بیوشیمی بالینی

روش های سنجش گلوکز

و

ارزیابی بیماری دیابت

Dr H.R.Joshaghani PhD

کربوهیدرات ها

- مقدمه
- هورمون هاي موثر در متابوليسم
- روشهاي اندازه گيري گلوکز

هورمون هاي موثر بر متابوليسم كربوهيدرات ها

- انسولين
- گلوكاگن
- هورمون رشد
- آدرنالين
- گلوكوكورتيكوئيدها (كورتيزول)

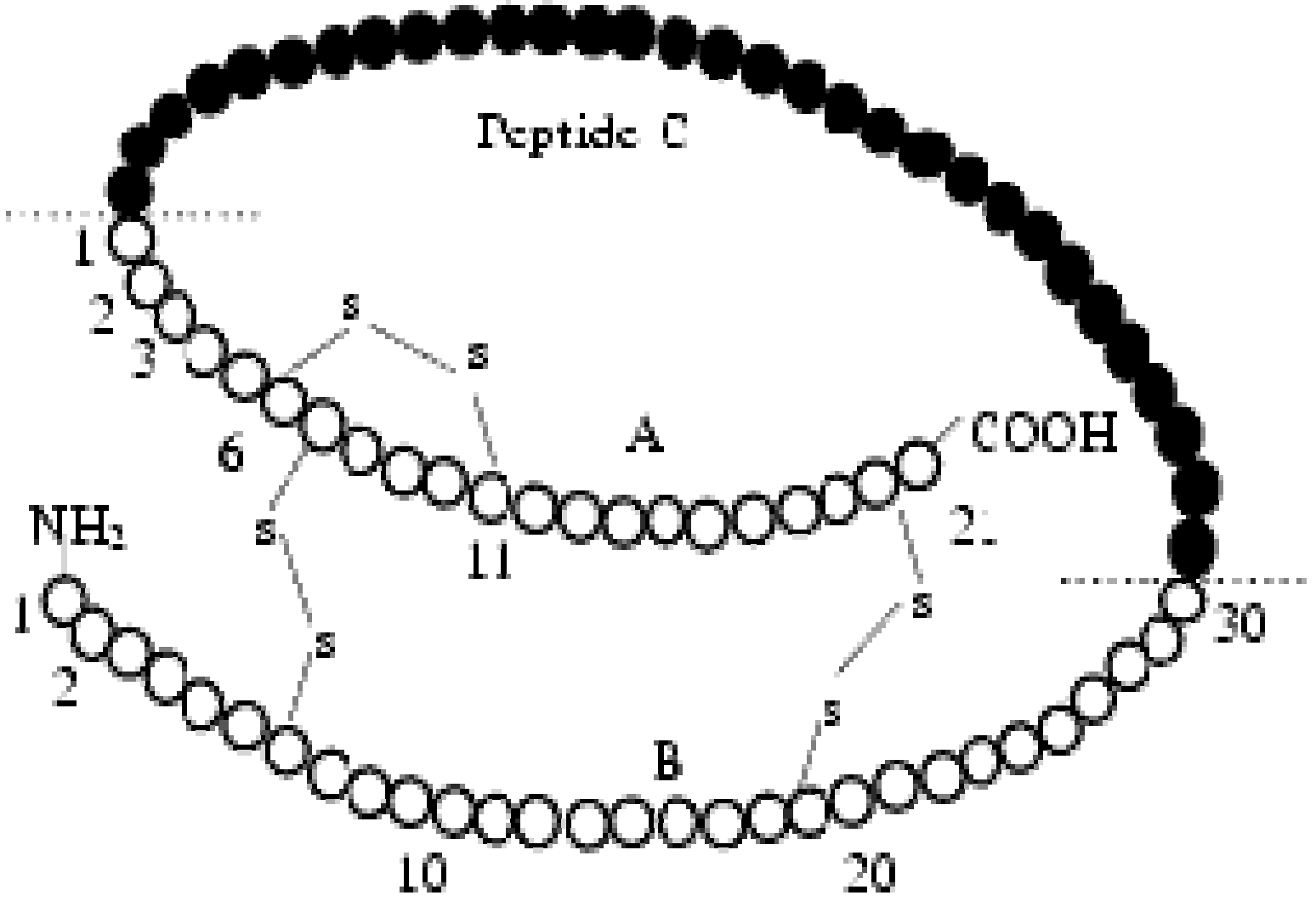
انسولين

- جزاير بتا لانگرهانس
- پپتيدي

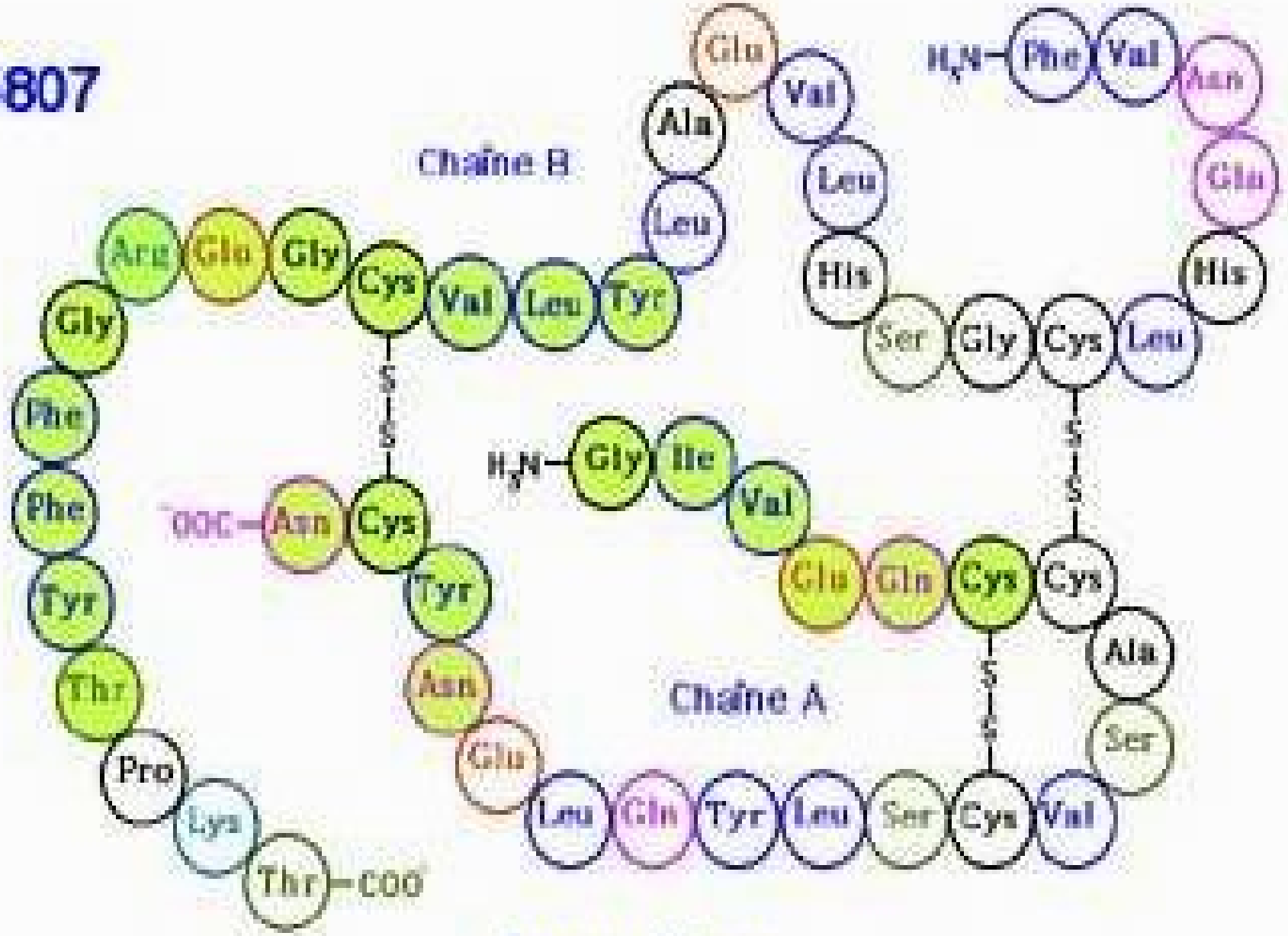
پره پرو انسولين ← پروانسولين ← انسولين

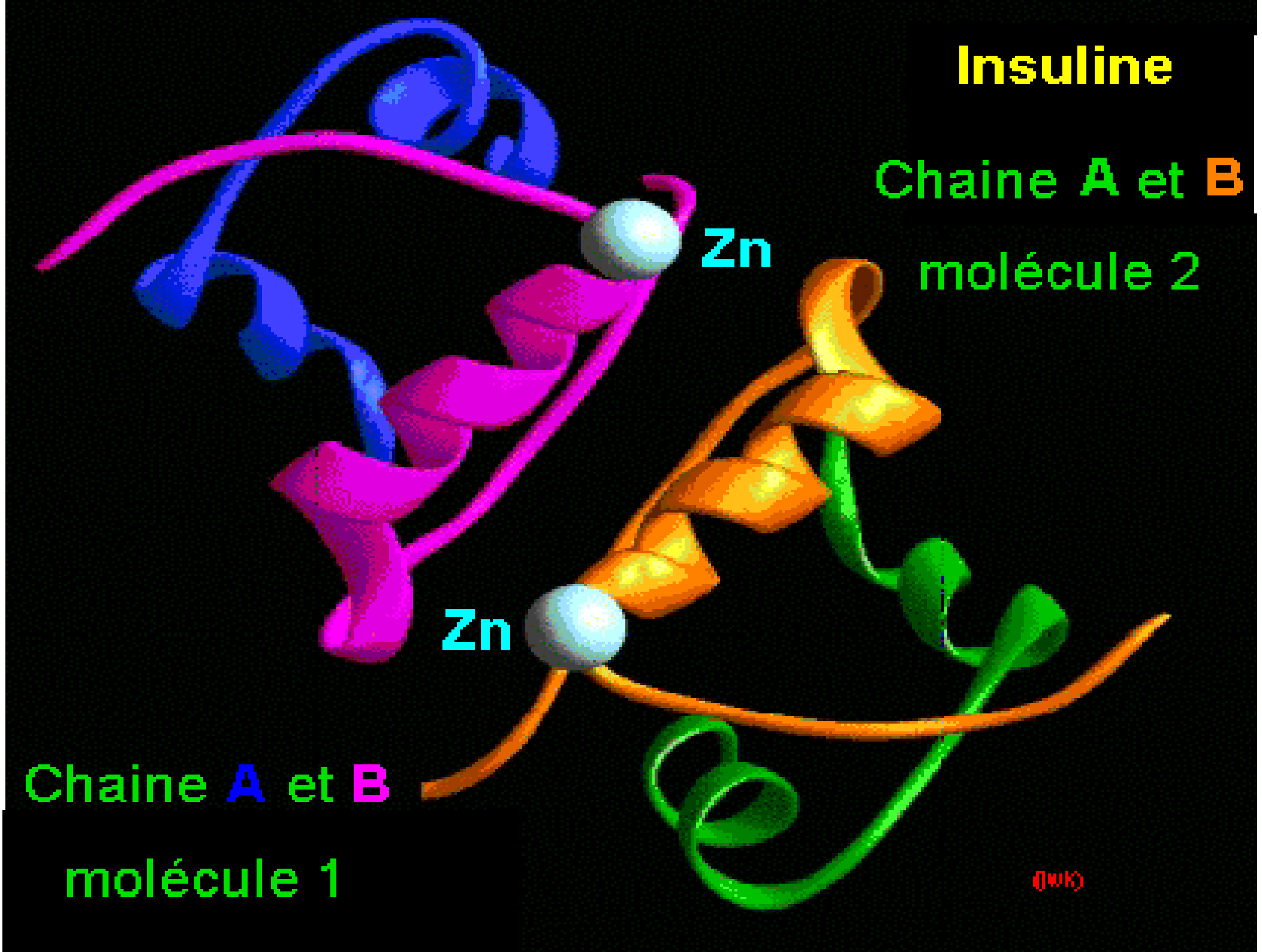
↓

پپتيد C

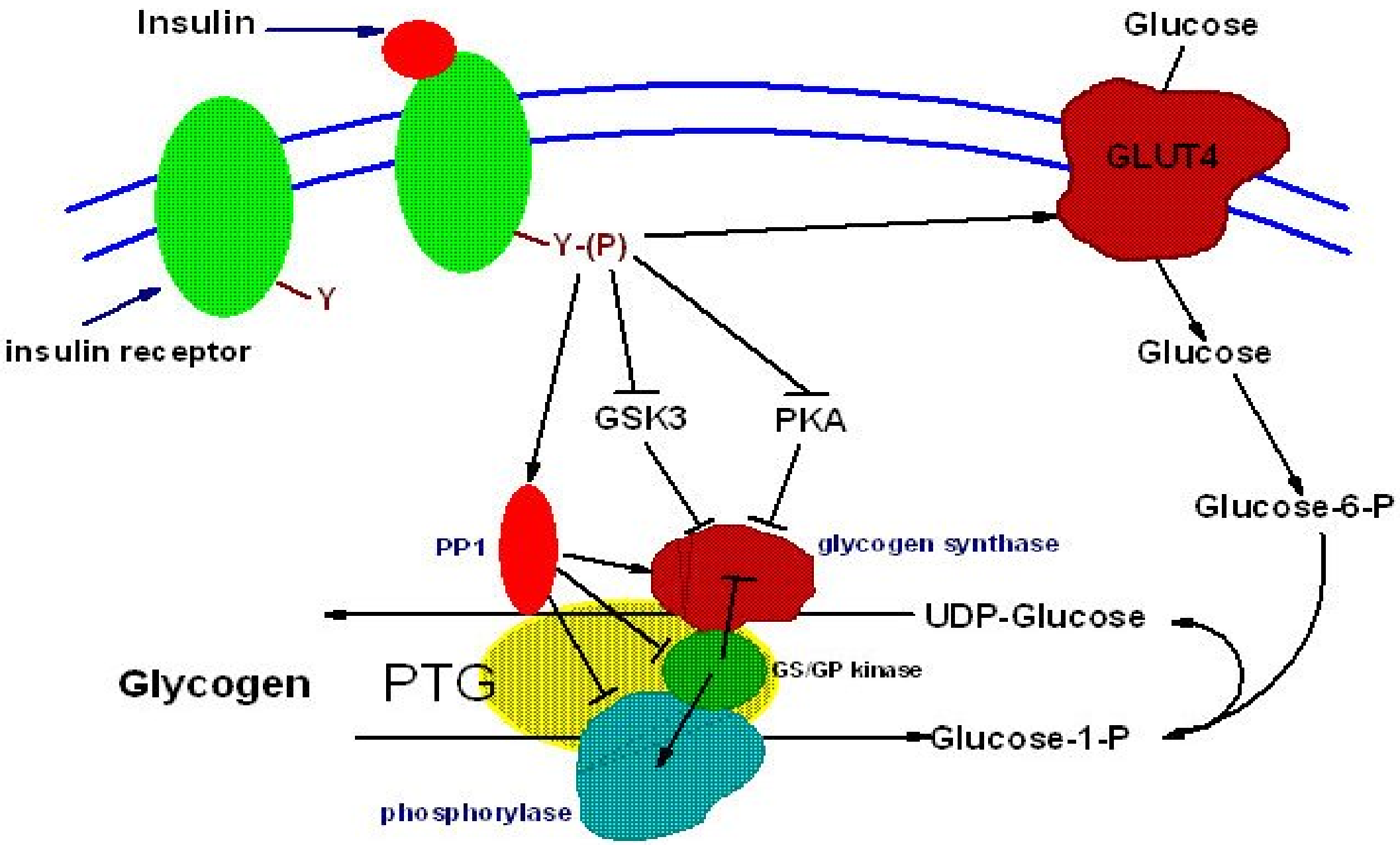

Peptide C
1
2
3
6
S
S
A
COOH
NH2
11
21
S
S
1
2
30
S
S
B
10
20

5807



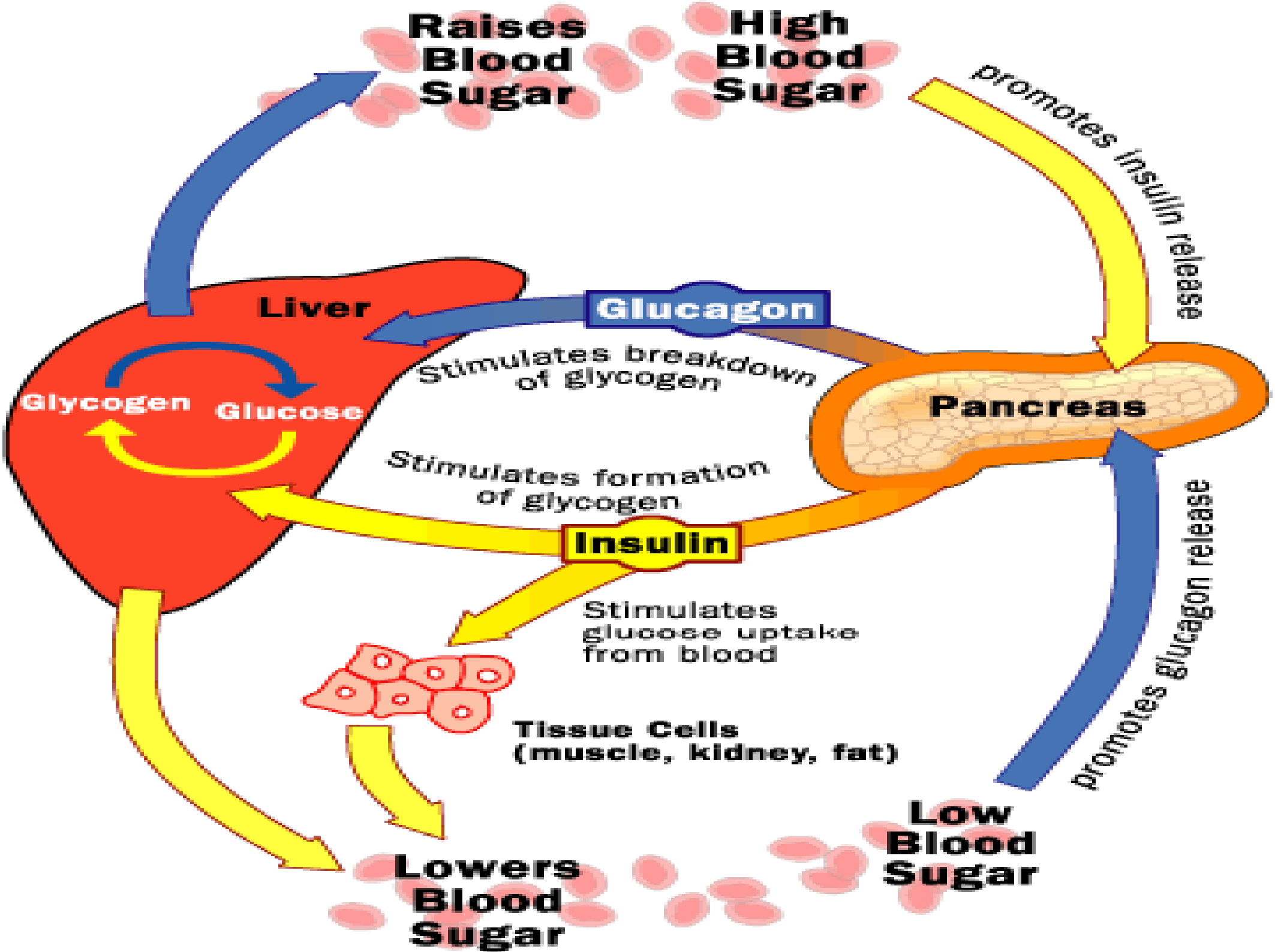

Insuline
Chaine A et B
molécule 2
Zn
Zn
Chaine A et B
molécule 1

Insulin-Mediated Regulation of Glycogen metabolism



گلوکاگن

- جزایر آلفا لانگرهانس
- پپتیدي

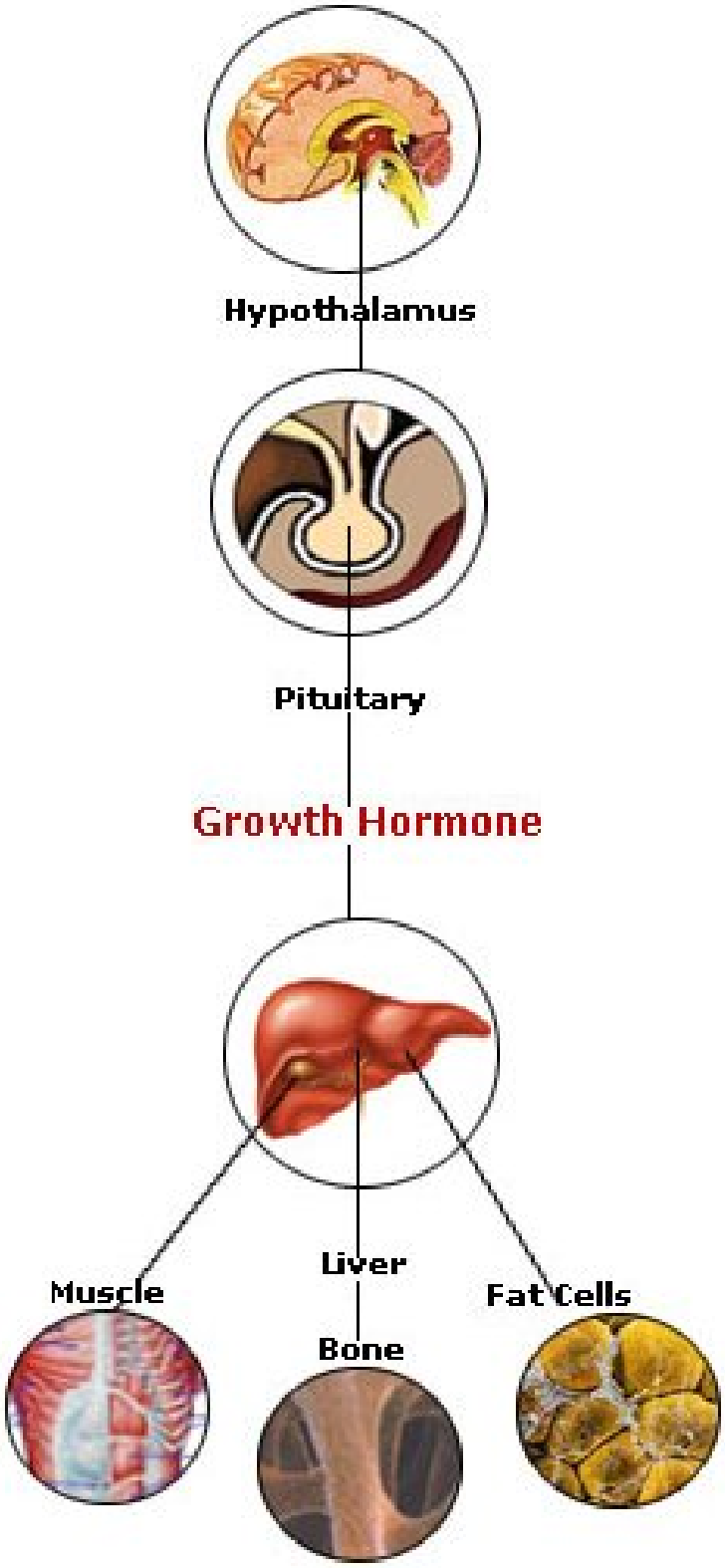

Raises Blood Sugar
High Blood Sugar
promotes insulin release
Liver
Glucagon
Stimulates breakdown of glycogen
Glycogen
Glucose
Pancreas
Stimulates formation of glycogen
Insulin
Stimulates glucose uptake from blood
Tissue Cells (muscle, kidney, fat)
promotes glucagon release
Low Blood Sugar
Lowers Blood Sugar

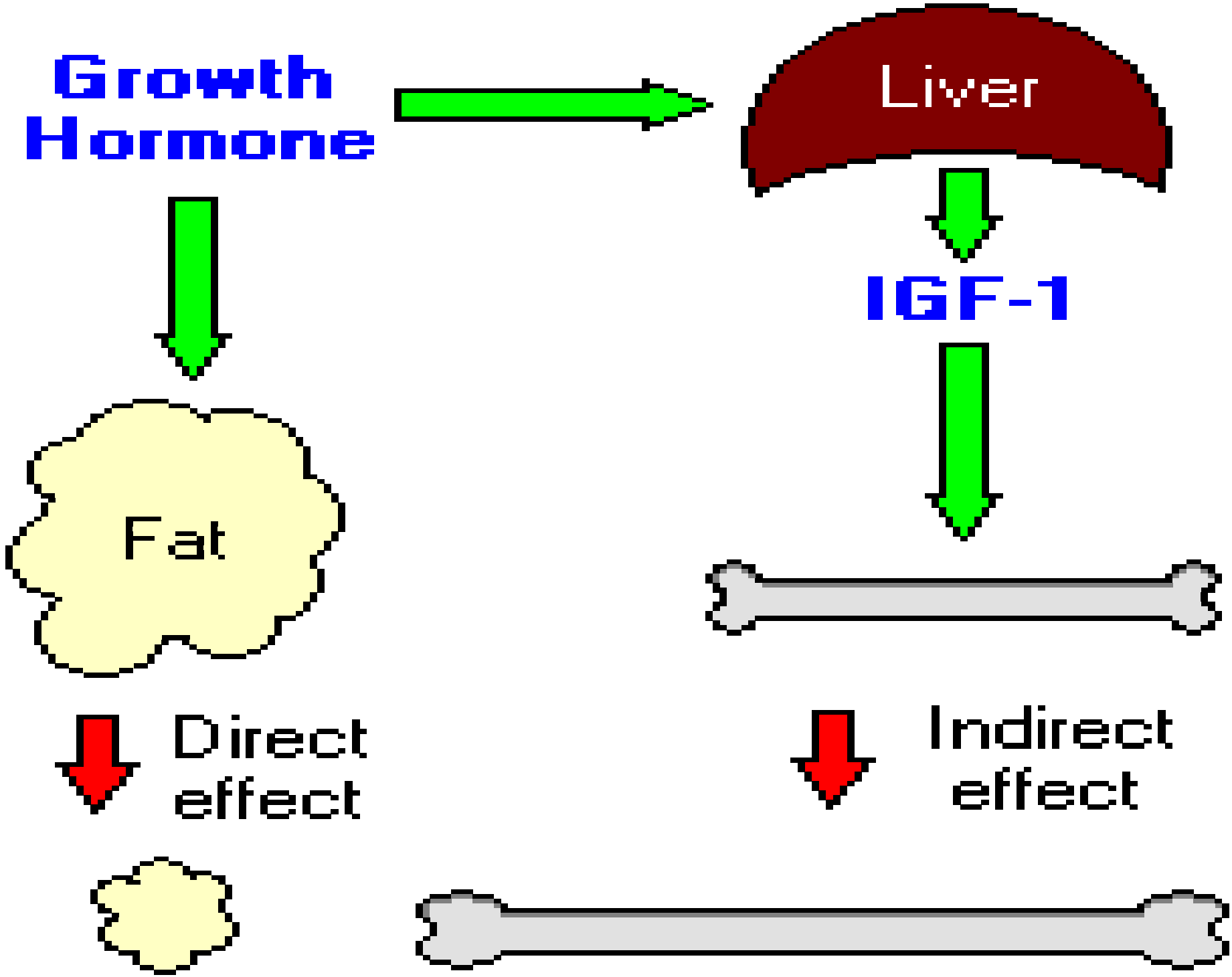
هورمون رشد (GH)

- بخش قدامي هيپوفيز
- پلي پپتيدي

- عوامل كنترل كننده:

1- GHRH
2- GRIH


Hypothalamus
Pituitary
Growth Hormone
Liver
Muscle
Fat Cells
Bone

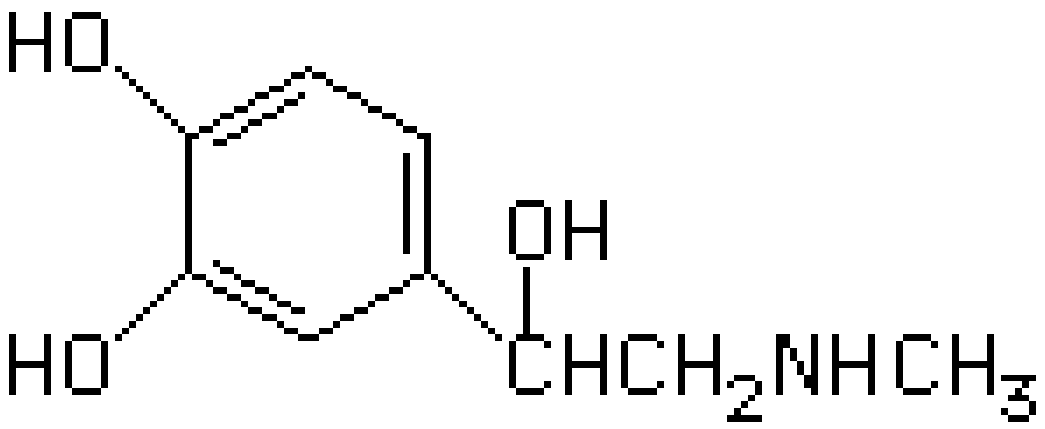

Growth Hormone
Liver
IGF-1
Fat
Direct effect
Indirect effect

آدرنالين

- بخش مرکزي غده فوق کليوي (آدرنال)
- مشتق از آمينواسيد (تيروزين)

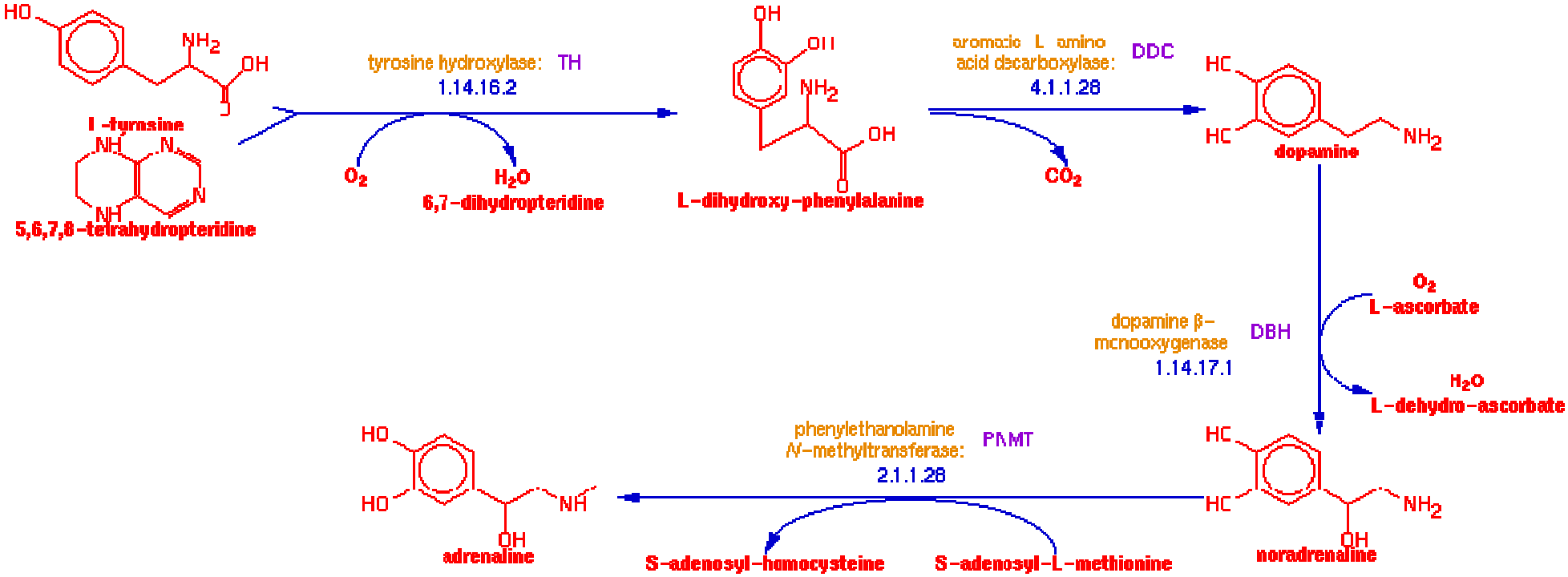
adrenaline

$C_9H_{13}O_3N$



also known as epinephrine

متابولیسم آدرنالین



اندازه گيري گلوكز

- نكات مربوط به نمونه گيري

  – ناشتا بودن
  – نمونه گيري
  – نگهداري نمونه

اندازه گيري گلوكز

- روش هاي اندازه گيري

-شيميايي:

- اورتوتولوئيدين
- فهلينگ

- آنزيمي

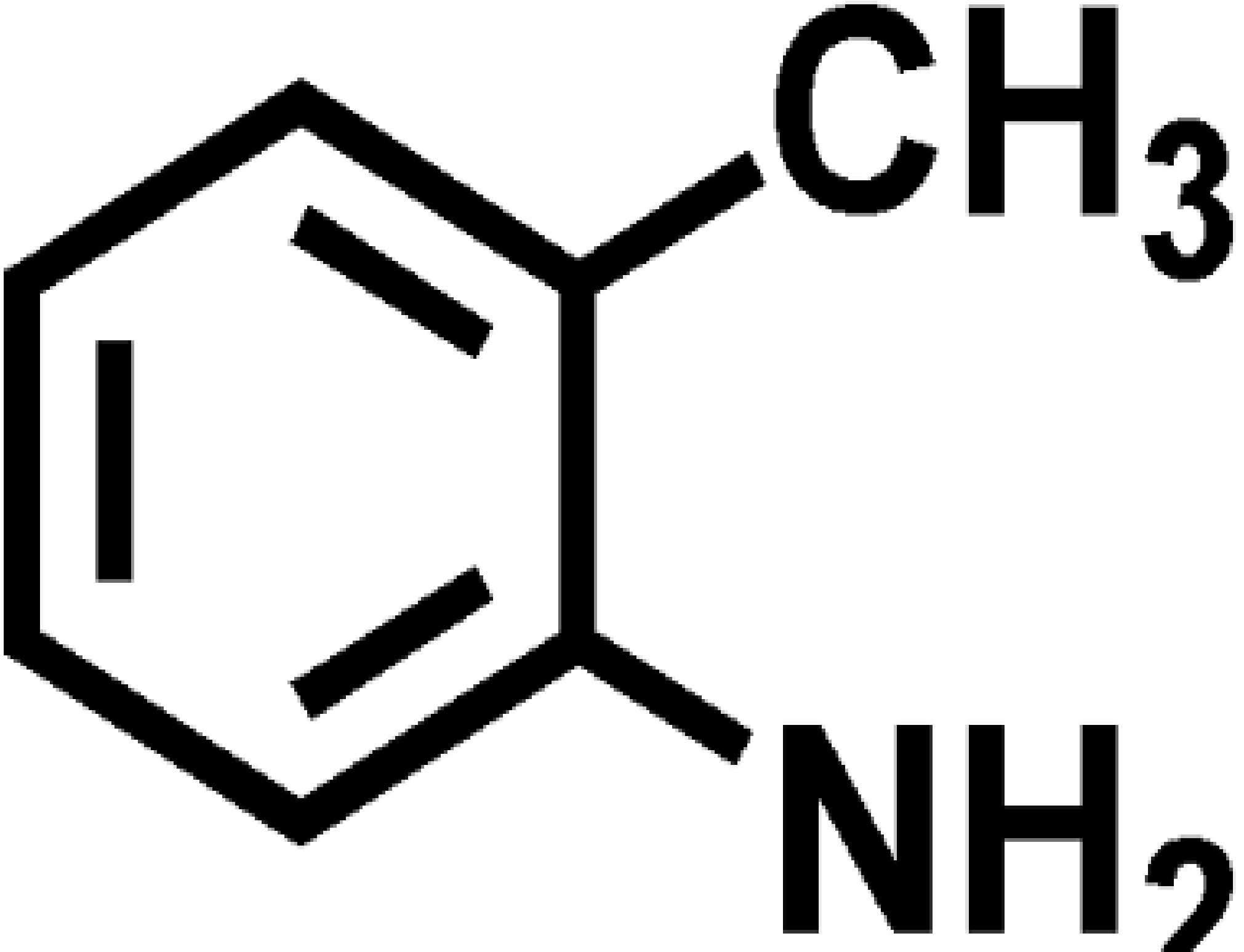
- هگزوكيناز
- گلوكز اكسيداز

روش اورتوتولوئیدین

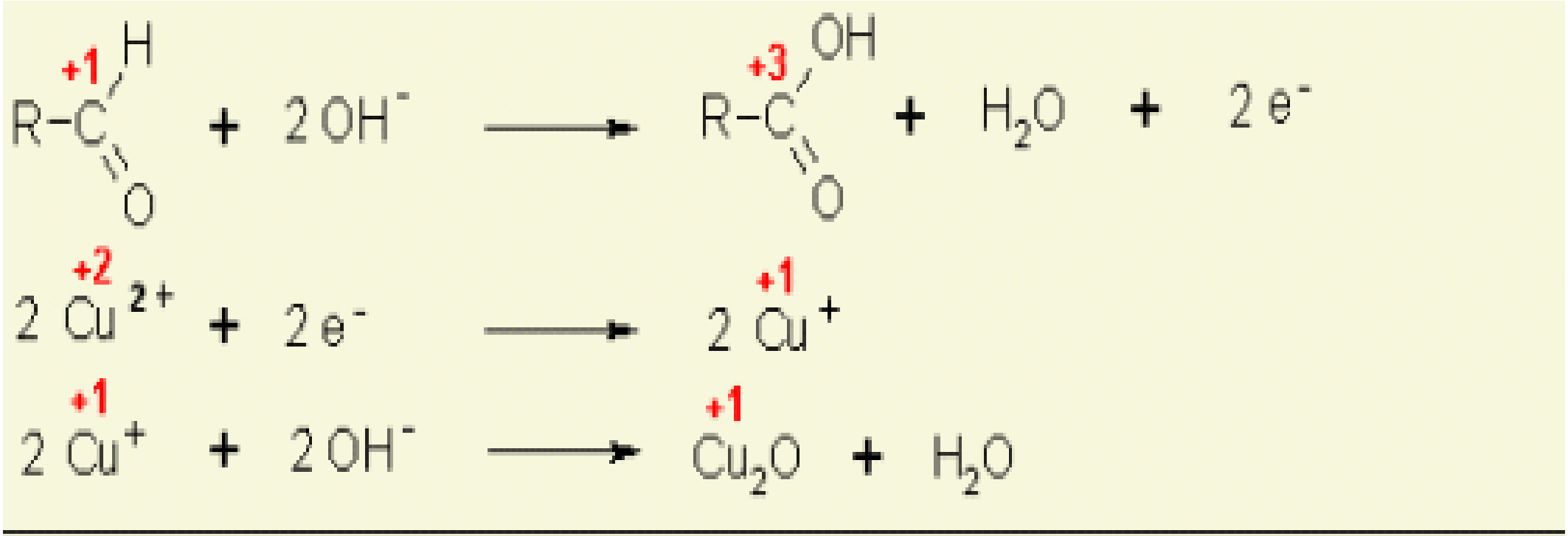
n o-Toluidine Method for Body-Fluid Glucose Determination

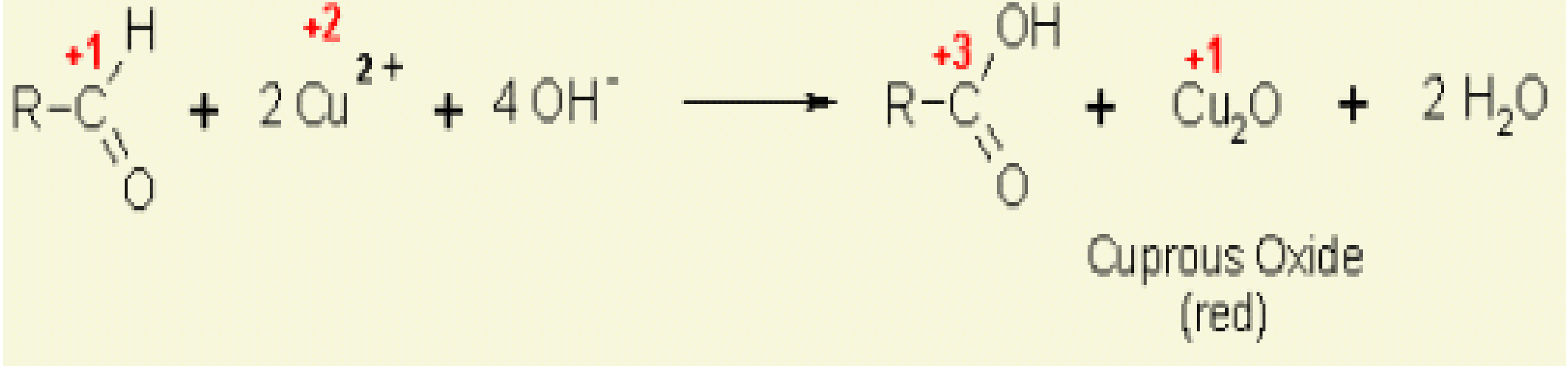
Kurt M. Dubowski

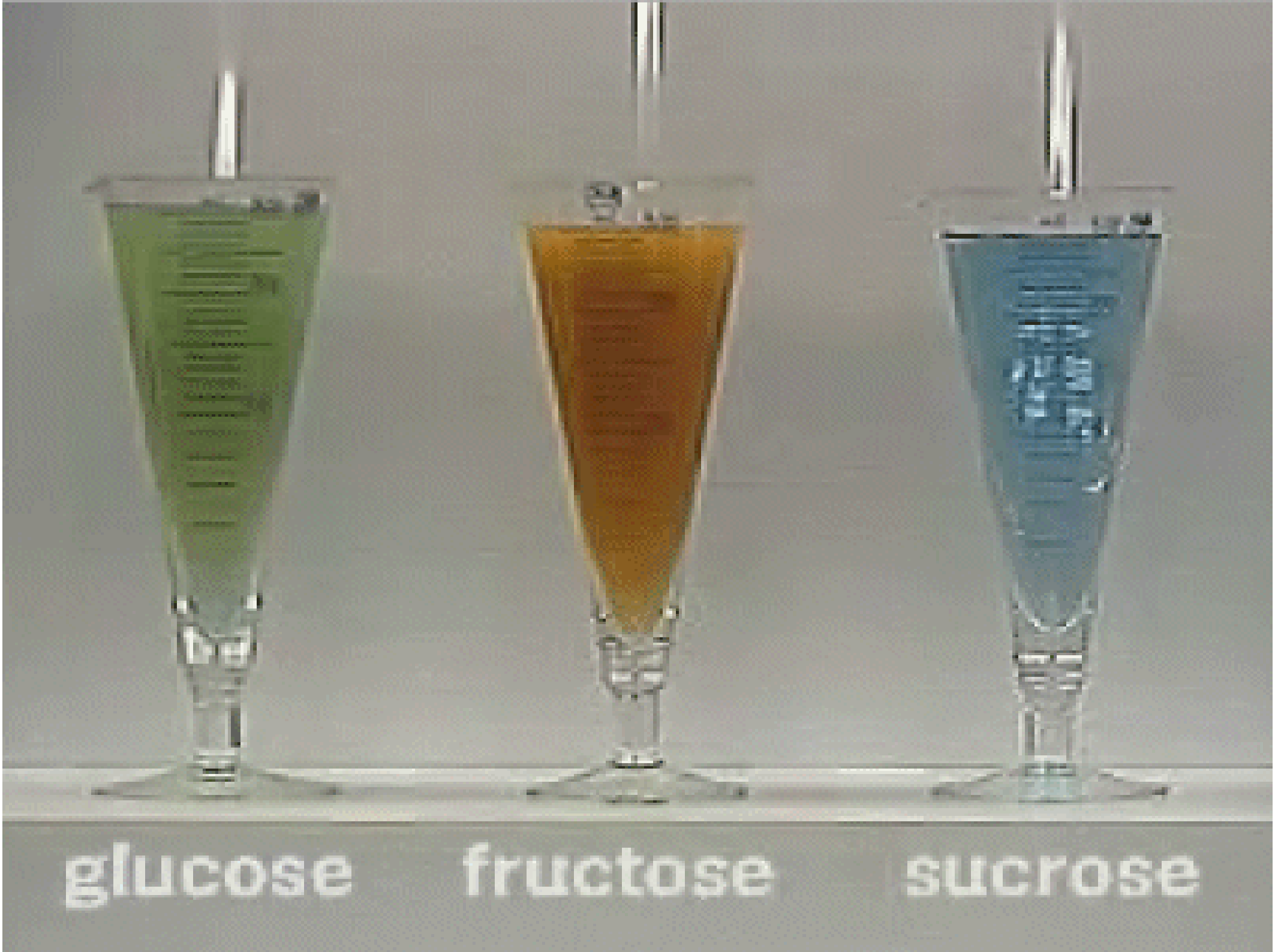
Clinical Chemistry, Vol 8, 215-235, **1962**


CH3
NH2

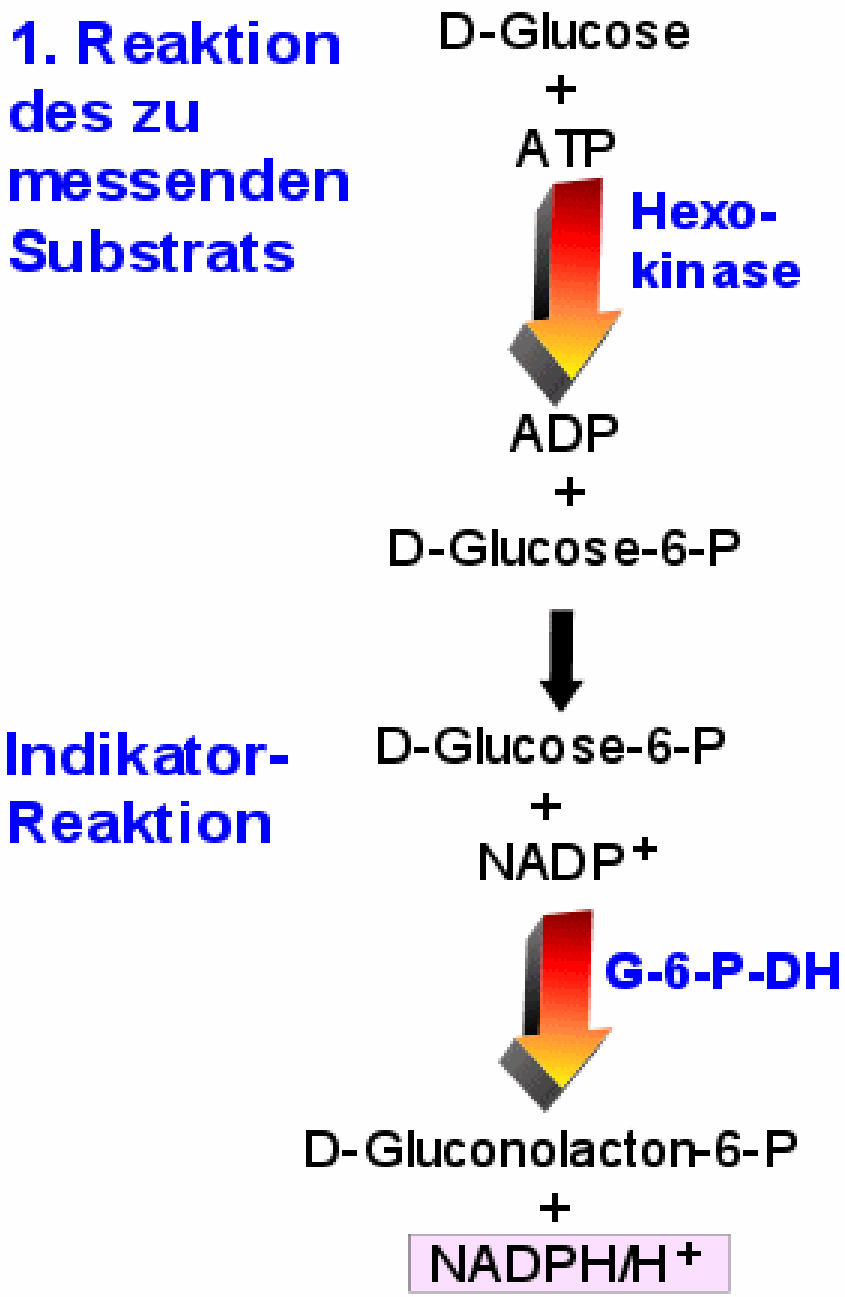
واکنش فهلینگ






glucose
fructose
sucrose

روش هگزوکیناز



روش گلوکز اکسیداز

B-D-glucose + H2O + O2 (glucose oxidase cat.) --> gluconate + H2O2

H2O2 + o-dianisidine (Peroxidase cat.)--> oxidized o-dianisidine

کربوهیدرات ها

- آزمایشات ارزیابي قند خون
- تستهاي تخصصي
- تداخلات

آزمایشات ارزیابی قند خون

- FBS (fasting blood sugar)
- BS
- 2hPP (2 hours postprandial)
- GTT (glucose tolerance test)
- HbA_1C

FBS

- Range normal:newborn 40-60 mg/dl
- adult 75-105 “

- Whole blood glucose are 90% of plasma

- Sodium floraide 9 mg/dl first 2h, stable after 2h

بيماري ها

- افزايش: ديابت مليتوس – تزريق آدرنالين – شوك – سوختگي

  فئوكروموسيتوم – تيروتوكسيكوز- آكرومگالي- ژيگانتيسم- كوشينگ سيستيك فيبروزيس- آنسفالوپاتي ورنيكه-

كاهش : مسموميت با آرسنيك ، كلروفرم- آديسون- فون ژيركه شربت افرا- گالاكتوزومي

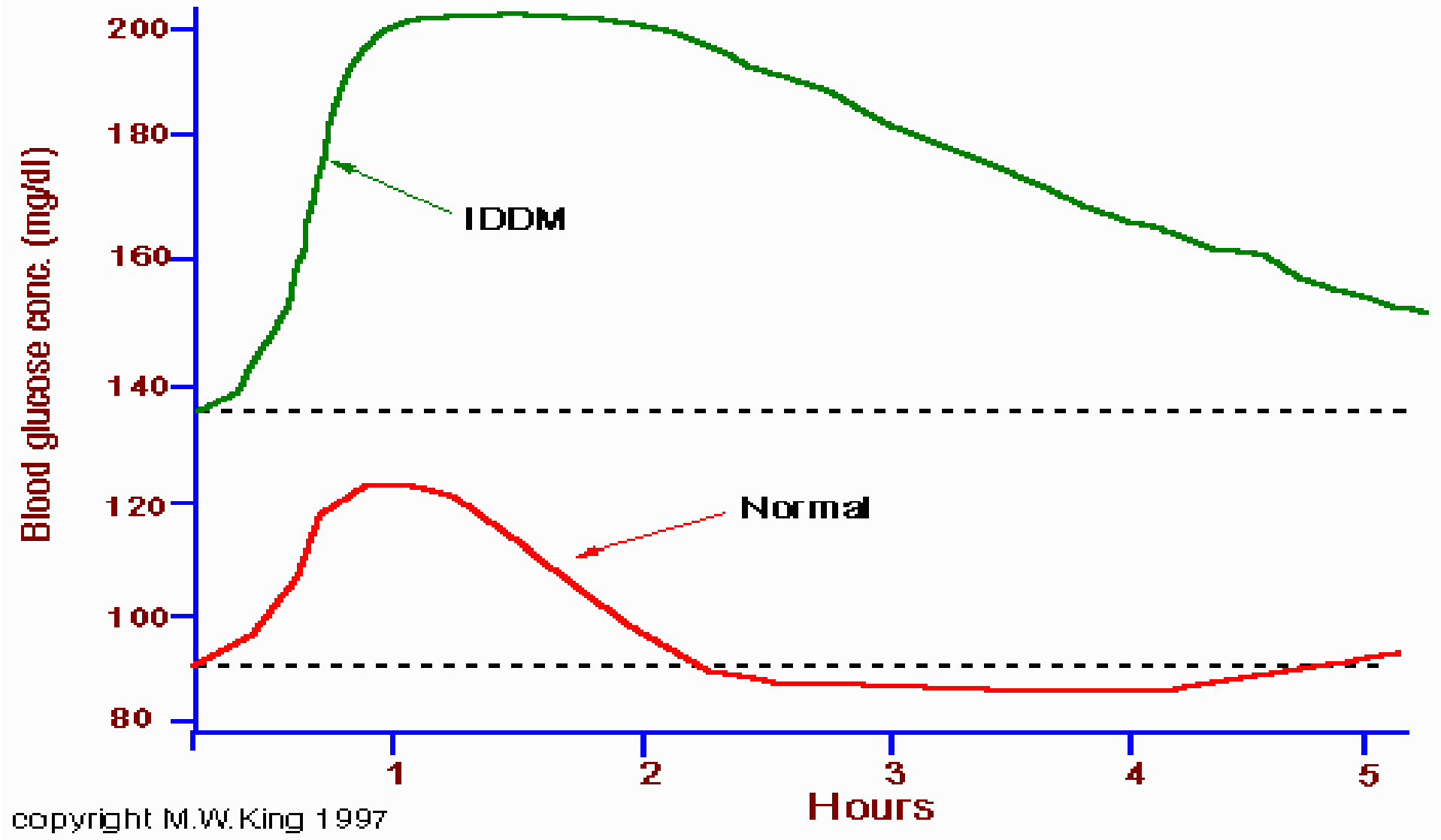
2hpp

- R.N < 120 mg/dl
- In diabetes melitus > 200 mg/dl

GTT

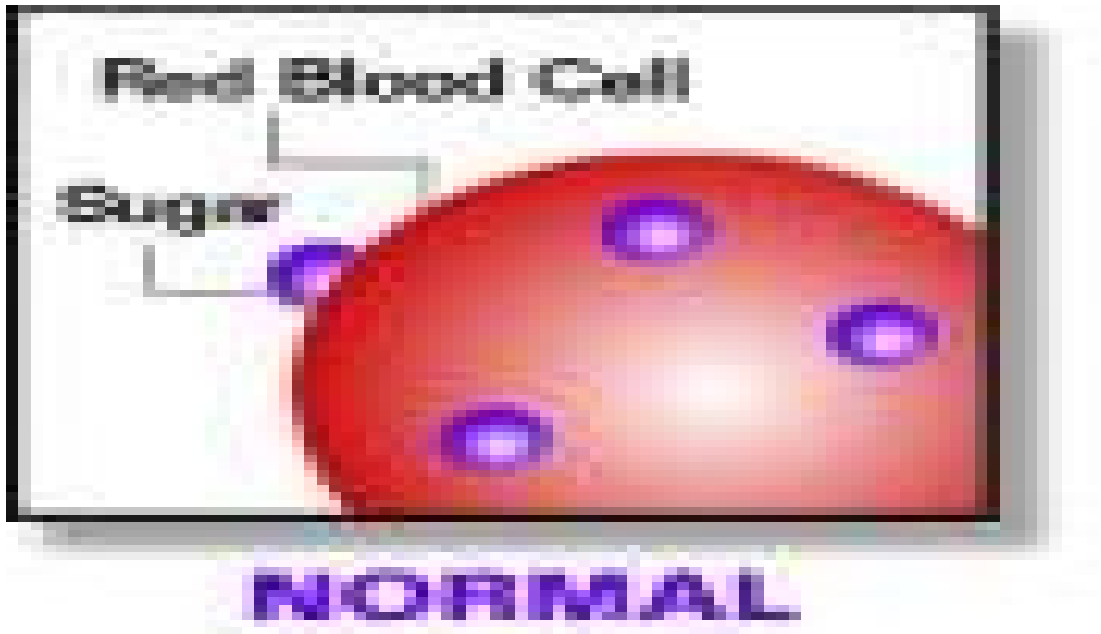
- Non pregnant adult 75 gr
- Pregnant adult 100 gr
- Child 1.75 g/kg up to 75gr
- R.N <140 mg/dl

GTT منحني


200
180
160
140
120
100
80
Blood glucose conc. (mg/dl)
IDDM
Normal
1
2
3
4
5
Hours
copyright M.W.King 1997

HbA1C

- B chin
- Valin
- 6-8 weeks


Red Blood Cell
Sugar
NORMAL

Diabetes Mellitus

Facts:

- Highest prevalence Rate
- Age – ½ Diabetes over 55 Y.O
- Race – at 65 Y.O
  - 33% Hispanics
  - 25% Blacks
  - 17% Whites
- Mortality
  - 1.5% death annually
  - Death of American women With D.M is 2X more than breast cancer

Controlling glucose by hormones

Decrease glucose :

- Insulin
- Somatomedin C

Controlling glucose by hormones

Increase glucose :

- Cortisol - Gluconeogenesis
- Glucagon – Gluconeogenesis + Glycogenolysis
- ACTH – Inhibit Glycolysis
- GH - Inhibit Glycolysis
- T4,T3 – Glycogenolysis
- Epinephrine, Norepinephrine – Glycogenolysis
- Somatostatin – Inhibition of glucagon & Insulin
- HPL

Classification

- Age – juvenile, Adult
- Treatment – 1979
  - Type I (IDDM)
  - Type II (NIDDM)
- Etiology – 1995,1997

Classification of Diabetes Mellitus (1997)

- Type 1 diabetes
  - Immune mediated
  - Idiopathic
- Type 2 diabetes
- Other specific types of diabetes
- Gestational diabetes mellitus (GDM)
- Impaired glucose tolerance (IGT)
- Impaired fasting glucose (IFG)

Immunological markers in type 1 D.M

- Islet cell antibodies (ICA) – 70% to 80% of type 1 newly diagnosed
- Insulin autoantibodies (IAA) – 50% of type 1 newly diagnosed
- Glutamic acid decarboxylase antibodies (GAD) – High incidence in type 1 , 10 years before type 1 presentation

  GAD → Gamma aminobutyric acid

  Anti GAD in type 2 → type 1
- Protein tyrosine phosphatase antibodies (IA-2)

Other specific types of D.M

- Genetic defects of ß-cell function
- Genetic defects in insulin action
- Disease of the exocrine pancreas
- Endocrinopathies (Cushing, Acromegaly)
- Drugs known to induce ß-cell dysfunction (Dilantin, Pentamidine)
- Drugs known to impair insulin action (Glucocorticoids, Thiazides, ß-Adrenergics)
- Infections
- Genetic syndroms (Down’s, Klinefelter’s, Porphyria)

Diagnosis of Diabetes Mellitus

- Classic symptoms of diabetes and casual plasma glucose concentration ≥ 200 mg/dL
- Fasting plasma glucose ≥ 126 mg/dL
- A 2-hour postload plasma glucose concentration ≥ 200 mg/dL during the OGTT

Impaired fasting Glucose

- Fasting plasma glucose between 100 and 125 mg/dL

Impaired Glucose Tolerance

- Fasting plasma glucose <126 mg/dL
- A 2-hour OGTT plasma glucose concentration between 140 and 199 mg/dL

GCT

- Perform between 24 and 28 weeks of gestation on all pregnant women ≥25 years of age (or <25 years of age with one risk factor)
- Administer 50-g oral glucose load without regard to time of the day or time of last meal
- Measure venous plasma glucose at 1 hour
- If glucose is ≥140 mg/dL , perform glucose tolerance test

Diagnosis of GDM

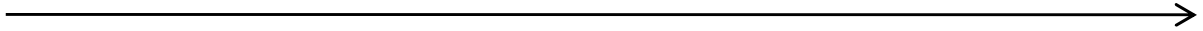
- Perform in the morning after an 8 to 14 hour fast
- Measure fasting venous plasma glucose
- Administer 100 g or 75 g of glucose orally
- Measure plasma glucose hourly for 3 hours
- At least two values must meet or exceed the following

	100 g	75 g
Fasting	95 mg/dL	95 mg/dL
1 hour	180 mg/dL	180 mg/dL
2 hours	155 mg/dL	155 mg/dL
3 hours	140 mg/dL	____

Glycosylated Hb (HbA1C)

By Amadori Rearrangement Binds to

- Glucose



NH2 Terminal of Valine Amino Acids
in β Chain of Hb

Hb A1C

- For monitoring Diabetic Patients
  - 4.5% - 6.2% Normal
  - 6.3% - 7.2% Goal
  - 7.2% - 9.1% Good Control
  - More than 9.2% Action suggested