
- The schedule of main meals, snacks, composition is observed;
- The meal times are synchronized with the insulin therapy regimen;
- The same carbohydrate intake is maintained at a certain meal each day and thus the large fluctuations in blood sugar are limited.

Time:	7	10	13	16	20	22
%:	20	10	30	10	20	10

Sweeteners

No food energy:

- Saccharin (E 954) (max 4 g / kg / day - NOT in children, pregnant women)
- Cyclamate (E952) (2.5 mg / kg / day)

Calorigen:

- fructose (0.5 mg / kg / day) promotes the increase of triglycerides;
- sorbitol (0.5 mg / kg / day) aggravates diabetic neuropathy;
- xylitol → as sweet as sucrose but having only two thirds of calories;
- aspartame (50 mg / day) is aspartic acid phenylalanine, 200 x sweeter than sucrose.

Glucides

Which can be consumed without restriction (not weighed): vegetables (content <5%);

Consumed foods weighed only: bread, flour, cereals, rice, potatoes, dried legumes, fruits, vegetables with a content> 5%, milk, cottage cheese, yogurt;

Prohibited foods: sugar, cakes, candies, chocolate, syrups, sugar biscuits, honey, ice cream, commercial sugary drinks (Cola, Pepsi, ...)

What is the glycemic index?

- The glycemic index (GI) is a value used to measure how much specific foods increase blood sugar levels.
- Foods are classified as low, medium, or high glycemic foods and ranked on a scale of 0–100.
- There are the three GI ratings:
  - Low: < 55
  - Medium: 56–69
  - High: >70

Glycemic Index

Low GI (<55), Medium GI (56-69) and High GI (70>)

Grains / Starchs		Vegetables		Fruits		Dairy		Proteins	
Rice Bran	27	Asparagus	15	Grapefruit	25	Low-Fat Yogurt	14	Peanuts	21
Bran Cereal	42	Broccoli	15	Apple	38	Plain Yogurt	14	Beans, Dried	40
Spaghetti	42	Celery	15	Peach	42	Whole Milk	27	Lentils	41
Corn, sweet	54	Cucumber	15	Orange	44	Soy Milk	30	Kidney Beans	41
Wild Rice	57	Lettuce	15	Grape	46	Fat-Free Milk	32	Split Peas	45
Sweet Potatoes	61	Peppers	15	Banana	54	Skim Milk	32	Lima Beans	46
White Rice	64	Spinach	15	Mango	56	Chocolate Milk	35	Chickpeas	47
Cous Cous	65	Tomatoes	15	Pineapple	66	Fruit Yogurt	36	Pinto Beans	55
Whole Wheat Bread	71	Chickpeas	33	Watermelon	72	Ice Cream	61	Black-Eyed Beans	59
Muesli	80	Cooked Carrots	39						
Baked Potatoes	85								
Oatmeal	87								
Taco Shells	97								
White Bread	100								

The reference food is glucose or white bread, whose GI is 100%.

Factors that affect the GI of a food

- The type of sugar it contains. There's a misconception that all sugars have a high GI. The GI of sugar ranges from as low as 23 for fructose to up to 105 for maltose.

- The structure of the starch. Starch is a carb comprising two molecules — amylose and amylopectin. Amylose is difficult to digest, whereas amylopectin is easily digested. Foods with a higher amylose content will have a lower GI.

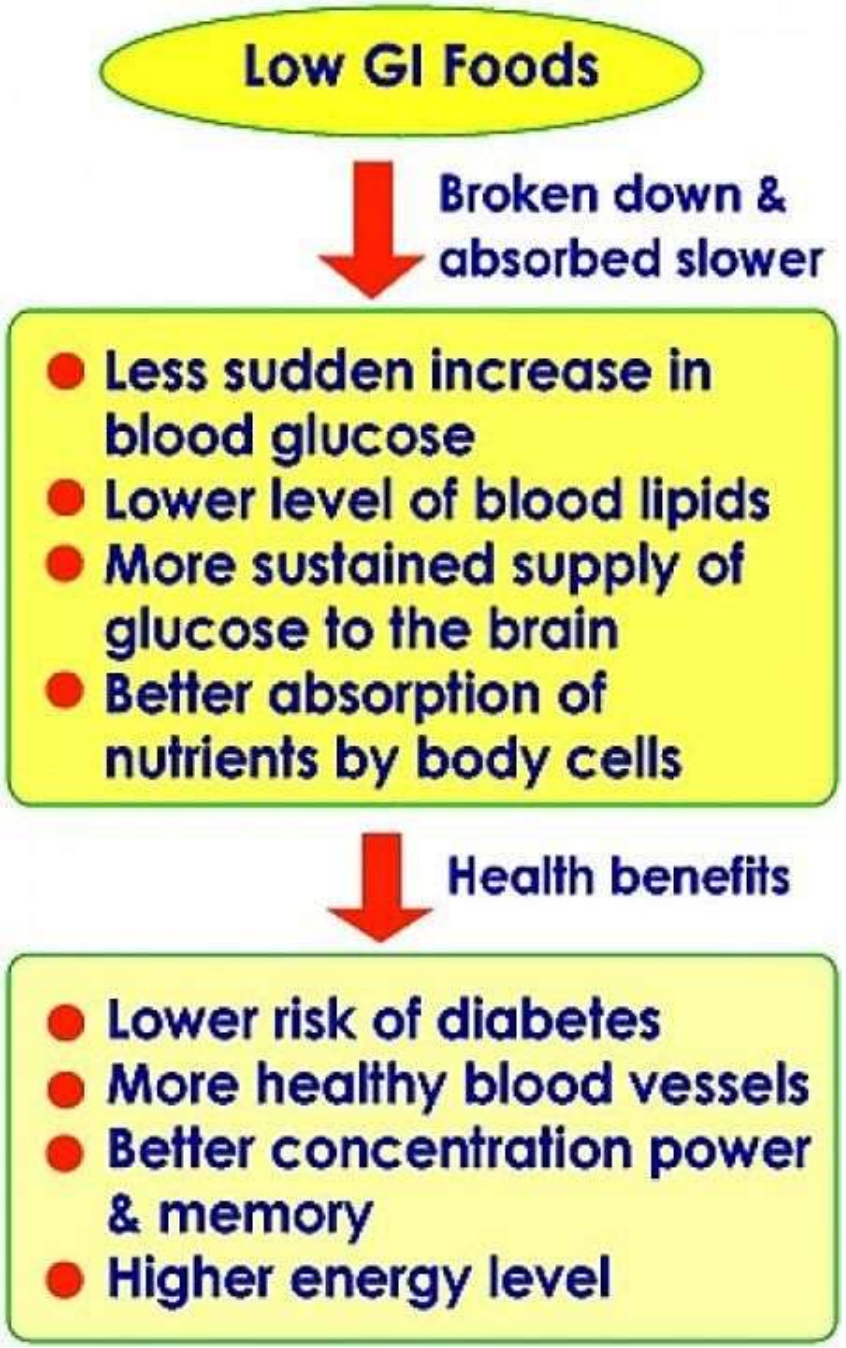
- Processing methods such as grinding and rolling disrupt amylose and amylopectin molecules, raising the GI. The more processed a food is, the higher its GI.

- Nutrient composition. Adding protein or fat to a meal can slow digestion and help reduce the glycemic response to a meal.

- Cooking method. Preparation and cooking techniques can affect the GI. The longer a food is cooked, the faster its sugars will be digested and absorbed, raising the GI.

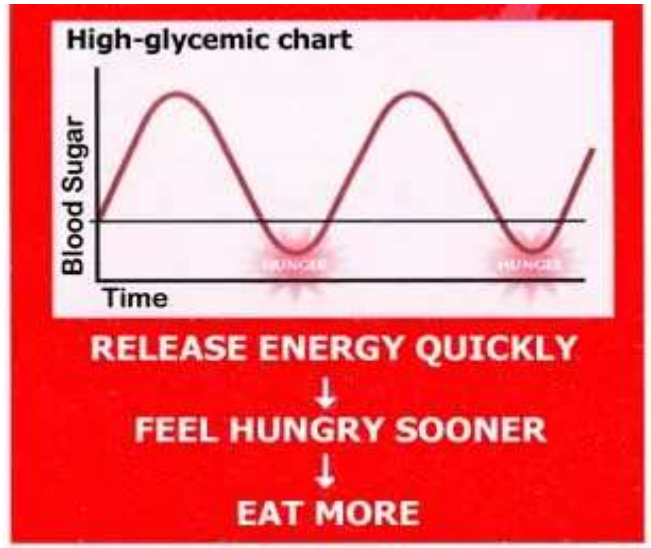
- Ripeness. Unripe fruit contains complex carbs that break down into sugars as the fruit ripens. The riper the fruit, the higher its GI. For example, an unripe banana has a GI of 30, whereas an overripe banana has a GI of 48.

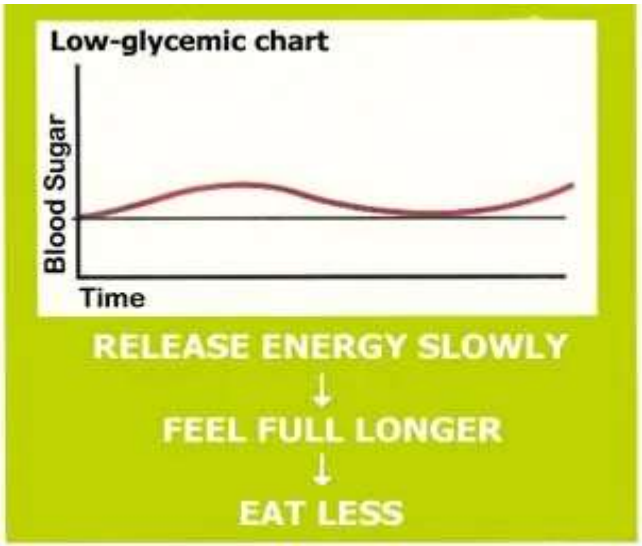
Benefits of low GI



Physiological benefits	Implications for Health
Improved metabolic modulation	Diabetes mellitus
Improved glucose tolerance	Cardiovascular disease
Prevention of hypoglycemia and hyperglycemia	Glycogen storage disease
Improved postprandial glycemic and insulinemic response	Dyslipidemia
Reduced blood lipid level	Cancer
Reduced cariogenic potential	Inflammation
Reduced glycosylation of body protein	Athletic performance
Prolonged satiety	Cognitive function
Prolonged physical performance during endurance exercise	Weight management
Delayed aging	Dental care

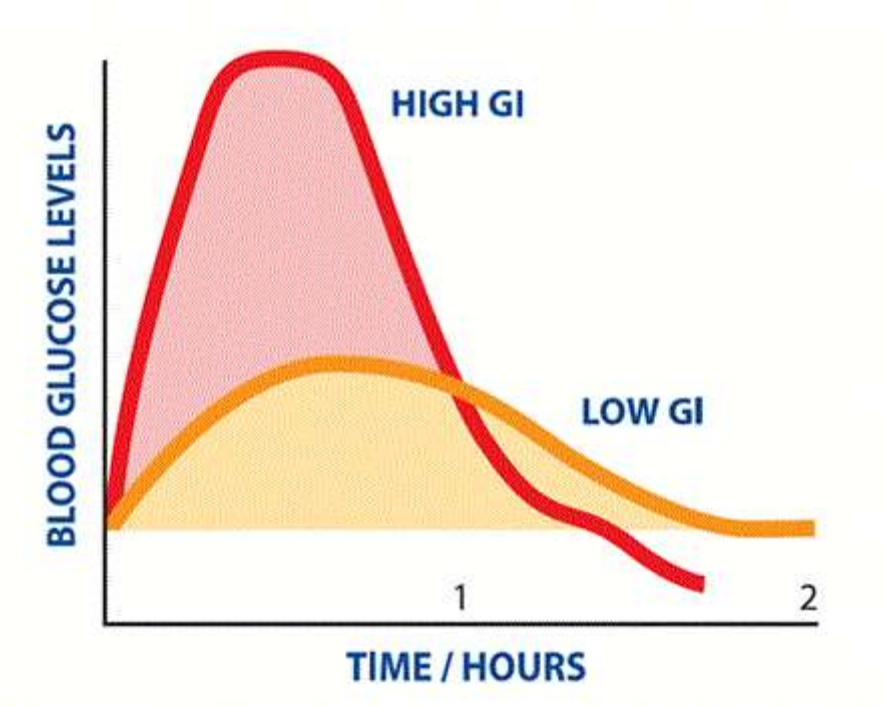
High GI vs Low GI





Sugar cravings	↓	Sugar cravings
Unable to mobilize fat	+	*Mobilizes fat*
↑ Inflammation, pain	↓	Inflammation, pain
Lack of post-meal satiety	+	Feel full after eating
Fatigue	+	Improve fatigue
Obesity	↓	Lose total body fat
Diabetes	↓	Blood sugar
Heart Disease	↓	Cardiac &stroke risk
Hypertension	↓	Blood pressure
Low energy, “crashes”	↑	Energy

What is the difference between glycemic index and glycemic load?

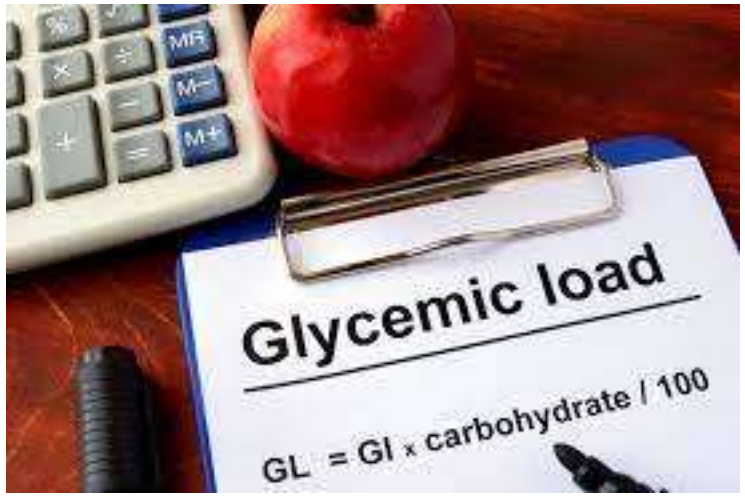


The glycemic index (GI) is a way of ‘ranking’ carbohydrate foods according to the speed at which they cause blood glucose levels to rise and fall.

Glycemic load (GL) is a measure that takes into account the amount of carbohydrate in a portion of food together with how quickly it raises blood glucose levels.

How is Glycemic load worked out?

GL = GI x carbohydrate / 100



To work with this equatio, you will need to know:

- The Glycemic Index (GI) of the food
- The amount of carbohydrate in that quantity of food

The formula for calculating glycemic load (GL)

GL= (GI x carbohydrates less fiber) / 100

The examples below are based on GL ranges of low, moderate, and high

Low GL < 10 **Moderate GL 10–14** **High GL > 15**

Example of a high-GI/low-GL food

A 120-gram serving of watermelon has a GI of 72 and the available carbohydrate is 6 grams (the amount of fiber contained in this serving does not warrant inclusion in the calculation). Therefore, the GL of watermelon is (72 x 6) / 100 = 4.3.

Example of a low-GI/high-GL food

A 180-gram serving of cooked whole wheat spaghetti has a GI of 37. The amount of available carbohydrate is 36 grams (42 grams of carbohydrate minus the approximate 6 grams of fiber content). Therefore, the GL of whole wheat spaghetti is: (37 x 36)/100 = 13

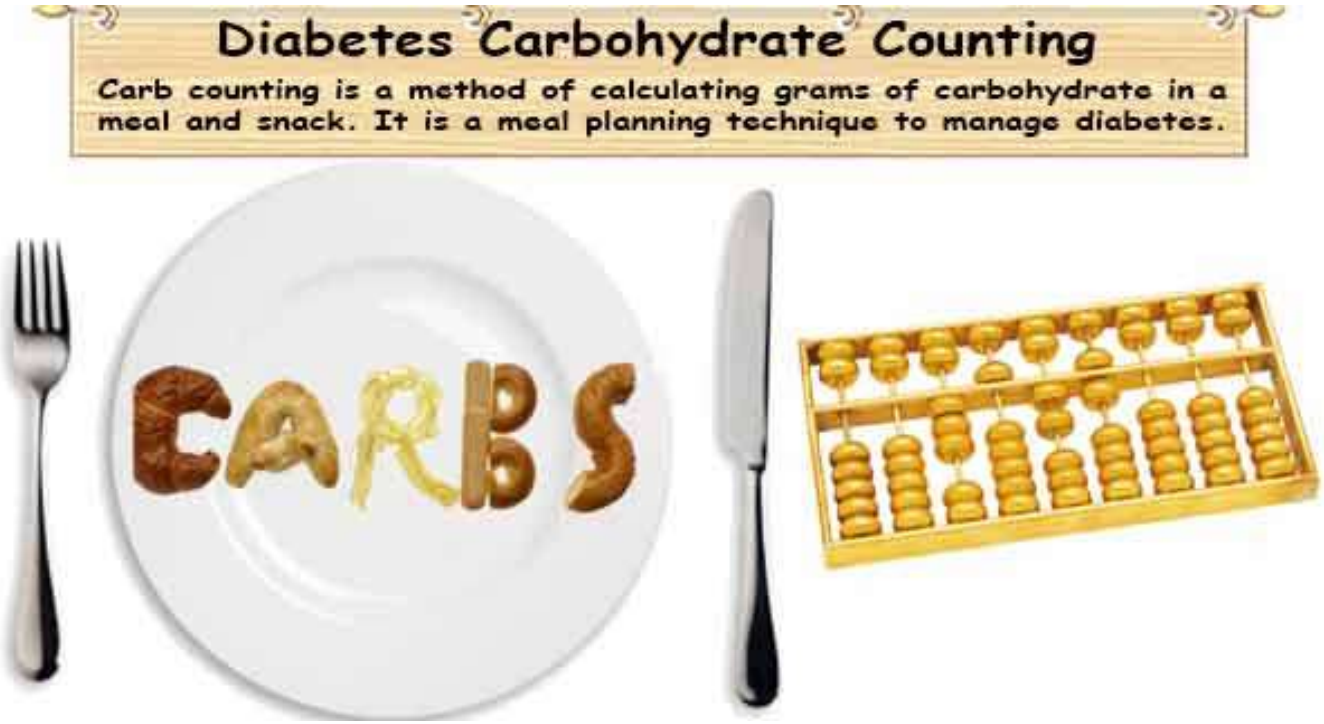
Example

Pumpkins have a glycemic index of 72 which makes them a high GI food, however, they only have 6 grams of carbohydrate per 100 gram serving.

Using the calculation above, we get a glycemic load of (6 x 72) / 100 = 4.32 which is less than 10.

Patient can eat pumpkin without having to worry about spikes in the blood sugar level.

Carbs Counting



To take the correct amount of insulin for the correct amount of carbs that patient eaten.

Insulin-to-carb ratio is 1 unit of insulin for every 10 grams of carbs.

Example: Person are having 60 grams of carbs at lunch.
Patient take 60 (amount of carbs eaten) divided by 10 (unit of insulin per 10 carbs) and will take 6 units of insulin before eat lunch.

Bread unit - what is it?

- A bread unit (or carbohydrate unit) is a conditional parameter for estimating the carbohydrate content of a particular food product.
- The term was introduced by German nutritionists to assess the diet of diabetics in the 1990s.

- One bread unit is equivalent to 10 g of simple carbohydrates in a product - or 12 g of carbohydrates including fiber.
- In terms of bread, one unit is a loaf of bread weighing 20-25 g.
- This amount of carbohydrates increases the level of glycemia by an average of 1.7 mmol/l.

Bread units table

Bread And Baking

Product gram for 1XE	Serving Size	
White bread	20 g	One piece
Rye bread	25 g	One piece
Sweet bun	20 g	Half
Salty cookies	15 g	Five pieces
Unsweetened crackers	15 g	Two pieces

Pasta and cereals

Product gram for 1XE		Serving Size
Pasta	15 g	Tablespoon
Buckwheat	15 g	Tablespoon
Kinoa	15 g	Tablespoon
Rice	15 g	Tablespoon
Millet	15 g	Tablespoon
Oatmeal	15 g	Tablespoon

Fruits

Product gram for 1XE		Serving Size
Banana	70 g	Half
Grapes	70 g	12 pieces
Pear	90 g	One middle
Melon	100 g	One piece
Grapefruit	170 g	Half large
Watermelon	270 g	One piece

Beverages

Product Volume for 1XE		Serving Size
Milk	200 ml	One glass
Kefir	200 ml	One glass
Coca Cola	100 ml	Half a glass
Fruit juice	100 ml	Half a glass
Morse	100 ml	Half a glass

How can we find out the amount of XE in the product?

For purchased products (pretzels, biscuits, other products) XE will be calculated according to the amount of carbohydrates indicated on the label.

Exemple:

100 g of pretzels contain 62 g of carbohydrates.

We will divide 62 by 10 and find out how many XE are in 100 g of pretzels, respectively 6.2 XE.

Informații nutriționale/ Nutritional Facts/ Средна хранителна информация	
	per 100g
Valoare energetică / Energy / Енергийна стойност	1928 kJ/ 460 kcal
Grăsimi / Fat / Мазнини	18 g
din care acizi grași saturați / of which saturates / от които наситени	2,3 g
Glucide / Carbohydrates / Въглехидрати	62 g
din care zaharuri / of which sugars / от които захари	1,5 g
Fibre / Fibers / Фибри	5,1 g
Proteine / Protein / Протеини	10 g
Sare / Salt / Сол	2,2 g

Cantitate netă/ Net weight/ Нето тегло:

100g e

How many XE contains 1 and 2?

01

02

Required quantity of bread units

Patients with normal weight	
Hard physical work	25-30
Moderate physical work	20-22
Easy physical work	16-18
Sedentary	12-15
Overweight or obese patients	
Hard physical work	20-25
Moderate physical work	15-17
Easy physical work	11-16
Sedentary	10
Patients with weight loss	25-30

Effort	Daily Calories
Rest	20 kcal/kg ideal weight
Sedentary	25 kcal/kg ideal weight
Moderate physical work	30-35 kcal/kg ideal weight
Hard physical work	40-45 kcal/kg ideal weight

Ideal body weight assessment

Broca Index (BI)	Standard Weight (kg) = Ht (cm) - 100 For females, the standard weight is 10% less
Lorentz-formula	Men: w = (height [cm]− 100) − ((height − 150)/4) Women: w = (height − 100) − ((height − 150)/2)
The Monnerot-Dumaine's formula	Ideal weight = (height - 100 + (4 * CW)) / 2 circumference of the wrist (CW)

https://www.omnicalculator.com/health/ideal-weight

Appreciate your ideal weight and calorie intake!

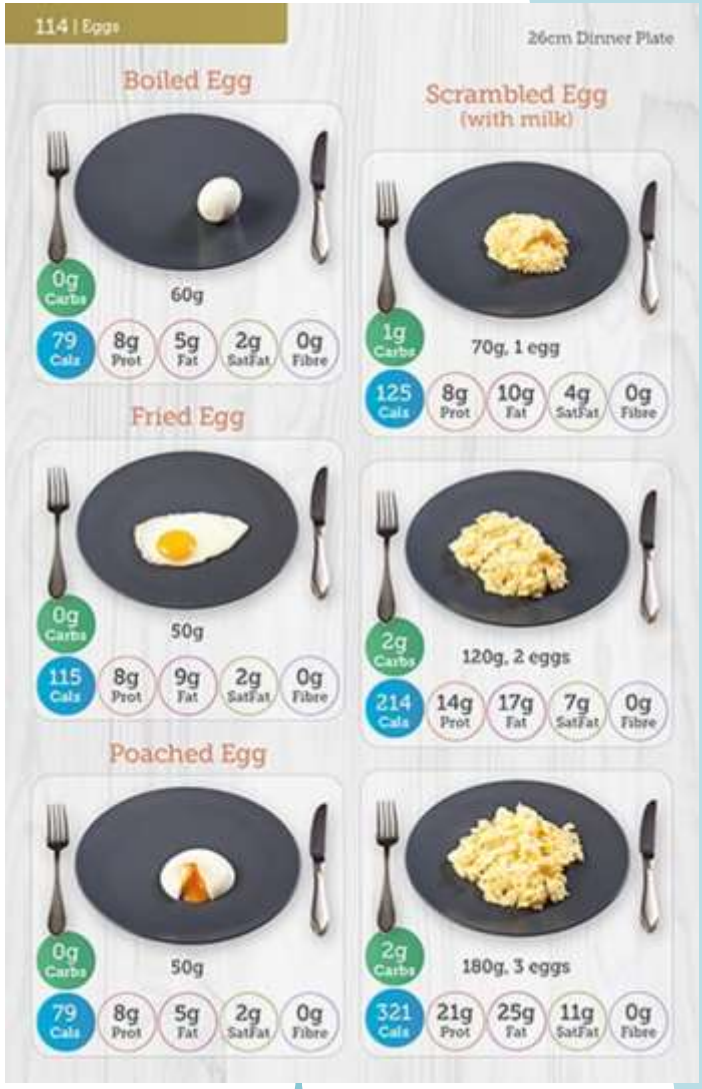
How to appreciate bread units for the food portion?

Initially, the total amount of XE will be calculated according to the ***daily caloric needs***

Example:

At a caloric requirement of 2000 kcal, carbohydrates will return 50%, 1000 kcal. Knowing that 1 g of carbohydrates will generate 4 kcal, their amount will be 250 g, which is 25 XE / day.

Applications



Physical activity - recomendation

- **Children and adolescents** - **60 min/day** or more of moderate- or vigorous-intensity aerobic activity, with vigorous muscle strengthening and bone-strengthening activities at least 3 days/ week.
- **Most adults** - **150 min/week** or more of moderate to vigorous-intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. Shorter durations (minimum 75 min/week) of vigorous intensity or interval training may be sufficient for younger and more physically fit individuals.
- **Adults** - 2–3 sessions/week of resistance exercise on nonconsecutive days.

Prolonged sitting should be interrupted every 30 min for blood glucose benefits.

Pre-exercise evaluation

- Providers should assess patients for conditions that might contraindicate certain types of exercise or predispose to injury.

- **Perform a careful history:**
  - assess cardiovascular risk factors,
  - uncontrolled hypertension,
  - untreated proliferative retinopathy,
  - autonomic neuropathy,
  - peripheral neuropathy, and a history of foot ulcers or Charcot foot.

- Certainly, high risk patients should be encouraged to start with short periods of low-intensity exercise and slowly increase the intensity and duration as tolerated.

Pre-exercise evaluation

Hypoglycemia

- insulin and/or insulin secretagogues,
- if the medication dose or carbohydrate consumption is not altered.
- need to ingest some added carbohydrate if pre-exercise glucose levels are < 90 mg/dL (5.0 mmol/L),
- **hypoglycemia after exercise** may occur and last for several hours due to increased insulin sensitivity.
- Patients need to be educated to check blood glucose levels before and after periods of exercise

Retinopathy

- Proliferative or severe nonproliferative diabetic retinopathy is present, then vigorous-intensity aerobic or resistance exercise may be contraindicated because of the risk of triggering vitreous hemorrhage or retinal detachment.
- Consultation with an ophthalmologist prior to engaging in an intense exercise regimen may be appropriate.

Diabetic Kidney Disease

- Physical activity can acutely increase urinary albumin excretion.

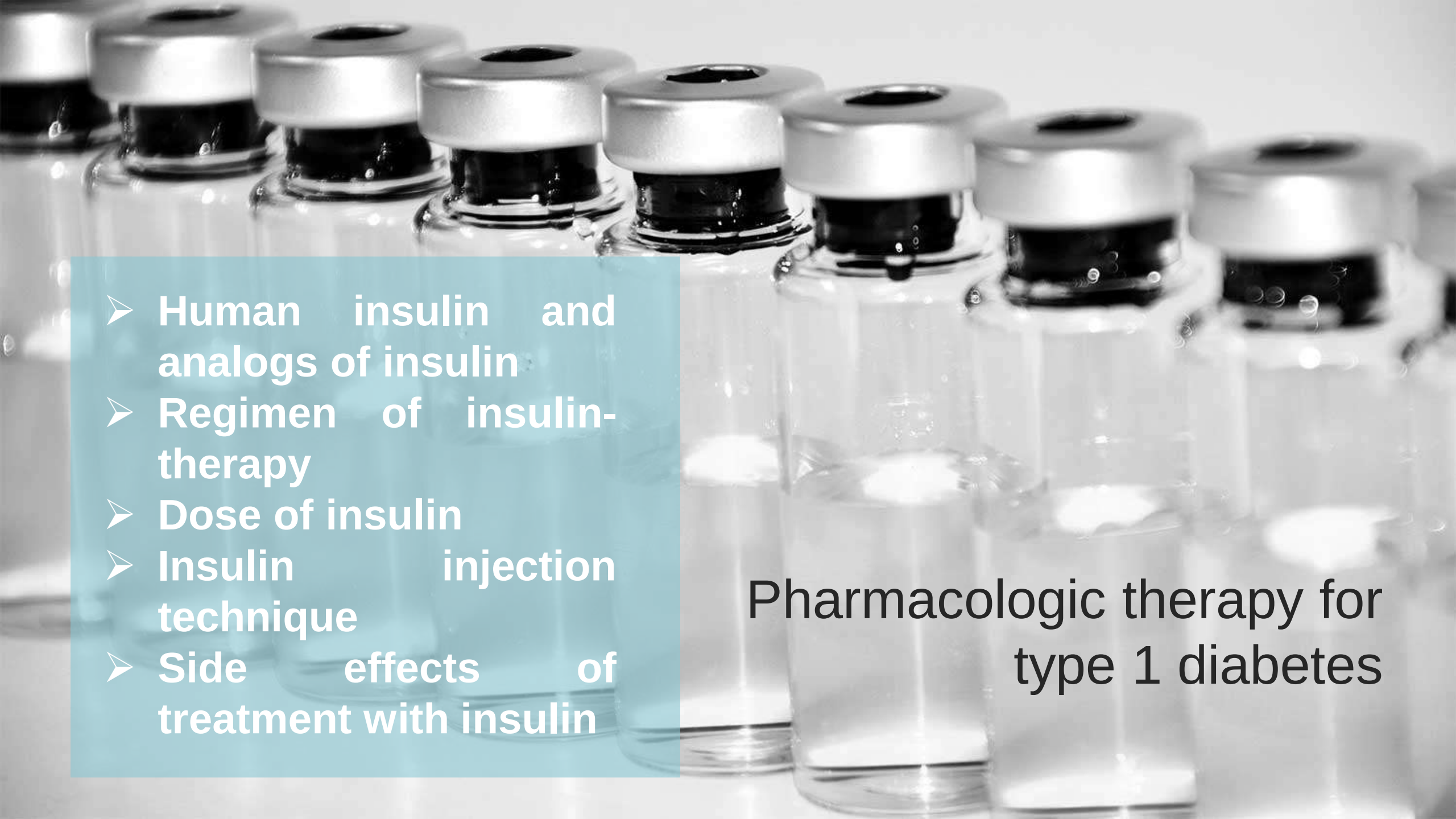
Pre-exercise evaluation (2)

Peripheral Neuropathy

- Decreased pain sensation and a higher pain threshold - increased risk of skin breakdown, infection, and Charcot joint destruction with some forms of exercise.
- assessment should be done to ensure that neuropathy does not alter kinesthetic or proprioceptive sensation during physical activity, particularly in those with more severe neuropathy.
- moderate-intensity walking may not lead to an increased risk of foot ulcers or reulceration in those with peripheral neuropathy who use proper footwear.
- 150min/week of moderate exercise was reported to improve outcomes in patients with prediabetic neuropathy
- All individuals with peripheral neuropathy should wear proper footwear and examine their feet daily to detect lesions early.

Autonomic Neuropathy

- can increase the risk of exercise-induced injury or adverse events:
  - decreased cardiac responsiveness to exercise,
  - postural hypotension,
  - impaired thermoregulation,
  - impaired night vision due to impaired papillary reaction,
  - and greater susceptibility to hypoglycemia.
- Cardiovascular autonomic neuropathy is also an independent risk factor for cardiovascular death and silent myocardial ischemia .
- Therefore, individuals with diabetic autonomic neuropathy should undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed.



Pharmacologic therapy for type 1 diabetes

- **Human insulin and analogs of insulin**
- **Regimen of insulin-therapy**
- **Dose of insulin**
- **Insulin injection technique**
- **Side effects of treatment with insulin**

Pharmacologic therapy for type 1 diabetes

- **Type 1 diabetes** - is absent or near-absent b-cell function**, insulin treatment is essential** for individuals with type 1 diabetes.

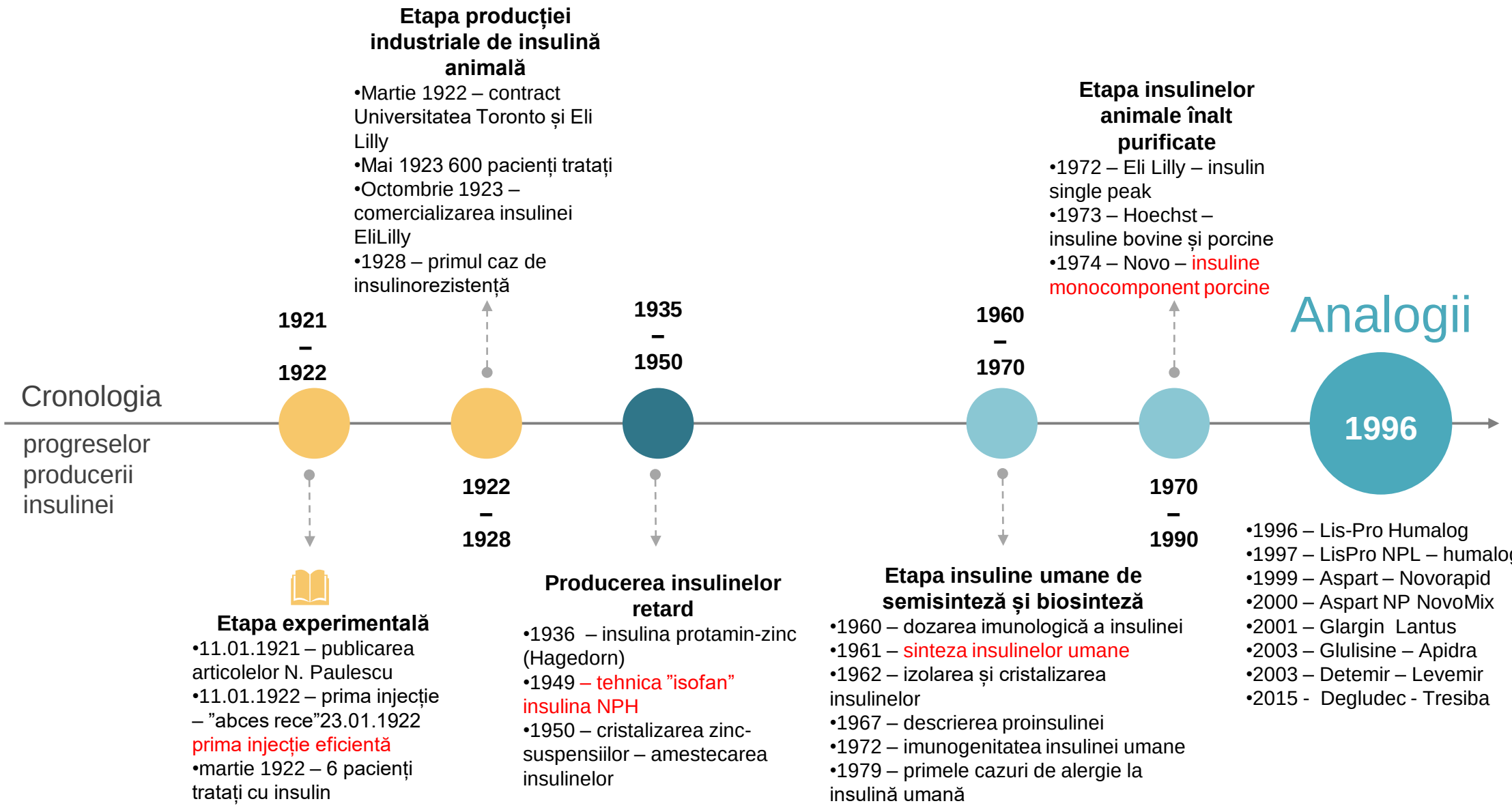
- **Insulinopenia can contribute:**
  - to hyperglycemia,
  - hypertriglyceridemia and
  - ketoacidosis.

- Over the past three decades, evidence has accumulated supporting more **intensive insulin replacement**, **using multiple daily injections** of insulin or **continuous subcutaneous administration through an insulin pump**, as providing the best combination of effectiveness and safety for people with type 1 diabetes.

Discovery of insulin1922

1921, Nicolae Paulescu, the discoverer of *pancreine* - later called insulin, published four papers at the Romanian Section of the Society of Biology in Paris

In February 1922, F. Banting and J. MacLeod , published their paper on the successful use of a different, alcohol based pancreatic extract for normalizing blood sugar levels in a human patient, a young boy.


Cronologia
progreselor producerii insulinei
1921 – 1922
1922 – 1928
1935 – 1950
1960 – 1970
1970 – 1990
1996
Analogii
Etapa producției industriale de insulină animală
•Martie 1922 – contract Universitatea Toronto și Eli Lilly
•Mai 1923 600 pacienți tratați
•Octombrie 1923 – comercializarea insulinei EliLilly
•1928 – primul caz de insulinorezistență
Etapa insulinelor animale înalt purificate
•1972 – Eli Lilly – insulin single peak
•1973 – Hoechst – insuline bovine și porcine
•1974 – Novo – insuline monocomponent porcine
Etapa experimentală
•11.01.1921 – publicarea articolelor N. Paulescu
•11.01.1922 – prima injecție – ”abces rece”23.01.1922 prima injecție eficientă
•martie 1922 – 6 pacienți tratați cu insulin
Producerea insulinelor retard
•1936 – insulina protamin-zinc (Hagedorn)
•1949 – tehnica ”isofan” insulina NPH
•1950 – cristalizarea zinc-suspensiilor – amestecarea insulinelor
Etapa insuline umane de semisinteză și biosinteză
•1960 – dozarea imunologică a insulinei
•1961 – sinteza insulinelor umane
•1962 – izolarea și cristalizarea insulinelor
•1967 – descrierea proinsulinei
•1972 – imunogenitatea insulinei umane
•1979 – primele cazuri de alergie la insulină umană
•1996 – Lis-Pro Humalog
•1997 – LisPro NPL – humalog Mix
•1999 – Aspart – Novorapid
•2000 – Aspart NP NovoMix
•2001 – Glargin Lantus
•2003 – Glulisine – Apidra
•2003 – Detemir – Levemir
•2015 - Degludec - Tresiba

Death

fear

longevity

Leonard Thompson

A 3-year-old boy before, and several weeks after becoming one of the first patients to receive insulin in 1922.

Normal Physiology of Insulin Secretion

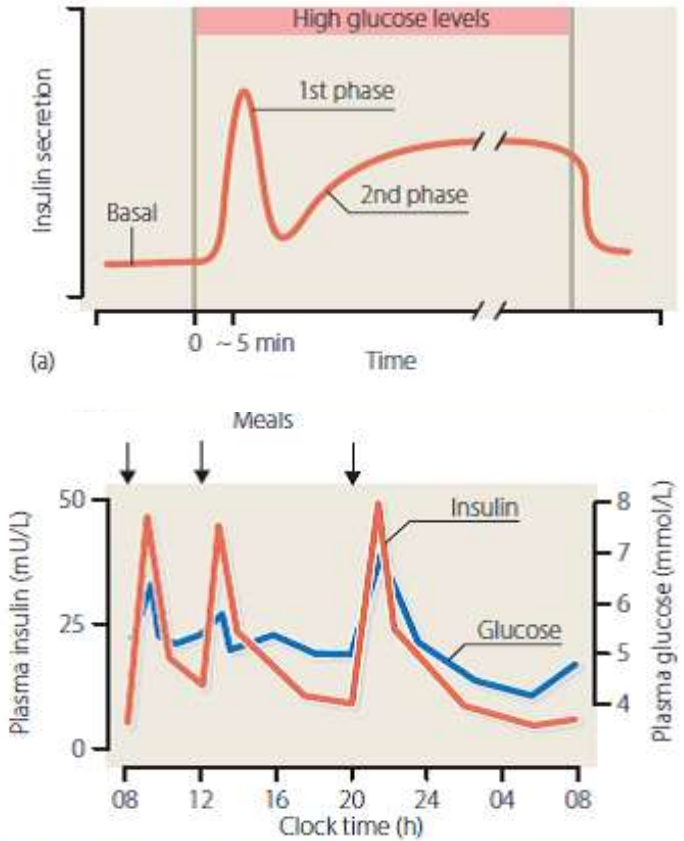


Figure 5.19 Profiles of plasma glucose and insulin concentrations in individuals without diabetes.

The amount of insulin secreted by the pancreas in 24 hours is about 48U.

Half is basal insulinemia and the other half is prandial insulinemia.

Glucose levels below 5 mmol/L (90 mg/dL) do not affect insulin release; half-maximal stimulation occurs at about 8 mmol/L (144 mg/dL).

Classification of insulin types

Type of Insulin	Appearance	Action times after injection (in hours)
Rapid-acting ▪ Lispro (Humalog) ▪ Glulisine (Apidra) ▪ Aspart (NovoRapid)	Clear 	 **Onset:** 10 to 15 mins **Peak:** 1 to 2 hours **Duration:** 3 to 5 hours
Intermediate-acting ▪ NPH (Humulin-N, Novolin-NPH)	Cloudy 	 **Onset:** 1 to 3 hours **Peak:** 5 to 8 hours **Duration:** up to 18 hours
Slow or long-acting ▪ Glargine (Lantus) ▪ Detemir (Levemir)	Clear 	 **Onset:** 90 mins **Peak:** None **Duration:** up to 24 hours

Different insulin regimens

- Once-daily insulin regimen
- Twice daily insulin regimen
- Basal-bolus regimen / multiple daily injection therapy
- Continuous subcutaneous insulin infusion / Insulin pump therapy

Physiologic Multiple Injection Regimens: The Basal-Bolus Insulin Concept

- Basal insulin
  - Controls glucose production between meals and overnight
  - Near-constant levels
  - Usually ~50% of daily needs

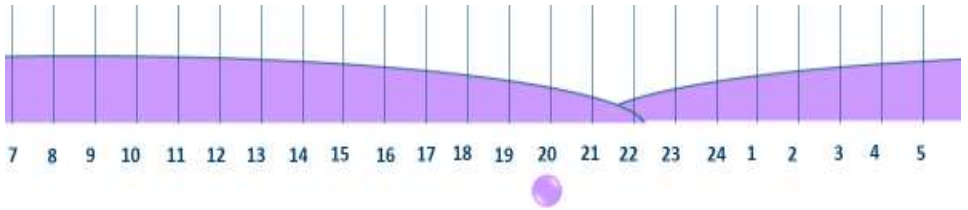
- Bolus insulin (mealtime or prandial)
  - Limits hyperglycemia after meals
  - Immediate rise and sharp peak at 1 hour post-meal
  - 10% to 20% of total daily insulin requirement at each meal

- For ideal insulin replacement therapy, each component should come from a different insulin with a specific profile or via an insulin pump (with 1 insulin)

Basal insulin

Onset – 2-4 h,
Peak – 6-10 h
Duration – 14-18 h

Onset – 2-4 h
duration – 20-24 h



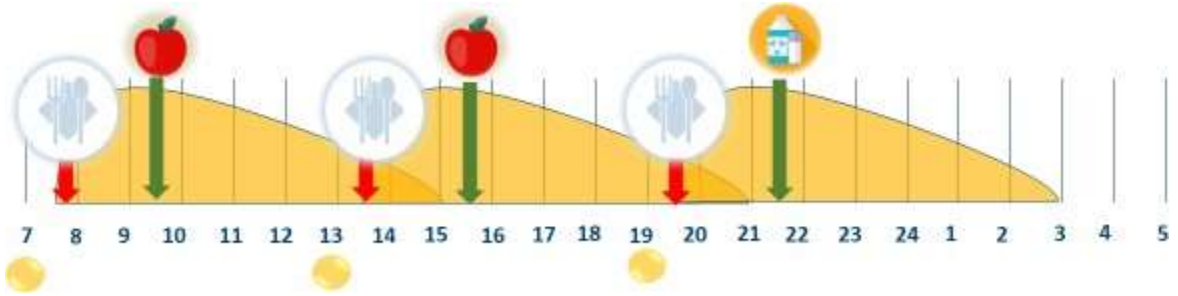
- **2 BID**
- **morning and evening**
- **Risk of hypoglycemia**

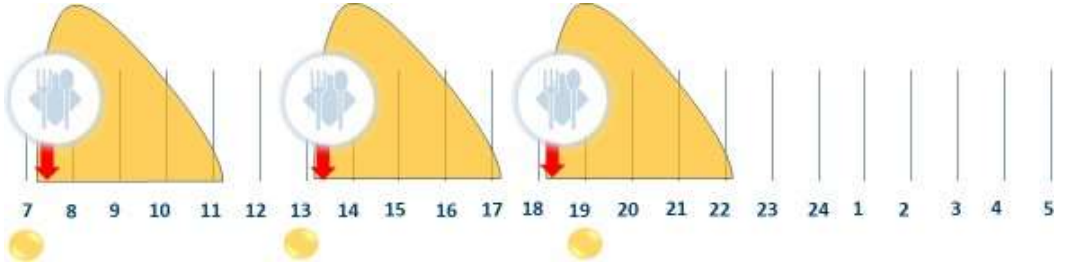
- **1 time - evening**
- **Low risk for hypoglycemia**

Prandial insulin

Onset – 30 min,
Peak – 2-3 h
Duration – 6-8 h

Onset – 15 min,
Peak – 0,5-1,0 h
Duration – 4-5 h



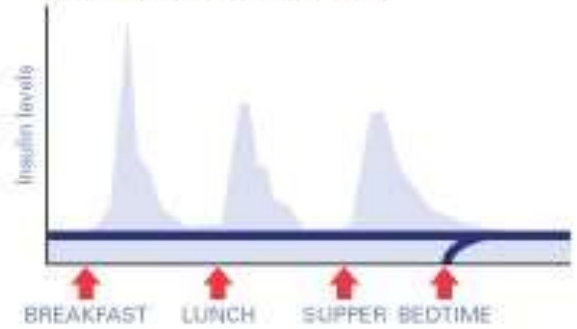


- **Meal after** 20-30’
- Snack in 2-3 h
- Risk of hypoglycemia

- **Meal after** 10-15’
- Low risk of hypoglycemia

BASAL (Lantus®)

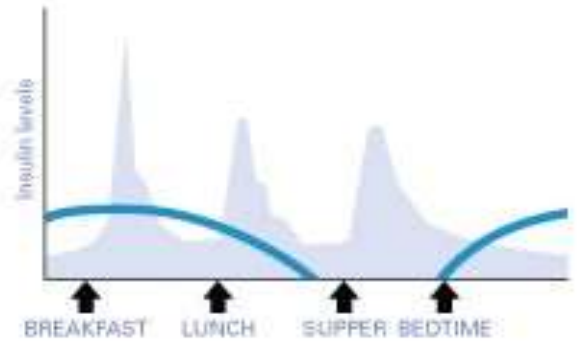
LONG-ACTING INSULIN



Onset
2-4 hours

Duration
24 hours

INTERMEDIATE-ACTING INSULIN (NPH)



Onset
0.5-1 hours

Duration
10-16 hours

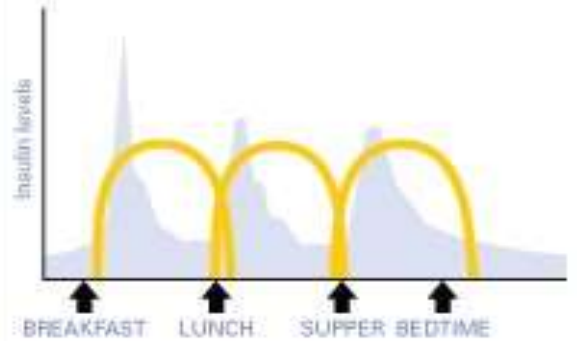
PRANDIAL

RAPID-ACTING INSULIN

Onset
~5 minutes

Duration
4-5 hours

SHORT-ACTING INSULIN (RHI)

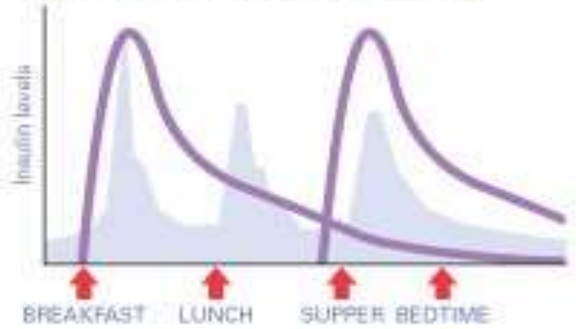


Onset
30 minutes

Duration
Up to 6 hours

PREMIX

PREMIXED INSULIN (ANALOG)



Onset
5-15 minutes

Duration
10-16 hours

PREMIXED INSULIN (HUMAN)

Onset
5-15 minutes

Duration
10-16 hours

Overview

- **Rapid-acting and long-acting insulin analogs** - have distinct pharmacokinetics compared with recombinant human insulins:
  - **basal insulin analogs**
    - have longer duration of action with flatter,
    - more constant plasma concentrations and activity profiles than NPH insulin;
  - **rapid-acting analogs (RAA)**
    - have a quicker onset and peak and
    - shorter duration of action than regular human insulin.

- **In people with type 1 diabetes**, **treatment with analog insulins** is associated with
  - less hypoglycemia
  - less weight gain
  - lower A1C compared with human insulins

Daily insulin requirments

Total daily insulin requirements can be estimated based on weight, with typical doses ranging from **0.4 to 1.0 units/kg/day**.

- **0.5 units/kg/day** as a typical starting dose in patients with type 1 diabetes who are metabolically stable,
  - 50% as **prandial insulin** given to control blood glucose after meals +
  - 50% as basal insulin to control glycemia in the periods between meal absorption

- **Higher amounts** are required during puberty, pregnancy, and medical illness.

Total daily insulin requirements

- The onset of diabetes - 0.5-0.6 IU / kgc / day under glycemic control;
- At discharge the need decreases by 10%;
- Prepuberty 0.6 - 1.0 IU / kgc / day;
- Puberty, intercurrences are administered 1.5 - 1.8 IU / kgc / day;
- "Honeymoon" <0.5 IU / kgc / day;
- Known diabetes 0.7 - 0.8 IU / kgc / day;
- Decompensation 1.0 - 1.5 IU / kgc / day.

Recommendations for prandial insulin dose (bolus)

- **Prandial insulin dose** administration should therefore be **individualized.**

- Physiologic insulin secretion varies with
  - glycemia,
  - meal size, and
  - tissue demands for glucose.

- **Education of patients** on how to adjust prandial insulin to account for carbohydrate intake, premeal glucose levels, and anticipated activity can be effective and should be offered to most patients.

Calculating Basal Insulin Dose

Example #1: Carbohydrate coverage at a meal

First, you have to calculate the carbo… using this formula:

CHO insulin dose =
Total grams of CHO in the meal
÷ grams of CHO disposed by 1 un
(the grams of CHO disposed of by 1 u… number or denominator of the Insulin…

For Example #1, assume:

- You are going to eat 60 grams of c…
- Your Insulin: CHO ratio is 1:10

To get the CHO insulin dose, plug the…

CHO insulin dose =
Total grams of CHO in the meal
÷ grams of CHO disposed by 1 un…

You will need 6 units of rapid acting insulin to cover the carbohydrate.

Example #2: High blood sugar correction dose

Next, you have to calculate the high blood sugar correction dose.

High blood sugar correction dose =

Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

†Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Correction dose =
Difference between actual and target blood glucose (100mg/dl)
÷ correction factor (50) = 2 units of rapid acting insulin

So, you will need an additional 2 units of rapid acting insulin to "correct" the blood sugar down to a target of 120 mg/dl.

Example #3: Total mealtime dose

…insulin dose, add the CHO insulin …d sugar correction insulin dose:

…n Dose

…se is 6 units of rapid acting insulin. …n dose is 2 units of rapid acting

…to calculate your total meal dose.

…e (6 units)
(2 units)

… 8 units of rapid acting insulin.

Total Daily Insulin Requirement

The general calculation for the body's daily insulin requirement is:

Total Daily Insulin Requirement(in units of insulin) = Weight in Pounds ÷ 4

Alternatively, if you measure your body weight in kilograms:

Total Daily Insulin Requirement (in units of insulin) = 0.55 X Total Weight in Kilograms

Example 1:

If you are measuring your body weight in pounds:

Assume you weigh 160 lbs:

TOTAL DAILY INSULIN DOSE = 160 lb ÷ 4 = 40 units of insulin/day

Example 2:

If you are measuring your body weight in kilograms:

Assume your weight is 70Kg:

TOTAL DAILY INSULIN DOSE = 0.55 x 70 Kg = 38.5 units of insulin/day

Basal and Bolus Insulin Doses

Basal/background insulin dose:

Basal/background Insulin Dose = 40-50% of Total Daily Insulin Dose

Example

Assume you weigh 160 pounds
Your total daily insulin dose (TDI) = 160 lbs ÷ 4 = 40 units.

Basal/background insulin dose = 50% of TDI (40 units) = 20 units
of either long acting insulin,(such as glargine or detemir) or rapid acting insulin.

Use pradial doses (PI) of 0.03-0.15 U / kg, and BI 0.2-0.25 U / kg.
The PI and BI ratio must be 50% / 50% or 60% / 40%.

Calculate the total insulin dose for the PI and BI ratio 60% / 40%

The carbohydate coverage ratio:

500 ÷ Total Daily Insulin Dose
= 1 unit insulin covers so many grams of carbohydrate

This can be calculated using the Rule of “500”: Carbohydrate Bolus Calculation

Example:

Assume your total daily insulin dose (TDI)
= 160 lbs ÷ 4 = 40 units

Carbohydrate coverage ratio
= 500 ÷ TDI (40 units)
= 1unit insulin/ 12 g CHO

This example above assumes that you have a constant response to insulin throughout the day. In reality, individual insulin sensitivity varies. Someone who is resistant in the morning, but sensitive at mid-day, will need to adjust the insulin-to-carbohydrate ratio at different meal times.

The high blood sugar correction factor:

Correction Factor = 1800 ÷Total Daily Insulin Dose = 1 unit of insulin will reduce the blood sugar so many mg/dl

This can be calculated using the Rule of “1800”.

Example:

Assume your total daily insulin dose(TDI) = 160 lbs ÷ 4 = 40 units
In this example:

Correction Factor
= 1800 ÷ TDI(40 units)
= 1 unit insulin will drop reduce the blood sugar level by 45 mg/dl

While the calculation is 1 unit will drop the blood sugar 45 mg/dl, to make it easier most people will round up or round down the number so the suggested correction factor may be 1 unit of rapid acting insulin will drop the blood sugar 40-50 mg/dl.

Insulin injection devices

- **Plastic syringes** - 12mm, 8mm, 6mm needles - minimal discomfort, can be used several times;

- **Pens** - devices for administering insulin in the form of a pen in which special cartridges are inserted, no need to aspirate insulin (needles 12-8-6-4mm);

- Insulin pumps - injection of insulin, only short-acting or fast-acting insulin analogues is continuous

The benefits of insulin pump therapy

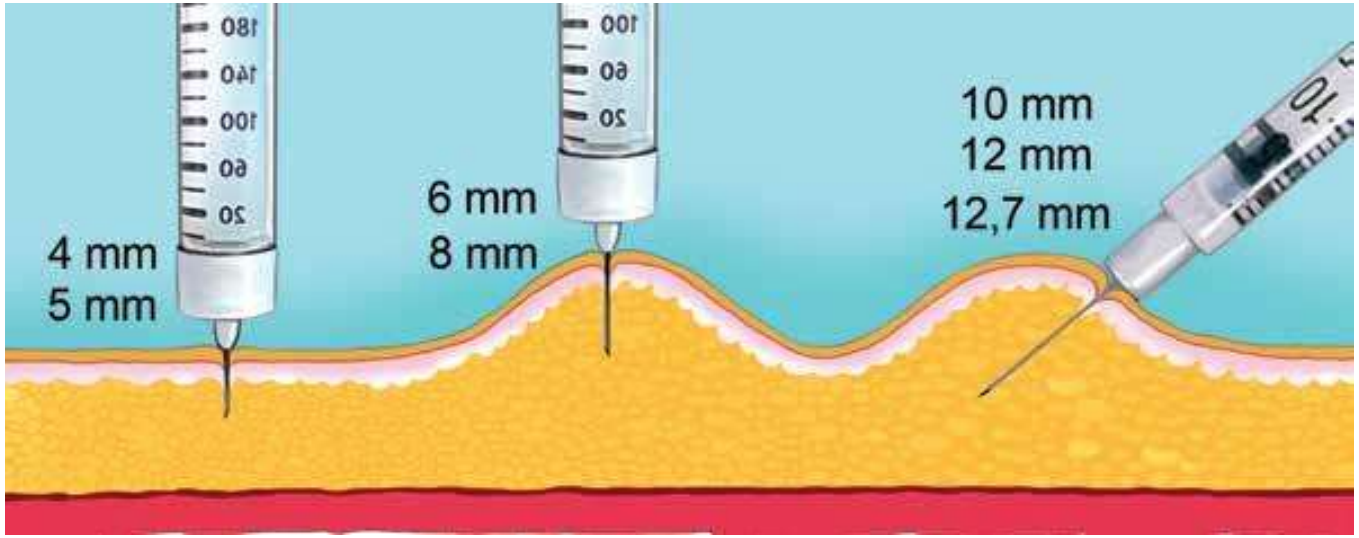
- Use only fast-acting insulin and analogues.
- The action of these insulins is more predictable than that of intermediate insulins which may show an uptake variation of up to 52%.
- Improves metabolic control, thus avoiding complications.
- In general, insulin requirements are lower than in multiple injection therapy.

Insulin injection technique

- **Correct insulin injection technique** is important to **optimize glucose control** and insulin use safety.

- **Insulin injection technique includes**
  - injecting into appropriate body areas,
  - injection site rotation,
  - appropriate care of injection sites to avoid infection or other complications, and avoidance of intramuscular (IM) insulin delivery.

Exogenous-delivered insulin should be injected into subcutaneous tissue, not intramuscularly.

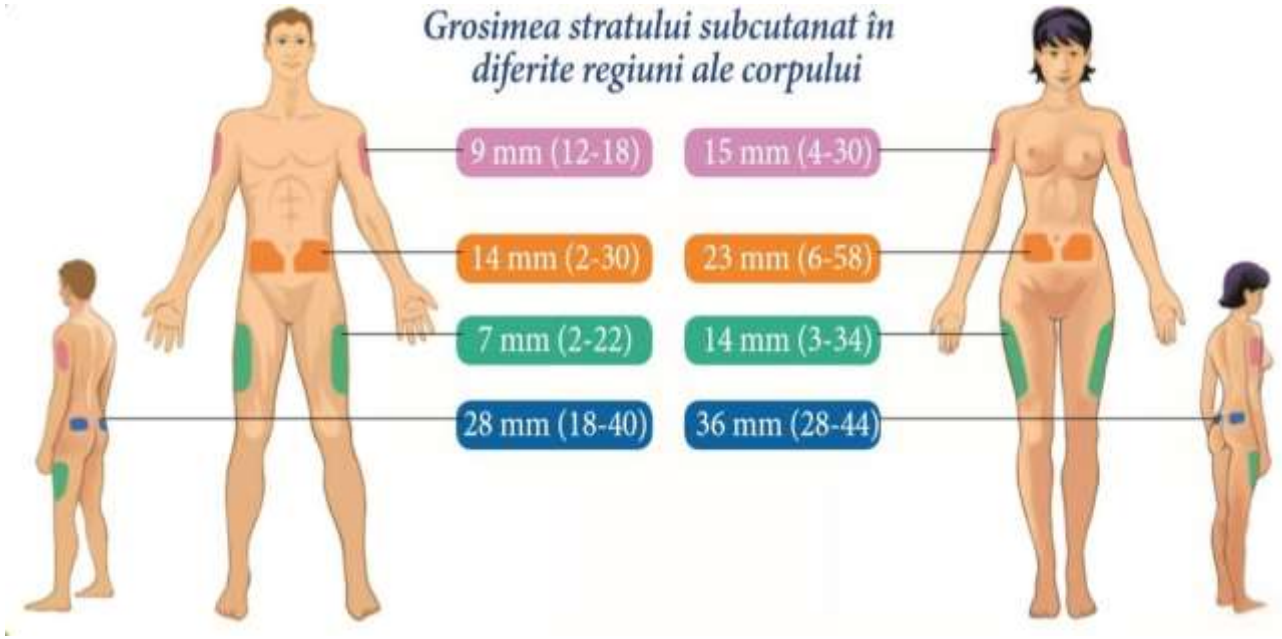


Insulin injection technique

- Recommended sites for insulin injection include the abdomen, thigh, buttock, and upper arm.

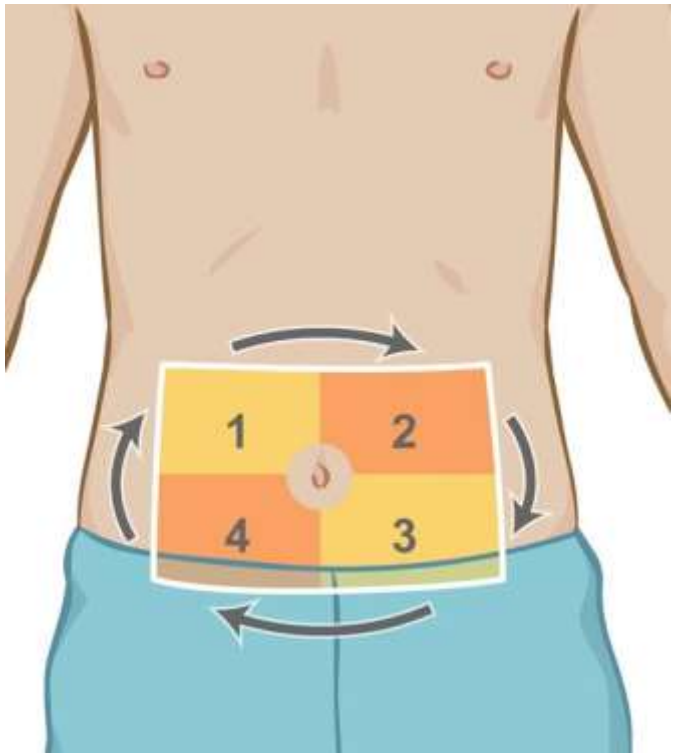
- Risk for IM insulin delivery is increased in younger, leaner patients when injecting into the limbs rather than truncal sites (abdomen and buttocks) and when using longer needles.

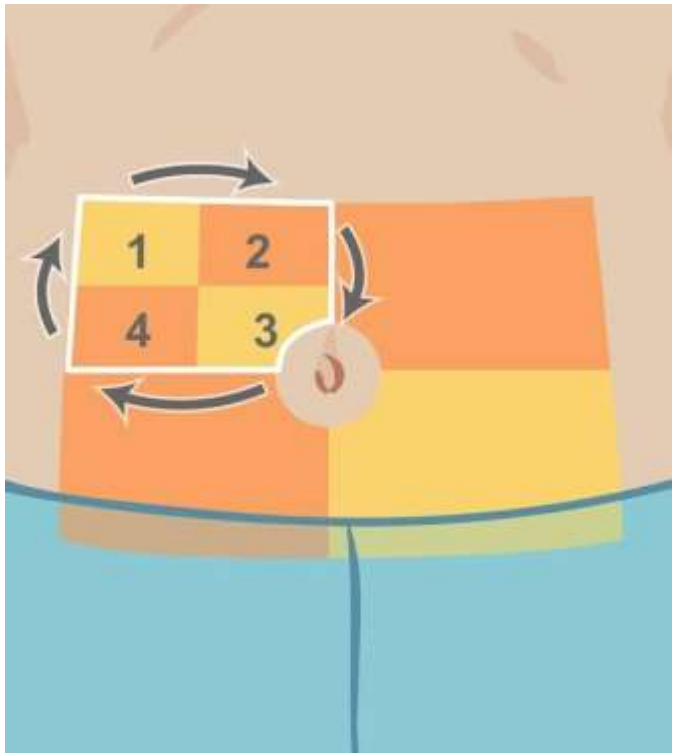
- Recent evidence supports the use of short needles (e.g., 4-mm pen needles) as effective and well tolerated when compared with longer needles, including a study performed in obese adults



Insulin injection technique

Injection site rotation is additionally necessary to avoid lipohypertrophy, an accumulation of subcutaneous fat in response to the adipogenic actions of insulin at a site of multiple injections.





??? Indication for insulin

Diabetes mellitus type 1

- Young people
- Sudden onset
- POLYURIA, POLYDIPSIA, WEIGHT LOSS
- Hyperglycaemia

Diabetes mellitus type 2

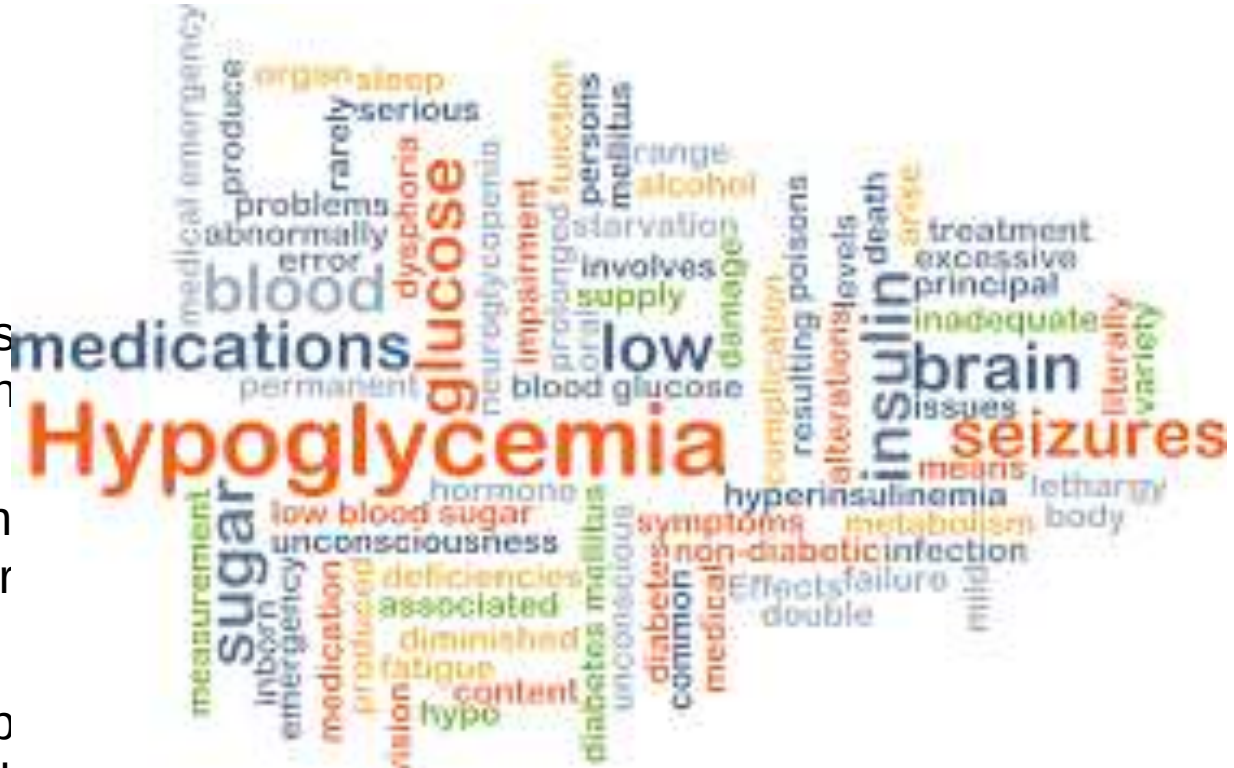
•Contraindication for atidiabetic agents
•Diabetes decompensation
•Surgery, infections
•Pregnancy

Gestational diabetes

OGTT 24-26 week
0 > 5,1 mmol/l
1 > 10 mmol/l
2 > 8,5 mmol/l

Side effects of insulin therapy

- Weight gain
- Insulin allergy
- Refractive disorders
  of the lens, it does n
- Insulin edema - tran
  in previously dehydr
- Lipodystrophies - lip
  which occur instead of insulin injection.

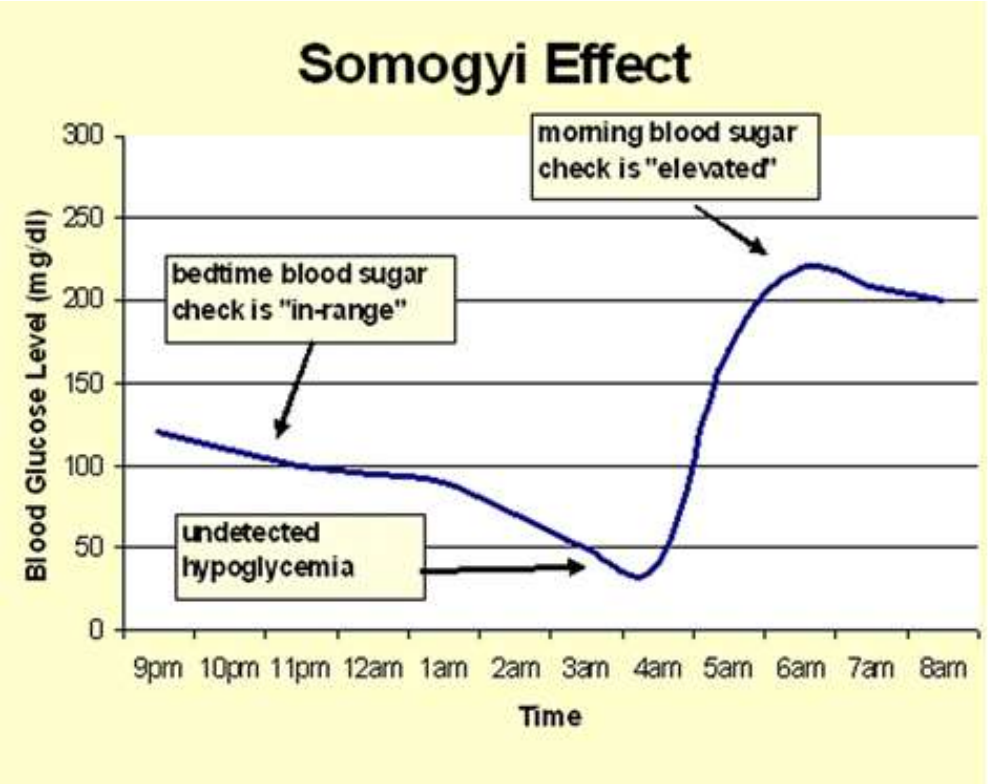


The Somogyi effect

- The Somogyi effect, also known as the "chronic Somogyi rebound," or "posthypoglycemic hyperglycemia," was a theory proposed in the 1930s by Dr. Michael Somogyi, who was an Hungarian-born professor at Washington University, St. Louis, MO, United States.

- He described the paradoxical tendency of the body to react to hypoglycemia by producing hyperglycemia.

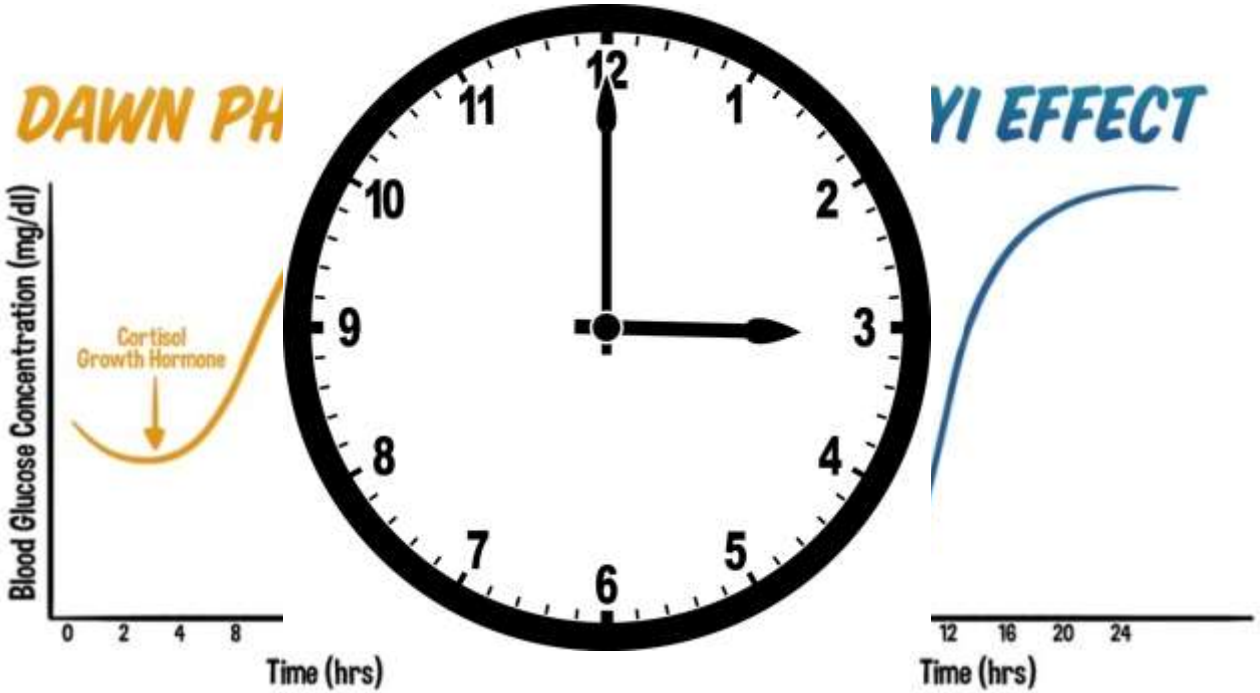
- Somogyi proposed, that when blood glucose levels drop too low during the late evening, activation of counterregulatory hormones such as adrenaline, corticosteroids, growth hormone, and glucagon may be observed, leading to activation of gluconeogenesis and resultant **hyperglycemia in the early morning**.



The dawn phenomenon

- A phenomenon known as the dawn phenomenon was introduced by Dr. Schimdt in the 1980s, stating that **morning hyperglycemia** is due to the decreased levels of endogenous insulin secreted at night.

- The dawn phenomenon is characterized by increased levels of fasting blood glucose or insulin requirements, or both, between 5 and 9 AM without preceding hypoglycemia.



Conclusion

- Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion.
- Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk.
- Patients with type 1 diabetes should be trained to match prandial insulin doses to carbohydrate intake, premeal blood glucose, and anticipated physical activity.

THANK YOU!