Can We Cure Atherosclerosis?

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What if you had a guide …

• To guarantee you a longer life?
• To prevent heart disease, stroke?
• To feel stronger and healthier now and later?
• To provide a better quality of life as you invest in your relationships and life goals?

Living Better with Life’s Simple 7™
Eat Better

- Eat healthy
- Get active
- Control weight
- Don’t smoke
- Control blood pressure
- Control blood sugar
- Control cholesterol

United States - Leading Causes of Death
Prevented by Lowering Cholesterol

1. Heart disease
2. Cancer
3. Chronic lung disease
4. Stroke
5. Accidents
6. Alzheimer’s disease
7. Diabetes
8. Kidney diseases
9. Influenza, pneumonia
10. Suicide
11. Septicemia
12. Chronic liver disease and cirrhosis
13. Hypertension and related renal disease
14. Parkinson’s disease
15. Pneumonitis

New cholesterol guideline

- Treat blood cholesterol to reduce cardiovascular (CVD) risk
- Healthy lifestyle is foundation
- Drug therapy for people most likely to benefit
  - Statins are first line
  - “Nonstatins” may benefit some
Net benefit from statins

- Clear net benefit in 4 groups
  - Already have cardiovascular disease
  - Genetic high cholesterol >190 mg/dl
  - Diabetes age 40-75 years
  - >7.5% 10-year cardiovascular risk age 40-75 years

Who might need more cholesterol lowering?

- Already have cardiovascular disease
- Genetic high cholesterol >190 mg/dl
- Intolerant to statins

New cholesterol drugs in the pipeline

- PCSK-9 monoclonal antibodies most promising
- Lower LDL-cholesterol ("bad") 50-65% when added to statins
- Commonly ↓ LDL-C levels <50 mg/dl
  - Often ↓ LDL-C levels <25 mg/dl
  - Average untreated LDL-C is 130 mg/dl
LDL-receptor removes LDL-C from blood
PCSK9 targets LDL-Receptor for breakdown

PCSK9 antibodies block PCSK-9
Increase LDL-Receptor Expression

⇒ Increase LDL-C removal from blood

So far appear safe & Reduce cardiovascular events

ODYSSEY
LONG TERM
• Alirocumab 150 mg every 2 weeks
• Average 1.5 year follow-up
• 48% reduction cardiovascular events
PCSK-9 inhibitors

Future directions

• “Stabilization” therapy – Clinical CVD
• Curing atherosclerosis – Primordial prevention

Atherosclerotic Cardiovascular Disease Progression Through the Lifespan

CVD EVENTS
- MI/Unstable angina
- Ischemic stroke/TIA
- Critical leg ischemia
- Intermittent claudication
- CV death

A new paradigm #1

Plaque stabilization

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Stabilization/Regression
PCSK-9 mAB Therapy

Stable Plaque

Atherosclerosis progression
Plaque stabilization

• CVD patients = Large burden atherosclerosis
• PCSK-9 antibodies $$$$$$
• Very low LDL-C = Plaque regression/stabilization in most patients
• Treat 2-3 years with PCSK-9 antibodies
• CVD risk reduction over 5-10+ years
  – Large "Legacy Effect"

New paradigm #2:
Cure atherosclerosis

• CVD remains the leading cause of death & major cause of morbidity in US & globally
• Population risk factor levels remain high
• If all forms of major CVD were eliminated, life expectancy could rise by almost 7 years
• CVD #1 cause of healthcare expenditures
  – Total CVD costs expected to triple by 2030 as US population ages

"Reverse" Atherosclerosis
"Reset the (Vascular Aging) Clock"

CVD EVENTS
MI/Unstable angina
Ischemic stroke/TIA
Critical leg ischemia
Intermittent claudication
CV death

NORMAL ARTERY
PCSK-9 mAb Therapy

Illustration Adapted from Libby P. Circulation. 2001;104:365-372.
Conclusions

- Healthy lifestyle is the best way to prevent CVD
- For those with bad luck (genes), unable, or unwilling $\Rightarrow$ Statin therapy prevents CVD & saves lives
- New cholesterol-lowering drugs may facilitate new prevention paradigms