Clinical Survival Guide

Unofficial Version 2019
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We sincerely thank all our medical student and physician editors for their hard work and dedication to this project. They are listed below.

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Hematology & Immunology
1.1 Vitamin B12 (Cobalamin) Deficiency

Typical Patient
- Elderly patient with neurological symptoms (see below)
- Adult with macrocytic anemia

Cause/Etiology (4 main categories)
Vitamin B12 → binds intrinsic factor secreted by gastric parietal cells → absorbed in terminal ileum
Takes 3-4 years to deplete B12 stores if no vitamin B12 is being supplied or absorbed
1. **Diet** — strict vegan, malnutrition, vegetarian in pregnancy, EtOH abuse
2. **Gastric** — gastritis, autoimmune mucosal atrophy, pernicious anemia, post-gastrectomy
3. **Intestinal Absorption** — crohn’s, celiac disease, pancreatic insufficiency, stagnant bowel, tapeworm, ileum resection, drugs
4. **Genetic** — transcobalamin II deficiency

Symptoms/Clinical Presentation
- Lemon yellow complexion (pallor and jaundice)
- If deficiency is severe, it can lead to thrombocytopenia, which can cause ecchymosis or purpura
- Glossitis: beefy, red, sore tongue
- Neurological symptoms
  - Cerebral – confusion, delirium, dementia
  - Cranial nerves – optic atrophy
  - Spinal cord – posterior columns: decreased vibration sense, proprioception and 2-point discrimination; pyramidal tracts: spastic weakness, hyperactive reflexes
  - Peripheral neuropathy – usually symmetrical affecting lower limbs more than upper limbs

Physical Exam
- Examine patient’s complexion
- Look for signs of thrombocytopenia
- Look at tongue for glossitis
- Perform neurologic exam

Investigations
- Macrocytic (oval) Anemia, reticulocyte count (inappropriately normal/low), blood smear → +/- hypersegmented neutrophils
- +/- neutropenia and thrombocytopenia (pancytopenia when severe)
- LDH/bilirubin (elevated due to break down of cells in bone marrow)
- Serum B12 and folate testing (often concurrently low)
- Serum or urine methylmalonic acid (MMA) levels (elevated)
- Serum or urine homocysteine levels (elevated)
- Bone marrow test (rare to do this)
  - Hypercellular bone marrow
  - Megaloblastic RBC maturation in bone marrow, giant band cells, hypersegmented neutrophils

Management/Treatment
- Identify the cause of the deficiency and address it
- Vitamin B12 supplements:
  - Oral supplementation (PO if intestinal absorption is intact). Consider limited high-dose oral supplementation initially (2 mg daily). Monitor potassium if anemia moderate/severe
  - Parenteral Intramuscular (IM) injection

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1. “The Anemias of Underproduction”, Isabelle Bence-Bruckler, October 5 2015, uOttawa Faculty of Medicine
2. Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.2 Iron Deficiency Anemia

Typical Patient
- Woman of childbearing age
- Most common cause of anemia worldwide

Cause
- Poor oral intake – rarely the sole cause
- Decreased gastrointestinal (GI) absorption – rarely the sole cause
- Increased iron requirement (ex. adolescence, pregnancy, lactation)
- Excessive iron loss (ex. blood loss: ulcer, gastritis, malignancy, menorrhagia)

Symptoms/Clinical Presentation
- Iron deficiency may cause fatigue before anemia develops
- Symptoms of anemia – fatigue, malaise, weakness, dyspnea, decreased exercise tolerance, palpitations, headache, dizziness, syncope
- Patient may present with a history of excessive bleeding; lack of overt bleeding does not rule out bleeding (e.g. occult GI bleeding from malignant or benign lesion)
- Pica – appetite for non-food substances (ice, dirt, paint, etc.)

Physical Exam
- Pallor
- Brittle hair and nails, and nail changes (koilonychia or spoon nails)
- Angular stomatitis, dysphagia, glossitis
- Flow murmur

Investigations
- Microcytic anemia, reticulocyte count (inappropriately normal/low), blood smear
- Iron indices
  - Serum iron
  - Total iron binding capacity
  - Transferrin saturation
  - Serum ferritin (ferritin is an acute phase reactant; therefore, may need to consider iron deficiency even in setting of reportedly normal range ferritin)
- Bone marrow sample stained for iron (Prussian Blue) – gold standard, rarely necessary for diagnosis
- Rule out nutritional deficit, gastrointestinal and genitourinary disease in iron deficiency anemia

Management/Treatment
- Identify the cause of the deficiency and address it; most importantly, consider whether investigations for GI malignancy are warranted
- Oral iron supplementation (tablets or liquid)
- Intravenous (IV) iron – if patient cannot tolerate or absorb oral iron (has increased adverse effects)
- Important to monitor patient’s response to iron supplementation

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3 “The Anemias of Underproduction”, Isabelle Bence-Bruckler, October 5 2015, uOttawa Faculty of Medicine
4 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.3 Hereditary Spherocytosis ⁵,⁶,⁷,⁸

Typical Patient
N/A

Cause
- Inherited deficiency/abnormality in the RBC membrane cytoskeletal proteins
- RBCs are spherically-shaped and less flexible; they are sequestered in the spleen, where they are destroyed (extravascular hemolysis)
- Autosomal dominant inheritance in majority of patients

Symptoms/Clinical Presentation
- General Symptoms of anemia – fatigue, pallor, etc.
- Jaundice, splenomegaly
- Cholelithiasis

Physical Exam
- Jaundice, splenomegaly

Investigations
- Blood film shows spherocytes - Loss of central pallor on blood smear (be familiar with the appearance)
- Increased osmotic fragility of RBCs
- Molecular analysis for genes encoding membrane proteins (ex. spectrin, ankyrin)

Management/Treatment
- Supportive care: consider folic acid
- In severe cases, splenectomy + vaccination against pneumococcus, meningococcus and *H. influenzae* type b (avoid in early childhood).

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⁵ “Hematopoiesis II: Red Cell and Platelets”, -Ruth Padmore, ND, uOttawa Faculty of Medicine
⁶ “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
⁷ Image from “vetbook.org”
⁸ Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.4 Hereditary Elliptocytosis\textsuperscript{9,10,11,12}

Typical Patient
N/A

Cause
- Inherited deficiency/abnormality in the RBC membrane cytoskeletal proteins
- Abnormality in spectrin interaction with other membrane proteins
- Usually autosomal dominant

Symptoms/Clinical Presentation
- Symptoms of anemia – fatigue, pallor, etc.
- Hemolysis (usually mild)

Physical Exam
- N/A

Investigations
- Blood film shows elliptocytes (25-75%)

Management/Treatment
- Supportive care: consider folic acid
- In severe cases, splenectomy + vaccination against pneumococcus, meningococcus and \textit{H. influenzae} type b (avoid in early childhood)

\textsuperscript{9} “Hematopoiesis II: Red Cell and Platelets”, Ruth Padmore, ND, -uOttawa Faculty of Medicine

\textsuperscript{10} “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine

\textsuperscript{11} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.

\textsuperscript{12} Image from “Medscape.com”
1.5 Folate Deficiency \(^{13,14}\)

**Typical Patient**
- Pregnant women, alcoholics, elderly patients, bariatric surgery, poor nutrition

**Cause (4 categories)**
Lack of folate (also known as vitamin B9), which takes weeks to months to develop depending on baseline stores. A well-balanced diet should contain enough folate to prevent folate deficiency, except during pregnancy. Folate supplements should be started at least one month prior to conception, and should be taken for the first trimester. This will help to prevent neural tube defects.

1. **Diet/deficiency** – alcoholism, substance abuse, elderly/infants, poor intake
2. **Malabsorption** – celiac disease, inflammatory bowel disease, infiltrative bowel disease, short bowel syndrome
3. **Drugs**
4. **Increased demand** – pregnancy, hemolysis, prematurity, hemodialysis, exfoliative dermatitis/psoriasis

**Symptoms/Clinical Presentation**
- Lemon yellow complexion (pallor and jaundice → latter secondary to hemolysis)
- If deficiency is severe, it can lead to thrombocytopenia which can cause ecchymosis or purpura
- Glossitis: beefy, red, sore tongue
- Angular stomatitis/cheilosis (corners of mouth inflamed)
- No neurological symptoms (unlike vitamin B12 deficiency)

**Physical Exam**
- Examine patient’s complexion
- Look for signs of thrombocytopenia
- Look at mouth and tongue for glossitis and/or angular stomatitis

**Investigations**
- Macrocytic anemia, reticulocyte count (inappropriately normal/low), blood smear
- +/- neutropenia and thrombocytopenia (pancytopenia when severe)
- LDH/bilirubin may be elevated
- Serum B12 – to check for concomitant deficiency
- Serum or urine homocysteine levels (elevated)
- Response to folate
- Bone marrow test (rarely necessary): same as B12 deficiency
  - Hypercellular bone marrow
  - Megaloblastic RBC maturation in bone marrow, giant band cells, hypersegmented neutrophils

**Management/Treatment**
- Identify cause if possible and treat it
- Folic acid supplementation – oral (PO) 1-5 mg for 1-4 months then 1 mg PO maintenance if cause is not reversible

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\(^{13}\) “The Anemias of Underproduction”, Isabelle Bence-Bruckler, October 5 2015, uOttawa Faculty of Medicine

\(^{14}\) Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.6 Sickle Cell Anemia\textsuperscript{15,16}

Typical Patient
- Patient from Equatorial Africa, Middle East, parts of India and Mediterranean – regions where there is a high incidence of \textit{Plasmodium falciparum} malaria (mutation has protective effect)

Cause
- Co-dominant inheritance
- Single amino acid substitution in the beta globin gene: glutamic acid to valine
- Heterozygote – HbAS (sickle cell trait) vs. homozygote – HbSS (sickle cell disease)
- Intracorpuscular hemolytic anemia

Symptoms/Clinical Presentation
- Vaso-occlusive phenomena: pain crises precipitated by fever, dehydration, infection, stress, pregnancy – can affect lungs (acute chest syndrome), brain (stroke), spleen; venous thromboembolism, priapism
- Infection
- Renal complications: hematuria, chronic kidney disease, renal medullary carcinoma

Physical Exam
- Dactylitis at young age
- Ulcers around the medial malleolus

Investigations
- Genetic testing (not required)
- Blood smear – normocytic normochromic RBCs, Howell-Jolly bodies, sickled cells, thrombocytosis due to functional asplenia
- Increased reticulocyte count, decreased haptoglobin
- Hemoglobin electrophoresis – visually detect HbS
- Chromatography – see a peak representing HbS

Management/Treatment
- Supportive care (i.e. during vaso-occlusive crises)
- Hydroxyurea to increase HbF levels
- Transfusions +/- chelating agent
- RBC exchange
- Bone marrow transplant if severe

\textsuperscript{15} “Hemoglobinopathies”, Lothar Huebsch, October 13 2015, uOttawa Faculty of Medicine
\textsuperscript{16} “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
1.7 Hemoglobin C

Typical Patient
- 40% of patients from areas in Africa

Cause
- Mutation on the beta gene on chromosome 11 – glutamic acid to lysine at position 6
- Homozygote CC is symptomatic, heterozygote AC is asymptomatic

Symptoms/Clinical Presentation
- HbSC – sickling syndrome, typically milder than HbSS
- HbS/β-thalassemia – depends on the quantity of β produced
- Hemolytic anemia, splenomegaly, cholecystitis

Physical Exam
- Assess splenomegaly

Investigations
- Blood smear: target cells >80%, spherocytes, red cell inclusion bodies
- Hemoglobin electrophoresis to detect HbC
- Chromatography – peak corresponds to HbC
- Confirm diagnosis by beta gene mapping

Management/Treatment
- Treat symptomatically based on mutations (i.e. treat for sickle cell or thalassemia)
- Consider bone marrow transplant if severe

---

17 "Hemoglobinopathies", Lothar Huebsch, October 13 2015, uOttawa Faculty of Medicine
1.8 Thalassemia

Typical Patient
- Patient typically from Northern Africa, Asia, or Mediterranean

Cause
- Alpha thalassemia – mutation on alpha gene located on Chromosome 11
  - $\alpha\alpha/\alpha\alpha = \text{normal}$
  - $\alpha\alpha/\alpha- = \text{silent carrier}$
  - $\alpha\alpha/- \text{ or } \alpha-\alpha- = \text{minor}$
    - $\alpha-\alpha- \text{ (trans mutation)}$
    - $\alpha\alpha/- \text{ (cis mutation, more common in individuals of Asian descent, risk of hydrops if partner has same mutation)}$
  - $\alpha-/- = \text{HbH}$
  - $--/-- = \text{Hb Bart (hydrops fetalis)}$
- Beta thalassemia – mutation on the beta gene located on Chromosome 16
  - $\beta\beta = \text{normal}$
  - $\beta^*\beta^* \text{ or } \beta^0\beta^0 = \text{Minor}$
  - $\beta^+\beta^+ = \text{intermedia}$
  - $\beta^0\beta^+ \text{ or } \beta^+\beta^0 = \text{major}$
- Hemoglobin chains are not made in the right amounts
- Microcytic hemolytic anemia, intracorpuscular hemolytic anemia, extravascular hemolytic anemia

Symptoms/Clinical Presentation
- Severity depends on the quantity of abnormal genes
- Beta thalassemia
  - Minor – asymptomatic
  - Intermedia – symptoms of iron overload (from chronic transfusions) at 20-40yo
  - Major – hepatosplenomegaly, pallor, jaundice, symptoms of iron overload at 2yo

Physical Exam
- Bone enlargement (axial skeleton, skull) due to marrow expansion

Investigations
- Increase in HbA₂ in beta thalassemia
- Increase in HbH in alpha thalassemia
- Blood smear – hypochromia, microcytosis, intracellular precipitate, extravascular hemolysis

Management/Treatment
- Chronic transfusions with chelating agent
- Bone marrow transplant
- Genetic consultation

---

18 “Hemoglobinopathies”, Lothar Huebsch, October 13 2015, uOttawa Faculty of Medicine
1.9 Warm Autoimmune Hemolytic Anemia

Typical Patient
- Autoimmune disease

Cause
- Antibodies (IgG) coating RBCs
- Extravascular hemolysis – phagocytes in spleen have Fc receptors for RBC destruction
- Triggers: medications, connective tissue diseases (ex. lupus), malignancies of the immune system (lymphoma, chronic lymphocytic leukemia (CLL)), idiopathic (50%)

Symptoms/Clinical Presentation
- Shortness of breath
- Pallor
- Jaundice
- Hemoglobinuria in severe cases

Physical Exam
- Assess splenomegaly

Investigations
- Low hemoglobin
- Blood Smear – spherocytes
- Coombs test positive (negative in <3%)
- High reticulocyte count
- High LDH
- High bilirubin
- Low haptoglobin

Management/Treatment
- Treat triggers
- Supportive transfusions if needed
- Glucocorticoids (ex. prednisone)
- Consider IVIG
- Second line: consider splenectomy, rituximab
- Folic acid

---

19 “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
1.10 Cold Autoimmune Hemolytic Anemia

**Typical Patient**
- Autoimmune disease

**Cause**
- Antibodies (IgM) that are activated at temperatures below 37°C
- IgM antibodies fix and activate the complement cascade
- Intravascular hemolysis –RBCs are destroyed in the circulation
- Triggers: infection, lymphoma, idiopathic

**Symptoms/Clinical Presentation**
- Shortness of breath
- Jaundice
- Acrocyanosis
- Hemoglobinuria

**Physical Exam**
- N/A

**Investigations**
- Low hemoglobin
- Blood Smear – agglutination (grape like appearance)
- Coomb’s test positive : positive anti-C3, usually negative anti-IgG
- Cold agglutinin titer and thermal range
- High reticulocyte count
- High LDH
- High bilirubin
- Low haptoglobin

**Management/Treatment**
- Treat underlying cause
- Avoidance of cold
- Supportive transfusions (warmed!) if needed
- Folic acid
- Plasmapheresis
- Consider Rituximab containing regimens for severe hemolysis

---

20 “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
1.11 Thrombotic Thrombocytopenic Purpura (TTP)\textsuperscript{21}

**Typical Patient**
- Immune (i.e. acquired, antibodies against ADAMTS13)
- Absence (i.e. congenital)
- Type of microangiopathic hemolytic anemia
  - With thrombocytopenia

**Cause**
- Decrease in ADAMTS13 (plasma protease that cleaves von Willebrand Factor (vWF) polymers) leading to an excess of large vWF multimers

**Symptoms/Clinical Presentation**
- Pentad of features
  - Thrombocytopenia (100%)
  - Microangiopathic hemolytic anemia (100%)
  - Fever (61%)
  - Renal impairment (44%)
  - Neurologic dysfunction (78%)
- Triad (anemia, thrombocytopenia, neurologic) in 78%
- Full pentad seen in 34% of patients
- Platelet rich thrombi

**Physical Exam**
- See above

**Investigations**
- Blood smear showing lysed RBCs (schistocytes) and thrombocytopenia
- Normal INR/ PTT

**Management/Treatment**
- Mainstay of treatment: plasma exchange using cryosupernatant – remove antibodies to ADAMTS13, remove vWF polymers, and replace with ADAMTS13
- Consider glucocorticoids.

\textsuperscript{21} “Abnormal Hemostasis”, Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.12 Disseminated Intravascular Coagulation (DIC)\(^{22}\)

**Typical Patient**
- Conditions associated with DIC: infections, obstetrical complications, tumours, trauma

**Cause**
- Tissue factor gets released into the circulation
- Activation of the coagulation cascade and the clot termination cascade at the same time, resulting in excessive bleeding with no fibrinogen left in the circulation

**Symptoms/Clinical Presentation**
- Oozing from venipuncture site
- Bleeding from mouth and nose
- Thrombosis leads to decreased perfusion of organs and tissues, which leads to end organ damage

**Physical Exam**
- N/A

**Investigations**
- INR – should be high
- PTT – should be high
- Fibrinogen levels – should be low
- Fibrinogen Degradation Products – should be high
- Platelet count – should be low
- Blood smear – red cell fragments (schistocytes)

**Management/Treatment**
- Treat the underlying cause
- Cryoprecipitate – to replace fibrinogen
- Supportive transfusion as necessary

---

\(^{22}\)“Abnormal Hemostasis”, Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.13 G6PD Deficiency

Typical Patient
- 10% of black males in US
- Patients from Mediterranean, Arab countries, South East Asia

Cause
- X-linked recessive
- RBCs deficient in G6PD are susceptible to free radical formation – premature destruction of the RBC membrane, hemoglobin, etc.

Symptoms/Clinical Presentation
- Hemolytic crises in response to illness, certain drugs (salicylates), certain foods (fava beans), diabetic ketoacidosis

Physical Exam
- N/A

Investigations
- Blood smear: bite cells, Heinz bodies
- Genetic testing
- G6PD assay: may be normal in acute hemolytic episode resulting in false negative result

Management/Treatment
- Treat hemolytic crises: hydration, transfusion as necessary
- Remove inciting agent

---

23 “Hemolytic Anemia”, Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
1.14 Approach to Hemolytic Anemia

Smear
- Look for cells that indicate a specific type of hemolytic anemia (i.e. spherocytes could be indicative of warm autoimmune hemolytic anemia)
- RBC fragmentation/schistocytes: **may be hematologic emergency** (i.e. TTP or ACUTE DIC)
  - Consider clinical presentation
  - Additional discerning laboratory investigations: coagulation profile, LDH

Reticulocyte Count
- Would expect a high reticulocyte count since the body’s response to a decrease in functional RBC count is to produce more RBCs but many of the cells that leave the bone marrow early to accommodate anemia would be immature (reticulocytes)

LDH
- Would expect a **high** LDH value since RBCs are being lysed and releasing their contents

Bilirubin
- Would expect a **high** bilirubin (indirect/unconjugated) value since RBCs are being lysed and more hemoglobin is being metabolized

Haptoglobin
- Would indicate whether or not the anemia is autoimmune and the type of autoimmune hemolytic anemia (i.e. warm vs. cold)

---

24 "Hemolytic Anemia", Karima Khamisa, October 13 2015, uOttawa Faculty of Medicine
1.15 Transfusion Associated Circulatory Overload (TACO)\(^{25}\)

**Typical Patient**
- Patient requiring transfusion
- Patients with cardiac or renal disease are predisposed
- Often the patient is not volume depleted

**Cause**
- Impaired cardiac or renal function
- Excessive rate or volume of transfusion

**Symptoms/Clinical Presentation**
- Dyspnea during or after transfusion

**Physical Exam**
- Check vitals
- Full respiratory exam

**Investigations**
- Check volume status

**Management/Treatment**
- **Treatment**
  - Stop the transfusion
  - Diuretic
- **Prevention**
  - Assess risk of TACO before transfusion
  - Give blood at a slower rate

\(^{25}\) "Abnormal Hemostasis", Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.16 Hemophilia

Typical Patient
- Patient with a family history of a bleeding disorder

Cause
- X-linked disorder
- Hemophilia A – deficiency of FVIII
- Hemophilia B – deficiency of FIX

Symptoms/Clinical Presentation
- Range depending on severity
  - >5% factor activity – mild hemophilia – excessive bleeding with challenge
  - 1-5% factor activity – moderate hemophilia – excessive bleeding with challenge, may have spontaneous bleeding
  - <1% level of activity – severe hemophilia – possibility of spontaneous bleeding
- Intracranial hemorrhage
- Soft tissue bleeds and bruising, iliopsoas bleeds, thigh/calf bleeds, deltoid/forearm bleed and bruising, buttock bleeds
- Neck swelling – emergency, possible airway compromise

Physical Exam
- Joint exam for hemarthrosis
- Neurologic exam for intracerebral hemorrhage (ICH)
- Other findings for soft tissue bleeding

Investigations
- High PTT – due to factor deficiency
- Factor assays to determine levels
- Family studies
- Genetic testing

Management/Treatment
- Factor first, think later!
- Prophylaxis – inject 2-3 times a week for people who bleed frequently, peri-procedural (around times of procedures, if a woman is delivering)
- Give factor concentrate – recombinant or human plasma derived
- DDAVP may work (may increase factor VIII levels)

26 “Abnormal Hemostasis”, Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.17 Von Willebrand Disease\textsuperscript{27}

Typical Patient

- Patient with a personal and family history of a bleeding disorder

Cause

- Deficiency or dysfunction of vWF
- Congenital disorder with multiple subtypes – autosomal dominant and autosomal recessive
- Type I – vWF works normally, but there is a low quantity of it in circulation
- Type II – vWF is present in normal quantities, but it does not function properly

Symptoms/Clinical Presentation

- Mucocutaneous bleeding – epistaxis, bruising, oral cavity bleeding, GI bleeding, menorrhagia

Physical Exam

- N/A

Investigations

- vWF antigen levels
- vWF activity assay – to determine functional activity of vWF
- Check factor VIII levels – vWF is a carrier protein for factor VIII

Management/Treatment

- Antifibrinolytics – tranexamic acid, prevents conversion of plasminogen to plasmin
- DDAVP – increases vWF release in vascular endothelium
- Human P/Wilate – plasma-derived vWF concentrates

\textsuperscript{27} “Abnormal Hemostasis”, Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.18 Synthetic Liver Dysfunction

Typical Patient
● N/A

Cause
● Acquired disorder
● See: “Causes of liver dysfunction”
● Liver synthesizes coagulation factors, fibrinolytic factors and natural anticoagulants

Symptoms/Clinical Presentation
● Many studies show no increased risk of bleeding in patients with liver disease and elevated INR

Physical Exam
● Stigmata of liver disease

Investigations
● INR – should be elevated
● Platelet count – should be low

Management/Treatment
● N/A

28 “Abnormal Hemostasis”, Dr. Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.19 Vitamin K Deficiency

Typical Patient
- Vitamin K deficient

Cause
- Malabsorption
- Antibiotic use
- Warfarin therapy
- Hemorrhagic disease of the newborn

Symptoms/Clinical Presentation
- Increased bleeding

Physical Exam
- N/A

Investigations
- INR – high

Management/Treatment
- Vitamin K replacement (oral or IV)
- Vitamin K injections given at birth for hemorrhagic disease of the newborn

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29 “Abnormal Hemostasis”, Eianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.20 Idiopathic/Immune Thrombocytopenia

Typical Patient
- N/A

Cause
- Most common acquired bleeding disorder
  - Childhood – self-limiting following viral illness
  - Adult – chronic disorder
- Autoimmune disorder

Symptoms/Clinical Presentation
- Increased bleeding

Physical Exam
- Petechiae (non-palpable)
- Wet purpura in mouth

Investigations
- Platelet count – should be low
- Hard to distinguish from TTP – use blood smear to distinguish (TTP is a microangiopathic hemolytic anemia)

Management/Treatment
- Immunosuppression – steroids, intravenous immunoglobulin (IVIG)
- Recombinant thrombopoietin
- Platelets are not usually given (unless platelet count is <20 or patient has serious bleeding)

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30 “Abnormal Hemostasis”, Elianna Saidenberg, October 19 2015, uOttawa Faculty of Medicine
1.21 Acute Lymphoid Leukemia (ALL)\textsuperscript{31,32}

Typical Patient

- 75% of ALL occurs in children < 6 yr old; second incidence peak at age 65

Cause

- Genetics, radiation, chemical exposure (ex. benzene), drugs (ex. chemotherapy), underlying hematologic disorder, retroviruses

Symptoms/Clinical Presentation

- Abrupt onset without a prodrome (i.e. patient was previously healthy)
- Signs and symptoms of bone marrow failure: anemia (fatigue), thrombocytopenia (bruising, petechiae, etc.), neutropenia (may have fever from infection, dry cough)
- Bone pain – sternal discomfort, low back pain
- Constitutional signs/symptoms – unwell, night sweats, fever, unintentional weight loss, chills, loss of appetite, etc.
- Lymphadenopathy and hepatosplenomegaly
- More likely to have central nervous system (CNS) involvement by leukemic cells

Physical Exam

- Look for signs of anemia, neutropenia (infection), and thrombocytopenia
- Look for lymphadenopathy and hepatosplenomegaly

Investigations

1. Complete blood count (CBC) + differential + smear (chest X-ray if person has fever to rule out infection)
2. Bone marrow aspirate and biopsy - must be done to diagnose
3. Histochemical staining (to distinguish between types of acute leukemia)
4. Stains relevant to ALL are:
   5. Periodic acid Schiff stain – lymphoblasts stain positive
   6. Terminal deoxynucleotidyl transferase stain (TdT) – positive in lymphoblasts, not myeloblasts
   7. Immunophenotyping (flow cytometry)
   8. Pre-B ALL: CD19, CD22, CD10
   9. Pre-T ALL: CD7, CD3
10. Cytogenetics (karyotype) – important \textbf{prognostic factor!}
11. PCR or FISH - to look for a specific mutations

Management/Treatment Options:

1. Chemotherapy
   - Induction chemotherapy +/- tyrosine kinase inhibitor (imatinib) (depends if patient is positive for t(9;22)
     - Goal of induction chemo is to achieve complete remission (<5% blasts in the bone marrow)
   - CNS prophylaxis (chemo given via lumbar puncture (intrathecal), radiate the head) → patients with AML do not get this unless they are symptomatic with CNS signs or symptoms
   - Intensification chemo – eliminate hidden cells
   - Maintenance chemo – low dose chemo for 2 years depending on protocol (patients with AML do not get maintenance chemo)
2. Allogenic stem cell transplant

\textsuperscript{31} “Leukemia”, Mitchell Sabloff, October 27 2015, uOttawa Faculty of Medicine
\textsuperscript{32} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.22 Acute Myeloid Leukemia (AML)\textsuperscript{33,34}

**Typical Patient**
- More common in adults (median age of onset is 65 yr old)
- Incidence increases with age
- Accounts for 10-15\% of childhood leukemias

**Cause**
- Genetics, radiation, chemical exposure (ex. benzene), drugs (ex. chemotherapy), underlying hematologic disorder, retroviruses

**Symptoms/Clinical Presentation**
- Abrupt onset without a prodrome (i.e. patient was previously healthy)
- Signs and symptoms of bone marrow failure: anemia (ex. fatigue), thrombocytopenia (ex. bruising, petechiae, etc.), neutropenia (ex. may have fever from infection, dry cough)
- Bone pain – sternal discomfort, low back pain
- Constitutional signs and symptoms – patient feels unwell, night sweats, fever, unintentional weight loss, chills, loss of appetite, etc.
- Unlike ALL, patients with AML do not usually have lymphadenopathy or hepatosplenomegaly

**Physical Exam**
- Look for signs of anemia, neutropenia (infection), and thrombocytopenia

**Investigations**
1. CBC + differential + smear (CXR if person has fever to rule out infection)
2. Bone marrow aspirate and biopsy - must be done to diagnose
3. Histochemical staining- Stains relevant to AML are:
   a. Myeloperoxidase stain positive
   b. Sudan black stain positive
   c. Combined esterase stain positive (granulocytes stain red, monocytes stain black)
4. Immunophenotyping (flow cytometry)
   a. Markers relevant to AML: CD13, CD33, Myeloperoxidase (MPO), CD34, HLA-DR
   b. Markers for Acute Promyelocytic Leukemia: MPO, CD13, CD33, CD34 negative, HLA-DR negative
5. Cytogenetics (karyotype) – important prognostic factor!
6. Polymerase Chain Reaction (PCR) to look for a specific mutations
7. Fluorescence In Situ Hybridization (FISH)

**Management/Treatment Options:**
1. Supportive therapy: blood transfusions (when RBCs and platelets get too low), antibiotics (neutropenia), hydration
2. Multi-agent chemotherapy
   a. Induction – rapidly kill off most leukemia cells, 7 day course, 1 cycle. Goal of induction is to achieve remission (<5\% blasts in bone marrow)
   b. Consolidation – eliminate hidden leukemic cell population, 2-4 additional cycles
   c. No maintenance chemo like in ALL
3. Hematopoietic stem cell transplantation
   a. Myeloablative chemotherapy and/or radiotherapy, followed by transplant from an allogeneic donor

\textsuperscript{33} “Leukemia”, Mitchell Sabloff, October 27 2015, uOttawa Faculty of Medicine
\textsuperscript{34} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.23 Chronic Lymphoid Leukemia (CLL)\textsuperscript{35,36}

**Typical Patient**
- Most common adult leukemia
- 2:1 ratio of males to females
- Most common in people >60 years old

**Cause**
- Clonal expansion of mature looking, functionally defective lymphocytes (not blasts like AML and ALL)

**Symptoms/Clinical Presentation**
- Often asymptomatic (25-40%)
- Patients may report being “well”
- If patient is symptomatic, they may report: weight loss, fevers and sweats, recurrent infections (lymphocytes are not functional)

**Physical Exam**
- Often physical exam is unremarkable
- Hepatomegaly
- Splenomegaly
- Check for lymphadenopathy
- Bone marrow failure occurs late in the disease
- Examine patient’s complexion
- Look for signs of thrombocytopenia (bruising, etc.) – rare

**Investigations**
- CBC → WBC count will be high
- Differential → > 5 x 10⁹ lymphocytes (too many)
- Peripheral blood smear → may see smudge cells, too many small, mature looking lymphocytes, not enough neutrophils
- Bone marrow aspiration and biopsy → not necessary
- Flow cytometry fingerprint for CLL: CD23+, CD5+
  - B-cell CLL: positive for CD19, CD20, CD 23
- CT scans for lymphadenopathy
- Cytogenetics (ex. FISH) are important for prognostics

**Management/Treatment**
- No cure
- No therapy given to patients who are asymptomatic
- Chemotherapy is given to symptomatic patients
- Small minority present with aggressive disease; usually associated with chromosomal abnormalities (ex. p53 deletion)
- Note: can transform to diffuse large B-cell lymphoma via Richter’s transformation

\textsuperscript{35} “Leukemia”, Mitchell Sabloff, October 27 2015, uOttawa Faculty of Medicine
\textsuperscript{36} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.24 Chronic Myeloid Leukemia (CML)$^{37,38}$

Typical Patient
- Middle aged to elderly patient

Cause
- Formation of hybrid gene, BCR-ABL oncogene, which encodes 210 kD fusion protein with tyrosine kinase activity, responsible for cellular transformation

Symptoms/Clinical Presentation
- Hypermetabolism: fever, weight loss, sweating, fatigue, gout
- Massive splenomegaly (not early on) → patient may report increasing abdominal weight or fullness

Physical Exam
- Assess weight loss and check for fever
- Splenomegaly

Investigations
- CBC → white blood cell (WBC) count will be high
- Differential → may have slightly elevated eosinophils and basophils
- Peripheral blood smear → heterogeneous mix of granulocyte precursors
- Bone marrow aspiration and biopsy → hypercellular with granulocytic predominance
- Cytogenetics, FISH, PCR to look for the BCR-ABL transcript
- Abdominal imaging for spleen size
- Detection of the bcr-abl fusion gene is a diagnostic test for CML (present in over 90% of patients).

Management/Treatment
- Bone marrow transplant is only known cure
- Synthetic tyrosine kinase inhibitor (ex. Gleevec/Imatinib)→ specifically inhibits activity of ABL tyrosine kinase (i.e. can get complete cytogenetic AND molecular remission with this drug)

$^{37}$ “Leukemia”, Mitchell Sabloff, October 27 2015, uOttawa Faculty of Medicine
$^{38}$ Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.25 Essential Thrombocytemia (ET)\textsuperscript{39,40}

Typical Patient
N/A

Cause
- ~50\% patients are JAK2V617F positive

Symptoms/Clinical Presentation
- Commonly asymptomatic
- May report erythromelalgia
- May have problems clotting or bleeding

Physical Exam
- Look for signs of bleeding – ecchymosis, etc.

Investigations
- CBC → sustained elevation in platelets
- Peripheral blood smear → too many platelets and mega-platelets
- Bone marrow → increased number of megakaryocytes
- Diagnosis of exclusion – must exclude causes of secondary thrombocytosis

Management/Treatment
- No need to treat someone who is asymptomatic unless >60 years old and/or there are comorbidities
- Hydroxyurea – best tolerated and most effective (cytoreductive therapy) or anagrelide as second-line agent
- Plateletpheresis for acute life threatening complications (i.e. in emergency) very temporary treatment because the half-life of platelets are very short
- Low dose aspirin (ASA)
- Splenectomy is NOT recommended

\textsuperscript{39} “Myeloproliferative and Myelodysplastic Disorders”, Carolyn Faught, October 28 2015, uOttawa Faculty of Medicine
\textsuperscript{40} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.26 Polycythemia Vera (PV)  

Typical Patient
- N/A

Cause
- ~95% of patients are JAK2V617F positive
- JAK2V617F is a constitutively active tyrosine kinase that is able to activate JAK-STAT signaling when co-expressed with the epo receptor, thrombopoietin receptor or G-CSF receptor, i.e. no EPO required to get production of RBCs

Symptoms/Clinical Presentation
- 80% of patients are symptomatic (secondary to increased blood viscosity)
- Bleeding complications – epistaxis, gingival bleeding, ecchymoses, GI bleeding
- Thrombotic complications – increased incidence of stroke and myocardial infarction, deep vein thrombosis, pulmonary embolism, etc.
- Erythromelalgia – burning pain in hands and feet and erythema of skin (pathognomonic microvascular thrombotic complication in PV and ET)
- Pruritus especially after warm bath or shower
- Epigastric distress
- Gout/hyperuricemia due to increased cell turnover

Physical Exam
- Splenomegaly
- Hepatomegaly
- Facial and/or palmar plethora
- Cutaneous ulcers (rare)
- Signs of digital infarction (rare)

Investigations
- CBC → Hemoglobin elevated or other marker of increased RBC volume (bone marrow)
- JAK2 mutation analysis
- Increased erythroid precursors in bone marrow (rarely done)
- Serum Erythropoietin (EPO) levels

Management/Treatment
- Phlebotomy to keep hematocrit below 45%
- Low-dose ASA\ to prophylax against thrombosis
- Myelosuppressive agents like hydroxyurea when phlebotomy is insufficient
- Patients may also need allopurinol or antihistamines

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41 “Myeloproliferative and Myelodysplastic Disorders”, Carolyn Faught, October 28 2015, uOttawa Faculty of Medicine
42 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.27 Myelodysplastic Disorders (MDS) 43,44

**Definition:** Heterogeneous group of malignant stem cell disorders characterized by dysplastic and ineffective blood cell production resulting in peripheral cytopenias

**Typical Patient**
- Older patient (>70 years old)
- Macrocytic anemia
- Usually presents as bone marrow failure in an elderly patient

**Cause**
- May be secondary to prior chemotherapy or radiation
- Old age
- Benzene or radiation exposure

**Symptoms/Clinical Presentation**
- Insidious onset
- Complications of any/all cytopenias
- Anemia
- Infection
- Bleeding

**Physical Exam**
- N/A

**Investigations**
- Complete blood count → any or all cytopenias, anemia is the most common finding
- Bone marrow aspiration and biopsy → necessary for diagnosis, see bizarre forms, dysplastic and often normocellular/hypercellular
- Cytogenetic analysis → partial or total loss of chromosomes: 5, 7, Y, or trisomy 8
- Peripheral blood smear → bizarre forms
  - Macrocytic anemia, oval shaped RBCs
  - Pseudo-Pelger-Huet cell (hypossegmented and hypergranular neutrophil)
  - Giant, hypogranular platelets
  - Ansio/poikilocytosis (unequal size and strange shapes)
  - May see peripheral blasts

**Management/Treatment**
- Depend on IPSS
  - Lower risk: correct cytopenias and improve quality of life
  - Higher risk: attempt to change natural history of disease with either transplant and/or hypomethylating agent
- Bone marrow transplant is the only cure, may be considered in younger patients
- Treatment is mainly supportive
- These patients are at risk for iron overload from chronic RBC transfusions, consider iron chelation
  - There is a high probability of MDS progression to leukemia

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43 “Myeloproliferative and Myelodysplastic Disorders”, Carolyn Faught, October 28 2015, uOttawa Faculty of Medicine
44 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.28 Myelofibrosis (MF)\textsuperscript{45,46}

**Typical Patient**
- Rare
- Median age at presentation is 65 years old

**Cause**
- Anyone who has had myeloproliferative neoplasms (MPN) for long time can develop MF

**Symptoms/Clinical Presentation**
- Anemia (severe fatigue is most common presenting complaint)
- Weight loss, fever, and night sweats secondary to hypermetabolic state
- Bone and joint pain secondary to osteosclerosis, gout
- Signs of extramedullary hematopoiesis (depends on organ involved)

**Physical Exam**
- Pallor
- Splenomegaly (extramedullary hematopoiesis) – may cause early satiety
- Hepatomegaly (may lead to portal hypertension)

**Investigations**
- CBC \(\rightarrow\) progressive anemia and pancytopenia
- Bone marrow aspiration is “dry tap”
- Bone marrow biopsy shows collagen fibrosis (needed for diagnosis)
- Peripheral blood smear \(\rightarrow\) tear drop shaped RBCs, may see nucleated RBCs and immature WBCs
- JAK2 PCR

**Management/Treatment**
- Supportive care: transfusions, hydroxyurea, steroids, androgens, EPO, thalidomide
- Radiation for symptomatic extramedullary hematopoiesis
- JAK2 inhibitor (Ruxolitinib) – very expensive
- Splenectomy if spleen is massive, causing symptoms, or person has large transfusion requirements (mortality is 10-20%)
- Only cure: allogeneic stem cell transplant in younger patients

\textsuperscript{45} “Myeloproliferative and Myelodysplastic Disorders”, Carolyn Faught, October 28 2015, uOttawa Faculty of Medicine
\textsuperscript{46} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
### 1.29 Hypersensitivity Summary Table

<table>
<thead>
<tr>
<th>Type</th>
<th>Pathophysiology</th>
<th>Skin test?</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type I</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylactic</td>
<td>Formation of IgE → release of immunologic mediators from basophils/ mast cells</td>
<td>Yes</td>
<td>Asthma</td>
</tr>
<tr>
<td></td>
<td>→ diffuse inflammation</td>
<td></td>
<td>Allergic rhinitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td><strong>Type II (ADCC)</strong></td>
<td>IgG antibodies from immune response bind antigens (self antigens or adsorbed</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>dependent cell mediated</td>
<td>antigens) on the host cell surface → macrophages or NK cells</td>
<td></td>
<td>ABO blood incompatibility</td>
</tr>
<tr>
<td>cytotoxicity</td>
<td>kill the tagged cell → tissue damage</td>
<td></td>
<td>Goodpasture’s syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Autoimmune hemolytic anemia</td>
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<td></td>
<td></td>
<td></td>
<td>Grave’s disease</td>
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<tr>
<td><strong>Type III</strong></td>
<td>IgG antibodies from immune response bind to antigens (self antigens or adsorbed</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Immune complex</td>
<td>antigens) on the host cell surface → complement cascade</td>
<td></td>
<td>Systemic Lupus Erythematosus (SLE)</td>
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<tr>
<td></td>
<td>triggered and destroy the cell with MAC</td>
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<td>Polyarteritis Nodosa</td>
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<td></td>
<td>Post-streptococcal glomerulonephritis</td>
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<tr>
<td></td>
<td>Formation of Antigen-Antibody (IgG) complexes get</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>deposited throughout the body (i.e. in vessels, serosa, glomeruli) → immune</td>
<td></td>
<td>Serum sickness</td>
</tr>
<tr>
<td></td>
<td>complexes activate complement and white blood cells → attract</td>
<td></td>
<td>Arthus reaction</td>
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<tr>
<td></td>
<td>inflammatory cells and release of cytokines → tissue injury</td>
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<td></td>
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<tr>
<td><strong>Type IV</strong></td>
<td></td>
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<tr>
<td>Delayed/cell-mediated</td>
<td>Macrophages take up antigen and present it on their MHC class II → helper T</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cells recognize the antigen in MHC II complex → release of cytokines by</td>
<td></td>
<td>Contact dermatitis – poison ivy, nickel allergy</td>
</tr>
<tr>
<td></td>
<td>sensitized T cells and T cell mediated cytotoxicity</td>
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<td>TB skin test</td>
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<tr>
<td></td>
<td>Takes 2-3 days to develop</td>
<td></td>
<td>Diabetes Mellitus Type I</td>
</tr>
<tr>
<td></td>
<td>*NOT antibody mediated</td>
<td></td>
<td>Hashimoto’s thyroiditis</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Graft rejection</td>
</tr>
</tbody>
</table>

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47 “Allergy Integrative Lecture”, Ham Pong, ND, uOttawa Faculty of Medicine
48 Adaptive Humoral Immunity, Lauren Segal, ND, uOttawa Faculty of Medicine
50 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1.30 Anaphylaxis

Typical Patient
- Family history of allergies
- Hygiene hypothesis
- Child following the atopic march

Cause
- Systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance
- An allergen elicits an antibody response by B cells – the antibody is attached to mast cells and circulating basophils = sensitization
- The mast cell responds to re-exposure of the specific allergen
- Common food allergens: peanut, tree nuts, cow’s milk, egg, wheat, soy, fish, shellfish, sesame seeds, sulfites, mustard seed
- Common non-food allergens: medications, insect sting, physical (ex: exercise, cold), latex, vaccines, hormones, seminal fluid, immunotherapy, skin tests, ragweed
- IgE-mediated: foods, some drugs (ex. penicillin), insulin, insect venom, latex, biologicals (ex. allergy serum)
- Direct mast-cell degranulation: radiocontrast material, tubocurarine, dextran, opiates
- Complement activation: incompatible drug transfusion, tissue plasminogen activator
- COX-1 inhibition: ASA, nonsteroidal anti-inflammatory drugs (NSAIDs)
- Unknown: idiopathic, local anaesthetics, physical, sulfites

Symptoms/Clinical Presentation
- Rash and swelling, urticaria (histamine-mediated)
- Angioedema
- Breathing difficulties
- Vomiting and diarrhea
- Heart failure and low blood pressure
- Possibly biphasic reaction – severe recurrence within 1-72 hours

Physical Exam
- N/A

Investigations
- Anaphylaxis is primarily a clinical diagnosis – plasma histamine peak at 5-10 min and undetectable by 60 min
- Serum tryptase level peaks at 1-2 hours
- Allergy testing for prevention

Management/Treatment
- Avoidance!
- Epinephrine is first line treatment – given as IM injection
- Antihistamines and bronchodilators can be given after epinephrine (and after transportation to hospital)

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51 “Anaphylaxis”, Antony Ham Pong, November 2 2015, uOttawa Faculty of Medicine
1.31 Severe Combined Immunodeficiency (SCID)\textsuperscript{52}

**Typical Patient**
- Young child that presents to hospital with an illness that is not improving (ex. a pneumonia that does not improve)
- Family history of losing a child due to an illness

**Cause**
- Mutation in a gene involved in T-cell development – most commonly X-linked
- Deficiency in adenosine deaminase (ADA) or purine nucleotide phosphorylase results in the accumulation of toxic metabolic products which damage T-cells

**Symptoms/Clinical Presentation**
- Any multiple of:
  - Thrush (i.e. fungal infection) in the mouth
  - White spots on tongue
  - Non-bloody diarrhea that worsens
  - Persistent diaper rash
- All of the symptoms last for multiple weeks

**Physical Exam**
- Head and neck examination, auscultation of the chest, neurological examination
- Delayed developmental milestones
- The physical exam results depend on the illness

**Investigations**
- Blood work – extremely low lymphocyte counts
- Serum immunoglobulins – low normal IgG, low IgM, low IgA
- Lymphocyte immunophenotyping – extremely low T, B and NK cells
- Chest X-ray – hyperinflation, atelectasis, absence of thymic tissue, bony abnormalities

**Management/Treatment**
- Avoidance of crowds and sick people
- Prophylactic antibiotics and antimycotics
- IVIg injections every 3-4 weeks
- Enzyme therapy for ADA deficiency
- Bone marrow or cord blood transplantation – this is currently the only cure for SCID
- Gene therapy – clinical trials are underway

\textsuperscript{52} “SCID” Self Learning Module, JA Roy, R Bell and A Jalali, 2015, uOttawa Faculty of Medicine
Musculoskeletal
2.1 Developmental Dysplasia of the Hip (aka. DDH)\(^1\)

**Typical Patient**
- Newborn infants and children who are either first-born, female, or have a family history of DDH

**Cause**
- Early – lax joint capsule (estrogens allow for joint flexibility; thus, laxity seen for the first couple weeks)
- Later – capsular constriction, muscle contractures, bony deformities
- DDH encompasses all dysplastic hip disorders, ranging from perinatal hip subluxation to dislocations

**Symptoms/Clinical Presentation**
- “Frank” breech
- Left hip twice as likely to be affected
- Avascular necrosis and early arthritis

**Physical Exam**
- Galeazzi sign
  - Infant lying supine, hips and knees bent, feet flat on bed
  - Knee height observed for symmetry (knee height should be lower on abnormal side)
- Thigh folds observation
  - Compare infant’s legs while extended on both anterior and posterior sides
  - Abnormal side has extra folds
- Ortolani test (sign of entry)
  - the infant is supine, and hips and knees are flexed to 90 degrees
  - Using index fingers, anterior pressure is placed on the greater trochanters, the legs are gently abducted using thumbs
  - Positive sign if a distinctive ‘clunk’ can be heard and felt as the femoral head slips into the acetabulum
  - Unreliable past 3-6 months of age due to tightening of joint capsule
- Barlow test (sign of exit)
  - Infant lying supine with hips and knees at right angles
  - Thighs adducted and posterior telescoping force applied
  - Positive if head of femur felt to slip out of acetabulum (remember to reduce if positive)
  - A positive Barlow test can be normal, whereas a positive Ortolani test is always abnormal

**Investigations**
- Ultrasound
  - Measurement of bony and cartilaginous components to assess formation of acetabulum
  - Look for alpha angle over 60 degrees, and beta angle under 77 degrees
  - Repeat U/S 4-8 weeks later after abnormal exam (most false positives will have developed well by this time)
- Avoid CT (radiation) and MRI (cannot immobilize infant)
- X-rays limited by extent of proximal femur ossification
  - However, can measure acetabular index (AI) – AI < 30 degrees is normal

**Management/Treatment**
- Birth to 6 months – Pavlik harness; closed reductions occasionally required
- 6 months to 18 months – Traction pre-reduction; closed reductions (non-forceful); open reductions
- 18 months to 3 years – Open reduction with soft tissues releases; may include osteotomy
- Greater than 3 years – Open reduction with osteotomy; if infant over 8 years of age with unilateral dislocation, do not reduce; if infant over 5 years of age with bilateral dislocation, do not reduce

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\(^1\) “MSK Congenital Disorders”, Ken Kontio, November 9 2015, uOttawa Faculty of Medicine
2.2 Metatarsus Adductus (aka. Metatarsus Varus)²

Typical Patient
- Pre-walking infants

Cause
- Intrauterine posturing, muscle imbalance, multifactorial genetics
- Associated with DDH in 10% of cases

Symptoms/Clinical Presentation
- Forefoot is adducted at tarso-metatarsal joints
- Hindfoot can be neutral or in a valgus position
- Deformities at the metatarsophalangeal joints with an overactive great toe abductor are referred to as “Dynamic Hallux Varus”

Physical Exam
- Assessed by abduction of forefoot to neutral position

Investigations
- Physical exam

Management/Treatment
- Majority of mild deformities will spontaneously correct in 2-3 years
- If foot is flexible past neutral position, no treatment
- If not flexible, foot should be put into a corrective cast
  - Stretch and re-cast for 4-6 weeks (change cast every 2 weeks)

² “MSK Congenital Disorders”, Ken Kontio, November 9 2015, uOttawa Faculty of Medicine
2.3 Talipes Equinovarus (aka. TEV/Clubfoot)³

Typical Patient
- Males twice as likely to be affected
- Can be seen from birth to adulthood
- Incidence of 1.24/1000 live births

Cause
- Complicated multifactorial genetic origin

Symptoms/Clinical Presentation
- CAVE
  - C – Midfoot cavus
  - A – Midfoot adductus
  - V – Hindfoot varus
  - E – Hindfoot equinus

Physical Exam
- Inspect for 4 aspects of CAVE

Investigations
- Primarily inspection/physical exam
- X-rays not often performed anymore

Management/Treatment
- Ponseti Treatment
  - Series of manipulative techniques designed to correct congenital clubfoot without invasive surgery
  - Involves weekly serial manipulation and casting which follows a certain order of correction
  - Success rate of 95-100%
- Surgery is rarely needed

³ “MSK Congenital Disorders”, Ken Kontio, November 9 2015, uOttawa Faculty of Medicine
2.4 Calcaneovalgus Foot Deformity (aka. Flexible Flatfoot)

Typical Patient
- Infants and young children

Cause
- Common and benign deformity caused by intrauterine positioning

Symptoms/Clinical Presentation
- Ankles are severely dorsiflexed, and anterior ankle structures are contracted

Physical Exam
- Inspection for dorsiflexed ankles
- Foot can be passively put into normal position

Investigations
- X-rays of the tibia (AP and lateral)
- X-rays of the foot in a plantarflexed position

Management/Treatment
- Observation (most cases resolve without treatment)
- Casting occasionally performed
- Orthotics are of no proven benefit
- Generally non-operative

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4 “MSK Congenital Disorders”, Ken Kontio, November 9 2015, uOttawa Faculty of Medicine
2.5 Conventional Osteosarcoma

Typical Patient
- 4-25 years of age
- Male:female ratio of 3:2

Cause
- Highly malignant spindle cell sarcoma characterized by production of osteoid matrix
- Etiology includes: genetic predisposition, hereditary retinoblastoma, Li-Fraumeni syndrome, viruses, and radiation

Symptoms/Clinical Presentation
- Tender and large mass
- Pain which waxes and wanes, and is often exacerbated by activity
- Over 50% of the time, onset of pain is related to an episode of trauma
- Restriction of function

Physical Exam
- Size of mass is generally large (over 5 cm)
- Often found in metaphysis of bones (diaphysis only 10% of the time)
- 50% of cases are found around the knee
- Distal femur, proximal tibia, proximal humerus, flat bones represent majority of cases

Investigations
- Blood work (increased alkaline phosphatase (ALP) and lactate dehydrogenase (LDH))
- X-rays
- CT
- Bone scan
- MRI
- Biopsy

Management/Treatment
- Combination of chemotherapy and resection surgery (can be either wide resection or radical resection)
- Amputation is common
- Rotationplasty is often seen

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5 “Clinical Approach to MSK Tumors” Natasha Holder, November 9, 2015, uOttawa Faculty of Medicine
2.6 Non-Ossifying Fibroma

Typical Patient
- Children 5-15 years of age

Cause
- Benign fibrogenic lesion
- Etiology unknown

Symptoms/Clinical Presentation
- Usually asymptomatic and found incidentally
- May present with pathologic fracture

Physical Exam
- May be cause of pathologic fracture
- Found in metaphysis of long bones
- 80% are found in the lower extremity of the body
- Common locations include the knee (distal femur and proximal tibia) and the distal tibia

Investigations
- X-rays

Management/Treatment
- Observation
- Cast any pathologic fractures
- Surgery (curettage and bone grafting) if large/symptomatic lesions

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6 “Clinical Approach to MSK Tumors” Natasha Holder, November 9, 2015, uOttawa Faculty of Medicine
2.7 Lipoma

Typical Patient
- Slightly more common in men
- Affects patients 40-60 years old
- Develops in sedentary individuals

Cause
- Common benign tumor of mature fats which may be subcutaneous, extra-muscular, or intra-muscular
- Tendency to develop lipomas is inherited

Symptoms/Clinical Presentation
- Usually a painless mass that has been present for a long time (commonly found in upper back, thighs, buttocks, shoulders, and arms)
- 5-10% of patients with a known superficial lipoma will have multiple lesions
- Size of lesions typically plateaus after initial growth

Physical Exam
- Palpable, mobile, painless lesions

Investigations
- X-rays
- MRI
- Biopsy (not often necessary as diagnosis can be made by MRI)

Management/Treatment
- Observation
- Marginal resection (indicated if lesions are symptomatic, rapidly growing, located deep to the fascia or in the retroperitoneum)

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7 “Clinical Approach to MSK Tumors” Natasha Holder, November 9, 2015, uOttawa Faculty of Medicine
2.8 Rotator Cuff Tendinopathy

Typical Patient
- Athletes and people who perform repetitive overhead activities with their arms

Cause
- Rotator cuff tendons (usually supraspinatus) are impinged as they pass through the subacromial space, causing mechanical irritation of rotator cuff tendons and swelling/damage
- Due to a combination of tendonitis, tendinosis, and tendon rupture
- Supraspinatus is the muscle that is almost always torn first
- Often caused by repetition/overuse of the shoulder in an overhead activity; can occasionally be due to a single event
- May be associated with laxity or instability of the shoulder

Symptoms/Clinical Presentation
- Pain with overhead activity
- Painful to sleep on shoulder
- Inability to lift arm (complete tear)

Physical Exam
- Painful arc (60-120 degrees of motion) during arm raise – supraspinatus
- Empty can test – supraspinatus
- Drop arm test – supraspinatus
- Lift-off test – subscapularis
- Cups test – infraspinatus and teres minor

Investigations
- Nothing (diagnosis made upon physical examination)
- X-rays
- Ultrasound
- MRI

Management/Treatment
- Protection, rest, medications
- Physiotherapy
- Corticosteroid injections (only good for short/medium term, not long term)
- Surgery (if traumatic full thickness tear)

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8 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.9 Biceps Tendon Rupture (aka. Popeye Sign)\(^9\)

**Typical Patient**
- Usually an older athlete or older patient

**Cause**
- Tear of the biceps muscle, either in the long head (connecting to the supraglenoid tuberosity of scapula) or short head (connecting to the coracoid process)
- Caused by excessive strain on the biceps muscle

**Symptoms/Clinical Presentation**
- Rupture commonly found in long head of biceps
- Accompanied by sharp pain
- Obvious deformity seen – Popeye sign (bulging of body of biceps due to rupture)
- Little loss of strength

**Physical Exam**
- Observe for Popeye sign
- Speed’s test
- Yergason’s test

**Investigations**
- X-rays

**Management/Treatment**
- Observation, with range of motion (ROM) therapy and strengthening
- Surgery (indicated if distal tear at insertion into radius)
  - Proximal tear causes little loss of strength, and surgery is only performed in those who perform power sports

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\(^9\) “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.10 Acromioclavicular Joint Separation/Injuries\textsuperscript{10}

Typical Patient
- Hockey players, football players, and skiers

Cause
- Separated shoulder caused by a fall or collision onto a single point of the shoulder

Symptoms/Clinical Presentation
- Point tenderness/pain
- Step deformity
- Painful at extreme abduction or flexion

Physical Exam
- Scarf test
- O’Brien’s test

Investigations
- X-rays at 15 degree cephalic tilt

Management/Treatment
- Depends on severity of injury
  - Type 1 – sling for 2-3 days
  - Type 2 – sling for a few weeks until pain improves; return to sports when there is full, pain-free ROM and no local tenderness
  - Type 3 – same as type 2, but surgery may be indicated if conservative treatment fails
  - Type 4 – surgery
  - Type 5 – surgery
  - Type 6 – surgery

\textsuperscript{10} “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.11 Adhesive Capsulitis (aka. Frozen Shoulder)

Typical Patient
- Patients who have previously suffered traumatic injury to the shoulder
- Patients suffering from diabetes, hypothyroidism, Dupuytren’s, or Parkinson’s
- Post surgery patients (from rotator cuff tears, fractures, or strokes)

Cause
- Fibrosis of the glenohumeral joint and profound loss of capsular volume

Symptoms/Clinical Presentation
- Early – pain with active and passive ROM; pain often radiates to deltoid insertion; pain at night
- Late – loss of active and passive ROM; ROM is completely lost in the glenohumeral joint
- Disorder is composed of 4 stages:
  - Inflammatory
  - Freezing (losing movement)
  - Frozen (movement is lost)
  - Thawing (regaining movement)

Physical Exam
- Unable to initiate arm raise/arc
- Isolate the glenohumeral joint by stabilizing the scapula to detect if scapular movement is compensating for limited shoulder abduction

Investigations
- Detect via physical exam

Management/Treatment
- Steroid injection (best efficacy in earlier stages)
- ROM exercise
- Physiotherapy (only beneficial once thawing phase has begun)
- Arthrographic glenohumeral hydrodilatation
- Manipulation of shoulder under anesthesia
- Surgical release of shoulder
2.12 Medial Epicondylitis (Golfer’s Elbow)\textsuperscript{12}

Typical Patient
- 30 years old
- Tennis player or golfer
- Tendinosis

Cause
- Overuse of muscles attaching to medial epicondyle (wrist flexors, finger flexors, forearm pronators)
- Throwing sports (golf, tennis)
- Recreational/occupational activities (snow shoveling, grocery bagging)

Symptoms/Clinical Presentation
- Pain along medial elbow
- Aching along volar forearm
- Impact on activities of daily living (ADL) if continual

Physical Exam
- Pain on palpation of common tendon and medial epicondyle
- Pain with resisted wrist flexion and forearm pronation
- Pain with passive wrist extension (stretching wrist flexors)

Investigations
- None necessary

Management/Treatment
- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
- Corticosteroid injection if acute flare
- Relative rest (identify and modify causative actions)
- Ice
- Stretching
- Strengthening
- Armband (to change point of tension when muscles contract)

\textsuperscript{12} “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.13 Lateral Epicondylitis (Tennis Elbow)

Typical Patient
- Patients who partake in racket sports, screwdriver use, knitting, brick laying, typists, etc.

Cause
- Injury due to overuse of muscles attaching to lateral epicondyle (wrist extensors, finger extensors, forearm supinators)

Symptoms/Clinical Presentation
- Pain along lateral elbow
- Aching along dorsal forearm
- Impact on ADL if continual

Physical Exam
- Pain on palpation of common tendon and lateral epicondyle
- Pain with resisted wrist extension and forearm supination
- Pain with resisted extension of third digit
- Pain with passive wrist flexion (stretch of wrist extensors)

Investigations
- None necessary

Management/Treatment
- NSAIDs
- Corticosteroid injection if acute flare
- Relative rest (identify and modify causative actions)
- Ice
- Stretching
- Strengthening
- Armband (to change point of tension when muscles contract)
- Eccentric contractions are of benefit in strengthening extensor origins and preventing recurrence

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13 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.14 De Quervain’s Tenosynovitis

Typical Patient
- Patients who partake in repetitive wrist deviation and forceful gripping with radial wrist deviation
- Video game players (repetitive use of thumbs)

Cause
- Inflammation of the first extensor compartment tendons (abductor pollicis longus and extensor pollicis brevis)

Symptoms/Clinical Presentation
- Swelling
- Crepitus
- Pain over radial styloid
- Pain with thumb movements (abduction and extension)

Physical Exam
- Pain with palpation of tendons along the radial distal wrist
- Finkelstein’s maneuver

Investigations
- None necessary

Management/Treatment
- Mild cases:
  - Ice
  - NSAIDs
  - Modifications of activities
- Intense/prolonged cases:
  - Corticosteroid injection along the tendon sheath
  - Thumb spica orthosis

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14 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.15 Carpal Tunnel Syndrome

Typical Patient
- Patients with repetitive use of hands (e.g. manual labour), abnormal finger/wrist postures, use of vibrating tools, rheumatoid arthritis, obesity, and pregnancy

Cause
- Median nerve compression at the wrist

Symptoms/Clinical Presentation
- Sensory changes in lateral 3.5 digits (burning/pins and needles/numbness)
- Symptoms often occur at night
- Symptoms can be dependent on hand position
- Relief with shaking hands
- Loss of strength (e.g. dropping objects)

Physical Exam
- Phalen’s maneuver
- Tinel’s sign
- Sensory abnormalities in median nerve territory
- Loss of strength of thumb abduction
- Wasting of thenar eminence

Investigations
- Nerve conduction studies
- Electromyography

Management/Treatment
- Activity modification/ergonomics
- Night splints (wrist placed in neutral position)
- Relative rest (breaks when involved in repetitive activity)
- Stretching (nerve and tendon gliding exercises)
- Steroid injection
- Surgery

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15 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.16 Trochanteric Bursitis\textsuperscript{16}

Typical Patient
- Contact sport athletes, runners, cross-country skiers, ballet dancers

Cause
- Irritation of the bursa at the greater trochanter of the femur

Symptoms/Clinical Presentation
- Burning, ache, or sharp pain in the buttocks/lateral hip, often radiating down the lateral thigh
- Often unable to sleep on affected side
- May have “snapping hip” as the tensor fasciae latae moves over the greater trochanter

Physical Exam
- Pain on palpation over the greater trochanter
- “Snapping hip” felt on hip flexion

Investigations
- None necessary

Management/Treatment
- Ambulation with cane/walking pole in contralateral hand
- Daily stretching of the iliotibial band
- Strengthening of gluteus medius
- Corticosteroid injection

\textsuperscript{16} “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.17 Iliotibial Band (ITB) Syndrome

Typical Patient

- Overuse injury common in runners or those who use step machines in the gym

Cause

- The ITB lies in front of the lateral epicondyle of the femur when the knee is fully extended
- When knee flexion occurs, the ITB moves behind the lateral epicondyle
- ITB syndrome occurs when the ITB is irritated by repetitive rubbing over the lateral epicondyle during knee flexion and extension
- Often precipitated by weak hip abductors or excessive pronation

Symptoms/Clinical Presentation

- Lateral knee pain
- May radiate up the lateral leg
- Pain is worse with repetitive knee flexion and extension

Physical Exam

- Pain on palpation over the lateral epicondyle
- Snapping of the ITB felt over the lateral epicondyle on palpation during knee flexion/extension
- Ober’s test

Investigations

- None necessary

Management/Treatment

- Rest and recovery
- Daily stretching of the ITB
- ITB friction/myofascial release/massage
- Strengthening of hip abductors
- Correction of excessive pronation using footwear (possibly orthotics)
- Ice
- Steroid injections (mainly for acute flares)
2.18 Anterior Cruciate Ligament (ACL) Injury

Typical Patient
- Athletes involved in sports which require jumping, pivoting, quick lateral movements, etc.

Cause
- Excessive forces to the knee (often valgus), causing tearing of the anterior cruciate ligament (ACL)

Symptoms/Clinical Presentation
- Patient will feel or hear a sudden pop
- Acutely painful injury, unable to return to play
- Rapid knee hemarthrosis (within an hour)
- Knee feels like it will give out
- Often times, medial collateral ligament (MCL), medial meniscus, and ACL are injured together (terrible triad)

Physical Exam
- Anterior drawer test
- Lachman test
- Exam for knee effusion, limited range of motion (ROM), limited weight bearing ability

Investigations
- X-rays
- MRI

Management/Treatment
- Physiotherapy for pain control, restoration of ROM, strengthening of hamstrings, and proprioception
- ACL brace
- Surgery (not always required; decision made based on presence of instability, activity level, patient age, associated knee injuries, etc.)
  - Significant rehabilitation time required with both non-operative and operative recovery (unable to play pivot sports for 9 months)
2.19 Posterior Cruciate Ligament (PCL) Injury

Typical Patient
- Patients who participate in sports with a high risk of impact to the front of the knee

Cause
- Posterior force applied to the tibia during knee flexion, causing tearing of the posterior cruciate ligament (PCL)
- Hyperextension with rotation on a planted foot
- May be associated with other knee injuries (e.g. meniscus)

Symptoms/Clinical Presentation
- Difficulty walking
- Knee feels unstable

Physical Exam
- Posterior drawer exam

Investigations
- X-rays
- MRI

Management/Treatment
- Rest and recovery
- Surgery usually not indicated, unless other accompanying injuries dictate surgery

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19 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.20 Medial Collateral Ligament (MCL) Injury

Typical Patient
- Patients who participate in sports involving bending, twisting, or a quick change of direction

Cause
- Valgus stress to the knee, usually while knee is partially flexed

Symptoms/Clinical Presentation
- Medial joint line tenderness along the MCL
- Possible moderate swelling

Physical Exam
- Pain and increased laxity upon applying a valgus stress to the knee while flexed at 30 degrees

Investigations
- None necessary

Management/Treatment
- Non-operative regardless of severity
- Rehabilitation focuses on range of motion (ROM), quadriceps and hamstring strengthening, and joint proprioception
- May benefit from hinged knee brace to facilitate early return to sport

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20 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.21 Lateral Collateral Ligament (LCL) Injury

**Typical Patient**
- Patients who participate in sports with a risk of direct-force trauma to the medial aspect of the knee

**Cause**
- Varus stress to the knee

**Symptoms/Clinical Presentation**
- Lateral joint line tenderness along the LCL

**Physical Exam**
- Pain and increased laxity upon applying a varus stress to the knee while flexed at 30 degrees

**Investigations**
- None necessary

**Management/Treatment**
- Non-operative for grades 1 and 2
- Grade 3 is operative and is usually associated with other instabilities, such as PCL ruptures

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21 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.22 Medial and Lateral Meniscus Injuries

Typical Patient
- Patients who participate in sports involving twisting or repetitive squatting
- Can also be seen in elderly patients and those with repetitive knee trauma

Cause
- Stress to the knee causes tearing of the medial or lateral menisci
- Menisci are most stressed when knee is near full flexion
- Twisting of the knee can also apply stress to the menisci
- Can be seen with anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) injuries

Symptoms/Clinical Presentation
- Pain that becomes worse with squatting
- Locking and clicking of the knee
- Buckling of the knee
- Swelling after activity

Physical Exam
- McMurray’s test
- Detection of effusion
- Loss of range of motion (ROM)
- Joint line tenderness

Investigations
- X-rays
- MRI

Management/Treatment
- Analgesics and conservative therapy
- Physiotherapy for ROM and strengthening
- Arthroscopic surgery if mechanical symptoms or pain persist after 6 weeks of conservative treatment

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22 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.23 Patellofemoral Pain Syndrome (aka. Chondromalacia Patella)\(^{23}\)

**Typical Patient**
- Patients who sit for prolonged periods of time
- More common in women than men
- Runners

**Cause**
- Linked to altered patellar tracking (patella moves too far laterally along the femur during knee flexion)
- Weak vastus medialis oblique
- Excessive pronation
- Weak hip abductors
- Tight iliobibial band
- Poor proprioception
- Increased Q angle

**Symptoms/Clinical Presentation**
- Pain in/around patella
- Worse with prolonged sitting or squatting
- Worse when climbing stairs

**Physical Exam**
- Crepitus
- Pain on palpation under the patella
- Pain with patellar stressing (patellar grind)

**Investigations**
- Often none necessary
- X-rays used to assess for osteoarthritis

**Management/Treatment**
- Analgesics
- Modify activity pattern
- Patellar stabilizing brace

\(^{23}\) “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.24 Plantar Fasciitis

Typical Patient
- Athletes participating in sports which require intense push-offs (running, dancing, etc.)
- Can occur in patients with increased load bearing (obesity, pregnancy, etc.)
- More prominent in those with pes planus (flatfoot) or pes cavus (high arched foot)

Cause
- Inflammation/irritation of the plantar aponeurosis, which inserts into the medial tuberosity of the calcaneus

Symptoms/Clinical Presentation
- Pain during the first few steps in the morning
- Prefer to bear weight on lateral heel/foot

Physical Exam
- Pain along course of plantar fascia, particularly at insertion on the calcaneus
- Pain with toe dorsiflexion

Investigations
- None necessary

Management/Treatment
- Activity modification
- Proper footwear/orthotics
- Stretching
- Night splinting to keep foot in neutral position
- Ice
- Massages
- NSAIDs
- Corticosteroid injections
- Extracorporeal shock wave therapy
2.25 Ankle Sprains

Typical Patient
- Athletes who participate in sports with quick changes of direction
- Hikers, runners, and people who walk on uneven ground

Cause
- Lateral ligament sprain (more common) – excessive inversion of ankle
  - Usually obtained through improper landing from a jump or walking on uneven ground
- Medial ligament sprain (less common) – excessive eversion of ankle
  - Usually obtained through quick changes in direction, and are associated with proximal fibular (Maisonneuve) fractures, disrupted interosseous membranes, and disrupted tibiofibular ligaments

Symptoms/Clinical Presentation
- Pain
- Swelling
- Point tenderness over ligaments
- Reduced ROM with increased ligamentous laxity

Physical Exam
- Anterior drawer test
- Lateral tilt test

Investigations
- X-rays according to the Ottawa Ankle Rules

Management/Treatment
- Reduction of pain and swelling
- Restoration of ROM
- Muscle conditioning
- Proprioception training
- Functional exercises
- Ankle braces

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25 “Approach to Soft Tissue Musculoskeletal Disorders”, Gerald Wolff, November 11 2015, uOttawa Faculty of Medicine
2.26 Ankylosing Spondylitis

Typical Patient
- Young male, 20-40 years old (3:1 male to female)
- Inflammatory back pain
- Limited spinal mobility
- Sacroiliitis
- +/- Uveitis
- Almost no peripheral arthritis

Cause
- Genetic/environmental factors
- Associated with the HLA-B27 gene

Symptoms/Clinical Presentation
- Pain and stiffness in lower back, hips, buttocks
- Bony fusion
- Pain in ligaments and tendons

Physical Exam
- Loss of lumbar lordosis
- Restricted chest expansion
- Finger to floor distance increased
- Schober’s test

Investigations
- X-rays of back and pelvis
- Measurement of chest while breathing
- HLA-B27 blood test

Management/Treatment
- Physical/occupational therapy
- Exercise
- NSAIDs
- Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
- Surgery in cases of advanced joint disease

26 “Seronegative Spondyloarthropathies”, Susan Humphrey-Murto, November 16 2015, uOttawa Faculty of Medicine
2.27 Psoriatic Arthritis

Typical Patient
- Male or female, 30-50 years old, but can present in children

Cause
- Genetic, HLA-B27 gene association
- Found in patients with psoriasis

Symptoms/Clinical Presentation
- Inflammatory arthritis: asymmetrical and distal interphalangeal joint (DIP) involvement
- Skin/nail changes
- Dactylitis (sausage digits)
- Enthesopathy
- +/- Asymmetrical sacroiliitis
- Onycholysis (loosening/separation of nail from nail bed)
- Nail pitting
- Enthesitis (inflammation of the entheses)
- Skin lesions (scaly plaques)

Physical Exam
- Observe for symptoms that fit clinical picture as listed above as well as symptoms of psoriasis
- Look for joint patterns
  - Asymmetrical oligoarticular arthritis
  - Symmetrical polyarthritis
  - Interphalangeal arthropathy
  - Arthritis mutilans
  - Spondylitis with or without sacroiliitis

Investigations
- None specific for psoriatic arthritis
- Can use radiologic imaging to rule out rheumatoid arthritis

Management/Treatment
- Treat the inflammation – NSAIDs/DMARDs
- Corticosteroid injections
- Consider TNF-α inhibitor if the above are ineffective

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27 “Seronegative Spondyloarthropathies”, Susan Humphrey-Murto, November 16 2015, uOttawa Faculty of Medicine
2.28 Gout/Pseudogout

Typical Patient
- Overweight, elderly, males who drink alcohol, and high purine diet

Causes
- Gout is caused by monosodium urate monohydrate crystals
- Pseudogout is caused by calcium pyrophosphate (CPP) crystals
- Elevated serum uric acid levels are the principal risk factor
- Primary gout is related to underexcretion or overproduction of uric acid (e.g. dietary excess, alcohol overuse)
- Secondary gout is related to medications or conditions that cause hyperuricemia (e.g. myeloproliferative diseases and treatment, renal failure, and lead poisoning)
- Pseudogout thought to be idiopathic/related to trauma; both conditions have some genetic component

Symptoms/Clinical Presentation
- Spontaneous onset of excruciating pain, edema, and inflammation in the metatarsal-phalangeal joint of the great toe
- Most common sites of gouty arthritis are the ankle, wrist, finger joints, and knee
- Pseudogout presents most commonly in the knee, wrist, elbow, or ankle
- Affected joints are erythematous and highly sensitive (e.g. brushing a bed sheet along joint causes excruciating pain)

Physical Exam
- Often a single joint with signs of inflammation
- Look for tophi (collections of urate crystals in the soft tissues)

Investigations
- Arthrocentesis — send joint fluid for fluid analysis, including cell count and differential, gram stain, culture and sensitivity, and microscopic analysis for crystals — gout will show strong birefringent yellow needle-shaped crystals; pseudogout will show weak negative birefringent blue rod-shaped crystals
- Requires synovial fluid analysis to rule out septic arthritis (must be diagnosed and treated promptly, because irreversible damage can occur within 4-6 hours)

Management/Treatment
- Need to treat acute episode (NSAIDs and colchicine)
- Provide prophylaxis against future flare-ups (colchicine/NSAIDs, lose weight if obese, stop drinking alcohol, avoid purine-rich foods)
- Lower urate stores to prevent tissue deposition of urate crystals (allopurinol, probenecid) — these drugs may cause an acute flare-up or make a flare-up worse; should only be used after 6 months of prophylactic colchicine

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2.29 Reactive Arthritis (Reiter’s Syndrome)\textsuperscript{29}

**Typical Patient**
- Young adults (20-40 years old)
- Equal prevalence in males and females

**Cause**
- Triggered within a month after having an infection elsewhere (commonly gastrointestinal/genitourinary tract)
- HLA-B27 association; disease more severe and chronic in carriers
- Can be due to an inflammatory reaction in response to a persistent organism/antigen (e.g. Chlamydia, Salmonella, Shigella)

**Symptoms/Clinical Presentation**
- Acute
- Asymmetric
- Oligoarticular
- Lower extremity
- +/- Sacroiliitis (SI)
- May become chronic or recurrent
- Clinical triad – urethritis, conjunctivitis, arthritis
- Enthesitis (inflammation of the entheses)
- Back pain from SI joint involvement

**Physical Exam**
- May see dactylitis
- Look for mouth ulcers, inflammation of the eye, circinate balanitis

**Investigations**
- Find out about previous infections, test for sexually transmitted infection (STI) (e.g. Chlamydia)
- HLA-B27 testing

**Management/Treatment**
- If due to bacterial cause, use appropriate antibiotics (e.g. Chlamydia – use azithromycin)
- NSAIDs for joint inflammation
- DMARDs in some cases

\textsuperscript{29} “Seronegative Spondyloarthropathies”, Susan Humphrey-Murto, November 16 2015, uOttawa Faculty of Medicine
2.30 Osteoarthritis (OA)\textsuperscript{30}

**Typical Patient**
- Middle-aged to elderly
- Symptoms that developed gradually

**Cause**
- Chronic degenerative disorder characterized by an adaptive response of synovial joints to a variety of stresses (e.g. overuse and trauma)
- Local inflammation in the synovium and the cartilage may contribute to pain and further joint damage

**Symptoms/Clinical Presentation**
- Pain in small and large joints (i.e. hips and knees), and spine in an asymmetric distribution throughout the body (worse with activity, relieved by rest)
- Insidious onset and generally slow progression
- Early morning stiffness (usually lasting less than 30 minutes)
- Joint swelling
- Impact on ADL

**Physical Exam**
- Warmth, swelling, tenderness, pain, and reduced ROM in the affected joints
- Nodes in the interphalangeal joints of the hand

**Investigations**
- Typically clinical diagnosis
- Joint aspiration (to rule out other forms of arthritis)
- X-rays
- MRI

**Management/Treatment**
- Pain and anti-inflammatory medications (NSAIDs, corticosteroids)
- Physical activity/strengthening
- Stretching
- Weight management
- Physical and occupational therapy (e.g. assistive devices)
- Surgery for patients with permanent damage that limits ADL

\textsuperscript{30} “Pathophysiology of osteoarthritis and juvenile idiopathic arthritis”, Roman Jurencak, November 23 2015, uOttawa Faculty of Medicine
2.31 Juvenile Idiopathic Arthritis (JIA)\textsuperscript{31}

**Typical Patient**
- Onset before the 16\textsuperscript{th} birthday
- Persists for more than 6 weeks
- Joint pain is often not the dominant symptom (instead, parents may notice their child limping)

**Cause**
- Unknown etiology

**Symptoms/Clinical Presentation**
- Early morning stiffness
- Joint swelling
- Limping
- Systemic JIA may present with skin rash, hepatosplenomegaly, lymphadenopathy, and constitutional symptoms (e.g. fever, fatigue, malaise, weight loss, and poor appetite)
- Uveitis

**Physical Exam**
- Evidence of active arthritis – joint effusion or two of joint line tenderness, pain on motion, limited ROM
- Enthesitis (inflammation of the entheses)
- Ulnar deviation, Boutonniere deformity, and swan-neck deformity
- Evidence of the extra-articular manifestations described above
- Growth abnormalities

**Investigations**
- Diagnosis of JIA is essentially a clinical one – no laboratory test confirms or rules out JIA
- Blood work [complete blood count (CBC), rheumatoid factor (RF), anti-citrullinated protein antibody (anti-CPP), positive C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)] may be used to support the clinical diagnosis
- X-rays
- Ultrasound
- MRI

**Management/Treatment**
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Steroids
- Disease-modifying anti-rheumatic drugs (DMARDs)
- Biologics
- Physical activity
- Physiotherapy
- Regular eye exams

\textsuperscript{31}Pathophysiology of osteoarthritis and juvenile idiopathic arthritis”, Roman Jurencak, November 23 2015, uOttawa Faculty of Medicine
2.32 Varicella (Chickenpox)\textsuperscript{32}

**Typical Patient**
- Children (especially those in daycare, school, etc.)

**Cause**
- Initial infection with varicella zoster virus (VZV)

**Symptoms/Clinical Presentation**
- 10-24-day incubation period (i.e. patient not contagious and usually asymptomatic before day 10 post-contact); children are less likely than adults to experience a prodromal, flu-like illness (fever, muscle aches, and pains) 1-3 days before the appearance of the rash
- Typical rashes – begin as papules, but rapidly progress to vesicles with surrounding erythema, eventually crusting within 2-3 days and are typically pruritic
- A low-grade fever, lassitude, malaise, and anorexia often accompany the rashes
- Lesions erupt over the course of 4-5 days and are mostly confined to the trunk and head; in severe infections, lesions may appear on the oral mucosa, pharynx, and genitalia – a characteristic feature of the varicella rash is the appearance of lesions in different stages of differentiation (papule, vesicle, pustule, and crusted)
- In adults and immunocompromised patients, the clinical evolution of the infection follows a more severe course and is more likely to be associated with complications, such as secondary infections (e.g. varicella pneumonitis)

**Physical Exam**
- Typical rash described above – generalized and pruritic

**Investigations**
- For the most part, primary varicella is a clinical diagnosis – the age, immune status, and presence of the typical vesicular rash are recognizable features of varicella; however, in immunocompromised patients or non-immune adults, disseminated varicella can be confused with disseminated herpes infections, and atypical presentations are possible
- For laboratory diagnosis, the optimal specimen is the vesicular fluid and/or skin scraping from the base of the lesion
- Several methodologies can be used to confirm VZV infection in the microbiology laboratory, including:
  - Direct fluorescent antibody
  - Culture in human cell lines
  - Polymerase chain reaction (PCR)
  - Serology (IgG antibodies are useful for determining the immune status; detection of IgM suggests recent infection)

**Management/Treatment**
- Childhood or mild varicella infections are typically not treated and are allowed to run their course; use of antivirals has minimal impact and is likely not justified given the cost of therapy and the increased risk of selecting for VZV resistant strains – treatment in these cases is usually symptomatic and aimed at minimizing pruritus with topical agents, reducing the fever with non-salicylic analgesics, and proper hygiene and skin care to reduce the risk of secondary bacterial infections
- In individuals over the age of 12 years, patients with congenital or acquired immunodeficiencies, or in severe cases, treatment with nucleoside analogues (e.g. acyclovir, famciclovir, and valacyclovir) can reduce the severity, minimize the risk of complications, and may shorten the duration of the infection
- There are two main approaches to the prevention of VZV – vaccination and post-exposure prophylaxis

\textsuperscript{32} “Varicella” Self Learning Module, Marc Desjardins, uOttawa Faculty of Medicine
2.33 Herpes Zoster (Shingles)\textsuperscript{33,34}

**Typical Patient**
- 65+ years old

**Cause**
- Reactivation of latent varicella zoster virus (VZV) and migration along sensory nerves back to the skin
- Associated with waning or loss of immunity, particularly cell-mediated immune responses

**Symptoms/Clinical Presentation**
- Localized skin eruptions that follow the involved dermatome (dermatomes T3 to L3 are the most commonly affected)
- Lesions appear in crops and progress from papules to vesicles and scabs; however, unlike primary varicella, they can coalesce into large lesions and persist for 2-3 weeks
- Cranial and eyelid involvement can lead to keratoconjunctivitis and corneal scarring
- Post-herpetic neuralgia can lead to debilitating pain up to one month following resolution of the rash
- Involvement of the geniculate nucleus can lead to herpes oticus or Ramsay Hunt syndrome; vesicular lesions can be seen in the external auditory canal, and compression of facial and auditory nerves secondary to inflammation can lead to deafness, unilateral facial palsy and vertigo
- In the immunocompromised host, VZV reactivation can become widespread, leading to disseminated cutaneous zoster – disease course tends to be more prolonged
- In HIV patients, shingles is often one of the first opportunistic infections encountered

**Physical Exam**
- Typical rash described above – dermatomal pattern

**Investigations**
- For the most part, primary varicella is a clinical diagnosis
- For laboratory diagnosis, the optimal specimen is the vesicular fluid and/or skin scraping from the base of the lesion
- Several methodologies can be used to confirm VZV infection in the microbiology laboratory including:
  - Direct fluorescent antibody
  - Culture in human cell lines
  - Polymerase chain reaction (PCR)
  - Serology (IgG antibodies are useful for determining the immune status; detection of IgM suggests recent infection)

**Management/Treatment**
- Antiviral therapy to hasten healing of cutaneous lesions and to decrease the duration and severity of acute neuritis; nucleoside analogues acyclovir, valacyclovir, and famciclovir are the preferred antivirals – whether antiviral therapy decreases the risk of post-herpetic neuralgia (PHN) is less clear
- Analgesia for patients with moderate to severe acute neuritis
- Herpes zoster vaccination can decrease the risk of developing herpes zoster and post-herpetic neuralgia among individuals ≥50 years of age

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\textsuperscript{33} “Varicella” Self Learning Module, Marc Desjardins, uOttawa Faculty of Medicine

\textsuperscript{34} Albrecht, MA. “Treatment of herpes zoster in the immunocompetent host”, Post, TW (Ed), UpToDate, Waltham, MA, 2016
2.34 Human Immunodeficiency Virus (HIV)

Typical Patient
- Individual that engages in high-risk sexual and drug practices
- Particularly prevalent among population of men who have sex with men

Cause
- Infection with the human immunodeficiency virus, most often via the anogenital mucosa
- HIV infected cells fuse with CD4+ T cells, leading to spread of the virus and gradual destruction of the immune system

Symptoms/Clinical Presentation
- An estimated 10-60% of individuals with early HIV infection will not experience symptoms
- In patients who have acute symptomatic infection, the usual time from HIV exposure to the development of symptoms is two to four weeks
- Symptoms include:
  - Constitutional symptoms – fever, fatigue, myalgia/arthralgia, weight loss, headache
  - Lymphadenopathy
  - Sore throat
  - Rash
  - Gastrointestinal symptoms: nausea, diarrhea, anorexia
- Opportunistic infections are usually associated with later stages of HIV disease (oral and/or esophageal candidiasis is the opportunistic infection most often seen in these patients)

Physical Exam
- Look for the signs and symptoms above

Investigations
- HIV virologic (viral load) test
- HIV antigen detection (p24 antigen test)
- Serologic studies (immunoassay)
- Drug resistance testing
- Screening for co-infections and prior exposures

Management/Treatment
- Certain patients who have had a very recent high-risk exposure (i.e. within 72 hours) may be candidates for post-exposure prophylaxis (PEP) against HIV
- Combination antiretroviral therapy (cART)

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35 Sax, PE. “Acute and early HIV infection: Clinical manifestations and diagnosis” Post, TW (Ed), UpToDate, Waltham, MA, 2016
Cardiology & Oncology
3.1 Left Heart Failure

Typical Patient
- Men = women
- Reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF)

Cause
- Impaired contractility (e.g. coronary artery disease, chronic volume overload, dilated cardiomyopathy)
- Increased afterload (e.g. advanced aortic stenosis, uncontrolled severe hypertension)
- Impaired diastolic filling (e.g. left ventricular hypertrophy, restrictive cardiomyopathy, myocardial fibrosis, transient myocardial ischemia, pericardial constriction or tamponade)

Symptoms/Clinical Presentation
- Dyspnea, orthopnea, paroxysmal nocturnal dyspnea (PND)
- Fatigue, nausea, weakness, exercise intolerance
- Dependent edema, weight gain, abdominal distension
- Cough
- Cool extremities

Investigations
- Physical exam for volume assessment, murmurs
- Blood work: Complete blood count (CBC), lyes, creatinine, liver function tests (LFTs), B-type natriuretic peptide (BNP), troponin
- Chest X-ray (cardiomegaly, pulmonary edema)
- Echo +/- MRI +/- coronary angiogram

Management/Treatment

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1 “Heart Failure”, Haissam A Haddad, January 11 2016, uOttawa Faculty of Medicine
NYHA Classification

Class I:
- No symptoms
- No limitations with ordinary activity

Class II:
- No symptoms at rest
- Mild limitation with strenuous activity

Class III:
- Minimal symptoms at rest
- Limitation with regular activity

Class IV:
- Symptoms at rest
- Limitation with any activity
3.2 Right Heart Failure

Typical Patient

- Could affect any age depending on the cause, but typically the elderly

Cause

Anything that prevents the right ventricle from effectively pumping blood to the lungs. There are 3 main categories:

- Cardiac cause:
  - Left heart failure - most common cause
  - Valvular: Pulmonary stenosis or regurgitation, tricuspid regurgitation
  - Right ventricular infarction

- Congenital:
  - Atrial septal defect, tetralogy of fallot
  - Pressure overload states
  - Cardiomyopathies
  - Pericardial processes, e.g. constriction

- Other:
  - Post cardiac surgery, acute respiratory distress syndrome (ARDS), sepsis
  - Pulmonary hypertension
  - All 5 groups

Clinical Presentation

- Abdominal pain, bloating, nausea, anorexia
- Shortness of breath – if accompanying left heart failure (LHF)
- Weakness, exercise intolerance
- Nocturia - urinating more frequently at night
- Significant increase in weight over a short period of time

Physical Exam

- Inspection:
  - Distension of external jugular vein, elevated Jugular Venous Pressure (JVP) with abdominal jugular reflux, positive Kussmaul’s sign, visible ascites.

- Palpation:
  - Right ventricular heave
  - Pitting edema
  - Hepatomegaly

- Auscultation: S3 heart sound. Possible murmur if accompanying valvular disease; possible loud S2 if pulmonary hypertension

Investigations

- Chest X-ray
- ECG
- Echocardiogram

- Basic blood work may be done including liver function and kidney function: CBC, electrolytes, blood urea nitrogen (BUN), creatinine, glucose, liver enzymes

Management/Treatment

- Treatment of underlying condition, e.g. pulmonary hypertension, valve disease that led to right heart failure (RHF)
- Diuretics for decongestion; Salt and fluid restriction
- Ventricular assist devices, heart transplant

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2 “Acute decompensated heart failure”, Sharon Chih, January 13 2016, uOttawa Faculty of Medicine
3.3 Anaphylactic Shock

Typical Patient
- Patient with Vasoplegia and increased capillary permeability due to an immunologic or chemical reaction

Cause
- Allergic reaction

Symptoms/Clinical Presentation
- Feeling anxious
- Chest discomfort or tightness
- Diarrhea
- Difficulty breathing, coughing, wheezing, or high-pitched breathing sounds
- Difficulty swallowing
- Dizziness or lightheadedness
- Hives, itchiness, redness of the skin
- Nasal congestion
- Nausea or vomiting
- Palpitations
- Slurred speech
- Swelling of the face, eyes, or tongue
- Unconsciousness

Physical Exam
- Low blood pressure
- Orthostatic hypotension
- Skin exam

Investigations
- Allergy

Management/Treatment
- Eliminate the triggering cause
- Intravenous anti-histamine and corticosteroids
- Blood pressure management: epinephrine and IV fluids if necessary

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3 “Shock”, Matthew Cameron, January 13 2016, uOttawa Faculty of Medicine
3.4 Cardiogenic Shock

Typical Patient
- Patient with left or right heart failure (mortality 40-80%)

Cause
- Left or right heart failure
- Myocardial infarction
- Abnormal heart rhythm

Symptoms/Clinical Presentation
- Chest pain or pressure
- Decreased urination
- Fast breathing
- Fast pulse
- Heavy sweating, moist skin
- Lightheadedness
- Loss of alertness and ability to concentrate
- Restlessness, agitation, confusion
- Shortness of breath
- Skin that feels cool to the touch
- Pale skin color or blotchy skin
- Weak (thready) pulse

Physical Exam
- Low blood pressure (most often less than 90 systolic)
- Blood pressure that drops more than 10 points when you stand up after lying down (orthostatic hypotension)
- Weak pulse

Investigations
- Cardiac catheterization
- Chest X-ray
- Coronary angiography
- Echocardiogram
- Electrocardiogram
- Nuclear scan of the heart
- Arterial blood gas, blood chemistry, complete blood count, cardiac enzymes

Management/Treatment
- Treat the underlying cause (e.g. dilation, bypass, cardiac transplantation)
- Medication
  - Dobutamine
  - Dopamine
  - Epinephrine
  - Levosimendan
  - Milrinone
  - Norepinephrine
- Electrical "shock" therapy (defibrillation or cardioversion)
- Implanting a temporary pacemaker

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4 “Shock”, Matthew Cameron, January 13 2016, uOttawa Faculty of Medicine
3.5 Hypovolemic Shock

Typical Patient
- Patient with insufficient intravascular volume (mortality <10%)

Cause
- Blood loss
- Burns
- Diarrhea
- Excessive perspiration, vomiting, dehydration
- Pancreatitis or bowel obstruction

Symptoms/Clinical Presentation
- Anxiety or agitation
- Cool, clammy skin
- Confusion
- Decreased or no urine output
- General weakness
- Pale skin color (pallor)
- Rapid breathing
- Sweating, moist skin
- Unconsciousness

Physical Exam
- Low blood pressure (most often less than 90 systolic)
- Blood pressure that drops more than 10 points when you stand up after lying down (orthostatic hypotension)
- Weak pulse

Investigations
- Cardiac catheterization
- Chest X-ray
- Coronary angiography
- Echocardiogram
- Endoscopy
- Electrocardiogram
- Nuclear scan of the heart
- Arterial blood gas, blood chemistry, CBC, cardiac enzymes

Management/Treatment
- Treat the underlying cause (e.g. hydration)
- Supportive medication
  - Dobutamine
  - Dopamine
  - Epinephrine
  - Levosimendan
  - Milrinone
  - Norepinephrine

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5 “Shock”, Matthew Cameron, January 13 2016, uOttawa Faculty of Medicine
3.6 Septic Shock

Typical Patient
- Patient with vasoplegia and microcirculation dysfunction due to toxins (mortality 40-50%)

Cause
- Bacterial, viral, or fungal infection
- Risk factors
  - Diabetes
  - Diseases of the genitourinary system, biliary system, or intestinal system
  - Diseases that weaken the immune system, such as AIDS
  - Indwelling catheters (those that remain in place for extended periods, especially intravenous lines and urinary catheters, and plastic and metal stents used for drainage)
  - Leukemia
  - Long-term use of antibiotics
  - Lymphoma
  - Recent infection
  - Recent surgery or medical procedure
  - Recent use of steroid medicines
  - Solid organ or bone marrow transplantation

Symptoms/Clinical Presentation
- Cool, pale arms and legs
- High or very low temperature, chills
- Lightheadedness
- Little or no urine
- Low blood pressure, especially when standing
- Palpitations
- Rapid heart rate
- Restlessness, agitation, lethargy, or confusion
- Shortness of breath
- Skin rash or discoloration
- Decreased mental status

Physical Exam
- Low blood pressure (most often less than 90 systolic)
- Blood pressure that drops more than 10 points when you stand up after lying down (orthostatic hypotension)
- Weak pulse

Investigations
- Urine culture
- Chest X-ray
- Nuclear scan of the heart
- Arterial blood gas, blood chemistry, CBC
- Blood culture

Management/Treatment
- Antibiotics
- Corticosteroids

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6 “Shock”, Matthew Cameron, January 13 2016, uOttawa Faculty of Medicine
3.7 Hypertrophic Cardiomyopathy (HCM) 7,8

Definition:
- Genetic cardiovascular disease with inappropriate right or left ventricular (often asymmetric with septal involvement) not solely explained by any cardiac or systemic cause.

Typical Patient
- Young male or female

Cause
- Genetic mutations mainly in genes encoding for sarcomeric proteins
- Familial (autosomal dominant pattern) inheritance, mainly due to abnormal sarcomeric genes

Symptoms/Clinical Presentation
- Dyspnea (the most common presenting symptom)
- Exertional limitations and shortness of breath
- Angina
- Syncope and presyncope
- Palpitations and arrhythmias
- Heart failure
- Sudden cardiac death (1%/year)

Physical Exam
- S4 Audible or palpable S4; ‘triple-ripple’ PMI
- Systolic ejection crescendo-decrescendo murmur
- Holosystolic murmur at the apex and axilla of mitral regurgitation
- Jugular venous pulse revealing a prominent a wave; carotid impulse has ‘spike and dome’ contour

Investigations
- Echocardiography: 1- left ventricular hypertrophy, 2- septal size >15 mm, 3- dilated left atrial size >4 cm, 4- systolic anterior movement of mitral valve with mitral regurgitation
- ECG may include the following characteristics: 1- left ventricular hypertrophy, 2- abnormal Q waves, 3- ST depressions, 4- T inversion, 5- P-R prolongation, 6- bundle branch block, 7- atrial enlargement
- Chest radiograph: normal or enlarged

Management/Treatment
- Beta-blocker, calcium channel blocker, diltiazem, amiodarone, and disopyramide
- Avoid positive inotropes, vasodilators, and dehydration
- ICD
- Avoid competitive sports
- Myectomy
- Heart transplant

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7 "Cardiomyopathy", Sharon Chih, Jan 14 2016, uOttawa Faculty of Medicine
8 Shah, SN. "Hypertrophic Cardiomyopathy: Practice Essentials, Background, Pathophysiology", Ooi, HH (ED), Medscape, 2016
3.8 Dilated Cardiomyopathy (DCM)\(^9\)

**Typical Patient**
- Adults M=F
- Most common cardiomyopathy in children
- Age variation dependent on etiology

**Cause**
- Idiopathic
- Genetic (autosomal dominant inheritance)
- Acquired (infectious myocarditis, peripartum, chemotherapy, alcoholic, sarcoidosis)

**Symptoms/Clinical Presentation**
- Progressively reduced exercise tolerance with dyspnea on exertion; eventually dyspnea at rest
- Orthopnea, PND
- Peripheral edema, ascites
- Mesenteric ischemia with pain postprandial, nausea, vomiting
- Arrhythmias with palpitations, syncope
- Sudden death

**Physical Exam**
- Auscultation may reveal presence of S3, S4
- Basal crackles on auscultation
- Elevated JVP, peripheral edema, ascites
- Weak peripheral pulses, hypotension (if low cardiac output)

**Investigations**
- ECG (sinus tachycardia, nonspecific ST and T wave segment changes, atrial enlargement)
- Chest X-ray (cardiothoracic ratio >0.5)
- Echo (abnormal LV function, mitral and/or tricuspid regurgitation)
- CBC, creatine kinase, BNP, troponin I and T

**Management/Treatment**
- Treat underlying cause
- Supportive therapy: sodium/fluid restriction, avoidance of alcohol
- Diuretics, vasodilators p.r.n.
- Long-term: ACEI, beta-blockers, aldosterone antagonists
- ICD implantation if high risk for ventricular arrhythmia

\(^9\) Goldman L, Schafer AI. Goldman’s Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.9 Restrictive Cardiomyopathy\textsuperscript{10,11}

Typical Patient
- More common in the elderly

Cause
- Inherited/hereditary
- Infiltrative:
  - Amyloidosis
  - Sarcoidosis
- Storage diseases: hemochromatosis, glycogen storage disease, Fabry disease
- Endomyocardial fibrosis
- Radiation (eg: radiation for breast cancer leading to fibrosis)

Clinical Presentation
Presentation mainly due to reduced cardiac output and congestion.
- Signs: Present with heart failure but preserved systolic function. In restrictive cardiomyopathy, there is diastolic dysfunction $\rightarrow$ increased pressures lead to congestion
  - Peripheral edema
  - Pulmonary edema
- Symptoms:
  - Dyspnea, orthopnea, PND
  - Exercise intolerance
  - Ascites, peripheral edema
  - Palpitations
- Specific presentations:
  - Amyloidosis:
    - May have rapid progression of heart failure
    - Presyncope or syncope from conduction blocks or arrhythmias
    - Systemic signs of amyloid deposition: neuropathy, orthostatic hypotension, macroGLOSSIA, abnormal nail beds, periorbital bruising
  - Haemochromatosis:
    - Arrhythmias (heart block)
  - Sarcoidosis:
    - Ventricular arrhythmias, complete heart block, heart failure

Physical Exam
- Inspection:
  - Elevated JVP with prominent x and y descents and positive Kussmaul’s sign
  - Other signs of heart failure – pitting edema, etc.
- Auscultation: May have S3 and S4 extra heart sounds. May have regurgitation murmurs. Crackles for pulmonary edema.

Investigations
- ECG
- Chest X-ray
- Echocardiography
- Endomyocardial biopsy if needed to determine etiology

Management/Treatment
- Need to exclude constrictive pericarditis, which has a similar presentation
- Need to treat underlying disease
- Treatment heart failure and arrhythmias

\textsuperscript{10} "Workshop on Cardiomyopathy", Sharon Chih, January 14, 2016, uOttawa Faculty of Medicine
\textsuperscript{11} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
3 Cardiology and Oncology

- Heart transplant

### 3.10 Stable Angina\textsuperscript{12,13}

#### Typical Patient
- Patients with chest pain due to imbalance in supply: demand of the heart (prevalence increases with age due to an increase in atherosclerosis)

#### Cause
- Decrease in myocardial supply: 1- coronary atherosclerotic lesion, 2- coronary spasm, 3- aortic stenosis, 4- hypertrophic cardiomyopathy
- Increase in myocardial demand: 1- LV hypertrophy, 2- hypertrophic cardiomyopathy, 3- increase in LV diastolic pressure, dilated cardiomyopathy, 4- tachycardia (ventricular and supraventricular)
- Systemic inflammatory or collagen vascular disease: 1- scleroderma, 2- systemic lupus erythematosus, 3- Kawasaki disease, 4- polyarteritis nodosa, 5- Takayasu arteritis
- Congenital cardiac anomalies

#### Symptoms/Clinical Presentation
- Chest pain or discomfort (pressure, squeezing, burning and heaviness)
- Shortness of breath
- Pain in neck, jaw, arm and shoulder
- Fatigue, nausea, vomiting and dizziness

#### Physical Exam
- Thorough medical history is critical for the diagnosis
- A positive Levine sign (clenched fist held over the chest) suggests angina pectoris

#### Investigations
- Exercise stress testing with ECG monitoring
- Stress echocardiography
- Coronary angiography

#### Management/Treatment
- Pharmacologic therapy: Beta-blocker, calcium channel blocker, ACE inhibitors, aspirin, clopidogrel, statins, and nitrates
- Lifestyle modifications: smoking cessation, treatment of risk factors (eg, hypertension, diabetes mellitus, obesity, hyperlipidemia)
- Procedures: Angioplasty and stenting, coronary artery bypass graft surgery

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\textsuperscript{12} Alaeddini, J. “Angina Pectoris: Practice Essentials, Background, Pathophysiology” Yang, EH, Medscape, 2016

\textsuperscript{13} Mayoclinic. “Angina” Mayoclinic, 2016.
3.11 Non-STEMI

Typical Patient
- 50 year old male
- Overweight/obese; hypertension
- Metabolic syndrome

Cause
- Acute thrombus formation/platelet aggregation secondary to rupture of atherosclerotic plaque
- Subsequent occlusion of coronary artery with subendocardial infarction
- Rarely, coronary artery vasospasm secondary to substance abuse or endothelial dysfunction

Symptoms/Clinical Presentation
- Typically, acute retrosternal chest pressure, squeezing, heaviness either intermittent or persistent
- Acute chest pain radiating to left arm, jaw
- Syncope, nausea, vomiting
- Atypically, aching chest pain, epigastric pain, indigestion, unexplained dyspnea

Physical Exam
- Most commonly unremarkable
- Auscultation may reveal basilar rales, ventricular gallop
- Beneficial to rule out other causes (e.g., costochondritis)

Investigations
- ECG (ST-depression, t-wave inversion in multiple leads; NO ST-elevation)
- Serum biomarkers (elevated troponin I, CK-MB)
- Coronary angiography (if high risk for MI/death in coming weeks to months)
- Exercise stress testing (if lower risk)

Management/Treatment
- If no ECG/biomarker abnormalities, reassess in 4-8 hours; if negative, perform stress test; if negative discharge with outpatient f/u
- If ECG/biomarker changes at outset or on 4 hour reassessment- admit and tx. ischemia
- If NSTEMI, administer to all patients: aspirin (ASA), beta-blocker/calcium channel blocker, nitroglycerin, statin
- If low-risk patient: unfractionated heparin (UFH) or enoxaparin + clopidogrel or ticagrelor
- If high-risk patient: Enoxaparin or UFH; pre-catheterization clopidogrel/ticagrelor or GP IIb, IIIa inhibitor; perform PCI post-angiography

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14 Goldman L, Schafer AI. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.12 ST-Segment Elevation Myocardial Infarction (STEMI)\textsuperscript{15}

Typical Patient
- More common in men than women before age 50 (after menopause, both men and women are equal)
- Usually have cardiac risk factors such as smoking, hyperlipidemia, high blood pressure, diabetes, family history of heart disease

Cause
- ST-elevation takes place if there is ischemia to the full thickness of the cardiac wall
- Ischemia mainly occurs due to atherosclerotic plaque rupture with complete occlusion of the coronary artery
- In rare cases could be due to vasospasm

Clinical Presentation
- Symptoms:
  - Intense pain / pressure in the chest (may describe as “elephant on chest”)
  - Pain often radiates to the neck, jaw, shoulder, or arm
  - Shortness of breath
  - Women may experience back pain
- Signs:
  - Diaphoresis
  - If severe STEMI with heart failure may see additional signs such as pedal edema, cyanosis, etc.

Physical Exam
- Vital signs:
  - Blood pressure may be increased due to sympathetic stimulation or decreased due to cardiogenic shock
  - May have tachycardia and tachypnea
  - Oxygen saturation may be low
- Inspection:
  - Tripod position
  - May have signs of heart failure if severe STEMI – pedal edema, cyanosis, high JVP
- Auscultation:
  - May have a S4 heart sound, but not always
  - May hear a regurgitation murmur if ischemia leads to papillary muscle dysfunction

Investigations
- 12 lead ECG: ST-elevations indicate the location of ischemia and therefore able to determine the coronary vessel that is affected
- Blood work: Cardiac biomarkers (troponin, creatine kinase), CBC, BUN, creatinine, electrolytes, glucose
- Chest X-ray

Management/Treatment
- Revascularization:
  - Percutaneous coronary intervention (PCI) – preferred management when symptom onset <12h
  - Fibrinolytics
  - Coronary artery bypass graft (CABG)
- Long-term medical treatment:
  - Clopidogrel (1 year only)
  - Aspirin
  - Statin
  - Beta-blocker
  - Nitrate – as needed (PRN)

\textsuperscript{15}“Acute Coronary Syndromes”, Marino Labinaz, January 20 2016, uOttawa Faculty of Medicine
3.13 Aortic Regurgitation

Typical Patient
- N/A but the prevalence increases with age due to degeneration of the valve

Cause
- Congenital (i.e. bicuspid valve is the most common congenital abnormality)
- Endocarditis
- Rheumatic fever
- Aortic root dilatation (Long standing uncontrolled hypertension is most common, syphilis)
- Degenerative aortic valve disease
- Collagen vascular disease (Marfan’s syndrome, Ehlers-Danlos)
- Traumatic/Post surgical

Symptoms/Clinical Presentation
- Dyspnea on exertion
- Fatigue
- Chest pain (angina)
- Heart failure
- Myocardial ischemia
- Palpitations/head pounding

Physical Exam
- Wide pulse pressure and associated peripheral manifestations, e.g. water hammer pulse
- Bounding pulses
- Early diastolic decrescendo best heard while patient leans forward at end exhalation (holodiastolic murmur in case of severe aortic regurgitation)
- Diastolic Austin flint murmur (functional mitral stenosis from jet of aortic regurgitation)

Investigations
- Echocardiography
- MRI (cardiac, aorta)
- Blood test depending on the etiology

Management/Treatment
- Diuretics if HF symptoms
- Calcium antagonists/ACEI to treat hypertension
- Surgical therapy (repair, replacement, Transcatheter aortic valve implantation (TAVI))

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16 “Valvular stenosis and insufficiency”, Kathryn Ascah, January 2016, uOttawa Faculty of Medicine
17 Wang, SS. “Aortic Regurgitation: Background, Pathophysiology, Etiology”, O’Brien, TX (ED), Medscape, 2016
3.14 Aortic Stenosis

Typical Patient
- 60-80 year old male or female
- History of hypertension, hyperlipidemia
- If bicuspid, usually male between ages 40-60 with or without above comorbidities

Cause
- Idiopathic thickening and calcification of the aortic valve (bicuspid or tricuspid)
- Congenital
- Secondary complication decades post-rheumatic fever

Symptoms/Clinical Presentation
- Angina
- Syncope
- Heart failure (e.g., peripheral edema, elevated JVP, etc.)

Physical Exam
- Auscultation reveals systolic ejection murmur radiating to neck
- Delayed upstroke, i.e. “pulsus tardus et parvus”
- Auscultation may reveal S4

Investigations
- ECG (may show left atrial enlargement (LAA), left ventricular hypertrophy (LVH))
- CXR (boot shaped heart, aortic valve calcification; commonly unremarkable however)
- Echo (LVH, elevated flow velocity)

Management/Treatment
- If asymptomatic, no treatment indicated
- If not a candidate for invasive surgery but symptomatic, offer supportive treatment (e.g., nitroglycerin for angina, diuretics for HF)
- Valve replacement surgery, percutaneous aortic valve replacement, or balloon aortic valvotomy, if candidate
- Vasodilators not recommended

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18 Goldman L, Schafer AI. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.15 Mitral Regurgitation

Typical Patient
N/A

Cause
- Ischemic
- Myxomatous mitral valve
- Rheumatic
- Congenital

Symptoms/Clinical Presentation
- Fatigue, weakness
- Dyspnea, orthopnea, PND
- Right heart failure

Physical Exam
- Apical pansystolic murmur radiating to the axilla
- Tachycardia
- Hypotension

Investigations
- ECG
- Cardiac function exam (e.g. left ventricular ejection fraction)
- Imaging (e.g. X-Ray, CT, MRI, ultrasound)
- Cardiac catheterization, angiography

Management/Treatment
- Afterload-reducing agents
- Diuretics
- Surgery
  - Repair
  - Replacement
- Mitral clip

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19 "Valvular Heart Disease" by Kathryn Ascah, January 25, 2016, uOttawa Faculty of Medicine
3.16 Mitral Stenosis

Typical Patient
- Mitral stenosis is usually seen in patients from developing countries as well as aboriginal populations, where there is limited availability of antibiotics
- Usually have a history of childhood strep infection and acute rheumatic fever

Cause
- Rheumatic disease (most common)
- Congenital (rare)
- Radiation fibrosis (eg: breast cancer)

Clinical Presentation
- Symptoms:
  - Fatigue
  - Palpitations
  - Orthopnea
  - Shortness of breath, especially with exertion
  - Hemoptysis - rupture of lung vessels due to increased pressure
- Signs of right heart failure may develop based on development of pulmonary hypertension
  - Peripheral edema
  - Liver congestion
  - Ascites
  - Pedal edema
- May experience systemic embolization due to development of atrial fibrillation (as a result of atrial enlargement)
  - Stroke
  - Myocardial infarction

Physical Exam
- Inspection:
  - High JVP if right heart failure
- Palpation:
  - Right parasternal lift associated with RVH
  - Diastolic thrill at apex (5th intercostal space) indicative of palpable murmur
- Auscultation:
  - Low pitch diastolic murmur at apex – best heard with bell in the left lateral decubitus position
  - Murmur follows an opening snap and occurs between S1 and S2
  - Loud S1 and loud P2

Investigations
- ECG: to assess atrial fibrillation, RVH, left atrial hypertrophy
- Chest X-ray: to assess left atrial enlargement, mitral valve calcification
- Echocardiography: decreased flow through stenotic mitral valve

Management/Treatment
- Treat atrial fibrillation and heart failure (e.g., anticoagulants to prevent thromboembolic events)
- Procedures if failure of medical therapy with persistent heart failure
  - Valve replacement
  - Percutaneous balloon valvuloplasty – there is risk of developing regurgitation
- Management of pulmonary edema - diuretics

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20 “Physiology of valvular heart disease”, Kathryn Aschah, January 25, 2016, uOttawa Faculty of Medicine
3.17 Tricuspid Regurgitation

Typical Patient
- Varies depending on the underlying etiology

Cause
- Most commonly dilation of the right ventricle secondary to hemodynamic load (e.g., elevated LV filling pressures, pulmonary hypertension)
- Infective endocarditis with damage to tricuspid valve proper (usually secondary to IV drug abuse)

Symptoms/Clinical Presentation
- Heart failure signs and symptoms if severe (e.g., elevated JVP, ascites, hepatic enlargement)

Physical Exam
- Auscultation may reveal holosystolic murmur heard along left sternal border
- Right parasternal lift
- Abdominal exam may reveal ascites, hepatomegaly, elevated JVP

Investigations
- ECG (may demonstrate right atrial enlargement, right ventricular hypertrophy)
- Echo (RV dilation, possible pulmonary hypertension, valve integrity)

Management/Treatment
- Treat underlying cause (e.g., pulmonary hypertension, LV failure)
- Ring annuloplasty or tricuspid valve repair, if concomitant left-sided valve surgery to be performed
- Very rarely, tricuspid valve replacement if severe deformity of valve

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21 Goldman L, Schafer AI. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.18 Tricuspid Stenosis

Typical Patient
- N/A (depending on the etiology)

Cause
- Rheumatic fever is the etiology in most cases
- Carcinoid heart disease
- Congenital tricuspid stenosis
- Infective endocarditis

Symptoms/Clinical Presentation
- Fatigue
- Edema in the periphery
- Dyspnea
- Distension in the abdomen/liver, abdominal pain and swelling
- May complain of prominent pulsations in the neck

Physical Exam
- Elevated JVP and prominent a wave
- Peripheral edema
- Diastolic murmur (low pitched and difficult to hear, louder with inspiration)

Investigations
- Echocardiography
- Chest radiography
- Blood test depending on the etiology

Management/Treatment
- Treatment of the etiology
- Surgical therapy
- Dietary Na restriction in case of right-sided HF

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22 “Valvular stenosis and insufficiency”, Kathryn Ascah, January 2016, uOttawa Faculty of Medicine
23 Mancini, MC. “Tricuspid Stenosis: Background, Pathophysiology, Epidemiology”, Lange, RA (Ed), Medscape, 2016
3.19 Pulmonary Regurgitation

Typical Patient
- Wide age range, based on etiology

Cause
- Pulmonary hypertension
- Rheumatic heart disease
- May be caused by repair of pulmonary stenosis

Clinical Presentation
- Symptoms:
  - Chest pain
  - Syncope
  - Fatigue
- Signs:
  - Venous congestion due to backwards flow of blood
  - Peripheral edema

Physical Exam
- Inspection:
  - High JVP
  - Peripheral Edema
  - Ascites
- Palpation:
  - Pedal edema
  - Abdominal tenderness
- Auscultation:
  - Early diastolic murmur at the left sternal border (may not hear as low pitch)
  - Often there is a systolic ejection murmur due to increased volume through the outflow tract

Investigations
- Chest X-ray
  - Right ventricle dilation
  - Signs of pulmonary hypertension if present - engorgement of pulmonary vessels
- ECG
- Echocardiography:
  - Diagnostic

Management/Treatment
- Pulmonary valve repair - preferred
- Pulmonary valve replacement
  - Mechanical valve – need Coumadin to prevent blood clots
  - Bioprosthetic valve - no anticoagulant needed, however high wear and tear
3.20 Pulmonic Stenosis

Typical Patient
- Patients with RVH

Cause
- Congenital
  - Valvular
  - Supravalvular
  - Subvalvular
- Rheumatic
- Carcinoid

Symptoms/Clinical Presentation
- Fatigue, weakness
- Dyspnea, orthopnea, PND
- Syncope
- Angina

Physical Exam
- Opening snap after S1 and systolic crescendo decrescendo (ejection) murmur at upper left sternal border
- Elevated jugular vein pressure
- Right ventricular lift
- Cyanosis

Investigations
- ECG
- Cardiac function exam (e.g. left ventricular ejection fraction)
- Imaging (e.g. X-Ray, CT, MRI, ultrasound)
- Cardiac catheterization, angiography

Management/Treatment
- Surgery
  - Repair
  - Replacement

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25 “Valvular Heart Disease”, Kathryn Asch, January 25, 2016, uOttawa Faculty of Medicine
3.21 Aortic Dissection

Typical Patient
- N/A (its prevalence increases with age) - typically occurs in patients between 50-70 years old

Cause
- There are various risk factors for the development of aortic dissection including:
  1. Conditions associated with increased aortic wall stress (hypertension, trauma, weight lifting, etc.)
  2. Conditions associated with aortic valve abnormalities

Symptoms/Clinical Presentation
- ~1% mortality per hour for 48 hours
- 5-20% mortality even with surgery
- Sharp, ‘tearing’ chest pain radiating to the back (rated 10 out of 10 by patients)
- Symptoms can be variable depending on location and extent of involvement of aorta and its branches
- Coronary Ischemia: chest pain
- Cerebrovascular ischemia: symptoms of stroke (loss of consciousness, aphasia, paralysis, etc)
- Visceral ischemia: abdominal pain
- Limb ischemia: cold, pulseless leg
- Pericardial tamponade: hypotension and cardiovascular collapse
- Acute aortic insufficiency: dyspnea and heart failure symptoms

Physical Exam
- Vitals: can be hypotensive or hypertensive
- Blood pressure differential in both upper limbs
- Cardiovascular: AI murmur, signs of pericardial tamponade
- Abdominal: pain, pulsatile abdominal mass
- Peripheral vascular exam: signs of acute limb ischemia (cold, dusky, pulseless leg)

Investigations
- ECG: may show signs of coronary ischemia or be non-specific
- CXR – signs of aortic dilation (widened mediastinum)
- CT-scan is diagnostic (high sensitivity and specificity, provides information about extent of involvement of aorta and its branches)
- Transesophageal echocardiography (High specificity; sensitivity slightly lower than CT-scan, provides information about cardiac and valvular function, limited information about extent of involvement of branch vessels)
- MRI – typically not used in the acute setting

Management/Treatment
- **Type A:** Stabilize patient, Surgical intervention
- **Type B:** Uncomplicated vs. complicated type B dissection
  - Uncomplicated – Medical therapy (Blood pressure control, monitoring for complications, surveillance imaging)
  - Complicated by malperfusion, aneurysm formation, rupture/impending rupture – evaluate for surgical or endovascular treatment

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26 “Aortic Pathology and Peripheral Arterial Disease”, Munir Boodhwani, February 6 2016, uOttawa Faculty of Medicine
3.22 Pulmonary Hypertension

Causes
- Type 1 (arterial): idiopathic, heritable, or drug-induced [female, 20-40 year-old]
- Type 2: due to left heart disease
- Type 3: due to lung disease, Cor pulmonale
- Type 4: due to thrombosis
- Type 5: unclear and/or multifactorial mechanisms

Symptoms/Clinical Presentation
- Chest pain
- Shortness of breath
- Fatigue
- Difficulty breathing with exertion
- Dizziness
- Rapid breathing
- Rapid heart rate
- Edema

Physical Exam
- Loud P2 sound on auscultation, and murmurs associated with tricuspid or pulmonic insufficiency
- Elevated jugular venous pressure
- Peripheral edema
- Ascites
- Hepatojugular reflux
- Clubbing

Investigations
- Echocardiogram
- Right heart catheterization

Management/Treatment
- Management of underlying causes
- Supportive care
  - Vasodilator therapy
  - Anticoagulation
  - Oxygen
  - Diuretics
- Prevent disease progression
  - IV prostacyclin
  - Phosphodiesterase inhibitors
  - Endothelin receptor antagonists
- Lung transplant

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27 "Pulmonary Hypertension", George Chandy, November 11 2015, uOttawa Faculty of Medicine
3.23 Endocarditis\textsuperscript{28,29}

Typical Patient
- Risk factors: prosthetic valves or intracardiac prosthetic material, previous endocarditis, intravenous drug user (IVDU)

Cause
- Infectious causes: Staph aureus, Staph epidermidis, Strep viridans, HACEK organisms
- Less commonly, non-infectious causes: malignancy, SLE

Symptoms/Clinical Presentation
- Fever
- New murmur or worsening of previous regurgitant murmur
- Heart failure
- Peripheral manifestations: Osler node, Nail-bed hemorrhages, Janeway lesions
- Stroke symptoms (embolization)

Physical Exam
- Peripheral stigmata (e.g., Osler nodes, Janeway lesions, splinter hemorrhages) may be noticeable
- Widened pulse pressure may indicate aortic insufficiency
- Funduscopic examination may reveal Roth spots
- Auscultation may reveal new murmur or worsening of existing regurgitant murmur

Investigations
- Blood cultures (at least 3 from separate sites, at least 1 hour apart)
- CBC with electrolytes (anemia of chronic disease, elevated WBC)
- Urinalysis (hematuria, proteinuria)
- CXR (may reveal consolidation, pleural effusion, septic emboli)
- ECG (may reveal AV-block with prolonged PR interval)
- Echo (mass attached to valve, abscess, dehiscence of prosthetic valve, new valvular regurgitation)
- Ancillary tests including elevated CRP, ESR, RF may be suggestive but not diagnostic
- Diagnostic probability based on Duke criteria

Management/Treatment
- Specific antibiotic treatment based on culture and antimicrobial susceptibility testing
- Clinically stable patients without complications do not necessarily require broad-spectrum antibiotic coverage prior to culture.
- Patients not clinically stable or suffering complications require broad-spectrum coverage while culture/susceptibility testing is performed
- Surgical management for heart failure, abscess formation, difficult to treat organisms (e.g. staph aureus, fungal), persistent infection

\textsuperscript{28} Goldman L, Schafer AI. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.24 Pericarditis\textsuperscript{30,31}

Typical Patient
- N/A as there is a variety in the etiology

Cause
- Idiopathic common
- Infections especially viral, TB
- Post-myocardial infarction (acute infarction, Dressler’s syndrome)
- Connective tissue disease (RA, SLE)
- Neoplastic, commonly metastases
- Metabolic disorders, such as renal failure, hypothyroidism, and hypercholesterolemia
- Miscellaneous causes (drug induced, radiation, postoperative, traumatic)

Symptoms/Clinical Presentation
- Chest pain (retrosternal/left pericardium, sharp-knife-like, pleuritic, positional)
- Fever
- Dyspnea

Physical Exam
- Pericardial friction rub (scratchy evanescent sound best heard with diaphragm while patient leans forward and exhales

Investigations
- Echocardiography: often normal with possibility of pericardial effusion
- ECG may include the following characteristics: 1- diffuse ST segment elevation (except AVR), 2- PR segment depression (except AVR)
- Blood test (CBC, electrolytes, BUN, CR, ESR, cardiac enzymes): increase in WBC level, increase in troponin level in myopericarditis
- Other tests may include chest x-ray, TST, ANA, RF, mammogram based on clinical etiology

Management/Treatment
- NSAID (ASA, Ibuprofen) and Colchicine
- Steroids (prednisone) if not responding to above combination therapy
- Treating the etiology (antibiotics, anti TB therapy, cancer therapy, dialysis)

\textsuperscript{30} “Pericardial disease”, Ian Burwash, January 27 2016, uOttawa Faculty of Medicine
\textsuperscript{31} Spangler, S. “Acute Pericarditis: Practice Essentials, Background, Anatomy”, O’Brien, TX (Ed), Medscape, 2016
3.25 Constrictive Pericarditis\textsuperscript{32}

Typical Patient
- Profound symptoms, potentially correctable condition

Cause
- Idiopathic or viral pericarditis
- Post cardiac surgery
- Post radiation therapy
- Post TB or bacterial pericarditis
- Connective tissue disease
- Malignancy
- Uremia

Symptoms/Clinical Presentation
- Fatigue, dizziness
- Right-sided HF; ascites, peripheral edema

Physical Exam
- Low blood pressure
- Elevated jugular venous pressure with prominent Y descent
- Kussmaul sign
- Pericardial knock
- Abdominal swelling, peripheral edema

Investigations
- Chest X-ray
- Echocardiogram
- Cardiac MRI
- Cardiac catheterization

Management/Treatment
- Treat HF symptoms with diuretics
- Pericardiectomy

\textsuperscript{32} “Pericardial disease”, Ian Burwash, January 27 2016, uOttawa Faculty of Medicine
### 3.26 Cardiac Tamponade

**Typical Patient**
- Sudden onset with severe distress/shock
- May have a history of pericarditis or pericardial effusion

**Cause**
Impaired diastolic filling of the heart due to increased intrapericardial pressure through fluid accumulation.
- Infection- viral, bacterial, TB
- Trauma
- Neoplasm
- Radiation
- Drug induced
- Uremia
- Proximal aortic dissection with rupture
- Cirrhosis
- Nephrotic syndrome

<table>
<thead>
<tr>
<th>Beck’s triad:</th>
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<tbody>
<tr>
<td>Hypotension</td>
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<tr>
<td>Elevated JVP</td>
</tr>
<tr>
<td>Muffled heart sounds</td>
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</tbody>
</table>

**Clinical Presentation**
- Signs:
  - Tachypnea
  - Peripheral edema
  - Hepatic congestion
- Symptoms:
  - Dyspnea
  - Pleuritic chest pain

**Physical Exam**
- Vitals:
  - Hypotension
  - Tachycardia
  - Tachypnea
  - Pulsus paradoxus – systolic BP drops > 10 mmHg with inspiration
- Inspection:
  - High JVP: “x” descent only, absent “y” descent
- Auscultation:
  - Muffled/decreased heart sounds
  - May hear pericardial rubs

**Investigations**
- ECG:
  - Low QRS voltage
  - QRS alternans (heart swinging in effusion)
  - Pericarditis finding (diffuse ST-elevation, PR segment depression)
- Echocardiogram:
  - Excessive pericardial effusion
  - Compression of cardiac chambers in diastole
  - Exaggerated respiratory movement of ventricular septum
  - Excessive respiratory variation in ventricular filling

**Management/Treatment**
- Echo guided pericardiocentesis
- Pericardiotomy
- IV fluids to increase cardiac output
- Treatment of underlying cause

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33 “Pericardial disease”, Ian Burwash, January 27 2016, uOttawa Faculty of Medicine
3.27 Atrial Fibrillation

Typical Patient
- Patients with irregular and rapid heart rate (its prevalence increases with age)
- More common in females

Cause
- Hemodynamic stress
- Cardiac structural abnormalities due to: 1- hypertension, 2- coronary artery disease, 3- valvular disease, 4- congenital abnormalities, 5- myocardial ischemia
- Sleep apnea
- Alcohol, caffeine, tobacco
- Family history
- Endocrine abnormalities such as overactive thyroid gland
- Sick sinus syndrome
- Inflammations and infections
- Lung diseases

Symptoms/Clinical Presentation
- Some patients are asymptomatic
- Palpitations
- Fatigue
- Exercise intolerance and shortness of breath
- Lightheadedness, dizziness, and confusion
- Presyncope and syncope

Investigations
- ECG: 1- Irregularly irregular, 2- Heart rate (typically in the 110-140 range, but rarely over 160-170)
- Holter monitor
- Echocardiography
- Cardiac MRI/CT
- Laboratory studies: CBC, cardiac enzymes, thyroid function studies, digoxin level when appropriate, serum electrolytes and BUN/creatinine for determining the underlying cause

Management/Treatment
- Pharmacologic therapy: antiarrhythmic therapy (rate control or rhythm control), antithrombotic therapy (warfarin, DOAC) to reduce the risk of stroke
- Electrical DC cardioversion
- Ablation therapy
- Surgical maze procedure

---

3.28 Atrial Flutter

Typical Patient
- Patients with irregular and rapid heart rate (no typical age; however, its prevalence increases with age)
- More common in females

Cause
- Hemodynamic stress
- Cardiac structural abnormalities due to: 1- hypertension, 2- coronary artery disease, 3- valvular disease, 4- congenital abnormalities, 5- myocardial ischemia
- Sleep apnea
- Alcohol, caffeine, tobacco
- Family history
- Endocrine abnormalities such as overactive thyroid gland
- Sick sinus syndrome
- Inflammations and infections
- Lung diseases

Symptoms/Clinical Presentation
- Some patients are asymptomatic
- Palpitations
- Fatigue
- Exercise intolerance and shortness of breath
- Lightheadedness, dizziness, and confusion
- Presyncope and syncope

Investigations
- ECG: 1- Irregularly irregular, 2- Heart rate (typically in the 110-140 range, but rarely over 160-170)
- Holter monitor
- Echocardiography
- Cardiac MRI/CT
- Laboratory studies: CBC, cardiac enzymes, thyroid function studies, digoxin level when appropriate, serum electrolytes and BUN/creatinine for determining the underlying cause

Management/Treatment
- Pharmacologic therapy: antiarrhythmic therapy (rate control or rhythm control), antithrombotic therapy (warfarin, DOAC) to reduce the risk of stroke
- Electrical cardioversion
- Ablation therapy
- Surgical maze procedure
3.29 Atrioventricular Block- First Degree\textsuperscript{37,36}

Typical Patient
- 40-60 year old male or female, though can occur in anyone
- Typically not accompanied by other arrhythmias/cardiac disease

Cause
- Reversible or structural
- Reversible: enhanced vagal tone, AV node ischemia, medications suppressing conduction through the AV node (e.g., Beta-blockers, CCB's)
- Structural: myocardial infarction, degenerative diseases of the conduction system (commonly due to aging)

Symptoms/Clinical Presentation
- Generally asymptomatic

Physical Exam
- None

Investigations
- ECG (prolongation of PR interval >0.2 seconds or >5 small squares)

Management/Treatment
- Generally a benign condition not requiring treatment
- May render susceptibility to more severe AV-block

\textsuperscript{37} Lilly, SL, “Pathophysiology of Heart Disease (6th ed.),” Philadelphia: Lippincott Williams & Wilkins, 2016
3.30 Atrioventricular Block- Second Degree- Type I (Wenckebach)\textsuperscript{38}

Typical Patient
- Patient descriptions will vary widely
- Can occur in children, athletes, and those with a high vagal tone
- Can also occur transiently in patients with myocardial infarction (MI)

Cause
- Impaired conduction through the AV node. Commonly, a result of heightened vagal tone (e.g., athletes) and AV node ischemia (e.g., MI)

Symptoms/Clinical Presentation
- Most commonly asymptomatic

Physical Exam
- None

Investigations
- ECG (repetition of progressively increasing PR interval with eventual block in conduction - i.e. p wave NOT followed by QRS)

Management/Treatment
- Generally a benign condition not requiring treatment
- Temporary treatment involves IV isoproterenol/atropine for transient improvement in AV conduction
- Occasionally, insertion of pacemaker if symptomatic and refractory to treatment

\textsuperscript{38} Lilly, SL, “Pathophysiology of Heart Disease (6\textsuperscript{th} ed.),” Philadelphia: Lippincott Williams & Wilkins, 2016
3.31 Atrioventricular Block - Second Degree - Type II

Typical Patient
- 60 year old male or female
- Often other cardiac comorbidities present

Cause
- Conduction block distal to AV node (bundle of His, Purkinje system)
- Often due to extensive myocardial infarction and/or chronic degeneration of the His-Purkinje system

Symptoms/Clinical Presentation
- Dizziness/lightheadedness
- Exertional dyspnea
- Presyncope/syncope
- Fatigue

Physical Exam
- None

Investigations
- ECG (sudden loss of QRS complex after P wave, without preceding gradual PR lengthening; often right or left bundle branch block)

Management/Treatment
- Requires pacemaker insertion even if asymptomatic

---

3.32 Atrioventricular Block - Third Degree (Complete Block)\textsuperscript{40}

Typical Patient
- 70-80 year old male or female
- Often other cardiac comorbidities present

Cause
- Complete failure of conduction from the atria to the ventricles
- Often result of extensive myocardial infarction (MI) and/or chronic degeneration of the conduction pathways due to aging

Symptoms/Clinical Presentation
- Dizziness/lightheadedness
- Exertional dyspnea
- Presyncope/syncope
- Fatigue

Physical Exam
- None

Investigations
- ECG (complete dissociation of P waves and QRS complexes)

Management/Treatment
- Requires pacemaker insertion even if asymptomatic

\textsuperscript{40}Lilly, SL, "Pathophysiology of Heart Disease (6\textsuperscript{th} ed.)", Philadelphia: Lippincott Williams & Wilkins, 2016
3.33 Ventricular Tachycardia

Typical Patient
- Monomorphic ventricular tachycardia – e.g. patient suffered from a myocardial infarction
- Polymorphic ventricular tachycardia

Cause
- Cardiomyopathy
- Myocardial infarction
- Heart failure
- Heart surgery
- Myocarditis
- Valvular heart disease

Symptoms/Clinical Presentation
- Angina
- Syncope
- Lightheadedness or dizziness
- Sensation of feeling the heart beat (palpitations)
- Shortness of breath

Physical Exam
- Absent pulse
- Loss of consciousness
- Normal or low blood pressure
- Rapid pulse

Investigations
- Continuous ambulatory electrocardiogram (Holter monitor)
- Electrocardiogram (ECG)
- Intracardiac electrophysiology study (EPS)
- Rhythm monitoring with a loop recorder or device

Management/Treatment
- Cardiopulmonary resuscitation (CPR)
- Electrical defibrillation or cardioversion (electric shock)
- Ablation
- Antiarrhythmic medications (such as lidocaine, procainamide, sotalol, or amiodarone) given through a vein

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41 “Cardiac Arrhythmia”, Mouhannad Sadek, February 4 2016, uOttawa Faculty of Medicine
3.34 Peripheral Artery Disease

Typical Patient
- Mostly the elderly
- Usually have cardiovascular risk factors such as smoking, hypertension, diabetes, high cholesterol, family history of vascular disease

Cause
- Acute ischemia are mainly due to occlusion by an in-situ thrombus or embolus (eg: atrial fibrillation)
- Chronic ischemia:
  - Atherosclerotic plaques
  - Inflammation - vasculitis (eg: Takayasu arteritis)
  - Degenerative (eg: Marfan’s disease)
  - Dysplastic (eg: fibromuscular dysplasia)

Clinical Presentation
- Acute presentation: think of the 5 P’s
  - Pain
  - Pulseless
  - Pallor
  - Paralysis
  - Paresthesia
- Chronic presentation:
  - Muscular pain induced by exertion and relieved by rest
  - Critical limb ischemia is indicated by pain at rest and night pain (more severe)

Physical Exam
- Asymmetry of blood pressure bilaterally - abnormal ankle brachial index
- Inspection (chronic changes):
  - Distal hair loss
  - Trophic skin changes – shiny skin
  - Hypertrophic nails
  - Ulcers
- Palpation:
  - Weak or absent pulse
- Positive Allen’s test for hand
- Auscultation:
  - May hear bruits indicative of turbulent flow in vessels

Investigations
- Duplex ultrasound
- CT angiogram (CTA)
- Magnetic resonance angiography (MRA)
- Contrast angiography

Management/Treatment
- Acute limb ischemia:
  - Urgent surgery/catheterization (thrombectomy, embolectomy, bypass)
  - Anticoagulation
  - Irreversible limb ischemia may lead to amputation
- Chronic limb ischemia:
  - Catheter based thrombolysis – tPA
  - Medication for symptom relief: vasodilation with phosphodiesterase inhibitor
  - Medical management of hypertension, diabetes, and high cholesterol
  - Antiplatelet therapy

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“Aortic Pathology and Peripheral Arterial Disease”, Munir Boodhwani, January 28 2016, uOttawa Faculty of Medicine
3.35 Acute Limb Ischemia

Typical Patient
- Those with risk factors of peripheral vascular disease (e.g. smoking, diabetes)

Cause
- Embolism, thrombosis
- Peripheral vascular disease
- Dissection or trauma (rare)

Symptoms/Clinical Presentation
- Pain
- Pallor
- Paresthesias
- Pulselessness
- Paralysis

Physical Exam
- Refer to the 5 P’s listed above
- Assess the heart for murmur or other abnormalities
- Assess all peripheral vessels
- Skin change
- Ankle-brachial index

Investigations
- Ultrasound
- Computed tomography angiography
- Magnetic resonance angiography

Management/Treatment
- Surgery
- Mechanical thrombolysis (e.g. ultrasound wave)
- Thrombolytic
3.36 Takayasu Arteritis\textsuperscript{44,45}

Typical Patient
- Often diagnosed in the 3rd decade of patient’s life
- Affecting women 10 times more than men
- More common in Asians

Cause
- Due to unknown inflammatory pathological process

Symptoms/Clinical Presentation
- Constitutional symptoms
- Upper extremity claudication
- Cerebrovascular insufficiency
- Aortic aneurysm
- Stenosis of abdominal aorta
- Bruit (most common location being the carotid artery)
- Decreased pulsation of one or both brachial arteries

Physical Exam (diagnostic criteria - high sensitivity/specificity when 3 criteria are present)
- Age of onset <40
- Intermittent claudication
- Diminished brachial artery pulse
- Subclavian artery or aortic bruit
- SBP variation of more than 10 mm Hg between arms
- Angiographic evidence of aorta or aortic branch vessel stenosis

Investigations
- Angiography
- Imaging CT, MRI
- Blood test

Management/Treatment
- Corticosteroid (anti-inflammatory)
- Immunosuppressive medications (methotrexate, azathioprine)
- Surgical treatment of aneurysmal or occlusive disease

\textsuperscript{44} “Aortic Pathology and Peripheral Arterial Disease”, Munir Boodhwani, February 6 2016, uOttawa Faculty of Medicine
\textsuperscript{45} Roberts, JR. “Takayasu Arteritis: Background, Pathophysiology, Etiology”, Diamond, HS (Ed), Medscape, 2016
3.37 Giant Cell Arteritis (Temporal Arteritis)\(^4\)

**Typical Patient**
- Elderly patient – usually presents in the 70s or 80s
- More common in Northern European ancestry
- More common in women than men (3:2)

**Cause**
- T cell mediated inflammation of arterial wall, initiating in the adventitia
  - This leads to formation of granulomas in the vessel walls, decreasing the integrity of the vessels

**Clinical Presentation**
- Symptoms:
  - Constitutional symptoms – fever, malaise, weight loss, fatigue
  - Cranial symptoms – headache, scalp tenderness, visual changes (monocular vision loss)
  - Jaw claudication
- May be associated with polymyalgia rheumatica, aortic aneurysm, or large vessel occlusions
- Diagnostic criteria (3 or more confer a sensitivity and specificity above 90%):
  - Older than 50 years
  - Recent-onset of localized headache
  - Temporal artery pulse attenuation or tenderness
  - Erythrocyte sedimentation rate greater than 50 mm/h
  - Arterial biopsy demonstrating necrotizing vasculitis

**Physical Exam**
- Assessment of the temporal arteries
  - Erythema
  - Pain on palpation
  - Thickening/nodularity
  - Reduced pulsation
- Ophthalmologic assessment
  - Change in visual acuity
  - Fundoscopy – edema of optic disc, vessel changes in the retina
- Neurological assessment

**Investigations**
- Temporal artery biopsy
- Blood work: ESR, CRP (will be increased – indicating inflammation)

**Management/Treatment**
- High dose corticosteroids for 1 to 2 years
- Immunosuppressive agents less effective
- Surgical treatment of aortic aneurysm

\(^4\) “Aortic Pathology and Peripheral Arterial Disease”, Munir Boodhwani, February 6 2016, uOttawa Faculty of Medicine
3.38 Aortic Aneurysm\(^{47}\)

**Typical Patient**
- 60 year old male with history of smoking, or family history, if abdominal aortic aneurysm
- 40 year old male with history of Marfan or Ehlers-Danlos syndrome, if ascending thoracic
- 60 year old male with history of smoking, chronic obstructive pulmonary disease (COPD) if descending thoracic

**Cause**
- Abdominal aortic and descending thoracic aneurysms: atherosclerosis, local vessel inflammation, and an imbalance between synthesis and degradation of extracellular matrix proteins
- Ascending thoracic aneurysms: cystic medial degeneration, with degradation of elastic fibers and accumulation of collagenous material in medial layer
- Ascending thoracic aneurysms develop in certain connective tissue disorders (e.g. Ehlers-Danlos syndrome)
- Aortic aneurysms generally can develop in certain vasculitides (e.g. Takayasu)

**Symptoms/Clinical Presentation**
- Asymptomatic in many cases
- Pulsation in abdomen (abdominal aortic aneurysm)
- Back pain (abdominal aortic)
- Symptoms of congestive heart failure (if ascending aorta involved)
- Cough, dyspnea (tracheal compression)
- Dysphagia (esophageal compression)
- Hoarseness (recurrent laryngeal nerve compression)
- Rupture

**Physical Exam**
- Palpation may reveal pulsatile abdominal mass
- Auscultation may reveal high-pitched early diastolic murmur heard best at left sternal border (aortic regurgitation) - if ascending aorta dilated
- Widened pulse pressure (if ascending aorta dilated)

**Investigations**
- Ultrasonography, contrast CT, MRI (dilation of aorta)

**Management/Treatment**
- Risk factor reduction (e.g. smoking, hypertension)
- Surgical treatment recommended for ascending aortic aneurysms >5.5-6.0 cm (>5.0 cm if patient has diagnosed Marfan syndrome)
- Surgical treatment recommended for descending thoracic aneurysms 6.5-7.0 cm
- Surgical treatment recommended for abdominal aortic aneurysms >5.5 cm
- Smaller aneurysms enlarging >1.0 cm/year recommended for surgery

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\(^{47}\)Goldman L, Schafer Al. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.39 Varicose Veins

Typical Patient
- Female
- Primarily in the lower extremities

Cause
- Dilatation and insufficiency of veins

Symptoms/Clinical Presentation
- Present as dilatation of lower extremity veins
- Bluish discoloration
- Associated pain and discomfort
- Worse with long periods of standing

Physical Exam
- Inspection (Swelling, erythema, atrophy, deformity, skin change)
- Palpation for temperature change and tenderness
- Edema

Investigations
- Not necessary

Management/Treatment
- Compression stockings
- Minimize long periods of standing
- Laser Therapy
- Sclerosing agents
- Vein removal or revascularization
3.40 Atrial Septal Defect

Typical Patient
- 50 year old adult
- May be accompanied mitral valve disease/arrhythmias

Cause
- Commonly, ostium secundum occurring in centre of interatrial septum due to enlarged foramen ovale or resorption of septum primum.
- Right atrial and ventricular dilation as result of left-to-right shunt

Symptoms/Clinical Presentation
- Typically minimally symptomatic before fifth decade of life
- Dyspnea on exertion, fatigue, exercise intolerance (secondary to pulmonary hypertension)
- Palpitations, syncope, stroke, if arrhythmia present
- Symptoms of right-heart failure (e.g., peripheral edema)

Physical Exam
- Auscultation reveals wide and fixed splitting of S2
- Delayed P2 due to right ventricular overload
- Soft mid-systolic murmur in second intercostal on left side due to high flow across pulmonic valve
- Mid-diastolic murmur on the lower left sternal border due to high flow across tricuspid valve
- Dilated pulmonary artery occasionally palpated over the left second intercostal space

Investigations
- ECG (characteristically incomplete RBBB; may also show prolonged PR, SVT arrhythmias)
- CXR (increased lung field markings bilaterally, prominent/dilated pulmonary vasculature)
- Echo (i.e. transesophageal- ostium primum and secundum defects)

Management/Treatment
- Usually operative if ASD does not resolve spontaneously
- If right-sided atrial or ventricular dilation, regardless of symptom profile, operative procedure recommended
- Percutaneous closure recommended for most patients
- If accompanying valve defects to be repaired, surgical closure recommended

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3.41 Ventricular Septal Defect$^{50,51}$

**Typical Patient**
- 1.5 to 3.5 per 1000 births

**Cause**
- Genetics
- Environmental

**Symptoms/Clinical Presentation**
- In 10% of infants with large defects
- Tachypnea
- Poor feeding
- Failure to thrive
- Frequent lower respiratory tract infections
- Can develop Eisenmenger syndrome

**Physical Exam**
- Holosystolic murmur best heard at left sternal border
- Systolic thrill
- Mid-diastolic rumbling murmur across the mitral valve

**Investigations**
- Chest radiography (cardiomegaly may be present)
- ECG findings may include: 1- left atrial enlargement, 2- left ventricular hypertrophy, 3- right ventricular hypertrophy later on if Eisenmenger syndrome develops
- Cardiac catheterization

**Management/Treatment**
- Spontaneous closure in 50% of small-moderate size VSDs by 2 years of age
- Percutaneous or Surgical closure

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$^{50}$ Lilly, SL. “Pathophysiology of Heart Disease (6th ed)”, Philadelphia: Lippincott Williams & Wilkins, 2016

$^{51}$ Mayo Clinic. "Ventricular septal defect (VSD)" Mayo Clinic, 2016
3.42 Patent Ductus Arteriosus (PDA)\textsuperscript{52,53}

**Typical Patient**
- Commonly seen in preterm infants; could also be seen in term infants
- Could present in any age – infancy, childhood, adulthood

**Cause**
- Main cause is premature delivery of the infant
  - Increased sensitivity to prostaglandin
  - Decreased sensitivity to oxygen
- Decreased oxygen levels in blood (hypoxemia): asphyxia, immature lungs, and high altitude

**Clinical Presentation**
- **Symptoms:** Typically asymptomatic
  - Decreased exercise tolerance
  - Pulmonary edema:
    - Shortness of breath/accessory muscle use
    - Coughing
    - Associated lower respiratory tract infections
- **Signs:**
  - Tachypnea
  - Failure to thrive and feeding difficulties in infants
  - In adults untreated PDA can lead to Eisenmenger syndrome where the left to right shunt reverses to a right to left shunt as a result of long-term pulmonary hypertension.
    - Cyanosis
    - Right heart failure

**Physical Exam**
- **Inspection:**
  - May appear normal or have lower birth weight
  - Unlikely to be cyanotic (cyanosis may be seen in adults) - normal blood oxygenation
- **Palpation:**
  - Bounding peripheral pulse and wide pulse pressure \(\rightarrow\) high ventricular stroke volume leads to increased systolic pressure and blood flowing through the PDA leads to low diastolic pressure
  - Thrills - indicative of murmur (blood flow through the PDA)
  - Laterally displaced apical beat \(\rightarrow\) dilation of the left ventricle due to \(\uparrow\) preload from lungs
- **Auscultation:**
  - Murmur (left infraclavicular region):
    - Less than 6 weeks of age – systolic murmur
    - More than 6 weeks of age – continuous machinery type murmur (murmur in systole and diastole as the pulmonary pressure has reached adult levels by 6 weeks)
  - May hear wheezes and crackles due to pulmonary edema

**Investigations**
- Chest X-ray: signs of pulmonary edema
- ECG
- Echocardiography: diagnostic

**Management/Treatment**
- Prostaglandin inhibitors such as NSAIDs (eg: indomethacin) to close the ductus arteriosus
- Larger PDA – surgical ligation
- Smaller PDA (usually in older children) - interventional catheter techniques

\textsuperscript{52} “An outline of congenital heart disease”, Suzie Lee, February 3 2016, uOttawa Faculty of Medicine
\textsuperscript{53} “Cardiovascular physiology in the fetus and newborn”, Suzie Lee, February 1 2016, uOttawa Faculty of Medicine
3.43 Tetralogy of Fallot

Typical Patient
- Congenital heart disease seen in infants

Cause
Often associated with other congenital abnormalities, 22q11 deletion syndrome clinical presentation
- Manifestation has 4 main components:
  - Pulmonary stenosis
  - Overriding aorta
  - RVH
  - Ventricular septal defect (VSD)
- Symptoms:
  - Difficulty with feeding
- Signs:
  - Failure to thrive
  - Cyanosis with exertion – based on the level of pulmonary stenosis and right to left shunting
  - Tetralogy spells: Sudden drop in oxygen saturation due to increased constriction of the pulmonary vessels during exertion

Physical Exam
- Inspection:
  - Decreased growth
  - Cyanosis of the lips and nail bed – occurs as the patent ductus arteriosus closes
  - May develop clubbing with time
- Palpation:
  - Thrills (palpable murmur) on the left sternal border - indicative of VSD
  - Right parasternal lift- indicative of RVH
- Auscultation:
  - Systolic ejection murmur at the left sternal border, 2nd intercostal space - indicative of pulmonary stenosis
  - Harsh holosystolic murmur of VSD

Investigations
- Hyperoxia test
  - Increased oxygen will have little effect on the oxygen saturation indicating intracardiac right-to-left shunting
  - Side note: diseases of the lung will respond positively to supplemental oxygen in Hyperoxia test
- Echocardiography
  - Able to identify the 4 defects that are characteristic to Tetralogy of Fallot
- Monitoring of blood gases
- Chest X-ray
  - Boot shaped heart - RVH
  - Decreased pulmonary vasculature
- ECG: RVH

Management/Treatment
- Infusion of prostaglandin- allows blood flow to the lungs and maintains oxygen saturation
- Surgical repair – usually done at 6 months, but can be earlier depending on severity
- Oxygen supplementation as needed

54 “An outline of congenital heart disease”, Suzie Lee, February 3 2016, uOttawa Faculty of Medicine
3.44 Transposition of Great Arteries

**Typical Patient**
- Found prenatally or during first hours to weeks of birth

**Cause**
- Exact cause unknown, but risk factors include:
  - Maternal age over 40
  - Alcoholism
  - Diabetes
  - Poor nutrition during pregnancy (prenatal nutrition)
  - Rubella or other viral illness during pregnancy
  - Two types: D-TGA (dextro-TGA where aorta and pulmonary artery transposed) and CC-TGA (congenitally corrected where LV connects to PA and RV connects to aorta)

**Symptoms/Clinical Presentation**
- Cyanosis
- Shortness of breath
- Lack of appetite
- Poor weight gain

**Physical Exam**
- Cyanosis
- Tachypnea
- Use of accessory muscles to breathe

**Investigations**
- Cardiac catheterization
- Chest x-ray
- Electrocardiogram (ECG)
- Echocardiogram (if done before birth, it is called a fetal echocardiogram)
- Pulse oximetry (to check blood oxygen level)

**Management/Treatment**
- Prostaglandin E1
- Balloon atrial septostomy
- Arterial switch operation for D-TGA

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55 “An Outline of Congenital Heart Disease”, Suzie Lee, February 3, 2016, uOttawa Faculty of Medicine
3.45 Congenital Aortic Stenosis

Typical Patient
- 10-15% patient less than 1 year old
- 80-85% presents with symptoms progressively in late childhood or adulthood
- Male

Cause
- Genetic or developmental defect
- Turner Syndrome

Symptoms/Clinical Presentation
- Shortness of breath
- Exercise intolerance
- Dizziness
- Chest pain
- Abnormal heart rhythms

Physical Exam
- Weak pulses throughout
- Low blood pressure
- Variable murmur
- Acyanotic

Investigations
- Continuous ambulatory electrocardiogram (Holter monitor)
- ECG
- Intracardiac electrophysiology study (EPS)
- Echocardiogram

Management/Treatment
- Prostaglandin E1
- Balloon valvuloplasty
- Surgical valvuloplasty

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56 “An Outline of Congenital Heart Disease”, Suzie Lee, February 3 2016, uOttawa Faculty of Medicine
### 3.46 Congenital Pulmonic Stenosis

#### Typical Patient
- Patient age will vary depending on the severity of stenosis
- Usually children with new onset cardiac symptoms and relevant clinical findings; however, can present in adulthood

#### Cause
- Congenital fusion of pulmonic valve cusps (i.e. develops during first 8 weeks of pregnancy)

#### Symptoms/Clinical Presentation
- Angina
- Syncope
- Right-heart failure symptoms (depending on severity of stenosis)

#### Physical Exam
- Auscultation reveals an early systolic ejection click followed by systolic ejection murmur radiating to the base of the heart
- Ejection click diminishes/disappears during inspiration
- If RVH develops, parasternal lift may be palpated

#### Investigations
- ECG (may demonstrate RVH, if severe)
- Echo (pulmonic stenosis, RVH, elevated transvalvular gradient)

#### Management/Treatment
- If asymptomatic with transvalvular gradient <25 mmHg, no treatment required
- If symptomatic or transvalvular gradient >50 mmHg, balloon commissurotomy recommended

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57 Goldman L, Schafer AI. Goldman's Cecil Medicine E-Book. Elsevier Health Sciences; 2011
3.47 Coarctation of the Aorta (CoA)\textsuperscript{58,59}

Typical Patient
- 1 per 6000 live births
- Often associated with bicuspid aortic valve
- Often occurs in patients with Turner syndrome (45, XO)

Cause
- Usually sporadic, but genetic influences seen: Turner’s (10-15% have CoA)

Symptoms/Clinical Presentation
- Symptoms of heart failure
- Hypertension in the young person
- Poor feeding
- Failure to thrive
- Difficulty breathing
- Pain in the lower extremity
- Lower extremity appears cyanotic
- If not severe, patient may be asymptomatic

Physical Exam
- Weak femoral pulses, radio-femoral delay
- Elevated upper body blood pressure (most common finding)
- Higher BP in arms than legs, > 20mmHg is significant
- Crescendo-decrescendo systolic murmur in scapular region
- Continuous murmur of collaterals

Investigations
- Chest radiography
- ECG, findings may include left ventricular hypertrophy
- Echo
- MRI or CT

Management/Treatment
- Prostaglandin to keep the patent ductus arteriosus patent until surgical treatment
- Surgical or percutaneous therapy

\textsuperscript{58} Lilly, SL. “Pathophysiology of Heart Disease (6th ed)”, Philadelphia: Lippincott Williams & Wilkins, 2016
\textsuperscript{59} Mayo Clinic. “Coarctation of the aorta”, Mayo Clinic, 2016
3.48 Eisenmenger Syndrome

**Typical Patient**
- Children with large untreated atrial septal defect/ventricular septal defect, atroventricular canal defects, or patent ductus arteriosus
- Adults with smaller known congenital defects as mentioned above

**Cause**
- Severe pulmonary vasculature obstruction initially a result of left-to-right shunting through a congenital heart defect
- Resulting pulmonary vasculature changes cause reversal of original shunt to right-to-left direction (with resultant systemic cyanosis)

**Symptoms/Clinical Presentation**
- Exertional dyspnea
- Fatigue
- Headaches, strokes (reduced hemoglobin with subsequent erythrocytosis)
- Hemoptysis (infarction/rupture of pulmonary vessels)

**Physical Exam**
- Cyanosis
- Digital clubbing
- Prominent a-wave in jugular vein pulse
- Auscultation reveals a loud P2

**Investigations**
- CXR (pulmonary artery dilation with peripheral tapering, calcification of pulmonary vessels)
- ECG (RVH, RAA)
- Echo (congenital cardiac defects, elevated pulmonary vasculature pressures)

**Management/Treatment**
- Avoidance of activities exacerbating shunt (e.g. strenuous exercise, high altitudes, peripheral vasodilators)
- Caution in women who are considering pregnancy (high maternal mortality rates)
- Supportive therapy to alleviate symptoms (e.g. phlebotomy, treating infections, arrhythmias)
- Pulmonary vasodilators (e.g. endothelin receptor antagonists, prostacyclin analogs, phosphodiesterase inhibitors)
- Cardiac/lung transplantation if refractory to treatment

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60 Lilly, SL. "Pathophysiology of Heart Disease (6th ed)", Philadelphia: Lippincott Williams & Wilkins, 2016
3.49 Colorectal Cancer

Typical Patient
- Usually after 50 years of age
- 1 in 14 men and 1 in 15 women develop colorectal cancer (CRC) in their lifetime

Causes/Risk factors
- Hereditary:
  - Personal or family history of sporadic cancer
  - Hereditary Nonpolyposis Colorectal Cancer (HNCC)
  - Familial Adenomatous Polyposis (FAP)
- Inflammatory Bowel Disease – Ulcerative Colitis
- Abdominal radiation (for instance, in survivors of childhood cancer)
- Age

Clinical Presentation
- Can be asymptomatic and discovered during screening
- Symptoms:
  - Abdominal pain
  - Change in bowel habits
  - Hematochezia (fresh blood in stools) or melena (black tarry stools)
  - Weakness
- Signs:
  - Iron deficiency anemia
  - Weight loss
  - Signs of bowel obstruction

Physical Exam
- Inspection:
  - May display signs of anemia (e.g. pallor)
- Palpation:
  - May have palpable mass
  - Tenderness to palpation
- Auscultation:
  - May have decreased bowel sounds

Investigations
- Fecal occult blood test in initial screening
- Colonoscopy
- Blood work: CBC, liver enzymes, etc.
- CT scan
- Optional liver MRI – if questions raised on CT
- Pelvic MRI for rectal cancer
- Final pathology assessment of the resected cancer

Management/Treatment
- Chemotherapy: fluorouracil, levamisole, oxaliplatin
- Surgical resection of the cancer with neoadjuvant and adjuvant chemotherapy
- Radiofrequency ablation (mainly in liver)
- Palliative care if needed

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61 “Colorectal cancer”, Tim Asmis, February 10 2016, uOttawa Faculty of Medicine
3.50 Lung Cancer

Typical Patient
- Small cell carcinoma
- Non-small cell carcinoma
  - Adenocarcinoma (female)

Cause
- Smoking
- Radon gas
- Asbestos
- Air pollutants (e.g. nitrogen dioxide)
- Genetics
- Multifactorial

Symptoms/Clinical Presentation
- Persistent cough
- Hemoptysis
- Shortness of breath
- Chest pain
- Wheezing
- Hoarseness
- Unintentional weight loss, muscle wasting
- Bone pain
- Headache
- Night sweat, fever

Physical Exam
- Look for signs/symptoms discussed above

Investigations
- Imaging (CXR, CT)
- PET scan
- Sputum cytology
- Tissue sample biopsy
- Bone scan

Management/Treatment
- Surgical removal
- Chemotherapy
- Radiation therapy
- Targeted drug therapy
  - Afatinib (Gilotrif)
  - Bevacizumab (Avastin)
  - Ceritinib (Zykadia)
  - Crizotinib (Xalkori)
  - Erlotinib (Tarceva)
  - Nivolumab (Opdivo)
- Palliative care

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62 “Multidisciplinary Approach to Management of Primary Lung Cancer”, Farid Shamji, March 21 2016, uOttawa Faculty of Medicine
3.51 Cutaneous Melanoma

Typical Patient
- More common among Caucasians.

Cause
- The risk factors for developing melanoma are both environmental and genetic.
  1. Sun exposure and UV radiation
  2. Fair skin with inability to tan
  3. Blue eyes
  4. Red hair
  5. >2 sun burns per year
  6. First degree relative with cutaneous melanoma
  7. New mole, pre-existing changing mole
  8. Dysplastic nevi, prior melanoma, and familial melanoma
  9. Patients who are immune suppressed

Symptoms/Clinical Presentation
- Asymmetry (one half doesn’t match the other half)
- Border irregularity (edges are ragged, notched, or blurred)
- Colour variation (pigmentation is not uniform; i.e. tan, brown, and black can be present together, special concern is the mixing of shades of red, white, and blue)
- Diameter (greater than 6 millimeters, sudden increase in size is of special concern, darkening of an existing mole, slow change is much more common)
- Enlargement or evolution of colour, shape or symptoms

Physical Exam
- abnormal or changing skin lesion, should carefully examine for possible in-transit disease or and clinical positive lymph nodes
- cardiovascular, respiratory, and abdominal examination likely unremarkable in localized disease
- Complete skin examination

Investigations
- Biopsy (excision preferred when possible)
- cauterization or freezing should not be performed on suspicious lesions
- TNM staging system,
- Molecular testing in high risk disease -BRAF status
- patients may have complete blood counts, serum LDH, CXR, or possible CT/MRI/PET scans depending on the stage of cancer (low yield in stage I and II asymptomatic patients)

Management/Treatment for localized disease
- Surgical wide local excision and sentinel lymph node evaluation when indicated
- Adjuvant systemic therapy usually considered for Stage IIb, III and resected IV (immune therapy and BRAF targeted therapy
- Consider adjuvant radiation therapy if high risk for local regional recurrence

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63 “Neoplasms” Case Based Learning, JA Roy, R Bell and A Jalali, 2015, uOttawa Faculty of medicine
3.52 Breast Cancer

Typical Patient
- 50 year old female
- May have family history of breast/ovarian/colon cancer
- Previous hormone replacement therapy (e.g. birth control pill)
- Previous precancerous biopsies

Cause
- Genetic (BRCA 1+, BRCA 2+)
- Genetic susceptibility with environmental triggers (e.g. alcohol intake, age, sedentary lifestyle, etc.)

Symptoms/Clinical Presentation
- Palpable breast mass
- Nipple changes/discharge
- Skin changes around breast (e.g. dimpling, peau d’orange)
- Palpable axillary lymph nodes
- Site specific metastatic symptoms (e.g. back pain if metastasized to bone)

Physical Exam
- Breast examination may reveal palpable breast lump or axillary nodes
- Nipple/skin changes may be present

Investigations
- Mammogram (clustered microcalcifications, soft tissue spiculated masses, architectural distortion)
- Ultrasound (examine mass and lymph node involvement)
- MRI (determine if multifocal disease present)
- Biopsy (determine if sentinel lymph node positive)

Management/Treatment
- Staging and clinical assessment (e.g. HER2, ER, PR+)
- Lumpectomy (including positive lymph nodes) and radiation
- Adjuvant chemotherapy (anthracyclines, taxanes)
- Adjuvant endocrine therapy: estrogen blockers (e.g. Tamoxifen), aromatase inhibitors, targeted monoclonal antibodies (e.g. Trastuzumab – anti-HER2 antibody)
- Mastectomy
- Palliative therapy
Respirology
4.1 Obstructive Sleep Apnea (OSA)\

**Typical Patient**
- More common in males, around 50 years old
- Risk factors: obesity, micrognathia, macroglossia, hypothyroidism, acromegaly, adenotonsillar hypertrophy, Asian heritage, Down Syndrome, neuromuscular syndromes, elevated Mallampati score, narcotic/sedative use

**Cause**
- Upper airway becomes partially or completely blocked during sleep (REM sleep causes relaxation and collapse of upper airways)

**Symptoms/Clinical Presentation**
- Snoring (more likely when supine)
- Periods of cessation of breathing at night (apneas), often noticed by partner of patient
- Daytime sleepiness/falling asleep inappropriately during the day, Epworth scale of >10-12
- Trouble concentrating
- Morning headaches, dry mouth, sore throat
- Nocturia (lack of antidiuretic hormone (ADH) secretion)
- Pedal edema
- Waking up suddenly feeling like one is choking/gasping for air
- Associated with other conditions like depression, fibromyalgia, arterial hypertension, pulmonary hypertension, higher glycemia in type 2 diabetes, atrial fibrillation, myocardial infarction and strokes
- Dyspnea and syncope if progression to pulmonary hypertension

**Physical Exam**
- High blood pressure
- Increased BMI/obesity (probably)
- Pedal edema
- High Mallampati score
- Increased neck circumference, increased size of tongue/jaw/tonsils
- Hypotonia of oropharyngeal muscles, micrognathia
- If progression to pulmonary hypertension, physical exam is often normal, but there can be a positive hepatojugular reflux, a pulmonary regurgitation and a right sided S3 gallop heard on auscultation

**Investigations**
- Overnight polysomnogram (determine apnea-hypopnea index (AHI))
  - Normal: AHI <5 events per hour
  - Light: AHI 5-15 events per hour
  - Moderate: AHI 15-30 events per hour
  - Severe: AHI >30 events per hour
- Epworth Sleepiness Scale
- CBC (hemoglobin, B12, folate)
- Check renal, liver, and thyroid function

**Management/Treatment**
- In adults: continuous positive airway pressure (CPAP); if more severe, bilevel positive airway pressure (BiPAP)
- Non-specific therapies: weight loss, positional therapy, avoidance of alcohol and sedatives
- Surgery (i.e. uvulopalatopharyngoplasty)

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1 “Obstructive Sleep Apnea” Self Learning Module, Judith Leech, uOttawa Faculty of Medicine
4.2 Obstructive Sleep Apnea (OSA) in children

Typical patient
- Young child
- Recurrent tonsillitis, high Mallampati score, or Down syndrome

Cause
- Relaxation of muscle during REM sleep causes upper airway collapse
- Risk factors: family history of apnea, micrognathia, macroglossia, hypothyroidism, acromegaly, adenotonsillar hypertrophy, Asian heritage, Down Syndrome, neuromuscular syndromes, high Mallampati score, narcotic/sedative use

Symptoms/Clinical Presentation
- Snoring and apnea episodes at night, usually reported by the patient’s parents
- Behavioral changes at school, mood swings
- Unexplained enuresis, mouth breathing during the day
- Morning headaches, dry mouth or sore throat
- Non-restorative sleep, frequent nightmares
- Hyperactivity, failure to thrive (growth problems)
- Associated with other conditions like arterial hypertension, pulmonary hypertension, weight gain due to insulin resistance, behavioral problems, academic and social problems
- Dyspnea and syncope if progression to pulmonary hypertension

Physical Exam
- Large neck circumference, high Mallampati score
- Obesity or low weight (growth deficiency)
- If progression to pulmonary hypertension, physical exam can be normal in many cases; in some cases there can be a positive hepatojugular reflux, pulmonary regurgitation heard on auscultation, and a right-sided S3 gallop

Investigations
- Overnight polysomnogram (determine apnea-hypopnea index (AHI))
  - Normal: AHI <5 events per hour
  - Light: AHI 5-15 events per hour
  - Moderate: AHI 15-30 events per hour
  - Severe: AHI >30 events per hour

Management/Treatment
- Tonsillectomy is the first line treatment
- Uvulopalatopharyngoplasty
- Need for continuous positive airway pressure (CPAP) is rare

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2 “Obstructive Sleep Apnea” Self Learning Module, Judith Leech, uOttawa Faculty of Medicine
4.3 Pleural Effusion

Typical Patient
- N/A

Cause
- Excess amount of fluid in the pleural space (normal volume = 10 mL)
- Disruption of normal equilibrium between hydrostatic and oncotic pressure (pleural fluid formation/entry and pleural fluid absorption/exit)

Symptoms/Clinical Presentation
- Often asymptomatic
- Dyspnea
- Cough
- Pleuritic chest pain
- Malaise

Physical Exam
- Inspection: trachea may deviate away from effusion, decreased chest wall expansion
- Percussion: decreased/absent tactile fremitus, dullness
- Auscultation: decreased breath sounds, bronchial breathing, egophony positive, pleural friction rub

Investigations
- CXR (PA and lateral decubitus): look for blunting of costophrenic angle, amount of fluid
- Thoracentesis: inspect for color, character, and odor of fluid
- Blood work: LDH, protein, glucose, pH, albumin
- Cell count, cytology
- Pleural biopsy: Gram stain, markers for TB
- Classify pleural effusion as transudate or exudate (distinguish using Light’s Criteria)

<table>
<thead>
<tr>
<th>Light’s Criteria</th>
<th>Albumin Gradient</th>
</tr>
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<tbody>
<tr>
<td>Protein – pleural fluid/serum</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td>LDH – pleural fluid/serum</td>
<td>&gt;0.6</td>
</tr>
<tr>
<td>Pleural Fluid LDH</td>
<td>&gt;2/3 upper normal serum limit</td>
</tr>
<tr>
<td><strong>Exudate = at least one criteria met</strong></td>
<td></td>
</tr>
</tbody>
</table>

*calculate albumin gradient if only one of Light’s Criteria met

Top 3 Causes

<table>
<thead>
<tr>
<th>Transudative Pleural Effusion</th>
<th>Exudative Pleural Effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>Neoplasm</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Infectious disease</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>Pulmonary embolus</td>
</tr>
</tbody>
</table>

Management/Treatment
- Thoracentesis
- Treat underlying cause
- Consider indwelling pleural catheter, pleurodesis, pleurectomy

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4 "Pleural Fluid Physiology and Non-Malignant Effusions", Kayvan Amjadi, March 23 2016, uOttawa Faculty of Medicine
4.4 Asbestos-Related Pleural Disease and Mesothelioma

Typical Patient
- Asbestos workers (e.g. insulation workers, shipbuilders)

Cause
- Benign manifestations of asbestos exposure
  - Benign asbestos pleural effusion: exudative effusion, typically ~10 yr after exposure, resolves
  - Pleural plaques, usually calcified: marker of exposure, usually an asymptomatic radiologic finding
- Mesothelioma
  - Primary malignancy of the pleura
  - Decades after asbestos exposure (even with limited exposure)
  - Smoking not a risk factor, but asbestos and smoking synergistically increase risk of lung cancer
- Histology: epithelial, sarcomatoid, mixed

Symptoms/Clinical Presentation
- Persistent chest pain (usually non-pleuritic)
- Dyspnea
- Cough
- Bloody pleural effusion
- Weight loss

Physical Exam
- Inspection/percussion/auscultation: look for signs of a pleural effusion

Investigations
- Bronchoscopy
- Needle biopsy/closed pleural biopsy
- CT thorax
- PET/CT

Management/Treatment
- Alleviate symptoms (e.g. therapeutic drainage of the effusion via thoracentesis or chest tube drainage)
- Prevent recurrence (e.g. chemotherapy/radiation)
- Chemical pleurodesis
- Chronic indwelling catheter
- Pleuroperitoneal shunt
- Pleurectomy
4.5 Pulmonary Emboli\textsuperscript{7,8,9}

**Typical Patient**
- Any risk factors associated with Virchow’s triad
  - Circulatory stasis: hospitalized patients (especially immobile, with recent surgery)
  - Hypercoagulable state: obstetric patient, patient on oral contraceptive, patient with cancer, patient with genetic predisposition to hypercoagulability
  - Vascular wall injury: delivery, atherosclerosis, indwelling catheters

**Cause**
- Obstruction of arterial inflow (95% from a previously existing deep vein thrombosis (DVT))
- Acute changes: obstruction, endothelial damage, and infarcted tissue
- Chronic changes: infarcted tissue will become fibrosed; multiple infarcted/fibrosed tissues may lead to pulmonary hypertension and ultimately to cor pulmonale

**Symptoms/Clinical Presentation**
- Pleuritic chest pain
- Dyspnea, hemoptysis
- Palpitations, faintness, syncope
- Symptoms of DVT: pain/tenderness of affected area, ache/cramping, dull to sharp pain, mild to severe, unilateral leg swelling (rarely bilateral), redness from inflammation

**Physical Exam**
- Increased heart rate, respiratory rate, JVP
- Normal heart auscultation
- Low oxygen saturation, respiratory distress, shock
- Signs of DVT

**Investigations**
- Tests for DDx: chest X-ray, ECG, arterial blood gas analysis
- Calculate Well’s score for PE
- CUS, D-Dimer, chest CT pulmonary angiography
- Ventilation/perfusion (V/Q) scan

**Management/Treatment (depends on cause)**
- Acute therapy: Direct oral anticoagulants (DOAC) in-home therapy
- Atrial fibrillation: Vitamin K antagonist (VKA), DOAC
- Acute VTE: Low molecular weight heparin (LMWH) +/- VKA, DOAC
- Mechanical valves: VKAs
- DVT prophylaxis: LMWH, pentasaccharide, VKAs, DOAC
- Cancer, pregnancy: LMWH only
- Renal failure: IV heparin followed by warfarin
- Duration: 3 months if transient risk factor; indefinite if due to cancer, unprovoked, or strong thrombophilia

---

\textsuperscript{7} “Pathology: Interstitial Lung Disease” Chi Lai, March 17 2016, uOttawa Faculty of Medicine
\textsuperscript{8} “Clot Preventers: The pharmacology and applications of anticoagulation”, Dimitri Scarvelis, April 5 2016, uOttawa Faculty of Medicine
\textsuperscript{9} “Deep vein thrombosis and pulmonary embolism”, Dimitri Scarvelis, April 5 2016, uOttawa Faculty of Medicine
4.6 Pulmonary Hypertension (PHT)\textsuperscript{10,11}

Typical Patient

- Type 1 PHT: female, 20-40

Types of PHT

- Type 1 (idiopathic): familial predisposition, meds (cocaine, anorexic drugs), collagen disease (scleroderma, lupus), HIV, congenital left-right shunts (Eisenmenger syndrome), ventricular communication, atrial communication, portal hypertension, chronic anemia
- Type 2 (left cardiopathy): left ventricular or atrial dysfunction, left valvular dysfunction (aortic or mitral stenosis)
- Type 3 (lung disease or hypoxia): problem with lung parenchyma (e.g. COPD, cystic fibrosis, interstitial fibrosis) or chronic hypoxia (e.g. sleep apnea, living at high altitudes, OSA, hypoventilation syndrome)
- Type 4 (thrombotic events): thrombosis causing pulmonary embolism or non-thrombotic embolism (tumor, parasite, foreign object) and destruction of vascular bed
- Type 5 (multifactorial): hematological disorders, sarcoidosis, metabolic disorders, physical compression of blood vessels (e.g. tumor)

Symptoms/Clinical Presentation

- Dyspnea, fatigue, syncope
- Peripheral edema
- Raynaud’s phenomenon

Physical Exam

- Asymptomatic until late disease
- Exertional breathlessness
- Loud P2, tricuspid regurgitation, S4 on right side, right ventricular heave, elevated JVP
- Peripheral edema, ascites

Investigations

- Right heart catheterization
  - Mean pulmonary arterial pressure >25 mmHg at rest or >30 mmHg with exercise
  - Wedge pressure from Swan-Ganz Catheter <15 mm Hg (if >15, could be LHF)
- Depending on cause: coronary angiography, pulmonary angiography, pulmonary function test, CT scan, connective tissue serology, sleep study
- Diagnosis of exclusion, typically made after 2.5 years

Management/Treatment

- Treat underlying cause
- Supportive initiating therapy: vasodilator, anticoagulant, oxygen, diuretic, potentially digoxin
- If idiopathic: endothelin receptor antagonists (e.g. Bosenten, Ambrisentan, Macitentan) to stop smooth muscle proliferation, PDE5 inhibitors (e.g. Sildenafil, Tadalafil) and IV prostacyclin (Flolan, Epoprostenol, Selexipag) for vasodilation and anti-proliferative effects
- Other: lung transplant
- Lifestyle: avoid heavy exercise, pregnancy, high altitude, surgery

\textsuperscript{10} “Pulmonary Hypertension”, George Chandy, January 25 2016, uOttawa Faculty of Medicine

\textsuperscript{11} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.7 Chronic Obstructive Pulmonary Disease (COPD)\textsuperscript{12,13,14}

**Chronic Bronchitis**

**Typical Patient**
- Individual >40 years old
- Current/former smoker
- Risk factors: smoking, age, biomass fuels, occupation, low socioeconomic status, tuberculosis, male gender

**Cause**
- Irritant-induced inflammation resulting in proliferation of smooth muscles and mucociliary dysfunction → loss of elasticity and an increase in air-flow resistance → evolutive and partially reversible obstruction of airways → predisposition to recurrent infections and bronchiectasis

**Symptoms/Clinical Presentation**
- Productive cough for more than 3 months, during 2 consecutive years
- Exacerbations and pulmonary infections that worsen with time
- Dyspnea, chest tightness
- Limitation of exercise, missing work
- Persistent wheeze, productive cough, hemoptysis
- Obesity

**Physical Exam**
- Barrel chest (hyperinflation), use of accessory muscles to breathe, pursed lips breathing
- Cyanosis, prolonged expiration, hypoxemia, hypercapnia
- Pulmonary hypertension and cor pulmonale in severe cases
- Respiratory examination: wheezing, diffusely decreased breath sounds, hyperresonance on percussion, prolonged expiration

**Investigations**
- Pulmonary Function Testing/Spirometry/Plethysmography: useful for diagnosis of COPD
- Arterial blood gas
- Culture of expectorations if suspect exacerbation because of infection
- Chest radiography
- Electrocardiogram

<table>
<thead>
<tr>
<th>Severity-Gold Classification 2007</th>
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<tr>
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<td>Stage 1 (light) FEV1 over 80%</td>
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<td>Stage 2 (moderate) FEV1 79% to 50%</td>
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</tr>
<tr>
<td>Stage 4 (very severe) FEV1 less than 30% or less than 50% with right sided heart failure</td>
</tr>
</tbody>
</table>

**Management/Treatment**
- Only options that prolong life: smoking cessation, oxygen therapy, vaccines
- Options to increase quality of life:
  - Non-pharmacologic: education, exercise (rehabilitation), smoking cessation

\textsuperscript{12} “COPD”, Shawn Aaron, February 29 2016, uOttawa Faculty of Medicine
\textsuperscript{13} “Respiratory pharmacology”, Krishna Sharma, February 29 2016, uOttawa Faculty of Medicine
\textsuperscript{14} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
Pharmacologic:
1) Education, smoking cessation
2) SABA
3) SABA + LABA ± anticholinergic
4) SABA + LABA ± pulmonary rehabilitation
5) LABA + anticholinergic + inhaled corticosteroids
6) Add oxygen

- For an acute exacerbation:
  - Acutely: short-acting beta-2 agonist, short-acting anticholinergic
  - Oxygen therapy
  - Systemic steroids (14-day course of prednisone)
  - Antibiotics if bacterial infection is present

**Emphysema**

**Typical Patient**
- Individual over 40 years old
- Current/former smoker
- Risk factors: smoking, age, biomass fuels, occupation, low socioeconomic status, tuberculosis, male gender

**Cause**
- Genetic cause (1%): α-1-antitrypsin deficiency causes diffuse (panlobular) destruction of the alveolar septum
- Inflammatory cause (99%): irritant causes centrolobular destruction of alveolar septum, mostly in superior regions of lungs
- Proliferation of smooth muscles and a muco-ciliary dysfunction → loss of elasticity and increase in air-flow resistance → evolutive and partially reversible obstruction of airways → predisposition to recurrent infections and bronchiectasis

**Symptoms/Clinical Presentation**
- Exacerbations and pulmonary infections that worsen with time
- Dyspnea, chest tightness, limitation of exercise, missing work
- Persistent wheeze, very little coughing, hemoptysis

**Physical Exam**
- Barrel chest (hyperinflation), use of accessory muscles to breathe, pursed lips breathing
- Pink skin, hypoxemia, hypercapnia, cachexia, lower diaphragmatic excursion
- Pulmonary hypertension and cor pulmonale in severe cases
- Pursed lips breathing
- Respiratory examination: wheezing, diffusely decreased breath sounds, hyperresonance on percussion, prolonged expiration

**Investigations**
- Pulmonary Function Testing/Spirometry/Plethysmography: useful for diagnosis of COPD
- Arterial blood gas
- Culture of expectorations if suspect exacerbation because of infection
- Chest radiography
- Electrocardiogram
- High-resolution CT (HRCT): emphysema has a radiological and/or pathological diagnosis

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</tbody>
</table>
Management/Treatment

- Same as chronic bronchitis

4.8 Asthma

Typical Patient

- Personal history of atopy (eczema, nasal polyps, allergies)
- Family history of asthma or atopy
- Child with a history of bronchiolitis or chronic bronchitis

Cause

- Airway inflammation after antigenic exposure

Symptoms/Clinical Presentation

- Dyspnea
- Chest tightness
- Wheezing (polyphonic, diffuse, biphasic)
- Expectoration, usually worse at night
- Limitation of activities of daily living (ADLs) like exercise, missing work
- Cough ± sputum production

Physical Exam

- Nasal polyps
- Wheeze Respiratory examination (wheeze)
- Barrel chest, cyanosis, usage of accessory muscles
- Pulsus paradoxus, difficulty talking, tachypnea, tachycardia in severe cases
- $O_2$ saturation <91% and loss of consciousness in extreme cases

Investigations

- Arterial gasometry and oxygen saturation
- Chest X-ray
- Spirometry/Pulmonary Function Testing (if over the age of 6)
  - Reversible if FEV1 increases by 12% or 200 mL after administration of bronchodilator or if administration of methacholine (histamine) drops FEV1 by 20%
- Trial of therapy (if under the age of 6)

Management/Treatment

<table>
<thead>
<tr>
<th>Relievers (rescue)</th>
<th>Controllers (preventers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Inhaled short-acting beta-2 agonists (SABA)</td>
<td>-Anti-inflammatory medications (inhaled glucocorticosteroids (ICS), leukotriene receptor antagonists)</td>
</tr>
<tr>
<td>-Relief of acute symptoms</td>
<td>-Some bronchodilators taken in addition to ICS (long-acting beta-2 agonists, theophylline)</td>
</tr>
<tr>
<td>-Used only on demand</td>
<td></td>
</tr>
</tbody>
</table>

- For an acute exacerbation:
  - SABA
  - Anticholinergic
  - Systemic steroid
  - Antibiotics (if infection is present)
- General steps for choosing medication:

15 "Asthma", Krishna Sharma, February 29 2016, uOttawa Faculty of Medicine
16 "Respiratory pharmacology", Krishna Sharma, February 29 2016, uOttawa Faculty of Medicine
17 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
1) SABA  
2) SABA with ICS  
3) 6-11 years: SABA with increase dose of ICS/ 12+ years: SABA + ICS + LABA  
4) 6-11 years: SABA + ICS + LABA / 12+ years: BACA + BALA + CSI + leukotriene receptor antagonist (LTRA)  
5) Add anti-IgE  
6) Prednisone

4.9 Exercise-Induced Bronchoconstriction

Typical Patient  
- 7-20% of general population  
- More common in children, and in athletes who play in cold-weather (e.g. hockey players)  
- Patient with asthma

Cause  
- Genetic  
- Pathway is inflammation via leukotrienes

Symptoms/Clinical Presentation  
- Presents like asthma but no other symptom of asthma (e.g. wheezing)  
  - No Dyspnea  
  - EIB can be present without asthma  
- Highest 10-15 min after exercise, resolves within 1 hr  
- Worse in dry, cold weather

Physical Exam  
- Normal at rest  
- Tachypnea and wheezing when symptomatic

Investigations  
- Negative methacholine challenge in pure EIB (exception: high-intensity athlete)  
- Exercise test followed by PFT: drop in FEV1 by 10% post-exercise  
- Issue: low sensitivity as exercise may not reproduce actual conditions

Management/Treatment  
- Warm up for longer  
- Face mask if cold air  
- Improve cardiovascular fitness  
- Rarely: SABA prophylactically or for relief, steroids and LTRA (long-acting reduces airway inflammation)

---

19 “Exercise Physiology and Exercise Testing”, Nha Voduc, February 25 2016, uOttawa Faculty of Medicine
4.10 Cystic Fibrosis\textsuperscript{20,21,22}

**Typical Patient**
- More common in Caucasians
- Patients usually receive diagnosis before age of 1, but some patients can have mild symptoms and only be diagnosed as an adult

**Cause**
- Autosomal recessive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, a chloride channel encoded on chromosome 7q (most common mutation is $\Delta F508$)
- CFTR normally transports chloride ions out of the cell, allowing sodium ions and water to follow passively, helping liquefy mucous lining the airways; CFTR mutation prevents this, leading to build-up of mucous that predisposes one to bacterial superinfection, and subsequent chronic lung damage

**Symptoms/Clinical Presentation**
- Newborn: ileus meconium, jaundice
- Infants: pancreatic failure (i.e. symptoms of fat-soluble vitamin deficiency), failure to thrive, anemia, hyponatremia
- Children: wheezing, chronic cough, recurrent lung infection, bowel obstruction (distal intestinal obstructive syndrome), hemoptysis, nasal polyps, rectal prolapse, finger clubbing
- Adults: obstructive lung disease, infertility (complete in men, diminished in women)
- In all cases: risk of pulmonary hypertension and cor pulmonale, focal biliary cirrhosis, type 1 diabetes, malnutrition, abdominal pain, rhinitis, sinusitis

**Physical Exam**
- Nasal polyps and rhinitis
- Tachypnea, wheezing, barrel chest, hyperresonance on percussion of lungs
- Coughing, cyanosis, clubbing, use of accessory muscles to breathe
- Abdominal exam: abdominal distension, rectal prolapse, hepatosplenomegaly
- Signs of deficiency in fat-soluble vitamins (i.e. Vitamins A, D, E, and K)

**Investigations**
- Sweat chloride test is the gold standard
- Genetic testing
- Newborn screening: dosage of trypsinogen (if positive, proceed to genetic testing or sweat chloride test)
- Culture of expectoration if suspected exacerbation because of infection
- Chest radiography

**Management/Treatment**
- Nutrition: high fat & high calorie diet, fat soluble vitamins, pancreatic enzymes, increased sodium in summer, ursodeoxycholic acid, insulin
- Chest assisted airway clearance: clapping, vest, positive end-expiratory pressure (PEEP) technique; oxygen for advanced cases
- Antibiotics: oral or IV for exacerbations, tobramycin for maintenance against \textit{P. aeruginosa}
- Dornase alpha
- CFTR gene modulators: Ivacaftor for G551D mutation
- Lung transplant when FEV1 < 30%
- Every 3 months: PFT, sputum culture, nutrition status
- Every year: blood work, CXR

\textsuperscript{20} “Cystic fibrosis lab”, Thomas Kovesi, March 2 2016, uOttawa Faculty of Medicine
\textsuperscript{21} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
\textsuperscript{22} Sharma, GD. “Cystic Fibrosis Clinical Presentation”, Haver K (Ed). Medscape, 2016.
4.11 Central Apnea: Congenital Central Hypoventilation Syndrome

Typical Patient
- Infants
- Onset at birth, rarely in childhood

Cause
- Absence of a central pattern generator due to gene mutation PHOX2B
- Predominance of volitional breathing control by RAS

Symptoms/Clinical Presentation
- Respiratory failure/arrest when patient falls asleep

Physical Exam
- Breathing: monotonous, slow, unresponsive to stimuli, hypercapnic, cyanosis upon arrest
- May see neural crest tumours
- Associated with bradycardia

Investigations
- Diaphragm: sniff test, EMG
- Maximum inspiratory and expiratory muscle strength measurements
- MRI for additional neurogenic tumours
- Sleep study: no abdominal movement resulting in no airflow

Management/Treatment
- Upon diagnosis at birth: tracheostomy, night time ventilation
- Diaphragmatic pacemaker

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23 “Ventilatory Control”, Author Unknown, February 22 2016, uOttawa Faculty of Medicine
4.12 Pneumonia²⁴,²⁵,²⁶

Typical Patient
- Elderly (age >65 yo)
- Diseases associated with immunosuppression (e.g. diabetes, HIV, transplant), weakens natural defenses of body (COPD/Emphysema, malignancy, renal insufficiency, alcohol abuse)
- Lifestyle that increases exposure (travel, animal contact, occupational, drugs such as PPIs or H2 blockers, steroids)

Cause
- Mode of transmission: 99% via inhalation, 1% gross aspiration, <1% hematogenous or transdiaphragmatic
- Community-acquired:
  - Viral: influenza, adenovirus (interstitial pneumonia)
  - Histoplasmosis if exposed to caves, bats or birds (interstitial pneumonia)
  - Typical bacteria: *S. pneumoniae* (majority, lobar pneumonia), *M. catarrhalis*, *H. influenzae* (lobar pneumonia or bronchopneumonia), *S. aureus* (complicated pneumonia)
- Nosocomial pneumonia: enteric bacteria, *P. aeruginosa*, *S. aureus* (MRSA)
- Aspiration pneumonia: loss of consciousness, sedatives, alcohol, dysphagia, intubation; infection by anaerobic, enteric, gram-negative bacteria (*E. coli*), *S. aureus*, *Klebsiella* or stomach contents can lead to abscess formation
- Pneumonia in immunocompromised patients: *P. jirovecii*, cryptococcus or other yeast, nocardia, virus (CMV, HSV), TB

Symptoms/Clinical Presentation
- Fever
- Cough and purulent discharge
- Pleuritic chest pain
- In older adults: confusion, loss of autonomy, incontinence, falls

Physical exam
- Fever, diaphoresis, cyanosis
- Tachypnea and tachycardia
- Dullness with percussion, crackles, tactile fremitus and egophony

Investigations
- CBC, CXR, C+S, ABG, CT (rarely)

Management/Treatment
- Oxygen, IV fluid
- Nebulized salbutamol if needed
- Antibiotics given depend on type and potential cause; minimum 5 days of treatment; should be afebrile within 48-72 hours (longer treatment if pseudomonas pathogen)
  - Community acquired: macrolide
  - Community acquired with comorbidities: fluoroquinolone or B-Lactam +macrolide
  - Aspiration: amoxiclavulin with or without macrolide

---
²⁴ “Community and Hospital Acquired Pneumonia”, Daniel Kobewka, March 14 2016, uOttawa de Medicine
²⁵ “Maladies Infectieuses – Laboratoire de pathologie”, Marcio Gomes, March 17 2016, uOttawa Faculté de Medicine
²⁶ Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
Nosocomial pneumonia: (piptazo or meropenem or levofloxacin)
- IF high risk of mortality or IV antibiotics in the last 90 days then pick 2 of (piptazo, aminoglycoside, levofloxacin, meropenem, ceftazedime)
- Narrow coverage if a causative organism is identified.
- Suspicion of MRSA: vancomycin or linezolid

4.13 Tuberculosis (TB)\textsuperscript{27,28}

Typical Patient
- Indigenous populations and immigrant populations (Asia, South America, Africa, Eastern Europe)
- Immunocompromised, recent travel to high risk countries, IVDU

Cause
- Exposure to droplets of \textit{Mycobacterium tuberculosis}
- TB becomes latent in 95% of cases; the other 5% of cases develop a primary TB; 5-10% of latent cases will reactivate, which is called a secondary TB

Symptoms/Clinical Presentation
- Latent TB: asymptomatic
- Primary and reactivation TB:
  - Constitutional symptoms: fever, night sweats, weight loss, loss of appetite
  - Pulmonary TB: chronic cough (initially dry and then productive), hemoptysis, pneumonia that does not resolve even with use of standard antibiotics
  - Extrapulmonary TB: enlarged lymph nodes, pleuritis, pericarditis, peritonitis, meningitis, osteomyelitis, adrenal infection, renal infection, ovarian infection
  - Miliary TB: hematogenous spread of TB to the lungs, indicates significant disease

Physical Exam
- Confusion, fever, weight loss, confusion, diaphoresis with cyanosis, dyspnea, tachypnea, and tachycardia
- Dullness on percussion, crackles, tactile fremitus and egophony present
- Extrapulmonary TB: depends on the site (ex. triphasic rub in pericarditis)

Investigations
- Latent TB: Mantoux skin test and radiography
- Active pulmonary TB: Sputum culture, acid fast stain, CXR
- Active extrapulmonary TB: biopsy of infected site
- Mantoux:
  - Positive if 0-4 mm in child of less than 5 years old
  - Positive if 5-9 mm in patients with HIV, a contact with TB that was less than 2 years ago, presence of fibronodular lesions on X-ray, immunosuppressive therapy (organ donation, anti TNF-\alpha, prednisone, etc.), kidney failure
  - Positive in all cases when over 10 mm
  - Mantoux test has downside: can be positive if the patient had a BCG vaccine
  - Mantoux test not used to diagnose active disease due to high false negative rate
- Chest X-ray:
  - Latent: granulomas (2 times higher risk of reactivation), blunting of the costophrenic angle (increases risk of reactivation), calcified lymph nodes (does not increase the risk of reactivation), apical fibronodular disease (increases risk by 9-19 times), apical capping (does not increase risk)
  - Active disease: upper lung zone cavitation/volume loss, cavitation (usually in inferior lobes if primary TB or apically if secondary TB), pleural effusion, mediastinal adenopathy, scars as proof of past TB infection

Management/Treatment

\textsuperscript{27} “Tuberculosis”, Gonzalo Alvarez, March 14 2016, uOttawa Faculty of Medicine.
\textsuperscript{28} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
Respirology

- Prevention via BCG vaccine: not efficient in adults, but efficient in 80% of cases in children to prevent miliary TB and meningitis primarily (only useful in high risk areas)
- Must isolate all cases of active TB and report them to Public health
- Latent TB: isoniazid (INH) for 9 months (or rifampin for 4 months if TB is INH-resistant)
- Active TB (4 for 2 and 2 for 4): INH, rifampin, pyrazinamide, ethambutol
  - All 4 medications for 2 months; if responding to medications, can drop 2 medications for the next 4 months

4.14 Interstitial Pneumopathy

Typical Patient
- Patients of all ages

Cause
- Diminished pulmonary compliance, increased respiratory workload, diminished lung volumes, diminished surface for gas exchange
- Differential diagnosis:
  - Pneumonia (virus or atypical bacteria give interstitial lesions on X-ray)
  - Lymphangitic carcinomatosis
  - Hypersensitivity pneumonia (exposure to organic compounds that irritate and cause inflammation)
  - Connective tissue disease
  - Pneumoconiosis (exposure to inorganic irritants)
  - Medication (e.g. amiodarone, nitrofurantoine, methodextrare, bleomycin)
  - Radiotherapy (fibrosis after 6-12 months post-treatment)
  - Idiopathic
  - Sarcoidosis

Symptoms/Clinical Presentation
Clinical presentation will vary depending on cause:
- Severe dyspnea, dry cough
- Uncommon to have chest pain or wheezing
- Connective tissue disease: joint pain, fever, swelling
- Pneumonia: fever, chills, sputum production
- Idiopathic: clubbing, cough
- Sarcoidosis: multisystemic symptoms (skin, eyes, brain, liver, etc.), no clubbing
- Pneumoconiosis: history of working with coal, silica, asbestos, etc.
- Hypersensitivity pneumonia: history of working with animals, wood, hay, food, etc.

Physical Exam
- Desaturation, tachycardia, tachypnea
- Crackles on auscultation (“Velcro” sound associated with idiopathic pneumopathy)

Investigations
- Radiography
- High-resolution computed tomography (HRCT)
- Pulmonary function test: restrictive pattern
- Blood work: factors associated with inflammation (RF, Anti-α), CBC
- Biopsy is not always necessary (except with cancer)

Management/Treatment
- Depends on cause

29 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
30 “Maladie pulmonaire interstitielle”, Tara Keays, March 14 2016, uOttawa Faculty of Medicine
4.15 Idiopathic Pulmonary Fibrosis (IPF)\textsuperscript{31,32}

**Typical Patient**
- More common after 50, incidence increases with age
- Men more commonly affected than women

**Cause**
- Progressive and irreversible fibrosis of pulmonary parenchyma, without any known cause

**Clinical Presentation**
- Dyspnea during effort
- Dry cough
- Weight loss, fever, chills, malaise
- Clinical history is very important because it is the key to differentiating between idiopathic fibrosis and other causes of fibrosis

**Physical Exam**
- Dyspnea, tachypnea, tachycardia, usage of accessory muscle in advanced cases
- Crackles at the base of lungs at the end of inspiration
- Velcro sound on auscultation
- Clubbing

**Investigations**
- CXR: reticular or reticulonodular lesions more important in inferior lobes; “honeycombing” in advanced cases
- CT: honeycombing
- HRCT: reticular lesions are predominantly present in inferior and peripheral zones of lungs, traction bronchiectasis, ground glass lesion, consolidation, honeycombing
- Biopsy: rarely necessary because honeycombing seen on imagery is enough to diagnose fibrosis; biopsy will show “temporal heterogeneity” with little inflammation and absence of proof of what is causing the inflammation
- PFT: restrictive pattern, provides information about severity of disease

**Management/Treatment**
- No cure (only lung transplant in advanced cases)
- Vaccination, smoking cessation, pulmonary rehabilitation
- Oxygen, palliative care
- Anti-fibrotic medications: pirfenidone (Esbriet) and nintedanib (Ofev) can slow evolution
- Give proton pump inhibitors empirically
- Prognosis: 3-5 years after diagnosis

\textsuperscript{31} “Maladie pulmonaire interstitielle”, Tara Keays, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{32} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.16 Pneumoconiosis

Asbestosis

Typical Patient
- Often symptoms develop >20 years after the period of initial exposure to asbestos

Cause
- Slowly progressive diffuse interstitial fibrosis induced by inhaled asbestos fibers
- Exposure risks: insulation, shipyards, construction, brake linings, pipefitters, plumbers

Symptoms/Clinical Presentation
- Usually insidious onset of shortness of breath and dry cough

Physical Exam
- Inspection: clubbing may be present (but in less than half of patients)
- Auscultation: crackles (in majority of patients, but depends on severity of fibrosis)

Investigations
- CXR: calcified and non-calcified pleural plaques, lower lobe > upper lobe involvement
- HRCT: reticulonodular pattern, pleural plaques usually present, honeycombing may develop in severe disease due to severe fibrosis
- Pathology
  - Microscopic examination reveals ferruginous bodies (aka asbestos bodies, rod-shaped structures that represent asbestos fibers coated in macrophages)
  - Pattern of fibrosis is similar to UIP (usual interstitial pattern), the pattern seen more commonly in IPF (idiopathic pulmonary fibrosis)

Complications
- Asbestos exposure also increases risk of lung cancer (the most common cancer in patients with previous asbestos exposure) and malignant mesothelioma (rare cancer, but seen almost exclusively in patients with asbestos exposure)

Treatment
- No specific treatment is available (patients may be eligible for workers’ compensation)
- Avoidance of further exposure
- Supportive measures (smoking cessation, pneumonia and flu vaccines, supplemental oxygen if qualify based on hypoxia, lung transplant if meet criteria)

Silicosis

Typical Patient
- Usually >15 years of silica exposure (though varies significantly depending on level/frequency of exposure)

Cause
- Inhalation of fine dust containing silica (quartz)

33 “Introduction to Interstitial Lung Diseases”, Nha Voduc, March 16 2016, uOttawa Faculty of Medicine.
34 “Interstitial Lung Disease”, Ashish Gupta, March 16 2016, uOttawa Faculty of Medicine
35 Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
Respirology

At-risk population: sandblasters, hard-rock miners, stonecutters, glass and ceramic production

Symptoms/Clinical Presentation
- Insidious onset of dyspnea and cough (over years, cough may be dry or productive)
- Rarely, patients can also present with rapidly progressive symptoms (over weeks) after a short period of very high level of silica exposure (i.e. “acute silicosis”)

Physical Exam
- A minority of patients will have crackles or wheeze on chest auscultation

Investigations
- CXR: upper > lower lobe; hilar lymph node enlargement is common
  - Early/mild: nodular disease (simple silicosis, no fibrosis)
  - Late/severe: nodules coalesce into larger masses in association with lung fibrosis (progressive massive fibrosis)
- HRCT: bilateral symmetric nodules (centrilobular), which may calcify
- PFT: may show a range of abnormalities depending on disease severity
  - In early/simple nodular disease, PFTs may be normal; in more severe fibrotic disease, can have decreased diffusion (DLCO), restriction (decreased TLC), but can also cause obstruction/COPD (decreased FEV1/FVC ratio)

Complications
- A minority of patients with silicosis have Caplan’s syndrome, which is the development of rheumatoid arthritis (inflammatory joint pains, positive RF and anti-CCP) associated with silicosis and more rarely with asbestosis or coal workers’ lung
- Silica exposure is a risk factor for TB, lung cancer, and COPD (tobacco smoke exposure further increases risks)

Management/Treatment
- Same as for asbestosis (i.e. supportive)

Coal Workers’ Pneumoconiosis (Black Lung)

Typical Patient
- Usually >10 years of frequent exposure to coal (i.e. coal miners)

Cause
- Small particles are inhaled, causing an inflammatory state, which damages pulmonary architecture
- Pulmonary nodules and progressive massive fibrosis can result
- Can present similarly to silicosis both clinically and radiologically, so history is usually the key to diagnosis
- Silica is also present in coal mines, and a significant minority of patients with coal workers’ lung also have evidence of silicosis on pathology

Symptoms/Clinical Presentation
- Progressive dyspnea
- Cough (often productive)

Physical Exam
- Besides nodules and fibrosis, coal dust also contributes to COPD (coal and tobacco have additive negative effects), so examine for COPD (Signs of hyperinflation, wheeze)

Investigations
- Compatible history (by far the most important factor)
- PFT: often obstructive pattern from COPD, decreased diffusion (low DLCO) due to lung destruction, and depending on level of fibrosis, may have restriction (decreased TLC)
- CXR: very similar to silicosis (small rounded opacities, can be present in all lung zones although traditional teaching is that they are most common in upper lobes)
- HRCT: if progresses to fibrosis, fibrosis is generally in the lower lung zones and may have a similar appearance to IPF (i.e. honeycombing)
Biopsy is rarely performed; clinical history (i.e. coal worker) and imaging/PFTs are usually enough to be fairly certain of the diagnosis.

- If open lung biopsy is performed (or on autopsy), classic pathology includes pigmented lesions in bronchioles, fibrosis, and emphysema.

**Management/Treatment**
- Reduce exposure, increase workplace controls (personal protective equipment and environmental controls)
- Consider eligibility for workers’ compensation
- Supportive care (see asbestosis section)
4.17 Sarcoidosis\textsuperscript{38,39,40,41}

Typical Patient
- Most common in ages 25-65 (median age at diagnosis is 45)
- Highest incidence among people of African descent; less common among people of Hispanic and Asian descent, relative to Caucasians

Cause
- Multisystem granulomatous disease of unknown etiology, characterized by the presence of non-caseating granulomas (tight clusters of organized macrophages and other inflammatory cells)
- Damage largely through granulomas compressing surrounding structures, hence greatest clinical significance if present in the eye, heart, or nerves
- There are 4 stages of pulmonary sarcoid, defined based on CXR:
  - Stage 1: hilar lymphadenopathy
  - Stage 2: hilar lymphadenopathy + pulmonary infiltrates
  - Stage 3: pulmonary infiltrates alone
  - Stage 4: with pulmonary fibrosis
- Note that the term “stage” is misleading, as patients rarely transition from one stage to another, but rather stay in the same stage

Symptoms/Clinical Presentation
- Highly variable, often asymptomatic (incidental finding on chest imaging)
- Progressive respiratory symptoms (dyspnea, cough), as the lung is the most commonly involved organ
- Classic presentations (rare, but common on exams)
  - Lofgren’s Syndrome (hilar lymphadenopathy, erythema nodosum, polyarthritis)
  - Heerfordt syndrome (fever, parotitis, uveitis, facial nerve paralysis)

Physical Exam
- Vitals: fever
- Cardiac: palpitations, arrhythmias, bradycardia (heart block), signs of heart failure (cardiomyopathy)
- Eyes: light sensitivity, redness (uveitis)
  - Ocular involvement can be silent, so should be seen by an ophthalmologist at least once after initial sarcoid diagnosis
- Lymph nodes: peripheral lymphadenopathy
- Joints: pain, swelling, stiffness
- Lungs: cough, possibly crackles (though typically chest sounds clear despite abnormal CXR)
- Skin: erythema nodosum, lupus pernio

Investigations
- CXR, CT chest, PFT (restrictive or mixed pattern), bronchoscopic lymph node FNA, bronchoscopic transbronchial biopsy (stage 2-3)
- Pathology shows non-caseating granulomas

Management/Treatment
- Corticosteroids (i.e. oral prednisone, usually ~0.5mg/kg tapered over several months)
- Most patients will not require therapy (>50% cases resolve spontaneously, especially stage 1), and therapy should NOT be started unless patient is symptomatic, has evidence of declining lung function,

\textsuperscript{38} “Introduction to Interstitial Lung Disease”, Nha Vodic, March 16 2016, uOttawa Faculty of Medicine
\textsuperscript{39} “Maladie pulmonaire interstitielle”, Tara Keays, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{40} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
\textsuperscript{41} “Sarcoidose - MAA”, Robert Dales, 3 octobre 2013, uOttawa Faculté de Medicine
significant radiographic progression, evidence of cardiac, ocular, or neurological involvement, hypercalcemia, or very bothersome skin involvement

- Methotrexate (and other immunomodulators) can be tried in severe cases when steroids cannot be successfully weaned; hydroxychloroquine can be helpful for skin involvement

### 4.18 Lung Cancer

#### Typical Patient
- Patient with exposure to cigarette smoking (accounts for more than 90% all lung cancers), second-hand smoke, asbestos, metals (e.g. arsenic, nickel, chromium), radon gas, polycyclic aromatic hydrocarbons, ionizing radiation, radiation therapy, genetics

#### Pathology and Prevalence Primary Lung Cancers [WHO 2015]¹

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Pathological Diagnosis</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-small cell lung cancer (NCSLC)</td>
<td>Adenocarcinoma</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>Adenosquamous cell carcinoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Squamous Cell Carcinoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large Cell Carcinoma</td>
<td></td>
</tr>
<tr>
<td>Small Cell Lung Cancer (SCLC) (i.e. Neuroendocrine Carcinomas)</td>
<td></td>
<td>15%</td>
</tr>
<tr>
<td>Sarcomatoid Carcinoma</td>
<td></td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

#### Symptoms/Clinical Presentation

<table>
<thead>
<tr>
<th>Intrathoracic Tumour Effects</th>
<th>Extrathoracic Metastatic Disease</th>
<th>Paraneoplastic Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough (50-70%)</td>
<td>Liver</td>
<td>Hypercalcemia</td>
</tr>
<tr>
<td>Hemoptysis (20-50%)</td>
<td>Bone</td>
<td>SIADH</td>
</tr>
<tr>
<td>Dyspnea (25-40%)</td>
<td>Brain</td>
<td>Lambert-Eaton Myasthenic Syndrome (LEMS)</td>
</tr>
<tr>
<td>Chest Pain (20-40%)</td>
<td>Adrenal</td>
<td>Hematological derangements (anemia, leukocytosis, thrombocytosis, eosinophilia, hypercoagulability)</td>
</tr>
<tr>
<td>Hoarseness</td>
<td></td>
<td>Hypertrophic osteoarthropathy (HPO)</td>
</tr>
<tr>
<td>Pleural involvement</td>
<td></td>
<td>Dermatomyositis and polymyositis</td>
</tr>
<tr>
<td>(thickening or effusion)</td>
<td></td>
<td>Cushing’s syndrome</td>
</tr>
<tr>
<td>SVC syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancoast syndrome (arm pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and Horner’s syndrome)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Physical Exam
- Vitals: oxygen saturation, hemodynamic stability
- Inspection: clubbing, tracheal deviation, respiratory distress
- Percussion: dullness (pleural effusions), tympanic (pneumothorax)
- Auscultation: reduced air entry, wheezing, findings of superimposed post-obstructive pneumonia
- Pancoast tumor: Horner’s syndrome (miosis, ptosis, anhydrosis)

#### Investigations
- Initial diagnosis
  - CBC, electrolytes, calcium, ALP, ALT, AST, total bilirubin, Cr (for paraneoplastic disease and organ involvement)
  - Imaging: CXR, CT chest and upper abdomen
  - Cytology: sputum, pleural effusion

---

Pathology: transthoracic needle biopsy, bronchoscopy, EBUS (for mediastinal LN staging)

Staging
- Imaging: whole body PET CT (if unavailable, bone scan and MRI brain)

Tumor genotyping
- EGFR mutation (common in Asians, females, adenocarcinomas, never smokers)
- ALK mutation (common in adenocarcinomas, never or light smokers)
- ROS1 translocation
- BRAF mutation

Management/Treatment

<table>
<thead>
<tr>
<th>SCLC</th>
<th>Stage</th>
<th>Definition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Limited</td>
<td>Confined to hemithorax and one radiation portal</td>
<td>Combined chemoradiation (cisplatin/etoposide)</td>
</tr>
<tr>
<td></td>
<td>Stage</td>
<td>Can include lymph nodes on either side of the mediastinum</td>
<td>Total of 4-6 cycles</td>
</tr>
<tr>
<td></td>
<td>Extensive</td>
<td>Extension beyond a single radiation portal</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Stage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NSCLC</th>
<th>Stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>I, II</td>
<td>Complete surgical resection +/- post-op adjuvant chemotherapy</td>
</tr>
<tr>
<td>Locally Advanced</td>
<td>IIIA, IIIB</td>
<td>Lymph nodes in mediastinum involved</td>
</tr>
<tr>
<td></td>
<td>“Wet” IIIB, IV</td>
<td>Systemic therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Molecularly targeted therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Symptom-based palliative management (radiation)</td>
</tr>
</tbody>
</table>

NSCLC:
- Platinum agents (cisplatin, carboplatin)
- Anti-microtubule agents (vinorelbine, taxanes)
- Antimetabolites (gemcitabine, pemetrexed)
- Targeted agents (EGFR tyrosine kinase inhibitors, e.g. gefitinib, erlotinib), bevacizumab
4.19 Respiratory Acidosis

Normal ABG Values: pH 7.36-7.44 (7.40 for simplicity), HCO₃⁻ 24mmHg, pCO₂ 40mmHg

1. Does the patient have an acidosis or an alkalosis?
   - Acidosis = low pH (<7.36)
   - Alkalosis = high pH (>7.44)

2. What is the primary problem – metabolic or respiratory?
   - Respiratory acidosis = high pCO₂
   - Metabolic acidosis = low HCO₃⁻

3. Is there any compensation by the patient?

<table>
<thead>
<tr>
<th>Respiratory Acidosis</th>
<th>ΔpCO₂ (mmHg) (normal ~40)</th>
<th>ΔHCO₃⁻ (mmHg) (normal ~24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>↑10</td>
<td>↑1</td>
</tr>
<tr>
<td>Chronic</td>
<td>↑10</td>
<td>↑4</td>
</tr>
</tbody>
</table>

*Increase in HCO₃⁻ in chronic respiratory alkalosis is really anywhere from 3.5-5; use increase of 4 for simplicity

Differential Diagnosis of Respiratory Acidosis:

- Acute
  - Respiratory centre/central nervous system depression (decreased RR)
  - Neuromuscular disorders (decreased vital capacity, e.g. ALS, Guillain-Barre syndrome, muscular dystrophy)
  - Acute obstruction of the lower and/or upper airway (e.g. asthma, COPD, foreign body, anaphylaxis, endobronchial tumor)
- Chronic
  - Chronic airway obstruction (COPD)
  - Mechanical hypoventilation (inadequate mechanical ventilation)
  - Chest wall disorders (severe kyphoscoliosis)
  - Obesity-hypoventilation syndrome
  - CNS depression (drugs, neurologic disorders, primary hypoventilation)
  - Chronic ventilator failure in neuromuscular disease
4.20 Respiratory Alkalosis

1. Does the patient have an acidosis or an alkalosis?
   - Acidosis = low pH (<7.36)
   - Alkalosis = high pH (>7.44)

2. What is the primary problem – metabolic or respiratory?
   - Respiratory alkalosis = low pCO2
   - Metabolic alkalosis = high HCO3

3. Is there any compensation by the patient?

<table>
<thead>
<tr>
<th>Respiratory Acidosis</th>
<th>ΔpCO2 (mmHg) (normal ~40)</th>
<th>ΔHCO3- (mmHg) (normal ~24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>↓10</td>
<td>↓2</td>
</tr>
<tr>
<td>Chronic</td>
<td>↓10</td>
<td>↓4</td>
</tr>
</tbody>
</table>

Differential Diagnosis of Respiratory Alkalosis

- CNS Causes of Hyperventilation
  - Pain, anxiety, psychosis
  - Hyperventilation syndrome
  - Fever
  - Cerebrovascular accident
  - Meningitis, encephalitis
  - Tumor
  - Trauma

- Hypoxia
  - High altitude
  - Right-to-left shunts

- Drugs (e.g. salicylates)

- Endocrine
  - Pregnancy
  - Hyperthyroidism

- Pulmonary
  - Pneumo/hemothorax
  - Pneumonia
  - Pulmonary edema
  - Pulmonary embolism
  - Aspiration
  - Interstitial lung disease
  - Asthma
  - Emphysema
  - Chronic Bronchitis

- Miscellaneous
  - Sepsis
  - Hepatic failure
  - Mechanical ventilation
  - Heat exhaustion
  - CHF
  - Anemia
4.21 Acute Rhinosinusitis

Typical Patient
- General risk factors: allergies, smoking, pollution, drugs
- Risk factors in children: increased viral load, developmental immaturity, adenoid hypertrophy, immunologic immaturity, tobacco smoke exposure, living conditions

Cause
- Obstruction of sinus drainage and retention of secretions due to preceding viral infection or epithelial injury
- Obstruction may be due to: mucosal swelling, abnormalities of cilia, structural abnormalities, overproduction of secretions
- Common bacteriology: *S. pneumonia*, *H. influenzae*, *M. catarrhalis*, *S. aureus*

Symptoms/Clinical Presentation
- **P** = facial pain/pressure/fullness
- **O** = nasal obstruction
- **D** = nasal purulence/discolored
- **S** = hyposmia/anosmia
- Symptoms >7 days = higher likelihood of bacterial infection, acute bacterial rhinosinusitis (ABRS) (requires confirmation of 2 major symptoms)

Physical Exam
- Need to examine area of middle meatus
- Look for evidence of purulence
- Evaluate for structural obstruction, polyps, foreign body

Investigations
- Clinical diagnosis
- CT only if severe ARS, immunocompromised patient, suspected complication
  - Sites of complications of acute rhinosinusitis: orbital, endocranial, osseous, etc.

Management/Treatment
- Mild/moderate ABRS = intranasal corticosteroids
- Severe ABRS = intranasal corticosteroids, antibiotics (first line amoxicillin x 7-14 d)
- Adjunct therapies: analgesics, decongestants (topical or oral), saline irrigation

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45 “Acute Rhinosinusitis”, Shaun Kilty, March 2 2016, University Ottawa Faculty of Medicine
4.22 Acute Tonsillitis\textsuperscript{46, 47}

**Typical Patient**
- Patient <25 yo with throat pain
- High Mallampati score

**Cause**
- Inflammation of the pharyngeal tonsils
- Bacterial tonsillitis: Group A β-hemolytic streptococci (most common), \textit{Mycoplasma pneumonia}
- Viral tonsillitis: rhinovirus (common in adults), EBV, CMV, adenovirus (common in children), influenza

**Symptoms/Clinical Presentation**
- Sore throat
- Dysphagia, odynophagia, trismus
- Malaise, fever
- Otalgia (referred)

**Physical Exam**
- Vitals: fever
- Inspection: tonsil erythema/edema, tonsil exudate
- Palpation: cervical lymphadenopathy

**Investigations**
- CBC
- Rapid Strep Test (Group A Strep only)
- Swab for culture
- Mono spot – less reliable in children <2 yo
- Centor Criteria
  - OLD = Age <15 (add 1 point)
  - C = Cervical lymphadenopathy
  - A = Absence of cough
  - F = Fever
  - E = Tonsil exudate

**Management/Treatment**
- Soft food diet, ample fluid intake
- Gargle with warm saline solution
- Analgesics and antipyretics
- Antibiotics
  - Only after appropriate swab for C&S
  - 1\textsuperscript{st} line penicillin or amoxicillin x 10d (erythromycin if penicillin allergy)
  - Rheumatic fever risk emerges approximately 9 d after the onset of symptoms (antibiotics are used to avoid this and to provide earlier symptomatic relief)

\textsuperscript{46} “Adenotonsillar Disease”, James P. Bonaparte, March 2 2016, uOttawa Faculty of Medicine
\textsuperscript{47} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.23 Oral Cavity Cancer

Typical Patient
- Mean age: 50-60
- M > F
- Smoker
- Heavy drinker
- Poor oral hygiene
- HPV infection

Cause
- Chronic exposure to carcinogens (e.g. cigarettes) causes changes to the entire mucosa
- Areas at most risk of cancer are the lateral tongue and floor of mouth (area where saliva filled with carcinogens pools)
- 95% are squamous cell carcinomas

Symptoms/Clinical Presentation
- Pain in oral cavity, referred otalgia
- Bleeding
- Dysarthria due to fixation of tongue
- Later: trouble swallowing, weight loss
- Neck mass

Physical Exam
- Examine mouth for lesions or ulcers that do not heal

Investigations
- CT scan
- Neck dissection/biopsy if tumor >2 cm or >4 mm deep or if lymph nodes involvement

Management/Treatment
- Primary surgery (local resection and/or reconstruction) and secondary radiation
- Small tumors: wedge excision and primary closure/secondary intention healing
- Larger tumors: resection, possible removal of part of mandible, reconstruction with radial forearm free flap (for soft tissue), reconstruction with fibular free flap (if segment of mandible needs to be replaced)
- Microvascular free tissue transfer (ideal reconstruction for oral cavity defects) - flaps have excellent vascular supply and can survive contact with oral flora and saliva

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48 “Head and Neck Malignancy”, Michael J. Odel, March 23 2016, uOttawa Faculty of Medicine
4.24 Oropharyngeal Cancer

Typical Patient
- Mean age: 50-70
- M:F = 4:1
- Risk factors: smoking, alcohol, HPV infection

Symptoms/Clinical Presentation
- Sore throat
- Neck mass
- Dysphagia
- Weight loss
- Dysarthria
- Bleeding
- Referred otalgia

Physical Exam
- Common sites: tonsil, base of tongue, posterior pharyngeal wall

Investigations
- Biopsy
- CT

Management/Treatment
- Radiation therapy
- Chemotherapy
- Surgery (only if radiation is unsuccessful)

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49 “Head and Neck Malignancy”, Michael J. Odell, March 23 2016, uOttawa Faculty of Medicine
4.25 Laryngeal Cancer\textsuperscript{50}

Typical Patient
- Mean age: 45-75
- M:F = 10:1
- Smoker
- Risk factors: alcohol, HPV 16 infection

Cause
- Larynx is narrowest part of airway and thus sees highest concentration of carcinogens (e.g. smoke) on the way to the lungs
- 90% are squamous cell carcinomas

Symptoms/Clinical Presentation
- Hoarseness
- Odynophagia
- Dysphagia
- Airway obstruction (stridor)
- Referred otalgia
- Neck mass
- Cough/hemoptysis

Physical Exam
- Inspect 3 common sites: glottic, supraglottic and subglottic
  - Tumors in glottic space have a better prognosis because they are detected early due to associated hoarseness
  - Tumors in supraglottic and subglottic sites can go undetected for years

Investigations
- Laryngoscopy
- CT/MRI

Management/Treatment
- Small T1 cancers (confined to one vocal cord): CO\textsubscript{2} laser, radiotherapy
- Large T1/T2 cancers (extension to both vocal cords): radiotherapy
- Supraglottic cancers: radiotherapy
- T3 (paralyzed vocal cord): radiotherapy and/or chemotherapy, total laryngectomy
- T4 (disease beyond larynx): total laryngectomy with adjuvant radiotherapy

\textsuperscript{50} “Head and Neck Malignancy”, Michael J. Odell, March 23 2016, uOttawa Faculty of Medicine
4.26 Differential Diagnosis for Hoarseness

Symptoms of Laryngeal Disease

- **Hoarseness**
  - Determine if intermittent or constant
  - Different characteristics of hoarseness: breathy, raspy, hot potato

- **Airway obstruction**
  - Stridor
  - Shortness of breath (especially with exertion)
  - Should be a very LATE finding

- **Dysphagia**
  - Mass may be large enough to block upper esophagus

- **Aspiration**
  - If protective function of larynx during swallowing is lost, may result in aspiration and aspiration pneumonia

Differential Diagnosis for Hoarseness

- **Laryngeal cancer**
  - Risk factors: smoking, alcohol
  - Early sign: hoarseness
  - Late signs: neck mass, airway obstruction, aspiration, dysphagia
  - Treatment: surgery vs. radiation therapy

- **Laryngeal papillomatosis**
  - Benign lesions caused by HPV
  - Can be seen in infancy (juvenile papillomatosis) or adulthood
  - Can cause significant hoarseness, if left unattended
  - Treatment: surgical removal

- **Unilateral vocal cord paralysis**
  - One cord remains fixed just lateral to midline
  - Causes: tumor growth into recurrent laryngeal nerve (RLN), iatrogenic trauma to RLN, idiopathic
  - Signs/symptoms: breathy voice, aspiration
  - Treatment: injection of cord with collagen

- **Bilateral vocal cord paralysis**
  - Causes: neurological (stroke, Guillain-Barre Syndrome), idiopathic, iatrogenic (surgery)
  - Inadequate airway leads to airway obstruction
  - Treatment: tracheostomy

- **Laryngeal nodules**
  - Overuse/abuse of the voice will cause strain on the vocal cords
  - Children: “screamer’s nodules” (bilateral nodules at junction of anterior 1/3 and posterior 2/3 of vocal cord)
  - Adults: may be unilateral or bilateral
  - Treatment: speech therapy, surgical removal (may recur if not treating underlying problem)

- **Granulomas of larynx**
  - Trauma to the vocal cord can result in the development of a granuloma
  - Common cause: intubation

- **Reinke’s edema**

---

51 “Physiology of Voice and Hoarseness”, Michael J. Odell, March 23 2016, uOttawa Faculty of Medicine
 Collection of fluid in Reinke’s space (loose connective tissue layer of true vocal cord)
 Floppy, swollen, edematous vocal cords
 Common cause: smoking
 Treatment: smoking cessation, surgical removal

4.26 Differential Diagnosis for Hoarseness - continued

- GERD
  - Most common cause of hoarseness
  - Usually happens at night while patient is supine
  - Symptoms: hoarseness is intermittent (often worse first thing in the morning)
  - Signs: erythema and edema of mucosa of posterior glottis on endoscopy (esophagus is posterior to glottis and reflux affects that portion of glottis primarily)
  - Treatment: proton pump inhibitors

- Vocal cord hematoma
  - Trauma to anterior larynx can cause compression of laryngeal cartilages and result in vocal cord hematoma
  - Symptoms: acute hoarseness after traumatic incident
  - Investigations: CT important to rule out laryngeal fracture
  - Treatment: usually resolves spontaneously

- Spasmodic dysphonia
  - Condition where excessive muscle tension in laryngeal muscle causes strangulation of voice
  - Very short phonation times, very difficult to create voice
  - Treatment: botox (very effective, needs to be repeated q6 months)
4.27 Subglottic Stenosis\textsuperscript{52,53,54}

Typical Patient
- Congenital cause (5%)
  - Newborns with a subglottic tracheal lumen of <4 mm in term infant, <3 mm in preterm infants
- Acquired (95%)
  - Iatrogenic (majority): patient with a long duration of endotracheal intubation
  - Infectious: tuberculosis, diphtheria, syphilis
  - Inflammation: sarcoidosis, GPA
  - Trauma: injury, irritant

Cause
- Congenital or acquired narrowing of the subglottic airway
  - Congenital: subglottic space of <4 mm at birth likely caused by incomplete canalization of the cricoid cartilage during development
  - Acquired: trauma or irritation of the endotracheal lining causes necrosis and scarring of subglottic space and cricoid cartilage

Symptoms/Clinical Presentation
- Biphasic stridor
- Respiratory distress
- Recurrent croup
- Less important stenosis may only cause stridor when exercising
- Voice changes
- Critical upper airway obstruction

Physical Exam
- Signs of respiratory distress: flaring nostrils, dyspnea, use of accessory muscles
- Fever, cough, expectoration due to increased susceptibility to infection, including croup
- Voice hoarseness or breathy voice can be associated with subglottic stenosis or GERD

Diagnostic Investigations
- Chest imaging (CXR or CT) can provide helpful information regarding associated conditions and potentially demonstrate stenosis; however, poor sensitivity
- PFTs may show blunting of the inspiratory and expiratory limbs of the flow volume curve (i.e. a fixed airway obstruction)
- Laryngoscopy and bronchoscopy for definitive diagnosis

Management/Treatment
- Observation if asymptomatic
- Prednisone for patients with symptomatic stenosis secondary to inflammatory etiologies (e.g. sarcoidosis, vasculitis)
- Treat the underlying cause
- Surgery or endotracheal dilatation for severe or symptomatic cases

\textsuperscript{52} “Détresse respiratoire aiguë et infections respiratoires aiguës chez les enfants”, Scott Kohlert, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{53} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.28 Laryngomalacia\textsuperscript{55,56}

Typical Patient
- Infants – usually before 2 weeks of age

Cause
- Most common congenital cause of stridor
- Stridor occurs due to the collapse of tissue above the vocal cords into the airway and can cause many problems (e.g. acid reflux, recurrent pneumonias, failure to thrive)
- Variety of congenital defects can lead to laryngomalacia:
  - Short aryepiglottic folds
  - Arytenoid prolapse
  - Omega-shaped epiglottis

Symptoms/Clinical Presentation
- Inspiratory stridor which is intermittent and variable in intensity
  - Worsens with agitation and feeding
  - Improves with prone position or neck extension
- If very severe (rare): apnea, cyanosis, failure to thrive, feeding difficulties
- Normal cry
- Recurrent upper respiratory tract infection
- Clinical course:
  - Begins at 2 weeks of age and progresses for the first few months of life
  - Then shows slow improvement with termination of symptoms at 18 months of age

Physical Exam
- Inspection:
  - Assess for cyanosis, failure to thrive, breathing difficulty
  - Pectus excavatum (seen in severe cases)
  - Assess for pneumonia and/or aspiration
- Auscultation:
  - Assess for equal air entry bilaterally
  - Assess severity of the stridor

Investigations
- May perform endoscopy

Management/Treatment
- Self-limiting disease but in severe cases may need surgery (i.e. supraglottoplasty)
- Treat GERD if present

\textsuperscript{55} “Acute Respiratory Distress and Acute Respiratory Infections in Children”, Tom Kovesi, Matthew Bromwich, Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{56} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.29 Epiglottitis\textsuperscript{57,58}

Typical Patient
- Usually in children age 2 to 12 years (or 1-4 years old)

Cause
- Inflammation of supraglottic structures (does not touch vocal cords, only epiglottis and aryepiglottic folds), because of infection by the \textit{H. influenzae} type b (HiB) bacteria
  - Rare since initiation of HiB vaccination in children

Symptoms/Clinical Presentation
- Rapid onset and progression
- Dysphagia due to severe pain; leads to drooling
- Child prefers sitting done, drools and sticks tongue out
- Dyspnea
- Dysphonia
- Muffled cough and voice
- High fever
- Inspiratory stridor
- Anorexia
- Anxious expression, toxic-looking patient
- Tend to sit leaning forward
  - There is a risk for the epiglottis to stick to the laryngeal structures causing complete obstruction of the airway and asphyxia

Physical Exam
- Always be ready for intubation before examining the patient
- Inspection:
  - Level of distress/urgency of the situation
  - Cyanosis
- Auscultation:
  - Inspiratory stridor
  - Lungs clear with decreased air entry

Investigations
- Must not use tongue depressor to examine the throat as this may compromise the airway
- X-ray: order only if the child is stable; “thumb sign” (swollen epiglottis) and thickened aryepiglottic folds
- Culture epiglottis (only after intubation)
- Blood work: CBC, blood culture

Management/Treatment
- Controlled intubation/emergency tracheostomy
- IV cefuroxime (second-generation cephalosporin)
- IV fluids as needed

\textsuperscript{57} “Acute Respiratory Distress and Acute Respiratory Infections in Children”, Tom Kovesi, Matthew Bromwich, Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{58} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.30 Croup (Viral Laryngotracheobronchitis)\textsuperscript{59,60}

**Typical Patient**
- Usually children 3 months to 5 years, presenting during autumn or spring

**Cause**
- Inflammation of infraglottic structures and mucous membranes, causing an exudate that compromises the upper respiratory tract
- Mucociliary dysfunction
- Viral infection:
  - Parainfluenza virus type III (most common)
  - Influenza virus
  - Respiratory syncytial virus (RSV)

**Symptoms/Clinical Presentation**
- Coryza (acute inflammation of the upper respiratory tract)
- Fever
- Voice loss or hoarseness
- Loud, barky cough
- Symptoms of upper respiratory infection before the attack
- Inspiratory stridor (can be biphasic)
- Patient seems less distressed/toxic than with epiglottitis – patient most often looks well
- Cyanosis if severe
- Symptoms worse at night

**Physical Exam**
- Inspection:
  - Child usually looks well
  - Assess for level of distress, cyanosis
  - In some cases: abnormal voice, dyspnea, expectoration, coughing, agitation, use of accessory muscles
- Auscultation:
  - May have inspiratory stridor
  - Usually normal air entry with normal pattern of breathing

**Investigations**
- Croup is a clinical diagnosis; therefore, does not require X-ray or other investigations
  - If neck X-ray done: “steeple sign” on AP view; can be normal in 50% of cases

**Management/Treatment**
- Self-limiting, therefore does not require treatment
- Oxygen supplementation if needed
- May use oral steroids (nebulized budesonide)
- Nebulized epinephrine if stridor at rest or increased difficulty breathing
- Proper hydration with systemic corticosteroids (symptoms should resolve after 7-14 days)
- Intubation and hospitalization if severe

\textsuperscript{59} “Acute Respiratory Distress and Acute Respiratory Infections in Children”, Tom Kovesi, Matthew Bromwich, Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{60} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.31 Pertussis (Whooping Cough)\textsuperscript{61,62}

Typical Patient

- Mainly in children <1 year old (not yet immune) or in teenagers (diminished immunity)

Cause

- Infection is usually caused by the gram-negative bacterium \textit{Bordetella pertussis}
  - Vaccine preventable disease (pertussis vaccination 90\% effective)
  - As vaccine effectiveness wanes over time, adults can remain reservoir and spread infection to children
- Highly contagious (mostly during catarrhal phase), transmissible through respiratory droplets released during coughing (incubation period of 6-20 days)
- Infection and toxin production by the bacterium leads to dysfunction and necrosis of cough receptors, causing intense bouts of coughing

Symptoms/Clinical Presentation

- Symptoms progress in 3 main stages:
  - Catarrhal phase (~ 1 week): most contagious phase, coryza, mild cough, sneezing
  - Paroxysmal phase (~ 6 weeks): severe paroxysms of coughing, facial plethora, vomiting, older children have inspiratory whoop at end of cough, small infants may develop apnea
  - Convalescent phase (up to 1 year): cough gradually improves but can be exacerbated or reactivate with viral infections, episodes of coughing are milder with reactivation

Physical Exam

- Inspection:
  - Fever is uncommon
  - Child usually looks well, but in some cases may be exhausted and/or cyanotic
  - Barking cough, bruising because of coughing, vomiting
- Auscultation:
  - Usually normal cardiac and respiratory examination
- The pressure from coughing can cause subconjunctival hemorrhage, rectal prolapse, epistaxis
- Pertussis infection increases the risk of sinusitis, pneumonia, aspiration, atelectasis, pneumomediastinum, pneumothorax, alveolar rupture, encephalopathy, intracranial hemorrhaging and convulsions

Investigations

- Clinical diagnosis
- Culture or PCR of nasopharyngeal aspirate
- Blood work:
  - CBC: lymphocytosis (leukemoid pattern)
  - Culture
- Chest X-ray:
  - Bronchopneumonia pattern

Management/Treatment

- Hospitalize patient if coughing is associated with cyanosis; give oxygen and saline
- Macrolide antibiotics shorten the period of infectivity
  - Macrolides can decrease cough when given early during the catarrhal phase
- Cough remedies have no effect
  - Cough improves as the cough receptors regenerate
- Macrolide antibiotics can be used as prophylaxis for close contacts

\textsuperscript{61} “Acute Respiratory Distress and Acute Respiratory Infections in Children”, Tom Kovesi, Matthew Bromwich, and Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine

\textsuperscript{62} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
4.32 Bronchiolitis\textsuperscript{63,64}

\textbf{Typical Patient}
- Mainly seen in infants (under 2 yo)

\textbf{Cause}
- Viral infection of the bronchioles (lower respiratory tract infection):
  - Respiratory syncytial virus (RSV) - most common
  - Influenza
  - Parainfluenza virus
  - Rhinovirus
  - Adenovirus
- Viral infection causes inflammation, edema, mucous production, and mucosal shedding of the bronchiolar epithelium; bronchospasm and atelectasis can follow
- Narrowing/obstruction of small airways leads to hyperinflation and atelectasis
- Anti-RSV IgE produced in response to infection increases risk of atopy in high-risk children; 50% of children that contract RSV bronchiolitis will have asthma later in life
- Contiguous spread into interstitium can lead to development of interstitial pneumonia
- Severe bronchiolitis cases can cause permanent legions (bronchiolitis obliterans, bronchiectasis, etc.)

\textbf{Symptoms/Clinical Presentation}
- Prodromal symptoms include coryza, fever, coughing
- Wheezing
- Feeding difficulty, irritability
- Tachypnea/ respiratory distress, tachycardia

\textbf{Physical Exam}
- Inspection:
  - Assess level of distress, pattern of breathing
  - Cyanosis if severe
  - Coryza, coughing, fever, lethargy, use of accessory muscle for breathing
- Auscultation:
  - Decreased air entry with wheezing
- Assess for signs and symptoms of asthma

\textbf{Investigations}
- Mostly a clinical diagnosis
- Viral culture or rapid testing immunofluorescence assay of nasopharyngeal aspirate
- Chest X-ray:
  - Hyperinflation
  - Bronchial wall thickening
  - May develop viral pneumonia (patchy atelectasis, interstitial infiltrates)

\textbf{Management/Treatment}
- Self-limiting disease
- 30-50% respond to bronchodilators (e.g. \(\beta_2\)-adrenergic agonists and nebulized epinephrine)
- Hypertonic saline through nebulizer to thin secretions by drawing water into mucus
- Use of oral steroids is controversial

\textsuperscript{63} "Acute Respiratory Distress and Acute Respiratory Infections in Children", Tom Kovesi, Matthew Bromwich, and Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine

\textsuperscript{64} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
Supplemental oxygenation, fluids, antipyretics, thickened feeds to decrease risk of micro-aspirations
Do not give antibiotics unless there is bacterial superinfection (secondary bacterial pneumonia)
In severe cases, give monthly dose of Ig-RSV or Palivizumad
Indications for hospitalization: \( O_2 \) saturation <92%, tachypnea even after bronchodilators, cardiac abnormalities, neuromuscular problems, immunocompromised patient, children <6 months, significant feeding difficulties

4.33 Peritonsillar Abscess\textsuperscript{65,66}

Typical Patient
- Most common in 15-35 yo
- Uncommon in children <10
- History of tonsilitis

Cause
- Cellulitis of space behind tonsils that progresses to soft palate, causing an abscess
- Group A streptococci (most common)
- Staphylococci
- Pneumococci
- May also be anaerobic bacteria or polymicrobial

Symptoms/Clinical Presentation
- Fever
- Recent history of pharyngitis
- Sore throat
- Dysphagia
- Odynophagia
- Fatigue and/or dehydration
- “Hot Potato” voice
- Trismus (due to inflammation and spasm of the medial pterygoid muscle)
- Ipsilateral otalgia

Physical Exam
- Abscess noticed in area close to the tonsils
  - Swollen and erythematous
  - May contain visible pus
  - Unilateral
- Soft palate: red and bulging
- May have deviated uvula if the abscess is large
- Examine for complications: acute rheumatic fever, scarlet fever, aspiration pneumonia, bacteremia

Investigations
- Usually clinical diagnosis
- CT scan in complicated and atypical cases
- Swab and cultures

Management/Treatment
- Make sure that airway is not compromised
- Symptomatic treatment (anti-inflammatories, pain control, hydration) with antibiotics
  - Antibiotics:
    - If positive for \textit{S. pneumoniae}: IV penicillin

\textsuperscript{66} “Adenotonsillar Disease”, James P. Bonaparte, March 2 2016, uOttawa Faculty of Medicine
If positive culture for anaerobic bacteria: clindamycin 300-450 mg QID, 7-10 days or metronidazole 500 mg BID, 7 days

- Incision and drainage
- May prescribe steroids

### 4.34 Tonsillar Phlegmonous Cellulitis\(^{67,68}\)

**Typical Patient**
- Patient <30 years old with throat sore
- High Mallampati score

**Cause**
- Tonsil infection that progresses to cellulitis
- Majority of cases due to *S. pneumoniae*, but many cases also due to anaerobic bacteria

**Symptoms/Clinical Presentation**
- Fever
- Odynophagia, dysphagia
- Throat pain
- Otalgia
- Malaise

**Physical Exam**
- One tonsil more erythematous than the other
- Inflammatory changes are bilateral, but one side worse than the other
- Midline uvula
- Normal or slightly modified voice (potato voice)
- Examine cervical lymph nodes
- Trismus, if present, is mild
- Examine for complications: rheumatic fever, scarlet fever, peritonsillar abscess

**Investigations**
- Clinical diagnosis
- Swab to screen for *S. pneumoniae*
- Rule out mononucleosis (if suspected, order FSC and monotest)

**Management/Treatment**
- Symptomatic treatment (anti-inflammatories, hydration, pain control) with antibiotics
- Antibiotics:
  - Penicillin-amoxicillin
  - Clindamycin 300-450 mg QID, 7-10 days
  - Metronidazole 500 mg BID, 7 days

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\(^{67}\) “Adéno-amygdalite”, Joe Marsan & Laurie McLean, March 2 2016, uOttawa Faculty of Medicine

4.35 Pulmonary Edema

Typical Patient
- Can be seen in patients of all ages ranging from infants to the elderly
- Usually seen in patients with cardiac disease

Cause
- Cardiogenic pulmonary edema
  - Left heart failure
  - Coronary artery disease with left ventricular failure
  - Cardiac arrhythmias
  - Cardiomyopathy
  - Obstructing valvular lesions
  - Myocarditis and infectious endocarditis
- Non-cardiogenic pulmonary edema (due to changes in capillary permeability)
  - Smoke/toxin inhalation
  - Acute respiratory distress syndrome (ARDS)
  - Head trauma
  - Overwhelming sepsis
  - Hypovolemic shock
  - Acute lung re-expansion
  - High altitude pulmonary edema
  - Disseminated intravascular coagulopathy (DIC)
  - Near-drowning
  - Overwhelming aspiration

Symptoms/Clinical Presentation
- Shortness of breath, in both activity and rest
- Orthopnea

Physical Exam
- Auscultation: crackles at the lung bases

Investigations
- Chest X-ray:
  - Kerley B lines (septal lines)
  - Pleural effusions
  - Thickening of the major and minor fissures
  - Peribronchial cuffing

Management/Treatment
- LMNOP:
  - L = Lasix
  - M = Morphine
  - N = Nitrates
  - O = Oxygen
  - P = Position (sitting up instead of lying down)

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69 “Acute Decompensated Heart Failure”, Sharon Chih, January 13 2016, uOttawa Faculty of Medicine
4.36 Acute Respiratory Distress Syndrome (ARDS)\textsuperscript{70}

Typical Patient
- Any patient who experiences acute exposure to a large amount of irritants

Cause
- Non-cardiogenic pulmonary edema due to leakage of fluid from the capillaries into the alveolar spaces and the interstitium, which progresses to lung inflammation and respiratory failure
- Aspiration of gastric contents
- Toxic inhalations: noxious gases/smoke
- Infections, severe pneumonia, sepsis (especially gram negative bacteria), DIC, shock
- Severe chest trauma
- Embolism (fat, amniotic fluid)
- Iatrogenic (transfusions, cardiopulmonary bypass, medications, radiation, mechanical ventilation)
- Other:
  - Neurogenic (head trauma)
  - Pancreatitis
  - Idiopathic

Symptoms/Clinical Presentation
- Severe lung dysfunction associated with hypercapnia as well as hypoxemic respiratory failure
- Severe dyspnea
- Cyanosis
- Rapid and shallow breathing
- May present with shock

Physical Exam
- Inspection: labored breathing with increased distress
- Auscultation: crackles at the lung bases
- Other organ dysfunction

Investigations
- Chest X-ray: pulmonary edema (bronchial wall thickening, interstitial infiltrates, patchy alveolar opacities)
- Normal wedge pressure indicates non-cardiogenic pulmonary edema

Management/Treatment
- Treat underlying disorder
  - Infection – antibiotics
  - Decrease exposure of irritants
- Treat pulmonary edema (LMNOP):
  - L = Lasix
  - M = Morphine
  - N = Nitrates
  - O = Oxygen
  - P = Position (sitting up instead of lying down)
- Mechanical ventilation to assist breathing
- Steroids controversial
- Careful fluid management to avoid worsening of pulmonary edema
- Treat secondary organ dysfunction – heart failure, fluid retention due to renal dysfunction

\textsuperscript{70} "Respiratory Failure" Tom Kovesi, February 24 2016, uOttawa Faculty of Medicine
4.37 Tracheomalacia\textsuperscript{71,72}

**Typical Patient**
- Infants and young children
- Patients 4-8 weeks old presenting with wheeze (expiratory or biphasic)

**Cause**
- Congenital disorder leading to flaccid tracheal cartilage and tracheal collapse
- Other, rarer causes: damage to trachea because of surgery, GERD, vascular problems or recurrent aspiration
- Associated with other cardiac and vascular congenital defects and GERD

**Clinical Presentation**
- Expiratory wheeze, becomes biphasic if severe
- In severe cases:
  - Apnea
  - Feeding difficulties
  - Failure to thrive
  - Recurrent pneumonias (due to reduced mucociliary clearance)
- Can lead to sleep apnea, failure to thrive, recurrent pneumonia

**Physical Exam**
- Possible intercostal indrawing
- Sign of reduced growth (failure to thrive)
- Auscultation: usually normal inspiration with expiratory wheeze

**Investigations**
- Chest X-ray: lung hyper-inflation and narrowing of tracheal lumen
- Endoscopy

**Management/Treatment**
- Symptoms often resolve spontaneously by 2 years of age
- Tracheostomy until maturation of cartilage
- May control infections with antibiotics
- May require surgical intervention
- Bronchodilators do not help (and even worsen) the situation

\textsuperscript{71} “Acute Respiratory Distress and Acute Respiratory Infections in Children” Tom Kovesi, Matthew Bromwich, Jean Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine
\textsuperscript{72} Concepcion, E. “Pediatric Tracheomalacia Clinical Presentation” Sharma, GD (Ed). Medscape, 2016.
4.38 Retropharyngeal Abscess\textsuperscript{73,74}

Typical Patient
- Occurs most often in children under 2 years of age, following an upper respiratory tract infection, tonsillitis, otitis, or adenitis
- Can also occur from penetrating injury to the posterior wall of the pharynx (e.g. fish bones, lollipop)

Cause
- Build-up of bacteria in the retropharyngeal space
  - Most common bacteria: Group A β-hemolytic streptococci

Symptoms/Clinical Presentation
- Difficulty and/or pain with breathing or swallowing (muffled voice, gurgling breathing, drooling)
- Fever
- Severe throat pain
- Stridor
- Torticollis
- Mass in posterior wall of pharynx (generally unilateral), hyperextended neck, enlarged cervical lymph nodes

Physical Exam
- Oral examination: look for lateral deviation of the uvula, swollen/red/inflamed tonsils
- Lymph node examination

Investigations
- Throat culture
- CBC
- X-ray or CT scan (usually unnecessary unless case is complicated or atypical)

Management/Treatment
- Antibiotics (IV penicillin)
- Incision and drainage
- Pain control
- Steroids (to control inflammation)

\textsuperscript{73} “Adenotonsillar Disease”, James P. Bonaparte, March 2 2016, uOttawa Faculty of Medicine
\textsuperscript{74} “Pediatric Stridor and Acute Respiratory Infections”, Thomas Kovesi, Matthew Bromwich, and Philippe Vaccani, March 14 2016, uOttawa Faculty of Medicine
4.39 Vocal Cord Paralysis\textsuperscript{75,76,77}

**Typical Patient**
- Patient with previous surgery near recurrent laryngeal nerve or with history of intubation, brain lesion (e.g. stroke), or neck mass (e.g. carcinoma of vocal cords, lymphoma, thyroid lesion)
- Patient with congenital paralysis (very rare)

**Cause**
- Organic lesion of nerve structures that participate in phonation: recurrent laryngeal nerve, vagus nerve (CNX), voice-producing area of brain

**Symptoms/Clinical Presentation**
- Unilateral: may have hoarseness, but most often breathy voice
- Bilateral: voice can remain normal, but there is often stridor
- Patients at high risk of aspiration (unilateral higher than bilateral) may also present with chest pain, cough, fever, dyspnea and/or expectorations due to aspiration pneumonia
- High risk of respiratory distress because of inability of vocal cords to move during breathing

**Physical Exam**
- Unilateral: vocal cord paralysis seen on endoscopy laterally
- Bilateral: both vocal cords are placed medially, causing risk of airway obstruction
- Respiratory distress (severe cases): cyanosis, use of accessory muscles to breathe, loss of consciousness
- Aspiration pneumonia: fever, dullness on percussion, crackles, tactile fremitus, egophony

**Investigations**
- Laryngoscopy
- EMG
- Blood count
- MRI, radiography: cervical and thoracic

**Management/Treatment**
- Unilateral:
  - Observation for majority of cases
  - Speech therapy
  - Injection laryngoplasty
  - Silastic medialisation
- Bilateral:
  - Observe if there are no breathing problems
  - Intubation and tracheostomy (reversible) for cases with breathing problems
  - Do not complete permanent surgical intervention until 1-2 years
  - 80% of cases need a tracheostomy before the age of 1, and 50% of cases resolve after 2 years without the need of a permanent surgical procedure

\textsuperscript{75}“Détresse respiratoire aiguë et infections respiratoires aiguës chez les enfants”, Scott Kohlert, March 14 2016, uOttawa Faculty of Medicine.
\textsuperscript{76}Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
\textsuperscript{77}Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.

4.40 Histoplasmosis

Typical Patient
- Lives in endemic area (St. Lawrence River, Ohio, Mississippi, lower Ottawa river valleys)
- Exposure to disturbed soil, soil contaminated with bird or bat feces

Cause
- Infection by the endemic fungus *Histoplasma capsulatum*

Symptoms/Clinical Presentation
- Majority are asymptomatic
- If symptomatic, presentation is similar to pneumonia (cough, fevers, chills, aches, dyspnea)
- ~10% also have rheumatologic symptoms (arthralgias)

Physical Exam
- General respiratory exam (inspection, percussion, auscultation)

Investigations
- CXR
- Consider bronchoscopy
- Histoplasma urine antigen test has sensitivity >90%

Management/Treatment
- Asymptomatic pulmonary nodules or mediastinal granulomas: no need for treatment
- Symptomatic: anti-fungal

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78 “Pathology: Air Exchange Diseases – Infectious Pneumonias”, Harman Sekhon, March 17 2016, uOttawa Faculty of Medicine
4.41 Hypersensitivity Pneumonitis

Typical Patient
- Patient who has been exposed to an antigen, often because of work: moldy hay, bird droppings, wood dust, paint, soy, insecticides, plastic, moldy cheese, popcorn, etc.
- History: hobbies; most studied is “Farmer’s Lung” (thermophilic actinomycetes in moldy hay) and “Bird Fancier’s Lung” (proteins from bird droppings)

Cause
- Hypersensitivity/allergic reaction to antigen, which can be almost anything (>200 organic antigens associated)
- Acute form: type 3 hypersensitivity reaction, within hours after exposure; subsides within a few days after removal of antigen
- Subacute form: over weeks and months; more common, try to prevent progression to chronic
- Chronic form: type 4 hypersensitivity reaction (rarest), over years, irreversible fibrotic changes in lung
- More common in those who do not smoke (tobacco is protective)
- Pathology:
  - Peribronchiolar interstitial pneumonitis = centrilobular lymphoplasmacytic inflammation = axial interstitium
  - Presence of poorly-formed, non-necrotizing granulomas (as opposed to sarcoidosis), giant cells, and septal thickening

Symptoms/Clinical Presentation
- Acute: cough, fever, chills, dyspnea 6-12 hours after exposure; resembles atypical pneumonia
- Subacute: chronic productive cough for a few weeks with progressive dyspnea; leads to cyanosis if untreated
- Chronic: present as primary ILD (dyspnea, weight loss, cough)

Physical Exam
- Acute: diffuse and bilateral crepitus, fever, tachycardia
- Subacute: same signs as chronic but shorter duration
- Chronic:
  - Low O₂ sat, tachycardia, tachypnea
  - Weight loss, use of accessory muscles
  - Crepitus, especially in lower lobes
  - Clubbing

Investigations
- X-ray can be normal: acute can show diffuse infiltrates, chronic can show reticulonodular lesions in upper lobes
- HRCT
- Bronchoalveolar cleaning (shows lymphocytosis)
- Biopsy as last resort (shows poorly-formed granulomas)

Management/Treatment
- May not have to quit work; avoid antigen (e.g. by wearing mask/filter, installing appropriate ventilation, mechanizing part of work where one interacts with antigen)
- Acute or subacute: prednisone 1 mg/kg per day for 3-6 weeks (necessary only if severe)
- Chronic: no definitive treatment, damage is irreversible; can do trial of prednisone 1 mg/kg for 3-6 weeks

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79 “Introduction to Interstitial Lung Diseases, Nha Voduc, March 16 2016, uOttawa Faculty of Medicine
80 “Occupational Lung Disease”, Sunita Mulpuru, March 16 2016, uOttawa Faculty of Medicine
4.42 Occupational Asthma

Typical Patient
- Worker exposed to potential irritants

Cause
- Variable airflow obstruction and/or airway hyper-responsiveness attributable to a particular work environment and not to stimuli encountered outside the workplace
- Usually new onset asthma, but can occur with pre-existing asthma
- Pathophysiology: IgE antibodies to high molecular weight or low molecular weight agents (e.g. latex, flour, animal allergens, dyes, resins) or physical irritants
- History gives high index of suspicion (take occupational history); symptoms improve when away from work, return when at work

Symptoms/Clinical Presentation
- Like asthma: airflow obstruction upon exposure to sensitizing agent

Physical Exam
- Like asthma: wheezing upon exposure to sensitizing agent

Investigations
- History is the most important
- Demonstrate asthma: PFT pre- and post-bronchodilator, or methacholine challenge (PC20 <4, 3-4x increase off work)
- Demonstrate work environment is cause:
  - Gold standard: specific inhalation challenges or occupational type of exposure tests
  - IgE of antigen: rarely done as rarely know precise antigen
  - Serial (4x daily) PEF 2 weeks on and 2 weeks off work: allowed to keep medications but avoid LABA
  - Serial methacholine challenge on and off work
- HRCT
- Bronchial lavage showing lymphocytosis
- Biopsy as last resort

Management/Treatment
- Reduce exposure to antigen (e.g. work area ventilation, change departments)
- Advise patient about workplace safety and insurance board (WSIB) compensation if appropriate
Lymphoma & Vascular
5.1 Myeloma

Typical Patient
- More common in: Elderly individuals & African Americans

Cause
- Chromosomal translocations cause lymphoproliferative disorders in the bone marrow
  
  Common translocations and FISH classifications for prognosis:

<table>
<thead>
<tr>
<th>High risk</th>
<th>Intermediate risk</th>
<th>Standard risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>FISH</td>
<td>FISH</td>
<td></td>
</tr>
<tr>
<td>Del 17p</td>
<td>t(4;14)</td>
<td>All others including:</td>
</tr>
<tr>
<td>t(14;16)</td>
<td>1q gain</td>
<td>● Trisomies</td>
</tr>
<tr>
<td>t(14;20)</td>
<td>Complex karyotype</td>
<td>● t(11;14)</td>
</tr>
<tr>
<td></td>
<td>Metaphase deletion 13 or hypodiploidy</td>
<td>● t(6;14)</td>
</tr>
<tr>
<td></td>
<td>High PC S-phase</td>
<td></td>
</tr>
</tbody>
</table>

Symptoms/Clinical Presentation
- Bone pain & fractures
- Anemia
- Recurrent infections from hypogammaglobulinemia
- Renal failure
- Hypercalcemia
- Fatigue, nausea, constipation, loss of appetite, weight loss (constitutional symptoms)

*NB: Most common symptoms = CRAB (Calcium elevation, Renal Failure, Anemia, Bone disease)*

Physical Exam
- Pallor (from anemia)
- Ecchymoses or purpura (from thrombocytopenia)
- Pathological fractures and/or bony tenderness
- Neurologic findings: e.g. loss of sensation (if spinal cord is compressed), neuropathy

Investigations
- Complete Blood Count (CBC), creatinine, calcium, albumin, and total protein
- Serum & urine protein electrophoresis and immunofixation
- Serum free light chain assay
- Bone marrow biopsy
- Skeletal survey (CANNOT do bone scan because lytic lesions will not take up tracer)
- Blood smear (look for Rouleaux formations - RBC stacking, background antibodies)
- +/- MRI if X-ray is negative and suspicion is high

Management/Treatment
- Chemotherapy
- +/- Autologous stem cell transplant (i.e. bone marrow transplant if eligible, <70 years old)
- Pain control (e.g. hydromorphone, palliative radiation therapy)
- Bisphosphonate (bone former)
- Internal fixation/orthopedic consultation for lytic lesions (prevents fractures)
- Blood transfusion (for anemia)
- IV fluids, dialysis (for renal failure)
- *Note that multiple myeloma is an incurable disease: treatments aim to relieve pain, prolong life, etc.*
5.2 Lymphoma

Typical Patient
- More common in elderly individuals

Cause
- Chromosomal translocations cause lymphoproliferative disorders
- Risk factors: Infection (e.g. Epstein-Barr virus), environmental factors (e.g. chemicals, chemotherapy, radiation exposure), immunodeficiency states, chronic inflammation
- Common translocations are:
  - t(14;18) for follicular lymphoma
  - t(8;14) for Burkitt’s lymphoma (implicates MYC oncogene)

Symptoms/Clinical Presentation
- Lymphadenopathy (painless, usually unilateral)
- Constitutional symptoms (fever, weight loss, night sweats)
- Cytopenias
- Alcohol-induced pain (uncommon, but very specific for Hodgkin’s lymphoma)
- Pruritus (more common in Hodgkin’s and T-cell Non-Hodgkin Lymphoma)

Physical Exam
- Palpable, painless lymphadenopathy (most often in neck, less common in axilla or inguinal regions)
- Splenomegaly and/or hepatomegaly (possibly)

Investigations
- CBC, electrolytes, albumin, calcium, creatinine, liver enzymes & function, lactate dehydrogenase, viral serology (HIV, HBV, HCV)
  - Characteristic histological finding: Reed Sternberg cells
- CT scan of: neck, chest, abdomen, pelvis
- PET scan useful for aggressive lymphomas
- Biopsy (of lymph node(s)) required for diagnosis
- +/- Bone marrow biopsy

Management/Treatment
- Chemotherapy
- +/- Radiation therapy and stem cell transplant (in younger patients)
- Post-treatment: PET-CT scan for restaging/reassessment
- Commonly used chemotherapy in Hodgkin’s Lymphoma is ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine). High success rate but increased risk of breast cancer, cardiac toxicity, and pulmonary toxicity.
- Aggressive lymphomas (diffuse large B cell and Burkitt’s) are the most curable
- Indolent lymphomas (follicular) are almost always incurable
- Hodgkin’s lymphoma has a better prognosis than Non-Hodgkin’s, but is less common

---

2 “Malignant lymphomas and multiple myeloma” Arleigh McCurdy, March 29 2015, uOttawa Faculty of Medicine
5.3 Deep Vein Thrombosis (DVT)\textsuperscript{3,4}

**Typical Patient**
- Acquired risk factors: Surgery/trauma, immobilization, active cancer, hormone replacement therapy/oral contraceptive use, pregnancy, age, myeloproliferative disorders, antiphospholipid antibody syndrome
- Inherited risk factors: Family history, genetic thrombophilias (factor V Leiden, prothrombin G20210A mutation, protein C/S deficiency, antithrombin deficiency)

**Cause**
- Blood clot forms in one or more of the deep veins in body (most commonly in the leg)
- Virchow’s Triad: (i) stasis of blood flow, (ii) endothelial injury, (iii) hypercoagulability

**Symptoms/Clinical Presentation**
- Pitting edema (most often unilateral)
- Pain in legs (ache/cramp)
- Redness
- Pain on palpation of veins
- Pain on forced dorsiflexion (Homan’s Sign)
- Difference in calf circumference (right vs. left)
- Superficial, non-varicose, venous dilatation
- Severe: Phlegmasia alba dolens (arterial spasm, cold and pale limb, weak pulse) and phlegmasia cerulea dolens (venous occlusion, severe edema, cyanosis, ischemia, etc)

**Physical Exam**
- Unilateral pitting edema
- Pain on palpation of legs, veins, forced dorsiflexion

**Investigations**
- Clinical Probability – Wells Score (for DVT)
- Compression Ultrasonography (CUS)
- D-Dimer - very sensitive, but not very specific

**Management/Treatment**
- Anticoagulation (e.g. unfractionated heparin, low molecular weight heparin, oral anticoagulants (warfarin, DOAC))
  - *Cancer patients: LMWH exclusively
  - *Pregnancy: LMWH
- Thrombolysis via catheter in severe cases (phlegmasia cerulea)
- Inferior vena cava filter (if anticoagulation is contraindicated)
- Compression stockings
- Treatment duration varies, but is 3 months for a transient risk factor, and usually indefinite otherwise

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\textsuperscript{3} “DVT and pulmonary embolism”, Dimitri Scarvelis, April 5 2015, uOttawa Faculty of Medicine
\textsuperscript{4} “Clot Preventers – The pharmacology and applications of anticoagulation”, Dimitri Scarvelis, April 5 2015, uOttawa Faculty of Medicine
5.4 Pulmonary Embolism (PE)\textsuperscript{5,6}

**Typical Patient**
- Acquired risk factors: surgery/trauma, immobilization, active cancer, hormone replacement therapy/oral contraceptive use, pregnancy, age, myeloproliferative disorders, antiphospholipid antibody syndrome
- Inherited risk factors: family history, genetic thrombophilias (factor V leiden, prothrombin G20210A mutation, protein C/S deficiency, antithrombin deficiency)
- Commonly present with no risk factor (idiopathic)

**Cause**
- Blood clot forms in one or more of the deep veins in body (most commonly in the leg), dislodges, and travels to the lungs
- Virchow’s Triad: (i) stasis of blood flow, (ii) endothelial injury, (iii) hypercoagulability

**Symptoms/Clinical Presentation**
- Shortness of breath
- Chest pain (pleuritic)
- Palpitations
- Faintness, syncope
- Hemoptysis
- DVT symptoms

**Physical Exam**
- Tachycardia, tachypnea, increased JVP due to RH strain
- Normal heart and lung sounds in most cases
- Low oxygen saturation
- Signs of DVT
- Respiratory distress, shock in severe cases

**Investigations**
- Wells PTP model for PE (then do investigations, as required)
- Compression ultrasonography to look for DVT if PE investigations are inconclusive or not possible
- D-Dimer
- CT pulmonary angiography → contraindicated in people w/ renal failure or allergy to contrast
- Nuclear ventilation-perfusion scan
- EKG, chest X-ray, arterial blood gases

**Management/Treatment**
- Anticoagulation (e.g. unfractionated heparin, low molecular weight heparin, oral anticoagulants (warfarin, DOAC))
- Thrombolysis in patients with hemodynamic failure
- PE with known precipitating event should be treated for a minimum of 3 months
- PE caused by cancer should be treated while the cancer is active
- PE with an unknown cause should be treated for over 3 months. Some patients may require lifelong treatment.

\textsuperscript{5} “DVT and pulmonary embolism”, Dimitri Scarvelis, Apr 5 2015, uOttawa Faculty of Medicine

\textsuperscript{6} “Clot Preventers – The pharmacology and applications of anticoagulation”, Dimitri Scarvelis, April 5 2015, uOttawa Faculty of Medicine
6.1 Urinary Incontinence

Typical Patient
- Varied based on cause of incontinence
- Risk factors: Caucasian race, FHx, anatomy (ie urinary fistula), age, obesity, UTI, CNS problems, pregnancy, vaginal delivery

Cause
- Reversible causes include:
  - D – Delirium
  - I – Infection
  - A – Atrophy (vaginal)
  - P – Pharmacological/Psychological
  - E – Excessive Fluid Intake
  - R – Restricted mobility
  - S – Stool Impaction

Symptoms/Clinical Presentation
- Stress incontinence—Loss of urine with exertion or sneezing or coughing
- Urge incontinence—Leakage accompanied by or immediately preceded by urinary urgency
- Mixed incontinence—Loss of urine associated with urgency and also with exertion, effort, sneezing or coughing
- Overflow incontinence—Leakage of urine associated with urinary retention
- Total incontinence—the complaint of a continuous leakage

Physical Exam
- Varies based on cause of incontinence

Investigations
- None necessary

Management/Treatment
- Varies based on cause of incontinence

---
1 “Basic Urology”, Jeremy Setterfield, May 6, 2016, uOttawa Faculty of Medicine
6.2 Urinary Retention

Typical Patient
- Varies based on cause of retention

Cause
- Can be caused by an urinary tract obstruction which can be either:
  - Supravesical or Infravesicular
  - Acute or Chronic
  - Unilateral or Bilateral
  - Extraluminal (lymph node, mass) or intraluminal (stone, blood clot, fungus ball) or intramural (transitional cell carcinoma, polyp)
  - Can occur at various anatomical sites: intrarenal, ureter, bladder, prostate, urethra
    - Most common in men:
      - Benign Prostate Hypertrophy (BPH)
    - Most common in women:
      - Pelvic prolapse (cystocele, rectocele, uterine), the prolapsing organ directly compressing the urethra, urethral stricture, urethral diverticulum, post-surgery for stress incontinence
  - Neurological
    - Spinal cord injury
    - Spina Bifida
    - Multiple Sclerosis

Symptoms/Clinical Presentation
- Frequency, urgency, nocturia, hesitancy, poor flow, an intermittent flow, and terminal dribbling
- Uremia—clinical signs and symptoms seen as a result of renal failure
  - Weakness
  - Fatigue
  - Abdominal and back pain
- Azotemia—elevated levels of nitrogen-containing compounds (e.g. urea, creatinine) in the blood
- Obstructive uropathy—reversible or irreversible renal dysfunction due to the effects of impaired renal drainage
- Hydronephrosis—dilation of the renal pelvis and calyces
- An obstruction would lead to thickening of the bladder wall
- Major issues:
  - Loss of renal function
  - Urinary tract infection/sepsis
  - Stones

Physical Exam
- Varies based on cause of retention
- If BPH, you would feel it on digital rectal exam (DRE)

Investigations
- DRE, ultrasound, blood urea, x-ray/CT for stones, urine test (to rule out urinary tract infection), neurological exam

Management/Treatment

---

2 “Basic Urology”, Jeremy Setterfield, May 6 2016, uOttawa Faculty of Medicine
6.3 Kidney Stones

Typical Patient
- 50 year old, otherwise healthy male
- Lives in a hot climate, works near heat (e.g. cook), obese, doesn’t drink a lot of water
- Complaining of colicky pain and displaying constant positional movements

Cause
- Supersaturated urine (increased calcium, oxalate, uric acid, cysteine) in the absence of urinary inhibitors (citrate, magnesium, some glycoproteins, phosphorus)
- Note: Most stones are calcium containing. Hypercalciuria can be caused by increased intestinal absorption, decreased renal reabsorption, hyperparathyroidism, or rare causes (malignancy, steroids, sarcoidosis).
- Note: Oxalate levels can be elevated due to a genetic disorder in glyoxylate metabolism, chronic diarrheal states, states of decreased fat absorption, overindulgence in oxalate rich foods, or it can be idiopathic

Symptoms/Clinical Presentation
- Renal colic – the pain may radiate across the flank anteriorly towards the upper abdomen and umbilicus and may be referred to the testis or labium
- Nausea and vomiting (caused by reflex stimulation of the celiac ganglion or proximity of other organs such as the colon or the gallbladder)
- Symptoms of vesical irritability
  - Frequency, urgency, suprapubic discomfort (usually associated with distal urethral stones)
- Hematuria
- Note: Fever and hemodynamic instability, if associated with an infection is an emergency and requires urgent decompression of the collecting system
- Note: If the patient has only one kidney, they may present with oliguria or anuria, increased creatinine, hypertension

Physical Exam
- Unremarkable abdominal exam with absence of peritoneal signs

Investigations
- CBC – white blood cells
- Urea, creatinine, electrolytes – kidney function
- Urinalysis – red blood cells, pH, nitrates, leukocyte esterase
- Urine culture
- Abdominal X-ray → not all stones are radiopaque; overlying structures can obscure stone
- Ultrasound (not very sensitive)
- Non-Contrast CT (gold standard – detects all stones except rare indinavir stones)

Management/Treatment
- Conservative:
  - Most will pass within 40 days (90% of stones under 5mm will)
  - Alpha 1 receptor blockers
  - NSAIDs for pain control

---

3 “Kidney Stone”, Annie-Claude Blouin, April 13 2016, uOttawa Faculty of Medicine
6 Nephrology

- Moderate amount of fluid intake
- Surgical: External shockwave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, open lithotomy
- For draining: Ureteral stent or Nephrostomy tube

6.4 Acute Kidney Injury - Prerenal

Typical Patient

- Volume contracted patient

Cause

- Acute kidney injury (AKI) is defined as a sudden reduction in renal function leading to the retention of products normally excreted by the kidney
- Causes can be classified as:
  - Prerenal
    - The kidney is intrinsically normal, but there is an inadequate delivery of blood to the kidney to be filtered
    - Intravascular volume depletion (vomiting, diarrhea, diuretics, cirrhosis, medications)
    - Decreased cardiac output (cardiomyopathy)
    - Renal artery disease

Symptoms/Clinical Presentation

- Prerenal
  - Signs of intravascular volume depletion or signs of decreased cardiac output
  - Benign urine sediment - no blood or proteins since there is no renal damage
  - Oliguria
  - Low fractional excretion of sodium (less than 1%)

Physical Exam

- Signs of low volume (cold, low BP)
- Signs of cardiac issues (high JVP)

Investigations

- Bloodwork
- Urinalysis with microscopy
- Fractional excretion of sodium if baseline Cr normal and patient is oliguric

Management/Treatment

- Intravenous fluid, usually normal saline
- Fix underlying cause

---

4 “Acute Kidney Injury”, Ann Bugeja, April 19 2016, uOttawa Faculty of Medicine
6.5 Acute Kidney Injury - Renal

Typical Patient
- N/A

Cause
- Acute kidney injury (AKI) is defined as a sudden reduction in renal function leading to the retention of products normally excreted by the kidney
- Causes can be classified as:
  - Renal
    - An abrupt cessation of renal function as a result of disease of the kidney parenchyma itself
  - Tubules and interstitium
    - Acute tubular necrosis (ATN)
      - Ischemia (congestive heart failure, cirrhosis, sepsis, acute pancreatitis)
      - Toxins (Antibiotics, other drugs)
    - Acute interstitial nephritis (AIN)
      - Caused by drugs, infection or idiopathic
  - Glomerulus
    - Vasculitis
    - IgA nephropathy
    - Proliferative glomerulonephritis related to infection
    - Proliferative glomerulonephritis related to lupus

Symptoms/Clinical Presentation
- Renal
  - ATN - muddy brown casts, normal urine sodium concentration
  - AIN – WBCs, WBC casts in urine (fever, rash, eosinophilia triad seen in less than 25%)
  - Glomerular - systemic symptoms, rapid creatinine rise, HTN, RBC cast, protein

Investigations
- Bloodwork
- Urinalysis with microscopy
- Consider Renal biopsy

Management/Treatment
- Treat cause
- Dialysis (AEIOU - acidosis, electrolyte issue, intoxication, overload, uremia (usually from pericarditis))
- Renal replacement therapy

---

5 “Acute Kidney Injury”, Ann Bugeja, April 19 2016, uOttawa Faculty of Medicine
6.6 Acute Kidney Injury - Postrenal

Typical Patient
- older male with BPH

Cause
- Acute kidney injury (AKI) is defined as a sudden reduction in renal function leading to the retention of products normally excreted by the kidney
- Causes can be classified as:
  - Post Renal
    - Renal injury as a result of impediment to urine flow due to structural or functional change occurring anywhere from the renal pelvis to the tip of the urethra
      - Congenital (posterior urethral valve, meningomyelocele)
      - Tumor (prostate, bladder, cervical)
      - Urologic (papillary necrosis, Bilateral kidney stones, Bladder stones, strictures)
      - Neurogenic bladder (multiple sclerosis, diabetes mellitus)
      - Retroperitoneal fibrosis

Symptoms/Clinical Presentation
- Postrenal
  - Note: presence of urine output does NOT rule out post-renal as a cause of AKI
  - Infrequent urination, weak stream

Physical Exam
- Palpable bladder

Investigations
- Bloodwork
- Urinalysis
- Imaging (Abdominal ultrasound to rule out hydrenephrosis)

Management/Treatment
- Relieve obstruction
- Treat underlying cause

---

6 “Acute Kidney Injury”, Ann Bugeja, April 19 2016, uOttawa Faculty of Medicine
6.7 Chronic Kidney Disease (CKD)\textsuperscript{7}

**Definition**
GFR <60ml/min for > 3 months

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (ml/min per 1.73m(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild decrease in GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Kidney damage with moderate decrease in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Kidney damage with Severe decrease in GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

**Cause**
Most common causes CKD are:
1. Diabetes
2. Hypertension

Other common causes:
- Prerenal (e.g. Macrovascular disease)
- Post renal- chronic obstruction (e.g. Prostate enlargement)
- Renal
  - Diabetes nephropathy
  - HTN nephrosclerosis
  - Chronic glomerulonephritis (e.g. lupus, IgA nephropathy)
  - Hereditary (e.g PCKD, Alports)
  - Tubulointerstitial nephritis from drugs, or connective tissue disease
  - others: malignancies etc.
  - Chronic infection, cancer (myeloma), glomerulonephritis, tubulointerstitial diseases, drugs etc.

**Acute vs Chronic Kidney disease**
Not always easy to tell if AKI or CKD. Diagnosis will be based on
1. History
2. Previous creatinine values- if available
3. Kidney size: large and dilated in AKI, shrunken in CKD (there are disease states that are exception to this rule)
4. Presence of complications of CKD (e.g. anemia, uremia, and bone disease)

**Symptoms/Clinical Presentation and Physical exam**
Symptoms will vary greatly depending on the degree of kidney dysfunction. Typically GFR <30ml/min is when electrolyte and hormonal consequences of CKD will occur.

**Complications of CKD:**
- Anemia- SOB, fatigue, pallor
- Uremic syndrome- pruritus, encephalopathy (confusion, asterixis), N/V, pericarditis, neuropathy
- Hyperkalemia: no physical finding, it can be picked up on ECG
- Acidosis- lethargic, tachypnea
- Bone disease: Renal osteodystrophy and osteomalacia, hyperparathyroidism
- CVD
- Malnutrition

\textsuperscript{7} “Basic Urology”, Jeremy Setterfield, May 6th, 2016, uOttawa Faculty of Medicine
• Volume overload- inspiratory crackles, tachypnea, hypoxia, peripheral pitting edema, increased JVP
• Platelet dysfunction- frequent, increase, or difficult to stop bleeding
• Hormonal imbalance- women with CKD will be infertile
• Hypertension

Investigations
• CBC, lytes, creatinine, BUN (blood urea nitrogen)- these will help determine GFR, extent of kidney disease, and bleeding issues
• Parathyroid hormone
• Renal ultrasound- determine if AKI or CKD
• Urine Albumin:Creatinine ratio /Urinalysis – proteinuria is a major indicator of treatment efficacy, and it also gives an idea of the extent of disease and potential causes of CKD
• Renal biopsy- done to determine cause of CKD, but only if diagnosis will change treatment plan
• ANCA, dsDNA, rheumatoid factor, anti GBM antibody test can all help rule out different autoimmune causes (rule out more common things before ordering these $$$ tests)

Management/Treatment
HTN is the 2nd most common cause of CKD, and 70% of patients with CKD will have hypertension that is caused or worsened by their CKD. Thus management of HTN is essential in CKD treatment.
Target BP is <140/90 for non-diabetic and 130/80 for diabetic patients or patients with proteinuria
• Pharmacologic
  o ACE Inhibitors /ARB:
    ■ Key in treatment of CKD
    ■ Will reduce proteinuria, which is correlated with longer preserved kidney function and better controlled HTN
  o Statins (due to high risk of CVD)
  o Low dose ASA
• Non-pharmacologic:
  o Diet, salt and protein restriction, smoking cessation, diabetes control

Management of Complications
• Anemia- Iron supplementation, synthetic EPO, transfusion
• Uremic syndrome- Dialysis
• Hyperkalemia: Glucose, calcium, insulin, ventolin, +/-bicarb, +/- kayexalate
• Acidosis- fluids, bicarb, dialysis, treat underlying cause (metabolic or respiratory)
• Bone disease: Calcitriol (Vitamin D analog), restrict phosphate intake, phosphate binders, parathyroidectomy
• Volume overload- Lasix and other diuretics. If no response, dialysis
• Platelet dysfunction- DDAVP, estrogen, cryoprecipitate

Renal Replacement Therapy
Once GFR <30ml/min there will be no recovery of renal function (5/6th nephrectomy theory) - RRT needed
• Dialysis:
  o Two main forms of dialysis are hemodialysis and peritoneal dialysis. Both have equal morbidity and mortality. PD generally provides a more comfortable lifestyle for patients
  o Dialysis will correct all complications of CKD except for the hormonal imbalances (estrogen/testosterone, PTH, EPO, and calcitriol), and does not improve GFR
  o Dialysis can be used in some acute situations: AEIOU
    ■ Acidosis
    ■ Electrolyte imbalance: Hyperkalemia
    ■ Intoxication (methanol)
    ■ Volume Overload (if non-responsive to Lasix)
Nephrology

- Uremia (pericarditis, encephalopathy). This is the only absolute indication for acute dialysis, the rest are relative indications
- Transplant:
  - Is the preferred treatment as it corrects all complications of CKD, including hormonal imbalance, and improves GFR
  - Only 20% of patients with end stage renal disease will be put on the transplant list - most patients with CKD have comorbidities that make them unsuitable donors

6.8 Urinary Tract Infection (UTI)\(^8\)

General Information
- More common in women (especially postmenopausal) due to shorter female urethra
- Sexual intercourse frequency is the strongest risk factor for recurrent UTIs in young women
- The most common causative organisms for community acquired uncomplicated urinary tract infections are *Escherichia coli* (85%) and *Staphylococcus saprophyticus* (10%)

Risk Factors
- Age, gender
- Behavioural - sexual intercourse, spermicide use
- Urinary tract - congenital anomalies, prostatic hypertrophy (most common cause in men), vesicoureteral reflux, urinary obstruction, neurogenic bladder
- Iatrogenic - Urinary catheterization, cystoscopy, nephrostomy, urinary stent
- Other - Diabetes mellitus, immunosuppression

Symptoms/Clinical Presentation

**Lower urinary tract Infection**
- Frequency
- Urgency
- Dysuria
- Hematuria

**Upper urinary tract infection**
- Fever, chills
- Back pain
- Nausea, vomiting
- Lower urinary tract symptoms

Physical Exam
- Fever may be present
- Costovertebral angle tenderness (if upper tract infection)

Investigations
- Blood culture if fever or chills
- Midstream urine test
  - Urinalysis and culture

Management/Treatment
- Positive urine cultures does not always mean antibiotics are necessary
- Decide if treatment needed based on bacteria count, presence/absence of symptoms, and type of bacteria
- Antibiotics tailored to local resistance patterns

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\(^8\) “Urinary Tract Infections”, Baldwin Toye, April 27 2016, UOttawa Faculty of Medicine
Shorter course recommended for lower infections
- If catheter associated, only treat if symptomatic
  - Avoid catheterization and remove catheter as soon as possible
- If recurrent infection with same organism (relapse), consider longer therapy; exclude urologic abnormalities
- If recurrent infection with new organism (reinfection), consider post-coital voiding, post-coital antibiotics
  - May consider antibiotic prophylaxis
  - Topical estrogen for postmenopausal women
  - Avoid diaphragm and spermicide

6.9 General Approach to Acid Base Problems

1) Look at the arterial pH:
   - pH = 7.40 is normal
   - pH < 7.40 suggests academia
   - pH > 7.40 suggests alkalemia

2) If the pH is abnormal, identify the type of disorder by looking at $[\text{HCO}_3^-]$ and pCO$_2$:
   - In metabolic acidosis, $[\text{HCO}_3^-]$ is low (<25)
     - If metabolic acidosis, determine whether it is an anion gap acidosis or not (anion gap = $[\text{Na}^-] - [\text{Cl}^-] - [\text{HCO}_3^-]$; normal AG= 8-12)
   - In respiratory acidosis, pCO$_2$ is high (>40)
   - In metabolic alkalosis, $[\text{HCO}_3^-]$ is high (>25)
   - In respiratory alkalosis, pCO$_2$ is low (<40)

3) Look for appropriate compensation in the other parameter
   - In general, for isolated acid base disorders, the other parameter compensates in the same direction that the parameter went to cause the imbalance

<table>
<thead>
<tr>
<th>Primary Disorder</th>
<th>Physiology</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Acidosis</td>
<td>Hyperventilation</td>
<td>Fall in pCO$_2$ of 1 – 1.2 mm Hg for each 1 mmol/L fall in $[\text{HCO}_3^-]$</td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td>Hypoventilation</td>
<td>Rise in pCO$_2$ of 0.7 mm Hg for each 1 mmol/L rise in $[\text{HCO}_3^-]$</td>
</tr>
<tr>
<td>Respiratory Acidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>HCO$_3^-$ production</td>
<td>Rise in $[\text{HCO}_3^-]$ of 1 mmol/L for each 10 mmHg rise in pCO$_2$</td>
</tr>
<tr>
<td>Chronic (&gt; 3 days)</td>
<td>Greater renal excretion of NH$_4^+$</td>
<td>Rise in $[\text{HCO}_3^-]$ of 3 mmol/L for each 10 mmHg rise in pCO$_2$</td>
</tr>
<tr>
<td>Respiratory Alkalosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>HCO$_3^-$ consumption</td>
<td>Fall in $[\text{HCO}_3^-]$ of 2 mmol/L for each 10 mmHg fall in pCO$_2$</td>
</tr>
<tr>
<td>Chronic (&gt; 3 days)</td>
<td>Lesser renal excretion of NH$_4^+$</td>
<td>Fall in $[\text{HCO}_3^-]$ of 5 mmol/L for each 10 mmHg fall in pCO$_2$</td>
</tr>
</tbody>
</table>

9 “Acid Base Workshop Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
**Additional Information**
- In all isolated acid base disorders except for chronic respiratory alkalosis, compensation never normalizes the pH to 7.40

### 6.10 Metabolic Acidosis

**Approach**
- Identify if metabolic acidosis is anion gap acidosis or non-anion gap acidosis
- Anion Gap = [Na⁺] – ([Cl⁻] + [HCO₃⁻])
- Normal is around 8-12 and roughly represents the negative charge on albumin
- Values above the normal range indicate metabolic acidosis is an anion gap acidosis (this assumes albumin levels are normal)

#### Anion Gap Acidosis
**Causes**
- Excessive acid intake
- Excessive acid generation
  - Lactic acidosis
  - Ketoacid accumulation (ex. diabetic ketoacidosis, starvation, ethanol)
  - Consumption of toxic alcohol (ex. methanol, ethylene glycol)
  - Renal failure (retention of organic ions)
  - Salicylate overdose

#### Non-Anion Gap Acidosis
**Causes**
- Excessive bicarbonate loss
  - Large volume diarrhea
  - Failure to reabsorb bicarbonate in proximal tubule
- Problems with renal acid excretion (ex. hyperkalemia affecting ammoniagenesis)

**Symptoms/Clinical Presentation**
- Non-specific symptoms
- Abdominal pain
- Fatigue

**Physical Exam**
- Tachypnea
- Kussmaul’s respiration (if severe)
- Lethargy, neurologic symptoms
- Hypotension if severe

**Investigations**
- Arterial blood gas
- Blood work (ex. determine if anion gap is increased, check potassium levels)
- Lab measurement of tCO₂ from venous plasma

**Management/Treatment**
- Address underlying cause (ex. insulin for diabetic ketoacidosis, hyperkalemia treatment)

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10 “Acid Base Workshop Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
- If severe, sodium bicarbonate therapy to stabilize pH to above 7.0 in meantime
- Preserve ventilation (avoid sedation, treat any pneumonias, intubate when necessary)

6.11 Metabolic Alkalosis

Causes
- Loss of acid from vomiting
- Excessive production of bicarbonate (ex. hypokalemia induced alkalosis)
- Excessive intake of bicarbonate

Symptoms/Clinical Presentation
- Non-specific symptoms
- Confusion

Physical Exam
- Hypoventilation

Investigations
- Arterial blood gas
- Blood work (ex. check potassium levels)
- Lab measurement of tCO₂ from venous plasma
- Urine electrolytes (confirm suspicions)

Management/Treatment
- Treat underlying cause (ex. restore potassium levels if hypokalemic)

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11 “Acid Base Workshop Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
6.12 Respiratory Acidosis

Causes
- Failure to excrete CO₂ (ventilation issues)
  - Chronic Obstructive Pulmonary Disease (COPD)
  - Upper or lower airway obstruction
  - Primary lung disease
  - Pneumonia, pulmonary embolus, fluid overload, pleural effusion, pneumothorax
  - Reduced respiratory drive from central nervous system depression (ex. narcotics overdose, primary CNS disease such as stroke or brain injury)
  - Neuromuscular disease
  - Obstructive sleep apnea

Symptoms/Clinical Presentation
- Dyspnea
- Confusion/altered level of consciousness
- Often associated with hypoxia and cyanosis
- Daytime somnolence

Physical Exam
- Examine for respiratory distress, accessory muscle use, barrel chest, clubbing suggestive of chronic respiratory disease, etc.
- Check for signs of hypoxia and cyanosis (lips, nail beds)
- Auscultate chest for wheezing, airway obstruction, etc.
- Examine for asterixis

Investigations
- Arterial blood gas
- Oxygen saturation measurement
- Chest X-ray
- CT head if primary CNS disease suspected
- Pulmonary function testing if respiratory disease workup

Management/Treatment
- ABCs in acute crisis, call for help
- Administer oxygen with caution (be cautious of oxygen administration in COPD)
- Medications for airway diseases (ex. Ventolin (albuterol))
- Airway support for ventilatory issues (intubation/ventilation or non-invasive support)
- Cessation of opioids and reversing of narcotic effects with naloxone

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12 “Acid Base Workshop Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
6.13 Respiratory Alkalosis

Causes
- Excessive excretion of CO\(_2\) (ex. hyperventilation)
  - Pneumothorax, pneumonia, pulmonary edema, pulmonary embolism, asthma, chronic obstructive pulmonary disease
  - Hypoxia
  - Drugs (ex. salicylates)
  - Pregnancy
  - Hyperthyroidism
  - Anxiety/panic attacks with hyperventilation

Symptoms/Clinical Presentation
- Dyspnea
- Chest tightness
- Neurological symptoms
  - Dizziness
  - Confusion
  - Seizures
  - Paresthesias

Physical Exam
- Auscultate for crackles, wheezing
- Assess for possible cyanosis
- Tachycardia
- Tachypnea
- Depressed consciousness

Investigations
- Arterial blood gas
- Chest X-ray
- CT if required

Management/Treatment
- Rarely life threatening
- Treat underlying cause
- In ventilated patients, reduce tidal volume or respiratory rate
- Monitor sedation and pain control
- Sedatives and antidepressants if conservative management has failed

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13 “Acid Base Workshop Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
6.14 Polyuria

Causes
- Urine is mostly water
  - Excessive water intake
  - Failure to concentrate urine: diabetes insipidus → central (no anti-diuretic hormone [ADH]) or nephrogenic
- Large urinary solute excretion
  - Salt
    - Large salt intake/extracellular fluid (ECF) volume overload
    - Diuretic use
    - Recovery from acute kidney injury (AKI)/after relief of urinary obstruction
  - “Osmotic”
    - Glucose: Hyperglycemia
    - IV Mannitol administration
    - Urea: large protein intake/catabolic state
- Nocturia in chronic heart failure (low output when upright, higher output when supine)

Symptoms/Clinical Presentation
- Frequent urination of normal/large volume each time
- Other symptoms depend on cause
  - Thirst (especially in Diabetes Insipidus)

Physical Exam
- No specific findings/depends on the cause
- ECF volume assessment: important to diagnosis of cause

Investigations
- Serum Na, glucose, urea, creatinine
- Random urine collection for osmolality, Na, K, Cl, glucose, urea
- 24 hour urine collection for volume, Na, K, Cl, glucose, urea

Management/Treatment
- Replace deficits & ongoing inappropriate losses of water or NaCl
- Treat underlying cause
- ADH (DDAVP) for central diabetes insipidus

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14 “Water Homeostasis”, Steven Nadler, May 4 2016, uOttawa Faculty of Medicine
6.15 Hypernatremia\textsuperscript{16,17,18}

Causes
- Excess of sodium (rare) e.g. drinking seawater
- Water deficit:
  - Defect in water intake: usually alteration in mental status impairing ability to request water; rarely damage to thirst center
  - Excessive losses:
    - Severe diarrhea, sweat, respiratory loss, osmotic diuresis (see polyuria section)
    - Central diabetes insipidus (cDI: deficient anti-diuretic hormone [ADH])
    - Nephrogenic DI (nDI: impaired response to ADH)

Symptoms/Clinical Presentation (more severe symptoms & signs with acute hypernatremia)
- Thirst (if no thirst, something is very wrong with brain!)
- +/- Polyuria
- Lethargy, irritability, confusion, seizures, coma, death
- Ataxia, tremors, muscle spasms

Physical Exam
- Hyperreflexia
- Neurologic deficits
- +/- ECF volume depletion: orthostatic hypotension, tachycardia

Investigations
- Serum sodium and osmolality (electrolytes)
- Serum glucose, urea, and creatinine
- Urine sodium and osmolality
  - If urine osmolality is low but increases after administering ADH, this suggests central diabetes insipidus
- If neurologic signs are present, consider neuroimaging

Management/Treatment
- For central DI, reduce urine water losses by giving exogenous ADH
- Administer fluid with a lower tonicity (Na + K) than urine to restore water levels
- Give water orally if possible; cannot give pure water intravenously due to osmotic lysis of red blood cells; hypotonic IV fluids include 5% Dextrose, “2/3:1/3”, 0.45% NaCl
- If ECF volume contracted as well, administer salt, but as hypotonic solution (e.g. 0.45% NaCl)
- Correct water deficit slowly to normalise serum Na over 2-3 days
- Monitor and adjust therapy often

\textsuperscript{16} “Water Homeostasis”, Steven Nadler, May 4 2016, uOttawa Faculty of Medicine
\textsuperscript{17} “Hypernatraemia”, The Royal Children’s Hospital Melbourne, December 2012, http://www.rch.org.au/clinicalguide/guideline_index/hypernatraemia
\textsuperscript{18} “Fluid & Water Homeostasis Workshop – Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
6.16 Hyponatremia\textsuperscript{19,20}

Causes
- Impairment of the kidney’s urine dilution mechanism
  - Reduced glomerular filtration rate
  - Thiazide or loop diuretics
  - Abnormal presence of anti-diuretic hormone (ADH)
- Excessive water intake

Symptoms/Clinical Presentation (more severe symptoms & signs with acute hyponatremia)
- Thirst, polyuria
- Cerebral edema: headache, lethargy, somnolence, disorientation, decreased level of consciousness (LOC), nausea, anorexia → seizures, coma, quadriplegia (due to brainstem herniation), death

Physical Exam – usually normal but with severe acute hyponatremia may have:
- Depressed deep tendon reflexes, abnormal sensorium, Cheynes-Stokes respiration
- Pseudobulbar palsy
- Extracellular fluid (ECF) volume assessment: may be normal, increased or low; important to diagnosis of cause

Investigations
- Serum sodium and osmolality (ensure that low plasma sodium represents low plasma osmolality)
- Serum glucose, urea, creatinine
- Urine sodium, chloride and osmolality
  - If urine osmolality appropriately low, suggests excessive water intake
  - If urine osmolality inappropriately high, indicates ADH is acting:
    - May be due to ECF volume depletion (check on physical exam, urine Na < 20)
    - May be due to decreased “effective arterial circulating volume” (cirrhosis, chronic heart failure)
    - +/- Do thyroid-stimulating hormone (TSH) and cortisol
    - If none of the above, may be syndrome of inappropriate anti-diuretic hormone secretion (SIADH); look up the many causes; do chest X-ray or CT chest
- If neurologic signs are present, consider neuroimaging

Management/Treatment
- Administer isotonic saline if volume contracted
- Ensure that current medications are not causing abnormally elevated ADH levels
- If patient is asymptomatic, do not treat aggressively
  - May not need any treatment if serum Na > 130
- Restrict water intake
- Aggressive therapy for symptomatic patients
  - Administer hypertonic saline to gradually increase plasma sodium
  - Monitor patient and sodium level often; avoid rapid correction – usually maximum 8 mmol/L/24 hours (rapid correction can cause brainstem demyelination!)
  - If plasma sodium concentration increases too fast, may give dilute IV solutions & ADH

\textsuperscript{19} “Water Homeostasis”, Steven Nadler, May 4 2016, uOttawa Faculty of Medicine
\textsuperscript{20} “Fluid & Water Homeostasis Workshop – Answers”, Author Unknown, May 5 2016, uOttawa Faculty of Medicine
6.17 Hypertension (HTN)\textsuperscript{21}

**Definition**
- Blood Pressure >140/90 for non-diabetics
- Blood Pressure >130/80 for diabetics
- Blood Pressure < 120/90 for high risk patients – age 55 plus non-diabetic CKD or CVD; age 75 and older

**Typical Patient**
- Overall prevalence of HTN in Canada is 23%, and increases with age
- >55 y/o
- Diagnosed at a younger age in men than women
- Common risk factors: Age, smoking, obesity, family history/genetic (female relative with hypertension diagnosed before 65 y/o or male relative with hypertension diagnosed before 55 y/o), dyslipidemia, diabetes, alcohol, poor diet

**Essential Vs Non-Essential Hypertension**
- 90% of hypertension is essential hypertension, 10% of HTN is due to secondary causes
- Essential hypertension is hypertension that is caused by multiple factors, including the ones listed above. There is a highly genetic component
- Secondary hypertension is hypertension caused by a specific disease state. Common causes of secondary hypertension include:
  1. CKD
  2. Sleep Apnea
  3. Primary hyperaldosteronism
  4. Renal artery stenosis
  5. Cushing’s syndrome
  6. Pheochromocytoma (catecholamine secreting tumor in the adrenal gland)
- There are certain factors that should lead you to think a patient is suffering from a secondary cause of HTN:
  1. HTN in young patients
  2. Sudden change in BP in a patient with previously controlled HTN
  3. HTN that is resistant to medication

**Complications of HTN**
- An important diagnostic and prognostic indicator of HTN is end organ damage
- Malignant hypertension will damage the eyes, heart, brain, peripheral vasculature, and kidneys
- This may lead to loss/changes of vision, MI, CAD, TIA, stroke, dementia, peripheral vascular disease, aortic dissection, CKD

**Symptoms/Clinical Presentation**
- ‘Silent killer’: People afflicted with HTN will not be aware of it until there is noticeable end organ damage
- Presentation varies from asymptomatic to massive hemodynamic instability in the setting of dissection or MI

**Physical Exam**
- Eye: AV-nicking, cotton wool spots, micro-hemorrhages
- CVD: sustained PMI, S4, renal artery bruits, carotid/femoral bruits, peripheral edema
- Lung: inspiratory crackles, SOB, tachypnea- in the setting of volume overload secondary to CKD

\textsuperscript{21} “Hypertension”, Marcel Ruzicka, May 11 2016, uOttawa Faculty of Medicine
Investigations
- An essential part of the workup for HTN is the assessment of Cardiovascular Risk Factors. These play an integral role in the assessment of the patient’s mortality over a 10-year period. See appendix for Framingham Cardiovascular Risk Assessment Tool
- CBC, lytes (K⁺ is important as low K⁺ may indicate primary hyperaldosteronism), creatinine, BUN (Blood urea nitrogen), urinalysis and ACR- assess kidney function
- Fasting glucose- screen for diabetes
- Fasting lipid profile (HDL, LDL, HDL/LDL, triglycerides), ECG-to assess CVD risk

Investigations for secondary causes of HTN
- Renal artery angiography to assess renal artery stenosis- this is the gold standard to investigate renal artery stenosis, however other modalities such as CT angiogram or MR angiogram could be used
- Renal biopsy- can determine different types of renal parenchymal disease 24-hr Urine for metanephrines and normetanephrines - catecholamine breakdown product, this for pheochromocytoma
- Sleep study for Obstructive Sleep Apnea
- 24-hr Urine for cortisol - for Cushing’s Syndrome
- Plasma Renin and Plasma Aldosterone for Conn’s syndrome (primary hyperaldosteronism)

Management/Treatment

Treatment Goal
- BP <140/90 for non-diabetic patients
- BP <130/80 for diabetic/nephrotic patients- these patients are already at higher cardiovascular risk
- BP< 120/90 for high risk patients – age 55 plus non diabetic CKD or CVD; age 75 and older

Non-pharmacological
- Diet: Salt and lipid restriction (protein restriction necessary if cause is CKD)
- Weight loss: Weight loss is key to HTN management. 1kg loss= 1mmHg systolic pressure drop. Exercise without weight loss is not beneficial for HTN management
- Diabetes management
- Smoking cessation

Pharmacological
- First line (used as monotherapy or in combination)
  - Thiazides
  - ACE inhibitor/ARB
  - Calcium channel blockers (dihydropyridines or diltiazem)
  - Beta-blockers
- Add-on BP meds not recommended as first line therapy (unless for specific indication e.g. aldosterone blockers for primary hyperaldosteronism)
  - Alpha blockers
  - Mineralocorticoid/aldosterone blockers
  - Central sympatholytics
  - Arterial vasodilators
Algorithm for Treatment of Hypertension

**Lifestyle Modifications**

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

**Initial Drug Choices**

**Without Compelling Indications**
- **Stage 1 Hypertension**  
  (SBP 140–159 or DBP 90–99 mmHg)  
  Thiazide-type diuretics for most.  
  May consider ACEI, ARB, BB, CCB, or combination.

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

**With Compelling Indications**
- **Drug(s) for the compelling indications**  
  Other antihypertensive drugs  
  (diuretics, ACEI, ARB, BB, CCB)  
  as needed.

**Not at Goal Blood Pressure**

Optimize dosages or add additional drugs  
until goal blood pressure is achieved.  
Consider consultation with hypertension specialist.
Gastroenterology
7.1 Early Childhood Caries

Typical Patient/Risk Factors
- Poor oral hygiene
- Prolonged exposure to sweetened beverages, particularly night-feeding
- Bacterial infection, high counts of S. Mutans
- Enamel defects, hypoplasia

Cause
- Bacteria adhere to protein coat on tooth enamel and ferment dietary carbohydrates, which produces acid and lowers the pH. Plaque buildup prevents buffering action of saliva. Demineralization of enamel exposes dentin to the acid, causing the dentin to erode and dental caries to reach the pulp. This stimulates nerve endings, signaling pain.

Symptoms/Clinical Presentation
- Early (begins soon after dental eruption)
  - Chalky white decalcification (typically on smooth surfaces)
- Advancing
  - Virulent caries with rapid progression
  - Enamel chips away as lesions advance
- Rampant
  - Progressively involves molar and cuspid teeth
  - Maxillary and mandibular lesions present
- Severe
  - Pulpal involvement
  - Abscess or fistula formation
  - At risk for cellulitis

Physical Exam
- Knee-to-knee examination (proper positioning for oral examination)

Investigations
- None necessary

Management/Treatment
- Risk assessment and prevention plan (i.e. behaviour modification (e.g. oral hygiene), tooth protection)
- Early caries detection, healing of early lesions
- Surgical restoration or extraction
- Sealants, fluoride varnish

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1 “Dental and periodontal pathology and odontogenic infections”, Caroline Fulop and Carol Janik, September 8 2016, uOttawa Faculty of Medicine
7.2 Periodontal Disease

Typical Patient/Risk Factors
- Smoking
- Hormones
- Stress
- Medications
- Clenching or grinding
- Diabetes
- Poor nutrition
- Iatrogenic dental restorations
- Crowded teeth
- Advanced age

Cause
- Inflammation of tissue around the teeth, leading to bone and tooth loss, if untreated
- **Common pathogens:** A. actinomycetemcomitans, P. gingivialis, P. intermedia, B. forsythus (predominantly gram-negative, anaerobic)

Symptoms/Clinical Presentation
- Red, shiny gums
- Gingival bleeding (spontaneous, brushing)
- Often painless
- Tender on palpation
- Swollen, discoloured gums
- Halitosis/bad taste
- Recession
- Mobility or drifting of teeth
- Abscess or purulence

Physical Exam
- Tone/texture/colour/contour
- Probing (bleeding, attachment levels)
- Calculus/plaque
- Gum recession
- Furcations
- Tooth mobility

Investigations
- Radiographic examination to assess bone loss

Management/Treatment
- Proper oral hygiene for plaque, calculus and halitosis control
- Regular professional care and monitoring
- Non-surgical management for minor cases (scaling/curettage)
- Surgical treatment for advanced cases (periodontal surgery/extractions)
- Medical assessment if oral cause ruled out

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2 “Dental and periodontal pathology and odontogenic infections”, Caroline Fulop and Carol Janik, September 8 2016, uOttawa Faculty of Medicine
7.3 Parapharyngeal Space Infection

Risk Factors
- Tonsilitis, pharyngitis
- Dental infection
- Salivary gland infection
- Secondary to instrumentation
- Presence of a foreign body
- Trauma
- IV drug use

Common Pathogens
- Polymicrobial
  - Most often streptococcal, staphylococcal, anaerobic bacteria
  - Gram-negative bacteria

Symptoms/Clinical Presentation
- Trismus
- Muffled voice
- Fever
- Odynophagia
- Dysphagia
- Drooling
- Nuchal rigidity
- Airway obstruction (in severe cases)

Physical Exam
- General appearance (stridor, respiratory distress, etc.), vitals
- Neck – check range of motion, lymphadenopathy,
- Oral cavity/oropharynx: assess trismus, look for source of infection
- Flexible laryngoscopy: assess for source of infection, location of abscess, assess for airway obstruction
- Complete cranial nerve exam

Investigations
- Complete blood count
- Lateral X-ray
- CT with contrast

Management/Treatment
- Consider patient’s airway (intubation or tracheostomy)
- Drainage of abscess
- Antibiotics
- Fluid resuscitation

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3 “Deep space neck infections” - Self Learning Module, Eric Henry, uOttawa Faculty of Medicine
7.4 Salivary Gland Neoplasms

Typical Patient
- Older

Cause
- Depends on type of tumor

Symptoms/Clinical Presentation
- Usually presents with palpable mass
- Usually slow growing
- **Signs suggesting malignancy:** facial nerve palsy, lymphadenopathy, skin involvement

Physical Exam
- General appearance
- Gland (which gland(s) is/are involved, skin changes)
- Oral cavity (look and palpate, floor of mouth swelling, calculi, duct secretions)
- Neck (lymphadenopathy, range of motion)
- Neurological impairment (VII, XII)

Investigations
- Fine needle aspiration
- Imaging
  - Ultrasound
  - CT/MRI important for staging and surgical planning in malignant disease

Management/Treatment
- Depends on pathology
  - Observation
  - Surgery (e.g. parotidectomy, either superficial or total)

Special Considerations
- The smaller the gland, the higher risk for malignancy
  - minor salivary gland > sublingual > submandibular > parotid gland

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4 “Taste and salivary glands”, James Bonaparte, September 6 2016, uOttawa Faculty of Medicine
7.5 Sialadenitis

Typical Patient/Risk Factors
- Post-operative patient, typically abdominal surgery (dehydrated, decreased oral intake)
- Poor oral hygiene
- Debilitated
- Stones/calculi
- Duct structure

Cause
- Bacteria infection:
  - Common pathogens: Staph aureus, Strep pneumonia, E. coli, H. influenza, Bacteriodes melaninogenicus, Strepto micros
- Viral etiology: HIV, Mumps, influenza

Symptoms/Clinical Presentation
- Sudden onset of diffuse enlargement of gland
- Induration
- Tenderness
- Warmth
- Trismus
- Purulent saliva at duct opening (upon massage)

Physical Exam
- General appearance
- Gland (which gland(s) is/are involved, skin changes)
- Oral cavity (look and palpate, floor of mouth swelling, calculi, duct secretions)
- Neck (lymphadenopathy, range of motion)
- Neurological impairment (VII, XII)
- Assess airway (especially if concerned about deep neck space infection ie. Ludwig’s Angina – submandibular space infection)

Investigations
- None, unless no improvement within 48 hours
- If worsens or fever persists, then CT neck with contrast to rule out abscess

Management/Treatment
- Hydration
- Improve oral hygiene
- Gland massage
- Sialogogues (ie. sour candies)
- C/S pus
- Antibiotics i.e. 1st gen cephalosporin

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5 “Taste and salivary glands”, James Bonaparte, September 6 2016, uOttawa Faculty of Medicine
7.6 Sialolithiasis

Typical Patient/Risk Factors
- Dehydration, decreased oral intake (ie. Post GI procedures)

Cause
- Calcium phosphate/carbonate precipitate and lead to stones in the salivary gland or duct (most→ least common: submandibular > parotid > sublingual gland)

Symptoms/Clinical Presentation
- Recurrent painful swelling worse with eating which resolves
- Some stones will pass spontaneously
- Occasionally may become infected

Physical Exam
- General appearance
- Gland (which gland(s) is/are involved, skin changes)
- Oral cavity (look and palpate, floor of mouth swelling, calculi, duct secretions)
- Neck (lymphadenopathy, range of motion)
- Assess airway (especially if concerned about severe infection)

Investigations
- Ultrasound
- Computed tomography
- Sialogram
- Sialendoscopy

Management/Treatment
- If not infected and stone not palpable
  - Massage gland
  - Hydration
  - Sialogogues (ie. sour candies)
  - Pain medication if needed
- If no infection and large stone
  - Same as above, however, can have chronic course and recurrent infections
  - Consider stone or gland excision
  - Lithotripsy
  - Sialendoscopy
- If infection (same as sialadenitis)
  - Hydration
  - Improve oral hygiene
  - Gland massage (helps drain the abscess)
  - Sialogogues (ie. sour candies)
  - C/S pus
  - Antibiotics i.e. 1st gen cephalosporin

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6 “Taste and salivary glands”, James Bonaparte, September 6 2016, uOttawa Faculty of Medicine
7.7 Sjogren’s Syndrome

Typical Patient
- Middle Aged Females
- Presence of other autoimmune disorders

Cause
- Autoimmune – lymphocytic infiltration of exocrine glands
- Primary: affects exocrine glands only
- Secondary: associated with another autoimmune disease (most commonly rheumatoid arthritis)

Symptoms/Clinical Presentation
- Keratoconjunctive sicca (dry eyes)
- Xerostomia (dry mouth)
- Intermittent bilateral parotid swelling
- Muscle aches
- Fatigue

Physical Exam
- Keratitis
- Dry mucosa

Investigations
- SSA (anti-Ro) and SSB (anti-La)
- Lip biopsy to assess minor salivary glands
- Schirmer test: Evaluates tear production

Management/Treatment
- Symptomatic (artificial tears and saliva)
- Monitor - Risk of non-Hodgkin’s lymphoma

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7 “Taste and salivary glands”, James Bonaparte, September 6 2016, uOttawa Faculty of Medicine
7.8 Dysphagia

Typical Patient
- Depends on etiology e.g. stroke, post intubation, malignancy, reflux, primary neuropathic process, etc.

Cause

<table>
<thead>
<tr>
<th>Oral Dysphagia</th>
<th>Pharyngeal Dysphagia</th>
<th>Esophageal Dysphagia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation/infection (tonsillitis, xerostomia)</td>
<td>Inflammation or infection</td>
<td>Infection (bacterial, viral, fungal) or inflammation (esophagitis, stricture)</td>
</tr>
<tr>
<td>Neoplasm (SCC of tongue, etc)</td>
<td>Neoplasm (SCC)</td>
<td>Neoplasm (esophagus, thyroid (large), lung,)</td>
</tr>
<tr>
<td>Degenerative</td>
<td>Central (neurocognitive, neuromuscular)</td>
<td>Degenerative (achalasia)</td>
</tr>
<tr>
<td>Aging (e.g. poor dentition, xerostomia)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Symptoms/Clinical Presentation
- Coughing or choking while eating
- Drooling or losing food from mouth (spillage)
- Pocketing of food
- Slow, effortful chewing or swallowing (lengthy meal times)
- Wet/gurgly voice; wet breath sounds
- Difficulty/pain with swallowing pills/foods; subsequent avoidance of certain solids or liquids
- Food sticking
- Globus sensation
- Reflux or heartburn
- Red flags: hoarseness, stridor, odynophagia, cough/aspiration, recurrent pneumonia, regurgitation, weight loss, otalgia

Physical Exam
- General appearance
- Head and neck exam (oral cavity, palpate neck for masses, crepitus, voice, larynx (mirror, fiberoptic nasolaryngoscopy))
- Neurological exam

Investigations
- Barium swallow → esophageal dysphagia
- Modified barium swallow
- Fiberoptic endoscopic evaluation of swallowing (FEES)
- Esophago-gastro-duodenoscopy (EGD)
- Esophageal manometry

Management/Treatment
- If esophageal treat the underlying cause. E.g. Antimicrobials, PPIs, stricture dilation, stent insertion, consider surgical options (e.g. excising Zenker’s diverticulum)
- If oropharyngeal then use passive compensatory techniques: texture (viscosity and consistency), positioning (sitting upright), presentation (rate, amount, alternating liquids with solids), restriction (bread, mixed consistency, dry particulates, straws), environment (distractors, talking while eating)
- Active compensatory techniques
  - Head positioning (chin tuck, head tilt/turn)
  - Specific maneuvers (supraglottic, super-supraglottic, effortful, Mendelsohn)
- NG/PEG/PEJ

---

8 “Physiology of swallowing and dysphagia”, Karen Mallett and Laurie McLean, September 7 2016, uOttawa Faculty of Medicine
7.9 Dysphagia: Achalasia

Typical Patient
- Age: 20-40 years

Cause
- ↓ inhibitory ganglions of myenteric plexus

Symptoms/Clinical Presentation
- Progressive dysphagia for solids and or liquids
- Weight loss
- Bland regurgitation
- Heartburn
- Chest pain
- Aspiration (cough, respiratory symptoms)

Physical Exam
- See P/E for dysphagia

Investigations
- Barium swallow (*bird’s beak* - classic and highly specific)
- Esophagogastroduodenoscopy (EGD) (to rule out other pathology that may mimic achalasia specifically ruling out distal malignancy)
- Manometry (to confirm diagnosis)

Management/Treatment
- Pharmacologic (unlikely to have significant effect)
  - Calcium channel blockers
  - Nitrates
  - Phosphodiesterase inhibitors (sildenafil)
- Endoscopic
  - Botulinum toxin injection of lower esophageal sphincter
  - Dilation (pneumatic or dilator assisted)
- Myotomy (*optimal therapy*)
  - either open surgical (Heller’s myotomy or endoscopic (POEM))
**7.10 Eosinophilic Esophagitis**

**Typical Patient**
- Age: 20s-30s (adult); 10.5 +/- 5.4 years (children)
- Male (3:1)
- Caucasian
- Atopic history

**Cause**
- Esophageal inflammation, fibrosis and dysphagia due to eosinophil activation upon exposure to a stimulus (e.g. food allergen)

**Symptoms/Clinical Presentation**
- Adult
  - Dysphagia
  - Food impaction * common first presentation
  - Heartburn
  - Non-cardiac chest pain
  - Odynophagia
  - Vomiting
  - Upper abdominal pain
- Children
  - Dysphagia
  - Vomiting
  - Abdominal pain
  - Feeding disorder
  - Food impaction

**Physical Exam**
- See P/E for dysphagia

**Investigations**
- Endoscopy
- Esophageal biopsy (2-4 from upper and lower esophagus)
- Trial of proton pump inhibition and repeat endoscopic biopsies (would show no improvement)

**Management/Treatment**
- Diet (i.e. avoid allergen or irritant)
- Medications (e.g. swallow inhaled corticosteroid)
- Dilation of esophagus (pneumatic or dilator assisted)

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10 “Clinical pathological conference: Barrett’s esophagus, carcinoma, eosinophilic esophagitis”, Jeffrey McCurdy and Celia Marginean, September 13 2016, uOttawa Faculty of Medicine
7.11 Esophageal Rings

Cause
- May be acid related but unclear

Symptoms/Clinical Presentation
- Type A Ring (symmetric, hypertrophied muscle covered by squamous epithelium; mostly proximal lower esophagus)
  - Usually asymptomatic
  - Rarely dysphagia
- Type B Ring (Schatzki’s) [thin, membranous ring covered by squamous epithelium; affects mainly squamous-columnar junction which typically overlies the gastroesophageal junction]
  - Intermittent, solid food dysphagia
  - Food bolus impaction

Physical Exam
- See P/E for dysphagia

Investigation
- Barium swallow
- Upper endoscopy

Management/Treatment
- A or B Ring
  - None if asymptomatic
  - If symptomatic
    - PPI
    - Bougie or pneumatic dilation
    - Botulinum toxin injection
7.12 Esophageal Webs

Cause
- Unclear

Symptoms/Clinical Presentation
- Asymptomatic
- Dysphagia for solids
- Associated with Plummer-Vinson syndrome (triad of iron deficiency anemia, esophageal webs, and dysphagia)

Physical Exam
- See P/E for dysphagia

Investigation
- Barium swallow
- Endoscopy

Management/Treatment
- Bougie or pneumatic dilation

12 “Esophageal Obstruction”, Amy Sharaf, September 16 2016, uOttawa Faculty of Medicine
7.13 Barrett's Esophagus

Typical Patient/Risk Factors
- Age ≥50 years
- Caucasian (uncommon among Black and Asian populations)
- Male (2:1)
- Chronic gastroesophageal reflux disease (GERD) (>10 years)
- Hiatus hernia
- Elevated BMI
- Intra-abdominal distribution of body fat

Cause
- Prolonged injury near the gastroesophageal junction leads to intestinal metaplasia (typical squamous mucosa of the esophagus is replaced by columnar mucosa with goblet cells); often a result of long-standing GERD

Symptoms/Clinical Presentation
- Symptoms of GERD
  - Heartburn, regurgitation
  - Chest pain, cough, sore throat, water brash
  - Esophagitis, esophageal ulcers, strictures
- Often asymptomatic

Physical Exam
- Not applicable

Investigations
- Upper endoscopy (mucosa looks orange, not pink)
  - Biopsy (should show intestinal metaplasia)

Management/Treatment
- Pharmacologic
  - Proton pump inhibitors
- Endoscopic removal of dysplastic tissue
  - Endoscopic mucosal resection (EMR)
  - Radiofrequency ablation (RFA)
- Surgical
  - Laparoscopic fundoplication
  - Esophagectomy

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13 “Clinical pathological conference: Barrett’s esophagus, carcinoma, eosinophilic esophagitis”, Jeffrey McCurdy and Celia Marginean, September 13 2016, uOttawa Faculty of Medicine
7.14 Esophageal Cancer

Typical Patient
- Age ≥ 50

Risk Factors
- Squamous cell carcinoma
  - Smoking
  - Alcohol
  - Diet
  - Pre-existing esophageal disorder e.g. achalasia
- Adenocarcinoma
  - Gastroesophageal reflux disease
  - Smoking
  - Obesity
  - Male gender (8:1)
  - Caucasian > African American (5:1)

Symptoms/Clinical Presentation
- Progressive solid food dysphagia
- Unintentional weight loss
- Anorexia
- Retrosternal discomfort
- Iron deficiency anemia
- Advanced stages – hoarseness, aspiration pneumonia, upper tract hemorrhage

Physical Exam
- See P/E for dysphagia

Investigations
- Upper endoscopy and biopsies
- Radiologic investigations (only adjunctive; mostly for staging)
  - CT chest and abdo scan
  - PET scan

Management/Treatment
- Curative (stage 0, I, IIa)
  - Surgical esophagectomy
  - Endoscopic removal techniques
  - Chemotherapy or radiation
  - Combination of the 3 above
- Palliative (Stage IV, incurable)
  - Radiation and/or chemotherapy
  - Esophageal dilation and/or stenting
  - Tumour ablation for debulking
  - Enteral feeding

14 “Clinical pathological conference: Barrett’s esophagus, carcinoma, eosinophilic esophagitis”, Jeffrey McCurdy and Celia Marginean, September 13 2016, uOttawa Faculty of Medicine
7.15 Gastroesophageal Reflux Disease

Typical patient/Risk factors
- Overweight, excessive alcohol use
- Diet (coffee, chocolate, fatty food)
- Smoking
- Eating 2-3 hours before bedtime

Cause
- Reflux of gastric acid into the esophagus causing irritation

Symptoms/Clinical Presentation
- Heartburn
- Regurgitation
- Dysphagia, odynophagia, chest pain, epigastric pain
- Nausea
- Hypersalivation
- Extraesophageal manifestations
  - Sore throat
  - Hoarseness
  - Cough
  - Shortness of breath
  - Wheezing
  - Globus sensation

Physical Exam
- General appearance, vitals
- Head and neck exam (oral cavity, palpate neck for masses, crepitus, voice, larynx (mirror, fiberoptic nasolaryngoscopy))
- Neurological exam
- Cardiac examination (to rule out MI, etc)
- Respiratory examination (to rule out infection, etc)

Investigations
- Blood work
- ECG
- Chest X ray
- Barium swallow
- Upper endoscopy
- 24-hour pH monitoring
- Manometry

Management/Treatment
- Proton pump inhibitor
- Lifestyle modifications (e.g. dietary modification, don’t eat late at night, HOB elevation, etc)
- Surgical

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15 “Gastro-esophageal Reflux Disease (GERD)” Case Based Learning, Ralph Lee (Ed), uOttawa Faculty of Medicine
7.16 Esophageal Ring: Peptic Stricture

Typical Patient:
- Gastroesophageal reflux disease (GERD)

Cause
- GERD → inflammation → collagen deposition → fibrosis

Symptoms/Clinical Presentation
- Progressive solid food dysphagia (without weight loss)
- Heartburn
- Food bolus impaction

Physical Exam
- See P/E for dysphagia

Investigations
- Barium swallow
- CT scan
- Biopsy
- Endoscopy

Management/Treatment
- Proton pump inhibitor
- Progressive dilation (Maloney, savary, balloon)
7.17 Peptic Ulcer Disease¹⁷

**Cause**
- H. pylori
- NSAID
- Gastric cancer
- Other, less common: chemotherapy/radiation, acid hypersecretion, crack cocaine

**Risk Factors**
- Smoking
- Alcohol
- NSAIDs

**Symptoms/Clinical Presentation**
- Sometimes asymptomatic
- Dyspepsia
- Upper abdominal pain (burning, gnawing)
  - Improves with food intake (duodenal ulcer)
  - Worsened by food intake (gastric ulcer)
- Nausea
- If complicated ulcer
  - Severe pain (perforation)
  - Vomiting (obstruction)
  - Coffee ground emesis, black stool (bleeding)

**Physical Exam**
- Abdominal exam (may show some epigastric tenderness; often unremarkable)
- DRE if concern for bleeding

**Investigations**
- Serology test for H pylori
- Urea breath test
- Endoscopy including biopsy

**Management/Treatment**
- Supportive care including withdrawal NSAID
- Medications e.g. proton pump inhibitor
- If bleeding may require endoscopic treatment (cauterize, hemoclips, epinephrine injection, hemospray)
- If H. pylori positive, then eradication
  - Quadruple therapy (PPI, tetracycline, bismuth, metronidazole) x 14 days and confirm eradication with urase breath test
- Rarely surgical removal of acid secreting part of stomach or vagotomy

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¹⁷ “Clinical pathological conference: H. Pylori, peptic ulcer disease, gastric cancer”, Navaaz Saloojee, Geoffrey Doherty and Terence Moyana, September 16 2016, uOttawa Faculty of Medicine
7.18 Pyloric Stenosis

Typical Patient
- Age: 2-8 weeks
- Male

Cause
- Narrowing of opening between stomach and duodenum due to hypertrophy of the pylorus

Symptoms/Clinical Presentation
- Progressive, projectile, non-bilious emesis
- Possible coffee grounds emesis
- Dehydration
- Jaundice

Physical Exam
- Hydration status (fontanelle, eyes, mucous membranes, skin turgor, urinary output)
- Palpable olive in the right upper quadrant or epigastrium
- Visible gastric peristaltic waves
- Gastric distension

Investigations
- Ultrasound
- Upper GI series (x-ray) with contrast if U/S non-diagnostic
- Electrolytes, pH, BUN, and creatinine

Management/Treatment
- Fluid resuscitation and correction of electrolyte and metabolic abnormalities
- Ramstedt’s pyloromyotomy

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18 “Pediatric gastrointestinal disorders”, Kyle Cowan, September 13 2016, uOttawa Faculty of Medicine


7.19 Gastric Carcinoma

Typical Patient/Risk Factors
- Advanced age
- Poor food hygiene
- H. pylori infection
- Heredity
- Environmental factors (H. pylori infection, tobacco use, socioeconomic status, diet)

Cause
- Loss of function mutation in a tumour suppressor gene and/or gain of function mutation in an oncogene

Symptoms/Clinical Presentation
- Weight loss (60%)
- Abdominal pain (50%)
- Fevers, night sweats
- Nausea and vomiting
- Anorexia
- Early satiety
- Melena
- Dysphagia
- Gastric outlet obstruction
- Paraneoplastic symptoms (rare)

Physical Exam
- Usually normal
- General appearance (cachexia, pallor)
- Abdominal exam (epigastric mass, hepatomegaly)
- Lymph node exam (Virchow’s node, Sister Mary Joseph’s node)
- Pelvic exam (Krukenberg tumor, mass in pouch of Douglas)

Investigations
- Complete blood count (often anemia)
- CT scan
- Upper endoscopy with biopsy

Management/Treatment
- Surgery
- Chemotherapy and/or radiation
Gastroenterology

7.20 Irritable Bowel Syndrome (IBS)²⁰

Putative Contributing Factors (cause unknown)
- Post-infectious
- Visceral hypersensitivity
- GI dysmotility
- Genetics
- Food sensitivity
- Abnormal central processing
- Brain-gut dysfunction
- Environmental factors
- Inflammation
- Psychological abuse history

Signs/Symptoms
- Recurrent abdominal pain
- Often improves with defecation
- Onset associated with change in form or frequency of stool (diarrhea OR constipation OR both)

Alarm Symptoms
- Melena
- Hematemesis
- Anemia
- Fever
- >5kg weight loss
- Recent major change in frequency or consistency of bowel movements
- First degree relative with CRC

Diagnostic (Rome) Criteria: Recurrent abdominal pain or discomfort ≥3 days/month in the last 3 months, + ≥2 of the following: 1. Improves with defecation, 2. Onset associated with change of frequency of stool, 3. Onset associated with change in form of stool

Physical Exam: Abdominal exam, no specific findings

Investigations
- Guided by patient symptoms
- Consider colonoscopy if other diagnosis is raised otherwise avoid endoscopy

Management/Treatment:
- Establish trusting doctor patient relationships (credibility, comfort, reassurance, placebo effect)
- Lifestyle changes (diet, exercise, decrease caffeine and alcohol intake, increase fiber intake)
- Check for food intolerances (e.g. lactose, gluten...)
- Psychological treatments (CBT (best evidence), psychotherapy, hypnotherapy, stress management, biofeedback, relaxation techniques)
- Pharmacotherapy: probiotics, loperamide (diarrhea), amitriptyline (chronic pain), bran, psyllium, mild laxatives (constipation), psychological medication, if depressed (TCAs)
- NOTE: Ladder approach to treatment
  - Mild IBS: Start with diet, lifestyle advice
  - Moderate IBS: Manage stress, pharmacotherapy
  - Severe IBS: Multidisciplinary approach, psychological treatment, improve functioning

²⁰ - Adult Functional Bowel Disease”- Self Learning Module, Grant Thompson, uOttawa Faculty of Medicine
7.21 Clostridium Difficile Associated Disease

Typical Patient:
- Exposure to antibiotics, hospitalization, institutions

Cause
- Most common: recent antimicrobial therapy (e.g. clindamycin) → dysbiosis of normal flora

Symptoms/Clinical Presentation
- Watery diarrhea
- Dysenteric illness
- Fever
- Shock

Physical Exam
- General appearance
- Vitals
- Abdominal exam

Investigations
- Stool for c diff toxin- most commonly available
- C Diff culture
- Tissue culture with neutralization
- Toxin detected by EIA
- Toxin B gene deletion by nucleic acid methods
- Abdominal XR to monitor for toxic megacolon

Management/Treatment
- Antibiotics: 1st line is Vancomycin x 14 days
- Rehydration
- Prevention (contact precautions until diarrhea controlled, hand washing, etc)
- If recur, consider extended course of antibiotics or fecal transplant

21 “Microbiology of the gut: Normal and abnormal”, Peter Jessamine, September 19 2016, uOttawa Faculty of Medicine
7.22 Ulcerative Colitis

Typical Patient:
- Age: two peaks 28-20s, 50-60

Cause
- Environmental, genetic, infectious, immunologic

Symptoms/Clinical Presentation
- Frequent loose bowel movements
- Blood in stool
- Hematochezia, mucus/pus
- Abdominal pain
- Urgency
- Failure to thrive
- Weight loss
- Extra-intestinal manifestations
  - Iritis
  - Oral ulceration
  - Joint pain
  - Sacroiliitis
  - Ankylosing spondylitis
  - Skin rashes - pyoderma gangrenosum, erythema nodosum

Key features:
- Continuous mucosal inflammation limited to the colon
- Rectum is always involved

Physical Exam
- Extra-intestinal manifestations: examination of eyes, mouth, skin, joints, etc, as necessary
- Abdominal exam

Investigations
- Blood work – including CBC, CRP
- Abdomen X ray
- Colonoscopy
- CT or MRI enterography (colonic wall thickening with contiguous spread)
- Stool testing to rule out infectious causes
- Biopsy

Management/Treatment
- 5-ASA- oral or rectal
- Antibiotics
- Immune-modulators
- Corticosteroids
- Biologic therapy (anti TNF-a, anti-integrins, etc)
- Surgery (total colectomy)
- Supportive therapy (e.g. hydration, Vitamin B12)

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22 “Clinical pathological conference: Inflammatory bowel disorders (IBD) and other colitides”, Richmond Sy, Celia Marginean and Cynthia Walsh, September 20 2016, uOttawa Faculty of Medicine
7.23 Crohn's Disease

Typical Patient:
- two peaks 28-20s, 50-60

Cause
- Environmental, genetic, infectious, immunologic

Symptoms/Clinical Presentation
- Frequent bowel movements (less so than UC)
- Diarrhea
- Bloody stool
- Significant abdominal pain
- Urgency
- Failure to thrive
- Weight loss
- Ulcers and fistulas
- Extra-intestinal manifestations
  - Ocular inflammation
  - Oral ulceration
  - Joint pain
  - Sacroiliitis
  - Ankylosing spondylitis

Physical Exam
- Extra-intestinal manifestations: examination of eyes, mouth, skin, joints, etc, as necessary
- Abdominal exam

Investigations
- Abdomen X ray
- Colonoscopy with biopsies
- CT or MRI enterography
- Anemia testing

Management/Treatment
- 5-ASA
- Antibiotics
- Immune-modulators
- Corticosteroids
- Surgery (removal of damaged segment)
- Supportive therapy (e.g. hydration, Vitamin B12)

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23 “Clinical pathological conference: Inflammatory bowel disorders (IBD) and other colitides”, Richmond Sy, Celia Marginean and Cynthia Walsh, September 20 2016, uOttawa Faculty of Medicine
7.24 Anal Fissures

Typical Patient/Risk Factors

- Local trauma
  - Hard stool
  - Prolonged diarrhea
  - Vaginal delivery
  - Anal sex

Cause

- Stretching of anal mucosa beyond its normal capacity → tear in the anoderm, distal to the dentate line

Symptoms/Clinical Presentation

- Bleeding on toilet paper
- Pain with passing stool
- Pruritus

Physical Exam

- Inspection

Investigations

- CBC

Management/Treatment

- Conservative therapy
- Medical therapy
  - Topical nitroglycerin
  - Topical Ca channel blockers
  - Botulinum toxin
- Surgery
  - Lateral sphincterotomy
  - Fissurectomy
  - Anal advancement flap
7.25 Appendicitis

Typical Patient
- Age: late teens, early 20s

Cause
- Obstruction of appendiceal lumen → bacterial overgrowth and distension from mucous secretion → venous obstruction → edema and ischemia → gangrene and perforation

Symptoms/Clinical Presentation
- Cramping periumbilical pain migrating to right lower quadrant (visceral pain → parietal pain, i.e. poorly localized to well localized)
- Anorexia
- Nausea and vomiting
- Diarrhea
- Chills
- Fever
- Sometimes dysuria (if bladder is irritated by the inflamed appendix)

Physical Exam
- General appearance, vitals
- Abdominal exam
  - Tenderness in RLQ and on rectal or pelvic exam
  - Percussion tenderness
  - Rebound, guarding
  - McBurney’s sign, Rovsing’s sign, psoas sign, obturator sign

Investigations
- CBC (elevated WBC)
- b-HCG (to rule out ectopic or regular pregnancy)
- Urinalysis (to rule out UTI, kidney stones)
- Ultrasound
- CT if ultrasound not sufficient

Management/Treatment
- Resuscitation with IV fluid and pre-operative antibiotics
- Appendectomy
- Non-operative management with perforation, delayed presentation, and associated phlegmon or abscess
- Post-operative antibiotics if appendix perforated
7.26 Diverticular disease

Typical Patient/Risk factors
- Older patient (>80 years) consuming a low fiber diet
- Obesity
- NSAID
- Physical inactivity
- Smoking

Cause
- Stasis or obstruction at the neck of the diverticulum may lead to bacterial overgrowth and local tissue ischemia

Symptoms/Clinical Presentation
- Left lower quadrant pain
- Fever, chills
- Change in bowel pattern
- Urinary urgency
- Fever
- Tachycardia
- Distended abdomen
- Diffuse peritonitis

Physical Exam
- General appearance, vitals
- Abdominal exam (may show rebound and guarding in LUQ/LLQ)

Investigations
- Blood work
- CT abdomen

Management/Treatment
- Uncomplicated
  - Outpatient treatment with oral antibiotics
  - Microbiology- blood cultures, stool cultures
- Complicated
  - Hospitalization, NPO, fluid
  - Drain abscess
  - IV antibiotics
  - Surgery if non resolving
7.27 Fistula-in-ano

Typical Patient/Risk factors
- Trauma
- Anal fissure
- Carcinoma
- Radiation therapy
- Infection

Cause
- Almost always caused by a previous anorectal abscess

Symptoms/Clinical Presentation
- Perianal discharge
- Pain
- Swelling
- Bleeding
- Diarrhea
- Skin excoriation
- External opening

Physical Exam
- Inspection of entire perineum
  - Look for external opening (sinus, granulation tissue)
  - DRE
  - Determine relationship between anus and position of tract
  - Assess anal tone and squeeze pressure

Investigations
- None required, unless complex perianal inflammation (in which case, CT, US, or MRI can be useful)
- Consider colonoscopy to evaluate for luminal disease

Management/Treatment
- Fistulotomy
- Fibrin sealant
- Insertion of seton or fistula plug or mucosal advancement flap

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27 “Surgical problems in GI – Part A”, Isabelle Raiche, September 20 2016, uOttawa Faculty of Medicine
7.28 Hemorrhoids

Typical Patient/Risk Factors
- Pregnancy
- Spinal injured population
- Straining, prolonged toilet time, inadequate fiber

Cause
- Swelling of the cushions through the anal canal → dilation of arteriovenous plexus → stretching of the suspensory muscles → prolapsing through anal canal

Symptoms/Clinical Presentation
- External hemorrhoids
  - Pain
  - Itchiness
  - Swelling
- Internal hemorrhoids
  - Bleeding
  - Swelling
  - Prolapsing

Physical Exam
- Abdominal examination
- Rectal examination, DRE

Investigations
- Anuscopy
- Sigmoidoscopy
- Digital rectal exam

Management/Treatment
- External
  - Conservative
    - Sitz baths
    - Analgesics
    - Stool softeners/fiber
    - Topical nifedipine
  - Surgical
- Internal
  - Conservative
    - Stool softeners/fiber
    - Topical treatments
  - Non-surgical
    - Sclerotherapy
    - Rubber band ligation
    - Infrared coagulation
  - Surgical
Typical Patient
- Dependent on the type of hernia
  - Indirect hernia: Male
  - Direct hernia: Older male
  - Femoral hernia: Female
  - Umbilical: post surgery

Cause
- Congenital predisposition (increased pressure combined with weak tissue)
- Iatrogenic (previous surgery with disruption of plane and creation of new space)

Symptoms/Clinical Presentation
- Pain, discomfort
- Limitations in certain activities
- Palpable lump, potentially reducible
- Digestive problems
- Esthetic concerns

Physical Exam
- Abdominal exam

Investigations
- Endoscopy
- Ultrasound
- CT abdomen

Management/Treatment
- Observation if asymptomatic (for inguinal hernia)
- Reduction if incarcerated
- Surgical repair +/- mesh
7.30 Ischemic Colitis

Typical Patient
- More common in women
- Advanced age

Risk Factors
- Congestive heart failure, cardiac arrhythmia, recent myocardial infarction
- Age
- Diabetes
- Hypotension
- Medication (vasopressor, digoxin)
- Underlying thrombophilia
- Pancreatitis, portal hypertension, cirrhosis
- Malignancy
- Coagulation disorders
- Chronic kidney disease
- Cocaine/amphetamine use

Cause
- Lack of oxygen and nutrient supply to an area of the colon, due to: hypoperfusion and reperfusion injury, decreased cardiac output, small vessel disease, etc

Symptoms/Clinical Presentation
- Sudden cramping abdominal pain
- Urgency
- Nausea
- Bright red blood per rectum
- Diarrhea

Physical Exam
- Abdominal exam (pain out of keeping with physical exam)
- Rectal exam, including DRE

Investigations
- Lab work (low hemoglobin and albumin; metabolic acidosis; high WBC and Lactate)
- Abdominal x-ray (thumb-printing in transverse colon image)
- CT with contrast
- CT angiography
- Colonoscopy with biopsies

Management/Treatment
- Most cases spontaneously resolve with conservative management (IV hydration, bowel rest, correct precipitating factors)
- Surgery if severely symptomatic (hypotension, tachycardia, severe abdominal pain) and presence of gangrene
- Antibiotics considered in moderate to severe cases

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30 “Clinical pathological conference: Inflammatory bowel disorders (IBD) and other colitides”, Richmond Sy, Celia Marginean and Cynthia Walsh, September 20 2016, uOttawa Faculty of Medicine
7.31 Microscopic Colitis

Typical Patient
- Age: 50-70 years old
- Female
- Smoker
- Celiac disease, arthritis, and/or autoimmune disorders

Cause
- Unknown
- Medications: SSRI, NSAIDs, PPI

Symptoms/Clinical Presentation
- Chronic watery, non-bloody diarrhea; average 8 stools/day + nocturnal episodes
  - Diarrhea can be fluctuating with remissions and exacerbations
- Abdominal cramps
- Bloating
- Nausea
- Fecal incontinence
- Symptoms are often reduced with fasting

Physical Exam
- Often normal
- Abdominal exam
- Rectal exam, including DRE

Investigations
- Blood work
- Colonoscopy with biopsy

Management/Treatment
- Budesonide (*best treatment*)
- Antidiarrheal agents (e.g. loperamide)
- Bulking agents (e.g. psyllium/fiber)
- Pepto Bismol
- Bile acid resins (cholestyramine)
- 5-ASA
- Probiotics
- Glucocorticoids
- Surgery

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31 “Clinical pathological conference: Inflammatory bowel disorders (IBD) and other colitides”, Richmond Sy, Celia Marginean and Cynthia Walsh, September 20 2016, uOttawa Faculty of Medicine
7.32 Perianal Abscess

Typical Patient/Risk factors
- Smoking
- Diabetes
- Obesity
- Male
- Previous episode

Cause
- Obstruction of anal crypts → stasis of glandular secretions → subsequent infection → suppuration → abscess formations

Symptoms/Clinical Presentation
- Dull perianal discomfort
- Pruritus
- Fever
- Pain with defecation or sitting
- Purulent discharge

Physical Exam
- Inspection, palpation, DRE +/- anoscope

Investigations
- None necessary
- Consider US

Management/Treatment
- Incision and drainage of abscess
- Antibiotics if
  - Diabetes
  - Immunosuppressed
  - Valvular disease
  - Cellulitis

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32 “Surgical problems in GI – Part A”, Isabelle Raiche, September 20 2016, uOttawa Faculty of Medicine
7.33 Anal Cancer

Typical Patient/Risk Factors
- Inflammatory bowel disease
- Anal sexual activity
- HPV (type 16 and 18)
- HIV
- Other chronic immunosuppression
- Smoking

Symptoms/Clinical Presentation
- Rectal bleeding (bright red blood, not melena)
- Change in bowel habits
- Prolapsing sensation
- Lump near the anus
- Incontinence
- Constitutional symptoms (fever, weight loss, night sweats)
- Itching or discharge

Physical Exam
- Perianal inspection, DRE
- Anoscopy or rigid sigmoidoscopy

Investigations
- Endoscopy with biopsy
- To rule out a proximal source:
  - Colonoscopy, flexible sigmoidoscopy, CT colonography
- CT chest/abdo/pelvis
- PET
- Gynecologic exam for women

Management/Treatment
- Surgery
- Combined modality
  - Chemotherapies- 5-fluorouracil, Mitomycin or cisplatin
  - Radiotherapy

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33 “Surgical problems in GI – Part A”, Isabelle Ralche, September 20 2016, uOttawa Faculty of Medicine
7.34 Colorectal Cancer (CRC)34

Typical Patient/Risk Factors
- Older age
- Living in developed countries
- Environmental (minor) — high fat, low fiber, high red meat, low Ca, low folate
- Adenomatous polyps
- Family history (first degree relative with colorectal cancer)
- Polyposis syndromes (FAP, HNPCC)
- IBD/Primary Sclerosing Cholangitis

Cause
- Polyposis Syndromes (Familial Adenomatous Polyposis, Lynch Syndrome, Peutz Jeghers, etc)
- Sporadic (usually begins with APC gene mutation)

Signs/Symptoms
- Often asymptomatic
- Constitutional symptoms- fever, weight loss, night sweats
- Abdominal pain
- Perforation/abscess
- Tenesmus/incomplete evacuation
- Proximal colon (right-sided)
  - Often start off asymptomatic
  - Occult blood loss, Fe-deficiency anemia (fatigue, SOB on exertion, exertional chest pain)
- Distal colon (left-sided)
  - Obstruction, rectal bleeding
  - Altered bowel pattern, pencil-thin stool

Physical Exam
- General appearance
- Abdominal exam
- DRE for distal masses

Investigations
- Colonoscopy with biopsy
- Radiology (ACBE, CT colonography)
- FOBT (screening)
- Bloodwork (liver enzymes, CEA)
- CXR, CT abdomen/pelvis – staging

Treatment
- Local endoscopic resection or surgery, if possible
- Adjuvant chemotherapy for stage 3 (and some stage 2)
- Chemotherapy for metastatic stage 4 disease
- Adjuvant radiation for rectal cancers
- Palliative stenting for obstructive tumors
7.35 Hirschsprung's Disease

Typical Patient/Risk Factors
- Neonate
- Male (4:1)
- Associated with Down’s Syndrome, cardiac malformations

Cause
- Interrupted development of myenteric nervous system, causing loss or absence of intestinal ganglion cells
- Results in failure of relaxation causing functional bowel obstruction

Symptoms/Clinical Presentation
- Neonatal presentation
  - Delayed passage of meconium (>48 hours after birth)
  - Bilious vomiting
  - Abdominal distension
  - Explosive diarrhea on rectal exam
- Beyond neonatal presentation
  - Chronic constipation
  - Abdominal distension
  - Malnutrition
  - Failure to thrive, short stature
- Enteroctitis as initial presentation (10%)

Physical Exam
- Abdominal exam
- Rectal exam

Investigations
- Abdominal X-rays (bowel distension)
- Contrast enema (transition zone, rectosigmoid ratio reversal, delayed evacuation of contrast)
- Manometry (infrequently used)
- Rectal biopsy ((i) absence of ganglion cells, (ii) hypertrophic nerve trunks, (iii) muscular hypertrophy)

Management/Treatment
- Fluid resuscitation
- Antibiotics
- Rectal washouts
- Surgical resection of the aganglionic colon
7.36 Intussusception

Typical Patient
- Age: 3-9 months

Cause
- majority are idiopathic
- Telescoping of bowel

Symptoms/Clinical Presentation
- Intermittent and colicky abdominal pain
- Non-bilious vomiting
- Abdominal mass
- Rectal bleeding ("red currant jelly")
- Can be non-specific early in its course

Physical Exam
- Abdominal exam - sometimes can feel mass in RUQ & epigastrium with empty RLQ

Investigations
- Abdominal ultrasound
  - Axial – target/doughnut sign
  - Transverse – pseudokidney sign
- Enema (air) via fluoroscopy

Management/Treatment
- Air enema
- Surgery – bowel resection if necrosis present or if air enema unsuccessful
7.37 Malrotation and Volvulus

Typical Patient
- Newborn (typically <1 month old)
- OR in elderly patients

Cause
- Babies- Improper embryological rotation of gut → angle of Treitz and cecum are side by side → gut twists around superior mesenteric vessels → ischemia
- Elderly- laxity of mesentery can allow for volvulus

Symptoms/Clinical Presentation
- Acute
  - Feeding problems
  - Bilious vomiting
  - Abdominal distension with tenderness or erythema and blood per rectum (late findings)
- Chronic
  - Frequent vomiting
  - Intermittent, crampy abdominal pain
  - Distension
  - Diarrhea or constipation
  - Hematemesis
  - Malabsorption and failure to thrive

Physical Exam
- Abdominal exam

Investigations
- X-ray of abdomen with contrast (Upper GI Series)

Management/Treatment
- Fluid resuscitation and antibiotics
- Consider endoscopic pneumatic decompression
- Surgery (derotation, divide Ladd’s bands, broaden base of mesentery, appendectomy)
7.38 Meckel’s Diverticulum

Typical Patient
- Age: <4 years

Cause
- Proximal portion of omphalomesenteric canal does not close completely

Symptoms/Clinical Presentation
- Bleeding with ulceration and no abdominal pain
- Bowel obstruction
- Inflammation

Physical Exam
- Abdominal exam

Investigations
- Depends on presentation but generally:
  - Hematocrit, hemoglobin
  - Stool smear for invisible blood
  - Abdominal X-rays / US / CT scan
  - Meckel’s (Technetium) scan

Management/Treatment
- Fluid resuscitation
- Surgery (if bleeding) to remove diverticulum
- Iron supplement (if anemic)
- Blood transfusion (if extensive blood loss)
7.39 Foreign Body Ingestion

Typical Patient
- Children (80%): 6 months – 6 years
- Any adults including those with cognitive disorders (inc dementia)

Risk Factors
- Esophageal pathology (e.g. Schatzki’s rings, peptic strictures)
- Adults: Psychiatric disorders, developmental delay, advanced age, dementia, intoxication, dentures/dental work

Symptoms/Clinical Presentation
- Dysphagia
- Odynophagia
- Chest pain
- Choking
- Sialorrhea
- Vomiting
- Respiratory compromise

Physical Exam
- General appearance
- Head & neck exam (crepitus, swelling, erythema)
- Respiratory exam (assess airways, respiratory distress, wheezing)
- Abdominal exam (tenderness, peritoneal signs)

Investigations
- Chest and abdominal X-rays
- Endoscopy
- Barium swallow – contra-indicated (risk of aspiration)

Management/Treatment
- None (> 80% will pass spontaneously)
- Assess airway – endotracheal intubation, PRN
- If symptomatic/severe: Esophagogastroduodenoscopy (contra-indicated if bowel perforation, obstruction, narcotic packet ingestion)
- If asymptomatic: surveillance with X-ray
- Surgery (last resort; required in 12-16% of cases)
  - Only if: complications, failure to progress, inability to be removed endoscopically, altered GI anatomy

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39 “Esophageal Obstruction”, Amy Sharaf, September 16 2016, uOttawa Faculty of Medicine
7.40 Small Bowel Obstruction

Typical Patient
- Prior surgery
- Malignancy

Causes
- Extrinsic
  - Adhesions (*most common*)
  - Hernia (*2nd most common*)
  - Neoplasm
- Intrinsic
  - Congenital
  - Inflammatory
  - Neoplastic (*3rd most common*)
  - Other (intussusception, endometriosis)
- Intraluminal
  - Foreign body
  - Bezoar
  - Gall stone

Symptoms/Clinical Presentation
- 5 classic symptoms: bloating, nausea and vomiting, constipation, obstipation, *crampy* abdominal pain
- Classic signs:
  - Afebrile
  - Distended abdomen
  - High-pitched bowel sounds
  - Hyper-resonant bowel
  - No localized tenderness

Physical Exam
- General appearance, vitals
- Abdominal exam - distension

Investigations
- Lab work
  - Normal or mildly elevated WBC
  - Hypochloremic, hypokalemic, metabolic alkalosis secondary to vomiting
- Imaging (abdominal X-ray, upright chest X-ray, CT)

Management/Treatment
- Hospitalization
- IV fluid
- NPO
- Nastrogastric tube
- Surgery if: (i) complete obstruction, (ii) adhesion, and/or (iii) hernia

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*“Surgical Problems in GI – Part B”, Melanie Paquin-Gobeil, September 21 2016, uOttawa Faculty of Medicine*
7.41 Large Bowel Obstruction

Typical Patient
- Colon cancer patient

Causes
- Intrinsic to intestinal wall
  - Colorectal cancer (*most common cause*)
  - Inflammation – diverticulitis, Crohn’s, Schistosomiasis, TB
- Extrinsic to intestinal wall
  - Colonic volvulus (*2nd most common cause*)
  - Adhesions
  - Hernias
  - Tumors in adjacent organs
  - Abscesses
- Intraluminal
  - Fecal impaction
  - Inspissated barium
  - Foreign bodies

Signs/Symptoms
- Similar to SBO – distension, obstipation, constipation, nausea, vomiting
- In addition, may have a history consistent with colorectal cancer
  - Melena, blood per rectum, change in bowel habit, decreased caliber of stool, incomplete emptying, soiling underwear

Physical Exam
- General appearance, vitals
- Abdominal exam including DRE

Investigations
- X-ray
  - “Picture frame”, look for haustra
  - Absence of gas in rectum
  - Closed loop (surgical emergency) versus open loop

Management/Treatment
- Hospitalization, NPO, IV fluids, NG suction
- Definitive treatment depends on cause of obstruction
- CT, colonoscopy, barium enema – if malignancy suspected
- Colonoscopic decompression for sigmoid volvulus followed by delayed sigmoid resection
- Surgery (hernias, closed loop obstructions)

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41 "Surgical Problems in GI – Part B", Melanie Paquin-Gobeil, September 21 2016, uOttawa Faculty of Medicine
7.42 Ileus

Typical Patient
- Post-operative

Cause
- Post-operative
- Metabolic and electrolyte disturbance
- Drugs
- Intra-abdominal inflammation
- Retroperitoneal hemorrhage or inflammation
- Intestinal ischemia
- Systemic sepsis

Symptoms/Clinical Presentation
- Distension
- No gas
- Constipation
- Nausea and vomiting

Physical Exam
- Abdominal exam

Investigations
- Abdominal X-ray

Management/Treatment
- Supportive
  - Nasogastric tube
  - IV fluid
- Treat the underlying cause
  - E.g. reduce opiate
  - Correct electrolyte abnormalities
  - Treat sepsis, intra-abdominal infection/inflammation
7.43 Pseudo-Obstruction (aka Ogilvie’s Syndrome)\(^{43}\)

**Typical Patient**
- Older, recent surgery

**Causes/Associations**
- Neuroleptic medications
- Opiates
- Severe metabolic illness
- Diabetes
- Uremia
- Lupus
- Parkinson’s
- Hyperparathyroidism
- Scleroderma
- Traumatic retroperitoneal hematomas

**Physical Exam**
- General appearance, vitals
- Abdominal exam

**Investigations**
- X-ray
- Gastrograffin enema – most useful test

**Treatment**
- Mostly conservative and supportive
  - NG tube, IV fluids, correct electrolyte abnormalities
- Consider endoscopic decompression
- Minimize medication that affect bowel motility (opiates)
- Neostigmine – generates high pressure and colonic decompression (side effect is bradycardia so this must be given in a monitored setting)

\(^{43}\)“Surgical Problems in GI – Part B”, Melanie Paquin-Gobeil, September 21 2016, uOttawa Faculty of Medicine
7.44 Upper GI Bleed

Typical Patient
- Male (2:1 M:F ratio)
- NSAID history (including ASA)

Cause
- Peptic ulcer disease (20-50%) *most common cause*
- Varices (5-20%)
- Mallory-Weiss tears (8-15%)
- Erosions (8-15%)
- AV malformations (5%)
- Tumours (5%)
- Dieulafoy’s lesions (1%)
- Other: gastric antral vascular ectasia, portal hypertension gastropathy, hemobilia, hemosuccus pancreatitis, aortoenteric fistulas, Cameron’s lesions/ulcers

Symptoms/Clinical Presentation
- Hematemesis – bright red; clots; “coffee ground” emesis
- Melena
- Increased bowel movement frequency (due to blood; indicator of rapidity of bleeding)
- Hemodynamic symptoms (presyncope, orthostatic dizziness/lightheadedness)
- Hematochezia (if rapid bleed)
- Chest pain
- Dyspnea
- Other: abdominal pain, heartburn, dysphagia, nausea and vomiting (depends on the cause of the bleed)

Physical Exam
- General appearance, vitals (hypotension, tachycardia, orthostatic changes)
- Hydration status, hemodynamic instability
- Altered mentation, jaundice
- Abdominal exam, including DRE

Investigations
- Bloodwork – CBC (hemoglobin, platelets), electrolytes, INR, BUN, creatinine, liver enzymes, liver function tests
- Nasogastric aspirate
- Esophagogastroduodenoscopy (EGD)
- RBC Scan (Tc tagged RBCs)

Management/Treatment
- INITIAL: ABC/s, resuscitation (IV access x2, fluids, NPO)
- Fluid management (IV crystalloids, colloids; RBC transfusion)
- Reverse anticoagulation (Increased INR → vitamin K, fresh frozen plasma, prothrombin complex concentrate; Decreased platelets → platelet transfusion)
- Pharmacotherapy (1. IV PPI if suspect ulcer; 2. Somatostatin if suspect varices (i.e. octreotide), IV
- EGD (within 24h, to diagnose, stratify risk, potentially treat): injection (vasoconstrictors), thermal therapy, mechanical therapy (hemoclips, rubber bands), hemospray
- If variceal bleed cannot be banded, can proceed with TIPS
- Mesenteric angiography (diagnose, therapeutic)
- Surgery as last resort

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“GI Bleeding”, Jeffrey McCurdy, September 23 2017, uOttawa Faculty of Medicine
Typical Patient

- Older age (mean age at presentation: 63-77 years old)

Cause

- Diverticulosis (25-65%) *most common cause*
- Cancers/polyps (17%)
- Colitis/ulcers (18%) – IBD, ischemic, vasculitis, infectious, radiation-induced, NSAID-induced
- Unknown (16%)
- Angiodysplasia (3-15%)  
- Other (8%) – post-polypectomy, stercoral ulcers, aorto-colonic fistulas
- Anorectal (24-64%) – fissures, hemorrhoids

Symptoms/Clinical Presentation

- Red blood per rectum (bright red → think left colonic; dark red/maroon → think right colonic, lower small bowel)
- Stool changes (increased frequency, diarrhea, location of blood)
- Melena (uncommon, but possible if bleed is in distal small bowel, cecum, right-sided colon)
- Other: fecal urgency, incontinence, tenesmus, abdominal pain, fever, chills, weight loss

Physical Exam

- General appearance, vitals (hypotension, tachycardia, orthostatic changes)
- Hydration status, hemodynamic instability
- Altered mentation, jaundice
- Abdominal exam, including DRE

Investigations

- Bloodwork – CBC (hemoglobin, platelets), electrolytes, INR
- BUN, creatinine
- Liver enzymes, liver function tests
- Nasogastric aspirate
- Colonoscopy (may do a flexible sigmoidoscopy in a young patient with no “red flags”)
- RBC Scan (Tc tagged RBCs)

Management/Treatment

- INITIAL: ABC/s, resuscitation (IV access x2, fluids, NPO)
- Fluid management (IV crystalloids, colloids; RBC transfusion)
- Reverse anti-coagulation (Increased INR → vitamin K, fresh frozen plasma, prothrombin complex concentrate; Decreased platelets → platelet transfusion)
- Colonoscopy
- Endoscopic hemostasis  
  - Injection (vasoconstrictors)
  - Thermal therapy
  - Mechanical therapy (hemoclips, rubber bands)
  - Hemospray
- Mesenteric angiography (diagnose, therapeutic)
- Surgery
- Note that there is no specific medication used for LGI bleeds

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45 “GI Bleeding”, Jeffrey McCurdy, September 23 2017, uOttawa Faculty of Medicine
7.46 Celiac Disease (CD)  

Typical Patient/Risk Factors
- Genetic susceptibility: HLA-DQ2/DQ8 (absence rules out CD)
  - Often comorbid with conditions with similar HLA haplotypes (Type 1 DM, dermatitis herpetiformis, hypothyroidism, rheumatoid arthritis, microscopic colitis, IBD, IgA deficiency, Down’s syndrome)
- Family history of celiac disease
- High prevalence in Western Europe, North America, Australia

Cause
- Abnormal immune reaction against gluten

Pathogenesis
- Gluten released from food sources in small bowel lumen → lamina propria → presentation of gliadin to APC → cytokine secretion → damage to intestinal lining and development of autoantibodies

Symptoms/Clinical Presentation
- Asymptomatic (most common)
- Amenorrhea, infertility*
- Iron-deficiency anemia (Iron absorbed in duodenum)*
- Osteopenia/osteoporosis (Calcium and Vitamin D malabsorption)*
- Delayed growth and puberty*
- Bloating, diarrhea (common)
- Steatorrhea, weight loss (rare)
- Extra-intestinal symptoms (rare): pruritis, skin rashes, non-specific hepatitis, neurologic symptoms (ataxia, neuropathies, seizures)
* Atypical presentation in symptomatic patients

Physical Exam
- General appearance including skin exam
- Abdominal exam

Investigations
- Bloodwork
- IgA endomysial, anti-tissue transglutaminase antibodies
- Endoscopy with tissue (small bowel) biopsy

Management/Treatment
- Gluten free diet
- Trial of steroids, immunosuppressants, elimination diets (if gluten free diet fails after 6-month trial)
- Future: drugs taken with meal to prevent gluten absorption by enterocytes
7.47 Gallstone Disease

**Cholecystitis** = inflammation of gallbladder (can be due to gallstones)
**Choledocholithiasis** = gallstone in the CBD
**Cholangitis** = infection of bile ducts due to bacteria (often in the presence of gallstones or any obstruction)

**Typical Patient:**
- Cholesterol stones: 5 Fs: Female, forty, fair, fertile, fat
- Pigment stones: hemolytic anemia, infection

**Cause**
- Stasis
- Bile composition: too much cholesterol, too much bilirubin, not enough bile acid

**Symptoms/Clinical Presentation**
- RUQ pain
- Nausea/vomiting
- Epigastric pain, often worse following meals
- Jaundice/scleral icterus
- Pain radiating to right shoulder/back
- Fever, chills
- May be asymptomatic

**Physical Exam**
- General appearance, vitals
- Abdominal exam

**Investigations**
- Basic bloodwork (CBC, electrolytes)
- INR, Creatinine, bilirubin, liver enzymes, lipase
- Abdominal ultrasound = 1st line imaging
- CT, MRCP, EUS may be done if cause is unclear

**Management/Treatment**
- ABCs, IV fluids, admit to hospital
- Blood cultures and repeat labs
- IV antibiotics
- Stone extraction (ERCP)
- Cholecystectomy (if indicated)
- Other: oral bile acids binders, sound wave lithotripsy + bile acids

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47 “Clinical Radiological Conference: Non-neoplastic biliary and pancreatic diseases”, Paul James and Wael Shabana, September 27 2016, uOttawa Faculty of Medicine
7.48 Acute Pancreatitis

Typical Patient:
- History of biliary colic and/or alcohol consumption

Cause
- Pneumonic I GET SMASHED (Idiopathic, Gallstones, EtOH, Trauma, Steroids, Mumps (+ other viruses: CMV, EBV), Autoimmune (SLE, polyarteritis nodosa), Scorpion sting, Hypercalcemia or hypertriglyceridermia, ERCP, Drugs (thiazides, sulfonamides, ACE-inhibitors, NSAIDs, azathioprine)
- Note: gallstones and alcohol are the two most common causes (60-70% of cases)

Symptoms/Clinical Presentation
- Sharp, epigastric pain radiating to the back
- Nausea/vomiting, may have a fever
- Dark urine
- Jaundice
- Pale stools
- Tachycardia
- Cullen’s sign (periumbilical bleed)
- Grey-Turner sign (flank bleed)

Physical Exam
- Vitals- may be hypovolemic
- Abdominal exam- epigastric tenderness

Investigations
- Bloodwork – CBC (increased WBCs), electrolytes, liver enzymes, bilirubin, lipase (increased)
- Pancreatic function test
- Ultrasound (to rule out gallstones in the bile duct)
- MRI
- Routine CT is NOT indicated. Only if complications or unknown diagnosis.

Management/Treatment
- Remove offending agent (e.g. gallstones, drugs, alcohol)
- Supportive care (admit, IV fluids & electrolytes, analgesia, nutritional support)
- Monitor for complications
- Consider antibiotics IF: 1. Cholangitis; 2. Infected necrosis; 3. Abscess; 4. Infected pseudocyst

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48 “Clinical Radiological Conference: Non-neoplastic biliary and pancreatic diseases”, Paul James and Wael Shabana, September 27 2016, uOttawa Faculty of Medicine
7.49 Chronic pancreatitis

Typical Patient:
- Recent onset diabetes
- Chronic alcohol use

Cause
- Alcohol (>80%)
- Idiopathic
- Rare: gallstones, hyperparathyroidism, autoimmune, congenital malformations, cystic fibrosis

Pathophysiology
- Irreversible parenchymal (acinar cell) destruction, leading to pancreatic dysfunction (exocrine and/or endocrine dysfunction)

Symptoms/Clinical Presentation
- Epigastric pain radiating to the back; aggravated by food, relieved by Tylenol with codeine
- Weight loss (due to malabsorption)
- Pale stools (steatorrhea – pale/fatty stools)
- Newly diagnosed diabetes

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Bloodwork – CBC (increased WBCs), electrolytes, liver enzymes, bilirubin, lipase (increased)
- Ultrasound (to rule out other causes of symptoms)
- CT (if normal, do EUS or MRCP – will see dilated pancreatic duct, lots of calcium deposits)
- Dilated main pancreatic duct (→ ERCP, endoscopic nerve block, surgery)
- Normal duct (→ endoscopic nerve block, pancreas islet cell transplant)

Management/Treatment
- Remove offending agent (e.g. discontinue alcohol)
- Analgesics
- Suppress secretion – drugs, supplement pancreatic enzymes (improves pain, diarrhea, nutrient absorption)
- Modify neural transmission – drugs, nerve block
- Relieve obstruction – surgery, stents
7.50 Fat Malabsorption

Typical Patient
- See causes below

Cause
- Excess gastric acid (denaturation of lipase) – e.g. Zollinger-Ellison Syndrome
- Impaired production/secretion of lipase or colipase – chronic pancreatitis; pancreatic duct obstruction (e.g. tumours, CF)
- Impaired bile acids (cholestasis, impaired enterohepatic recirculation, inborn errors of bile acid synthesis)
- Loss of enterocyte surface area or function (inflammatory disease (e.g. Crohn’s, celiac), chronic infections, deposition diseases, intestinal lymphoma, small bowel resection or bypass)
- Impaired lymphatic transport (primary or secondary lymphangiectasia)

Symptoms/Clinical Presentation
- Steatorrhea
- Crampy abdominal pain, bloating
- Weight loss, loss of subcutaneous fat
- Oxalate kidney stones
- Osteoporosis/osteomalacia/Rickett’s (if unable to absorb fat-soluble, vitamin D)
- Blindness (if unable to absorb fat-soluble, vitamin A)
- Coagulopathy (if unable to absorb fat-soluble, vitamin K)

Physical Exam
- General appearance- low BMI, vitals
- Abdominal exam

Investigations
- 72-hour fecal fat assessment, while on a high fat diet (*for steatorrhea*)
- Spot stool analysis
- Investigations are targeted to evaluate for causes of fat malabsorption

Management/Treatment
- Depends on underlying cause – e.g. replacement of pancreatic enzymes in CF
7.51 Carbohydrate Malabsorption

Typical Patient:
- See causes below

Cause
- Excess gastric acid (denaturation of amylase)
- Impaired production/secretion of pancreatic amylase – chronic pancreatitis; pancreatic duct obstruction (e.g. tumours, CF)
- Loss of enterocyte surface area or function (inflammatory disease (e.g. Crohn’s, celiac), chronic infections (SIBO), deposition diseases, intestinal lymphoma, small bowel resection or bypass)

Symptoms/Clinical Presentation
- Watery diarrhea (due to osmotic force)
- Crampy abdominal pain
- Bloating, flatulence

Physical Exam
- General appearance- low BMI, vitals
- Abdominal exam

Investigations
- Stool pH <6
- High 24-hr urine d-xylose following administration of 25g oral d-xylose
- High H$_2$ or $^{13}$CO$_2$ breath tests following ingestion of lactose, fructose...
- Lactose intolerance test

Management/Treatment
- Depends on the underlying cause of CHO malabsorption

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51 “Malabsorption”, Alaa Rostom, September 27 2016, uOttawa Faculty of Medicine
7.52 Pancreatic Insufficiency (PI)²

Typical Patient
- History of pancreatic damage (tumour, CF, pancreatitis, or otherwise)

Cause
- >80-90% loss of pancreatic cells
- Obstruction of pancreatic ducts (tumors, CF)
- Inactivation of pancreatic enzymes (ZES)

Signs/Symptoms
- Steatorrhea, diarrhea
- Abdominal pain, bloating
- Fatigue, weight loss
- Chronic, recurrent abdominal pain (chronic pancreatitis)
- B12 malabsorption (can’t cleave R protein in duodenum)

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Direct tests
  - Secretin stimulation challenge (gold standard)
  - Stool chymotrypsin, elastase (low in PI)
- Indirect tests
  - Fecal fat assessment (assess for malabsorption)
  - Imaging (MRI, MRCP)
  - Trial of pancreatic replacement enzymes

Treatment
- Low fat diet
- Exogenous pancreatic lipase
- Treat underlying cause of PI
  - Remove alcohol
  - ERCP and stent or lithotripsy if obstruction
  - Pancreaticojejunostomy if chronic obstruction
  - Surgery if obstructing pancreatic tumour

²“Malabsorption”, Alaa Rostom, September 27 2016, uOttawa Faculty of Medicine
Typical Patient
- 1.3:1 males to female
- More common in black population (~2x)
- Age >45 years

Risk Factors
- Elderly
- Diabetes Mellitus (DM) (usually within 2 years of cancer diagnosis)
- Smoking
- Chronic pancreatitis
- Hereditary pancreatitis
- Familial pancreatic cancer
- Hereditary cancers (pS3, BRCAZ, k-ras)
- Pancreatic cysts

Cause
- Loss of function mutation in a tumour suppressor gene or gain of function mutation in an oncogene

Signs/Symptoms
- Painless jaundice
- Pruritis (+/- scratchmarks)
- Malaise in epigastric area, which may radiate to back
- Scleral icterus
- Weight loss, anorexia
- Dark urine
- Thirsty/frequent urination (DM)

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Bloodwork (CBC, INR, electrolytes, AST, ALT, ALP, Tbil)
- Ultrasound abdomen
- CT abdomen – “double duct” sign
- MRI (if contraindications to use of CT)
- ERCP (mainly therapeutic for stent placement)
- Biopsy – for staging

Treatment
- Surgery (if resectable)
- ERCP (unresectable, stenting)
- +/- chemo, radiation
- Pancreatic enzymes
7.54 Biliary Tract Carcinoma

Typical Patient
- Older age
- Women (gallbladder cancer)
- Men (cholangiocarcinoma)

Risk Factors
- Gallbladder cancer: obesity, high carbohydrate intake, gallbladder polyps > 1 cm in size, porcelain gallbladder, anomalous pancreato-biliary ductal junction
- Cholangiocarcinoma: Primary sclerosing cholangitis, ulcerative colitis, intraductal stones, smoking
- Ampulla: Adenomas, especially villous type (e.g. FAP), AIDS

Cause
- Loss of function mutation in a tumour suppressor gene or gain of function mutation in an oncogene

Signs/Symptoms
- Jaundice (pale stool, tea-coloured urine, pruritus)
- Pain (less in cholangiocarcinoma)
- Hepatomegaly
- Lymphadenopathy
- Fatigue, malaise, weight loss
- Scleral icterus
- Occasionally: cholecystitis, cholangitis, pancreatitis, gastric outlet obstruction, diabetes, steatorrhea

Physical Exam
- General appearance (jaundice, icterus), vitals
- Lymph node exam (lymphadenopathy)
- Abdominal exam (hepatomegaly, palpable gallbladder, abdominal mass)

Investigations
- Bloodwork
  - LFTs – ALP, AST, ALT, GGT (increase ALP, GGT, increase AST/ALT)
  - Bilirubin, INR, albumin (elevated INR due to vitamin K deficiency)
  - Diabetes
  - CA-19 (tumor marker)
- Abdominal Ultrasound
- CT
- MRCP
- ERCP +/- duct brushing +/- stenting (therapeutic)
- EUS +/- FNA (for staging)
- PET (for staging)

Treatment
- Gallbladder: Laparoscopic cholecystectomy (or open if advanced)
- Pancreatobiliary (distal common bile duct, ampulla of vater, pancreatic)
  - Whipple (surgery)
  - Radiation/chemo if unresectable
  - Stents (for obstruction)
  - Narcotics, celiac-axis block for pain

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54 “Clinical Pathological Conference: Pancreatic and biliary tumours”, Harinder Dhaliwal, Goo Lee and Wael Shabana, September 30 2016, uOttawa Faculty of Medicine
7.55 Acute Hepatitis

Causes
- Hepatitis A, B, C, D, E
- CMV, EBV (mono), HSV
- Medications - tylenol
- Wilson’s disease
- Autoimmune hepatitis
- CBD stone
- Celiac disease
- Alpha-1 antitrypsin deficiency

Signs/Symptoms
- Nausea, anorexia, mild right upper quadrant discomfort
- Jaundice (rare), dark urine (rare)
- Low grade fever
- ALT very high (100s or 1000s)
7.56 Hepatitis A Virus (HAV) 56

Cause
- Fecal-oral spread

Typical Patient
- Military personnel
- Food handlers, common in travellers
- Healthcare/childcare/sanitation workers

Physical Exam
- General appearance (jaundice), vitals
- Abdominal exam

Investigations/Diagnosis
- Enzymes (ALT)
- Antibodies to HAV (IgM (acute) vs IgG (previous or immune))

Prevention
- Hep A vaccine

Treatment
- None – will clear on its own

56 “Acute and chronic liver disease – Part 1”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.57 Hepatitis B Virus (HBV)\textsuperscript{57}

Typical Patient/Risk Factors
- IVDU\textsuperscript{*}, immigrants\textsuperscript{*} from high-risk countries, hemodialysis patients, MSM, frequently transfused patients

Cause
- Mother-to-baby most common route of infection
- Transfusion, fluids (blood, semen), contamination needles (also common)

Physical Exam
- General appearance (jaundice), vitals
- Abdominal exam

Investigations/Diagnosis
- HBsAg, HBeAg, anti-HBC (IgM, IgG), anti-HBs, anti-HBe
- HBV DNA-gold standard test for infectivity

Indications for Treatment
- HBsAg positive, HBV DNA positive
- Persistent elevation of ALT
- Significant liver fibrosis (biopsy/fibroscan)
- Infected healthcare worker
- Complications: progression to HCC

Treatment
- Non-specific (avoid alcohol and hepatotoxic drugs)
- Immunize active and passive contacts – infants of infected moms, MSM, IVDU, travelers, hemodialysis patients, healthcare worker
- Antivirals (tenofovir, entecavir)
- Monitor for cirrhosis

\textsuperscript{57} “Clinical Pathological Conference: NASH, alcohol and other hepatitides - clinical portion”, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
Typical Patient/Risk factors
- IVDU, hemophiliacs, renal dialysis patient, MSM, endemic areas

Cause
- Injection with contaminated needles (*most common*)

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations/Diagnosis
- HCV antibody positive
- HCV RNA-PCR based assay
- Liver biopsy or fibroscan – determines degree of fibrosis
- ALT
- Specific signs: Hep C causes cryoglobulinemia/leukocytoclastic vasculitis, porphyria cutanea tarda

Indications for Treatment
- Age
- ALT -> 1.5x normal
- Significant fibrosis on biopsy/fibroscan
- Presence of associated conditions
- No current alcohol or drug abuse
- Note- if the patient also has cirrhosis or has an indication for transplant, this is sometimes done prior to treating the HepC

Treatment
- Pegylated interferon and fibavirin
- New antivirals (eg. Harvoni)
- Newest agent: Epclusa (sofosbuvir and velpatasvir)

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58 “Clinical Pathological Conference: NASH, alcohol and other hepatitides - clinical portion”, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
Typical Patient

- Chronic alcoholic

Cause

- Environmental (alcohol intake)
- Genetics

Sign/Symptoms

- Sudden jaundice
- Right upper quadrant pain
- Nausea, fever
- If cirrhosis
  - Spider nevi, palmar erythema
  - Edema
  - Ascites

Physical Exam

- General appearance, vitals
- Look for stigmata of chronic liver disease
- Abdominal exam

Investigations

- Bloodwork
  - Elevated total bilirubin, macrocytosis, increased WBC (PHNs), decreased platelets, decreased albumin
  - AST>ALT, but usually only mild-moderately elevated

Treatment

- Admit to hospital. Stop alcohol/nutritional support/thiamine/vitamins
- Look for infection (test for Hep B and C)
- Alcoholic hepatitis score: Maddrey discriminant function: Bilirubin and INR; > 32
  - If high treat with Prednisolone
- Liver transplant
7.60 Wilson’s Disease

Typical Patient
- Young patient at presentation (5-30 years) with a family history of Wilson’s disease

Cause
- Autosomal recessive genetic condition → Cu deposits in liver and basal ganglia

Signs/Symptoms
- Present at age 5-30 with neurology or hepatic disease
- May present as:
  - Abnormal LFTs
  - Fulminant hepatic failure
  - Chronic active hepatitis
  - Cirrhosis (less common)
- CNS features (e.g. Tremor, psychiatric abnormalities)

Physical Exam
- Eye exam including slit lamp
- Abdominal exam
- Neurological exam

Investigations
- Decreased ceruloplasmin in blood (Cu-binding protein)
- Increased urinary copper (do a 24-hr urine)
- Kayser-Fleisher Rings (slit lamp exam)

Treatment
- D-penicillamine (binds copper)

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60 “Acute and chronic liver disease – Part 2”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.61 Hereditary Hemochromatosis

Typical Patient
- Northern European

Cause
- Autosomal recessive disorder → excess iron absorption and deposition in several organs

Signs/Symptoms
- Hyperpigmented skin
- Arthritis (joint pain)
- Fatigue, weakness
- Hypopituitary symptoms- hypothyroidism etc.
- Abdominal pain

Physical Exam
- General appearance, vitals
- MSK exam
- Cardiovascular exam
- Abdominal exam

Investigations
- Serum transferrin saturation
- Serum ferritin
- Liver function tests
- MRI liver (quantify iron)
- Biopsy

Treatment/Management
- Phlebotomy
- Gene testing for family screening
- Screen for hepatoma every 6 months ONLY in cirrhotics

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61 “Acute and chronic liver disease – Part 2”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
3.62 Autoimmune Hepatitis

Typical Patient
- Young women or menopausal women

Signs/Symptoms
- Fatigue
- Jaundice
- Hepatomegaly
- Joint pain
- Skin rashes
- Spider angiomas

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Bloodwork
  - Increased AST, ALT, IgG
  - ANA positive in 80%
  - Anti-smooth muscle antibody
- Liver biopsy

Treatment
- Corticosteroids as first line (Prednisone)
- Add Azathioprine when stable with the plan of tapering off steroids

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62 "Acute and chronic liver disease – Part 2", Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.63 Primary Biliary Cirrhosis (PBC)\(^63\)

**Typical Patient**
- Middle-aged women

**Cause**
- Cell-mediated damage to small intrahepatic ductules

**Signs/Symptoms**
- Fatigue
- Hepatomegaly
- +/- pruritus
- Xanthomas
- Pigmentation
- Jaundice/Scleral icterus

**Physical Exam**
- General appearance, vitals
- Abdominal exam

**Investigations**
- Bloodwork
  - Increased alkaline phosphate
  - Positive anti-mitochondrial antibodies
  - Positive IgM

**Treatment**
- Ursodeoxycholic acid
- Liver transplant
- Cholestyramine for treatment of pruritus

\(^63\) “Acute and chronic liver disease – Part 2”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.64 Primary Sclerosing Cholangitis (PSC)\textsuperscript{64}

Typical Patient
- Male
- History of ulcerative colitis

Cause
- Autoimmune damage of medium size intra- and extra-hepatic bile ducts

Signs/Symptoms
- Fatigue
- Itching
- Pain in upper right part of abdomen
- Fever, chills, night sweats
- Hepatomegaly
- Jaundice

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Bloodwork – LFTs, Bili, ANCAs
- MRI of bile ducts (MRCP)
- Liver biopsy

Treatment
- No effective treatment
- ERCP dilatation of tight strictures
- Liver transplant in some cases

\textsuperscript{64} “Acute and chronic liver disease – Part 2”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.65 Budd-Chiari Syndrome

Typical Patient
- Patient with hypercoagulation

Cause
- Blockage of hepatic veins (thrombosis, or otherwise)

Signs/Symptoms
- Abdominal pain
- Acute onset ascites
- Hepatomegaly

Physical Exam
- Abdominal exam

Investigations
- Bloodwork
- US Liver Doppler
- MRI of blood vessels (MRA) or CT if Doppler is unclear

Treatment
- Anticoagulation
- +/- Tipps (shunt in liver)
- +/- liver transplant

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65 "Acute and chronic liver disease – Part 2", Linda Scully, October 4 2016, uOttawa Faculty of Medicine
7.66 Acetaminophen Overdose (Liver Toxicity)

Typical Patient/Risk Factors
- Substance abuse
- Underlying liver disease
- Certain medications (inc. ETOH)

Cause
- Ingestion of toxic levels of acetaminophen
  - Typical Dose to Cause Overdose
    - >250 mg/kg in single ingestion
    - >12 g over 24 hours

Signs/Symptoms
- Initially asymptomatic
- Nausea and vomiting, malaise
- Right upper quadrant pain
- Confusion → cerebral edema
- Bruising, bleeding (hematemesis)
- Dilated pupils
- Jaundice

Physical Exam
- General appearance, vitals
- Abdominal exam
- Neurological exam

Investigations
- Bloodwork
  - Increased INR
  - Increased Bilirubin
  - Increased creatinine
  - Hypoglycemia
  - ALT, AST > 1000
  - Tylenol levels
- Clinical history important for diagnosis

Treatment
- N-acetyl cysteine (NAC) (can use nomogram if single ingestion)
  - 100% hepatoprotective if given <8 hours post ingestion
- If severe damage and not responding to NAC, liver transplant

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66 “Clinical Pathological Conference: NASH, alcohol and other hepatitis - clinical portion”, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
7.67 Alcoholic Liver Disease (ALD)\textsuperscript{67,68}

- Dose-responsive relationship between amount of alcohol consumed and risk of ALD
- Women: <2 drinks/day, 10/week
- Men: <3 drinks/day, 15/week

Types of ALD
- Alcoholic fatty liver disease
- Alcoholic hepatitis
- Alcoholic cirrhosis

\textsuperscript{67} “Acute and chronic liver disease – Part 1”, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
\textsuperscript{68} “Clinical Pathological Conference: NASH, alcohol and other hepatitis - clinical portion”, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
**7.68 Alcoholic Steatohepatitis**

**Typical Patient**
- Chronic, heavy alcohol consumption

**Cause**
- Continued heavy alcohol consumption -> liver inflammation due to cytokines, oxidative stress

**Signs/Symptoms**
- Jaundice
- Anorexia
- Fever
- Tender hepatomegaly
- Confusion
- Possible ascites

**Physical Exam**
- General appearance, vitals
- Abdominal exam

**Investigations**
- Based on appropriate clinical history
- Bloodwork
  - AST>ALT (2:1 pattern)
  - Elevated GGT
  - Biopsy (although not required for diagnosis) – ballooned hepatocytes, Mallory neutrophils, fat droplets

**Treatment**
- General
  - Abstinence (from EtOH)
  - Treatment of alcohol withdrawal
  - Nutritional support – high calorie meals, thiamine
  - Surveillance for infection
  - Prevention of AKI
- Less evidence but could consider
  - Prednisolone
  - Pentoxifylline
  - NAC

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69 “Clinical Pathological Conference: NASH, alcohol and other hepatitides - clinical portion”, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
7.69 Non-Alcoholic Fatty Liver Disease\textsuperscript{70,71}

Typical Patient/Risk Factors
- Obese (69-100%); especially central obesity
- Diabetic (34-75%)
- Hyperlipidemic (20-80%)
- Bariatric surgery patients

Cause
- Unknown

Signs/Symptoms
- Often clinically silent disease with non-specific signs/symptoms
- Look for signs of cirrhosis

Physical Exam
- General appearance, vitals
- Abdominal exam

Investigations
- Bloodwork - liver enzymes, Bili, full workup to rule out other causes of increased LFTs
- Non-invasive testing - US
  - Fibroscan to look for cirrhosis and degree of inflammation
  - Can also consider CT, MRI, CAP
- Liver biopsy = gold standard

Treatment (NASH)
- First line
  - Lifestyle modification (weight loss, exercise)
  - Drug therapy of metabolic syndrome complications (dyslipidemia, HTN, diabetes)
- Second line
  - Pharmacotherapy (glitazones, vitamin E)
- Third line
  - Farnesoid X receptor agonists, GFT505, LOXL2

\textsuperscript{70} Acute and chronic liver disease – Part 1, Linda Scully, October 4 2016, uOttawa Faculty of Medicine
\textsuperscript{71} Clinical Pathological Conference: NASH, alcohol and other hepatitides - clinical portion, Cynthia Tsien, October 7 2016, uOttawa Faculty of Medicine
**7.70 Ascites**

**Typical Patient**
- See causes below

**Causes**
- 1 chronic liver disease (*most common cause*)
- Malignancy (ovarian, gastric)
- Heart failure
- TB

**Pathogenesis**
- Decreased albumin → decreased oncotic pressure → leakage of fluid into interstitium

**Signs/Symptoms**
- Bulging flanks
- Abdominal pain, discomfort
- Shortness of breath

**Physical Exam**
- General appearance, vitals
- Abdominal exam
- Stigmata of chronic liver disease
- Test for shifting dullness
- Fluid wave test
- Peripheral edema (most sensitive)

**Investigations**
- Paracentesis
  - Cell count, culture, gram stain, albumin, total protein pH
  - Glucose, LDH, amylase, gram stain, TB smear, cytology, TG
  - $[\text{Albumin}]_{\text{serum}} - [\text{Albumin}]_{\text{ascites}} = \text{serum-ascites albumin gradient}$
    - High > 11g/L
    - Low < 11 g/L
- US

**Treatment**
- Na restriction (<1.5g/d)
- Diuretics
  - Spironolactone +/- furosemide at 5:2 ratio
  - Stepwise increase as needed, to maximal doses
- Large volume paracentesis
- Refractory ascites: TIPS, liver transplant

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72 “Complications of Cirrhosis”, Linda Scully, October 7 2016, uOttawa Faculty of Medicine
7.71 Hepatic Encephalopathy

Typical Patient
- Hepatic failure
- Portosystemic shunting

Cause
- Buildup of ammonia in the brain, leading to reversible neuropsychiatric abnormalities
- Precipitants: Infection, excess protein, TIPS, surgery, sedatives, hypnotics, over-diuresis with diuretics, nonadherence to lactulose

Signs/Symptoms
- 1st sign is reversal of sleep wake cycle
- Asterixis
- Aggressive/hostile
- Mercaptan (sweet) smell
- Confusion
- Comatose, drowsy

Physical Exam
- General appearance, vitals
- Assess for asterixis
- Abdominal exam, including abdominal and peripheral stigmata of chronic liver disease
- Neurological exam

Investigations
- Number connection test, clock drawing, handwriting – micrographia
- Bloodwork – elevated ammonia- useful to do once, do not trend
- Abnormal EEG

Treatment
- Lactulose – a laxative, can be used multiple times daily to target 2-3 loose stools/day
- Rifaximin – antibiotic

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73 “Complications of Cirrhosis”, Linda Scully, October 7 2016, uOttawa Faculty of Medicine
7.2 Cirrhosis

Typical Patient
- See causes below

Causes
- Hepatitis A-E
- Alcoholic hepatitis
- Autoimmune hepatitis/liver disease (PSC, PBC)
- Genetic: Wilson’s, hemochromatosis, alpha-1-antitrypsin deficiency
- Non-alcoholic steatohepatitis
- Cryptogenic

Signs/Symptoms
- Jaundice, scleral icterus
- Palmar erythema
- Dupuytren’s contracture
- Leukonychia
- Bruising
- Ascites and peripheral edema
- Proximal muscle wasting
- Terry’s nails
- Gynecomastia, testicular atrophy
- Spider nevi, caput medusa
- Parotid (bilateral) enlargement and temporal muscle wasting

Physical Exam
- General appearance, vitals
- Inspection for stigmata of chronic liver disease
- Abdominal exam

Investigations
- LFTs
- INR, albumin, bilirubin
- CBC
  - Thrombocytopenia, neutropenia – splenic sequestration
  - Mild anemia and macrocytosis (due to alcohol)

Treatments
- Liver transplant is only curative option (allocated by meld score – INR, bilirubin, creatinine)
- Monitor for
  - Bleeding secondary to esophageal varices with EGD
  - HCC with q6month abdominal imaging- US or MRI
  - Hepatic encephalopathy- treat with lactulose or rifaxamin

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74 “Complications of Cirrhosis”, Linda Scully, October 7 2016, uOttawa Faculty of Medicine
Endocrinology
8.1 Type 1 Diabetes

Typical Patient
- Can occur at any age – 50% of new type 1 diabetes cases develop after age 30
- Peak age of diagnosis 14 years
- May present in ketoacidosis with symptoms of metabolic decompensation
- 0.4% of general population

Cause
- Autoimmune destruction of the insulin-producing β-cells of the pancreas
  - Insulin autoantibodies (IAA), tyrosine phosphatase-like protein (IA2), antibodies to glutamic acid decarboxylase (GAD), islet cell cytoplasm antibodies (ICA)
- Genetic susceptibility
  - Class II MHC antigens DR3 and/or DR4
  - Nonaspartic acid at position 57 of DQ-B chain
  - 5% if sibling affected, 4% if mother affected, 6% if father affected

Symptoms/Clinical Presentation
- 3 P’s: polyuria, polydipsia, polyphagia ± weight loss, fatigue
- Severe: ketoacidosis from inability to use CHO as energy source
- Risk of micro/macrovacular complications (see 8.3 and 8.4)

Physical Exam
- Blood pressure (BP), heart rate, weight
- Screen for micro/macrovacular complications

Diagnosis
- Hemoglobin A1c (reflects long-term glucose, not used for <18yo)
  - 6.0-6.4% – prediabetes
  - ≥6.5% – diabetes
- Fasting Plasma Glucose (FPG)
  - 6.1-6.9 mmol/L – impaired fasting glucose
  - ≥7.0 mmol/L – diabetes
- 75g Oral Glucose Tolerance Test (OGTT)
  - 7.8-11.0 mmol/L – impaired glucose tolerance
  - ≥11.1 mmol/L – diabetes
- Random Plasma Glucose (RPG)
  - ≥11.1 mmol/L – diabetes
- Further investigations to rule out micro/macrovacular complications

Management/Treatment
- Initial stabilization
  - Control hyperglycemia through insulin and diet
  - IV fluids not required unless in DKA
- Insulin and self-management – manage diet, activity, insulin levels
- Education
- Goals of therapy
  - Blood sugar control
  - Avoidance of complications
  - Optimize quality of life

1 “Introduction to Diabetes”, Erin Keely, October 11 2016, uOttawa Faculty of Medicine
8.2 Type 2 Diabetes

Typical Patient
- Metabolic syndrome: abdominal obesity, hypertension, high blood sugar, high triglycerides and low high-density lipoprotein levels

Cause
- Diabetes that ranges from insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance

Symptoms/Clinical Presentation
- May present with micro/macrovascular complications – eye changes, kidney disease, foot ulcers, heart attack, stroke
- Can present with polyuria and polydipsia
- Associated diseases:
  - Polycystic ovarian syndrome, acanthosis nigricans, obstructive sleep apnea, psychiatric disorders (bipolar disorder, depression, schizophrenia), HIV infection
- Drugs associated with diabetes:
  - Glucocorticoids
  - Atypical antipsychotics
  - Highly active antiretroviral therapy (HAART)

Physical Exam
- Blood pressure, heart rate, weight, waist circumference
- Screen for micro/macrovascular complications (see 8.3 and 8.4)

Diagnosis:
- Hemoglobin A1c (reflects long-term glucose, not used for <18yo)
  - 5.7-6.4% – prediabetes
  - ≥6.5% – diabetes
- Fasting Plasma Glucose (FPG)
  - 6.1-6.9 mmol/L – impaired fasting glucose
  - ≥7.0 mmol/L – diabetes
- 2h Postprandial Glucose
  - 7.8-11.0 mmol/L – impaired glucose tolerance
  - ≥11.1 mmol/L – diabetes
- Random Plasma Glucose (RPG)
  - ≥11.1 mmol/L – diabetes

Management/Treatment
- Lifestyle – diet and exercise
  - Dietary fibre, low glycemic index foods
- Oral agents
  - Biguanides (e.g. metformin), sulfonylureas (e.g. gliclazide), GLP-1 receptor agonists (e.g. liraglutide), DPP-4 inhibitors, SGLT2 inhibitors, α-glucosidase inhibitors
- Insulin
8.3 Microvascular Complications of Diabetes

Typical Patient
- Any patient with diabetes mellitus
- Screen at diagnosis for type 2 diabetes, and after five years with type 1 diabetes

Cause
- Clearly related to blood glucose, but also genetics
- Proposed pathways:
  - Aldose Reductase Pathway, Advanced Glycation Endproduct Pathway, Reactive Oxygen Intermediate Pathway, Protein Kinase C Pathway

Symptoms/Clinical Presentation
- Diabetic retinopathy
  - Nonproliferative Retinopathy
    - Microaneurysms, dot hemorrhages, exudates, retinal edema
  - Proliferative Retinopathy
    - Growth of new capillaries and fibrous tissue within the retina and into the vitreous chamber
- Diabetic nephropathy
  - Elevated urine albumin:creatinine ratio
- Diabetic neuropathy
  - Peripheral neuropathy: stocking-glove pattern (most common form) – longer nerves are especially vulnerable, hence impact on the foot
  - Autonomic neuropathy: can affect BP and pulse, GI activity, bladder function, erectile function

Physical Exam
- Direct fundoscopy
- 10g monofilament testing or 128-Hz vibration sense

Investigations
- Urine albumin:creatinine ratio (ACR) – need two of three positive tests (≥2 mg/mmol)
- Serum creatinine

Management/Treatment
- Diabetic retinopathy
  - Annual eye examination
  - Argon photocoagulation and focal treatment of new vessels reduce severe visual loss
  - Anti-VEGF or injection of bevacizumab (Avastin) can stop the growth of new blood vessels
- Diabetic nephropathy
  - Annual urine ACR, serum creatinine
  - Refer to Nephrology if chronic, progressive loss of kidney function, urine ACR persistently ≥60 mg/mmol, eGFR <30 mL/min, adverse effects of renal-protective therapies (e.g. ACE inhibitor or ARB), unable to achieve target BP
  - For end stage renal disease: hemodialysis and/or renal transplantation
- Diabetic neuropathy
  - Annual 10g monofilament exam
  - Consider nerve conduction studies to rule out other causes of neuropathy
  - Pain management for neuropathic pain

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3 “Acute Emergencies and Chronic Complications of Diabetes”, Amel Arnaout, October 13 2016, uOttawa Faculty of Medicine
8.4 Macrovascular Complications of Diabetes

**Typical patient:**
- Chronic type 1 or type 2 diabetes

**Cause**
- Not as clearly related to blood glucose
- Other risk factors
  - Hypertension
  - Elevated LDL-C
  - Hyperinsulinemia/insulin resistance
  - Hypercoagulable state
  - Smoking

**Symptoms/Clinical Presentation**
- Coronary artery disease
- Peripheral vascular disease
  - Ischemia of the lower extremities
- Cerebrovascular disease
- Ulcers

**Physical Exam and Investigations**
- Check all risk factors (metabolic syndrome)
  - Abdominal obesity: waist circumference >88 cm for F; >102 cm for M
  - Elevated blood pressure: >130 mmHg systolic and/or >85 mmHg diastolic
  - Elevated fasting plasma glucose: >5.6 mmol/L
  - High serum triglycerides: >1.7 mmol/L
  - Low HDL levels: <1.0 mmol/L in F; <1.3 mmol/L in M
- Cardiovascular examination
  - Carotid bruits
- Peripheral vascular examination
  - Pedal pulses
- Consider exercise ECG for typical or atypical cardiac symptoms (e.g. unexplained dyspnea, chest discomfort)

**Management/Treatment**
- Cardiovascular protection
  - Statin therapy for patients with diabetes, age ≥40 or age ≥30 with ≥15 years of diabetes, regardless of baseline LDL-C
  - Target LDL-C ≤2.0 mmol/L
- Peripheral vascular disease
  - Prevention of foot injury
  - Control of risk factors such as blood pressure, glucose levels, smoking cessation
  - Patients should be advised to seek immediate medical care if a diabetic foot ulcer develops

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4 “Acute Emergencies and Chronic Complications of Diabetes”, Amel Arnaout, October 13 2016, uOttawa Faculty of Medicine
8.5 Hypoglycemia

Typical Patient – Whipple’s Triad (requires all 3):
- Autonomic or neuroglycopenic symptoms
- Low plasma glucose level, <2.8 mmol/L (<4.0 mmol/L for patients treated with insulin or an insulin secretagogue)
- Symptoms responding to the administration of carbohydrate

Cause
- Non-diabetic
  - Insulin excess – insulinoma, postprandial hypoglycemia
  - Non-insulin mediated – adrenal insufficiency, severe liver disease, malignancy
  - Factitious – exogenous insulin, oral agents
- Diabetic
  - Excess insulin
  - Inadequate oral intake – illness (nausea/vomiting), gastroparesis
  - Exercise – increased insulin sensitivity, increased glucose utilization

Symptoms/Clinical Presentation
- Adrenergic
  - Diaphoresis, tremor, palpitations, anxiety, hunger, paresthesias
- Neuroglycopenic
  - Cognitive impairment, psychomotor abnormalities, visual changes, seizure, coma
- Hypoglycemic unawareness
  - Lack of symptoms despite hypoglycemia

Physical Exam
- N/A

Investigations
- Mixed meal test – check critical sample following ingestion of meal that usually brings on symptoms
  - Critical sample: serum glucose, insulin, c-peptide, β-hydroxybutyrate – can help determine cause

Management/Treatment
- Mild-moderate hypoglycemia: 15g carbohydrate choices (glucose tablets, table sugar dissolved in water, juice or soft drink, Life Savers, honey)
- Postprandial hypoglycemia: dietician consult, small frequent meals, well-balanced diet, avoid/limit high glycemic index foods
- Insulinoma: surgical resection

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5 “Hypoglycemia Cases”, Irena Druce, October 13 2016, uOttawa Faculty of Medicine
8.6 Hyperosmolar Hyperglycemic State (HHS)\textsuperscript{6}

Typical Patient
- Type 2 diabetes

Cause
- Stressor – ↑insulin resistance
- Relative insulin deficiency
- ↑glucose production, ↓utilization
  - ↓renal excretion of glucose (2\textsuperscript{nd} to renal disease, aging kidneys)
    - Unable to undergo osmotic diuresis: can’t get rid of glucose through urine, therefore very hyperglycemic

Symptoms/Clinical Presentation
- Severe hyperglycemia
- Dehydration
- Serum hyperosmolality
- Lack of significant ketosis
  - It takes less insulin to prevent ketosis than it does to stop hyperglycemia
  - If there is some insulin around, ketosis will not occur

Physical Exam
- Look for any signs of dehydration
  - Orthostatic hypotension and tachycardia
  - Supine tachycardia
  - Dry mucous membranes

Investigations
- Hyperglycemia
- Serum creatinine, $\beta$-hydroxybutyrate

Management/Treatment
- Correct serum osmolality
  - IV fluids
- Decrease blood glucose
  - Blood sugar should fall in response to fluid repletion
- Correct hypernatremia
  - If Na>155 mmol/L, start 0.45% NS as initial fluid
- Insulin
  - Insulin infusion if persistent hyperglycemia after fluid repletion

\textsuperscript{6} “Acute Emergencies and Chronic Complications of Diabetes”, Amel Arnaout, October 13 2016, uOttawa Faculty of Medicine
8.7 Diabetic Ketoacidosis

Typical Patient
- Type 1 diabetes

Cause
- Insulin deficiency → Decreased peripheral glucose utilization → Increased glucose production →
  Increased ketogenesis → Increased lipolysis in adipocytes → Increase FFAs for ketone production →
  Increased glycerol for gluconeogenesis
- Excess counter-regulatory hormones

Symptoms/Clinical Presentation
- Symptoms of metabolic decompensation (polyuria, polydipsia, weight loss, fatigue)
- Metabolic acidosis with compensatory respiratory alkalosis

Physical Exam
- Features of volume depletion
- Clinical features of lactic acidosis: marked hyperventilation, mental confusion

Investigations
- Anion gap metabolic acidosis
  - Anion gap >12
  - pH ≤ 7.3
  - Bicarbonate <18 (can use venous blood gas (VBG))
- Positive serum β-hydroxybutyrate
  - Urine ketones may be absent in early stages
- Hyperglycemia
  - Usually ≥ 14 mmol/L but can be lower or normal (younger patients and/or SGLT2 inhibitor use)

Management/Treatment
- Main goals:
  - Replace volume loss
  - Stop ketone production
  - Replace K+ loss
  - Correct acidosis
- Fluid:
  - Normal saline (NS) if glucose >15 mmol/L
  - Will need to replace between 1-4 L
  - CHANGE TO D5/NS WHEN GLUCOSE DROPS <15 mmol/L
- Potassium:
  - Start when K is 4.0-5.5 in serum - 20 mmol/L in replacement fluid
  - IF <3.3 mmol/L, REPLACE K BEFORE STARTING INSULIN
- Insulin:
  - Infusion 0.1 units/kg/hour
  - Capillary blood glucose q1h, VBG and electrolytes q2-4h
  - Adjust IV insulin rate and IV fluids based on investigations
  - DO NOT STOP INSULIN INFUSION UNTIL ACIDOSIS/ANION GAP CORRECTED
- Bicarbonate:
  - Can consider giving sodium bicarbonate if pH <7.0

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7 “Acute Emergencies and Chronic Complications of Diabetes”, Amel Arnaout, October 13 2016, uOttawa Faculty of Medicine
8.8 Familial Hypercholesterolemia

Typical Patient
- MI <60 yo
- Prevalence: 1 in 260-500

Cause
- Autosomal dominant: LDLR – 93%, ApoB, PCSK9 (gain of function)
- Autosomal recessive: LDLRAP1

Symptoms/Clinical Presentation
- Early coronary artery disease
- Tendon xanthomata (yellow deposits of cholesterol-rich fat on the tendons)
  - Particularly in the Achilles and patellar tendons and in the extensor tendons of the hands
- Corneal arcus (yellow deposits of cholesterol-rich fat in the outer margin of the iris)
- Xanthelasma (yellow deposits of cholesterol-rich fat on the eyelids)

Physical Exam
- As above

Investigations
- Very high LDL-C
- Genetic testing for LDL receptor mutations and ApoB mutations

Management/Treatment
- Diet and lifestyle
- Statin
- Ezetimibe
- Bile acid sequestrant
- PCSK9 inhibitor
8.9 Familial Dysbetalipoproteinemia

Typical Patient
- N/A

Cause
- Mutation in ApoE – most common is ε2/ε2 (wild type is ε3/ε3)
- Cys→Arg mutation at 158 on ε3 + one additional factor (“second hit”)
- Decreased uptake of chylomicrons and VLDL-C from liver resulting in increased uptake by macrophages in peripheral tissue

Symptoms/Clinical Presentation
- Tubero-eruptive xanthomas
  - Tend to occur on extensor surfaces, especially elbows and knees
- Xanthoma striata palmaris
- Premature CAD, PVD

Physical Exam
- See above

Investigations
- High triglycerides, high LDL-C

Management/Treatment
- Manage diet
  - Reduced intake of cholesterol, fat and alcohol
- Treat secondary causes
8.10 Familial Combined Hypercholesterolemia¹⁰

Typical Patient
- 1 in 100, most common lipid disorder

Cause
- Unknown
- Autosomal dominant

Symptoms/Clinical Presentation
- Family history of lipid disorders, early MI history

Physical Exam
- N/A

Investigations
- High triglycerides and high LDL-C, low HDL-C

Management/Treatment
- Treat secondary causes
- Lifestyle
- Statin
  - Can add ezetimibe, fenofibrate, bile acid sequestrant if needed

¹⁰ “Introduction to Lipoprotein Metabolism and Genetic Disorders of Lipoprotein Metabolism”, Ruth McPherson, October 17 2016, uOttawa Faculty of Medicine
8.11 Chylomicronemia Syndrome

Typical Patient
- N/A

Cause
- Lipoprotein lipase (LPL) deficiency, Apo CII deficiency – autosomal recessive
- Medical conditions – uncontrolled diabetes
- Majority are unknown

Symptoms/Clinical Presentation
- Recurrent pancreatitis
  - Watch out for symptoms, such as: N/V, sweating, pain in upper abdomen or pain radiating to the back
  - Risk of pancreatitis increases in pregnancy and lactation or during the administration of estrogenic steroids
- Eruptive xanthomas
- Hepatosplenomegaly
- Lipemia retinalis

Physical Exam
- As above

Investigations
- Very high triglycerides
- Cream layer (lipemic serum)

Management/Treatment
- Goal: maintain triglycerides <10 mmol/L
- Diet and lifestyle
  - Low in fat, low in simple carbohydrates (intake of fat should be <10% of total calories)
  - Consult with dietician regarding use of Medium Chain Triglyceride (MCT) oil
- Lipid-lowering drugs
  - Fibrates
  - Statins
8.12 Hypothyroidism

**Typical Patient**
- More common in women
- Often have family history of hypothyroidism

**Cause**
- Chronic autoimmune thyroiditis (Hashimoto’s) – most common cause in developed world
- Iodine deficiency
- Other: medications, thyroidectomy, central hypothyroidism (pituitary disorder)

**Symptoms/Clinical Presentation**
- Impairment of growth and development in infants
- CNS deficits (intellectual impairment, tiredness, depression, psychosis, slow mentation)
- Muscle/nerve deficits (weakness, cramps, delayed tendon reflexes)
- Cardiovascular symptoms (bradycardia, cardiomegaly, pericardial effusion, hypertension)
- Cold intolerance, dry/coarse/thick/pale skin, puffiness of face and body, coarse/brittle hair or hair loss, enlarged tongue, hoarseness, hemorrhagia, constipation, hyperlipidemia

**Physical Exam**
- Inspection for clinical signs of hypothyroidism
- Palpation of the thyroid gland for nodules or goiters

**Investigations**
- Thyroid stimulating hormone (TSH) - most sensitive marker
- Consider free T4 only if suspecting central hypothyroidism
- Choosing Wisely Canada recommendations:
  - Do NOT use Free T4 or T3 to screen for hypothyroidism or to monitor and adjust levothyroxine (T4) dose in patients with known primary hypothyroidism
  - Do NOT order thyroid ultrasound unless palpable abnormality of the thyroid
  - Do NOT routinely test for Anti-Thyroid Peroxidase Antibodies (anti-TPO)

**Management/Treatment**
- Levothyroxine (synthetic T4)
  - Initiate treatment if TSH is >10 mU/L, or if TSH elevated and patient has symptoms of hypothyroidism

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12 "Thyroid Disorders: Hyper and Hypothyroidism", Amel Arnaout, October 28 2016, uOttawa Faculty of Medicine
8.13 Hyperthyroidism

Typical Patient
- More common in women
- Often seen in patients with a family history of thyroid problems (i.e. Graves’ disease) or other autoimmune diseases

Cause
- Graves’ disease
- Autonomous thyroid nodule(s)
- Thyroiditis
- Excess exogenous levothyroxine

Symptoms/Clinical Presentation
- Anxiety, heat intolerance, insomnia, diaphoresis, diarrhea
- Restlessness, warm/moist skin, tremor, proximal muscle weakness
- Rare: dermopathy, onycholysis, periodic paralysis

Physical Exam
- Inspection for clinical signs of hyperthyroidism
- Palpation of the thyroid gland for nodules or goiters
- Auscultate the thyroid gland for bruits (pathognomonic for Graves’ disease)

Investigations
- TSH
- Free T4
- Free T3
- Thyroid uptake and scan

Management/Treatment
- Dependent on cause
- Anti-thyroid drugs (e.g. methimazole, propylthiouracil), radioactive iodine, surgery

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13 “Thyroid Disorders: Hyper and Hypothyroidism” by Amel Arnaout, October 28 2016, uOttawa Faculty of Medicine
8.14 Hashimoto’s Thyroiditis

Typical Patient
- More common in women
- More likely to affect people between the ages of 30 and 50
- Often seen in patients with other autoimmune diseases
- May have family history of thyroid diseases

Cause
- Antibodies react to thyroid peroxidase (TPO) enzyme resulting in autoimmune destruction and lymphocytic infiltration into the thyroid gland
- Leads to fibrosis and destruction of the thyroid gland

Symptoms/Clinical Presentation
- Commonly no local symptoms
- Goiter may be present
- Clinical features of hypothyroidism

Physical Exam
- Inspection for clinical signs of hypothyroidism
- Palpation of the thyroid gland for goiter

Investigations
- TSH

Management/Treatment
- Levothyroxine

14 “Thyroid Physiology”, Amel Arnaout, October 25 2016, uOttawa Faculty of Medicine
8.15 Graves' Disease

Typical Patient
- More common in women than men (4:1)
- Often seen in patients younger than 40 years of age
- Often seen in patients with other autoimmune diseases
- May have family history of thyroid diseases
- May have history of emotional or physical stress

Cause
- Antibody-mediated autoimmune reaction to TSH receptor

Symptoms/Clinical Presentation
- Clinical symptoms of hyperthyroidism
- Ophthalmopathy (periorbital swelling, lid retraction, lid lag, proptosis, edema, conjunctival chemosis, ophthalmoplegia) – often bilateral
- Pretibial myxedema

Physical Exam
- Inspection for clinical signs of hyperthyroidism
- Inspection for ophthalmopathy and pretibial myxedema
- Palpate thyroid gland for diffuse enlargement
- Auscultate thyroid gland for bruit

Investigations
- TSH
- Free T4
- Free T3
- Thyroid uptake and scan

Management/Treatment
- Anti-thyroid drugs (e.g. methimazole, propylthiouracil)
- Radioactive iodine
- Subtotal thyroidectomy

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15 “Thyroid Physiology”, Amel Arnaout, October 25 2016, uOttawa Faculty of Medicine
8.16 Thyroiditis

**Typical Patient**
- More common in women than men
- Often seen in patients with other autoimmune diseases
- May have family history of thyroid diseases

**Cause**
- Inflammation of the thyroid causing release of pre-formed thyroid hormone

**Symptoms/Clinical Presentation**
- Patients may describe viral prodrome followed by neck pain and/or tenderness
- 3 phases:
  - Hyperthyroidism
  - Hypothyroidism
  - Recovery phase

**Physical Exam**
- Inspection for clinical signs of hyperthyroidism or hypothyroidism
- Palpate thyroid gland for pain or tenderness

**Investigations**
- TSH
- Free T4
- Free T3
- Thyroid uptake and scan if diagnosis unclear

**Management/Treatment**
- For pain: NSAID or prednisone
- Beta-blocker for hyperthyroid symptoms
- Follow serial thyroid function tests (e.g. q6-8 weeks) to ensure resolution

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16 “Thyroid Physiology”, Amel Arnaout, October 25 2016, uOttawa Faculty of Medicine
**8.17 Thyroid Nodular Disease**

**Typical Patient**
- More common in women than men

**Cause**
- 95% of all thyroid nodules are benign
- Cyst, colloid nodule, benign neoplasm
- Papillary carcinoma
- Granulomatous thyroiditis, infections, follicular/medullary/anaplastic carcinoma, metastatic lymphoma (uncommon)

**Symptoms/Clinical Presentation**
- Asymptomatic
- 5% of the general population have a palpable thyroid nodule
- Compressive symptoms (dysphagia, dysphonia, dyspnea when supine)
- If autonomous thyroid nodule, may present with clinical symptoms of hyperthyroidism

**Physical Exam**
- Inspect for clinical signs of hyperthyroidism
- Palpate the thyroid gland for nodules and cervical lymph nodes

**Investigations**
- TSH
- Ultrasound if TSH is normal or high
  - Fine needle aspiration biopsy of nodule depending on presence of suspicious features
- Thyroid uptake and scan if TSH is low

**Management/Treatment**
- Low-risk nodules: observation
- High-risk nodules: refer to Otolaryngology for surgical opinion
- Anti-thyroid drugs, radioactive iodine, surgery (toxic nodule)
8.18 Thyroid Cancer

Typical Patient
- More common in women than men
- More likely to be malignant in men than women
- May have family history of thyroid cancer

Cause
- Generally unknown
- May be linked to radiation exposure to the neck (e.g. treatment of lymphoma)

Symptoms/Clinical Presentation
- Lump/swelling in neck (most common symptom)
- Pain in neck and ears, dysphagia, trouble breathing, hoarse voice

Physical Exam
- Inspection for clinical signs of hyperthyroidism
- Palpate the thyroid gland for nodules
- Physical findings correlated to high risk of malignancy:
  - Size >4cm
  - Male
  - Age between 20 to 60 years
  - Rapid growth of tumour
  - Presence of lymphadenopathy, hoarse voice, voice changes, or vocal cord paralysis
  - Mass is fixed and does not move with swallowing

Investigations
- TSH
- thyroglobulin
- Ultrasound
  - High-risk of malignancy if:
    - Irregular margins
    - Microcalcifications
    - Taller than wide
    - Extrathyroidal extension
  - Intermediate-risk of malignancy if:
    - Hypoechoic
  - Multiple features confer higher risk
- Decision for fine needle aspiration biopsy can be guided by Cancer Care Ontario
- If medullary thyroid cancer: serum calcitonin, genetic screening of family (autosomal dominant)

Management/Treatment
- Thyroidectomy (lobectomy, hemithyroidectomy, total thyroidectomy)
  - ± post-thyroidectomy if considered high risk
- Levothyroxine – aim for TSH suppression
- Regular follow-up with endocrinologist (follow serum thyroglobulin levels, anti-thyroglobulin antibodies, surveillance ultrasounds)

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18 “Thyroid Cancer”, Self Learning Module, Heather Lochnan, uOttawa Faculty of Medicine
8.19 Thyroid Storm

Typical Patient
- Patients with hyperthyroidism who have recently experienced trauma, surgery, severe emotional distress, stroke, diabetic ketoacidosis, congestive heart failure, pulmonary embolism
- Most common in patients with Graves' Disease

Cause
- Life-threatening condition associated with under-treated hyperthyroidism, resulting in decompensation of end organs

Symptoms/Clinical Presentation
- Hyperpyrexia, tachycardia, cardiac dysrhythmia
- Dehydration and dry skin, restlessness, anxiety, delirium
- Goiter with or without exophthalmos
- Stupor, coma, shock
- Systolic hypertension, widened pulse pressure
- GI effects (diarrhea, nausea, vomiting)

Physical Exam
- Measure vital signs (heart rate, respiratory rate, temperature, blood pressure) and level of consciousness
- Inspection for clinical signs of hyperthyroidism

Investigations
- TSH, T4, T3
- Leukocytosis
- Calcium levels
- AST, ALT, ALP, LDH, CK

Management/Treatment
- ABCs, cardiac monitor – usually need ICU
- Lower temperature (e.g. cooling blanket)
- Beta-blockers
- Anti-thyroid medications
- Hydrocortisone
- Super saturated potassium iodide (SSKI)
- Plasmapheresis
- Thyroidectomy if refractory to above
- Treat precipitating event

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19 “Thyroid Disorders: Hyper and Hypothyroidism”, Amel Arnaout, October 28 2016, uOttawa Faculty of Medicine
8.20 Hypercalcemia

Typical Patient
- Women >50 years of age

Cause
- Parathyroid hormone (PTH)-dependent: e.g. primary hyperparathyroidism
- PTH-independent: e.g. hypercalcemia of malignancy, medications (thiazides)

Symptoms/Clinical Presentation
- Weakness
- Hypertension, valve and arterial calcifications
- Constipation, anorexia, nausea, vomiting, pancreatitis
- Kidney stones, renal insufficiency, nephrogenic diabetes insipidus (rare)
- Bone pain
- Altered mental status

Physical Exam
- Measure blood pressure to detect hypertension
- Inspection for nervous system findings (confusion, hypotonia, hyporeflexia, paresis, coma)
- Inspection for signs of renal failure
- Inspection for fecal impaction, pancreatitis
- Inspection for band keratopathy
- Auscultate for arrhythmias

Investigations
- Serum calcium, albumin, phosphate, magnesium, PTH, creatinine, alkaline phosphatase (ALP)
- Ionized serum calcium if STAT result needed (severe hypercalcemia requiring admission to hospital)

Management/Treatment of Acute Hypercalcemia
- IV fluids
- Furosemide (if volume overloaded)
- Bisphosphonates – onset of action 48-72 hr
- Calcitonin – tachyphylaxis seen within 1-2 days
- Steroids – if granulomatous disease is the cause
- Calcium sensing receptor antagonist (for primary hyperparathyroidism)
- Dialysis if refractory to above
8.21 Primary Hyperparathyroidism

Typical Patient
- More common in women than men (present in 2-3% of post-menopausal women)

Cause
- Excessive PTH secretion leading to increased bone resorption and increased reabsorption of calcium from the kidneys
- Caused by:
  - Solitary adenoma
  - Primary hyperplasia
  - Parathyroid carcinoma

Symptoms/Clinical Presentation
- Muscle weakness, lethargy, fatigue, depression
- Kidney stones, frequent urination, abdominal pain, nausea, vomiting, confusion, impaired memory, constipation, bone thinning and fractures

Physical Exam
- Generally unremarkable
- Examine for muscle weakness and depression

Investigations
- For diagnosis: PTH (can be high or normal), serum calcium, albumin, phosphate, 24-hour urine calcium
- For surgical planning: parathyroid scan (negative test does not rule out primary hyperparathyroidism), thyroid ultrasound
- Bone density scan

Management/Treatment
- Parathyroidectomy
- Medical therapy (i.e. bisphosphonates, cinacalcet) as bridge to surgery
8.22 Malignancy-associated Hypercalcemia

**Typical Patient**
- Most commonly seen in patients with breast cancer, lung cancer, renal cell carcinoma, lymphomas, and multiple myeloma (rare in colon, gastric, and thyroid carcinoma)
- Most common cause of hypercalcemia in hospitalized patients

**Cause**
- Secondary to humoral effects of increased tumour-derived factors (i.e. parathyroid hormone-related protein in most cases)
- Lymphomas may also be associated with increased vitamin D levels

**Symptoms/Clinical Presentation**
- Clinical symptoms of hypercalcemia

**Physical Exam**
- Weakness
- Hypertension, valve and arterial calcifications
- Constipation, anorexia, nausea, vomiting, pancreatitis
- Kidney stones, nephrogenic diabetes insipidus, renal insufficiency
- Bone pain
- Altered mental status

**Investigations**
- PTH, serum calcium, albumin, phosphonate, magnesium
- ALP
- Imaging (e.g. CT) to look for malignancy if not previously diagnosed

**Management/Treatment**
- Treat the primary tumour
- Treatment of acute hypercalcemia (see 8.20)
8.23 Hypocalcemia\textsuperscript{23}

Typical Patient
- Post-thyroid or parathyroid surgery (75% of cases)
- Patients with a vitamin D or magnesium deficiency
- Patients with a history of GI disorders, pancreatitis, kidney failure, liver failure, or anxiety disorders

Cause
- Hypoparathyroidism
- Severe vitamin D deficiency
- Drug-induced (calcitonin, furosemide)
- Pseudohypoparathyroidism

Symptoms/Clinical Presentation
- Paresthesia
- Laryngospasm
- Seizures
- Carpopedal spasm
- Hyperreflexia
- Mental status changes

Physical Exam
- Neurological exam for paresthesia and hyperreflexia
- Chvostek’s sign and Trousseau’s sign
- Psych evaluation for mental status changes

Investigations
- Serum calcium, albumin, PTH, magnesium, ALP
- Serum 25-OH vitamin D

Management/Treatment
- Manage ABCs
- Replenish calcium levels (calcium gluconate IV, oral calcium administration)
- Treat hypomagnesemia if present
- May require vitamin D supplementation including calcitriol
- Correct any underlying causes

\textsuperscript{23} “Calcium Metabolism”, Dora Liu, October 25 2016, uOttawa Faculty of Medicine
8.24 Osteoporosis

Typical Patient
- Will be experienced by 1 in three women and 1 in five men (lifetime risk)
- Commonly seen in patients ≥65 yo
- Previous history of falls and fractures

Cause
- Primary osteoporosis: metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to bone fragility
- Secondary osteoporosis: a result of a variety of chronic conditions/medication use/nutritional deficiencies leading to bone mineral loss
- Osteogenesis imperfecta: genetic disorder characterized by excessively fragile bones that are prone to fracture
- Idiopathic juvenile osteoporosis: unknown pathophysiology

Symptoms/Clinical Presentation
- Asymptomatic
- Fragility fractures (low-energy or non-traumatic, e.g. fall from standing height)
- Height loss – 2/3 of vertebral fractures are asymptomatic

Physical Exam
- Weight under 51 kg
- Tooth count <20
- Rib-pelvis length <2 finger breadths
- Wall-occiput distance >0 cm
- Self-reported hump back

Investigations
- DEXA (dual energy X-ray absorptiometry)
- Calcium (corrected for albumin), CBC, creatinine, ALP, TSH, SPEP (if vertebral fractures present), vitamin D (after 3-4 months of supplements)

Management/Treatment
- Low risk: lifestyle interventions
- Moderate risk: lifestyle interventions with pharmacological treatment depending on patient preference or if other significant risk factors are present
- High risk: lifestyle interventions and pharmacological treatment
- For post-menopausal women:
  - 1st line pharmacotherapy – Alendronate/Risendronate/Zoledronic acid (bisphosphonates), Denosumab (RANK ligand inhibitor), Raloxifene (SERM)
  - If vasomotor symptoms present – hormone replacement therapy
  - If intolerant of 1st line treatment – Etidronate, potentially Teriparatide
- For men:
  - 1st line pharmacotherapy – Alendronate, Risendronate, Zoledronic acid, Denosumab
  - NOT recommended to take testosterone
- Surgical intervention – vertebroplasty (for acute, painful vertebral fractures within 6 weeks)
8.25 Pituitary Masses

Typical Patient
- Variable depending on cause of pituitary mass

Cause
- Pituitary adenomas
- Craniopharyngiomas
- Meningiomas
- Gliomas
- Metastatic lesions
- Aneurysms

Symptoms/Clinical Presentation
- Headache
- Bitemporal hemianopsia (superior compression of optic chiasm)
- Cranial nerve palsies (lateral compression of cavernous sinus)
- Rhinorrhea (inferior compression of sphenoid sinus)
- If functional pituitary adenoma, can also see symptoms of Cushing’s disease, hyperprolactinemia (galactorrhea, impaired sexual function), acromegaly, hyperthyroidism (TSHomas are rare)

Physical Exam
- Neurological exam for clinical symptoms – visual fields by confrontation, CNs III-VI

Investigations
- Serum cortisol, electrolytes, follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, insulin-like growth factor 1 (IGF-1), testosterone/estradiol, TSH, free T4 – best done at 8am
- If hypercortisolemia suspected - dexamethasone suppression test, 24-hour urine free cortisol
- Visual fields – if large mass with suspected optic chiasm involvement
- MRI

Management/Treatment
- Prolactinomas: dopamine agonist therapy
- Surgery (especially if there is compression of the optic chiasm)
- Radiation (if contraindications to surgery exist)
- Post-op treatment with hormone replacement if surgery causes hypopituitarism

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25 “Physiology of the Hypothalamic/Pituitary Axis (HPA)”, Erin Keely, October 31 2016, uOttawa Faculty of Medicine
Typical Patient
- Variable depending on cause
- Can be seen in patients with genetic syndromes (e.g. MEN1, MEN4, McCune-Albright Syndrome)

Cause
- Tumours – pituitary adenoma, craniopharyngioma, pituitary apoplexy
- Granulomas – sarcoid, TB, syphilis
- Vascular – postpartum necrosis (Sheehan’s disease), carotid aneurysm
- Traumatic – stalk section, radiation
- Infiltration – hemochromatosis, amyloid, histiocytosis
- Autoimmune
- Empty sella syndrome
- Congenital deficiencies
- Hypothalamic disease

Symptoms/Clinical Presentation
- Reduced levels of circulating hormones correlate with clinical findings as follows:
  - CRH/ACTH – adrenal insufficiency
  - GnRH/LH/FSH – delayed puberty, decreased libido, impotence, body hair changes, eunuchoidal habitus, azospermia,amenorrhea, infertility
  - TRH/TSH – hypothyroidism
  - GHRH/GH – short stature, pale skin tone, decreased muscle mass, fine wrinkled skin, lowered energy levels
  - Prolactin – failure to lactate post-partum
  - Oxytocin – no clinical effects
  - ADH – diabetes insipidus

Physical Exam
- Inspection for clinical signs indicative of specific hormone deficiencies

Investigations
- Biochemical: measure anterior pituitary and target organ hormones, or stimulation studies (e.g. ACTH stimulation test, arginine stimulation test)
- MRI of sella

Management/Treatment
- Replace pituitary hormone or target organ product
  - ACTH – cortisol
  - GH – GH
  - TSH – thyroid hormone
  - LH/FSH – testosterone or estrogen
  - ADH – DDAVP

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26 “Pituitary and Adrenal Disorder Cases”, Stephanie Dizon, November 1 2016, uOttawa Faculty of Medicine
8.27 Hypersecretion of the Pituitary

Typical Patient
- Variable depending on cause
- Can be seen in patients with genetic syndromes (e.g. MEN1, MEN4, McCune-Albright Syndrome)

Cause
- Functioning pituitary adenoma
- Decrease in normal inhibitory factors
- Excess stimulation (e.g. stress, drugs)
- Ectopic production of stimulatory factors or hormone itself
- Decrease in clearance of active hormone (e.g. chronic renal failure)

Symptoms/Clinical Presentation
- Prolactin – galactorrhea, infertility, amenorrhea, impotence, libido changes
- GH – acromegaly, gigantism
- ACTH – Cushing’s syndrome
- TSH (rare) – hyperthyroidism

Physical Exam
- Inspection for clinical signs indicative of specific hormone excess

Investigations
- Biochemical (baseline hormone measurements, suppressive tests)
- MRI of sella

Management/Treatment
- Treat underlying cause
- 3 options for pituitary adenoma:
  - Medical (e.g. Bromocriptine, Cabergoline) – may prevent growth in non-prolactinomas
  - Radiation
  - Surgery
- For prolactinoma
  - Dopamine agonist therapy
  - Surgery usually not required unless significant mass effect
- For acromegaly:
  - Surgical, medical (e.g. Somatostatin, Cabergoline, Pegvisomant), radiation

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27 “Pituitary and Adrenal Disorder Cases”, Stephanie Dizon, November 1 2016, uOttawa Faculty of Medicine
8.28 Cushing’s Syndrome

**Typical Patient**
- High blood pressure
- Obesity
- Diabetes
- Osteoporosis
- Virilization syndrome (hirsutism) with menstrual disorders

**Cause**
- Constellation of symptoms and signs that result from excessive glucocorticoid action
- Causes can be:
  - ACTH-dependent (pituitary Cushing’s disease, ectopic ACTH syndrome, ectopic CRH syndrome)
  - ACTH-independent (adenoma, carcinoma, adrenal hyperplasia, glucocorticoid administration)
- Pituitary (Cushing’s disease) is most common endogenous cause of hypercortisolism

**Symptoms/Clinical Presentation**
- Fat redistribution/weight gain
- Metabolic effects (diabetes, hypertension, hypokalemia)
- Catabolic effects (thinning of skin, easy bruising, abdominal striae, poor wound healing, osteoporosis, proximal myopathy, limb asthenia)

**Physical Exam**
- Supraclavicular fat pad
- Dorsal fat pad (buffalo hump)
- Moon facies, facial plethora
- Check vitals for hypertension
- Inspect for brittle skin, bruises, abdominal striae
- Physical exam for osteoporosis

**Investigations**
- Step 1 – screening test to document hypercortisolism (24-hour urinary free cortisol, overnight dexamethasone suppression test, plasma cortisol for diurnal rhythm)
- Step 2 – determine cause of hypercortisolism (plasma ACTH and DHEA-S, high dose dexamethasone suppression test, inferior petrosal sinus sampling)
- Step 3 – imaging (MRI of pituitary, CT of adrenals, image the site of ectopic ACTH production)

**Management/Treatment**
- Pituitary ACTH-dependent: trans-sphenoidal resection of tumour, bilateral adrenalectomy, radiotherapy, medical therapy (adrenal enzyme inhibitors, ACTH suppressors, glucocorticoid receptor antagonists)
- Adrenal Cushing’s syndrome: surgical resection of adrenal tumour, radiotherapy, adrenal enzyme blockers, Mitotane
- Ectopic ACTH syndrome: treatment of primary tumour, adrenal enzyme blockers, Mitotane, bilateral adrenalectomy
8.29 Primary Adrenal Insufficiency

**Typical Patient**
- Patients with cancer, tuberculosis, or autoimmune diseases (e.g. type 1 diabetes, Graves’)
- Patients who are on anticoagulants
- Patients who have had previous surgeries to remove any part of their adrenal gland

**Cause**
- Autoimmune (Addison’s disease)
- Tuberculosis
- Acute adrenal infarction
- Adrenalectomy
- Medications – prolonged steroid use, opioids
- Others (viral, adrenal hemorrhage, metastases, infiltrative disorders)

**Symptoms/Clinical Presentation**
- Hyperpigmentation (nail beds, palmar crease, mouth, skin)
- Nausea and vomiting, fatigue, hypotension, hypoglycemia
- Hyponatremia, hyperkalemia

**Physical Exam**
- Vitals
- Hyperpigmentation

**Investigations**
- Sodium
- Potassium
- Cortisol
- ACTH
- ACTH stimulation test

**Management/Treatment**
- Glucocorticoids (hydrocortisone, cortisone acetate, prednisone, dexamethasone)
- Mineralocorticoids (fludrocortisone) – if primary adrenal insufficiency
- Prevention of adrenal crisis (increase dosage when under stress)
- Ensure patient wears medic alert bracelet

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29 “Adrenal Disorders”, Erin Keely, November 1 2016, uOttawa Faculty of Medicine
8.30 Congenital Adrenal Hyperplasia

Typical Patient
- Often seen in patients whose parents both have congenital adrenal hyperplasia or are both carriers of the genetic defect for the disorder
- More prevalent in Ashkenazi Jews, Hispanics, Italians, Yugoslavians, and Yupik Inuits

Cause
- Group of autosomal recessive disorders resulting from deficiency of one of the 5 enzymes required for steroidogenesis
- Leads to decreased negative feedback inhibition of cortisol on pituitary ACTH secretion
- This results in deficient synthesis of cortisol (and sometimes aldosterone) as well as excess secretion of precursors
- 21-hydroxylase deficiency (90% of all cases of CAH) – cortisol deficiency leads to high ACTH, leading to overproduction of adrenal androgens and resultant virilization
- 2/3 of patients also have mineralocorticoid deficiency
- 11-hydroxylase deficiency – similar to 21-hydroxylase deficiency, but with increased risk of hypertension due to accumulation of 11-deoxycorticosterone (weak mineralocorticosteroid)
- p450 deficiency and 3B-hydroxysteroid dehydrogenase deficiency – death in utero

Symptoms/Clinical Presentation
- Common symptoms: compromised final adult height, osteoporosis, obesity, decreased fertility, changes in sexual function, hyperinsulinemia

Physical Exam
- Measure vitals to check for hypertension
- Inspection for clinical signs such as hyperpigmentation, dehydration, signs of virilization/ambiguous genitalia in females (fusion of labioscrotal folds)
- Precocious development of pubic hair/phallic enlargement/accelerated growth and skeletal maturation in males

Investigations
- Sodium
- Potassium
- 21-hydroxylase deficiency – measure serum 17-alpha-hydroxyprogesterone (precursor)

Management/Treatment
- Replace glucocorticoids and potentially mineralocorticoids as well
- Suppress ACTH and androgen production

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30 “Adrenal Disorders”, Erin Keely, November 1 2016, uOttawa Faculty of Medicine
8.31 Primary Aldosteronism (Conn’s Syndrome)\textsuperscript{31}

Typical Patient
- Higher prevalence in persons of African origin
- More common in women than men, particularly those aged 30-50
- Leading cause of secondary hypertension

Cause
- Caused by adrenal aldosterone-producing adenoma or hyperplasia leading to a high aldosterone-to-renin ratio (ARR)

Symptoms/Clinical Presentation
- Hypertension
- Hypokalemia
- Metabolic alkalosis
- Suppressed plasma renin activity
- High and non-suppressible plasma aldosterone
- Normal plasma and urine cortisol

Physical Exam
- Measure vitals to check for hypertension
- Inspection of abdominal distention
- GI exam to determine if presence of ileus from hypokalemia
- Strength test to determine if muscle weakness is present

Investigations
- Serum electrolytes, renin, aldosterone
- If high ARR, can confirm with saline infusion test
- Anti-hypertensive medications can affect ARR
- Imaging (CT or MRI of adrenals, iodo-cholesterol scan, selective venous sampling of blood for aldosterone measurement)

Management/Treatment
- Aldosterone-producing adenoma: surgical resection may decrease need for anti-hypertensives
- Bilateral adrenal hyperplasia: aldosterone receptor antagonist (e.g. spironolactone, Eplerenone)

\textsuperscript{31} "Adrenal Disorders", Erin Keely, November 1 2016, uOttawa Faculty of Medicine
8.32 Adrenocortical Tumours\textsuperscript{32,33}

**Typical Patient**
- Often discovered incidentally – adrenal incidentaloma incidence increases with age (7% above age 70)
- Can be seen in patients with rare genetic syndromes (e.g. LiFraumeni, Von Hippel-Lindau, MEN1/MEN2, Beckwith-Wiedemann syndrome)

**Cause**
- Functional – Cushing’s syndrome, Conn’s syndrome, hyperandrogenism syndromes
- Non-functional – many are discovered incidentally
- 90% of adrenal incidentalomas are benign and non-functional

**Symptoms/Clinical Presentation**
- Often asymptomatic
- Abdominal pain and mass
- Weight loss, weakness, fever
- Altered mental status
- Lymphadenopathy, hepatomegaly
- Hypertension
- Endocrine manifestations

<table>
<thead>
<tr>
<th>Function</th>
<th>Symptoms</th>
<th>Screening Labs</th>
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<tbody>
<tr>
<td>Non-secreting (90%)</td>
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<tr>
<td>Cushing’s syndrome (5%)</td>
<td>Truncal obesity, easy bruising</td>
<td>24-hr urine free cortisol</td>
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<td></td>
<td>Hypertension, diabetes</td>
<td>1 mg dexamethasone suppression test</td>
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<tr>
<td>Pheochromocytoma (5%)</td>
<td>Can be asymptomatic hypertensive,</td>
<td>24-hr urine metanephrines</td>
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<td>diaphoresis, palpitations,</td>
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<tr>
<td></td>
<td>headaches</td>
<td></td>
</tr>
<tr>
<td>Primary aldosteronism (1%)</td>
<td>Hypokalemia</td>
<td>Serum renin and aldosterone</td>
</tr>
</tbody>
</table>

**Malignant**
- Malignant (3%)
- Primary versus Metastasis
- Can be functional
- CT adrenal

<table>
<thead>
<tr>
<th>Physical Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure vitals for hypertension and fever</td>
</tr>
<tr>
<td>GI exam for abdominal mass/pain</td>
</tr>
<tr>
<td>Lymph node exam</td>
</tr>
<tr>
<td>Strength test to detect muscle weakness</td>
</tr>
</tbody>
</table>

**Investigations**
- Dexamethasone suppression test
- 24-hour urine metanephrines
- Serum electrolytes, renin, aldosterone if hypertensive
- CT adrenals

**Management/Treatment**
- Surgery
- Radiation
- Chemotherapy

\textsuperscript{32} “Adrenal Disorders”, Erin Keely, November 1 2016, uOttawa Faculty of Medicine

8.33 Pheochromocytoma

Typical Patient
- Common in early to middle adulthood
- Often genetically inherited
- Patients may have other genetic conditions (e.g. Von Hippel-Lindau disease, neurofibromatosis type 1, MEN2)

Cause
- Tumour of chromaffin cells leading to excess production of catecholamines

Symptoms/Clinical Presentation
- Hypertension
- Sweating, tachycardia, arrhythmia, pallor, weight loss
- Headaches, palpitations, nervousness, nausea and vomiting, chest and abdomen pain

Physical Exam
- Measure vitals for hypertension and heart rate
- Inspection for diaphoresis and pallor

Investigations
- Biochemical – 24-hour urine metanephrines/normetanephrines, serum catecholamines
- Localization – CT adrenals; metaiodobenzylguanidine (MIBG) scan (i.e. nuclear imaging) if extra-renal source suspected

Management/Treatment
- Alpha-adrenergic receptor blockade
- Beta-adrenergic receptor blockade
- Surgery
- Post-operative treatment

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34 “Adrenal Disorders”, Erin Keely, November 1 2016, uOttawa Faculty of Medicine
8.34 Multiple Endocrine Neoplasia Syndrome 1 (MEN1)\textsuperscript{35}

**Typical Patient**
- Age of onset of endocrine tumours is usually in teenage years, but symptoms may not appear until the fourth decade of life
- Cutaneous tumours may appear in teenage years

**Cause**
- Mutation of tumour suppression gene MEN1 on chromosome band 11q13
- Mutations in both alleles are required for tumour formation

**Symptoms/Clinical Presentation**
- Hyperparathyroidism and hypercalcemia
- Pancreatic neuroendocrine tumours
- Pituitary adenomas (galactorrhea, acromegaly, Cushing’s syndrome, mass effect of tumour)

**Physical Exam**
- Inspection for clinical symptoms of hypercalcemia, galactorrhea, Cushing’s, etc.
- Neurological exam to determine presence of mass effect

**Investigations**
- Hyperparathyroidism: serum calcium, PTH, 24-hour urinary calcium, neck ultrasound, parathyroid scan
- Pancreatic neuroendocrine tumours: fasting hormone levels (for islet cell tumours), MRI, endoscopic ultrasound
- Pituitary adenomas: electrolytes, serum prolactin, morning cortisol levels, morning GH levels, LH, FSH, IGF-1, testosterone, 24-hour urinary free cortisol, glucose loading tests (for acromegaly), MRI

**Management/Treatment**
- Hyperparathyroidism: surgical removal of parathyroid tissue
- Pancreatic neuroendocrine tumours: surgical resection, surveillance, chemotherapy
- Pituitary adenomas: medication for prolactinoma, surgical resection for other hormone over-producing adenomas or mass effect tumours
- Screening post-diagnosis
  - Annual fasting gastrin, pancreatic polypeptide, calcium PTH
  - Periodic prolactin/pituitary hormones
  - Periodic MRI/CT of abdomen/chest/pituitary

\textsuperscript{35} “Multiple Endocrine Neoplasia”, Self Learning Module, Claire Gavin, uOttawa Faculty of Medicine
8.35 Multiple Endocrine Neoplasia Syndrome 2 (MEN2)\textsuperscript{36}

Typical Patient
- May have family history of MEN2
- No difference in prevalence between genders or race

Cause
- Autosomal dominant RET gene mutations
- MEN2A cardinal features – medullary thyroid cancer, pheochromocytoma, parathyroid tumours
- MEN2B cardinal features – medullary thyroid cancer, pheochromocytoma, mucosal neuromas, marfanoid habitus, and ganglioneuromas

Symptoms/Clinical Presentation
- Medullary thyroid cancer – thyroid mass, neck pain, calcitonin-related diarrhea, raised calcitonin
- Pheochromocytoma/ganglioneuroma
- Parathyroid tumours (2A)

Physical Exam
- Thyroid exam for mass/pain

Investigations
- Calcitonin levels
- Thyroid biopsy and ultrasound
- 24-hour urine metanephrines
- CT adrenals
- MIBG scan if extra-adrenal pheochromocytoma suspected

Management/Treatment
- Medullary thyroid cancer: surgical thyroidectomy and central lymph node dissection, treatment with tyrosine-kinase inhibitors (if there is metastasis), follow up with calcitonin levels
- Pheochromocytoma/ganglioneuroma: surgical resection, alpha- and beta-adrenergic blockade
- Parathyroid tumours: surgical resection
- Screening
  - Periodic assessment for pheochromocytoma and hyperparathyroidism (2A)
  - Genetic testing

\textsuperscript{36} “Multiple Endocrine Neoplasia”, Self Learning Module, Claire Gavin, uOttawa Faculty of Medicine
9.1 Approach to Antenatal and Postpartum Care\textsuperscript{1,2}

**Preconception Care**
- Gather full obstetrical history
- Determine maternal factors for high risk pregnancy and reduce risk/optimize:
  - Medical conditions: diabetes, hypertension, cardiac disease, renal disease, anemia, thyroid disease
  - Obesity or low body weight
  - Grand multipara (>5 pregnancies)
  - Social factors: substance abuse, smoking, domestic abuse, financial insecurity, housing, mental health
  - Infectious diseases and immunization: gonorrhea, chlamydia, HIV, syphilis, hepatitis B, tuberculosis, lacking varicella and rubella immunity
  - Occupational exposure: radiation, pathogens such as parvovirus B19, physical demands
  - Inherited disorders: thalassemia, sickle cell
  - Pelvic anatomical factors
  - Family history of genetic diseases
  - History of stillbirth, neonatal death, premature delivery
  - Advanced maternal age (>35 years old)
  - In vitro fertilization pregnancy
  - Multiple gestation
  - Rh immunization
- Medication adjustments (e.g., valproic acid)
- Optional genetic counselling
- Folate: dose in accordance with risk (0.4-4 mg/day); take 2-3 months before conception and during pregnancy
- Multivitamins: take 2-3 months before conception and during pregnancy

**Antenatal Care**
- Ontario Antenatal Record 1 and 2 used to document prenatal visits
- First visit: establish gestational age using Naegele’s rule (EDD = LMP + 1yr – 3mo + 7d) or the pregnancy wheel
- First trimester (weeks 0-12 gestation)
  - Prenatal visit every 4 weeks
  - Physical exam:
    - Blood pressure
    - Body mass index
    - Heart sounds
    - Thyroid exam
    - Breast exam
    - Pelvic exam (Hegar’s sign, Chadwick’s sign, uterus size, herpes)
    - Peripheral vascular exam
    - Fetal heart rate
  - Routine testing:
    - Hemoglobin and MCV
    - ABO, Rh, and antibody screen
    - Rubella immunity
    - HBsAg, HIV, and VDRL
    - Pap smear, if needed
    - *N. gonorrhoeae*, *C. trachomatis*, *Trichomonas vaginalis*, bacterial vaginosis
    - Urine culture & stain
    - Sickle cell and hemoglobin electrophoresis in high risk populations

\textsuperscript{1} “Antenatal Care and Prenatal Screening”, Daisy Moores, November 16 2016, uOttawa Faculty of Medicine
\textsuperscript{2} “Postpartum et Allaitement”, Steve Ballou, November 25 2016, uOttawa Faculty of Medicine
Screening for birth defects (see below)

Dating ultrasound (5-12 weeks gestation)

**Second trimester (weeks 12-24 gestation)**
- Prenatal visit every 4 weeks
- History: bleeding, rupture of membranes, fetal movement, contractions
- Physical exam:
  - Blood pressure
  - Body weight
  - Fetal heart rate
  - Fetal lie
  - Symphyseal fundal height
- Routine testing:
  - 24-28 weeks gestation: Hemoglobin, ABO, Rh, and antibody screen
  - 24-28 weeks gestation: gestational diabetes screen
  - Urine protein
- Screening for birth defects (see below)

**Third trimester (weeks 24 gestation to delivery)**
- Prenatal visit every 2 weeks from 28-36 gestation, then every week until delivery
- History and physical exam (same as second trimester)
- Group B Streptococcus testing at 35-37 weeks gestational age ± intrapartum antibiotics
- Screening for birth defects
  - Non-invasive screening
    - Integrated prenatal screening if presented by 11-14 weeks gestation
      - Part 1: ultrasound + pregnancy-associated plasma protein
      - Part 2: Free βHCG, Alpha-fetoprotein (AFP), unconjugated estriol
    - Maternal serum screening if presented by 15-20 weeks gestation
  - Invasive screening (if tested positive in any of the above screens)
    - Chorionic villus sampling (11-13 weeks gestation)
    - Amniocentesis (15-22 weeks gestation)

**Immunization:**
- Get influenza vaccines
- Avoid live vaccines

**Nutrition**
- Extra 300 kcal per day
- Adequate iron, calcium, vitamin D, omega 3 and 6 fatty acids
- Avoid uncooked and unpasteurized foods

**Exercise:** 30 min aerobic activity 3-5 times weekly (depends on pre-conception baseline)

**Medications:** Tylenol and antihistamines are preferred instead of non-steroidal anti-inflammatories

**Mental health**

**Postpartum Care**

**Mother:**
- Uterine involution
- Lochia rubra, lochia serosa, and lochia alba
- Perineal tears
- Vital signs
- Laboratory investigations

**Neonate:**
- APGAR scale (appearance, pulse, grimace, activity, respirations)
- Anticipate the need for neonatal resuscitation
- Newborn full physical exam
- Skin-to-skin
- Newborn medications: vitamin K, ophthalmic erythromycin

**Breastfeeding:**
- Educate on many benefits and on technique (position, latch, following baby’s feeding schedule)
- Colostrum is the first breast milk production that is filled with antibodies
9.2 Polyps

Typical Patient
- Pre- and post-menopausal women

Cause
- Hyperplastic overgrowth of endometrial glands and stroma around a hypervascular core
- Sessile or pedunculated structure
- One of the most common causes for abnormal genital bleeding in both pre- and post-menopausal women

Risk Factors
- Tamoxifen, obesity, hormone replacement therapy

Risk Factors for Malignancy (~5% of polyps)
- Polyp size >1.5cm, Tamoxifen use, post-menopausal

Symptoms/Clinical Presentation
- Abnormal uterine bleeding – regular cycle with intermenstrual bleeding
- Can be single, multiple, various sizes, and may be asymptomatic

Physical Exam
- Pelvic exam

Investigations
- Transvaginal sonography
- Saline infusion sonohysterography

Management/Treatment
- If symptomatic: excise all cases
- If asymptomatic: decision to excise depends on the likelihood of malignancy of the polyp and whether it is indicated due to infertility
  - Pre-menopausal women:
    - Polyp > 1.5 cm diameter
    - Multiple polyps
    - Polyp prolapsing through cervix
    - Infertility
    - Risk factors for endometrial cancer (see section 5.4)
  - Post-menopausal women:
    - All polyps are removed

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3 “Abnormal Uterine Bleeding”, Olga Bougie, November 8 2016, uOttawa Faculty of Medicine
9.3 Adenomyosis and Endometriosis\(^4,5\)

Typical Patient
- Women aged 40-50 years (although newer reports suggest they may also be the cause of some chronic pelvic pain and dysmenorrhea in younger reproductive-age women)

Cause
- Ectopic endometrial glands and stroma within the myometrium (uterine musculature) that induce hypertrophy and hyperplasia of surrounding myometrium, resulting in a diffusely enlarged uterus or focal nodules (adenomyomas)
- Develop during reproductive years and regress after menopause
- Pathogenesis is not fully understood

Risk factor
- Parity, Age, Tamoxifen therapy

Symptoms/Clinical Presentation
- Abnormal uterine bleeding – regular cycle with heavy bleeding
- Dysmenorrhea (painful menses)
- Chronic pelvic pain
- Enlarged globular uterus
- May be asymptomatic

Physical Exam
- Pelvic exam: enlarged globular uterus, that may be tender

Investigations
- Magnetic resonance imaging
- Transvaginal sonography
- Definitive diagnosis on histopathology following hysterectomy (preoperative diagnosis made clinically)
- Pathognomonic feature is the presence of endometrial tissue within the myometrium

Management/Treatment
- Definitive treatment is hysterectomy, which is the treatment of choice for women who have completed childbearing or who have significant symptoms
- Hormonal options (for women who wish to remain fertile):
  - Progestin therapy (e.g., Levonorgestrel-releasing intrauterine device)
  - Gonadotropin releasing hormone analogs
  - aromatase inhibitors
  - Oral combined hormonal contraceptives (albeit there is a lack of consensus on their efficacy)
  - \(N.B.,\) Symptoms return within 6 months after cessation.
- Conservative surgical options (for women who wish to remain fertile):
  - Endometrial ablation or resection
  - Laparoscopic myometrial electrocoagulation
  - Excision of adenomyosis
  - Uterine artery embolization

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\(^4\) "Abnormal Uterine Bleeding", Olga Bougie, November 8 2016, uOttawa Faculty of Medicine

9.4 Leiomyoma (Fibroids or Myomas)⁶

Cause
- Benign, well-circumscribed monoclonal tumors arising from smooth muscle cells of the myometrium
- Most common pelvic tumor in women
- Occur during reproductive years and regress after menopause

Classification
- Intramural myomas
- Submucosal myomas: types 0 (completely intracavity), I (<50% invading uterine wall), and II (>50% invading uterine wall)
- Subserosal myomas
- Cervical myomas

Risk Factors
- African American ethnicity (2 to 3 times more common, occur earlier, and fibroids are larger)
- Increased number of menses:
  - Early menarche (<10 years old)
  - Nulliparity
  - Frequent menses/shorter cycles
- Others – hypertension, family history of fibroids, diabetes
- Age 40-50 years

Symptoms/Clinical Presentation
- Abnormal uterine bleeding – regular cycle with heavy bleeding
- Pelvic pain or pressure/heaviness (bulk-related symptoms)
- Reproductive dysfunction (infertility or adverse pregnancy outcomes)
- The majority are asymptomatic

Physical Exam
- Pelvic exam: may find an asymmetrically enlarged yet mobile uterus on bimanual exam, or a prolapsed submucosal fibroid or change in cervical contour on speculum exam

Investigations
- Transvaginal ultrasound
- Sonohysterography (Saline infusion sonography)
- Diagnostic hysteroscopy
- Endometrial biopsy in women aged >40 years with abnormal uterine bleeding to rule out malignancy
- Magnetic resonance imaging occasionally for preoperative planning

Management/Treatment
- Prophylactic therapy is not recommended, unless it is a large submucosal myoma in a woman planning a pregnancy, or the fibroid is causing urethral compression with moderate to severe hydronephrosis
- Expectant / non-interventional
- Hormonal therapies: combined hormonal contraceptives, Levonorgestrel–releasing intrauterine device (Mirena®), progestin injections (Depo-Provera®) or pills (Micronor®), gonadotropin-releasing hormone agonists (Lupron ®), selective progesterone receptor modulators (ulipristal acetate)
- Surgical options: uterine artery embolization, myomectomy (preserves fertility), hysterectomy

⁶ “Abnormal Uterine Bleeding”, Olga Bougie, Nov 8 2016, uOttawa Faculty of Medicine
9.5 Endometrial Hyperplasia and Carcinoma

Causes
- Chronic estrogen stimulation unopposed by progesterone

Pathology and Progression
- Proliferation of endometrial glands that may progress to or coexist with endometrial carcinoma
  - Simple hyperplasia without atypia: increased number of glands
  - Complex hyperplasia without atypia: greater thickness than simple hyperplasia, but cells appear histologically normal
  - Simple atypical hyperplasia: cells with nuclear atypia that line glands that are separated by significant amounts of normal stroma
  - Complex atypical hyperplasia: crowding of glands lined with atypical cells
  - Carcinoma: congruent glands with loss of stroma

Risk Factors
- Age >40 years
- BMI >30
- Nulliparity
- Polycystic ovarian syndrome (PCOS)
- Diabetes
- Hereditary nonpolyposis colorectal cancer
- Early menarche, late menopause
- Tamoxifen / unopposed estrogen therapy
- Family history of breast, colon, or gynecological cancer
- Estrogen secreting tumour

Symptoms/Clinical Presentation
- Abnormal uterine bleeding – irregular/unpredictable cycle

Physical Exam
- Pelvic exam

Investigations
- Transvaginal sonography to exclude another etiology of abnormal uterine bleeding
- Diagnosed by histology of endometrial biopsy
  - Indications for endometrial biopsy: Age >40 years, risk factors listed above, failure of medical treatment, or significant intermenstrual bleeding

Management/Treatment
- Atypical hyperplasia:
  - Treatment of choice for women not planning a future pregnancy is hysterectomy
  - High dose progestin therapy for pre-menopausal women who wish to preserve their fertility
- Carcinoma: staging and total hysterectomy

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7 “Abnormal Uterine Bleeding”, Olga Bougie, November 8 2016, uOttawa Faculty of Medicine
9.6 Cervical Cancer

Typical Patient
- Women aged 20-49 years

Cause
- Invasive carcinoma arising in the cervical transformation zone that takes ~10 years to develop from dysplasia
- Persistent infection with human papillomavirus (HPV) causes >90% of cases, and the most common high risk oncogenic types are HPV-16 and HPV-18
- Cytological types: squamous cell carcinoma (>95% of cases), adenocarcinoma, and other rare types (small cell carcinoma, clear cell carcinoma)

Risk Factors
- Risks for HPV infection:
  - High number of sexual partners
  - Early age at onset of sexual intercourse
  - Number of partners of the male sexual partner
  - Sexual partners who are HPV carriers
- Co-factors for neoplastic transformation:
  - Smoking and second-hand smoke exposure
  - Use of oral contraceptives >5 years
  - >5 full-term pregnancies
  - Poor diet
  - Immunosuppression

Symptoms/Clinical Presentation
- Asymptomatic in early stages
- Vaginal bleeding (irregular, postcoital, or postmenopausal)
- Pelvic or back pain

Physical Exam
- Pelvic exam (visual inspection of cervix for friability, changes in colour or contour)

Investigations
- Pap test* for cervical cytology *Decision-making
- If indicated based on Pap test results, colposcopy for cervical biopsy (loop electrosurgical excision or cone)
- If indicated, imaging for treatment decisions

Management/Treatment
- Therapeutic options depend on pathology
- Surgery: trachelectomy or hysterectomy, ± lymphadenectomy
- Further treatment options: radiotherapy, chemoradiation, chemotherapy

Prevention
- The use of condoms and safe sex practices
- Regular Pap testing as per Screening Guidelines Ontario
- Vaccination against HPV ideally before sexual intercourse onset: Gardasil® or Cervarix®
9.7 Benign Breast Disease

Palpable lump
- Physical examination benign
  - Smooth, round, mobile, rubbery
- Physical examination malignant
  - Hard, irregular, non-mobile at times, fixed to skin or pectoralis muscle, less well-defined borders
- History
  - Age at menarche and menopause, birth control pill use, hormone use, history of breast cancer in the family, parity, age of first live birth, previous biopsies and investigations
- Investigations
  - Mammography: first line women ages >35; Ultrasound: first line women <35, second line women >35; MRI: use if dense breast and high suspicion
  - Aspiration or biopsy
- Management/Treatment
  - Close observation (usually every 3 to 6 months for 2 years and then back to regular screening)
  - Surgical excision

Clinical Presentation/Investigations/Treatment
- Fibroadenoma – most common benign neoplasm
  - Age 15-30
  - Palpable lump or on imaging, size > 5cm
  - Mammography with calcification
  - Treatment: observe, biopsy, U/S follow-up, excise if diagnostics uncertain or severe symptoms
- Papilloma – benign neoplasm
  - Located close to areola (size < 1cm)
  - Bloody nipple discharge
  - 2 types: 1) Solitary – more common: age 60-70, large, central papilloma, nipple discharge, can be a mass or intracystic
  - 2) Multiple: age 40-50 (younger), micropapilloma, more peripheral, less nipple discharge
  - Investigation: U/S
  - Treatment: terminal duct excision
- Mastitis +/- abscess
  - Hot, red, hard, tender breast, fever (Staph. aureus)
  - Treatment: Cephalexin or Erythromycin/Clavulin or Erythromycin + Flagyl, breastfeed/pump, warm compress, repeated aspiration, percutaneous drainage, NSAID for pain and swelling
- Breast abscesses peripheral non-lactational
  - Diabetes, rheumatoid arthritis, immunocompromised, usually pre-menopausal
  - Mammogram once resolved
- Granulomatous mastitis
  - Young, Asian, within 5 years pregnancy, non-smoker
  - Treatment: steroids helpful, spontaneously resolve
- Peri-areolar infection (Zuska disease) – breast abscess
  - Young female around age 32, smokers, periductal mastitis, mammary duct fistula
  - Treatment: ensure no underlying DCIS or other pathology with mammogram and ultrasound
- Fibrocystic breast disease
  - Age 40-59
  - 60-90% of breasts but 10% present clinically
  - Pre-menstrual cyclic mastalgia
  - Breast changes: become firm with palpable nodule
  - Mammography: dense breast tissue

9“Benign Breast Disease”, Susan J. Robertson and Erin Cordeiro, November 22 2016, uOttawa Faculty of Medicine
• Breast cysts – non-proliferative
  o Age 40-49
  o 25% of masses overall; risk of developing more than one during lifetime
  o Complex cysts: can be associated with mass
  o Simple cysts: aspirate if symptomatic
  o Treatment: aspirate, excise, observe
• Sclerosing adenosis: proliferative (no atypia, benign)
  o Increasing number of small terminal ductules or acini
  o Small calcifications; mass
  o Treatment: excise
• Fat necrosis
  o Causes: trauma, surgery, radiation. Can be spontaneous
  o Induration, skin retraction, can be cystic or calcified
• Phyllodes tumours (rare)
  o High risk: women > 40, larger than 4cm, history of recent growth
  o Treatment: core biopsy to triage for the next step - watch, excise, or excise with wider margin
• Gynecomastia
  o Affects 25 to 64 % of males
  o Associated with certain medications
    ■ Ranitidine, Omeprazole, Amiodarone, Digoxin, Spironolactone, anabolic steroids, Domperidone, marijuana
  o Associated with certain medical conditions
    ■ Obesity, hyperthyroidism, liver cirrhosis, chronic renal failure, Klinefelter syndrome
9.8 Breast Cancer

Causes
- Pre-invasive cancer: Lobular Carcinoma in Situ – LCIS, Ductal Carcinoma in Situ – DCIS
- Invasive cancer: Invasive ductal carcinoma (most common), Invasive lobular carcinoma

Symptoms/Clinical Presentation
- Ductal Carcinoma in Situ - DCIS
  - Mass, often non-palpable; present radiologically and include calcifications
- Paget’s disease
  - Eczema of the nipple, bloody discharge, itchiness of the nipple
  - If palpable mass, likely invasive; if not palpable likely DCIS
- Invasive cancer
  - Painless mass or via screening; irregular rather than round, hard; palpable axillary nodes
  - Non-mobile or causing distortion or nipple inversion or skin changes including dimpling or peau d’orange.
  - Rare case inflammatory carcinoma swollen red thickened skin, rapidly progressing
- Inflammatory breast cancer
  - Erythema, edema, warmth, peau d’orange

Investigations/Management/Treatment
- Mammogram; Compression views; US and biopsy; BiRADS; Breast MRI
  - Invasive lobular carcinoma: difficult to see on mammogram – Indication for MRI
- Lobular Carcinoma in Situ - LCIS
  - Localized: lumpectomy + radiation
  - Widespread: mastectomy with or without reconstruction, no radiation
  - Axilla: no sentinel node biopsy unless mastectomy due to 15% upgrade risk to cancer or UOQ lesion – technical considerations
  - When LCIS on biopsy for an imaging abnormality: if discordant, excisional biopsy
- Paget’s disease
  - Steroid cream; needs follow up, if it doesn’t improve, requires punch biopsy
  - Mammogram and US:
    - If negative, MRI to ensure no associated lesion (DCIS or invasive)
    - If associated lesion, treat as an invasive cancer or DCIS
- Early stage breast cancer
  - Breast: lumpectomy + radiation, mastectomy with or without reconstruction
  - Axilla (non-palpable nodes): sentinel node biopsy
- Locally advanced breast cancer
  - Tumour greater than 5cm; inflammatory breast cancer; many nodes positive and palpable
  - Breast: lumpectomy + radiation (small tumour, multiple nodes positive
  - Axilla: palpable nodes - axillary dissection (level I and II); non-palpable nodes - sentinel node biopsy
  - Unresectable cancer: neoadjuvant chemotherapy for downstaging of disease to make surgery possible
- Inflammatory breast cancer
  - Always chemo first. If no response – 2nd line chemo; If no response – radiation
  - In responders: total mastectomy and axillary dissection with no reconstruction
- Adjuvant radiation: all lumpectomies and if mastectomy, 4 or more nodes positive or tumour ≥ 5 cm
- Adjuvant chemotherapy: node positive, HER2-positive (≥5mm-1cm), Triple Negative (≥5mm-1cm), patients under 40 years-old (relative)

10. “Breast Cancer”, Susan J. Robertson and Erin Cordeiro, November 22 2016, uOttawa Faculty of Medicine
9.9 Ovulatory Dysfunction

Cause
- Absence of cyclic production of progesterone
- Underlying causes
  - Hypothalamic disorder:
    - psychological stress
    - obesity
    - low body weight
    - elite athletes / excessive physical activity
  - Endocrinopathy
    - thyroid disorder
    - polycystic ovarian syndrome (PCOS)/hyperandrogenic disorder
    - hyperprolactinemia
    - luteal out-of-phase events (perimenopause)
  - Idiopathic

Symptoms/Clinical Presentation
- Abnormal uterine bleeding – irregular/unpredictable cycle
- Variable amounts of bleeding during menses

Management/Treatment
- Treat underlying cause

11 “Abnormal Uterine Bleeding”, Olga Bougie, November 8 2016, uOttawa Faculty of Medicine
9.10 Infertility

Definition
- Failure to conceive after 1 year of unprotected intercourse
- Age and fertility:
  - Decline in follicle numbers and oocyte quality with age
  - Miscarriage rates increase with age
- Risk factors
  - Females
    - Over 35 years of age, Oligo/amenorrhea
    - Pelvic Inflammatory Disease/ STIs
    - Endometriosis
    - Previous treatment for cancer
    - Previous abdominal/pelvic surgery
    - Extremes of body weight
  - Males
    - Over 40 years of age
    - Undescended testes
    - Previous cancer therapy
    - Previous urogenital surgery (testicular and hernia)
    - Recreational drugs, smoking, alcohol
    - Genetic disorders (Klinefelter’s, Cystic fibrosis, Y-microdeletion)
    - Heat exposure, lubricant
    - Exogenous hormone use

Cause
- Amenorrhea
  - Primary – absence of menarche by age 15
  - Secondary – absence of menses for 6 months when previously menstruating
- Oligomenorrhea – cycles >35 days; Hypermenorrhea – cycles <21 days
- When oligomenorrhea or anovulation suspected
  - Hypothalamic amenorrhea (hypogonadotropic hypogonadism):
    - Physical exercise, nutrition or psychological stress; congenital or acquired GnRH deficiency
  - Polycystic ovary syndrome-PCOS (normogonadotropic)
  - Premature ovarian insufficiency (hypergonadotropic hypogonadism)
  - Other: prolactinoma, thyroid dysfunction, pregnancy, uterine adhesions (Asherman’s Syndrome)

Investigations
- Primary care evaluation
  - Age of woman and partner
  - Duration of unprotected intercourse
    - Timing and frequency of intercourse: 2-3 times per week around mid-cycle (day 11-22)
    - Determine if appropriate understanding of time of ovulation
  - Focused history from both partners
  - Examination of both partners
- Evaluation of infertility
  - Assessment of ovulation
    - History: regular, predictable periods every 21-35 days
      - If irregular cycles: TSH screening, prolactin level, day 3 FSH
    - Basal body temperature charting

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12 “The Infertile Couple”, Aaron Jackson, October 10 2016, uOttawa Faculty of Medicine
- Urine LH detection kits
- Detecting saliva ferning
- Luteal phase progesterone (serum): day 21-23
  - Assessment of Tubal Patency: hysterosalpingogram or laparoscopy
  - Semen analysis (WHO criteria)
    - 1. Vol >1.5 mL
    - 2. Concentration > 15 million/mL
    - 3. Motility >40% progressive
    - 4. Morphology >30% normal

Management/Treatment
- Ovulation induction/Superovulation ± intrauterine insemination (IUI); In Vitro Fertilization
- When to refer:
  - If obvious abnormality in history, physical exam or investigations – immediate referral
  - If no obvious abnormality: Age <35 - after 12 months of trying, Age 35-39 - after 6 months of trying, ≥ 40 years - immediate fertility assessment
9.11 Approach to Abnormal Uterine Bleeding (AUB)

Definitions
- Normal cycle: Regular cycle every 28±7 days, menses lasting 3-8 days with blood loss <80cc
- AUB: Menstrual bleeding of abnormal quantity, duration, or schedule
  - Oligomenorrhea: cycle duration >35 days
  - Polymenorrhea: cycle duration <21 days
  - Menorrhagia: regular cycles with >80cc blood loss or menses lasting >8-10 days
  - Metrorrhagia: irregular cycles with normal blood loss and duration of menses
  - Menometrorrhagia: irregular cycles with >80cc blood loss or menses lasting >8-10 days

Classification of Causes
- By age
- Structural vs non-structural
- Ovulatory vs anovulatory

Approach to AUB in Reproductive Age Women
- Rule out pregnancy
- Rule out infection, trauma, coagulopathy, systemic diseases, iatrogenic causes, medications
- Determine if anovulatory or ovulatory
  - Anovulatory: most common cause in reproductive age women (see section 5.5); evaluate for underlying causes and for endometrial pathology
  - Ovulatory: evaluate for uterine pathology

Approach to AUB in Peri-Menopausal Women
- Rule out infection, trauma, coagulopathy, systemic diseases, iatrogenic causes, medications
- Evaluate for endometrial pathology (hyperplasia, carcinoma, polyps, fibroids)

Approach to AUB in Menopausal Women
- Rule out hormone replacement therapy (HRT) use, especially if started <6 months ago (recommend that AUB is re-evaluated if persistent after 9 months on HRT)
- Evaluate for endometrial pathology
- Evaluate for other neoplasia (vagina, cervix, ovary, fallopian tube, bladder, rectum)

Investigations
- βHCG
- Transvaginal ultrasound or saline infusion sonography
- Hysteroscopy ± endometrial biopsy
- If coagulopathy suspected: CBC, peripheral blood smear, ferritin, coagulation panel ± Von Willebrand (VW) panel (VW factor antigen, Ristocetin cofactor, factor VIIIa activity)
- If thyroid disorder suspected, check TSH levels
- If pituitary disorder suspected, check prolactin levels

General Management
- Medication is 1st line treatment for non-structural causes of AUB
- Non-hormonal medication (for regular cycles with heavy menses ± dysmenorrhea): NSAIDS, antifibrinolytics (tranexamic acid)
- Hormonal medication (for irregular cycles ± heavy menses ± dysmenorrhea): combined hormone contraceptive, progestins (oral, injection, or intrauterine system), gonadotropin-releasing hormone agonists, selective progesterone receptor modulators, Danazol
- Surgery is 2nd line for non-structural causes: endometrial ablation, hysterectomy

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13 “Abnormal Uterine Bleeding”, Olga Bougie, November 8 2016, uOttawa Faculty of Medicine
9.12 Amenorrhea

Clinical Presentation
- Primary amenorrhea: never reached menarche
  - No menses by age 14, and has no signs of pubertal development
  - No menses by age 16, despite the presence of signs of pubertal development
- Secondary amenorrhea: previously menstruating but menses have stopped for 3 cycles or 6 months at age <40

Cause
- Physiologic: pregnancy, lactation, menopause
- Hypothalamic: Tumour, functional (chronic disease, weight loss, eating disorder, stress, excessive exercise, obesity), constitutional delay, gonadotropin releasing hormone agonist, traumatic brain injury, radiation, Kallmann syndrome
- Pituitary: prolactinoma, radiation, surgery, infiltrative diseases (hemochromatosis, sarcoidosis), medications (antidepressants, antipsychotics, antihypertensives, opiates)
- Thyroid: hyper- or hypothyroidism
- Adrenal: cushing’s disease, Addison disease, congenital adrenal hyperplasia, androgen-secreting tumour
- Ovary: polycystic ovarian syndrome (see section 5.8), primary ovarian insufficiency (see section 5.9), tumour, surgery
- Outflow tract obstruction: congenital causes (complete androgen resistance, imperforate hymen, Mullerian agenesis, transverse vaginal septum), acquired causes (Asherman syndrome, cervical stenosis)

Consequences
- Primarily infertility

Physical Exam
- Primary amenorrhea: growth, thyroid exam, genetic stigmata, skin and hair (thyroid, hyperandrogen, Cushing’s), Tanner staging, abdominal exam (masses), external genitalia (low estrogen or hyperandrogen signs)
- Secondary amenorrhea: thyroid exam, skin and hair (thyroid, hyperandrogen, Cushing’s), abdominal exam (masses), pelvic exam (low estrogen or hyperandrogen signs)

Investigations
- Primary amenorrhea: growth charts, bone age (for constitutional delay), progesterone withdrawal challenge, BHCG, FSH, LH, TSH, prolactin, E2, 17-OHP, pelvic and abdominal ultrasound, genetic testing, MRI if tumour suspected
- Secondary amenorrhea: progesterone withdrawal challenge, BHCG, FSH, LH, TSH, prolactin, androgen panel, 24-hour free urine cortisol, pelvic and abdominal ultrasound, MRI if tumour suspected

Management/Treatment
- Treat underlying cause

14 “Amenorrhea and Polycystic Ovarian Syndrome”, Case Based Learning, Tania Dumont, November 10 2016, uOttawa Faculty of Medicine
9.13 Polycystic Ovarian Syndrome (PCOS)\(^{15}\)

**Cause**
- Precise etiology unknown
- Pathogenesis:
  - Insulin resistance decreases sex hormone-binding globulin thereby increasing free testosterone that causes features of hyperandrogenism
  - High levels of LH stimulate testosterone production, leading to follicular atresia and anovulation; excess testosterone is converted to estrogen that induces endometrial proliferation unopposed by progesterone (without ovulation there is no corpus luteum)

**Risk factors**
- Family history, metabolic syndrome

**Clinical Presentation**
- Irregular cycles, oligomenorrhea, or amenorrhea
- Hyperandrogenism (acne & hirsutism)
- Obesity
- Infertility

**Physical Exam**
- Skin and hair (hirsutism, acne, androgenic alopecia, acanthosis nigricans) and pelvic exams (assess ovarian size)

**Investigations**
- To rule out other causes: BHCG, FSH, LH, TSH, prolactin, 24-hour free urine cortisol, abdominal ultrasound
- Tests that may point to PCOS: progesterone withdrawal challenge, androgen panel, pelvic ultrasound

**Rotterdam Diagnostic Criteria**
Two of the following three:
- Hyperandrogenism (hirsutism or biochemical evidence of hyperandrogenism)
- Ovulatory dysfunction (oligomenorrhea or amenorrhea)
- Polycystic ovaries on ultrasound

**N.B.,** PCOS is a diagnosis of exclusion.

**Consequences**
- **Short term:**
  - Fertility issues
  - Irregular cycles
  - Hyperandrogenism
  - Metabolic syndrome
- **Long term:**
  - Type 2 diabetes
  - Endometrial hyperplasia and cancer
  - Cardiovascular disease

**Management/Treatment**
- Restore menses and reduce risk of endometrial hyperplasia / carcinoma:
  - If contraception needed: combined hormonal contraception (CHC), patch, ring, intrauterine system
  - If contraception is not needed: cyclic progesterone
- Acne: CHC, cyproterone acetate (Diane-35\(^{®}\)), topical treatments, antibiotics, isotretinoin
- Hirsutism: CHC, cyproterone acetate, spironolactone, 5-alpha-reductase, laser, waxing, threading
- Metabolic syndrome: work up and follow up with diabetes screening, lipid profile, blood pressure, and waist circumference & BMI measurements; manage/treat with lifestyle modification (diet, exercise), weight loss, metformin (for insulin resistance

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\(^{15}\) “Amenorrhea and Polycystic Ovarian Syndrome”, Case Based Learning, Tania Dumont, November 10 2016, uOttawa Faculty of Medicine
Primary Ovarian Insufficiency (POI)

**Cause**
- POI is the loss of oocytes and surrounding stroma before the age of 40 years, resulting in no ovarian-made estrogen and progesterone.
- There are many possible causes:
  - Congenital: gonadal dysgenesis, Turner syndrome, Fragile X, complete androgen insensitivity syndrome, congenital adrenal hyperplasia, aromatase deficiency
  - Acquired: autoimmune destruction particularly associated with hypothyroidism, iatrogenic (chemotherapy, radiation, pelvic surgery, mumps infection)
  - Idiopathic

**Risk Factors**
- Treatment of malignancy with chemotherapy or radiotherapy

**Symptoms/Clinical Presentation**
- POI manifests as primary or secondary amenorrhea

**Physical Exam**
- Primary amenorrhea: growth, thyroid exam, genetic stigmata, skin and hair (thyroid, hyperandrogen, Cushing’s), Tanner staging, abdominal exam (masses), external genitalia (low estrogen or hyperandrogen signs)
- Secondary amenorrhea: thyroid exam, skin and hair (thyroid, hyperandrogen, Cushing’s), abdominal exam (masses), pelvic exam (low estrogen or hyperandrogen signs)

**Investigations**
- Specific for POI: two serum FSH of >40 on two separate occasions, separated by at least 1 month
- Other tests: LH, E2, TSH, prolactin, androgen panel, abdominal and pelvic ultrasounds, genetic testing (karyotype)
- Also to consider for primary amenorrhea: growth chart and bone age (wrist X-ray)

**Diagnosis**
- Amenorrhea, serum FSH of >40 on two separate occasions separated by at least 1 month, and age ≤40

**Consequences**
- Increased risk of cardiovascular disease
- Increased risk of osteoporosis
- Infertility

**Treatment/Management**
- To prevent endometrial hyperplasia/carcinoma:
  - If pubertal development is completed: combined hormonal contraceptive (CHC)
  - If no signs of puberty: low dose of estrogen, slowly ramping up over 2 years, then add progesterone via CHC
- For contraception, redressing normal menses, and fertility: CHC, patch, vaginal ring, copper intrauterine device + HRT, intrauterine system + estrogen replacement therapy; not medroxyprogesterone acetate (Depo-provera®)
- For cardiovascular health: adopting a healthy lifestyle (diet and exercise, avoiding smoking), hormone replacement therapy (HRT), follow up on blood pressure annually, follow up cholesterol levels every 5 years
- For bone health: weight bearing exercise, adequate intake of vitamin D and calcium, bone mineral density scan
- For mental health: psychological support

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16 “Amenorrhea and Polycystic Ovarian Syndrome”, Case Based Learning, Tania Dumont, November 10 2016, uOttawa Faculty of Medicine
9.15 Menopause

**Definition**
- Menopause: one day in life after exactly 12 months of amenorrhea following the last menses; occurs between 45-55 years of age (on average, at 51.4 years)
- Early menopause: menopause that occurs between the ages of 40-45 years
- Late menopause: menopause that occurs after 55 years of age
- Primary ovarian insufficiency: menopause that occurs before the age of 40 years (see section 5.9)
- Post-menopause: the period in life after menopause
- Peri-menopause: the symptomatic period (2-8 years) leading into menopause

**Cause**
- It is due to the ageing-related loss of physiological ovarian function
- Perimenopause is associated with fluctuating hormonal levels, leading to irregular cycles, periods of anovulation, symptoms of estrogen (E) excess/insufficiency, and narrowing of the thermoneutral zone (vasomotor symptoms)

**Symptoms/Clinical Presentation**
- Menstrual cycles that progress from normal, to shortened, to irregular cycles, and then cycles cease
- Vasomotor symptoms: hot flashes, night sweats, cold spells
- Urogenital symptoms: urinary frequency and urgency, vaginal dryness, diminished sex drive and response
- Sleep disturbance, poor concentration, poor memory, Irritability and/or emotional lability, Depression
- Fatigue, myalgia and arthralgia, episodic breast tenderness

**Physical Exam**
- Vitals, weight, BMI, cardiac and respiratory exam, breast exam, abdominal exam, pelvic exam (pelvic masses, vulvovaginal atrophy, decreased vaginal calibre)

**Investigations**
- Diagnosis is clinical, investigations are rare; serum FSH, LH, E2 to confirm
- Workup: pap test, fasting lipids, fasting glucose, mammogram, bone mineral density scan ± pelvic ultrasound

**Consequences of Low Estrogen**
- Dyslipidemia and an increased risk of cardiovascular disease (the #1 cause of death in women)
- Osteoporosis
- Colorectal cancer
- Quality of life concerns

**Treatment**
- Vasomotor symptoms: lifestyle changes (reduce weight if obese, smoking cessation, avoid triggers such as alcohol, warm environments, hot drinks) ± hormone replacement therapy (E+progesterone, E alone, or progesterone alone) in the form of pills, gels, or patches at the lowest possible dose that control symptoms
- Urogenital symptoms: local vaginal E (cream, suppository, ring)

**Prevention**
- Cardiovascular disease: lifestyle changes (smoking cessation, exercise, moderate alcohol)
- Osteoporosis: weight bearing exercise and balance training; adequate daily calcium and vitamin D intake

---

17 “Menopause”, Yaa Amankwah, November 12 2016, uOttawa Faculty of Medicine
5.16 Sexual Dysfunction in Women

Sexual Response
1. Desire: Sexual drive for sexual activities, sexual beliefs and values, and sexual motivation that reflects the emotions to engage in sexual activities
2. Arousal: Physical and emotional stimulation leading to vaginal and vulvar congestion, increases in vaginal lubrication, breast and vaginal vasodilation, and clitoral engorgement
3. Orgasm: Repetitive contractions of the pelvic floor at 0.8s intervals, generalized muscle contractions, carpopedal spasm, uterine contractions
4. Resolution: Release of muscular tension with a return to the unaroused state

Common sexual dysfunctions
1. Sexual interest/desire disorder: difficulty with or lack of interest in sexual activity
2. Sexual arousal disorder: difficulty or lack of the usual physiologic response to sexual stimuli
3. Orgasm disorder: significantly diminished intensity of, or complete lack of orgasm, despite self-report of adequate sexual arousal
4. Sexual pain disorder: genital pain with sexual activity

Prevalence
- Sexual interest/desire disorder: 64%
- Orgasm disorder: 35%
- Dyspareunia: 26%

Most difficulties last less than 6 months, but one third may persist longer.

Causes
- Sexual interest/desire disorder
  - Psychological and emotional: depression; fatigue from medical conditions such as anemia, thyroid dysfunction; sexual aversion with anxiety and/or disgust of sexual activity
  - Social factors: relationship or occupation
- Sexual arousal disorder
  - Absent or impaired genital sexual arousal such as minimal vulvar swelling or vaginal lubrication (e.g. menopause, postpartum hypoestrogenism)
  - Medication (e.g. SSRI, sedatives, narcotics, alcohol, drugs, antihypertensives, antipsychotics); pelvic pain and physical inability (e.g. arthritis, fibromyalgia, multiple sclerosis)
- Orgasm disorder
  - Lack of orgasm, diminished orgasm intensity or delay of orgasm despite sexual arousal
  - Medications, dyspareunia (e.g. vulvovaginal atrophy, dermatoses)
- Dyspareunia
  - Function disorder called vaginismus; vulvodynia, vaginal atrophy (e.g. menopause)
  - Pelvic disorders (e.g. pelvic inflammatory disease (PID), endometriosis, tumours or cysts)
  - Skin conditions or infections and irritants
  - Vulvar vestibulitis: associated with history of frequent yeast infections

Treatment/Management
- Address the medical issues such as medications, chronic disease or acute problems that might result in sexual dysfunction
- Do not hesitate to refer to a therapist or counselor who specializes in the assessment of sexual issues
- Relationship therapy for sexual interest/desire disorder, sexual arousal disorder
- Educate on the expectations; try different sexual positions or tools

---

18 “Female Sexual Function”, Case Based Learning, Jonathan D. Huber, uOttawa Faculty of Medicine
For dyspareunia: Kegel and reverse Kegel exercises, local moisturization, estrogen cream, remove local irritants, change in contraceptive methods, psychotherapy or other behavioural techniques, pain clinic

9.17 Bacterial Vaginosis (BV)

Cause
- A polymicrobial infection of anaerobes that replaces the normal vaginal flora of hydrogen-producing lactobacilli
- Anaerobes include: Gardnerella (most common), Prevotella, Mobiluncus, Ureaplasma, and Mycoplasma
- It is not a sexually transmitted infection (STI)

Risk Factors
- African American ethnicity
- Changing a sexual partner
- Having a lesbian partner with BV
- Douching
- Intrauterine systems
- Antibiotic use
- Having a co-existing STI

Symptoms/Clinical Presentation
- Most commonly asymptomatic
- Increased discharge and malodour

Physical Exam
- Pelvic exam (vaginal discharge, malodour)

Investigations/Diagnosis with AMSEL’s Criteria
- Require 3 of the 4 following criteria:
  - Thin, white homogenous discharge
  - Clue cells on microscopy (cells covered with anaerobes, and the absence of lactobacilli)
  - Vaginal fluid pH > 4.5
  - Positive Whiff test (a fishy odour with 10% KOH)

Consequences
- Increased risk of contracting a STI: HIV, gonorrhea, chlamydia, herpes simplex virus-2 (HSV-2)

Treatment
- Recommended 1 of 3 regimens:
  - Metronidazole 500 mg PO BID for 7 days
  - Metronidazole gel 0.75% intravaginal
  - Clindamycin cream 2% intravaginal
- Alternate regimens:
  - Clindamycin 300 mg PO BID for 7 days
- Recommended 1 of 3 regimens if during pregnancy:
  - Metronidazole 500 mg PO BID for 7 days
  - Metronidazole 250 mg PO TID for 7 days
  - Clindamycin 300 mg PO BID for 7 days
- Treatment not required for sex partner

19 “Fluide vaginal”, Hélène M. Gagné, November 12 2016, uOttawa Faculty of Medicine
9.18 Vulvovaginal Candidiasis

**Cause**
- Also called yeast infection
- Fungal infection of the vulva and/or vagina
- Responsible pathogens:
  - *Candida Albicans* (95% of cases)
  - Non-Albicans species: *Candida Glabrata, C. Parapsilosis, C. Krusei, Saccharomyces cerevisiae*

**Risk Factors**
- Low risk groups:
  - Menopause
  - Prepubertal
- High risk groups:
  - Immunocompromised
  - Diabetic
  - Pregnant

**Clinical Presentation, Investigations and Diagnosis**
- Diagnosed by the following:
  - Pruritus
  - Burning
  - Discharge that is thick, white, and has the classic “cottage cheese” appearance
  - Fissures
  - Satellite lesions are pathognomonic for Candida Vulvitis
  - Vaginal culture

**Physical Exam**
- Pelvic exam

**Treatment**
- First line treatment options:
  - Topical azoles available over-the-counter
    - Clotrimazole
    - Miconazole
    - Terconazole
  - Fluconazole 150 mg PO single dose
- Resistant or atypical infection treated with boric acid 600 mg PV QHS for 14 days
- Alternate regimens: Gentian violet, lactobacilli / probiotics, garlic tampons, tea tree oil, Echinacea, Yeast-gard suppositories

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20 "Écoulement vaginal", Hélène M. Gagné, November 12 2016, uOttawa Faculty of Medicine
9.19 Trichomoniasis Infection

**Cause**
- Sexually transmitted infection (STI) of the urogenital tract with the unicellular flagellated parasite *Trichomonas Vaginalis*

**Risk Factors**
- No condom use

**Symptoms/Clinical Presentation**
- Symptoms develop one week after contact with infected partner:
  - Green, frothy discharge
  - Malodour
  - Pruritus
  - Dysuria
  - Dyspareunia
  - Postcoital bleeding
- Asymptomatic in ~50% of cases

**Physical Exam**
- Pelvic exam *(see above, can have “strawberry cervix”, which is pathognomonic for trichomoniasis)*

**Investigations**
- Vaginal swab for microscopy
- Rapid antigen test *(not available in Canada)*

**Consequences**
- Trichomoniasis is a marker for high risk sexual activity and it is common to find a co-infection with other STIs
- Rarely causes pelvic inflammatory disease

**Treatment/Management**
- This STI is non-reportable
- Treatment regimen options:
  - Metronidazole 500 mg PO BID for 7 days
  - Metronidazole 2 g PO in 1 dose
- Treat partner(s)
- Do not have sexual intercourse for 1 week as the risk of re-infection is elevated

---

21 “Écoulement vaginal”, Hélène M. Gagné, November 12 2016, uOttawa Faculty of Medicine
## 9.20 Chlamydia, Gonorrhea, and Syphilis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Symptoms</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>• Often asymptomatic</td>
<td>• Specific culture or urinary assay (often gonorrhea co-infection)</td>
<td>• Reportable disease&lt;br&gt;• Azithromycin 1 g PO 1 dose OR Doxycycline 100 mg PO BID for 7 days&lt;br&gt;• Treat partner(s)&lt;br&gt;• Abstain from intercourse for 1 week&lt;br&gt;• Reinfection possible</td>
</tr>
<tr>
<td>Neisseria</td>
<td>• Often asymptomatic</td>
<td>• Specific culture or urinary assay (often chlamydia co-infection)</td>
<td>• Reportable disease&lt;br&gt;• Azithromycin 1 g PO 1 dose + either Ceftriaxone 250 mg IM or Cefixime 400 mg PO 1 dose&lt;br&gt;• Treat partner(s)&lt;br&gt;• Abstain from intercourse for 1 week&lt;br&gt;• Reinfection possible</td>
</tr>
<tr>
<td>Treponema</td>
<td>• Primary: painless chancre&lt;br&gt;• Secondary: flu-like symptoms, miliary rash, arthralgia&lt;br&gt;• Latent: asymptomatic (can last 1-30 years)&lt;br&gt;• Tertiary: major destruction of brain, skin, joints, eyes, ears, cardiovascular system</td>
<td>• Swab lesion and microscopy or VDRL blood test</td>
<td>• Reportable disease&lt;br&gt;• Penicillin&lt;br&gt;• Abstain from intercourse until cure confirmed&lt;br&gt;• Reinfection possible</td>
</tr>
</tbody>
</table>

### Risk Factors
- Sex with an untreated partner
- Lack of mutual monogamy
- Having unsafe sex
- Rapid partner turnover
- Douching after sex

### Prevention
- Condom use
- Harm-reduction behaviour

---

22 "Sexually Transmitted Infections", Karen Visser, December 2 2016, uOttawa Faculty of Medicine
### 9.21 Viral Sexually Transmitted Infections

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Symptoms</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Genital Herpes**             | • Primary outbreak: fever and tingling prodrome, dysuria, many painful vesicles that rupture leaving erosions without scarring  
                              | • Recurrent outbreaks, mild symptoms                                     | • Viral culture of lesion or tissue sample                                 | • Incurable                                                                |
| **Human Immunodeficiency Virus (HIV)** | • Asymptomatic for many years  
                              | • Fatigue, night sweats, diarrhea, weight loss  
                              | • Acquired immune deficiency syndrome (AIDS)                               | • Reportable disease  
                              | • Incurable                                                                |
| **Human Papillomavirus (HPV)** | • Genital warts (condylomata acuminata) that can clear then recur later | • Clinical                                                                | • Physical modalities: excision, laser, cryotherapy, electrosurgery  
                              |                                                                          | • Immunologic modalities: Imiquimod  
                              |                                                                          | • Chemical modalities: trichloroacetic acid, podophyllin, podofilox |

**Risk Factors**
- Sex with an untreated partner
- Lack of mutual monogamy
- Having unsafe sex
- Rapid partner turnover
- Douching after sex

**Prevention**
- Condom use (less protective for HSV)
- Harm-reduction behaviour
- Gardasil® or Cervarix® vaccines for HPV

---

23 "Sexually Transmitted Infections", Karen Visser, December 2 2016, uOttawa Faculty of Medicine
### 9.22 Pregnancy Infections

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Presentation</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Toxoplasmosis** | ● >90% asymptomatic  
● Viral symptoms  
● Maternal-fetal transmission: 1-4 months after placental colonization  
● Fetal  
   ○ Classic triad: chorioretinitis, hydrocephalus, intracranial calcifications  
● Long-term risks: retinal diseases, major neurological abnormalities, problems with psychomotor development | ● IgG and IgM for toxoplasmosis  
● Screening in amniotic fluid | ● Based on the amniocentesis  
● Spiramycin or Pyrimethamine + sulfadiazine + leucovorin |
| **Rubella** | ● Rash  
● 25-50% asymptomatic  
● 60-70% polyarthritis-polyarthralgia  
● Risk of congenital deformities up to 20 weeks of pregnancy only  
   ○ 16-20 weeks: sensorineural hearing loss  
● Neonatal  
   ○ Sensorineural hearing loss  
   ○ Heart defect, CNS defects, retinopathy, cataract, congenital glaucoma | ● IgG and IgM for rubella | ● Immunoglobulin  
● Discuss termination  
● Rubella vaccine  
   ○ Live attenuated vaccine  
   ○ Contraindicated in pregnancy  
   ○ Administered postpartum in non-immunized patients |
| **CMV** | Most common cause of intrauterine infection  
● Asymptomatic  
● Viral symptoms  
● Neonatal:  
   ○ Sensorineural hearing loss; mental retardation/delayed development; vision problems | ● IgG and IgM for CMV  
● Screening in amniotic fluid | ● Tx: None recommended  
○ Immunoglobulins not useful  
● Discuss termination |
| **Herpes** | ● Genital ulcers and prodrome  
● Painful  
● Congenital infection (1-5%) – Acquisition in utero: symptoms < 48h  
● Neonatal: symptoms > 48h after birth  
   ○ Exposure via maternal genital tract (85%) – during birth  
   ○ Iatrogenic/familial transmission after birth via skin lesions (10-15%)  
   ○ Infection of skin, eyes, mouth  
   ○ CNS infection  
   ○ Disseminated disease | ● Viral culture vesicles  
● Type specific herpes IgG test - controversial | ● Suppressive treatment at 36 weeks of pregnancy  
○ Acyclovir 400 mg PO TID or 200 mg PO QID  
○ Valacyclovir 500 mg PO BID  
● Neonatal: Acyclovir IV |

---

24 “Infections in pregnancy”, Marie-Ève Roy-Lacroix, November 21 2016, uOttawa Faculty of Medicine
<table>
<thead>
<tr>
<th>Group B Streptococcus</th>
<th>Rectovaginal culture between 35-37 weeks of pregnancy - GBS screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>● 20% of asymptomatic women</td>
<td>● Penicillin G 5 million units IV as initial dose, then 2.5 million units every 4 hours until delivery</td>
</tr>
<tr>
<td>● Without intervention: 50% of newborns will be colonized and 1% will develop sepsis</td>
<td>● Alternatives: ampicillin, clindamycin, vancomycin</td>
</tr>
<tr>
<td>● Maternal:</td>
<td>● Treat if:</td>
</tr>
<tr>
<td>○ Chorioamnionitis (maternal fever)</td>
<td>o Culture positive for GBS</td>
</tr>
<tr>
<td>○ Endometritis</td>
<td>o GBS bacteriuria</td>
</tr>
<tr>
<td>● Neonatal:</td>
<td>o Past history of GBS infected child*</td>
</tr>
<tr>
<td>○ First week of life (often in the first 48h)</td>
<td>o &lt;37 weeks pregnant*</td>
</tr>
<tr>
<td></td>
<td>o Rupture membranes &gt; 18 hours*</td>
</tr>
<tr>
<td></td>
<td>*if culture result is unknown</td>
</tr>
</tbody>
</table>

**Investigations**

- Ultrasound markers of infection in pregnancy
  - Intracranial calcifications
  - Microcephaly
  - Hydrocephalus
  - Ascites
  - Hepatosplenomegaly
  - Severe intrauterine growth restriction (IUGR)
9.23 Diabetes in Pregnancy

**Cause**
- Pre-diabetes
- Gestational diabetes
- Carbohydrate intolerance with onset or first recognition in pregnancy
  - Prevalence = 2-4% of pregnancies
  - Same risk factors as Type 2 diabetes

**Symptoms/Clinical Presentation**
- **Physiological changes**
  - Fasting glucose levels fall in pregnancy; 3.5 mmol/L in 1st trimester
  - Increased hypoglycemia unawareness
  - Increased Insulin resistance
  - Increased risk of DKA; high risk of fetal mortality
- **Comorbidities**
  - Type 1: Autoimmune attack, thyroid disorders
  - Type 2: Hypertension, obesity, PCOS, coronary artery disease
- **Complications:**
  - Retinopathy: worse with pregnancy
  - Nephropathy: normally increase GFR 50%
    - If serum Cr > 125 mmol/L = risk of permanent/prolonged worsening
    - High risk of preterm delivery
- **Impact on fetus**
  - Sacral agenesis: very small lower body with very large upper body
  - Birth weight: macrosomia > 4.5kg or 95% for gestational age, or small for gestational age-20% of deliveries
  - Fetal loss: first trimester or late pregnancy loss
    - Increased risk in: 1) poor control 2) fetal macrosomia 3) fetal interventricular septal hypertrophy

**Diagnosis**
1. 50g glucose challenge test with plasma glucose 1 hour later (1hPG) ≥11mmol/L
   or 1hPG 7.8-11.0mmol/L + 75g OGTT with FPG ≥5.3mmol/L, 1hPG ≥10.6mmol/L, 2hPG ≥9.0mmol/L
   Or
2. 75g OGTT FPG ≥5.1mmol/L, 1hPG ≥10.0mmol/L, 2hPG ≥8.5mmol/L
   o If 1 value is met or exceeded, gestational diabetes

**Investigations**
- All women screened at 24-28 weeks
- Reasons to look for gestational diabetes
  - Index pregnancy: macrosomia, hypoglycemia in neonate, fetal loss
  - Offspring: type 2 diabetes, obesity
  - Maternal: type 2 diabetes

**Management/Treatment**
- Treatment target HBA1C <7%
- Folate supplementation recommendation: 5mg for diabetes and for BMI >35kg/m²
- Need laser treatments before pregnancy and stable for 6 months for the retinopathy
- Need to stop ACE inhibitor; worsens microalbuminuria

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25 “Medical problems of pregnancy”, Erin Keely, November 17 2016, uOttawa Faculty of Medicine
9.24 Urinary Tract Infections (UTI) in Pregnancy

**Cause**
- Physiological changes
  - Progesterone: causes ureters/urethra to loosen at gestational age week 7
  - Compression of urinary collecting system = stasis of urine
  - Changes in urine pH and increased glycosuria
- Effect of pregnancy on UTI
  - Untreated asymptomatic bacteriuria more likely to persist and more likely to result in pyelonephritis (up to 20-30%)
  - Acute pyelonephritis more likely to be complicated
    - Increased risk of Acute Respiratory Distress Syndrome (ARDS)
  - Impact on choice of antibiotics
    - Penicillins, Cephalosporin, Clindamycin, Nitrofurantoin
    - AVOID Fluoroquinolones, Erythromycin, Tetracycline

**Symptoms/Clinical Presentation**
- Effect of UTI on pregnancy
  - Increased risk of preterm delivery
  - Increased risk of low birthweight

**Investigations**
- All women should have urine dip test at every visit

**Management/Treatment**
- If positive urine dip test, treat even if asymptomatic

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26 “Medical problems of pregnancy”, Erin Keely, November 17 2016, uOttawa Faculty of Medicine
9.25 Asthma and Anemia in Pregnancy

**Asthma**

**Cause**
- Effect of pregnancy on asthma
  - Exacerbations between gestational age 17 to 24 weeks
  - Increased risk of reflux (GERD) and sinusitis as trigger
- Effect of asthma on pregnancy
  - Well-controlled asthma does not confer increased risk

**Symptoms/Clinical Presentation**
- Physiological changes
  - Shortness of breath
  - Respiratory alkalosis
  - Hypoxemia
  - Change in plasma lung volumes

**Investigations**
- Spirometry not affected

**Management/Treatment**
- Effective therapy should not be stopped

**Anemia**

**Causes**
- Iron deficiency – most common
- Malaria
- Folate/B12 deficiency
- Thalassemia

**Symptoms/Clinical Presentation**
- Physiological changes
- Increase in total plasma volume Dilutional anemia of pregnancy

**Complications**
- Maternal
  - Death in severe anemia
  - Fatigue
- Fetal
  - Iron deficiency in neonate
  - Low birth weight
  - Placental hypertrophy

**Investigations**
- Normal hemoglobin for pregnancy is 110 g/L

**Management/Treatment**
- Iron supplementation

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27 “Medical problems of pregnancy”, Erin Keely, November 17 2016, uOttawa Faculty of Medicine
9.26 Cardiac Diseases in Pregnancy

Cause
- Prevalence = 1% of pregnancies
- Women previously undiagnosed may present in pregnancy
- Different types of cardiac disease affect pregnancy outcomes
  - Congenital valvular heart disease (e.g. rheumatic fever mitral stenosis)
  - Valve replacement (usually mechanical)
  - Cardiomyopathy – dilated or hypertrophic
  - Ischemic heart disease
- Peripartum cardiomyopathy – a unique condition presenting in the 3rd trimester
  - Left ventricular systolic dysfunction; between last month of pregnancy and 5 months postpartum
  - Risk factors:
    - African descent
    - >30 years of age
    - Multiple gestation

Symptoms/Clinical Presentation
- Physiological changes
  - Increase in preload, cardiac output, oxygen consumption
  - Decrease in afterload
- Type/severity of heart disease
  - Volume overload lesions are well tolerated (e.g. aortic insufficiency) and pressure overload lesions are poorly tolerated (e.g. mitral stenosis)
  - Cyanotic and ischemic heart disease poorly tolerated
  - Some have higher than normal risk of maternal mortality e.g. Eisenmenger syndrome and pulmonary hypertension – up to 50% maternal mortality rate
- Labour and delivery
  - Physiologic changes
    - Cardiac output increases 10-15% with each contraction
    - Valsalva increases afterload, decreases preload, decreases cardiac output
      - May need an assisted second stage i.e. no pushing
  - Immediately postpartum
    - Autotransfusion of 300-500 cc for 24-48 hours postpartum
    - Cardiac output increases 65% = loss of low resistance placental bed, decrease vascular compliance

Management/Treatment
- Need to change medications
  - e.g. Mechanical valves and warfarin
  - e.g. ACE inhibitors in heart failure
- Peripartum cardiomyopathy
  - Recovery rates:
    - 30-50% recover LV function
    - 10% require cardiac transplant
    - 35% risk of recurrence in subsequent pregnancy – especially if LV function has not recovered

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28 “Medical problems of pregnancy”, Erin Keely, November 17 2016, uOttawa Faculty of Medicine
9.27 Isoimmunisation in Pregnancy

**Cause**
- Maternal-fetal red cell incompatibility

**Symptoms/Clinical Presentation**
- Hemolytic Disease of Fetus and Newborn (HDFN)
  - Maternal RBC antibodies cross the placenta and destroy fetal RBCs = fetal and/or neonatal anemia
  - Clinical circumstances at risk for HDFN
    - Early pregnancy loss/termination
      - Spontaneous or induced abortion
      - Ectopic pregnancy
      - Molar pregnancy
    - Antepartum Hemorrhage
      - Abdominal trauma
      - External cephalic version
      - Fetomaternal hemorrhage
    - Invasive fetal procedures
      - Amniocentesis
      - Chorionic villus sampling
      - Cordocentesis
    - Peripartum fetomaternal hemorrhage
  - Pregnancy at risk for HDFN
    - Mother has RBC antibodies known to cause HDFN e.g. anti-D antibody
    - AND Fetus has RBC antigen
      - If father is homozygous for the antigen then the fetus is at risk
      - If father is heterozygous then the fetus may not be at risk; fetal DNA testing at 8-12 weeks
  - Most common cause of hemolytic disease in the newborn = incompatibility of the ABO group
    - Most anti-A and anti-B antibodies are IgM, which cannot cross the placenta
    - Anemia usually mild; typically have neonatal anemia and jaundice and do not have erythroblastosis fetalis

**Investigations**
- All pregnant women should have blood group and antibody screen prior to pregnancy
  - Identify Rh(D) negative women at risk of developing anti-D antibody
  - Identify women with antibody at risk for HDFN

**Management/Treatment**
- Prevention
  - First dose of anti-D immunoglobulin at 28 weeks i.e. WinRho to Rh (D) negative women with no anti-D antibody; Earlier dose if termination, trauma or invasive procedure
  - Second dose is given after delivery (within 72 hours postpartum) if the infant is Rh (D) positive
- Monitoring pregnancy at risk
  - Maternal antibody titer monthly; increasing or high titer suggests fetus at risk of hemolysis
  - MCA Doppler Assessment: indirect measure of hemoglobin level
    - Other imaging technique = ultrasound for hydrops fetalis
  - Cordocentesis: fetal blood sampling to measure the fetal hemoglobin directly
- Postpartum management
  - RBC transfusion; phototherapy – most neonates with HDFN
9.28 Varicocele

Typical Patient
- Male adult or adolescent

Cause
- Dilation of the pampiniform plexus veins of the spermatic cord due to incompetent venous valves
- It is hypothesized that the resultant increase in testicular temperature is responsible for fertility issues in ~35% of cases

Symptoms/Clinical Presentation
- Painless or throbbing pain that is worse with prolonged standing/activity and aggravated by valsalva maneuver
- Discomfort or heaviness often relieved with scrotal support or when supine
- Infertility in ~35% of cases
- Mostly left-sided (85%), sometimes bilateral (15%), and rarely right-sided (red flag, investigate further)

Physical Exam
- Genitourinary exam:
  - Classic “bag-of-worms” on palpation
    - Grade 0: Non-palpable and only visible on ultrasound (does not necessitate treatment)
    - Grade 1: Palpable with valsalva maneuver only
    - Grade 2: Palpable without valsalva maneuver
    - Grade 3: Visible
  - Note testicular volume (may see atrophy of affected testicle(s))
- Abdominal exam (search for mass)

Investigations
- Scrotal ultrasound to assess testicular volume (may be reduced)

Management/Treatment
- Indications for surgery:
  - Palpable veins
  - And 1 of the following:
    - Infertility with abnormal semen analysis
    - Symptomatic
    - Ipsilateral testicular atrophy
- Surgical options:
  - Microsurgical varicocelectomy preferred
    - Inguinal
    - Subinguinal
  - Traditional open varicocelectomy
    - Retroperitoneal
    - Inguinal
    - Open
  - Laparoscopic
  - Transvenous embolization

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30 “Scrotal Pathology”, Ravin Bastiampillai, November 29 2016, uOttawa Faculty of Medicine
9.29 Hydrocele

Typical Patient
- Male infant (communicating hydrocele)
- Male adult or adolescent (simple/non-communicating hydrocele)

Cause
- Collection of serous fluid between the two layers of the tunica vaginalis
- Two types:
  - Congenital (in children): patent tunica vaginalis after testicles have descended, resulting in a communicating hydrocele with the peritoneum
  - Acquired (in adults):
    - Primary / idiopathic
    - Secondary (i.e. due to testicular disease such as defective lymph hemostasis, or reactive subsequent to trauma, infection, rarely tumor)

Symptoms/Clinical Presentation
- Painless unless very large
- Scrotal size variation throughout the day suggests a communicating hydrocele
- There may be other symptoms in the case of a secondary hydrocele

Physical Exam
- Genitourinary exam:
  - Palpable fluid
  - Transillumination of scrotal mass indicates fluid
  - Fluid may be reducible in a communicating hydrocele
  - Testicle may not be palpable with large hydroceles

Investigations
- Scrotal ultrasound

Management/Treatment
- Indications for treatment:
  - Children: most cases resolve within 1 year; treat if persists >1 year due to the risk of hernia
  - Adults: treat if symptomatic, for cosmetic concerns, or if there is an underlying pathology
- Mainstay of treatment is surgery:
  - Inguinal approach in children
- Scrotal approach in adults

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31 "Scrotal Pathology", Ravin Bastiampillai, November 29 2016, uOttawa Faculty of Medicine
9.30 Spermatocele

Typical Patient
- Male aged 40-60 years (but can be present at any age)

Cause
- Cystic dilation at caput region of an epididymal tubule that contains seminal fluid
- Typically occurs after puberty

Symptoms/Clinical Presentation
- Painless scrotal mass located on the posterior-superior aspect of the testicle

Physical Exam
- Genitourinary exam:
  - Spermatocele usually distinguished from testis on palpation (marble sensation)
  - Spermatocele may transilluminate

Investigations
- Scrotal ultrasound

Management/Treatment
- No treatment (rarely necessary to treat)
- Spermatocelectomy using a scrotal approach if cyst is large and symptomatic
- Surgery can lead to epididymal obstruction and infertility, so ideally delay treatment until after the patient has children
9.31 Acute Orchitis, Epididymitis, and Epididymo-orchitis

**Cause**
- Inflammation of the epididymis
- The testis is often implicated, hence the term epididymo-orchitis
- Two types:
  - Infectious: caused by retrograde ascent of a pathogen
    - Bacterial: typically associated with a sexually transmitted infection (STI) in men aged ≤35 years (common pathogens are *N. gonorrhea*, *C. trachomatis*, and *E. coli*) or with a urinary tract infection in men aged >35 years (common pathogen is *E. coli* or other *KEEPS* organisms)
    - Non-bacterial: viral infections (note that mumps in children has the risk of infertility), tuberculosis
  - Non-infectious: Idiopathic, traumatic, autoimmune

**Symptoms/Clinical Presentation**
- Gradual onset testicular pain, swelling, and redness
- Fever, occasionally sepsis
- Recent instrumentation
- Sexual activity
- Lower urinary tract symptoms/UTI symptoms

**Physical Exam**
- Genitourinary exam:
  - Swollen and tender epididymis ± testis on palpation
  - Urethral discharge
  - Assess for inguinal lymphadenopathy
  - Positive Prehn sign
  - Cremasteric reflex intact
- Abdominal exam and digital rectal exam if assessing for bladder outflow obstruction

**Investigations**
- CBC, urinalysis and culture & sensitivity, and urethral swab for STI
- Tuberculosis workup if suspected
- Scrotal ultrasound to rule out testicular torsion

**Complications**
- Abscess
- Chronic pain
- Venous thrombosis
- Epididymitis progressing to orchitis

**Management/Treatment**
- Rest with scrotal support
- Analgesics
- Antibiotics if bacterial infection:
  - Men aged ≤35 years: Ceftriaxone 250 mg IM x1 + Doxycycline 100 mg PO for 10 days *Treat sexual partner(s) as well*
  - Men aged >35 years: Levofloxacin 750 mg PO for 10-14 days

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33 *“Scrotal Pathology”, Ravin Bastiampillai, November 29 2016, uOttawa Faculty of Medicine*
### 9.32 Testicular Torsion

**Typical Patient**
- Boy aged 12-18 years

**Cause**
- Rotation of the testicle causes twisting of the spermatic cord, resulting in disruption of blood flow to the testicle
- Two different mechanisms:
  - Extravaginal torsion (neonatal): Complete torsion of the spermatic cord before fusion of the tunica vaginalis with the dartos fascia
  - Intravaginal torsion (pubertal): Torsion of the spermatic cord with the visceral layers only; bell-clapper deformity

**Symptoms/Clinical Presentation**

- **Extravaginal torsion:**
  - Red and swollen scrotum at birth
  - Often asymptomatic

- **Intravaginal torsion:**
  - Sudden onset scrotal pain
  - Nausea and vomiting in 98% of cases
  - History of ipsilateral pain
  - Redness and swelling of the scrotum

**Physical Exam**
- **Genitourinary exam:**
  - **Extravaginal torsion:**
    - Indurated testis
    - Scrotal erythema
    - Scrotal swelling, sometimes associated with a hydrocele
  - **Intravaginal torsion:**
    - Tender, erythematous, swollen testicle
    - Bell-clapper deformity
    - High riding, transverse position of testicle
    - Negative Prehn sign
    - Loss of cremasteric reflex is most specific for testicular torsion

**Investigations**
- Scrotal Doppler ultrasound if diagnosis is not obvious on physical exam (if diagnosis obvious, do NOT get ultrasound since this will delay surgical treatment)

**Consequences**
- Risk of testicular loss becomes important 6 h from the onset of pain
  - >97% of cases are salvageable if treated within 6 h
  - <10% of cases are salvageable if treated at 24 h
- Hormonal and fertility issues if contralateral testicle is also involved
- Necrosis and/or abscess

**Management/Treatment**
- This is a surgical emergency
- Surgical exploration ± untwist cord, and bilateral orchiopexy or orchiectomy if there is necrosis

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34 “Scrotal Pathology”, Ravin Bastiampillai, November 29 2016, uOttawa Faculty of Medicine
9.33 Testicular Cancer

**Typical Patient**
- Male aged 15-34 years (most common cancer in this age range)

**Cause**
- Tumour arising in the testis
- Types:
  - Germ cell tumours (95% of testicular tumours)
    - Seminoma (most frequent but best prognosis)
    - Non-seminoma
  - Non-germ cell/stromal tumours
    - Gonadoblastinoma
    - Lymphoma

**Risk factors**
- Family history (relative risk of 8-10 if brother affected, and 4-6 if father affected)
- Past history of testicular cancer
- Genetic factors: Down syndrome, Klinefelter syndrome, gonadal dysgenesis
- Intra-tubular germ cell neoplasia
- Cryptorchidism

**Symptoms/Clinical Presentation**
- Testicular mass with possible swelling and discomfort
- Systemic symptoms: abdominal pain, back pain, lymphadenopathy, dyspnea (suggests metastasis)

**Physical Exam**
- Genitourinary exam (mass does not transilluminate); full physical exam

**Investigations**
- Serum markers: \( \beta \)HCG, alpha fetoprotein, lactate dehydrogenase
- Scrotal ultrasound (reveals a hypoechoic vascular mass)
- Pelvic/abdominal CT scan for staging
- Chest X-ray or CT scan

**Management/Treatment**
- Radical orchiectomy (bilateral if gonadoblastinoma or lymphoma) ± prosthesis and confirm histopathology for staging to guide further treatment
- Following orchiectomy, surveillance with frequent follow up (serum markers, chest X-ray, pelvic / abdominal CT scan)
- Further treatment options for high risk tumors or if evidence of metastasis: Retroperitoneal lymph node dissection, chemotherapy, radiotherapy depending on histology and stage

**Staging**
- Stage I: Tumour is confined to the testis
- Stage II: Cancer has metastasized to the retroperitoneal lymph nodes
- Stage III: Cancer has metastasized beyond the retroperitoneal lymph nodes

**Biopsychosocial Impact**
- Self-esteem, infertility, future cancer risk increased

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35 “Scrotal Pathology”, Ravin Bastiampillai, November 29 2016, uOttawa Faculty of Medicine
9.34 Erectile Dysfunction (ED)\(^{36}\)

**Typical Patient**
- Male aged 40 years or older with cardiovascular disease risk factors

**Definition**
- The inability to attain and/or maintain penile erection of sufficient quality for satisfactory sexual performance

**Causes by Classification**
- **Organic causes**
  - Vasculogenic (arterial)
  - Neurogenic (sensory, motor, autonomic, neurotransmitters)
  - Hormonal (testicular, pituitary, thyroid)
  - Anatomic (cavernosal, trauma)
  - Medications and drugs
- **Psychogenic causes** (performance anxiety, stress)
  - Generalized
  - Situational

**Clinical Presentation**
- Organic causes: gradual onset and progressive loss of erectile function; absent or weak nocturnal erections
- Psychogenic causes: sudden and complete loss of erectile function that is situational; presence of normal nocturnal erections

**Risk Factors**
- Aging
- Diabetes mellitus
- Cigarette smoking
- Obesity
- Cardiovascular disease
- Hypertension
- Dyslipidemia
- Depression
- Benign prostatic hyperplasia
- Spinal cord injury
- Neurodegenerative conditions
- Renal insufficiency
- Medications (e.g., histamine-2 blockers, antihypertensives, antidepressants)
- Obesity
- Benign prostatic hyperplasia
- Cardiovascular disease

**Physical Exam**
- Vitals, weight and waist circumference
- Genitourinary exam (penile deformity, testicular atrophy), cardiovascular exam ± neurological exam

**Investigations**
- Lipid panel, fasting glucose or HbA1C, total testosterone, ± bioavailable testosterone, TSH, prolactin

**Consequences**
- ED is a predictor of future cardiovascular disease and is strongly associated with metabolic syndrome

**Management/Treatment**
- Education
- Modify reversible causes: medication adjustment, lifestyle (diet, exercise, smoking cessation, moderate alcohol), treat any contributing underlying cause and optimise comorbidities
- First line therapies: psychotherapy, phosphodiesterase-5 inhibitors* (sildenafil, vardenafil, tadalafil)
  - Contraindicated in patients taking nitrates
- Second line therapies: intra-cavernosal injections, intra-urethral suppository, vacuum erection device

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\(^{36}\)“Testosterone Deficiency and Erectile Dysfunction”, Ravin Bastiampillai and Tony Bella, November 29 2016, uOttawa Faculty of Medicine
9.35 Testosterone Deficiency Syndrome (TDS)\textsuperscript{37}

**Definition**
- Also known as late-onset hypogonadism, TDS is a clinical and biochemical syndrome of testosterone (T) deficiency

**Cause**
- Age-related decline in hypothalamic and testicular function: declining production of gonadotropin-releasing hormone and luteinizing hormone results in fewer and less sensitive Leydig cells, and thus lower levels of T
- Two types: primary and secondary hypogonadism

**Risk Factors**
- Metabolic syndrome
- Obesity
- Diabetes
- Chronic obstructive pulmonary disease
- Kidney failure
- Hemochromatosis
- HIV infection

**Symptoms/Clinical Presentation**
- Decreased libido
- Decreased vitality
- Fatigue
- Mood changes
- Insomnia
- Anemia
- Hot flashes
- Delayed ejaculations
- Erectile dysfunction
- Decreased muscle mass
- Weakness
- Increased body fat, gynecomastia
- Testicular atrophy
- Osteopenia/osteoporosis
- Loss of facial, body, and pubic hair

**Physical Exam**
- General appearance: increased body fat, decreased muscle mass
- Skin and hair exam: loss of facial/body/pubic hair
- Genitourinary exam: testicular atrophy

**Investigations**
- T profile (total T, bioavailable T, sex hormone binding globulin), LH, FSH
- Further testing as needed: prolactin, ferritin, karyotype testing, magnetic resonance imaging

**Consequences**
- Quality of life issues
- Metabolic syndrome
- Cardiovascular disease
- Diabetes mellitus
- Osteoporosis

**Management/Treatment**
- Non-hormonal therapies: lifestyle changes targeting modifiable risk factors, psychotherapy or antidepressants PRN, bisphosphonates PRN
- T replacement therapy: transdermal patch or gel, injections, buccal, or oral (rarely)*
- Monitor every 3, 6, then 12 months: T levels, digital rectal exam, prostate specific antigen, hematocrit, lipids

\textsuperscript{37}“Testosterone Deficiency and Erectile Dysfunction”, Ravin Bastiampillai and Tony Bella, November 29 2016, uOttawa Faculty of Medicine
Note contraindications and risks of T therapy
10.1 Major Depressive Disorder (MDD)\textsuperscript{1,2}

**Symptoms/Diagnostic Criteria (MSIGECAPS)**
- At least 2 weeks (1 week for children/adolescents) of depressed mood (M) or loss of interest (I) along with at least 4 other symptoms:
  - Mood changes (depressed mood)
  - Sleep changes
  - Interest loss
  - Guilt/worthlessness
  - Energy loss/fatigue
  - Cognition/concentration difficulties
  - Appetite loss
  - Psychomotor changes (e.g. agitation)
  - Suicidal ideation

**Physical Exam**
- If clinical suspicion, examine as appropriate for possible contributory medical conditions (e.g. vitamin B12 deficiency, hypothyroidism)

**Investigations**
- If clinical suspicion, rule out contributory medical conditions

**Management/Treatment**
- Use the biopsychosocial approach
- If mild to moderate: psychotherapy (cognitive behavioural therapy (CBT) or interpersonal psychotherapy (IPT)) or antidepressants
- If moderate to severe: medication ± psychotherapy
- If psychotic depression: combination treatment with antipsychotic and antidepressant or electroconvulsive therapy (ECT)
- Antidepressant treatment:
  - Start with selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI)
  - Start at lowest possible dose and titrate up gradually every 5 half-lives until intolerable side effects, full response, or maximal dose achieved
  - Monitor regularly (expect clinical response within 4-6 weeks and maintain treatment for 6 months-1 year if first episode, 2 years if second episode, etc.)
  - Choose an antidepressant that will maximize compliance

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\textsuperscript{1} “Differential Diagnosis of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine

\textsuperscript{2} “Psychopharmacology of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.2 Disruptive Mood Dysregulation Disorder (DMDD)\textsuperscript{3,4}

**Symptoms/Diagnostic Criteria**
- Severe temper outbursts (verbal/behavioural) with underlying persistent angry or irritable mood, inconsistent with developmental level
  - Duration of at least 12 months
  - \(\geq 3\) temper outbursts a week
  - Present in 2 of 3 settings (home, school, peers) and severe in at least 1 of these settings
  - Onset before age 10 but do not diagnose before age 6
  - Cannot diagnose for the first time after age 18

**Physical Exam**
- If clinical suspicion, examine as appropriate for possible contributory medical conditions (e.g. ADHD, ODD, conduct disorder)

**Investigations**
- If clinical suspicion, rule out contributory medical conditions

**Management/Treatment**
- As per MDD
- Other medications to consider:
  - Lithium
  - Clonidine
  - Antipsychotics
  - Anticonvulsants
  - Psychostimulants

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\textsuperscript{3} “Differential Diagnosis of Mood Disorders”, Sinhuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
\textsuperscript{4} “Psychopharmacology of Mood Disorders”, Sinhuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.3 Persistent Depressive Disorder (Dysthymia)\textsuperscript{5,6}

**Symptoms/Diagnostic Criteria (MSIGECAPS)**
- At least 2 years (1 year for children/adolescents) of depressed mood along with at least 2 other symptoms:
  - Appetite change
  - Sleep change
  - Low energy
  - Low self esteem
  - Decreased concentration
  - Hopelessness
- May include episodes of major depressive episodes (double depression)

**Physical Exam**
- If clinical suspicion, examine as appropriate for possible contributory medical conditions (e.g. vitamin B12 deficiency, hypothyroidism)

**Investigations**
- If clinical suspicion, rule out contributory medical conditions

**Management/Treatment**
- Same as Major Depressive Disorder

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\textsuperscript{5} “Differential Diagnosis of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine

\textsuperscript{6} “Psychopharmacology of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.4 Premenstrual Dysphoric Disorder (PMDD)\textsuperscript{7,8}

**Symptoms/Diagnostic Criteria**
- At least 5 symptoms in the week prior to menses; symptoms minimal or absent in the week after menses
  - Of the 5 symptoms, $\geq 1$ must be from category B:
    - Affective lability
    - Irritability
    - Depressed mood
    - Anxiety/tension
  - Of the 5 symptoms, $\geq 1$ must be from category C:
    - Poor concentration
    - Decreased interest
    - Fatigue or low energy
    - Appetite change
    - Hypersomnia/insomnia
    - Overwhelmed (feeling that one is losing control)
    - Physical symptoms (e.g. pain in breasts, bloating, muscular pain)
- Significant affective symptoms emerging in the week prior to menses and quickly disappearing with the onset of menses
- Present in all menstrual cycles in the past year and documented prospectively for at least 2 cycles

**Physical Exam**
- If clinical suspicion, examine as appropriate for possible contributory medical conditions

**Investigations**
- If clinical suspicion, rule out contributory medical conditions

**Management/Treatment**
- Same as Major Depressive Disorder
  - SSRI during luteal phase
  - Lifestyle changes
  - Light therapy
- Contraceptive medications
- NSAIDS for pain

\textsuperscript{7} “Differential Diagnosis of Mood Disorders”, Sinhuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
\textsuperscript{8} “Psychopharmacology of Mood Disorders”, Sinhuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.5 Depressive Disorder due to Medical Causes

Symptoms/Diagnostic Criteria
- Acute onset
- Absence of previous psychiatric history
- Atypical presentation of known psychiatric disorders
- Refractory to treatment
- Fever
- Weight loss despite appropriate nutrition
- Past medical history or family history of relevant medical conditions

Causes
- Neurologic (E.g. stroke, dementia, Parkinson’s disease, multiple sclerosis, seizure)
- Endocrine/Metabolic (E.g. hyperthyroidism, hypothyroidism, electrolyte abnormalities)
- Neoplastic
- Hematologic (E.g. anemia (deficiencies in vitamin B12, iron, folate))
- Cardiovascular (E.g. coronary artery disease)
- Rheumatologic
- Sleep disorders (E.g. obstructive sleep apnea)
- Medications (E.g. steroids, anti-hypertensives, oral contraceptives, accutane)
- Substances (E.g. alcohol, cannabis, amphetamines, opioids)
- Heavy metals and toxins

Physical Exam
- As appropriate based on DDx

Investigations
- As appropriate based on DDX

Management/Treatment
- As appropriate based on diagnosis

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9 “Differential Diagnosis of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10 “psychopharmacology of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.6 Bipolar Disorders\textsuperscript{11,12}

**Symptoms/Diagnostic Criteria for Bipolar I (GIDDINESS)**
- Mania: at least 1 week of euphoria (E) with at least 3 other symptoms, or irritability (I) with at least 4 other symptoms:
  - Grandiosity
  - Increased goal directed activity
  - Decreased judgment
  - Distractibility
  - Irritability
  - Need for sleep decreased
  - Euphoria
  - Speedy thoughts
  - Speedy talk

**Symptoms/Diagnostic Criteria for Bipolar II**
- Hypomania + major depressive episode
  - Hypomania: same diagnostic criteria as mania, except:
    - 4-day duration
    - No psychosis
    - No severe impairment
    - No hospitalization
- No manic episodes

**Physical Exam**
- If clinical suspicion, examine as appropriate for possible contributory medical conditions

**Investigations**
- If clinical suspicion, rule out causes of similar presentations
  - Medical conditions (e.g. hyperthyroidism, malignancy, renal failure, stroke, multiple sclerosis)
  - Medications (e.g. steroids, immunosuppressants, antidepressants)
- If clinical suspicion for substance use (e.g. alcohol, amphetamines), investigate as appropriate

**Management/Treatment**
- Use the biopsychosocial approach
- Psychotherapy: CBT, IPT, social rhythm therapy, family therapy
- For acute mania: lithium, valproic acid, atypical antipsychotics
  - Taper and discontinue antidepressants
- For acute bipolar depression: lithium, lamotrigine, quetiapine
  - Do not use antidepressants exclusively
- For maintenance therapy: lithium, valproic acid, lamotrigine, atypical antipsychotics
- Monitor for side effects
- For medical causes, manage and treat as appropriate

\textsuperscript{11} “Differential Diagnosis of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
\textsuperscript{12} “psychopharmacology of Mood Disorders”, Sinthuja Suntharalingam, January 5 2017, uOttawa Faculty of Medicine
10.7 Schizophrenia\textsuperscript{13,14}

**Epidemiology**
- Male to female ratio = 1.4:1
- Prevalence = 1%, preserved across cultures
- Mean age of onset is 21 in males and 27 in females

**Symptoms/Diagnostic Criteria**
- ≥2 of the following symptoms present for a significant time during a 1 month period (less if successfully treated); at least 1 symptom must be the first three:
  - Delusions
  - Hallucinations (auditory most frequent)
  - Disorganized speech
  - Grossly disorganized or catatonic behaviour
  - Negative symptoms (i.e. avolition, apathy, affective flattening, anosognosia)
- Social/occupational dysfunction
- Duration of at least 6 months (including prodrome), with 1 month of the first criterion being met
- Other criteria:
  - If present, depressive and/or manic symptoms are brief compared to the total duration of illness
  - Exclusion of substances and medical conditions
- Other symptoms:
  - Cognitive symptoms: deficits in attention, memory, executive functions
  - Mood symptoms: dysphoria, suicidality (5% die by suicide, 20% attempt suicide), hopelessness
  - Thought disorder: loosening of associations, derailment, circumstantiality, tangentiality, word salad, echolalia, mutism, clanging, verbigeration, incoherence, flight of ideas, thought blocking

**Physical Exam**
- If clinical suspicion, examine as appropriate for contributory medical conditions
- Full neurological exam, eye exam

**Investigations**
- CBC, electrolytes, BUN, creatinine, AST, ALT, ALP, Ca, PO4, TSH, B12, folate, EKG, fasting glucose and lipids
- If clinical suspicion, rule out contributory medical conditions or substance use (e.g. urinalysis, drug screen)
- Radiological investigations as clinically indicated

**Management/Treatment**
- Second-generation antipsychotics (i.e. 5HT2A/D2 antagonists) for 1 year
  - Consider starting with weight-neutral antipsychotics
  - Lower doses for prevention of relapse once stabilized; consider gradual supervised discontinuation if patient has good insight and is symptom-free after 1 year
- Individualize medications and route of administration based on side effect profile and history of efficacy
- Monitor for side effects such as extrapyramidal symptoms (i.e. tremor, rigidity, akinesia, stooped posture), akathisia, tardive dyskinesia, symptoms of hyperprolactinemia (e.g. sexual dysfunction, galactorrhea)
- Monitor for potential life-threatening complications (e.g. neuroleptic malignant syndrome)
- If 2 antipsychotic trials fail at full dose for 8 weeks, or if severe suicidal behaviour, consider clozapine
  - On clozapine, monitor blood weekly for possible agranulocytosis (1% prevalence)
- Psychotherapy: CBT, family therapy, supportive therapy, assertive community treatment (ACT), social skills training
- Encourage cessation of smoking and drugs/alcohol
- Diminish psychosocial stressors (e.g. financial strain, housing)
- ALWAYS evaluate risk of aggressiveness towards oneself or others

\textsuperscript{13} “Schizophrenia: The Schizophrenias”, Sharman Robertson, January 9 2017, uOttawa Faculty of Medicine
\textsuperscript{14} “Neurotransmitters and Psychosis”, Elliott Lee, January 11 2017, uOttawa Faculty of Medicine
10.8 Substance Use Disorder

Symptoms/Diagnostic Criteria

- A problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by the presentation of ≥2 of the following symptoms within a 12 month period:
  - Substance is often taken in larger amounts or over a longer period than intended
  - Persistent desire or unsuccessful effort to cut down or control substance use
  - A great deal of time spent on activities necessary to obtain the substance, use the substance, or recover from its effects
  - Craving or a strong desire/urge to use the substance
  - Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
  - Continued substance use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
  - Important social, occupational, or recreational activities are given up or reduced because of the substance use
  - Recurrent substance use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by substance use)
  - Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
  - Tolerance, as defined by either of the following:
    - A need for markedly increased amounts of substance to achieve intoxication or the desired effect
    - A markedly diminished effect with continued use of the same amount of the substance
  - Withdrawal, as manifested by either of the following:
    - The characteristic withdrawal syndrome for the substance
    - The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

Physical Exam

- Examine as appropriate for physical signs of substance use, including intoxication and withdrawal, depending on the substance in question

Investigations

- Blood work
- Drug toxicology testing: urinalysis, screening immunoassay
- Associated markers: AST, ALT, GGT, MCV for alcohol
- Liver function tests: albumin, bilirubin, INR
- Infectious disease testing: hepatitis C, hepatitis B, HIV, sexually-transmitted infections

Management/Treatment

- Manage as appropriate depending on the substance in question

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15 “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
16 “Substance Intoxication and Withdrawal”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.9 Alcohol/Benzodiazepine Intoxication\textsuperscript{17,18}

**Symptoms/Diagnostic Criteria**
- Recent use of substance
- Clinically significant maladaptive behavioural or psychological changes that developed during, or shortly after use (e.g. inappropriate sexual or aggressive behaviour, mood lability, impaired judgement)
- ≥1 of the following signs or symptoms developing during, or shortly after use
  - Slurred speech
  - Incoordination
  - Unsteady gait
  - Nystagmus
  - Impairment in cognition (e.g. attention, memory)
  - Stupor or coma
- Signs or symptoms not attributable to another medical condition, mental disorder, including intoxication with another substance

**Physical Exam**
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- Blood work (e.g. blood alcohol concentration, CBC, vitamin B1, B12, glucose)
- Associated markers: MCV for alcohol
- Liver function tests: albumin, bilirubin, INR
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- Monitor in-hospital for liver failure, cardiomyopathy, ED, various cancers, cognitive deficits, diabetes, GI problems
- Maintain patent airway and ensure respiration
- Thiamine (vitamin B1) replacement to prevent Wernicke’s encephalopathy and Korsakoff syndrome
  - Symptoms: confusion, ataxia, nystagmus, CN VI palsy
- Hemodialysis if concentrations dangerously high
- Symptomatic treatment
- Address alcohol/benzodiazepine use
- For chronic alcohol use, recommend Alcoholics Anonymous

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\textsuperscript{17} “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine

\textsuperscript{18} “Substance Intoxication and Withdrawal”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.10 Alcohol/Benzodiazepine Withdrawal\textsuperscript{19,20}

**Symptoms/Diagnostic Criteria**
- Cessation of (or reduction in) substance use that has been prolonged
- ≥2 of the following developing within several hours to a few days after cessation of (or reduction in) substance use
  - Autonomic hyperactivity (e.g. sweating or pulse rate greater than 100)
  - Increased hand tremor
  - Insomnia
  - Nausea or vomiting
  - Transient visual, tactile, or auditory hallucinations or illusions (e.g. formications)
  - Psychomotor agitation
  - Anxiety
  - Grand mal seizures
- Signs and symptoms in the second criterion cause clinically significant distress or impairment in social, occupational or other important areas of functioning
- Signs and symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance

**Physical Exam**
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- Blood work
- Associated markers: MCV for alcohol
- Liver function tests: albumin, bilirubin, INR
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- For alcohol use:
  - Peak intensity of symptoms usually after 24-72 hours; improves by 4-5 days
  - Thiamine replacement to prevent Wernicke’s encephalopathy and Korsakoff syndrome
  - Benzodiazepines such as diazepam for management of withdrawal symptoms unless oversedated
    - Consider oxazepam, temazepam, lorazepam for patients with liver disease
  - If severe or repeated seizures: IV diazepam (dosage based on algorithm - commonly CIWA protocol)
    - If treatment not initiated for withdrawal, seizures occur within 2-3 days and/or delirium tremens in 3-5 days
  - To prevent relapse, provide anti-craving medications: antabuse, naltrexone, acamprosate; off-label medications include topiramate, gabapentin, baclofen
  - Monitor medications accordingly for efficacy and side effects
  - Motivational interviewing and group therapy: Alcoholics Anonymous
  - Harm reduction strategies e.g. outpatient, intensive outpatient, residential, medically-supervised treatment
  - Discuss stages of change to determine appropriate treatment
- For benzodiazepine use:

\textsuperscript{19} “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
\textsuperscript{20} “Substance Intoxication and Withdrawal”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
○ Taper accordingly with benzodiazepines, preferably longer-acting agents such as diazepam
○ Dispense medications based on patient reliability
○ For lower tapering doses, outpatient management is preferred
○ Monitor for recurrence, rebound, and side effects

10.11 Opioid Intoxication\textsuperscript{21,22}

\textbf{Symptoms/Diagnostic Criteria}
\begin{itemize}
  \item Recent use of an opioid
  \item Clinically significant, problematic behavioural or psychological changes developing during or shortly after use (e.g. initial euphoria followed by apathy, dysphoria, psychomotor agitation or retardation, impaired judgement)
  \item Pupillary constriction (or pupillary dilation due to anoxia from severe overdose) and \(\geq 1\) of the following signs or symptoms:
    \begin{itemize}
      \item Drowsiness or coma
      \item Slurred speech
      \item Impairment in attention or memory
    \end{itemize}
  \item Signs and symptoms not attributable to another medical condition or mental disorder, including intoxication with another substance
\end{itemize}

\textbf{Physical Exam}
\begin{itemize}
  \item Vitals
  \item Neurologic exam
  \item Examine for neurologic and cardiorespiratory depression
  \item If clinical suspicion, examine as appropriate for other causes
\end{itemize}

\textbf{Investigations}
\begin{itemize}
  \item Blood work
  \item If clinical suspicion, investigate as appropriate for other causes
\end{itemize}

\textbf{Management/Treatment}
\begin{itemize}
  \item Symptoms normally last for several hours
  \item Prompt administration of naloxone as warranted
  \item Advanced cardiac life support as warranted
  \item Assess for substance use disorder
    \begin{itemize}
      \item If present, recommend Narcotics Anonymous
    \end{itemize}
\end{itemize}

\textsuperscript{21} “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
\textsuperscript{22} “Substance Intoxication and Withdrawal”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.12 Opioid Withdrawal\textsuperscript{23,24}

**Symptoms/Diagnostic Criteria**
- Presence of either of the following:
  - Cessation of (or reduction in) opioid use that has been heavy and prolonged
  - Administration of an opioid antagonist after a period of opioid use
- \geq 3 of the following developing within minutes to several days after the first criterion:
  - Dysphoric mood
  - Nausea or vomiting
  - Muscle aches
  - Lacrimation or rhinorrhea
  - Pupillary dilation, piloerection, or sweating
  - Diarrhea
  - Yawning
  - Fever
  - Insomnia
- Signs and symptoms in the second criterion cause clinically significant distress or impairment in social, occupational or other important areas of functioning
- Signs and symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance
- Other subjective complaints include anxiety, restlessness, an achy feeling often located in the back and legs, craving and drug-seeking behaviour, irritability and increased sensitivity to pain

**Physical Exam**
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- Blood work
- Clinical Opioid Withdrawal Scale to assess severity
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- Likely will require supportive medications ± opioids
- Tailor treatment choice to the patient:
  - Abstinence
  - Non-opioid management
    - Clonidine
    - Antidiarrheals (e.g. loperamide), antinauseants (e.g. dimenhydrinate), analgesics (e.g. NSAIDs)
  - Taper using long-acting opioid such as oxycontin
    - Ensure adequate monitoring
  - Opioid substitution therapy
    - Methadone taken orally as a liquid
    - Suboxone taken sublingually
    - Ensure adequate monitoring
  - Harm reduction strategies
  - Narcotics Anonymous

\textsuperscript{23} “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
\textsuperscript{24} “Substance Intoxication and Withdrawal”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.13 Stimulant Intoxication

Symptoms/Diagnostic Criteria
- Recent use of amphetamine-type substance, cocaine, or other stimulant
- Clinically significant, problematic behavioural or psychological changes (e.g. euphoria or affective blunting; changes in sociability, hypervigilance, interpersonal sensitivity, anxiety, tension or anger; stereotyped behaviours; impaired judgement) that developed during or shortly after stimulant use
- ≥2 of the following signs or symptoms, developing during or shortly after stimulant use:
  - Tachycardia or bradycardia
  - Pupillary dilation
  - Elevated or lowered blood pressure
  - Perspiration or chills
  - Nausea or vomiting
  - Evidence of weight loss
  - Psychomotor agitation or retardation
  - Muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias
  - Confusion, seizures, dyskinesias, dystonias, or coma
- Signs and symptoms are not attributable to another medical condition, mental disorder, or intoxication with another substance

Physical Exam
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work
- Drug toxicology testing
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Symptomatic management
- Assess for possible substance use disorder
- Harm reduction strategies

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25 “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.14 Stimulant Withdrawal

Symptoms/Diagnostic Criteria
- Cessation of (or reduction in) prolonged amphetamine-type substance, cocaine, or other stimulant use
- Dysphoric mood and ≥2 of the following physiological changes, developing within hours to several days after criterion A:
  - Fatigue
  - Vivid, unpleasant dreams
  - Insomnia or hypersomnia
  - Increased appetite
  - Psychomotor retardation or agitation
- Signs and symptoms cause clinically significant distress and impairment in social, occupational, or other important areas of functioning
- Signs and symptoms not attributable to another medical condition, mental disorder, or intoxication or withdrawal from another substance

Physical Exam
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work
- Drug toxicology testing
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- No medications required
- Assess for possible substance use disorder
- Harm reduction strategies

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26 “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
10.15 Cannabis Intoxication

Symptoms/Diagnostic Criteria
- Recent use of cannabis
- Clinically significant, problematic behaviour or psychological changes (e.g. impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgement, social withdrawal)
- ≥2 of the following signs or symptoms developing within 2 hours of cannabis use:
  - Conjunctival injection
  - Increased appetite
  - Dry mouth
  - Tachycardia
- Signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance

Physical Exam
- Vitals
- Neurologic exam
- If clinical suspicion, examine for other causes

Investigations
- Blood work
- Drug toxicology testing (cannabis remains in urine for 20-30 days)
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Symptomatic management
- Can result in possible precipitation of psychotic disorder, amotivational syndrome, etc.
- Assess for possible substance use disorder
- Harm reduction strategies

10.16 Cannabis Withdrawal

Symptoms/Diagnostic Criteria
- Cessation of (or reduction in) cannabis use that has been heavy and prolonged
- ≥3 of the following signs and symptoms develop within approximately 1 week of criterion A:
  - Irritability, anger or aggression
  - Nervousness or anxiety
  - Sleep difficulty (insomnia, disturbing dreams)
  - Decreased appetite or weight loss
  - Restlessness
  - Depressed mood
  - ≥1 of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache

Physical Exam
- Vitals
- Neurologic exam
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work
- Drug toxicology testing

27 “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine

28 “Substance Use Disorders”, Melanie Willows, January 10 2017, uOttawa Faculty of Medicine
• If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
• No medications required
• Typically resolves in a couple of weeks
• Assess for possible substance use disorder
• Harm reduction strategies
10.17 Dystonia\textsuperscript{29,30}

Typical Patient
- Young male <30 years old
- On a course of potent antipsychotics
- Symptoms usually present within 1 week of starting treatment

Symptoms
- Torticollis
- Swollen tongue
- Trismus
- Oculogyric crisis
- Opisthotonos
- Dystonic hyper pronation
- Laryngeal adductor spasm

Physical Exam
- Examine for symptoms
- If clinical suspicion, examine as appropriate for other causes

Investigations
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Oral anticholinergics: benztropine, procyclidine (IV or IM if life-threatening)
- Oral or IV diphenhydramine
- Oral or IV benzodiazepine
- Review need for and dose of antipsychotic
- Maintain anticholinergics or benzodiazepine for 4-6 weeks

\textsuperscript{29} “Movement Disorders and Extrapyramidal Symptoms”, Alain Labelle, January 11 2017, uOttawa Faculty of Medicine
\textsuperscript{30} “psychopharmacology of Psychotic Illness”, Elliott Lee, January 14 2017, uOttawa Faculty of Medicine
10.18 Parkinsonism\textsuperscript{31,32}

Typical Patient
- Elderly female
- History of neurological problems
- On a high dose, high potency antipsychotic
- Onset within 30 days of starting treatment

Symptoms
- Bradykinesia
  - Diminution of background motor activity
  - Slowed execution of movements with difficult initiation
  - Progressive fatiguing and diminishing amplitude of movements
  - Interruption of flow of consecutive movements
- Rigidity
  - Increase in resting muscle tone
- Tremor

Physical Exam
- Neurologic exam: examine for symptoms
- If clinical suspicion, examine as appropriate for other causes

Investigations
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Modify antipsychotic regimen
  - Trial of newer generation antipsychotic
    - Clozapine
- Anticholinergics: benztropine, kemadrin
- Dopamine agonists: L-dopa, bromocriptine, lisuride, pergolide
  - Typically avoid in patients with psychotic symptoms and parkinsonism from medications
- Serotonin (5HT2) antagonists

\textsuperscript{31} “Movement Disorders and Extrapyramidal Symptoms”, Alain Labelle, January 11 2017, uOttawa Faculty of Medicine
\textsuperscript{32} “Psychopharmacology of Psychotic Illness” Elliott Lee, January 14 2017, uOttawa Faculty of Medicine
10.19 Akathisia\textsuperscript{33,34}

**Typical Patient**
- Middle-aged female
- On a course of potent antipsychotics
- Variable onset of symptoms

**Symptoms**
- Restlessness
- Dysphoria
- Apprehension
- Anxiety
- Tension
- Impatience
- Irritability

**Physical Exam**
- Examine for symptoms
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- Modify antipsychotic regimen
  - Trial of newer generation antipsychotic
  - Clozapine
- Beta-blockers: propranolol
- Benzodiazepines: lorazepam, clonazepam
- Anticholinergics
- Serotonin (SHT2) antagonists

\textsuperscript{33} “Movement Disorders and Extrapyramidal Symptoms”, Alain Labelle, January 11 2017, uOttawa Faculty of Medicine
\textsuperscript{34} “psychopharmacology of Psychotic Illness” Elliott Lee, January 14 2017, uOttawa Faculty of Medicine
10.20 Tardive Dyskinesia^35,36

**Typical Patient**
- Older female
- On a prolonged course of potent antipsychotics (>3 months of use)
- Variable onset of symptoms

**Symptoms**
- Abnormal, repetitive, involuntary motor movements in one or more body parts after prolonged exposure to antipsychotics
  - E.g. protrusion and rolling of the tongue, sucking and smacking movements of the lips, chewing motion, facial dyskinesia, involuntary movements of the body and extremities

**Physical Exam**
- Examine for symptoms
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- Modify antipsychotic regimen
  - Smallest effective dose?
  - Trial of newer generation antipsychotic
  - Clozapine
- Tetrabenazine (VMAT2 inhibitor)
- Clonazepam
- Botulinum toxin
- Propranolol
- Reserpine
- Ondansetron
- Vitamin E
- Treat antipsychotic withdrawal

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^35 “Movement Disorders and Extrapyramidal Symptoms”, Alain Labelle, January 11 2017, uOttawa Faculty of Medicine
^36 “Psychopharmacology of Psychotic Illness” Elliott Lee, January 14 2017, uOttawa Faculty of Medicine
10.21 Neuroleptic Malignant Syndrome (NMS)\textsuperscript{37,38}

**Risk Factors**
- Antipsychotic use
- Rapid dose increase
- Extreme psychomotor abnormalities
- Dehydration
- Affective disorder
- IM medication usage
- Male
- Medical illness

**Symptoms (FRAME)**
- Fever
- Rigidity
- Autonomic instability: higher heart rate, unstable blood pressure, diaphoresis
- Mental status changes
- Extra: lab changes (e.g. higher white blood cell count)

**Physical Exam**
- Vitals
- Neurological exam
- If clinical suspicion, examine as appropriate for other causes

**Investigations**
- Blood work
- If clinical suspicion, investigate as appropriate for other causes

**Management/Treatment**
- Hospitalize
- Discontinue all antipsychotics
- Supportive treatment: antipyretics, hydration
- Dopamine agonists: bromocriptine, amantadine
- Muscle relaxants: dantrolene

\textsuperscript{37} “Movement Disorders and Extrapyramidal Symptoms”, Alain Labelle, January 11 2017, uOttawa Faculty of Medicine

\textsuperscript{38} “psychopharmacology of Psychotic Illness” Elliott Lee, January 14 2017, uOttawa Faculty of Medicine
10.22 Anorexia Nervosa

Epidemiology
- Predominantly females (90%)
- Young age of onset (13-20 years old); peaks at 14 and 18 years of age
  - Only 5% present after 20 years of age
- Often have comorbid depression, obsessive compulsive disorder, generalized anxiety disorder, or social phobia; suicidal ideation common and must be monitored

Symptoms/Diagnostic Criteria
- Restriction of intake leading to significantly low body weight
- Intense fear of gaining weight
- Distorted body image
  - Undue influence of weight on self-worth
  - Denial of seriousness of low weight
- Further specified as restricting type or binge-eating/purging type
- Associated symptoms:
  - Excessive exercising
  - Restlessness
  - Self-induced vomiting
  - Use of diet pills and laxatives

Physical Exam
- Vitals, weight/height, hydration status
- Examine skin for dryness, hands for Russell’s sign, parotid glands for enlargement, muscles for wasting, teeth for dental erosion
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work (e.g. glucose, extended electrolytes, LFTs, BUN, Cr, TSH)
- Electrocardiogram
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Thorough biopsychosocial assessment
- Reversal of effects of starvation and medical monitoring
  - Refeeding
  - Meal plan
- No medications found to be effective (atypical antipsychotics, specifically olanzapine, may decrease distress)
- Psychological treatment
  - Family-based therapy for children and adolescents
  - CBT, IPT, motivational therapy
- Support, education on illness
- Treat comorbidities (note: SSRIs are not effective in malnourished patients)

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39 “Eating Disorders”, Leanna Isserlin, January 14 2017, uOttawa Faculty of Medicine
10.23 Bulimia Nervosa

Epidemiology
- Predominantly females
- Young age of onset (16.5-19 years old)
- Often have comorbid depression, generalized anxiety disorder, social phobia, substance abuse; suicidal ideation is common and must be monitored

Symptoms/Diagnostic Criteria
- Recurrent binge eating:
  - Eating a large amount of food in a discrete period of time
  - Lack of control during binge episodes
- Recurrent compensatory behaviour to prevent weight gain
  - Vomiting
  - Laxatives
  - Fasting
  - Over-exercise
- Criteria one and two occur at least once a week for 3 months
- Self-worth unduly influenced by shape and weight
- Not anorexia nervosa

Physical Exam
- Vitals, weight/height, hydration status
- Examine skin, teeth for dental erosion
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work (e.g. glucose, extended electrolytes, LFTs, BUN, Cr, TSH)
- Electrocardiogram
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Thorough biopsychosocial assessment
- Reversal of effects of starvation and medical monitoring
  - Refeeding
  - Meal plan
- High-dose SSRIs
  - Fluoxetine 50-80 mg/day
- Psychotherapy
  - Family-based therapy for children and adolescents
  - CBT, IPT
- Support, education on illness
- Treat comorbidities

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"Eating Disorders", Leanna Isserlin, January 14 2017, uOttawa Faculty of Medicine
10.24 Binge Eating Disorder

Epidemiology
- More equal female: male ratio than other eating disorders (3.5:2)
- Typically presents in adolescence and adulthood

Symptoms/Diagnostic Criteria
- Binges at least once a week for 3 months
- Binges associated with ≥3 of the following:
  - Eating rapidly
  - Eating until uncomfortably full
  - Eating large amounts when not hungry
  - Eating alone
  - Feeling disgusted, depressed or guilty afterwards
- No compensatory behaviour
- Not anorexia nervosa or bulimia nervosa

Physical Exam
- Vitals
- If clinical suspicion, examine as appropriate for other causes

Investigations
- Blood work
- If clinical suspicion, investigate as appropriate for other causes

Management/Treatment
- Psychotherapy
  - CBT (individual or group)
  - IPT
  - Dialectical behaviour therapy (DBT)
- Medications
  - Sertraline
  - Imipramine
  - Citalopram
  - Escitalopram
  - Topiramate
10.25 Anxiety and Stress

Typical Patient
- Acute
  - Panic attacks
  - Autonomic arousal
- Chronic
  - Tension
  - Exhaustion
  - Unexplained somatic symptoms

Causes
- Genes
- Environment
- Threat
- Personality

Separation Anxiety Disorder
- Marked fear or anxiety of separation from attachment figures to a degree that is developmentally inappropriate
  - Main fear: harm to or death of loved one or untoward event occurring to oneself
- Nightmares and physical symptoms of distress
- 4-week duration is required for diagnosis in childhood; longer duration (typically at least 6 months) is required for diagnosis in adulthood

Specific Phobia
- Marked fear, anxiety, or avoidance of circumscribed objects or situations out of proportion to the danger posed

Social Anxiety Disorder
- Marked fear, anxiety, or avoidance of social interactions and situations that involve being scrutinized or being the focus of attention (e.g. being observed while speaking, eating, or performing in front of others) and that is out of proportion to the threat posed
  - Main fears: potentially embarrassing or humiliating oneself, being rejected

Agoraphobia
- Marked fear, anxiety, or avoidance of ≥2 of the following situations: public transportation, open spaces, enclosed spaces, queues or crowds, or being outside of home alone
  - Main fear: escape might be difficult or help might not be available if panic or other embarrassing symptoms occur

Panic Disorder
- Recurrent unexpected panic attacks (i.e. abrupt surge of intense fear or discomfort that reaches a peak within minutes and includes ≥4 specified symptoms, including autonomic arousal and other physical and cognitive symptoms
- Persistent concern or worry about further panic attacks or maladaptive avoidance behaviours for at least 1 month

Generalized Anxiety Disorder
- Marked anxiety and worry, more days than not, about various domains, such as finances, work and school
- Viewed as excessive and uncontrollable by patient
- Lasts for at least 6 months

42 “Anxiety and Stress: Overview”, J. Shilk, January 16 2017, uOttawa Faculty of Medicine
- ≥3 physical symptoms: restlessness or feeling keyed up or on edge, easily fatigued, difficulty concentrating, irritability, muscle tension, sleep disturbance

### Features of Anxiety Disorders Across Lifespan

<table>
<thead>
<tr>
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<th>Adulthood</th>
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<td>Depression, another anxiety disorder</td>
<td>Depression, another anxiety disorder, substance abuse</td>
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### Management/Treatment

- Education and reassurance
- Psychotherapy
  - CBT
  - Exposure therapy
- Medications
  - SSRIs or SNRIs
  - Benzodiazepines (for short-term only)
  - Other antidepressants
  - Antipsychotics, mood stabilizers (if comorbid bipolar disorder or as adjunct to antidepressant)
10.26 Attention-Deficit/Hyperactivity Disorder (ADHD)

Typical Patient
- School-aged children (4-16 years old)

Causes
- Genetics (0.76 variance)
- Non-genetic factors (e.g. low birth weight/prematurity, maternal smoking or drinking alcohol in pregnancy, psychosocial adversity)
- Catecholamine dysfunction (norepinephrine and dopamine)

Symptoms/Diagnostic Criteria
- Inattentive symptoms (≥6/9) and/or hyperactive-impulsive symptoms (≥6/9) have persisted for at least 6 months
  - Note: for older adolescents and adults (≥17 years), ≥5 symptoms are required
- Several symptoms must have been present before age 12
- Several symptoms must be present ≥2 settings
- Clear interference in functioning (e.g. school, social, family, work)
- Symptoms are not better explained by another mental health disorder or medical condition

Comorbidities
- Any mood disorder (e.g. MDD)
- Any anxiety disorder (e.g. social phobia, generalized anxiety disorder)
- Any substance disorder

Assessment in Children and Adolescents
- Parent interview including developmental history (including any recent major changes or stressors in child’s life)
- Child/adolescent interview
- Collateral information from teachers and other sources

Assessment in Adults
- Focused biopsychosocial history
- Brief childhood history and childhood ADHD symptoms
- Assess lifelong and current ADHD symptoms

Investigations
- Hearing, vision assessment
- Sleep assessment
- Assess for head injuries and seizures

Treatment
- Non-pharmacological:
  - Psychoeducation
  - Behavioral parent management training
  - Behavioral social and academic intervention
  - Psychotherapy (e.g. CBT)
- Pharmacological:
  - Methylphenidate (Ritalin, Concerta, Biphentin)
  - Amphetamines (Adderall, Vyvanse)
  - Non-stimulants (e.g. atomoxetine)

43 “ADHD, Oppositional Defiant Disorder, Conduct Disorder”, Dhiraj Aggarwal, January 17 2017, uOttawa Faculty of Medicine
10.27 Conduct Disorder

Typical Patient
- School aged children (4-16 years old)

Cause
- Multifactorial = genetics and environment

Diagnostic Criteria
- Repetitive and persistent pattern of behavior
  - Basic rights of others or major age-appropriate societal norms/rules are violated
  - >3 of 15 in past 12 months (&1 in past 6 months)
- Disturbance causes clinically significant impairment (social, academic, occupational, legal)
- If >18 years, criteria not met for anti-social personality disorder

Co-morbidities
- Learning Disorder
- Anxiety
- Mood disorders – depressive or bipolar
- Substance-related disorders

Treatment
- Non-Pharmacological:
  - Cognitive problem solving skills training
  - Parent management training
  - Family therapy
  - Multisystemic therapy
- Treat co-morbid conditions:
  - ADHD – stimulants
  - Depression – SSRIs, bupropion
  - Anxiety – SSRIs, buspirone
- Treat CD symptoms alone:
  - Impulsivity/aggression: mood stabilizers, neuroleptics, alpha-2 agonists
  - Hyperactivity: stimulants, alpha-2 agonists

44 “Disruptive Behavior Disorders”, C. Robertson, January 17 2017, uOttawa Faculty of Medicine
10.28 Oppositional Defiant Disorder (ODD)\textsuperscript{45}

Typical Patient
- School-aged children (4-16 years old)

Cause
- Multifactorial: temperament, genetics, and environment (e.g. adverse childhood experiences)

Symptoms/Diagnostic Criteria
- Pattern of (a) angry/irritable mood, (b) argumentative/defiant behavior, or (c) vindictiveness lasting at least 6 months, as evidenced by ≥4 symptoms from any category, during interactions with ≥1 person (who is not a sibling)
- Disturbance in behaviour is associated with distress in the individual or others in the individual’s immediate social context or causes clinically significant impairment in functioning
- Behaviours do not occur exclusively during the course of a psychotic, substance use, depressive or bipolar disorder

Comorbidities
- ADHD
- Increased risk of anxiety disorders and MDD
- Learning disabilities
- CD

Treatment
- Non-pharmacological:
  - Parent training
  - Parent-child interaction therapy
  - Individual psychotherapy
  - Family psychotherapy
  - Social skills training
- Pharmacological:
  - ODD + ADHD: use 1\textsuperscript{st}-line ADHD medications
  - ODD alone: stimulants do not reduce symptoms

\textsuperscript{45} “Disruptive Behavior Disorders”, C. Robertson, January 17 2017, uOttawa Faculty of Medicine
10.29 Insomnia\textsuperscript{46}

Typical Patient
- All age groups, but most common first presentation is between ages 30–50
- Predominantly females

Cause
- Stressful personal events
- Impending stressors (e.g. exams, legal issues)
- Acute illness
- Can be “constitutional” (i.e. lifelong shallow sleeper, easily awakened, with persistent hyperarousal)

Symptoms/Diagnostic Criteria
- Present for at least 3 months and occurs at least 3 nights per week
- Not better explained by a psychiatric illness (e.g. anxiety disorder, substance abuse (especially alcohol and cocaine), mood disorder, psychosis)
- Not better explained by a disruptive chronic medical condition (e.g. diarrhea), a diagnosable sleep disorder (e.g. sleep apnea), or a substance (e.g. drug of abuse, medication)
- Possibly explained by a misperception of sleep need or misperception of the amount of sleep that is actually occurring

Investigations
- Psychiatric history is critical
  - Amount of insomnia (at least 30 min 3x/week)?
  - When did it begin (e.g. recent life events and stressors)?
  - Is there daytime napping?
    - Many “insomnia” patients are not objectively sleepy during the day, whereas sleep apnea patients are
  - Is there shift work and if so, do shifts change more often than every 2 weeks?
  - In what part of the night does insomnia occur (early = anxiety; late = depression)?
  - Is the insomnia associated with physical or environmental causes?
  - Is there alcohol consumption after 7pm or caffeine consumption after 2pm?

Treatment
- Acute insomnia (i.e. lasting <3 months): reassurance, support, medications for short-term (i.e. 2 weeks) use (e.g. trazodone, doxepin, temazepam, lorazepam, clonazepam, zopiclone, zolpidem)
- Chronic insomnia: ask questions about substance abuse, depression, anxiety, sleep hygiene, naps, caffeine, shift work
  - Treat psychiatric illness if present or refer to psychiatrist
  - Refer to sleep lab if suspect sleep disorder
  - Suggest CBT for insomnia (CBTi) from a psychologist
  - Improve sleep hygiene: limiting caffeine and alcohol in the evening, decreasing stimulation and screen time before bed, waking up at the same time everyday regardless of amount of sleep

\textsuperscript{46} “Insomnia”, Alan B. Douglass, January 18 2017, uOttawa Faculty of Medicine
10.30 Trauma and Stress-Related Disorders

Typical Patient
- Experienced or witnessed a stressor that the individual perceives as horrible or uncontrollable
- Learning about something horrible that has happened to a loved one
- Repeated or extreme exposure to aversive details of a trauma (e.g. first responder or investigator)

Acute Stress Disorder
- Re-experiencing (e.g. memories, dreams, dissociative flashbacks, prolonged psychological or physical distress in response to internal or external cues)
- Negative mood (e.g. emotional numbing)
- Hyperarousal
- Avoidance
- Dissociation
  - Reduction in awareness of surroundings
  - Amnesia
- ≥9/14 symptoms for >2 days but <1 month

Post-Traumatic Stress Disorder (PTSD)
- 4 symptom clusters:
  - Intrusive symptoms (e.g. re-experiencing)
  - Avoidance (at least one symptom)
  - Negative cognitions and mood (at least two symptoms)
  - Hyperarousal (at least two symptoms)
- ≥1 symptom from each of the first 2 clusters and ≥2 symptoms from each of the last 2 clusters; symptoms persist for >1 month
- Symptoms cause clinically significant impairment in social, occupational or other important areas of functioning
- Symptoms not better explained by another diagnosis

Investigations
- Psychiatric history in a comfortable, private place
  - Type of trauma
  - Age at time of trauma
  - Reaction to trauma
  - Risk factors (e.g. childhood abuse, female gender, dissociation at time of trauma, lack of psychosocial supports)
  - Protective factors
  - Assess functional level

Management/Treatment
- Stage 1: stabilization
  - Goal is symptom management (e.g. sobriety, parasuicidal behaviour, treatment of comorbidities)
  - Pharmacotherapy
    - Core medications:
      - SSRIs (paroxetine, sertraline, fluoxetine)
      - SNRIs (venlafaxine)
    - Augmenting medications:
      - Insomnia: trazodone, mirtazapine, zopiclone, seroquel
      - Nightmares: prazosin, nabilone
  - Psychoeducation

47 “Trauma-Stressor Related Disorders”, Helene Cadotte, January 18 2017, uOttawa Faculty of Medicine
DBT adapted for PTSD: usually for PTSD related to childhood abuse or if PTSD is comorbid with borderline personality disorder

- Stage 2: trauma-focused treatment, grief work, making meaning of trauma
  - Goal is living in the present and not being stuck in the past
  - Psychotherapy
    - Prolonged exposure therapy
    - Cognitive processing therapy and narrative storytelling
    - Eye movement desensitization and reprocessing (EMDR)

- Stage 3: reconnection with friends, community, and work-related activities

**Treatment for acute trauma:**

- Provide basic needs as required (e.g. housing, food)
- Psychoeducation and social support
- Critical incident debriefing is controversial
  - No evidence supporting efficacy of widespread single or multiple session psychological debriefing
  - May interfere with course of natural recovery
- Monitor symptoms carefully
- Screen for PTSD risk factors, though most will not develop PTSD
10.31 Personality Disorders

Typical Patient
- Late adolescence to early adulthood
- Significant interpersonal difficulties

Causes
- Genetic heritability of personality disorders similar to heritability of personality
- Adverse childhood events (e.g. abuse, neglect)

Symptoms/Diagnostic Criteria
- Impairment in personality functioning and has established pattern
- ≥1 pathological personality traits:
  - Antisocial
  - Borderline
  - Schizotypal
  - Avoidant
  - Obsessive-compulsive
  - Narcissistic
- Impairments are relatively inflexible and pervasive across a broad range of personal and social situations
- Impairments are relatively stable over time; can be traced back to adolescence or early adulthood

Cluster A Personality Disorders
- All have a genetic link to schizophrenia, with schizotypal having the strongest relationship
- Schizoid
  - Detachment from social relationships
  - Restricted range of expression of emotions in interpersonal settings
- Schizotypal
  - Acute discomfort with, and reduced capacity for, close relationships
  - Cognitive or perceptual distortions (e.g. odd beliefs)
  - Eccentricities of speech or behaviour
- Paranoid
  - Distrust and suspiciousness of others
  - Others’ motives are interpreted as malevolent

Cluster B Personality Disorders
- Histrionic
  - Excessive emotionality (i.e. rapidly shifting and seemingly shallow)
  - Attention-seeking (e.g. inappropriate seductive or provocative behaviour, exaggerated physical appearance, impressionistic speech, dramatic/theatrical)
- Antisocial
  - Disregard for, and violation of, the rights of others
  - Occurring since age 15 (would have received diagnosis of CD)
  - Must be at least 18 years
- Narcissistic
  - Grandiosity – fantasy or behaviour
  - Need for admiration and sense of entitlement
  - Lack of empathy and interpersonally exploitative
- Borderline
  - Instability of interpersonal relationships, self-image, and affect
  - Marked impulsivity

48 “Personality Disorders”, Deanna Mercer, January 19 2017, uOttawa Faculty of Medicine
Cluster C Personality Disorders

- Obsessive-compulsive
  - Orderliness, perfectionism, and mental and interpersonal control at the expense of flexibility, openness, and efficiency
  - Not to be confused with obsessive-compulsive disorder
- Avoidant
  - Social inhibition
  - Feelings of inadequacy
  - Hypersensitivity to negative evaluation
- Dependent
  - Pervasive and excessive need to be taken care of that leads to submissive and clinging behavior and fears of separation

Complications

- Functional impairment
  - Large negative impact on quality of life
- Elevated risk of suicide
- Reduced life expectancy by 15-20 years
- Increased risk of other mental disorders (e.g. depression, anxiety, substance use disorder)

Investigations

- Psychiatric and psychosocial history

Management/Treatment

- Psychotherapy
10.32 Borderline Personality Disorder (BPD)\(^{49}\)

**Typical Patient**
- Late adolescence to early adulthood

**Cause**
- Genetic heritability of personality disorders similar to heritability of personality
- Adverse childhood events (e.g. physical/emotional/sexual abuse, physical/emotional neglect)

**Symptoms/Diagnostic Criteria**
- Pervasive pattern of instability of interpersonal relationships, self-image and affect and marked impulsivity
  - Relationships: Chaotic, idealizing/devaluing, fear of abandonment
  - Cognitive/self-image: Emptiness, unstable sense of self, mild psychotic symptoms under stress, dissociation
  - Affect: Emotional lability, problems with anger
  - Behaviour: Suicide and self-harm, Impulsivity (e.g. promiscuity, binge eating, driving fast, finances)

**Comorbidities**
- Mood disorders
  - MDD, PDD, bipolar disorder
- Eating disorders
  - Anorexia nervosa, bulimia nervosa, obesity
- Anxiety disorders
- PTSD (full or residual symptoms)
- Dissociative disorders
- Substance use disorders

**Investigations**
- Psychiatric history

**Management/Treatment**
- Psychotherapy: DBT or good psychiatric management (GPM)
- Hospitalization for acute crises (e.g. serious suicide attempt, psychosis/severe disorganization)
- Medications for comorbid mental disorders (e.g. depression, anxiety) and for sleep (short-term only)

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\(^{49}\) “Personality Disorders”, Deanna Mercer, January 19 2017, uOttawa Faculty of Medicine
10.33 Autism Spectrum Disorder (ASD)\(^50\)

**Typical Patient**
- School-aged children (4-16 years old)

**Cause**
- **Genetics**
  - Known genetic syndromes, defined mutations, de novo copy number variations
  - Single gene disorders (e.g. fragile X syndrome, tuberous sclerosis, Prader-Willi syndrome, neurofibromatosis)
- **Environmental factors**
  - Advanced parental age (especially >40 years)
  - Maternal anticonvulsants

**Symptoms/Diagnostic Criteria**
- Persistent deficits in social communication and social interaction across multiple contexts. Manifested by:
  - Deficits in social-emotional reciprocity
  - Deficits in nonverbal communicative behaviors used for social interaction
  - Deficits in developing, maintaining and understanding relationships
- Restricted, repetitive patterns of behaviours, interests, or activities, as manifested by:
  - Stereotyped or repetitive motor movements, use of objects, or speech
  - Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior
  - Highly restricted, fixated interests that are abnormal in intensity or focus
  - Hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment
- Symptoms must be present in the early developmental period
- Symptoms cause clinically significant impairment in social, occupational or other important areas of functioning
- Symptoms are not better explained by intellectual disability or global developmental delay

**Physical Exam**
- Identify dysmorphic features (neurological exam, head circumference, vision and hearing assessment)

**Investigations**
- Psychiatric history
- Observation of child, including play
- Collateral information about child in social settings
- Psychological evaluation: cognitive testing, adaptive skills
- Speech/language/communication assessment
- Evaluation by occupational therapist (i.e. sensory/motor)
- Genetic testing: chromosomal microarray analysis, molecular DNA for fragile X syndrome
- Comorbidities: Intellectual disability, ADHD, Specific language impairment, Anxiety, Depression, OCD, Motor disorder

**Management/Treatment**
- Non-pharmacological:
  - Applied Behaviour Analysis (ABA)
  - Intensive behavioural intervention
- Pharmacotherapy:
  - Risperidone and aripiprazole approved for irritability in children/adolescents with ASD

\(^{50}\) “Autism Spectrum Disorder”, Dhiraj Aggarwal, January 20 2017, uOttawa Faculty of Medicine
10.34 Delirium

**Typical Patient**
- Elderly

**Causes (IWATCHDEATH)**
- Infection
- Withdrawal (i.e. substance intoxication/withdrawal)
- Acute metabolic derangements
- Trauma
- CNS pathology
- Hypoxia
- Deficiencies
- Endocrine
- Acute vascular/myocardial infarction
- Toxins (i.e. medication-induced)
- Heavy metals

**Symptoms/Diagnostic Criteria**
- Disturbance of attention and awareness
- Acute, change from previous, and fluctuating
- One other disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, perception)
- Not better explained by another neurocognitive disorder and not in context of severely decreased LOC
- Due to direct physiological consequence of a medical condition, substance, toxin, or multiple etiologies
- Specify if acute/persistent and hypoactive/hyperactive/mixed

**Risk Factors**
- Top 4 independent risk factors: vision impairment, any severe illness, cognitive impairment, high BUN/Cr
- Demographics/medical history: male, age >75, long-term care, sensory impairment
- Psychiatric history: history of delirium, other neurocognitive disorders, depression, bipolar disorder, schizophrenia, drugs/alcohol
- Medications: polypharmacy, anticholinergic medications, serotonin medications
- Other: dehydration, malnutrition, sleep deprivation, pain, IV line, catheters, restraints

**Investigations**
- Vitals, physical exam, hydration status
- Basic labs: CBC, electrolytes, BUN/Cr, glucose, TSH, B12, LFTs, Ca, albumin
- Infection workup: urinalysis, CXR ± blood cultures
- Primarily a clinical diagnosis based on assessment of attention (e.g. serial 7’s, orientation, Confusion Assessment Method (CAM))

**Consequences**
- Prolonged length of stay in hospital
- Worse rehabilitation/functional outcomes
- Higher institutionalization rates
- Increased risk of cognitive decline
- Higher mortality rates

**Management/Treatment**
- Ensure accurate diagnosis (hypoactive delirium is often misdiagnosed as depression)

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51 “Neurocognitive Disorders”, Soojin Chun, January 4 2017, uOttawa Faculty of Medicine
52 “Acute Confusion in the Elderly”, Barbara Power, March 31 2017, uOttawa Faculty of Medicine
- Reverse psychotic signs and symptoms (e.g. haldol to treat severe agitation)
- Identify and treat underlying cause(s)
  - Note: about 10% have no identifiable underlying cause
Ophthalmology
11.1 Cataracts$^{1,2,3}$

**Typical Patient**
- Elderly
- Diabetic

**Cause**
- Age-related: most common
  - Increased risk depending on genetic, presence of oxidative damage (smoking, diet) and environmental hazards (UV light, radiation)
- Drugs: Steroids
- Trauma
- Childhood: congenital, metabolic, infectious

**Symptoms/Clinical Presentation**
- Gradual painless loss of vision
- Reading difficulty/glasses prescription changing frequently
- Glare (patient avoids driving at night)
- Colour desaturation (sees yellow tinge)
- Monocular diplopia (double vision) (‘ghosting’ of images)
- Myopic shift (‘second sight’)

**Physical Exam**
- Lens opacification
- Reduced red reflex with ophthalmoscope

**Investigations**
- Lens opacities visible on slit lamp examination

**Management/Treatment**
- Indications for treatment
  - Pediatric: immediate referral to prevent amblyopia (importance of screening)
  - Adult: patient decision, unable to meet driving standards, ophthalmologist unable to visualize retina, very large cataract causing glaucoma (rare)
- Surgery
  - Phacoemulsification: US breaks cataract which are subsequently aspirated followed by insertion of an intraocular lens (99% of the time), spectacles or contact lenses
- For a congenital cataract, the lens is replaced with an external lens as children’s eyes continue to grow until 2-4 years old
  - Laser-assisted: laser makes the incision, followed by US
  - “Extracapsular” techniques: lens removed without use of above, more in developing countries

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$^1$ “Chronic Visual Loss”, Julia Baryla, January 23 2017, uOttawa Faculty of Medicine

$^2$ “Ophthalmic Emergencies in the first three months of life”, Michael D. O’Connor, January 24 2017, uOttawa Faculty of Medicine

$^3$ Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
11.2 Age-related Macular Degeneration (AMD)\(^4\)

**Typical Patient**
- Elderly patient with long history of smoking and poor diet
- Acute worsening of central vision often due to wet AMD, responsible for 80% of AMD-related blindness

**Cause**
- Age
- Smoking
- Genetics
- Ultraviolet light

**Types**
- Dry AMD/Non-vascular/Non-exudative → 90% of cases
- Wet AMD/Neovascular/Exudative

**Clinical Presentation**
1) **Dry AMD**
   - Gradual loss of central vision (cannot read or recognize faces), often bilateral and symmetric
   - Peripheral vision often maintained (does not lead to total blindness)
2) **Wet AMD**
   - Often severe, sudden central visual loss on a background of dry AMD

**Physical signs**
1) **Dry AMD**
   - Drusen: Small yellowish deposits due to accumulation of lipid between Bruch’s membrane and RPE
   - Macular pigment changes: Hypo/hyperpigmentation
2) **Wet AMD**
   - Neovascular membrane, retinal pigment epithelial elevation due to intravascular leakage

**Investigations**
1) **Dry AMD**: Amsler grid test shows scotoma (blank spots) mapping loss of central visual fields.
2) **Wet AMD**: Amsler grid test shows scotoma and metamorphopsia (central visual distortion)

**Management/Treatment**
1) **Dry AMD**: Antioxidants and mineral supplementation (Vitamins C & E, Zinc and Copper), smoking cessation, diet control (dry AMD has no treatment, just options to delay progression)
2) **Wet AMD**
   - Intraocular injections of anti-VEGF (vascular endothelial growth factor) agents
     - Ranibizumab (Lucentis\(^®\))
     - Bevacizumab (Avastin\(^®\))
     - Aflibercept (Eylea\(^®\))
   - Prognosis: Few improve, most stabilize, some worsen

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\(^4\)“Chronic Visual Loss” Julia Baryla, January 23 2017, uOttawa Faculty of Medicine
11.3 Diabetic Retinopathy

Typical Patient
- Working-age patient of obese BMI with 10+ year history of type 2 diabetes (T2D)
- Type 1 diabetic (T1D) after puberty not appropriately screened

Causes/Risk factors
- Poorly controlled diabetes: HbA1C > 7.0
- Hyperlipidemia (hard exudates), Nephropathy, Pregnancy

Note: Poorly controlled high blood pressure (>130/80) would cause hypertensive retinopathy

Types
- Non-proliferative diabetic retinopathy (NPDR), Proliferative diabetic retinopathy (PDR)

Screening Guidelines
- T1D: If adult, begin 5 years after diagnosis; if child, begin at puberty
- T2D: Begin at time of diagnosis
- Subsequent screening depends on presence and degree of retinopathy. Additional screening if pregnant.

Clinical Presentation
- Chronic, often painless visual loss

Physical Exam (Fundoscopy)
1) NPDR
   - Retinal edema
   - Microaneurysms, Dilation/beading of retinal veins
   - Hemorrhages: Dot-and-blot intraretinal, and flame (although this is more consistent with hypertensive retinopathy)
   - Capillary non-perfusion due to BM thickening
   - Macular ischemia: Due to intraretinal capillary closure
   - Macular edema due to increased vascular permeability (main cause of loss of vision)
   - Hard exudates: Lipid and protein leaking out of weak vessels
   - Nerve fibre layer infarcts, Cotton wool
2) PDR: Growth of new fragile blood vessels
   - Vitreous hemorrhage (boat shaped hemorrhage)
   - Carry fibrous tissue → "Scarring" → Retinal traction, holes and detachment
   - Neovascular glaucoma

Management/Treatment
- Diabetes control
- Laser: Panretinal photocoagulation to stop retinal neovascularization (albeit concurrently reducing visual field), focal or grid laser
- Intraocular injections of Anti-VEGF therapy, in select situations (and to treat macular edema)
- Surgery for complications (vitreous hemorrhage, retinal detachment)
11.4 Open Angle Glaucoma

Typical Patient
- Elderly patient
- West African patient
- Patient with family history of glaucoma
- Thin cornea

Cause
- Primary: idiopathic, dysfunction of trabecular meshwork resulting in increased intraocular pressure (IOP)
- Secondary
  - Trauma (hyphema, damage to meshwork or RBC clog up meshwork)
  - Inflammation: uveitis, WBC clog up meshwork, or scarring if chronic inflammation
  - Steroids: esp. if already have glaucoma or have family history
  - Neovascularization (such as diabetes): new vessels block drainage

Types
- Normal pressure glaucoma: open angle, pressure normal, but optic nerve damage
- Open angle glaucoma: open angle, high pressure, optic nerve damage (most common)
- Glaucoma suspect: open angle, high pressure, no optic nerve damage

Clinical presentation
- Slow progressive visual field loss (tunnel vision)
- Often painless and picked up on screening exam

Physical Signs (Fundoscopy)
- Increased cup to disc ratio due to permanent loss of axons
  - Note: tends to thin out in the vertical direction first

Treatment/Management
- Irreversible loss, focus on prevention by reducing IOP and with periodic screening
- Medications to reduce IOP
  - Decrease fluid production: carbonic anhydrase inhibitor, beta blockers
  - Increase outflow: prostaglandin analogues
  - Both decreased production and increased outflow: alpha agonists
- Laser Trabeculoplasty: increase outflow
- Surgery to increase outflow: Trabeculotomy, Glaucoma drainage device

6 “Glaucoma”, Garfield Miller, January 23 2017, uOttawa Faculty of Medicine
11.5 Acute Primary Angle Closure Glaucoma

Typical Patient
- Elderly female
- Inuit or Asian ethnicity
- Hyperopia (smaller eyes are predisposed due to more crowded anterior chambers)
- (No history of cataract surgery)

Cause
- Primary/idiopathic
- Resistance to flow at ciliary body → cannot get past the iris → P ↑ behind iris → iris bows forward

Clinical Presentation
- Pressure feeling around orbit
- Corneal edema
- Pain
- Redness
- Blurred vision
- Halos around lights
- Headache, nausea, vomiting (due to high IOP)

Physical Exam
- High intraocular pressure: very high pressure → rapid visual loss (hours)
- Edematous hazy cornea
- Fixed mid-dilated pupil

Investigations
- Slit lamp exam gonioscopy: shallow anterior chamber (due to Pressure behind iris)

Management/Treatment
- Emergency
- Urgently unblock the pupil and lower the pressure: pilocarpine eye drops, acetazolamide, glycerine, isosorbide, mannitol
- Re-establish flow: laser peripheral iridotomy (definitive treatment)

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7 “Glaucoma”, Garfield Miller, January 23 2017, uOttawa Faculty of Medicine
11.6 Congenital Glaucoma

**Typical Patient**
- Infant with great big eyes, although kept closed most of the time

**Cause**
- Insufficient aqueous drainage

**Symptoms/Clinical Presentation**
- Big “beautiful” eye(s): as pediatric tissues are elastic, eye expands under pressure
- Cloudy cornea: cells under high pressure → corneal endothelium cannot pump water out
- Blepharospasm: keep eyes closed as light scatters in the eye
- Photophobia: due to light scattering in eye
- Tearing

**Physical Exam/Investigations**
- High intraocular pressure

**Management/Treatment (depends on cause)**
- Surgical (vs adults, where glaucoma treatment is primarily laser and drops)

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8 “Ophthalmic Emergencies in the first three months of life”, Michael D. O’Connor, January 24 2017, uOttawa Faculty of Medicine
11.7 Retinal Causes Of Sudden Loss Of Vision\textsuperscript{9,10}

Typical Patient
- Patient with HTN, high IOP, or blood dyscrasia (retinal vein occlusion)
- Patient at high risk of emboli (retinal artery occlusion)

Types
- Central retinal artery occlusion (CRAO)
- Branch retinal artery occlusion (BRAO)
- Central retinal vein occlusion (CRVO)
- Branch retinal vein occlusion (BRVO)

Cause
- Retinal artery occlusion: secondary to embolic phenomena, often carotid or cardiac
- Retinal vein occlusion: associated with hypertension, blood dyscrasia, high IOP

Symptoms/Clinical Presentation
- Sudden monocular loss of vision, often painless
- Central retinal artery occlusion: Amaurosis Fugax (curtain coming down)

Physical Sign
- Central retinal artery occlusion: pale fundus with cherry red spot
- Branch retinal artery occlusion: emboli in smaller vessels with cotton wool spots, retinal edema
- Central retinal vein occlusion: diffuse hemorrhage and cotton wool spots ("blood and thunder")
- Branch retinal vein occlusion: hemorrhage and cotton wool spots

Management/Treatment
- Emergency
- Restore blood flow by massaging globe for management of retinal artery occlusion
- Decrease IOP: Beta blockers, drain aqueous fluid
- Intra-arterial or intravenous thrombolysis

\textsuperscript{9} “Sudden painless loss of vision”, Walter T Delpero, January 23 2017, uOttawa Faculty of Medicine
\textsuperscript{10} Vojvodic, M., Young, A. Toronto Notes. Toronto, ON: Type & Graphics Inc. 2014.
11.8 Optic Neuritis\textsuperscript{11,12} 

Type of Anterior Inflammatory Optic Neuropathy

Typical Patient
- Often younger patient
- Associated with multiple sclerosis (MS) in 75% F and 35% M over 15 years

Cause
- Viral infection
- Inflammatory autoimmune

Symptoms
- Subacute central visual field loss
- Symptoms worsen with increased body temperature
- Prognosis: Vision worsens over 1-2 weeks with slow improvement in 4 to 12 weeks. Vast majority improve to 20/40 or better.

Physical Exam
- Fundoscopy: optic disc margins raised and swollen with cup obliterated, often unilateral
  - Indistinguishable from papilledema
  - Exception: in retrobulbar optic neuritis, the fundus exam is normal
- Red reflex and ICP normal
- Systemic findings of neurological impairment

Investigations
- Colour desaturation test positive
- Relative afferent pupillary defect (RAPD) positive

Management/Treatment (depends on the cause)
- Controversial
- No oral prednisone. Use IV methylprednisolone for the first 3 days. Mainstay treatment is still tincture of time (observation).

\textsuperscript{11} “Sudden painless loss of vision”, Walter T Delpero, January 23 2017, uOttawa Faculty of Medicine

\textsuperscript{12} “Imaging of the optic nerve”, Danah Albreiki, January 25 2017, uOttawa Faculty of Medicine
11.9 Temporal Arteritis\textsuperscript{13,14,15} Also called Giant Cell Arteritis (GCA), Cranial Arteritis

Type of arteritic anterior ischemic optic neuropathy

Typical Patient
- Elderly (>55) Caucasian woman

Cause
- Systemic vasculitis
- Autoimmune activation of dendritic cells in vessel wall which recruit T cells and macrophages, forming large multinucleated “giant” cells. This inflammatory process results in intimal hyperplasia, vessel occlusion and thus sudden loss of blood supply to optic nerve.

Symptoms/Clinical Presentation
- Acute vision loss (sudden blindness) or reduced visual acuity
- Headache, tender scalp, jaw claudication
- Often associated with polymyalgia rheumatica: generalized malaise, fatigue, weight loss, loss of appetite, hip/shoulder pain
- Systemically can affect the heart, brain, and kidneys

Physical Exam
- Fundoscopy: optic nerve edema, swollen disc indistinguishable from papilledema, mostly unilateral, cherry red spot if retinal artery occlusion, cotton wool spots, hemorrhage
- Tender palpable temporal arteries (may be pulseless)

Investigations
- Optic nerve dysfunction (RAPD)
- Lab work: ESR $\uparrow$, CRP $\uparrow$, CBC (increased PLAT)
- Definitive diagnosis confirmed with temporal artery biopsy
  - Potential for false negatives due to patchy involvement
  - Treatment begun immediately upon suspicion, before biopsy results

Management/Treatment (depends on cause)
- Immediate high dose steroids (oral prednisone, IV solumedrol)
- No recovery, aim to preserve remaining function

\textsuperscript{13} “Sudden painless loss of vision”, Walter T Delpero, January 23 2017, uOttawa Faculty of Medicine
\textsuperscript{14} “Imaging of the optic nerve”, Danah Albreiki, January 25 2017, uOttawa Faculty of Medicine
\textsuperscript{15} “The eye and systemic disease”, Michael Dollin, January 27 2017, uOttawa Faculty of Medicine
11.10 Amblyopia

Typical Patient
- Child before age of 9-10 with condition affecting normal brain visual development
- If causes not addressed early, results in decreased visual acuity even when all other eye problems have been corrected
- Most common cause of unilateral visual loss in childhood

Causes
- No image provided by eye to the brain = media opacity or mass
  - Eyelid tumour (Eg. capillary hemangioma)
  - Cataract
- Blurry image reaching brain = refractive error
  - Unequal refractive errors are especially poorly tolerated
- Confusing image reaching brain, causing brain to ignore input from one eye = strabismus (eye misalignment)
  - Eye turned outward: exotropia
  - Eye turned inward: esotropia
  - Even a small angle deviation can be an issue

Symptoms/Clinical Presentation
- Parental concerns
- Ocular family history
- Failed vision screening
- Regular screening to be done by family physician is key as it is almost always preventable and patient may be pre-verbal. If screening results are concerning, follow with fundoscopy and refer.
- May be unilateral or bilateral

Physical Exam/Investigations
- Red reflex: absent if obstruction (leukocoria due to congenital cataract)
  - Refer if poor red reflex in one or both eyes
- Visual acuity: objection to occlusion, ability to maintain fixation, eye chart
  - Refer if asymmetric or diminishing visual acuity
- Ocular alignment - Cover test
  - Refer if constant or acute-onset strabismus
- Fundoscopy: only if above screening tests concerning

Treatment (depends on cause)
- If media opacity, clear media (example cataract)
- If blurry image, correct refractive error
- If confusing image, use penalization therapy (force patient to look with eye that does not see well)
  - Occlusion (patching)
  - Pharmacologic (blur the ‘good’ eye with cyclopia)
  - This fixes the amblyopia but not the strabismus
- Earlier treatment works better as the brain is more plastic.
11.11 Papilledema

**Typical Patient**
- Patient with hypertension, or space occupying lesion in the brain

**Cause**
- HTN
- Space occupying lesion: Tumor, hemorrhage, edema (mechanical obstruction)
- Hydrocephalus
- Infection (meningitis)
- Idiopathic intracranial hypertension: young female, recent weight gain (dx of exclusion)

**Symptoms/Clinical Presentation**
- Enlarged ASx blind spot
- Normal optic nerve function if acute
- May have headache

**Physical Exam/Investigations**
*Findings bilateral on fundoscopy*
- Optic disc
  - Colour: hyperemia if acute, gray/gliosis if chronic due to scarring
  - Cup to disc ratio very small (cup obliterated)
  - Margins elevated
- Vessels (vascular features): hemorrhage, tortuosity
- Choroidal or retinal folds on retina

**Management/Treatment (depends on cause)**
- Urgent blood pressure management and neuroimaging

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17 “Imaging of the optic nerve”. Danah Albreiki, January 25 2017, uOttawa Faculty of Medicine
11.12 Conjunctivitis\textsuperscript{18}

**Typical Patient**
- History of contact with other people with red eye
- History of atopy (allergic)
- History of multiple sexual partners (chlamydia, gonorrhea)

**Cause**
- Viral
- Bacterial (eg. chlamydial, gonococcal)
- Allergic

**Symptoms/Clinical Presentation**
- Non-painful red eye, swollen eyes, sticky eyelids, burning or foreign body sensation, tearing
- Viral: bilateral, non-purulent, clear mucoid discharge, often with history of upper respiratory tract infection
- Bacterial: unilateral mucopurulent discharge. Suspect gonorrhea if hyperacute/hyperpurulent
- Chlamydia: unilateral mucopurulent discharge, tearing much more pronounced than viral cause
- Allergy: unilateral or bilateral, non-purulent, clear mucoid discharge, often with pronounced itching

**Physical Exam/Slit lamp exam**
- Viral: conjunctival follicles, tender preauricular nodes, diffuse injection
- Bacterial: conjunctival papillae, no preauricular nodes, diffuse injection
- Chlamydia: conjunctival follicles, lid crusting, diffuse injection, non-tender preauricular nodes
- Allergy: papillary follicles, edematous (conjunctival chemosis), milder diffuse injection,

**Investigations**
- Swab for bacterial/chlamydia

**Management/Treatment (depends on cause)**
- Viral: self limiting, resolution often within 2 weeks. Topical artificial tears for lubrication. Cool compress. Counsel on hand hygiene. Highly contagious up to 2 weeks post-onset.
  - If significant pain suggesting corneal abrasion, refer
- Allergy: cool compress, artificial tears for lubrication, oral antihistamines (diphenhydramine), topical mast cell stabilizer, topical mild steroid (only prescribed by ophthalmologist)
- Bacterial: topical antibiotic with appropriate coverage. If suspect gonococcal, refer urgently to ophthalmologist and treat with IV ceftriaxone, topical ciprofloxacin, saline irrigation and treat for possible co-chlamydia infection.
- Chlamydia: systemic doxycycline or azithromycin +/- topical erythromycin, treat sexual partners

\textsuperscript{18} “The Red Eye”, Case Based Learning, Rishi Gupta, Michael Dollin, Michael O’Connor, January 23 2017, uOttawa Faculty of Medicine
11.13 Acute Anterior Uveitis (Iritis)\textsuperscript{19}

**Typical Patient**
- Patient with HLA-B27 seronegative condition: Psoriatic arthritis, Ankylosing spondylitis, Inflammatory bowel disease, Reactive arthritis (use the pneumonic “PAIR”)

**Cause**
*Ciliary body inflamed due to:*
- Idiopathic (~50%)
- Autoimmune
- Infectious
- Inflammatory
- Neoplasm

**Symptoms/Clinical Presentation**
- Pain
- Redness
- Photophobia: whenever iris dilates and constricts, it irritates inflamed ciliary body
- Lack of corneal staining or corneal infiltrate to suggest corneal pathology
- Lack of follicles or discharge to suggest conjunctivitis

**Physical Exam**
- Ciliary flush
- Decreased vision: due to WBC floating in anterior chamber, vitreous debris, macular edema, or underlying etiology of uveitis
- Keratic precipitates
- Hypopyon: collection of neutrophilic exudates inferiorly in the anterior chamber
- Back pain if ankylosing spondylitis

**Investigations**
- Slit lamp exam: cells and flare in anterior chamber
- Ocular pressure may be low, normal, or mildly elevated

**Management/Treatment (depends on cause)**
- Steroid drops or ointment (prescribed by ophthalmologist): resolve inflammation
- Cycloplegic: prevent posterior synechiae
- Note whether patient meets driving standards (Ontario standards: at least 20/50 with both eyes open, continuous visual field of 120° horizontally and 15° vertically)

\textsuperscript{19} \textit{“The Red Eye”, Case Based Learning, Rishi Gupta, Michael Dollin, Michael O'Connor, January 23 2017, uOttawa Faculty of Medicine}
12.1 Glioblastoma Multiforme (Grade IV Astrocytoma)

Typical Patient
- 40-60 year old M/F

Cause
- Tumor arising from astrocytes with anaplasia, high cellularity, round and pleomorphic cells, nuclear atypia, vascular proliferation, and necrosis (note the last 2 characteristics do not occur in anaplastic astrocytoma - grade III)

Symptoms/Clinical Presentation
- Headache
- Seizures
- Focal neurologic deficits
- Mental status changes

Physical Exam
- Neurological exam

Investigations
- CT/MRI with contrast (solitary brain lesion with contrast enhancement and edema)

Management/Treatment
- Maximal possible surgical resection with radiation and adjuvant chemotherapy (e.g., temozolomide)
- Anti-angiogenic agents (e.g., bevacizumab) with stereotactic radiosurgery for local recurrences
- Steroids (dexamethasone) may help reduce some of the edema and improve symptoms temporarily

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Typical Patient
- 80% of stroke is ischemic in origin
- Sudden onset of focal neurological symptoms based on region of the brain affected, usually unilateral.
- Usually have vascular risk factors such as diabetes, HTN, hyperlipidemia, family history and smoking.

Causes
- Large vessel thrombosis – Atherosclerosis (ex: carotid artery stenosis)
- Small vessel thrombosis – Diabetes, HTN (causes lipohylanized vessels)
- Cardioembolic – Atrial fibrillation, valvular disease, congestive heart failure
- Systemic hypoperfusion (global cerebral ischemia) – mainly affects the watershed areas (border between MCA and the ACA or PCA territories)
- Other (much less common) – carotid artery dissection, malignancy, cocaine-induced vasospasm, etc

Clinical Presentation – based on the area of the brain affected
- Middle Cerebral Artery (most commonly affected) – contralateral facial and arm weakness/sensory deficit with legs less affected, contralateral visual field defects; aphasia if left sided, neglect if right sided
- Anterior Cerebral Artery – contralateral leg weakness/sensory deficit, cognitive deficits
- Posterior cerebral artery – contralateral visual field defects
- Small penetrating vessels deep in the brain – lacunar stroke (can affect the basal ganglia, internal capsule) – hemi-body symptoms (motor, sensory or both; face/arm/leg equally affected)

Physical Exam
- Vitals: HR, RR, BP
- Assessment of level of consciousness
- Complete neurological examination

Investigations
- Mainly a clinical diagnosis (history and physical examination), investigations guide treatment
- Non-contrast CT head to exclude intracranial hemorrhage
- Blood vessel imaging – CT angiogram or MR angiogram of the neck and head
- Additional investigations:
  - BP – if >185/110 need to administer Labetolol before TPA administration
  - CBC, BUN, creatinine, electrolytes, PT/INR, CK, TnI
  - Blood glucose – hypo/hyperglycemic can mimic neurological condition by inducing seizure
  - ECG

Management/Treatment
- Acute treatment: Urgent treatment needed to rescue the penumbra of brain tissue.
  - TPA administration after reviewing contraindications – onset <4.5h
  - Absolute contraindication = intracranial bleed, coagulopathy (INR >1.7, PLT < 100, DOAC use)
  - Mechanical thrombectomy/endarterectomy if onset <6h
- Secondary prevention of stroke (address cause):
  - Small vessel disease: antiplatelet, anti-hypertensives, glycemic control, statins
  - Large vessel disease:
    - Carotid Endarterectomy / Carotid Stent for >50% ipsilateral stenosis
    - Antiplatelet, statin, glycemic control, anti-hypertensives
    - Cardioembolic (Atrial fibrillation, A flutter): anti-coagulants
    - All subtypes: smoking cessation, diet, exercise, weight loss
- Long term treatment - rehabilitation and prevention of future strokes as above
12.3 Subarachnoid Hemorrhage (SAH)³

Typical Patient
- Subtype of hemorrhagic stroke
- History of smoking, excessive alcohol use and HTN (higher risk for aneurysm)
- History of previous similar presentation (sentinel bleed)
- Associated with Polycystic Kidney Disease (PKD)

Cause
- Trauma (most common)
- Aneurysm rupture: 2nd most common cause, saccular/berry aneurysm more likely to rupture if >7mm, often found at artery bifurcations, especially anterior circle of Willis.
  - Cocaine
  - Vasculitis
  - Coagulopathy
  - Infectious (endocarditis)

Clinical Presentation
- Thunderclap Headache: Maximal at onset, severe (10/10) in intensity
- Nausea/vomiting
- Acute loss of consciousness
- Seizures
- Neurological deficits if pressure is high enough to injure surrounding tissue

Physical Exam
- Vitals: HR, RR, BP
- Assessment of Glasgow Coma Scale (GCS)
- Complete neurological examination: Cranial nerves, Gait, Coordination, Sensory, Motor

Investigations
- Mainly a clinical diagnosis (history and physical examination)
- Non-contrast CT head: 1st line, 95% sensitivity esp if < 6 hours. Hyperdense lesion in subarachnoid space
  - If CT normal and suspect SAH, do lumbar puncture 12h to 1 week after onset of symptoms. Positive if non-traumatic tap shows blood or xanthochromia.
- Vessel imaging if SAH confirmed (CTA, MRA, DSA) to find aneurysm
- Additional investigations:
  - CBC, BUN, creatinine, electrolytes, glucose
  - INR

Management/Treatment
- Acute
  - Decreased level of consciousness: airway protection
  - Address cerebral aneurysm: Endovascular coiling, Surgical clipping
  - Address any cardiac issues such as arrhythmia, seizure
- Follow up for potential delayed complications
  - Rebleeding
  - Hydrocephalus
  - Vasospasm, leading to ischemic stroke: prevent with avoiding hypotension and using calcium channel blockers
- Long term treatment:
  - Rehab program
  - Long-term medications based on risks – anti-hypertensives, smoking cessation, alcohol reduction

³ “Hemorrhagic Stroke”, Grant Stotts, February 7 2017, uOttawa Faculty of Medicine
12.4 Intracerebral Hemorrhage (ICH)\(^4\)

Typical Patient

- Subtype of hemorrhagic stroke
- Older patients with hypertension, smoking, excess EtOH (risk of microaneurysm), dementia (lobar)
- Familial forms less common, associated with Polycystic Kidney Disease (PKD) and Alzheimer’s disease

Cause

ICH subtypes

- Subcortical: microaneurysms (Charcot-Bouchard) of small vessels that are at risk of bleeding
- Lobar
  - Anticoagulant or coagulopathy associated
  - Bleed into a tumor
  - Bleed after ischemic infarct
  - Amyloid angiopathy – related to Alzheimer’s disease, elderly

Clinical Presentation

- Acute onset of neurological deficits (similar to ischemic stroke)
- In addition, symptoms of increased intracranial pressure:
  - Headache
  - Nausea/Vomiting
  - Progressive deterioration of level of consciousness

Physical Exam

- Vitals: HR, RR, BP
- Assessment of Glasgow Coma Scale (GCS)
- Complete neurological examination: Cranial nerves, Gait, Coordination, Sensory, Motor

Investigations

- Mainly a clinical diagnosis (history and physical examination)
- Non-contrast CT
- Vessel Imaging: CTA or MRA
- CBC, BUN, creatinine, electrolytes
- Blood glucose – hypoglycemia or hyperglycemia can mimic neurological condition
- INR/PTT

Management/Treatment

- Acute treatment:
  - Limit progression of hematoma: stop and reverse anticoagulants such as Warfarin, control blood pressure
  - Investigate underlying cause of hemorrhage
    - Eg: vascular malformations can be identified using CTA or MRA
    - In most cases, no lesion identified as a small vessel is involved
  - Supportive care
  - Surgical decompression if applicable (posterior fossa or superficial large hemispheric)
- Long term treatment:
  - Rehab program
  - Long-term medications based on risks – anti-hypertensives, glycemic control
  - Lifestyle modifications – proper diet, smoking cessation, EtOH reduction

\(^4\)“Hemorrhagic Stroke”, Grant Stotts, February 7 2017, uOttawa Faculty of Medicine
12.5 Spinal Cord Injury

Typical Patient
- Typically younger male (due to increased risk of traumatic injury), however may occur to any individual

Cause
- Trauma to the neck or back (most commonly from motor vehicle accidents or athletic activities)

Symptoms/Clinical Presentation
- Hyperreflexia and extensor plantar responses below the level of injury (mimics an UMN injury)
- Flaccid weakness and complete absence of deep tendon reflexes after trauma (spinal shock)
- Spasticity develops over days to weeks
- Loss of sensory/motor function below the level of the lesion

Physical Exam
- Full neurological exam (e.g., Babinski, assessment of weakness, pin-prick, etc.)

Investigations
- CT Spine (bony structures) / MRI Spine (spinal cord)

Management/Treatment
- Immobilization
- ABC’s
- High doses of methylprednisolone if spinal cord compression (controversial)
- Surgical decompression is of uncertain benefit, but may be performed for appropriate patients

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12.6 Traumatic Brain Injury (TBI) - Concussion

Typical Patient
- Children and young adults
- Athletes

Cause
- Usually head trauma resulting from MVA or sporting activities

Symptoms/Clinical Presentation
- Alteration/LOC subsequent to head trauma
- Headache
- Disorientation
- Dizziness
- Nausea
- Retrograde/anterograde amnesia

Physical Exam
- Level of consciousness (Glasgow Coma Scale)
- Complete neurological examination (rule out more serious injury),
- Mental status, can consider cognitive test batteries (sideline – SCAT, office – ACE tool)

Investigations
- Canadian CT Head Rule – image if GCS < 15 at 2 hours, suspected skull fracture, signs of basal skull fractures, vomiting 2 or more times, age > 65, pre-impact amnesia > 30 minutes, dangerous mechanism

Management/Treatment
- Primarily supportive (e.g., NSAIDS, rest with gradual progression to normal activities)
- Guidelines exist regarding concussion protocol; Example from American Academy of Neurology
- If no LOC and symptoms persisting <15 minutes, athlete may return to play, but second event that day requires 1 week of rest
- If no LOC but symptoms lasting >15 minutes, athlete should be evaluated very carefully for first 48 hours and may return to play after a minimum of 1 week rest without symptom recurrence
- If LOC, urgent evaluation is necessary with hospital admission until symptoms dissipate; athlete may return to play after a week symptom free; a second event requires a minimum 1 month rest
- Note there are several guidelines to manage concussions in athletes, UpToDate may provide the most current guidelines; local guidelines - Ontario Guidelines for Concussion / mild TBI (http://concussionsontario.org/resources/adult-concussion-guidelines/)

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12.7 Traumatic Brain Injury (TBI) - Epidural Hematoma

Typical Patient
- M>F
- Younger adults and the elderly

Cause
- Trauma resulting in temporal bone fracture and laceration of the middle meningeal artery (less frequently, middle meningeal vein or dural sinus)

Symptoms/Clinical Presentation
- Classically lucid interval after the initial impact, with subsequent rapid deterioration in LOC as hematoma enlarges (known as the “talk and die” phenomenon)

Physical Exam
- Vitals and Glasgow Coma Scale
- Trauma examination (e.g: signs of skull fracture, other injuries)
- Complete neurological examination

Investigations
- CT (lens-shaped, hyperdense lesion between the skull and dura mater)

Management/Treatment
- Surgical evacuation if required

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12.8 Traumatic Brain Injury (TBI) - Subdural Hematoma

Typical Patient
- Acute - younger adults, history of acute head trauma
- Chronic - elderly, anticoagulated patients, potential history of mild head trauma

Cause
- Head trauma resulting in rupture of bridging veins connecting the brain and dural sinuses

Symptoms/Clinical Presentation
- Headache
- Contralateral hemiparesis
- Seizures
- Increased intracranial pressure if large hematoma

Physical Exam
- Vitals and Glasgow Coma Scale
- Complete neurologic examination

Investigations
- CT (crescent-shaped hyperdensity between the brain parenchyma and skull)

Management/Treatment
- Surgical evacuation if necessary
- Discontinuation of anticoagulation

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12.9 Encephalitis

Typical Patient
- Any age

Cause
- Inflammation of brain parenchyma in association with clinical evidence of neurological dysfunction
- Infectious (HSV, VZV, West Nile, Mumps, etc.), autoimmune, or post-infectious
- If meninges are involved, then it is classified as meningoencephalitis

Symptoms/Clinical Presentation
- Prodrome: myalgia, fever, anorexia
- Headache
- Personality changes, bizarre behavior (esp. if HSV)
- Focal neurological signs
- Decreased LOC
- Seizures
- Coma

Physical Exam
- Vitals
- Complete neurological examination
- Kernig/Brudzinski/nuchal rigidity (meningitis)

Investigations
- CT / MRI
- LP for cell count, glucose, protein, routine culture / stains, HSV PCR
- EEG

Management/Treatment
- Supportive
- Treat underlying etiology (e.g., if HSV, give IV acyclovir)
12.10 Meningitis

Typical Patient
- Adults over 50 years of age or children less than 2 years of age

Cause
- Meningeal inflammation secondary to bacterial/viral/fungal infection
- Bacterial most commonly Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae

Symptoms/Clinical Presentation
- Prodrome: malaise, URTI
- Classic triad: fever, headache, stiff neck
- Photophobia
- Lethargy or coma
- Seizures
- Cranial nerve abnormalities
- Infants and neonates may additionally present with poor feeding/vomiting, lethargy, irritability, seizures, etc.

Physical Exam
- Kernig’s sign (pain on thigh flexion at the hip and knee at 90 degrees, and subsequent extension of the knee)
- Brudzinski’s sign (Neck flexion results in involuntary lifting of legs on examination table)
- Complete neurological examination (rule out focal findings)

Investigations
- CT Scan
- Lumbar puncture (bacterial = high protein, low glucose, PMNs; viral = high protein, normal glucose, lymphocytes; TB/Fungal = high protein, low glucose, lymphocytes)
- If LP is contraindicated, obtain blood cultures + stain

Management/Treatment
- Stabilize patient: manage seizures, aspiration, control intracranial pressure
- Start appropriate antibiotics (if bacterial) +/- dexamethasone; tailor antibiotics once results of culture are available
- Avoid delays in beginning empiric antibiotics

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10 “Infections of the Central Nervous System”, Baldwin Toye, February 21 2017, uOttawa Faculty of Medicine
12.11 Prion Diseases

aka Transmissible Spongiform Encephalopathies

Types
- Creutzfeldt-Jakob Disease
- Variant Creutzfeldt-Jakob Disease
- Kuru disease

Typical Patient
- Creutzfeldt-Jakob disease: 45-75 yo (older patients), global
- Variant Creutzfeldt-Jakob Disease: 20s (younger), eating infected cattle, higher incidence in UK and France
- Kuru disease: cannibalism, eating infected humans

Cause
- Prion proteins induces abnormal folding of normal proteins, causing spongiform (vacuolar) changes in the brain, leading to prion protein deposition, neuronal loss, gliosis, and degeneration
- Sporadic (85%) → eating infected cattle, vCJD
- Familial – autosomal dominant (15%) → CJD
- Iatrogenic (<1%)
  - Corneal transplant
  - Dural mater graft
  - Human growth hormone

Clinical Presentation
- Rapidly progressive dementia
- Myoclonus
- Spasticity
- Cortical blindness
- EPS (basal ganglia)
- Ataxia (cerebellum)
- Psychiatric abnormalities, esp. vCJD

Physical Exam
- Complete neurological assessment, symptoms depending on affected neuronal functions

Investigations
- EEG – periodic synchronous bi- or triphasic sharp wave complexes in 67-95%
- MRI
- Lumbar puncture – CSF protein markers like 14-3-3 protein and tau protein
- Definitive diagnosis is through brain biopsy

Management/Treatment
- No current treatment available – leads to 100% mortality
- Supportive care
- Palliative care

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11 “Infections of the Central Nervous System”, Baldwin Toye, February 21 2017, uOttawa Faculty of Medicine
12.12 Multiple Sclerosis

Typical Patient
- Peak onset age 25 and average onset age 30 (age range 15-50)
- More common in females than males (2:1)
- Highest in North America and Europe

Cause
- Autoimmune attack on oligodendrocytes leads to demyelination of the central nervous system, slowing of nerve conduction and conduction block, and eventual axon loss
- Main subtypes:
  - Relapsing – Remitting MS (Most common)
  - Primary Progressive
  - Secondary Progressive
  - Clinically Isolated Syndrome – One episode of symptoms that suggest MS, but not yet diagnosed
  - Radiologically Isolated Syndrome – incidental finding on MRI, no symptoms yet

Clinical Presentation
- Recurrent attacks of various neurological symptoms with periods of improvement
- Optic neuritis: loss of vision in one eye, pain upon eye movements, often the first symptom
- Limb weakness, limb paresthesia, limb numbness
- Transverse myelitis with sensory dysfunction
- Bladder dysfunction
- Brainstem/ cerebellar syndrome = vertigo +/- cranial nerve symptoms (diplopia, dysphagia, etc)

Physical Exam (Full neurological and eye exam)
- Fundoscopy: Relative Afferent Pupillary Defect (RAPD), diplopia, visual field defect
- Sensory assessment: may show sensory level, numbness, tingling
- Motor exam: upper motor neuron weakness
- Posture/Gait: imbalance, dizziness
- Coordination
- Cranial nerves
- Lhermitte’s sign = electrical-type sensation down the spine with neck flexion
- Uthoff’s sign = worsening of symptoms with increased temperature (i.e: blurrier vision) that resolves after temperature normalizes

Investigations
- Combined clinical and radiologic diagnosis - McDonald Criteria (2010, 2017)
- LP: normal RBC and glucose, normal or mildly elevated protein, mildly elevated WBC (5 to 20), oligoclonal bands
- MRI – white matter lesions in multiple areas (juxtacortical, peri-ventricular (Dawson’s finger), brainstem, spinal cord
- Evoked potentials – visual >> somatosensory, brainstem auditory

Management/Treatment
- Treat attacks (average duration of 6 weeks)
  - Methylprednisolone 1000mg IV x 3-5 days OR Prednisone 1200mg PO daily x 3-5 days
- Treat symptoms: depending on the patient
- Relapsing MS: prevent attacks and delay disability with disease modifying agents (most often managed by MS specialist)
  - 1st line – interferons such as Betaseron, Rebif, etc.
  - 2nd line – natalizumab, ocrelizumab, rituximab, fingolimod, etc.
  - 3rd line – chemotherapy, bone marrow transplant, etc.

12 “Multiple Sclerosis”, Heather MacLean, February 23 2017, uOttawa Faculty of Medicine
Progressive MS: few treatments are effective (ocrelizumab is the first approved treatment)

12.13 Amyotrophic Lateral Sclerosis (ALS)

Typical Patient
- Adult disease
- Usually after age 40 - Median age of onset is 54 years with median survival of 3 years
- Slight male predominance

Cause
- Degeneration of both upper motor neurons (UMN) and lower motor neurons (LMN) along with intraneuronal inclusions called Bunina bodies, resulting in neuronophagia, fiber atrophy, fascicle atrophy
- Sporadic – most common (>90%)
- Familial – autosomal dominant, ex: gain of function mutation in the superoxide dismutase (SOD) enzyme

Clinical Presentation – combination of LMN and UMN signs
- LMN
  - Progressive atrophy and weakness of distal extremities (limbs) – asymmetric
  - Fasciculations
- UMN
  - Progressive spasticity
  - Hyperreflexia
  - Babinski
- Absence of significant sensory deficits
- Dysarthria and dysphagia due to corticobulbar affect
- General: weight loss
- ‘Emotional incontinence’ (laugh and cry at smallest triggers) due to pseudobulbar affect, often later
- Eventual respiratory failure (cause of death)

Physical Exam
- Complete neurological examination
- Motor – positive findings of muscle atrophy, fasciculations, spasticity, weakness, hyperreflexia, increased tone
- Sensory: absent of significant sensory deficits
- Often also spares cognition, sphincter control, and eye movements

Investigations
- ALS is a diagnosis of exclusion, therefore need further investigations
- MRI to rule other conditions such as nerve compression, spondylarthrosis, and spinal stenosis (present with both UMN + LMN signs)
- Electromyography/Nerve conduction study: involvement of LMN, denervation

Management/Treatment
- Riluzole (glutamate antagonist) has been shown to extend survival by 3 months
- Respiratory assistance - BiPAP
- Nutritional support
- Muscle relaxant for spasticity
- Multidisciplinary approach: physiotherapy, occupational therapy, social work, speech therapy, group support, research trials, palliative care
- Average survival 3 years, a small subset (<10%) survive 10 years+

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13 “Amyotrophic Lateral Sclerosis” Self Learning Module, Jocelyn Zwicker, Pierre Bourque, uOttawa Faculty of Medicine
12.14 Huntington’s Disease (HD)\textsuperscript{14}

**Typical Patient**
- 35-45 year old M/F
- Positive family history

**Cause**
- Autosomal dominant neurodegenerative disorder of HTT gene affecting the basal ganglia (e.g., atrophy of caudate and putamen), and cerebral cortex (layer 3)
- Formation of deposits in nucleus, and induction of cell death

**Symptoms/Clinical Presentation**
- Triad of chorea, behavioural/personality changes, and dementia (may precede each other by years)

**Physical Exam**
- Full neurological exam (e.g., abnormal movements)

**Investigations**
- CT/MRI
- MMSE/MOCA
- Genetic testing (increased CAG repeats in huntingtin gene)

**Management/Treatment**
- Pharmacological management of dementia/chorea (e.g., dopaminergic antagonists- tetrabenazine, haloperidol, etc.)
- Genetic counseling (autosomal dominant, anticipation)

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12.15 Essential Tremor

Typical Patient
- Can be present at any age
- Usually have a family history of essential tremor
- 10X more common than Parkinson’s disease

Cause
- Idiopathic

Clinical Presentation
- Progressively worsening of kinetic and postural tremor which is long standing (most common in hands)
- Tremor is relieved by rest or when walking
- No resting tremor
- Improved with alcohol consumption
- Worsened with stress
- Also possible head and voice tremor, legs rarely affected

Physical Exam (Neurological exam)
- Bilateral high frequency fast kinetic/postural tremor, variable amplitude
- Usually bilateral but asymmetric
- Normal gait assessment (sometimes slight difficulty with tandem)
- Normal postural stability
- No rigidity, cogwheeling only
- Normal facial expression
- Handwriting: markedly affected by tremor (spiral test)
- Cup-pour test: increased spilling due to tremor

Investigations
- Clinical diagnosis (history and physical examination)

Management/Treatment
- Pharmacological
  - Beta blockers:
    - 1st line = propranolol
    - 2nd line = atenolol
  - Anticonvulsant:
    - 1st line = primidone
    - 2nd line = gabapentin, topiramate
- Deep brain stimulation if very severe

15 “Movement disorders”, D. A Grimes, February 13 2017, uOttawa Faculty of Medicine
16 “Neurodegenerative Disorders” Case Based learning, David A. Grimes, uOttawa Faculty of Medicine
12.16 Parkinson’s disease\textsuperscript{17,18}

Typical Patient
- Male > Female, 1-3% of patients >65 years of age

Cause
- Degeneration of dopaminergic neurons especially in the substantia nigra
- Idiopathic/sporadic = Most common
- Familial

Clinical Presentation
- T – Tremor (low frequency and slow): resting and postural. Usually no intention tremor.
  - Can have chin and leg tremor
  - If head tremor present - NOT Parkinson’s disease!
- R – Rigidity: with or without cogwheeling, may present initially as ‘frozen shoulder’
- A – Akinesia/Bradykinesia: slowness of movement with difficulty in initiating movement, hypomimia, decreased blink reflex
- P – Postural instability: stooped, shuffling gait, falls (usually >3-5yrs after diagnosis)
- Psychiatric and cognitive impairment: dementia, apathy, depression, anxiety
- REM sleep disorder
- Postural hypotension (d/t autonomic dysfunction)

Physical Exam (Full neurological exam, especially motor exam)
- Vitals: postural hypotension
- Inspection:
  - Unilateral resting tremor
  - Decreased blink rate
  - Masked facies
  - Decreased phonation (whispering/soft voice)
- Tone: Rigidity of limbs
- Bradykinesia: slowed and reduced amplitude of alternating wrist pronation/supination, finger tap, foot tap
- Posture: positive retropulsion test (‘pull test’) = decreased postural stability causes the patient to take more than 2 steps to regain balance
- Gait assessment:
  - Slowness and shuffling gait, difficulty initiating walk, festination, en-bloc turns, decreased arm swing, tremor increases with walking
- Micrographia
- MMSE may show cognitive deficits

Investigations
- Clinical diagnosis (History and physical examination)

Management/Treatment
- Pharmacological:
  - If > 70: 1st line Sinemet (Levodopa/Carbidopa) (possible side effects: orthostatic hypotension, delirium)
  - If < 60: 1st line Sinemet OR dopamine agonist such as ropinirole (Requip), pramipexole (Mirapex)
  - Adjuncts: MAO inhibitor (Selegiline), anticholinergics (only in younger patients), COMT inhibitor (Entacapone)

\textsuperscript{17} “Movement disorders”, D. A Grimes, February 13 2017, uOttawa Faculty of Medicine
\textsuperscript{18} “Neurodegenerative Disorders” Case Based learning, David A. Grimes, uOttawa Faculty of Medicine
12 Neurology

- Exercise
- Assessment and treatment of depression and sleep disorders
- Severe - deep brain stimulation

12.17 Guillain Barré Syndrome (GBS)

Typical Patient
- Any age, Male > Female (3:2)
- 2/3 have history of viral or bacterial (mainly campylobacter) infection (respiratory or diarrheal) days to weeks before onset of symptoms

Cause
- Often follows antecedent illness a few weeks before, especially respiratory or diarrheal, potentially resulting in molecular mimicry and selective autoimmune attack of the Schwann cells
- Most common subtype is acute inflammatory demyelinating polyradiculoneuropathy (AIDP)

Clinical Presentation
- Sensory: often 1st symptom of deep aching pain/paresthesia in lower back
- Motor: symmetric ascending paralysis spreads from legs then arms, proximal muscles more affected
- Facial weakness often bilateral
- Areflexia
- Can progress to respiratory failure requiring ventilation
- Autonomic dysregulation:
  - Blood pressure dysregulation
  - Cardiac arrhythmias
  - Bladder dysfunction
  - Constipation
- Develops over days/weeks, nadir usually within 3 weeks

Physical Exam
- Vitals: BP, HR, RR, O2 saturation, Temperature
- Neurological examination
  - Motor weakness
  - Sensory dysfunction may be present, but a sharp spinal level suggests an alternate diagnosis

Investigations
- Primarily clinical diagnosis (History and physical examination)
- Bedside spirometry (MIP, MEP, SVC)
- If spinal sensory level present, may need a MRI to r/o spinal cord lesion
- Lumbar puncture: albuminocytological dissociation (high protein, normal WBC)
- Electromyography and nerve conduction study: often normal/minimally abnormal initially, abnormalities develop in 2-3 weeks

Management/Treatment
- Immunomodulatory: IVlg, Plasmapheresis, No corticosteroids
- Supportive
  - MUST: Close monitoring of respiration with hourly bedside spirometry (NOT oximetry or blood gases) and ventilation as needed
  - Pain management
  - Blood pressure monitoring
- General
  - DVT prophylaxis
  - Control nosocomial infection
  - Bowel routine

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19 “Disorders of peripheral Nervous system”, Elizabeth Pringle, February 14 2017, uOttawa Faculty of Medicine
12.18 Diabetic Neuropathy

Typical Patient
- 50-65 year old M/F (may be younger if Type I)
- History of type I/type II diabetes (typically >5 years onset)
- Poor glycemic control

Cause
- Multifactorial
- Microvascular disease
- Elevated intracellular glucose leading to disruption of protein function, activation of protein kinase C, and activation of polyol pathway

Symptoms/Clinical Presentation
- Many clinical patterns
- Most common pattern is chronic length-dependent sensory (> motor) axonal distribution
- Distal tingling/numbness
- Distal muscle cramps
- If small fiber predominant - burning pain, autonomic neuropathy
- If large fiber predominant - little/no pain, prominent ataxia (‘diabetic pseudobulbs’), due to loss of proprioception
- Autonomic neuropathy (e.g., tachycardia, postural hypotension, bladder dysfunction, etc.)
- Diabetic third nerve palsy (ptosis, diplopia, sparing pupils) - ‘down and out’ eye

Physical Exam
- Motor/Sensory exam (i.e., vibration, temperature, pin-prick)
- Gait assessment
- Cranial nerve exam (particularly CN III, IV, VI for ocular assessment)

Investigations
- CBC
- Fasting glucose + HbA1C
- Oral glucose tolerance test if not previously performed

Management/Treatment
- Lifestyle modifications
- If refractory, oral medications (e.g., metformin)
- If refractory, injectable insulin
- Regular follow-up to check glucose/ensure appropriate control
- Neuropathic pain agents:
  - Topical: capsaicin, isosorbide dinitrate, Lidoderm patch
  - Oral: pregabalin, gabapentin, amitriptyline, duloxetine, opioids if refractory

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20 “Disorders of the Peripheral Nervous System Part 1: Overview, radiculopathies, neuropathies”, Elizabeth Pringle, February 14 2017, uOttawa Faculty of Medicine
12.19 Myasthenia Gravis

Typical Patient
- Can occur at any age but 2 peaks of occurrence – women in their 3rd decade and men in their 5th decade.
- Women more affected than men (3:2)
- May have other associated autoimmune disorders (thyroid disorders, diabetes, pernicious anemia)

Cause
- Autoimmune attack of the acetylcholine receptors in the neuromuscular junction, resulting in fatigue and inability of muscle to sustain force of contraction

Clinical Presentation
- Variable degree of fatigue, depend on initial strength and disease severity
- Muscle fatigue asymmetric, alternating and fluctuating
- 70% have hyperplastic changes of the thymus. 10% have thymoma.
- Muscle fatigue and weakness worse by the end of the day or with exertion
  - Improves with rest
  - Worsens in hot environments
- Usual muscles involved:
  - Ocular – ptosis, double vision, cannot keep eyes open as day progresses, and frontalis contraction to compensate in attempting to keep eyes open, resulting in a worried/surprised look
  - Bulbar – facial weakness, trouble smiling resulting in a snarl, dysarthria (slurring), difficulty speaking loudly for sustained periods of time, dysphagia, easily tired of chewing, neck weakness, dyspnea if severe
  - Limbs/ trunk - cannot keep arm extended upwards for sustained periods of time

Physical Exam
- Neurological exam, Motor assessment:
  - Ask them to look at you or look at ceiling, note eyelid gradually falls down
  - Ask them to extend arm upwards, note arm gradually falls down

Investigations
- Ice pack test: Apply for 2 minutes to ptotic eyelid, improves ptosis temporarily
- Tensilon test (historic) – blocks acetylcholinesterase enzyme, which results in temporary relief of symptoms
- Electrophysiological test – repetitive nerve stimulation, Single fibre EMG
- Anti-ACh receptor antibody: specific but low sensitivity, especially if ocular. Concentration does not correlate with disease severity, course, or prognosis.
- Anti-MuSK antibody: detects some of the false negative cases from the Anti-ACh receptor antibody test

Management/Treatment
- Symptom management → Anticholinesterase inhibitor (Mestinon/Pyridostigmine)
- Immunosuppression
  - Corticosteroids, Azathioprine, Mycophenolate, Cyclosporine, IVIG, Plasmapheresis
- CT of thymus for all cases to detect any thymoma
- Thymectomy for patients with thymoma or selected patients with generalized myasthenia
- Avoid medications that can worsen myasthenia (aminoglycosides, macrolides, fluoroquinolones, magnesium, beta-blockers, calcium channel blockers, botulinum toxin)

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21 “Neuromuscular junction and muscle”, Elizabeth Pringle, February 14 2017, uOttawa Faculty of Medicine
12.20 Dermatomyositis

Typical Patient
- Female > Male adult
- Acute/subacute onset
- Potential history of autoimmune disorders

Cause
- Autoimmune B-cell mediated attack against blood vessels in muscle and skin
- 10-20% of cases associated with underlying malignancy (e.g., lung, breast, ovary, colon)

Symptoms/Clinical Presentation
- Typically painless weakness (proximal muscles > distal, neck flexors > extensors, eye muscles spared)
- Heliotrope rash
- Gottron’s papules
- Calcinosis
- Dilated nail bed loops
- Systemic symptoms consisting of:
  - Respiratory: interstitial pneumonitis and fibrosis
  - Cardiac: cardiomyopathy, conduction defects
  - Gastrointestinal: dysphagia, perforated viscus

Physical Exam
- Gait assessment
- Motor exam (particularly proximal muscles)
- Skin survey
- Auscultation of heart and lungs

Investigations
- Serum CK measurement
- Antibody testing (anti-Jo1, anti-Mi2, etc.)
- EMG (abnormal spontaneous activity, myopathic changes)
- Biopsy (inflammatory infiltrate around vessels, perifascicular atrophy)
- Screen for underlying malignancy (CT chest/abdo/pelvis; PET)

Management/Treatment
- Corticosteroids (e.g., prednisone)
- Immunosuppressants (e.g., azathioprine, methotrexate, cyclophosphamide, IVlg)
12.21 Inclusion body Myositis

**Typical Patient**
- Male (>50 years old)
- Potential history of autoimmune disorders (e.g., Sjogren syndrome, sarcoidosis, thrombocytopenia)

**Cause**
- Multifactorial – both autoimmune and primary degenerative hypotheses

**Symptoms/Clinical Presentation**
- Proximal=distal weakness, predilection for finger/wrist flexors, knee extensors (e.g., quadriceps atrophy)
- Weakness/wasting of muscles
- Dysphagia

**Physical Exam**
- Gait assessment
- Motor exam (particularly proximal muscles)

**Investigations**
- Serum CK
- Muscle biopsy

**Management/Treatment**
- No available treatment (no immunotherapy has shown to be effective)
- Supportive care (e.g., physical therapy, exercise as able to, etc.)
12.22 Polymyositis

**Typical Patient**
- Female > Male adult
- Acute/subacute onset
- Potential history of autoimmune disorders

**Cause**
- Autoimmune
  - T-cell mediated attack against muscle fibers themselves

**Symptoms/Clinical Presentation**
- Typically painless weakness (proximal muscles>distal, neck flexors>extensors, eye muscles spared)
- Dysphagia
- Systemic symptoms consisting of:
  - Respiratory: interstitial pneumonitis and fibrosis
  - Cardiac: cardiomyopathy, conduction defects
  - Gastrointestinal: dysphagia, perforated viscus

**Physical Exam**
- Gait assessment
- Motor exam (particularly proximal muscles)
- Auscultation of heart and lungs

**Investigations**
- Serum CK measurement
- Antibody testing (anti-Jo1, anti-Mi2, etc.)
- EMG (abnormal spontaneous activity, myopathic changes)
- Biopsy (inflammatory infiltrate invading muscle fibres)
- Screen for underlying malignancy (CT chest/abdo/pelvis; PET)

**Management/Treatment**
- Corticosteroids (e.g., prednisone)
- Immunosuppressants (e.g., azathioprine, methotrexate, cyclophosphamide, IVIg)
12.23 Duchenne’s Muscular Dystrophy\textsuperscript{25,26}

**Typical Patient**
- Young boys show signs by age 2 and usually wheelchair-bound by age 12.

**Cause**
- X-linked disorder = 1 in 3300 live male births
- Nonsense frameshift mutation in dystrophin gene leads to absence of dystrophin production – causes increased muscle wear and tear over time

**Clinical Presentation**
- Delayed motor milestones
- Toe walking
- Bulky calf muscles
- Protuberant abdomen
- Proximal muscle weakness which is worse in legs than arms

**Physical Exam**
- Full neurological exam
  - Motor: proximal muscle weakness, pseudohypertrophy of calf muscles (d/t replacement of muscle with adipose tissue)
  - Gait assessment: lordotic and waddling gait, toe walking
  - Gower’s sign
- Cardiac exam: dilated cardiomyopathy, esp. in female carriers

**Investigations**
- Elevated CK (usually 1000’s) present at birth, eventual decline as muscle atrophies
- EMG: to confirm myopathy and extent of involvement
- Muscle biopsy: degeneration, fiber necrosis, hypercontracted fibers, absent dystrophin stains
- Molecular genetic studies
- Pedigree analysis

**Management/Treatment**
- Supportive care
  - Physiotherapy
  - Mobility aid
- May use steroids (may stabilize membranes)
- Medication for cardiomyopathy
- Periodic pulmonary function tests and support
- Research trial enrollment

\textsuperscript{25} “Neuromuscular junction and muscle”, Elizabeth Pringle, February 14 2017, uOttawa Faculty of Medicine
\textsuperscript{26} “Duchenne Muscular Dystrophy” Case Based learning, Nikkel, Jackie Carnegie, uOttawa Faculty of Medicine
Typical Patient
- Bimodal distribution – children, elderly, but affects all ages
- May occur as part of a syndrome in younger patients (e.g., Juvenile Myoclonic Epilepsy)

Cause
- Epileptic Seizure – Abnormal and excessive hypersynchronous discharge of brain neurons causing a temporary disrupion of brain function
- Epilepsy – 2 unprovoked seizures > 24 hours apart OR 1 unprovoked seizure and a high chance for more seizures (based on EEG, MRI)
  - Causes are multifactorial (genetic, environmental, prior brain injury from stroke/tumor/infection)
- Provoked Seizure – due to an acute, reversible brain disturbance with no ongoing risk for seizures (EtOH withdrawal, metabolic derangement, CNS infection, etc.)

Symptoms/Clinical Presentation
- Depends on the area of brain affected and the extent of spread of seizure activity
- Focal seizures:
  - Temporal lobe: automatisms, eye/head deviation, sensory hallucinations, fear/panic, déjà vu, epigastric rising sensation, etc.
  - Frontal Lobe: clonic limb movements, eye/head deviations, bicycling, “fencing posture”, etc.
- Generalized seizures:
  - Tonic-clonic: generalized stiffening of muscles (accompanied by ictal scream/cry, tongue biting), followed by rhythmic clonic movements of the limbs
- Typical seizures last seconds to a few minutes (emergency if beyond 5 minutes); often stereotyped (multiple of the same episode)
- Classify based on focal/generalized, motor/non-motor, aware/non-aware

Physical Exam
- Neurological exam (e.g., may identify Todd’s paresis, meningitis as underlying cause, etc.)
- If status epilepticus – vitals, ABCs, etc.

Investigations
- CT/MRI
- EEG
- CBC, electrolytes and extended electrolytes +/- tox screen (rule out underlying cause)

Management/Treatment
- Specific treatment dependent on the underlying cause
- Antiepileptic medications (e.g., phenytoin - partial seizures, ethosuximide - absence seizures, valproic acid - partial/generalized seizures)
- Status epilepticus /Aborting seizures: benzodiazepines followed by phenytoin or other AEDs (valproic acid, levetiracetam, etc.), can use general anesthetics if refractory (propofol, barbiturates, etc.)
12.25 Migraine - With/Without Aura

Typical Patient
- 20-50 years old
- Before puberty M=F, after puberty F>M
- May have a positive family history of migraines

Cause
- Multifactorial (genetic with environmental contributions)
- During aura phase - spreading depression (neural and glial depolarization)
- During headache phase
  1) activation of primary sensory trigeminal neurons innervating the meninges and blood vessels
  2) primary disturbance of central pain pathways producing allodynia

Symptoms/Clinical Presentation
- Aura: transient neurological symptoms (e.g., visual scotoma, scintillations) lasting 5-60 minutes
- Moderate/severe, throbbing, unilateral headache lasting 4-72 hours, aggravated by physical activity
- Nausea/vomiting
- Photophobia/phonophobia
- Vasomotor autonomic symptoms (e.g., lightheadedness, vertigo, etc.)

Physical Exam
- None necessary

Investigations
- CT or MRI may be necessary depending on differential diagnosis (none needed for typical cases)

Management/Treatment
- Acute (abortive): Aspirin/NSAIDS; Triptans - Sumatriptan, Rizatriptan, etc.; Ergot alkaloids - ergotamine/caffeine; Narcotics (only if refractory); Antiemetics - chlorpromazine, metoclopramide, etc.)
- Prophylactic: TCAs - amitriptyline; Beta blockers - propranolol, atenolol; Anticonvulsants - topiramate, valproic acid; Calcium channel blockers - verapamil, flunarizine; Nutraceuticals - magnesium, riboflavin)
- Do not combine ergot alkaloids with triptans

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12.26 Tension Headaches

**Typical Patient**
- F>M
- 20-40 years old

**Cause**
- Unknown

**Symptoms/Clinical Presentation**
- Non-throbbing
- Bilateral occipital head pain lasting hours to days (may feel like a band around the patient’s head)
- Not associated with vomiting, nausea, visual disturbance

**Physical Exam**
- Pain on palpation of musculotendinous structures is common

**Investigations**
- CT/MRI depending on clinical differential (none needed for typical cases)

**Management/Treatment**
- Acute attacks: ASA, acetaminophen, NSAIDS, triptans
- Prophylactic: TCAs - amitriptyline, nortriptyline; Beta-blockers - propranolol, atenolol
12.27 Cluster Headaches

Typical Patient
- 25-40 years old
- M>F
- Rarely a family history

Cause
- Unknown
- fMRI of patients demonstrates ipsilateral hypothalamic activation

Symptoms/Clinical Presentation
- Prodrome: burning over the lateral aspect of nose, pressure behind the eye
- Unilateral, constant throbbing headache lasting 15 minutes – 3 hours
- Occur commonly at night when awakening from sleep; recur in clusters of weeks to months with headaches every other day up to 8 times per day
- Between episodes, symptom free
- Associated symptoms: conjunctival injection, lacrimation, nasal stuffiness, Horner’s syndrome

Physical Exam
- None necessary

Investigations
- None required, if atypical presentation MRI / MRA brain scan to rule out vascular and/or hypothalamic/sellar lesion

Management/Treatment
- Acutely: inhalation of 100% oxygen for 15-20 minutes or IV sumatriptan for pain relief
- Other abortive options include: intranasal sumatriptan, lidocaine, etc.
- Prophylactic: first line - verapamil; second line - gabapentin, lithium, topiramate

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12.28 Trigeminal Neuralgia

Typical Patient
- Adult disease > 50 yo
- More common in females than males

Cause
- Idiopathic
- Multiple sclerosis (young patient)
- Neurovascular compression (elderly patient)

Clinical Presentation
Age --> arteries bend with age like old rivers --> push against nerve root --> pressure --> demyelination --> 'short circuit' to nearby nerve fiber (C fiber, pain) --> sensory signal now interpreted as intense pain!!!
- Sudden electric/ shooting pain along one or more branches of the trigeminal nerve distribution
  - Very short – seconds to minutes, several times a day
  - Unilateral pain
  - Severe
  - Sharp
  - Pain can be triggered/precipitated by mechanical stimuli over the trigeminal nerve distribution (light touch, brushing teeth, cold wind, etc.)
  - V2 and V3 > V1

Physical Exam
- Neurological examination:
  - Cranial nerves assessment (motor and sensory)

Investigations
- Meets diagnostic criteria (clinical diagnosis)
- MRI as necessary to r/o nerve compression or MS: In young patients need to rule out multiple sclerosis!

Diagnostic Criteria
A. At least 3 attacks of unilateral facial pain fulfilling criteria B and C
B. Occurring in 1+ divisions of the trigeminal nerve, with no radiation beyond its distribution
C. Pain has a minimum of 3 out of 4 characteristics:
  a. Recurrent paroxysmal attacks lasting max 2 minutes
  b. Severe intensity
  c. Electric shock-like, shooting, stabbing, or sharp in quality
  d. Precipitated by innocuous stimuli to the affected side of the face
A. No clinically evident neurological deficits
B. Not better accounted for by another ICHD-3 diagnosis

Management/Treatment
- First line: carbamazepine
- Second line: oxcarbazepine, gabapentin, lamotrigine, baclofen, botox
- Consider surgical treatment for medically refractory trigeminal neuralgia (microvascular decompression)
12.29 Narcolepsy

Typical Patient
- M/F late teens/early 20s

Cause
- Loss of hypocretin secreting neurons in the hypothalamus

Symptoms/Clinical Presentation
- Excessive daytime somnolence
- Cataplexy (sudden loss of muscle tone often during laughter or presence of strong emotions)
- Sleep paralysis
- Hypnagogic hallucinations (occurring upon falling asleep)

Physical Exam
- None

Investigations
- Multiple sleep latency test (MSLT) - sleep latency < 8 minutes with > 2 episodes of REM at sleep onset is diagnostic
- LP with CSF analysis for hypocretin levels (<110pg/ml) – usually not necessary

Management/Treatment
- Modafinil
- Amphetamines (e.g., methylphenidate/dextroamphetamine)
- Cataplexy may be treated with TCA’s (e.g., clomipramine), fluoxetine, venlafaxine, sodium oxybate

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