Diabetes Summary Notes

Given a symptomatic or asymptomatic patient at high risk for diabetes (e.g., patients with gestational diabetes, obese, certain ethnic groups, and those with a strong family history), screen at appropriate intervals with the right tests to confirm the diagnosis.

Signs and Symptoms

- Diabetic ketoacidosis (automatic diagnosis of diabetes as this is symptomatic hyperglycemia),
- Polyuria/polydipsia/polyphagia and weight loss, most often seen in type 1 diabetes
- Acanthosis nigricans (particularly in children and adolescents with type 2 DM), and
- Obesity
- And more

Screening

- The general population should be screened for type 2 DM after age 40 at an interval of every 3 years using either fasting plasma glucose OR hemoglobin A1c (HbA1c);
    - you can use random plasma glucose but you'll need to confirm using a second DIFFERENT test.
- All individuals should be evaluated annually for type 2 diabetes RISK on the basis of demographic and clinical criteria.
- Can use the **CANRISK** as a risk scoring tool
    - cANRISK or The Canadian diabetes risk questionnaire which includes age, sex, activity and diet, family history and other risk factors.
- If at high risk (>33% chance in developing diabetes over 10 years), start screening earlier using the same q3 years minimum frequency,
    - you may screen more frequently (e.g. every 6 or 12 months) for those at very high risk.
- Note: screening is not done for T1DM

Risk Factors

- Previous gestational diabetes mellitus (up to 50% will develop diabetes later on)
- Prediabetes
- Family history of T2DM
- Abdominal obesity/being overweight
- Metabolic syndrome (3 of the following:
    - Elevated waist circumference,
    - Elevated TGs >=1.7 or treatment for elevated TGs,
    - Decreased HDL <1.3 in women, <1.0 in men,
    - Elevated BP with SBP >=130 or DBP >=85 or treatment for elevated BP,
    - Elevated FPG >=5.6 or treatment of elevated glucose)
- Hypertension
- Ethnicities including South Pacific Islanders, Asian people, Indigenous North Americans, Black people
- Smoking history
- Associated diseases including:
    - PCOS, Acanthosis nigricans, history of pancreatitis, hyperuricemia/gout, non-alcoholic steatohepatitis, psychiatric disorders (e.g. bipolar disorder, depression, schizophrenia), HIV infection, obstructive sleep apnea, cystic fibrosis
- Medications such as
    - Glucocorticoids, atypical antipsychotics, statins, highly-active anti-retroviral therapy, anti-rejection drugs, alpha-interferon, beta-adrenergic agonists, calcineurin inhibitors, diazoxide, dilantin, fluoroquinolones, nicotinic acid, pentamidine, thiazides, thyroid hormone, vacor (rodenticide)

Screening In Pregnant Patients

- Screened with 1hr OGTT between 24 and 28 weeks GA
- Confirmation is with the 2hr test

Positive Test Results

- Fasting plasma glucose level > 7.0, or
- Random plasma glucose >= 11.1, or
- HbA1c >= 6.5%
- 2h Oral Glucose Tolerance Test with FPG >7.7, 2hr Gluc >= 11.1
- You should confirm any of these results with a second test of the same type on another day
    - Unless the first test is random glucose reading and then you need to confirm with A1c or FPG; you may also use FPG + A1c together or 2hOGTT as a confirmatory test. If the results of 2 tests are both above threshold, the diagnosis is made.
    - If a patient presents with symptomatic hyperglycemia then the diagnosis of diabetes is made.

Given a patient diagnosed with diabetes, either new-onset or established, treat and modify treatment according to disease status (e.g., use oral hypoglycemic agents, insulin, diet, and/or lifestyle changes).

Lifestyle Changes

- 5% reduction in bodyweight can help reduce risk of diabetes
- Diets high in fibre, low in saturated fat, low in fat, and low in calories can help achieve weight loss goals
- The Mediterranean diet is recommended for DM prevention.
- Benefit has also been seen with:
    - DASH diet
    - Alternate Healthy Eating Index (AHEI), and
    - diets high in: whole grains, fruits, vegetables, legumes, olive oil, white meat/ seafood, little or moderate alcohol, and reduced intake of red and processed meats and sugar-sweetened beverages. Diets emphasizing whole grain and dairy product consumption are associated with lower risk of diabetes.
- Benefits are noted with 300-400g of dairy intake a day, up to 120 to 140 g/day of yogurt and ~50 g/day of cheese.
- Physical activity 150 mins per week of moderate to vigorous activity are recommended.
    - People with twice the activity time (300 minutes or more per week) had even lower risk of developing diabetes mellitus.

Medications

First Line Agent

Metformin

- Increased body's tissue sensitivity to insulin and reduces glucose production in liver
- Cardiac benefits
- Low cost
- No weight gain
- Side effects: nausea, and diarrhea
- Contraindicated with low renal function and hepatic failure

Second Line Agents

Sulfonulyreas

- Cheap
- Minimal to moderate hypoglycemia risk
- Weight gain

SGLT2 inhibitors

- Weight loss
- Low risk of hypoglycemia
- Costly
- Some side effects

Meglitinide

- A bit costly
- Less weight gain

DPP4 Inhibitors

- Weight neutral
- Very costly
- Low risk hypoglycemia

Injectables

- Low risk of hypoglycemia
- Weight loss
- Very costly

Insulins

- Many available

Third Line Agents

Thiazoledinediones

- May prevent progression of diabetes
- Associated with many adverse outcomes

Alpha Glucosidase Inhibitors

- Costly
- Negligible risk of hypoglycemia
- Weight neutral
- GI side effects common

Orlistat

- Very costly
- Negligible risk of hypoglycemia
- Promotes weight loss
- Associated with GI side effects

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.)

- Certain medications should be held on days with GI symptoms of diarrhea and vomiting or poor fluid and food intake
- This avoids risk of dehydration, kidney injury and hypoglycemia
- Medications to adjust: SADMANS
    - Sulfonylureas, ACE inhibitors, Diuretics, Metformin, ARBs, NSAIDs, SGLT2 inhibitors

Hypoglycemia

- The development of autonomic or neuroglycopenic symptoms in the setting of a low plasma glucose level
    - <4.0 mmol/L for people with diabetes treated with insulin or an insulin secretagogue
    - And symptoms respond to the administration of a carbohydrate
- Patients at high risk and their families should be counselled about their risk, prevention and treatment of hypoglycemia
    - Including prevention of driving and industrial accidents through self-monitoring and taking appropriate precautions
    - Patients should carry a glucose load of 15 g and wear a MedicAlert bracelet
- Hypoglycemic episodes are most common in patients with T1DM then patients with t2DM managed with insulin, then in patients with T2DM managed with insulin secretagogues
- Severity can be estimated based on symptoms
    - Mild: autonomic symptoms present, individual is able to self-treat
    - Moderate: autonomic and neuroglycopenic symptoms are present, individual is able to self-treat
    - Severe: individual requires the assistance of another person, may be unconscious. Plasma glucose is typically <2.8 mmol/L
- Symptoms
    - Neurogenic (autonomic)
        - Trembling
        - Palpitations
        - Sweating
        - Anxiety
        - Hunger
        - Nausea
        - Tingling
    - Neuroglycopenic
        - Difficulty concentrating
        - Confusion, weakness, drowsiness, vision changes
        - Difficulty speaking, headache, dizziness
- Complications
    - Short term
        - Accidents
        - Inability to maintain consciousness
    - Long term
        - Prolonged coma
        - Mild intellectual impairment
        - Rare but permanent neuro sequelae including: hemiparesis, pontine dysfunction
        - Hypoglycemia unawareness
        - Associated with cognitive disorders
        - Increased mortality
        - Prothrombotic states
        - Changes in heart function
- Treatment
    - Mild to moderate: 15 g of carbs required to produce increase in blood gluc of 2.1 mmol/L within 20 mi
    - Severe in awake patient: Oral gluc load of 20 g will increase blood gluc by about 3.6 mmol/L at 45 minutes
    - Severe in unconscious patient:
        - No IV access-> glucagon 1 mg SQ or IM x 1, intranasal 3mg, call emergency services
        - IV access-> 10-25 g (20-50 mL of D50W) of glucose over 1-3 minutes

Hyperglycemia

- Diabetic ketoacidosis and hyperosmolar hyperglycemic state should be suspected in all diabetic patients who are all

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.

- Appropriate interprofessional team engagement including pharmacist, diabetic nurse educator, endocrinologist, wound care nurse PRN, diabetic foot care nurse, social work or financial aid
- Group education can be helpful
- Encourage Eating Well with Canada's Food Guide and to undergo nutrition therapy with a registered dietition
- Self-management training:
    - Individuals using insulin more than once a day: check glucose levels at least 3 times/day (should include pre and post prandial measurements)
    - Individuals using once daily insulin and other non-insulin antihyperglycemics: check glucose once daily at variable times
    - Individuals not using insulin: frequency of self-monitoring of blood glucose should be individualized
        - If patients are achieving appropriate glycemic control and are not using antihyperglycemics, it is appropriate to do infrequent self-monitoring of blood glucose
        - More frequent monitoring may be need to better understand what changes should be made to ensure proper glycemic control
    - Flash glucose monitoring may be used in both T1DM and T2DM
    - Meters should be checked against lab reading at least annually
    - Follow up: check HbA1c every 3 months when making treatment changes or when glycemic controls are not stable, may stretch to 6 months of at target and stable
- Physical activity is important to increase muscle usage of glucose-> increasing glycemic control over time
    - Recommendations: 150 minutes of aerobic exercise and 2 sessions of resistance training per week
    - Individuals with certain conditions 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; pre-proliferative 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.
    - People with severe peripheral neuropathy can safely do weight bearing exercise if they do not have active foot ulcers
    - Consider exercise prescriptions
    - No more than two consecutive days without exercise should be accumulated
    - For patients with T1DM, matching carb intake to insulin therapy with activity can be difficult
        - Strategies to avoid hypoglycemia include
            - Consumption of extra carbs for exercise
            - Limiting pre-prandial bolus insulin doses
            - Reducing basal insulin rate for CSII
            - 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.

Glycemic Management of Adults with T1DM

- Insulin should be started on immediately on diagnosis, can use basal bolus insulin either as multiple daily injection (MDI) or continuous subcutaneous insulin infusion (CSII)
    - Both are first line but CSII is indicated if targets are not being considered and in other conditions such as
        - Significant glucose variability, frequent severe hypoglycemia, hypoglycemia unawareness, rise of blood glucose early in morning, low insulin requirements, suboptimal treatment satisfaction and quality of life, women considering pregnancy
- Individuals appropriate for CSII must be motivated, on optimized basal-bolus injection therapy, be willing to monito blood glucose, understand sick day management and attend follow-up visits
- Basal bolus regimen should be tailored to an individual's treatment goals, lifestyle, diet, age, general health, motivation, hypoglycemia awareness and ability for self-management
- All individuals should be counselled about risk, prevention and treatment of hypoglycemia
- Note: insulin requirements tend to increase then stabilize over time
- Continuous glucose monitoring may be offered to those not meeting targets

Pharmacological Management of Adults with T2DM

- A1C<1.5% above target: pharmacotherapy added if glycemic targets not achieved within 3 months of initiating healthy behaviour interventions
- A1C ≥ 1.5% above target: antihyperglycemic pharmacotherapy added with healthy behaviour interventions
- Insulin added if there is either metabolic decompensation and/or symptomatic hyperglycemia
    - Signs and symptoms: marked hyperglycemia, ketosis, unintentional weight loss
    - Can be tapered or discontinued if stability is achieved
- Metformin is first choice in absence of metabolic decompensation or symptomatic hyperglycemia
- Dose adjustments/additional agents added to achieve A1C target in 3-6 months
    - Targets:
        - <7% for most adults
        - <6.5% to reduce risk of CKD or microvascular complications
        - 7.1-8% in those who are functionally dependent
        - 7.1-8.5% in those who are frail or with limited life expectancy
- Second choice pharmacotherapy is made based on patient characteristics, glucose lowering efficacy, contraindications, patient preference, hypoglycemic risk, affordability/access, benefit for comorbidity management and effect on weight
    - Patients with clinical CV disease not meeting targets may benefit from antihyperglycemics with proven CV benefit i.e. SGLT2i
    - Patients without CV disease not meeting targets may prefer DPP4i, GLP1 agonist or SGLT2i
    - Patients on insulin not meeting targets should consider adding DPP4i, GLP1 agonist or SGLT2i before increasing insulin

In patients with established diabetes, look for complications and refer as necessary to deal with complications

CVD

- Resting ECG every 3-5 years for all individuals with any of the following
    - Older than 40, older than 30 and have had diabetes for >15 years, evidence of end organ damage, have one or more CVD risk factor, over 40 years and planning on undertaking very vigorous or prolonged exercise
- Monitor for hypertensions and treat
    - Target blood pressure for diabetic patients: 130/80 mmHg
- Refer: If symptomatic or abnormal ECG findings
    - Exercise stress test
        - For those who have typical or atypical cardiac symptoms, signs or symptoms of PAD, carotid bruits or TIA, stroke, resting abnormalities on ECG, coronary artery calcium >400 Agatston score
    - Pharmacological stress echo or nuclear imaging in those whom resting ECG abnormalities preclude use of exercise ECG stress test
    - Refer to cardiology if individuals with diabetes demonstrates ischemia at low exercise capacity (<5 METs) on stress testing

Retinopathy

- Risk factors: Longer duration of DM, elevated A1C, increased BP, dyslipidemia, anemia, pregnancy (T1DM), proteinuria, severe retinopathy
- T1DM
    - 5 years post diagnosis ≥ 15 years: yearly assessment by optho for retinopathy
- T2DM
    - At diagnosis, assessment every 1-2 years
- If present: diagnose severity and monitor at intervals less than 1 year
- Refer:
    - Optho for retinopathy for laser, pharmacological or surgical treatment
    - Review glycemic, BP and lipid control, adjust treatment to reach targets

Neuropathy

- Test with a 10g monofilament on dorsal aspect of great toe bilaterally or vibration sensation with 128 Hz tuning fork starting at diagnosis of T2DM, annually after. For T1DM screening should begin after 5 years post-pubertal duration of diabetes
- Treat with intensified glycemic control to prevent onset and progression
- May use anticonvulsants, antidepressants, topical nitrate spray, opioids if not responsive

Chronic Kidney Disease

- Screening w random urine albumin: creatinine ratio with serum creatinine converted to an eGFR starting at diagnosis of T2DM or 5 years after diagnosis in T1DM, repeated yearly
- Diagnosis of CKD:
  - eGFR <60 and/or random ACR $\geq$ 2.0 mg/mmol on at least 2/3 samples over a 3 month period
- Treat with ACEi or ARB
  - Patients should be treated with an ACEi or ARB should be monitored with a serum Cr and K+ level at baseline, within 1-2 weeks of initiation or titration of therapy and during times of acute illness
- Adults with DM and CKD need to be given sick day list of meds to avoid
- May consider SGLT2i for people with T2DM and clinical CVD with eGFR >30
- Refer to nephrology if
  - Chronic, progressive loss of kidney function
  - Urine ACR persistently > 60mg/mmol
  - eGFR <30 mL/min
  - Unable to remain on renal protective therapies due to adverse effects
  - Unable to achieve target BP

Hypogonadism in Men with DM

- Hypogonadotropic hypogonadism is common in men with T2DM -> prevalence up to 40%
- Hypogonadal men with diabetes have a higher risk of CV mortality
- Screening for symptomatic hypogonadism in men with T2DM is recommended
  - Test with morning serum total testosterone drawn before 11 AM
- Refer
  - To fertility expert if interested in fertility options

Other Referrals

- Endocrinology
  - If poor control of sugars despite optimal therapy and lifestyle changes or if frequent hyperglycemia or hypoglycemia or if concomitant endocrine disorders
- Neurology or physiatry
  - If any stroke or neuro symptoms including peripheral neuropathy
- Vascular surgery
  - If any need for assessment of PVD and potential treatment
- GI
  - May consider screening for celiac disease in T1DM

Foot Ulcers

- Foot exams should be done at least annually and more frequently for those at high risk
- Assess for: neuropathy, skin changes, peripheral arterial disease, structural abnormalities
- People at high risk should receive foot care education and professionally fitted footwear
- Refer
  - People with foot injuries or complications should be referred to health care professionals trained in foot care
  - Refer for assessment and management if needed for any foot ulcers to prevent recurrent ulcers and amputation
  - Refer for debridement PRN

Sexual Dysfunction

- All adult men with diabetes should be screened for erectile dysfunction with sexual function history
- Current mainstay of therapy: PDE-5 inhibitors
  - If unresponsive: consider investigations for hypogonadism
- Sexual dysfunction may be an early marker of CVD

Prevention Measures: Vaccinations

- Influenza vaccine
- Pneumococcal vaccine
  - Initially when over the age of 18 and again when over the age of 65 (if initial vaccine < 65 years and over 5 years ago), one time over the age of 65
- Herpes zoster vaccine
  - Should consider for patients $\geq$ 60
- Hepatitis B vaccine
  - Recommended for all children and those in high risk groups

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

- 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 (i.e. polyuria, polydipsia, polyphagia, nausea, vomiting)
- A normal or mildly elevated glucose does not rule out DKA in certain conditions
- If a patient is presenting with hyperglycemia, there is often and underlying cause (i.e. an infection, a stressor on the body, insulin omission, or another insult to homeostasis)

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

- ABCs and DEFG (Don't Ever Forget Glucose)
- If comatose-> airway management is important first
- Patients will need fluid, likely in the volume of litres
- DKA requires IV insulin administration
    - CANNOT use subcutaneous insulin for DKA until the anion gap is closed
- Bicarbonate therapy may be considered for extreme acidosis (i.e. pH $\leq$ 7.0)