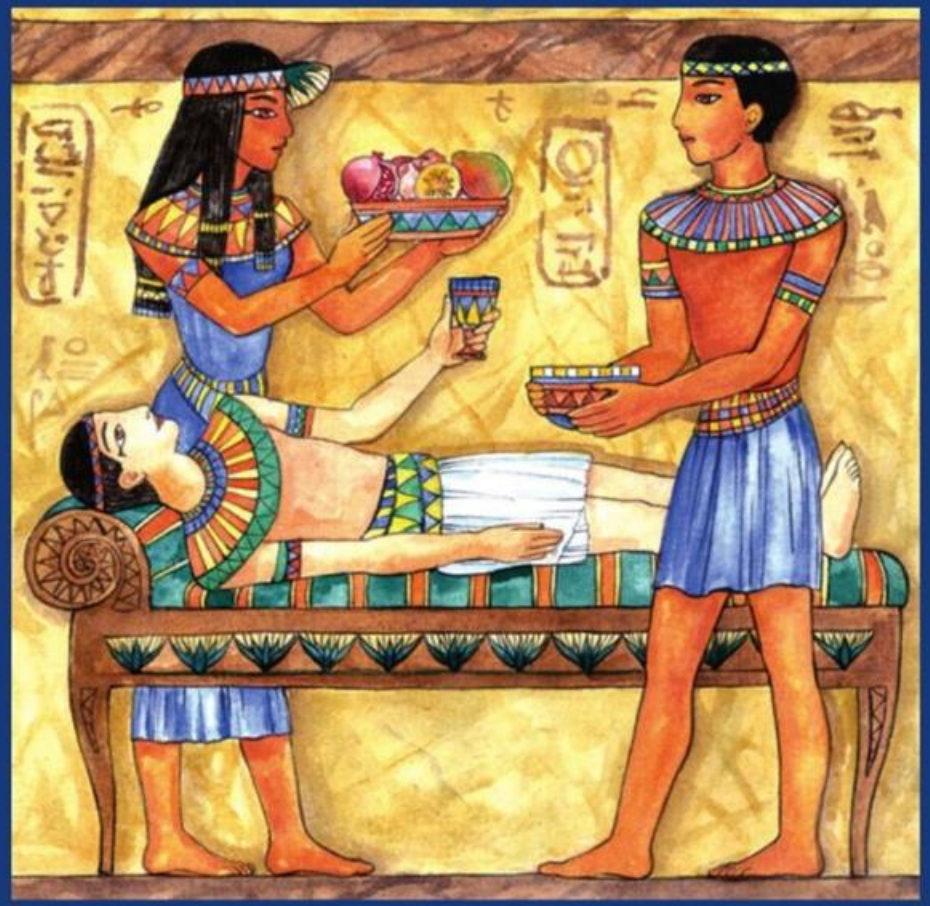
HISTORY OF DIABETES

The Young Doctors Collection™

The Story of the Discovery of

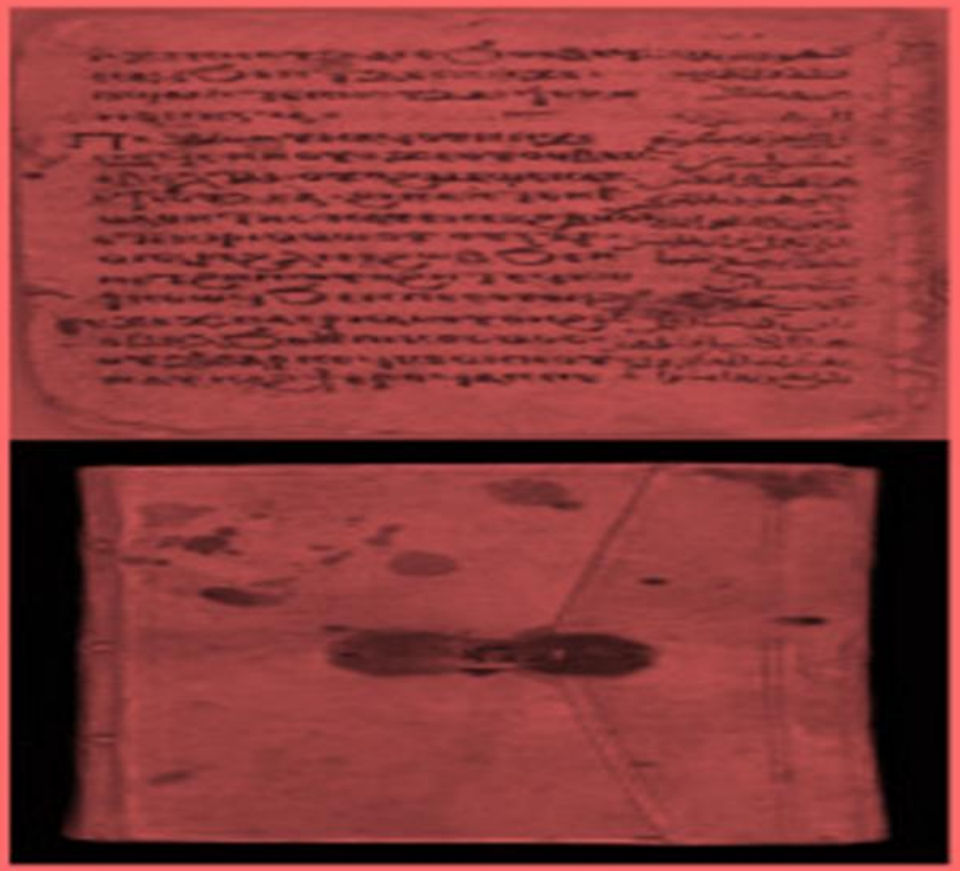
Insulin



By Kun Yan, M.D., Ph.D.
Illustrated by Olga Zakharova

DIABETES

- One of the first diseases described with an EGYPTIAN MANUSCRIPT from1500BC.
  mentioning "too great emptying of the urine"



HISTORY

HISTORY

- Greek physicians and ancient Hindu physicians, used to taste the patient's urine to detect abnormal constituents.
- This unpleasant practice perhaps enabled them to detect diabetic patients.

Ramachandran A, A K Das. Diabetology. In Shah SN eds. API Textbook of Medicine. 7th ed. The Association of Physicians, Mumbai; 1097-1136.

History of Diabetes

First known reference comes from an Egyptian papyrus dating back to 1550 BC

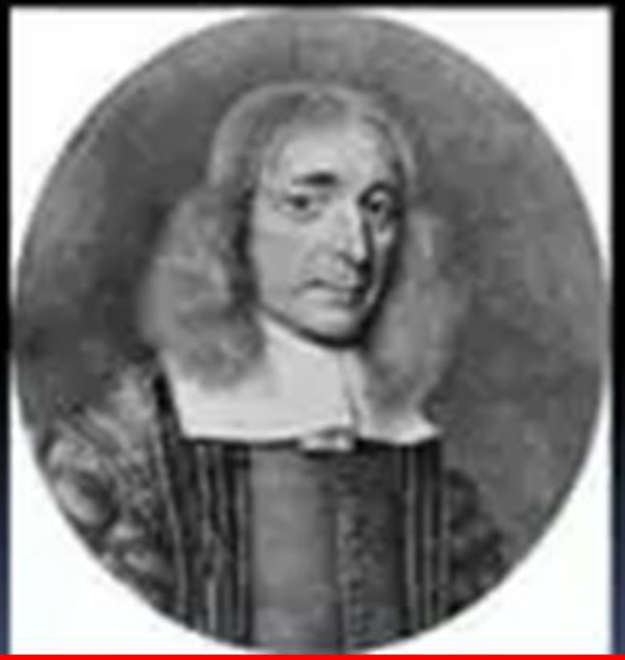
Diabetes was named by the Greek physician Aretaeus between 30 and 90 AD

Additional History About Diabetes

- 17th century AD: Thomas Willis, physician to King Charles II, rediscovered the sweetness in the urine of subjects with diabetes.
- 1776: Matthew Dobson showed that urinary sweetness was caused by sugar and was associated with a rise in blood sugar.

- 1674 AD: Dr Thomas Willis, Physician of King Charles-I first used the word "Diabetes Mellitus"

Mellitus → (Latin)
honey sweet

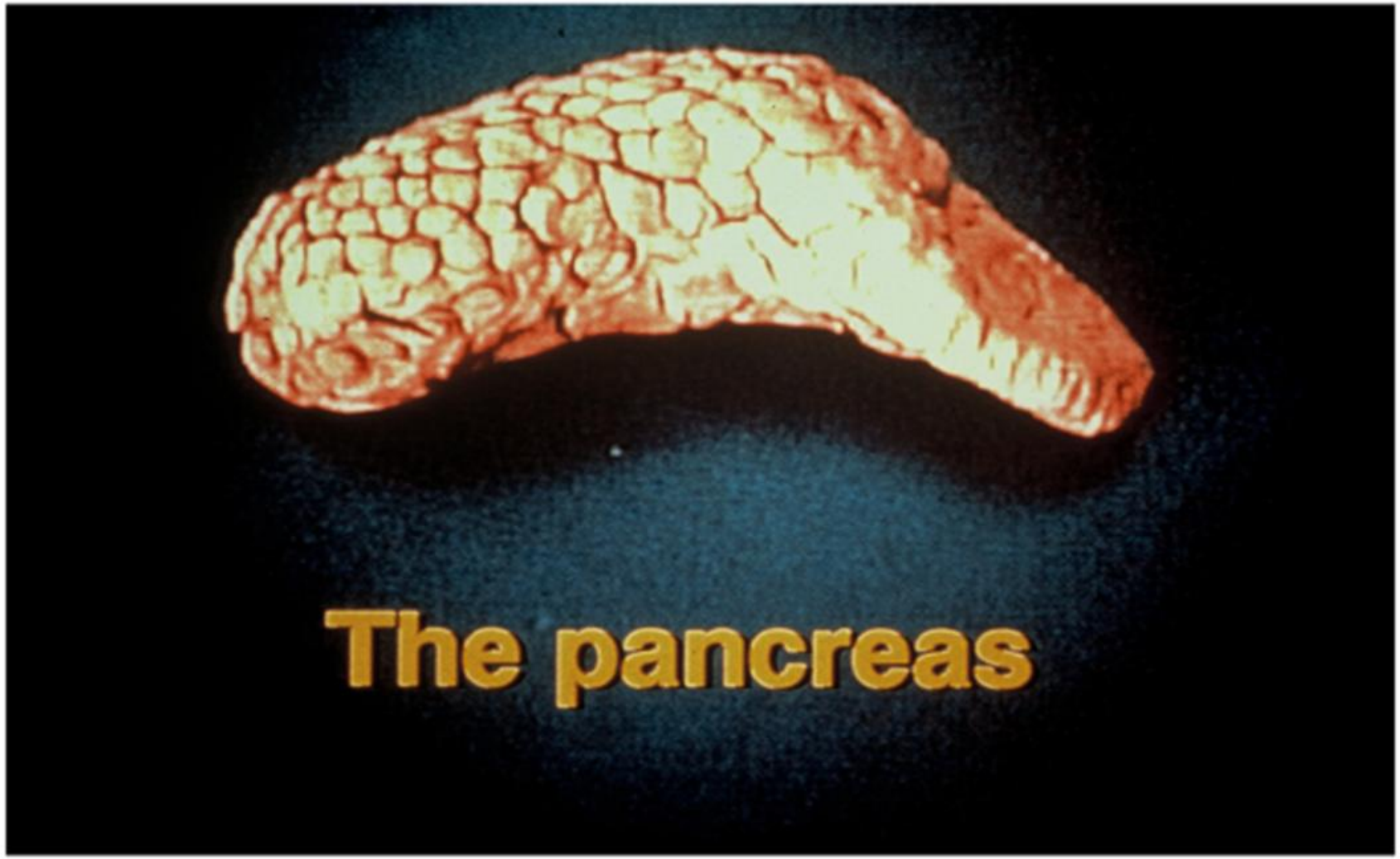


1869

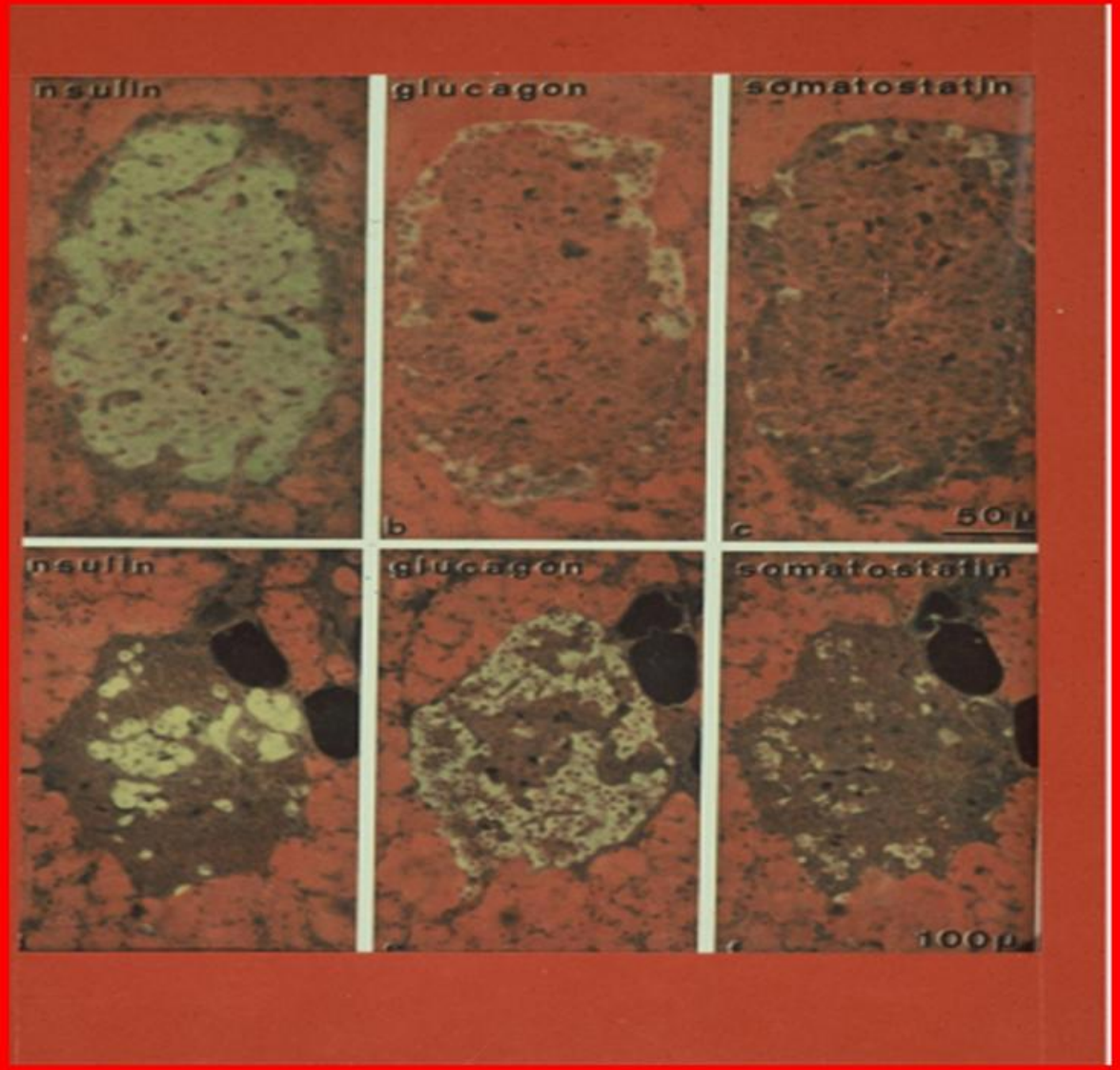
Diabetes R&D

Paul Langerhans, a medical student in Berlin, discovers a collection of unknown pancreatic cells, which would later play a central role in the discovery of insulin.

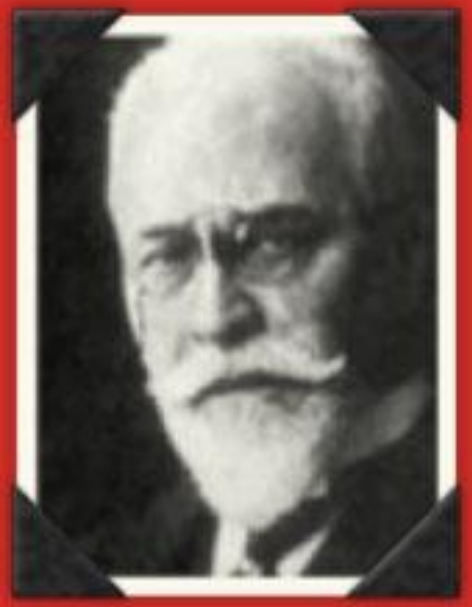
Lilly


The pancreas

ISLETS OF LANGERHANS



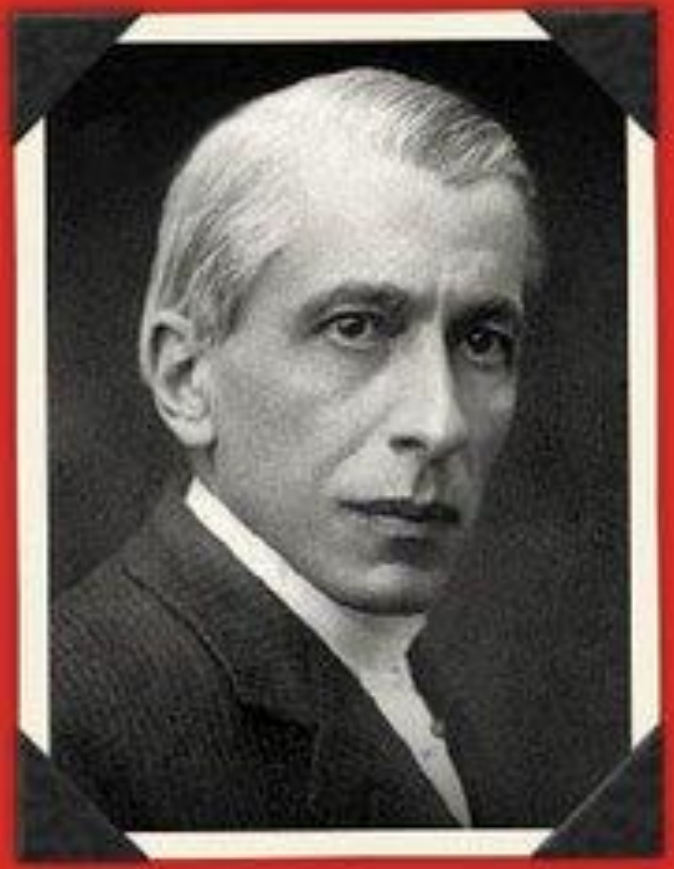
1889 Discovery of Insulin



Drs. Minkowski & von Mering conclude that the cluster of pancreatic cells discovered by Paul Langerhans produces a substance, later known as insulin.

Lilly

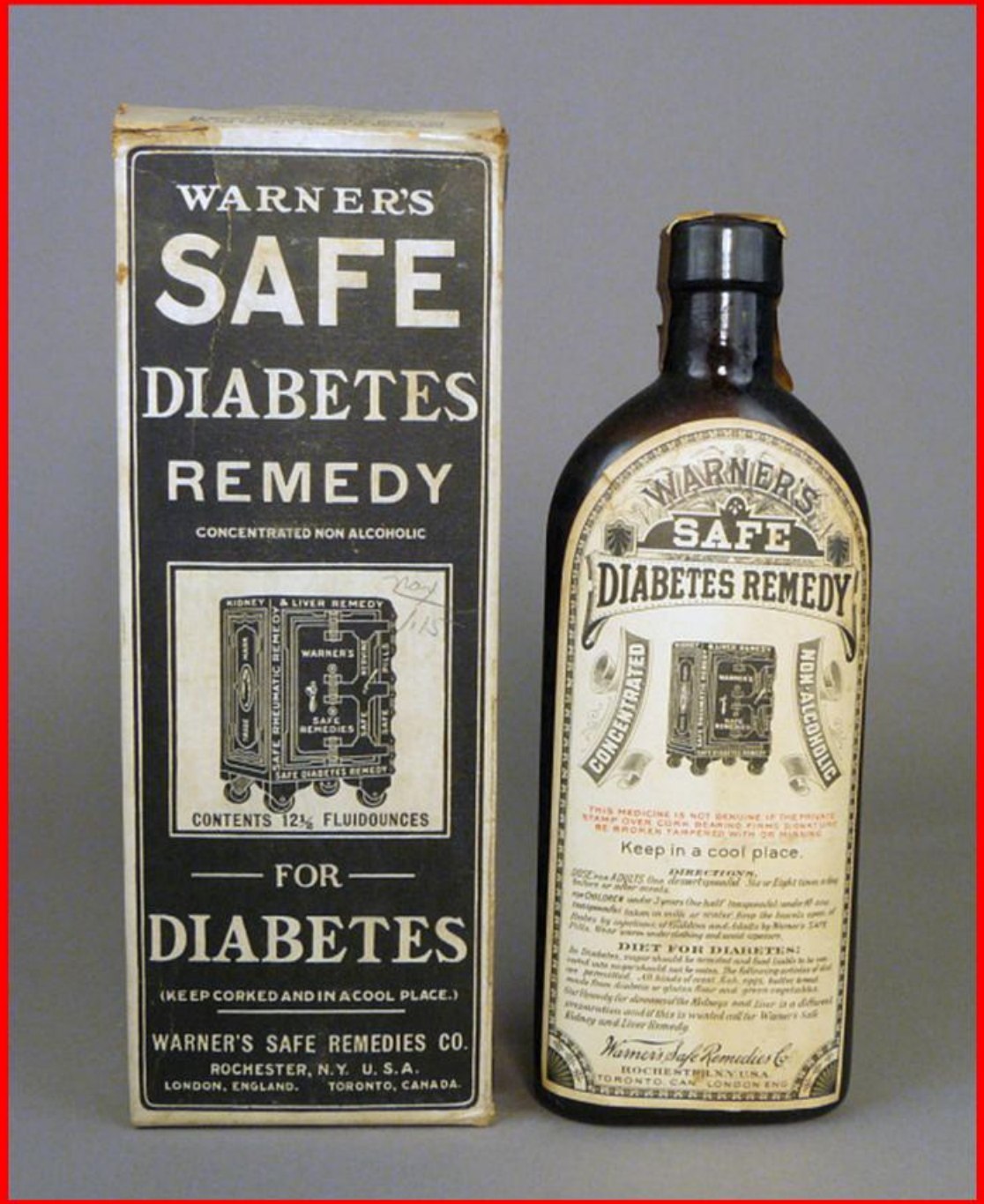
1916 Insulin R&D Efforts Continue



Romanian Professor Nicolae Paulescu develops an extract of the pancreas showing that it lowers blood sugar in dogs with diabetes.

Lilly


AMAZING
TIME-TRAVEL DRINK
ONE SIP! Just one sip of Time Travel Fluid will accelerate you immediately through time! Instant ~ positive relief ~ from the present. INCLUDED Free easy to read Dosage Chart *helps* you control time direction and distance.
The PURE ESSENCE OF TIME
Science IN A BOTTLE
GUARANTEED TO BE 100% FREE FROM *MOST* TEMPORAL PARADOXES
SINCE 1948
Pure TIME TRAVEL DRINK
New EFFERVESCENT TAR-COAL FLAVOR!


WARNER'S
SAFE
DIABETES
REMEDY
CONCENTRATED NON ALCOHOLIC
KIDNEY & LIVER REMEDY
SAFE RHEUMATIC REMEDY
WARNER'S
SAFE REMEDIES
SAFE DIABETES REMEDY
CONTENTS 12½ FLUIDOUNCES
FOR
DIABETES
(KEEP CORKED AND IN A COOL PLACE.)
WARNER'S SAFE REMEDIES CO.
ROCHESTER, N.Y. U.S.A.
LONDON, ENGLAND. TORONTO, CANADA.
WARNER'S
SAFE
DIABETES REMEDY
CONCENTRATED
NON ALCOHOLIC
Keep in a cool place.
DIRECTIONS.
DIET FOR DIABETES:
Warner Safe Remedies Co.
ROCHESTER N.Y. U.S.A.
TORONTO, CAN. LONDON ENG.

Dr. Banting and Best with Marjorie at University of Toronto

One by one, the scientists moved through the ward, injecting each child with insulin. As the hours passed, the quiet, deathly still room began to transform. Children who had been comatose were sitting up, talking, and eating for the first time in days.

The first (human) patient treated with insulin

Leonard Thompson
(1908 – 1935)

Dying from diabetes, he was the first human to get the extract in January 1922

Survived until the age of 27.

Banting FG, Best CH, Macleod JJR. *Am J Physiol.* 1922;59:479.

DEAR DR. BANTING,

I WISH YOU COULD COME TO SEE ME. I AM A FAT BOY NOW AND I FEEL FINE. I CAN CLIMB A TREE. MARGARET WOULD LIKE TO SEE YOU.

LOTS OF LOVE FROM

TEDDY RYDER

CHARLES EVANS HUGHES AND MARY HUGHES

DAUGHTER OF U.S. SECRETARY OF STATE TRIES NEW TORONTO DISCOVERY.

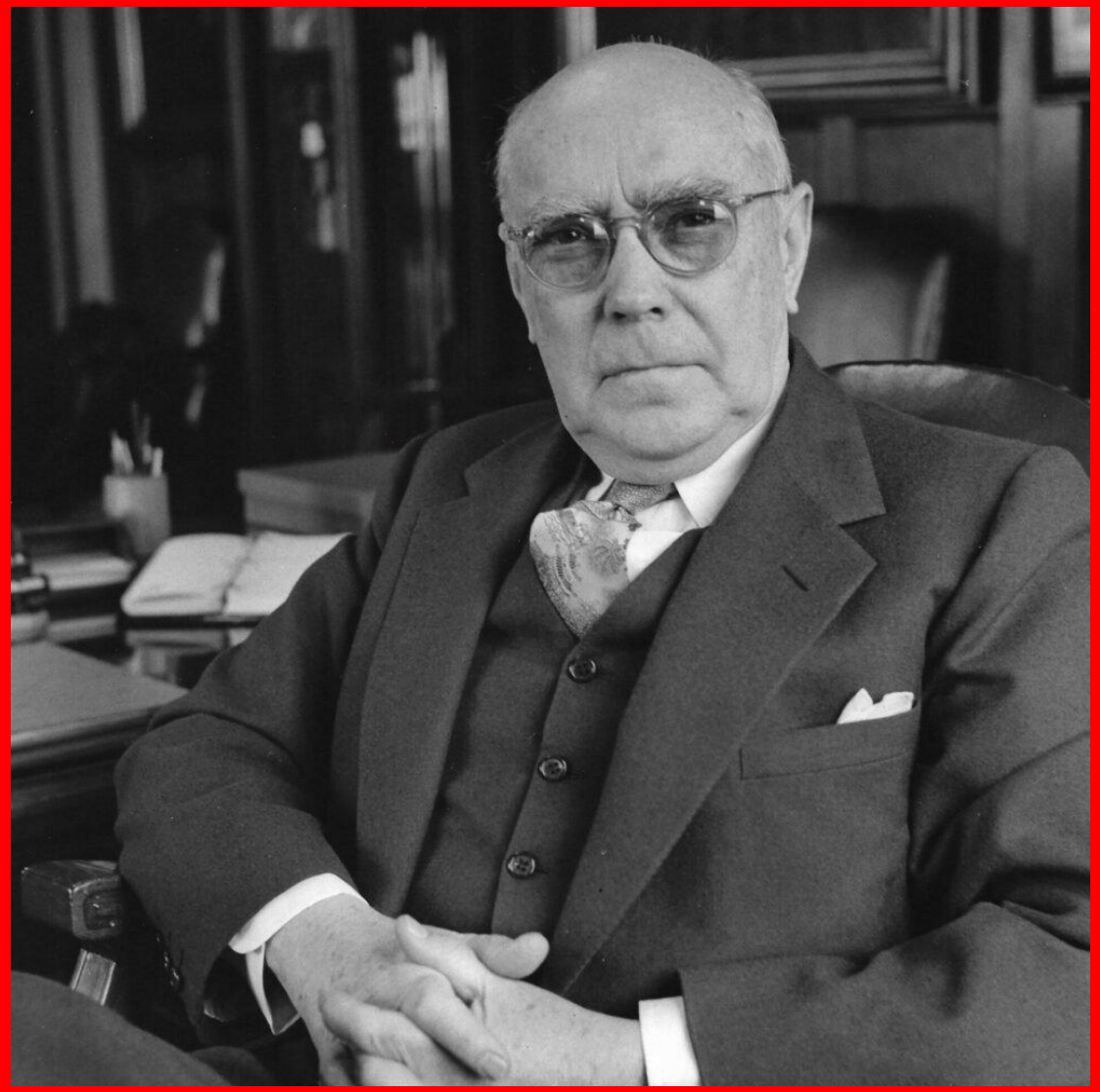
On the left is Mrs. Charles Evans Hughes, who accompanied her daughter to Toronto this week to take a new treatment for diabetes, which has been worked out at the University of Toronto. In the centre is her fifteen-year-old daughter, who is here to take the treatment. On the right is Dr. F. G. Banting, 140 Bloor street west, who is the originator of the insulin treatment for diabetes, and who for over a year has been doing research work along with Mr. C. H. Best, of Toronto. The new treatment has already prolonged the lives of many sufferers from the disease.

“

Insulin does not belong to
it belongs to the world.’

FREDERICK BANTING

ELI LILLY

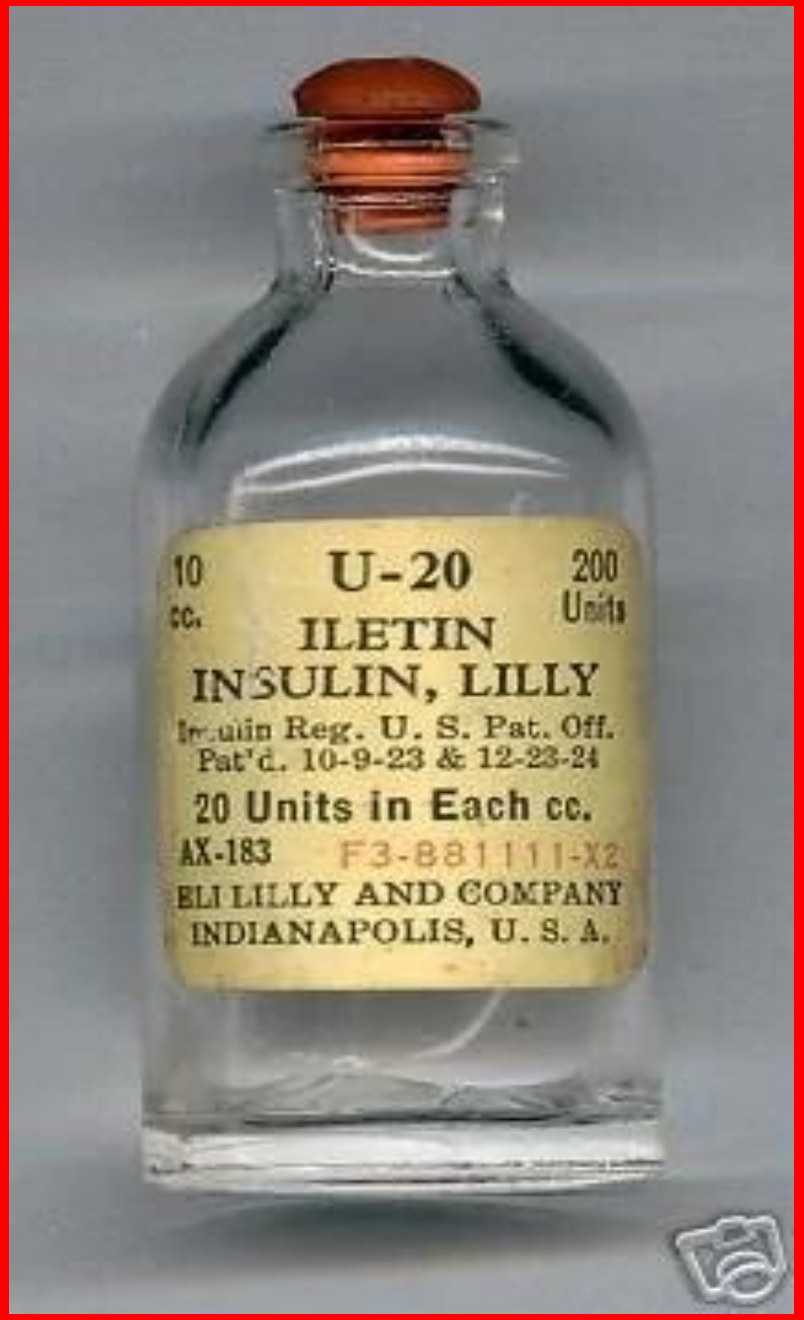


ELLIOT JOSLIN

HANS CHRISTIAN HAGEDORN


INSULIN

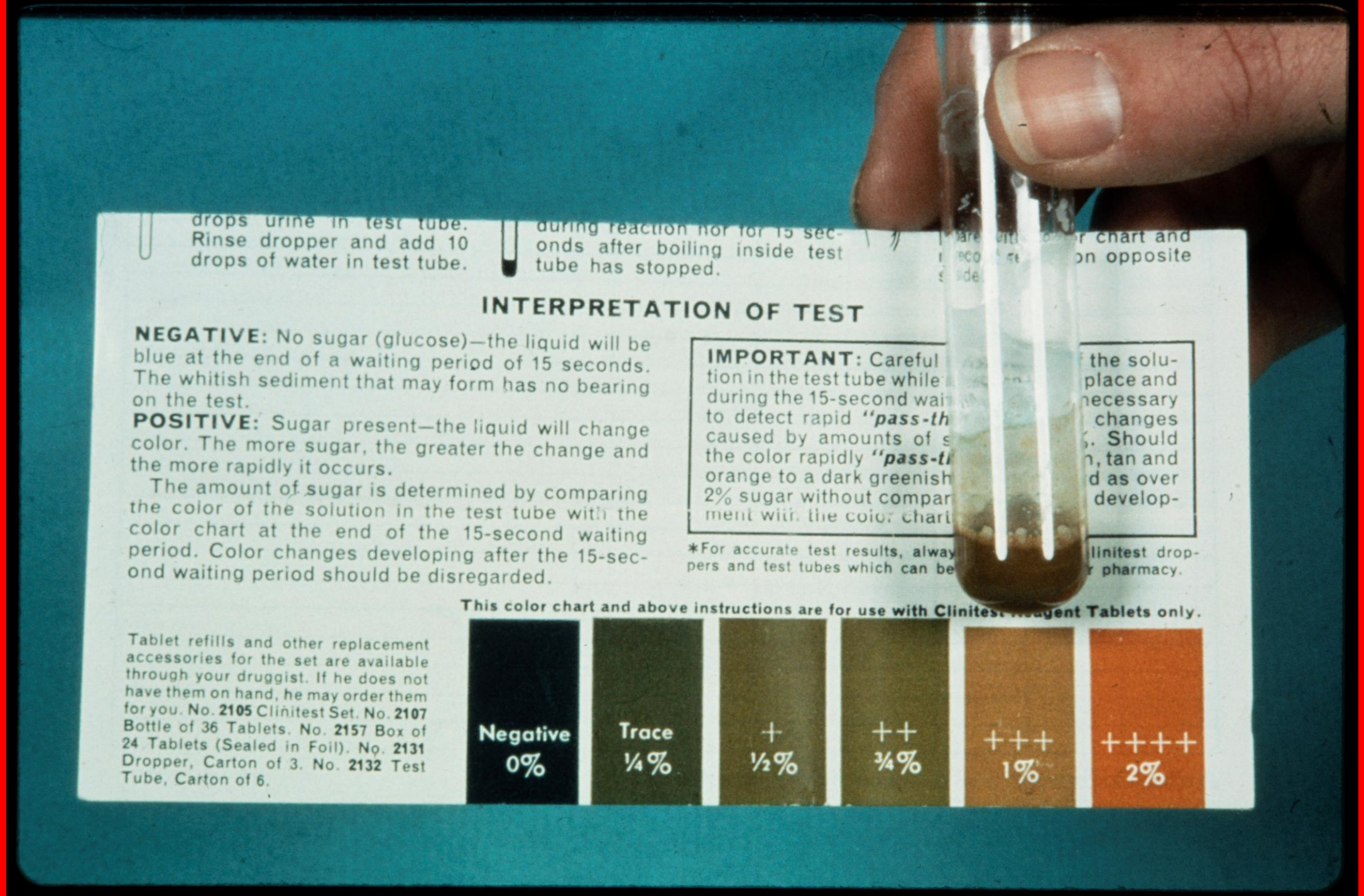
INSULIN FROM ANIMAL PANCREASES


10
cc.
U-20
200
Units
ILETIN
INSULIN, LILLY
Insulin Reg. U. S. Pat. Off.
Pat'd. 10-9-23 & 12-23-24
20 Units in Each cc.
AX-183
ELI LILLY AND COMPANY
INDIANAPOLIS, U. S. A.


10 ml
Novolin L
Zinc Suspension
recombinant DNA origin
10 ml
Novolin N
NPH, Human Insulin
Isophane Suspension
recombinant DNA origin

Diabetes in the 1950s


LOT 1495648-45F
Urine Glucose Test
REF 998575 34X
DATE OF USE 17.05.25


drops urine in test tube. Rinse dropper and add 10 drops of water in test tube.
during reaction for 15 seconds after boiling inside test tube has stopped.
chart and
on opposite
INTERPRETATION OF TEST
NEGATIVE: No sugar (glucose)—the liquid will be blue at the end of a waiting period of 15 seconds. The whitish sediment that may form has no bearing on the test.
POSITIVE: Sugar present—the liquid will change color. The more sugar, the greater the change and the more rapidly it occurs.
The amount of sugar is determined by comparing the color of the solution in the test tube with the color chart at the end of the 15-second waiting period. Color changes developing after the 15-second waiting period should be disregarded.
IMPORTANT: Careful
the solution in the test tube while
place and
during the 15-second wai
necessary
to detect rapid "pass-th
changes
caused by amounts of s
. Should
the color rapidly "pass-ti
n, tan and
orange to a dark greenish
d as over
2% sugar without compar
develop-
ment with the color chart
*For accurate test results, alway
linitest drop-
pers and test tubes which can be
r pharmacy.
This color chart and above instructions are for use with Clinitest Reagent Tablets only.
Tablet refills and other replacement accessories for the set are available through your druggist. If he does not have them on hand, he may order them for you. No. 2105 Clinitest Set. No. 2107 Bottle of 36 Tablets. No. 2157 Box of 24 Tablets (Sealed in Foil). No. 2131 Dropper, Carton of 3. No. 2132 Test Tube, Carton of 6.
Negative 0%
Trace ¼%
+ ½%
++ ¾%
+++ 1%
++++ 2%

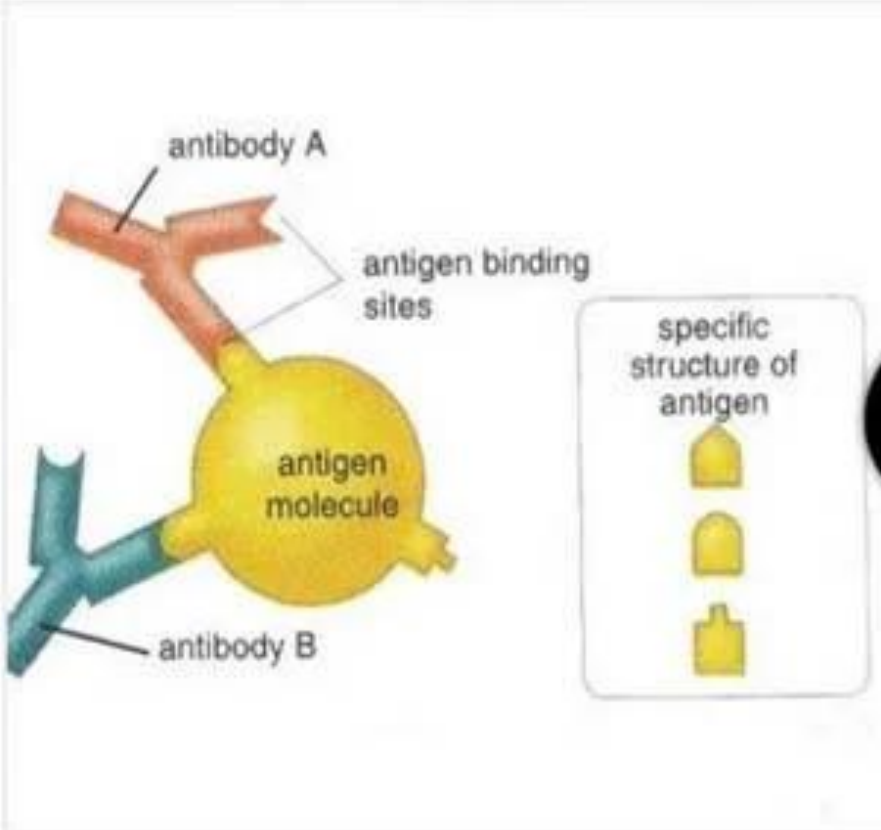

TES-TAPE
Rapid
Convenient
Tes-Tape


OZ
OZ
OZ BY 1/4

SYRINGES AND NEEDLES

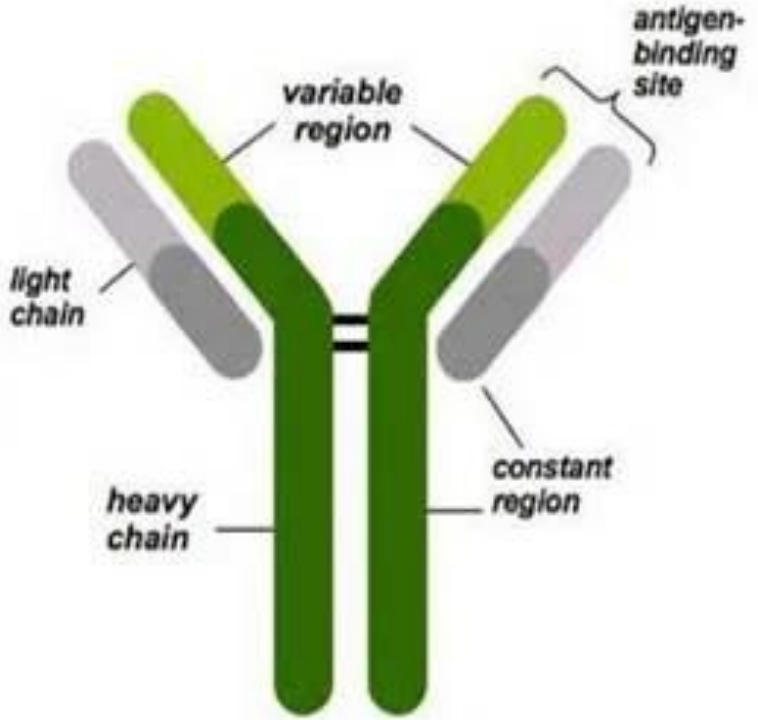
INSULIN INJECTION COMPLICATIONS

Antigens



VS

Antibody

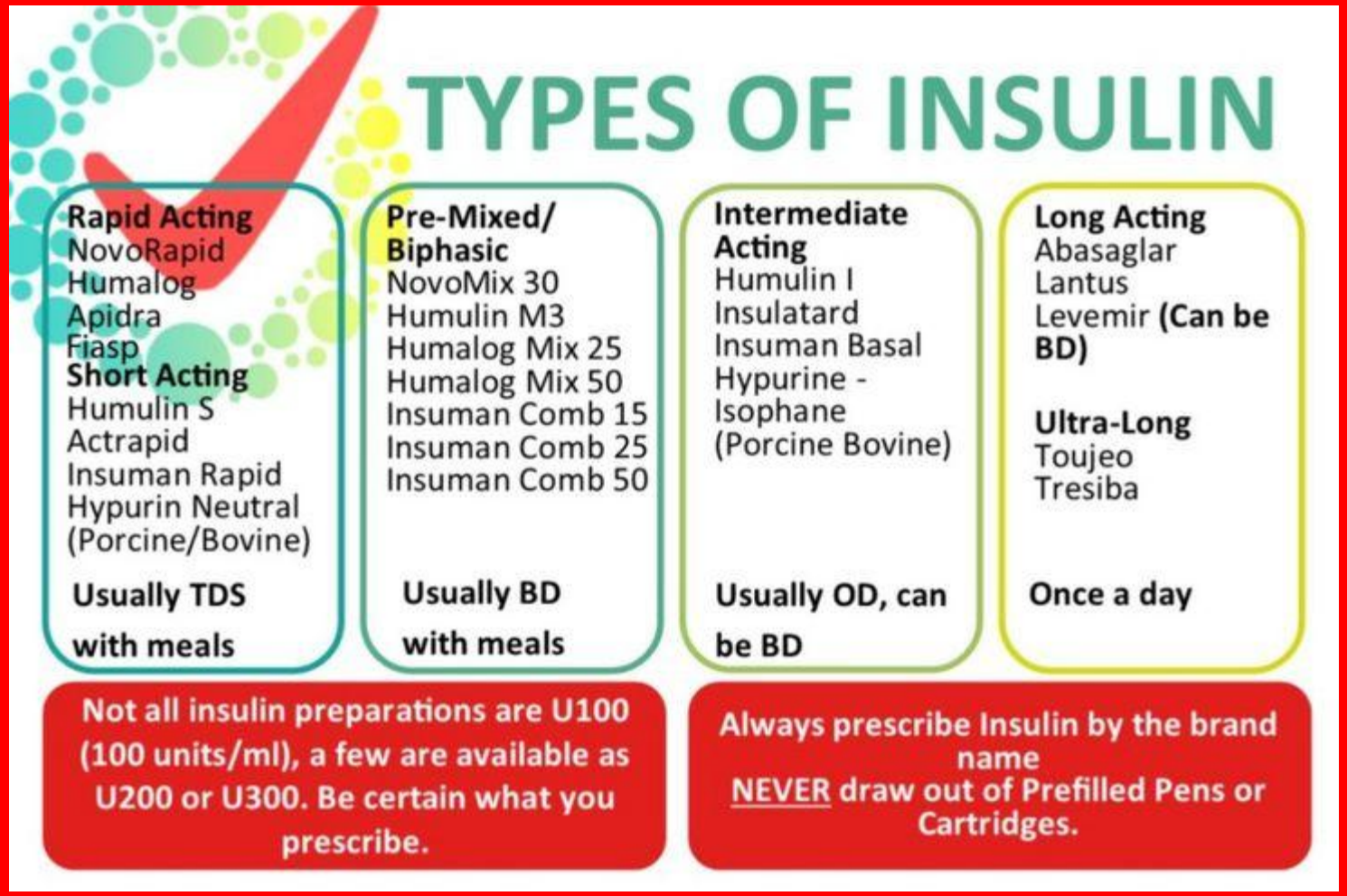



Human insulin production
by
Recombinant DNA technology
www.onlinebiologynotes.com


A
Lantus
insulin glargine
injection
100 units/mL
10mL vial
Aventis Pharmaceuticals
50019386
B
Humalog
insulin lispro injection
U-100
Humalog Mix75/25
Humalog Mix50/50
Humulin N
Humulin 70/30
Humulin R
C
Apidra®
insulin glulisine
(rDNA origin) injection
100 units/mL
(U-100)
FOR USE ONLY IN OPTICLIK® INSULIN DELIVERY DEVICE
FOR SUBCUTANEOUS USE ONLY
USE ONLY IF SOLUTION IS CLEAR AND COLORLESS WITH NO PARTICLES VISIBLE
℞ ONLY
sanofi aventis
D
Levemir®
Insulin detemir
(rDNA origin) Injection
100 units/mL (U-100)
10 mL
Important: See insert
Avoid freezing

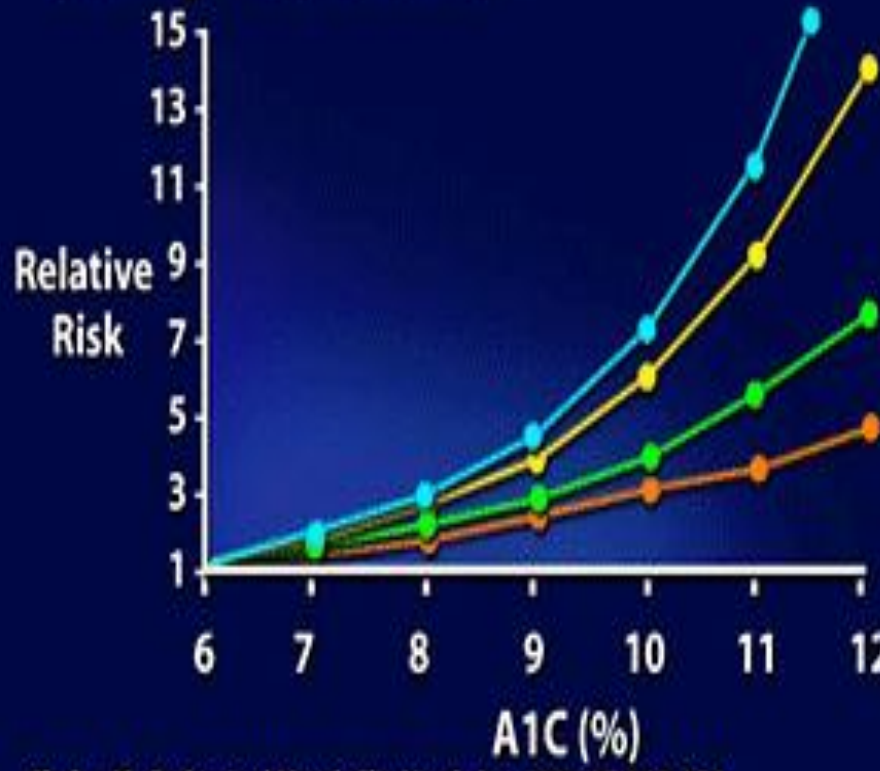

INSULIN
Lantus
insulin glargine
100
LANTUS
LONG-ACTING INSULIN


ONCE WEEKLY USE


TYPES OF INSULIN
Rapid Acting
NovoRapid
Humalog
Apidra
Fiasp
Short Acting
Humulin S
Actrapid
Insuman Rapid
Hypurin Neutral
(Porcine/Bovine)
Usually TDS
with meals
Pre-Mixed/
Biphasic
NovoMix 30
Humulin M3
Humalog Mix 25
Humalog Mix 50
Insuman Comb 15
Insuman Comb 25
Insuman Comb 50
Usually BD
with meals
Intermediate
Acting
Humulin I
Insulatard
Insuman Basal
Hypurine -
Isophane
(Porcine Bovine)
Usually OD, can
be BD
Long Acting
Abasaglar
Lantus
Levemir (Can be
BD)
Ultra-Long
Toujeo
Tresiba
Once a day
Not all insulin preparations are U100 (100 units/ml), a few are available as U200 or U300. Be certain what you prescribe.
Always prescribe Insulin by the brand name
NEVER draw out of Prefilled Pens or Cartridges.

ORAL INSULIN

DCCT: A1C and Microvascular Complications



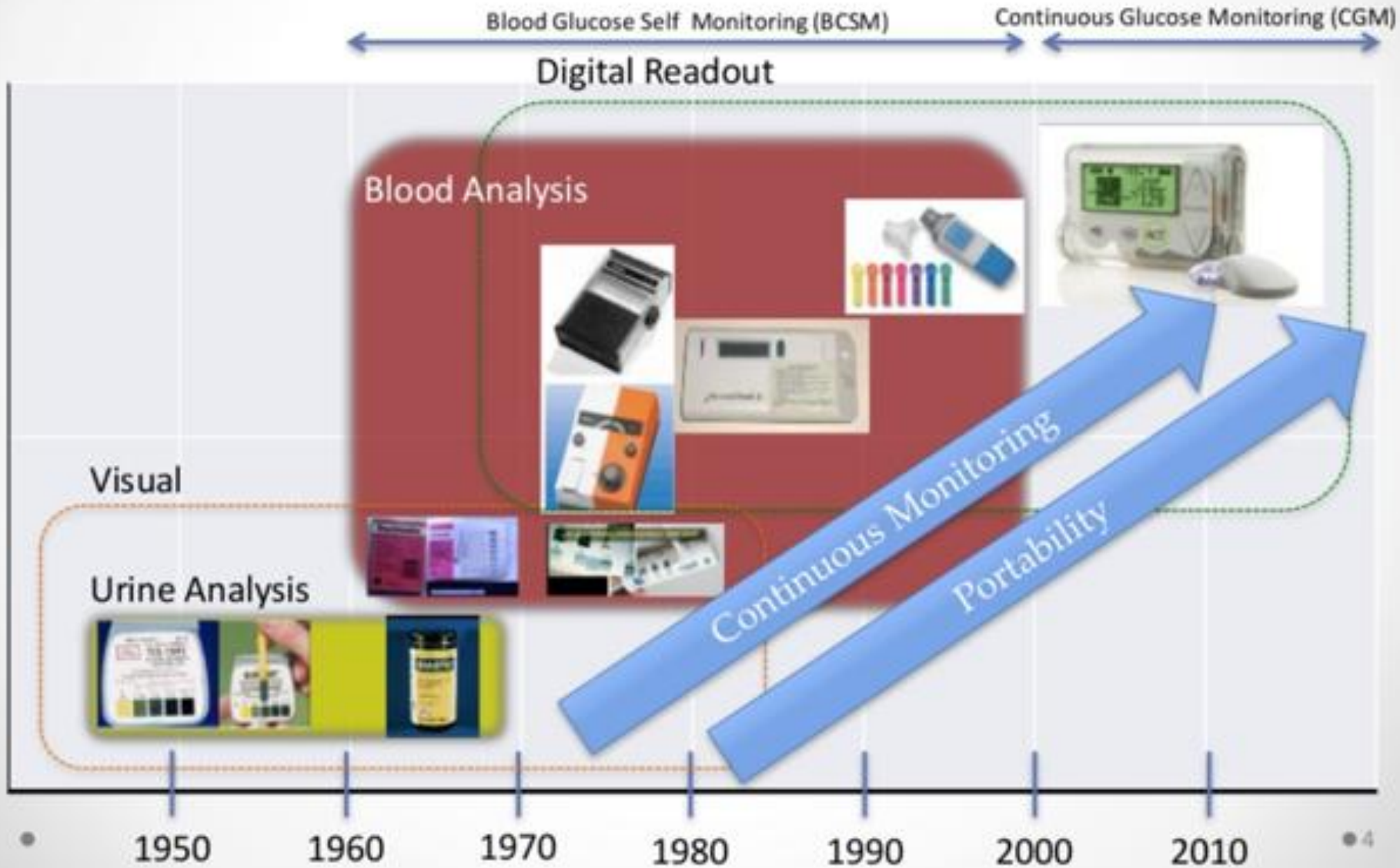
Skyler JS. *Endocrinol Metab Clin North Am.* 1996;25:243-254.

UKPDS: Overview

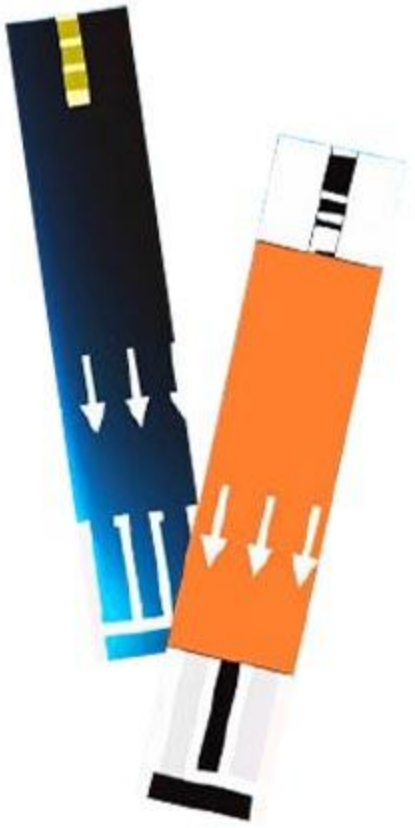
- 20-year, multicentre, prospective, randomised, intervention trial
- 5102 people with newly diagnosed Type 2 diabetes
- FPG >6 mmol/l (108 mg/dl)
- Mean follow-up: 11 years

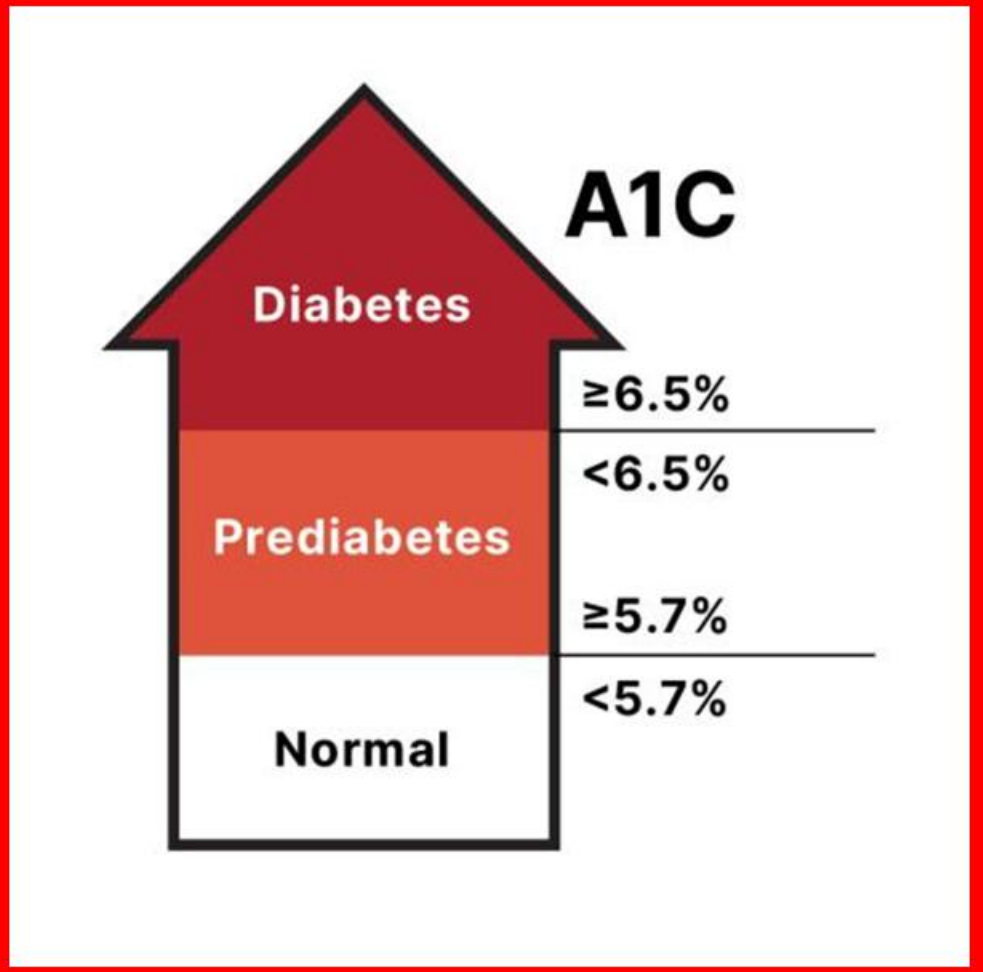
UKPDS Group. Lancet. 1998;352:837–853.

Glucose Meter Evolution



AMES REFLEXOMETER




A1C
Diabetes
≥6.5%
<6.5%
Prediabetes
≥5.7%
<5.7%
Normal


6,3
+0,1


CGM
CONTINUOUS
GLUCOSE
MONITOR
dexcom
10:09 AM
110
8 AM
9 AM
Now
110
8AM
9AM
Now
Events
Settings


DEXCOM
218
mg/dL
12:35
Last
Updated
12:35 PM
3HR
200
80

Early Insulin Pumps


ayto
syringe
Your text here

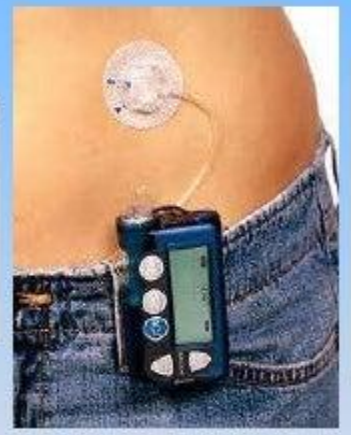

ML
SYRINGE
DISPOSABLE


100%
5:30 PM
14 Nov
300
250
200
150
100
50
INSULIN ON BOARD
OPTIONS
0.1 u
BOLUS
3
HRS

Insulin Pump Evolution

1970s-
early 1980s

1980s



1990s – 2000s

Present

Global Insulin Patch Pumps Market

Richard Lillehei and William Kelly – First successful pancreas transplant - *December 16, 1966*

Dr. Lillehei, transplant of hormonal dis

another co

The ap topic allo operating pendent re conducted sota Hosp lehei and Kelly desc of the prog diabetic uremia pr poor-risk either for dialysis."

First Tran

In the kidney tra transplant the same Kelly bega ago. In coo K. Merkel transplant organ is d tion, whe vein joins the portal pancreatic end overs pancreatic operative tinues to of the pa operation reducing damage to the time th anesthesia.

The ap is professo work begu 1962. Asso Drs. Felix Francisco man, John Idezuki. La

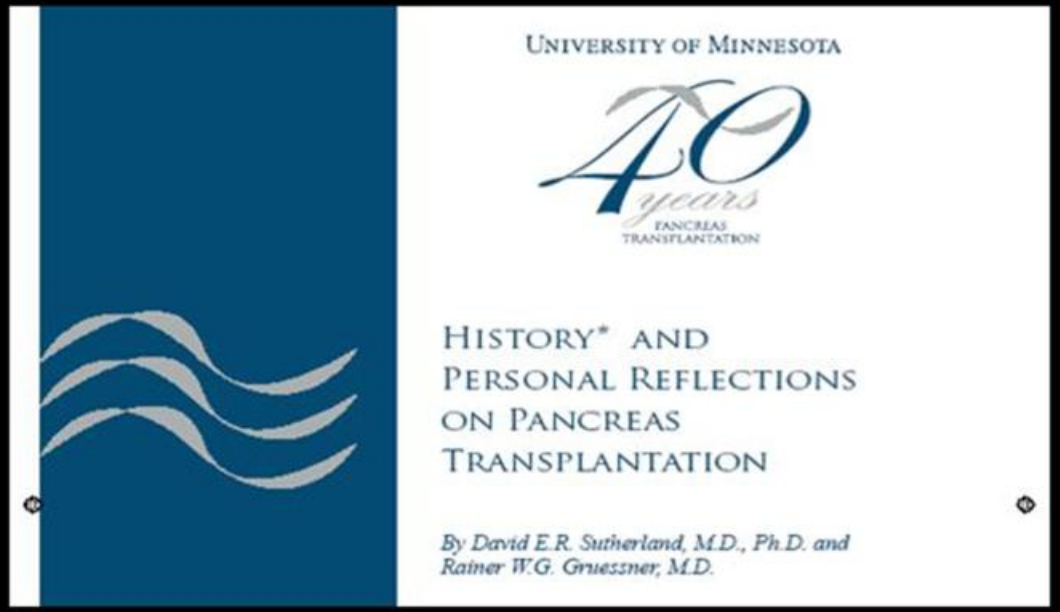
Transplant Of Pancreas Succeeds

Cadaver organ secretes insulin in female diabetic

Minnesota surgeons Richard C. Lillehei and William D. Kelly appear to have achieved the first successful transplantation of a pancreas to a human being. As a result of an operation

tion, she has needed no insulin. A cadaver kidney was implanted in her right iliac fossa at the same time, and she has regained urinary function.

In a procedure developed by Dr. Lillehei, which ensures preservation and control of both exocrine and endocrine functions, the surgical team transplanted an entire pancreas along with its attached duodenum, constituting the whole pancreaticoduodenal system. Drs. Lillehei and Kelly believe that this procedure, along with a separate technique devised by Dr. Kelly in which only part of the pancreas is transplanted and the organ's function is later controlled by postoperative irradiation, may have wide therapeutic use. After further refinement, the operations could not only be useful in treat-



News Alert

FDA Approves First Drug That Can Delay Onset of Type 1 Diabetes

"Teplizumab is the first drug approved as a disease modifying therapy for type 1 diabetes. We at DRI have been working nearly 40 years on trying to develop disease modifying therapies. We participated in the studies of teplizumab, and continue to be involved in multiple studies in this space."

DR. Jay S. Skyler, MD, MACP
Professor of Medicine, Pediatrics, & Psychology, in the Division of Endocrinology Diabetes & Metabolism, Department of Medicine, University of Miami Leonard M. Miller School of Medicine

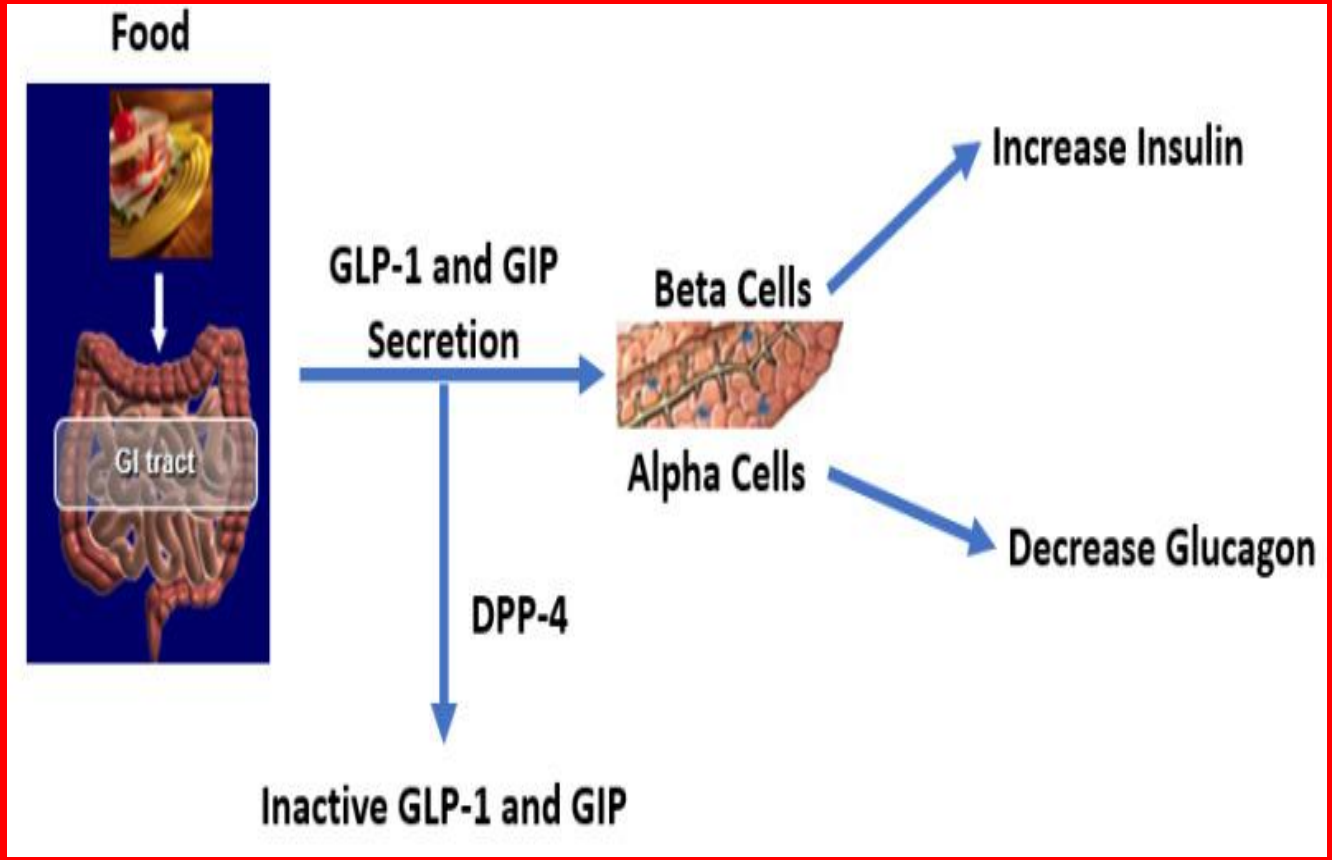
ORAL DIABETES MEDICATIONS

CLASS	DRUG ACTION
BIGUANIDES (METFORMIN)	• Improves insulin sensitivity • Decreases glucose production in liver
THIAZOLADINIDIONES	• Improves insulin sensitivity • Reduces glucose production in liver
DPP-4 INHIBITORS	• Increases pancreatic insulin secretion • Decreases glucagon levels
SULFONYLUREAS	• Increases pancreatic insulin secretion
MEGLITINIDES	• Increases pancreatic insulin secretion
ALPHA GLUCOSIDASE INHIBITORS	• Slows glucose absorption in GI tract
SGLT-2 INHIBITORS	• Increases renal glucose excretion
DOPAMINE-2 AGONISTS	• Decreases glucose production in liver
GLP-1 RECEPTOR AGONISTS	• Increases insulin secretion • Decreases glucagon production

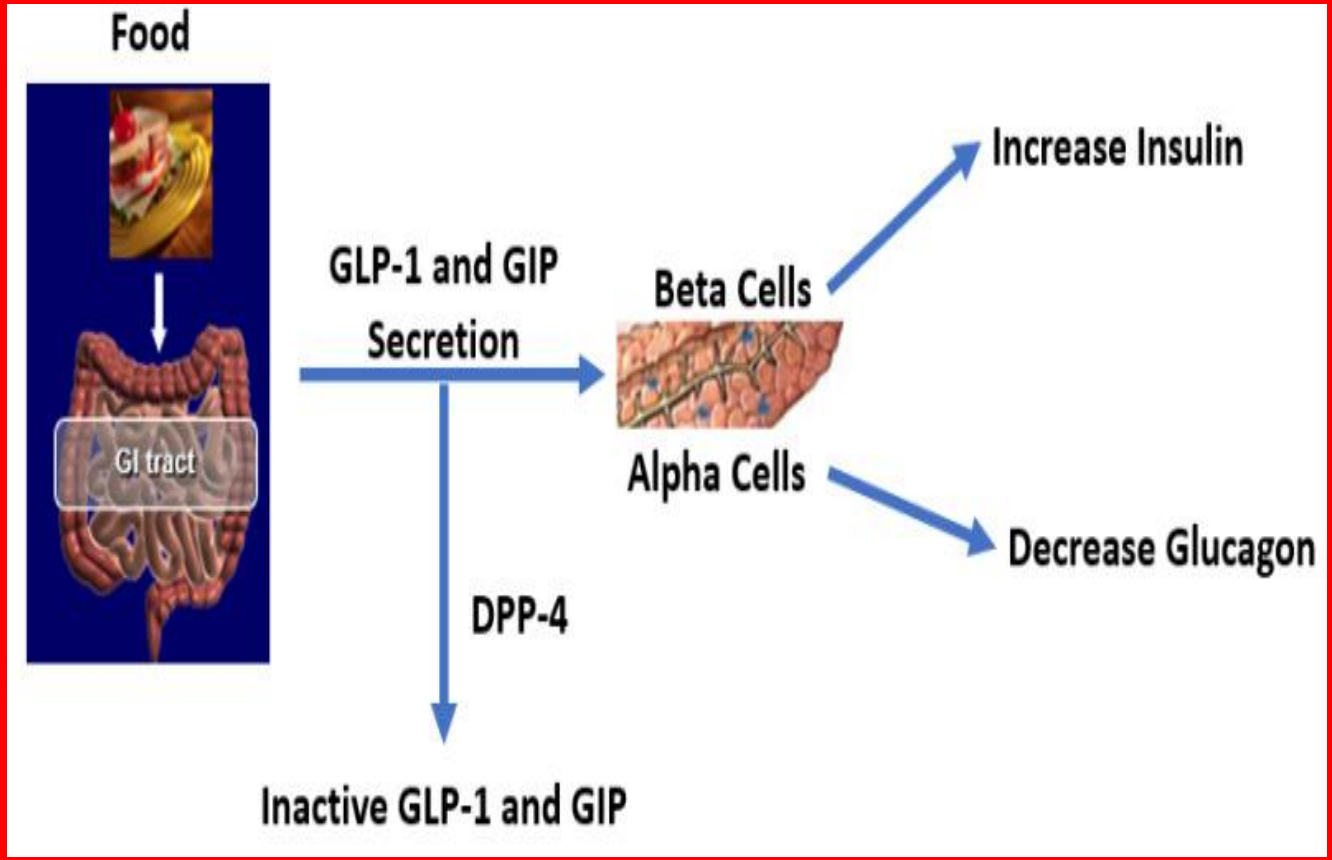
DIETITIANS ON DEMAND

What are my options? American Diabetes Association. https://diabetes.org/healthy-living/medication-treatments/oral-medication/what-are-my-options. Accessed March 8, 2023.
DeFronzo RA. Bromocriptine: A sympatholytic, D2-dopamine agonist for the treatment of type 2 diabetes. Diabetes Care. 2011;34(4):789-794. doi:10.2337/dc11-0064

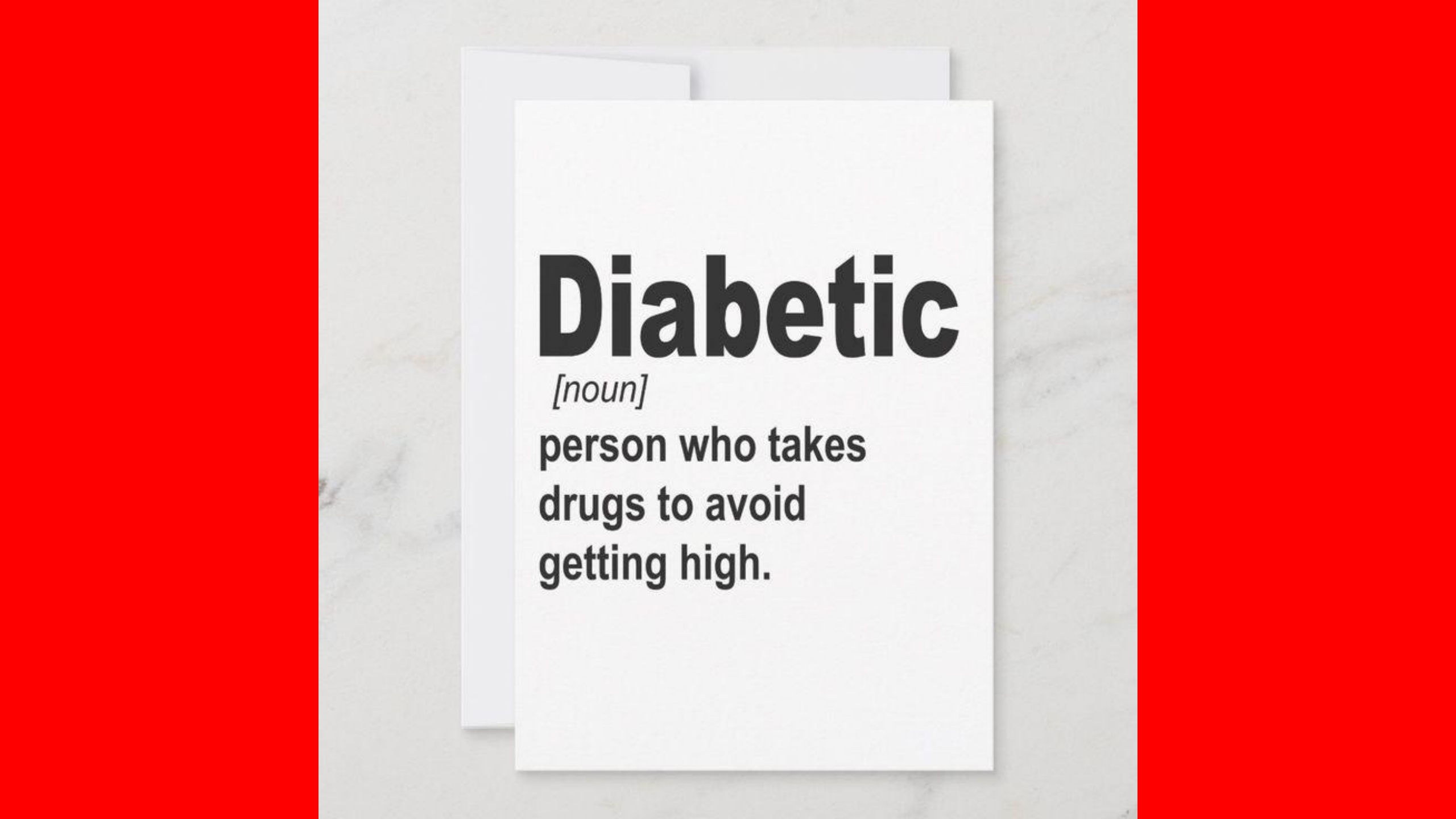
GLP-1 AND GIP AGONISTS



GLP-1 AND GIP AGONISTS

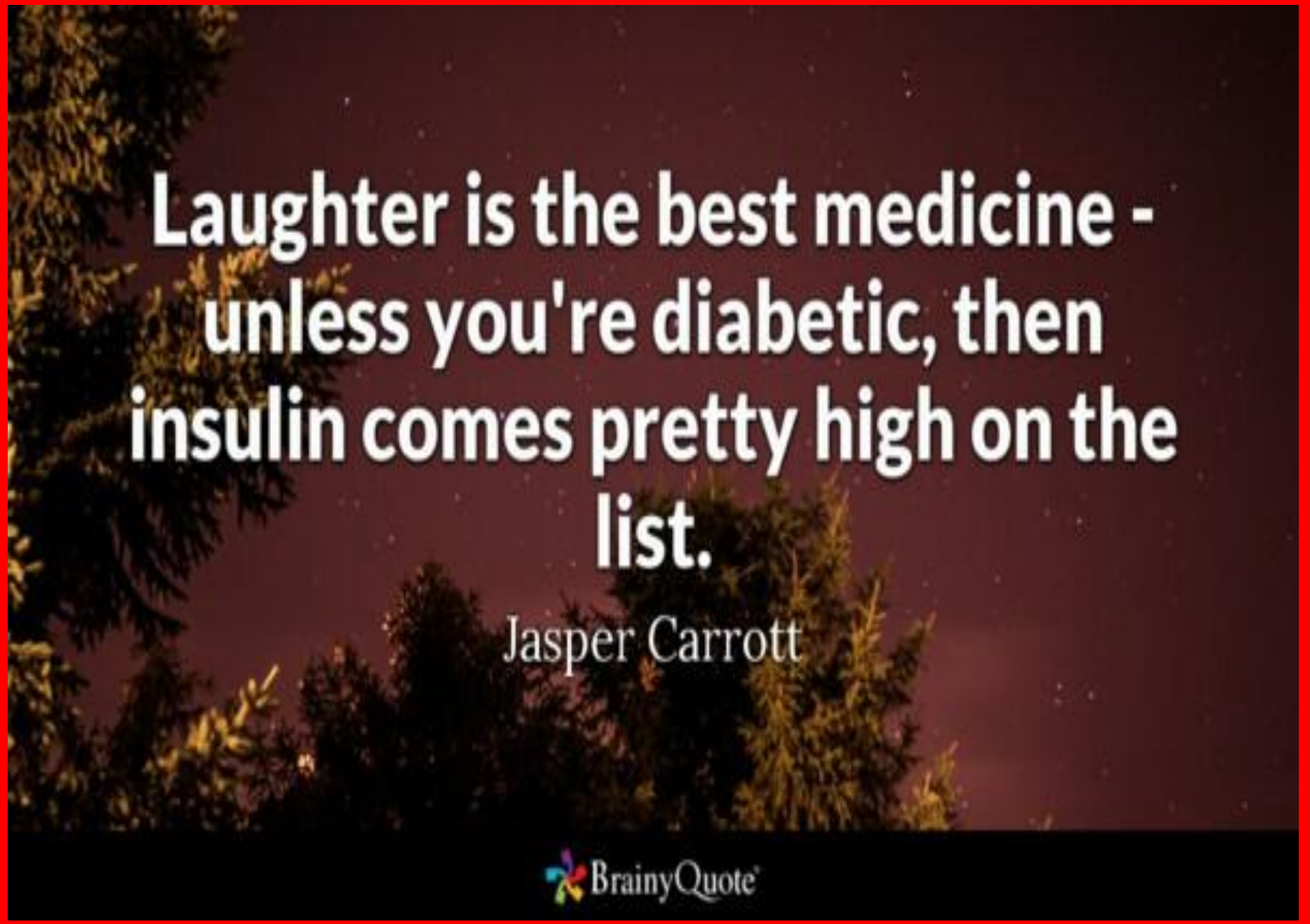


SLG2 INHIBITORS


Diabetic
[noun]
person who takes drugs to avoid getting high.

Diabetes is a FULL-TIME job.

Except you don't get paid, you never get vacation time, and you can't quit.


Laughter is the best medicine - unless you're diabetic, then insulin comes pretty high on the list.
Jasper Carrott
BrainyQuote