DISCLOSURES

No Conflicts of Interest
OBJECTIVES

Diabetes

• a. Identify the role of new oral agents in the management of diabetes mellitus.

• b. Consider the current function and use of insulin pumps including indications and safe usage.

• c. Discuss the signs and symptoms of the various aspects of diabetic neuropathy
COMMITMENTS TO CHANGE

✓ I WILL COMMIT TO HAVE A PERSONALIZED APPROACH TO THE TREATMENT OF HYPERGLYCEMIA IN TYPE 2 DIABETES, BY UNDERSTANDING THE MECHANISM OF ACTION, PROS AND CONS OF ORAL AGENTS

✓ I WILL COMMIT TO COUNSEL MY PATIENTS INTERESTED IN INSULIN PUMP THERAPY ON THE CHALLENGES, AND ADVANTAGES OF THIS THERAPY OPTION. I WILL SELECT IDEAL CANDIDATES BASED ON THEIR MOTIVATION AND ABILITY TO CARRY OUT THE TASKS REQUIRED TO USE THIS COMPLEX AND TIME CONSUMING THERAPY SAFELY AND EFFECTIVELY

✓ I WILL COMMIT TO INCORPORATE A 5-MINUTE ROUTINE FOOT EXAMINATION AND RAPID RISK STRATIFICATION INTO MY PRIMARY CARE OF PATIENTS WITH DIABETES
IDENTIFY THE ROLE OF NEW ORAL AGENTS IN THE MANAGEMENT OF DIABETES MELLITUS
CLASSES OF GLUCOSE LOWERING AGENTS FOR TREATING TYPE 2 DIABETES
MAIN PATHOPHYSIOLOGICAL DEFECTS IN T2DM

HYPERGLYCEMIA

- Decreased incretin effect
- Decreased pancreatic insulin secretion
- Increased pancreatic glucagon secretion
- Increased hepatic glucose production
- Decreased peripheral glucose uptake
- Increased glucose absorption

Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011
MAIN PATHOPHYSIOLOGICAL DEFECTS IN T2DM

- Hyperglycemia
  - Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011

**MAIN PATHOPHYSIOLOGICAL DEFECTS IN T2DM**

- **Gut carbohydrate delivery & absorption**
  - **Incretin effect**
  - **Pancreatic insulin secretion**
  - **Pancreatic glucagon secretion**

**PERGLYCEMIA**

- **Energy balance**

  - **Hepatic glucose production**
  - **Glucose absorption**
  - **Peripheral glucose uptake**

**Pharmacological Agents**

- **Sulfonlureas**
- **Meglitinides**
- **GLP-1 agonists**
- **DPP4 inh.**
- **GLP-1 agonists**
- **Amylin**
- **Metformin**
- **TZD's**
- **GLP-1 agonists**
- **Amylin**
- **Bromocriptine**
- **SGLT-2 Inhibitors**

**Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011**
<table>
<thead>
<tr>
<th>Initial drug monotherapy</th>
<th>Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (↓ HbA1c)</td>
<td>high</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>low risk</td>
</tr>
<tr>
<td>Weight</td>
<td>neutral/loss</td>
</tr>
<tr>
<td>Side effects</td>
<td>GI/lactic acidosis</td>
</tr>
<tr>
<td>Costs</td>
<td>low</td>
</tr>
</tbody>
</table>
# Diabetes Management Options

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Dual Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong>*</td>
<td>high</td>
</tr>
<tr>
<td><strong>Hypo risk</strong></td>
<td>low</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>neutral / loss</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>GI / lactic acidosis</td>
</tr>
<tr>
<td><strong>Costs</strong>*</td>
<td>low</td>
</tr>
</tbody>
</table>

If A1C target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

<table>
<thead>
<tr>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>Thiazolidinedione</td>
<td>DPP-4 inhibitor</td>
<td>SGLT2 inhibitor</td>
<td>GLP-1 receptor agonist</td>
</tr>
<tr>
<td>high</td>
<td>high</td>
<td>intermediate</td>
<td>intermediate</td>
<td>high</td>
</tr>
<tr>
<td>moderate risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
</tr>
<tr>
<td>gain</td>
<td>gain</td>
<td>neutral</td>
<td>low</td>
<td>low</td>
</tr>
<tr>
<td>hypoglycemia</td>
<td>edema, HF, fxS</td>
<td>rare</td>
<td>GU, dehydration</td>
<td>GI</td>
</tr>
<tr>
<td>low</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>high</td>
</tr>
</tbody>
</table>
SGLT-2 INHIBITORS

Canagliflozin *(invokana)*
Dapagliflozin *(Farxiga)*
Empagliflozin *(Jardiance)*

Glucosuria
Effect of Inhibiting SGLT2 on Renal Threshold for Glucose Excretion

Non-diabetes: ~ 180 mg/dl

Type 2 diabetes: ~ 250 mg/dl

SGLT2 inhibitor in type 2 diabetes: ~ 70-90 mg/dl
Glucose Reduction

SGLT2 Inhibitors Added to Metformin (Absolute Changes from Baseline; Not Head-to-Head Trials)

<table>
<thead>
<tr>
<th></th>
<th>Canaglifozin</th>
<th>Dapaglifozin</th>
<th>Empaglifozin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline A1C (%)</td>
<td>7.8</td>
<td>7.9</td>
<td>7.9</td>
</tr>
<tr>
<td>ΔA1C (%)</td>
<td>-0.93</td>
<td>-0.52</td>
<td>-0.77</td>
</tr>
</tbody>
</table>

# SGLT-2 INHIBITORS

<table>
<thead>
<tr>
<th>Once daily dosing</th>
<th>Polyuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ A1c ~0.5-0.9%</td>
<td>Dehydration</td>
</tr>
<tr>
<td>↓ FPG, PPG</td>
<td>Hypotension</td>
</tr>
<tr>
<td>↓ Weigh</td>
<td>UTI’s</td>
</tr>
<tr>
<td>combination with other OA and/or insulin</td>
<td>Genital infections</td>
</tr>
<tr>
<td>Minimal GI s/e</td>
<td>↑ LDL and non-HDL</td>
</tr>
<tr>
<td>↓ BP</td>
<td>Require near normal GFR</td>
</tr>
<tr>
<td>Potential ↓ uric acid</td>
<td>Diabetic ketoacidosis</td>
</tr>
<tr>
<td></td>
<td>Cost/Insurance</td>
</tr>
</tbody>
</table>
DKA develops when insulin levels are too low or during prolonged fasting. DKA most commonly occurs in patients with T1DM, usually accompanied by hyperglycemia. The FAERS cases were somewhat atypical (most had T2DM and their glucose levels, when reported only slightly increased compared to typical cases of DKA)
SGLT2 Inhibitors: the unknowns with any new medication

CV Safety

Blood pressure
TGC, ↑LDL AND NON-HDL-C

SGLT2 Inhibitors

Bone health

Canagliflozin
(invokana)

Dapagliflozin
(Farxiga)

Empagliflozin
(Jardiance)

Chronic glycosuria
Bladder Ca surveillance (dapa)

Malignancy
<table>
<thead>
<tr>
<th>Ideal candidates</th>
<th>Do not consider:</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2DM and HTN</td>
<td>H/o UTI’s or genital infections</td>
</tr>
<tr>
<td>Overweight or obese</td>
<td>Immunocompromised patients: post-transplant, or on immunosuppressant agents</td>
</tr>
<tr>
<td>Patients with frequent hypoglycemia and/or weight gain on other agents (sulfonylureas)</td>
<td>eGFR &lt;45 for Cana &lt;60 for Dapa)</td>
</tr>
<tr>
<td>Patients with s/e to other drugs (GI s/e, h/o pancreatitis)</td>
<td>Frailty, elderly prone to falls and/or dehydration</td>
</tr>
</tbody>
</table>
Natural History of Type 2 Diabetes

BP = blood pressure.
Consider initial dual combination therapy if A1C target not achieved.

Begin with these options if metformin contraindicated.

- **Bromocriptine**
  - Intermediate risk
  - Neutral GI
  - Low

- **Colesevelam**
  - Intermediate risk
  - Neutral GI
  - Low

Triple therapy:

- **Bromocriptine**
- **Colesevelam**

Combination injectable therapy:

- **Bromocriptine**
- **Insulin (basal)**

---

Diabetes Care 2015;38:S41-S48
BROMOCRIPTINE

Energy balance

- Early morning hypothalamic dopamine levels in diabetes
- Bromocriptine
- Hypothalamic SNS activity
- HGP
- Lipolysis/FFA
- Lipogenesis/TG
- Glucose intolerance
- Insulin resistance
- Dyslipidemia
- Cardiovascular disease

- Early Morning
- Morning hypothalamic dopamine levels
- SNS activity
- HGP
- Lipolysis/FFA
- Lipogenesis/TG
- Glucose tolerance
- Insulin sensitivity
- Plasma FFA/TG
- Vascular pathology
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study sample</th>
<th>Study design</th>
<th>Study treatment, n</th>
<th>Baseline A1c</th>
<th>ΔA1c%</th>
<th>ΔFPG mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>T2DM; overweight/obese; drug naïve; A1c 7.5-11.0%</td>
<td>Randomized DB, 24 weeks</td>
<td>BQR, 1.6-4.8 mg, n = 80 PBO, n = 79</td>
<td>8.95</td>
<td>8.75</td>
<td>−0.56&lt;sup&gt;a&lt;/sup&gt; −31 vs. PBO&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Monotherapy Trials</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>T2DM; overweight/obese; current treatment with SU; A1c 7.8-12.5%</td>
<td>Randomized DB, 24 weeks</td>
<td>BQR, 1.6-4.8 mg, n = 244 PBO, n = 250</td>
<td>9.3</td>
<td>9.4</td>
<td>−0.55&lt;sup&gt;d&lt;/sup&gt; −23 vs. PBO&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Add-on Trials</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>T2DM; diet alone (12%), or ≤2 OHA, or insulin + ≤1 OHA; A1c 7.5-10.0%</td>
<td>Randomized DB, 52 weeks</td>
<td>BQR, 1.6-4.8 mg, n = 341 PBO, n = 174</td>
<td>8.3</td>
<td>8.3</td>
<td>−0.69% (&lt;0.97% &lt;sup&gt;c,e&lt;/sup&gt;, −0.41%) ---</td>
</tr>
</tbody>
</table>

<sup>a</sup> Data from the study mentioned in the reference.
BROMOCRIPTINE

Once daily dosing
- ↓ A1c ~0.69%
- Minimal hypoglycemia
- Weight neutral
- Favorable CV profile

- Nausea* (32.2%)
- Dizziness (~15%)
- Fatigue (~14%)
- Headache (11.4%)

- Small clinical trial database

* Similar in short-term placebo controlled trials
BILE ACID SEQUESTRANTS (BAS): COLESEVELAM

The exact mechanism regulating the glycemic effect of a BAS remains not fully understood

- ↓ endogenous glucose production
- May affect secretion of incretin hormones: GLP-1 and GIP
SUMMARY OF THE CLINICAL EFFECTS OF COLESEVELAM IN PATIENTS WITH TYPE 2 DIABETES

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Duration (weeks)</th>
<th>Background therapy</th>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Treatment difference: HbA1c (%)</th>
<th>Treatment difference: LDL cholesterol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bays et al. (17)</td>
<td>316</td>
<td>26</td>
<td>Metformin-based therapy</td>
<td>Colesevelam 3.75 g/day (n = 159); Placebo (n = 157)</td>
<td>8.1</td>
<td>-0.54†</td>
<td>-15.9†</td>
</tr>
<tr>
<td>Fonseca et al. (18)</td>
<td>461</td>
<td>26</td>
<td>Sulfonylurea-based therapy</td>
<td>Colesevelam 3.75 g/day (n = 230); Placebo (n = 231)</td>
<td>8.2</td>
<td>-0.54†</td>
<td>-16.7†</td>
</tr>
<tr>
<td>Goldberg et al. (19)</td>
<td>287</td>
<td>16</td>
<td>Insulin-based therapy</td>
<td>Colesevelam 3.75 g/day (n = 147); Placebo (n = 140)</td>
<td>8.3</td>
<td>-0.50†</td>
<td>-12.8†</td>
</tr>
<tr>
<td>Goldfine et al. (25)</td>
<td>509</td>
<td>52</td>
<td>Metformin-, sulfonylurea-, or insulin-based therapy</td>
<td>Colesevelam 3.75 g/day (n = 509)</td>
<td>8.2</td>
<td>-0.3*</td>
<td>Not reported</td>
</tr>
<tr>
<td>Rigby et al. (42)</td>
<td>169</td>
<td>16</td>
<td>Metformin monotherapy</td>
<td>Colesevelam 3.75 g/day (n = 57); Rosiglitazone 4 mg/day (n = 56); Sitagliptin 100 mg/day (n = 56)</td>
<td>8.1</td>
<td>-0.3*†</td>
<td>-11.6**†</td>
</tr>
</tbody>
</table>

Treatment difference = colesevelam – placebo. *Mean change from baseline. †P < 0.001 vs. placebo. **P ≤ 0.001 vs. baseline. ††P < 0.05 vs. baseline.
<table>
<thead>
<tr>
<th>Benefits</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once daily dosing</td>
<td>Constipation</td>
</tr>
<tr>
<td>↓ A1c ~0.5%</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>Minimal hypoglycemia</td>
<td>Flatulence</td>
</tr>
<tr>
<td>Weight neutral</td>
<td>Nausea</td>
</tr>
<tr>
<td>Favorable effects in lipids</td>
<td></td>
</tr>
<tr>
<td>Not systemically absorbed, ok</td>
<td></td>
</tr>
<tr>
<td>in CKD, hepatic impairment</td>
<td></td>
</tr>
<tr>
<td>or heart failure</td>
<td></td>
</tr>
</tbody>
</table>
CONSIDER THE CURRENT FUNCTION AND USE OF INSULIN PUMPS INCLUDING INDICATIONS AND SAFE USAGE
WHAT IS AN INSULIN PUMP?

A programmable electromechanical device capable of delivering variable doses of insulin (rapid acting) through a temporarily implanted catheter

HOW DOES AN INSULIN PUMP FUNCTION?
ANATOMY OF AN INSULIN PUMP
MYTHS ABOUT INSULIN PUMPS

• Pump therapy is easier than many injections a day
• I don’t have to prick my fingers to test my blood sugars
• The pump will test my blood sugars and will give me insulin automatically
IS INSULIN PUMP THERAPY BETTER THAN SHOTS?

• Endocrinologist response....

...It depends...
# IS INSULIN PUMP THERAPY BETTER THAN SHOTS?

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Objectives</th>
<th>Studies included</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weissberg-Benchell et al, 2003</td>
<td>Metabolic and psych impact</td>
<td>52 (37 paired, 4 randomized cross over, 11 parallel, N=1,547)</td>
<td>Improvement in glycemic control, ↓ hypoglycemia but potential ↑ risk of DKA</td>
</tr>
<tr>
<td>Jeitler et al, 2008</td>
<td>Glycemic control, hypoglycemia, insulin requirements, adverse events</td>
<td>22 RCT’s (17 in T1DM and 2 T2DM, 3 pediatric)</td>
<td>Greater A1c ↓, ↓ insulin requirements, ☞ in hypoglycemia No conclusive benefits in T2DM</td>
</tr>
<tr>
<td>Fatourechi et al, 2009</td>
<td>Glycemic control and hypoglycemia</td>
<td>15 RCT (T1 n=669; T2 n=239)</td>
<td>Greater A1c ↓, unclear effect on hypoglycemia, outcomes similar en T2</td>
</tr>
<tr>
<td>Pickup and Sutton, 2008</td>
<td>Glycemic control and severe hypoglycemia</td>
<td>22 RTC’s (T1 n=1,414)</td>
<td>Greater A1c ↓, ↓ risk of severe hypoglycemia</td>
</tr>
<tr>
<td>Monami et al, 2009</td>
<td>Glycemic control and hypoglycemia</td>
<td>11 RCT’s (T1 n=444 vs MDI n=439)</td>
<td>Greater A1c ↓, ☞ risk of severe hypoglycemia</td>
</tr>
</tbody>
</table>
## INSULIN PUMP THERAPY

### Challenges
- Being attached to a device 24/7
- Remembering to use it properly: testing glucose 4x/day, change sites frequently, taking care of supplies
- Not thinking enough before using it
- Troubleshooting technical issues
- Technology

### Advantages
- Flexibility
- Better management in changes in routine
- Eliminate need for insulin injections
- When used properly: better glucose control
CONSENSUS STATEMENT BY THE
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/
AMERICAN COLLEGE OF ENDOCRINOLOGY

INSULIN PUMP MANAGEMENT TASK FORCE
CONSENSUS STATEMENT SUMMARY

• Justified in Patients with type 1 diabetes, on basal bolus insulin therapy

• Only providers whose practice can assume full responsibility for a comprehensive pump management program should offer this technology

• Appropriate patient selection is necessary and must include a thorough assessment of the patient’s knowledge of diabetes management principles
ASSESSING CANDIDACY FOR INSULIN PUMP THERAPY

Ideal Candidate

- Patient with T1 or intensively managed insulin dependent type 2
- SMBG ≥ 4 times/day, sustainable
- Motivated to achieve optimal blood glucose control
- Willing and able to:
  - carry out the tasks required to use this complex and time consuming therapy safely and effectively
  - maintain frequent contact with their health care team

Not recommended

- Unable or unwilling to:
  - Perform >3-4 insulin injections daily
  - SMBG ≥ 4 times/day
  - Lack of motivation
  - h/o non-adherence to insulin injection protocols
  - Serious psychological or psych conditions
  - Substantial reservations about pump usage interfering with lifestyle
  - Unrealistic expectations (belief that it eliminates the need to be responsible for diabetes management)
When should it not be used?

Pump therapy is not recommended for people:

• who are unwilling or unable to perform a minimum of four blood glucose finger tests per day.

• who are unwilling or unable to maintain contact with their healthcare professional.

• whose vision or hearing does not allow recognition of pump signals and alarms.
In addition to a basal continuous infusion of insulin, insulin pumps have sophisticated features to bolus for food:

- **Insulin-to-Carb Ratio (ICR)**: 1 unit of insulin to be delivered for “X” amount of carbohydrates.
- **Insulin Sensitivity Factor (ISF)**: The number of mg/dl one unit of insulin lowers glucose.
- **Target Range**: BG used in the correction formula when calculating a correction dose.
- **Active Insulin Time**: Insulin remaining from previous boluses that continues to have a pharmacodynamic effect and potential to lower glucose.
VGO INSULIN DELIVERY SYSTEM

• Basal-bolus insulin delivery device to help control blood glucose in adults with Type 2 diabetes
• Continuous preset basal rate of insulin throughout the day and night—during a full 24-hour period—as well as on-demand bolus doses
• Disposable
• 3 pre-set basal rates: 20U, 30U and 40U/24 hrs.
• No electronics, no battery
• No programming
• Bolus types: delivered in 2 unit increments: 36 u in 2 u increments

www.go-vgo.com/
DISCUSS THE SIGNS AND SYMPTOMS OF THE VARIOUS ASPECTS OF DIABETIC NEUROPATHY
## Classification Diabetic Neuropathy

<table>
<thead>
<tr>
<th>Diffuse</th>
<th>Focal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal symmetric: sensorimotor neuropathy</td>
<td>• Mononeuropathies</td>
</tr>
<tr>
<td>A) Large fiber</td>
<td>• Entrapment neuropathies</td>
</tr>
<tr>
<td>B) Small fiber</td>
<td>• Truncal neuropathies</td>
</tr>
<tr>
<td>• Autonomic</td>
<td>• Cranial neuropathies</td>
</tr>
<tr>
<td>• Symmetric proximal lower limb motor neuropathy (amyotrophy)</td>
<td>• Focal amyotrophy</td>
</tr>
</tbody>
</table>
# Diabetic Neuropathy

<table>
<thead>
<tr>
<th>Sensory Symptoms</th>
<th>Motor Symptoms</th>
<th>Autonomic Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative Symptoms: lack of function</strong>&lt;br&gt;Numbness, loss of balance</td>
<td>Distal, proximal or focal weakness: Impaired coordination: opening jars, tripping, difficulty climbing up and down stairs, getting up from seated position, difficulty raising arms.</td>
<td><strong>CV system</strong>: persistent sinus tachycardia, orthostatic hypotension, sinus arrhythmia, heart variability to deep breathing, near syncope</td>
</tr>
<tr>
<td><strong>Positive Symptoms: abnormal function</strong>&lt;br&gt;Tingling, electric-shock like, tightness, hypersensitivity</td>
<td></td>
<td><strong>GI system</strong>: gastroparesis, dysphagia, nausea, vomiting, incontinence, diarrhea/constipation, malabsorption</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>GU system</strong>: poor stream, incomplete voiding, emptying, ED</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Sweat glands</strong>: heat intolerance, sweating of head, neck and trunk with anhidrosis of lower trunk and extremities, gustatory sweating</td>
</tr>
</tbody>
</table>
THE NEUROLOGIC EXAM

Semmes-Weinstein Monofilament

Right Foot

Left Foot

J Fam Pract. 2014;63:646-656
WHAT TO ASK (1 MINUTE)

History of:
- Previous leg/foot ulcer, amputation or surgery
- Angioplasty, stent or leg bypass surgery
- Foot wound requiring >3 weeks to heal
- Smoking or nicotine use
- Diabetes control measures

Does the patient have:
- Burning or tingling in legs and feet
- Leg or foot pain with activity or at rest?
- Changes in skin color or skin lesions
- Loss of sensation

Has the patient established regular podiatric care?

*J Fam Pract.* 2014;63:646-656
WHAT TO LOOK FOR (1 MINUTE)

The dermatologic exam

- Discolorations, calluses, wounds, fissures, macerations, nail dystrophy, or paronychia.
- Skin discoloration or loss of hair growth
- Calluses and hypertrophic skin often are precursors to ulcers
- Search for fungal, ingrown, or elongated nails
- Examine the areas between the toes, where deeper lesions may go unnoticed
WHAT TO LOOK FOR (1 MINUTE)

Musculoskeletal exam
• Range of motion of the joints
• Obvious deformities?
• Is the midfoot hot, red or inflamed?

Vascular exam
• Is hair growth decreased?
• Are the Dorsalis pedis and posterior tibialis palpable?
• Temperature difference between the calves and feet, or between the left and right foot?
Diabetic sensorimotor polyneuropathy is the most common complication of diabetes and affects up to 50% or more of all patients.

- Therapeutic challenge, pathophysiology not yet fully understood.
- The pharmacological treatments, with exception to those targeted to the glycemic control, are symptomatic, not focused on the pathophysiological mechanisms.

**DISTAL SYMMETRICAL PAINFUL NEUROPATHY (PN)**

- Exclude other causes of painful diabetic neuropathy
- Improve glycemic control as a prophylactic therapy
- Alleviate the pain

- Diabetic sensorimotor polyneuropathy is the most common complication of diabetes and affects up to 50% or more of all patients.
DISTAL SYMMETRICAL PAINFUL NEUROPATHY (PN):

EXCLUDE:

- Treatment-induced neuropathy, in the setting of rapid glycemic control
- Diabetic neuropathy in the setting of unintended severe weight loss (diabetic neuropathic cachexia)
- Diabetic neuropathy that is seen with intentional weight loss (diabetic anorexia)

Severe neuropathic pain, autonomic dysfunction, and a potentially reversible course that may last for many months
<table>
<thead>
<tr>
<th>Pharmacological Treatment of Painful Diabetic Neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticonvulsants</strong></td>
</tr>
<tr>
<td>Pregabalin</td>
</tr>
<tr>
<td>Gabapentin</td>
</tr>
<tr>
<td>Valproic Acid</td>
</tr>
<tr>
<td>300-600 mg/day</td>
</tr>
<tr>
<td>900-3600 mg/day</td>
</tr>
<tr>
<td>500-1200 mg/day</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
</tr>
<tr>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Duloxetine</td>
</tr>
<tr>
<td>Amitriptyline</td>
</tr>
<tr>
<td>75-225 mg/day</td>
</tr>
<tr>
<td>60-120 mg/day</td>
</tr>
<tr>
<td>25-100 mg/day</td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
</tr>
<tr>
<td>Dextrometorphan</td>
</tr>
<tr>
<td>Morphine sulfate</td>
</tr>
<tr>
<td>Tramadol</td>
</tr>
<tr>
<td>400 mg/day</td>
</tr>
<tr>
<td>Up to 120 mg/day</td>
</tr>
<tr>
<td>210 mg/day</td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Alpha-lipoic acid</td>
</tr>
<tr>
<td>Acetyl-L-carnitine</td>
</tr>
<tr>
<td>600-1800 mg/day</td>
</tr>
<tr>
<td>1000 mg/TID</td>
</tr>
<tr>
<td><strong>Topical Agents</strong></td>
</tr>
<tr>
<td>Isosorbide spray</td>
</tr>
<tr>
<td>Capsaicin</td>
</tr>
<tr>
<td>Lidocaine patch</td>
</tr>
<tr>
<td>0.075% QID</td>
</tr>
</tbody>
</table>

WHICH OF THE FOLLOWING IS NOT AN EFFECT OF THE SGLT2 INHIBITORS?

a)↑ HDL-C
b)↑ LDL-C
c)↓ NON-HDL-C
d)↑ NON-HDL-C
CASE STUDIES

Sandy is 25 yo, she has type 1 diabetes, otherwise healthy

- She performs SMBG on average 6 times a day
- A1c 6.6%
- No complications secondary to diabetes, but has had 2 episodes of confusion secondary to hypoglycemia

Bella is 18 yo, she has type 1 diabetes, and an eating disorder (bulimia)

- She has had many ER visits secondary to dehydration, secondary to severe hyperglycemia.
- 2 hospitalizations in the last year secondary to DKA
- A1c 14%
- She “hates” to give injections and test her glucose levels
CASE STUDIES QUESTION #1

• Both of these patients with type 1 diabetes are interested in an insulin pump.
• Who is a better candidate for insulin pump therapy?

A. Sandy
B. Bella
CASE STUDIES QUESTION #2

PATIENTS WITH TYPE 1 DIABETES ON INSULIN PUMP THERAPY ARE AT INCREASED RISK OF DIABETIC KETOACIDOSIS

a) TRUE
b) FALSE
Routine foot examination and rapid risk stratification is often difficult to incorporate into busy primary care settings.

- Routine foot examination in patients with diabetes is adequately evaluated ________ of the time.
  - A) 4-10%
  - B) 12-20%
  - C) 35-45%

• Up to _____ of patients with diabetes who have significant sensory loss due to neuropathy may be completely asymptomatic of lower extremity complications.

• A) 10%
• B) 30%
• C) 50%

Asymptomatic patients fail to search for early signs of infection, skin breakdown, ulcer formation, skin temperature changes and inadequate vascular perfusion, which may allow complications to develop.

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THANK YOU FOR YOUR INTEREST IN DIABETES

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