Diabetes Pathophysiology

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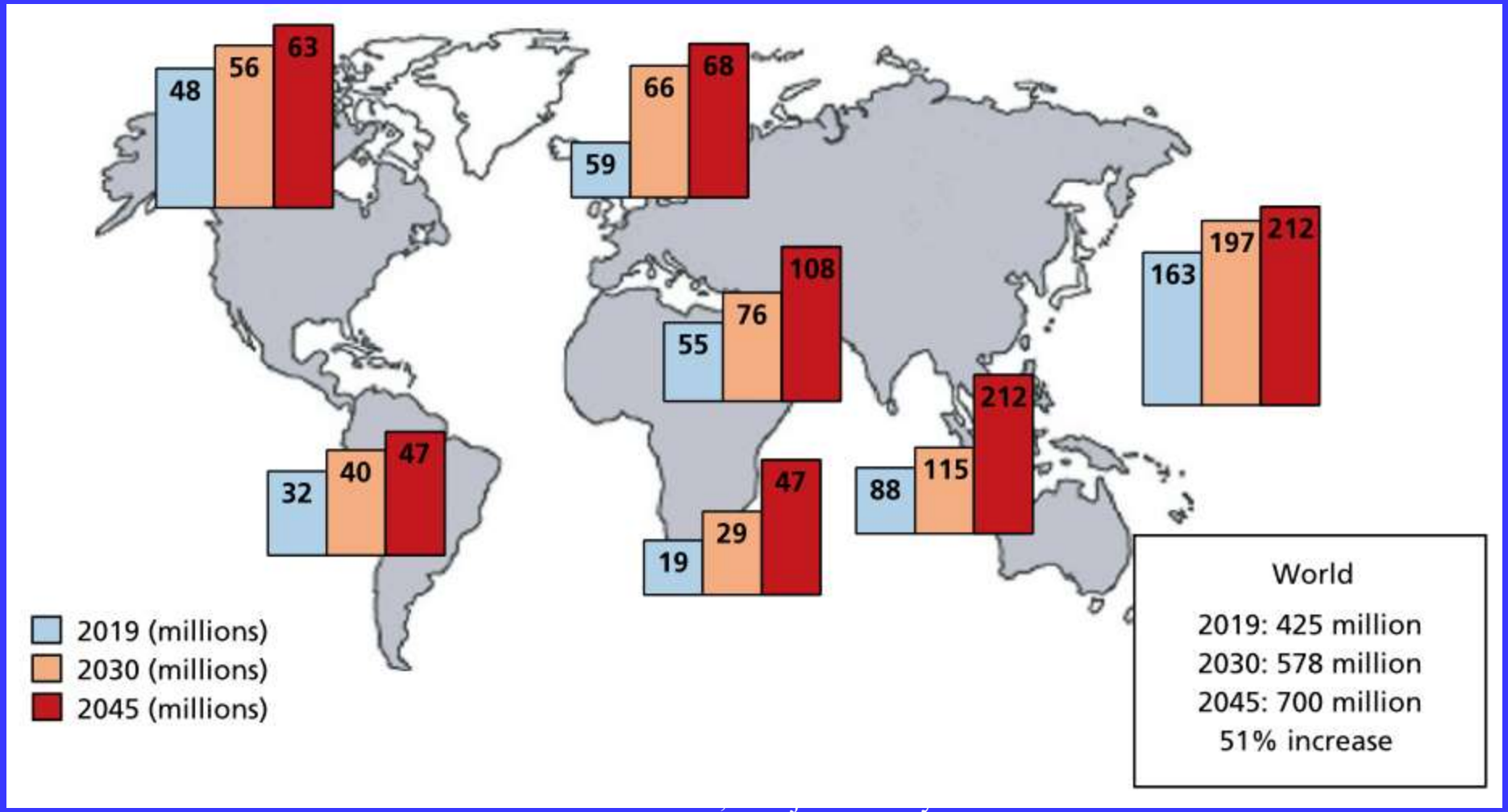
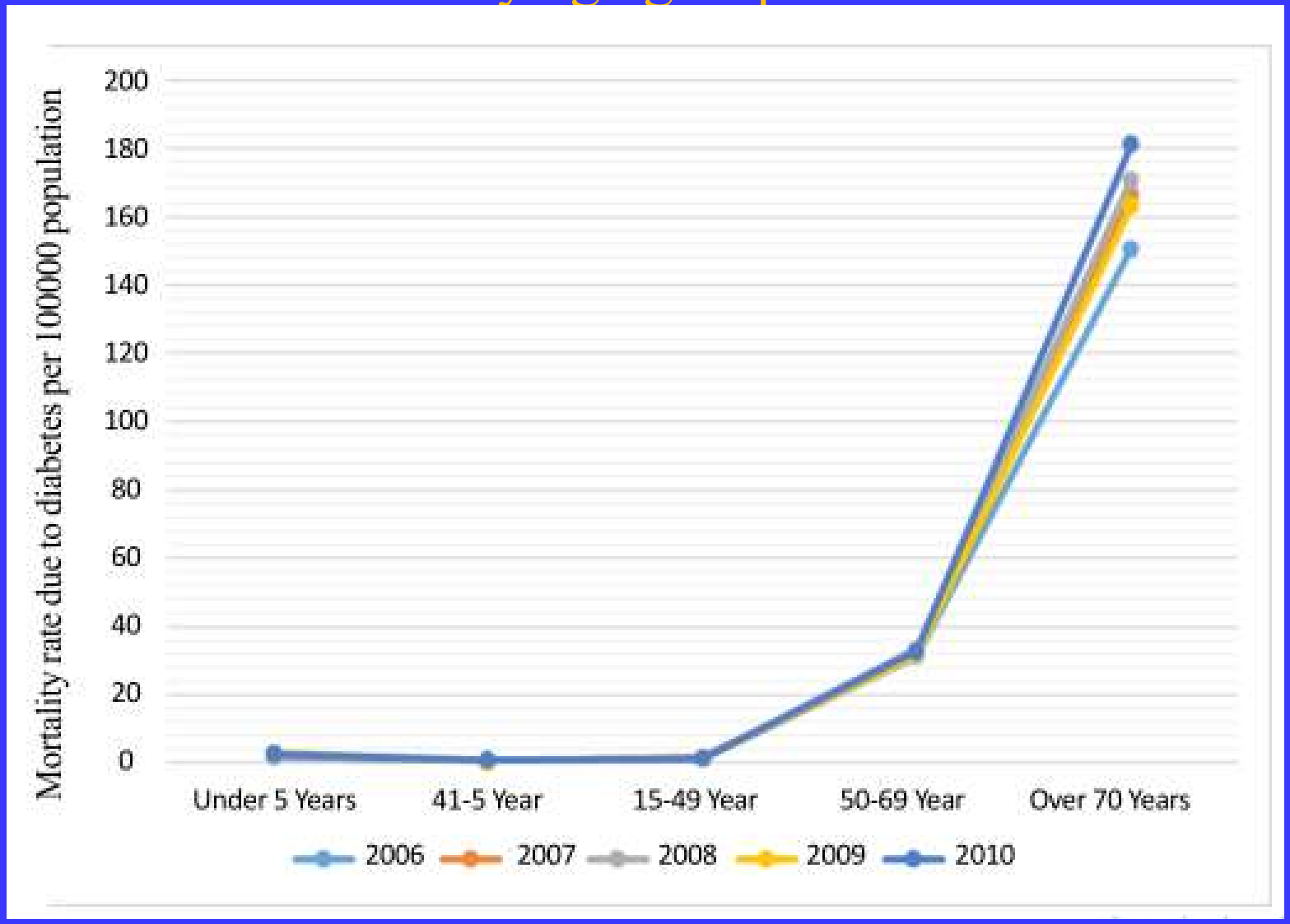
Worldwide prevalence of diabetes



Mortality rate due to diabetes per 100000 population by age groups



میزان مرگ ومیر به دلیل دیابت در ایران

Year	No. (%)			The Rate per 100000			Sex Ratio (Male/Female)	Residence (Rate per 100000)		Average Age (Years)
	Female	Male	Total	Female	Male	Total		Village	City	
2006	2858 (53.2)	2517 (46.8)	5375	10.17	8.69	9.42	0.88	5.91	10.07	67.7
2007	2920 (54.6)	2432 (45.4)	5352	11.15	9.05	10.09	0.83	6.32	11.03	69.3
2008	3163 (57.3)	2354 (42.7)	5517	11.94	8.66	10.03	0.74	6.31	11.41	68.8
2009	2898 (54.4)	2428 (45.6)	5326	10.79	8.82	9.79	0.84	6.63	10.6	68
2010	3214 (55)	2634 (45)	5848	11.78	9.44	10.6	0.82	6.93	11.6	66.6
Total	15053 (54.9)	12365 (45.1)	27418				0.82			68.1

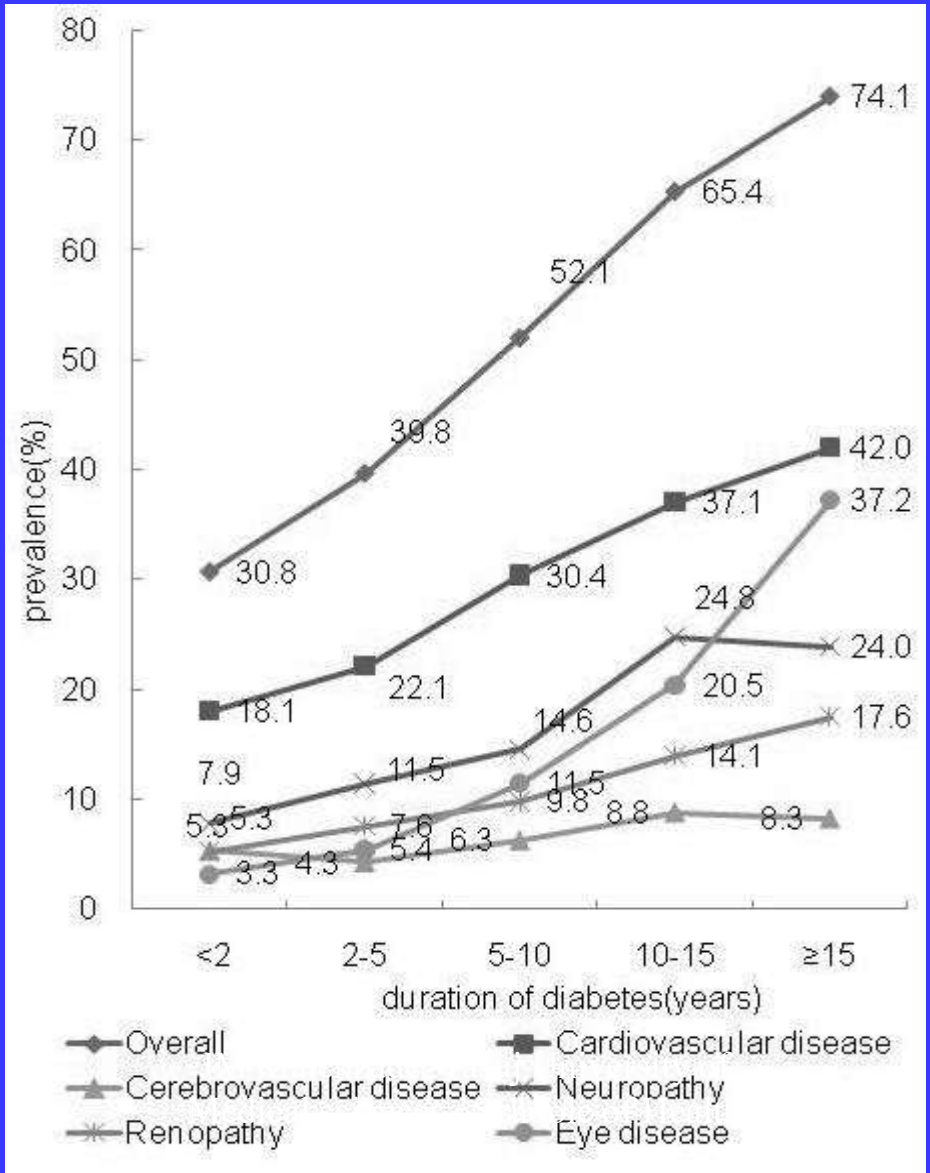
Quarterly of
The Horizon of Medical Sciences

JM Malekzade, Yasuj University of Medical sciences Schoole of Health

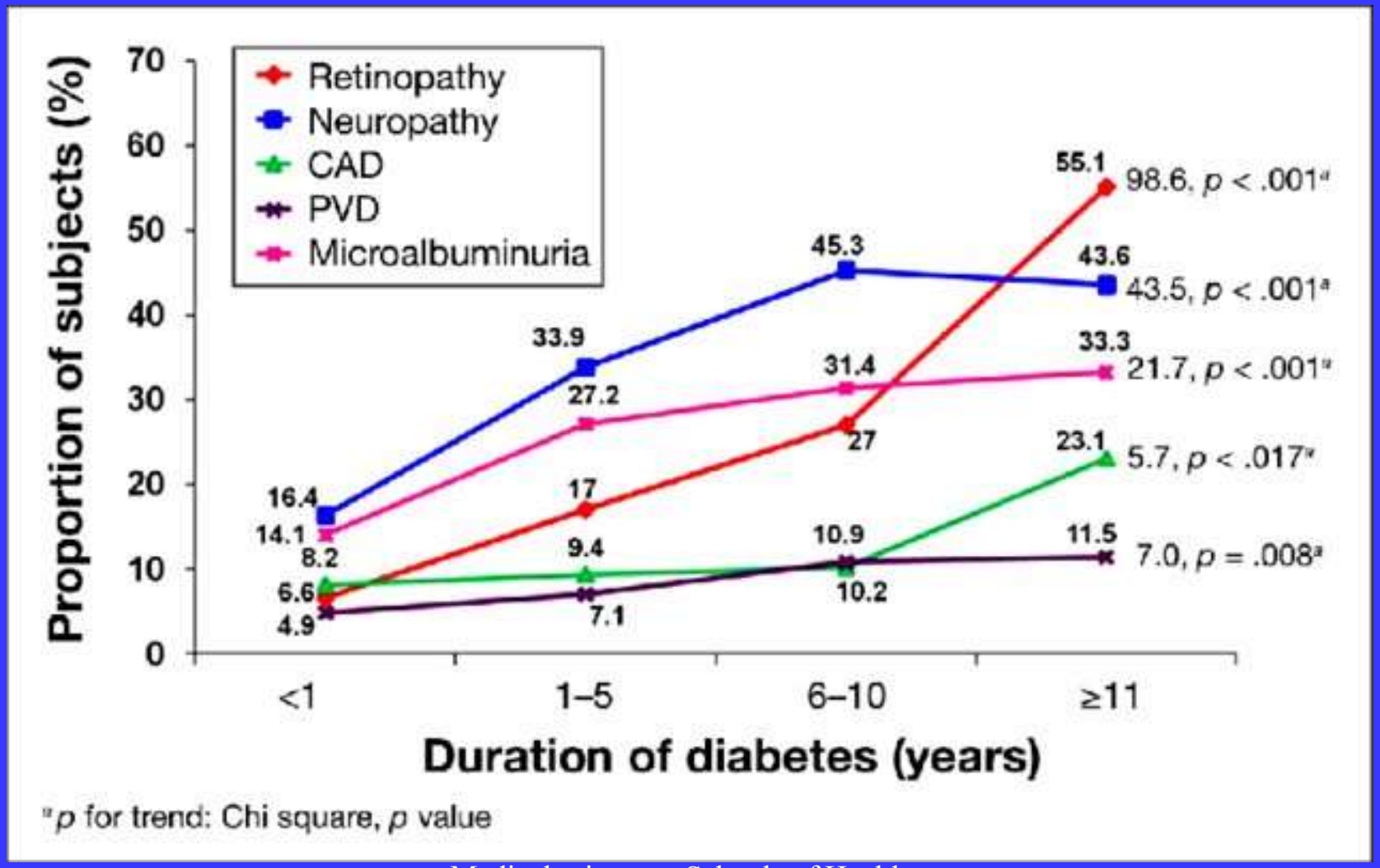
In Yazd, Iran

- Of the 9965 individuals recruited, the crude self-reported prevalence of DM was 14.1% (95% CI: 13.4–14.7). The prevalence was higher in women than men (15.6 vs.12.4%), significantly. The age-standardized prevalence of DM was 8%.

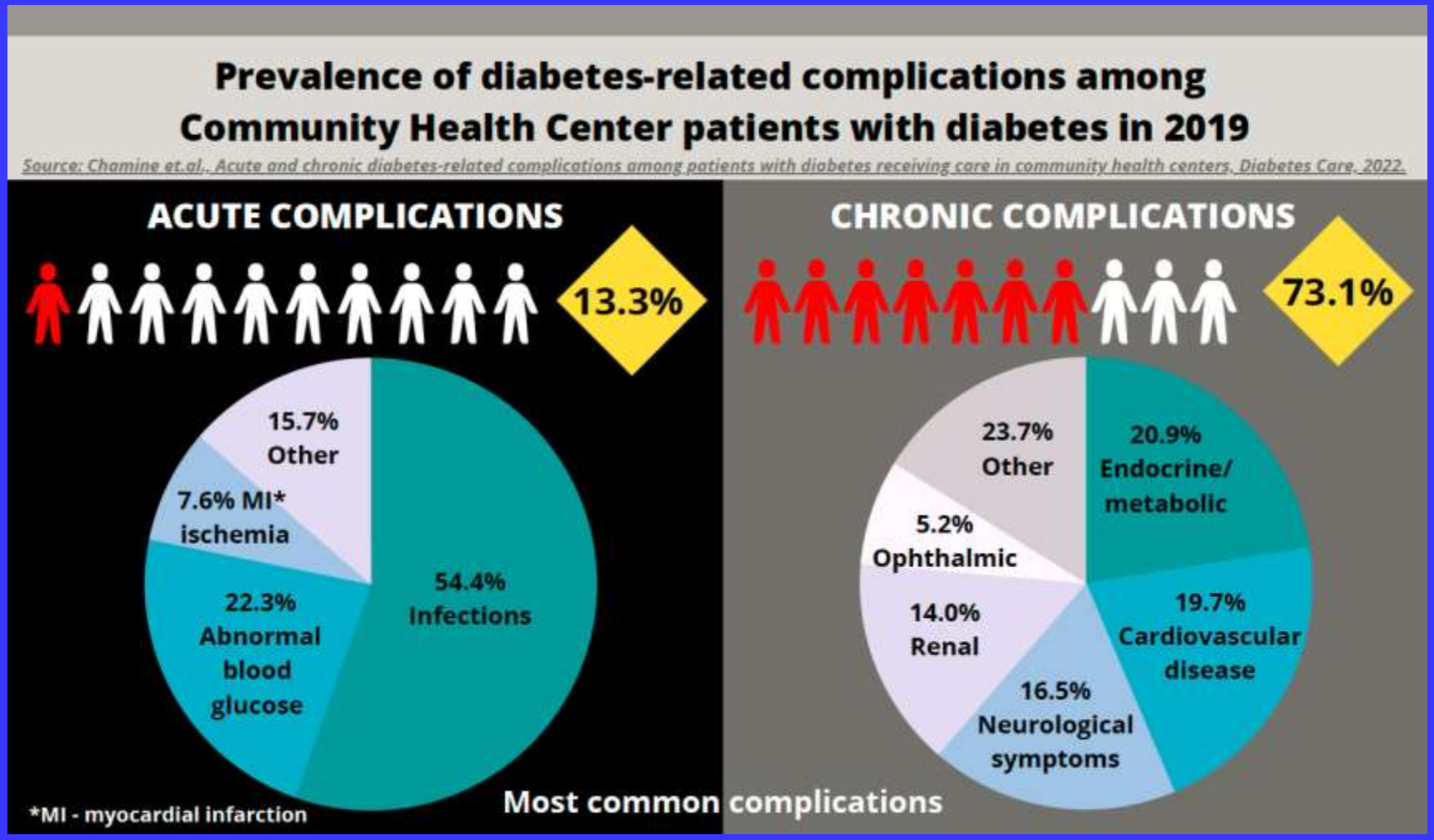
prevalence of chronic complications of T2DM in 1524 urban Chinese



Prevalence of diabetes complications in relation to duration of diabetes india



[a] p for trend: Chi square, p value



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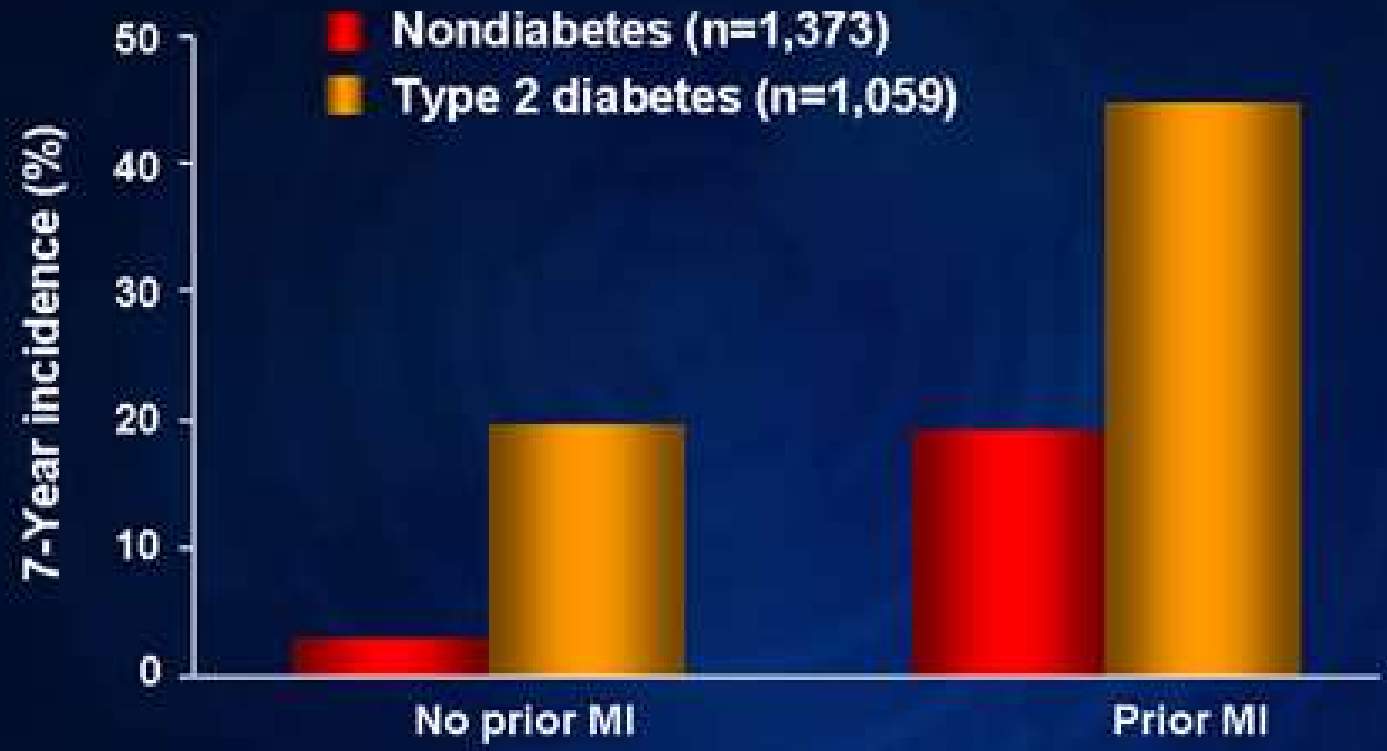
Incidence of Myocardial Infarction in People with Type 2 Diabetes



Haffner SM et al. *N Engl J Med.* 1998;339:229-234.

Prevalence

- Increases with age
- Gender Difference
- Racial, Ethnic – Disproportionate prevalence

Mortality Risk

- Duration of Diabetes
- Lack of Blood Glucose Control
- Cardiovascular Risk Factors such as
  - Smoking
  - Hypertension
  - Abnormal Lipid Levels
  - Physical Inactivity
  - Central Obesity

Benefits of good blood glucose control in type 1 and type 2 diabetes (Diabetes Control and Complications Trial 1993; UK Prospective Diabetes Study 1998):

- New eye disease risk reduced by 76%
- Worsening of existing eye disease reduced by 54%
- Early kidney disease risk reduced by 54%
- More serious kidney problems reduced by 39%
- Nerve damage risk reduced by 60%
- Heart disease risk reduced by 56%
- Stroke risk reduced by 44%
- Kidney disease risk reduced by up to 33%

Pathophysiology

- Genetic
- Obesity
- Sedentary Lifestyle
- Aging

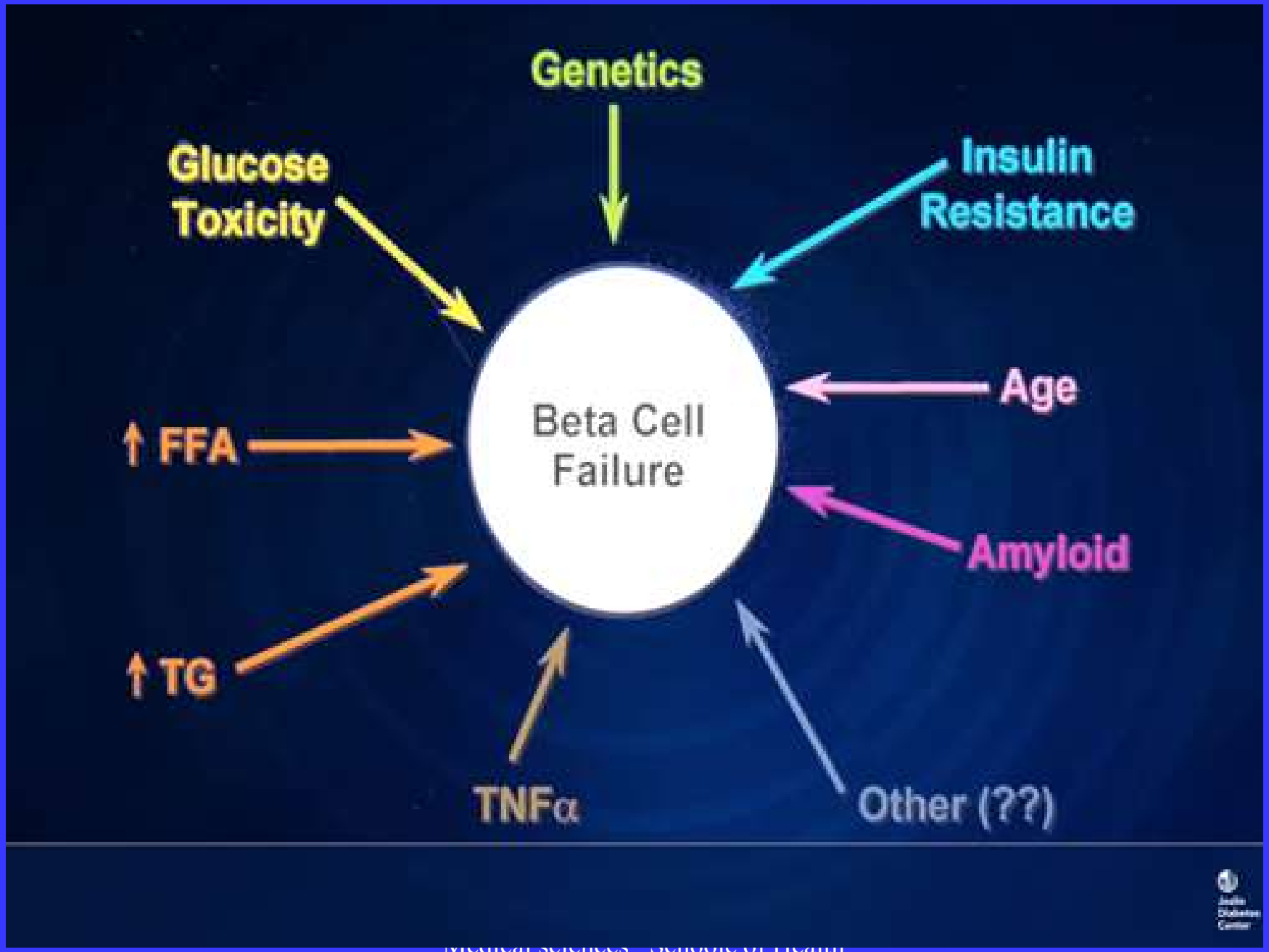
Identifying Individuals at High Risk for Type 2 Diabetes

- Clinical
  - Age
  - Ethnicity
  - Family history
  - Obesity
  - Blood pressure
  - Lipid profile
- Biochemical
  - Hyper/euglycemic clamp
  - IGT
  - FPG
  - GDM
  - Matsuda ins sensitivity/ins resistance Index

Diabetes Care. 2007:30:1544.

Risk Factors for Asymptomatic Patients

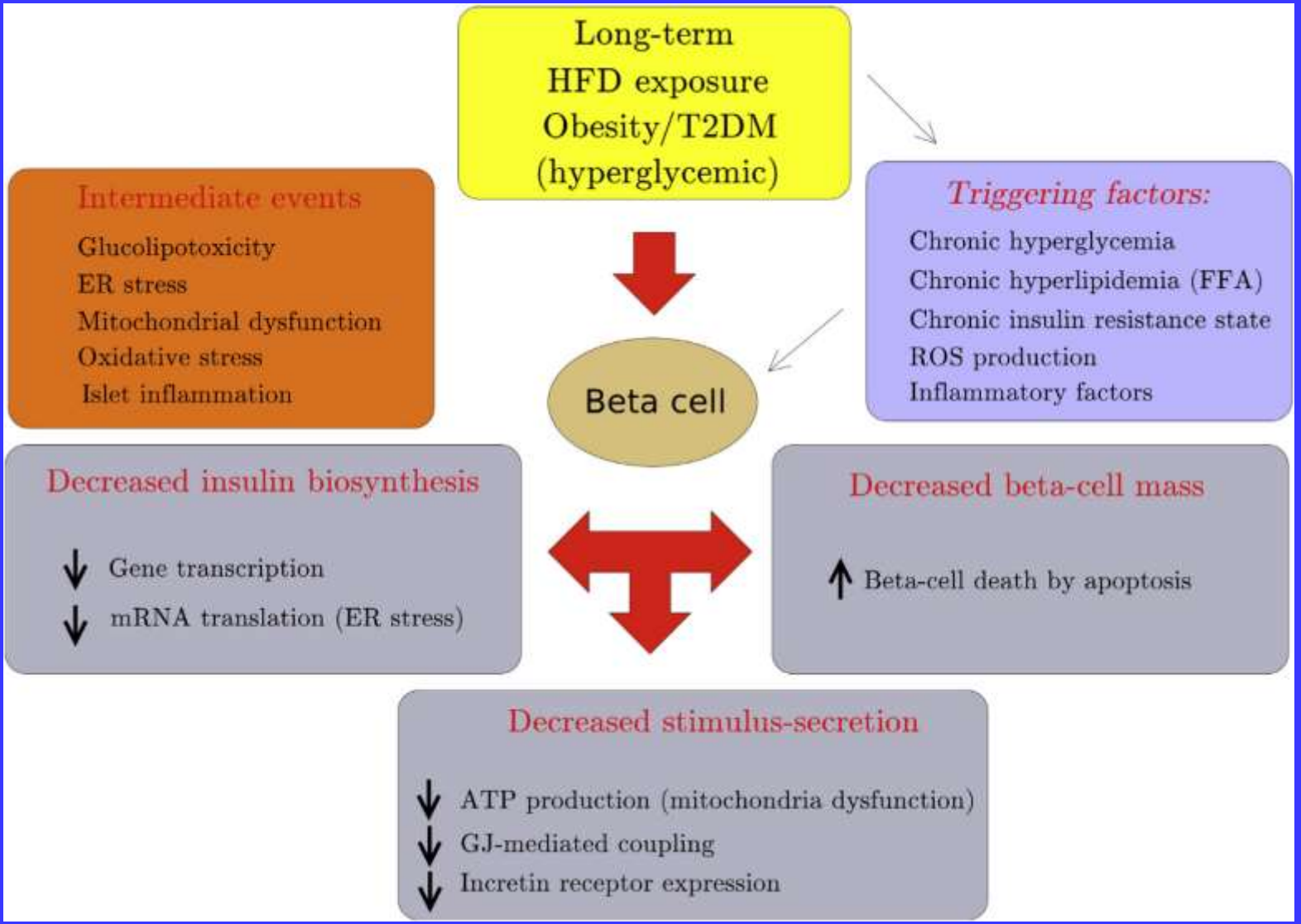
- Strong Family History
- Obesity
- Certain Races
- Women with previous GDM
- Previous IGT
- Hypertension or hypertriglyceridemia
- 40 years old with any of the above


Genetics
Glucose Toxicity
Insulin Resistance
Beta Cell Failure
↑ FFA
Age
Amyloid
↑ TG
TNFα
Other (??)

The Growing Epidemic of Type 2 Diabetes in Relation to Obesity

Mokdad AH et al. *Diabetes Care*. 2000;23:1278-1283; Mokdad AH et al. *JAMA*. 1999;282:1519-1522; Mokdad AH et al. *JAMA*. 2001;286:1195-1200.

Prolonged high-fat diet-induced β-cell failure and death

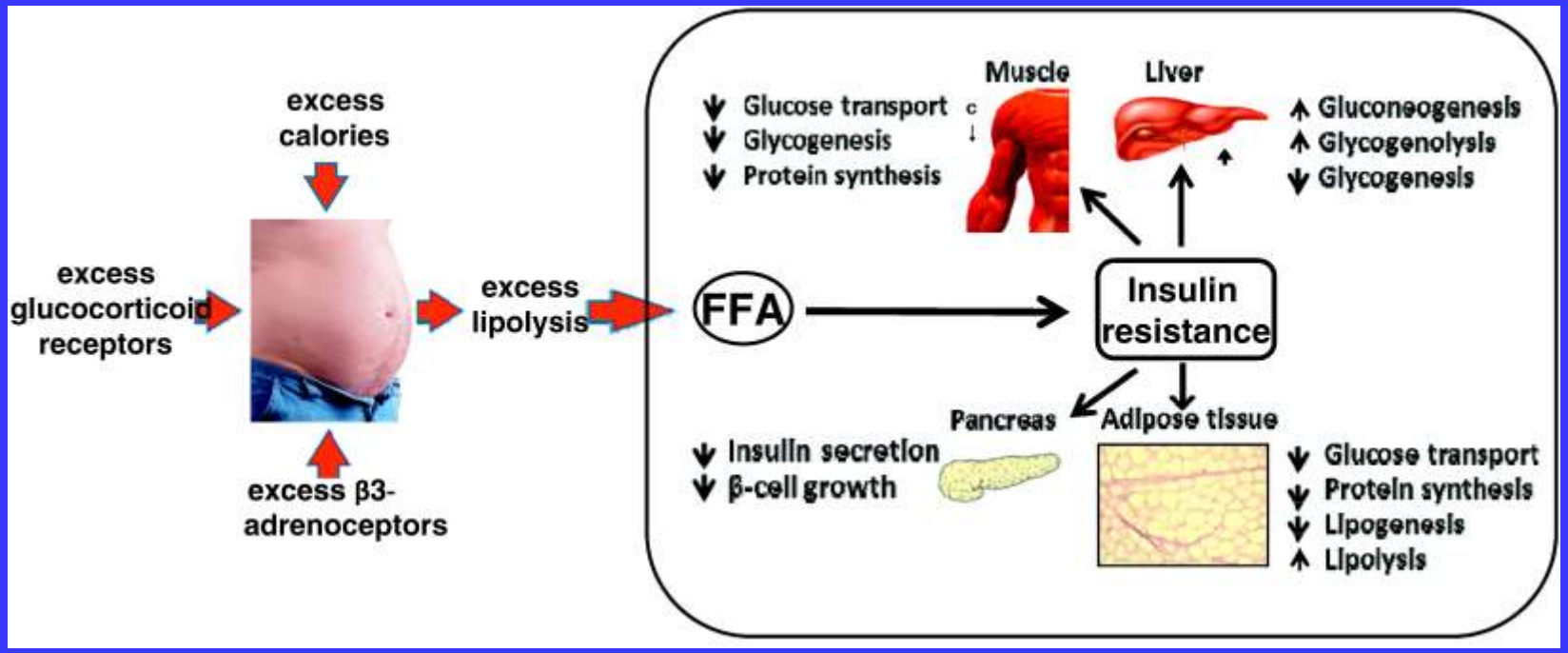


High-Fat Diets and b-Cell Dysfunction: Molecular Aspects, in Molecular Nutrition and Diabetes

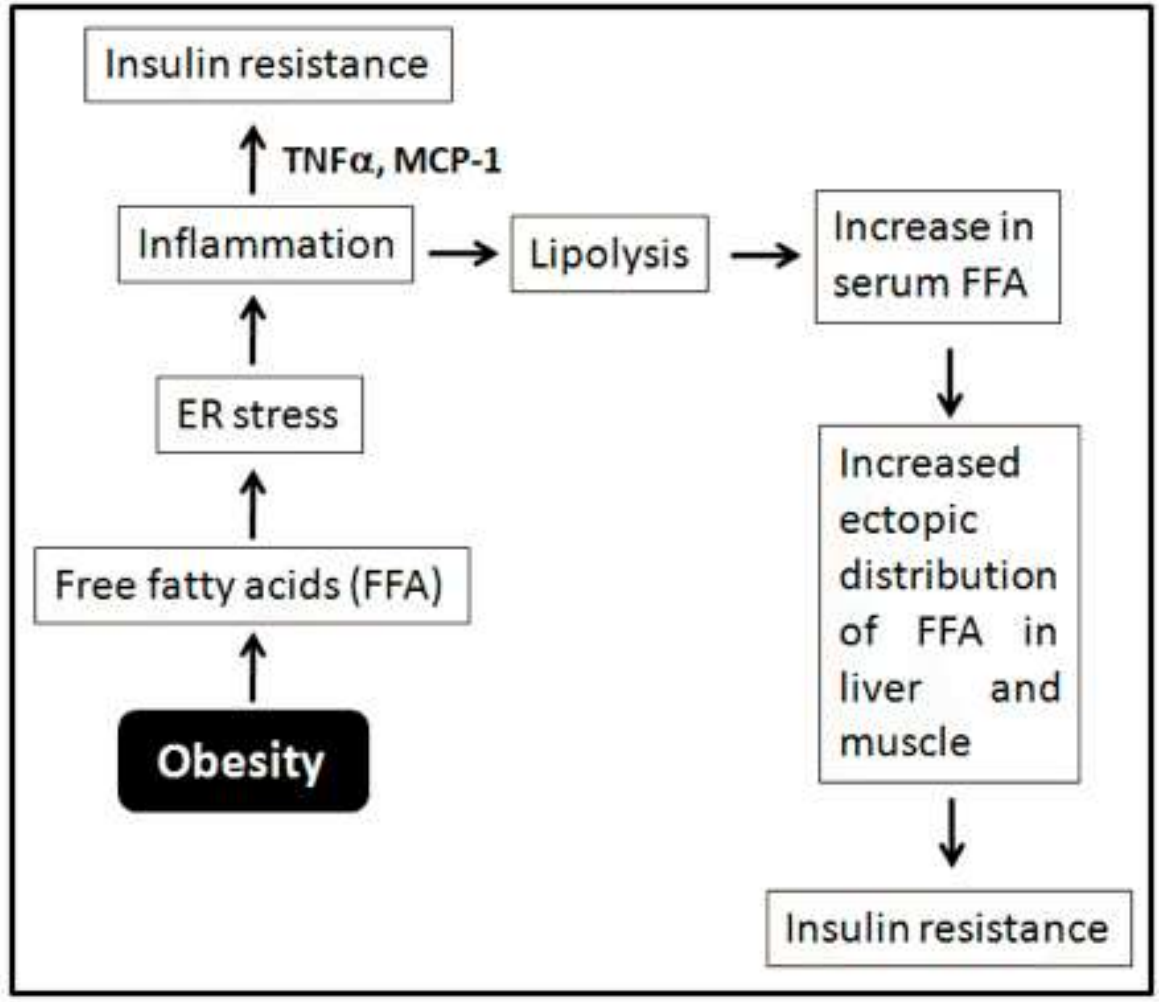
اسیدهای چرب ازاد و دیابت

- FFAبا مهار سیگنال دهی انسولین از طریق فعال شدن سرین کینازها باعث مقاومت به انسولین می شود

چاقی، اسیدهای چرب ازاد و دیابت

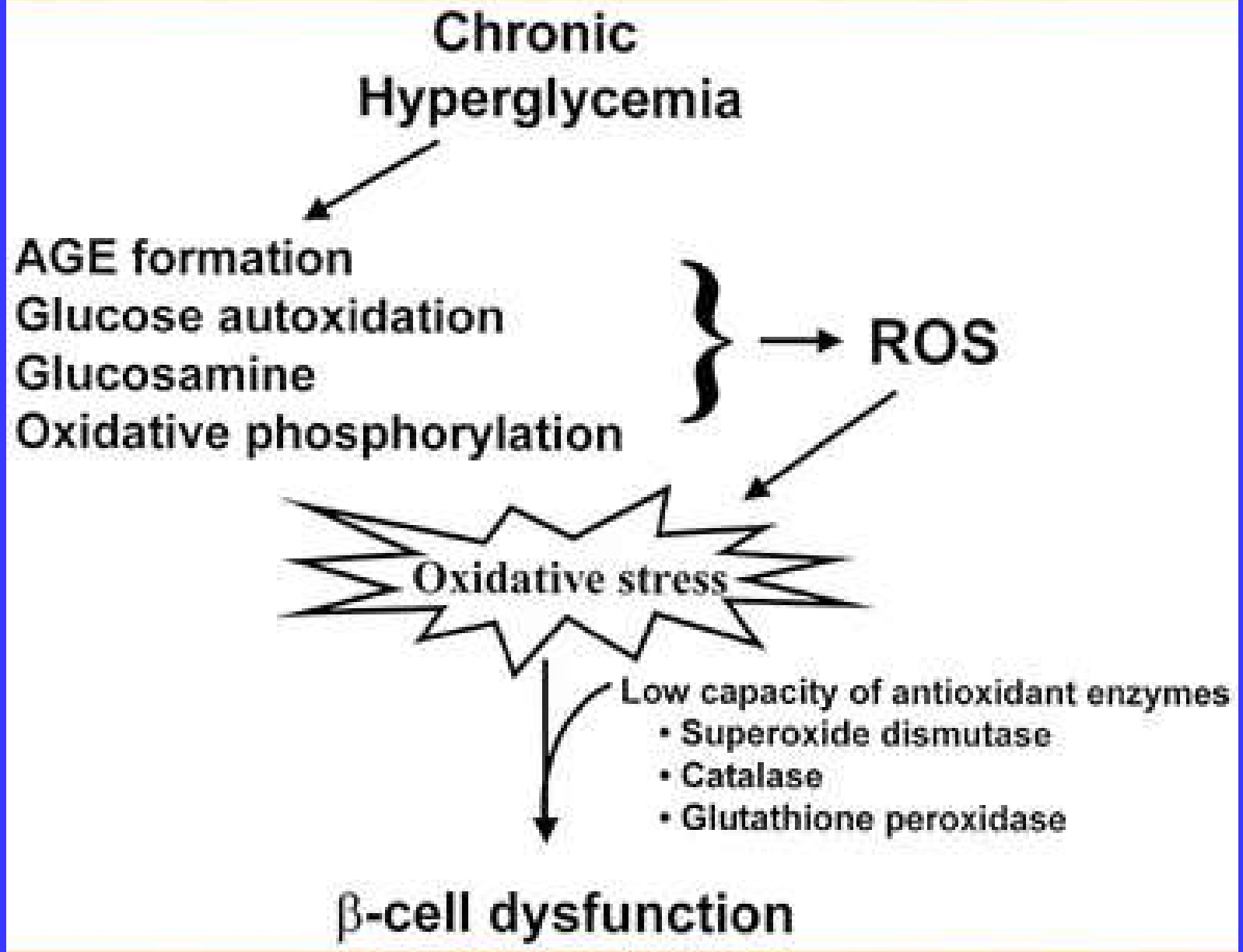


چاقی، اسیدهای چرب ازاد و دیابت



Glucose Toxicity

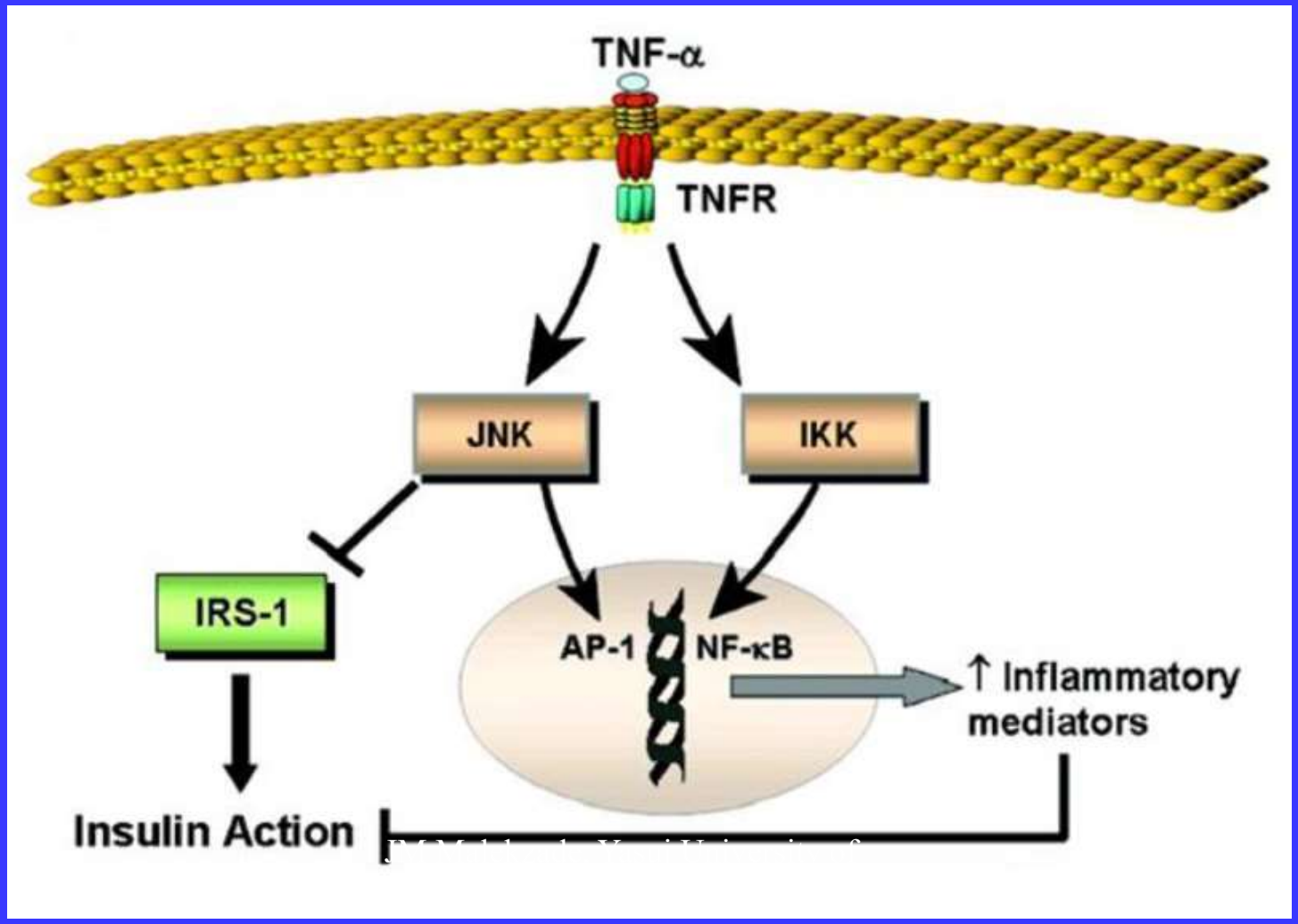
- اثرات نامطلوب غلظت های بالاتر از طبیعی گلوکز بر سلول ها و بافت ها
- مقادیر نسبتا کم آنزیم های آنتی اکسیدانی جزایر پانکراس
- هیپرگلیسمی طولانی مدت= اکسیداسیون جزایرلانگرهانس
- در نتیجه گلوکز اضافی ترشح و عملکرد انسولین را مختل میکند



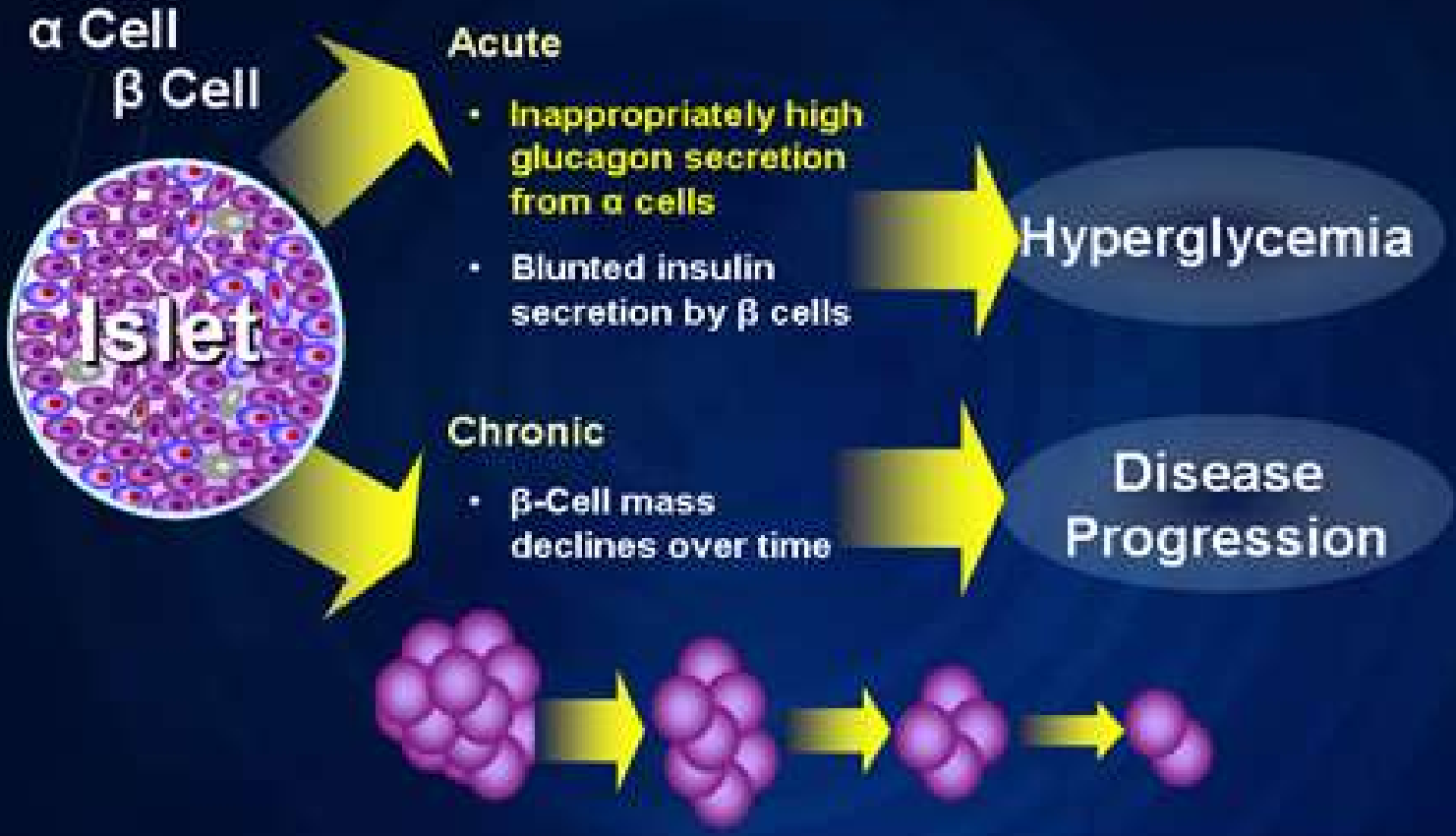
TNF-α

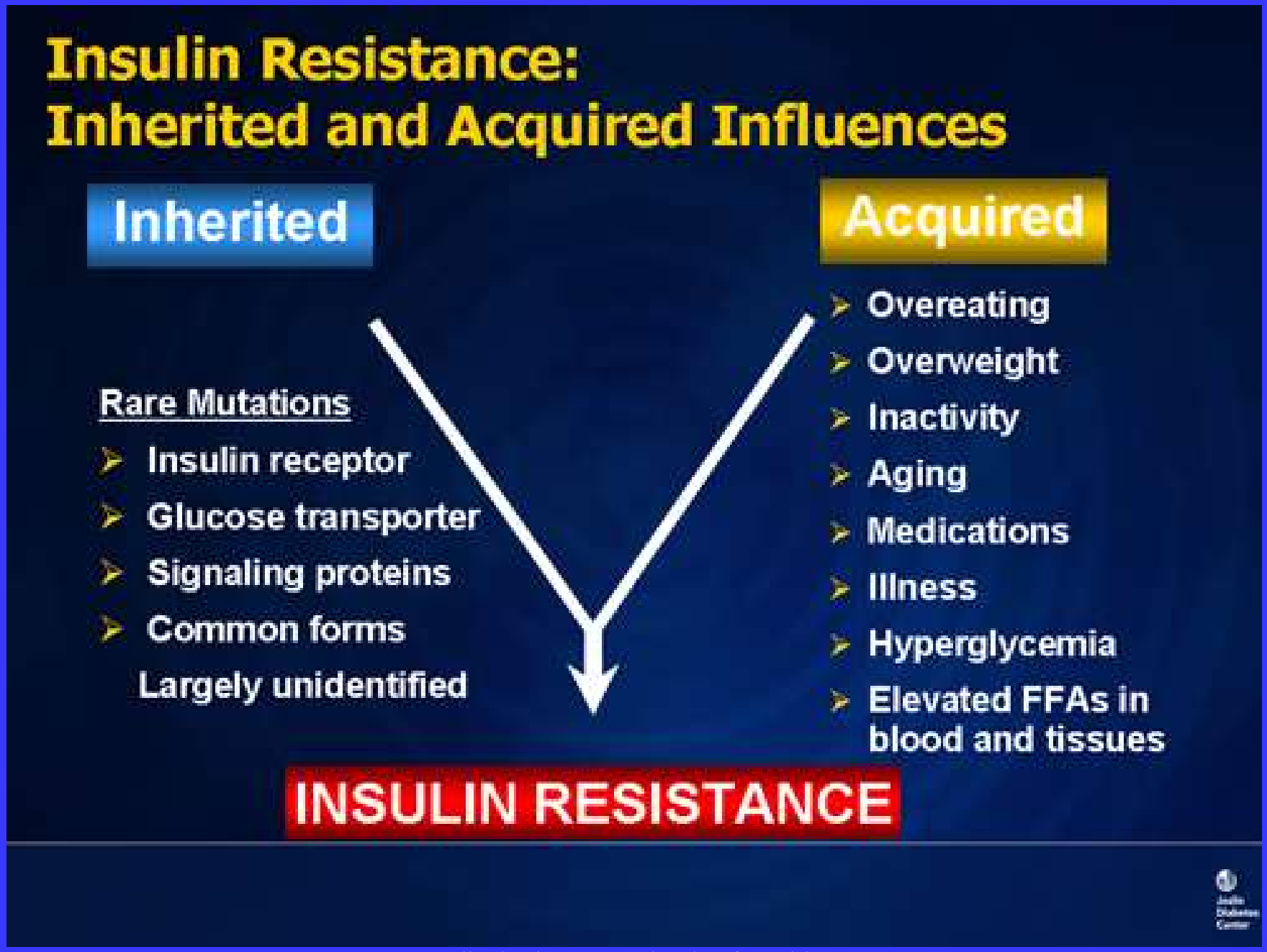
- باعث التهاب جزایر پانکراس والقای آپوپتوز در سلول های βجزایر پانکراس می شود
- TNF-αبا فعال کردن فاکتور NF-κB باعث مرگ سلول های پانکراس می شود
- کاهش TNF-α ممکن است اثرات مفیدی داشته باشد

TNF-alpha and Insulin Resistance



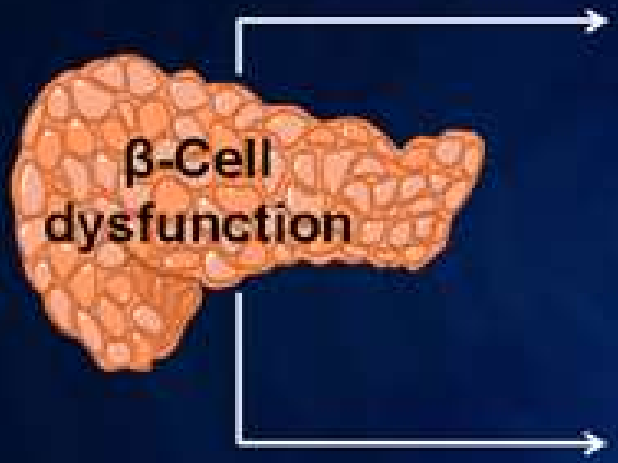
Islet Dysfunction Contributes to Both Acute and Chronic Aspects of Type 2 Diabetes




Insulin Resistance:
Inherited and Acquired Influences
Inherited
Rare Mutations
Insulin receptor
Glucose transporter
Signaling proteins
Common forms
Largely unidentified
Acquired
Overeating
Overweight
Inactivity
Aging
Medications
Illness
Hyperglycemia
Elevated FFAs in blood and tissues
INSULIN RESISTANCE

- 25 درصد از افراد تا حدی به انسولین مقاوم هستند، اما اگر سلول های بتا سالم داشته باشند، دیابتی نمی شوند
- . برخی داروها (به عنوان مثال، استروئیدها)، هایپرگلیسمی و افزایش اسیدهای چرب آزاد در خون نیز می توانند بر حساسیت به انسولین تأثیر منفی بگذارند

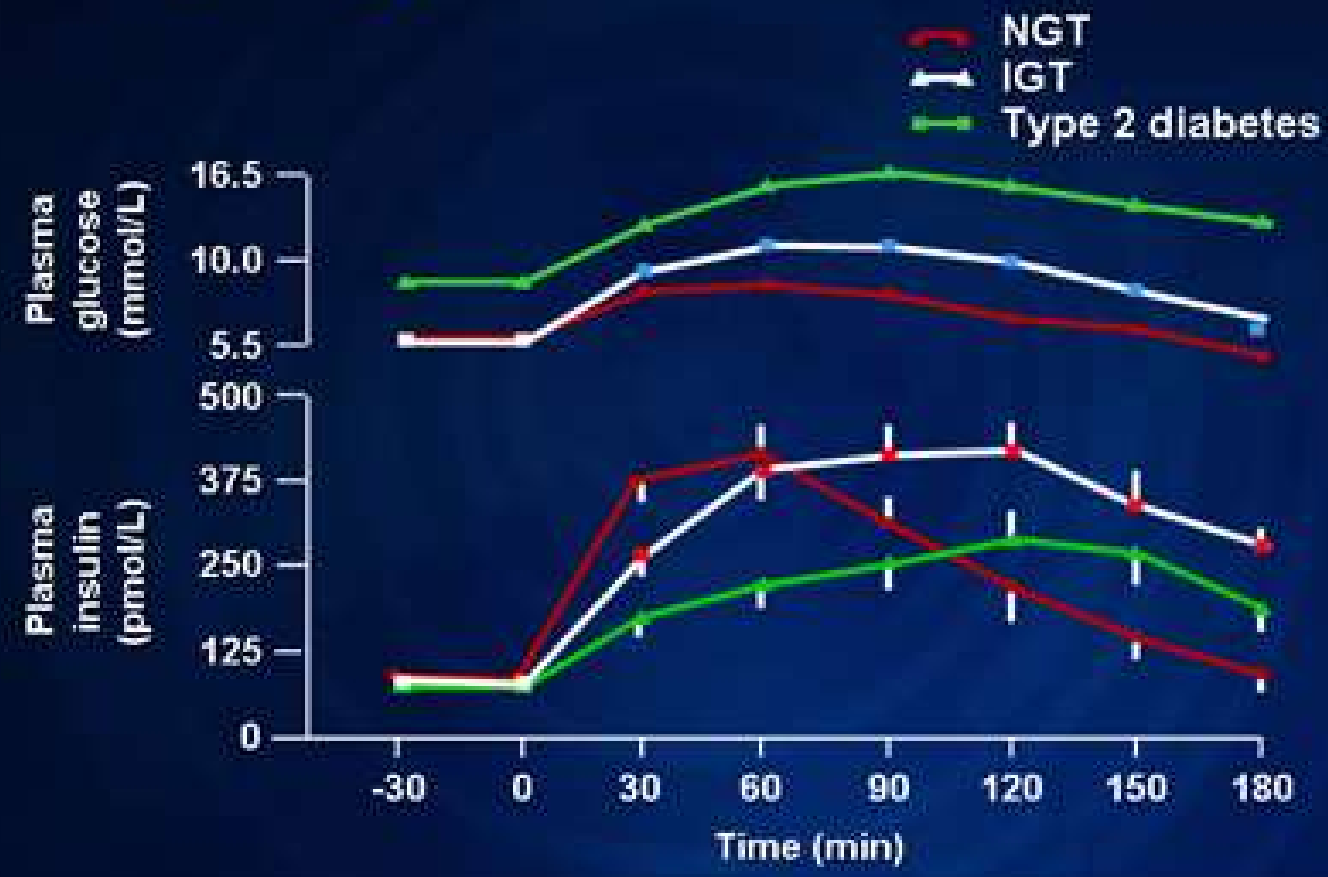
Abnormalities of β-Cell Function in Type 2 Diabetes



- Disrupted pulsatile insulin response[1]
- ↓ First phase
- ↑ Proinsulin/insulin ratio[1]
- ↓ β-cell responsiveness to glucose[2,3]
- ↓ Insulin production[4]
  - ↓ insulin
  - ↓ insulin granules

1. Buchanan TA. *Clin Ther.* 2003;25(suppl B):B32-B46. 2. Buse JB et al. In: Larsen PR et al. *Williams Textbook of Endocrinology*. 10th ed. Saunders; 2003;1427-1493. 3. Ward WK et al. *J Clin Invest.* 1984;74:1318-1326. 4. Marchetti P et al. *J Clin Endocrinol Metab.* 2004;89:5535-5541.

Plasma Glucose and Insulin Responses in Patients With Normal Glucose Tolerance, Impaired Glucose Tolerance, and Type 2 Diabetes



Adapted from Gerich JE. *Horm Metab Res.* 1996;28:404-412.

Classification

- Diabetes Mellitus and Other Categories of Glucose Intolerance
  - DM (with four subclasses)
  - Impaired Glucose Tolerance
  - Gestational DM

Categories of Altered Glucose Regulation

- Impaired glucose tolerance (IGT)
  - Plasma glucose concentration >140 mg/dL but <200 mg/dL 2 hours after an oral glucose tolerance test (OGTT)
- Impaired fasting glucose (IFG)
  - Fasting plasma glucose (FPG) concentration >100 mg/dL but <126 mg/dL
- Type 2 diabetes
  - 2-h OGTT plasma glucose ≥200 mg/dL or
  - FPG ≥126 mg/dL
  - Symptoms of diabetes and a casual plasma glucose ≥200 mg/dL

Types of DM

- Type I DM (Insulin Dependent)
- Type II DM (Non-Insulin Dependent)
- Maturity-onset diabetes of the young (MODY)
- Secondary/other types of diabetes associated with certain conditions
- Malnutrition related DM

Type I DM

- Presence of ketosis
- Severe lack or Almost complete lack of insulin
- Autoimmune Cause
- Patients commonly lean

Type II DM

- Most Common
- Strong Genetic Basis
- Absence of Ketosis
- Inadequate Insulin Secretion
- Obesity a strong factor

maturity-onset diabetes of the young (MODY)

- **Genetic mutations in:**
  - Glucokinase
  - Hepatic nuclear factor 1α

Secondary/Other Type

- Related to certain diseases, conditions or drugs
- Known or probable cause
- Treatment of underlying disorder may ameliorate the diabetes
- Hyperglycemia present at level diagnostic of diabetes

- **Diabetes secondary to endocrine disease**
  - Acromegaly
  - Cushing syndrome
  - Phaeochromocytoma
- **Diabetes secondary to drugs and chemicals**
  - Glucocorticoids
  - Thiazide diuretics
  - Antipsychotics
  - β-adrenergic receptor blockers

❑•Infections

- ➢Congenital rubella
- ➢Cytomegalovirus
- ➢Mumps

Malnutrition Related Diabetes Mellitus

- Mostly in developing countries
- Among 10 to 40 year olds
- Hyperglycemia present without ketoacidosis
- Role of malnutrition as a causal factor is unknown.

Impaired Glucose Tolerance

- Higher than normal plasma glucose but lower than the diagnostic values for DM
- Precursor for Type II
- about 25% develop into type II and rest go back to normal
- Patients are more susceptible to macrovascular diseases.

Gestational DM

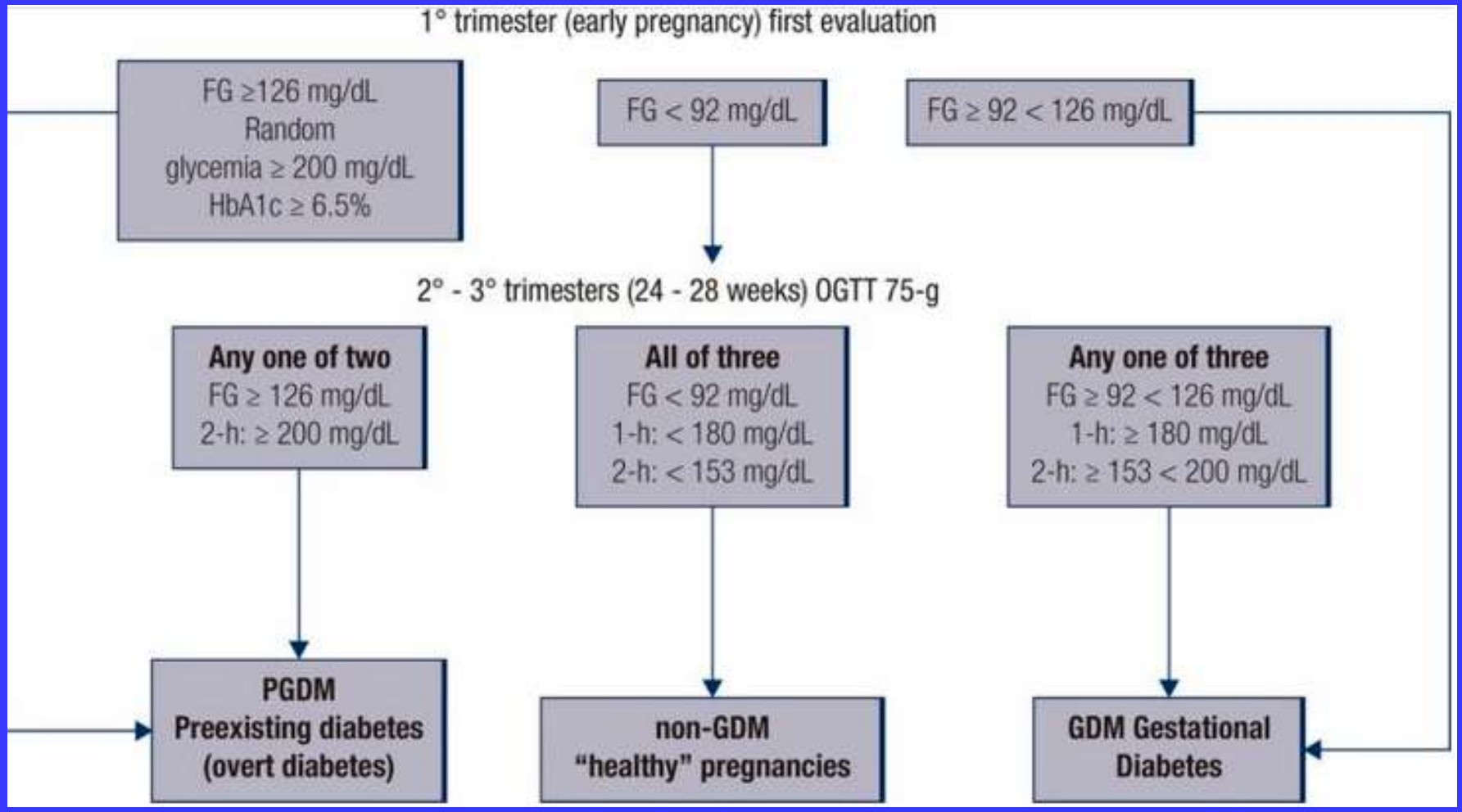
- 2-4% during second or third trimester
- Onset of DM with pregnancy
- More common in older women with family history of DM
- Higher chance of developing NIDDM and IGT

Diagnosis of Diabetes

- Polydipsia – Increased thirst
- Polyuria – Increased frequency of urination
- Fatigue
- Polyphagia – Increased Fatigue
- Weight Loss
- Abnormal Healing
- Blurred Vision
- Increased occurrence of infections

معیارهای تشخیص دیابت و پیش دیابت

Diagnosis	Criteria
Diabetes	A1C ≥6.5%* OR FPG ≥126 mg/dl (≥7.0 mmol/L)* OR 2-h PG ≥200 mg/dl (≥11.1 mmol/L) during an OGTT* OR In patients with classic symptoms of hyperglycemia or hyperglycemic crisis, a random PG ≥200 mg/dL (≥11.1 mmol/L)
Prediabetes	FPG 100-125 mg/dL (5.6-6.9 mmol/L) [Impaired fasting glucose] OR 2-hPG in the 75-g OGTT 140-199 mg/dl (7.8-11.0 mmol/L) (Impaired glucose tolerance) OR A1C 5.7-6.4%
Normal	FPG <100 mg/dL (<5.6 mmol/L) 2-hPG <140 mg/dL (<7.8 mmol/L) A1C 4 to 5.6%


1° trimester (early pregnancy) first evaluation
FG ≥126 mg/dL
Random
glycemia ≥ 200 mg/dL
HbA1c ≥ 6.5%
FG < 92 mg/dL
FG ≥ 92 < 126 mg/dL
2° - 3° trimesters (24 - 28 weeks) OGTT 75-g
Any one of two
FG ≥ 126 mg/dL
2-h: ≥ 200 mg/dL
All of three
FG < 92 mg/dL
1-h: < 180 mg/dL
2-h: < 153 mg/dL
Any one of three
FG ≥ 92 < 126 mg/dL
1-h: ≥ 180 mg/dL
2-h: ≥ 153 < 200 mg/dL
PGDM
Preexisting diabetes
(overt diabetes)
non-GDM
"healthy" pregnancies
GDM Gestational
Diabetes

مهم

قند پلاسمای زن باردار در هر زمانی مساوی یا بیشتر از 126= دیابت

و اگر بین 105-126 باشد بایستی GCT انجام شود.

Nutrition Therapy

- Nutrition Therapy – The Most Fundamental Component of the Diabetes Treatment Plan
- Goals:
  - Near Normal Glucose Levels
  - Normal Blood Pressure
  - Normal Serum Lipid Levels
  - Reasonable Body Weight
  - Promotion of Overall Health

The ADA's glycemic treatment goals for persons with diabetes

TABLE 30-3 Recommendations for Glycemic Control for Adults with Diabetes

Glycemic Control	Criteria
A1C	<7.0%*
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)

TABLE 30-4 Recommendations for Lipid and Blood Pressure for Most Adults with Diabetes

Lipids/Blood Pressure	Criteria
LDL cholesterol	<100 mg/dl (<2.6 mmol/l)*
HDL cholesterol	
Men	>40 mg/dl (>1.1 mmol/l)
Women	>50 mg/d (>1.4 mmol/l)
Triglycerides	<150 mg/dl (<1.7 mmol/l)
Blood pressure	<140/90 mm Hg

Comparison of HbA_{1c} and plasma glucose levels:

HbA_{1c} (%)	Average glucose levels (mg/dL)
6	126
7	154
8	183
9	212


با تشکر از صبر و
حوصله شما