

# PREVALENCE AND CAUSALITY OF OBESITY

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*Venus of Věstonice*  
30.000 B.C.

**OBESITY  
IN THE  
MANKIND  
HISTORY**

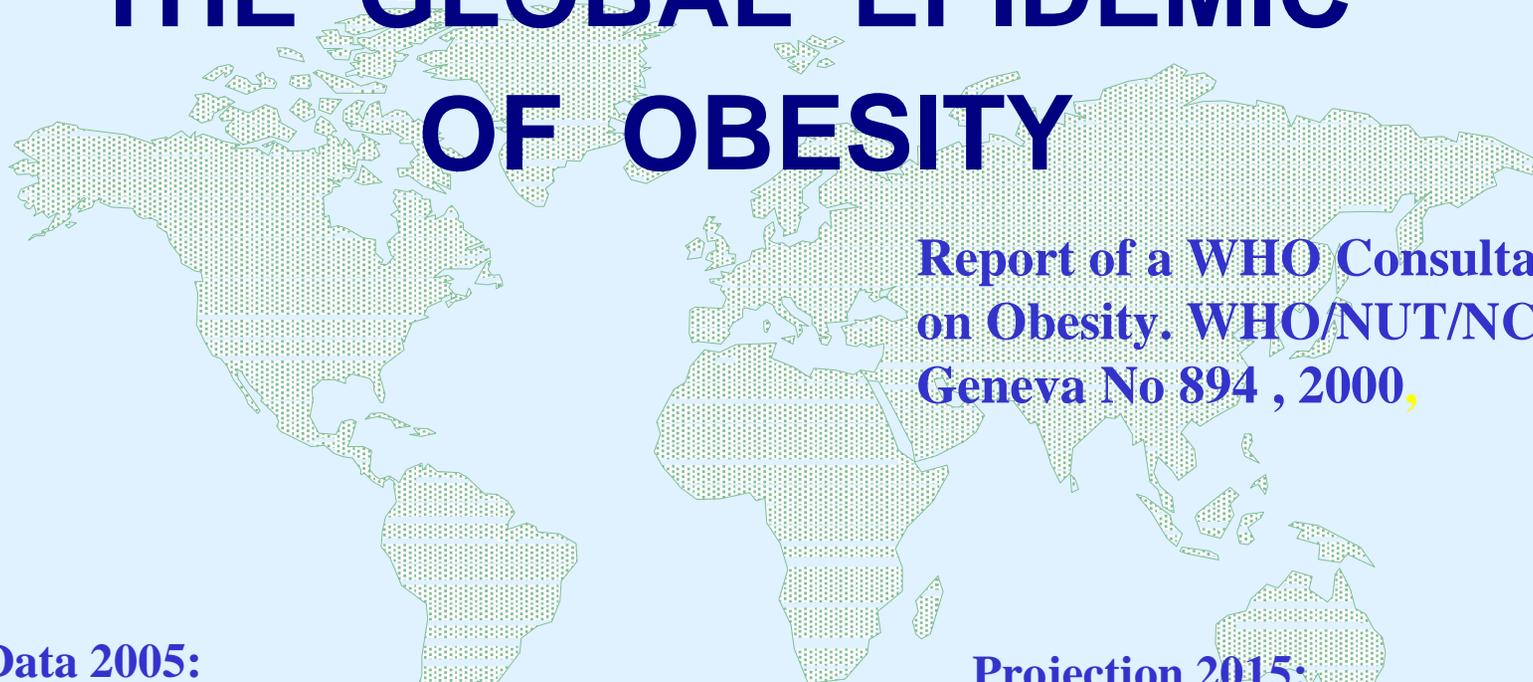


*Baroque sculpture*  
17. century

# WHO/IOTF REPORT 2000

## OBESITY: PREVENTING AND MANAGING THE GLOBAL EPIDEMIC

### THE GLOBAL EPIDEMIC OF OBESITY



Report of a WHO Consultation  
on Obesity. WHO/NUT/NCD,  
Geneva No 894 , 2000,

**Data 2005:**  
400 mill. adults obese (BMI $\geq$ 30)  
1.6 billion adults overweight (BMI $\geq$ 25)

**Projection 2015:**  
700 million adults obese  
2.3 billion adults overweight



# **CHARACTERISATION OF OBESITY AND DEFINITION OF BODY MASS INDEX (BMI)**

- **Obesity is a chronic disease characterised by an increase of body fat stores (>25% in men, >30% in women)**
- **In clinical practice, body fatness is assessed by the body mass index**
- **Body mass index (BMI) is calculated:  
measured body weight (kg)/measured height (m<sup>2</sup>)**

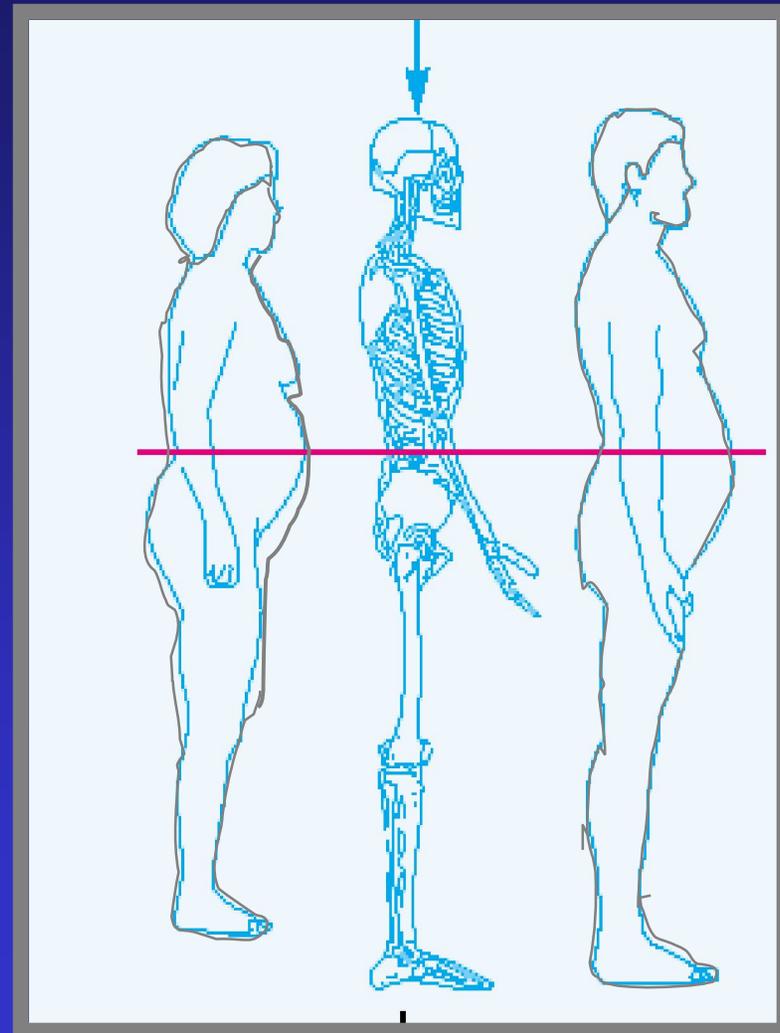
# CLASSIFICATION OF OVERWEIGHT AND OBESITY (BMI) AND BODY FAT DISTRIBUTION (WAIST CIRCUMFERENCE)

CLASSIFICATION	BMI kg/m <sup>2</sup>	DISEASE RISK* Waist Circumference	
		<102 cm (men) <88 cm (women)	≥102 cm (men) ≥88 cm (women)
Underweight	<18.5	Increased	Increased
Normal range	18.5 – 24.9	Low	Increased
Overweight	25.0 – 29.9	Increased	High
Obesity (grade I)	30.0 – 34.9	High	Very High
Obesity (grade II)	35.0 – 39.9	Very High	Very High
Obesity (grade III)	>40.0	Extremely High	Extremely High

\* International Diabetes Federation (2005) declares more strict cut-off points for waist circumference: ≥94 cm in men and ≥80 cm in women

# WAIST CIRCUMFERENCE AS A MEASURE OF VISCERAL FAT

Waist circumference  
is measured midway  
between the upper iliac  
crest and the lower rib



# COUNTRY-/ETHNICITY- SPECIFIC VALUES FOR WAIST CIRCUMFERENCE DEFINING ABDOMINAL OBESITY

*International Diabetes Federation (2005)*

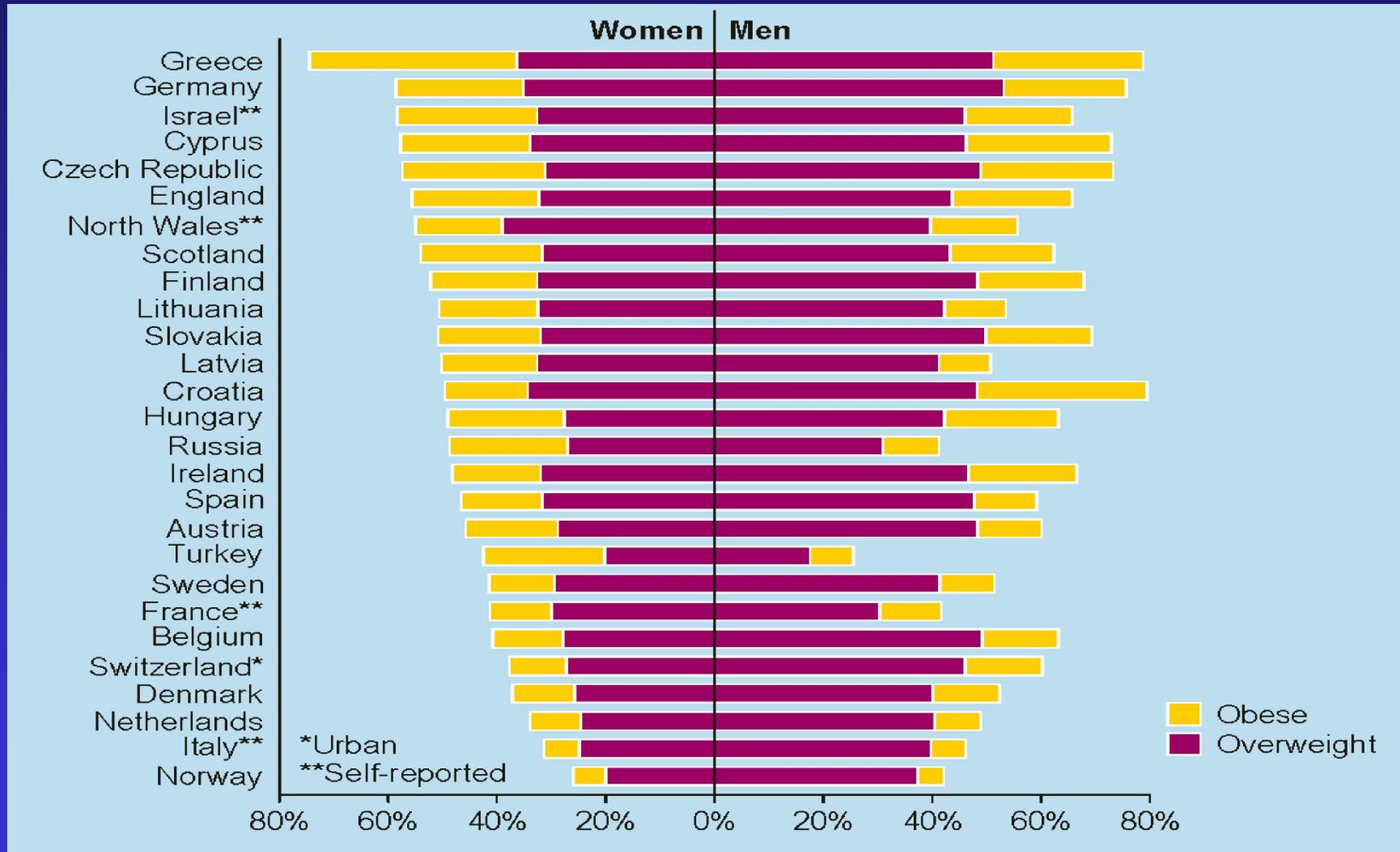
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	Men	Women
<b>Europids</b>	<b><math>\geq 94</math> cm</b>	<b><math>\geq 80</math> cm</b>
<b>South Asians</b>	<b><math>\geq 90</math> cm</b>	<b><math>\geq 80</math> cm</b>
<b>Chinese</b>	<b><math>\geq 90</math> cm</b>	<b><math>\geq 80</math> cm</b>
<b>Japanese</b>	<b><math>\geq 85</math> cm</b>	<b><math>\geq 90</math> cm</b>

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# PREVALENCE OF OBESITY

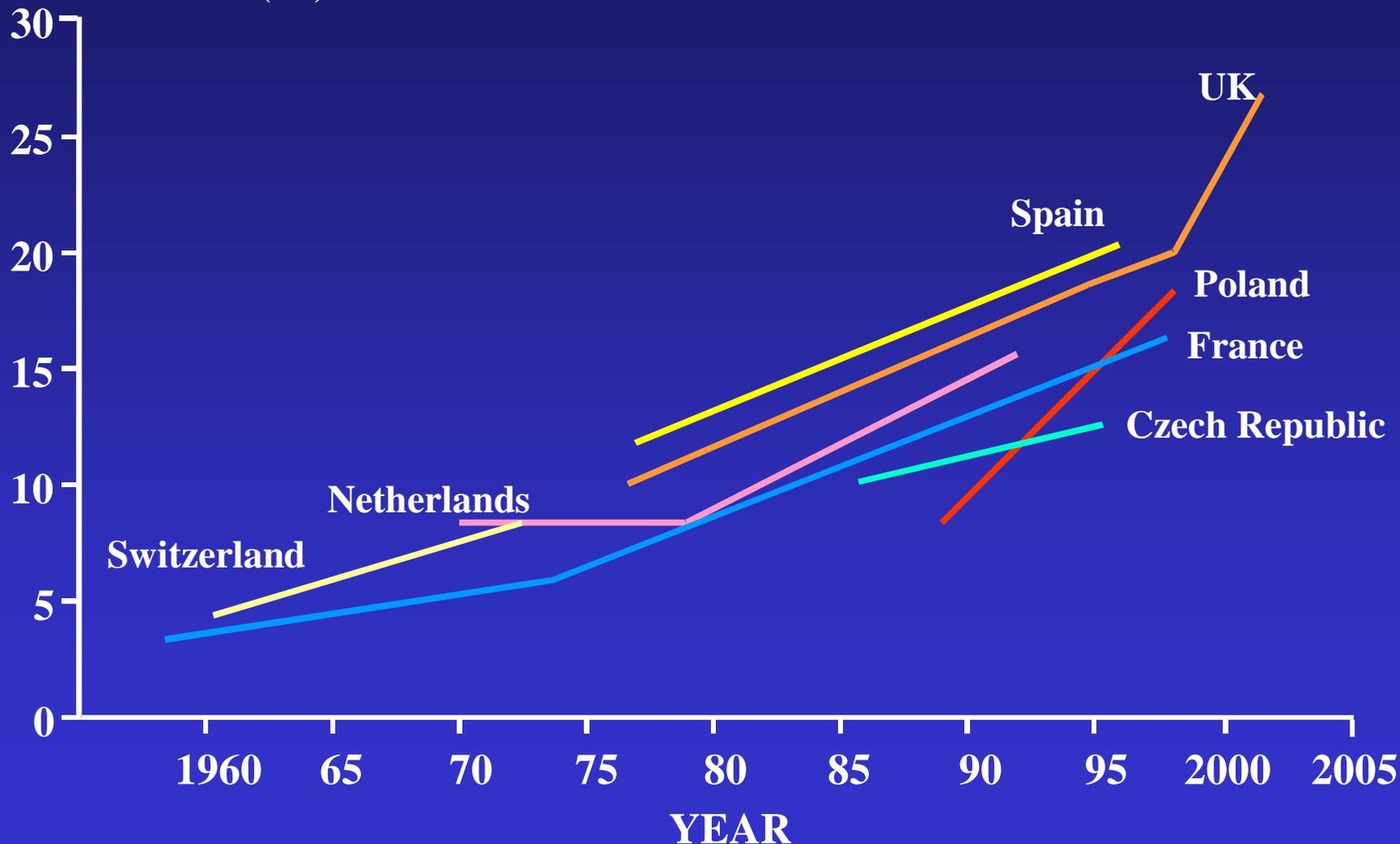
in most European countries is in the range 10-20% in men and 15-30% in women (*IOTF 2005*)



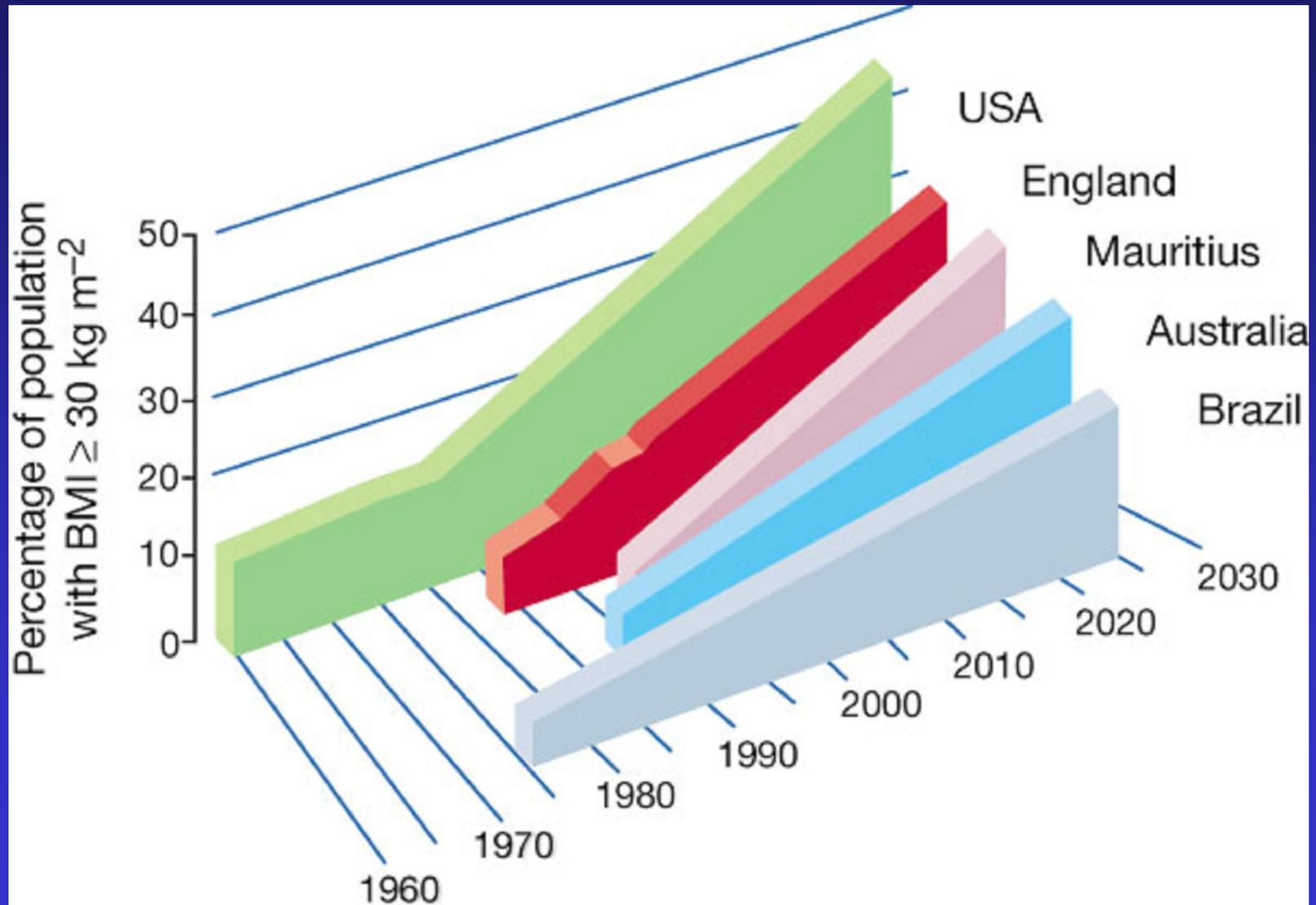
# PREVALENCE OF OVERWEIGHT IN CHILDREN AND ADOLESCENTS IS INCREASING

*IOTF/EASO Obesity in Europe Report 2002; IOTF 2004*

PREVALENCE (%)



# TRENDS IN OBESITY PREVALENCE (IOTF 1999)



# HEALTH RISKS OF OBESITY

**Obesity - besides smoking, the most important cause of death which could be prevented**

## METABOLIC

- Diabetes type 2
- Dyslipidaemia
- Hyperuricaemia, gout

## CARDIOVASCULAR

- Hypertension
- CHD, heart failure
- Cerebral stroke
- Thromboembolism

## BRONCHOPULMONARY

- Asthma
- Sleep apnoea syndrome
- Hypoventilation syndrome

## OBESITY PREVENTS

- Osteoporosis

## GASTROINTESTINAL

- Gastroesophageal reflux disease
- Non-alcoholic hepatic steatosis
- Hernias

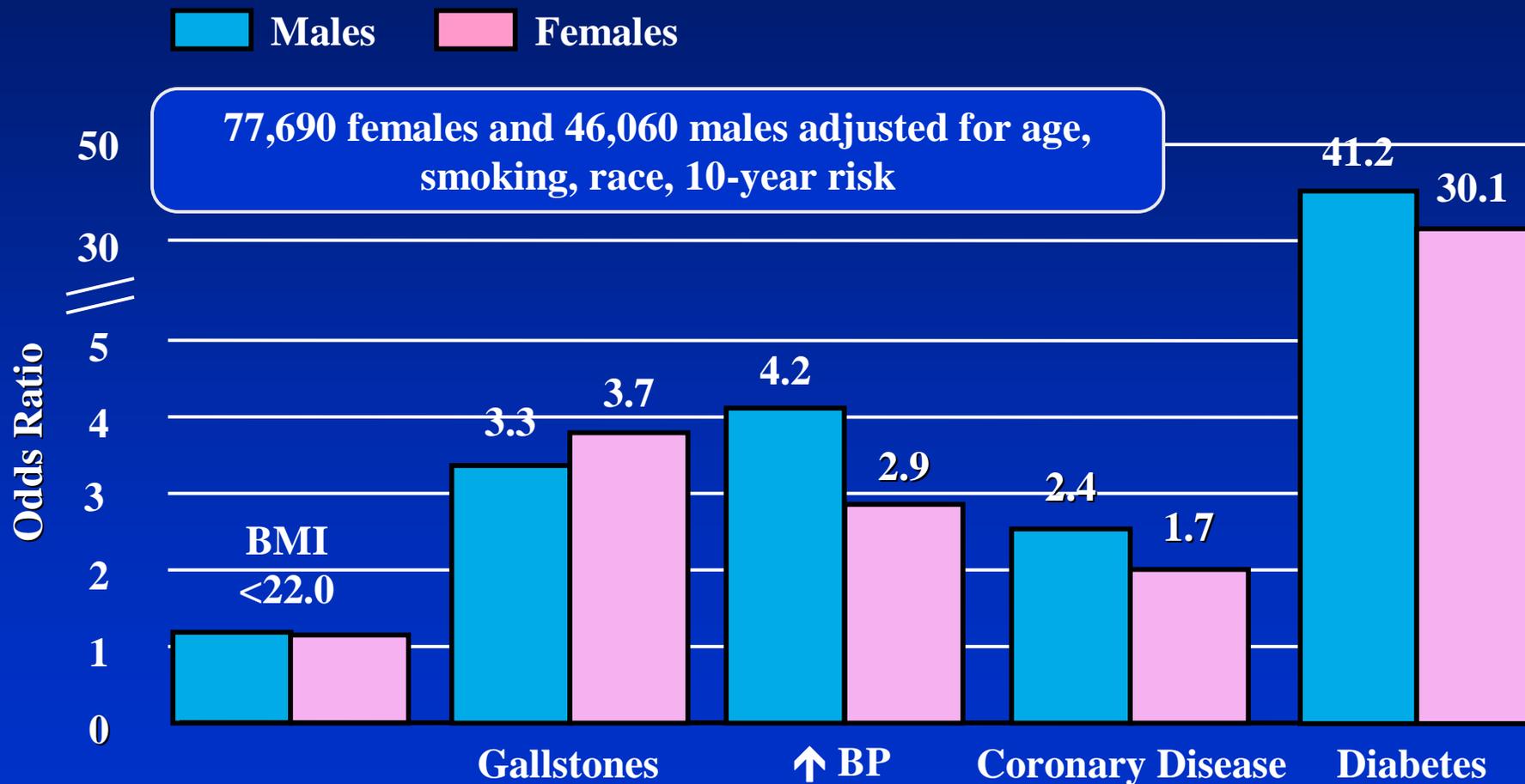
## TUMOURS

- Breast, uterine, ovarian cancer
- Colon cancer, prostatic cancer

## OTHERS

- Polycystic ovary syndrome
- Infertility/amenorrhoea
- Urinary incontinence
- Osteoarthritis, spondylitis
- Depression, anxiety
- Eating disorders
- Dermatological diseases

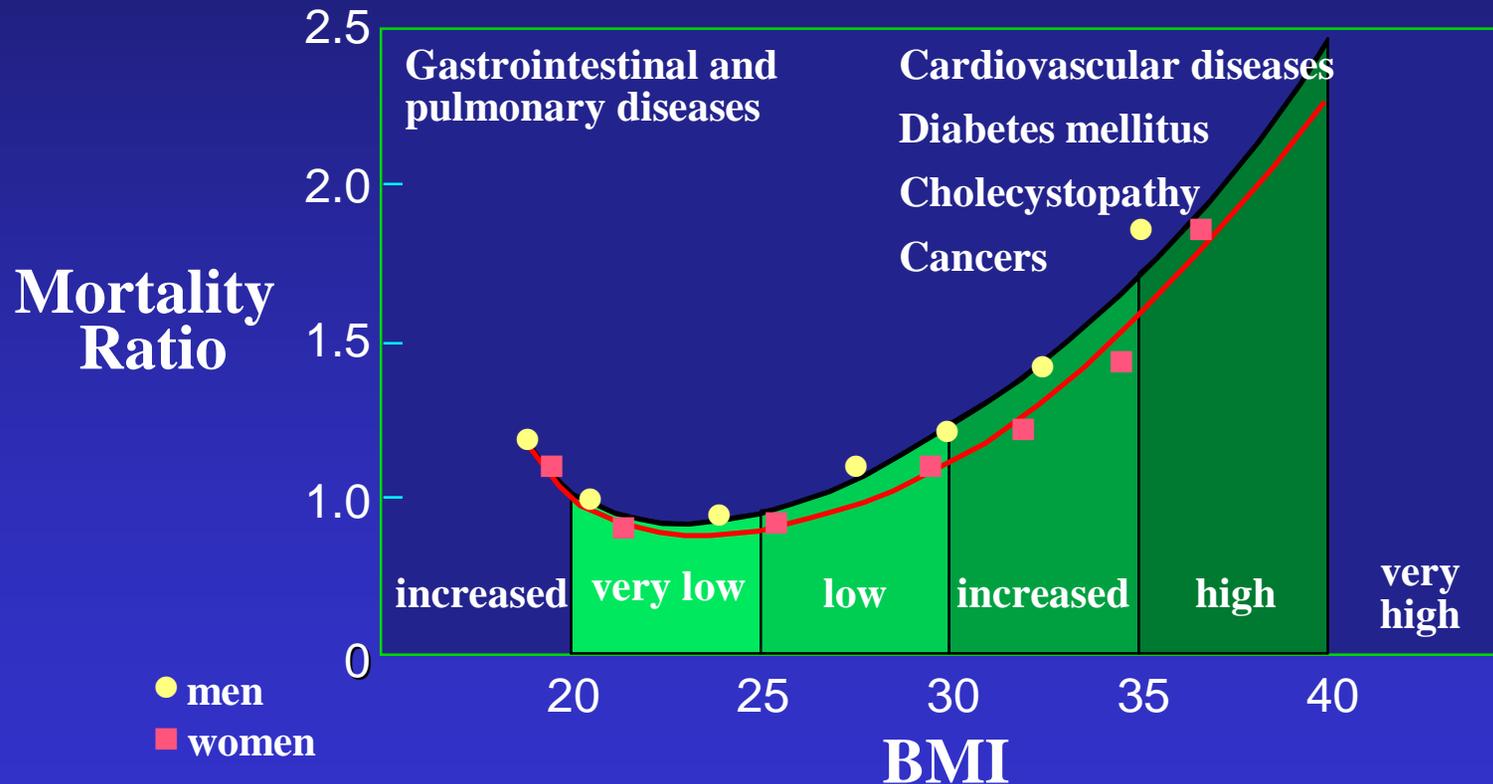
# OBESITY INCREASES RISK FOR DM2 MOST (BMI $\geq 35$ vs $<22$ kg/m<sup>2</sup>)



Field AE, Arch Intern Med 2001; 161: 1581-1586

# RELATIONSHIP BETWEEN BMI AND MORTALITY

## American Cancer Society Prevention Study



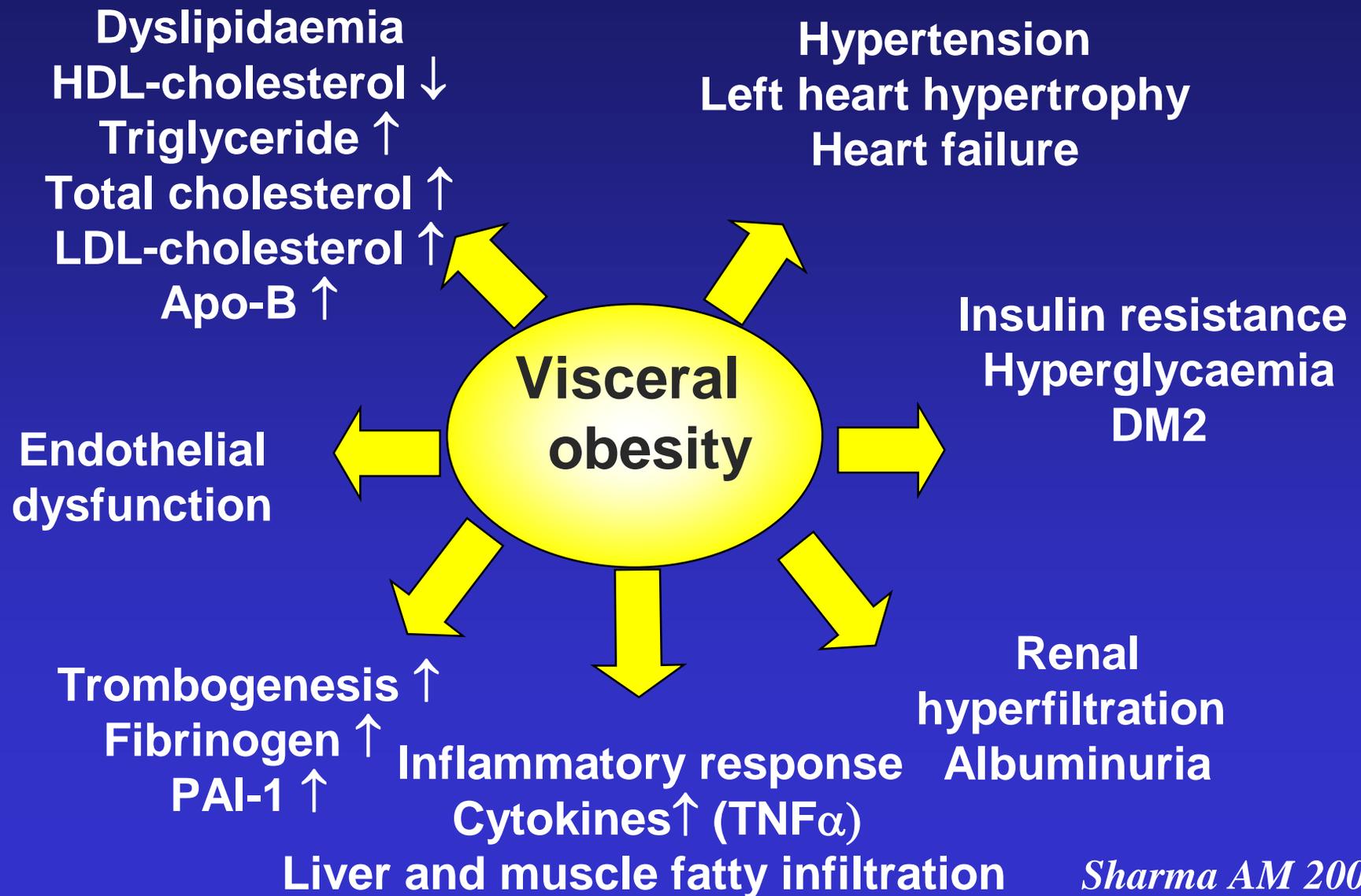
Gray. *Med Clin North Am.* 1989;73(1):1-13, based on statistical information from Lew et al. *J Chron Dis.* 1979;32:563-576.

# METABOLIC SYNDROME WORLDWIDE DEFINITION

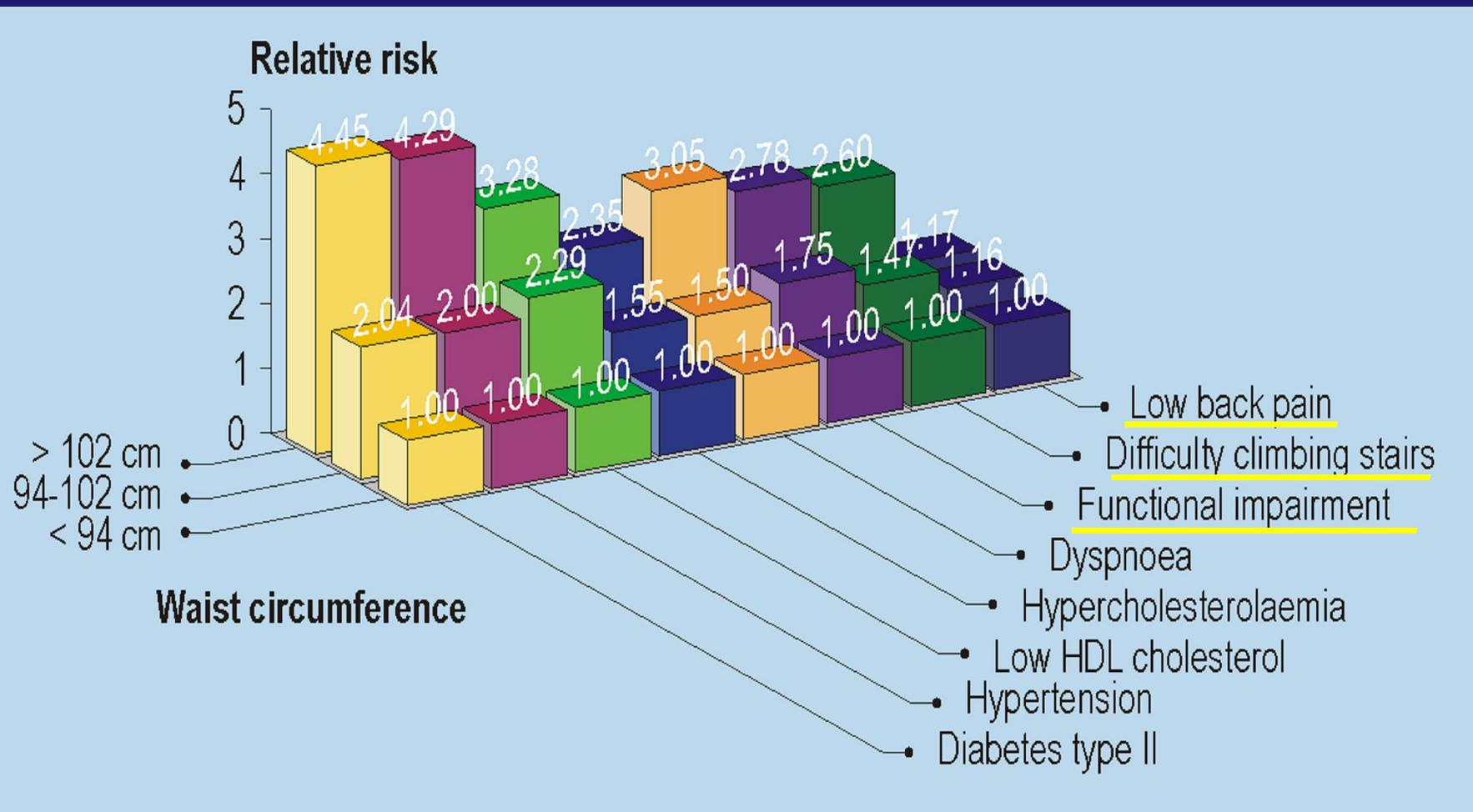
*International Diabetes Federation (2005)*

- **↑ Waist circumference (ethnicity specific)**  
+ Any two of the following
- **↑ Triglycerides  $\geq 1.7$  mmol/l (150 mg/dl) or treated dyslipidaemia**
- **↓ HDL-cholesterol or treated dyslipidaemia**
  - Males  $< 1.0$  mmol/l (40 mg/dl)
  - Females  $< 1.3$  mmol/l (50 mg/dl)
- **↑ Blood pressure  $\geq 130 / \geq 85$  mm Hg or treated hypertension**
- **↑ fasting plasma glucose  $\geq 5.6$  mmol/l (100 mg/dl) or previously diagnosed type 2 diabetes**

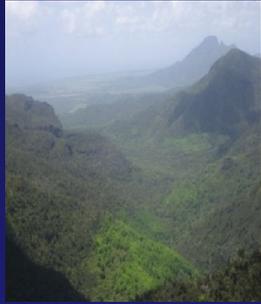
# ABDOMINAL (VISCERAL) OBESITY AND CARDIOVASCULAR HEALTH RISKS



# SYMPTOMS AND SECONDARY DISORDERS ASSOCIATED WITH ABDOMINAL OBESITY EVALUATED BY WAIST CIRCUMFERENCE IN MEN



*Lean M et al. Lancet 1998; 351: 853-856*



# HIGH PREVALENCE OF TYPE 2 DM AND METABOLIC SYNDROME IN MAURITIUS

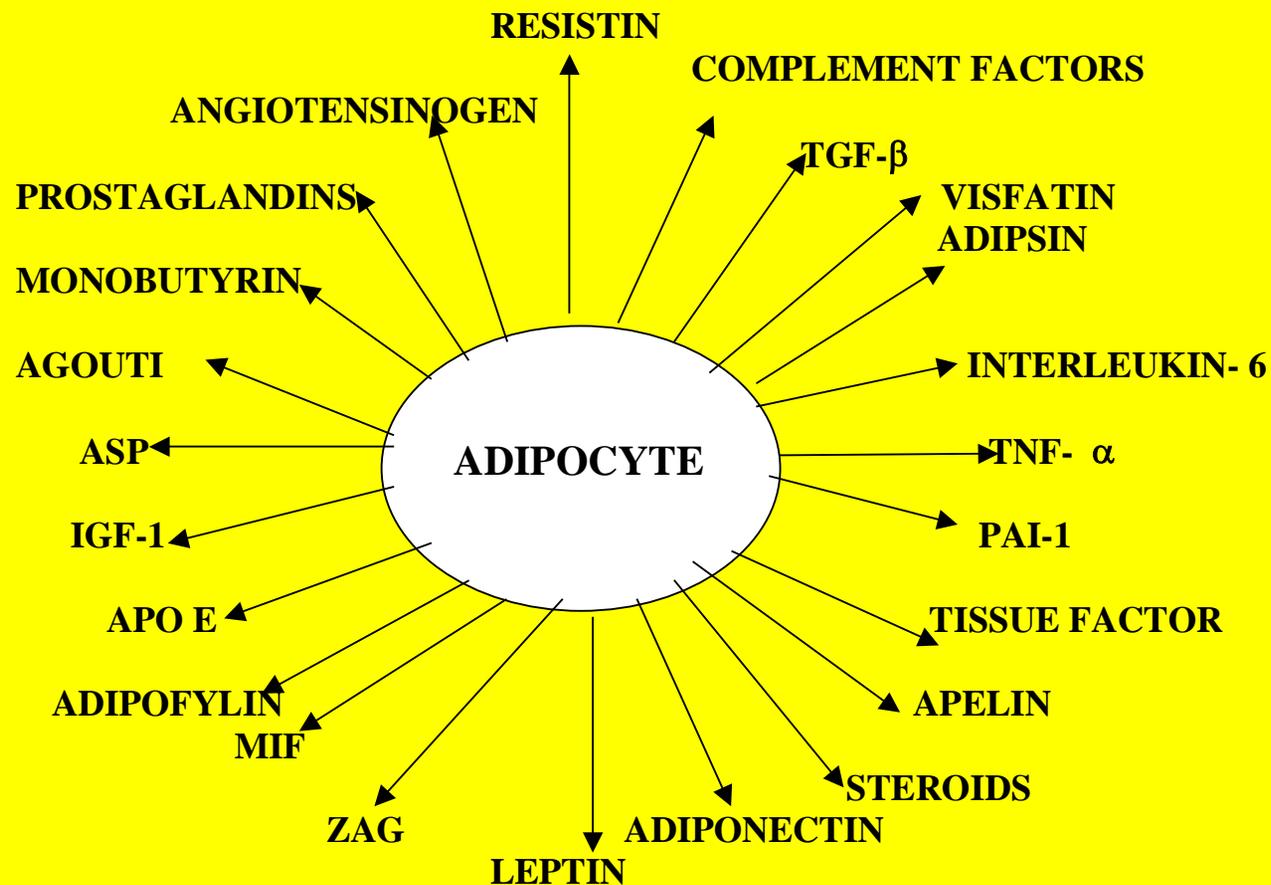
## Recent Studies



- Nyamdorj R et al.: BMI Compared With Central Obesity Indicators as a predictor of Diabetes Incidence in Mauritius. *Obesity* 2008 Nov 13
- Cameron AJ et al.: Central Obesity as a Precursor to the Metabolic Syndrome in the AusDiab Study and Mauritius *Obesity* 2008 Sept 25
- Nyamdorj R et al.: Comparison of Body Mass Index With Waist Circumference, Waist-to-Hip Ratio, and Waist-to-Stature Ratio as a Predictor of Hyperension Incidence in Mauritius *J Hypertens* 2008; 26: 866-870
- Cameron AJ et al.: The Metabolic Syndrome as a Predictor of Incident Diabetes Mellitus in Mauritius. *Diabet Med* 2007; 24: 1460-1469

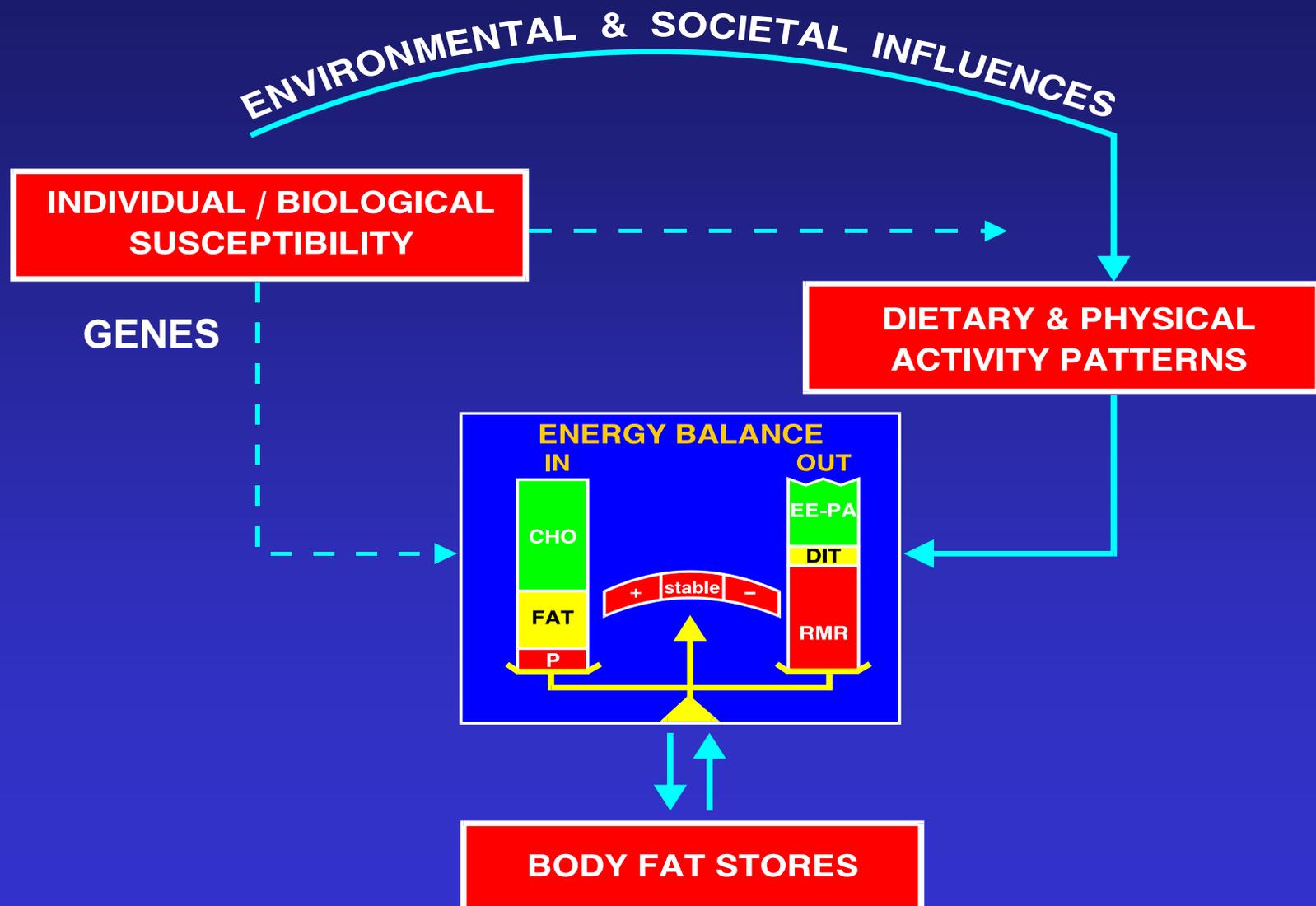
# ADIPOSE TISSUE

**LARGEST ENDOCRINE ORGAN IN THE BODY  
CYTOKINES PRODUCED BY ADIPOCYTE ARE RELATED TO  
THE RISKS OF METABOLIC SYNDROME**

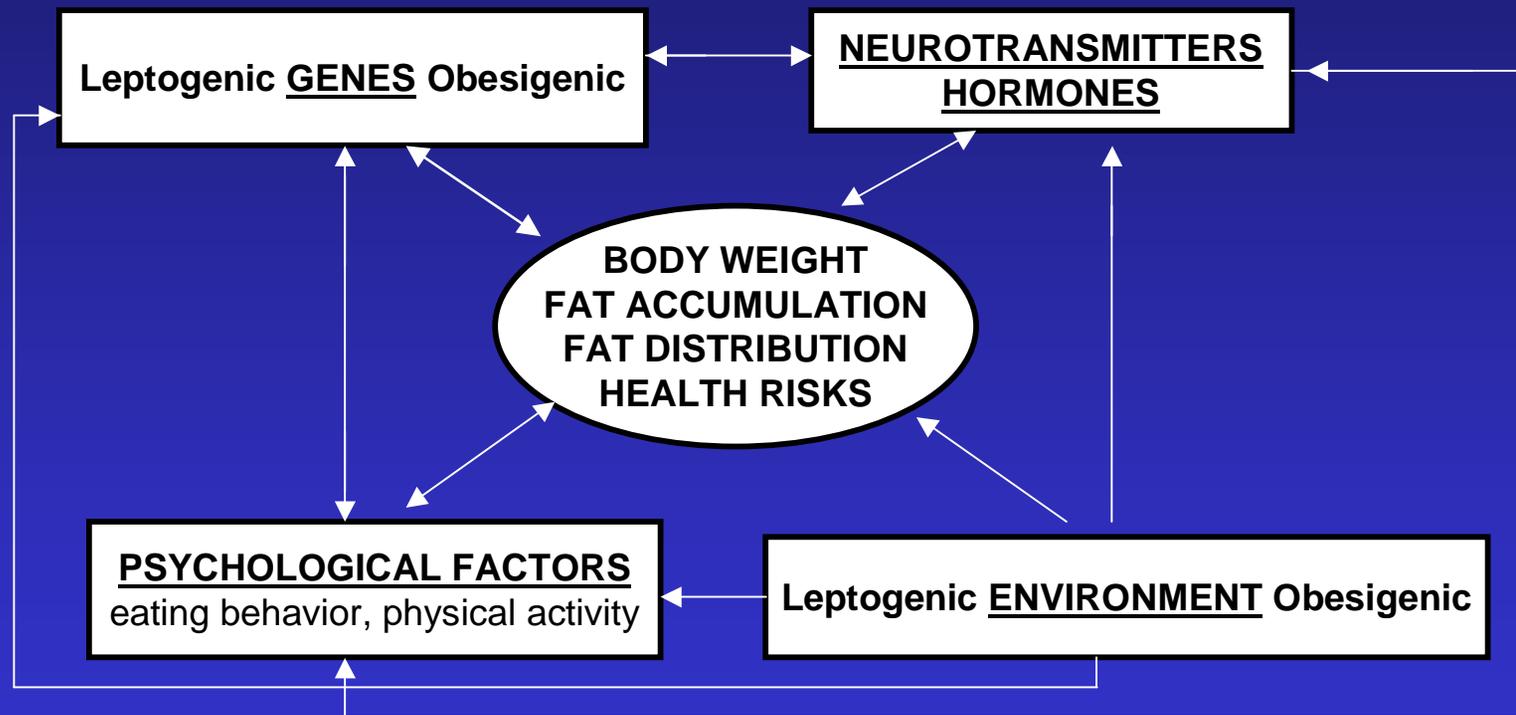


# PATHOGENESIS OF OBESITY

ACCUMULATION OF BODY FAT STORES RESULTS FROM IMBALANCE  
BETWEEN ENERGY INTAKE AND ENERGY EXPENDITURE



# INTERACTION BETWEEN BIOLOGICAL (GENES, HORMONES ETC.), PSYCHOBEHAVIOURAL AND ENVIRONMENTAL FACTORS IN BODY WEIGHT REGULATION AND HEALTH RISKS OF OBESITY



# THE HUMAN OBESITY GENE MAP

*Obes. Res. 2006, 14: 529*

## OBESITY RELATED TO MENDELIAN SYNDROMES - RARE

- Prader-Willi (prevalence 1:25,000), Bardet-Biedl etc.
- 2005 - 49 loci relevant to human obesity have been mapped

## OBESITY DUE TO SINGLE-GENE MUTATIONS - RARE

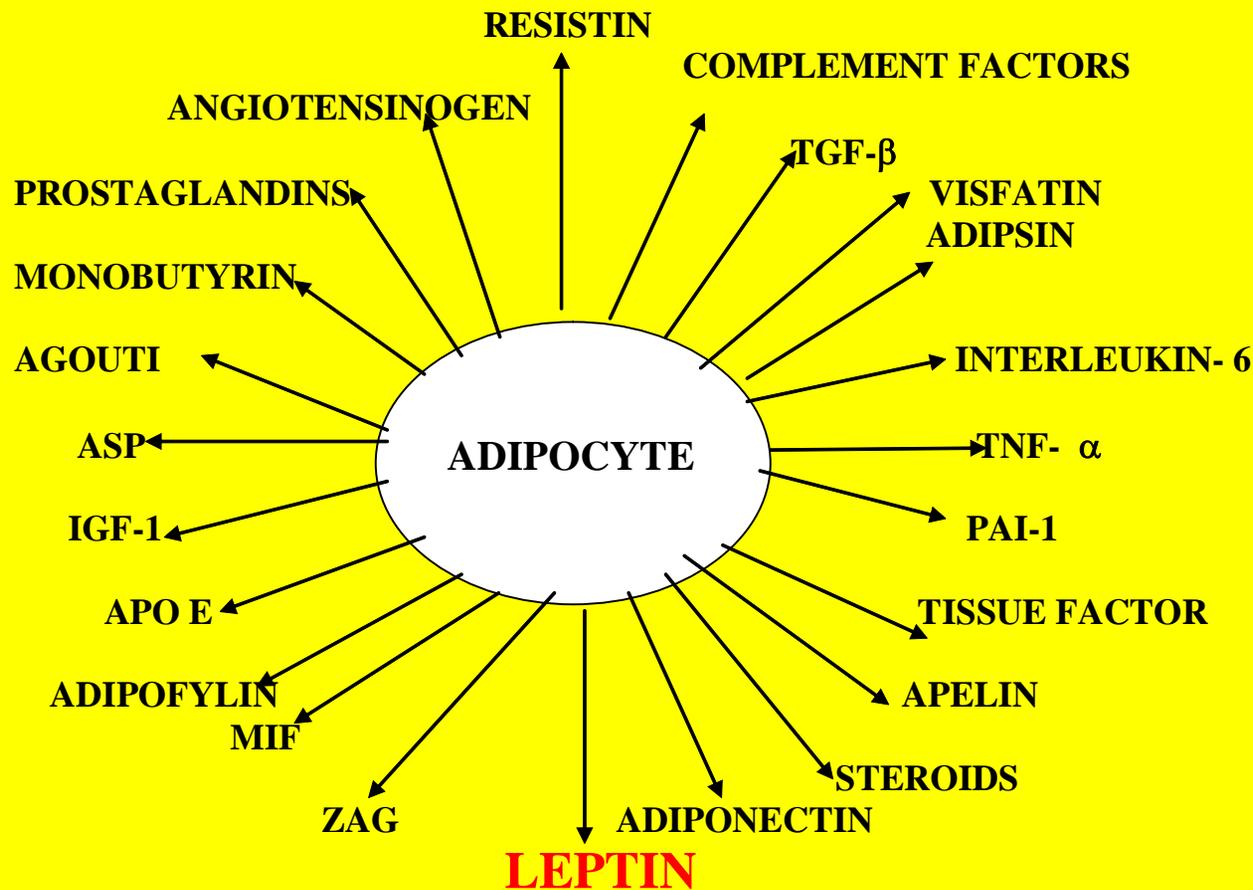
- 1997 - 3 cases involving mutations in two genes
- 2000 - 47 cases involving mutations in six genes
- 2002 - 89 cases involving mutations in six genes
- 2005 – 173 cases involving mutations in 10 genes

## OBESITY DETERMINED BY MULTIPLE GENES: POLYGENIC - COMMON

- More than 600 genes, markers, and chromosomal regions have been associated or linked with human obesity phenotypes
- Genetic variations in the first intron of the *FTO* gene (Frayling TM et al. 2007) and downstream of the *MC4R* gene (Loos RJ et al. 2008) - might greatly contribute to the general predisposition to obesity

# ADIPOSE TISSUE

**LARGEST ENDOCRINE ORGAN IN THE BODY  
CYTOKINES PRODUCED BY ADIPOCYTE ARE RELATED TO  
THE RISKS OF METABOLIC SYNDROME AND REGULATION  
OF ENERGY BALANCE**



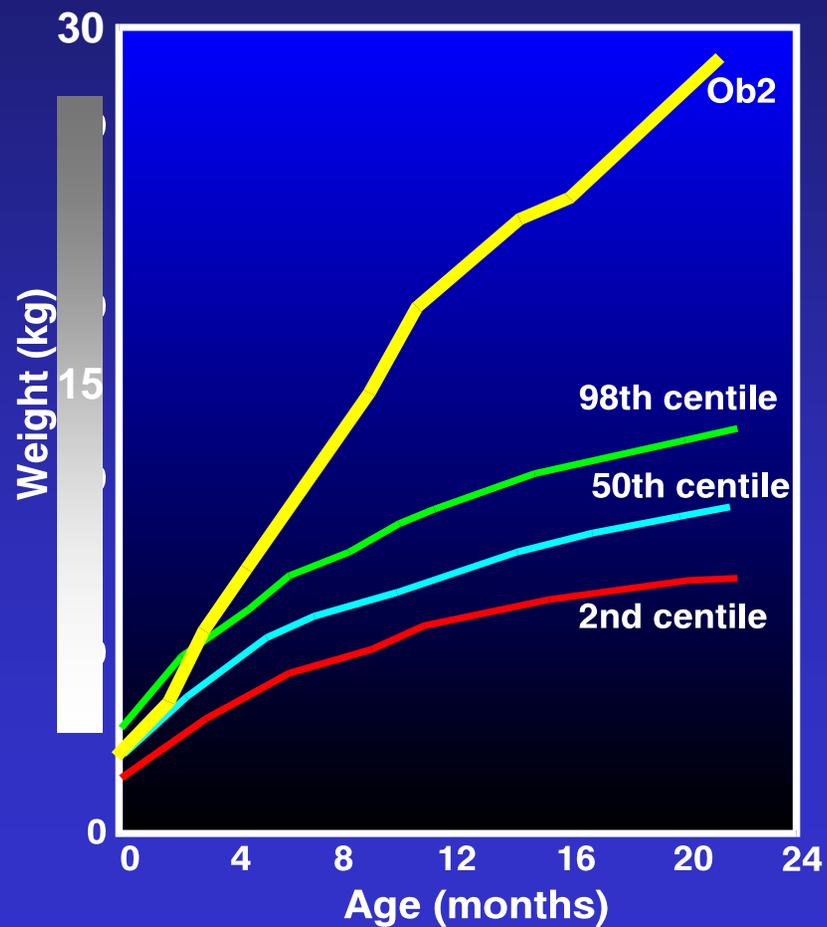
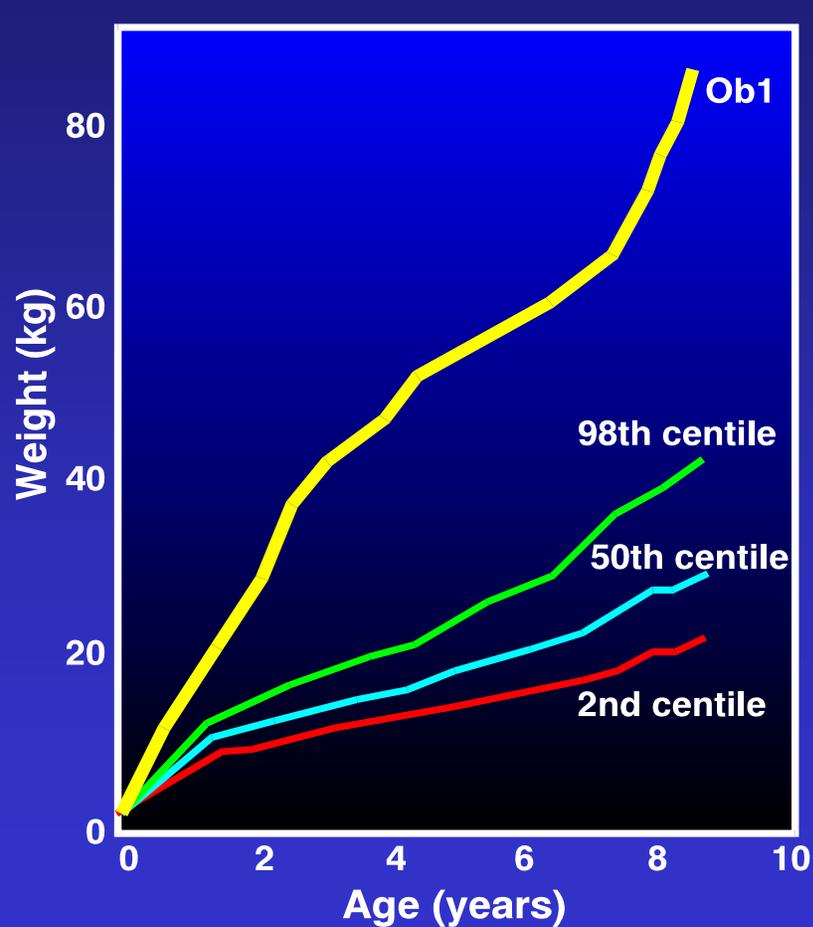
# **ADIPOSE TISSUE HORMONE LEPTIN REGULATES ENERGY BALANCE AND REPRODUCTION**

## **LEPTIN**

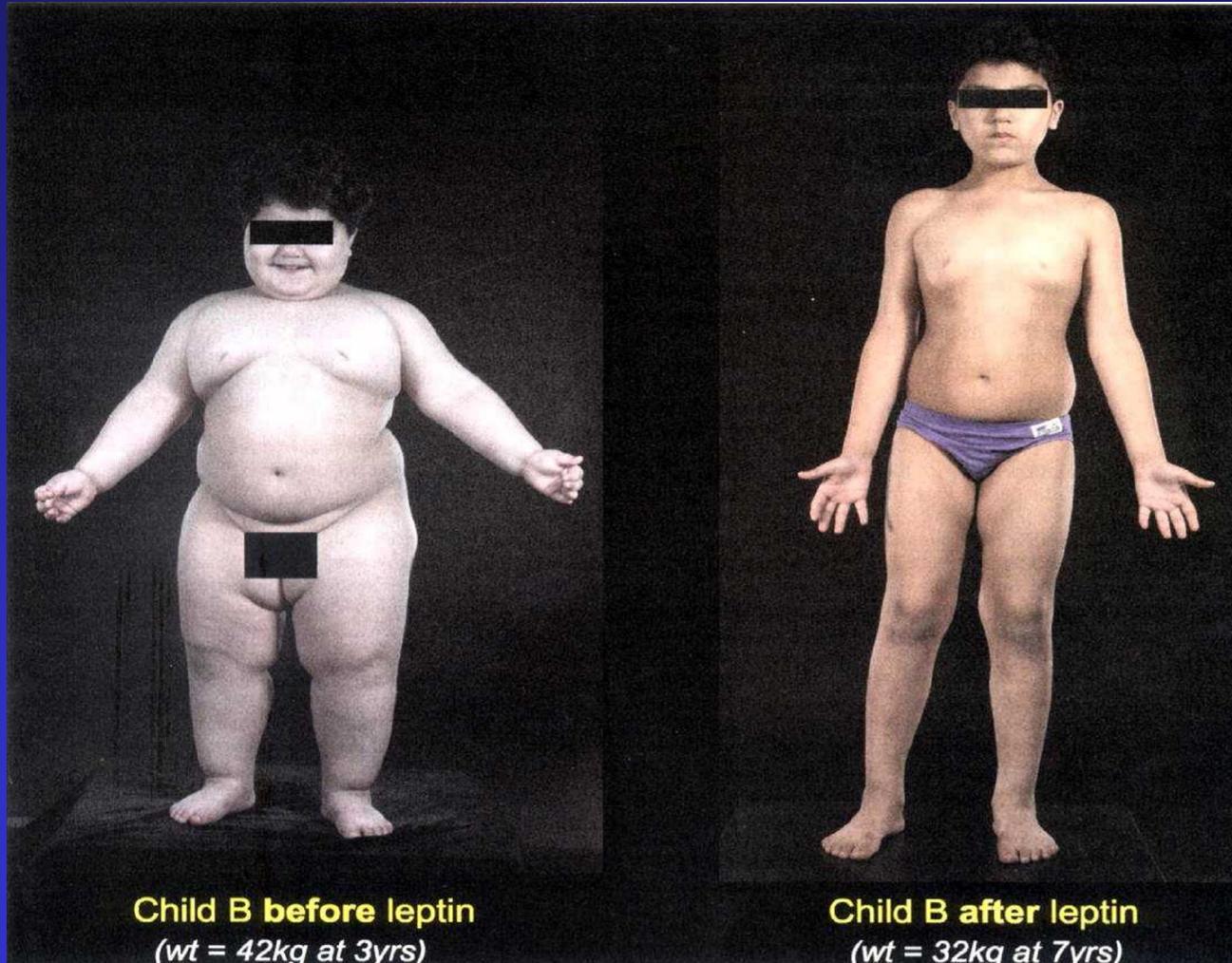
- **Increases thermogenesis by activateing SNS**
- **Decreases food intake by**
  - **by inhibition of orexigenic pathway: neuropeptide Y (NPY) and Agouti Related Peptide (AGRP)**
  - **by activation of anorexigenic pathway: proopiomelanocortin – corticoliberin – MSH – MC4R**
- **Initiates puberty and facilitate fertility by activating gonadoliberin secretion (LHRH)**

# MUTATION OF LEPTIN GENE

CONGENITAL LEPTIN DEFICIENCY IS ASSOCIATED WITH SEVERE EARLY - ONSET OBESITY IN HUMANS



# TREATMENT OF INBORN LEPTIN DEFICIENCY BY RECOMBINANT LEPTIN



# MUTATION OF MELANOCORTIN4 RECEPTOR (MC4R) GENE



9 yr - homzygote

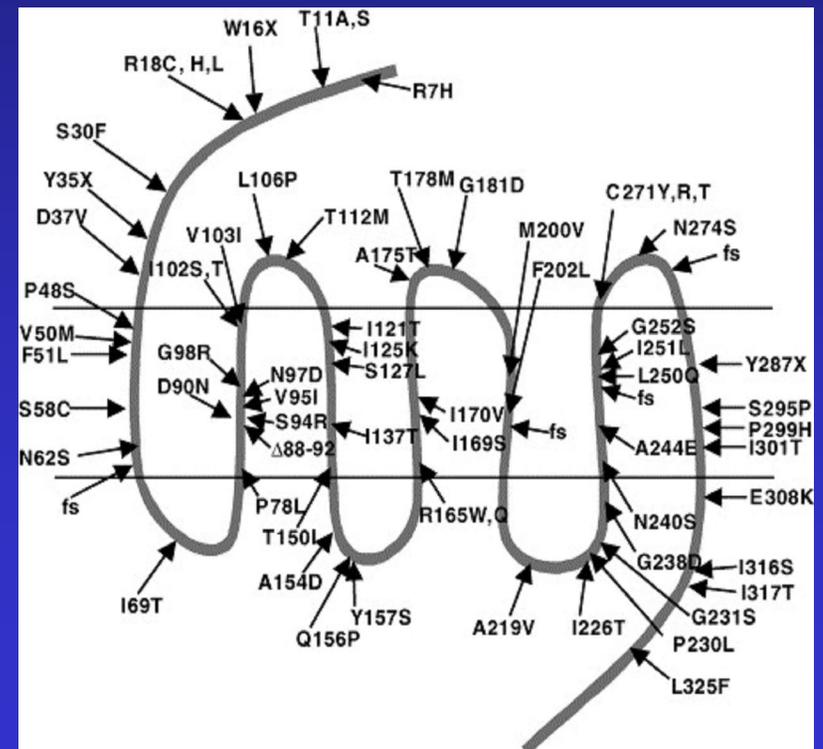
16 yr – his brother  
without mutation

# MUTATION OF MELANOCORTIN4 RECEPTOR (MC4R)

- most frequent form of monogenic obesity
- prevalence in early onset obesity 0.5-6.0 %, Czech cohort: 2.4%
- missense, frameshift, in frame deletion, nonsense mutations (> 70)

MC4R MUTATION IN CZECH COHORT (I. Hainerová *J Clin Endocrinol Metab* 2007)      MC4R MUTATIONS UNTIL 2005 (YX Tao 2005)

Mutation	Gender (F/M)	Age (years)	Onset (years)
<b>Arg7Cys*</b>	M	17	5
Ser19fsdelA	F	11	3
<b>Cys84Arg*</b>	F	13	11
Gly181Asp	M	15	<1
Phe51Leu	M	14	3
Phe51Leu	F	17	3
Ser127Leu	M	6	3



\* new

**ESTIMATES OF HERITABILITY OF COMMON FORMS OF OBESITY RANGE FROM 40 to 70%.**

**THE FOLLOWING FACTORS ARE GENETICALLY DETERMINED**

- **Control of food intake (appetite regulation)**
- **Perception of hunger and satiety**
- **Eating behavior (dietary disinhibition)**
- **Hormones controlling food intake, energy expenditure and fat stores**
- **Food preferences**
- **Food ingestion**
- **Nutrient absorption and oxidation**
- **Energy expenditure (metabolic rate, diet-induced thermogenesis, spontaneous physical activity)**
- **Nutrient deposition in energy stores**

# GENES ASSOCIATED WITH COMMON OBESITY IN HUMANS

Association confirmed by  $\geq 5$  studies:

ACE_(6 studies)	ADRB2_(20)	ADIPOQ_(11)
ADRB3_(29)	APOE_(5)	AR_(5)
DRD2_(5)	FABP2_(5)	FOXC2_(7)
GNB3_(15)	HTR2C_(12)	IL6_(10)
IL6R_(6)	INS_(10)	LDLR_(5)
LEP_(13)	LEPR_(19)	LIPC_(5)
LIPE_(6)	MC4R_(8)	NROB2_(5)
NR3C1_(12)	PLIN_(9)	PPARG_(30)
PPARGC1A_(8)	RETN_(5)	TNFA_(11)
UCP1_(11)	UCP2_(14)	UCP3_(15)
VDR_(7)	FTO_(6)	

*The Human Obesity Gene Map*

# CANDIDATE GENES OF COMMON OBESITIES

## RELATION TO PHENOTYPE

( supported by  $\geq 5$  studies)

**THRIFTINESS**

**ADRB $\beta$ 2, ADRB $\beta$ 3, UCP1, UCP2, UCP3**

**HYPERPHAGIA**

**DRD2, HTR2C, LEP, LEPR, MC4R,  
NR3C1**

**SEDENTARISM**

**DRD2, MC4R**

**LOW FAT  
OXIDATION**

**ACE, ADIPOQ, GNB3, IL6, INS,  
LDLR, LIPE, RETN, TNFA**

**ADIPOSE TISSUE  
HYPERPLASIA**

**PPAR $\gamma$ , VDR**

*According to Bouchard C. 2006*

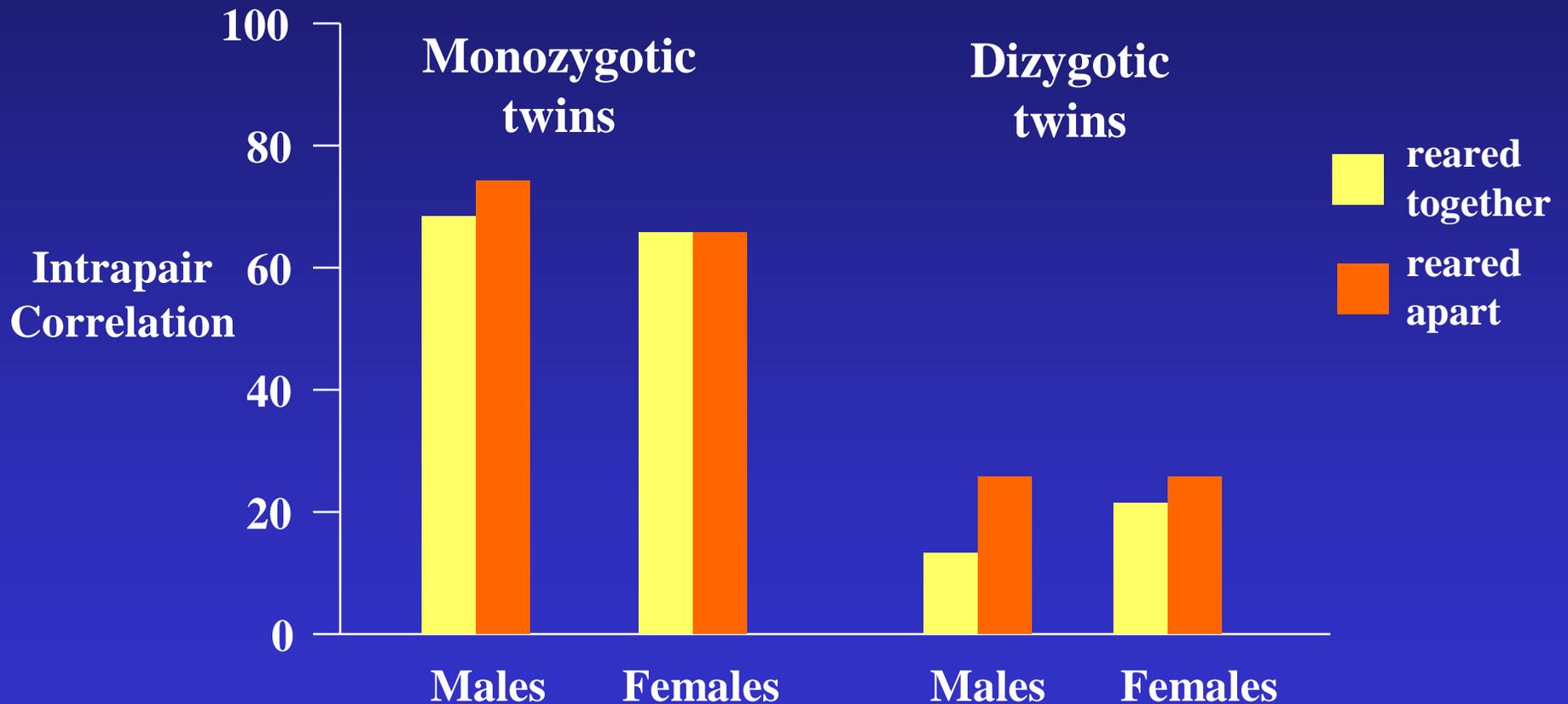
# FAMILY BACKGROUND OF OBESITY

Mean BMI 39.9 kg/m<sup>2</sup>

Obesity in family	Men n = 206	Women n = 782
Father	42.7%	30.4%
Mother	56.3%	54.0%
Both parents	23.3%	15.9%
One or both parents	<b>72.8%</b>	<b>68.5%</b>
Brother	18.4%	14.6%
Sister	21.4%	14.8%
None	15.5%	18.4%

*V.Hainer et al., 1998*

# INTRAPAIR CORRELATION OF BMI IN TWINS REARED TOGETHER AND APART



*Stunkard AJ et al., N Engl J Med 1990; 322: 1483*

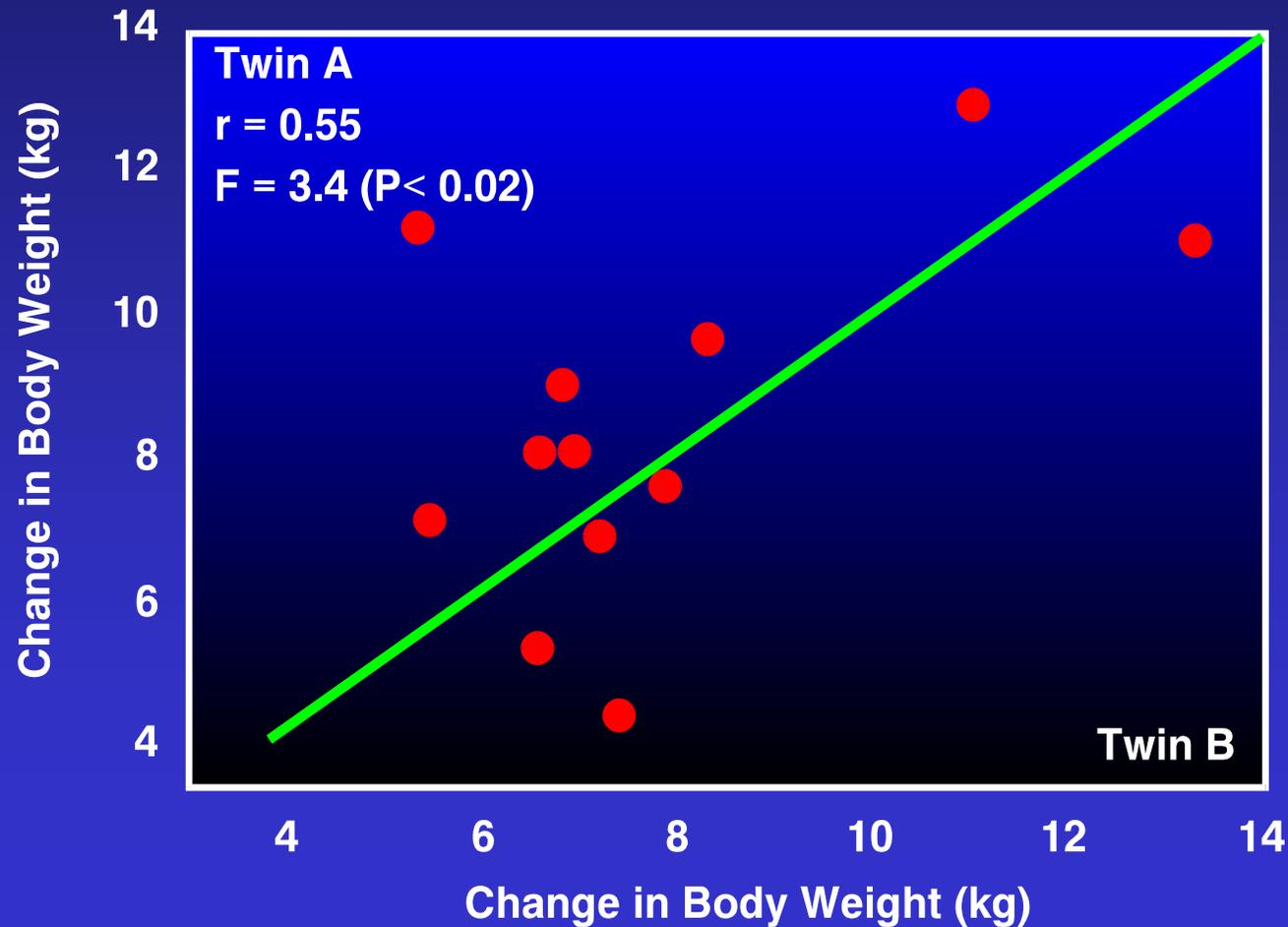
# **STUDIES ON GENES x ENVIRONMENT INTERACTION CONDUCTED IN IDENTICAL TWINS**

- **Response to positive energy balance induced by overfeeding in male normal weight identical twins**  
*C. Bouchard et al. New Engl.J. Med. 1990, 322:1477-1482*
- **Response to negative energy balance induced by exercise in male identical twins with modestly elevated weight**  
*C. Bouchard et al. Obes. Res. 1994, 2:404-410*
- **Response to negative energy balance induced by VLCD in female obese identical twins**  
*V. Hainer et al. Int. J. Obes. 2000, 24:1051-1057*  
*V. Hainer et al. Int. J. Obes. 2001, 25:533-537*  
*V. Hainer et al. Horm. Metab. Res. 2001, 33:417-422*

# STUDIES IN IDENTICAL TWINS DEMONSTRATED THAT GENES AFFECT WEIGHT GAIN IN RESPONSE TO A POSITIVE ENERGY BALANCE

*Bouchard C et al N Engl J Med 1990; 322: 1477-1482*

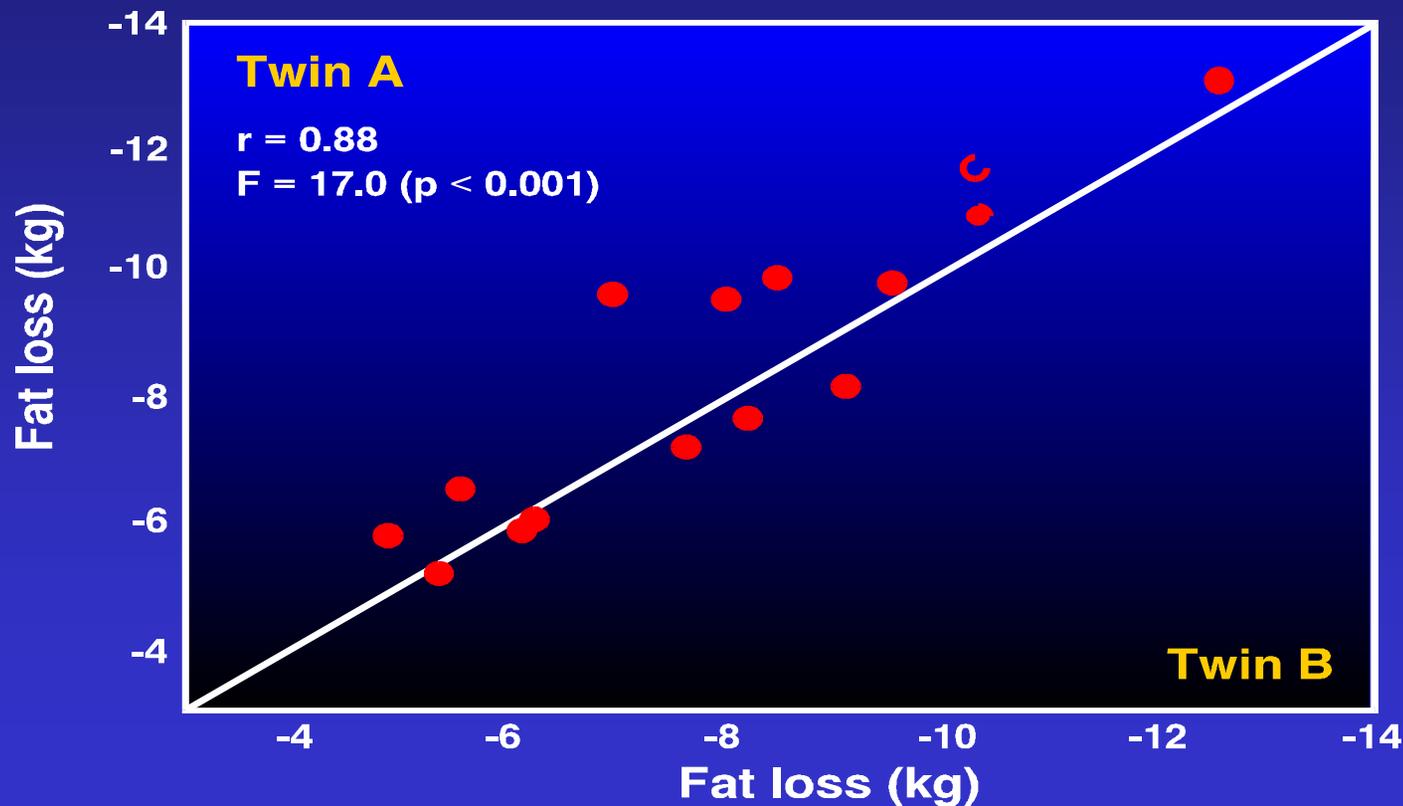
**SIMILARITY WITHIN PAIRS WITH RESPECT TO CHANGES IN BODY WEIGHT IN 12 PAIRS OF MALE TWINS IN RESPONSE TO 100 DAYS OF OVERFEEDING**



# STUDIES IN IDENTICAL TWINS DEMONSTRATED THAT GENES AFFECT FAT LOSS IN RESPONSE TO A NEGATIVE ENERGY BALANCE

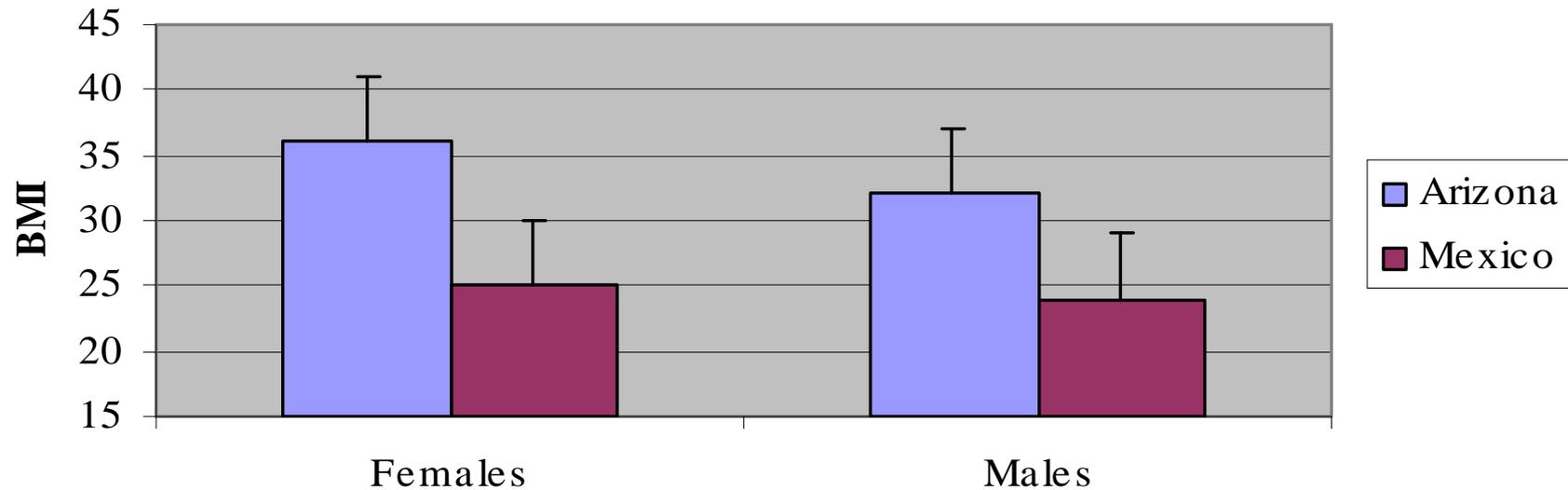
*Hainer V et al. Int. J. Obes. 2000, 24:1051*

## INTRAPAIR RESEMBLANCE IN VLCD - INDUCED FAT LOSS



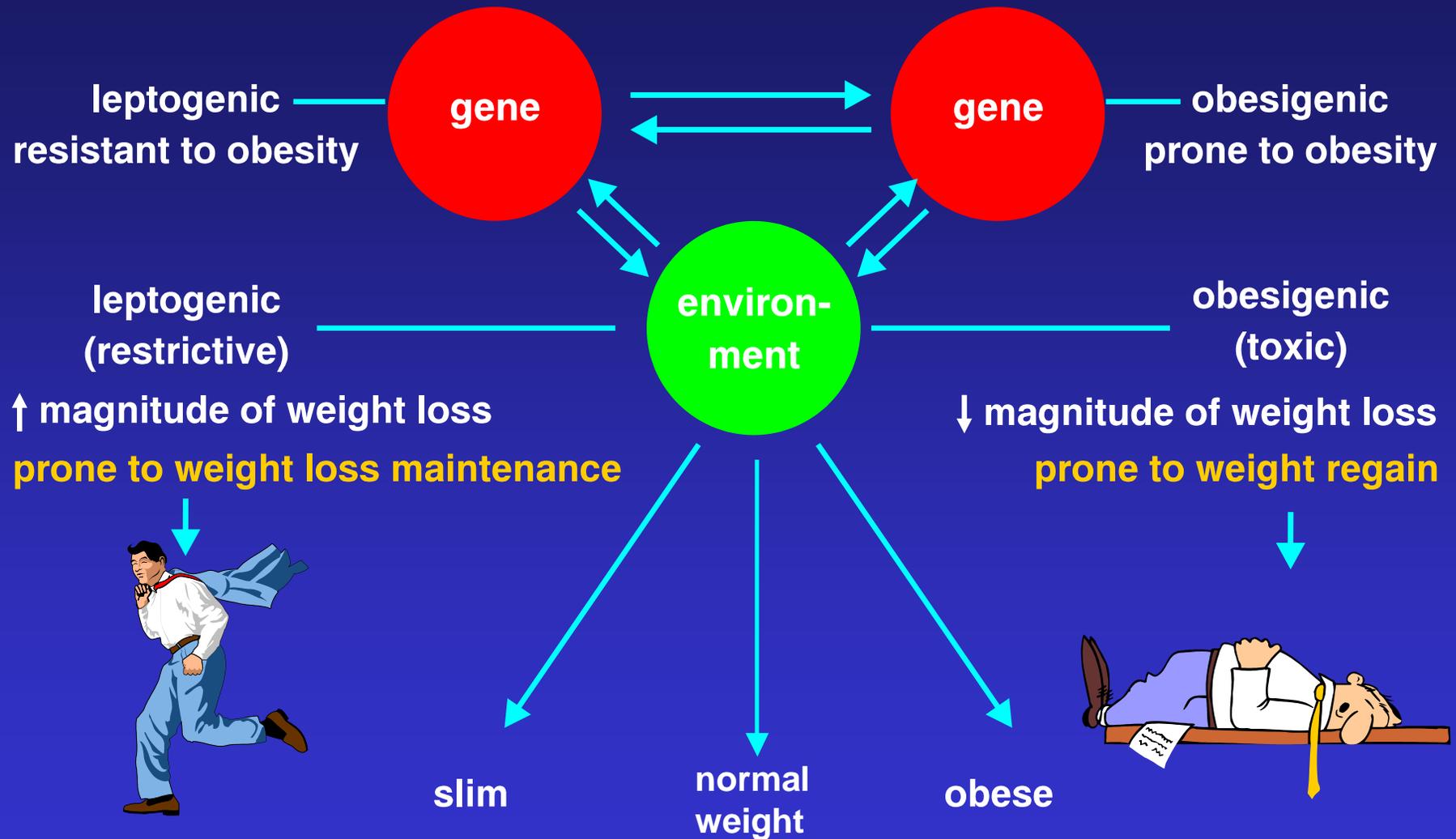
# ENVIRONMENT STRONGLY AFFECTS BMI IN OBESITY PRONE INDIVIDUALS: MEAN BMI IN AGE-MATCHED PIMA INDIANS LIVING IN ARIZONA AND MEXICO

p<0.001 Arizona vs. Mexico



*Ravussin E. Metabolism 1995, 9 (Suppl. 3): 12*

# GENE - GENE INTERACTION GENE(S) - ENVIRONMENT INTERACTION



*Hainer V et al. Essentials of Clinical Obesity, Grada-Avicenum, Prague, 2004*

# **CURRENT EPIDEMIC OF OBESITY**

- **cannot be explained by changes in genes during the past two decades although they do play an important role in individual susceptibility to development of obesity**
- **reflects the failure of human genes to cope with an obesigenic (toxic) environment characterized by a positive energy balance due to**
  - **high energy density diet**
  - **low physical activity and adoption of a sedentary lifestyle**

# OBESIGENIC ENVIRONMENT: HIGH ENERGY DENSITY DIET

- Increased consumption of fatty items
- Increased consumption of soft drinks and sweetend juices
- Decreased consumption of fruits and vegetables
- Decreased consumption of low fat dairy products

## FAST FOOD



3335 kJ

traditional Czech



3344 kJ

Mc Donald's

# **DIETARY FAT IS A MAJOR RISK FACTOR FOR WEIGHT GAIN AND OBESITY**

- **High energy density (fat: 38 kJ/g vs. carbohydrate or protein: 17 kJ/g)**
- **Weak satiety**
- **Low postprandial thermogenesis (Diet Induced Thermogenesis – DIT)**
- **Taste preferences for fat (and sugar - high palatability substances) – hedonic responses**

# EFFECTS OF MACRONUTRIENTS ON SATIETY AND DIET-INDUCED THERMOGENESIS

- proteins +++
- carbohydrates ++



- fats +



# OBESIGENIC ENVIRONMENT

**DIMINISHES HABITUAL PHYSICAL ACTIVITY AND CONTRIBUTES TO DEVELOPMENT OF OBESITY IN SUSCEPTIBLE INDIVIDUALS**

## TRANSPORTATION

- private cars
- motorcycles
- elevators
- escalators
- moving sidewalks
- automatic door openers

## COMMUNICATIONS

- mobile phones
- e-mail
- fax

## WORK SITE ACTIVITIES

- computers
- automatisisation
- robotisation
- remote control

## BODY CARE

- electric shavers
- hair dryers
- massage apparatus

## COOKING, HOMEWORK AND HOUSEKEEPING

- food processors
- electric knives, juicers, can openers
- electric beaters and blenders vysavače
- microwaves
- dish washers
- washing machines and dryers
- vacuum cleaners
- snow blowers
- electric drills and screwdrivers

## GARDENING

- motor or electric saws
- motor or electric lawnmowers
- electric sanders

## ENTERTAINMENT

- TV and video sets
- remote control of TV/audio/video
- video games

# HIGH - TEC PROMOTES WEIGHT GAIN

*Rossner, 2002*



Cellular phones and remote controls deprive us from walking!

20 times daily x 20 m = 400 m

Walking distance lost/year  
 $400 \times 365 = 146,000$  m

146 km = 25 h of walking

1 h of walking = 113-226 kcal

Energy saved = 2800-6000 kcal

→ + 0.4-0.8 kg adipose tissue per year

# **FACTORS CONTRIBUTING TO OBESITY EPIDEMIC BESIDES HEREDITARY PREDISPOSITION & EXCESS INTAKE OF ENERGY DENSE FOOD WITH SEDENTARISM**

- **Intrauterine programming and epigenetic events**
- **Epigenetic events during postnatal life**
- **Assortative mating**
- **Smoking cessation**
- **Infection (adenovirus)**
- **Decrease (or increase) in the number of hours of sleep**
- **Increase in home temperature during winter**
- **Air conditioning availability in warm climates**

# CONCLUSION

- **Obesity is associated with increased morbidity, mortality and impaired quality of life**
- **Production of hormones and inflammatory cytokines by adipose tissue contributes to development of the cardiometabolic health risks**
- **Obesity epidemic reflects the failure of human genes to cope with an obesigenic environment characterized by a positive energy balance**
- **Involvement of hereditary factors in the development of obesity is estimated about 40 – 70%**

## **CONCLUSION**

- **Common obesity is polygenic disease determined by interaction of multiple genes with environmental factors; among them consumption of energy dense food and sedentary lifestyle play a crucial role**
- **Obesity has been included in the International Classification of diseases more than half a century (code E66)**
- **General public, health policy makers and many health care providers do not accept obesity as a serious health problem although its pathogenesis, prevalence and health consequences are comparable with other complex diseases as hypertension.**

# THE EUROPEAN ASSOCIATION FOR THE STUDY OF OBESITY (EASO)

**Established in 1986 to promote  
obesity research and actions that  
tackle the current epidemic of obesity**

**EASO**

European Association for the Study of Obesity

# EASO INCLUDES 29 MEMBER COUNTRIES

- Austria
- Belgium
- Bulgaria
- Croatia
- Czech Republic
- Denmark
- Finland
- France
- Germany
- Greece
- Georgia
- Hungary
- Iceland
- Ireland
- Israel
- Italy
- Netherlands
- Norway
- Poland
- Portugal
- Republic of Macedonia
- Romania
- Serbia
- Slovakia
- Spain
- Sweden
- Switzerland
- Turkey
- United Kingdom

Northern Region

Middle Region

Southern Region

EASO

European Association for the Study of Obesity

# ECO IS THE MOST IMPORTANT ANNUAL SCIENTIFIC EVENT ON OBESITY IN EUROPE

The ECO provides information about recent research advances in the field of obesity.

## PREVIOUS ECOS

- 1988 Stockholm, Sweden
- 1989 Oxford, England
- 1991 Nice, France
- 1992 Noordwijkerhout, Netherlands
- 1993 Ulm, Germany
- 1995 Copenhagen, Denmark
- 1996 Barcelona, Spain
- 1997 Dublin, Ireland
- 1999 Milan, Italy
- 2000 Antwerp, Belgium
- 2001 Vienna, Austria
- 2003 Helsinki, Finland
- 2004 Prague, Czech Republic
- 2005 Athens, Greece
- 2007 Budapest, Hungary
- 2008 Geneva, Switzerland

## FUTURE ECOS

- 2009 Amsterdam, Netherlands
- 2011 Istanbul, Turkey

**EASO**

European Association for the Study of Obesity

# TO REALIZE ITS GOALS THE EASO ESTABLISHED THREE TASK FORCES AND ITS OFFICIAL JOURNAL

- **OBESITY MANAGEMENT & EDUCATION TASK FORCE (OMTF)**
- **OBESITY PREVENTION AND PUBLIC HEALTH TASK FORCE**
- **CHILDHOOD OBESITY TASK FORCE**
- **OBESITY FACTS HAS BEEN LAUNCHED AS AN EASO OFFICIAL JOURNAL THIS YEAR**

**EASO**

European Association for the Study of Obesity

# **EASO OBESITY MANAGEMENT & EDUCATION TASK FORCE (OMTF)**

- **Creation of network of obesity specialists across the EASO member countries**
- **Implementation of educational programmes on obesity management**
- **Guidelines on bariatric surgery (developed together with the European Chapter of the International Federation for the Surgery of Obesity) - published in the International Journal of Obesity, Obesity Surgery and Obesity Facts**
- **Updated version of the European Guidelines on Obesity Management in Primary Care - published in the 2<sup>nd</sup> issue of Obesity Facts**
- **Continuous monitoring of obesity management strategies in the EASO member countries**
- **Definition of the EASO Collaborating Centres in Obesity Management**

**EASO**

European Association for the Study of Obesity

## **EASO CHILDHOOD OBESITY TASK FORCE (COTF)**

- **Promotion of educational activities for healthcare providers dealing with obese children across Europe**
- **Current goal: To prepare a template for childhood obesity management**
- **Satellite symposia at ECOs**
- **Collaboration with other childhood obesity groups (EAROC, ECOG, ECOPA)**

**EASO**

European Association for the Study of Obesity

# EASO PREVENTION AND PUBLIC HEALTH TASK FORCE

- **Joint action with WHO Europe ‘Lifestyle Strategies for Primary Care for the Prevention of Overweight and Obesity’ (workshop at ECO in Geneva)**
- **Establishing a network of public health experts and epidemiologists representing the national associations for the study of obesity in Europe**
- **Participation in the EU Platform on Diet, Physical Activity and Health**
- **Monitoring overweight and obesity in Europe**
- **Improvement of the epidemiological perspective on obesity in Europe**

**EASO**

European Association for the Study of Obesity

# INVITATION

**WELCOME TO THE 17<sup>th</sup> ECO IN  
AMSTERDAM, MAY 6-9<sup>th</sup> 2009**

**EASO**

European Association for the Study of Obesity

# *Greetings from Prague - Castle*

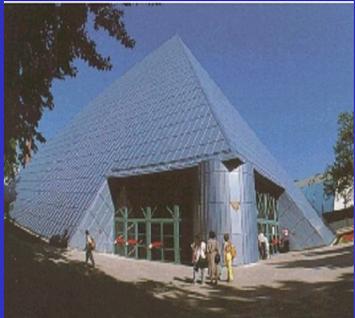
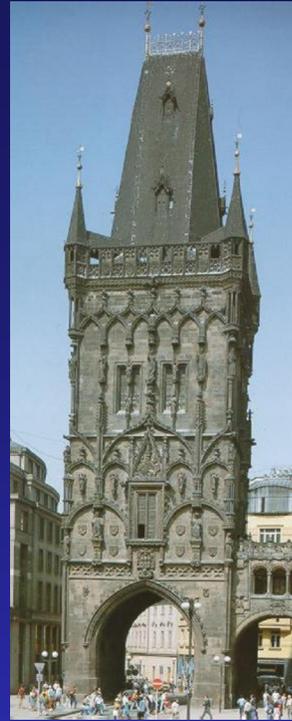


# Prague

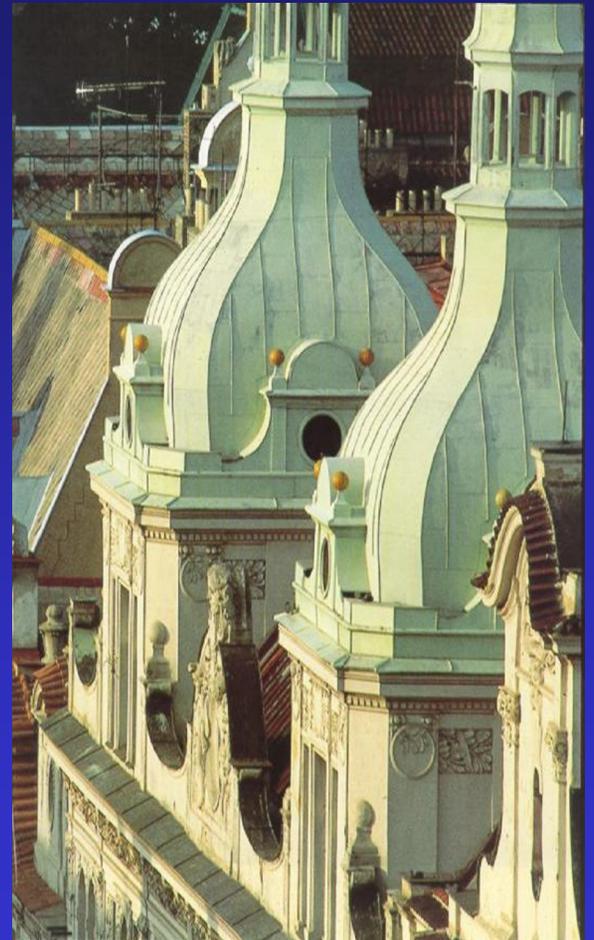
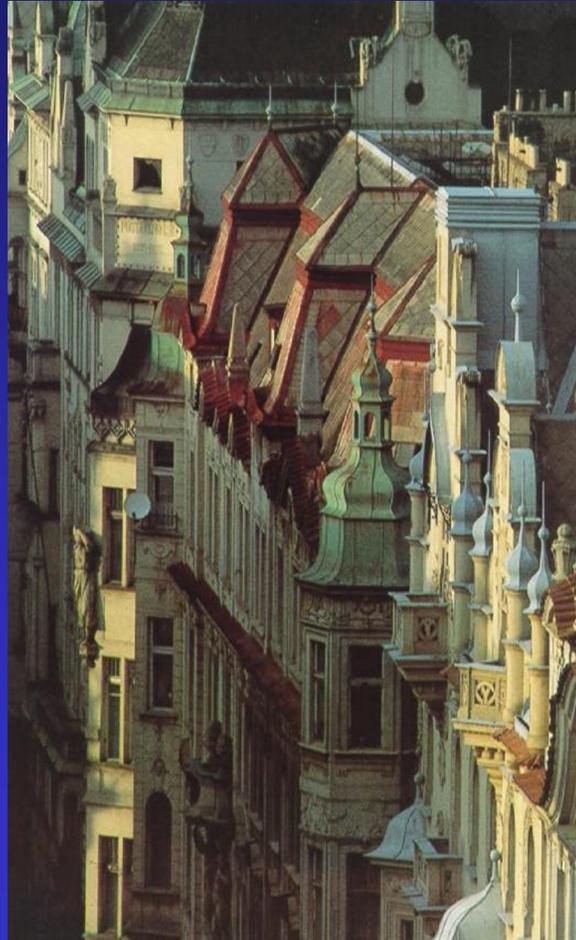
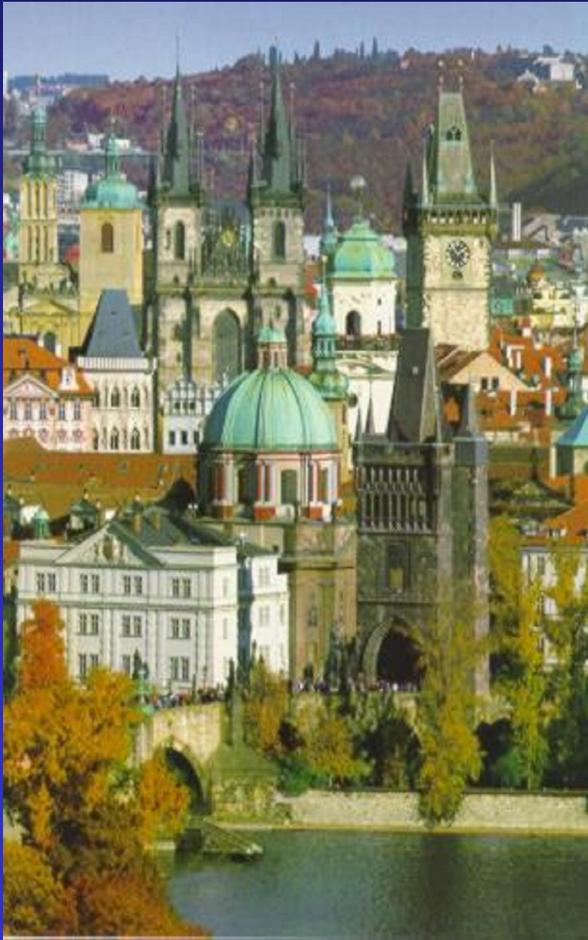
## seat of the Charles University

1348  
*Universitas Carolina*

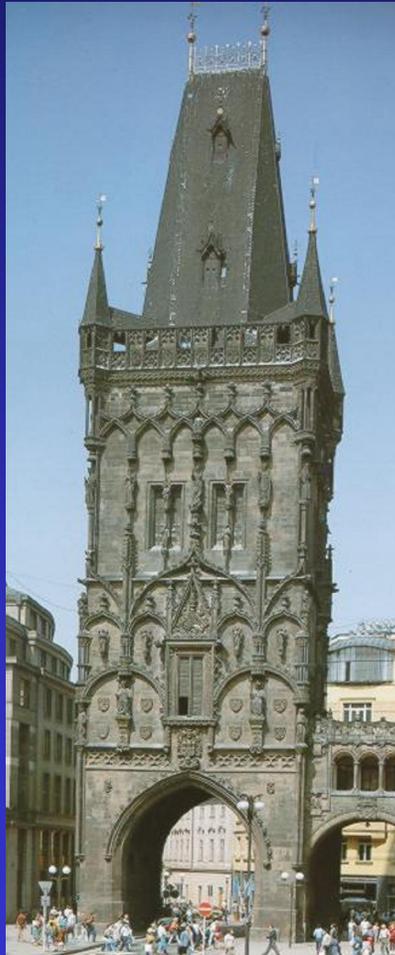




# ***"Golden", "steepled" ...***



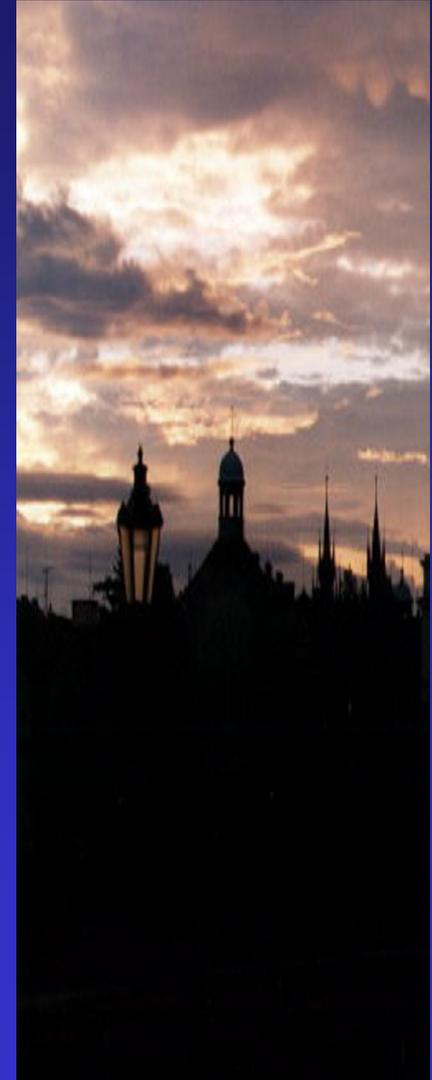
# *Prague – historical city*



# *Prague – city of churches...*



# *Prague by night*



# *Old Town Square Christmas tree 2008*



**Thanks for your attention!**



**Prague – Charles Bridge**