THE PREVALENCE AND PICTURE OF FAMILIAL HYPERCHOLESTEROLEMIA

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Disclosures

- Nurse Advisory Board – Genzyme
- Speaker’s Bureau - Abbott
Objectives

Discuss the prevalence of heterozygous and homozygous familial hypercholesterolemia.

Describe the clinical presentation of the individual with familial hypercholesterolemia.
The prevalence of FH in the USA is:

A. 1:150 individuals
B. 1:500 individuals
C. 1:750 individuals
D. 1:1,000 individuals
Individuals with heterozygous familial hypercholesterolemia must have xanthomas in order to be positively identified as having the disorder.

A. True
B. False
**Characteristics of Patients**

*Most common and serious monogenic disorder of lipid metabolism*

- Elevated LDL cholesterol
- Severe risk for Coronary Heart Disease
- Genetic disorder / Patients afflicted since birth
Recognition of FH

- Recognizable from features in:
  - Family and personal history
  - Physical examination
  - Analysis of lipid profile
Clinical Spectrum of Familial Hypercholesterolemia

Mean LDL-C in US Adults 100 – 200 mg/dl.

LDL-C Range for Untreated Heterozygous Familial Hypercholesterolemia Patients: 200 – 450 mg/dl.

LDL-C Range for Untreated Homozygous Familial Hypercholesterolemia Patients: 450 – 1000+ mg/dl.
Estimated Prevalence

- Heterozygous FH – 1:500
  More likely 1:300 - 500

- Homozygous FH – 1:1,000,000
Founder Effect

Accounts for higher prevalence than seen in the general population.

French Canadians
Christian Lebanese
South African Afrikaners and Ashkenazi Jews
## Estimated Frequencies of FH

<table>
<thead>
<tr>
<th>Region</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td></td>
</tr>
<tr>
<td>South Africa/Afrikaners</td>
<td>1:100</td>
</tr>
<tr>
<td>South Africa/Indians</td>
<td>1:72</td>
</tr>
<tr>
<td>South Africa/Ashkenazi Jews</td>
<td>1:67</td>
</tr>
<tr>
<td><strong>French Canadians</strong></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>1:500</td>
</tr>
<tr>
<td><strong>Middle East</strong></td>
<td></td>
</tr>
<tr>
<td>Lebanese Christian</td>
<td>1:85</td>
</tr>
<tr>
<td><strong>Japan/Japanese</strong></td>
<td></td>
</tr>
<tr>
<td>1:900</td>
<td></td>
</tr>
</tbody>
</table>
Meet Scott...

- Husband
- Retired teacher
- Father
- Active volunteer at church
- Golfer
Meet Scott...

- 61-year-old male diagnosed with hypercholesterolemia in college.
- Early treatment included bile acid sequestrants and ultimately statins.
- Intolerant with fatigue, myalgias, and myopathy
- After 1 year off statins, rechallenged with Crestor 10mg twice weekly, with return of symptoms
Meet Scott...

- Anginal symptoms at 56 years of age.
- Positive stress test.
- Quadruple coronary artery bypass surgery.
- Restenosis of \( \frac{3}{4} \) grafts, with multiple stenting procedures.
- Most recent stent placement, 2009
Meet Scott...

- **Family History**

  Twin brother with hypercholesterolemia and MI at 56 years of age.

  Daughter without hypercholesterolemia.

  Mother, 89, with hypercholesterolemia and coronary disease with onset at 59 years of age.
Meet Scott...

- Evaluated in lipid clinic, 3/2010
- TC 337mg/dl
- LDL-C 261mg/dl, Apolipoprotein B 169mg/dl
- Total LDL particles >3500nmol/l
- Small LDL particles 2845nmol/l
- HDL 26mg/dl
- Triglycerides 248mg/dl
Physical Examination

- Bilateral ear creases
- Bilateral corneal arcus
- Tendon xanthomas on both knuckles
- Carotids +2 with brisk upstroke and no bruits
- Normal S1 and S2 with 1/6 SEM MLSB
- No hepatosplenomegaly
Meet Scott...

- Bilateral
- premature
- corneal arcus
First evaluated at 3 years of age.

Lipid Profile

TC – 697 mg/dl.
LDL-C – 565 mg/dl.
Triglycerides – 420mg/dl.
HDL – 20 mg/dl.

Brief treatment with lovastatin 5 mg/day and cholestyramine 2 tablespoons per day.
Medications discontinued due to poor response
No tendon xanthomas or corneal arcus.
Cardiovascular examination normal.
Meet Megan

- 20-year-old with HoFH and untreated LDL of 800 mg/dl.
  - Mother - 52 with HeFH. TC 387 mg/dl and LDL 292 mg/dl
  - Father - 54 with HeFH. TC 350 mg/dl and LDL 294 mg/dl
  - Maternal grandmother – TC 300 mg/dl.
  - Maternal grandfather - died at 36 years of age from myocardial infarction
  - Paternal grandfather - died at 38 years of age from myocardial infarction
Megan’s Clinical Course

- Treated with statin therapy, intensified over time, with addition of cholesterol absorption inhibitor, niacin, and aspirin
- Throughout childhood and adolescence, monitored for aortic valve and coronary disease, with echocardiograms, coronary calcium scoring, and 64-slice CT scan with coronary angiography – all NEGATIVE results.
- At 15 years of age, developed planar xanthomas between webbings of her fingers
Xanthomas in Finger Webbings

Xanthoma on patient's both hands.

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Appearance of Achilles Tendon Xanthomas at Age 17
Calcification of Achilles Tendon Xanthomas
OPEN HOUSE WEEKEND

UNDERGRADUATE OPEN HOUSE
Saturday, September 24, 2011
908.737.KEAN / www.kean.edu
There will be another Open House on Sunday, November 6.

GRADUATE OPEN HOUSE
Sunday, September 25, 2011
908.737.GRAD / www.kean.edu/~keangrad/
facebook.com/keanuniversity
Megan’s Clinical Picture

- Current lipid profile:
  - Total cholesterol: 380 mg/dl
  - Triglycerides: 41 mg/dl
  - HDL: 64 mg/dl
  - LDL-C: 310 mg/dl
Playing soccer in college
DEVELOPED LESIONS AT 3 MONTHS OF AGE, TREATED AS MOLLUSCUM

- Diagnosed at 3 years of age after xanthomas noted on knees and thighs and yellow plaques on finger webs and toes.
- Biopsy confirmed xanthomas
Lipid profile: TC 899mg/dl, LDL 850mg/dl and HDL 23 mg/dl
Mother – 32 – Untreated total cholesterol greater than 800 mg/dl. Started on statin, but never had any followup. + premature corneal arcus.

Maternal grandmother with elevated cholesterol levels.

Father’s lipid values unknown.
Physical Findings

- Extensive tuberous xanthomas on anterior aspect of both knees
- None in popliteal fossae
- No palmar planar xanthomomas in creases of palms
- No tendon xanthomas
Physical findings
Planar xanthomas in gluteal folds
Planar xanthomas on thighs, arms, and buttocks