Objective Three:
Given a patient with established diabetes, advise about signs and treatment of hypoglycemia/hyperglycemia during an acute illness or stress (i.e., gastroenteritis, physiologic stress, decreased intake.)

- **a.** The patient should be aware of sick-day adjustments to make to their medications. If you're a mnemonic person, one you can use is SADMANS =
  - **i.** Sulfonylureas
  - **ii.** ACEi
  - **iii.** Diuretics
  - **iv.** metformin
  - **v.** ARBs
  - **vi.** NSAIDs
  - **vii.** SGLT2is
    1. Medications should be held on days with gastro or poor fluid and food intake to avoid risk of dehydration, hypoglycemia, and kidney injury

- **b. HYPOGLYCEMIA**
  - **i.** Definition:
    "The development of autonomic or neuroglycopenic symptoms in the setting of a low plasma glucose level"
    1. this is <4.0 mmol/L for people with diabetes treated with insulin or an insulin secretagogue,
    2. and symptoms respond to the administration of a carbohydrate.
  - **ii.** People at high risk of severe hypoglycemia should be counselled about their risk, along with their families, about preventing and treating hypoglycemia (including the use of glucagon), preventing driving and industrial accidents through self-monitoring blood glucose levels, and taking appropriate precautions prior to activity
    1. Patient's experience with hypoglycemia should be reviewed at every visit including discussion of cause, frequency, symptoms, recognition, severity, and treatment, as well as risk of driving with hypoglycemia.
  - **iii.** Patients should also document BG readings during sleeping hours.

iv. Hypoglycemic episodes are most common in patients with T1DM, then in patients with T2DM managed with insulin, then in patients with T2DM managed with insulin secretagogues (e.g. sulfonylurea or meglitinide)
v. Severity:
    1. Mild: autonomic symptoms are present and the individual is able to self-treat.
    2. Moderate: Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat.
    3. Severe: The individual requires assistance of another person. Unconsciousness may occur. Plasma glucose is typically <2.8 mmol/L.
vi. Hypoglycemia signs:
    1. Confusion
    2. Weakness
    3. Shaking/ tremor/trembling
    4. Seizure activity
    5. Altered level of of consciousness/coma
    6. Vision changes
    7. Difficulty speaking
    8. Headache
    9. Dizziness
    10. Diaphoresis
    11. Anxiety
    12. Palpitations
    13. Hunger
    14. Nausea
    15. Tingling
    16. Difficulty concentrating
    17. Not all symptoms have to be present and some patients may have other or no symptoms
vii. Patients at risk of hypoglycemia should always carry with them a glucose load of 15 g minimum for treatment of hypoglycemia and wear a MedicAlert bracelet.
viii. Complications of hypoglycemia:
    1. Short-term:
        a. Accidents (industrial, driving)

b. Inability to maintain consciousness while caring for other people

2. Longer-term:

a. Prolonged coma may be associated with transient neurological symptoms.

i. Paresis

ii. Convulsions

iii. Encephalopathy

b. Mild intellectual impairment

c. Permanent neuro sequelae

i. Hemiparesis

ii. Pontine dysfunction

iii. (both rare, only reported in case studies)

d. Hypoglycemia unawareness.

e. A clear association exists between hypoglycemia and cognitive disorders as well but the nature of that relationship unclear.

i. Patients with cognitive disorders are at higher risk of future hypoglycemia, possibly due to med errors.

f. Increased mortality with severe hypoglycemia in patients with established or very high risk for CVD

i. Uncertain mechanism; severe hypoglycemia may merely be an indicator of vulnerability

g. Acute hypoglycemia is proinflammatory, increases platelet activation, and decreases fibrinolysis therefore leading to a prothrombotic state; there are also numerous changes induced in heart function (rhythm, rate, electrical conduction) with hypoglycemia.

ix. Treatment of hypoglycemia:

1. Mild-to-moderate:

a. 15 g of carbs required to produce increase in blood gluc of 2.1 mmol/L within 20 mins, with adequate relief for most people (not well-studied in patients with gastroparesis)

i. 15 g of glucose in glucose tab

ii. 15 mL or 3 packets of table sugar dissolved in water
iii. 5 cubes of sugar
iv. 150 mL of juice or regular soft drink (NOT diet or zero sugar – duh!)
v. 6 Life Savers (1 LS = 2.5 g of carbs)
vi. 15 mL of honey

b. Retest 15 mins after glucose load, if not >4.0 mmol/L, redose. ***
c. The above does not apply in children and I refer you to the DC Guideline to review the same – they recommend IV dextrose in the hospital setting or IM glucagon in the home setting. http://guidelines.diabetes.ca/cpg/chapter34#sec8

2. Severe hypoglycemia in awake patient:
   a. Oral gluc load of 20 g will increase blood gluc by about 3.6 mmol/L at 45 minutes
   b. Treat with oral ingestion of 20 g carb, preferably as glucose tabs or equivalent.
   c. Recheck BG in 15 mins, retreat if BG < 4.0 mmol/L
3. Severe hypoglycemia in unconscious person with diabetes:
   a. No IV access:
      i. Glucagon 1 mg SQ or IM x 1 (support persons should be taught how to administer glucagon!)
      ii. Call emergency services
      iii. Discuss with healthcare team as soon as possible after episode resolved
   b. IV access:
      i. 10-25 g (20-50 mL of D50W) of glucose should be given over 1-3 minutes

c. HYPERGLYCEMIA

i. Dangerous hyperglycemic states include diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS). These have been addressed in episode 23, Chronic Diseases. As a reminder, hyperglycemia needs to be

suspected in all diabetic patients who are ill. If either DKA or HHS is present, precipitating factors should be sought and rectified if possible.

Objective Four:
In a patient with poorly controlled diabetes, use effective educational techniques to advise about the importance of optimal glycemic control through compliance, lifestyle modification, and appropriate follow-up and treatment.

d. Appropriate interprofessional team engagement including pharmacist, diabetic nurse educator, endocrinologist, wound care nurse PRN, diabetic foot care nurse, social work or financial aid team to help with med coverage as needed, psychologist PRN, dietitian
e. Group education can be helpful if employing adult education skills.
f. Intensive Lifestyle Intervention programs should be considered for patients to help with nutrition and physical activity although the effects seem to attenuate after 8 years so may not be effective to reduce risk of CV events over time.
g. Encouraged to follow Eating Well with Canada's Food Guide and to undergo nutrition therapy with a registered dietitian.
h. Self-management training; for individuals using insulin more than once a day, they should check their glucose levels at least 3 times a day, and should include both pre- and post-prandial measurements
i. For patients on once-daily insulin in addition to other non-insulin antihyperglycemics, checking gluc once daily at variable times is recommended.
j. For patients not using insulin, frequency of SMBG should be individualized to the patient based on the specific agents being used, their risk of hypoglycemia, and level of glycemic control
    i. In patients not receiving good glycemic control, they should implement SMBG AND have teaching on how to adjust health behaviours in response to readings.
k. If patients are achieving appropriate glycemic control/are at target AND are also not using antihyperglycemics that put them at risk of hypoglycemia, it is appropriate to do infrequent SMBG.
l. In many patients with diabetes, more frequent SMBG may need to be undertaken to better understand what therapeutic changes

must be made to ensure proper glycemic control (including decreasing the risk of hypoglycemia)

m. In patients with T1DM who have not achieved their target for glycemic control, it is appropriate to consider continuous glucose monitoring for both improvement of glycemic control and to reduce the time spent in a hypoglycemic state
n. Flash glucose monitoring may be used in T1DM and T2DM to reduce time spent in hypoglycemic state
o. Meters should be checked against lab readings at least annually and if A1c and home readings don't match
p. Appropriate follow-up – check HbA1c q3 months when making treatment changes or in anyone whose glycemic control is not stable; may stretch to 6 months if at target and stable with healthy lifestyle modifications and treatment. May check more frequently with pregnant patients or people who have had significant therapy changes.
q. Physical activity is important in glycemic control as it increases muscle usage of glucose and therefore improves the glycemic control over time when done consistently at appropriate intensities
    i. 150 minutes of aerobic exercise per week PLUS 2 sessions of resistance training per week recommended, but benefits are noted with less activity.
    ii. Individuals who should be screened prior to initiation of an exercise program: people with symptoms of coronary ischemia or with typical/atypical chest discomfort, unexplained dyspnea, PAD, carotid bruits, or history of angina, MI, stroke, TIAs, or syncope (resting ECG and an EST should be considered) if they wish to do more intense exercise than brisk walking; middle-aged and older individuals wanting to undertake very vigorous or prolonged exercise (e.g. long-distance running, HIIT at maximal effort, competitive racing) should be assessed for conditions that may put them at increased risk of adverse events; preproliferative or proliferative retinopathy should be treated and stabilized prior to commencement of vigorous exercise; and people with severe peripheral neuropathy should check their feet daily especially on days they are physical active, and should be advised to wear appropriate footwear.

iii. People with severe peripheral neuropathy can safely do weight-bearing exercise provided they do not have active foot ulcers. People who do daily weight-bearing exercise with peripheral neuropathy are actually at lower risk of ulceration than people who are sedentary.
iv. Consider exercise prescriptions.
v. No more than two consecutive days without exercise should be accumulated in order to maintain glycemic control.

r. In T1DM, matching carb intake to insulin therapy with activity is difficult and can be a barrier to exercising. Encourage some strategies to avoid hypoglycemia including:
   i. Consumption of extra carbs for exercise
   ii. Limiting preprandial bolus insulin doses
   iii. Reducing basal insulin rate for CSII
   iv. Reducing prandial insulin by 25% to 75% for exercise within 2 hours after a meal, but heavy reductions may cause hyperglycemia so they need to monitor their glucose levels.

2. **Glycemic Management of Adults with T1DM**
   a. May use basal-bolus (multiple daily injection or continuous subcutaneous insulin infusion). If targets not met with MDI, CSII may be considered. Insulin must be started immediately on diagnosis of T1DM.
   b. CSII and MDI both first line but CSII indicated if:
      i. Not reaching targets despite optimized basal-bolus injection therapy
      ii. Significant glucose variability
      iii. Frequent severe hypoglycemia
      iv. Hypoglycemia unawareness
      v. Significant "dawn phenomenon" with rise of BG early in the morning
      vi. Very low insulin requirements
      vii. Adequate glycemic control but suboptimal treatment satisfaction and quality of life or women contemplating pregnancy.
   c. Picking appropriate individuals for CSII important; should be motivated, currently on optimized basal-bolus injection therapy, willing to frequently monitor BG, understand sick-day management and attend F/U visits as required by the health-care team.

d. Basal-bolus methodology requires selection of a regime and comprehensive diabetes education. The regimen should be tailored to individual's treatment goals, lifestyle, diet, age, general health, motivation, hypoglycemia awareness stats, and ability for self-management.
e. All individuals with T1DM should be counselled about the risk, prevention, and treatment of hypoglycemia.
f. Patients may experience honeymoon period initially after insulin initiation, but requirements usually increase then stabilize over time
g. Continuous glucose monitoring (CGM) may be offered to people not meeting glycemic targets who will wear the devices the majority of the time in order to improve glycemic control. CGM seems to afford better A1c control without excess hypoglycemia; in adults with poor hypoglycemia awareness, it reduces time spent in hypoglycemic state.

3. **Pharmocologic Management of Adults with T2DM**
   a. In people with T2DM with A1C < 1.5% above target, antihyperglycemic pharmacotherapy should be added if glycemic targets not achieved within 3 months of initiating healthy behaviour interventions.
   b. In people with T2DM >= 1.5% above A1c target, antihyperglycemic agents should be initiated concomitantly with healthy behaviour interventions; consideration can be given to initiating combination treatment with 2 agents at this time
   c. Insulin should be initiated immediately in patients with either metabolic decompensation and/or symptomatic hyperglycemia.
      i. Signs/ symptoms of this would be: marked hyperglycemia, ketosis or unintentional weight loss, or symptoms previously discussed in key feature 3.
      ii. Insulin may eventually be tapered or discontinued if stability achieved
   d. In absence of metabolic decompensation or symptomatic hyperglycemia, metformin (a biguanide) should be first-choice agent for initiation unless contraindicated.
   e. Dose adjustments or additional agents should be added to achieve A1C target within 3 to 6 months (<7% for most adults, <6.5% to reduce risk of CKD or microvascular complications in people with long life expectancy, 7.1-8.0% for functionally dependent, 7.1-8.5%

in people who are frail or with limited life expectancy, at high risk of hypoglycemia, multimorbidity, or patient preference).

f. Second choice of pharmacotherapy should be made based on patient characteristics, glucose-lowering efficacy, contraindications, patient preference, hypoglycemic risk, affordability/access, benefit for comorbidity management, and the effect on weight.
g. In patients with clinical CV disease who are not achieving A1c targets, addition of an antihyperglycemic with proven CV benefit should be considered (e.g. SGLT2i)
h. In patients without CV disease in whom targets are not met, they may prefer a DPP4i or GLP1 agonist (incretin analogues) or an SGLT2i because these improve control of sugars with low risk of hypoglycemia and weight gain.
i. In patients on insulin not reaching targets, consider adding SGLT2i, DPP4i, or GLP1 agonist before increasing insulin because it may offer comparable glycemic control with lower or comparable risk of hypoglycemia and low risk of weight gain.

5. **In patients with established diabetes:**
   a) Look for complications (e.g., proteinuria).
   a. <u>Retinopathy</u>
      i. Risk factors for development or progression of diabetic retinopathy are:
         1. Longer duration of DM
         2. Elevated A1c
         3. Increased BP
         4. Dyslipidemia
         5. Anemia
         6. Pregnancy (T1DM)
         7. Proteinuria
         8. Severe retinopathy itself
      ii. T1DM: Starting at 5 years post-dx in all individuals >=15 yo, q1yearly assessment by ophtho for retinopathy
      iii. T2DM: Starting at diagnosis for people of all ages, q1-2 years to assess for retinopathy
      iv. If retinopathy is already present, diagnose severity and establish appropriate monitoring intervals (1 year or less).
   b. <u>Cardiovascular disease</u>

i. Resting ECG should be repeated q3-5years for all individuals with diabetes with any of the following characteristics:
    1. If they are older than 40 years
    2. Or, if they're older than 30 and have had diabetes for more than 15 years
    3. If there is evidence of end organ damage, thinking microvascular or macrovascular
    4. if they have one or more CVD risk factor
        a. current smoking,
        b. hypertension,
        c. fam hx of premature CVD in 1st degree rel [men < 55, women <65],
        d. CKD,
        e. obesity BMI > 30,
        f. erectile dysfunction
    5. If they are over 40 years and planning to undertake very vigorous or prolonged exercise, such as competitive running, long-distance running, or high-intensity interval training

ii. Monitor for hypertension and treat if blood pressure is above target
    1. Generally, the target blood pressure is < 130 mmHg SBP and < 80 mmHg DBP for patients with diabetes to reduce the risk of cardiovascular and microvascular disease over time.

c. Chronic Kidney Disease
    i. Screening with random Urine Albumin:Creatinine ratio should be performed with serum creatinine converted to an eGFR starting at diagnosis of T2DM or 5 years after diagnosis of T1DM in adults and repeated yearly thereafter.
    ii. Diagnosis of CKD made only if:
        1. eGFR < 60 and/or random ACR >= 2.0 mg/mmol on at least 2 of 3 samples over a 3 month period (need to rule out AKI if initial values elevated)
    iii. Treat with ACEi or ARB for patients with CKD and either hypertension or albuminuria
    iv. Patients treated with an ACEi or ARB should be monitored with a serum Cr and K+ level at baseline and then within 1 to

2 weeks of initiation or titration of therapy, and during times of acute illness

v. Adults with DM and CKD need to be given "sick-day" list of meds to avoid during times of acute illness as noted above.
vi. May consider SGLT2-I for people with T2DM and clinical CVD in whom glycemic targets are not achieved with existing antihyperglycemic meds and with eGFR > 30

d. Neuropathy
    i. Test with 10 g monofilament on dorsal aspect of great toe bilaterally OR vibration sensation with 128 Hz tuning fork starting at diagnosis for T2DM and then annually thereafter; T1DM, screening should begin after 5 years post-pubertal duration of diabetes.
    ii. Treat with intensified glycemic control to prevent onset and progression
    iii. May use anticonvulsants (pregabalin grade A, gabapentin grade B, valproate grade B), antidepressants (amitriptyline, duloxetine, venlafaxine), topical nitrate spray, opioids if not responsive to rest above.
e. Foot ulcers:
    i. Foot exams should be done in patients with diabetes at least annually and more frequently for people at high-risk.
    ii. Assess for neuropathy, skin changes (e.g. calluses, ulcers, infection), peripheral arterial disease (e.g. pedal pulses, skin temp) and structural abnormalities (e.g. ROM of ankles and toe joints, bony deformities).
    iii. People at high risk should receive foot care education and professionally fitted footwear.
f. Sexual dysfunction
    i. All men with diabetes (adults) should be regularly screened for erectile dysfunction with sexual function history
    ii. Current mainstay of therapy is PDE-5 inhibitors
    iii. Sexual dysfunction may be an early marker of cardiovascular disease
    iv. If unresponsive to PDE-5i, consider investigations for hypogonadism.
g. Hypogonadism in Men with DM

i. Hypogonadotropic hypogonadism is common in men with type 2 diabetes, with a prevalence up to 40%
ii. Hypogonadal men with diabetes have a higher risk for CV mortality than eugonadal men with DM
iii. Screening for symptomatic hypogonadism in men with T2DM is recommended – test with morning serum total testosterone drawn before 11 am

h. Preventative measures such as vaccinations should be considered and recommended
    i. Influenza
    ii. Pneumococcal – initially when over the age of 18, and again when over the age of 65 if initial vaccine was < 65 yo and over 5 years ago; one-time over the age of 65. Health Canada recommends Pneu-P-23. Some experts recommend pneumococcal conjugate vaccine FOLLOWED by Pneu-P-23 a minimum of eight weeks later. If someone has been given Pneu-P-23 but Pneu-C-13 still recommended (immunocompromise or >= 65 yo as per CDC), need to wait 1 year before administration.

i. Herpes Zoster – Should consider for patients >= 60 as the vaccine wanes in effectiveness within 5 years BUT the risks are higher above 60; people with diabetes have lower cell-mediated immune responses

j. Hepatitis B Vaccination recommended for all children and those in "high-risk groups" by National Advisory Committee on Immunization (Canada) but diabetes NOT specified in this recommendation (as per the Diabetes Canada guidelines). The patient's personal risk for HBV infection should be taken into account when deciding on whether or not to administer the vaccine.

b) Refer them as necessary to deal with these complications

a. Retinopathy:
    i. Ophtho for retinopathy for laser, pharmacological, or surgical treatment
    ii. Review glycemic, BP, and lipid control, and adjust tx to reach targets as per guidelines

b. Cardiovascular disease: if symptomatic or abnormal ECG findings on screening:

i. Exercise Stress Test
    1. People with DM should undergo EST for investigation of CAD as initial test in presence of any of the following:
        a. Typical or atypical cardiac symptoms (e.g. unexplained dyspnea, chest discomfort)
        b. Signs or symptoms of associated diseases
            i. PAD (abnormal ankle-brachial index)
            ii. Carotid bruits
            iii. Transient ischemic attack
        c. Stroke
        d. Resting abnormalities on ECG e.g. Q waves
        e. Coronary Artery Calcium > 400 Agatston score

ii. Pharmacological Stress Echo or nuclear imaging should be used in diabetic patients in whom resting ECG abnormalities preclude the use of exercise ECG stress testing (e.g. LBBB, ST-T abnormality).
    1. People who require stress testing but cannot exercise should also undergo pharmacological stress echo or nuclear imaging

iii. Individuals with diabetes who demonstrate ischemia at low exercise capacity (<5 METs) on stress testing should be referred to cardiology

c. Nephropathy

i. Referral to nephrology for CKD if:
    1. Chronic, progressive loss of kidney function
    2. Urine ACR persistently >60 mg/mmol
    3. eGFR < 30 mL/min
    4. Unable to remain on renal-protective therapies due to adverse effects, such as hyperkalemia or a >30% increase in serum Cr within 3 months of starting an ACEi or ARB
    5. Unable to achieve target BP

d. Foot care

i. People with foot injuries or complications should be referred to health-care professional trained in foot care

ii. Referral for assessment and management if needed for any foot ulcers to prevent recurrent ulcer and amputation
iii. Off-load ulcer, refer for debridement PRN

e. Hypogonadism
i. If interested in fertility options, refer to fertility expert (REI, endocrinology)

f. Endocrinology if poor control of sugars despite optimal therapy and lifestyle changes, or if frequent hyperglycemia or hypoglycemia, or if concomitant endocrine disorders e.g. Addison's, thyroid disorders, etc.

g. Neurology or physiatry if any stroke/ neuro symptoms including peripheral neuropathy

h. Vascular surgery if any need for assessment of PVD and potential treatment of same, including amputation secondary to ulcers

i. GI – may consider screening for celiac disease in T1DM patients and subsequent referral to GI for biopsy if necessary.

Objective Six:
In the acutely ill diabetic patient, diagnose the underlying cause of the illness and investigate for diabetic ketoacidosis and hyperglycemia.

k. T1DM patients should be instructed on how to check for ketones when pre-prandial glucose is >14 consistently and if there are symptoms of DKA (polyuria, polydipsia, polyphagia, nausea, vomiting)
l. A normal or mildly elevated gluc does NOT rule out DKA in certain conditions – e.g. pregnancy, SGLT2-I use
m. Always remember if a patient is presenting with hyperglycemia, there is often an underlying cause – an infection, a stressor on the body, insulin omission, or another insult to homeostasis.
n. See episode 23 on Chronic Disease for review of DKA and HHS

Objective Seven:
Given a patient with diabetic ketoacidosis, manage the problem appropriately and advise about preventing future episodes

o. ABCs as always, and the other cardinal rule DEFG - don't ever forget glucose!

p. If comatose, airway management is important first.

q. Patients will NEED fluid as they are all dehydrated, likely in volume of litres.

r. DKA requires IV insulin administration – CANNOT USE SUBCUT INSULIN FOR DKA UNTIL ANION GAP CLOSED.

s. Bicarbonate therapy may be considered only for extreme acidosis e.g. pH <= 7.0

t. For a more comprehensive review of DKA management, please see episode 23 on Chronic Disease.

personal reflections from Dr Karin Winston:

"diabetes is so much harder than it looks on paper. The guidelines make it look like it should be as simple as "a little more of this and a little less of this" but in truth it is very difficult for most people to get their sugars to target and it is incredibly emotionally and psychologically draining. Diabetes takes a toll on people and health care providers need to be sensitive to this when choosing what words to use with people.

- if anyone plans on seeing a lot of diabetes as part of their practice, they should see if there is an opportunity to work at a diabetes camp in their province - we run summer camps for kids with T1DM and the learning as to the practicalities of living with diabetes as well as the humility of never quite being able to get it right! I have been the camp director for D-Camps in Alberta for a few years and love having family doctors or family medicine residents come out to join us. (*we have linked to the Diabetes Canada link as well to enable you to reach out to them if you're interested in helping)*

- there is a great concept of the balance of burden and capacity for chronic disease and I am attaching a paper from Mayo clinic that talks about capacity coaching. Your listeners will undoubtedly be working with a lot of people with various chronic diseases and may benefit from understanding this framework, even if they don't end up taking any further training in capacity coaching."

Resources Used

- Diabetes – Obtained from the Diabetes Canada Clinical Practice Guidelines (Full update in 2018, select updates in 2020)
  Diabetes Canada Clinical Practice Guidelines Expert Committee. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*. Can J Diabetes. 2018;42(Suppl 1):S1-S325.
- The app (DC CPG) is super helpful for a quick reference!
- CanRisk https://health.canada.ca/apps/canrisk-standalone/pdf/canrisk-en.pdf
- Canada's Food Guide https://food-guide.canada.ca/en/