Macrovascular complications
Coronary heart disease, peripheral arterial disease, and cerebrovascular disease
At conclusion of the lecture the participant will be able to:

1. Identify different types of macro-vascular complications of diabetes
2. Identify modifiable and non-modifiable risk factors
3. Compare lifestyle modifications, treatments and goals for prevention of complications
4. Identify appropriate individualized treatment goals
Short term tight glucose control doesn’t really make a big difference in macrovascular CV outcomes (it is good short term for microvascular - i.e. eyes, kidneys, feet) YES!

Long term glucose control does for risk reduction in macrovascular complications
Blood Glucose, A1C, and CVD

- ACCORD, ADVANCE, VADT
  No improvement in CVD outcomes
  - with A1C less than ~6.0%-6.5%
- ADVANCE
  - less microvascular disease (nephropathy) if tightly controlled
- Lower A1C (UKPDS, DCCT)
  - less microvascular disease (nephropathy, neuropathy, retinopathy

Cardiovascular disease (CVD)
- Myocardial infarction (MI)
- Peripheral arterial disease (PAD)
- Stroke

Dyslipidemia

Hypertension

Tight Glycemic Control
- Delays the onset of macro vascular complications
MACROVASCULAR COMPLICATIONS

Inflammation

Glucose + Dyslipidemia

Other factors (dyslipidemia, insulin resistance, hypertension, smoking, CKD)

Time (years in humans)

Early lesions
Intermediate lesions
Advanced lesions

CVD

American Diabetic Association’s 74th Scientific Sessions®, June 13-17, 2014, Bierman Award: Uncomplicating the Macrovascular Complications of Diabetes given by Karin E. Bornfeldt, PhD
## SCREENING

**Maintain lipid levels as follows:**
- LDL <100 mg/dL (<70 mg/dL if established CVD)
- HDL >40 mg/dL in men and >50 mg/dL in women
- Non-HDL cholesterol <130 mg/dL (<100 mg/dL if established CVD)
- Triglycerides <150 mg/dL

**Additional preventive strategies include:**
- Aspirin therapy in diabetic patients at very high cardiovascular risk
- Screening for diabetic retinopathy every 2 years (and exams every year if retinopathy is present)
- Annual screening for neuropathy; comprehensive foot-care program
- Annual screenings for nephropathy
- Medical nutrition therapy, aerobic and strength-training exercise, weight reduction/control
- Smoking cessation

Abbreviations: CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
TRENDS IN AGE-STANDARDIZED RATES OF DIABETES-RELATED COMPLICATIONS AMONG U.S. ADULTS WITH DIABETES, 1990-2010.

Gregg, Edward; Li, Yanfeng; Wang, Jing; Burrows, Nilka; Ali, Mohammed; Rolka, Deborah; Williams, Desmond; Geiss, Linda.
DOI: 10.1056/NEJMo1310799

MI ↓ 68%
(-67.8%; 95% confidence interval [CI], -76.2 to -59.3)

Stroke ↓ 53%
(-52.7%; 95% CI, -64.4 to -40.9)
CVD and Diabetes → Major cause of:
- Morbidity
- mortality

Risk factors for CVD
- Hypertension
- dyslipidemia

Diabetes itself confers independent risk
RISK OF CVD EVENTS

Stroke
Heart Attack

Two to four times higher in persons with diabetes

65% of deaths → CVD
More recent studies suggest that this is perhaps only true for those with fairly long-standing diabetes – duration over ten years.

Heart Disease Facts

- **Heart disease**
  - 1 to 6 deaths/year
  - leading cause of death

- **MI**
  - 715,000 Americans/year
  - 525,000 1st MI
  - 190,000 repeat MI

CDC’s Division of Heart Disease and Stroke Prevention.
SWEET NEWS FOR BABY BOOMERS ON THE HORIZON?

- Middle aged adults may find cardiovascular benefits by eating chocolate
Non-Modifiable
- Age
- Race/ethnicity
- Gender
- Family history

Modifiable
- Overweight
- Abnormal lipid metabolism
- Inflammation
- Hypertension
- Smoking
- Physical inactivity
- Unhealthy diet
- Insulin resistance
Loaded Gun Theory
The risk exists-do you pull the trigger?
Age-Race Ethnicity Gender Family History!

Cardiometabolic Risks
Global diabetes and CVD Risk
Obesity

>65% of American adults are overweight or obese

Contributes to insulin resistance and cardiometabolic risk
RECOMMENDATIONS: BARIATRIC SURGERY

- Surgery considered when BMI > 35 kg/m² & type 2 diabetes, especially if diabetes or associated comorbidities are difficult to control by lifestyle & pharmacological therapy.
- Life-long lifestyle support & medical monitoring is necessary.
The beneficial effects of statins in reducing macrovascular complications in diabetics is well established.

Risk if high-density lipoprotein cholesterol < 35 mg/dL, or triglyceride level > 250 mg/dL
GOAL: LDL-C< 100 MG/DL

Moderate dose statin in patient with diabetes age 40-75 years-old
- Moderate dose
  - Atorvastatin 10-20 mg
  - Fluvastatin 80 mg
  - Lovastatin 40 mg
  - Pitavastatin 2-4 mg
  - Pravastatin 40-80 mg
  - Rosuvastatin 5-10 mg
  - Simvastatin 20-40 mg
** STATINS REDUCE CORONARY EVENTS **

**Diabetic Patients**

- Placebo: 45
- Simvastatin: 23
- Risk Reduction: 55%

**Nondiabetic Patients**

- Placebo: 27
- Simvastatin: 19
- Risk Reduction: 32%

*CHD death or nonfatal MI

COMMON ANTI-LIPID MEDICATIONS

- **Statins**
  - Potent
  - Lower total cholesterol, LDL most effectively
  - Cut CVD risk by ~30%

- **Fibrates**
  - Target triglycerides
  - Often used in combo with Statins
  - Benefit uncertain in TG’s <400?

- **Niacin**

- **Omega-3 fish oils**
Peripheral Arterial Disease

- Blood vessels narrowed or blocked by fatty deposits
- Increased risk
  - Heart attack
  - Stroke
  - Amputation
- Affects >33% diabetes over 50 y/o
Contributing to amputations

- ~60% of lower limb amputations occur in people with diabetes
- ~71,000 lower limb amputations annually
- Amputation rate is 10 times higher
PAD DIAGNOSIS

- Brachial index (ABI)
- Contrast angiography with dye
- Ultrasound test
- Magnetic Resonance Angiography (MRA)
- Computed Tomography Angiography (CTA) tests
PERIPHERAL ARTERY DISEASE: AVOIDANCE

- A1C <7%
- Treat same risk factors as heart attack and stroke
  - Treat to target blood pressure
  - Treat to target cholesterol
  - Daily aspirin
PERIPHERAL ARTERIAL DISEASE: TREATMENT

- “Bypass” surgery (usually femoral artery to popliteal artery)
- Medications
  - Aspirin daily
  - Clopidogrel
- Amputation for severe disease
  - Tissue death
  - Severe infection ("gangrene")
“You can enjoy diabetes, high cholesterol and hypertension or you can suffer from good health.”
Cardiometabolic Risks Global diabetes and CVD Risk

- Smokers are 30-40% more likely to develop type 2 diabetes
  - Hypercoagulativity
  - Inflammation
- Recommended Adult activity: 150 minutes/wk

Smoking, Physical Inactivity, Unhealthy Eating
## Glycemic Target Levels for Nonpregnant Adults

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>HbA1c</th>
<th>Fasting Plasma Glucose Concentration</th>
<th>2-Hour Postprandial Glucose Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Association of Clinical Endocrinologists (AACE)</td>
<td>≤6.5%</td>
<td>&lt;110 mg/dL</td>
<td>&lt;140 mg/dL</td>
</tr>
<tr>
<td>International Diabetes Federation</td>
<td>&lt;7.0%</td>
<td>&lt;115 mg/dL</td>
<td>&lt;160 mg/dL</td>
</tr>
<tr>
<td>American Diabetes Association</td>
<td>&lt;7.0%</td>
<td>80–130 mg/dL</td>
<td>&lt;180 mg/dL</td>
</tr>
</tbody>
</table>
Type 2 Diabetes: UKPDS

UKPDS: 1% A1C Decrease and Reduced Risk of Complications

Lower-extremity amputation or fatal peripheral vascular disease†

Microvascular disease†

Cataract extraction†

Heart failure*

Myocardial infarction†

Stroke*

Cardiovascular complications

*P<.05; †P<.0001.
UKPDS=United Kingdom Prospective Diabetes Study.
Goals for people with diabetes and hypertension

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>&lt;140 mmHg</td>
</tr>
<tr>
<td>Diastolic</td>
<td>&lt;90 mmHg</td>
</tr>
</tbody>
</table>

- Lower targets (<130 mmHg, <80 mmHg) may be appropriate for certain individuals (younger patients) if it can be achieved without undue treatment burden.
Screening and diagnosis

- Blood pressure measured at every routine visit
- Elevated blood pressure
  - Confirm on a separate day

Goal is > 140/90

ADA. 8. Cardiovascular Disease and Risk Management. Diabetes Care 2015;38(suppl 1):S49
Recommendations: Hypertension/Blood Pressure Control

Treatment

- Patients with blood pressure >140/80 mmHg should be advised on lifestyle changes to reduce blood pressure B
- Patients with confirmed blood pressure higher than 140/90 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely subsequent titration of pharmacological therapy to achieve blood pressure goals A

ADA. 8. Cardiovascular Disease and Risk Management. Diabetes Care 2015;38(suppl 1):S49
Recommendations: Hypertension/Blood Pressure Control

Treatment (2)
- Lifestyle therapy for elevated blood pressure
  - Weight loss if overweight
  - DASH-style dietary pattern including reducing sodium, increasing potassium intake
  - Moderation of alcohol intake
  - Increased physical activity
Pharmacological therapy for patients with diabetes and hypertension comprise a regimen that includes:
- either an ACE inhibitor or angiotensin II receptor blocker B;
- if one class is not tolerated, substitute the other C

Multiple drug therapy (two or more agents at maximal doses) generally required to achieve blood pressure targets B

later-line alternatives-
- Beta-blockers—remember BB mask hypoglycemic responses....CAUTION
CARDIOVASCULAR DISEASE

Risk:
- Stroke 2 to 4 times higher
- Heart Disease 2 to 4 times higher

~75% of diabetes patients have high blood pressure (hypertension)

~75% of people with diabetes have a dyslipidemia (cholesterol disease)
CARDIOVASCULAR DISEASE

- Heart disease and stroke ~65% of diabetes deaths
- Routine screening of asymptomatic not recommended
- Treat risk factors (lipids, BP, smoking, etc)

Diabetes Care January 2011; 34 (Supplement 1)
COMMON ANTI-HYPERTENSIVES

- **ACEI**: Lisinopril (Prinivil), Ramipril (Altace), others
- **ARB**: Valsartan (Diovan), Losartan (Cozaar), others
- **Beta-Blockers**: atenolol, metoprolol (Toprol), carvedilol (Coreg-mixed function), others
COMMON ANTI-HYPERTENSIVES

- Calcium Channel Blockers- Amlodipine (Norvasc), Verapamil (Covera, Verelan), Diltiazem (Cardizem), others
- Diuretics- Hydrochlorothiazide, others
**HYPERTENSION MEDICATIONS**

- ACEI and ARB medications are initial drugs of choice for HTN in DM
- Benefit of lowering blood pressure, reducing heart attack, stroke, and kidney disease
- ACE and ARB’s
  - act on kidney
  - kidney protective
Aspirin Therapy is likely indicated for most Diabetes Patients over the age of 50 or 10 year CVD risk >10% (consider risk of GI bleed, etc.)

- 75-325mg daily depending on risk factors and co-morbidities
- CV risk reduction 15-50%
- Smoking cessation
- Meal planning

Diabetes Care January 2011; 34 (Supplement 1)
ULTIMATE GOAL-HEALTH!