Diabetes Mellitus and the individual with I/DD part 2

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### Complications of Diabetes


<table>
<thead>
<tr>
<th>Complications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>Leading cause of diabetes related deaths</td>
</tr>
<tr>
<td>Stroke</td>
<td>Risk is increased by two to four times</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>97% have lipid abnormalities contributing to higher rates of cardiovascular disease</td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>Incidence is 73%</td>
</tr>
<tr>
<td>Blindness</td>
<td>Retinopathy is the leading cause of new blindness in adults aged 20-74 years</td>
</tr>
<tr>
<td>Kidney Disease</td>
<td>Nephropathy is the leading cause of end stage renal disease (44% of new cases)</td>
</tr>
<tr>
<td>Nervous System Disease</td>
<td>60% to 70% have mild to severe form of damage</td>
</tr>
<tr>
<td>Amputations and Peripheral Neuropathy</td>
<td>Leading nontraumatic cause of lower limb amputations and foot ulcerations</td>
</tr>
<tr>
<td>Acute-Life Threatening Events</td>
<td>Diabetic ketoacidosis, hyperosmolar nonketonic coma, more susceptible to infections (e.g. pneumonia and influenza)</td>
</tr>
</tbody>
</table>
• Cardiovascular Disease
  – HTN
  – Dyslipidemia
• Kidney disease
• Neuropathy/amputation
• Eye problems
• Peridonal issues
• Immunizations
Cardiovascular Disease Risk Factors

- Hypertension*
- Cigarette smoking
- Obesity* (BMI ≥30 kg/m2)
- Physical inactivity*
- Dyslipidemia*
- Diabetes mellitus*
- Microalbuminuria or estimated GFR <60 mL/min
- Age (older than 55 for men, 65 for women)
- Family history of premature CVD (men under age 55 or women under age 65)

*Components of metabolic syndrome

Cardiovascular Disease and Diabetes

- 52% of annual diabetes costs
- 65% of people with diabetes die from heart disease or stroke
- Risk of stroke increases 2 to 4 times
- Same risk for heart attack as people without diabetes and a history of heart attack
- Smoking doubles the risk
- 97% of those with diabetes have lipid abnormalities
- 70% of those with diabetes have high blood pressure
Prevention of Cardiovascular Disease

- Stop smoking
- Reduce blood pressure
- Cholesterol management
- Glucose control
- Weight management
- Antiplatelet agents
- Aspirin therapy
Antiplatelet Therapy and CVD

- Aspirin 81–162 mg/day
- Primary prevention for men/women with diabetes:
  - Age over 40 years
  - Additional risk factors for cardiovascular disease
    - Family history of cardiovascular disease (CVD)
    - Hypertension
    - Smoking
    - Dyslipidemia
    - Albuminuric
- Secondary prevention for men/women with diabetes with:
  - History of myocardial infarction
  - Vascular bypass procedure
  - Stroke or transient ischemic attack
  - Peripheral vascular disease
  - Claudication
  - Angina
Aspirin Therapy

Contraindications
- Aspirin allergy or intolerance
- Recent gastrointestinal bleeding or other hemorrhagic states

Precautions
- Bleeding tendency
- On anticoagulant therapy
- Clinically active hepatic disease
- Age under 21 years
  - Increased risk of Reye’s syndrome

Conditions Associated with Hypertension

- Obese
- Decreased arterial compliance
- Endothelial dysfunction
- Abnormal glucose metabolism
- Neurohormonal dysfunction
- Renal function changes
- Abnormal lipid metabolism
- Accelerated atherogenesis
- LVH/dysfunction
- Abnormal insulin metabolism
- Blood-clotting mechanism changes
# Lifestyle Modifications to Lower Blood Pressure

<table>
<thead>
<tr>
<th>Modification*</th>
<th>Recommendation</th>
<th>Approximate Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI 18.5-24.9 kg/m$^2$)</td>
<td>5-20 mmHg/10 kg weight loss</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Regular aerobic physical activity such as brisk walking (at least 30 min/day, most days of the week)</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

*For overall cardiovascular risk reduction, stop smoking
**Nutritional Modifications to Lower Blood Pressure**

<table>
<thead>
<tr>
<th>Modification*</th>
<th>Recommendation</th>
<th>Approximate Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adopt dietary approaches to stop hypertension</td>
<td>Diet consisting of vegetables, lowfat dairy products, fruits, reduced saturated and total fat</td>
<td>8-14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to 2.4 g sodium per day (6 g sodium chloride)</td>
<td>2-8 mmHg</td>
</tr>
</tbody>
</table>

*For overall cardiovascular risk reduction, stop smoking
Pharmacologic Management of Hypertension

- Antihypertensive Drugs
  - Angiotensin-converting enzyme inhibitors (ACEIs)
  - Angiotensin receptor blockers (ARBs)
  - Alpha-blockers
  - Beta-blockers
  - Diuretics
  - Calcium channel blockers
  - Combination therapies
ACE Inhibitors

- Slows progression of
  - Nephropathy
  - Cardiovascular events
  - Mortality
- Hypertensive patients with diabetes +/- microalbuminuria
- Blood pressure lowering effects seen by 4-6 weeks
- Evaluate protein lowering effects after 3 months
- Decrease mortality and morbidity in patients
  - With congestive heart failure
  - Post-myocardial infarction
- Reductions in cardiovascular end points
- Monitor serum potassium for development of hypoperkalemia; watch for drug interactions
ARBs

- Decrease proteinuria
- Prevent progression of nephropathy when microalbuminuria or more advanced stages of nephropathy present in patients with type 2 diabetes
- Cardiovascular data limited
- Not associated with a cough, like ACE inhibitors
- Combination of ACEIs and ARBs reduce blood pressure and urinary albumin levels more than either medication alone
- Monitor serum potassium for development of hyperkalemia; watch for drug interactions

ACEs or ARBs?

**ACE Inhibitors**
- drugs of choice over ARBs for prevention and treatment of proteinuria in patients with type 1 diabetes (Level 1 evidence)\(^1\)\(^-\)\(^3\)
- drugs of choice for acute MI, congestive heart failure, hypertension (Level 1 evidence)

**ARBs**
- drugs of choice for first-line renoprotective therapy in hypertensive type 2 diabetic patients with microalbuminuria (Level 1 evidence)\(^4\)\(^-\)\(^6\)
- recommended in patients who are candidates for renin-angiotensin blockade but demonstrate intolerance to ACEIs

References
• Atenolol
  – Reduces proteinuria and glomerular filtration rate
  – Equally effective as ACEI in decreasing risk of diabetes-related end points and microvascular events
• Demonstrated efficacy following myocardial infarction (with acebutalol, atenolol, metoprolol, propranolol, timolol)
• Reductions in mortality of ~25%
• May prolong or blunt hypoglycemia
  – Avoid use in insulin-using patients with history of severe hypoglycemia
  – In other patients with diabetes, especially those with recent myocardial infarction, benefits appear to outweigh potential risks related to hypoglycemia

Thiazide Diuretics

- May be considered first-line therapy in patients without additional cardiovascular risk factors or proteinuria
- Effect on the progression of diabetic nephropathy compared with other drugs is unknown
- Demonstrated efficacy in reducing the risk of stroke and heart failure in subjects with mild-to-severe hypertension
- In elderly patients with systolic hypertension:
  - A low-dose thiazide diuretic reduces cardiovascular event rate by 34% when compared with placebo
  - Absolute risk reduction twice as great for subjects with diabetes vs. subjects without diabetes
- Renal function issues (not useful when GFR<20ml/min)

Second Line Antihypertensive Agents

- If target blood pressure goal not obtained with initial doses of 1\textsuperscript{st} line drugs
  - Increase dose
  - Add second drug from different group
- Less effective in preventing complications
- Other classes of drugs without long-term data on efficacy in improving outcomes can be used when:
  - There is intolerance to other classes
  - There are specific indications for use
  - Additional drugs are required to reach target blood pressure

**NDCCBs**

- Non-dihydropyridine calcium-channel blockers (NDCCBs) (e.g., diltiazem, verapamil) used when:
  - ACEIs, ARBs, or beta-blockers not tolerated or contraindicated
  - 2nd or 3rd drug is required
- Less effective in preventing complications
  - Myocardial infarction
  - Heart failure
  - Nephropathy

effects of antihypertensive agents in hypertensive diabetic patients


<table>
<thead>
<tr>
<th>Class</th>
<th>Effects on progression of renal disease</th>
<th>Effects on coronary event rates</th>
<th>Effects on stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Beneficial</td>
<td>Beneficial</td>
<td>Beneficial</td>
</tr>
<tr>
<td>ARBs</td>
<td>Beneficial</td>
<td>Unknown</td>
<td>Unknown</td>
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<tr>
<td>Beta-blockers</td>
<td>Beneficial</td>
<td>Beneficial</td>
<td>Beneficial</td>
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<tr>
<td>Thiazide diuretics</td>
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<td>Beneficial</td>
<td>Beneficial</td>
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<tr>
<td><strong>Second-line agents</strong></td>
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<td></td>
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<tr>
<td>NDCCBs</td>
<td>Beneficial</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>DCCBs</td>
<td>Controversial</td>
<td>Controversial</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Alpha-blockers</td>
<td>Unknown</td>
<td>Controversial</td>
<td>Unknown</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Centrally acting adrenergic agents</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Algorithm for Treatment of Hypertension

Not at Goal Blood Pressure (<140/90 mmHg) (<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 Hypertension (SBP 140–159 or DBP 90–99 mmHg) Thiazide-type diuretics for most. May consider ACE, ARB, BB, CCB, or combination.

Stage 2 Hypertension (SBP ≥160 or DBP ≥100 mmHg) 2-drug combination for most (usually thiazide-type diuretic and ACE, or ARB, or BB, or CCB)

With Compelling Indications

Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE, ARB, BB, CCB) as needed.

Lifestyle Modifications

Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.
### Goals For Hypertensive Patients with Diabetes


<table>
<thead>
<tr>
<th>Goal (mmHg)</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral therapy alone (maximum of 3 months) then add pharmacologic treatment</td>
<td>130-139</td>
<td>80-89</td>
</tr>
<tr>
<td>Behavioral therapy + pharmacologic treatment</td>
<td>≥ 140</td>
<td>≥ 90</td>
</tr>
</tbody>
</table>
• 70-97% of individuals with diabetes have dyslipidemia
• “Diabetic dyslipidemia” is a triad of abnormalities
  – Increase in triglycerides
  – Decrease in HDL cholesterol
  – Small, more dense LDL particles
• Carries a cardiovascular risk equivalent to an LDL concentration 150-220 mg/dL

Treatment of Dyslipidemia

- Lifestyle modification
  - Weight loss/BMI reduction
  - Increase physical activity
  - Smoking cessation
  - Reduce intake of saturated fat/cholesterol
  - Improved glycemic control
- Pharmacological therapy
  - Statins
  - Fibrates (e.g. gemfibrozil-Loid®, fenofibrate-Tricor®)
  - Niacin
- Combination therapy
LIPID TREATMENT ALGORITHM FOR TYPE 1 AND TYPE 2 DIABETES MELLITUS IN ADULTS

Consider statin therapy in all diabetics > age 40 with total cholesterol > 135 mg/dL to achieve an LDL-C reduction of ~ 30% (and LDL-C < 100 mg/dL) irrespective of initial LDL-C levels (Heart Protection Study. Lancet 361:2005-16; 2003). Use with caution in patients with diabetes. Need to closely follow self-monitoring blood glucose (SMBG) as may worsen glycemic control. Recheck FLP and ALT 2–3 months after drug therapy initiation/titration. If patient develops myalgias, hold lipid-lowering drug and check CPK as soon as possible. If TG > 200 mg/dL.

1. Determine last lipid profile (FLP) yearly.

Abnormal FLP: TLC; control diabetes; evaluate and treat secondary causes of dyslipidemia: alcohol, estrogens, anabolic steroids, corticosteroids, hypothyroidism, hepatic disease, nephritic syndrome, chronic renal failure. If LDL-C elevated = primary treatment target, unless TG > 400 mg/dL, which then becomes the primary treatment target.

- Elevated LDL-C 7160 mg/dL
  - Start Statin, titrate to goal LDL-C
  - Reinforce TLC
  - If LDL-C remains > 100 mg/dL, Add Bile acid resin-binder or Ezetimibe or Orlistat
  - Refer to Lipid Specialist

- Elevated TG 7150 mg/dL
  - TLC
  - If TG remains > 200 mg/dL, Add Niacin or Statin or Orlistat

- Isolated low HDL-C < 40 mg/dL (LDL-C < 100 mg/dL & TLC)
  - Consider Fibrate, Niacin or Statin

- Elevated LDL-C 7100 mg/dL
  - TLC & Calculate Non-HDL-C
  - LDL-C > 100 mg/dL, Start Fibrate or Niacin

- Elevated TG 7100 mg/dL
  - TLC & Start Fibrate, titrate to goal TG

- LDL-C < 100 mg/dL, Start Fibrate or Niacin

- LDL-C < 100 mg/dL, follow elevated LDL-C algorithm

- TLC & Calculate Non-HDL-C
  - LDL-C > 100 mg/dL, Start Fibrate or Niacin

- TLC
  - LDL-C > 100 mg/dL, Start Fibrate or Niacin

Legend
TLC = Therapeutic Lifestyle Changes
Statin = HMG Co-A Reductase Inhibitor
TG = Triglycerides
Non-HDL-C = Total Cholesterol minus HDL-C
FLP Goals:
- LDL-C < 100 mg/dL
- HDL-C > 40 mg/dL (men)
- HDL-C > 50 mg/dL (women)
- TG < 150 mg/dL

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Statin = HMG Co-A Reductase Inhibitor
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Goals of Treatment (ADA)

- Lower LDL cholesterol to < 100 mg/dL
- Lower triglycerides to < 150 mg/dL
- Raise HDL cholesterol to:
  - > 40 mg/dL in men
  - > 50 mg/dL in women
# CHD Risk Reduction and Lipid Lowering Agents

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diabetes</td>
<td>25147</td>
<td>27%*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2443</td>
<td>31%*</td>
</tr>
<tr>
<td>Younger age</td>
<td>19119</td>
<td>33%*</td>
</tr>
<tr>
<td>Older age</td>
<td>16549</td>
<td>30%*</td>
</tr>
</tbody>
</table>
• Secondary prevention of cardiovascular mortality and morbidity
  – For all patients with known coronary artery disease and type 2 diabetes
• Primary prevention against macrovascular complications
  – In patients with type 2 diabetes and other cardiovascular risk factors
• Patients with Type 2 diabetes
  – Moderate doses of a statin
  – Routine monitoring of liver function tests of muscle enzymes not recommended except for those in specific circumstances

Kidney Disease and Diabetes

- Diabetes most common single cause of end-stage renal disease (ESRD) in the US and Europe
- Diabetic nephropathy accounts for 40% of all new cases in the US
- 20% of patients with diabetes have microalbuminuria
  - 20-40% of these develop nephropathy
  - 20% progress to ESRD
- Albuminuria is a marker for increased cardiovascular morbidity
- Nearly 142,963 patients with diabetes required dialysis/kidney transplant in 2001
- 1997 cost for treatment of patients with ESRD was more than $15.6 billion
Signs of Diabetic Nephropathy

• Albumin in urine (microalbuminuria)

<table>
<thead>
<tr>
<th>Category</th>
<th>Spot collection (μg/mg creatinine)</th>
<th>24-h collection (mg/24 h)</th>
<th>Timed collection (μg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 30</td>
<td>&lt; 30</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-299</td>
<td>30-299</td>
<td>20-199</td>
</tr>
<tr>
<td>Clinical albuminuria</td>
<td>≥ 300</td>
<td>≥ 300</td>
<td>≥ 200</td>
</tr>
</tbody>
</table>

• Reduction in glomerular filtration rate (GFR)
  – Can be estimated by determining creatinine clearance rate except when renal function is <5-10% of normal

Calculating Creatinine Clearance

- **Cockcroft-Gault equation**
  - In men:
    \[
    CrCl (\text{mL/min}) = \frac{(140 - \text{age}) \times \text{weight in kg}}{(72 \times \text{serum creatinine mg/dL})}
    \]
  - Multiply by 0.85 for women
  - Use adjusted body weight if > 30% above IBW
  - Use serum creatinine of 1 if cachetic and actual serum creatinine is < 0.8 mg/dL

Treatment of Diabetic Nephropathy

- Glycemic control
- Hypertension management
- Cholesterol management
- Lifestyle modifications
  - Weight loss
  - Diet modification (reduce salt, alcohol, protein, phosphate)
  - Exercise
Diabetic Neuropathy

- Refers to a group of nerve disorders caused by diabetes
- Affects 50-60% of patients with diabetes
- Foot ulcers occur in 15%
- >60% of nontraumatic limb amputations
- 67,000 amputations/year (1993-1995)
- 82,000 amputations/year (2000-2001)
- Cost of a diabetes-related amputation: $27,000
Types of Diabetic Neuropathy

- **Peripheral neuropathy** - pain or loss of feeling in the toes, feet, legs, hands, and arms
- **Autonomic neuropathy** - changes in digestion, bowel and bladder function, sexual function, and perspiration. It can also affect the nerves that serve the heart and control blood pressure
- **Proximal neuropathy** - pain in the thighs, hips, or buttocks and leads to weakness in the legs
- **Focal neuropathy** - sudden weakness of one nerve, or a group of nerves, causing muscle weakness or pain
Signs and Symptoms of Diabetic Neuropathy

• Numbness, tingling, or pain in the toes, feet, legs, hands, arms, and fingers
• Wasting of the muscles of the hands or feet
• Indigestion, nausea or vomiting
• Diarrhea or constipation
• Dizziness or faintness due to a drop in postural blood pressure
• Impotence or vaginal dryness
• Incontinence
• Weakness
Treatment of Diabetic Neuropathy

- **GLYCEMIC CONTROL!**
- Tricyclic antidepressants (TCAs)
  - desipramine, amitriptyline
- Selective serotonin-reuptake inhibitors (SSRIs)
  - paroxetine, citalopram
- Anticonvulsants
  - gabapentin, carbamazepine, phenytoin
- Opioid analgesics and nonsteroidal antiinflammatory drugs (NSAIDs)
  - oxycodone, tramadol, ibuprofen
Factors Contributing to Foot Amputation

- Peripheral neuropathy
- History of ulcers
- Peripheral vascular disease
- History of amputation
- Bony deformity
- Increased pressure
- Severe nail pathology
- Altered biomechanics

• **Annual foot exam with assessment of:**
  - Protective sensation
  - Neurological status
  - Foot structure
  - Biomechanics
  - Vascular status
  - Skin integrity
  - Pedal pulses

• **Patient education**
  - Wear well-fitting shoes
  - Good glycemic control
  - Smoking cessation
  - Implications of sensory loss
  - Importance of daily foot exam, monitoring and proper care
  - Report nonhealing injuries

Eye problems associated with diabetes include retinopathy, glaucoma, and cataracts.

Retinopathy affects 80%–97% of patients with diabetes of ≥15 years’ duration.

Diabetes is the leading cause of new cases of blindness* in adults aged 20-74 years.

Diabetic retinopathy accounts for the majority of cases:
- Causes 12,000 to 24,000 new cases each year.
- Minimum cost of blindness for working-age adult is estimated at $12,769 per year.

*Blindness is defined as visual acuity ≤ 20/200.

Diabetic Retinopathy

- Prevent or delay progression
  - Glycemic control
  - Blood pressure control
- Treatment - laser photocoagulation
- Ophthalmological evaluation
  - Initial: Dilated and comprehensive eye exam
    - Type I diabetes: Within 3-5 years of diabetes onset
    - Type II diabetes: Shortly after diagnosis
  - Subsequent: Repeated annually
  - More often for diabetic women who are pregnant (not gestational diabetes)
Periodontal Disease and Diabetes

- 90% of adults have gum disease in their lifetime
- Diabetes and poor blood glucose control increases the risk of gum disease
- About 1/3 of people with diabetes have severe periodontal diseases with loss of attachment of the gums to the teeth measuring 5 millimeters or more
- Up to 44% of the elderly have gingivitis
- Periodontal disease is linked to cardiovascular disease
- Smoking increases the risk of periodontal disease in patients with diabetes almost 10 times
Immunizations and Diabetes

- Patients with diabetes have abnormalities in immune function
- At increased risk of morbidity and mortality from infection
- Effective immunizations strategies
  - Are multidimensional and target the patient, provider, support staff/family/friends, and the health system
- Goal to immunize all patients with diabetes against influenza and pneumococcal disease
Influenza Vaccine and Diabetes

- Recommended yearly for all adults with diabetes
- Specific populations requiring systematic intervention strategies for influenza prevention (e.g., standing orders)
  - >64 years of age
  - Residents of nursing homes or other facilities
  - Require regular medical follow-up or hospitalization
  - Have additional secondary chronic disorders of the cardiopulmonary system
- Healthy People 2010 aim to vaccinate
  - 90% of diabetic adults >65 years by 2010
  - 60% of diabetic adults <65 by 2010
Pneumococcal Vaccine and Diabetes

- One time revaccination for people
  - >64 years of age and previously immunized when they were <65 years of age and if vaccination was more than 5 years ago
  - Age 2-64 years who have chronic illness (including diabetes) or other risk factors
- Other indications for repeat vaccination
  - Nephrotic syndrome
  - Chronic renal disease
  - Other immunocompromised states, (e.g., post-organ transplantation or receiving corticosteroids)
- People with diabetes at increased risk
CEU Questions?

For information: Contact Jose Polanco at Education@tarrytownexpocare.com