Familial Hypercholesterolemia

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Faculty Disclosures

Claire Rice has no disclosures except that she loves to catch fish.
Learning Objectives

1. Identify the prevalence of heterozygous and homozygous familial hypercholesterolemia

2. Describe the clinical presentation of individuals with familial hypercholesterolemia

3. Summarize current therapies available for patients with familial hypercholesterolemia
These patients have a long-standing history of severe hypercholesterolemia dating back to childhood.

If an acute coronary event has not already occurred, symptoms consistent with ischemic heart disease are not uncommon, especially if other cardiovascular risk factors (especially smoking) are present.

Past or present symptoms of recurrent Achilles tendonitis or arthritic complaints may be present.
Premature CAD and severe hypercholesterolemia are present in one or more first-degree relatives.

If carefully questioned, patients with either homozygous or heterozygous FH may describe first-degree relatives who had visible tendon xanthomas on their hands.

- Compared 47 FH/70 without FH, > 50 years of age
- Exclusion: Stroke and TIA
- FH high incidence of mild cognitive impairment compared with those without FH (21.3% vs 2.9%; P = .00).
- Prior studies demonstrated older patients with sporadic hypercholesterolemia do not show a higher incidence of mild cognitive impairment.
- These findings suggest that early exposure to elevated cholesterol or LDL receptor dysfunction may be risk factors for mild cognitive impairment.
Clinical Presentation
Children with HoFH

- May have symptoms consistent with ischemic heart disease, peripheral vascular disease, cerebrovascular disease, or aortic stenosis which may be confused with benign conditions unless diagnosis of HoFH is considered.
- May have articular symptoms such as tendonitis, arthralgias or unusual skin lesions.
- May be diagnosed as early as age 2. May start on LDL–C apheresis as early as 3 years of age.
- May have CV events when they are a very young age and may result in death if goes untreated.
Physical characteristics of FH

- Xanthelasma of the eyelid in hetero-FH
- Achilles tendon xanthoma in hetero-FH
- Arcus corneae and xanthelasma of the eyelid in hetero-FH
- Xanthoma on extensor tendons of the hand in hetero-FH
- X-ray measurement of Achilles tendon thickness
Combination Lipid Therapy
Some homozygotes exhibit partial response to statins
Portocaval shunting (high morbidity and mortality)
Liver transplantation—limited applicability / high morbidity
Gene therapy has been disappointing (*Nat Med.* 1995;1:1148–1154)
Low-density lipoprotein apheresis

2013 ACC/AHA Guideline for Management of Blood Cholesterol

Figure 2. Major recommendations for statin therapy for ASCVD prevention

ASCVD Statin Benefit Groups
Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

- Adults age ≥21 y and a candidate for statin therapy
  - Yes
  - Clinical ASCVD
    - Yes
      - Age <75 y
        - High-intensity statin (Moderate-intensity statin if not candidate for high-intensity statin)
    - No
      - Age >75 y OR if not candidate for high-intensity statin
        - Moderate-intensity statin

- LDL-C ≥190 mg/dL
  - Yes
    - High-intensity statin (Moderate-intensity statin if not candidate for high-intensity statin)
  - No
    - Diabetes Type 1 or 2
      - Yes
        - Moderate-intensity statin
      - No
        - Estimated 10-y ASCVD risk ≥7.5%*
          - High-intensity statin

- Estimated 10-y ASCVD risk with Pooled Cohort Equations*
  - ≥7.5% estimated 10-y ASCVD risk and age 40-75 y
    - Yes
      - Moderate-to-high intensity statin
  - No
    - ASCVD prevention benefit of statin therapy may be less clear in other groups
      In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.
Statin Treatment in Children With FH
The Younger, the Better


186 of the original 214 children available for follow up.
Ages 8–18 years
Randomized to Pravastatin 20 mg or 40 mg vs placebo.

Conclusions: Data indicate early initiation of statin treatment delays the progression of carotid IMT in adolescents and young adults and exhibits for the first time that early initiation of statin therapy in children with familial hypercholesterolemia might be beneficial in the prevention of atherosclerosis in adolescence.
LDL Apheresis– EUH
Age 23, male, senior graphic arts major, presented in mid January 2012 with complaints of squeezing chest discomforts at rest and with exertion when working out with a trainer.

- **PMH:** Diagnosed with FH age 3, followed at local pediatric heart center.

- **Family History:** Father MI and CABG age 43 (obesity and hyperlipidemia); Mother hyperlipidemia, 5 siblings with FH and 1 sibling normal lipids.

- **MEDICATION:** Prior use of Vytorin and Lipitor. Currently, tolerating Crestor 40 mg qd. Admitted to inconsistency with taking medications.

- **Laboratory:** LDL 249, Total chol 303, TG 155, HDL 23, Non–HDL 280, Lp a 35, TSH 2.23.
Physical Exam:
- BP 121/75 mmHg, HR 89 bpm.
- Ht 67 in, wt 187.8 lbs, BMI 29.5.
- HEENT: Slight arcus at corneal ridge,
- I/VI systolic ejection murmur at the base.
- Extremities: Mild Xanthomas present on extensor tendons of hands.
Exercise stress test:
  - At 5 mins on Bruce Protocol, + chest discomfort and dyspnea, 1.5 mm ST–T wave depression that persisted in recovery.

Cardiac cath:
  - 90%Prox LAD; 99% 1st Dg, 100% RCA. EF 50%

CABG X 4: later January 2012
  - LIMA LAD, SVG 1st Dg, left radial artery to mid OM RIMA PDA

19 year old sister had aortic valve surgery within the same time period.
## CASE STUDY

### JL

<table>
<thead>
<tr>
<th>Date</th>
<th>Total chol</th>
<th>LDL</th>
<th>HDL</th>
<th>Non HDL</th>
<th>TG</th>
<th>Medications</th>
</tr>
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<tbody>
<tr>
<td>1/2012</td>
<td>303</td>
<td>249</td>
<td>23</td>
<td>280</td>
<td>155</td>
<td>Crestor 40 + Zetia 10 mg –14.8 lbs Folic Acid 1 mg, CRehab,</td>
</tr>
<tr>
<td>2/2012</td>
<td>161</td>
<td>116</td>
<td>25</td>
<td>136</td>
<td>101</td>
<td>+2 gm Omega 3 PUFA and diet consult</td>
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<tr>
<td>3/2012</td>
<td>183</td>
<td>129</td>
<td>33</td>
<td>150</td>
<td>107</td>
<td>Alarm reminder for meds Encouraged diet and ex.</td>
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<tr>
<td>4/2012</td>
<td>208</td>
<td>145</td>
<td>34</td>
<td>174</td>
<td>144</td>
<td>Declined meds, wanted to increase ex.</td>
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<tr>
<td>6/2012</td>
<td>177</td>
<td>122</td>
<td>31</td>
<td>146</td>
<td>119</td>
<td>+Niaspan 500 mg</td>
</tr>
<tr>
<td>7/2012</td>
<td>255</td>
<td>174</td>
<td>34</td>
<td>221</td>
<td>235</td>
<td>Finals off diet/ex.</td>
</tr>
<tr>
<td>1/2013</td>
<td>283</td>
<td>225</td>
<td>29</td>
<td>254</td>
<td>143</td>
<td>+Welchol 1250 mg bid</td>
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<td>7/2013</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Next treatment options for JL

- a. Add one of the recently FDA-approved novel therapies such as MTP inhibitor (Lomitapide) or ApoB antisense (Mipomersen)
- b. Portocaval shunting
- c. Liver transplantation
- d. Low-density lipoprotein apheresis
- e. A and D
- f. None of the above.
A. MTP inhibitor (Lomitapide) or ApoB antisense (Mipomersen) (need frequent Monitoring of LFTs in first year).
B. Portocaval shunting (high morbidity and mortality)
C. Liver transplantation– limit applicability / high morbidity
D. Low–density lipoprotein apheresis
E. A or D (consider at some point in the future when patient is more adherent to therapy.
F. None of the above.
CASE STUDY FP

- 42 year old male, presented for routine cardiac follow up in 2010.
- PMH: STEMI 2003 with PCI and stent to RCA age 31.
- Diagnosed with FH 2004. Highest total cholesterol was > 500.
- Family History:
  - Mother with elevated cholesterol, follows vegan diet. Maternal grandfather deceased age 42 with MI and maternal uncle deceased age 37 with MI.
  - Age 13 daughter and age 15 son normal cholesterol levels.
CASE STUDY FP
Objective 2012

- BP 120/80 mmHg, Pulse 68 bpm. Weight 210 lbs. BMI 31.

- HEENT: No arcus corneaeae or xanthelasmas of the lids.

- Cardiac: RRR, Normal S1, S2. No murmurs, rubs or gallops.

- Extremities: No extensor tendon xanthomas of hands or Achilles tendon. Present prior to LDL–C apheresis.
Lipid lowering meds:
- Atorvasatin 20 mg qd, Zetia 20 mg qd, Niaspan 2000 mg qhs, Omega 3 PUFA
- Undergoing LDL–C apheresis since 2005 at Emory. Takes 3 & ½ hrs every other week.
- Has not been seen in clinic in over one year.
- Was No–show for his exercise stress test.
- Admits he is not exercising as he has in past.
- Continues to struggle with weight loss.
### FP Case Study

#### Pre and Post LDL–C Apheresis

<table>
<thead>
<tr>
<th>DATE</th>
<th></th>
<th>Total chol</th>
<th>LDL</th>
<th>HDL</th>
<th>Non HDL</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/2014</td>
<td>Pre</td>
<td>238</td>
<td>188</td>
<td>35</td>
<td>203</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>79</td>
<td>44</td>
<td>31</td>
<td>48</td>
<td>22</td>
</tr>
<tr>
<td>8/2013</td>
<td>Pre</td>
<td>357</td>
<td>303</td>
<td>38</td>
<td>319</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>108</td>
<td>44</td>
<td>32</td>
<td>76</td>
<td>43</td>
</tr>
<tr>
<td>12/2012</td>
<td>Pre</td>
<td>404</td>
<td>339</td>
<td>34</td>
<td>370</td>
<td>153</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>110</td>
<td>71</td>
<td>29</td>
<td>81</td>
<td>50</td>
</tr>
</tbody>
</table>
What do you recommend for the next therapeutic recommendations for FP

A. Follow up with provider
B. Maximize medical therapy
C. Increase exercise
D. Diet consult for weight loss.
E. All of the above.
F. A, C & D.
What do you recommend for the next therapeutic recommendations for FP
A. Follow up with provider (he has not been in clinic in over a year and was no show for his EXT.
B. Increase statin
C. Increase exercise.
D. Diet consult for weight loss.
E. All of the above.
F. A, C & D.
Low-density lipoprotein apheresis

Liposorber Treatment
Indications for Use

- \( \text{LDL-C} \geq 200 \text{ mg/dL with documented CHD} \)
- \( \text{LDL-C} \geq 300 \text{ mg/dL} \)
Liposorber Treatment Frequency

- **LDL–C Level**
  - 200–299 mg/dL
    - Regimen: Q 2 weeks
  - > 300 mg/dL
    - Regimen: Q week
Example of Liposorber Sites

- Cedars–Sinai Medical Center, CA
- Transfusion Medicine Associates, CA
- Oregon Health Sciences University, OR
- Harborview Medical Center, WA
- University of Nebraska, NE
- Medcenter One, ND
- Endo & Diabetes, IL
- St. Vincent Hospital, IN
- Diabetes & Lipid of Alaska, AK
- Vanderbilt University, TN
- Parkland Hospital, TX
- Oklahoma Cardiovascular, OK
- University of Michigan, MI
- Mayo Clinic Jacksonville, FL
- University of Utah, UT
- Mary Washington Hospital, VA
- Christianacare, DE
- Preventative Cardiology Boca Raton, FL
- University of Rochester Medical Center, NY
- John Theurer Cancer Center, NJ
- Emory University, GA
- Institute for Transfusion Medicine Pittsburgh, PA
- Hartford Hospital, CT
- Cleveland Clinic, OH
- New York–Presbyterian Hospital / Rogosin Institute, NY
- Millennium Physicians Group, Naples, FL
- Virginia Nephrology Group, Fairfax, VA
- The Reading Hospital, PA
- The Heart Group, Lancaster, PA
- University of Pennsylvania, PA
The FHF national patient registry

CASCADE FH REGISTRY

www.theFHfoundation.org

“What’s measured improves”
Peter F. Drucker

Long term goal is to have
90% of FH patients
DIAGNOSED and TREATED
FH Screening

- General population
  - Family history
  - Universal cholesterol screening
- Cascade screening in affected families
  - Do you use DNA testing?
    - 80% have \( LDLR \) mutation
    - With rare exception you don’t manage patients differently based on mutation
Work To Be Done

- 1/500 have FH.
- 20% of patients with FH have been identified.
- 80% of patients with FH are undiagnosed.
Message to FH Patients

- FH is treatable (Novel therapies)
- FH is common (1/500)
- Partner with a provider that understands the disease and is aggressive with treatments.
- Early screening and treatment for family members (50% chance of children, siblings, and parents have it too).
PCNA Patient Education Materials

What You Need to Know

Familial Hypercholesterolemia (FH)

What is Familial Hypercholesterolemia?
- FH is an inherited high blood cholesterol condition. If a person has FH, their body is unable to properly remove cholesterol from the body. As a result, cholesterol builds up in the arteries, increasing the risk of heart disease.

Reasons why you may need to be tested for FH
- If your family has FH, you may need to be tested. It is important to identify individuals with FH early on to prevent development of heart disease.

What You Need to Know

If You Have FH: What You Can Do
- Know your cholesterol levels and other risk factors.
- Make lifestyle changes, such as eating a healthy diet and getting regular exercise.
- Take cholesterol-lowering medications as prescribed by your doctor.

If You Have FH: What You Can Do
- Remember that FH is not curable. However, you can lower your risk of heart disease.
- Focus on a healthy lifestyle to manage your cholesterol levels.
- Check your cholesterol levels regularly to monitor your progress.

Reasons why your nurse or doctor may want to test for FH
- If your total cholesterol is above 200 mg/dL, your LDL cholesterol is above 130 mg/dL, or your HDL cholesterol is below 40 mg/dL, you may have FH.
- If you have a family history of FH, you may be at increased risk.

available @PCNA.net
National Lipid Association

FAMILIAL HYPERCHOLESTEROLEMIA