

LIPIDS (AND ENDOTHELIAL DYSFUNCTION)

Jan Pitha

MANAGEMENTS OF DYSLIPIDEMIA

Strategy

- To offer better and longer life

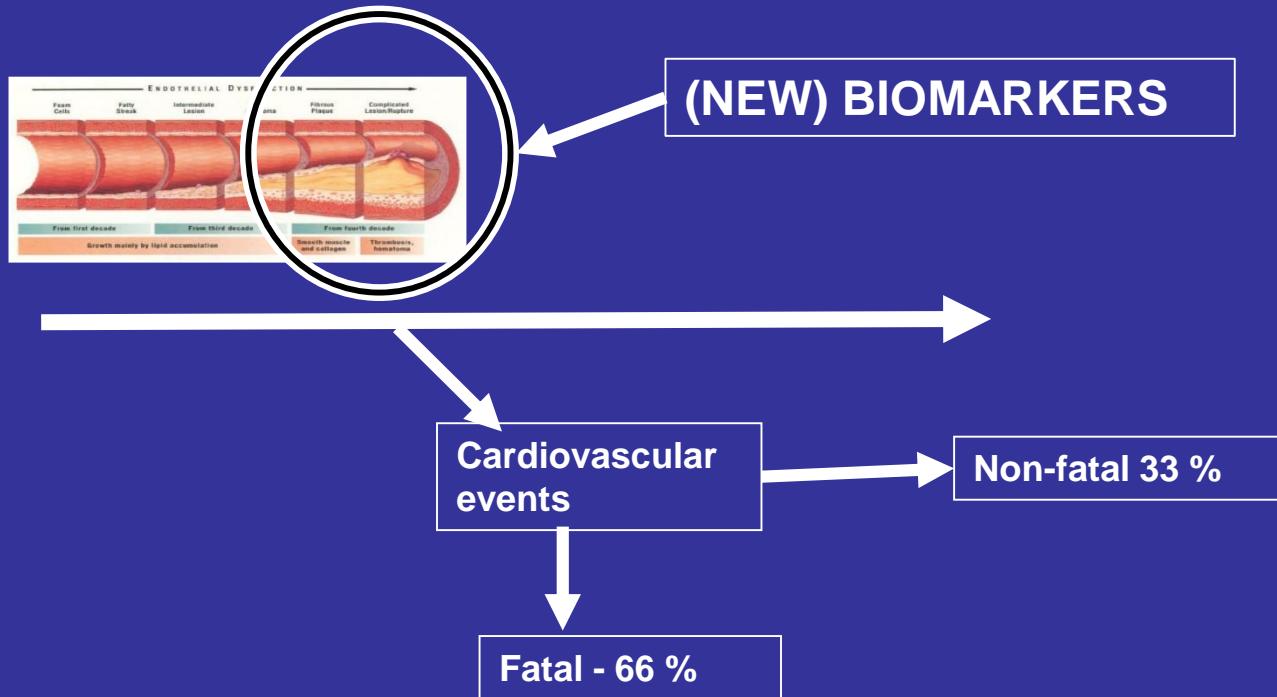
Tactics

- Find (out) and remove as much of CV risk as possible

DYSLIPIDEMIAS IN DISEASE

	Atherosclerotic CVD	NAFLD/NASH	Pancreatitis
Type of dyslipidemia	Isolated Hyper- Cholesterolemia	Mixed dyslipidemia	Isolated Hyper- Triglyceridemia
Total cholesterol (mmol/l)	8-15	5.5-8	5-6
Triglycerides (mmol/l)	1.0-1.7	1.8-5	More than 11
HDL cholesterol (mmol/l)	1.1-1.3	0.8-1.0	-
LDL cholesterol (mmol/l)	6-12	3-5	-

DEVELOPMENT OF ATHEROSCLEROSIS



Chambless L et al, Population versus clinical view of case fatality from acute coronary heart disease: results from the WHO MONICA Project 1985-1990, Multinational MONitoring of Trends and Determinants in CArdiovascular Disease, Circulation, 1997;3849-59,

MAIN RISK FACTORS FOR CVD

NON-MANAGEABLE

- 1) AGE**
(45y m, 55y w)
- 2) MALE GENDER**
- 3) GENETICS**
(Fam. history – 60 y m, 65 y w)

MANAGEABLE

- 1) SMOKING**
- 2) DYSLIPIDEMIA**
- 3) HYPERTENSION**
(140/90 mm Hg and above)
- 4) DIABETES M.**
(fasting/nonfasting glycemia more than 7/11 mmol/l)
- 5) *RENAL DISEASE***

INFORMATION:

- **(Family) history**
- **Physical examination**
- **Standard biochemical analyses**
- **Novel biomarkers/algorhitms**

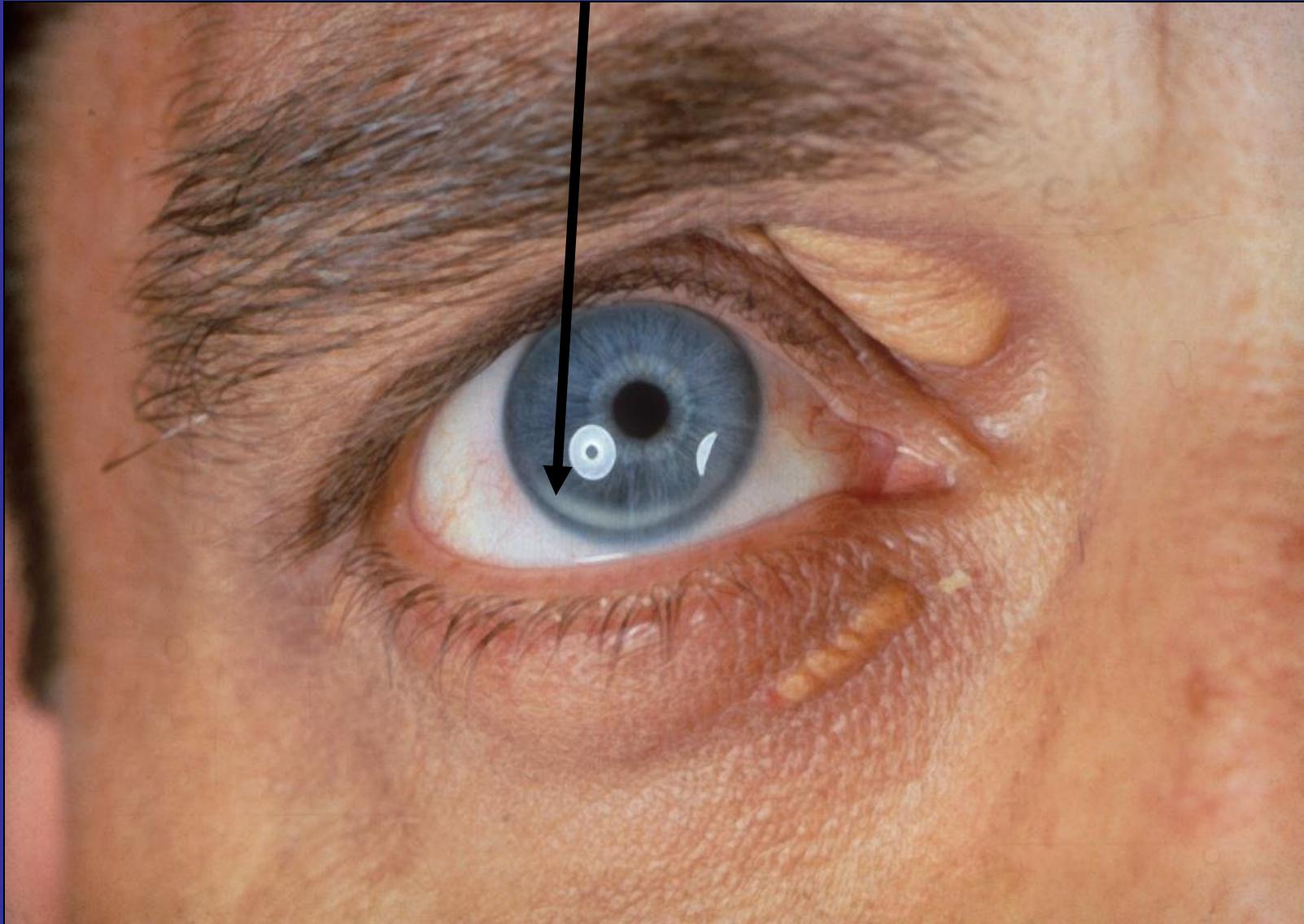
(FAMILY) HISTORY

- Age
- Ethnicity
- CV Risk factors – family history, history of CVD atherosclerotic origing, smoking, hypertension, diabetes mellitus, dyslipidemia, renal disease – duration of all of them
- Pregnancy, menstrual cycle in women
- Other diseases
- Drugs

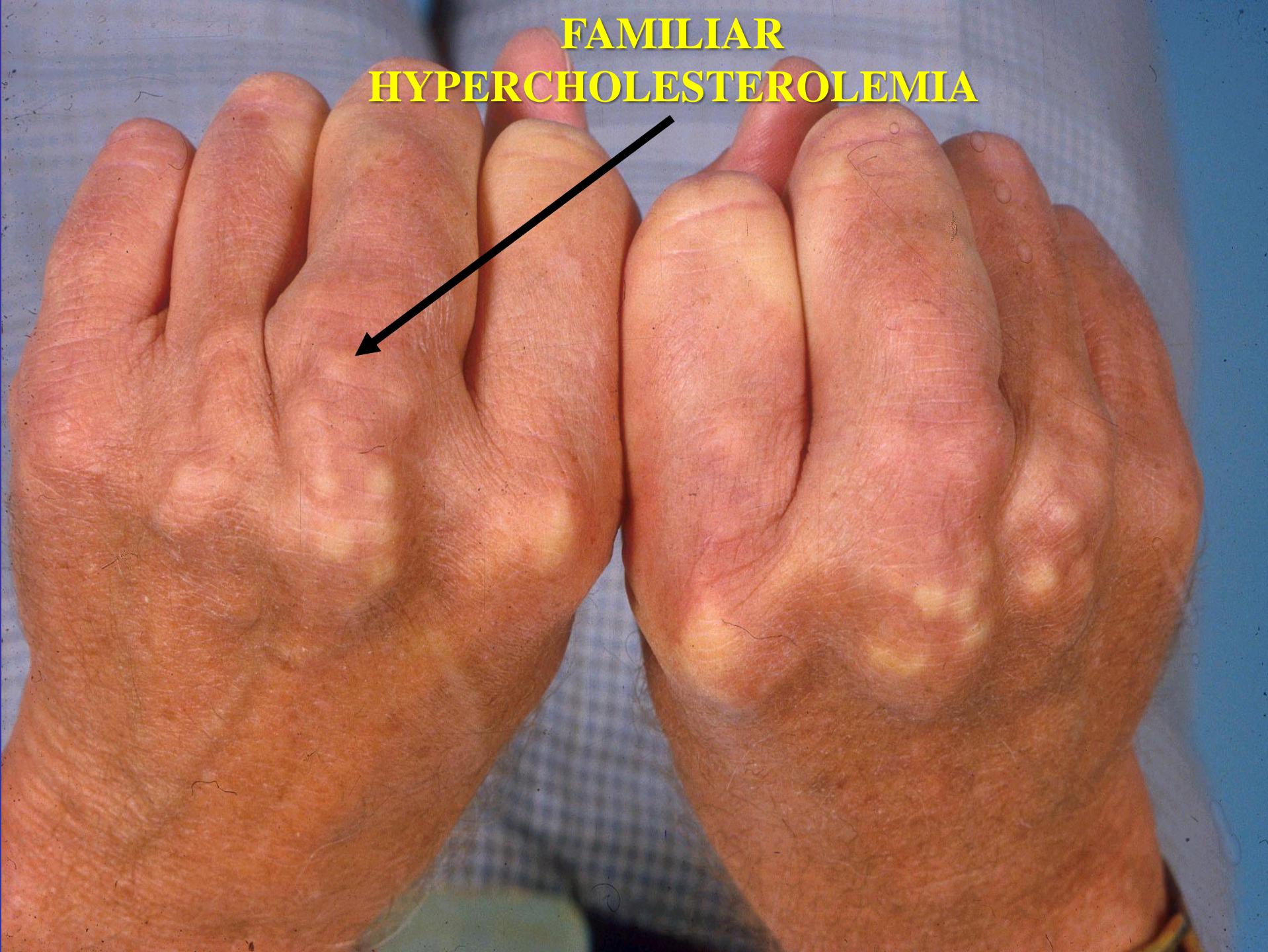
PHYSICAL EXAMINATION

- BMI
- Waist/Hip circumference
- Thigh circumference
- Blood pressure
- Bruits
- Xanthelasma
- Xanthomas
-

ALL DLP



**FAMILIAR
HYPERCHOLESTEROLEMIA**



FAMILIAR HYPERCHOLESTEROLEMIA

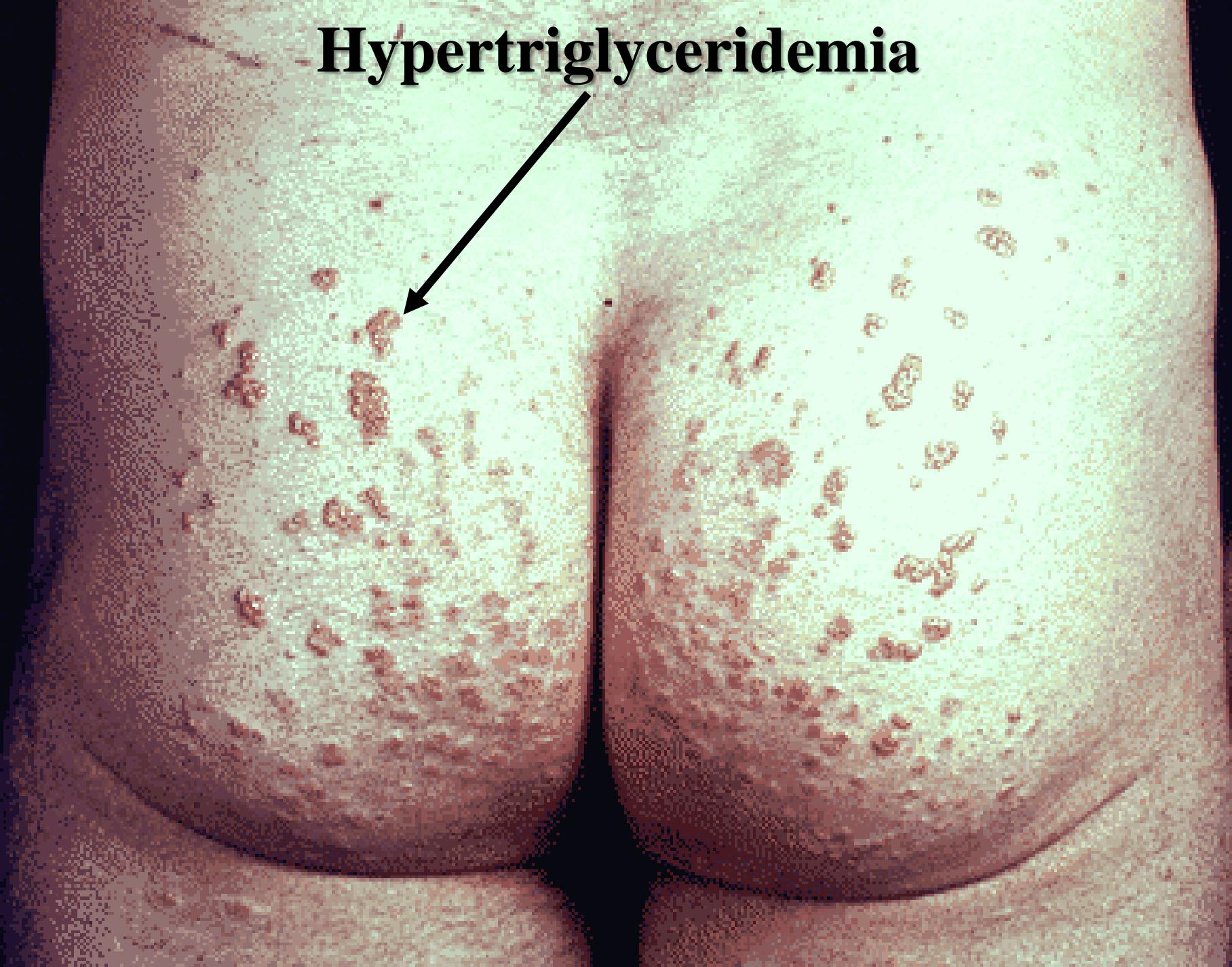


DYSBETALIPOPROTEINEMIA



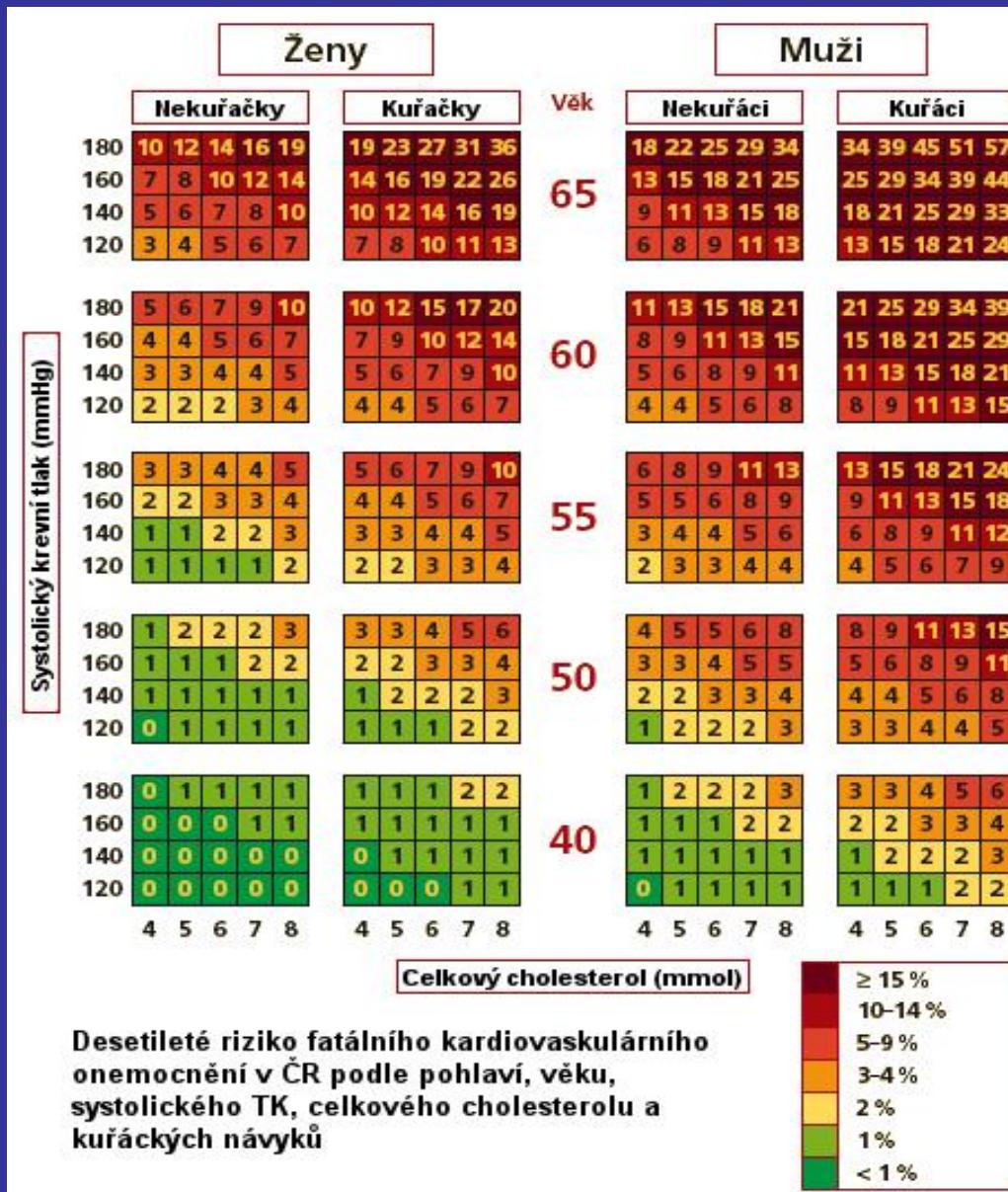
Courtesy Jana Franekova

Hypertriglyceridemia



COMMON BIOCHEMICAL VALUES

- LDL cholesterol
- Triglycerides
- HDL cholesterol
- Total cholesterol
- Fasting glycemia
- Renal tests
- Liver tests
- Creatine kinase
- TSH



IMAGING/FUNCTIONAL METHODS

Function of endothelium

- 1. Barrier**
- 2. Regulation of Vasoactivity**
- 3. Antithrombotic**
- 4. Auto-, para- a endocrine (NO, endothelin, ..)**

Risk stratification

aCVD present

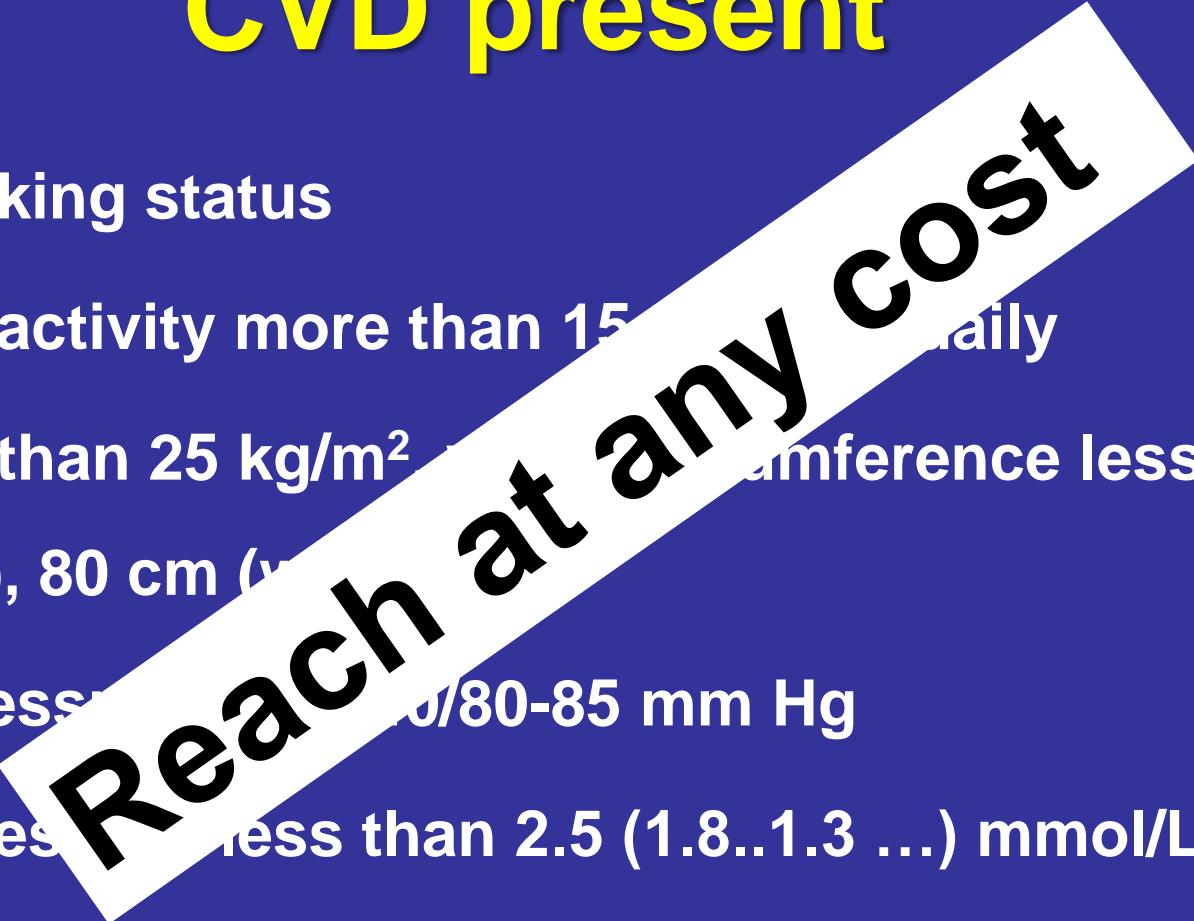
x

aCVD absent

CVD present

- Non-smoking status
- Physical activity more than 15 minutes daily
- BMI less than 25 kg/m², waist circumference less than 94 cm (men), 80 cm (women)
- Blood pressure 130-140/80-85 mm Hg
- LDL cholesterol less than 2.5 (1.8..1.3 ...) mmol/L
- *HDL more than 1.1 mmol/L (men) 1.2-1.3 mmol/L (women)*
- Triglycerides less than 2.0 (1.7) mmol/L

CVD present

- Non-smoking status
 - Physical activity more than 150 min weekly
 - BMI less than 25 kg/m² or waist circumference less than 94 cm (men), 80 cm (women)
 - Blood pressure less than 120/80-85 mm Hg
 - LDL cholesterol less than 2.5 (1.8..1.3 ...) mmol/L
 - *HDL more than 1.1 mmol/L (men) 1.2-1.3 mmol/L (women)*
 - Triglycerides less than 2.0 (1.7) mmol/L
- 

CVD absent

- Non-smoking status
- Physical activity more than 15 minutes daily including brisk walk
- BMI less than 25 kg/m², waist circumference less than 94 cm (men), 80 cm (women)
- Blood pressure 130-140/80-85 mm Hg
- LDL cholesterol less than 3.4 (1.8 ?) mmol/L
- HDL more than 1.1 mmol/L (men) 1.2-1.3 mmol/L (women)
- Triglycerides less than 2.0 (1.7) mmol/L

THERAPY OF DYSLIPIDEMIAS

- 1. Exclude secondary cause
(hypothyroidism, diabetes mellitus, ...)**
- 2. Establish actual risk (lifestyle measures x
pharmacotherapy)**
- 3. Focus on LDL cholesterol – treat by statins
(iHMGCoA reductase)**
- 4. Avoid untoward effects**

DYSLIPIDEMIAS

	SECONDARY DLP	PRIMARY DLP
ELEVATED ONLY CHOLESTEROL	HYPOTHYROSIS NEPHROTIC SYNDROME	FAMILIAR HYPERCHOLESTEROLEMIA POLYGENIC HYPERCHOLESTEROLEMIA
ELEVATED ONLY TRIGLYCERIDES	DECOMPENSATED DIABETES MELLITUS TYPE 1+2 HIGH INTAKE OF ALCOHOL	LPL DEFICIENCY FAMILIAR HYPERTRIGLYCERIDEMIA
ELEVATED CHOLESTEROL AND TRIGLYCERIDES + LOWER HDL	COMPENSATED DIABETES MELLITUS TYPE 2 RENAL INSUFFICIENCY	DYSBETALIPOPROTEINEMIA (REMNANT REMOVAL DISEASE) FAMILIAR COMBINED HYPERLIPIDEMIA + LOW HDL: LCAT DEFICIENCY HYPOALPHALIPOPROTEINEMIA

PRIMARY DLP

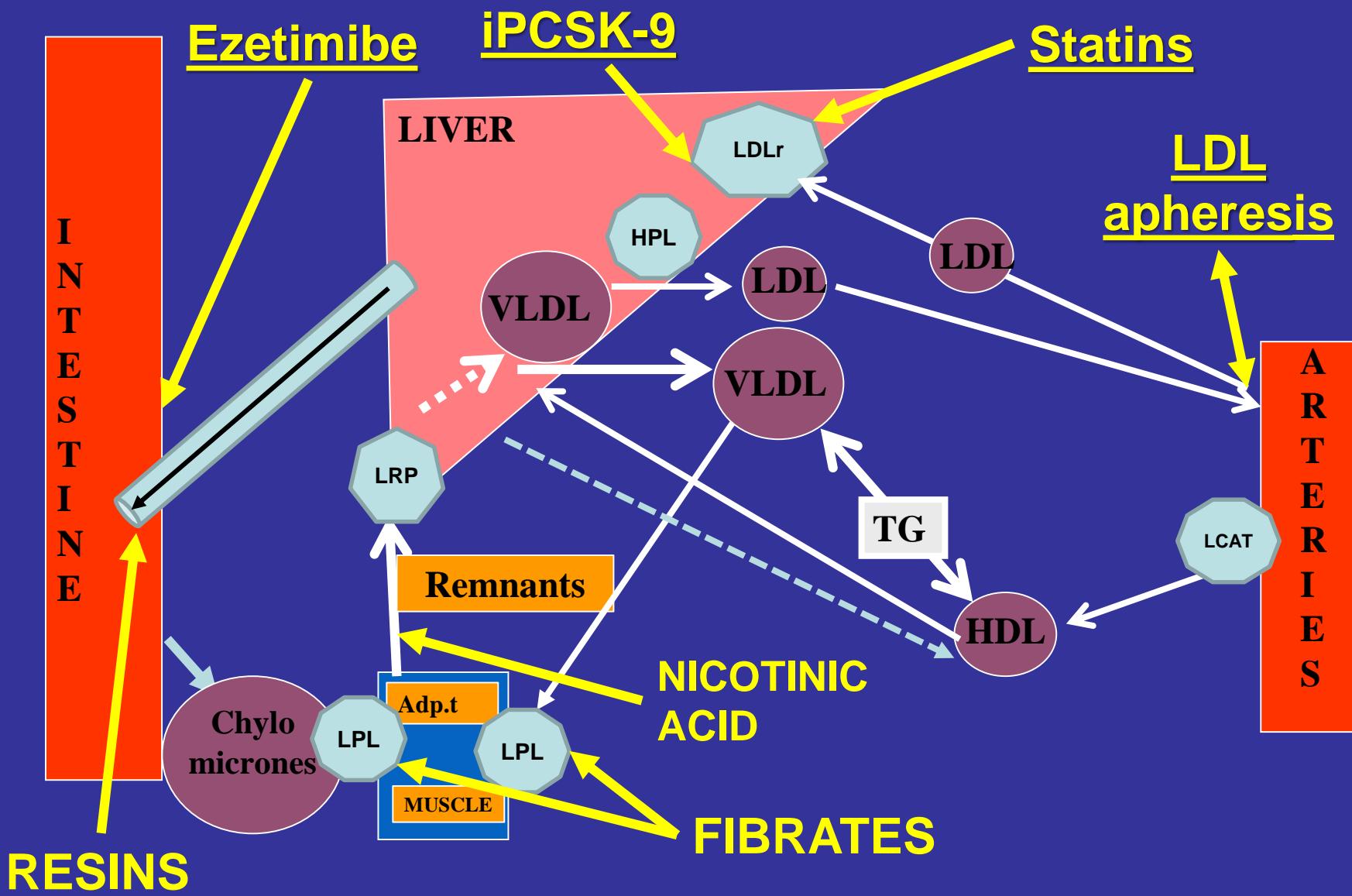
- High cholesterol (familiar hypercholesterolemia
– heterozygote/homozygote)
- High triglycerides (Lipoprotein lipase deficiency)
- High cholesterol + triglycerides
(dysbetalipoproteinemia, familiar mixed DLP) +
low HDL cholesterol

Therapy of dyslipidemias

- 1) Lifestyle
- 2) Pharmacotherapy
- 3) LDL apheresis
- 4) Liver transplant
- 5) Gene therapy

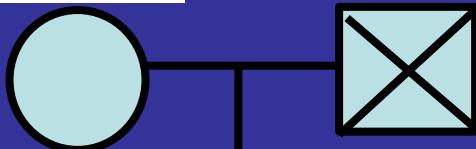
MANAGEMENT OF LDL CHOLESTEROL

	LDL cholesterol	Decrease of Clinical Events	Non-Lipid effects
Lifestyle, diet	5-30 %	+-	Antiinflammatory effect
Statins	30-60 %	+++	Antiinflammatory, antiapoptotic effect
Ezetimibe (+ statins)	15-20 %	+	Lowering of glucose ?
LDL/Lp(a) apheresis	60-80 %	++ ? (non-randomized studies)	Lowering of Lp(a) 60-80 %, fibrinogen,
PCSK9 inhibitors (cumabs)	60 %	+	?
Fibrates, Niacin, ...	10-20 %	-	Improvement of lipid spectrum (HDL/TG), fibrates microangiopathies



Woman, white, 41 yrs

MI, 59 y, non-smoker

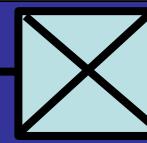
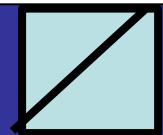


CABG, 66 y, non-smoker

MI, 59 y, smoker

CABG, 57 y, smoker

Carcinoma, died at 48 y



MI, 51 y, smoker



48 y, smoker

Our patient

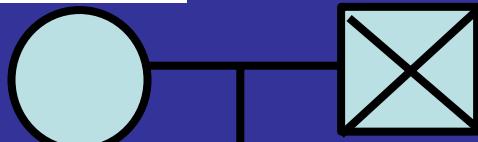
History/RF:

???



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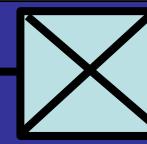
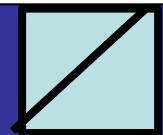


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History/RF:

CVD-0

Smoking – 10 years nonsmoker

DM -0

DLP - ?

HT -0

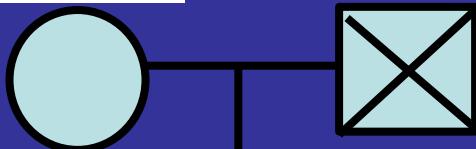
Pregnancy – no problems

Diet – healthy/appropriate

Physical activity - low

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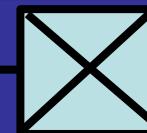
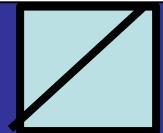


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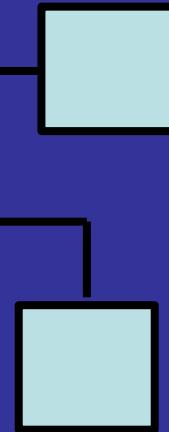
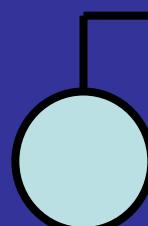
48 y, smoker

Our patient



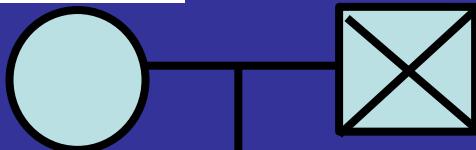
Physical exam:

???



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CABG, 57 y, smoker

Carcinoma, died at 48 y

Physical exam:

Body mass index: 25.8 kg*m⁻²

Waist circumference: 78 cm

Thigh circumference: NA

BP: 103/69 mmHg

No signs of dyslipidemia

Woman, white, 41 yrs

MI, 59 y, non-smoker

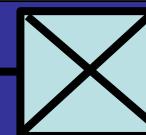
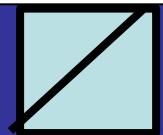


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Our patient

Regular Biochemistry:

???



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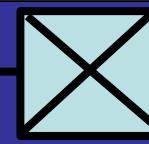
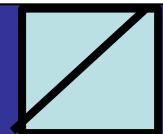


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48 y, smoker

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Regular Biochemistry:

LDL cholesterol - 1.5 mmol/l

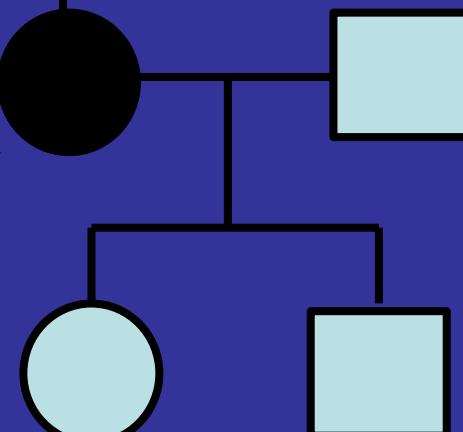
HDL cholesterol – 1.23 mmol/l

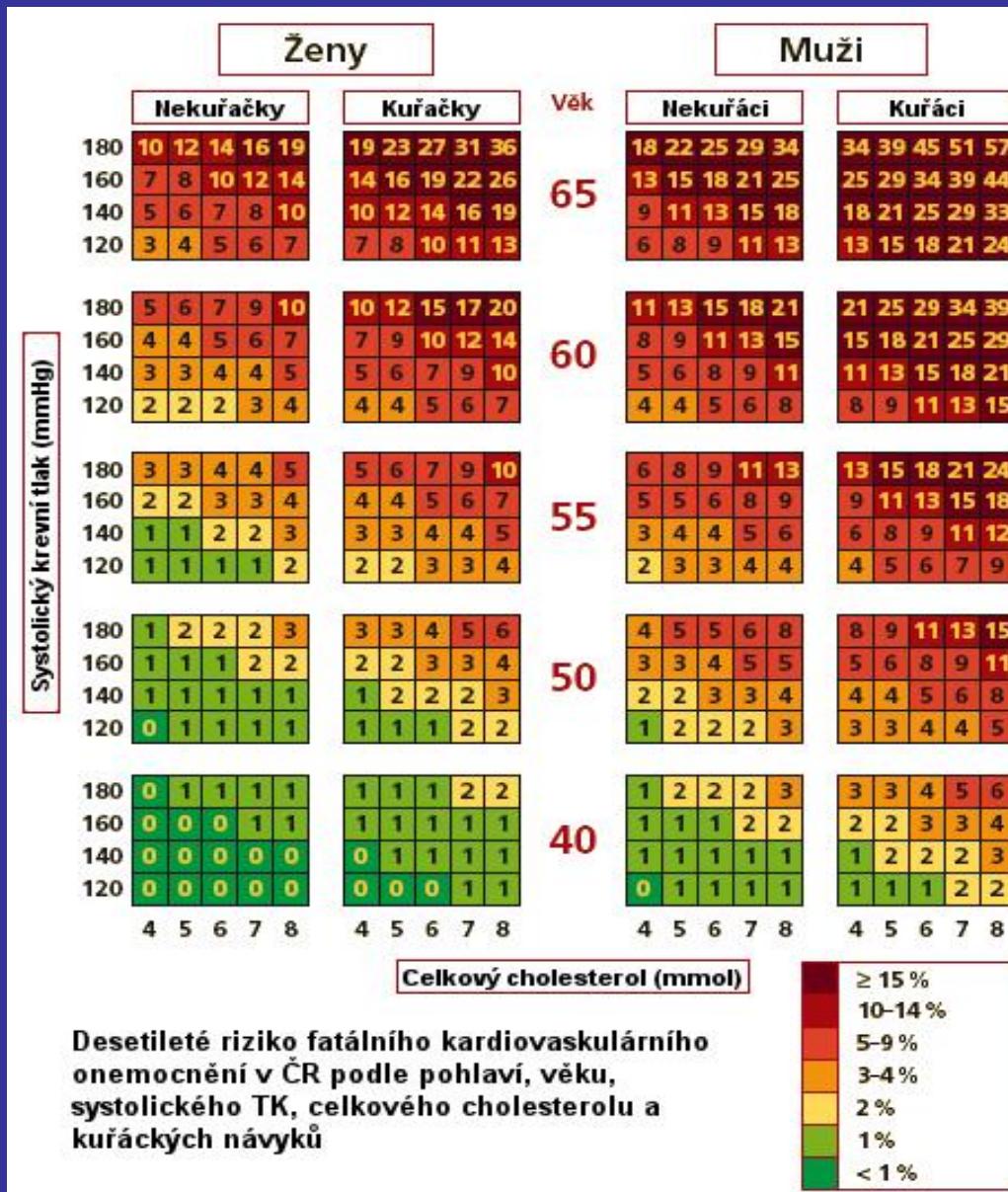
Triglycerides – 0.90 mmol/l

Total cholesterol – 3.20 mmol/l

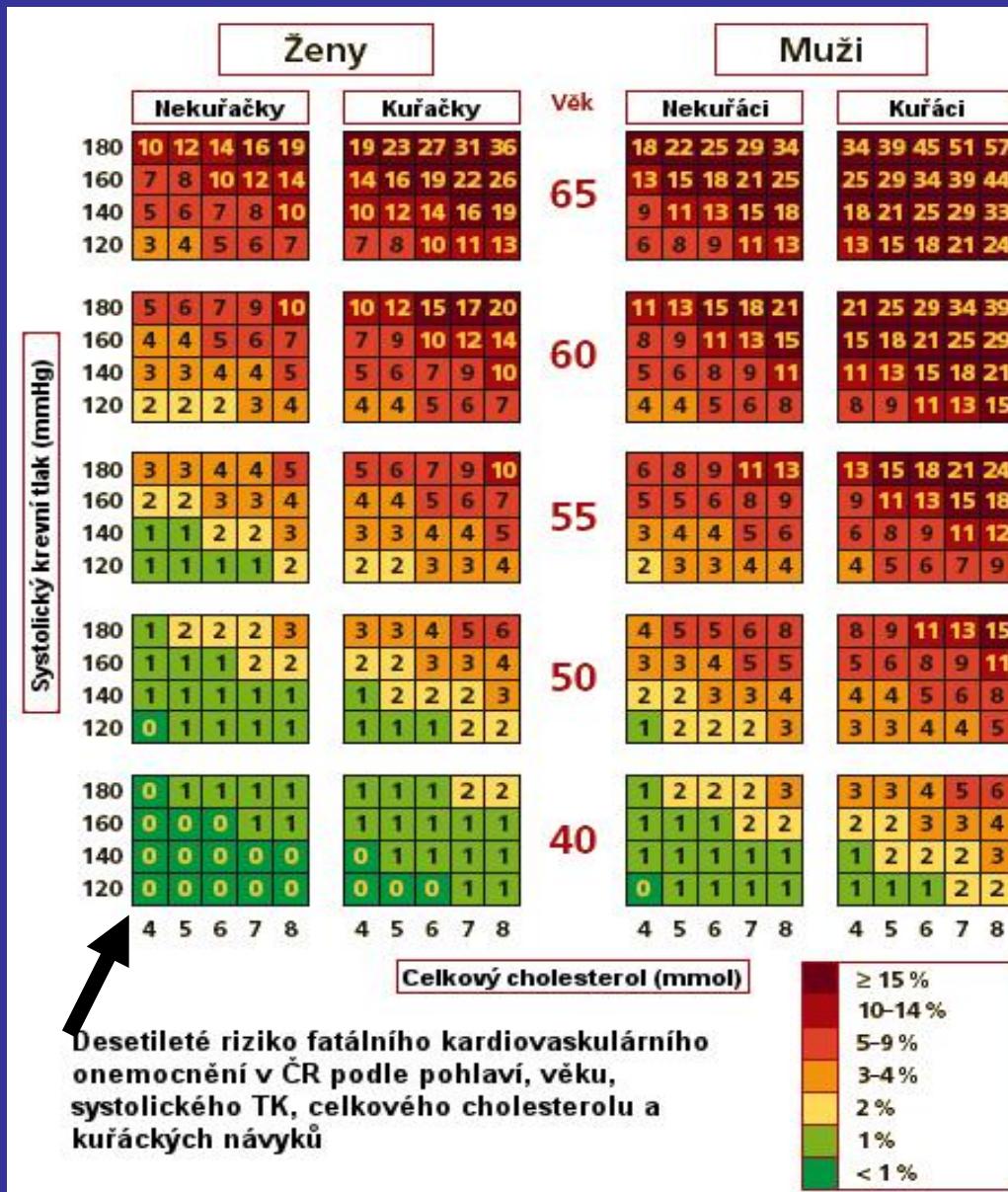
Glycemia – 4.1 mmol/l

TSH – normal values





Desetileté riziko fatálního kardiovaskulárního onemocnění v ČR podle pohlaví, věku, systolického TK, celkového cholesterolu a kuráckých návyků



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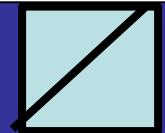


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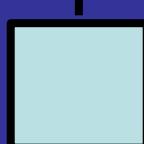
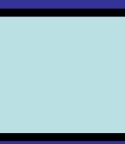
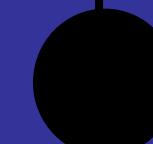


MI, 51 y, smoker



48 y, smoker

Our patient



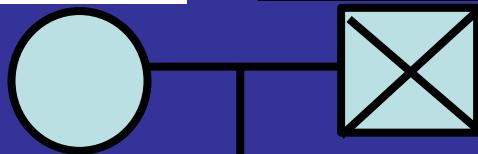
Any other proposal(s)

???



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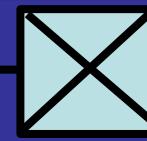
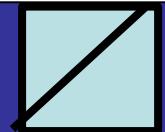


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Carcinoma, died at 48 y



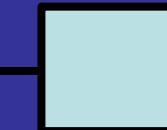
MI, 51 y, smoker



48 y, smoker



Our patient



Duplex ultrasound of carotid arteries:

CIMT less than 0.8 mm in all segments

Belcaro score – 1*

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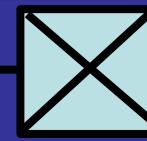
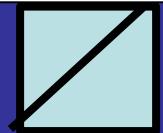


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48 y, smoker

Our patient

Conclusion(s)

?



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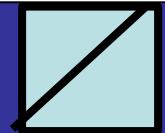


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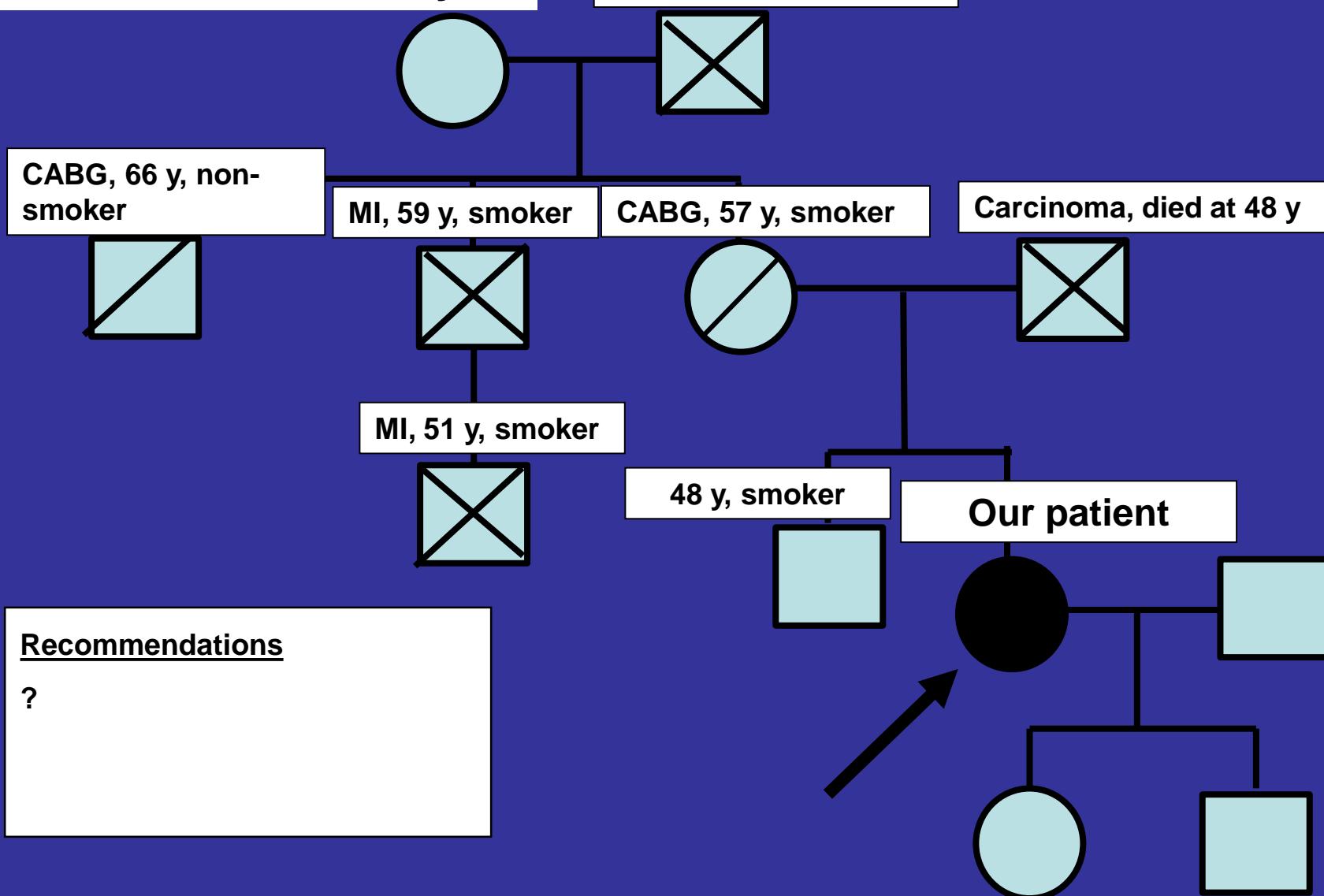
Conclusions:

Patient without signs of aCVD, with strongly positive family of aCVD, without dyslipidemia, signs of preclinical atherosclerosis

Familiar hypercholesterolemia in family

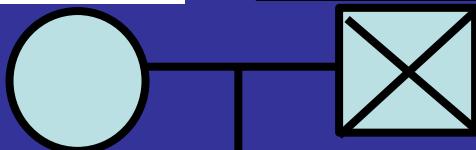
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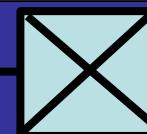
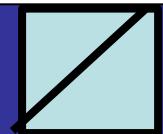


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48 y, smoker

Our patient



Recommendations

Sustain healthy lifestyle

+ Examination of her brother

Woman, white, 41 yrs

MI, 59 y, non-smoker

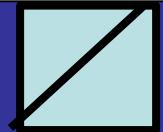


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Recommendations

+ do not start smoking in
transition to menopause

