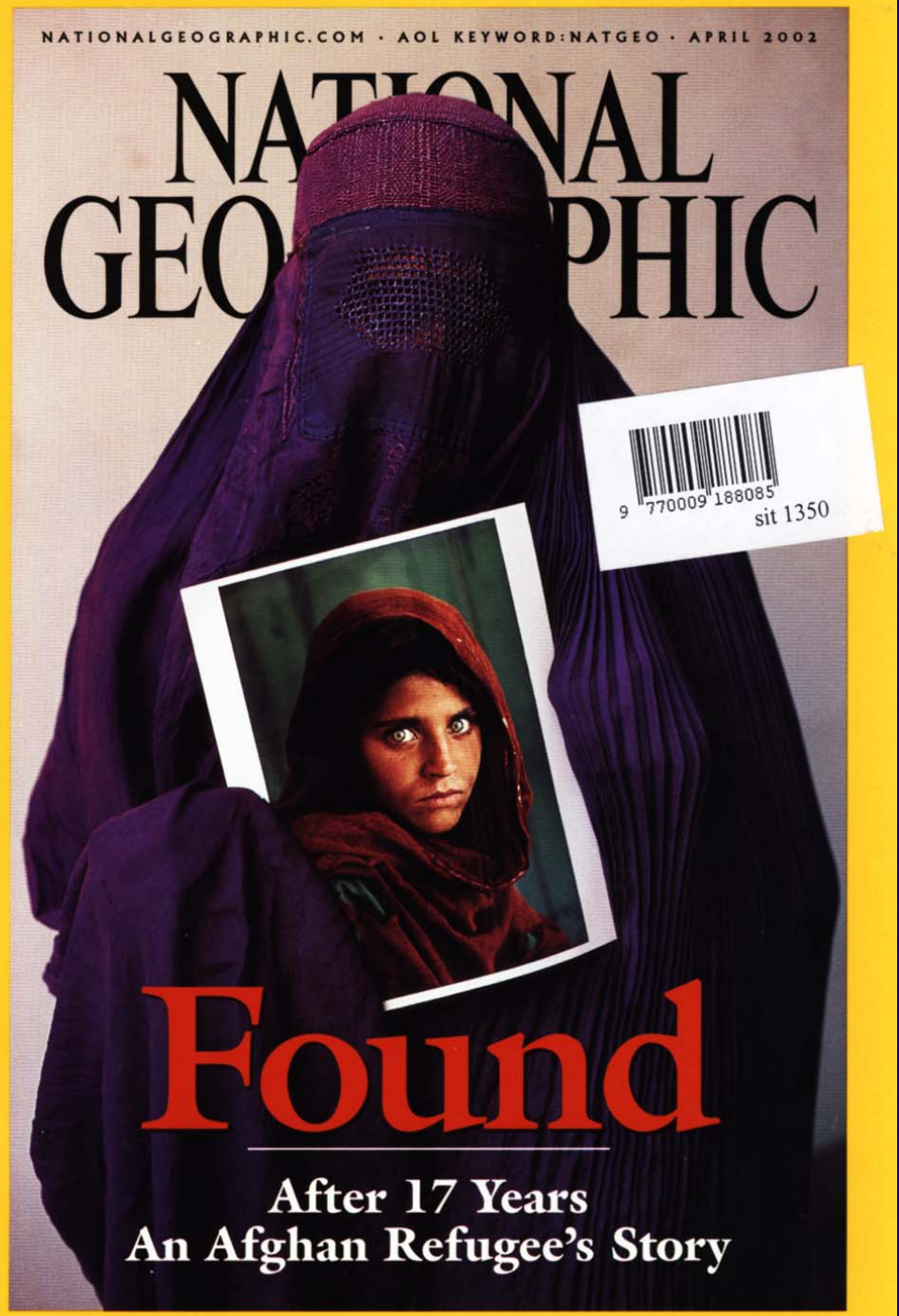
Sladkorna bolezen

Doc.dr. Andrej Janež, dr.med.

Klinika za endokrinologijo, diabetes in bolezni presnove.
Klinični center Ljubljana


NATIONALGEOGRAPHIC.COM · AOL KEYWORD:NATGEO · APRIL 2002
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9 770009 188085
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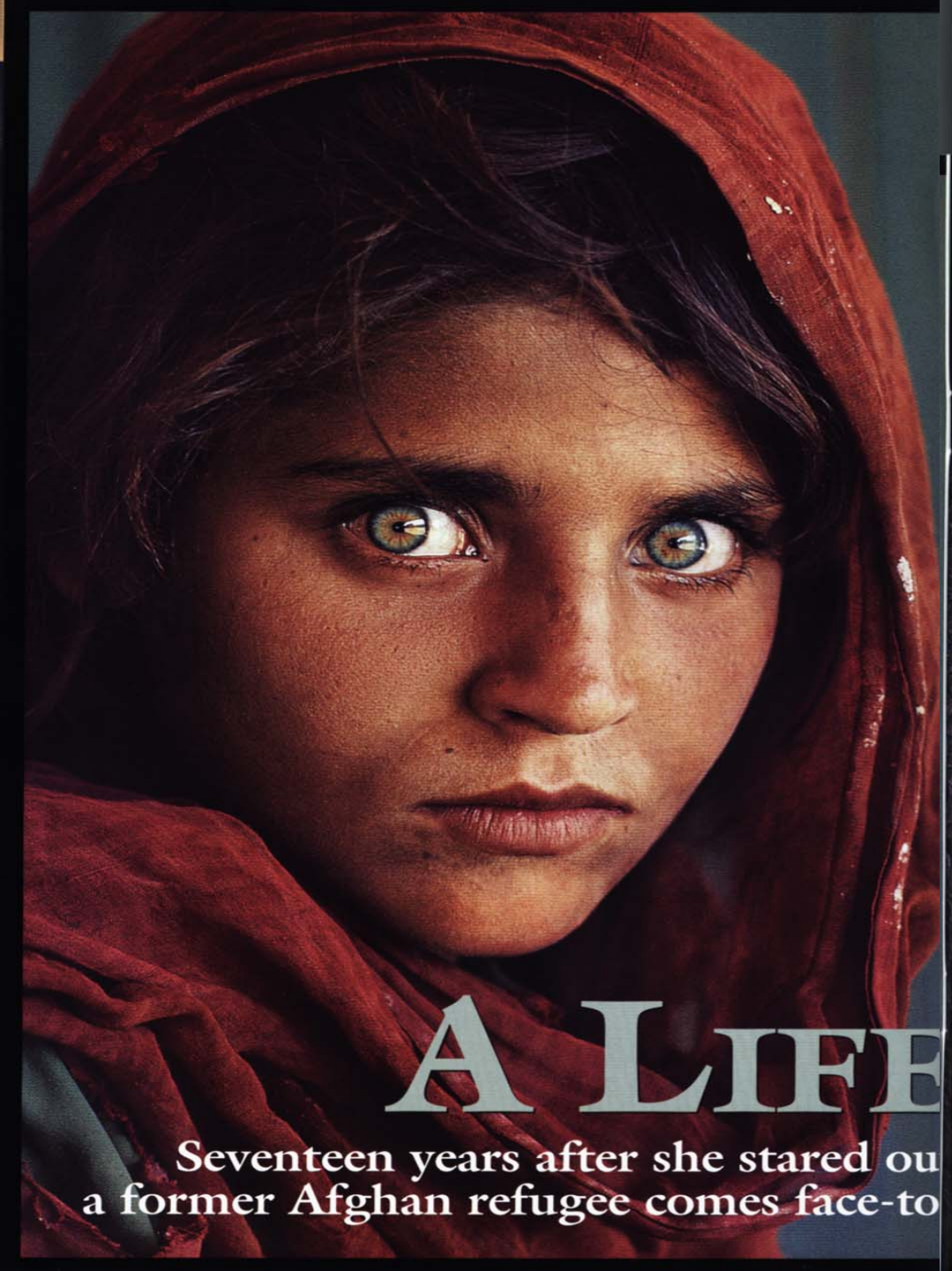
Found
After 17 Years
An Afghan Refugee's Story

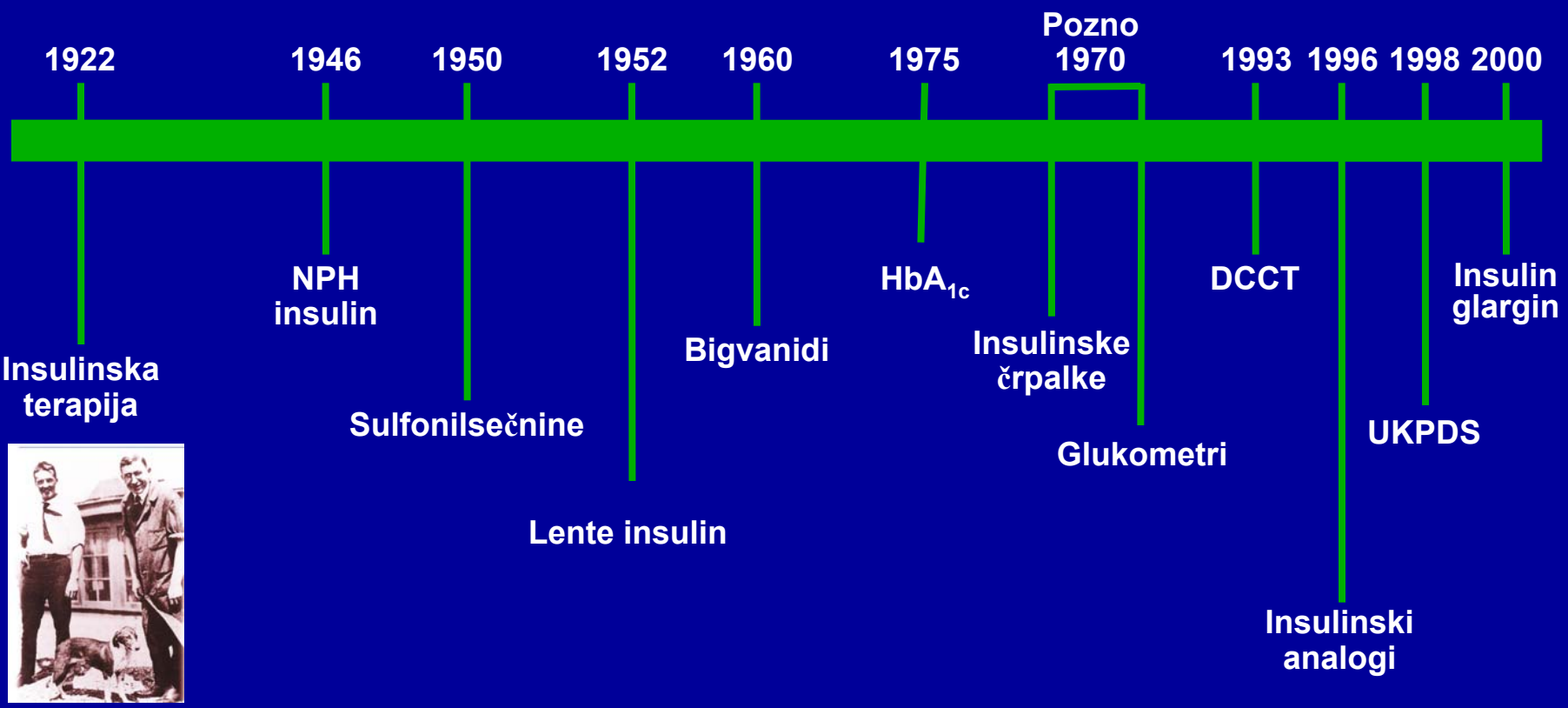


A LIFE REVEALED

Seventeen years after she stared ou
a former Afghan refugee comes face-to

from the cover of National Geographic,
face with the world once more.

Mejniki v diabetologiji

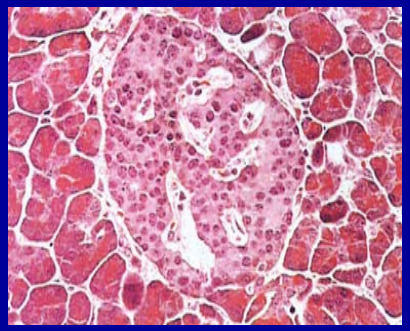


ČUDEŽ INSULINA

Bolnik J.L., December 15, 1922

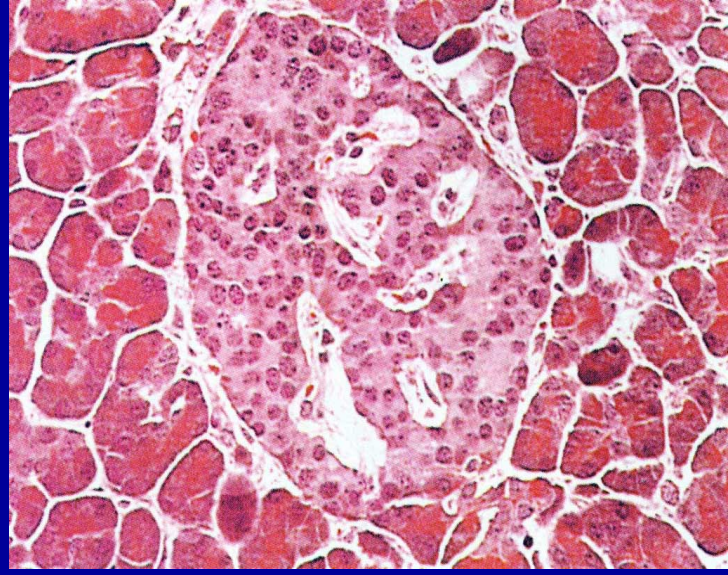
Februar 15, 1923

Oblike sladkorne bolezni



- SLADKORNA BOLEZEN TIP 1
- SLADKORNA BOLEZEN TIP 2
- NOSEČNOSTNA SLADKORNA BOLEZEN
- SEKUNDARNA SLADKORNA BOLEZEN

KRVNI SLADKOR



3.9 - 6.0 mmol/l

DIAGNOZA

Na tešče $\geq$ 7.0 mmol /l

Po obroku $\geq$ 11.1 mmol/l

SLOVENIJA 4%

100.000 oseb

2002 → 150 mio

2025 → 300 mio

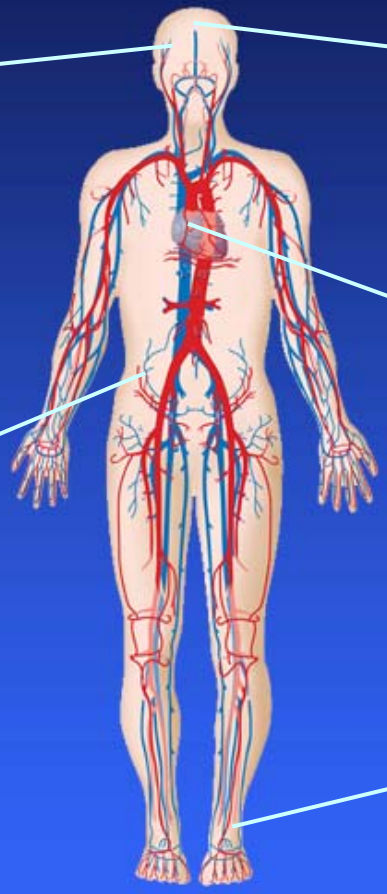
Sladkorna bolezen je težka bolezen

Diabetična retinopatija

Vodilni vzrok slepote

Diabetična nefropatija

Vodilni vzrok končne odpovedi ledvic



Možganska kap

2 to 4x povečano tveganje

Srčno-žilne bolezni

8/10 diabetikov umre za SŽB

Diabetična nevropatija

Vodilni vzrok netravmatske amputacije

LIVING WITH DIABETES

NICOLE JOHNSON

Miss America 1999

Nicole Johnson

"Nicole has captured the emotion, courage, and drama known to everyone who has diabetes. Her journey of limitless possibilities will touch your heart."

—LEEZA GIBBONS

ENERGIZING EXERCISE | ALPHA-LIPOIC ACID | FROZEN DESSERTS

Diabetes Forecast

THE HEALTHY LIVING MAGAZINE OF THE AMERICAN DIABETES ASSOCIATION FOR 50 YEARS

JULY 2001

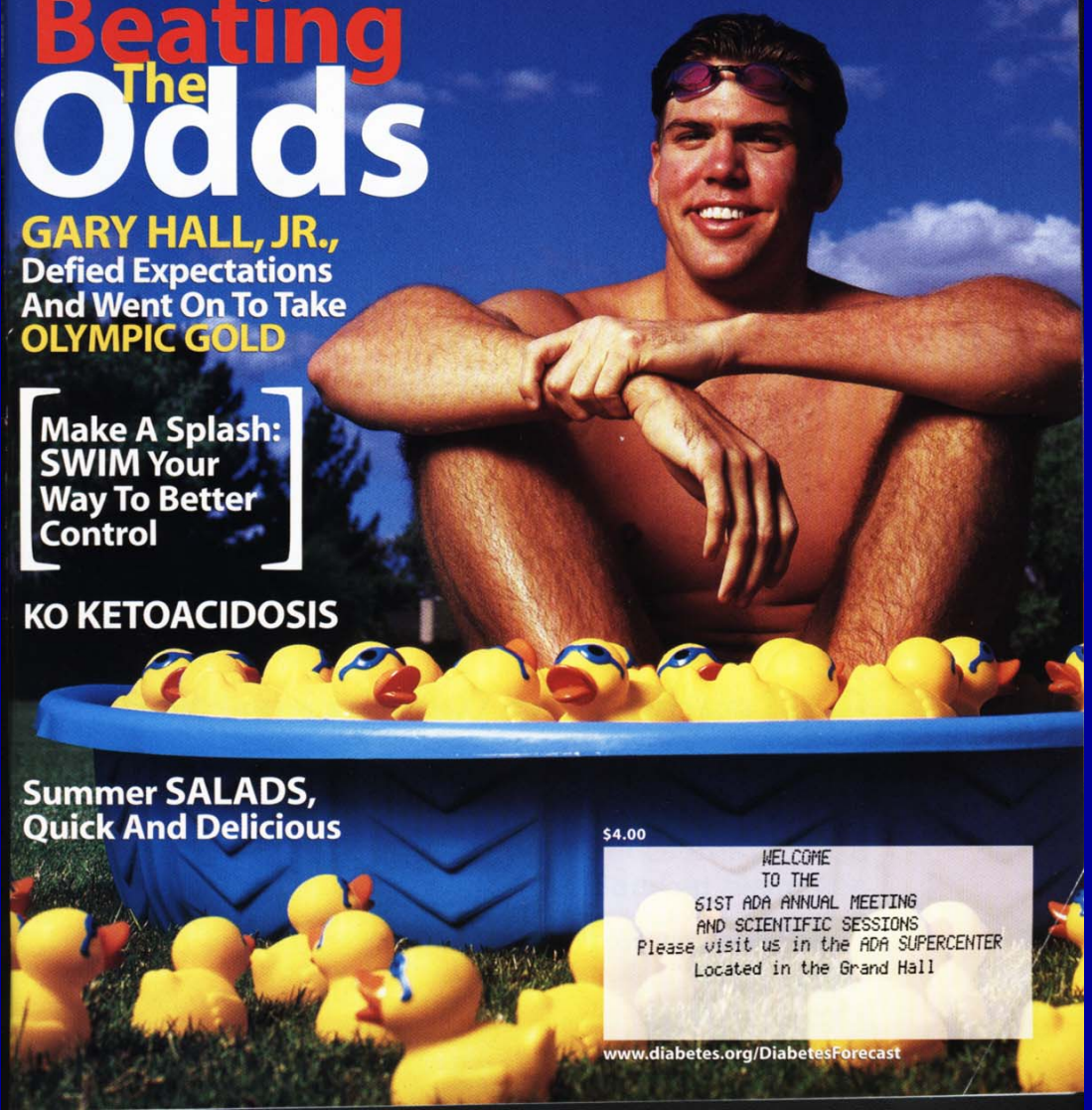
Beating The Odds

GARY HALL, JR., Defied Expectations And Went On To Take OLYMPIC GOLD

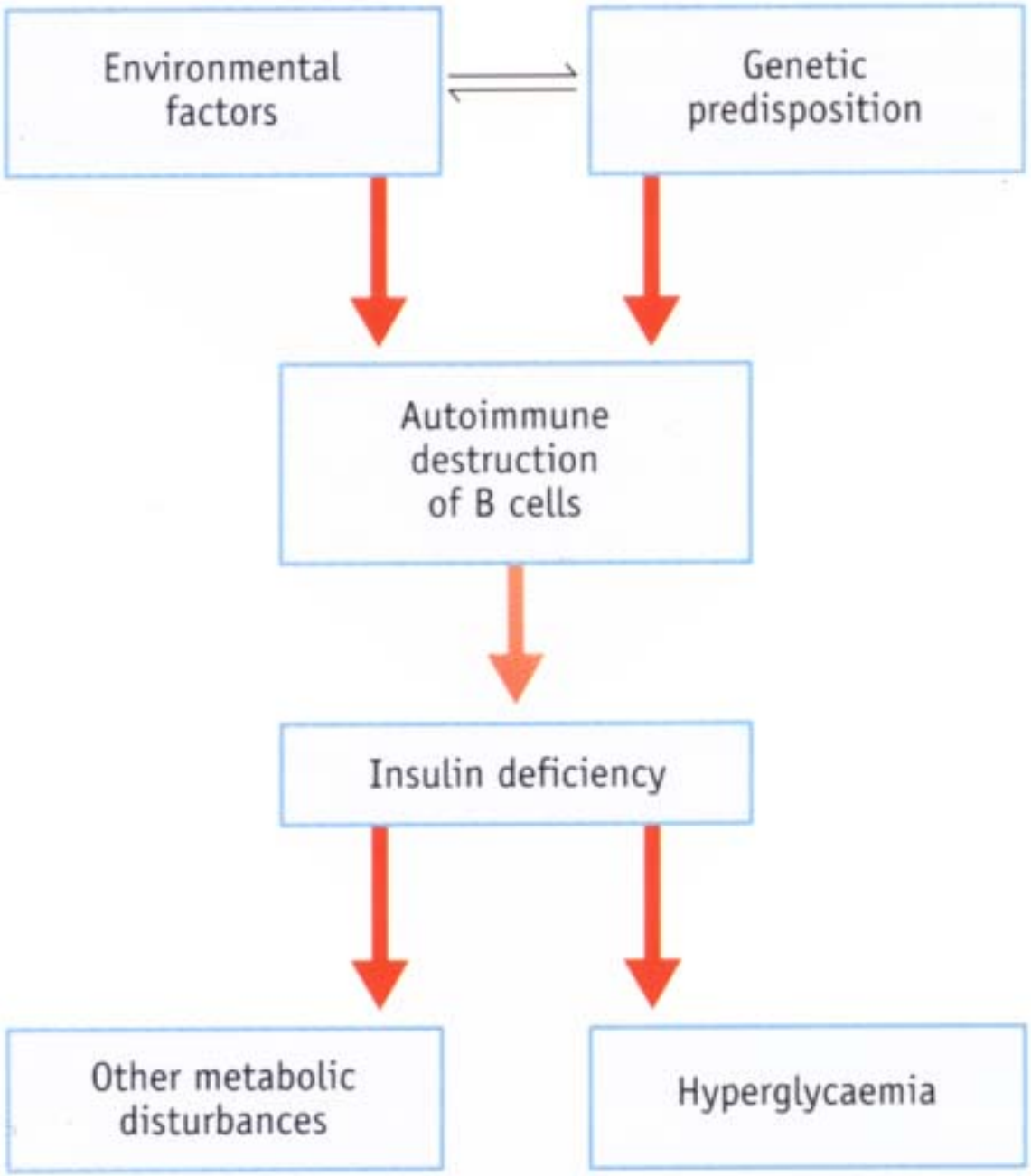
Make A Splash: SWIM Your Way To Better Control

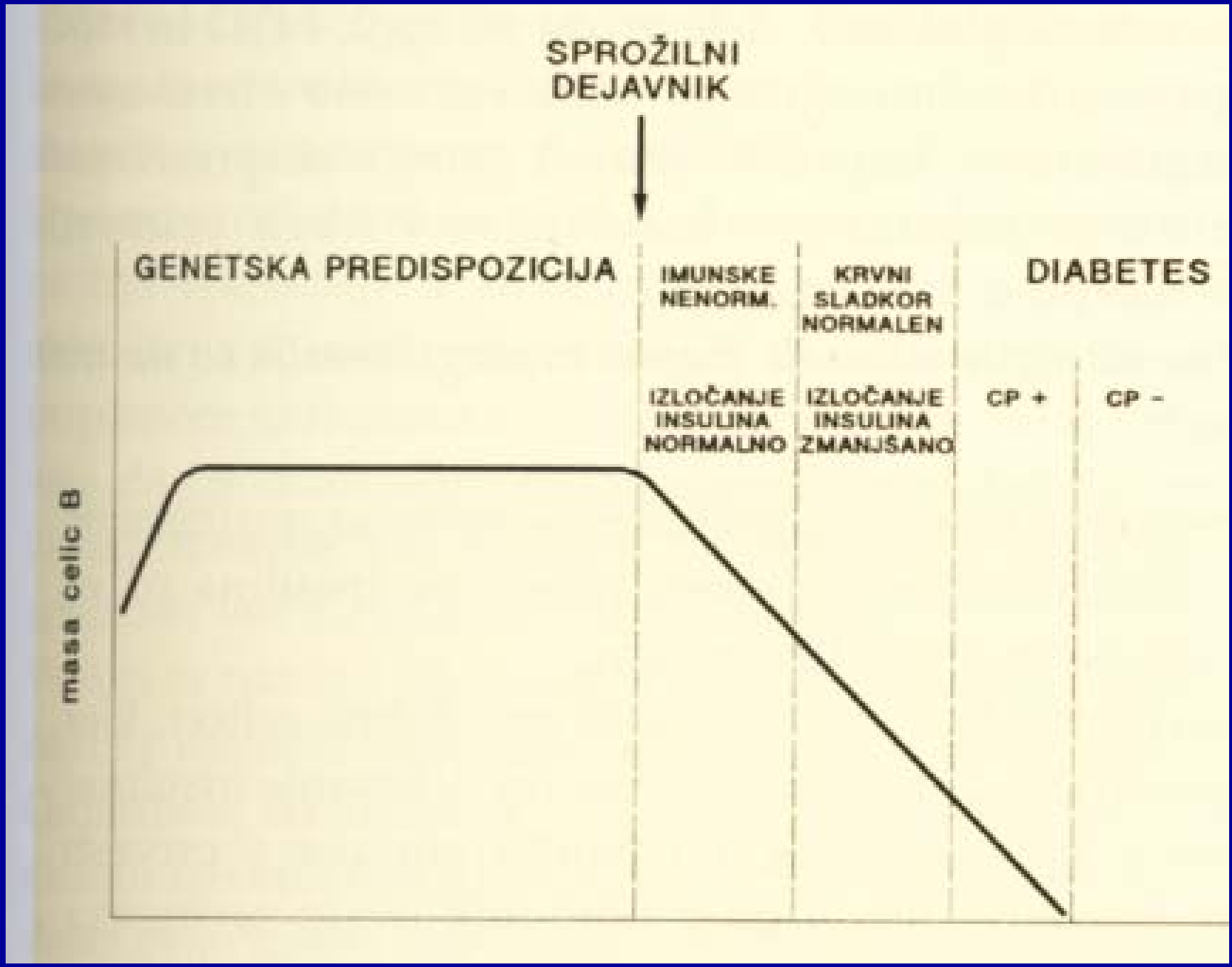
KO KETOACIDOSIS

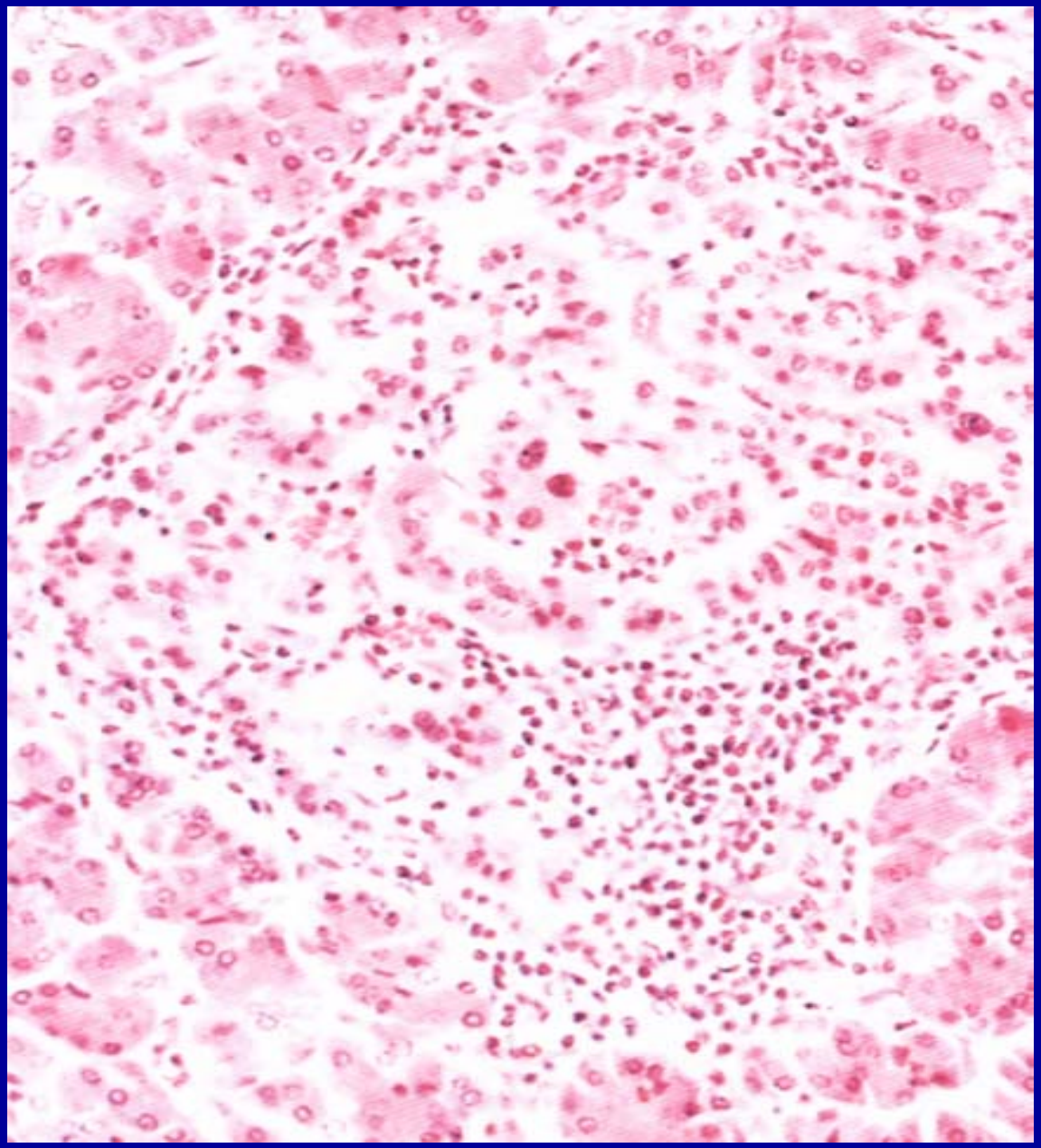
Summer SALADS, Quick And Delicious



www.diabetes.org/DiabetesForecast


Environmental factors
Genetic predisposition
Autoimmune destruction of B cells
Insulin deficiency
Other metabolic disturbances
Hyperglycaemia

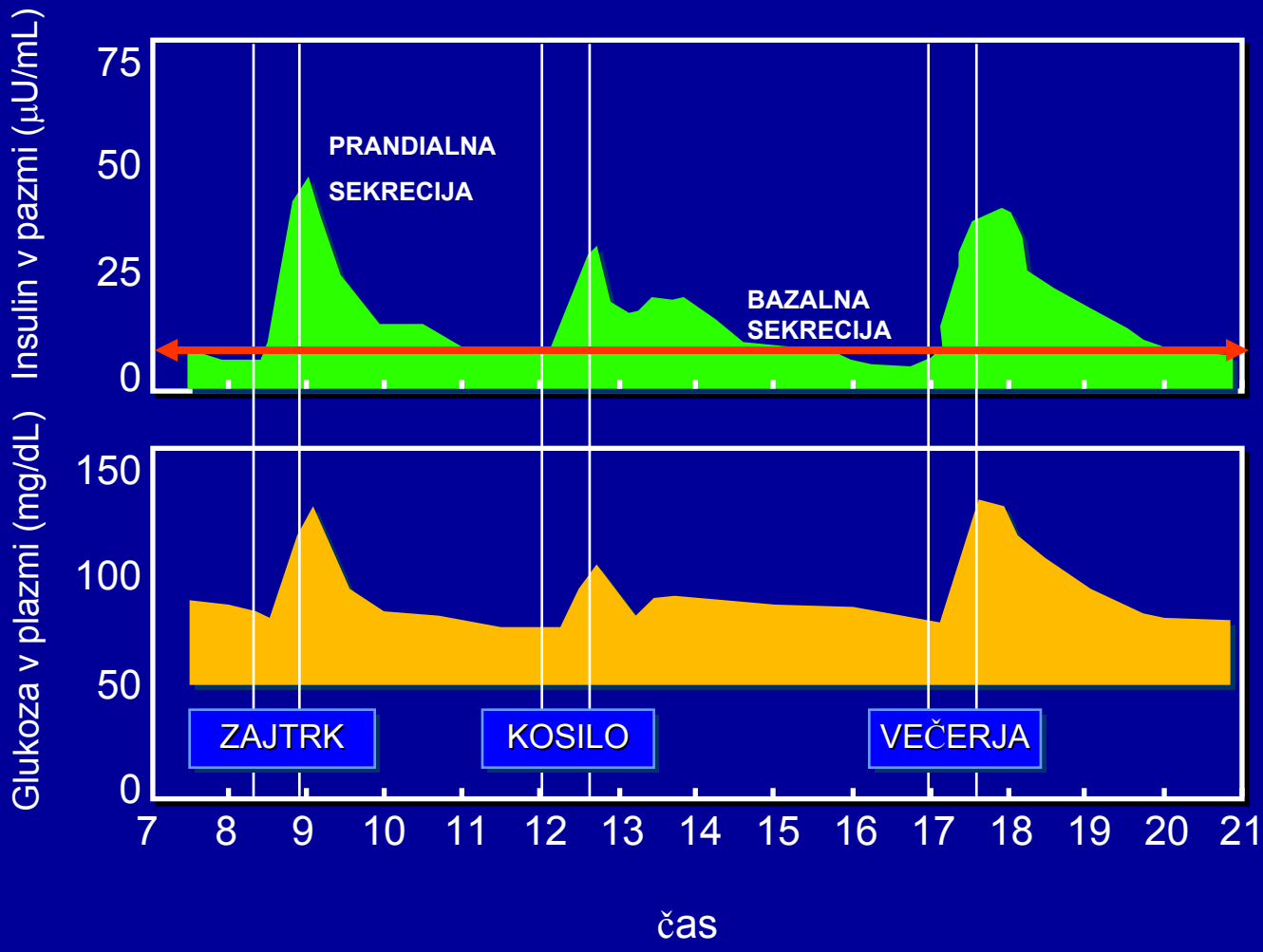

SPROŽILNI
DEJAVNIK
GENETSKA PREDISPOZICIJA
IMUNSKE
NENORM.
KRVNI
SLADKOR
NORMALEN
DIABETES
IZLOČANJE
INSULINA
NORMALNO
IZLOČANJE
INSULINA
ZMANJŠANO
CP +
CP –
masa celic B



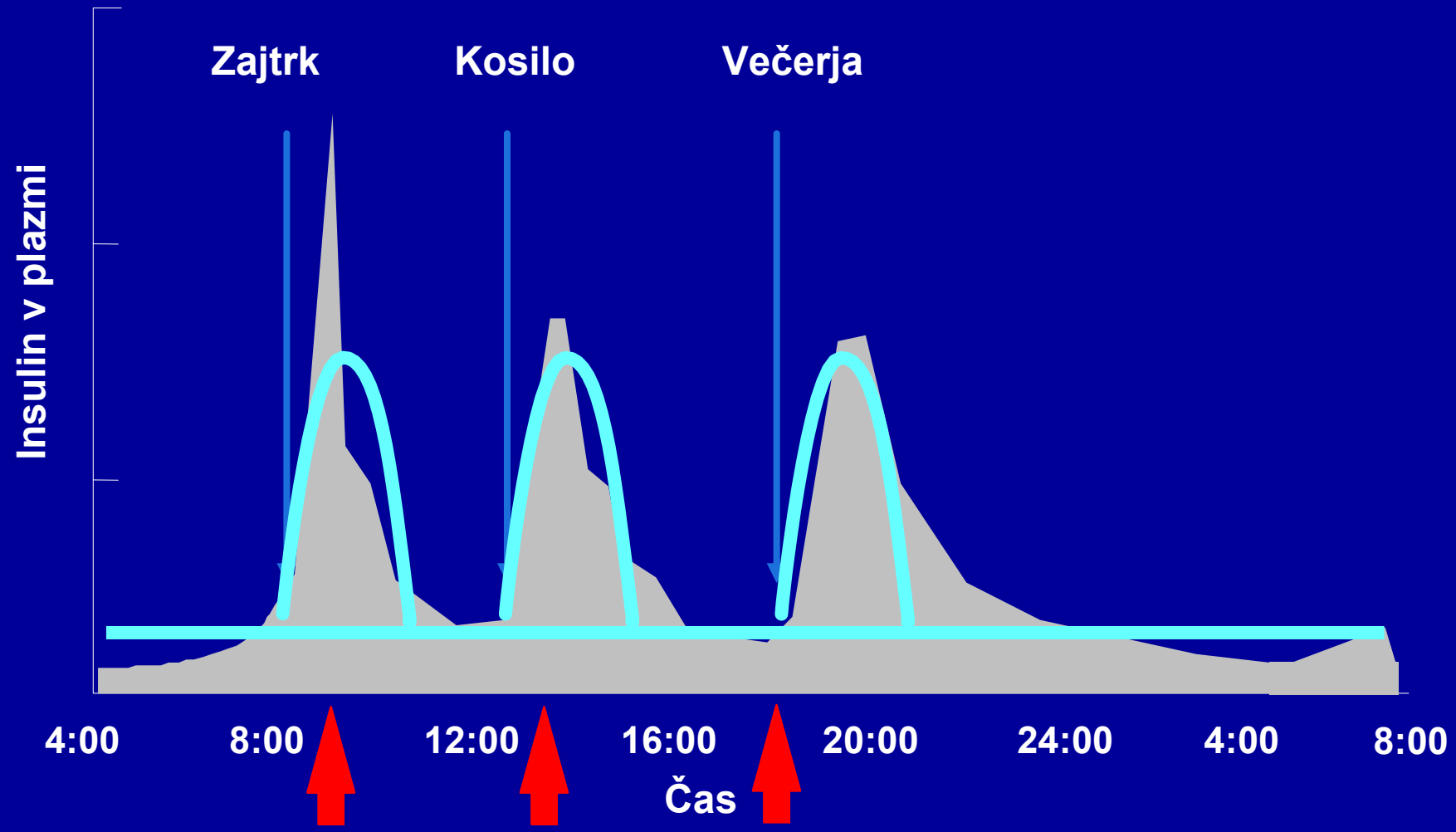
	Diagnostic			Predictive value	
Antibody	**Abbreviation**	**Sensitivity**	**Specificity**	**First-degree relatives**	**General population**
Islet-cell antibodies	ICA	80–90%	96–99%	20–50%	20–30%
Islet-cell surface antibodies	ICSA	30–60%	95%	ND	ND
Cytotoxic islet-cell antibodies	C'AMC	40–60%	95%	ND	ND
Insulin autoantibodies	IAA	40–70%	99%	<50%	ND
Glutamate decarboxylase (GAD65)	GAD65AB	70–90%	99%	>50%	ND

INSULINI?

Insulin v plazmi in profil glukoze pri zdravem



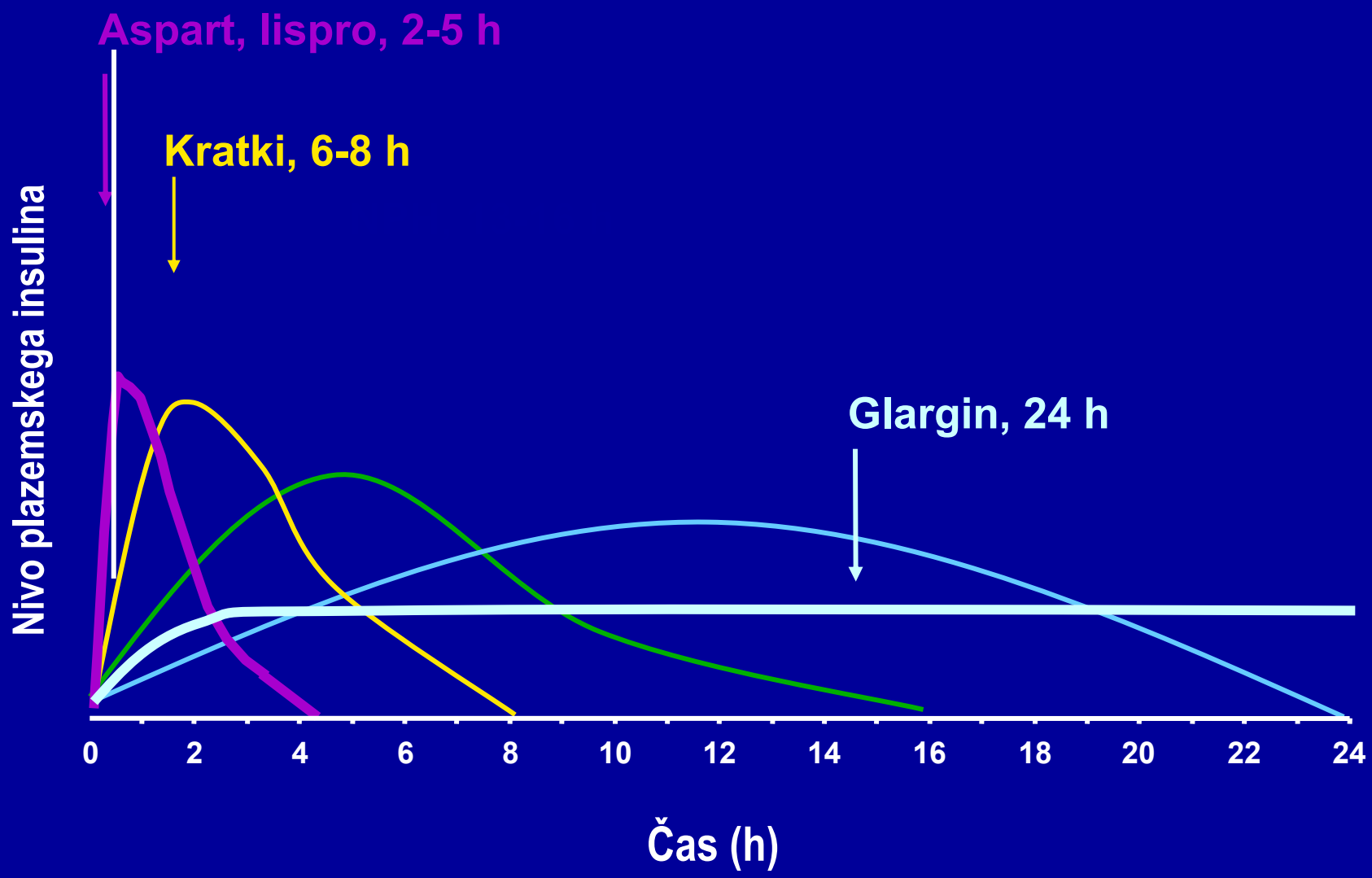
Bazalni/Bolusni Insulin



Delovanje insulinov

Insulin	Začetek delovanja	Vrh delovanja	Trajanje delovanja
Ultra-kratkodelujoči			
Kratki	30-60 min	2-4 h	6-8 h
Lispro	15 min	1-2 h	2-5 h
Aspart	10-20 min	1-3 h	3-5 h
Srednjedolgo delujoči			
NPH	1-3 h	5-7 h	13-16 h
Detemir	—	4-6 h	20 h
Dolgodelujoči insulin			
Glargin	1-2 h	Brez vrha	~24 h
Pre-mix insulini			
Insulin lispro 75/25	10 min	1-4 h	10-20 h
Insulin aspart 70/30	10 min	1-4 h	16-20 h

Delovanje insulinov



Insulinski analogi

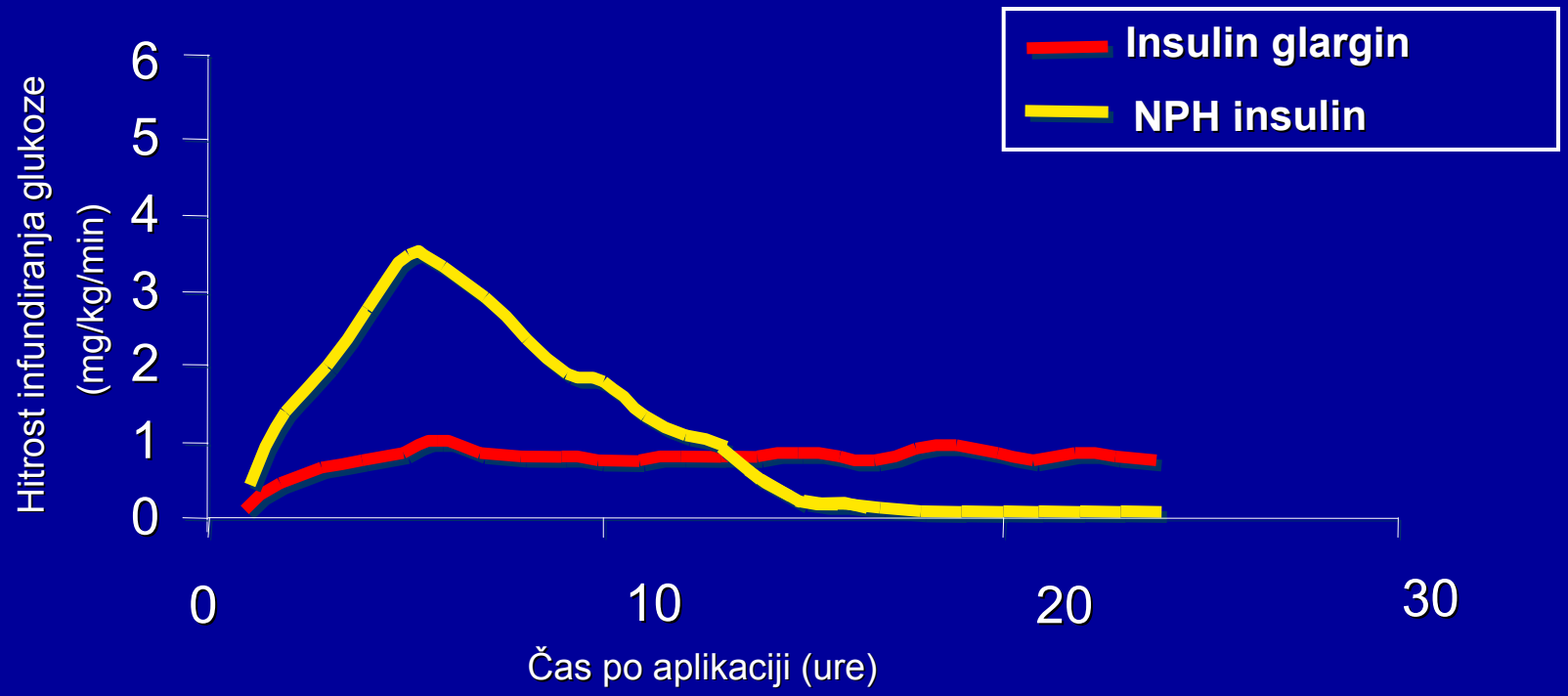
Humani Insulin

Aspart

Lispro

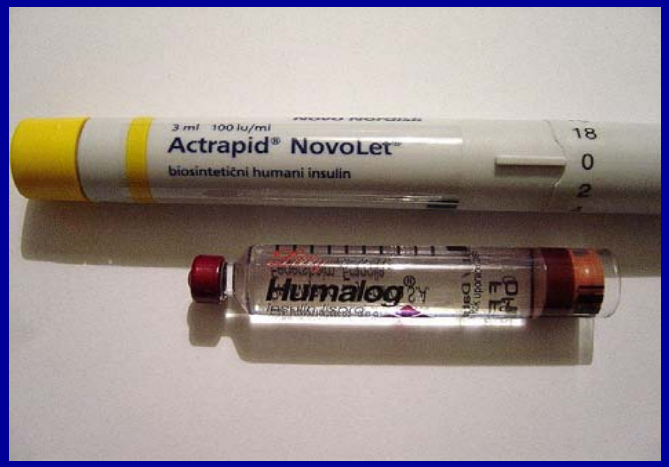
Glargin

Delovanje bazalnih insulinov



Povzeto po Lantus® (insulin glargin) EMEA Summary of Product Characteristics 2002.

INSULIN

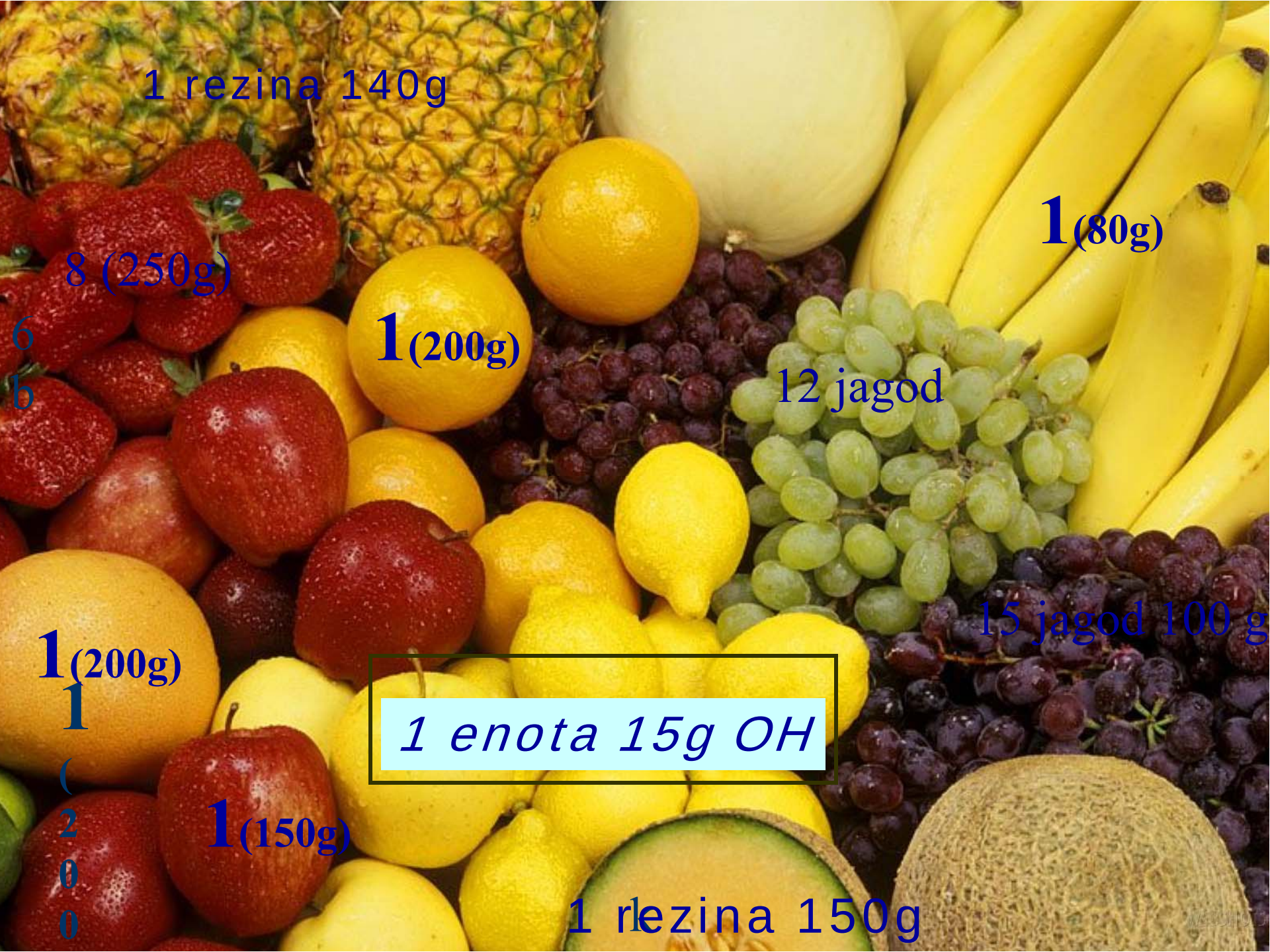

3 ml 100 iu/ml
Actrapid® NovoLet™
biosintetični humani insulin
18
0
2
Humalog®

NovoRapid®
FlexPen®
Insulatard®
FlexPen®

NovoMix® 30
FlexPen®

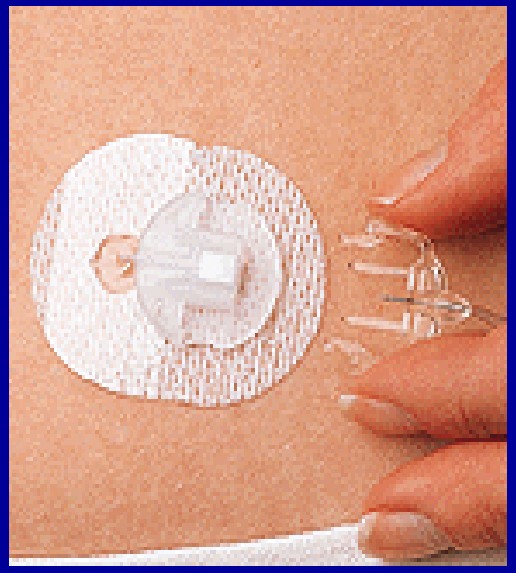
OptiPen® Pro1

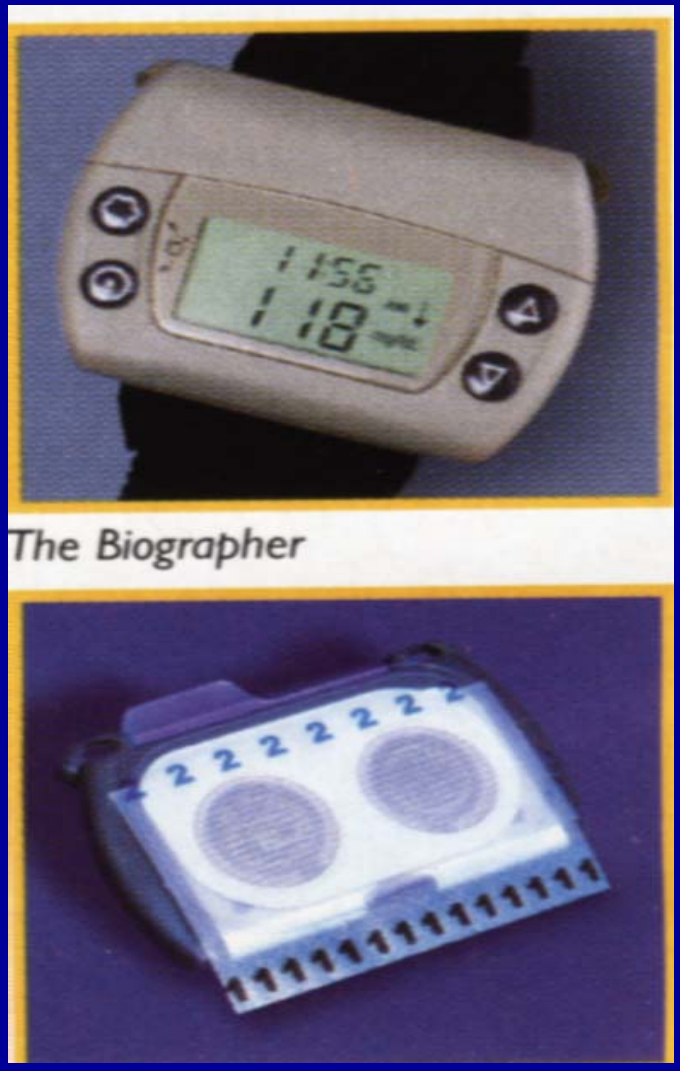
Mixtard® 30 NovoLet®
Biosynthetic Human Insulin
Shake well and inject
18
0
2


1 rezina 140g
8 (250g)
6
b
1 (200g)
1 (80g)
12 jagod
15 jagod 100 g
1 (200g)
1
(
2
0
0
1 (150g)
1 enota 15g OH
1 rlezina 150g

MiniMed 508
12:43 PM
sel
act

Infuzijski seti




The Biographer

MiniMed Solutions: CGMS Sensor

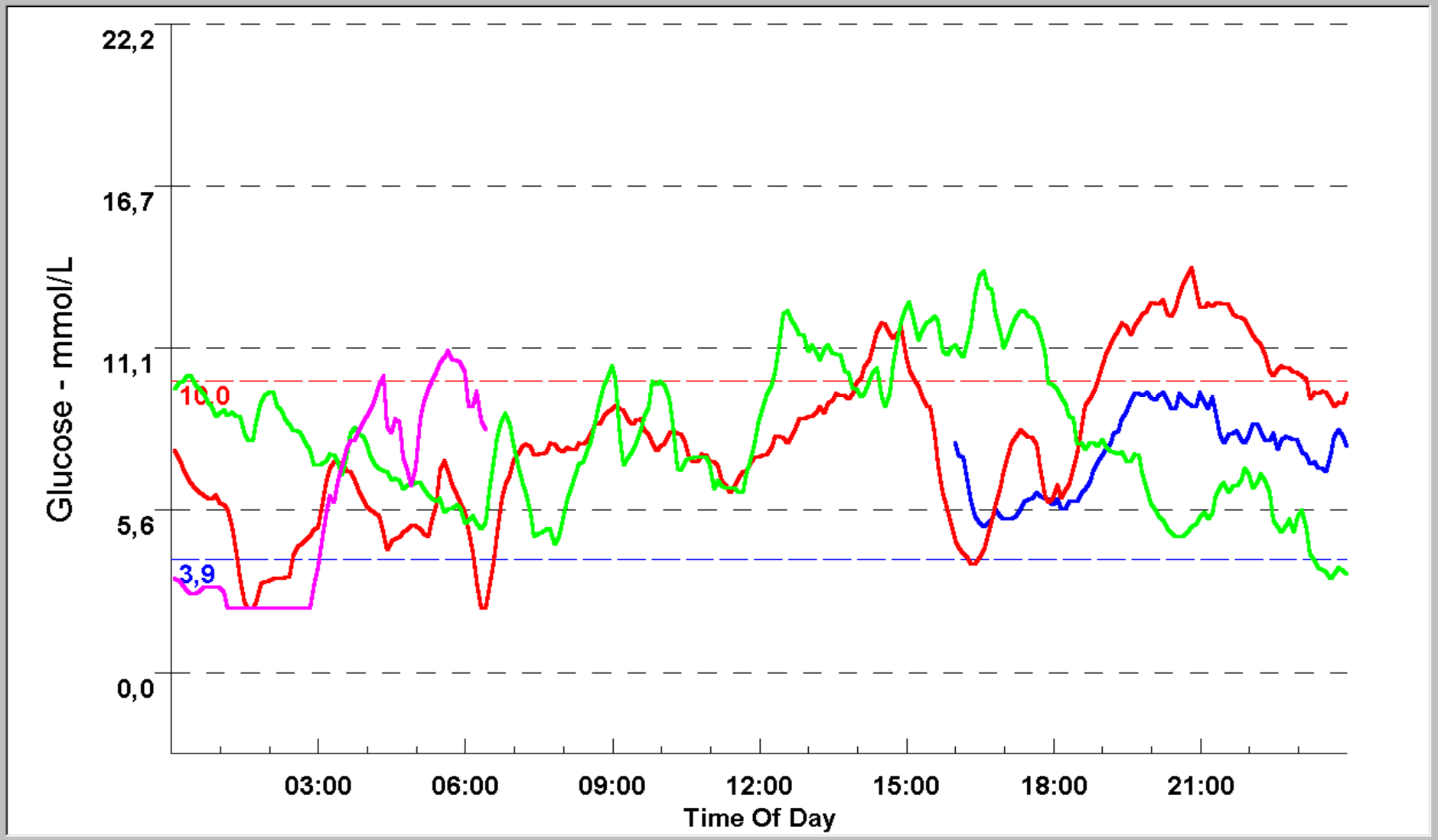
File Download Data Reports Help

Sensor Modal Day

Patient: MATEJA MALEŠ

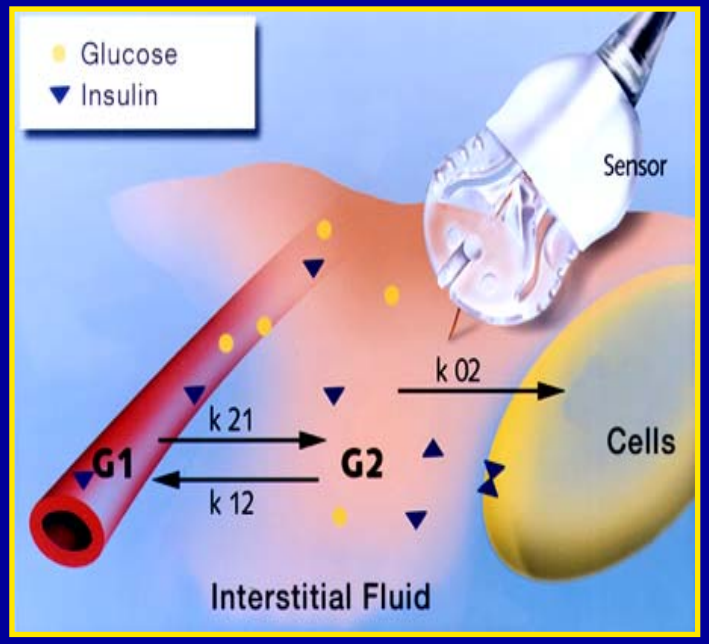
ID: 0124283

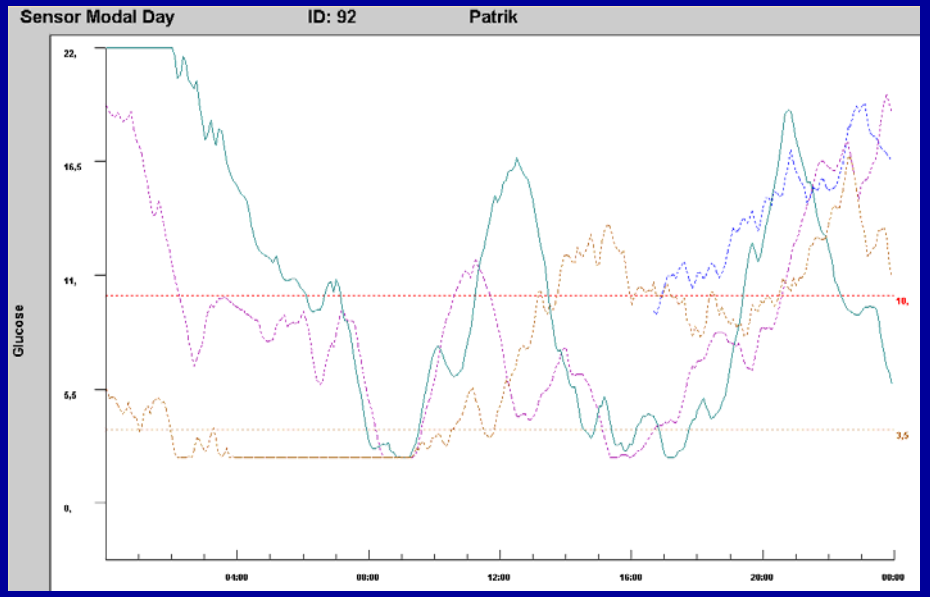
Legend | Close



Click sensor plot line to read data value

CAPS NUM INS 5.1.05 9:12


Glucose
Insulin
Sensor
k 02
k 21
G1
G2
Cells
k 12
Interstitial Fluid


Sensor Modal Day
ID: 92
Patrik
Glucose
22,
16,5
11,
5,5
0,
10,
3,5
04:00
08:00
12:00
16:00
20:00
00:00

MiniMed
SEL
ACT

Glikiran hemoglobin-HbA_{1c}

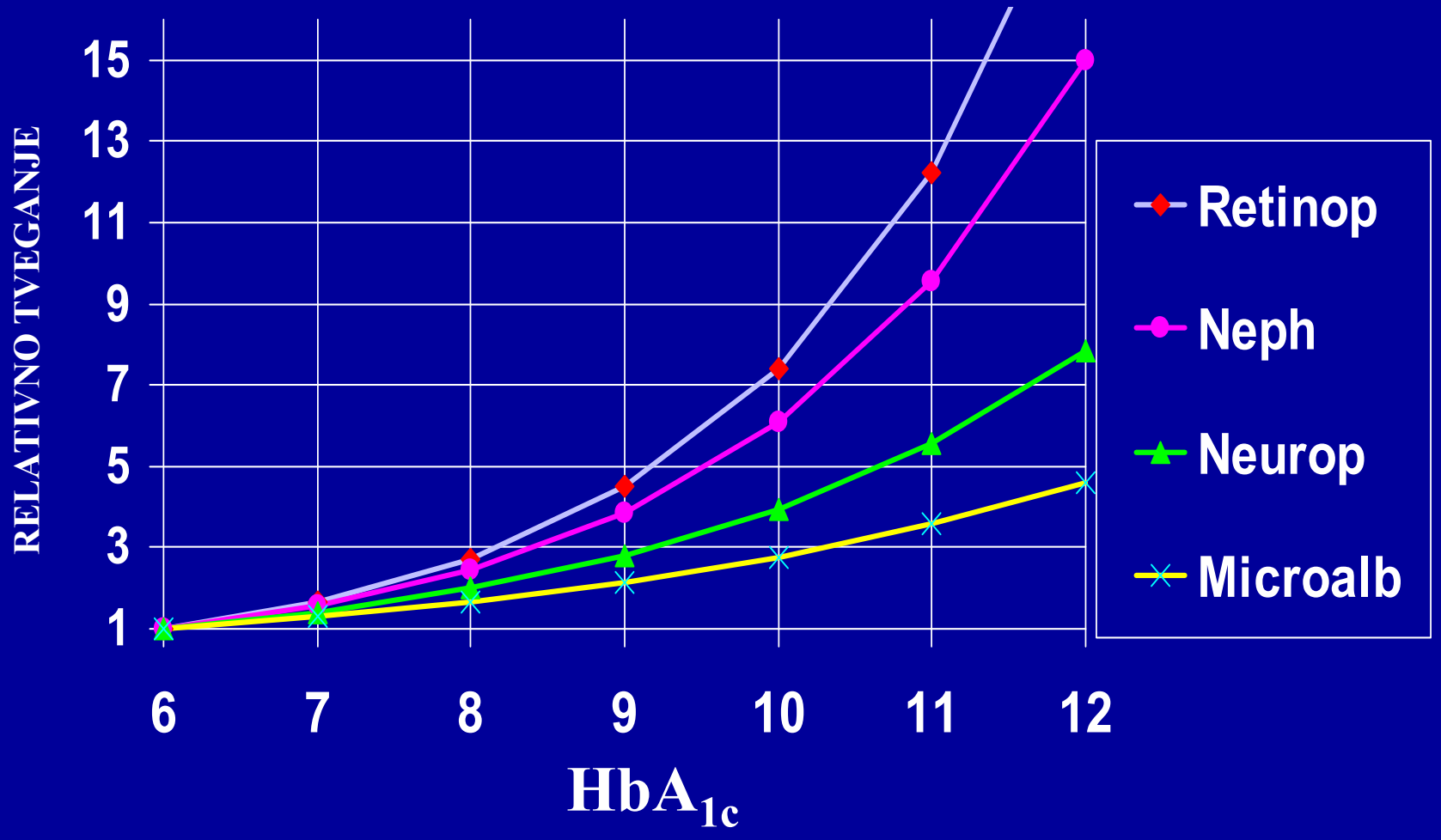
Merilo urejenosti diabetesa

Povprečje: 8-10 tednov

Meja: 7 %

2xHba1c - 6

Tveganje za pozne zaplete sladkorne bolezni



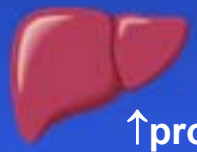
Skyler: Endo Met Cl N Am 1996

Sladkorna bolezen tip 2: vpliv genov in okolja

Genetska dovzetnost
debelost, “sedeč” način
življenja

Insulinska rezistenca

↓ privzem glukoze



↑produkcija
glukoze v jetrih

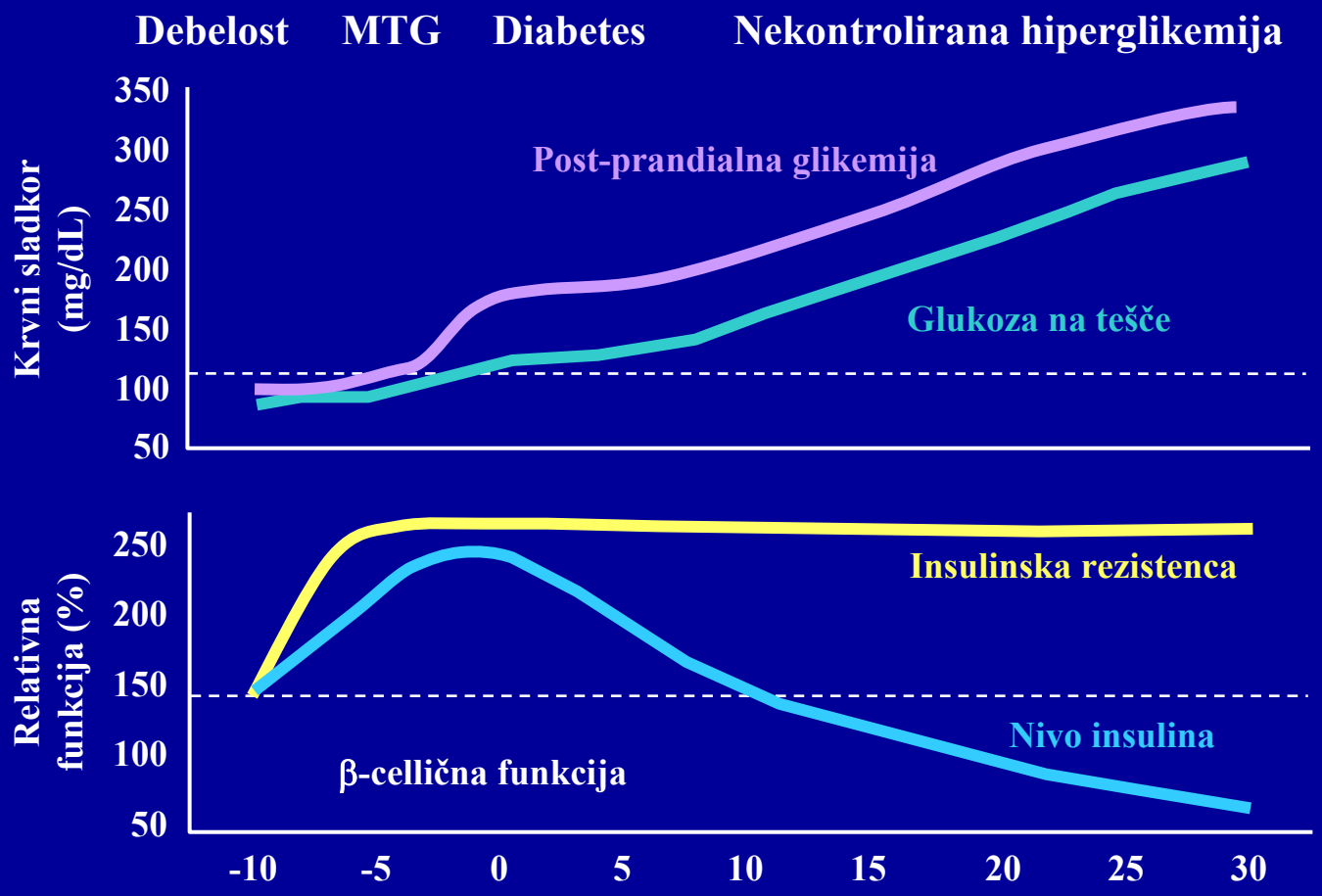
β-celična disfunkcija

moteno izločanje
insulina

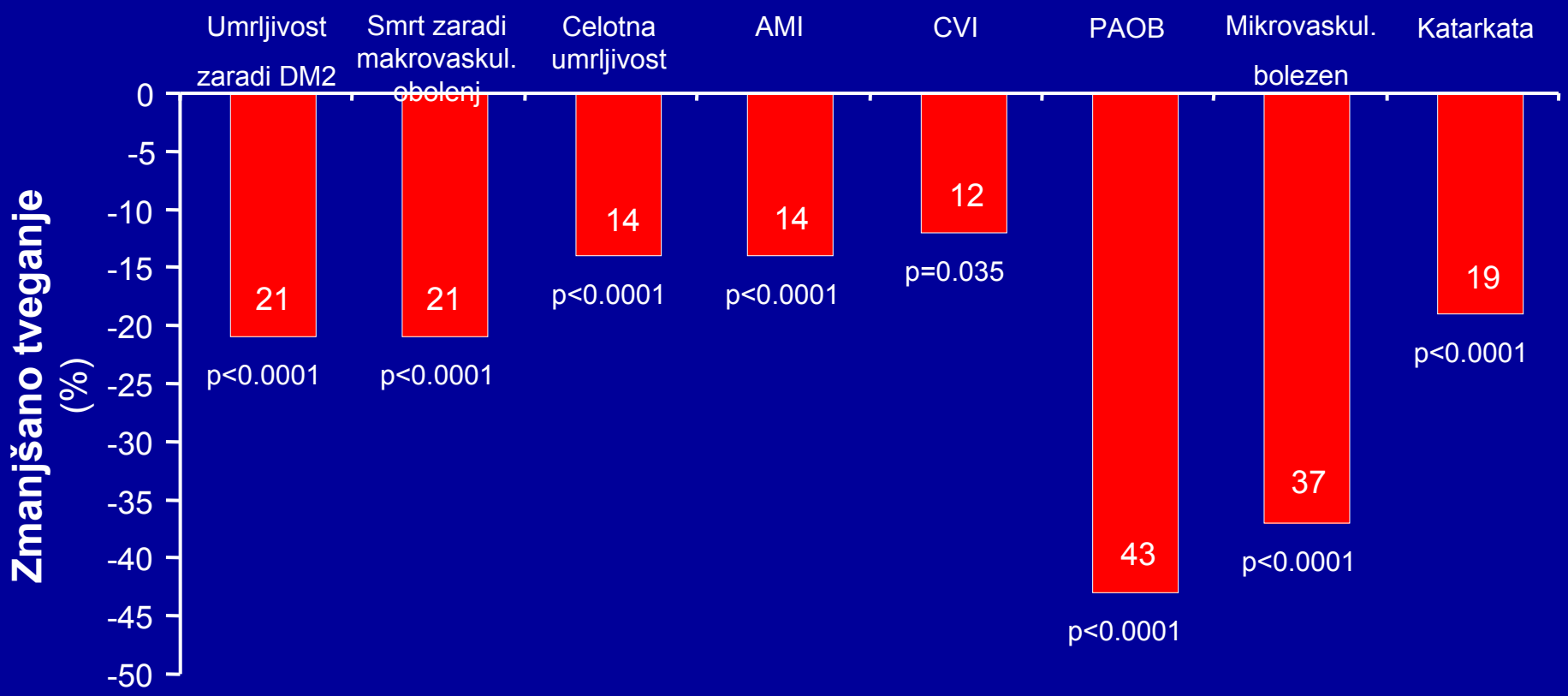
Sladkorna bolezen tip2

De Fronzo J. *Diabetes* 1998; 37:667–687.

Naravni potek sladkorne bolezni tip 2

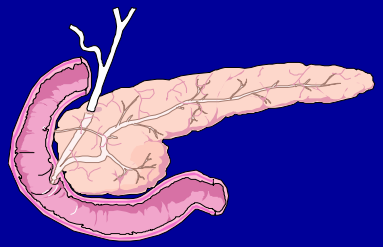


Dobra urejenost sladkorne bolezni zmanjšuje kronične komplikacije



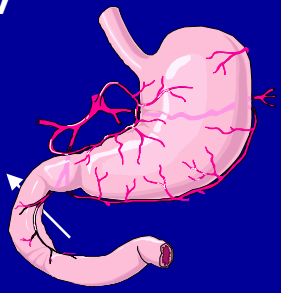
Stratton IM *et al* (UKPDS 35). *BMJ* 2000; 321: 405-412

Moteno izločanje insulina



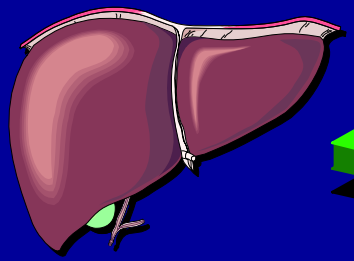
Insulinski sekretagogi
(sulfonilsečnine, glitinidi)

Metabolizem ogljikovih hidratov



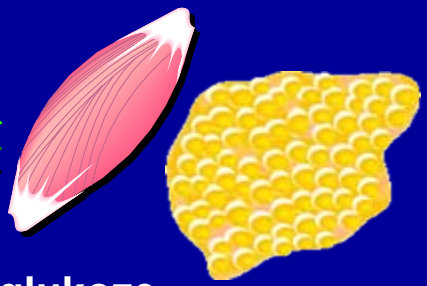
α-glukozidazni inhibitorji

Hiperglikemija



↑ producije glukoze v jetrih

Bigvanidi

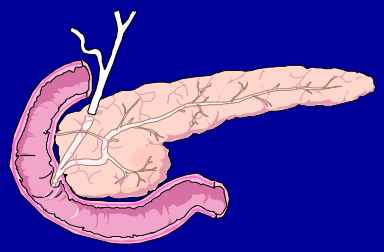


↓ privzem glukoze

Tiazolidindioni

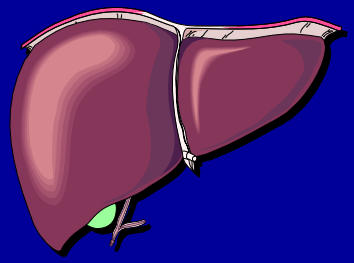
Sulfonilsečnine
Glitinidi

Glibenklamid
(Glibenklamid, Daonil, Euglucon)
Gliklazid
(Diaprel, Diaprel MR)
Glikvidon
(Glurenorm)
Glimepirid
(Amaryl)
Glipizid
(Antidiab, Glucotrol XL)



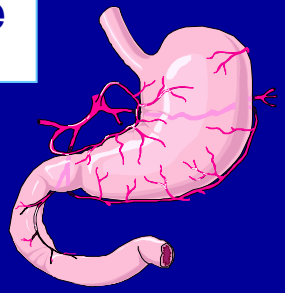
Repaglinid
(NovoNorm)

Bigvanidi



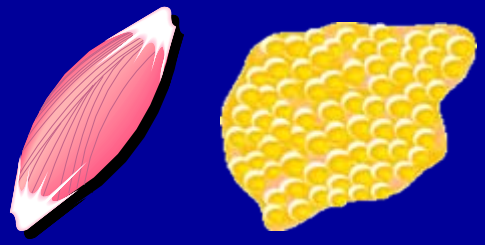
Metformin
(Glucophage, Aglurab, Gluformin)

Inhibitorji α-glukozidaze



Akarboza
(Glucobay)

Tiazolidindioni



Rosiglitazon (Avandia)

Peroralni antidiabetiki: delovanje in učinkovitost

Razred	Delovanje	Znižanje HbA_{1c} %
Insulinski sekretagogi (sulfonilsečnine, glitinidi)	Spodbujajo izločanje insulina	1.0-2.0
Bigvanidi (metformin)	Zavirajo produkcijo glukoze v jetrih	1.0-2.0
Tiazolidindioni	Spodbujajo delovanje insulina v mišicah, maščevju in jetrih	0.5-1.0
α-glukozidazni inhibitorji	Upočasnijo GI absorbcijo OH	0.5-1.0

Nathan DM. *N Engl J Med.* 2002;347:1342-1349.

Peroralni antidiabetiki: fiziološki učinki

	Insulinski sekretagogi	Metformin	α-glukozidazni inhibitorji	TZD
Vpliv na KS_t / HbA_{1c}	↓	↓	↓	↓
Vpliv na plazemski insulin	↑	↓	-	↓
Vpliv na LDL-holesterol	-	↓	-	↑
Vpliv na HDL-holesterol	-	↑/-	-	↑
Vpliv na trigliceride	-	↓/-	-	↓/-

DeFronzo RA. *Ann Int Med* 1999; 131:281–303.
Freed MI, *et al*. *Am J Cardiol* 2002; 90:947–952.

Peroralni antidiabetiki: stranski učinki

Razred	Stranski učinki
Insulin sekretagogi (sulfonilsečnine, glitnidi)	Porast telesne teže, hipoglikemija
Bigvanidi (metformin)	Gastrointestinalni; laktacidoza
Tiazolidindioni	Porast telesne teže, zadrževanje tekočin-edemi,dilucijska anemija; kongestivno srčno popuščanje;hipoglikemija v komb. s sulfonilsečnino
α-Glukozidazni inhibitorji	Flatulenca; redko hepatična nekroza

*

Peroralni antidiabetiki: stranski učinki

	Insulinski sekretagogi	Metformin	α-glukozidazni inhibitorji	TZD
Hipoglikemija	✓	-	-	-
Porast teže	✓	-	-	✓
GI učinki	-	✓	✓	-
Laktacidoza	-	✓	-	-
Edemi	-	-	-	✓
Anemija	-	✓	-	✓

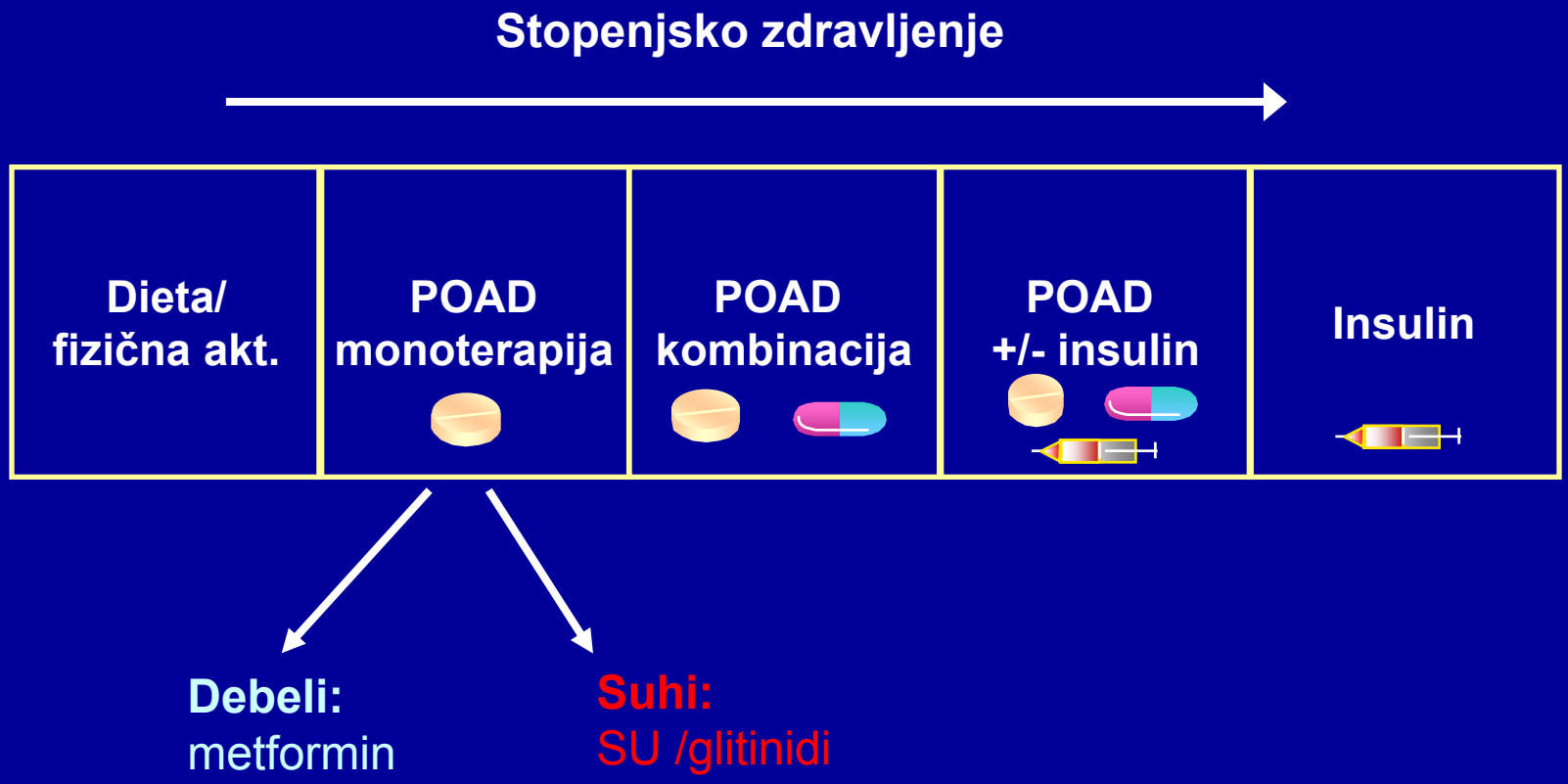
DeFronzo RA. *Ann Int Med* 1999; 131:281–303.

Učinkovitost peroralnih antidiabetikov

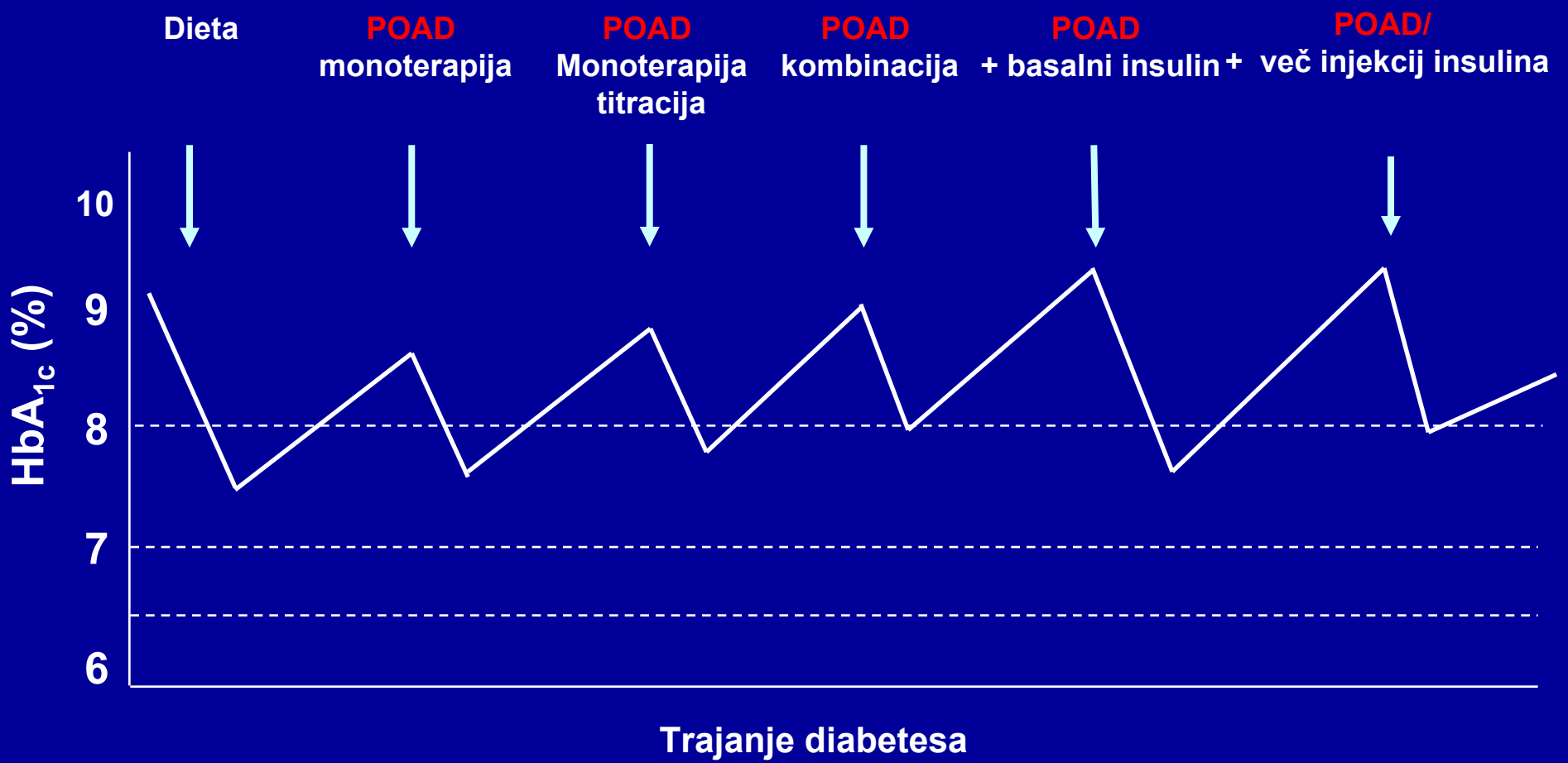
Monoterapija

	HbA_{1c}
Sulfonilurea	1 % do 2 %
Metformin	1% do 2 %
Pioglitazon	0.6 % do 1.9 %
Rosiglitazon	0.7 % do 1.8 %
Repaglinid	0.8 % do 2 %
Akarboza	0.5 % do 1.0%

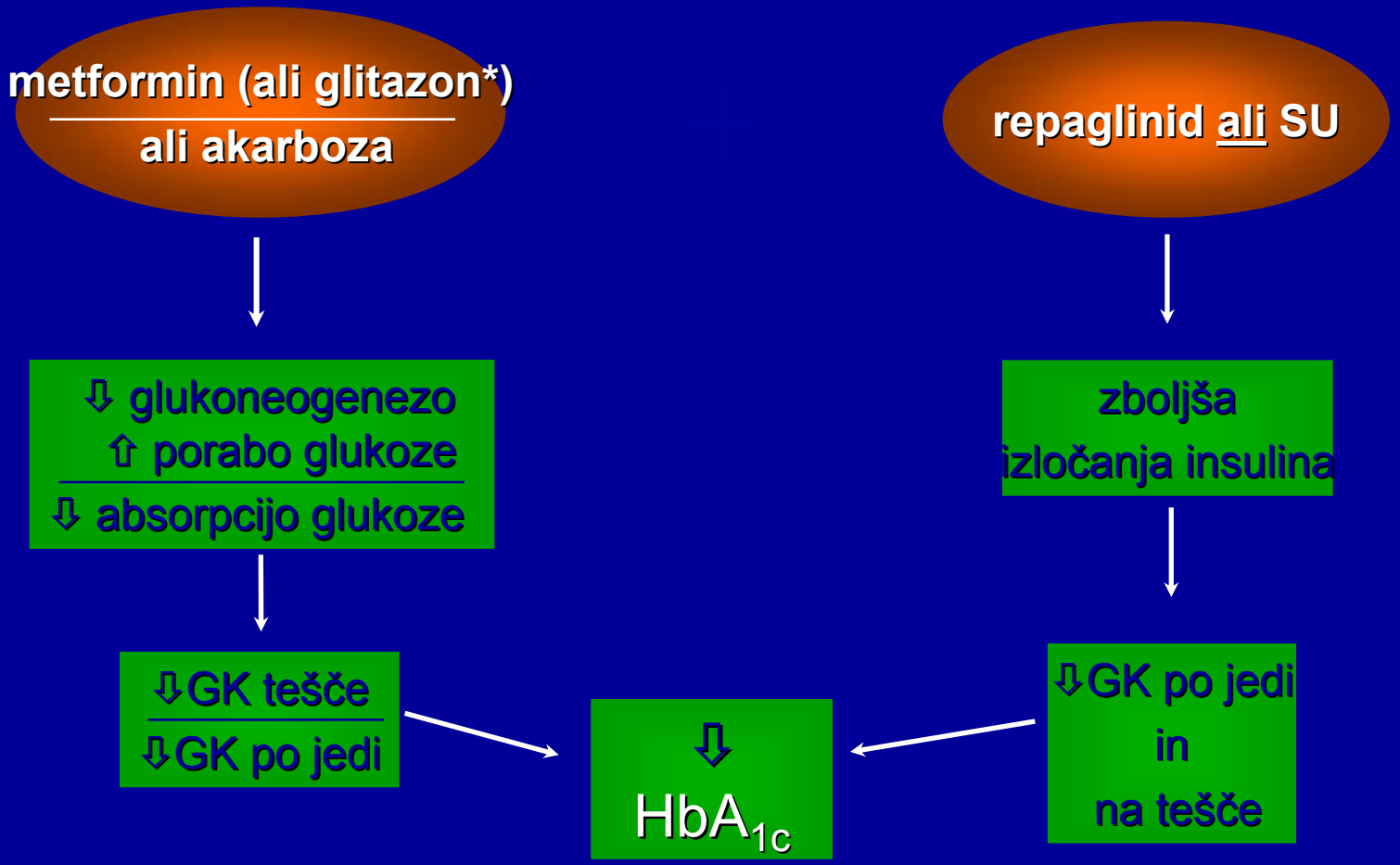
Zdravljenje sladkorne bolezni tip 2



Tradicionalni pristop v zdravljenju sladkorne bolezni tip 2



Kombiniramo zdravila z različnimi načini delovanja



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Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

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ABSTRACT

BACKGROUND

Cardiovascular morbidity is a major burden in patients with type 2 diabetes. In the Steno-2 Study, we compared the effect of a targeted, intensified, multifactorial intervention with that of conventional treatment on modifiable risk factors for cardiovascular disease in patients with type 2 diabetes and microalbuminuria.

METHODS

The primary end point of this open, parallel trial was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, revascularization, and amputation. Eighty patients were randomly assigned to receive conventional treatment in accordance with national guidelines and 80 to receive intensive treatment, with a stepwise implementation of behavior modification and pharmacologic therapy that targeted hyperglycemia, hypertension, dyslipidemia, and microalbuminuria, along with secondary prevention of cardiovascular disease with aspirin.

RESULTS

The mean age of the patients was 55.1 years, and the mean follow-up was 7.8 years. The decline in glycosylated hemoglobin values, systolic and diastolic blood pressure, serum cholesterol and triglyceride levels measured after an overnight fast, and urinary albumin excretion rate were all significantly greater in the intensive-therapy group than in the conventional-therapy group. Patients receiving intensive therapy also had a significantly lower risk of cardiovascular disease (hazard ratio, 0.47; 95 percent confidence interval, 0.24 to 0.73), nephropathy (hazard ratio, 0.39; 95 percent confidence interval, 0.17 to 0.87), retinopathy (hazard ratio, 0.42; 95 percent confidence interval, 0.21 to 0.86), and autonomic neuropathy (hazard ratio, 0.37; 95 percent confidence interval, 0.18 to 0.79).

CONCLUSIONS

A target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and microalbuminuria reduces the risk of cardiovascular and microvascular events by about 50 percent.

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N Engl J Med 2003;348:383-93.

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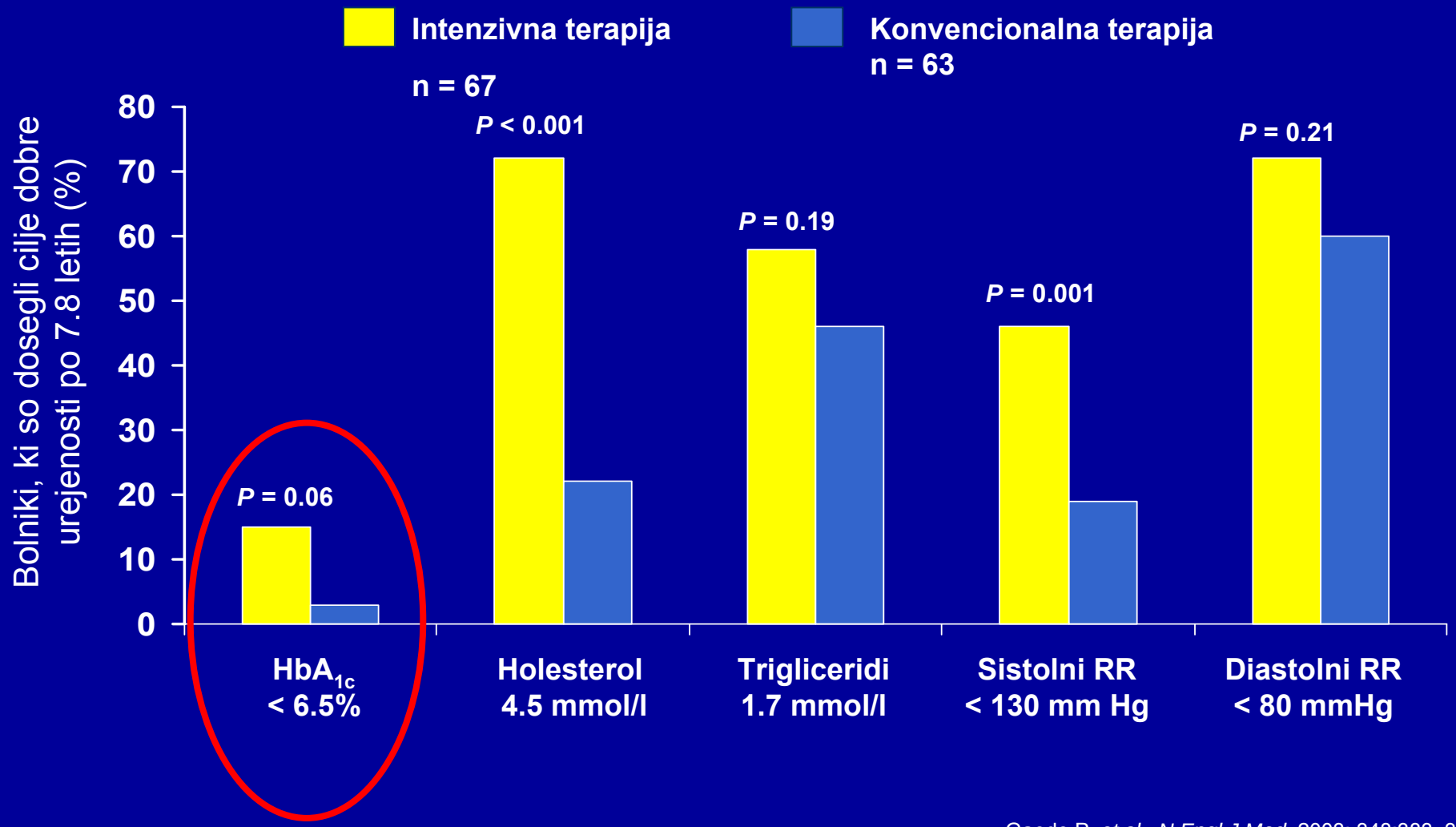
GLUKOZA

LIPIDI

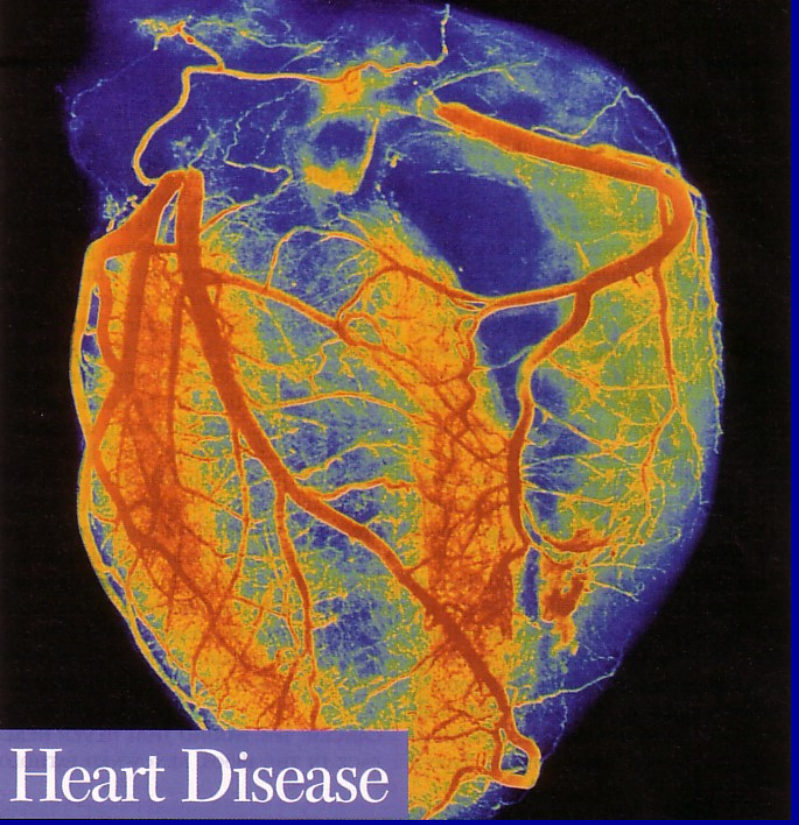
Steno-2: učinki intenzivne, celostne obravnave diabetikov



Gaede P, *et al*. *N Engl J Med* 2003; 348:383–393.

Dejavniki tveganja za koronarno bolezen pri diabetiku tipa 2

1. LDL
2. HDL
3. HbA1c
4. Sistolni RR
5. Kajenje



- 75-80% DM2 umre zaradi IBS, CVI
- IBS 2-4x pogostejša kot nediabetiki
- 1od 4 bolnikov z AMI ima DM2

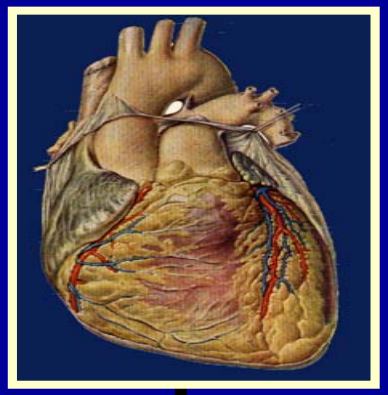
Diabetes je močan dejavnik tveganja!

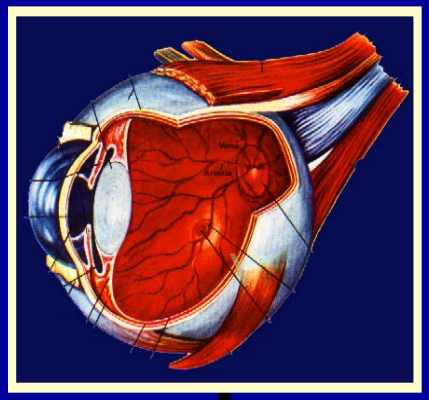
Terapevtični cilji pri osebah s sladkorno boleznijo 2005

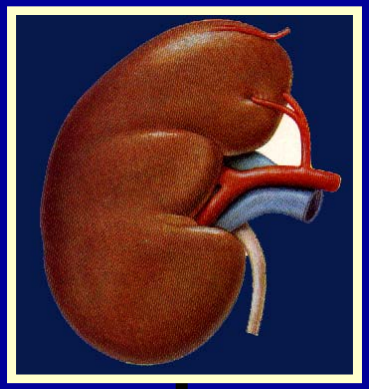
Parameter	Vrednost
HbA1c (DCCT stand.)	≤ 6,1 %
KS na tešče	≤ 6,0 mmol/l
Samok. KS na tešče	4,0 - 5,0 mmol/l
Samok. KS pp	4,0 - 7,5 mmol/l
Krvni tlak	< 130 / 80 mmHg
Holesterol	< 4,5 mmol/l
LDL holesterol	< 2,5 mmol/l

European guidelines on cardiovascular disease prevention in clinical practice.
Konsenz združenj: IDF Euro, EASD, EAS, EHN, ESC, ESH, ISBM, ESGP/FM.
European Heart Journal 2003; 24:1601-10, ADA 2005

Kronične okvare: obravnava







Detekcija

Detekcija

Detekcija

Detekcija

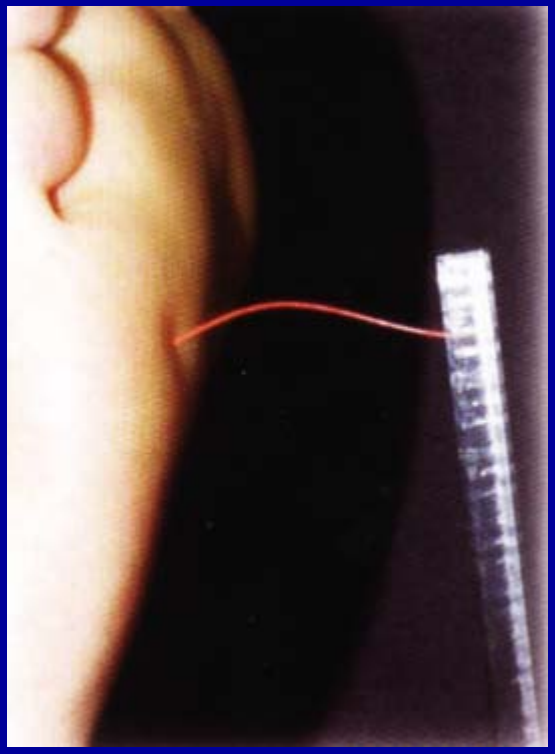
Anamneza
EKG

Fundi

PU, µAU

Presejalni test
-Pulz?
-Inspekcija
-Senzibiliteta?

Terapija + obravnava z ustreznimi specialisti, če je potrebno

Pregled očesnega ozadja

Varovanje nog