

e.g. in China HA low even w/ high smoking and BP
Yuna Indians have 50% IDDM but not NHA

Clot Phages -

- hang 30 minutes to prove non-haem
 - #1 cause of death = sneezing
 - but real cause is clot phaging
- } like cholesterol
chol = clot

So why do so many US people have high LDL?

6 year old girl born w/ LDL = 1000. - develop NHA at 18 months

1968
at NIH

- develop Xanthomas = chol. deposits - b/c scavengers cannot remove chol. after injuries

So maybe this can say something about HA.

So... took cells into tissue ~~culture~~ culture

Found that "normal" cells did not make any cholesterol b/c they take it from plasma using LDL receptors (acceptor \rightarrow pit \rightarrow lysosome)

Child's cells could not make receptors. Cells turn on back-up pathway.

Can block cholesterol synthesis
which leads to ↑ in LDL T/A

Block HMG CoA Reductases - STATINS

3 studies

15,000 people - 5 yrs
plasma LDL ↓ 26-35%
MI's ↓ 25-30%
death ↓ 30% (45 study)
death by MI ↓ 42%

?? 80-90% of plaques contain Chlamydia pneumoniae

- can be found in lots of tissues
- does Chlamydia cause any problems?
- no evidence.

?? does ETOH affect ability of liver. **NO!**

?? does parent entry affect child?

Wanted to say on part some Lamarck
but corrected self.

Europe + NA - born like world

- gradually creep up over years
due to high FAT diet

Japanese Men

Living in JAPAN vs CALIFORNIA

Evidence... diet rich in chol. + fat
raises level in blood

Med Students fed TONS of cholesterol

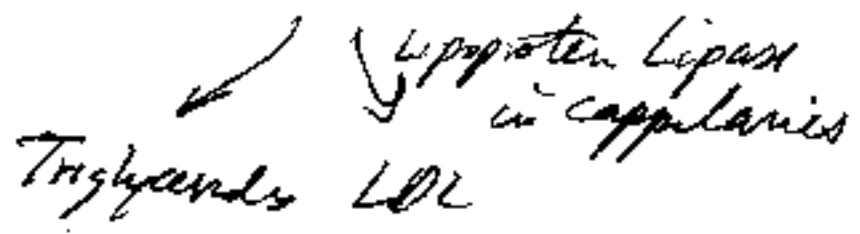
- leads to NO increase over 24 hours
- but w/ time the amt of cholesterol
in liver increases.
- flaw in Nature... liver doesn't tell
brain to ↓ cholesterol
- so liver decreases receptors

SREBP - attached to membrane - needs to
be cleaved for tx. factor to go to nucleus.
(two proteases needed)

Protease inhibited w/ lots of cholesterol

In body

- LDL receptors (x) primarily in LIVER
- Liver makes VLDL

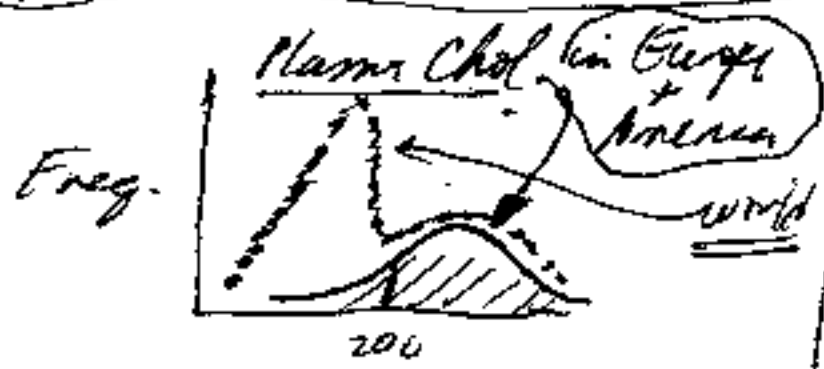


remove by binding to LDL receptors

In FH - LDL not removed from blood, how long to?

	t/t	t/FH	FH/FH
freq		1/500	1/200,000
plasma LDL		$\uparrow 2.5x$	$\uparrow 6x$
age of MI		35-45	5-15

@ disrupt same gene in mice
 @ FH + mouse shows much incr. in LDL even in low cholesterol diet. Even work in high cholesterol human.
 @ also same type of deposits
 @ correct defect w/ adenovirus w/ LDL receptor gene. but not ready for humans.



200/500 people die of MI or stroke but only 1/500 have FH.
why?

Europe + NA cholesterol v. high relative to world