Laboratory Testing: The Basics

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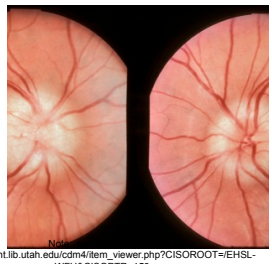
Case

- 48 yr old white female presents with acute loss of vision in her right eye and decreased vision in her left
  - She was scheduled 2 weeks previously for an eye exam on a referral from her PCP but had fallen and was unable to make that appointment
  - She reports that her vision in her right eye seems to be getting worse over the past several weeks.
  - Was diagnosed with diabetes 1.5 years ago
    - BS control has been erratic with range between between 6.7-13.3 (120-240)
    - Last A1C: 9.1

Entrance Skills/Health Assessment

VA: OD: finger count
OS: 20/40 (6/12)
CVF: OD: unable to assess
OS: temporal hemianopsia
Pupils: sluggish reactivity with a 2+ RAPD OD
SLE: corneal arcus noted, no other significant findings
IOP: 16, 16 mmHG OD, OS
DFE: see photos



http://content.lib.utah.edu/cdm4/item_viewer.php?CISOROOT=/EHSL-WFH&CISOPTR=159

Physical Presentation

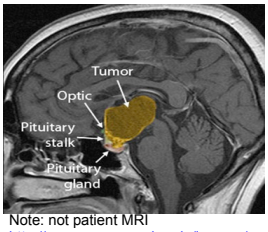
- Upon entering the room I noted that her right hand was twitching
  - I asked her how long that had been going on and she said about 2-3 weeks
  - I asked her if she experienced headaches, to which she said she had bad headaches that even woke her up at night

Referral

- Contacted her PCP who reported that she had examined the patient 3 weeks prior and had not noted any of these findings
- Referred the patient for an immediate MRI
  - wasn't able to be scheduled until the next day

Imaging/Surgery Referral

- MRI revealed large mass in her brain
  - Patient was diagnosed with a Craniopharyngioma
- She was referred for immediate surgery
  - Neurosurgeon reported that she removed a tangerine sized Craniopharyngioma
  - was the largest tumor she has ever removed



Note: not patient MRI
http://neurosurgery.ucla.edu/images/Pituitary%20Program/Craniopharyngioma/Cranio_Sag_Preop_fullylabeled.jpg

Craniopharyngioma

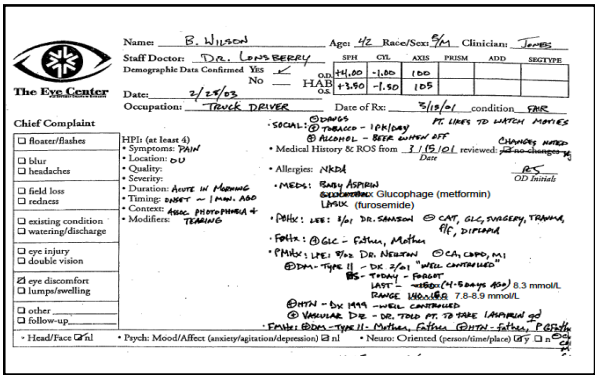
- Presenting signs and symptoms of increased intracranial pressure (80%)
  - Headache
  - Vomiting
  - Papilledema
  - Loss of vision and visual field (60%)
  - Diabetes (15%)
  - Mental deterioration or personality change (26%)

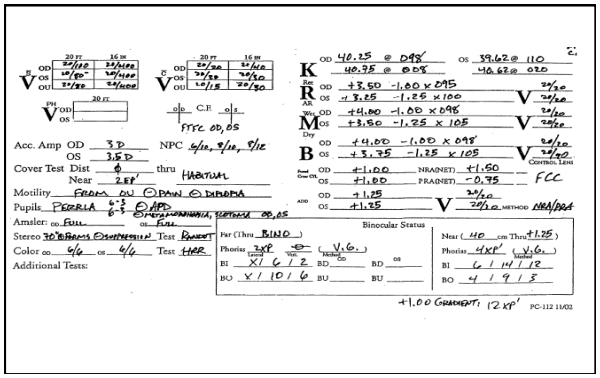
Craniopharyngioma

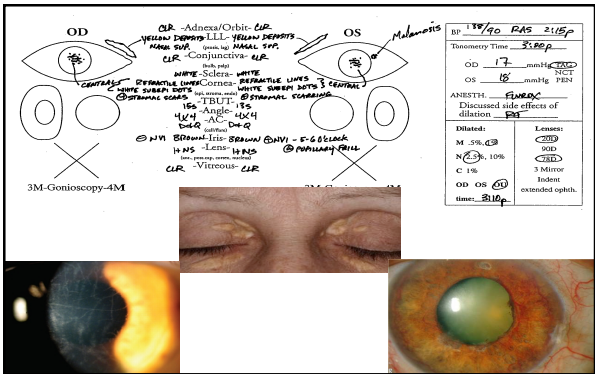
- Treatment:
  - Therapy is often unsatisfactory
  - Total resection often results in major functional deficits
  - Partial resection followed by conventional radiation therapy as a more conservative approach has been recommended

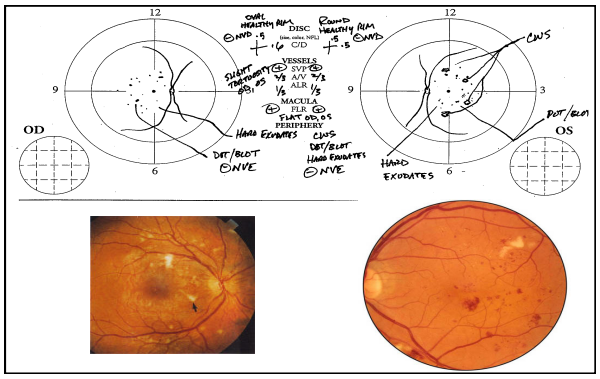
Pituitary Adenomas

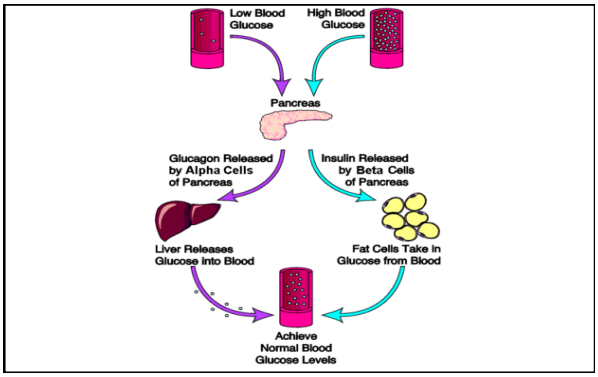
- The most common symptoms include:
  - Headaches
  - Vision problems that cannot be easily explained
  - Menstrual cycle changes in women
  - Mood swings or behavior changes
  - Erectile dysfunction
  - Weight change











In a normal person, the blood glucose concentration is narrowly controlled

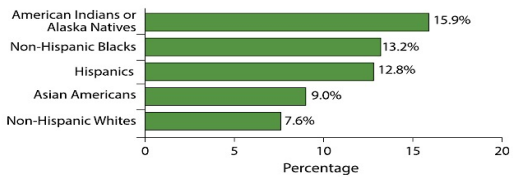
Fasting levels: 4.44-5.0 mmol/L

After meal: 6.67-7.78 mmol/L

Feedback systems for blood glucose rapidly return the blood glucose back to control levels within 2 hours

Important mechanisms for tight control:
- Liver function
- Glucagon & Insulin

Compared to non-Hispanic whites, members of ethnic minority groups are more likely to have diagnosed diabetes



National Health Interview Survey, 2010-2012, and the Indian Health Service's National Patient Information Reporting System, 2012.

Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism

Type 1 diabetes, or insulin-dependent diabetes mellitus (IDDM)

Type 2 diabetes, or non–insulin-dependent diabetes mellitus (NIDDM)

Gestational Diabetes

Other causes: medication, neonatal diabetes, chemical-induced diabetes

DM Type I is caused by autoimmune destruction of β cells in the pancreatic islets

3–5% of cases of diabetes mellitus and usually presents in children

Autoantibodies detected in 85-90% of DM I

However, a small minority of these patients have no known etiology (idiopathic DM)
- Most are of African or Asian ancestry
- No evidence of autoimmunity
- Strong family history

The risk factors for the development of DM I are environmental and genetic

Genetic risk

0.4% risk with no family history

30% risk with both parents Dx with DM I

Environmental risk

Demonstrated in a increase in the incidence of DM Type I in multiple populations

Blood Sugar

- Throughout a 24 hour period blood sugar typically maintained between 3.9-7.8 mmol/L (70-140 mg/dL)
- [A1c (%) x 1.59] – 2.59 = average Blood Glucose (in mmol/L)

DIAGNOSIS OF PREDIABETES & DIABETES

Test	Result	Dysglycemia category
FPG (mmol/L) No caloric intake for at least 8 hours	6.1 – 6.9	IFG
	≥7.0	Diabetes
2hPG in a 75 g OGTT (mmol/L)	7.8 – 11.0	IGT
	≥11.1	Diabetes
A1C (%) Standardized, validated assay, in the absence of factors that affect the accuracy of A1C and not for suspected type 1 diabetes	6.0 – 6.4	Prediabetes
	≥6.5	Diabetes
Random PG (mmol/L)	≥11.1	Diabetes

Diabetes Lab Testing

- Comprehensive medical panel will include:
  - Serum glucose
  - Electrolytes
  - Liver enzymes
  - Kidney function:
    - BUN and creatinine
      - Elevated in renal failure
    - Glomelular filtration rate
      - Reduced in chronic kidney disease/renal failure

Kidney function

- Urinalysis can be used in conjunction with blood testing to help confirm systemic etiology of conditions
  - **Urine Glucose**
    - Any glucose in the urine is abnormal
  - **Urine Protein**
    - Proteinuria is an important indicator of renal disease
  - **Urine Ketones**
    - Ketones are byproducts of body fat metabolism formed in the liver
    - Ketonuria occurs in patients with diabetes

Kidney Function Tests:

Serum Creatinine:

- waste product that comes from the normal wear and tear on muscles of the body.
  - Kidney impairment results in rise of creatinine level in the blood

BUN (blood urea nitrogen):

- If kidneys cannot filter wastes out of the blood due to disease or damage, then the level of urea in the blood will rise

Liver Tests

- Liver tests (LTs) are blood tests used to reflect the presence of damage or inflammation.
- **alanine aminotransferase (ALT)** and aspartate **aminotransferase (AST)** are the most commonly used tests
- These enzymes normally found in the blood when liver cells are injured.

Liver Tests

- The ALT is felt to be a more specific indicator of liver inflammation as AST is also found in other organs such as the heart and skeletal muscle.
- In acute injury to the liver, as in viral hepatitis, the level of the ALT and AST may be used as a general measure of the degree of liver inflammation or damage.

Liver Tests

- Bilirubin is the main bile pigment in humans which, when elevated causes the yellow discoloration of the skin called jaundice.
  - the bilirubin may be elevated in many forms of liver or biliary disease, it is relatively non-specific
- Allbumin is a major protein which is formed by the liver.
  - chronic liver disease causes a decrease in the amount of albumin produced

Blood Chemistry: Lipid Profiles

Consists of:

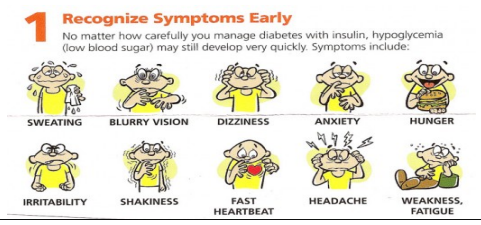
- Serum lipids,
- Cholesterol,
  - High density lipoproteins (HDL) – "good" cholesterol
  - Low density lipoproteins (LDL) – "bad" cholesterol
  - Very-low density lipoproteins (VLDL) – dangerous cholesterol
- triglycerides

Current Recommended Lipid Levels

Cholesterol Levels		
	US (mg/dL)	Canada (mmol/L)
Total Cholesterol		
Ideal	<200	<5.2
Borderline high	201-239	5.2-6.1
High	<240	<6.2
LDL Cholesterol		
Ideal	<100	<2.6
Middle range	100-159	2.7-4.1
High	160-189	4.2-4.9
Very high	>190	>4.9/5.0
HDL Cholesterol		
Low	<40	<1.0
High	>60	>1.6

Blood Sugar

- Hypoglycemia is typically defined as plasma glucose 3.9 mmol/L (70 mg/dL) or less
  - patients typically become symptomatic of hypoglycemia at 2.8 mmol/L (50 mg/dL) or less



Action Item

- Optometrists should have a rapid-acting carbohydrate (glucose gel or tablets, sugar-sweetened beverage or fruit juice) in their offices for use with diabetic patients who experience acute hypoglycemia during an eye examination

Hypoglycemia

Always have a rapid-acting carbohydrate in the office (juice, sugared soda, glucose gel) for pts on meds that can cause low blood glucose….

Insulin
Sulfonylureas

15gm CHO will ↑BG ~ 30-40 mg/dl (1.7-2.2 mmol/L)

Hypoglycemia is an acute metabolic complication of diabetes

Mismatching insulin levels to the patient's physiologic state causes hypoglycemia

Sulfonylureas and parenteral insulin are the primary causes of drug-induced iatrogenic hypoglycemia

- <3.89 mmol/L alert the caregiver or patient
- 2.78-3.33 mmol/L symptomatic for hypoglycemia
- 1.11-2.22 mmol/L potentially dangerous

Hypoglycemia can have severe consequences

Deficient supply of glucose to the brain:

- Dizziness, confusion, fatigue, difficulty with speaking, headache, inability to concentrate, seizures, and coma

Triggering the sympatho-adrenal system by hypoglycemia:

- Palpitations, tremor, anxiety, sweating, hunger, paresthesias

To correct for hypoglycemic state, the patient needs an intake of glucose

Most mild or moderate episodes of hypoglycemia can be self-treated by ingestion of fast-acting carbohydrates: glucose tablet, glucose gels, or food

If a patient is unable to ingest food, intravenous administration of glucose is recommended

It takes 10-20 minutes for the blood sugar levels to rise

Mortality rate from hypoglycemia ranges from 4-10%

Type 1 Diabetes Treatment

- The new HbA1c target of less than 7.5% across all pediatric age groups
- The adult HbA1c target of less than 7%
  - Less stringent A1C goals (such as <8%)
    - history of severe hypoglycemia,
    - limited life expectancy,
    - advanced microvascular or macrovascular complications,
    - and extensive comorbid conditions and in those with longstanding diabetes in whom the general goal is difficult to attain
  - <6.5 for recent diagnosed or long life expectancy

Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism

Type 1 diabetes, or insulin-dependent diabetes mellitus (IDDM)

Type 2 diabetes, or non–insulin-dependent diabetes mellitus (NIDDM)

Gestational Diabetes

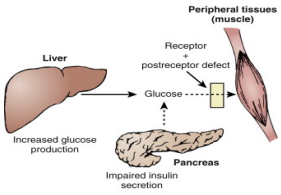
Other causes: medication, neonatal diabetes, chemical-induced diabetes

DM II is caused by dysregulation of insulin release from β cells and insulin resistance in peripheral tissues

Resistance to the actions of insulin in the peripheral tissues: fat, muscle, and liver

Increased glucose production by the liver

Defective insulin secretion, particularly in response to glucose stimulus



Olefsky, Jerrold M. "Type 2 Diabetes Mellitus." *Endocrinology: Adult and Pediatric*. By Christopher J. Hupfeld. 7th ed. N.p.: n.p., 2010. 691-714.

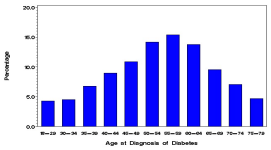
DM II accounts for ~90-95% of DM

Onset: 40-64 yo, average 54 yo

- >1/4 of adults age 65 and older have diabetes

Prevalence: 9%

Incidence rate parallels the rise of the overweight and obese



Data Source: Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, Division of Health Interview Statistics, data from the National Health Interview Survey. Data computed by personnel in CDC's Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion

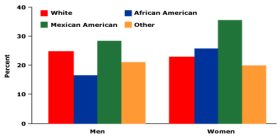
Risk of developing DM II depends on genetics and health factors

- Increases with age
- Lack of physical activity
- Hx of gestational DM or delivering a baby weighing > 9 lbs
- Women with polycystic ovarian syndrome
- Genetics
  - One parent: 40% risk
  - Both parents: 70% risk
- Metabolic Syndrome

Metabolic syndrome is a group of risk factors that raises the risk of health problems like heart disease, diabetes, and stroke

You need a least 3 of the following risk factors to be diagnosed with metabolic syndrome

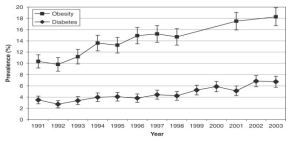
- Large waistline
- High triglyceride levels
- Low HDL
- Hypertension
- High fasting blood sugar



Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002; 287:356.

Obesity is the most important clinical indicator of DM II

- The relationship between DM II and BMI is linear
- Increased risk with body fat distribution to the waist
  - Strong predictor for Asian populations
- Increase in adipose tissue impairs insulin action



Chittleborough, C.r., J.f. Grant, P.j. Phillips, and A.w. Taylor. "The Increasing Prevalence of Diabetes in South Australia: The Relationship with Population Ageing and Obesity." *Public Health* 121.2 (2007): 92-99

Diagnostic tests for DM: A1C

A1C shows the average level of blood glucose over the previous 3 months

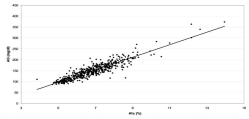
Other names: HbA1C, Glycated hemoglobin, glycosylated hemoglobin, glycohemoglobin

Normal: Less than 6.0%

Pre-diabetes: 6.0-6.4%

Diabetes: 6.5% or higher

Goal is individualized, but commonly <7%



A1C (%)	mg/dl*	mmol/l†
5	97 (76–120)	5.4 (4.2–6.7)
6	126 (100–152)	7.0 (5.5–8.5)
7	154 (123–185)	8.6 (6.8–10.3)
8	183 (147–217)	10.2 (8.1–12.1)
9	212 (170–249)	11.8 (9.4–13.9)
10	240 (193–282)	13.4 (10.7–15.7)
11	269 (217–314)	14.9 (12.0–17.5)
12	298 (240–347)	16.5 (13.3–19.3)

Data in parentheses are 95% CIs. *Linear regression eAG (mg/dl) = 28.7 × A1C − 46.7. †Linear regression eAG (mmol/l) = 1.5944 × A1C − 2.5944.

Nathan, D. M., J. Kuenen, R. Borg, H. Zheng, D. Schoenfeld, and R. J. Heine. "Translating the A1C Assay into Estimated Average Glucose Values." *Diabetes Care* 31.8 (2008): 1473-478.

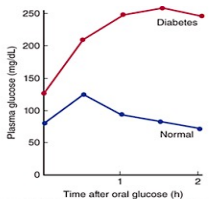
Diagnostic tests for DM: OGTT

Oral glucose tolerance test (OGTT) is commonly done to check for gestational diabetes

Adults are given 75 g of glucose in 300 mL of water

After 2 hours, the plasma glucose is measured:

Normal after OGTT: <7.8 mmol/L
Impaired glucose tolerance: 7.8-11.1 mmol/L
Diabetes after OGTT: > 11.1 mmol/L



Ganong's Review of Medical Physiology, 25e > Endocrine Functions of the Pancreas & Regulation of Carbohydrate Metabolism

Diagnostic test for DM: Fasting BS

Fasting blood sugar can be assessed after 8 hours of fasting

Normal: 3.9-7.8 mmol/L

Impaired fasting glucose (IFG): ≥5.56 to 6.94 mmol/L

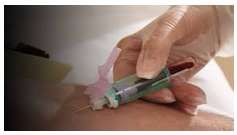
Diabetes: ≥7 mmol/L

If confirmed by another test on a different day unless classic symptoms of DM are present

Diagnostic test for DM: Random Plasma Glucose

This test is typically done to confirm diabetes with severe diabetes symptoms

Random plasma glucose is done at an time to get a "snapshot" of the glucose concentration in the bloodstream



Normal: 3.89-6.1 mmol/L

Diabetes: >11.1 mmol/L and classic symptoms of diabetes

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

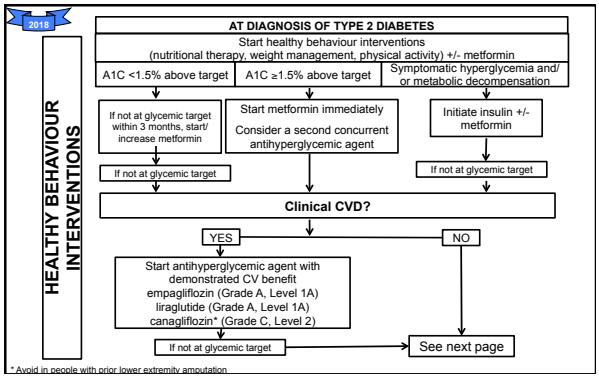
Pharmacotherapy in Type 2 Diabetes Checklist

- ✓ CHOOSE initial therapy based on glycemia
- ✓ START with metformin +/- others
- ✓ INDIVIDUALIZE your therapy choice based on characteristics of the person with diabetes and the agent
- ✓ REACH TARGET within 3-6 months of diagnosis

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Initial choice of therapy

A1C <1.5% over target	Initiate healthy behavior interventions and start metformin if not at target in 3 months OR Start metformin with healthy behavior interventions
A1C ≥ 1.5% over target	Start metformin with healthy behavior interventions AND Consider second concurrent agent



2018

Clinical CVD?

NO

Add additional antihyperglycemic agent best suited to the individual based on the following

CLINICAL CONSIDERATIONS	CHOICE OF AGENT
Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy	DPP-4 inhibitor, GLP-1 receptor agonist or SGLT2 inhibitor
Other considerations: Reduced eGFR and/or albuminuria Clinical CVD or CV risk factors Degree of hyperglycemia Other comorbidities (CHF, hepatic disease) Planning pregnancy Cost/coverage Patient preference	see Renal Impairment Appendix See Table Below

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- Healthy behaviour interventions should be initiated in people newly diagnosed with type 2 diabetes
- If glycemic targets are not achieved within 3 months of initiating healthy behaviour interventions, antihyperglycemic pharmacotherapy should be added
- Dose adjustments and/or additional agents should be instituted to achieve target A1C within 3 to 6 months

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- In people with type 2 diabetes with A1C <1.5% above the person's individualized target, antihyperglycemic pharmacotherapy should be added if glycemic targets are not achieved within 3 months of initiating healthy behaviour interventions
- In people with type 2 diabetes with A1C ≥1.5% above target, antihyperglycemic agents should be initiated concomitantly with healthy behaviour interventions, and consideration could be given to initiating combination therapy with 2 agents

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- Insulin should be initiated immediately in individuals with metabolic decompensation and/or symptomatic hyperglycemia
- Otherwise, metformin should be the initial agent of choice in people with newly diagnosed with type 2 diabetes, unless contraindicated
- Choice of second-line antihyperglycemic agents should be made based on individual patient characteristics, patient preferences, any contraindications to the drug, glucose lowering efficacy, risk of hypoglycemia, affordability/access, effect on body weight, and other factors

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- In people <u>with</u> clinical CVD in whom A1C targets are not achieved with existing pharmacotherapy, an antihyperglycemic agent with demonstrated CV outcome benefit should be added to antihyperglycemic therapy to reduce CV risk

CV, cardiovascular; *CVD*, cardiovascular disease

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- In people <u>without</u> clinical CVD in whom A1C target is not achieved with current therapy, if affordability and access are not barriers, people with type 2 diabetes and their providers who are concerned about hypoglycemia and weight gain may prefer an incretin agent (DPP-4 inhibitor or GLP-1 receptor agonist) and/or an SGLT2 inhibitor to other agents as they improve glycemic control with a low risk of hypoglycemia and weight gain

CVD, cardiovascular disease

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages

- In people receiving an antihyperglycemic regimen containing insulin, in whom glycemic targets are not achieved, the addition of a GLP-1 receptor agonist, DPP-4 inhibitor, or SGLT2 inhibitor may be considered before adding or intensifying prandial insulin therapy to improve glycemic control with less weight gain and comparable or lower hypoglycemia risk

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages for People with Diabetes

- Some people who have type 2 diabetes can achieve their target blood glucose levels with nutrition guidance and physical activity alone, but most also need glucose lowering medications. The decision about which medications are best for you depends on many factors, including your blood glucose level, symptoms, and any other health problems you have. Your health-care provider may even combine medications that act differently on your body to help you control your blood glucose

2018 Diabetes Canada CPG – Chapter 13. Pharmacologic Glycemic Management of Type 2 Diabetes

Key Messages for People with Diabetes

- First-line glucose-lowering medication
- Metformin:
  - generally the first choice for people with type 2 diabetes because of its safety, low cost, and possible heart benefits
  - It works by making your body respond better to insulin so that your body uses insulin more effectively
  - Metformin also lowers glucose production from the liver
  - Nausea and diarrhea are possible side effects and usually go away within 1 to 2 weeks as your body gets used to the medicine
  - It is associated with a low risk of hypoglycemia and does not cause weight gain

Medications are categorized as those that enhance insulin availability and those that enhance insulin action

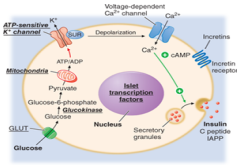
Insulin sensitizers
- Metformin
- Thiazolidinediones
  - pioglitazone & rosiglitazone

Insulin Secretagogues
- Sulfonylureas
  - glipizide, glyburide, and glimepiride
- Meglitinides
  - repaglinide & nateglinide

Dipeptidyl Peptidase-4 (DPP-4) Inhibition
  - Sitagliptin

Glucagon-Like Peptide-1 (GLP-1) Analog
  - Exenatide

Insulin



30 YR WM

- Patient calls from his PCP office asking if we can see him today because he has had red/painful eyes for over a week and has not resolved
- Medical history:
  - Past week has been experiencing painful urination and discharge
  - New sexual partner apprx 10 days ago, who also had developed a red eye
  - Chlamydia and gonorrhea testing were negative
  - Has tested positive for HSV2 but no current flare up

59

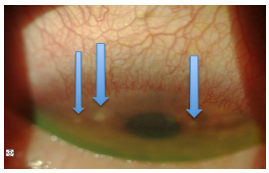
30 YO WM

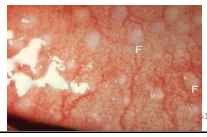
- Medications:
  - In the past week patient:
    - 2 courses of azythromycin (1 gram each)
    - Injection of rocephin
    - Injection of penicillin G
    - Currently taking doxycycline 100 mg bid
    - Valtrex 1 gram 3 times per day for 7 days (d/c 1 day ago)
    - Was on Vigamox qid for 7 days (d/c 1 day ago)
- VA: 6/7.5 (20/25) OD, OS
- Entrance skills unremarkable though some pain on eye movement

60

30 YO WM

- SLE:
  - 2+ injection conjunctival both eyes
  - 1-2+ lid edema
  - Mixed papillary and follicular response
  - 1-2+ diffuse SPK (no staining noted above infiltrates)
  - No cells or flare noted





61

30 YO WM

- AdenoPlus:
  - Performed on the right eye (patient felt that was the worst eye)
  - Negative

62

30 YO WM

- Started patient on the miracle drop
  - Tobradex 4 times per day and scheduled patient to come back the next day
- 1 day f/u
  - Patient was feeling better
  - Less redness and much reduced photophobia and discomfort
  - No improvement on painful urination or discharge and is now seeing blood in his urine
  - Continue tobradex 4 times per day and RTC in 4 days for f/u with dilation and told to contact PCP to update on the blood in the urine

63

30 YO WM

- 4 day f/u:
  - Patient says his eyes are doing great and that all of his urogenital problems abruptly stopped on Saturday
  - Discussion with PCP: Kidney stone
  - What was going on with the eye?
    - Viral conjunctivitis likely EKC

What did we learn from this?

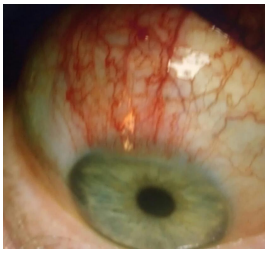
64

STI Lab Testing

- STI's:
  - Chlamydia and gonorrhea: nucleic acid amplification test (NAAT)
  - Syphilis:
    - Non-treponemal: CMIA/RPR/VDRL
    - Treponemal: FTA-Abs/VDRL

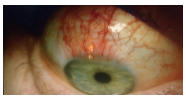
Question

A 50YOWF patient presents with eye pain and the following presentation. What lab testing should be considered first?



Superior Limbic Keratoconjunctivitis (SLK)

- inflammation of the superior bulbar conjunctiva with predominant involvement of the superior limbus
- adjacent epithelial keratitis and a papillary hypertrophy of the upper tarsal conjunctiva.
- association between thyroid abnormalities and SLK
  - 33% of patients with superior limbic keratoconjunctivitis (SLK) has Graves' disease



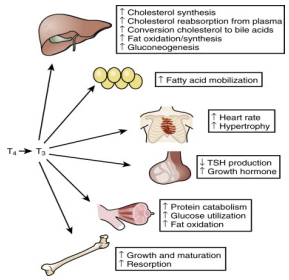
Superior Limbic Keratoconjunctivitis (SLK)

- mimicking disorder has been encountered in soft contact lens (SCL) wearers, typically with exposure to thimerosal-preserved solutions
- middle-aged people and women are predominantly affected
- Much higher prevalence in Graves patients than normal population
- Treatment: aggressive lubrication, cyclosporine A, surgery

Actions of Thyroid Hormone

Thyroid hormones exert an effect on almost all tissues

- Increase metabolism
- Decrease serum cholesterol levels
- Increase in lipolytic events
- Increase cardiac contractions and heart rate
- Negative feedback on TSH and TRH production. Increase GH.
- Increase skeletal muscle expenditure and muscle catabolism
- Required for normal bone growth brain development, and normal skin function



DeGroot, Leslie J., and J. Larry. Jameson. "Thyroid Hormone Action." *Endocrinology: Adult and Pediatric*. Philadelphia: Saunders/Elsevier, 2010

Hyperthyroidism

Epidemiology

- More common in women than in men 5-10x
- Peaks in 3rd to 4th decade
- Prevalence:
  - Subclinical 10-40/1000
  - Overt 0.5-1/1000

Associated Conditions

- Myasthenia gravis
- SLE
- Type I DM
- Rheumatoid Arthritis

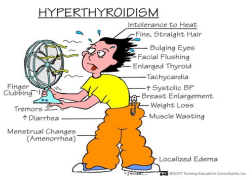
Hyperthyroidism

Causes

- Graves disease (most common cause)
- Toxic multinodular goiter
- Toxic uninodular goiter
- Medications: Amiodarone
- Pituitary adenoma (rare)

Hyperthyroidism Symptoms

- Anxiety/irritability
- Weakness
- Tremors
- Difficulty sleeping
- Palpitations
- Increased bowel movements
- Fatigue
- Weight loss
- Hyperkinetic movements
- Heat intolerance



Hyperthyroidism

Signs/Symptoms

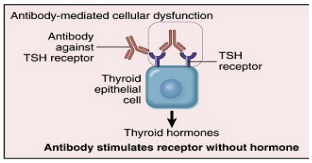
- Increased metabolism, elevating basal body temperature
- Tachycardia and cardiac hypertrophy
- Fatigue, dyspnea
- Upper and lower lid retraction
- Warm, moist skin
- Thin hair
- Physical development is normal but fertility is reduced
- Plummer's nails (onycholysis)
- Tremor and insomnia

Mangione, Salvatore. *Physical Diagnosis Secrets*. 2nd ed. N.p.: Elsevier, 2008.

Graves' Disease is an autoimmune disorder

Thyroid stimulating hormone receptor autoantibodies (TRAbs) stimulate the thyroid to secrete T_4 and T_3

- Classic presentation: hyperthyroidism, diffuse goiter, exophthalmos



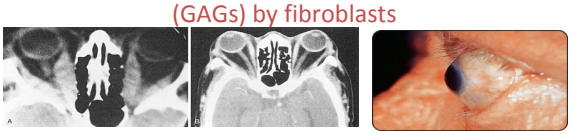
Graves' Ophthalmopathy

a.k.a. thyroid eye disease, graves' orbitopathy

Clinical signs or symptoms of ophthalmopathy are present in ~50% of patient's with Graves' disease with a wide variability of disease severity

- Although a systemic disease, ocular involvement can be asymmetric
- Smoking increases risk of developing ophthalmopathy by 7-8 times

EOMs and connective tissues are infiltrated by lymphocytes leadings to inflammation, edema, and excess secretion of glycosaminoglycans (GAGs) by fibroblasts

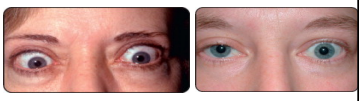


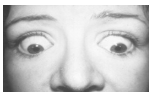
Proptosis secondary to increase in volume of EOMs, adipose tissue, and connective tissue in the orbit

Kanski, Jack K. "Orbit." Clinical Ophthalmology: A Synopsis. 2nd ed. N.p.: Elsevier, 2009. 93-112.
Peter Laurberg, and Rebecca S. Bahn. "Hyperthyroid Disorders." *Williams Textbook of Endocrinology*. By Terry F. Davies. 13th ed. N.p.: n.p., 2015. 369-415

Graves' ophthalmopathy frequently presents with lid retraction

- Kocher's sign: lid retraction on attentive fixation
- Dalrymple's sign: lid retraction in primary gaze
- Van Graefe's sign: lid lag on downgaze
- Conjunctival hyperemia and chemosis

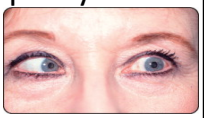


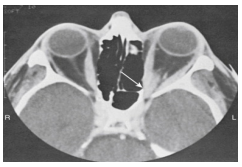


Kanski, Jack K. "Orbit." *Clinical Ophthalmology: A Synopsis*. 2nd ed. N.p.: Elsevier, 2009. 93-112.
Mangione, Salvatore. *Physical Diagnosis Secrets*. 2nd ed. N.p.: Elsevier, 2008.

Graves' Ophthalmopathy

- Diplopia
- Increased IOP
- Optic nerve compression by surrounding structures
  - Optic edema and subsequent atrophy
- Decrease visual acuity
  - Optic atrophy, dry eyes





Bahn, Rebecca S. "Graves' Ophthalmopathy." *Endocrinology: Adult and Pediatric*. By Henry B. Burch. 2016. 1465-477.
Kanski, Jack K. "Orbit." Clinical Ophthalmology: A Synopsis. 2nd ed. N.p.: Elsevier, 2009. 93-112.

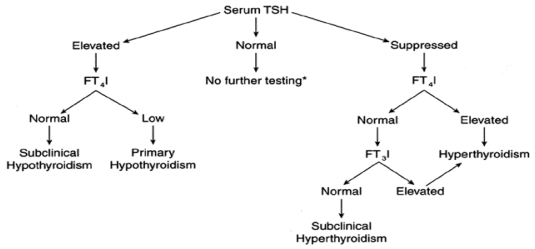
Diagnosis of hyperthyroidism is based off presenting signs/symptoms and lab tests

Patient history and signs/symptoms

Lab tests:

- TSH (abnormal then test t4/t3)
- T_4 & T_3
- TRAb assay (receptors)
- Radioactive iodine uptake (RAIU) with thyroid imaging

Thyroid Testing Algorithm



Thyroid Gland

- T4 is the major hormone produced but has low activity in stimulating metabolism
  - T_4 has a longer half-life, much higher levels of T_4 than T_3 are in the circulation
  - T_4 considered a prohormone and is metabolized primarily in liver (87% of T3 in circulation is formed from T4)
- T3 is 3-4 times metabolically more active than T4

Testing recommendations?

Patients with no symptoms of thyroid disease and no obvious risk factors have a low likelihood of thyroid disease.

In most situations, TSH is the more sensitive indicator of thyroid status. If further thyroid function tests are indicated they can be subsequently added by the laboratory, or the GP usually without the need to retest the patient.

Key points about Grave's disease:

- ❖ Most common cause of eyelid retraction
- ❖ Most common cause of bilateral or unilateral proptosis.
- ❖ More common in women
- ❖ Associated with hyperthyroidism in 90% of patients; 6% are euthyroid
- ❖ Smoking is associated with increased risk and severity of ophthalmopathy.

Grave's disease/Thyroid Ophthalmopathy

Clinical signs

- Eyelid retraction- most common sign
- Lid lag
- Proptosis
- Restrictive extraocular myopathy
- Optic neuropathy

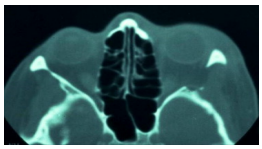
Other clinical features:

- Most frequent ocular symptom is pain or discomfort (30%)- often the result of dry eyes
- Diplopia- 17%
- Lacrimation/photophobia- 15-20%
- Blurring of vision- 7.5%

Proper management of hyperthyroidism requires co-management with other specialties

Team approach: endocrinology, radiology, radiotherapy, otolaryngology, neurosurgery, ophthalmology/optometry

- Methimazole (antithyroid drug)
- Oral/IV steroids
- Radiotherapy
- Surgical therapy
  - Orbital decompression
  - Cosmetic management



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