What is Familial Hypercholesterolemia - FH?

FH is genetic disorder that affects the livers capacity to collect excess LDL cholesterol from the blood stream.

It is passed from parent to child - FH Patients are born with the condition. There is no cure but it is treatable.

Children establish their baseline LDL levels by age 2

1- 300/500 humans (on average) have Heterozygous FH
1 - 1,000,000 have Homozygous FH

Left undiagnosed and untreated FH Patients will develop Heart Disease and may die young from a heart attack or a stroke.

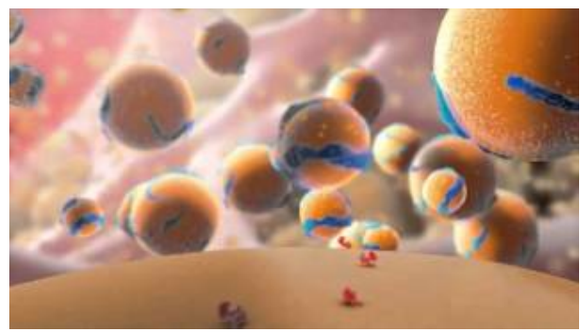
Why is FH dangerous?

LDL Cholesterol is a wax-like, fatty substance that can build up in the walls of blood vessels.

Every cell in the human body requires LDL Cholesterol

On average, the body sends LDL Cholesterol in to the blood stream every ten minutes

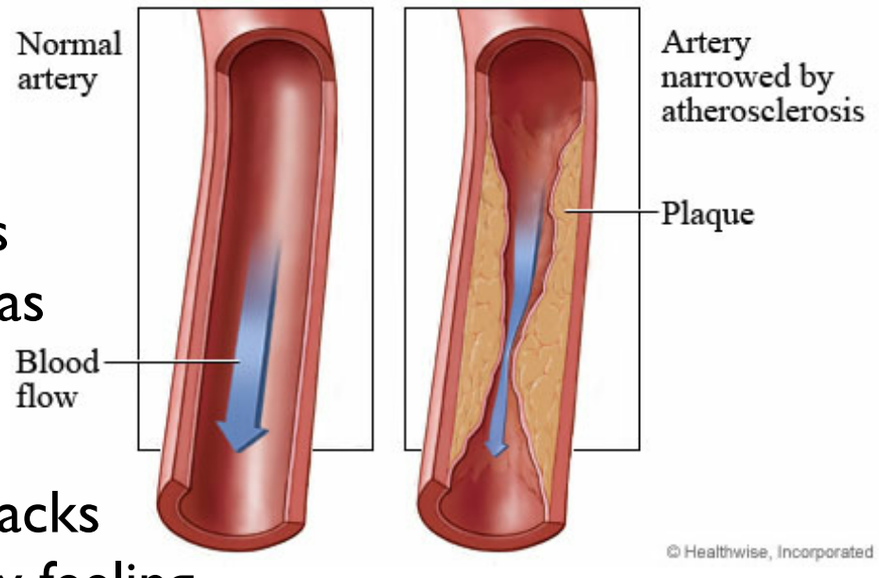
Cells that need it, absorb it in through the cell wall
- those that don't, deposit the LDL on the outside of the cell wall



Receptor Video

As the blood flows through the liver, receptors grab the excess LDL and dispose of it through waste

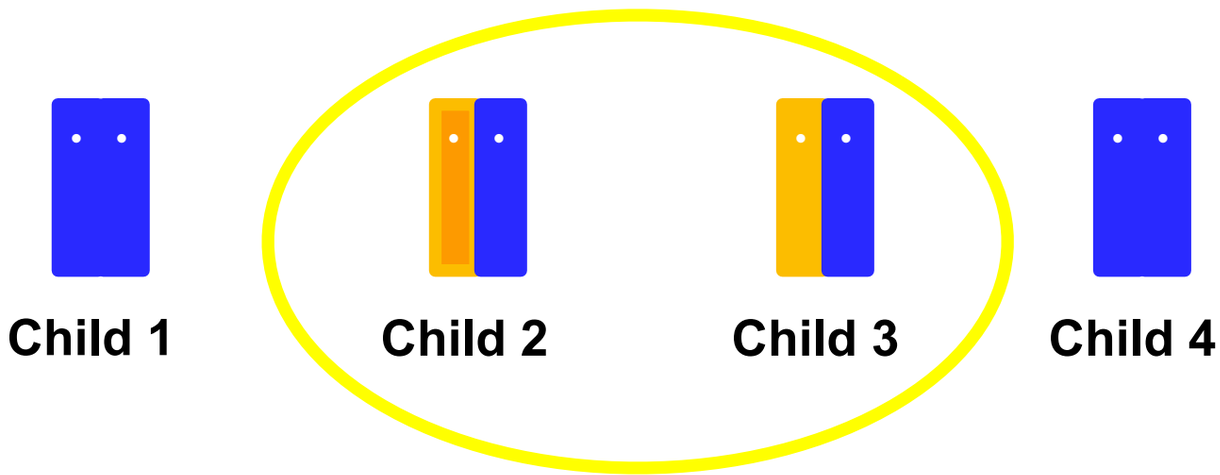
An FH Patient has broken receptors therefore most of the LDL is NOT collected and it deposits through out the body on tendons as zanthomas, in eyes as arcus and in arteries and vessels.



Narrowed and blocked arteries and blood vessels cause heart attacks and strokes in otherwise healthy looking and most of time, healthy feeling people.

Heterozygous FH

(One Copy; 1 in 300/500)



50% Chance the Child Will Have the Disorder

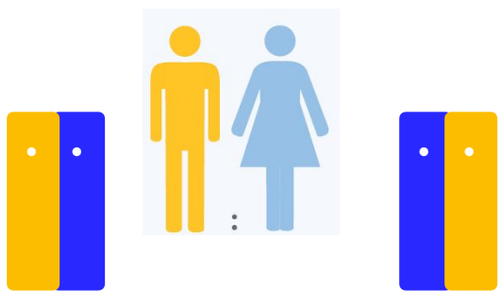
LDL levels 180-400 mg/dL

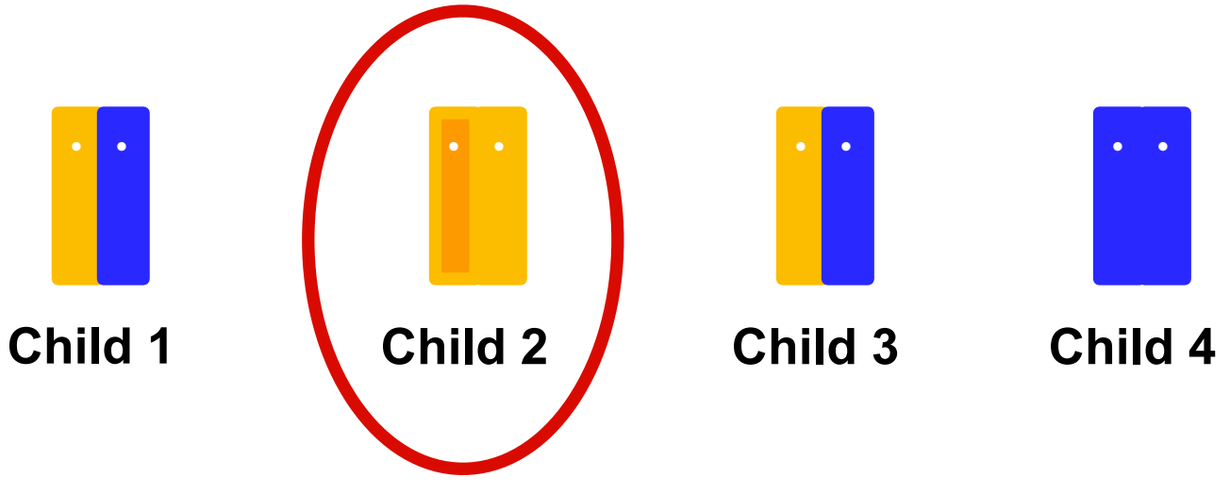
Homozygous FH

(Two Copies; 1 in 1,000,000)

Chromosome with FH mutation

Chromosome without FH mutation





LDL Levels 500-1000 mg/dL
Heart Disease in Childhood

Familial Hypercholesterolemia(s)

Definition:
Severe hypercholesterolemia with autosomal dominant inheritance pattern

Primary Autosomal Dominant forms:
- *LDLR (classic FH) ~85-90% cases*
  Homozygous (1:1,000,000); TC 650-1000mg/dl
  Heterozygous (1:500); TC 350-550mg/dl
- *APOB (Agr3500Gln) ~5-10% cases*
- *PCSK9 (gain-of-function) ~5% cases*

20% have no known genetic mutation

***620,000 - 1,000,000 Possible FH patients in US**
(10-20% diagnosed)

Total cholesterol >290 or LDL >190 mg/dl in adult,
or total cholesterol >260 or LDL>160mg/dl in child

AND

Definite: Tendon xanthoma in patient or relative

Probable:
Family history of premature heart attack, OR
Hypercholesterolemia in 1st or 2nd degree relative

* www.google.com/publicdata
311,591,917 - Jul 2011
Source: U.S. Census Bureau

* **Goldberg AC et al. J Clinic Lipid 2011;5:S1-S8**

Current Treatment for FH

Statins

Diet

Modify other risk factors

Additional drugs (Niacin, Bile acid resins, ezetimibe)

LDL apheresis

Possible Treatment for FH

PCSK9 inhibitors

Mipomersen - APO b antisense

CETP inhibitors

MTP inhibitors