

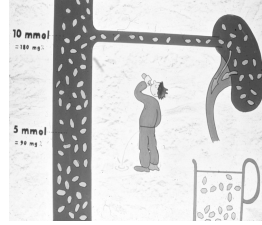
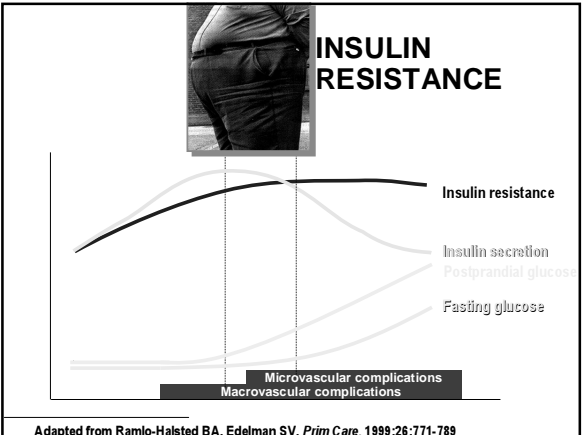
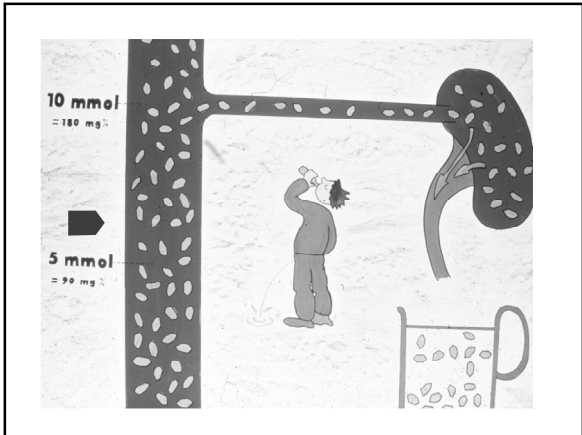
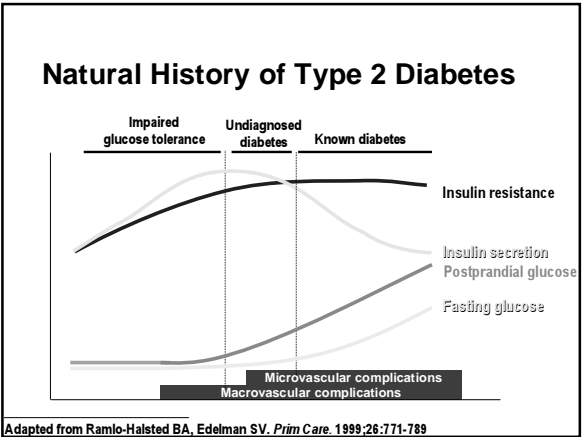
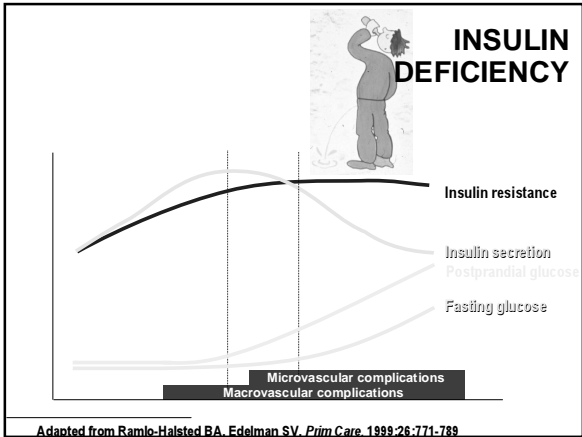
LE PREDIABETE

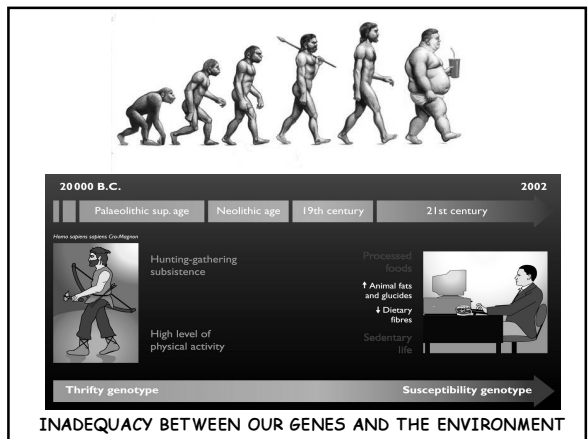
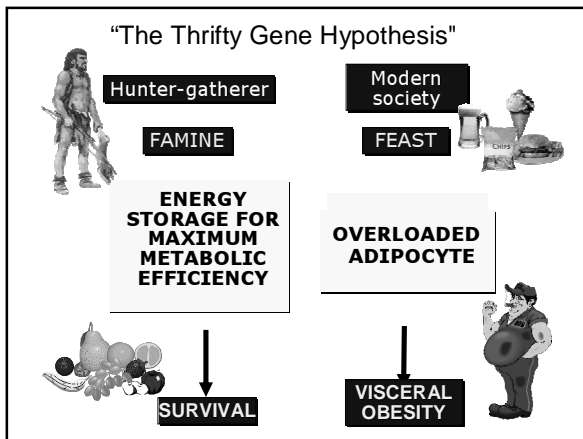
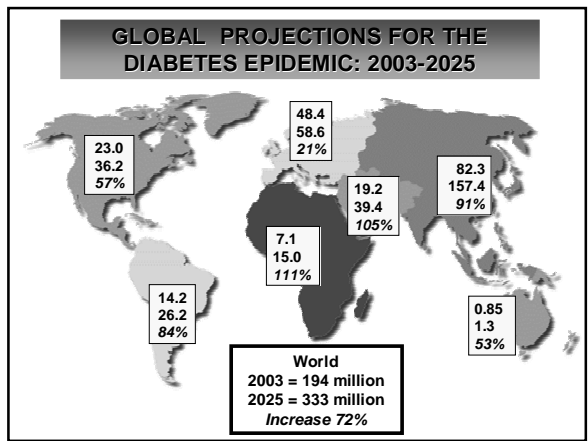
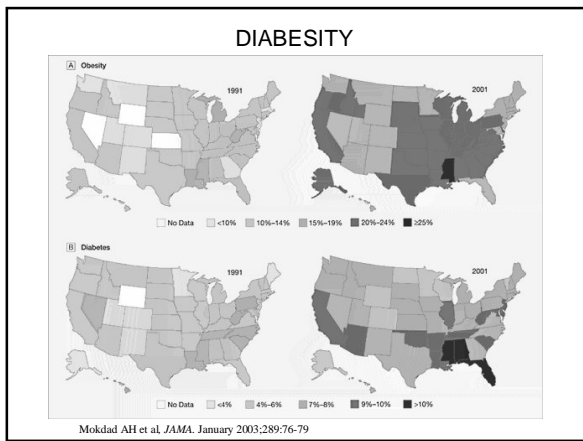
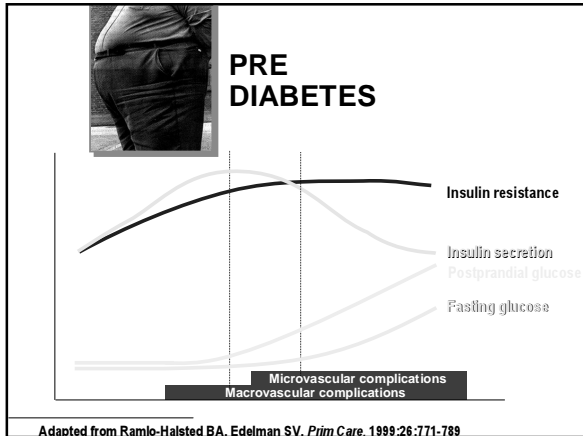
DIABETOLOGIST

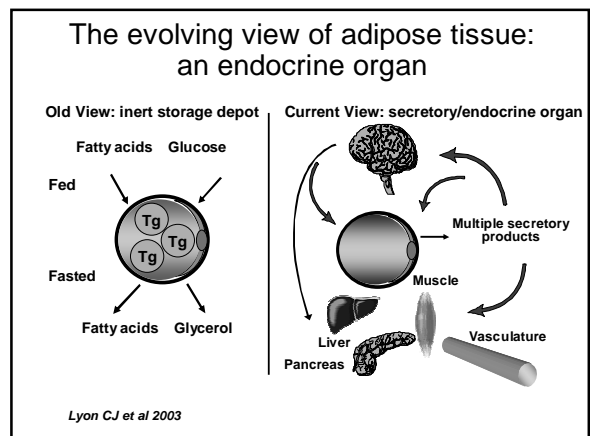
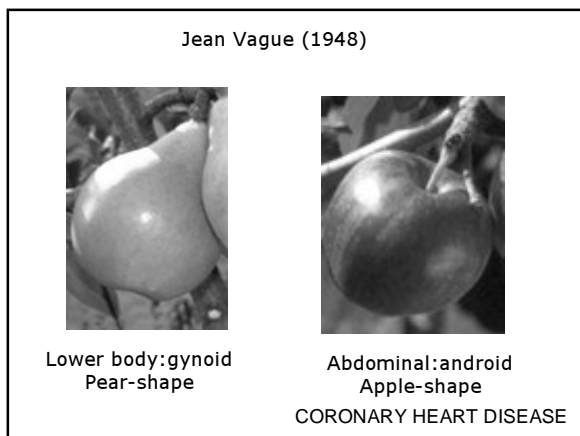
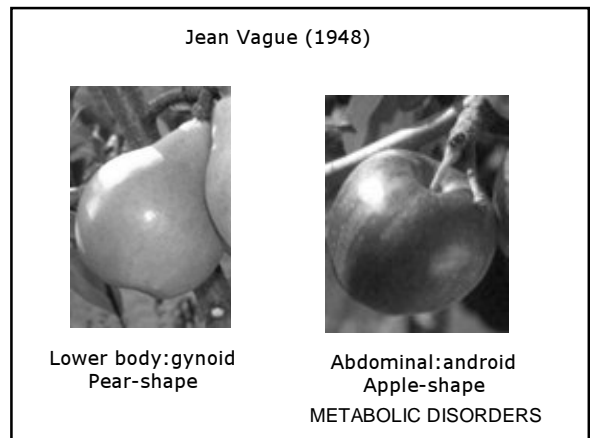
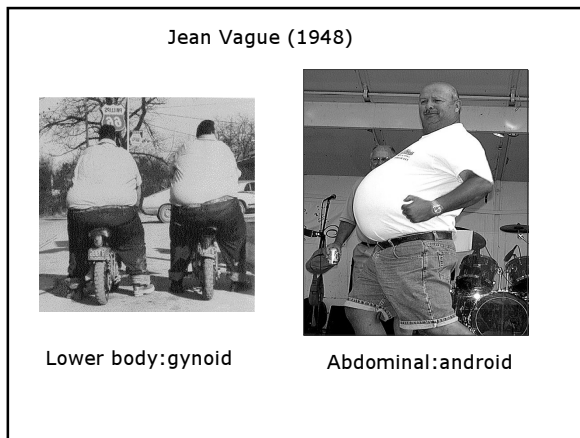
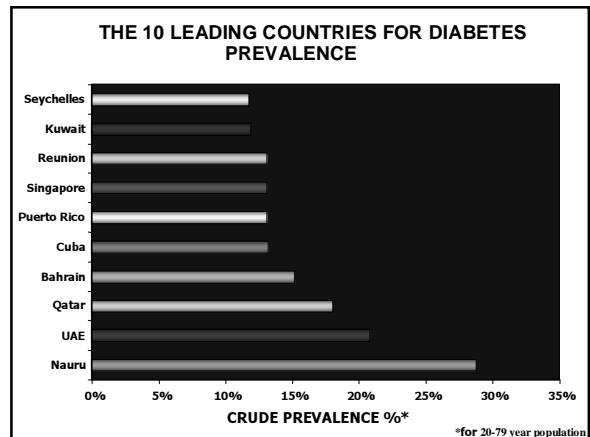
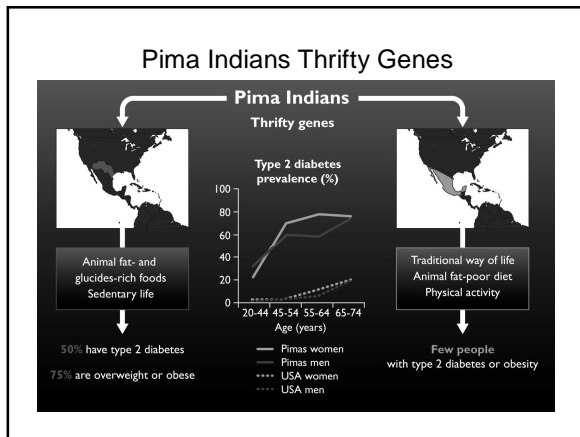
Pr. Selim Jambart
 Chef du Service d'Endocrinologie et des Maladies Métaboliques
 Hotel Dieu de France

**Type 2 diabetes:
 vascular complications at diagnosis**

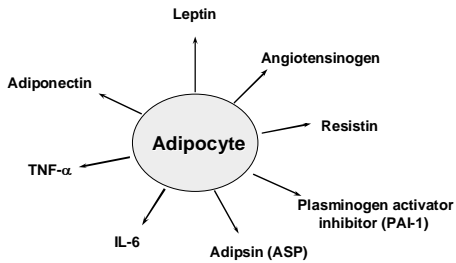
- 20–30% diabetic retinopathy
- 10–20% microalbuminuria
- 30–40% hypertension
- 50–80% dyslipidaemia

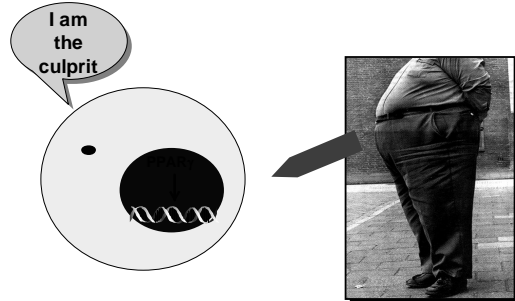




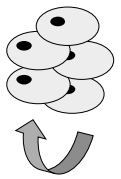
Adipose Tissue as Endocrine Cells



OVERLOADED VISCERAL ADIPOSE TISSUE BECOMES INSULIN RESISTANT



OVERLOADED ADIPOCYTE

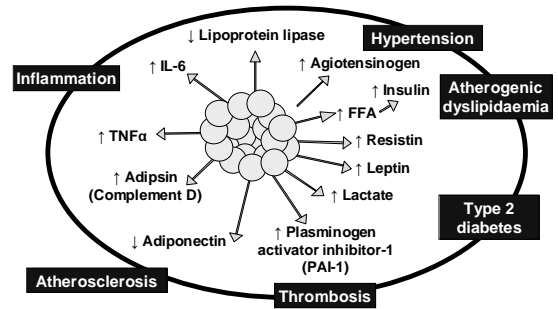


These amplifying signals increasingly impair adipocyte insulin signaling and eventually cause systemic insulin resistance in liver and muscles

TNF α
IL-6

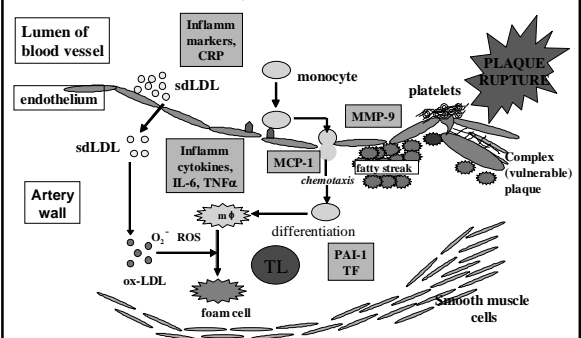
INSULIN RESISTANCE

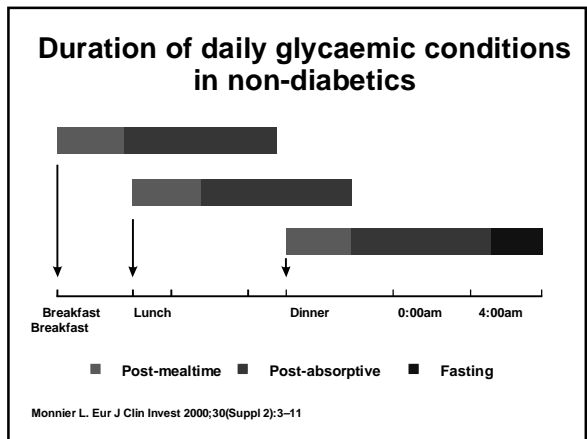
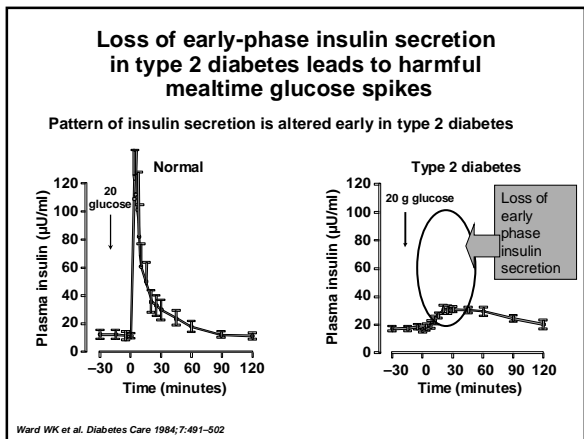
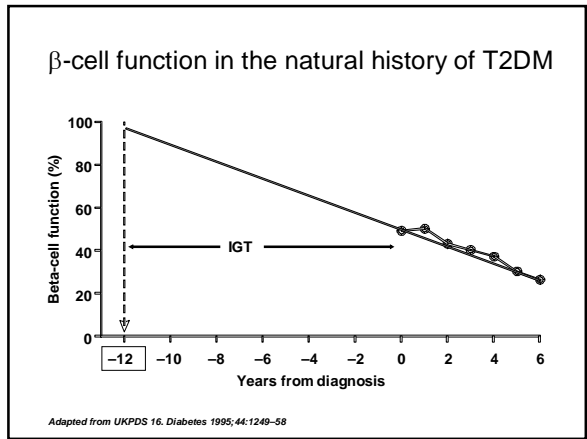
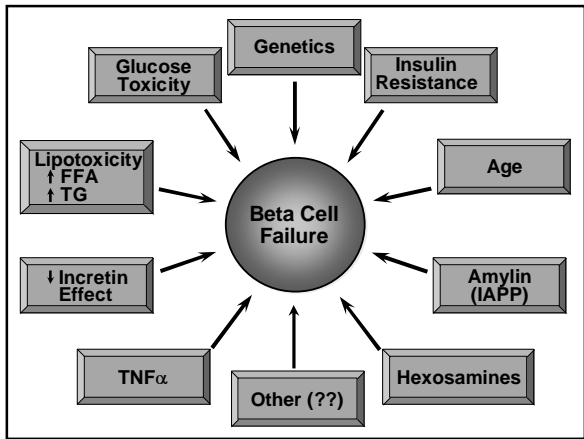
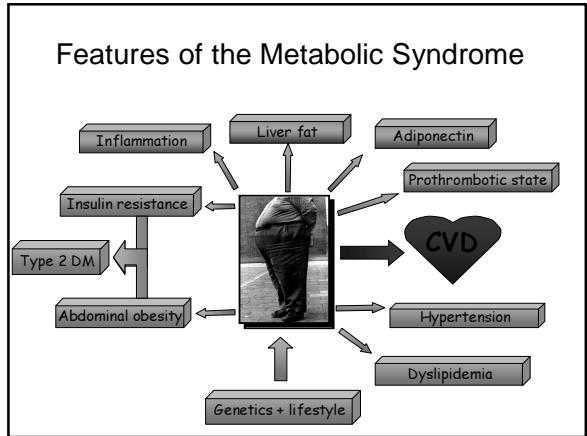
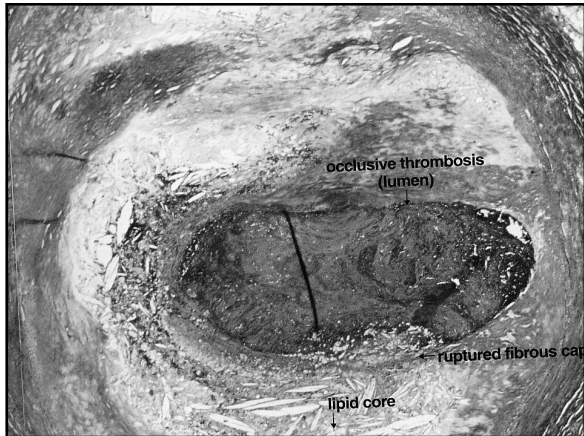
Adverse cardiometabolic effects of products of adipocytes



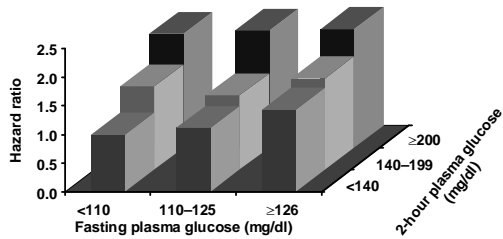
Lyon 2003; Trayhurn et al 2004; Eckel et al 2005

The inflammatory atherosclerotic process





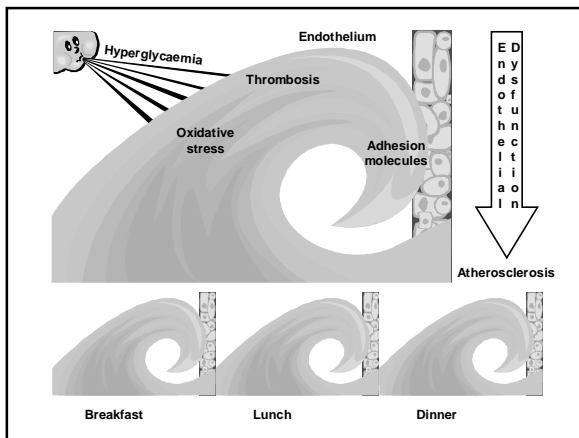
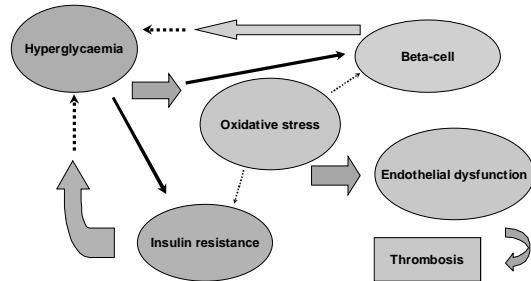
DECODE: risk for all-cause mortality



Adjusted for age, center, sex, cholesterol, body mass index (BMI), systolic blood pressure (SBP), smoking

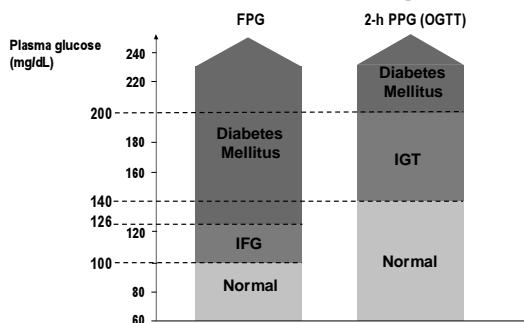
Adapted from DECODE Study Group. Lancet 1999;354:617-21

Hyperglycemia: the role of oxidative stress?



Need for early detection of type 2 diabetes and for a strict control of blood glucose in diabetic patients in order to avoid vascular events

Glucose Tolerance Categories



American Diabetes Association. Diabetes Care. 2004;27(suppl 1):S5-S10

Clinical identification of the metabolic syndrome (ATP III)

AT LEAST THREE OF THE FOLLOWING

- Waist circumference
 - Men > 102 cm
 - Women > 88 cm
- Triglycerides = > 150 mg/dl
- HDL-Cholesterol
 - Men < 40 mg/dl
 - Women < 50 mg/dl
- Blood pressure = >130/ = >85 mm Hg
- Fasting glucose = >110 mg/dl

Clinical identification of the metabolic syndrome (IDF- April 2005)

VISCERAL OBESITY

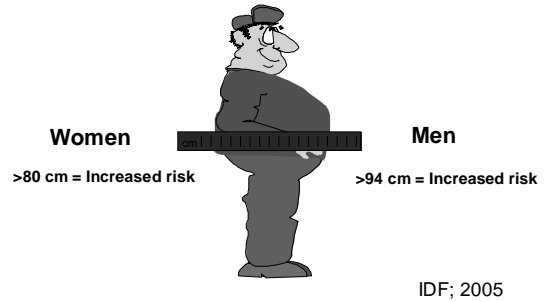
- Waist circumference (ethnic specific)
 - Men > 94 cm
 - Women > 80 cm

+

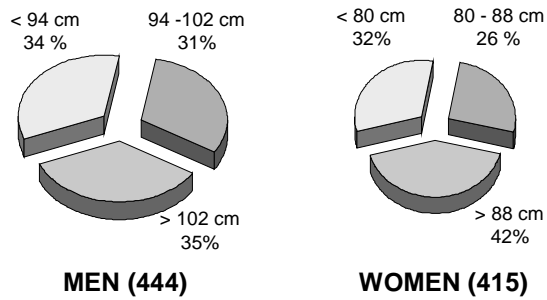
AT LEAST TWO OF THE FOLLOWING

- Triglycerides = > 150 mg/dl
- HDL-Cholesterol
 - Men < 40 mg/dl
 - Women < 50 mg/dl
- Blood pressure = >130/ = >85 mm Hg
- Fasting glucose = >100 mg/dl

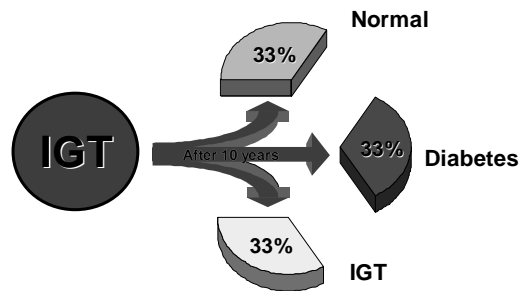
Waist circumference is a surrogate marker of visceral fat



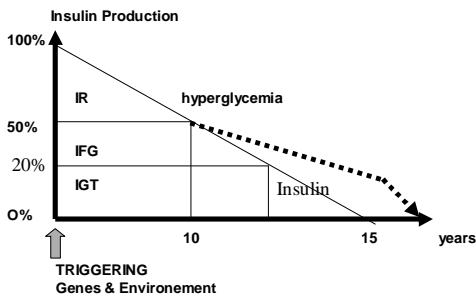
WAIST CIRCUMFERENCE - LEBANON



NATURAL HISTORY OF IGT



Can type 2 diabetes be prevented ?



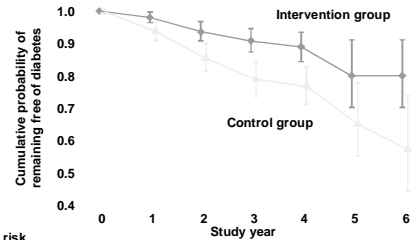
Goals behind treating pre-diabetes

- Avoiding β -cell dysfunction will allow a delayed progression from pre diabetes to diabetes
- Treating individuals at risk of developing diabetes will translate into improved CVD outcomes and mortality rate

PRE DIABETES INTERVENTIONAL TRIALS

- Lifestyle intervention
- Pharmacotherapy

Prevention of type 2 diabetes by lifestyle changes in 522 persons with IGT



Subjects at risk	Study year					
Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

Tuomilehto J et al. NEJM 2001;344:1343

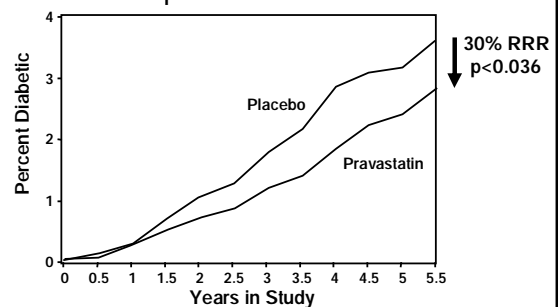
Prevention of Type 2 Diabetes Pharmacotherapy for IGT

Reduction in progression
to diabetes (%)

Diabetes Prevention Program N=3234, 2.8 years Metformin 850 mg bid	31
STOP-NIDDM trial N=1429, 3.3 years Acarbose 100 mg tid	25
TRIPOD study N=236, 2.5 years Troglitazone 400 mg qd	>50

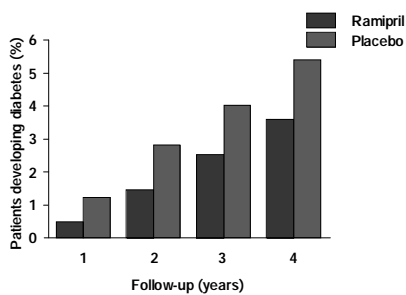
DPP Research Group. *N Engl J Med.* 2002;346:393-403; Chiasson J-L et al. *Lancet.* 2002;359:2072-2077; Buchanan TA et al. *Diabetes.* 2002;51:2796-2803

WOSCOPS: Effect of Pravastatin on Development of Diabetes



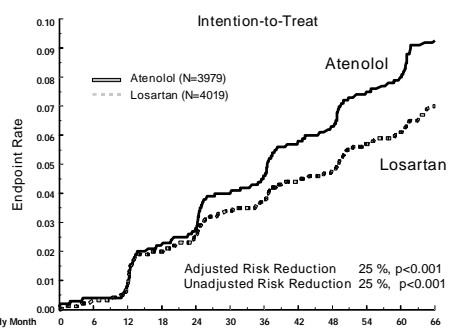
Freeman DJ et al. *Circulation* 2001;103:357-362.

HOPE – onset of new diabetes



Yusuf S *AHA* 72nd Session, Atlanta, USA, November 1999.

LIFE: New-Onset Diabetes



B. Dahlöf at the American College of Cardiology, Atlanta, GA, March 17-20, 2002.

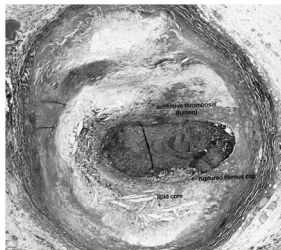
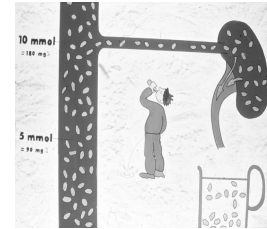
Potential Underlying Mechanisms of Benefit

- Modulation of inflammatory cytokines
 - By reducing IL-6 & TNF- α , lipoprotein lipase activity is increased & lipolysis in adipose tissue decreased
 - Interruption of natural progression from central obesity to insulin resistance
- Improvement of endothelial function
 - Improved capillary recruitment & insulin resistance
 - Improved tissue perfusion & glucose & insulin transport
- Improvement of beta cell function
 - Decreased gluco and lipo toxicity
 - Decreased oxidative stress
 - Decreased beta cell apoptosis

Freeman DJ et al. Circulation 2001;103:357-362

Type 2 Diabetes Mellitus: the classical approach

- «chronic hyperglycemia suspected by the presence of excessive thirst and polyuria »
- Goals of management : avoid symptoms related to this hyperglycaemia



Type 2 Diabetes Mellitus: the new approach

- atherosclerotic vascular disease, with a high blood glucose
- Goals of management: prevent, delay, arrest vascular complications

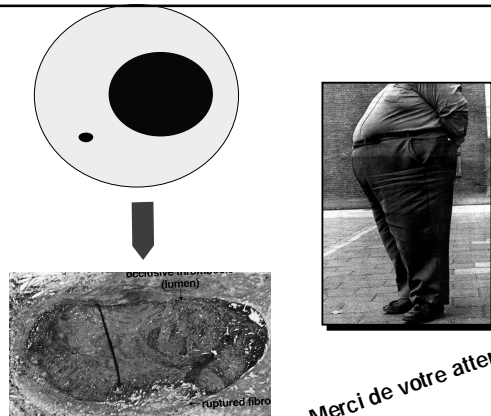
- Le prédiabète est un état d'obésité viscérale et de l'insulinorésistance qui en découle
- Le risque vasculaire est présent dès ce stade à cause de la sécrétion d'adipokines inflammatoires et pro-thrombotiques, et de la dyslipidémie et de l'hypertension, souvent déjà présentes
- L'évolution vers l'hyperglycémie est un épiphénomène qui dépend de la performance des cellules bêta

Le concept de syndrome métabolique ne doit pas être perçu comme:

- Une anomalie supplémentaire par rapport aux différents éléments qui le composent
- Un plus dans la prise en charge des désordres métaboliques

Mais comme

- Un moyen de dépister au plus tôt dans une population donnée les personnes à risque et leur proposer une prévention adéquate



Merci de votre attention