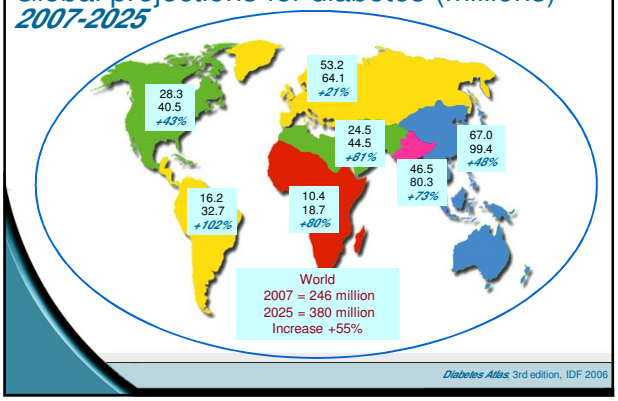
T2DM MED 341 FEB 2017

AlMaatouq MA, MD

OBJECTIVES:

1. SCOPE OF DIABETES
2. MAKING THE DIAGNOSIS
3. PATHOPYSIOLOGY
4. DISEASE CONSEQUENCES
5. MANAGEMENT
6. CONCLUSION

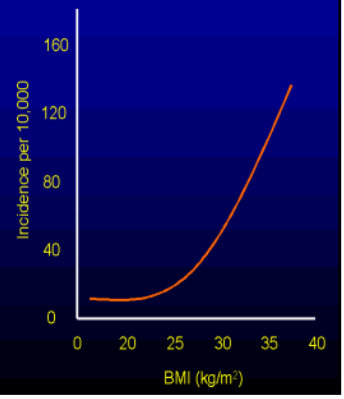
Global projections for diabetes (millions) *2007-2025*



Diabetes Atlas, 3rd edition, IDF 2006

Obesity and type 2 diabetes

- Elevated BMI (> 25) is associated with an increased risk for the development of Type 2 diabetes.
- Prevalence of Type 2 diabetes closely matches the prevalence of obesity.
- Elevated TNF-α levels may be partly responsible.



Obesity in Saudi Arabia

Mansour M. Al-Nozha, Yaqoub Y. Al-Mazrou, Mohammed A. Al-Maatouq, et al

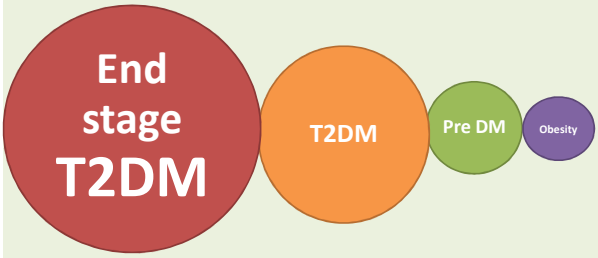
Methods: This study is a community-based national epidemiological health survey, conducted by examining Saudi subjects in the age group of 30-70 years of selected households over a 5-year period between 1995 and 2000 in KSA.

Results: Data were obtained by examining 17,232 Saudi subjects from selected households who participated in the study. The prevalence of **overweight was 36.9%.** Overweight is significantly more prevalent in males (42.4%) compared to 31.8% of females (p<0.0001). The age-adjusted **prevalence of obesity was 35.5%** in KSA with an overall prevalence of 35.6% [95% CI: 34.9-36.3], while severe (gross) obesity was 3.2%. Females are significantly more obese with a prevalence **of 44%** than males **26.4%** (p<0.0001).

Conclusion: Obesity and overweight are increasing in KSA with an overall obesity prevalence of **35.5%**.

Saudi Med J. 2007 Apr ;28 (4):559-68

Costs of T2DM 2030

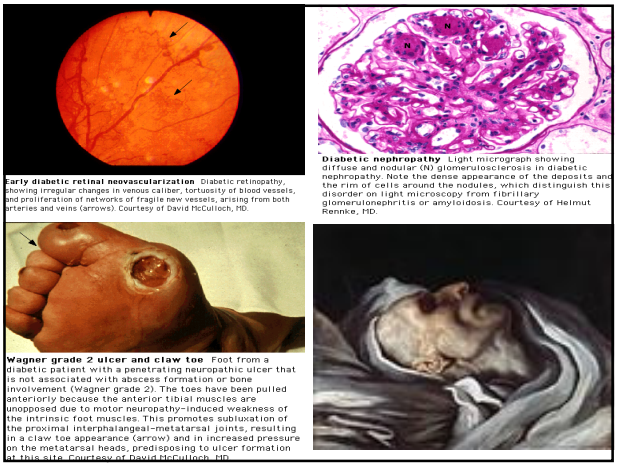


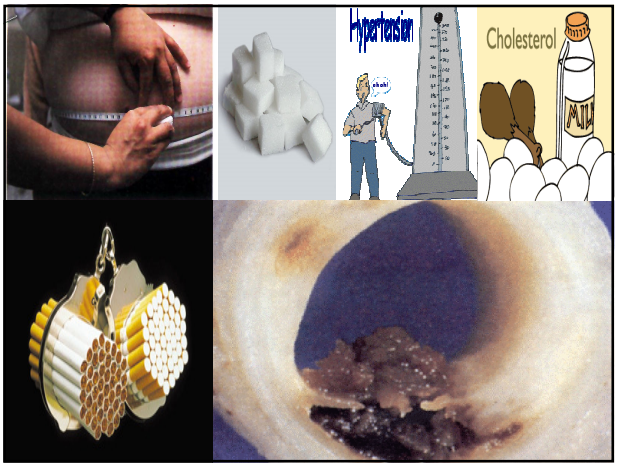
Diabetes mellitus in Saudi Arabia

Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, et al

- OBJECTIVE: Diabetes mellitus (DM) is a major public health problem worldwide, and it is a known risk factor for coronary artery disease (CAD). New recommendations for the diagnosis of diabetes have changed the epidemiology of DM. Therefore, we designed this study with the objective to determine the prevalence of DM among Saudis of both sexes, between the ages of 30-70-years in rural as well as urban communities. This work is part of a major national project: Coronary Artery Disease in Saudis study (CADISS) that is designed to look at CAD and its risk factors in Saudi population.
- METHODS: This study is a community-based national epidemiological health survey, conducted by examining Saudi subjects in the age group of 30-70-years of selected households over a 5-year period between 1995 and 2000. Data were obtained from history, fasting plasma glucose levels, and body mass index. The data were analyzed to classify individuals as diabetic, impaired fasting glucose and normal, using 1997 American Diabetes Association (ADA) criteria, which was adopted by the World Health Organization (WHO) in 1998, to provide prevalence of DM in the Kingdom of Saudi Arabia (KSA).
- RESULTS: A total of 17232 Saudi subjects were selected in the study, and 16917 participated (98.2% response rate). Four thousand and four subjects (23.7%), out of 16917 were diagnosed to have DM. **Thus, the overall prevalence of DM obtained from this study is 23.7% in KSA.** The prevalence in **males and females were 26.2% and 21.5% (p<0.00001)**. The calculated age-adjusted prevalence for Saudi population for the year 2000 is 21.9%. Diabetes mellitus was more prevalent among Saudis living in **urban areas of 25.5% compared to rural Saudis of 19.5%** (p<0.00001). Despite the readily available access to healthcare facilities in KSA, a large number of diabetics 1116 **(27.9%) were unaware of having DM.**
- CONCLUSION: The overall prevalence of DM in adults in KSA is 23.7%. A national prevention program at community level targeting high risk groups should be implemented sooner to prevent DM. We further recommend a longitudinal study to demonstrate the importance of modifying risk factors for the development of DM and reducing its prevalence in KSA.

Saudi Med J. 2004 Nov;25(11):1603-10.





What is the

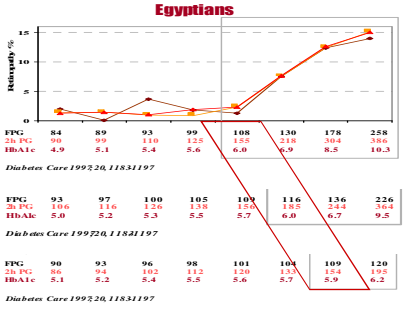
GOLD standard

for the Diagnosis of Diabetes?

Etiologic classification of diabetes mellitus

Impaired glucose tolerance IGT
Impaired fasting glucose IFG

Prevalence of Retinopathy by Deciles
Egyptians



FPG	84	89	93	99	108	130	178	258
2h PG	90	99	110	125	155	218	304	386
HbA1c	4.9	5.1	5.4	5.6	6.0	6.9	8.5	10.3

Diabetes Care 19:720, 11831197

FPG	93	97	100	105	109	116	136	226
2h PG	106	116	126	138	150	185	244	364
HbA1c	5.0	5.2	5.3	5.5	5.7	6.0	6.7	9.5

Diabetes Care 19:720, 11831197

FPG	90	93	96	98	101	104	109	120
2h PG	86	94	102	112	120	133	154	198
HbA1c	5.1	5.2	5.4	5.5	5.6	5.7	5.9	6.2

Diabetes Care 19:720, 11831197

Diagnostic criteria for T2DM

1. 8 hours fasting plasma glucose value ≥ 126 mg/dL (7 mmol/L)

OR

2. Polyuria, polydipsia, unexplained weight loss and random plasma glucose value ≥ 200 mg/dL (11.1 mmol/L)

OR

3. 2 hour plasma glucose during a (75 g anhydrous glucose) OGTT ≥ 200 mg/dL (11.1 mmol/L)

OR

4. HbA1c ≥ 6.5 %

1, 3 & 4 to be confirmed by repeat testing on a different day if no unequivocal hyperglycemia

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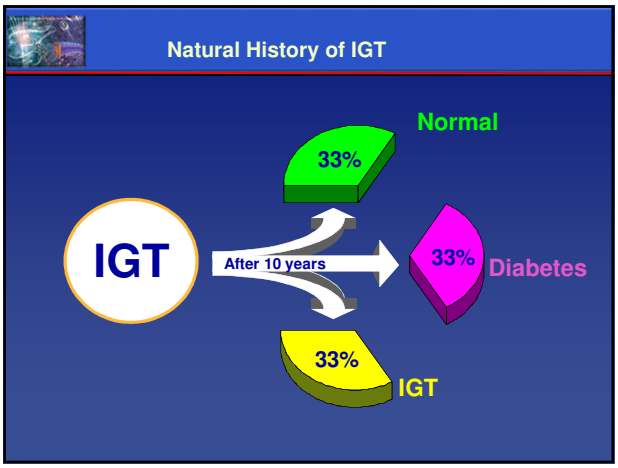
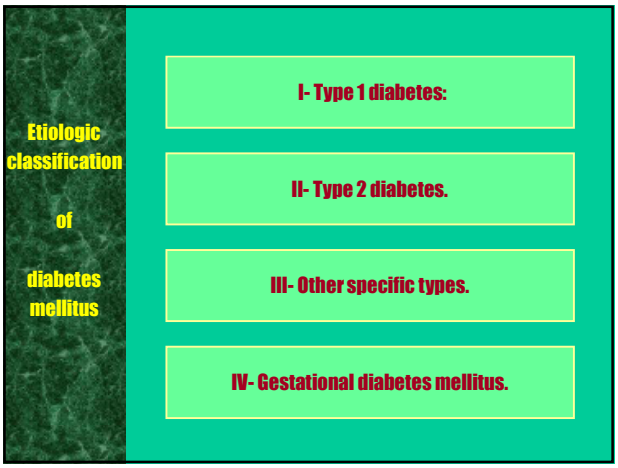
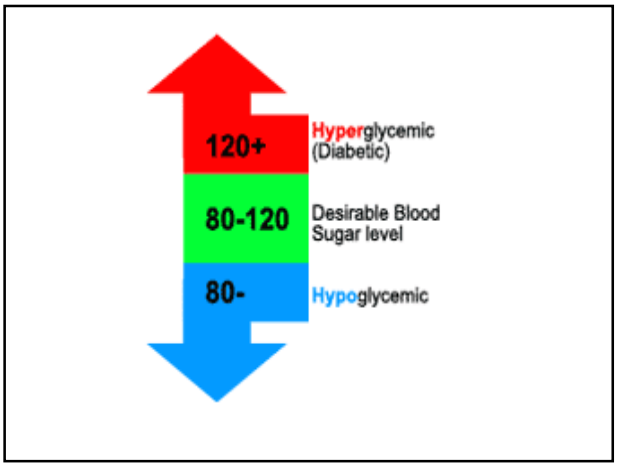
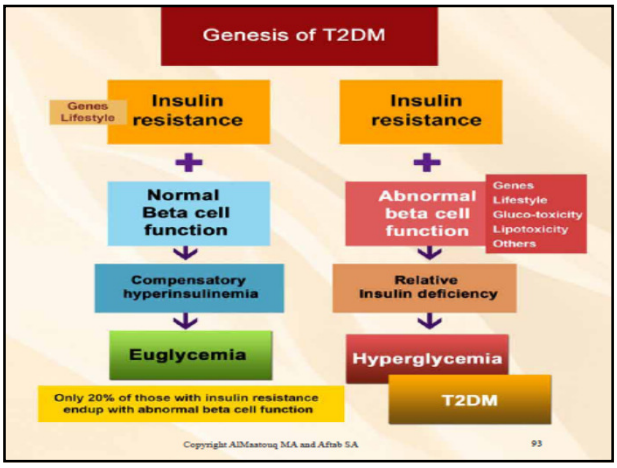

Natural History of IGT
Normal
33%
IGT
After 10 years
33%
Diabetes
33%
IGT


Etiologic classification of diabetes mellitus
I- Type 1 diabetes:
II- Type 2 diabetes.
III- Other specific types.
IV- Gestational diabetes mellitus.


120+
Hyperglycemic (Diabetic)
80-120
Desirable Blood Sugar level
80-
Hypoglycemic


Genesis of T2DM
Genes
Lifestyle
Insulin resistance
Normal Beta cell function
Compensatory hyperinsulinemia
Euglycemia
Only 20% of those with insulin resistance endup with abnormal beta cell function
Insulin resistance
Abnormal beta cell function
Genes
Lifestyle
Gluco-toxicity
Lipotoxicity
Others
Relative Insulin deficiency
Hyperglycemia
T2DM
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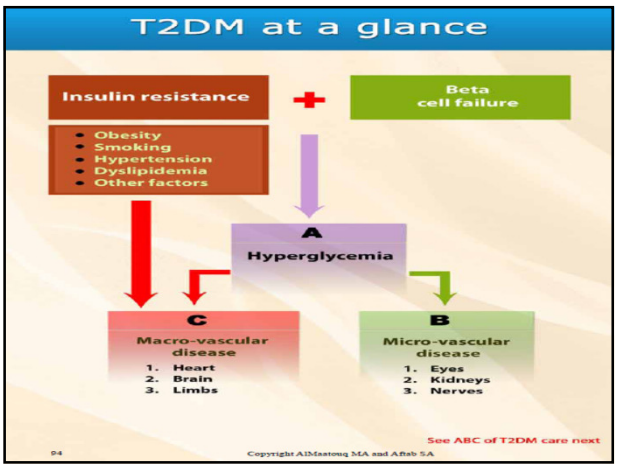
T2DM at a glance
Insulin resistance
Obesity
Smoking
Hypertension
Dyslipidemia
Other factors
Beta cell failure
A
Hyperglycemia
C
Macro-vascular disease
1. Heart
2. Brain
3. Limbs
B
Micro-vascular disease
1. Eyes
2. Kidneys
3. Nerves
See ABC of T2DM care next
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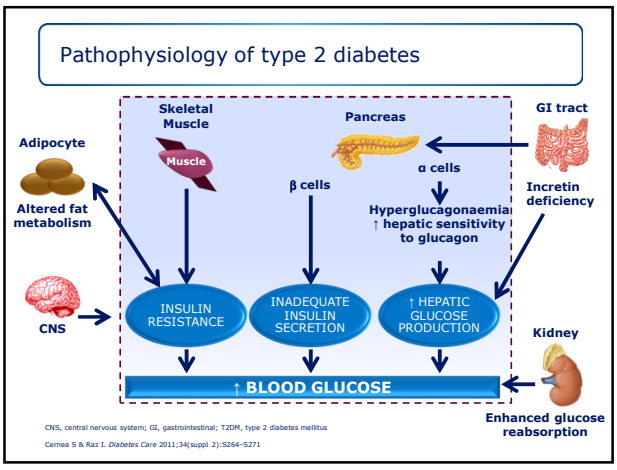
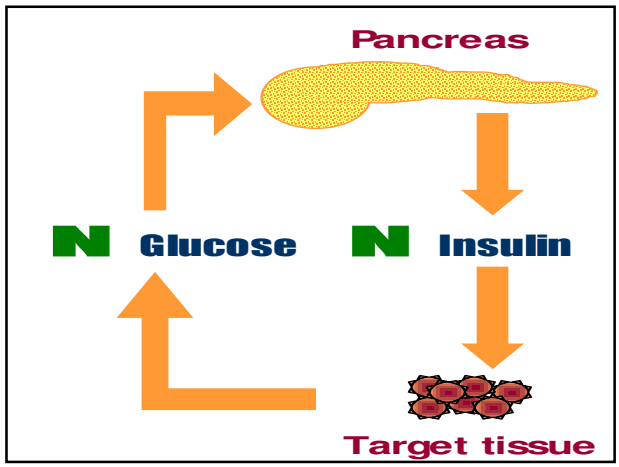
Copyright AlMaatouq MA and Aftab SA

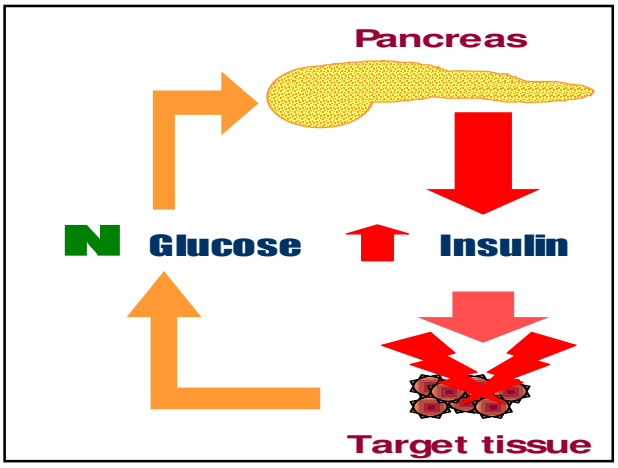

Pathophysiology of type 2 diabetes
Skeletal Muscle
Muscle
Adipocyte
Altered fat metabolism
Pancreas
α cells
β cells
Hyperglucagonaemia
↑ hepatic sensitivity to glucagon
GI tract
Incretin deficiency
CNS
INSULIN RESISTANCE
INADEQUATE INSULIN SECRETION
↑ HEPATIC GLUCOSE PRODUCTION
Kidney
↑ BLOOD GLUCOSE
Enhanced glucose reabsorption
CNS, central nervous system; GI, gastrointestinal; T2DM, type 2 diabetes mellitus
Cernea S & Raz I. Diabetes Care 2011;34(suppl 2):S264–S271

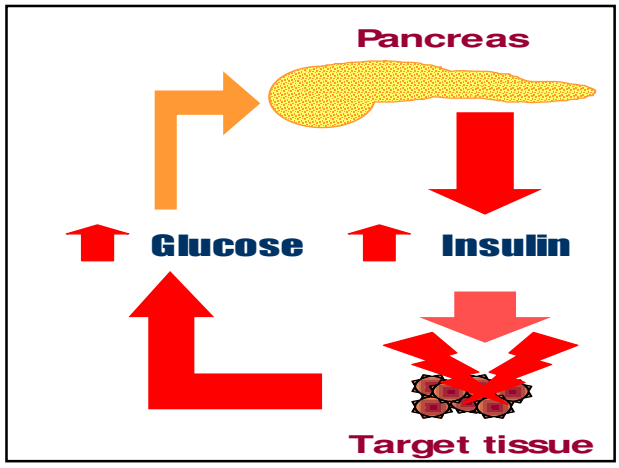
TNF-alpha may induce insulin resistance in obesity

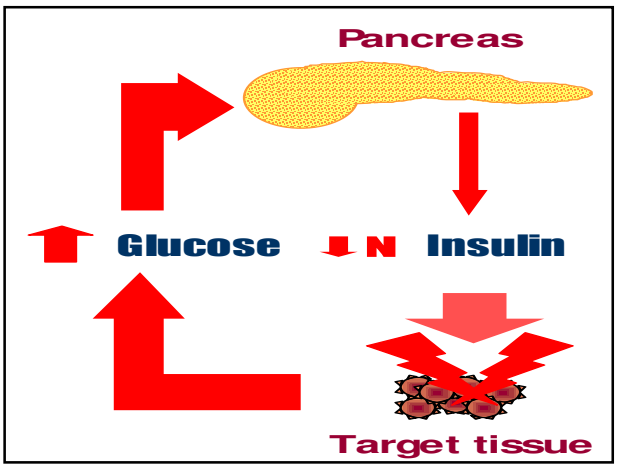
The cytokine tumour necrosis factor-α (TNF-α) is produced from adipose tissue, and TNF-α levels are often elevated in obesity.

- Administration of TNF-α leads to insulin resistance.
- Over-expression of TNF-α in adipose and muscle of obese, insulin resistant diabetic subjects is positively correlated with insulin resistance.
- Polymorphisms at the TNF-α locus correlate with insulin resistance.
- TNF-α inhibits insulin receptor signalling in adipocytes.
- TNF-α deficiency (knockout mice) prevents diet-induced insulin resistance.









Patients with type 2 diabetes are at heightened risk of disabling complications versus non-diabetics

Complication	Relative Risk*
Blindness	↑ 20
End-stage renal disease	↑ 25
Amputation	↑ 40
Myocardial Infarction	↑ 2-5
Stroke	↑ 2-3
Lifespan	↓ 6 years

* Diabetics versus non-diabetics

Ryden L. Eur Heart J. 2007; 28: 88-136

Burden of Type 2 Diabetes

15 Years Follow-up

Complications

Heart attacks	27 patients
Stroke	10 patients
Retinopathy	23 patients

Premature Mortality

Diabetes deaths	28 patients
Life expectancy	5-7 years ↓

100 Patients - Age 55

UKPDS 33. Lancet 1998; 352: 837-53

The ABC of T2DM care

Glycemic control is important.
Non glycemic factors are even more important towards outcome

- Glycemic control
- HbA1c/HBGM
- Hypos / illness
- Work / leisure
- Special events

Glucose **A**

- Kidneys
- Eyes
- Feet
- Nerves
- Erectile Dysfunction

Micro vascular **B**

- BP
- Lipids
- Aspirin
- Smoking cessation
- Diet / Exercise

Macro vascular **C**

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Lessons from UKPDS: Better control means fewer complications

EVERY 1% reduction in HBA_{1C}

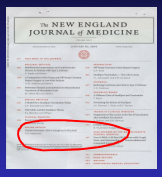
	REDUCED RISK*
Deaths from diabetes	-21%
Heart attacks	-14%
Microvascular complications	-37%
Peripheral vascular disorders	-43%

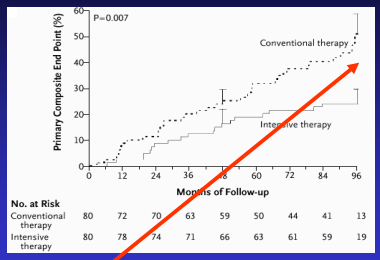
1%

*p<0.0001

UKPDS 35. BMJ 2000; 321: 405-12

Benefits of intervention to reduce multiple risk factors – Danish Steno 2 Study

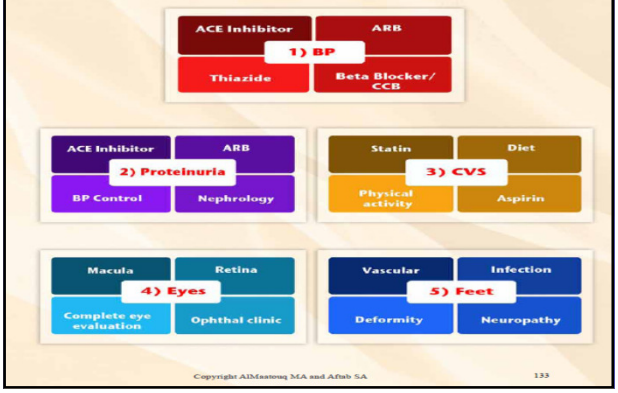




53% Risk Reduction with Intensive Therapy

Gaede P et al. NEJM 2003; 348: 383-393
Gaede P et al. NEJM 2008; 358: 580-591

T2DM: 2nd FU OPD visit Consolidation of therapy



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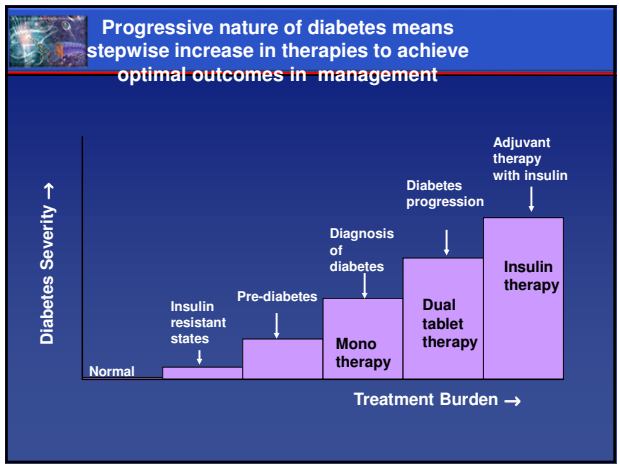
Lessons from major trials

1. DM complications are present at diagnosis
2. DM complications progress with time
3. DM control predicts rate and state of complications
4. Early and sustained control limits complications
5. Management is multifaceted and complex
6. Majority of patients are NOT at target

Guidelines need to address all concerns

Targets

1. HgbA1c: 7% Early Young No AT
2. HgbA1c: 8% Late Old W AT



PATHOPHYSIOLOGIC-BASED (DEFRONZO) ALGORITHM

Lifestyle +
TRIPLE COMBINATION:

Metformin + PIO + GLP-1 Analogue

HbA_{1c} < 6.0%

CONSENSUS

Saudi Arabia, Kuwait, Egypt, Lebanon, UAE, Jordan

Optimising the medical management of hyperglycaemia in type 2 diabetes in the Middle East: pivotal role of metformin

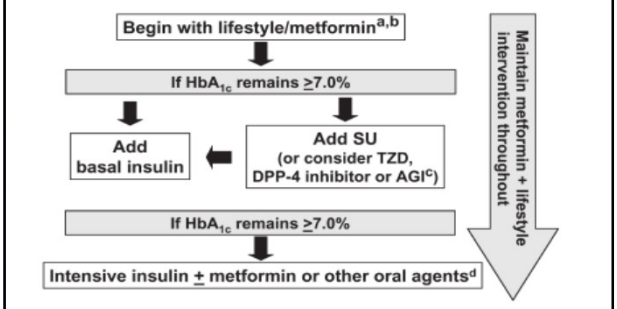
M. Al-Maatouq,[1] M. Al-Arouj,[2] S. H. Assaad,[3] S. N. Assaad,[3] S. T. Azar,[4] A. A. K. Hassoun,[5] N. Jarrah,[6] S. Zatari,[7] K. G. M. M. Alberti[8]

The burden of diabetes is high in the Middle East

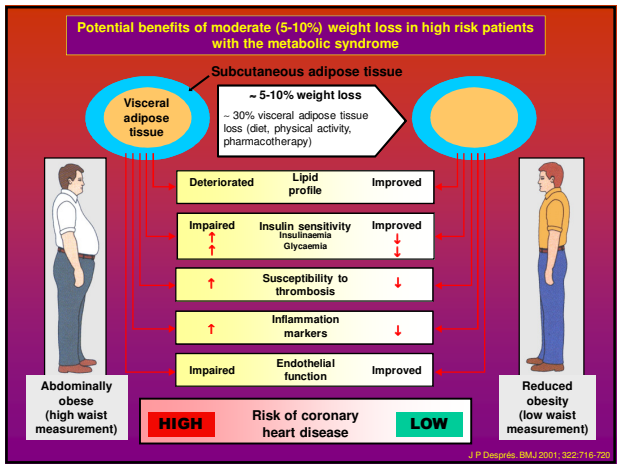
The Middle East has largely been overlooked by guideline writers

Al-Maatouq M. Int J Clin Pract 2010; 64: 149-159

Recommended treatment algorithm for the Middle East



AlMaatouq MA. Int J Clin Practice 2010; 64: 149-159



Practical dietary advice

1. Salad: 1hour BEFORE the meal
2. ¼ - ½ what you are used to. No cheating.
3. 1 Fruit per meal (juice is fruit)
4. 2 DATES BID (1 extra date BID)
5. No Communal eating
6. Avoid what you can live without.

Make Your Diabetic Patients Walk

Long-term impact of different amounts of physical activity on type 2 diabetes

Chiara Di Loreto, MD
Carmine Fanelli, MD
Paola Lucidi, MD
Giuseppe Murdolo, MD
Arianna De Cicco, MD
Natascia Parlanti, MD
Anna Ranchelli, MD
Cristina Fatone, MD
Chiara Taglioni, MD
Fausto Santeusanio, MD
Pierpaolo De Feo, MD

Western and developing countries face two serious health problems: the rising prevalence of obesity and diabetes and the fact that people no longer need to be physically active in their daily lives (1–4). Many studies

- T2D
- n = 182
- 2 year follow up
- HbA1c baseline: 7.6%
- Diabetes duration: 7.6 years
- Advice for physical activity: moderate, aerobic endurance training (30-60% of max. HF), aim: > 10 MET/ h /wk)
- 7 visits, total of ca 2 h counseling, 1 visit every 3 Month

Di Loreto et al , Diabetes Care, 2005

Effects of physical activity in T2DM

	Walking / Hours / Week*					
	0	1,5	4	5,5*	7,5	12
Weight (kg)	+ 0,8	+ 0,6	+ 0,1	- 2,2	-3,0	-3,2
Waist (cm)	+ 1,0	+ 1,0	- 0,9	- 3,8	- 5,5	- 7,1
HbA_{1c} (%)	+ 0,03	- 0,06	- 0,44	- 0,8	- 1,11	- 1,19
BD syst. (mmHg)	- 1,8	- 1,5	- 6,4	- 5,5	- 6,6	- 9,2
BD diast. (mmHg)	- 4,6	- 2,4	- 2,9	- 4,8	- 5,3	- 7,1
Chol. (mg/dl)	- 3,8	- 5,6	- 10,2	- 10,7	- 7,4	- 10,9
LDL-Chol. (mg/dl)	- 4,5	- 7,1	- 3,4	- 5,3	- 6,3	- 7,7

* e.g. 21-30 MET- 45 min walking (4 mph) /day, ca. 5 km/day

p <0,05

Tuomilehto C. et al. Diabetes Care (2005)28:1295-1302

Complications of Bariatric Surgery

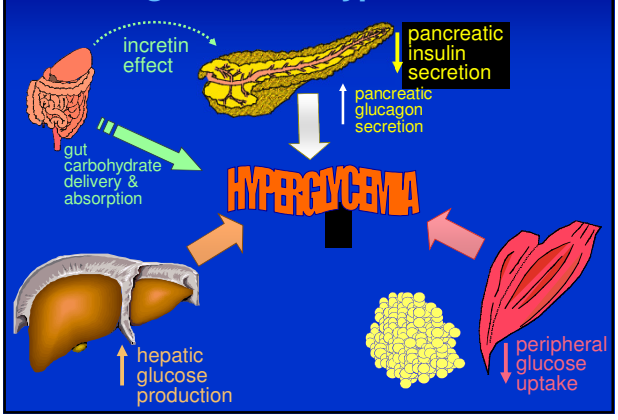
All procedures:
- Atelectasis and pneumonia
- Deep vein thrombosis
- Pulmonary embolism
- Wound infection
- Gastrointestinal bleeding
- Gallstones
- Failure to lose weight
- Intractable vomiting/kwashiorkor (B1)
- Mortality (0.1%–2%)

Gastric bypass:
- Anastomotic leak with peritonitis
- Stomal stenosis
- Marginal ulcers
- Staple line disruption
- Nutrient deficiencies (iron, calcium, folic acid, vitamin B12)
- Dumping syndrome
- Small bowel obstruction
  - Internal hernia
  - Adhesions

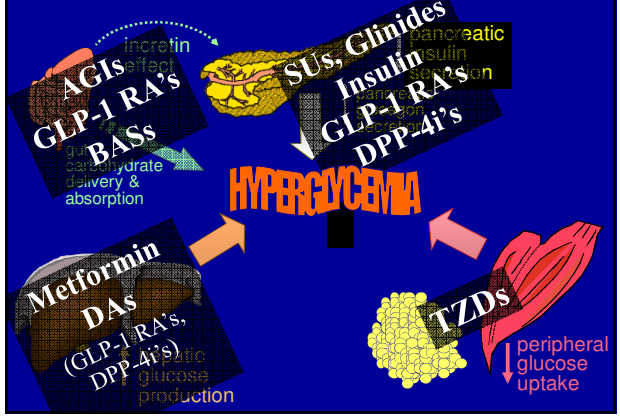
Gastric banding procedure:
- Band slippage
- Band erosion
- Esophageal dilatation
- Band or port infections
- Port disconnection
- Port displacement

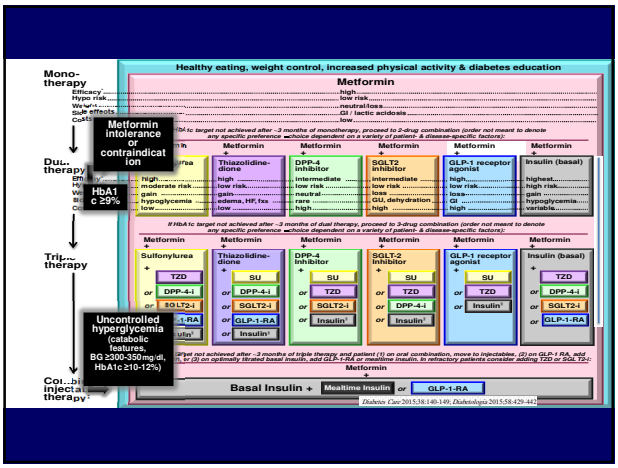
Biliopancreatic diversion:
- Anastomotic leak with peritonitis
- Protein-calorie malnutrition
- Calcium, iron, folic acid, fat soluble vitamin (A,D,E,K) deficiencies
- Dehydration
- Steatorrhea
- Small bowel obstruction
  - Internal hernia
  - Adhesions

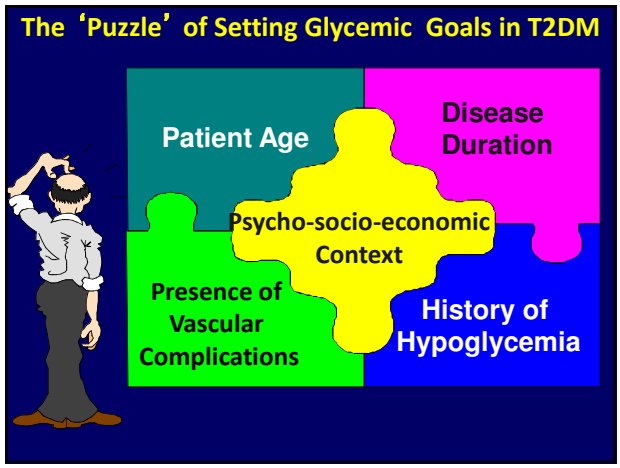
Pathogenesis of Type 2 Diabetes

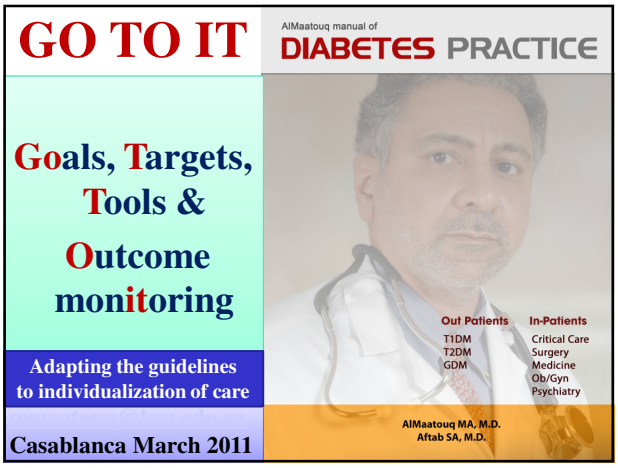


Therapy of Type 2 Diabetes




Healthy eating, weight control, increased physical activity & diabetes education
Metformin
Mono-therapy
Metformin intolerance or contraindication
HbA1c ≥9%
Uncontrolled hyperglycemia (catabolic features, BG ≥300-350mg/dl, HbA1c ≥10-12%)
Basal Insulin +
Mealtime insulin
or
GLP-1-RA


The 'Puzzle' of Setting Glycemic Goals in T2DM
Patient Age
Disease Duration
Psycho-socio-economic Context
Presence of Vascular Complications
History of Hypoglycemia


GO TO IT
AlMaatouq manual of
DIABETES PRACTICE
Goals, Targets, Tools & Outcome monitoring
Adapting the guidelines to individualization of care
Casablanca March 2011
Out Patients
T1DM
T2DM
GDM
In-Patients
Critical Care
Surgery
Medicine
Ob/Gyn
Psychiatry
AlMaatouq MA, M.D.
Aftab SA, M.D.